Asymmetric Aldol Reactions Using Boron Enolates

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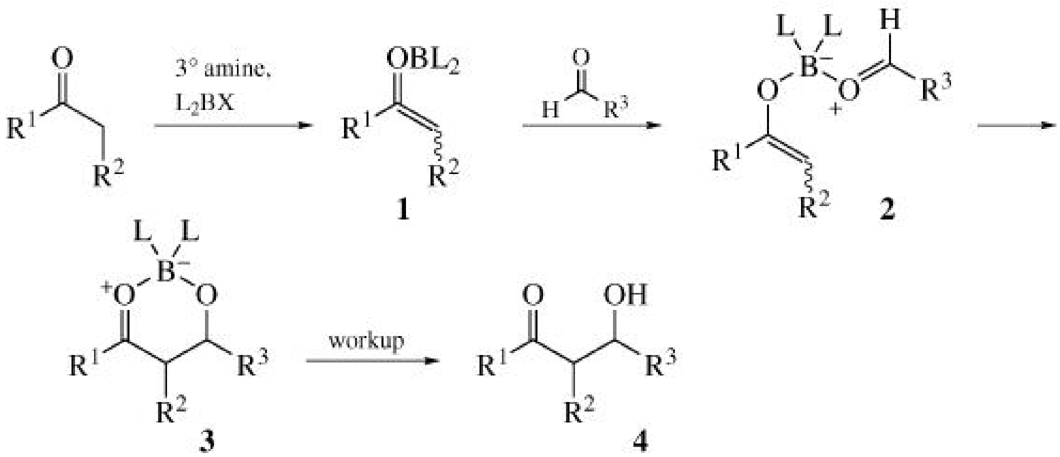
1. Introduction

The directed aldol reaction allows the construction of new carbon–carbon bonds in a regio-, diastereo-, and enantioselective manner. The kinetically controlled, boron-mediated aldol reaction is particularly powerful for the efficient synthesis of β -hydroxy carbonyl compounds. Compared to other metal enolates, the boron–oxygen bond in boron enolates is relatively short which, on addition to aldehydes, leads to tight cyclic transition states and highly stereoselective carbon–carbon bond formation. Moreover, variation of the steric demands of the ligands on boron allows discrimination between competing transition states. Chiral auxiliaries attached to the boron enolate are frequently employed to control the relative and absolute stereochemistry of the aldol products. Asymmetric reactions using chiral ligands on boron are also possible and these produce useful enantiomerically enriched adducts. The utility of boron-mediated aldol reactions has been demonstrated in numerous total syntheses of complex polyoxygenated natural products, and several of these are highlighted in the Application to Synthesis section of this chapter.

Several reviews of the directed aldol reaction are available, (1-8) including the *Organic Reactions* chapter by Mukaiyama in 1981. (9) The material covered in this review concerns only the asymmetric formation of β -hydroxy carbonyl compounds using boron enolates and surveys the literature from 1981 until the end of 1995. (10)

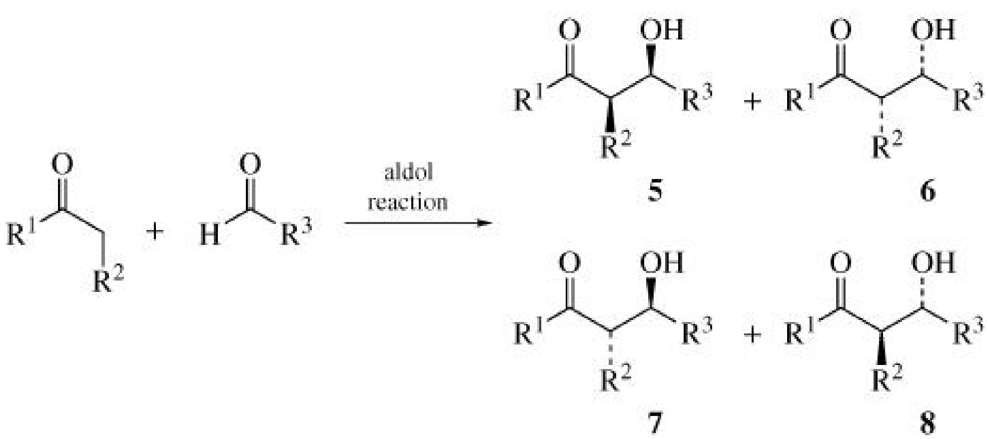
2. Mechanism and Stereochemistry

In the boron-mediated aldol reaction, enolization of a carbonyl compound with a Lewis acidic boron reagent (L_2BX; X = OTf, Cl, Br) generates a boron enolate **1**, which combines with an aldehyde to form a reactive ate-complex **2** (Eq. 1). This complexation then facilitates bond reorganization via a six-membered cyclic transition state, thus affording the boron aldolate **3** which, upon hydrolytic workup, gives the aldol product **4**.



(1)

A stereorandom aldol reaction between a carbonyl compound (R^2 ¹ H) and an aldehyde (R^3 ¹ H) creates a new carbon–carbon bond and two stereocenters and gives rise to four possible products: a pair of syn stereoisomers (**5** and **6**) and a pair of anti stereoisomers (**7** and **8**) (Eq. 2). If the R^1, R^2, and R^3 groups do not

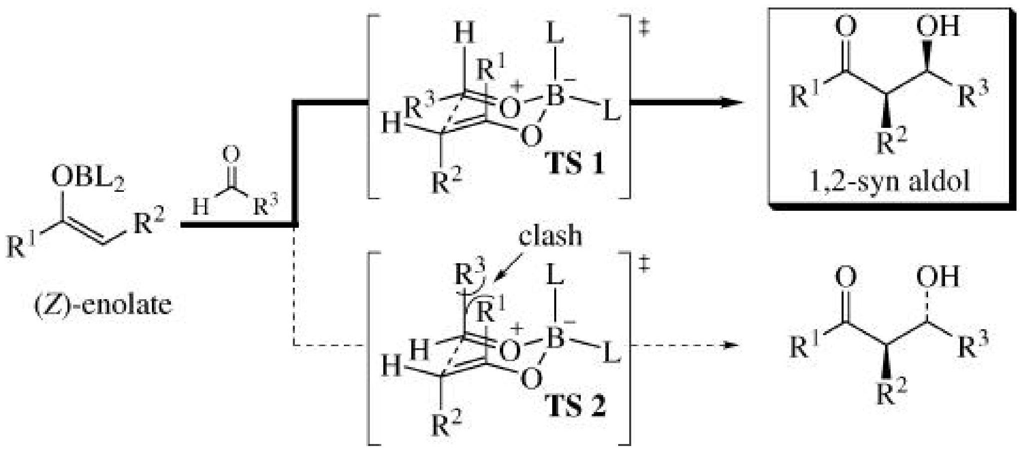


(2)

contain any further stereocenters, then compounds **5** and **6** will be enantiomers, as will compounds **7** and **8**. The selective formation of any one of these four stereoisomers constitutes an asymmetric process. In such an aldol reaction there will be two stereochemical issues operating: relative and absolute stereocontrol.

2.1. Relative Stereocontrol Arising from Enolization Selectivity

Most boron-mediated aldol reactions are considered to proceed through a chair-like transition state, where (*Z*)-boron enolates[*] give syn aldol products (Eq. 3) and (*E*)-boron enolates[*] afford anti aldol products (Eq. 4). (10a,b) The controlling influence



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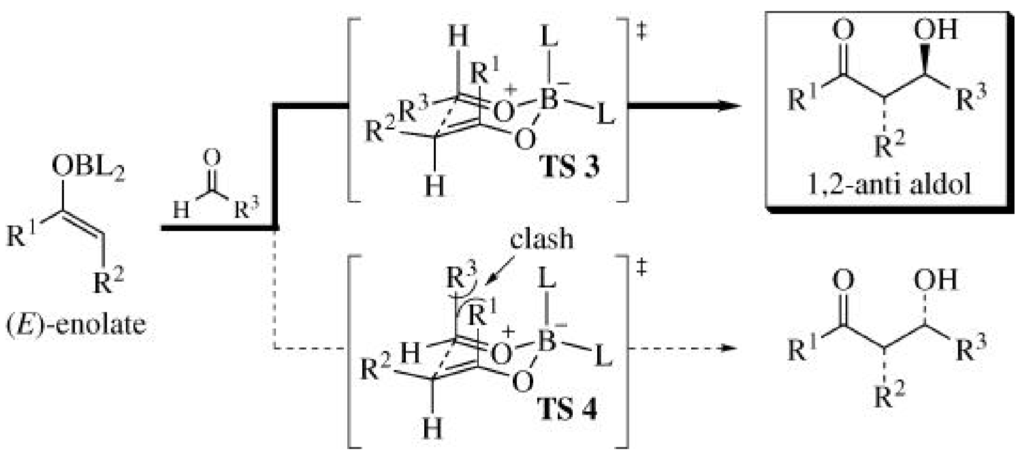
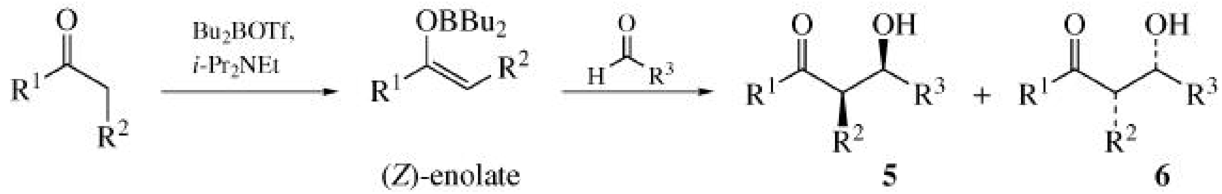


(4)

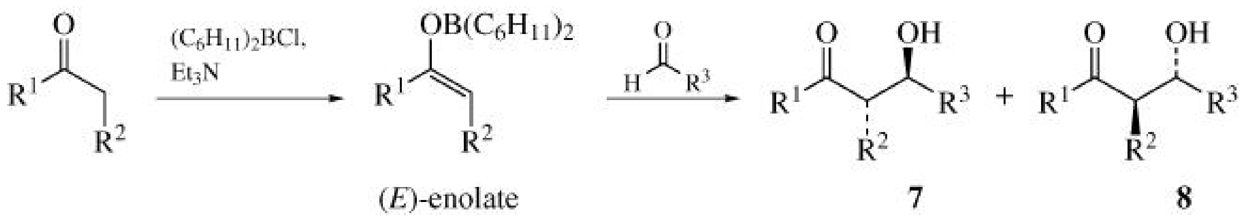
in these reactions is the avoidance of severe 1,3-diaxial interactions in the cyclic transition states (**TS 1** vs. **TS 2** and **TS 3** vs. **TS 4**). It is also unlikely that transition states such as **TS 2** and **TS 4** would be accessible because this requires the formation of an unfavorable cis geometry about the ate-complex **2**.

As the boron enolate geometry is faithfully translated into aldol product stereochemistry, enolization selectivity is crucially important. In the case of direct boron enolate formation, it is usually possible to selectively prepare either (*E*)- or (*Z*)-boron enolates by enolization of simple ethyl ketones (R^2 = Me). (10-13) A combination of small ligands on boron (e.g., *n*-butyl), a good leaving group (e.g., triflate), and a bulky amine base (e.g., diisopropylethylamine) usually leads to (*Z*)-selective enolization (Eq. 5). On the other hand, use of sterically demanding



(5)

ligands on boron (e.g., cyclohexyl), a poor leaving group (e.g., chloride), and a small amine base (e.g., triethylamine) usually promotes (*E*)-enolate formation (Eq. 6). (11,12,14–17) Two explanations have been proposed for this enolization behavior. (18,19)



(6)

2.2. Absolute Stereocontrol Arising from p -Facial Selectivity

In an aldol reaction, absolute stereocontrol is the selective production of either syn aldol products **5** or **6** and, similarly, the production of either anti products **7** or **8**. Control of the absolute stereochemistry requires facial discrimination of either the boron enolate or aldehyde π -systems. This π -facial discrimination can be achieved by one or more of the following methods:

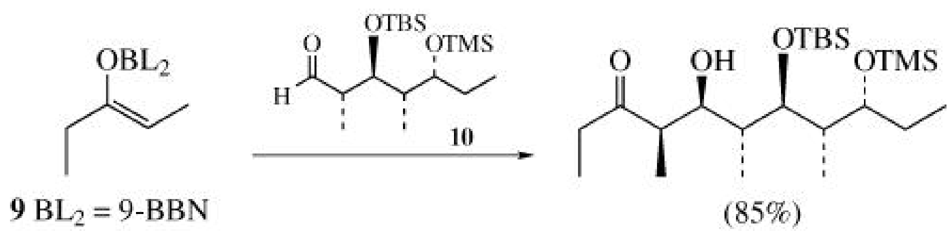
1. The use of chiral aldehydes where R^3 is a stereogenic group
2. The use of auxiliary control from the enolate where R^1 is a stereogenic group and is subsequently removed
3. The use of substrate control from a chiral enolate where R^1 is a stereogenic group but is retained in subsequent steps
4. Reagent control by the use of chiral boron reagents

A more detailed discussion of these individual effects and their combined influence is outlined in the following section.

3. Scope and Limitations

3.1. Asymmetric Induction from Chiral Aldehydes

Reactions of achiral enolates with chiral aldehydes represents the simplest method of asymmetric aldol synthesis. Control of the boron enolate geometry generally determines the syn versus anti diastereoselectivity; it therefore follows that if a good level of facial selectivity can be imparted by a chiral aldehyde, a useful asymmetric aldol reaction will be possible. The selectivity induced by a chiral aldehyde can fluctuate, and changing either the ligands on boron, (20) the solvent used, (21) or the protecting group on a β-oxygenated stereocenter (20) can have a significant effect. When these variables are optimized, a synthetically useful reaction can result. For example, reaction of boron enolate **9** with aldehyde **10** proceeds in high yield to afford a single observed syn aldol adduct (Eq. 7). (22) Interestingly, the aldol reaction of aldehyde **11** was initially performed using a chiral auxiliary, but it was subsequently found that the facial bias of the aldehyde was enough to use the achiral enolate **12** (Eq. 8). (23)



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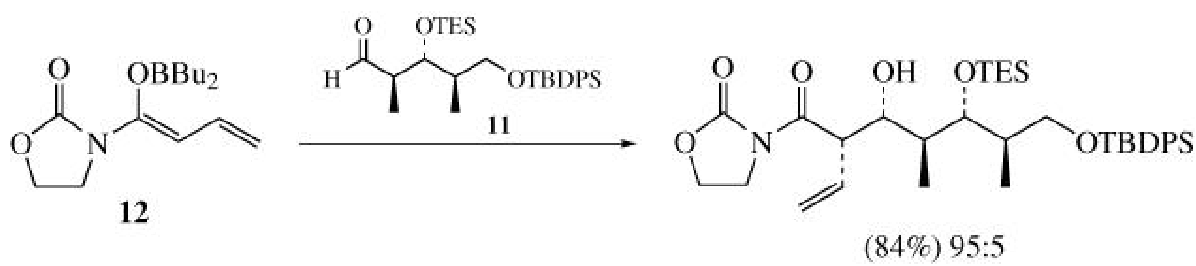
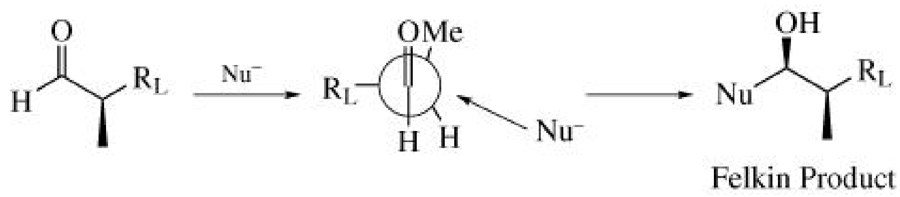


(8)

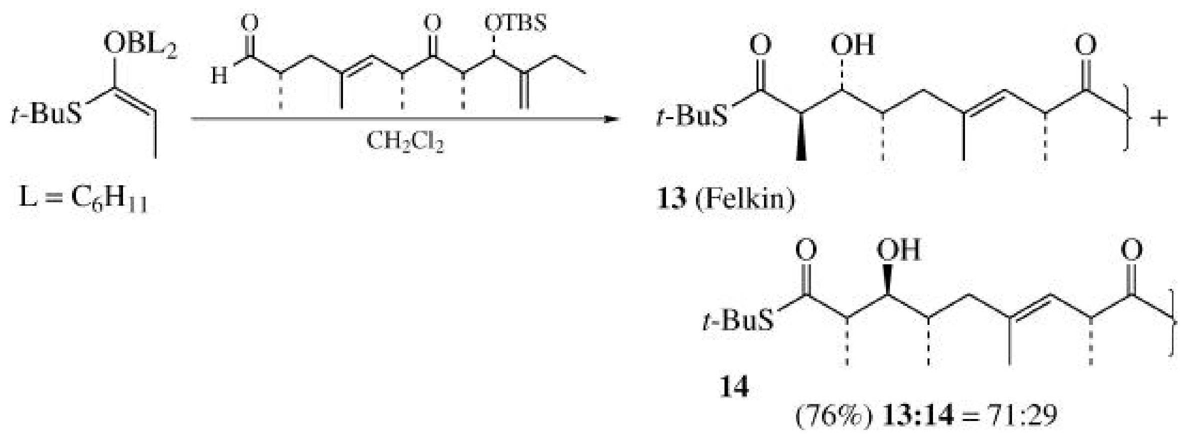
3.1.1. α -Chiral Aldehydes and Influence of Enolate Geometry

Aldol reactions of achiral boron enolates and α-substituted chiral aldehydes are the most thoroughly studied systems. The Felkin–Anh model for nucleophilic attack on α -chiral aldehydes predicts the product stereochemistry indicated in Eq. 9, where R_L is either the largest group or the group with the lowest lying σ * orbital. (24,25)



(9)

When a reaction takes place through an acyclic transition state, the Felkin–Anh model generally holds. However, boron-mediated aldol reactions usually proceed through a highly ordered cyclic transition state where other factors have an influence on the selectivity. Thus, while (*E*)-boron enolates usually favor formation of the Felkin adduct, as in Eq. 10, (21, 26) (*Z*)-boron enolates normally lead to anti-Felkin products, as in Eq. 11. (27)



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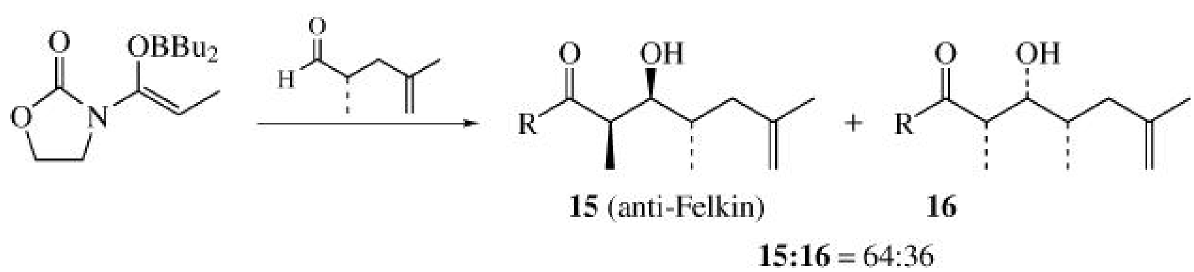
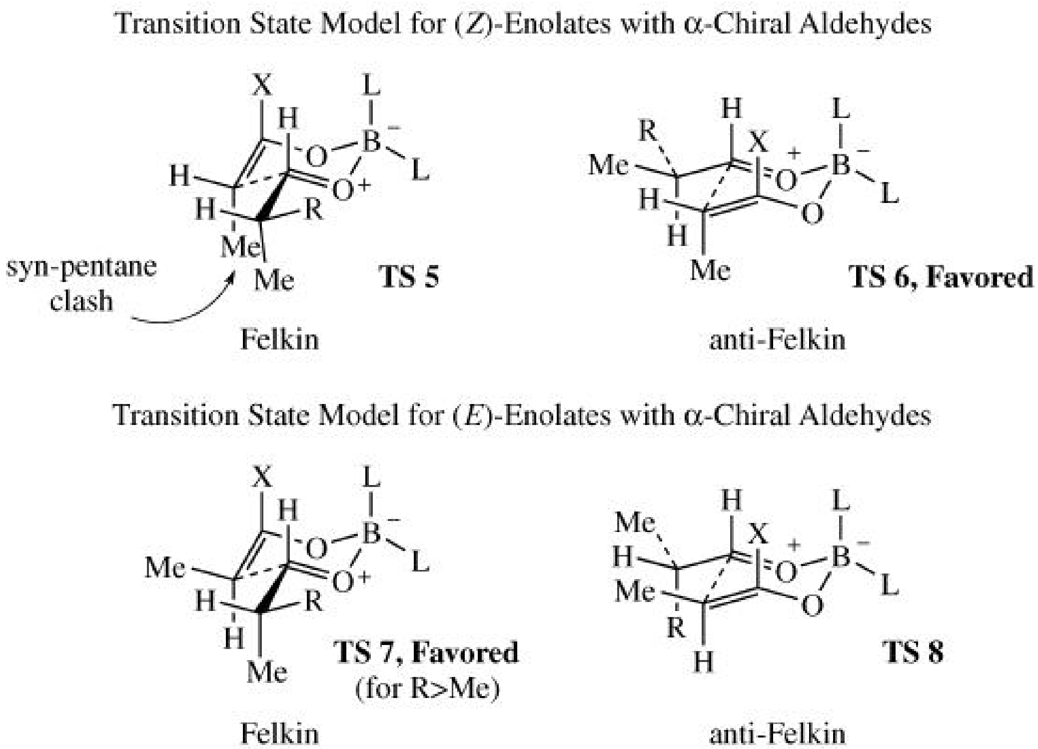


(11)

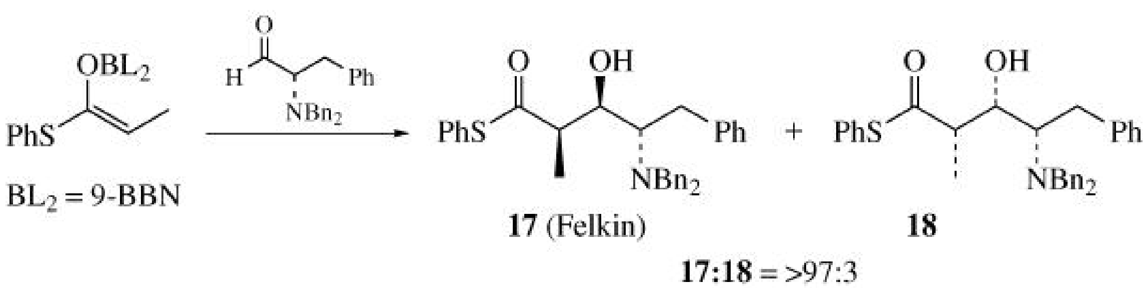
This anomalous behavior of (*Z*)-boron enolates has been attributed to a destabilizing syn-pentane steric interaction in the cyclic chair transition state **TS 5** leading to the Felkin product (Fig. 1). (28, 29) This interaction is avoided in the diastereomeric transition state **TS 6** leading to a preference for anti-Felkin attack. For (*E*)-boron enolates, the aldol addition favors the

Felkin-type **TS 7** over **TS 8**.

Fig.1.

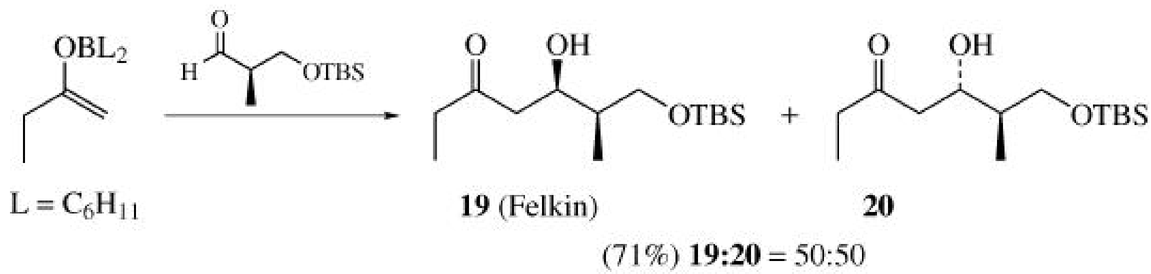


There are exceptions to this generalization; for example, an α-heteroatom may provide an especially strong facial bias leading to Felkin-type selectivity (Eq. 12). (30)



(12)

Few examples of boron-mediated aldol reactions of methyl ketones or thioesters with α -chiral aldehydes which do not possess a β -stereocenter have been reported. (31) It would appear, however, that the asymmetric induction from an α -methyl group alone is negligible (Eq. 13). (32)

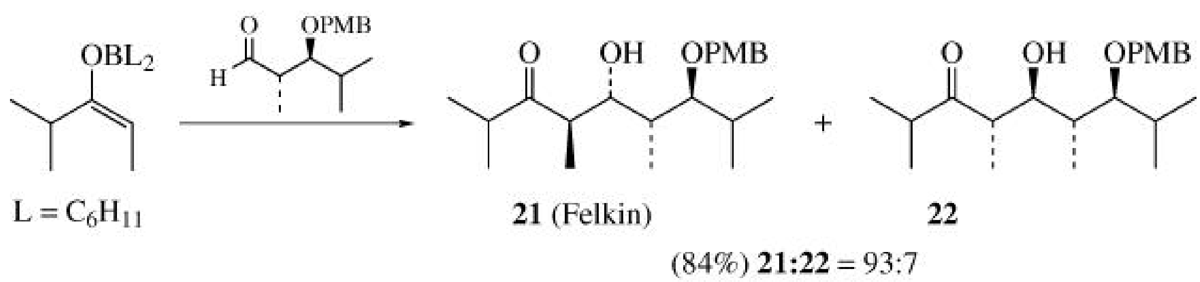


(13)

3.1.2. Stereochemical Trends for β -Alkoxy Aldehydes

The boron-mediated aldol reactions of ketones with chiral aldehydes having a β -alkoxy substituent have been studied in detail. (20, 33-39) In the majority of cases, the aldehyde also possesses an α stereocenter which complicates the analysis. For dialkyl boron reagents, a chelation-controlled reaction is not possible, but the β -alkoxy stereocenter has steric and electronic contributions. There are many variables in these reactions, including the β -oxygen protecting group, the choice of ligands on boron and, of course, the structure of the enolate concerned.

The β -alkoxy stereocenter of an aldehyde may exert an electronic or opposed dipoles effect resulting in the production of a 1,3-anti diol relationship. (37, 39) Such an effect is strongest for reactions that proceed through an open transition state, such as the Mukaiyama aldol reaction. In the examples of Eqs. 14 and 15, the selectivity



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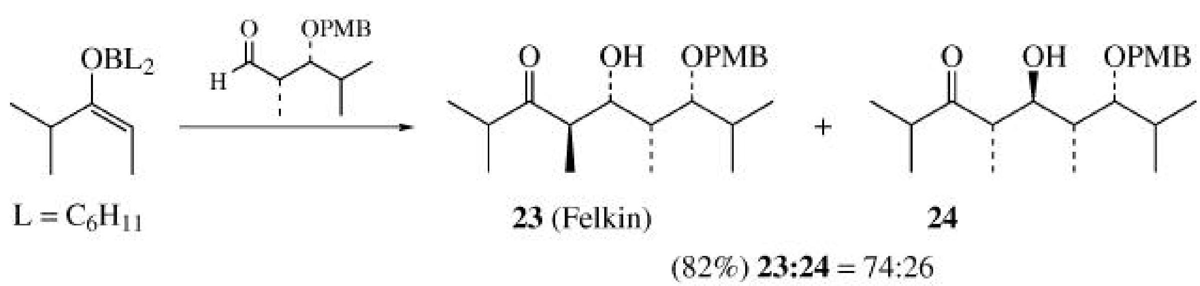
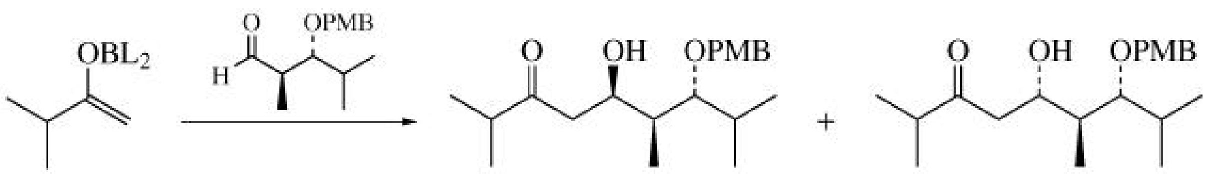


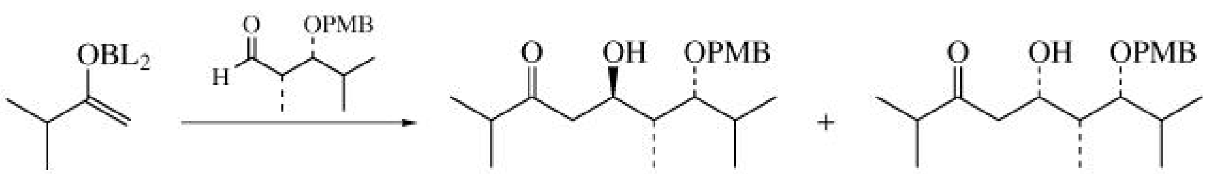
(15)

of the aldol reaction deteriorates when the aldehyde β -stereocenter is inverted, indicating some contribution to the reaction. (38) The bias of the aldehyde is still dominated by the α -chiral methyl group however, showing that the effect of the β -stereocenter is only moderate.

The analogous methyl ketone aldol reaction of α -methyl- β -alkoxy aldehydes has been extensively studied. (20, 34, 35, 38-40) As already indicated (Eq. 13), boron-mediated aldol reactions of methyl ketones are not greatly influenced by the α -chiral methyl group of an aldehyde, and from the results reported to date, the β -stereocenter can play a significant role. For example, the 1,3-anti product is obtained independent of the configuration of the α -methyl group of the aldehyde (Eqs. 16 and 17). (39)

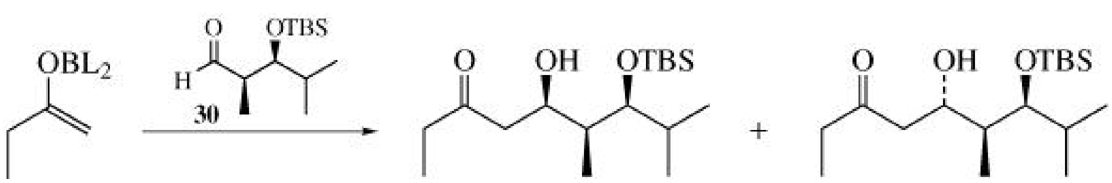


BL_2 = 9-BBN   **25** (Felkin)   **26**   **25:26** = 69:31   (16)

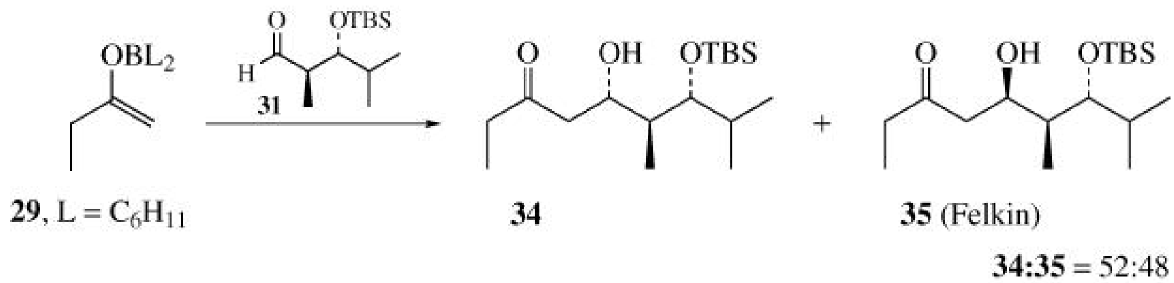


BL_2 = 9-BBN   **27**   **28** (Felkin)   **27:28** = 77:23   (17)

In contrast, the reaction of boron enolate **29** with aldehydes **30** and **31** leads to a small preference for the 1,3-syn product (Eqs. 18 and 19). (34)

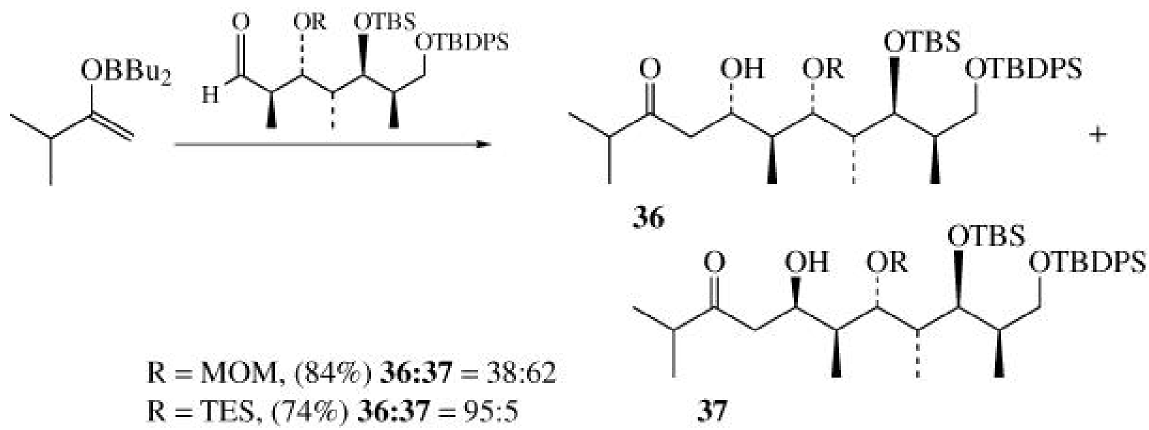


29, L = C_6H_{11} **32** (Felkin)   **33**   **32:33** = 76:24   (18)



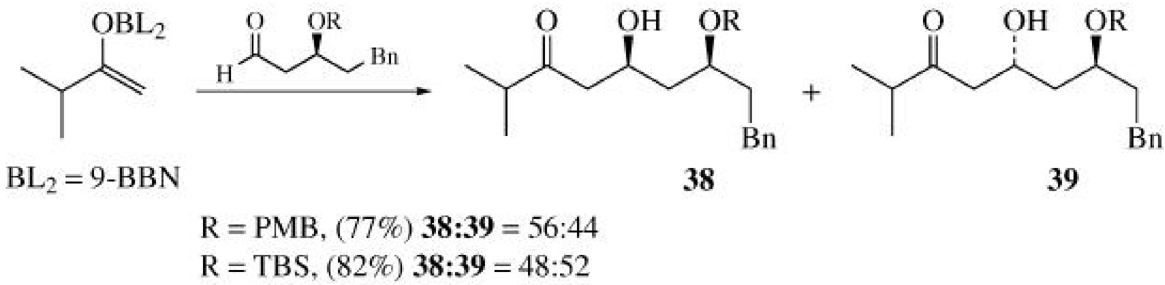
(19)

In the previous examples, the choice of β -alkoxy protecting group controls the selectivity of the reaction. This effect has also been observed in more complicated systems. The exchange of a methoxymethyl ether protecting group for a silyl group caused the reaction depicted in Eq. 20 to show a strong preference for anti-Felkin attack leading to a 1,3-syn diol arrangement. (20)



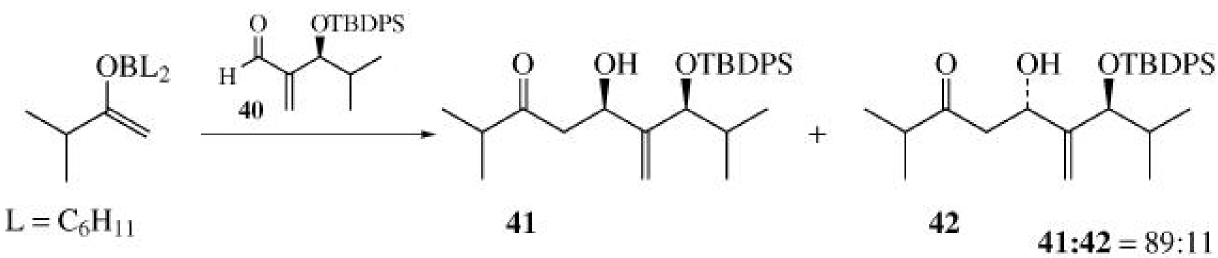
(20)

The selectivity of these reactions may be due to a steric interaction of the β -alkoxy protecting group in the chair transition state, causing the reactions to proceed through a boat transition state. (20) A contributing factor could also be the simple alteration in conformational bias of the aldehyde as the β-alkoxy protecting group is changed. It should be noted that the same trends do not appear to be followed for α -unsubstituted chiral aldehydes, where limited induction is observed (Eq. 21). (37)



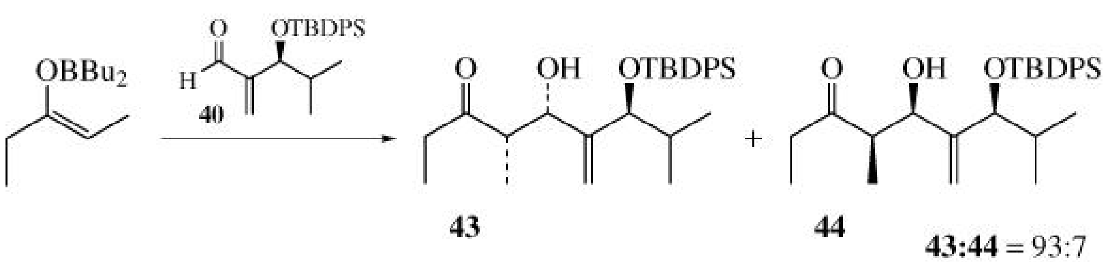
(21)

A more pronounced example of 1,3-induction is observed for α -methylene- β -oxygenated aldehydes, where the selectivity is dependent upon the structure of the boron enolate. (33) Methyl ketones add to these aldehydes in a 1,3-syn manner, especially when the protecting group on the β -oxygen substituent is large, as in aldehyde **40** (Eq. 22). In contrast, syn aldol reactions of ethyl ketones with this



(22)

aldehyde show high selectivity for the formation of 1,3-anti diols, as shown in Eq. 23. (33)



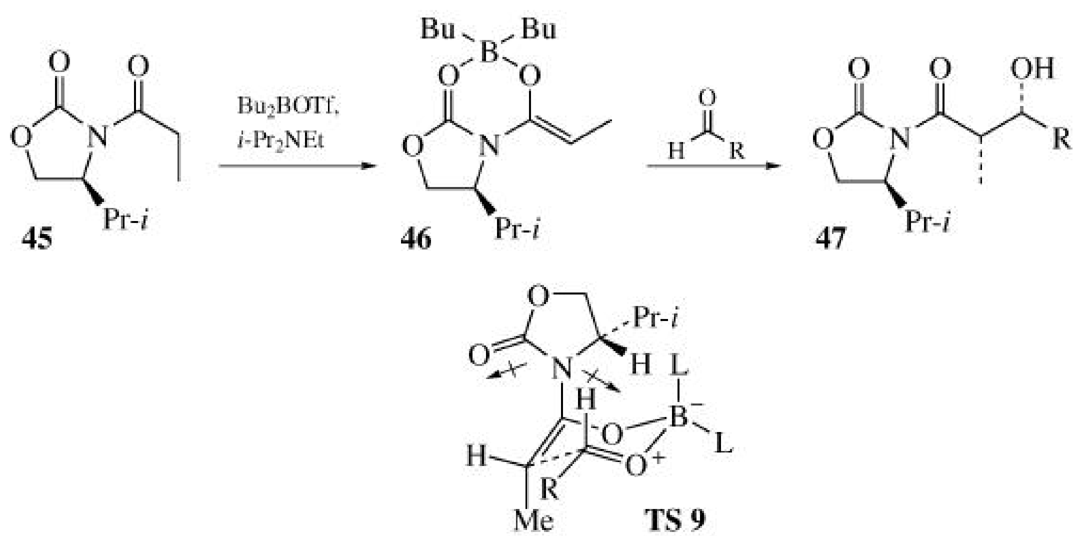
(23)

In summary, the level of induction imparted by a chiral aldehyde with a boron enolate is usually moderate, and control from a chiral enolate becomes necessary to achieve more synthetically useful levels of selectivity. Still, the contribution from the aldehyde is important for double stereodifferentiation because it can make the difference between a matched aldol reaction and a potentially unsuccessful, mismatched reaction. (8)

3.2. Auxiliary-Mediated Aldol Reactions

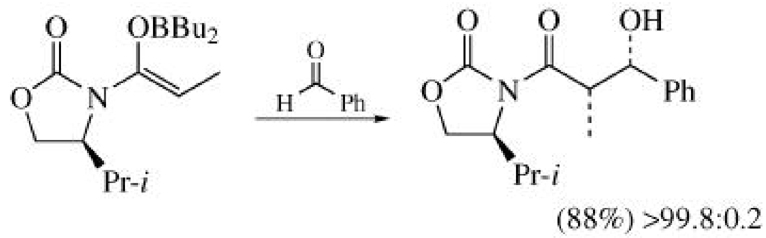
3.2.1. Heterocycle Auxiliaries

Boron aldol reactions mediated by a covalently attached chiral auxiliary are powerful tools for acyclic stereocontrol. The most widely used chiral auxiliaries are those based on oxazolidinone heterocycles. There are many variations on this theme, but the most popular are the Evans auxiliaries. (41, 42) The (*Z*)-boron enolate is prepared in the usual manner by enolization of the parent imide **45** with a boron triflate reagent in conjunction with a hindered tertiary amine base (commonly diisopropylethylamine) in dichloromethane (Eq. 24). This method normally gives exclusive formation of the (*Z*)-enol borinate **46**, which leads to syn aldol products of the type **47** with diastereoselectivities of up to 500:1. (27, 43)



(24)

The observed selectivity is accounted for by coordination of the aldehyde to the boron enolate **46** followed by transition state **TS 9** where the dipoles of the enolate oxygen and the carbonyl group of the auxiliary are opposed. (44) Some examples of this reaction for achiral aldehydes are given (Eqs. 25, (41) 26, (45, 46) and 27 (47)).



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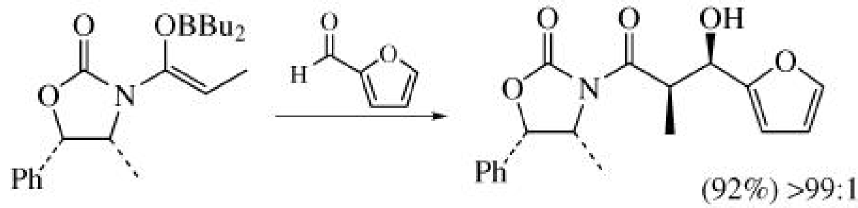

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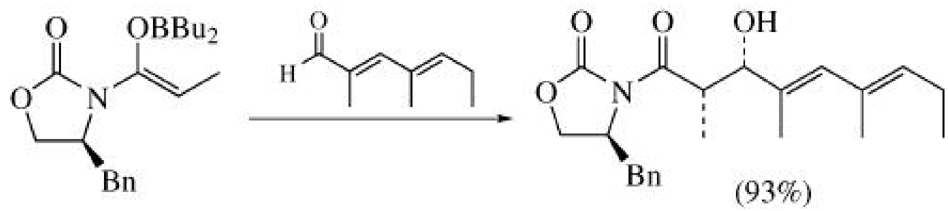
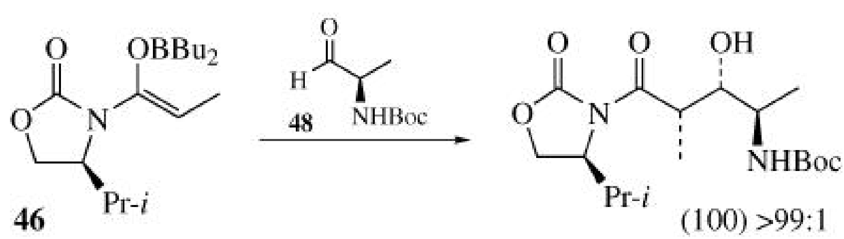


(27)

The facial bias of these enolates overrides any inherent π -facial selectivity of chiral aldehydes in all but a few cases. For example, the boron-mediated aldol reaction of aldehyde **48** with either boron enolate **46** or its enantiomer **ent-46** leads to auxiliary control of the newly generated stereocenters (Eqs. 28 and 29). (48-50)



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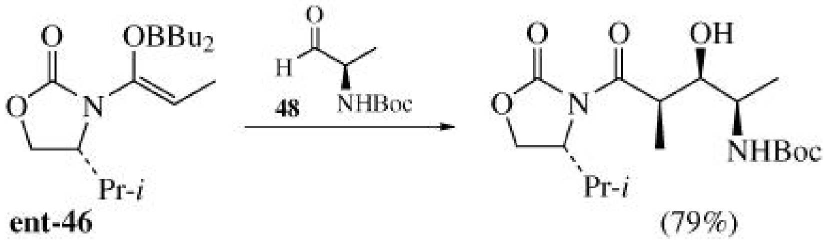
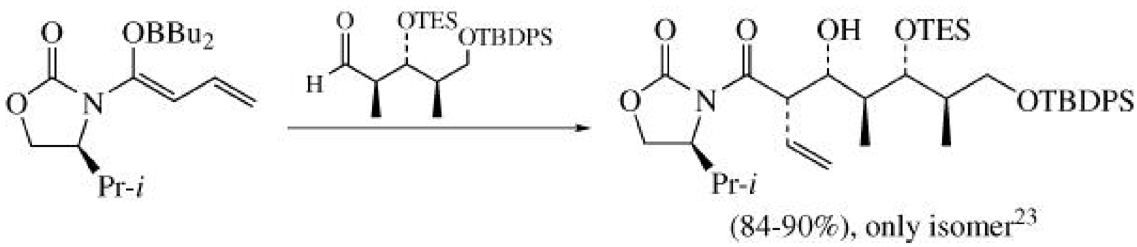


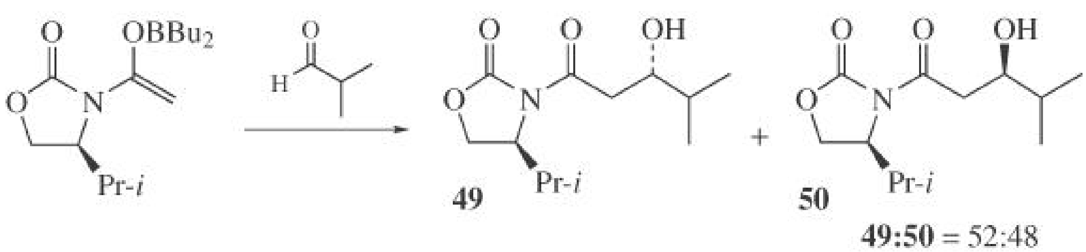
(29)

A wide variety of alkylated imides have been successfully used in the boron-mediated aldol reaction of oxazolidinone auxiliaries. By far the most common is the propionimide which acts as a propionate building block for polyketide systems. The crotyl imides are also popular (e.g., Eq. 30), and the products of these reactions have been used in approaches to several natural products. (23,51–54)



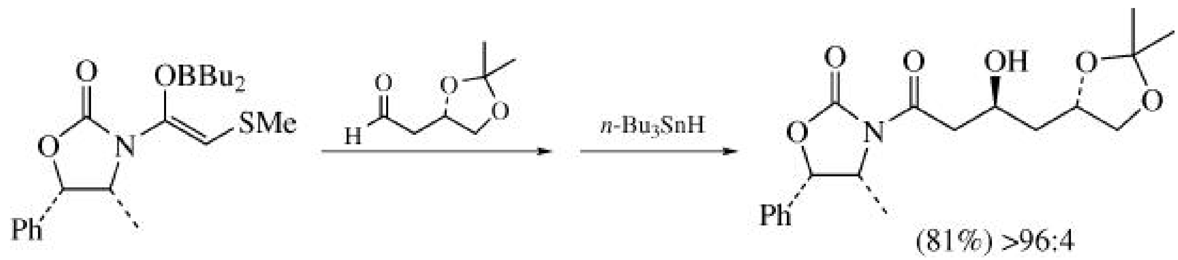
(30)

In contrast, the parent *N*-acetyl imide is unselective in its aldol reactions, giving approximately equal amounts of the two aldol diastereomers **49** and **50** (Eq. 31). (41, 44) This result may be attributed to competition of boat transition states. (55)



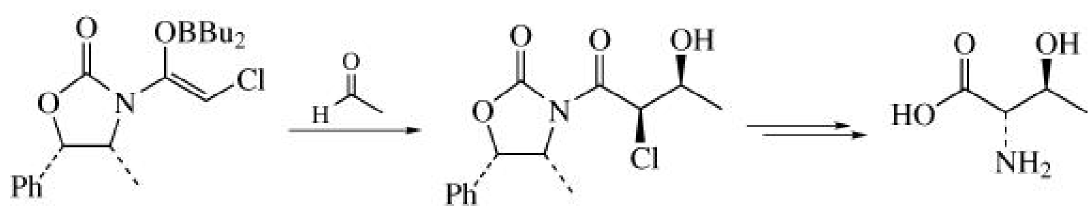
(31)

The lack of selectivity for unsubstituted enolates can be overcome, usually by the temporary incorporation of a heteroatom substituent. (41) For example, a thioalkyl group can be reductively removed after the aldol reaction; this tactic has been employed in a synthetic approach to rhizoxin (Eq. 32). (56)



(32)

Another example of this protocol is the incorporation of a halogen atom, which was used in a synthesis of the immunosuppressant FK-506. (57) The aldol products from such reactions are also interesting building blocks for other purposes. For example, synthesis of amino acids via an azide displacement step (Eq. 33) (58) and the synthesis of epoxides have also been reported from both chlorides and bromides (Eq. 34). (59, 60) It should be noted that enolization of these systems apparently provides ~25% (*E*)-enolate, which does not interfere with the aldol reaction because it reacts more slowly than the corresponding (*Z*)-enolate. (58)



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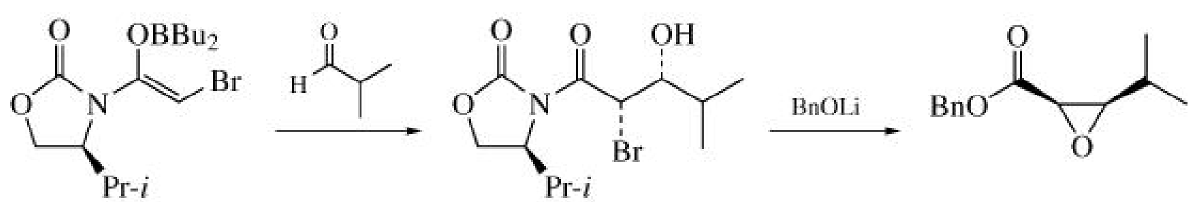
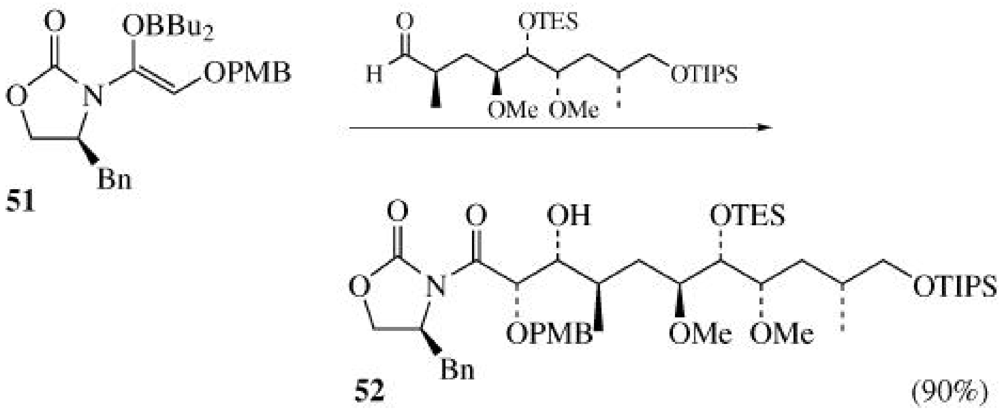


(34)

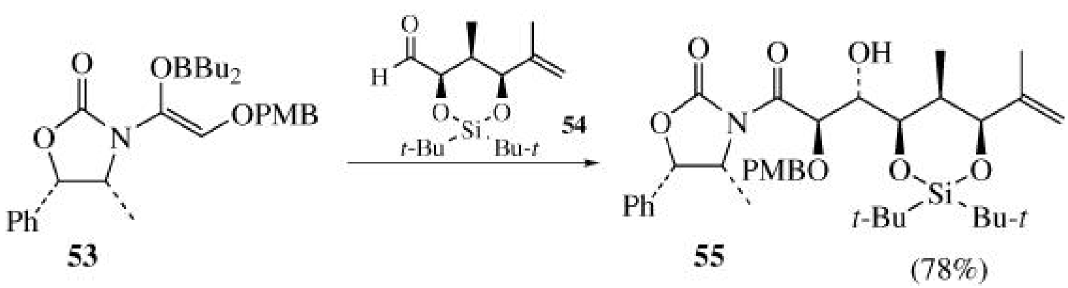
The use of α -oxygenated *N*-acetyl imides has also been well studied. The (*Z*)-enolate **51** from the *p*-methoxybenzyloxy substituted imide reacts with typical behavior, producing aldol product **52** in high yield and selectivity (Eq. 35). (57) This



(35)

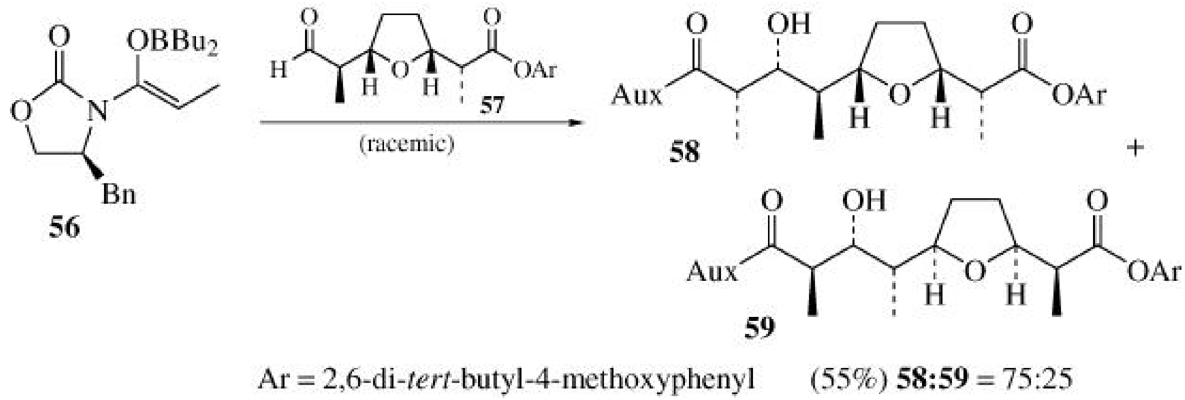
same conversion is not possible when protecting groups sensitive to the Lewis acidic enolization conditions are used; triethylsilyl, *tert*-butyldimethylsilyl, and 3,4-dimethoxybenzyl groups are all removed under the enolization conditions. Such protecting groups on the aldehyde segment pose no such problem in boron-mediated aldol reactions. Moreover, careful attention to the quality and quantity of reagents employed ensures that most common protecting groups can be tolerated in the enolate component.

A notable exception to the impressive syn-selectivity of these auxiliaries is the reaction of dibutylboron enolate **53** with aldehyde **54** which affords the anti adduct **55** as the exclusive product (Eq. 36). (61) This result is unusual and may be explained by the strong Felkin bias of the aldehyde.



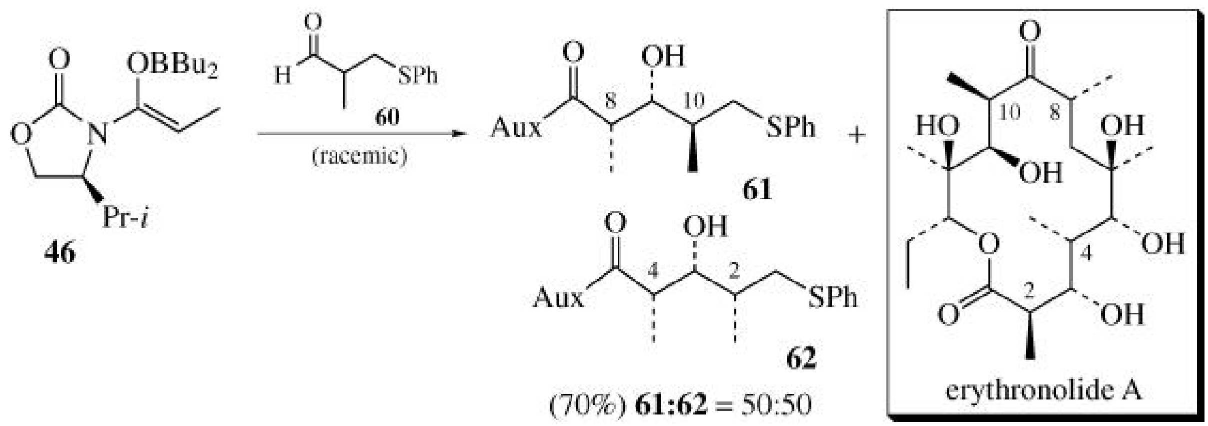
(36)

One area where the auxiliary-controlled aldol reaction has been underutilized is in the production of enantiomerically pure products from racemic aldehydes. (57,62–65) The kinetic resolution reaction of the boron enolate **56** with two equivalents of racemic aldehyde **57** gives the major syn aldol adduct **58** from a matched case (Eq. 37). (65) Here, the minor product is the anti aldol adduct **59** obtained from the mismatched reaction, which may result from an acyclic transition state.



(37)

Another example (Eq. 38) is the aldol reaction of boron enolate **46** with the racemic aldehyde **60**. (63) Both enantiomers of the aldehyde react with similar rates

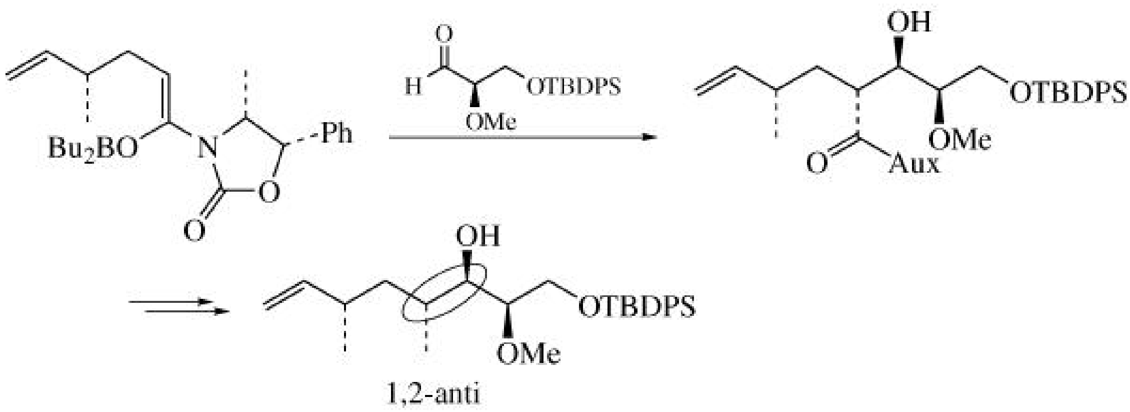


(38)

to give an equimolar mixture of syn aldol products **61** and **62**. These compounds were separated and used in an approach toward the synthesis of the macrolide antibiotic erythromycin, where this single aldol reaction provides five of the ten stereocenters required in erythronolide A (C_9 will be oxidized).

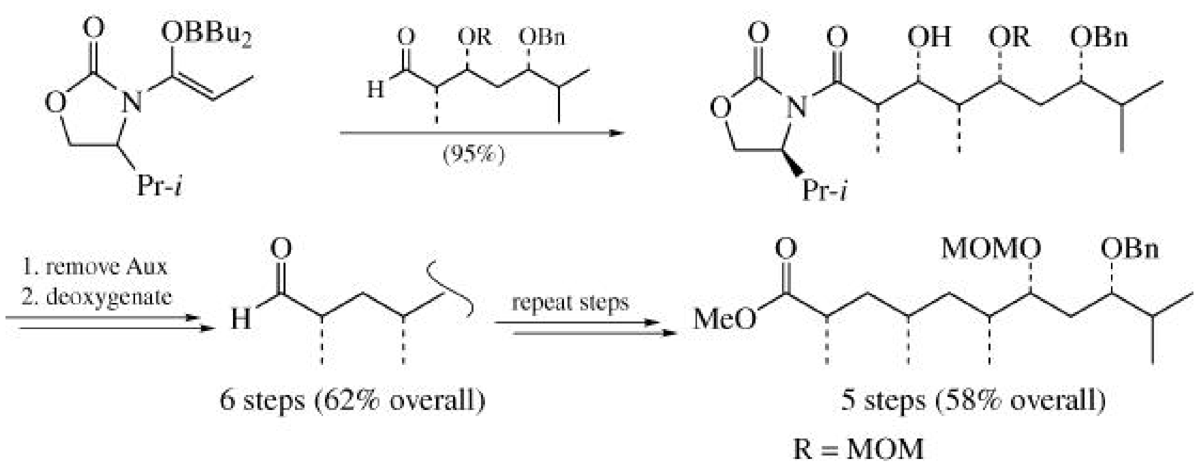
One of the advantages of these oxazolidinone auxiliaries is that they may be elaborated in many ways. Nondestructive hydrolysis of the imides is possible, (66) usually using lithium hydroperoxide. (67) Transamination to the synthetically versatile Weinreb amide is also a common transformation, (68) as is the reductive removal of the auxiliary. (51, 69-71) This latter approach may be followed by a deoxygenation step, which allows the syn aldol reaction to be used as an apparent anti aldol reaction, and this protocol has been used in several polypropionate natural product syntheses (53, 72) including rapamycin (Scheme 1). (73)

Scheme 1.



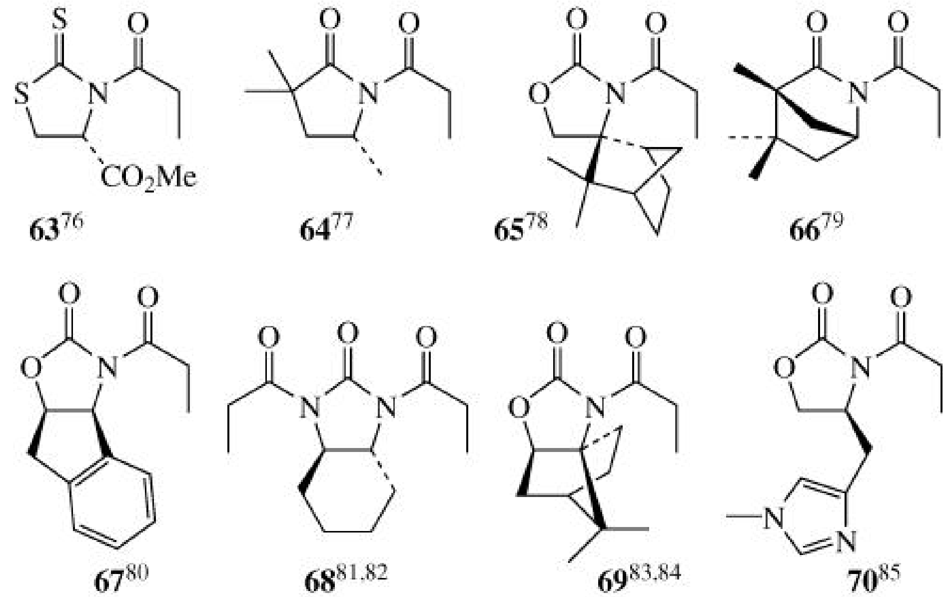
Deoxygenation of the aldol products themselves allows access to 1,3-dimethylated systems, and such an approach, with two sequential iterations, has been used in the synthesis of the marine natural product doliculide (Scheme 2). (74, 75)

Scheme 2.



While the heterocyclic auxiliaries introduced by Evans are by far the most widely used, many variations have been reported. A selection of those imides, **63–70**, which have been utilized in boron-mediated aldol additions, is shown in Fig. 2.

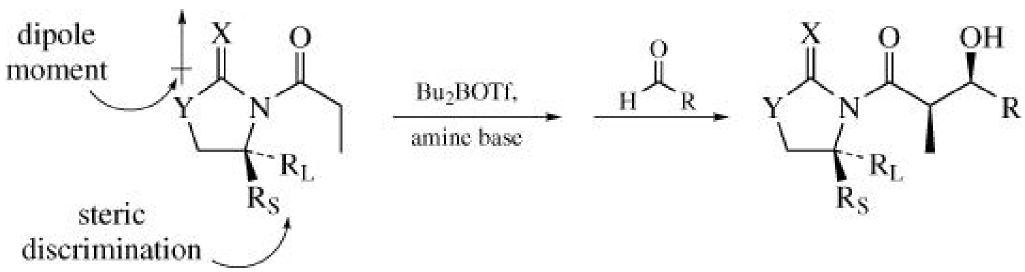
Fig.2.



63[76] **64**[77] **65**[78] **66**[79] **67**[80] **68**[81,82] **69**[83,84] **70**[85]

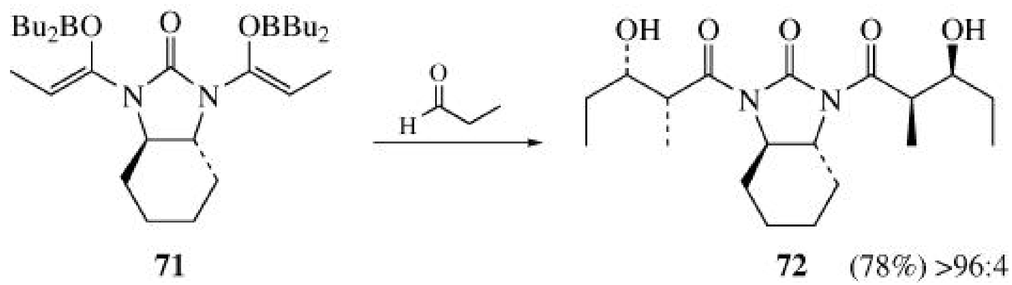
All of these auxiliaries function along similar lines, producing the same major product based on the Evans aldol transition state model (see **TS 9**). Each of the auxiliaries acts as a molecular scaffold with a carbonyl group acting as a strong dipole and a large and small group supplying facial selectivity (Eq. 39).

Only a few of these second-generation auxiliaries offer advantages over the original design. For example, the cysteine-derived auxiliary **63** confers excellent



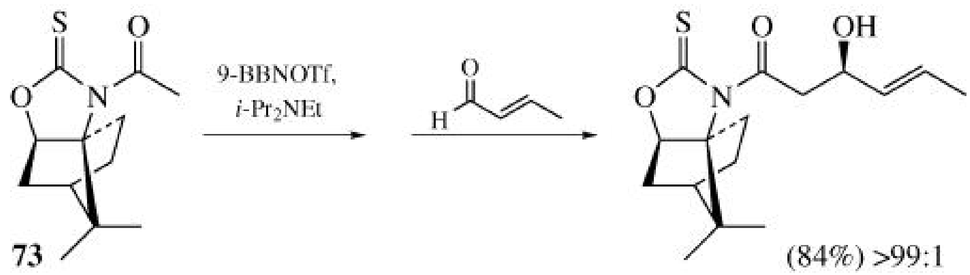
(39)

selectivities in syn aldol reactions (76, 86) and has found use in natural product synthesis. (87-89) Aminolysis (86, 90) and direct reduction to an aldehyde is possible, (87, 89) but a nonoxidative aldol workup is necessary because competitive oxidation of sulfur is problematic. (76) The “quat” chiral auxiliary **64** offers the advantage of improved exocyclic selectivity in its hydrolytic removal. (77) The bifunctional, C_2-symmetric reagent **71** undergoes simultaneous two-directional chain extension to give bis-adduct **72**, thus facilitating atom economy (Eq. 40). (81, 82)



(40)

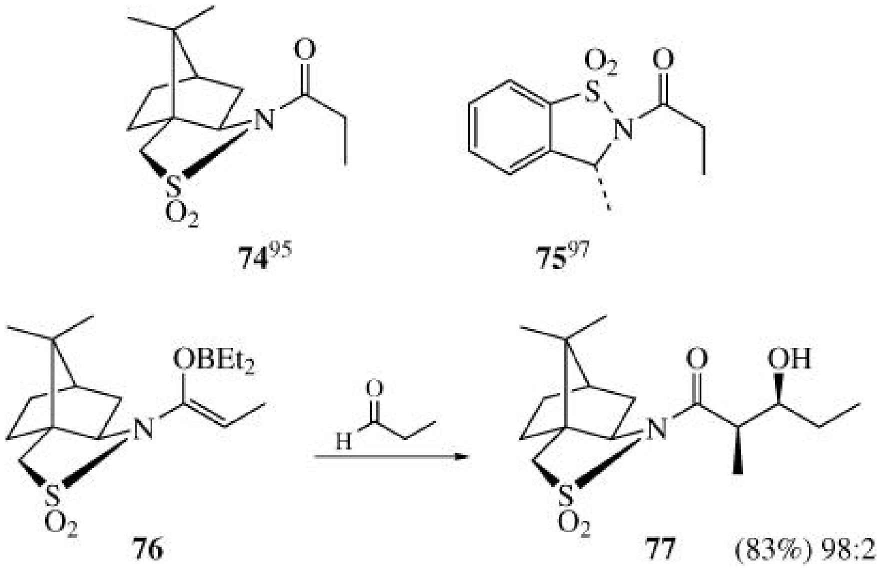
Several of these second-generation auxiliaries contribute useful levels of facial bias to unsubstituted enolates. (91, 92) The best of these would appear to be thioimide **73**, which gives good control in the methyl series as shown in Eq. 41. (93, 94) The absolute



(41)

configuration of the hydroxy stereocenter in these reactions is opposite to that predicted from the typical chair model, suggesting that a boat-like transition state is now dominant.

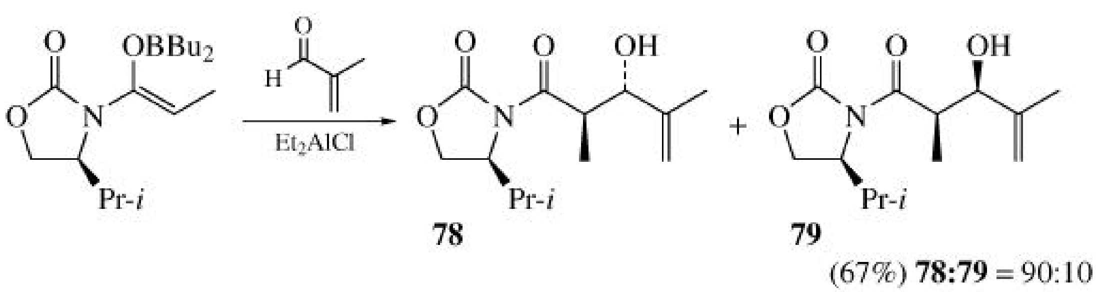
The Oppolzer sultams **74** and **75** have also been used in boron-mediated aldol reactions, providing selectivities which compete with the oxazolidinone auxiliaries. (95-98) One experimental difference with these auxiliaries is that the reaction of the sultams proceeds better when using in situ generated diethylboron triflate as opposed to dibutylboron triflate. Again, enolization selectively gives the (*Z*)-boron enolate **76** and this, in turn, reacts to afford the syn aldol product **77** via a



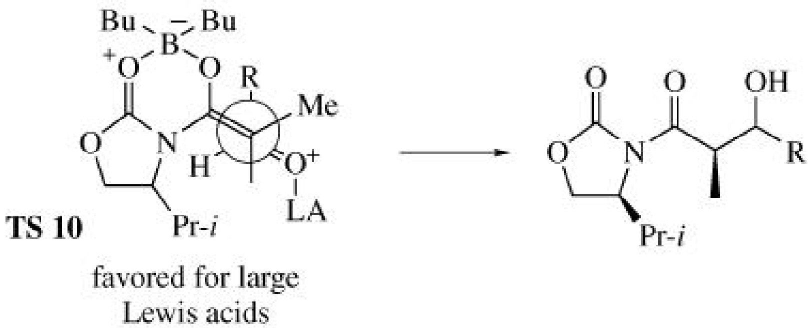
(42)

transition state that relies on preorganization due to opposed dipoles. (98-100) Removal of these auxiliaries by hydrolysis is common, and “transesterification” with allyl alcohol in the presence of $Ti(OEt)_4$ is possible. (101)

The foregoing auxiliaries offer excellent levels of asymmetric induction in syn aldol reactions via the preferential formation of (*Z*)-boron enolates. Note that the analogous (*E*)-enolates should afford anti aldol adducts. However, owing to the steric bulk of the auxiliaries, (*E*)-enolates cannot be formed preferentially on enolization. The generation of anti aldol products is possible by diverting the (*Z*)-boron enolate from a cyclic transition state. This is usually accomplished by pre-complexation of the aldehyde with a Lewis acid such as Et_2AlCl, thereby leading to an open transition state. (102, 103) When a bulky Lewis acid is used, these aldol reactions favor a single anti aldol product with the minor isomer, usually a syn diastereomer (Eq. 43). A transition-state model **TS 10** which explains the formation of the anti aldol products is shown (Eq. 44). (103)

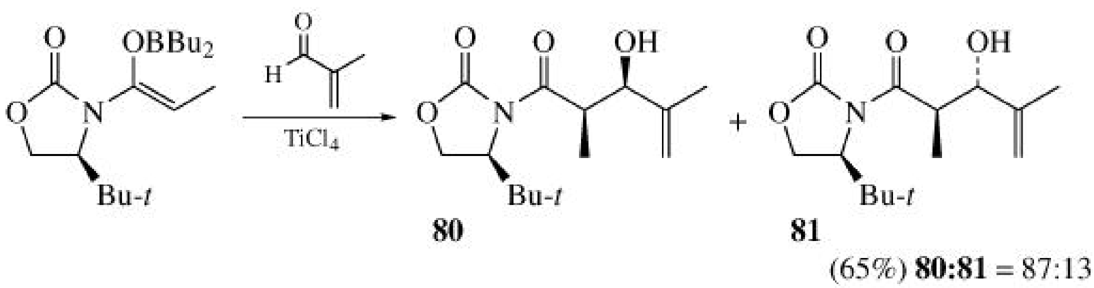


(43)



(44)

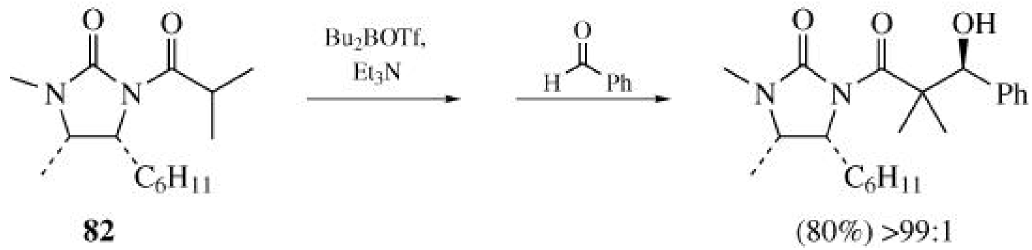
The reaction can also be adapted to provide the "non-Evans" syn aldol adduct as the major product by using nonsterically demanding Lewis acids such as $TiCl_4$ (Eq. 45). (103) It should be noted that the premixing of sensitive aldehydes with Lewis acids may lead to side reactions.



(45)

In certain cases, excess dibutylboron triflate can act as a Lewis acid, thus diverting the usual syn-selective reaction to an anti aldol reaction. (102, 104) A loss in selectivity when using an excess of dibutylboron triflate is indicative of this competing reaction pathway. Note that when triethylamine is used rather than diisopropylethylamine, this effect should be less important since triethylamine coordinates more strongly to dibutylboron triflate, thus minimizing any erosion of stereocontrol. (10, 102)

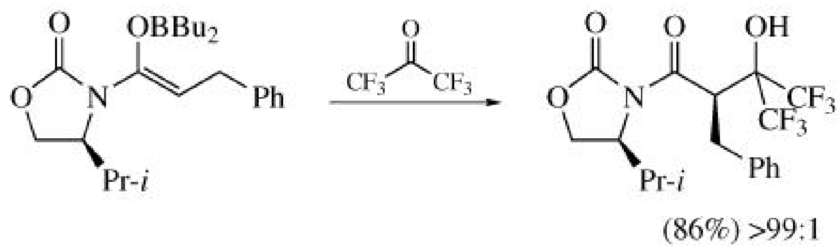
With the successful generation of anti aldol products, one area that still requires study is the asymmetric synthesis of quaternary centers. (105) The reaction of tetra-substituted enolates of typical oxazolidinones proceeds poorly, (106) but the use of the related ephedrine-derived imidazolidinone **82** is reported to be successful, as shown in Eq. 46. (345) It remains to be seen whether this can be extended to the asymmetric synthesis of quaternary stereocenters.



82

(46)

Another method of establishing quaternary stereocenters involves the aldol reaction of a boron enolate with an unsymmetrical ketone. However, boron enolates are usually unreactive to ketones, and other metal enolates such as tin(II) would be better suited to this transformation. (5) The only successful examples of such an asymmetric, boron-mediated reaction are with highly electrophilic ketones such as hexafluoroacetone (e.g., Eq. 47), which probably proceed through an open transition state. (107)

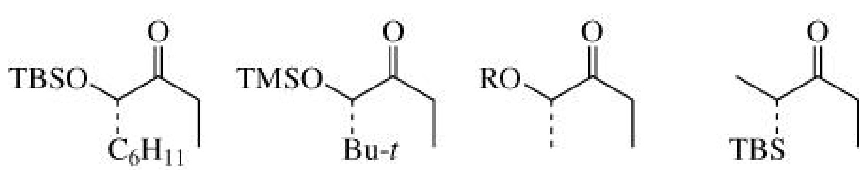


(47)

3.2.2. α -Oxygenated Ketone Auxiliaries

Chiral auxiliaries unrelated to heterocyclic imides and sultams are also known. The most common of these are the α -oxygenated ketones **83**, (108) **84**, (109) **85**, (110) and **86**, (110) although the α-silyl ketone **87** (111) is also known (Fig. 3). While these are simple chiral ketones, the aldol products are manipulated in such a way that they are best considered as chiral auxiliaries.

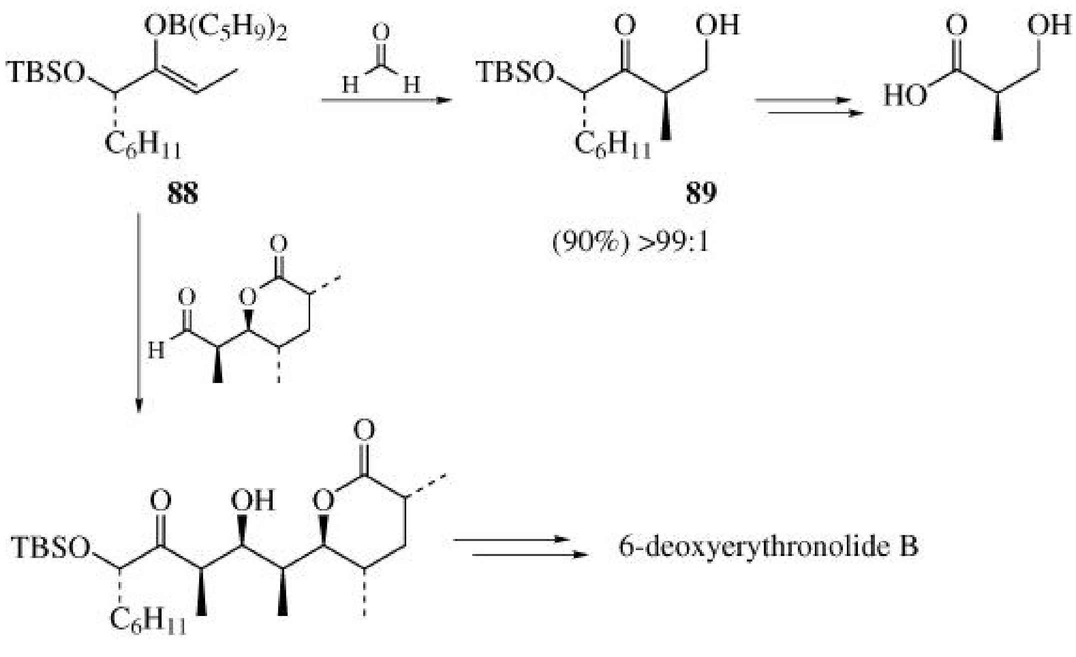
Fig.3.



83[108] **84**[109] **85**, R = Bn[110] **86**, R = Bz[110] **87**[111]

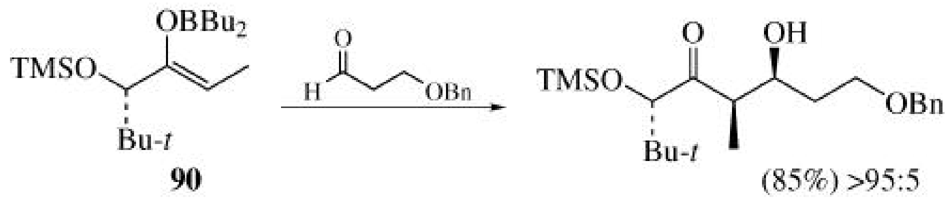
The ethyl ketone **83** and its enantiomer are derived from (*S*)- and (*R*)-mandelic acid respectively. (108) The derived enolates of these ketones undergo highly selective syn aldol reactions using sterically demanding ligands on boron. The major aldol products are desilylated and then oxidatively cleaved to reveal the enantiomerically pure carboxylic acids. The reaction of enolate **88** even proceeds with formaldehyde to generate adduct **89**; (112) related reactions have been used in several synthetic efforts (113-115) including the synthesis of 6-deoxyerythronolide B (Scheme 3). (116)

Scheme 3.



An analogous system employs the auxiliary **84**, which is likely to be of limited synthetic utility because it is obtained from the expensive (L)-*tert*-butylglycine. (109) The derived boron enolate **90** reacts with the same sense of induction as enolate **88**, again giving syn aldol products with useful levels of diastereoselectivity, as indicated in Eq. 48.

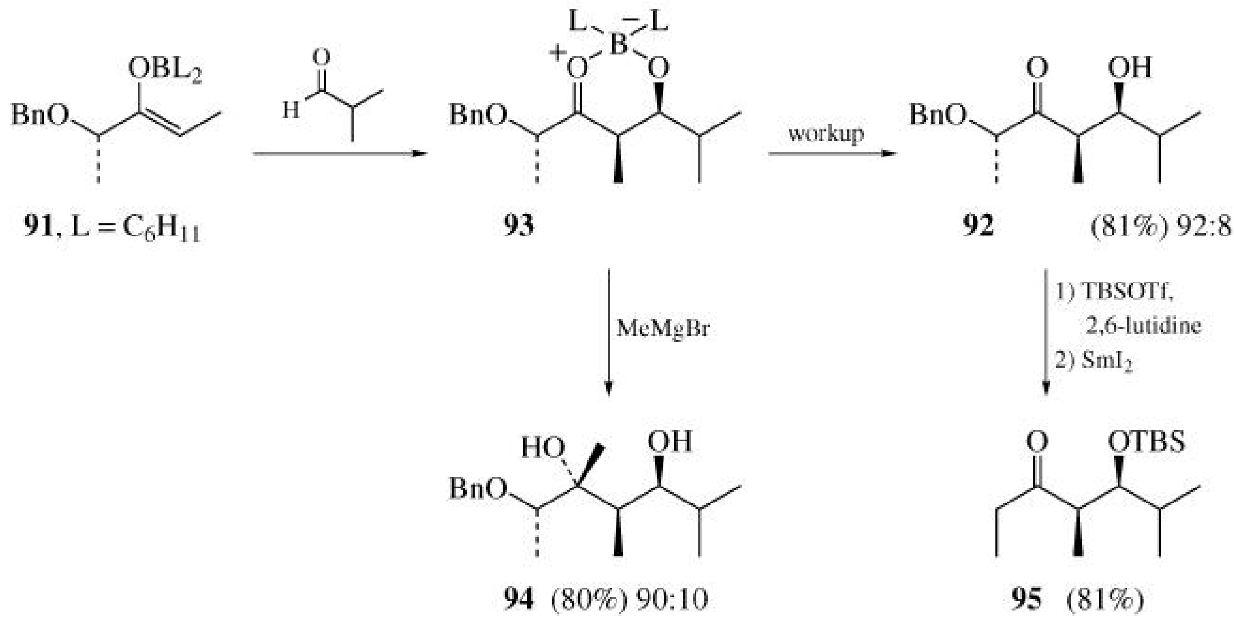
The third of these auxiliaries is the lactate-derived ketone **85** (Fig. 3); its (*Z*)-boron enolate **91** also undergoes selective syn aldol reactions (Scheme 4). (110, 117) The aldol products, such as **92**, can be manipulated via an oxidative cleavage step to reveal synthetically useful compounds. This process has been extended to the in situ addition of carbon nucleophiles to the aldolate intermediate **93** to give a stereochemically defined diol product **94**. (117) Ethyl ketones, for example, compound **95**, can also be prepared using samarium diiodide (SmI_2) to remove the α-benzyloxy group of ketone **92**. Potentially, this can be used as an “auxiliary-free”



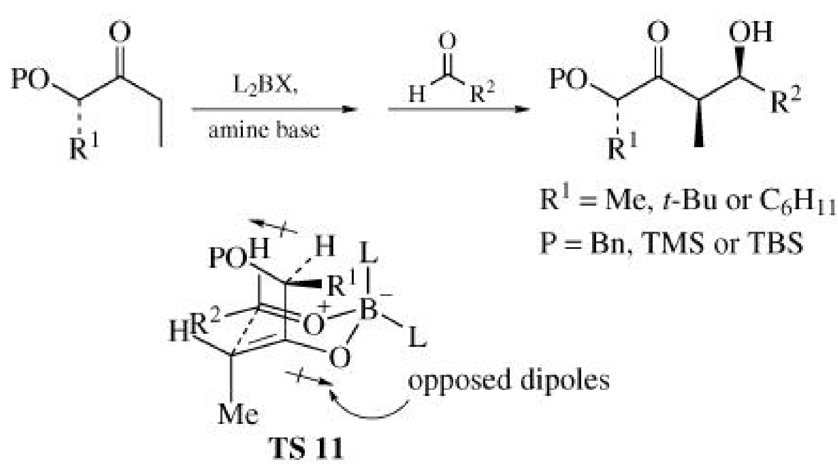
(48)

system with the methyl group of the products retained (cf. the cyclohexyl or *tert*-butyl groups of the previous auxiliaries). Another advantage is that both enantiomers are easily obtained from the inexpensive (*S*)-ethyl and (*R*)-isobutyl lactate esters.

Scheme 4.



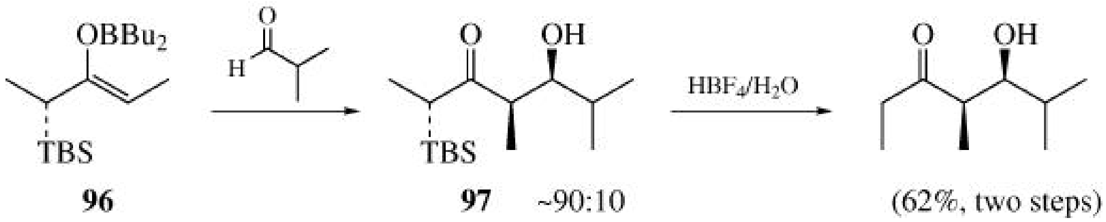
The three previously described auxiliaries lead to the same sense of asymmetric induction, as indicated in Eq. 49. In each case, the (*Z*)-enolate reacts via chair



(49)

transition state **TS 11** with the bulky alkyl group positioned to avoid steric congestion and the alkoxy group aligned so as to oppose the dipole associated with the enolate oxygen. The moderate loss of selectivity when changing from the cyclohexyl or *tert*-butyl groups to the α -methyl group of compound **85** is noteworthy.

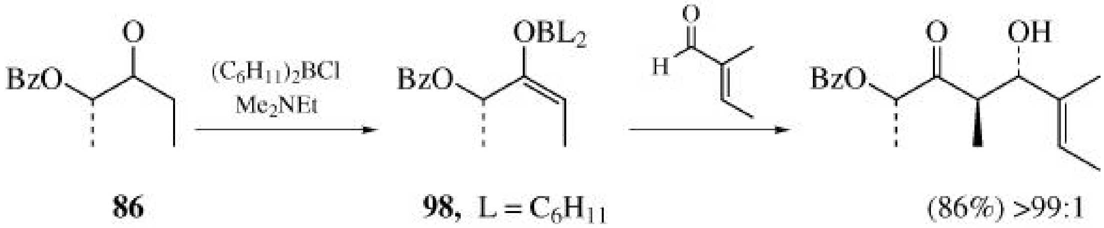
An alternative to the previously mentioned α -oxygenated auxiliaries is the α -silyl ketone **87**, whose synthesis depends upon the use of a RAMP or SAMP auxiliary. (111) The (*Z*)-boron enolate **96** shows high levels of asymmetric induction in aldol reactions, again giving syn aldol adducts (Eq. 50). The diastereoselectivity



(50)

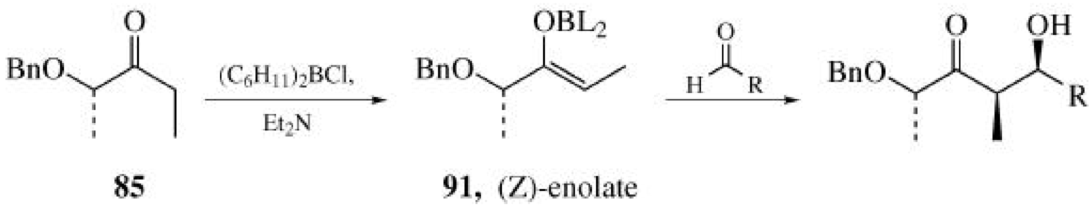
of the reaction matches the (*Z*):(*E*) selectivity of the enolization, so further improvement to the enolization selectivity would be profitable. The aldol products, such as ketone **97**, can be desilylated with tetrafluoroboric acid to give the corresponding ethyl ketones, a transformation analogous to theα -deoxygenation of aldol adduct **92**, Scheme 4.

The foregoing examples again show how syn aldol products of defined absolute configuration can be successfully constructed using auxiliary control. However, the synthesis of anti aldol products without using strong Lewis acids to divert reactions away from cyclic transition states is desirable. One solution to this problem is the benzoate-protected, lactate-derived ketone **86**. (110) The (*E*)-enolate **98** adds to aldehydes with almost complete π -face selectivity to give anti adducts, where the minor product (<2%) is a syn aldol isomer (Eq. 51). (110, 118)

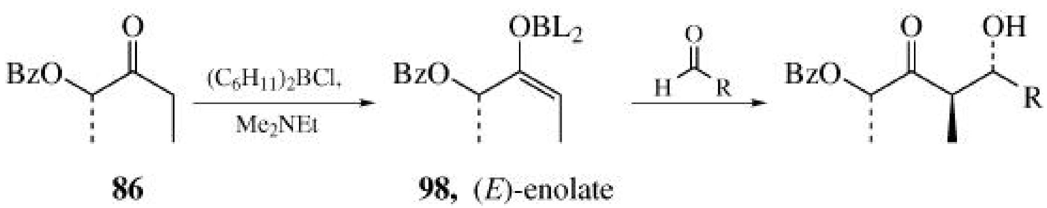


(51)

The anti selectivities from this reaction depend on formation of the (*E*)-boron enolate **98** by enolization of ketone **86** with the bulky dicyclohexylboron chloride reagent in conjunction with a small amine base (typically dimethylethylamine). Note that the conditions for the formation of this (*E*)-enolate (Eq. 53) are almost identical to the conditions for the formation of the (*Z*)-enolate **91** of the benzyl protected ketone **85** (Eq. 52). The benzyl protecting group of the αoxygen in compound **85** allows chelation of the boron reagent before deprotonation, leading to the formation of a (*Z*)-enolate **91**. In contrast, the benzoate-protected system **86** does not facilitate chelation, and the (*E*)-enolate **98** is formed.

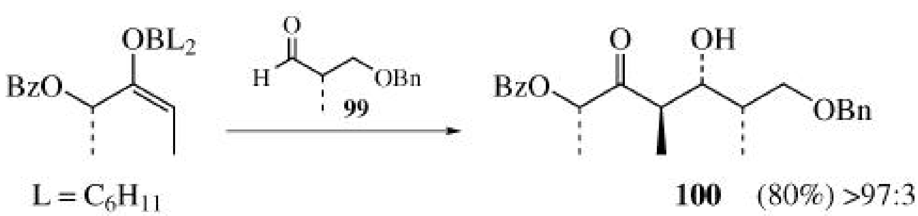


(52)

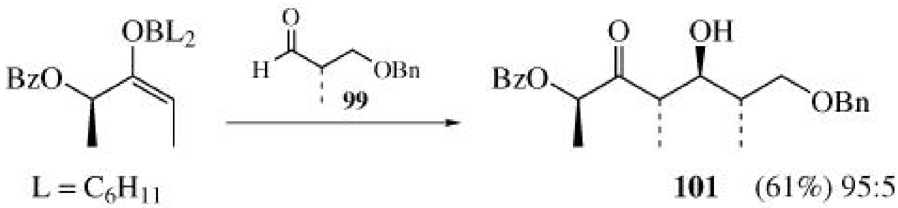


(53)

Reagent control is possible in this anti aldol reaction, as demonstrated by the reaction of each enantiomer of the ketone with the same α -chiral aldehyde **99** (Eqs. 54 and 55). (110) Here, the enolate facial selectivity dominates that of the aldehyde leading to the Felkin **100** or anti-Felkin product **101**, respectively.

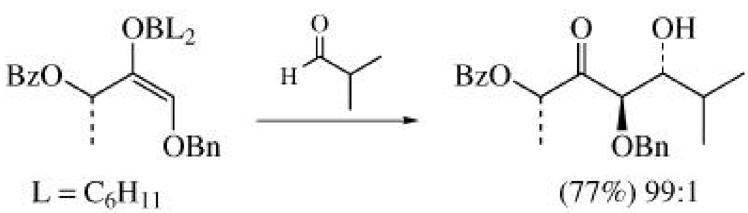


(54)



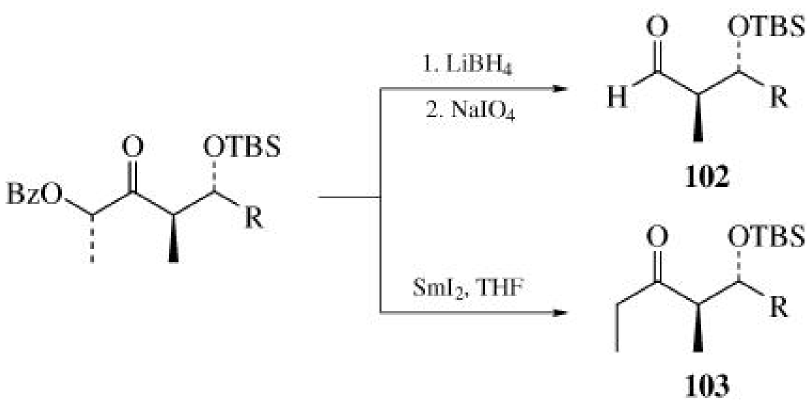
(55)

This anti aldol reaction has also been extended to propyl and α -alkoxymethyl ketones with similarly high diastereoselectivities (Eq. 56). (110)



(56)

The synthetic utility of the anti aldol products is similar to those already discussed. Hence, a two-step protocol (lithium borohydride followed by sodium periodate) affords aldehydes of general structure **102**, while removal of the α -benzoate group with samarium diiodide gives ethyl ketones **103**, Eq. 57. (117)



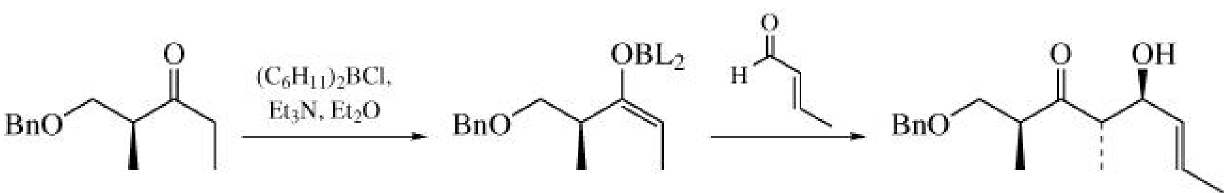
(57)

3.3. Substrate-Mediated Aldol Reactions Using Chiral Ketones

The asymmetric induction imparted by chiral aldehydes alone is usually insufficient to lead to highly selective boron-mediated aldol reactions (vide supra). Hence, it is usually necessary to impart stereocontrol from a chiral enolate. This has already been demonstrated for the auxiliary-mediated aldol reaction where the auxiliary group is subsequently removed. This section outlines reactions of chiral ketones where the controlling stereocenter(s) is retained, not just in the aldol product, but also in the target molecule. Such an approach is often more direct than using auxiliary control, as steps to install and then remove the auxiliary are not required.

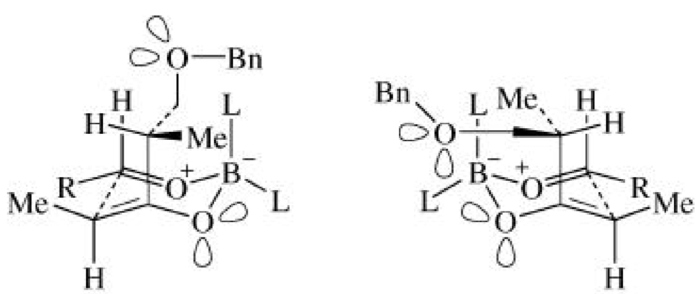
3.3.1. α -Chiral Ketones

One of the most simple and effective chiral ketones for use in asymmetric aldol reactions is ethyl ketone **104**, which acts as a dipropionate equivalent for the synthesis of polypropionate natural products. (119-121) It is synthesized in three steps from commercially available (*S*)-methyl 3-hydroxy-2-methylpropionate. (122) The same route is followed in the enantiomeric series starting from the (*R*)-ester. The (*E*)-boron enolate **105** of this ketone, generated by reaction with ($C_6H_{11})_2BCl$ /Et_3N, reacts with aldehydes to give anti-anti aldol adducts with high levels of diastereoselectivity (>95% ds) (Eq. 58). (120, 122)



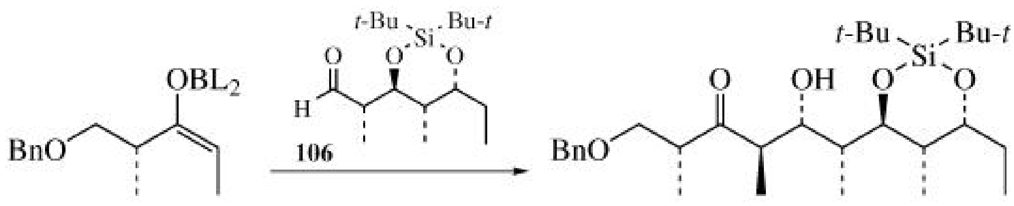
(58)

Transition-state structure **TS 12** accounts for the selectivity of this anti aldol reaction. (6) The benzyloxymethylene unit of the ketone faces into the transition state, and this contra-steric arrangement is explained by the avoidance of lone-pair repulsion between the enolate oxygen and that of the benzyl ether substituent (cf. **TS 13**). If the ether oxygen is replaced by a methylene group, the enolate face selectivity is greatly reduced.



TS 12　　**TS 13**

This aldol reaction is particularly well suited to the synthesis of complex polyketide natural products and has been used in the synthesis of swinholide A, (208, 213) denticulatins A and B, (123, 124) oleandolide, (122, 125) and muamvatin. (126) For the last, the chiral enolate **ent-105** was added to the chiral aldehyde **106** to give anti adduct **107**, resulting from a matched aldol reaction (Eq. 59). Note that the benzyl



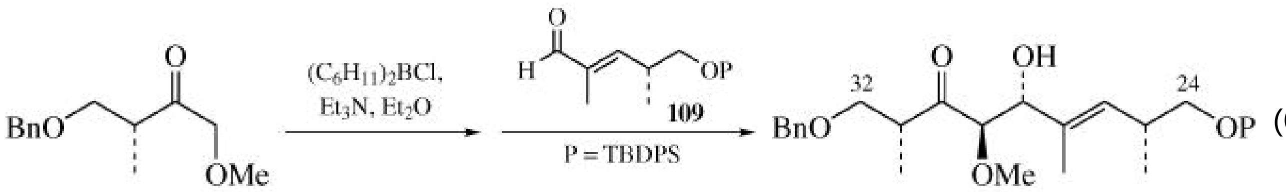
ent-105, L = C_6H_{11} **107** (91%) >98:2 (59)

protecting group of the ketone can be varied to include PMB and TIPS, although the latter leads to reduced selectivity.

The reaction has also been extended by the in situ reduction of the initially formed boron aldolate, thus affording syn 1,3-diols selectively in a single operation (Eq. 60). (123, 124, 127)

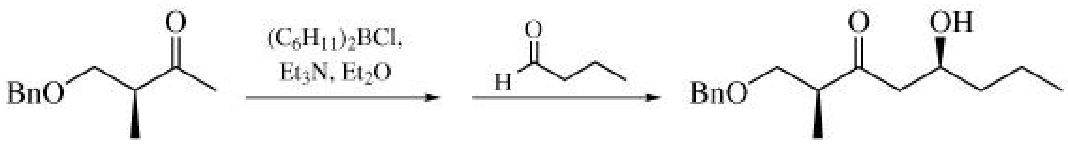
L = C_6H_{11} (91%) 97:3 (60)

The analogous α -alkoxymethyl ketones are equally successful in anti aldol reactions. The aldol addition of chiral ketone **108** with aldehyde **109** proceeds with high stereocontrol (97% ds) to afford adduct **110**, a C(24)–C(32) subunit of the macrolide rapamycin. (128)



108 110 (94%) 97:3

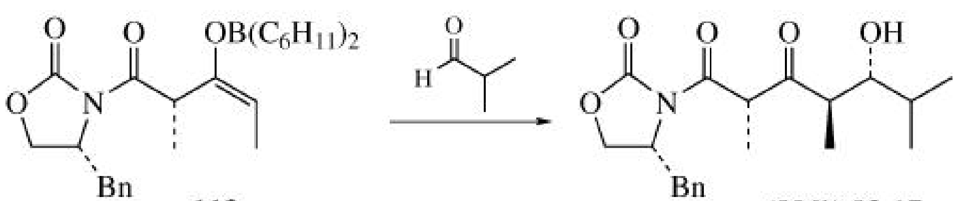
Chiral methyl ketone **111** undergoes aldol reactions with useful levels of 1,4-asymmetric induction to give β -hydroxy ketone **112** preferentially (Eq. 62). (120) The diastereoselectivity of this reaction is improved by the use of chiral ligands on boron; this is discussed further in the next section.



(62)

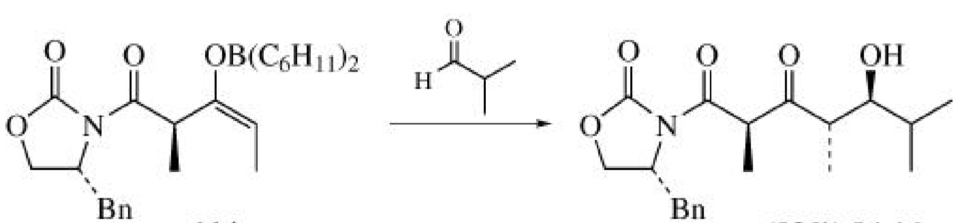
111 112 (84%) 88:12

A related anti aldol reaction, which again uses dicyclohexylboron chloride for enolization, is that of β -keto imides (Eqs. 63 and 64). (129) In these systems, the α -methyl group is the controlling asymmetric influence; the auxiliary stereocenter of the enolates **113** and **114** has little effect.



(63)

113 (89%) 83:17

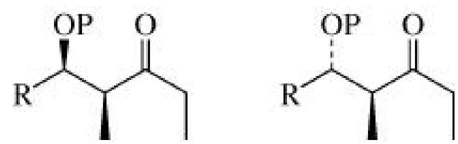


(64)

114 (93%) 84:16

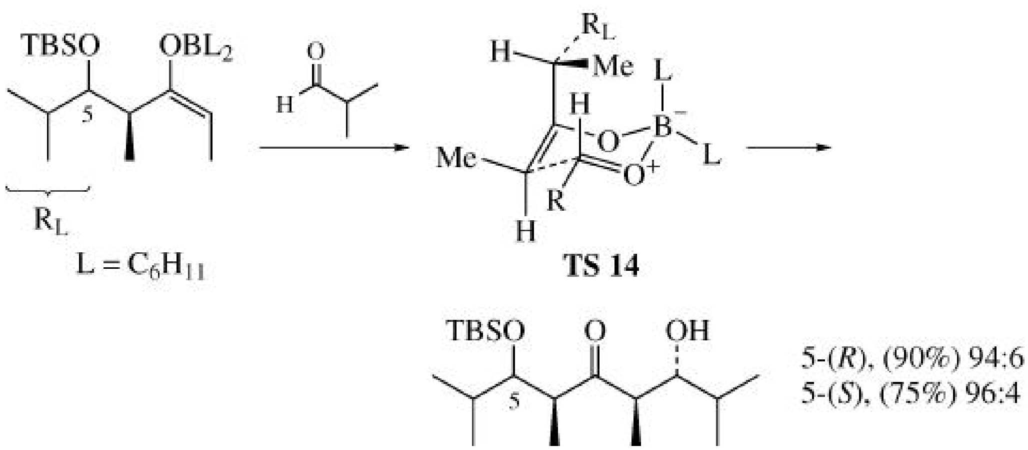
3.3.2. β -Alkoxy Chiral Ketones

Another well-studied group of chiral ethyl ketones are compounds **115** and **116**. (21, 26, 38, 129-133) It is possible to generate selectively either the (*E*)- or (*Z*)-enolate of these α-methyl- β -alkoxy systems, which then display high levels of asymmetric induction with achiral aldehydes.



115 **116**

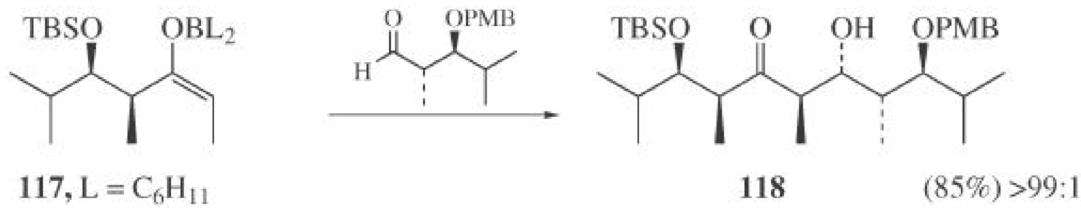
Results indicate that the β -stereocenter of the ketone plays a limited role in these reactions because the compounds epimeric at this stereocenter lead to similar levels of asymmetric induction in anti aldol reactions (Eq. 65). (129) Therefore,



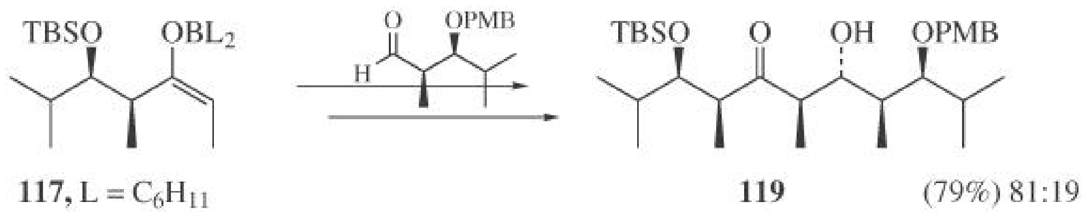
(65)

the α -methyl group is the principal controlling influence which acts in the opposite sense to the previously mentioned anti aldol examples (cf. enolates **105**, **113**, and **114**). This has been rationalized by a steric model **TS 14**, where the large group (R_L) occupies the outside position in the chair transition state and A(1,3)-strain is minimized. (6, 129, 134)

The reaction of the (*E*)-boron enolate **117** has also been studied with chiral aldehydes. (38) These reactions proceed with good levels of control when the enolate is matched with the aldehyde in a Felkin sense as in product **118**. The dominant influence in these reactions is from the enolate, and even the mismatched case giving adduct **119** proceeds in good yield, although with lower levels of asymmetric induction (81% ds). (38)

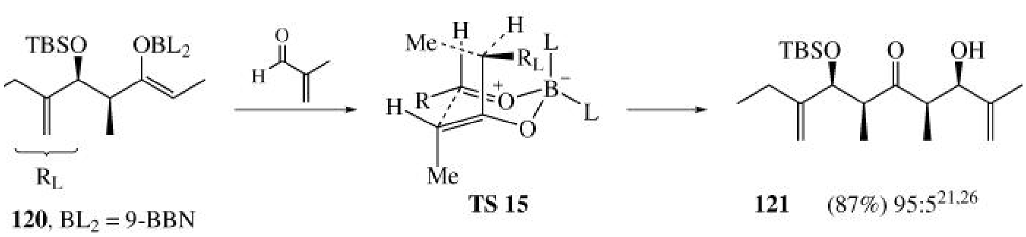


(66)



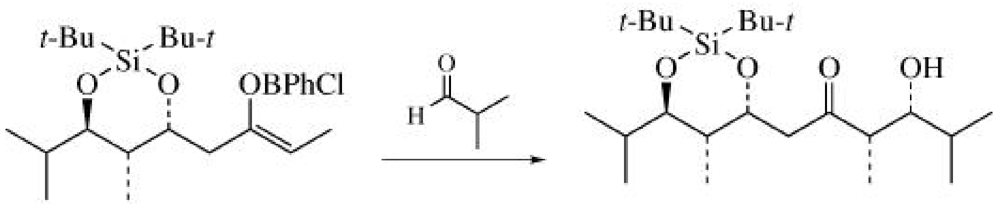
(67)

The analogous syn aldol reaction of these systems is also synthetically useful (130, 132, 135) and has been applied to the synthesis of ebelactones A and B (see Application to Synthesis section). (21, 26) Again, the β-alkoxy group of the enolate **120** plays a limited role in the reaction; the steric transition state model **TS 15** accounts for preferential formation of product **121** (Eq. 68). (6, 134)



(68)

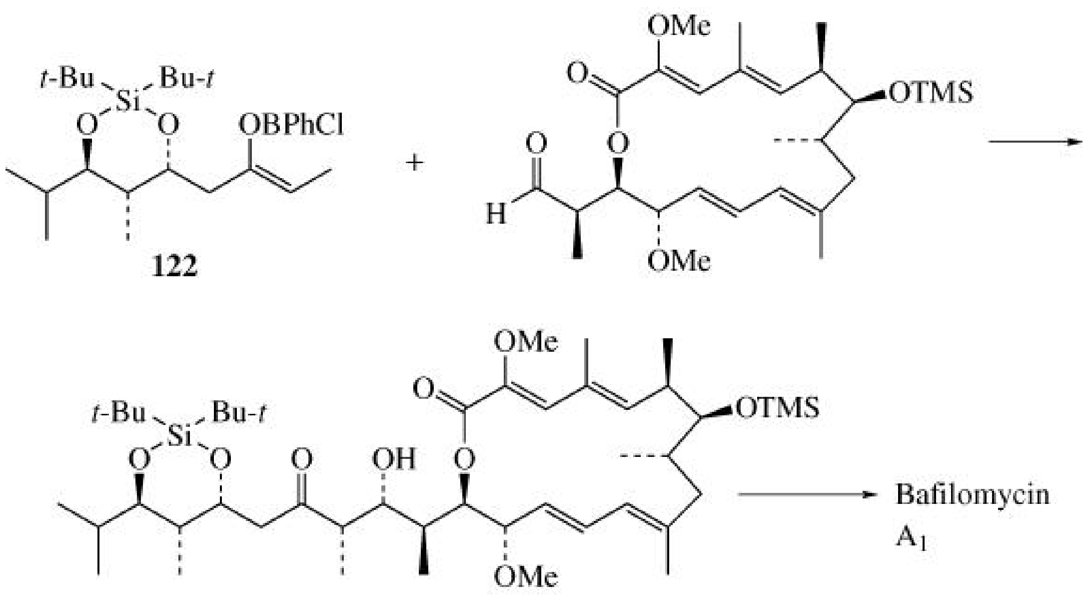
In the preceding examples, the α -methyl group of the enolate controls the selectivity of the aldol reactions. (*Z*)-Enol borinate **122**, where such an α -methyl group is absent, reacts with achiral aldehydes with high levels of 1,4-asymmetric induction giving, for example, adduct **123** (Eq. 69). (136)



122 123 (72%) >99:1 (69)

When this reaction was applied to the synthesis of the macrolide bafilomycin A_1, it again performed well, affording the desired aldol product **124** exclusively (Scheme 5). (136) These aldol reactions are notable for the utilization of the uncommon chlorophenylboron enolate. (137)

Scheme 5.



122

124 (60%) >95:5

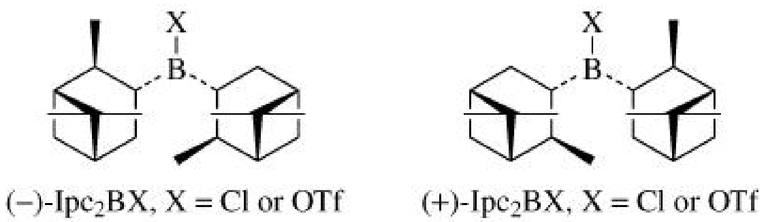
This last example highlights the benefit of developing reaction conditions whereby the stereochemistry of the aldol substrates can be used to advantage in the concise synthesis of complex systems. There are times, however, when the inherent facial bias of the enolate and the aldehyde are mismatched. The use of chiral ligands on boron then offers the possibility of enhancing the required selectivity, and this is discussed in the following section.

3.4. Ligand-Mediated Aldol Reactions Using Chiral Boron Reagents

The use of chiral ligands on boron for stereochemical control in aldol reactions of ketones and thioesters with aldehydes corresponds to reagent control. This contrasts with the substrate control provided by chiral ketones or chiral aldehydes. A significant advantage of this class of boron-mediated aldol reactions is that it produces enantiomerically enriched synthetic intermediates from simple prochiral starting materials. It also provides the possibility of using a chiral reagent to reinforce and perhaps even overturn the inherent stereochemical bias of a chiral ketone or aldehyde.

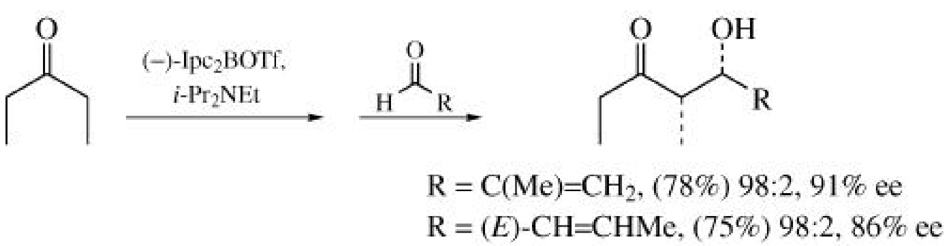
3.4.1. Isopinocampheyl (Ipc) Ligands on Boron

Among the most common reagents used are the two enantiomeric forms of diisopinocampheylboron chloride, Ipc_2BCl, which is a commercially available crystalline solid. (138) This reagent



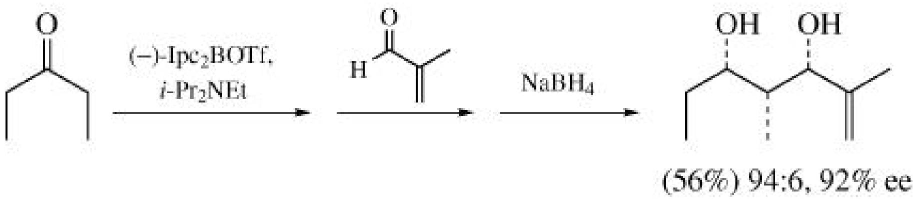
was introduced for the asymmetric reduction of ketones; (139, 140) the corresponding boron triflate was first used for the asymmetric aldol reaction of an azaenolate. (141, 142) The boron chloride can itself be a useful chiral reagent for aldol reactions, or the corresponding diisopinocampheylborane (Ipc_2BH) can be used to prepare the triflate. (121, 141)

The use of the boron triflate in conjunction with the hindered base diisopropylethylamine leads to the formation of (*Z*)-enolates from ethyl ketones and subsequently to syn aldol products. (133) As can be seen from Eq. 70, the asymmetric



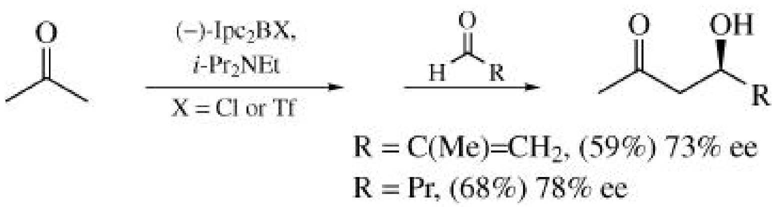
(70)

aldol reaction of diethyl ketone with aldehydes facilitated by (–)-Ipc_2BOTf proceeds in good yield to afford aldol products with enantiomeric excesses up to 93%. (121, 143) The in situ reduction of the boron aldolates of these reactions provides enantiomerically enriched 1,3-diols in moderate yield (Eq. 71). (144)



(71)

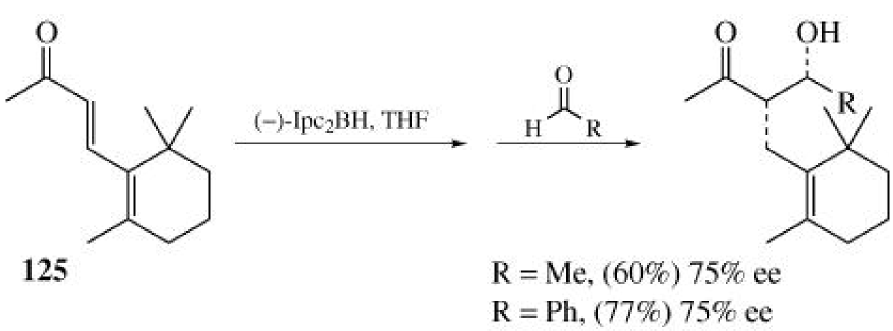
The corresponding methyl ketone aldol reaction (Eq. 72) with the same reagent system affords aldol adducts which are lower in enantiomeric purity and,



(72)

surprisingly, of opposite aldehyde facial selectivity than the ethyl ketone reaction. (121,145) This is explained by the ethyl ketone reaction proceeding through a chair-like transition state, with the methyl ketone reaction preferring a twist-boat arrangement. (146)

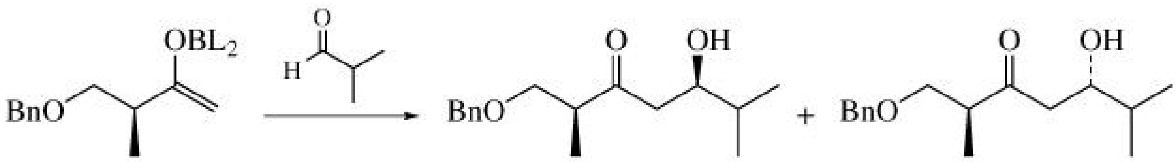
An extension of this work uses Ipc_2BH, which reacts with enones in a conjugate fashion, thus generating a chiral boron enolate. (147, 148) This reaction has the advantage of controlling the regiochemistry of enolate formation and, at times, leading to the preparation of otherwise inaccessible enolates. (149, 150) An example is the reaction of β -ionone (**125**) with Ipc_2BH and subsequent aldol addition to either acetaldehyde or benzaldehyde (Eq. 73). Under standard enolization conditions, the exclusive formation of this particular (*Z*)-boron enolate would not be possible. (147, 148)



125

(73)

The Ipc_2BOTf and Ipc_2BCl reagents have also been used in conjunction with chiral ketones in double stereodifferentiating aldol reactions. For example, the aldol reaction of enolate **126** with achiral ligands on boron affords adduct **127** with reasonable selectivity. When chiral ligands on boron are chosen in a matched sense, the selectivity and yield of the reaction improve considerably. (120, 151)*



126, L = Bu
129, L = (–)-Ipc

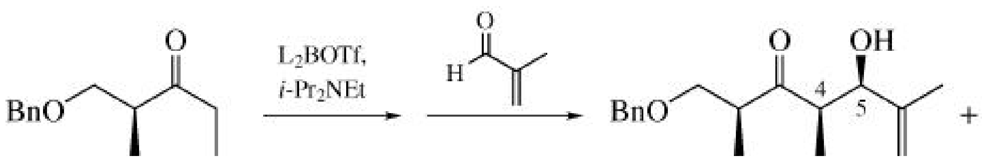
127

128

L = Bu, (45%) I:II = 84:16
L = (–)-Ipc, (91%) I:II = 95:5*

(74)

An informative example of this concept is the aldol reaction of chiral ketone **104** (Eq. 75). Using an achiral boron reagent the reaction was nonselective, giving

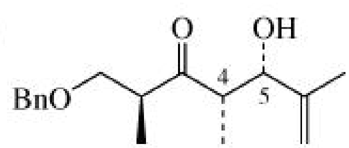


104

130

(75)

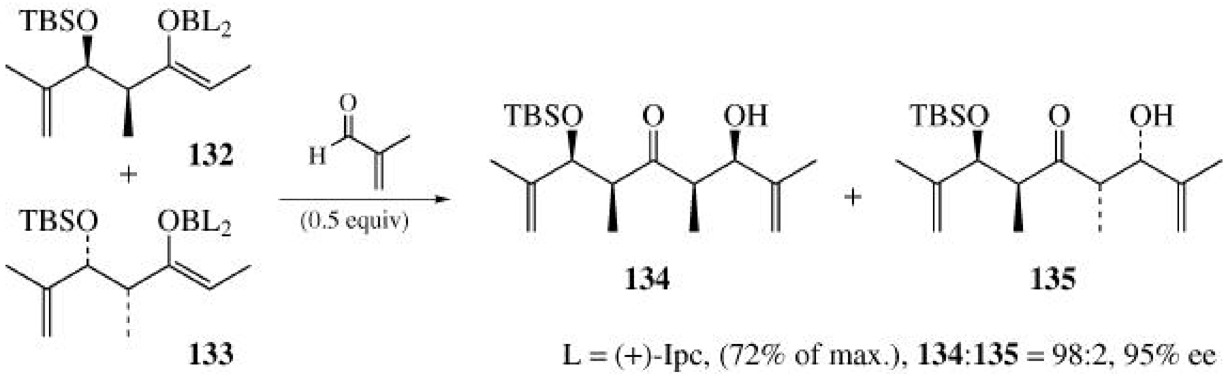
L = Bu, (76%) **130**:**131** = 54:46 (+ 8% 4,5-anti adducts)
L = (+)-Ipc, (74%) **130**:**131**= 93:7
L = (–)-Ipc, (62%) **130**:**131**= 7:93



131

a mixture of syn aldol isomers **130** and **131** in approximately equal amounts. (119) However, with the use of either (+)- or (–)-Ipc_2BOTf, either of the syn adducts can be produced with high stereocontrol. (119)

A kinetic resolution process using an asymmetric boron aldol reaction has also been performed with Ipc_2BOTf. (131, 133) Enolization of racemic chiral ketones with (+)-Ipc_2BOTf affords diastereomeric enolates, which may react with aldehydes at different rates. In Eq. 76, reaction of the diastereomeric enolates **132** and **133** with half an equivalent of methacrolein affords enantiomerically enriched aldol products (95%ee) from the faster reacting, matched enolate **132**.

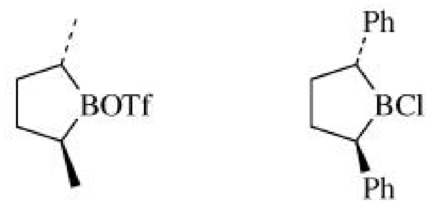


(76)

L = (+)-Ipc, (72% of max.), **134**:**135** = 98:2, 95% ee

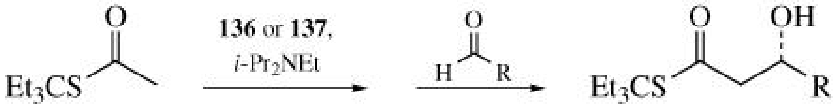
3.4.2. Borolane Reagents

Two chiral boron reagents which are structurally related to each other are the C_2-symmetric triflate **136** (152, 153) and chloride **137**, (154-156)



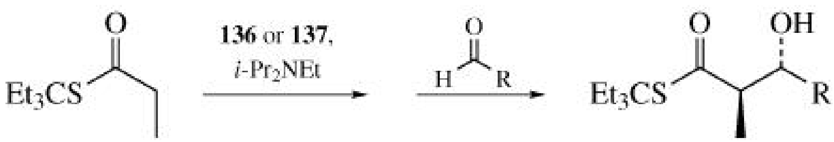
(*S*,*S*)-reagent, **136** (*R*,*R*)-reagent, **137**

both of which are prepared by a resolution procedure. These borolane reagents are efficient for asymmetric thioester aldol reactions, including reactions of acetates which are difficult to control using chiral auxiliary protocols (Eq. 77). (152, 155)



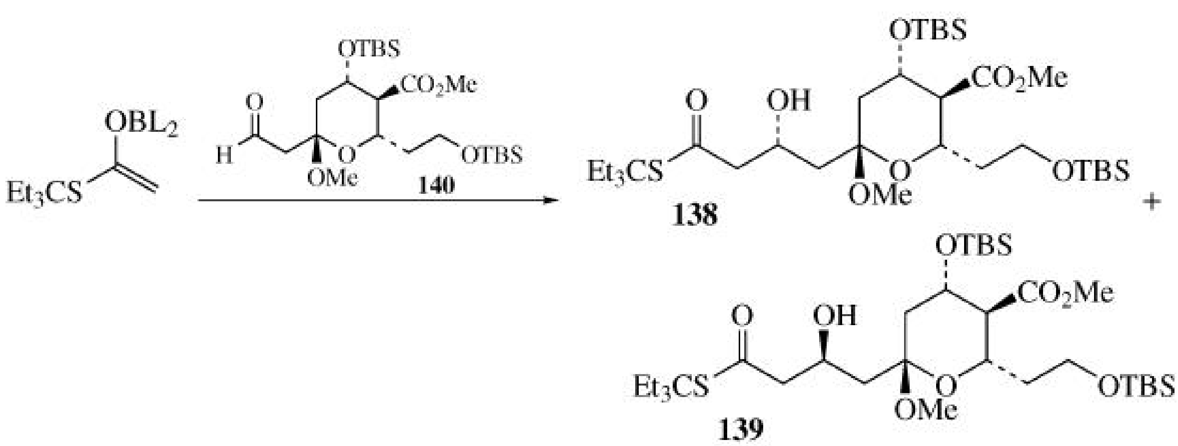
Reagent (**136**), R = *i*-Pr, (81%) 86.9% ee[152] (77)
" (**137**), R = *i*-Pr, (72%) 92% ee[155]
" (**136**), R = C_6H_{11}, (95%) 85.6% ee[152]
" (**137**), R = C_6H_{11}, (87%) 95% ee[155]

These reagents have also been used successfully in anti aldol reactions of α -substituted thioesters with aldehydes. With the use of a bulky group on sulfur, generation of the (*E*)-enolate is favored, which then leads to the formation of anti aldol adducts with high diastereo- and enantioselectivity (Eq. 78). (152, 155)



Reagent (**136**), R = *i*-Pr, (85%) 95.4% ee[152] (78)
" (**137**), R = *i*-Pr, (82%) 99% ee[155]
" (**136**), R = C_6H_{11}, (82%) 93.1% ee[152]
" (**137**), R = C_6H_{11}, (58%) 98.7% ee[155]

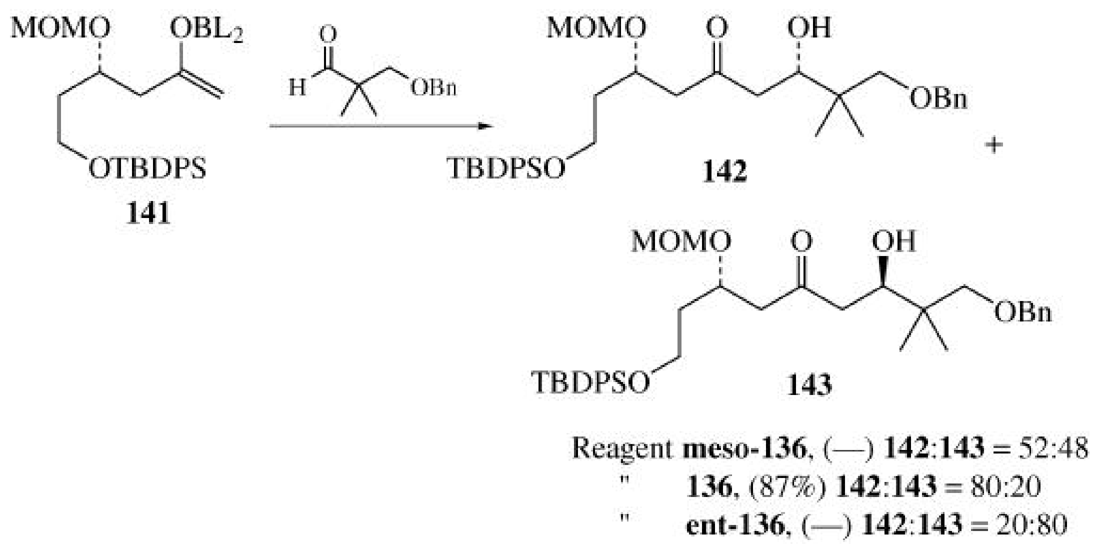
This work has been extended to reagent control in aldol additions to chiral aldehydes. (157) The strong induction from the boron enolate is effective in over-turning any existing facial bias of the aldehyde. For example, either of the two diastereomeric products **138** or **139** is prepared in good yield from aldehyde **140** by appropriate choice of chiral boron reagent (Eq. 79). (158)



(79)

Reagent **136**, (88-93%) **138**:**139** = 91:9
" **ent-136**, (88-93%) **138**:**139** = 11:89

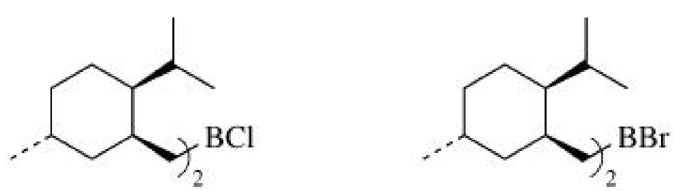
Reagent **136** has been successfully applied to the aldol reaction of ketone substrates as well as thioesters. The example shown in Eq. 80 is from the total synthesis of bryostatin 7. (153, 159, 160) Use of an achiral boron reagent indicated that the β -oxygenated chiral enolate **141** has little facial bias, and hence the use of chiral ligands on boron was necessary for a synthetically useful reaction.



(80)

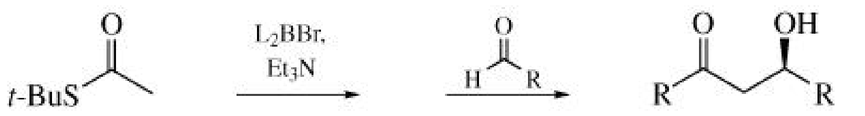
3.4.3. Menthone-Derived Ligands

Another series of boron reagents for aldol reactions are the computer-designed reagents **144** (161) and **145**, (162, 163) both of which



[(–)-(Menth)CH_2]$_2$BCl, (**144**) [(–)-(Menth)CH_2]$_2$BBr, (**145**)

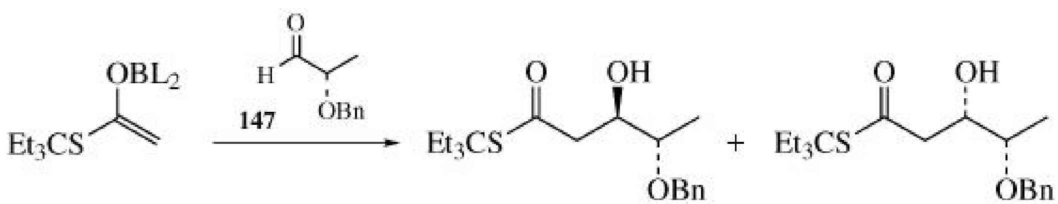
are derived from the methylenation and subsequent hydroboration of menthone. While the boron chloride **144** does not promote efficient enolization of thioesters, the bromide reagent **145** is sufficiently reactive, leading to products **146** of high enantiomeric purity (Eq. 81). (162)



146 (81)

L = (–)-(Menth)CH_2, R = *i*-Pr, (75%) 95.2% ee[162]
L = (–)-(Menth)CH_2, R = C_6H_{11}, (88%) 93.4% ee[162]

The selectivity obtained from this reagent overrides the influence of several chiral aldehydes in aldol additions, thus providing an example of double stereo-differentiation. (164, 165) Aldol reaction using either of the enantiomeric reagents with α -benzyloxy aldehyde **147** overturns any inherent facial bias of the aldehyde (Eq. 82). (164)

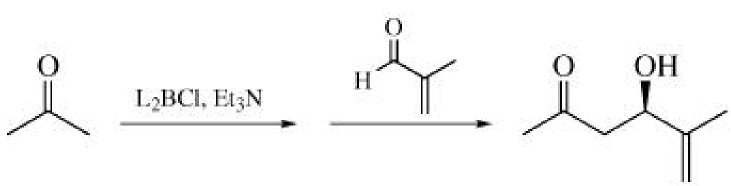


(82)

148 149

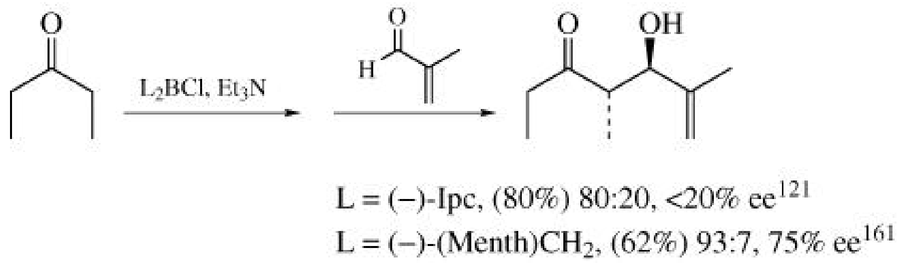
L = (–)-(Menth)CH_2, (75%) **148**:**149** = 93:7
L = (+)-(Menth)CH_2, (65%) **148**:**149** = 6:94

Use of the boron chloride reagent [(–)-(Menth)CH_2]$_2$BCl for the aldol reaction of methyl ketones (161) leads to enantioselectivities comparable to those obtained with the Ipc_2BCl reagent (Eq. 83). (121) On the other hand, the anti aldol reaction of diethyl ketone using [(–)-(Menth)CH_2]$_2$BCl is greatly superior to the same reaction using Ipc_2BCl (Eq. 84).



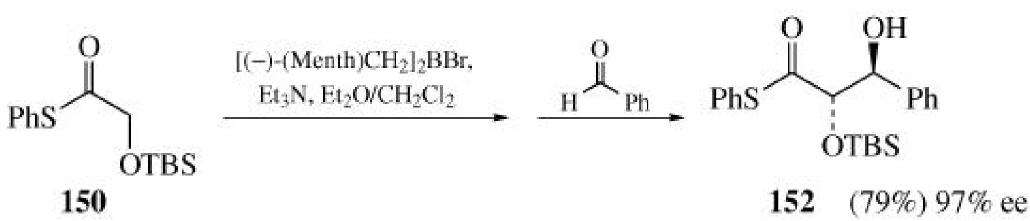
(83)

L = (–)-Ipc, (67%) 62% ee[121]
L = (–)-(Menth)CH_2, (65%) 58% ee[161]

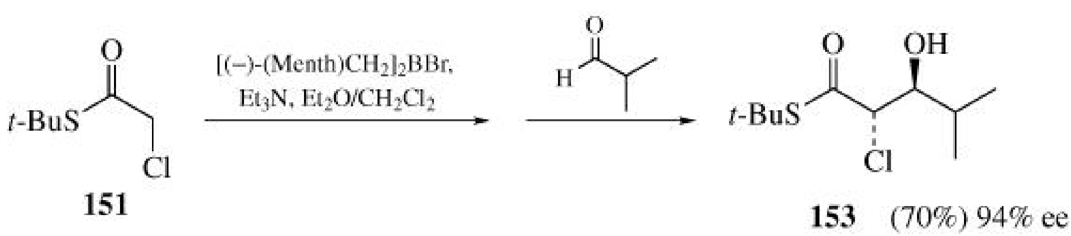


(84)

A useful extension of this work has involved the anti aldol reaction of a variety of α -substituted thioesters, for example, compounds **150** and **151**, which proceed with high levels of asymmetric induction to afford products **152** and **153**, respectively (Eqs. 85 and 86). (163)



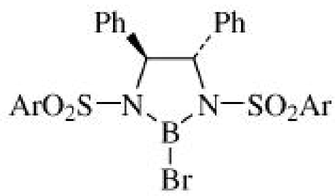
(85)



(86)

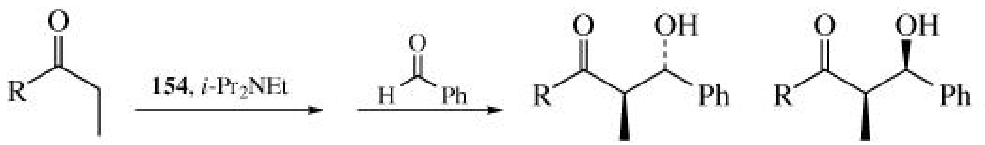
3.4.4. Diazaborolidine Reagents

While several chiral boron reagents are successful for the asymmetric aldol reaction of thioesters, only reagent **154** has been used for the corresponding reaction of esters. The boron bromide **154** is effective for the asymmetric anti aldol reaction of *tert*-butyl esters (19, 166-168) and for the syn aldol reaction of phenyl thioesters (Eq. 87). (19, 168, 169)



Ar = 3,5-$(CF_3)_2C_6H_3$, **154**
Ar = *p*-MeC_6H_4, **155**

(87)



156 **157**

R = OBu-*t*, (89%) **156**:**157** = 96:4, 94% ee[168]
R = SPh, (90%) **156**:**157** = 1:99, 97% ee[168]

It is worth noting that the reaction of diethyl ketone and benzaldehyde with the related diazaborolidine reagent **ent-155** affords aldol product **158** with an enantiomeric excess higher than any previous results for this reaction. (169, 170)

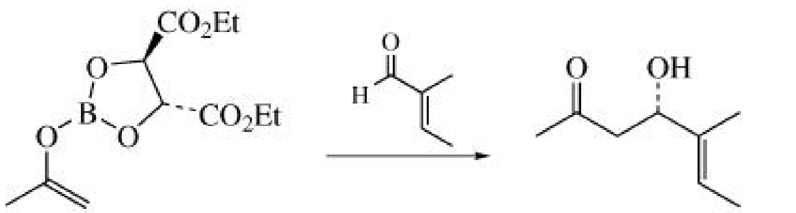
(88)

158 (95%) 97% ee

3.4.5. Boronates

Chiral enol boronates which utilize tartrate-derived ligands on boron have also been used in boron-mediated aldol reactions. α -Unsubstituted enolate **159** reacts with aldehydes to afford adducts, **160** for example, with moderate enantiocontrol (Eq. 89). (171)

In contrast to enol borinates of ethyl ketones, (*E*)- and (*Z*)-enol boronates of ethyl ketones add to aldehydes in a stereo-convergent manner to give syn aldol products. (31, 172-176) With this in mind, it is interesting that (*E*)-enol boronate (*E*)-**161** affords greater asymmetric induction than the corresponding (*Z*)-enol



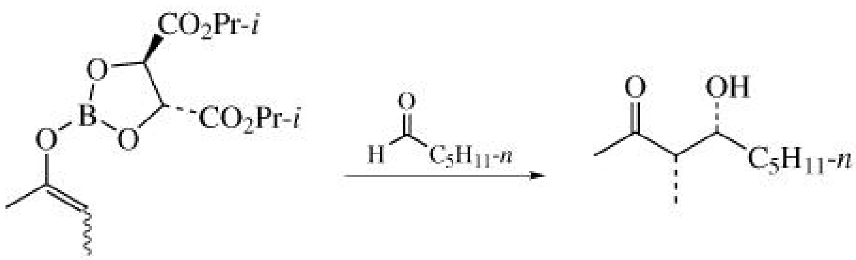
159

160

(64%) 57% ee

(89)

boronate (*Z*)-**161** (Eq. 90). (177) It should be noted that these enolates are not formed by direct enolization of 2-butanone.



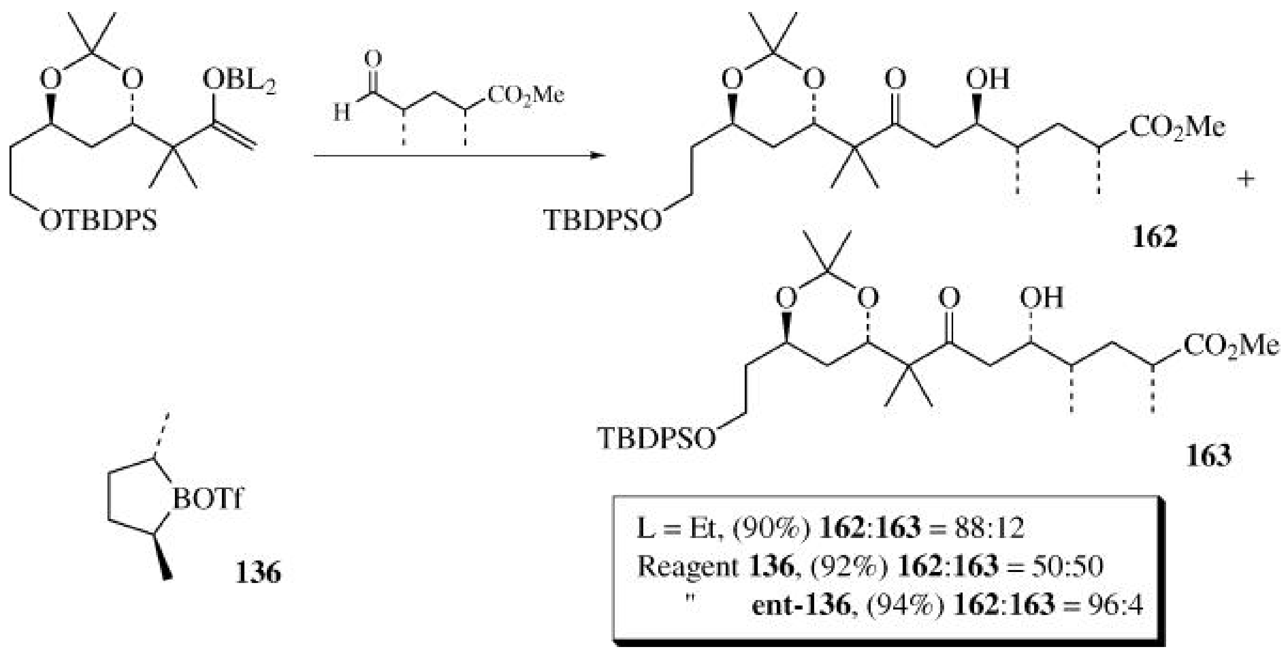
(*E*)-and (*Z*)-**161**

(*E*)-boronate, (74%) >95:5, 72% ee
(*Z*)-boronate, (45%) >95:5, 30% ee

(90)

3.5. Triple Asymmetric Induction

The most complicated aldol couplings are those between chiral ketones and chiral aldehydes mediated by chiral boron reagents. There have only been a few reported examples of these triple stereodifferentiating aldol reactions; (35, 178-180) this area of research will provide many interesting results in the future. To date, only methyl ketones have afforded reasonable yields; the enolization of sterically demanding ethyl ketones with bulky chiral boron reagents is problematic. It appears that the intrinsic facial selectivities of the components combine in an additive fashion. (8) One such example is shown and indicates that when the individual components of the reaction complement each other in a matched sense, as in the formation of **162**, highly selective reactions are possible. (178)



OBL2
CO2Me
H
O
OTBDPS
TBDPSO
OH
162
163
+
BOTf
136
L = Et, (90%) 162:163 = 88:12
Reagent 136, (92%) 162:163 = 50:50
" ent-136, (94%) 162:163 = 96:4

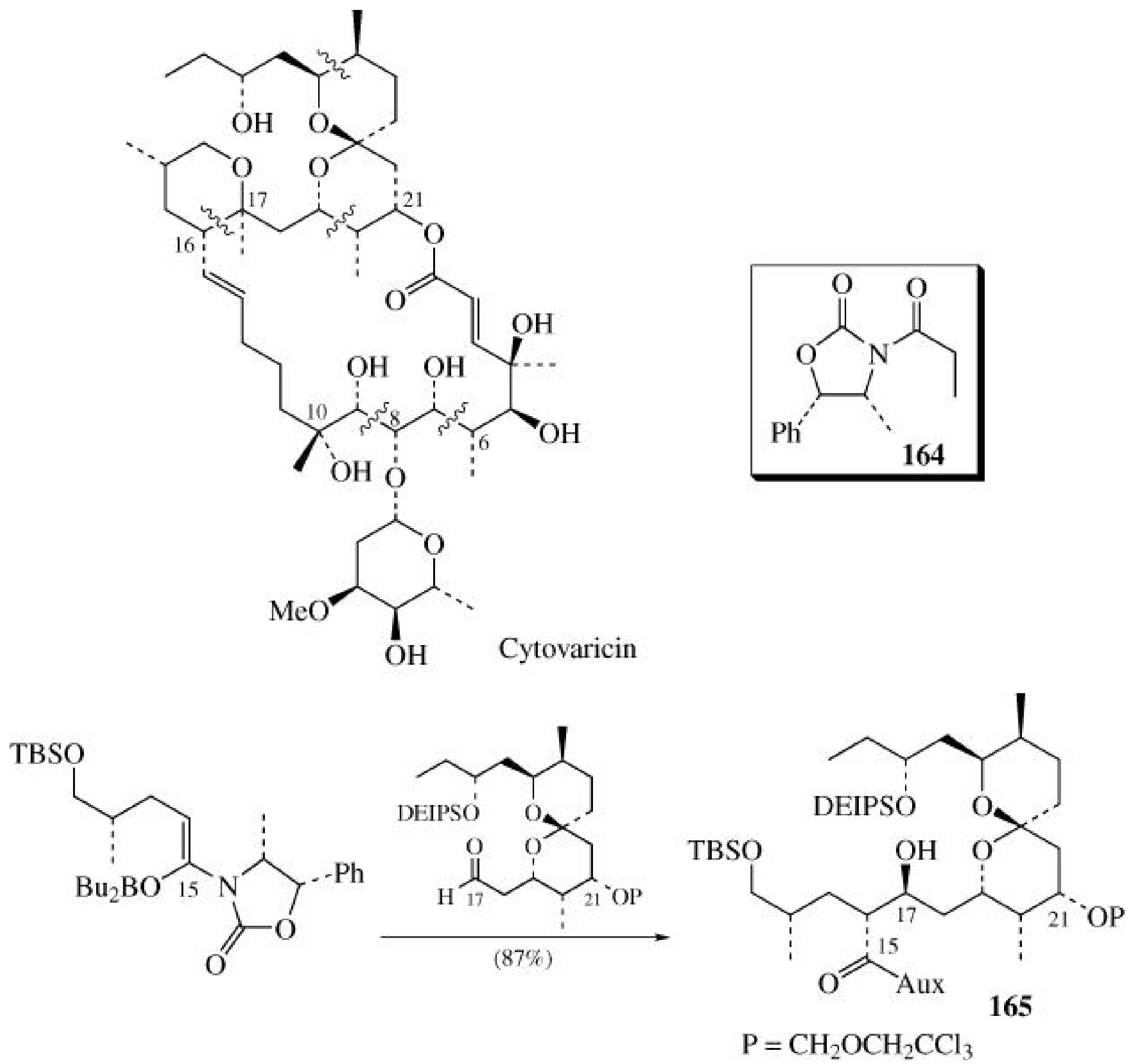
(91)

4. Application to Synthesis

The excellent levels of selectivity and high yields obtained in the boron-mediated aldol reaction have ensured that it has become the cornerstone of many total syntheses. The auxiliary-mediated reaction has commonly been used for the enantiocontrolled synthesis of subunits and also as a reliable method for the introduction of functionality at a late stage. A more concise approach is the use of chiral ketones in aldol reactions for the stereocontrolled synthesis of complex fragments. The coupling of these units may also use a boron-mediated aldol reaction, and chiral boron reagents allow the possibility of enhancing the required selectivity.

4.1. Cytovaricin

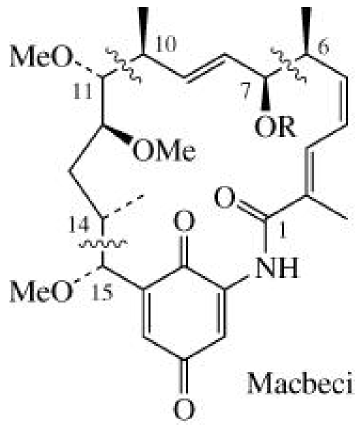
In the synthesis of the macrolide cytovaricin, the Evans syn aldol reaction is used five times in all. (61) Three of the boron-mediated aldol reactions were performed with chiral imide **164** and achiral aldehydes, while two were performed on more complicated substrates, including the example shown in Eq. 92, which afforded compound **165** as a single stereoisomer in 87% yield.



(92)

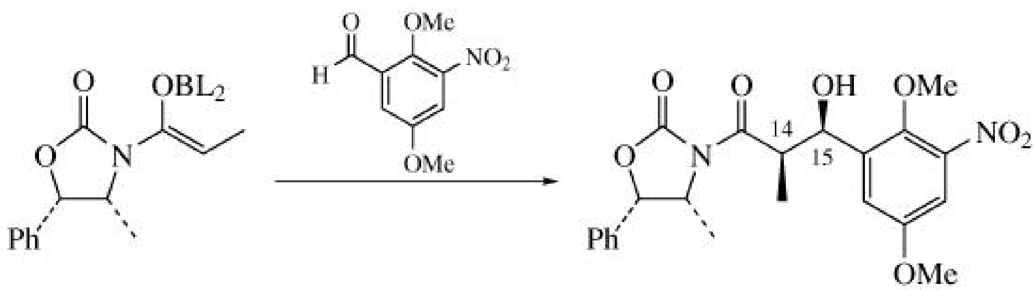
4.2. Macbecin I

The efficiency of the oxazolidinone aldol reaction has sometimes stimulated similar synthetic approaches to a target. In the Baker (181-184) and Evans (185, 186) syntheses of macbecin I, both groups use the same auxiliary-mediated syn aldol reaction to build the C(14)–C(15) bonds (Eq. 93). Similarly, both use a boron aldol reaction to build the C(6)–C(7) bond, and Evans also uses such a reaction to introduce the C(10)–C(11) stereocenters. Subsequently, Martin (46) has completed a formal total synthesis of macbecin I, which again uses a boron-mediated aldol reaction to form the C(6)–C(7) and C(10)–C(11) bonds.



Macbecin I, R = C(O)NH$_2$

(93)



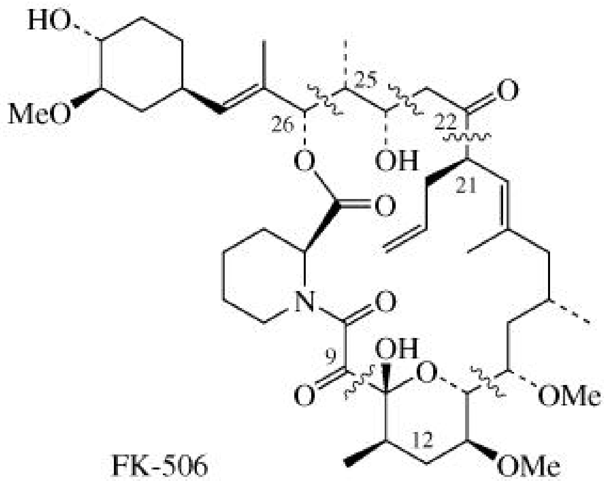
L = Et, (88%)[181-184]
L = Bu, (80%) >97% ds[185,186]

4.3. FK-506

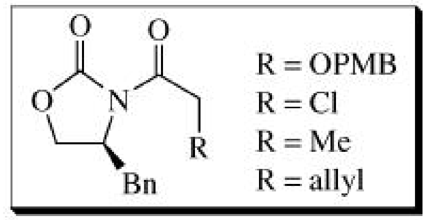
The utility of boron-mediated aldol reactions is readily apparent from synthetic efforts toward the immunosuppressant FK-506. In the Merck synthesis, the four different chiral imides shown are used in five auxiliary-mediated aldol reactions. (57, 187, 188)

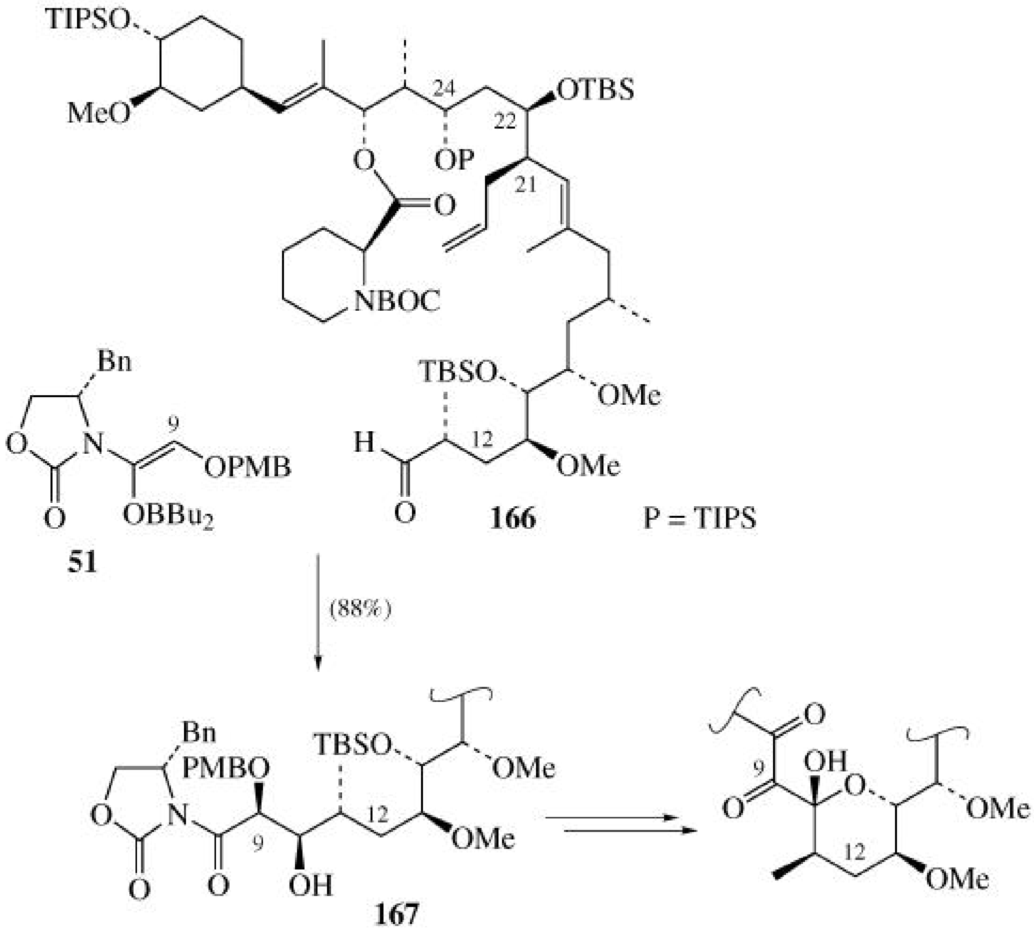
The reliability of the boron-mediated aldol reaction for the stereocontrolled formation of carbon–carbon bonds is highlighted in this synthesis. A key step is the reaction of boron enolate **51** with complex aldehyde **166**, which proceeds in 88% yield to give adduct **167** (Scheme 6). The two newly generated stereocenters from this reaction become part of the tricarbonyl unit of FK-506 and hence the aldol reaction is important, not for the stereocenters generated, but instead as an efficient carbon–carbon bond-forming step. It is also notable that several groups incorporate the C(21) allyl group via a boron-mediated aldol reaction. Again, this generates a stereocenter at C(22) which is subsequently lost through oxidation. (57, 189-191)

Scheme 6.

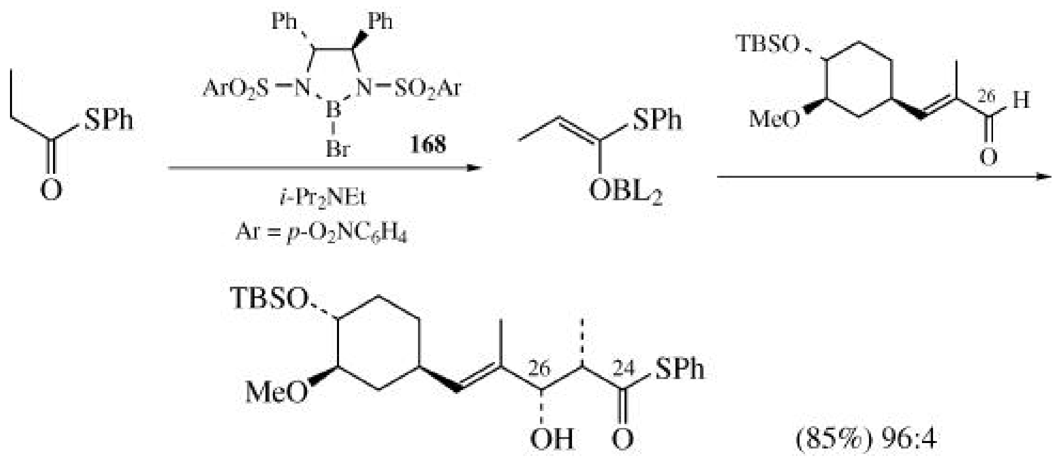


FK-506





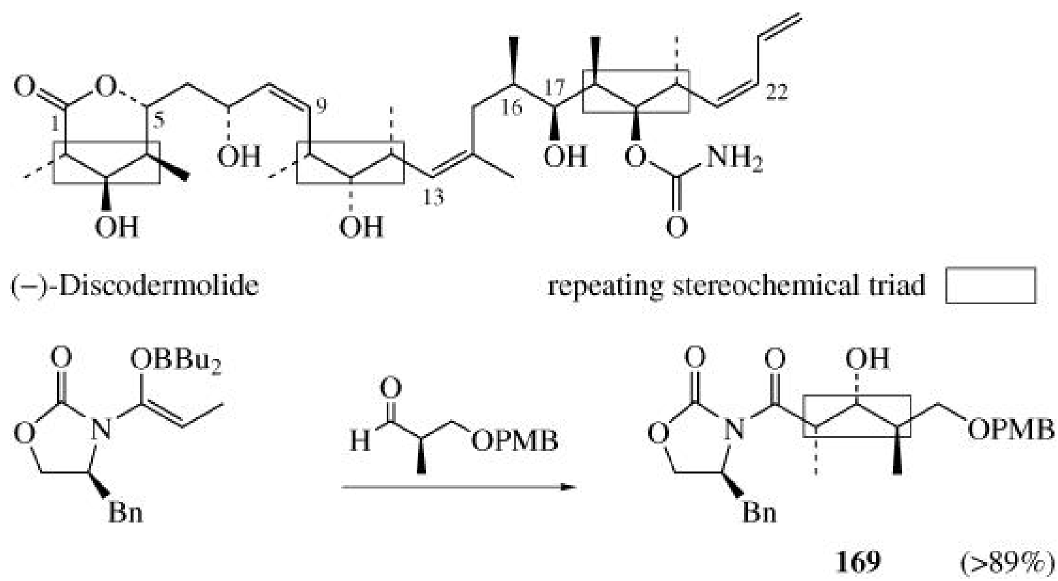
Apart from those already mentioned, several other synthetic approaches to FK-506 have used boron-mediated aldol reactions; (192-194) an interesting variation is the use of the chiral boron reagent **168** which was used in the stereocontrolled construction of a C(18)–C(35) segment (Eq. 94). (195)



(94)

4.4. Discodermolide

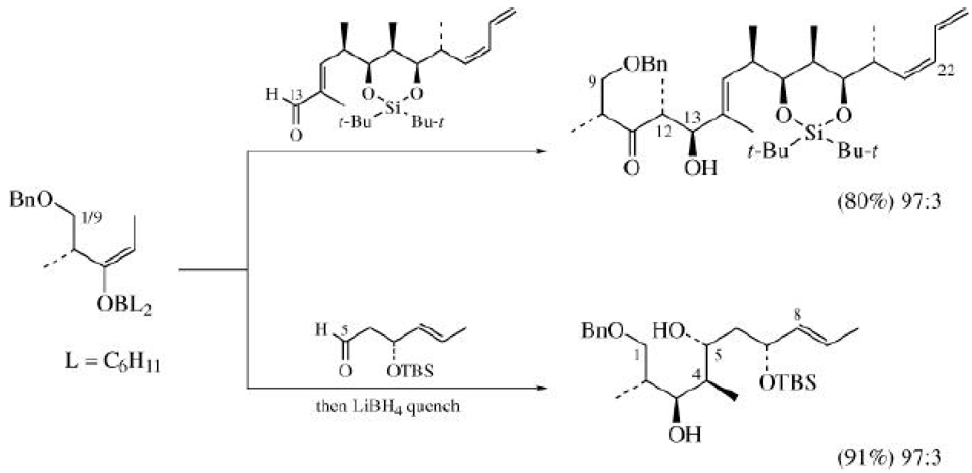
Another demanding synthetic target with immunosuppressant activity is discodermolide. One synthesis of this molecule relied upon Evans syn aldol reactions generating eight of the thirteen stereocenters. (196) The observation of a common stereochemical triad in discodermolide resulted in the aldol product **169** being used for three separate segments in the Smith total synthesis. A further boron aldol reaction provided the C(16)–C(17) unit.



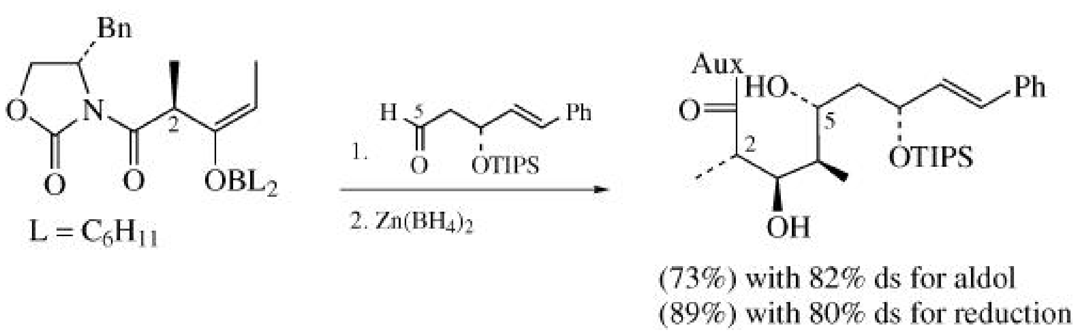
(95)

Other approaches to discodermolide have also used boron-mediated aldol reactions. In the Paterson approach (Scheme 7), two anti aldol reactions under substrate control were used to construct the C(4)–C(5) and C(12)–C(13)

bonds. (127, 197) Here, the former bond construction was followed by in situ reduction of the boron aldolate to introduce the C(3) stereocenter.
Scheme 7.



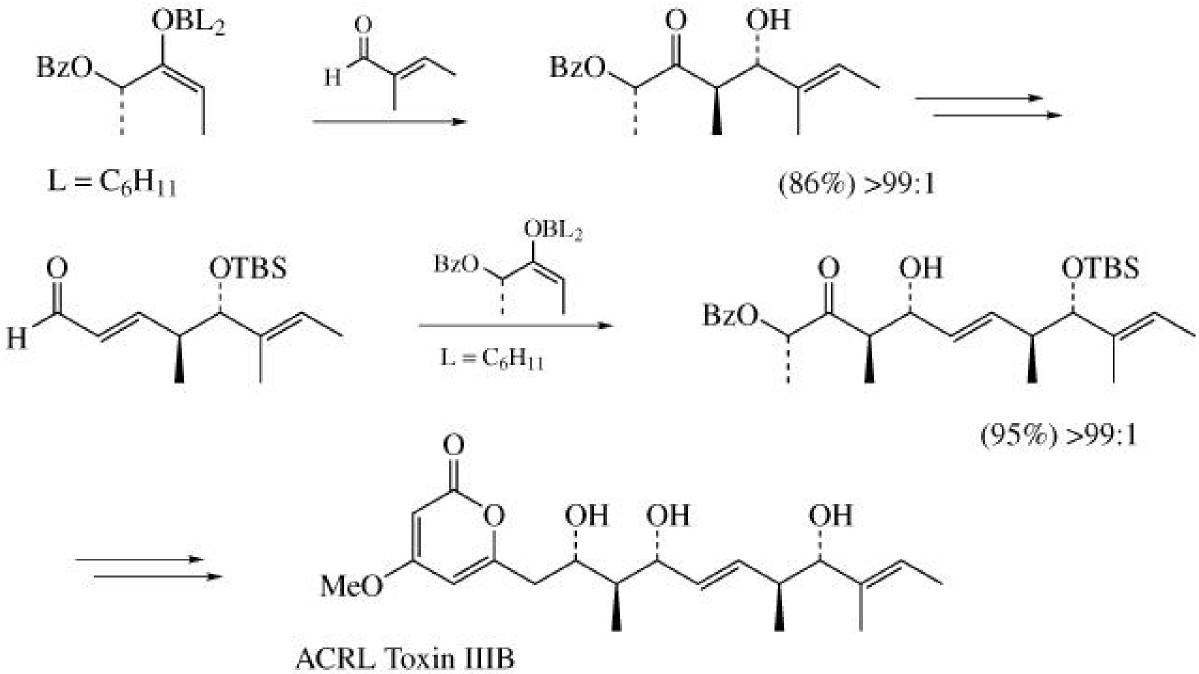
A third approach to discodermolide uses an anti aldol reaction for the C(4)–C(5) bond, while an Evans syn aldol reaction is again used to construct the C(11)–C(12) bond. The anti aldol/reduction sequence is used to establish the four contiguous stereocenters of the δ -lactone portion (Eq. 96). (198, 199)



(96)

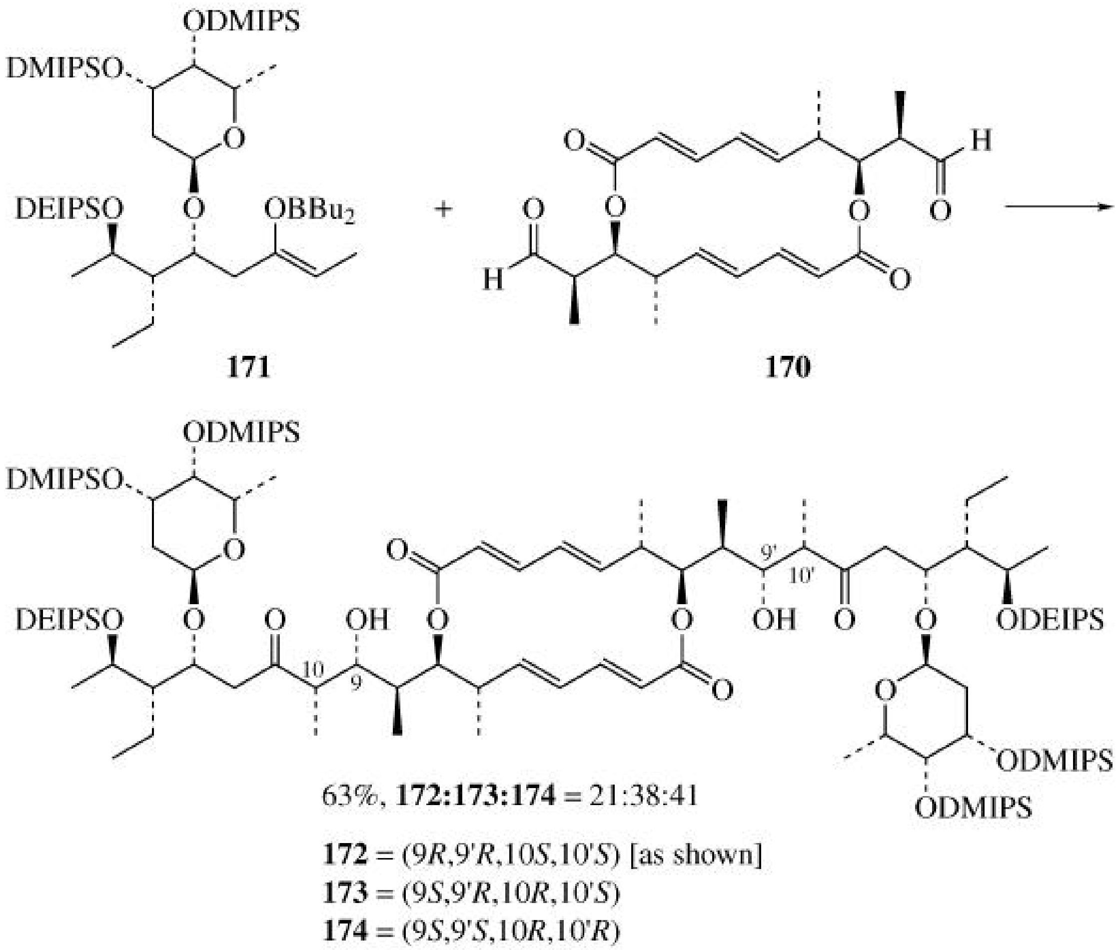
4.5. ACRL Toxin IIIB

While the use of syn aldol reactions has become common practice, there are few examples of *auxiliary*-controlled anti aldol reactions. A notable exception is the synthesis of ACRL toxin IIIB (Scheme 8), where two anti aldol reactions both proceed with high diastereoselectivity (>99%ds). (118)
Scheme 8.



4.6. Elaiophylin

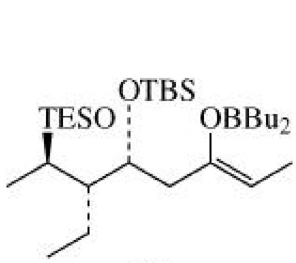
An advanced intermediate in the synthesis of the C_2-symmetric antibiotic elaiophylin was obtained from a double aldol reaction of dialdehyde **170** with two equivalents of the (*Z*)-boron enolate **171** (Eq. 97). (180, 200) This aldol reaction is notable in that it accommodates an acid-sensitive glycosidic linkage in the ketone



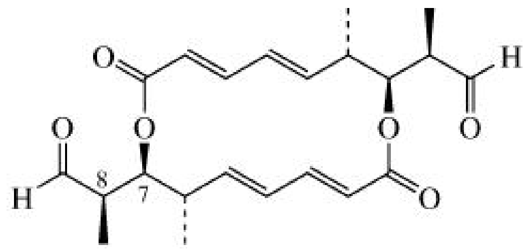
(97)

portion. Unfortunately, the desired product was obtained as the minor isomer in only 13% yield. The use of chiral ligands on boron failed to overturn the substrate selectivity observed in this aldol reaction.

A synthesis of an elaiophylin aglycone again utilizes a double boron-mediated aldol reaction of dialdehyde **170**. (201-203) In this case, the construction of the dialdehyde included an Evans syn aldol reaction to install the C(7)–C(8) bond. Reaction of compound **170** with an excess of (*Z*)-boron enolate **175** afforded the required aldol adduct in just 9% yield, again as the minor product of the reaction.



175

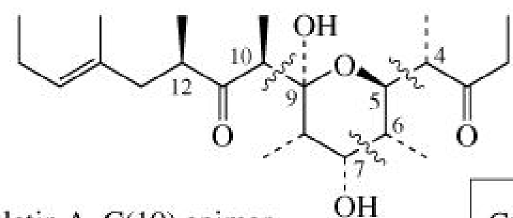


170

It might be anticipated that in the two previous examples, the addition of a (*Z*)-boron enolate would favor the formation of the desired anti-Felkin product, but this was not the case. It is interesting that the same stereochemical motif is found in bafilomycin A_1 (see page 31); an aldol reaction with substrate control was successful in obtaining the desired anti-Felkin product as the sole observed stereoisomer. (136)

4.7. Denticulatin A and B

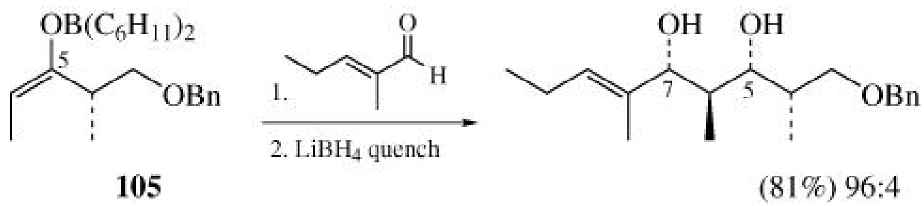
Denticulatins A an B are challenging polypropionate synthetic targets and several total syntheses of these compounds have been reported. (123, 124, 204-207) The targets are well suited to the use of boron aldol reactions for bond construction, and three different examples are now highlighted.



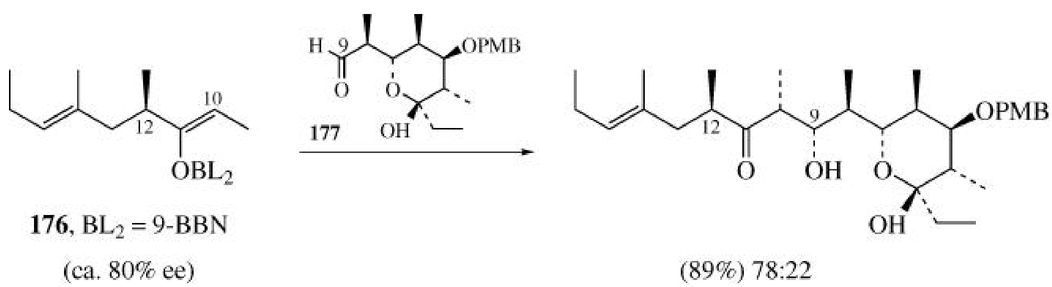
Denticulatin A, C(10) epimer
Denticulatin B

C(4)-C(5) disconnection, Oppolzer[207]
C(6)-C(7) disconnection, Paterson[123,124]
C(9)-C(10) disconnection, Hoffmann[205,206]

Paterson uses an anti aldol reaction of chiral enolate **105**, followed by an in situ reduction of the boronate intermediate, to set up four of the required stereocenters of the natural products (Eq. 98). (123, 124) Hoffmann uses a syn aldol reaction as the penultimate step to couple the two halves **176** and **177** of the denticulatins, where the minor product is epimeric at C(12) resulting from the presence of the enantiomeric enolate (Eq. 99). (205, 206) A third synthesis of the denticulatins, reported by Oppolzer, (207) uses meso-dialdehyde **178** in a symmetry-breaking,

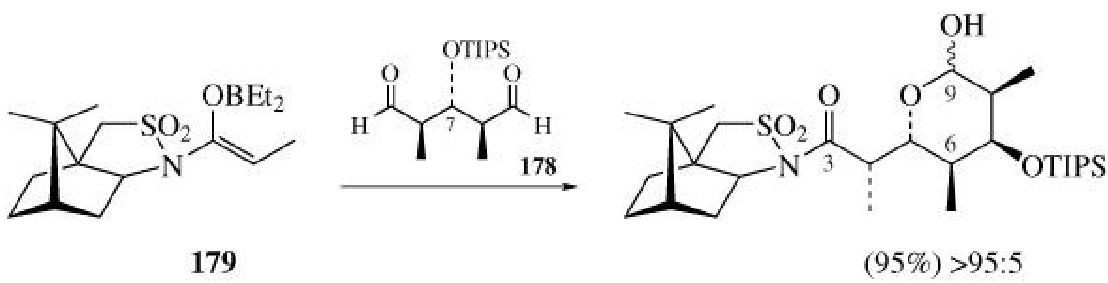


(98)



(99)

boron aldol reaction (Eq. 100). Addition of boron enolate **179** with dialdehyde **178** gives a major aldol product corresponding to a matched, anti-Felkin reaction.

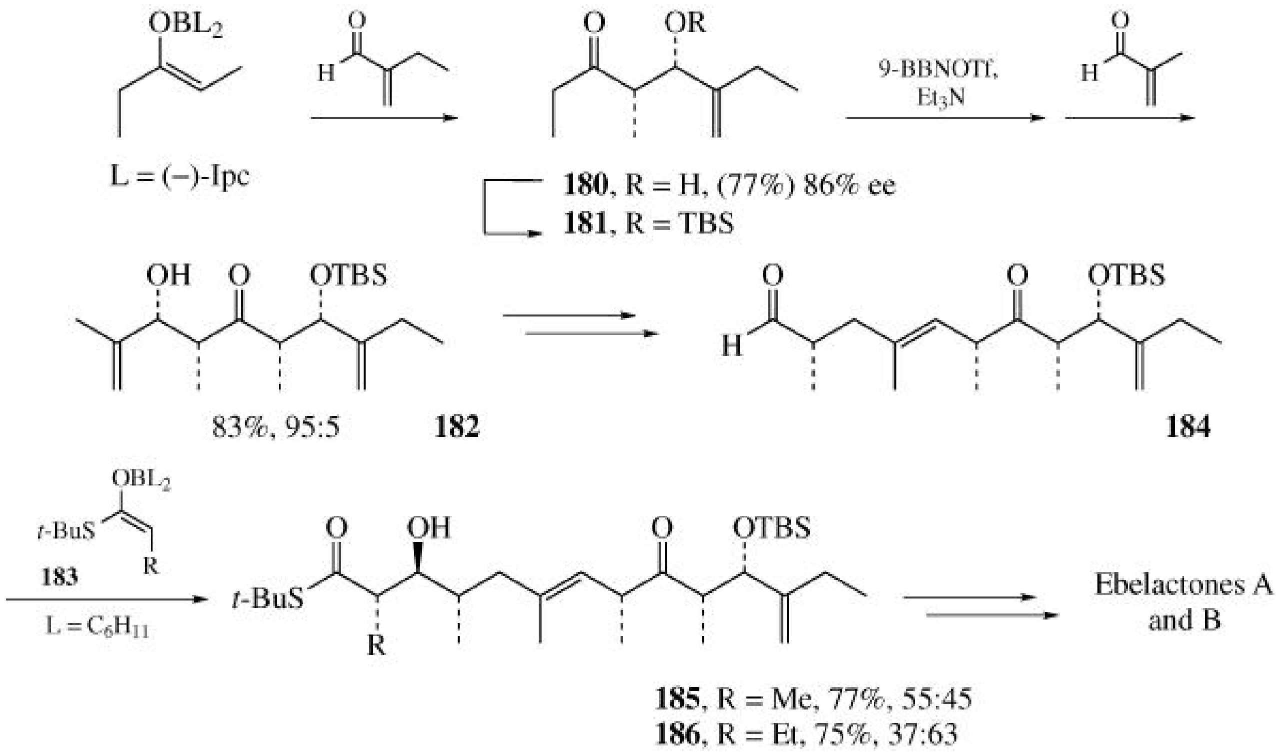


(100)

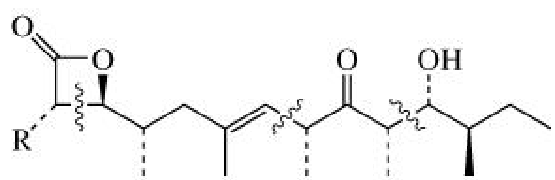
4.8. Ebelactone A and B

A synthesis of the enzyme inhibitors ebelactone A and B utilizes three different boron-mediated aldol reactions (Scheme 9). (21, 26)

Scheme 9.



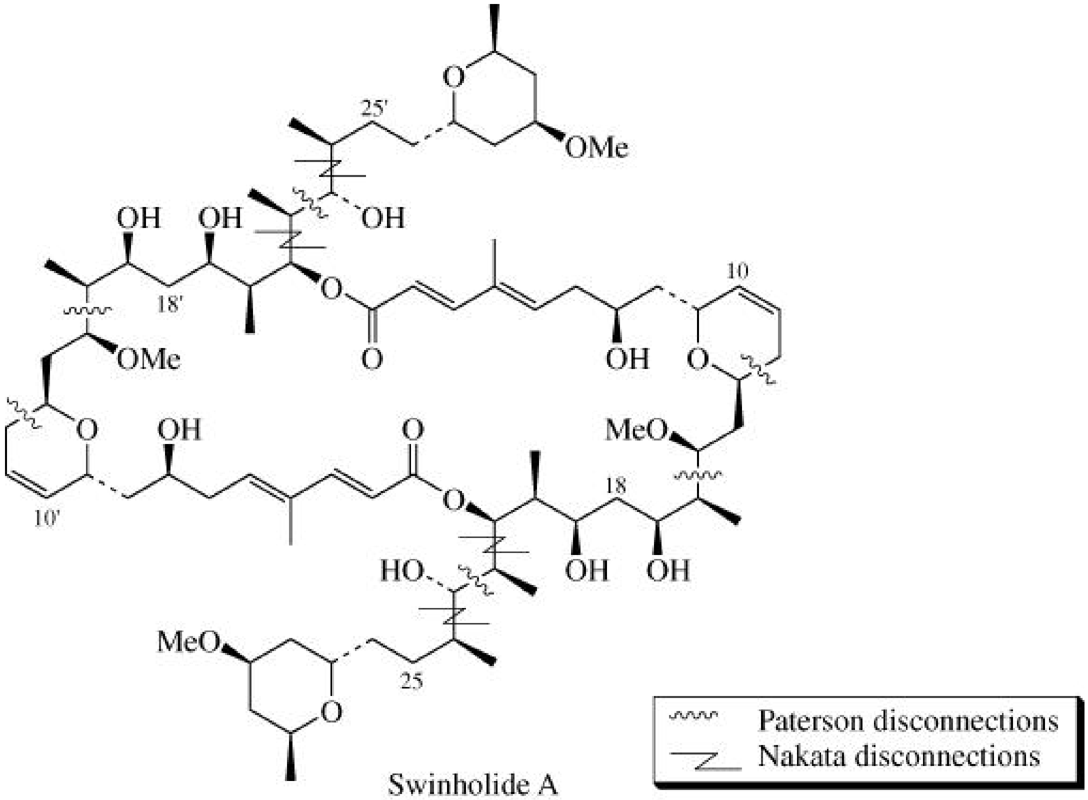
The first is controlled by chiral ligands on boron to afford adduct **180** in 86% ee. The second uses substrate control from the chiral ketone **181** to give the syn product **182** with high selectivity (95% ds). Finally, anti aldol addition of (*E*)-boron enolate **183** (R = Me or Et) to chiral aldehyde **184** affords the ebelactone A and B precursors **185** and **186**, respectively.



Ebelactone A, R = Me
Ebelactone B, R = Et

4.9. Swinholide A

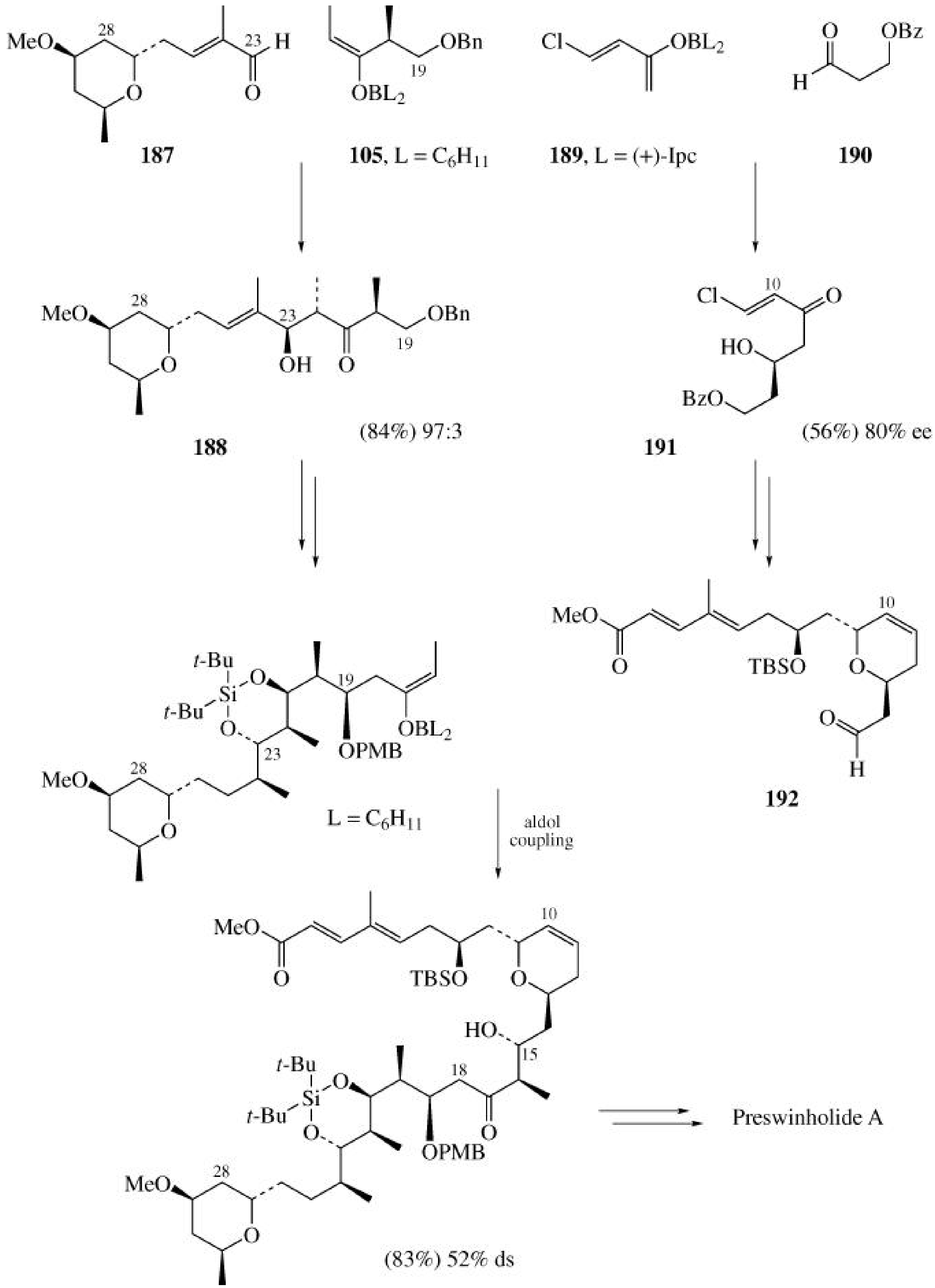
Swinholide A is a cytotoxic marine polyketide with a 44-membered macrodiolide structure. Two groups have reported approaches to this compound which rely upon boron-mediated aldol reactions. (35, 208-212)



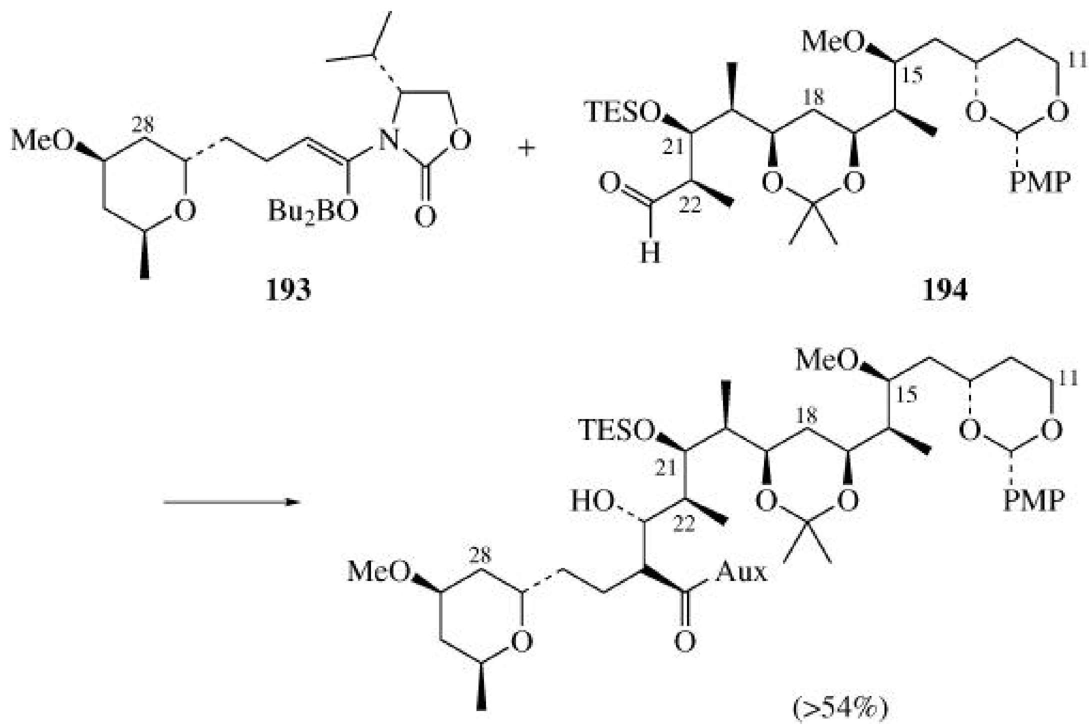
Swinholide A

In the Paterson total synthesis, (210) the anti aldol reaction of the (*E*)-boron enolate **105** with enal **187** gives aldol adduct **188** with ³97% diastereoselectivity (Scheme 10). (208, 213) An aldol reaction of chiral enolate **189** with aldehyde **190** affords adduct **191** (80% ee), which is then transformed into the dihydropyran unit of the natural product. (209, 214) A third boron aldol reaction was used in the first synthesis of preswinholide A (the monomeric form of swinholide A). (35, 215) Because aldehyde **192** undergoes unwanted si-face attack with (*Z*)-boron enolates, an anti aldol reaction with the isomeric (*E*)-boron enolate was employed with inversion of the C(15) stereocenter at a later stage. Unfortunately, attempts at triple asymmetric induction by using chiral ligands on boron had little effect apart from lowering the yield of the required aldol adducts. (35)

Scheme 10.


MeO
28
23
H
O
OBn
19
OBL$_2$
Cl
OBz
187
105, L = C_6H_{11}
189, L = (+)-Ipc
190
OH
10
HO
BzO
188
(84%) 97:3
191
(56%) 80% ee
t-Bu
Si
TBSO
OPMB
L = C_6H_{11}
192
aldol
coupling
15
18
Preswinholide A
(83%) 52% ds

Nakata's approach to swinholide A uses two auxiliary-controlled boron aldol reactions in the synthesis of the C(11)–C(32) unit (Eq. 101). (211, 212) The first introduces the C(21)–C(22) stereocenters and the second aldol coupling unites two advanced fragments **193** and **194**.

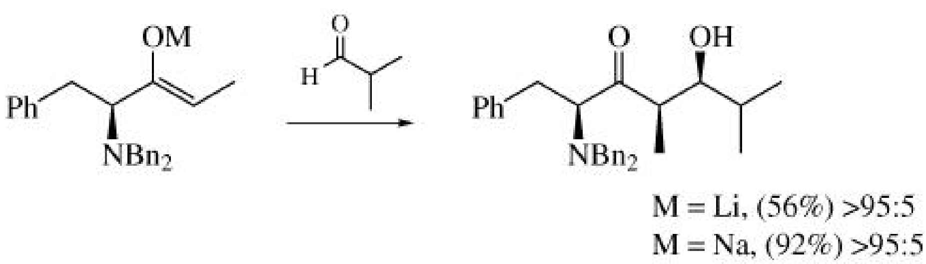


5. Comparison with Other Methods

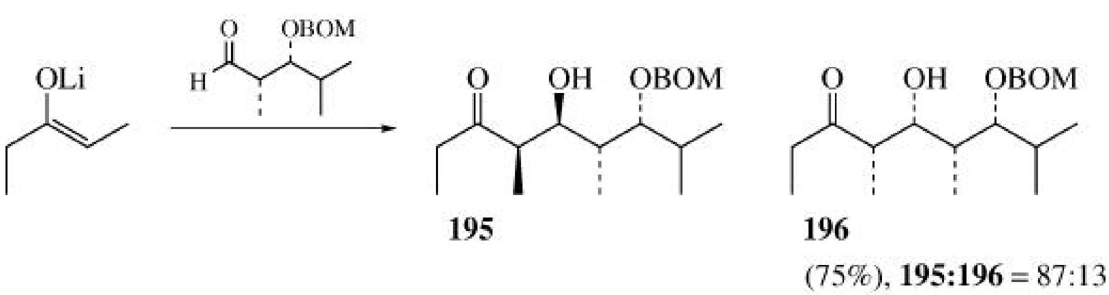
While boron enolates are easily formed and frequently react with aldehydes to afford β -hydroxy carbonyl compounds with high levels of stereocontrol, other metal enolates can act in a complementary fashion. The Mukaiyama aldol and allylation/crotylation reactions are closely related to metal-mediated aldol reactions and these are also briefly discussed in this section.

5.1. Use of Other Metals in Asymmetric Aldol Reactions

Because of their ease of formation by enolization of ketones, esters, and thioesters, lithium-mediated aldol reactions are commonly exploited in synthetic endeavors. (1-8) However, compared with boron enolates, lithium enolates are more basic, and aldol selectivity is generally lower and less easy to predict. It is more difficult to control lithium enolate geometry and also, for ketones, the enolate regiochemistry. Moreover, the geometry of a specific lithium enolate may no longer be faithfully translated into the relative stereochemistry of the aldol product (i.e., syn versus anti selectivity). Nevertheless, stereoselective lithium-mediated aldol reactions are possible, as seen in Eqs. 102 (216) and 103. (217)

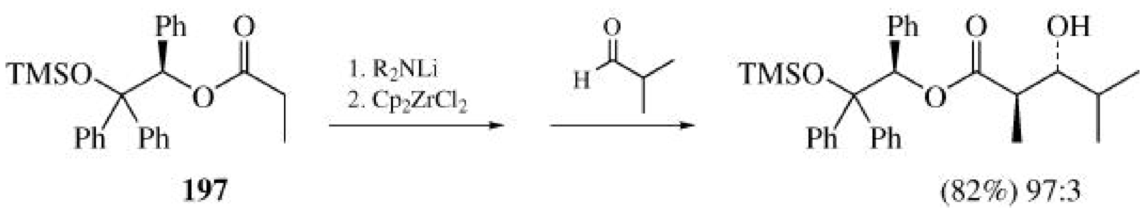


(102)



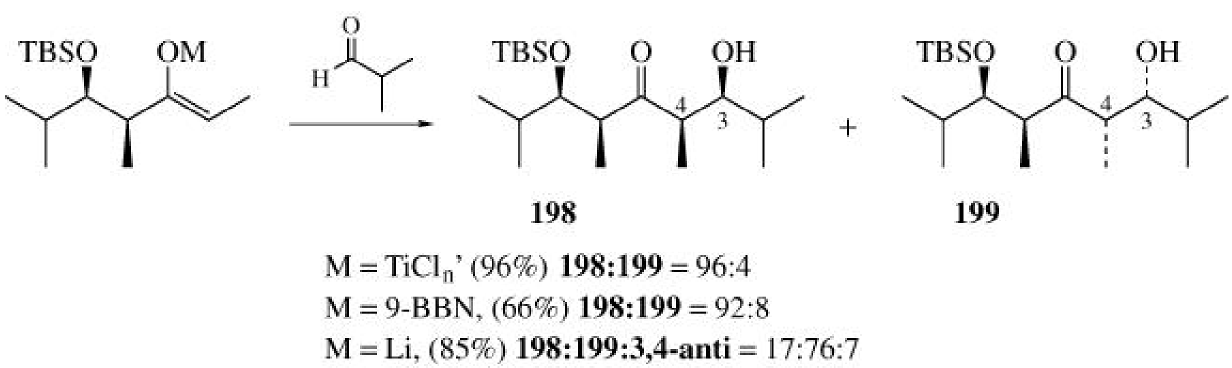
(103)

Titanium and zirconium enolates normally afford highly syn-selective aldol reactions, irrespective of their enolate geometry. (2, 218) This stereoconvergent behavior is rationalized by (*Z*)-enolates reacting through chair transition states, while (*E*)-enolates favor boat transition states. An exception to this generalization is the zirconium-mediated, anti-selective aldol reaction of ester **197** (Eq. 104). (219)



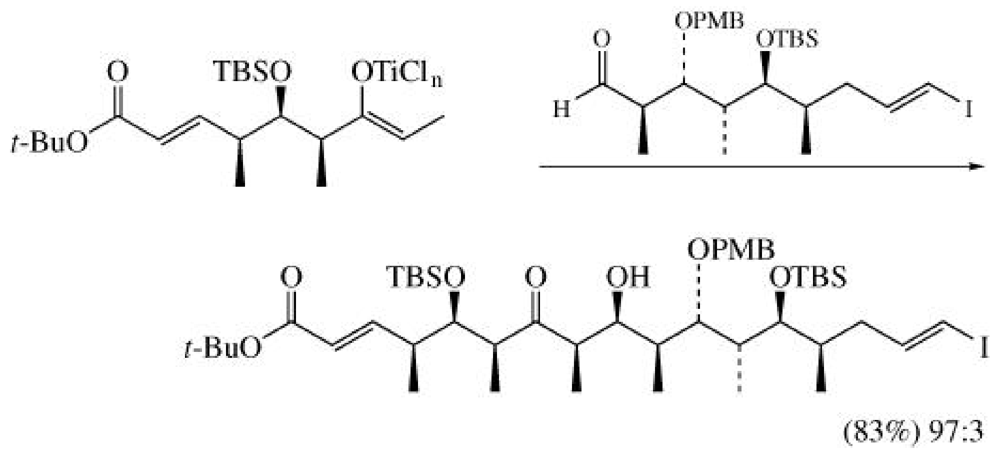
(104)

Titanium-mediated aldol reactions can proceed with high levels of substrate control and sometimes in higher yield than their boron counterparts. In Eq. 105, the titanium (220) and boron (135) enolates favor production of the same syn aldol product **198**, while lithium favors the diastereomeric syn product **199**. (221)



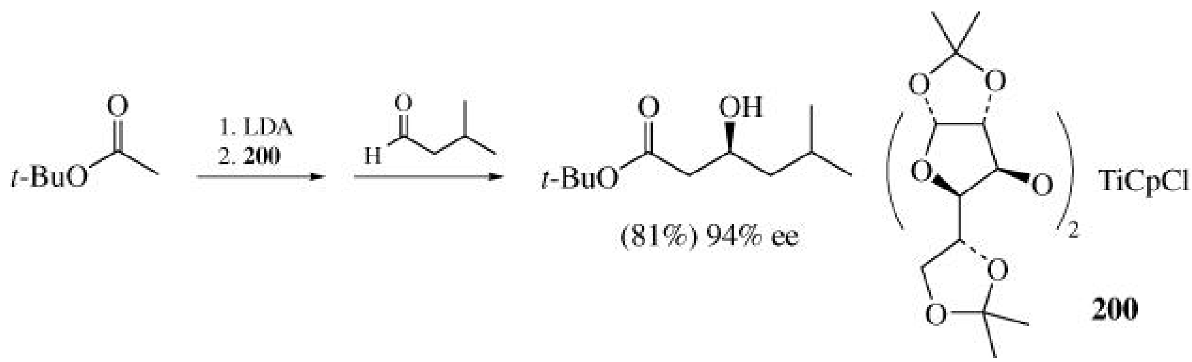
(105)

Like enol borinates, titanium enolates offer a good method for the stereocontrolled coupling of complex fragments in total syntheses. Such a reaction is seen in the synthesis of the macrolide antibiotic rutamycin B (Eq. 106). (222, 223)



(106)

Chiral ligands on titanium can promote enantioselective aldol reactions. Transmetallation of the lithium enolates of acetate and propionate esters with chlorotitanium reagent **200** leads to useful levels of reagent-based asymmetric induction (Eq. 107). (224, 225)

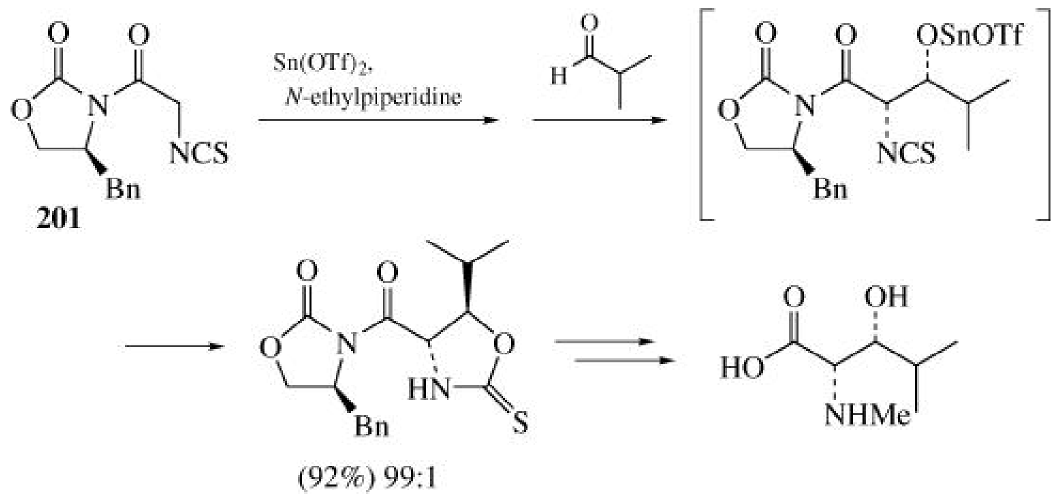


(107)

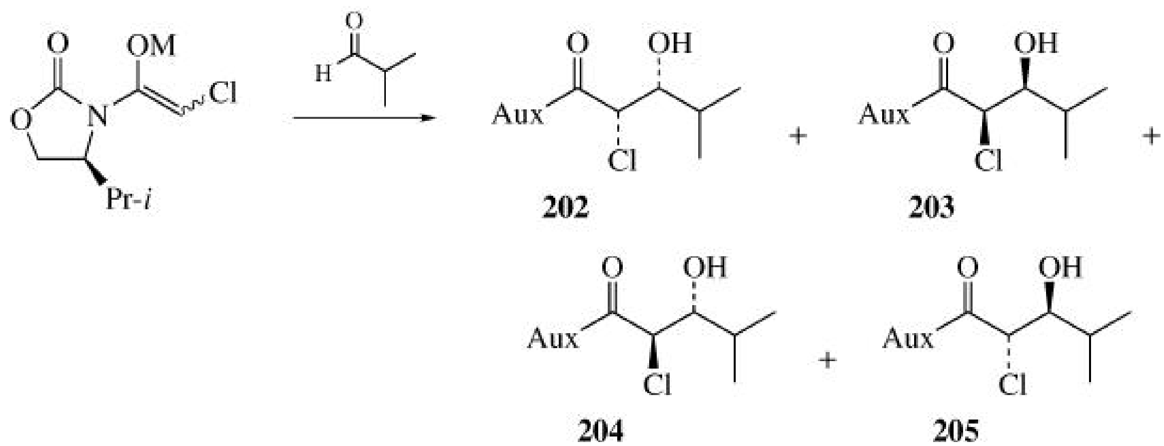
200

Tin(II) enolates are readily prepared by reaction of certain carbonyl compounds and tin(II) triflate in the presence of an amine base. (5) These enolates are more reactive than boron enolates and can afford high levels of selectivity in aldol reactions. Whereas the boron and lithium enolates of imide **201** give low selectivities upon reaction with aldehydes, the tin(II) enolate is highly successful (Scheme 11). (226)

Scheme 11.



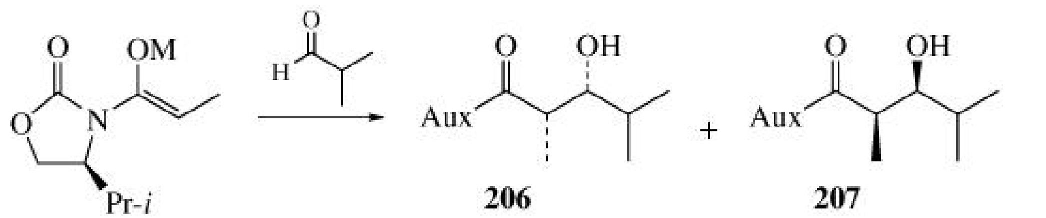
A comprehensive study which examined five different metal enolate derivatives of α -chloro- and α -bromoacetimides offers an insight into the different selectivities of this system (Eq. 108). (59, 60)



(108)

M = Li, (46%) **202:203:204:205** = 17.5:53:17.5:12
M = ZnCl, (68%) **202:203:204:205** = 10.5:84:5:0.5
M = SnOTf, (77%) **202:203:204:205** = 78:19:1.5:1.5
M = $SnBu_3$, (66%) **202:203:204:205** = 10.5:74:13:2.5
M = BBu_2, (52%) **202:203:204:205** = >98:<2:0:0

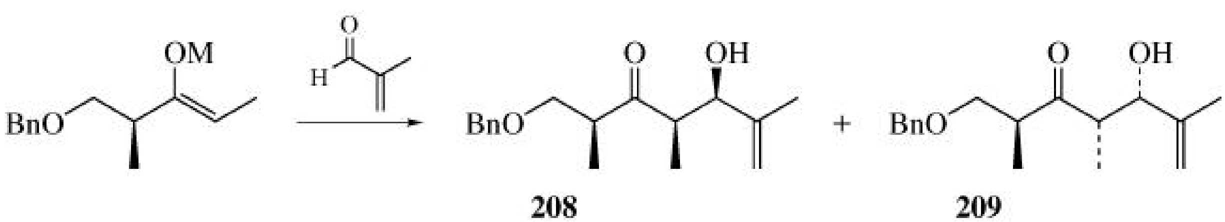
From these results, it was concluded that lithium, zinc, and tin(IV) favor a transition state with chelation of the oxazolidinone carbonyl to the metal center, while boron and tin(II) do not. A similar argument has been used to account for the selectivity of the titanium-mediated aldol reaction of a related oxazolidinone (Eq. 109). (227, 228)



(109)

M = Ti(OPr-i)$_3$, (72%) **206:207** = 9:91 (5% anti isomers)[227,228]
M = BBu$_2$, (78%) **206:207** = 99.8:0.2[41,43]

There are many examples where different metal enolates react in a complementary fashion. While the (*E*)-boron enolate of the chiral ketone **105** shows high levels of substrate control in anti aldol reactions (see Eq. 58, page 27), (120) chiral ligands on boron are necessary for synthetically useful levels of control in the syn aldol reaction of the (*Z*)-boron enolate reaction (Eq. 110). (119, 122) On the other hand, the tin(II) (*Z*)-enolate shows good selectivity in favor of the syn aldol product **208** (Eq. 110). (229)

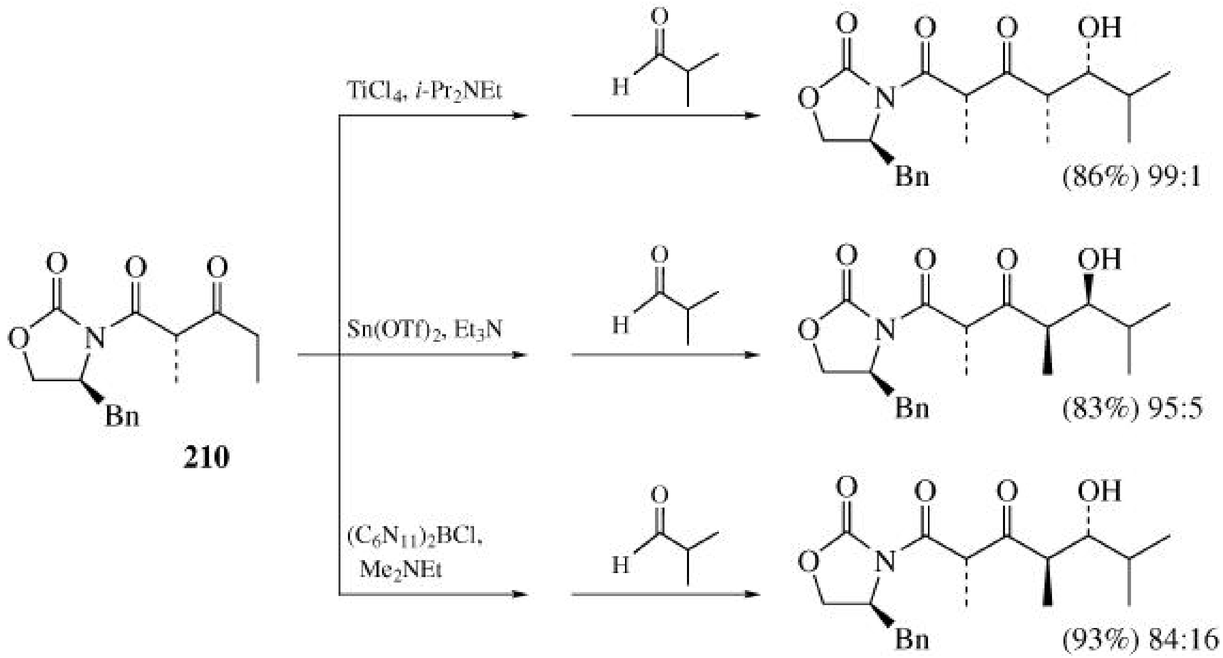


(110)

M = BBu$_2$, (76%) **208:209** = 54:46 (8% 4,5-anti adducts)
M = B(−)-Ipc$_2$, (62%) **208:209** = 7:93
M = SnOTf, (92%) **208:209** = 93:7 (<1% anti isomers)

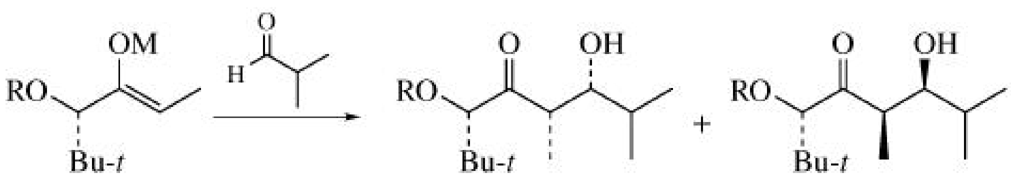
A similar example of the complementary behavior of different metal enolates concerns the chiral ketone **210** (Scheme 12). Reaction of the tin(II) and titanium enolates both afford syn aldol products, but in the opposite relative sense. (230) As already mentioned, the (*E*)-boron enolate of this system affords anti aldol products with synthetically useful levels of control. (129)

Scheme 12.



210

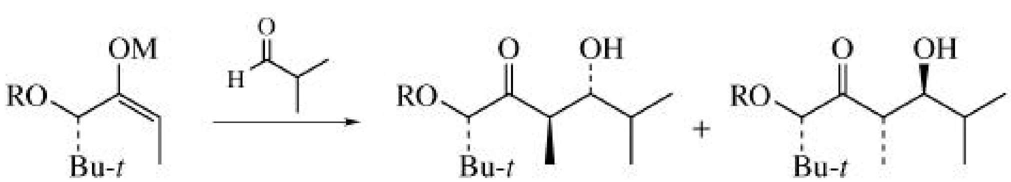
In an impressive example of the differing behavior of various metal enolates, each of the four possible diastereomeric aldol products (**211-214**) of related chiral ketones is formed by appropriate choice of metal enolate. (109) Hence, the lithium and boron (*Z*)-enolates both give syn aldol products, with lithium favoring a chelation pathway (Eq. 111). Similarly, generation of the (*E*)-magnesium and titanium enolates leads to the two different anti aldol products (Eq. 112). (109)



211 **212**

M = Li, R = TMS, (70%) **211:212** = >95:5
M = BBu$_2$, R = TMS, (70%) **211:212** = <5:95

(111)



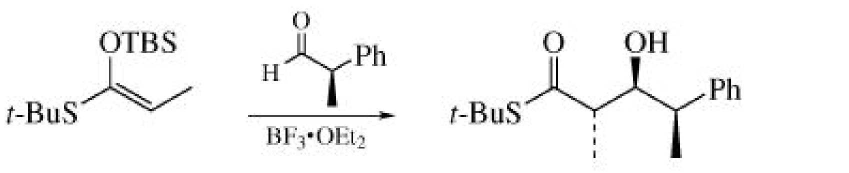
213 **214**

M = MgBr, R = TMS, (75%) **213:214** = ca. 93:7
M = Ti(OPr-*i*)$_3$, R = TBS, (85-88%) **213:214** = <5:95

(112)

5.2. Mukaiyama Aldol Reactions

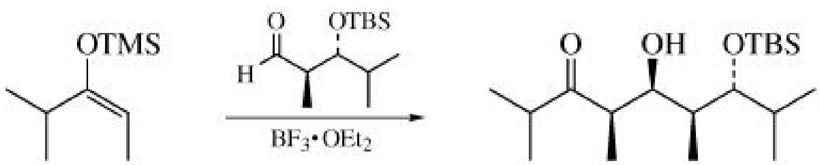
In contrast to most boron-mediated aldol reactions, the Lewis acid catalyzed reaction of silyl enol ethers with aldehydes proceeds through an open transition state where the geometry of the enol ether may not be reflected in the aldol product stereochemistry. Felkin–Anh control from the aldehyde component is particularly strong in Mukaiyama aldol reactions (Eq. 113), (231) and similarly,



(113)

(75%) 91:9

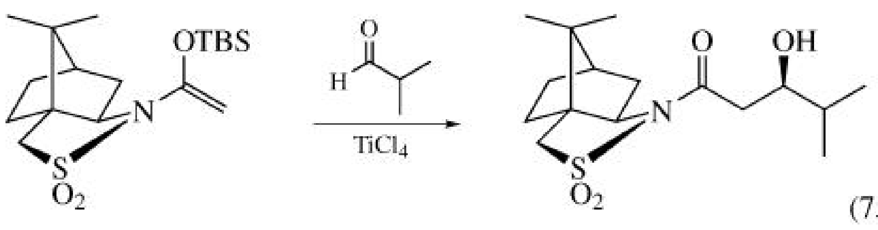
β -oxygenated stereocenters of aldehydes imply a strong facial bias (Eq. 114). (232, 233)



(114)

(95%) 95:5

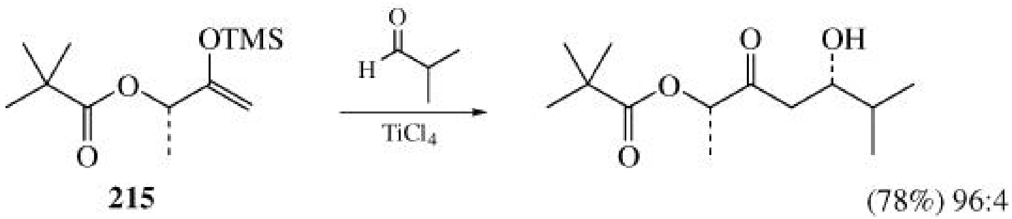
Auxiliary control from the enol ether is possible in the Mukaiyama aldol reaction, as can be seen from the example in Eq. 115. (234) Excluding auxiliary controlled



(115)

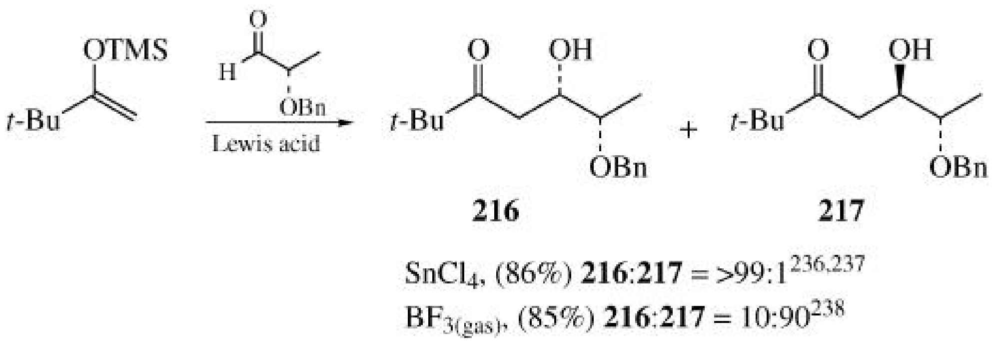
(75%) 96:4

reactions, induction from a chiral enol ether is less common. A notable exception is the 1,4-diastereoselectivity observed for the chiral enol ether **215** (Eq. 116). (235)



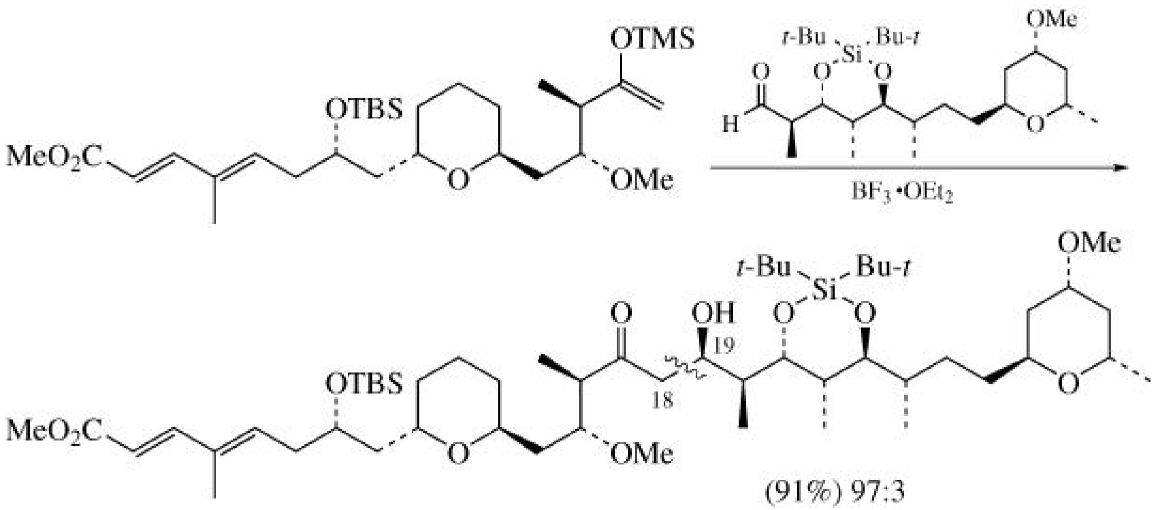
(116)

The Mukaiyama aldol reaction is versatile in that choice of either a chelating (e.g., $SnCl_4$) or nonchelating (BF_3•OEt_2) Lewis acid can give either diastereomeric product if the aldehyde has a suitable chelating group in the α or β position (Eq. 117). (236-238)



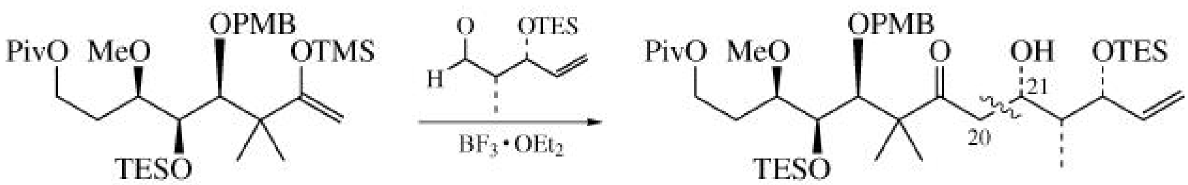
(117)

When Felkin control from α -methyl chiral aldehydes is desired, the Mukaiyama aldol reaction is the method of choice; such a reaction is common in natural product synthesis. One example is the key fragment coupling step in the synthesis of swinholide A (Eq. 118). (35)



(118)

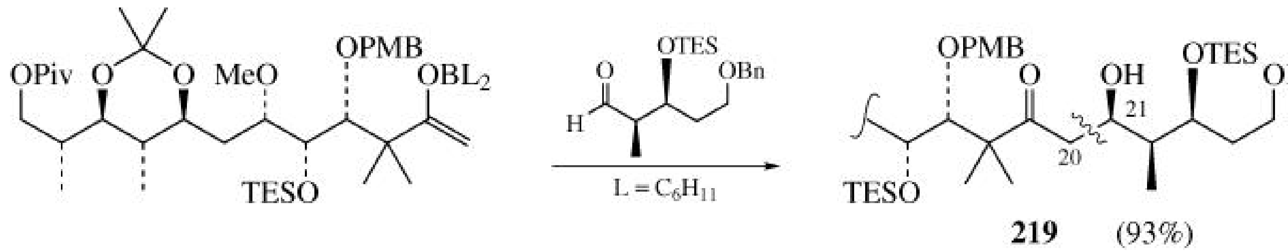
A stereocontrolled Mukaiyama aldol coupling reaction is also found in the synthesis of (+)-calyculin A. (40, 239) Again, Felkin control leads to the desired product **218** in good yield as the only observed diastereomer (Eq. 119). In a subsequent

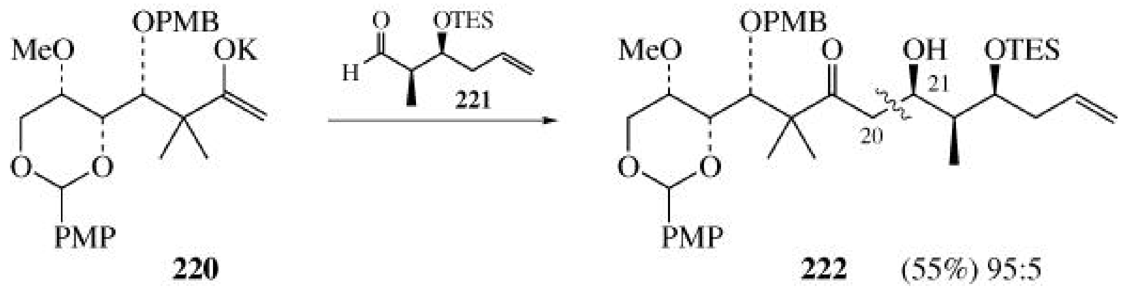


(119)

218 (80%)

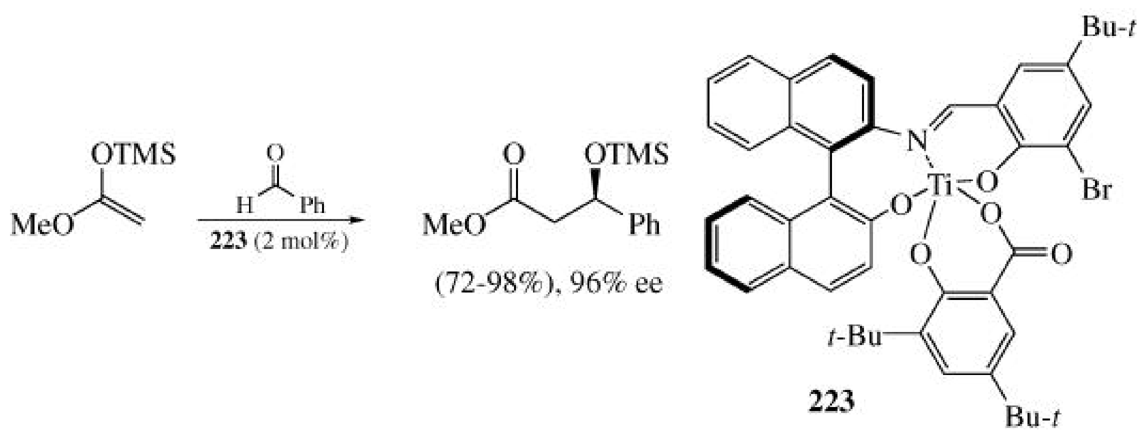
synthesis of (–)-calyculin A, a similar Mukaiyama aldol reaction to form the C(20)–C(21) bond proved too slow to be synthetically useful. (240) On this occasion, a boron-mediated aldol reaction was superior and, using bulky ligands on boron, afforded exclusively the desired product **219** in excellent yield (Eq. 120). A third synthesis of calyculin utilized the reaction of potassium enolate **220** with aldehyde **221**; this again gave the desired product **222** as the major isomer (95% ds). (241) These examples highlight the versatility of the aldol reaction in acyclic situations and show how a reaction can be tuned to afford the desired stereochemistry by appropriate choice of enolate.





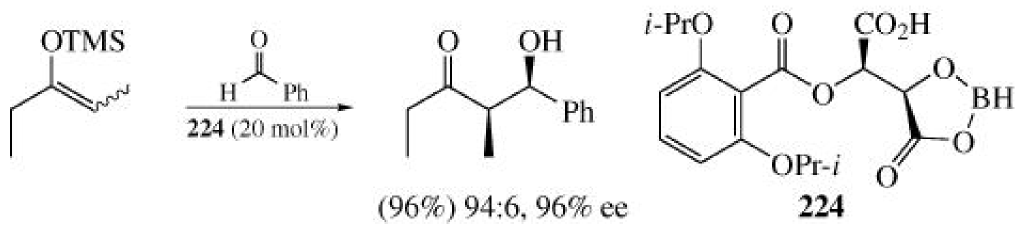
(121)

An important point concerning the use of silyl enol ethers is that the Mukaiyama aldol reaction allows chiral modification of the Lewis acid promoter. For example, titanium(IV) complex **223** catalyzes (2 mol%) the reaction of silyl ketene acetals with aldehydes to afford silylated aldol products in good yield and high enantiomeric excess (94–97% ee) (Eq. 122). (242)



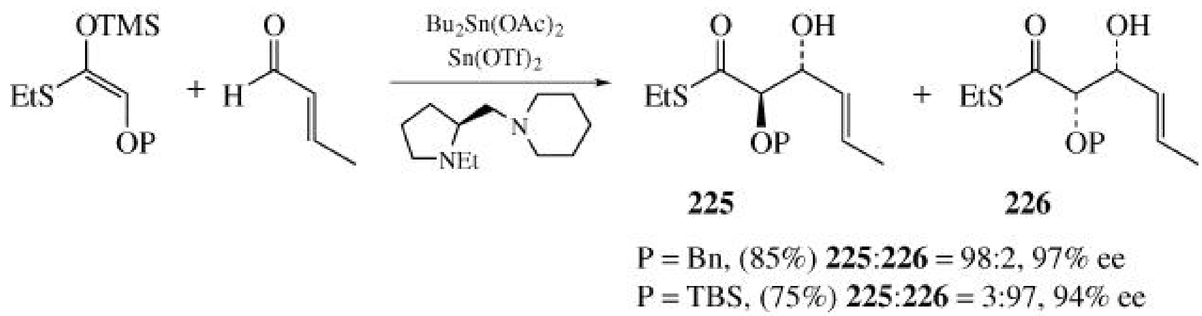
(122)

The tartaric acid derived chiral (acyloxy)borane complex **224** catalytically (20 mol%) promotes the addition of silyl enol ethers and ketene acetals with various aldehydes (Eq. 123). (243, 244)



(123)

The use of chiral diamines with Sn(II) species efficiently promotes asymmetric Mukaiyama aldol reactions. By choice of protecting group, the asymmetric synthesis of either syn or anti 1,2-diol units is achieved with high levels of enantioselectivity (Eq. 124). (245)

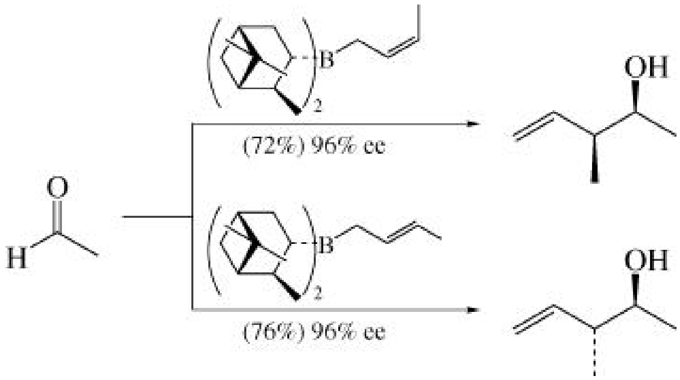


(124)

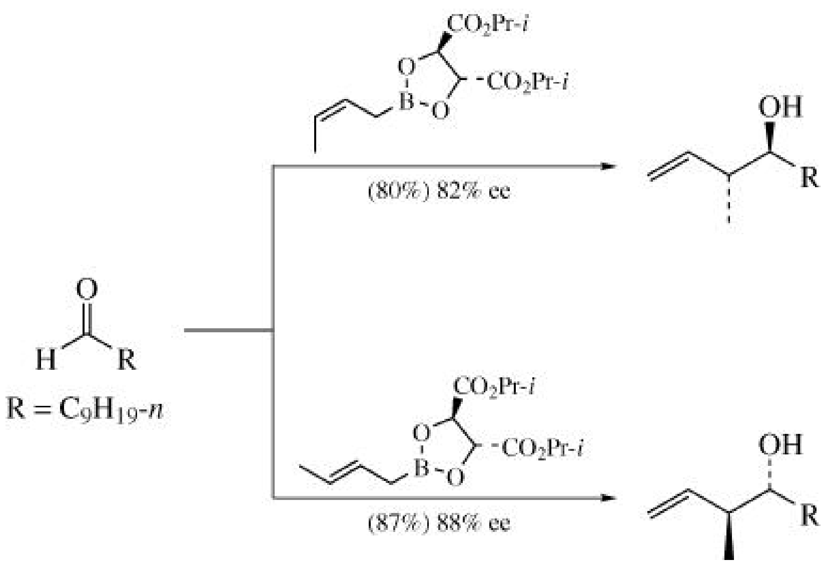
5.3. Asymmetric Allylations and Crotylations

Allylation and crotylation reactions are closely related to aldol reactions and are often used to synthesize similar polyketide-derived natural product fragments. While several different allyl and crotylmetal reagents are available, boron is frequently the metal of choice, and cyclic transition states are again operative. (246) As in the boron-mediated aldol reaction, crotylboration reactions show a strong relationship between reagent geometry and product stereochemistry. Again, (*Z*)-reagents give syn products with anti-Felkin selectivity and (*E*)-reagents afford anti products with moderate Felkin control. (247) Transition states similar to those already depicted for boron-mediated aldol reactions have been proposed to explain the selectivity of the reaction. (246) It should be noted that allylor crotylboron reagents are apparently more reactive with aldehydes than the corresponding boron enolates. Another important difference between the reactions is that removal of the boron during workup is usually more difficult for allyl/crotylborations.

Chiral ligands on boron are successful in controlling the allylation/crotylation reaction. Isopinocampheyl- (Eq. 125) (248-250) and tartrate- (Eq. 126) (251-254) derived

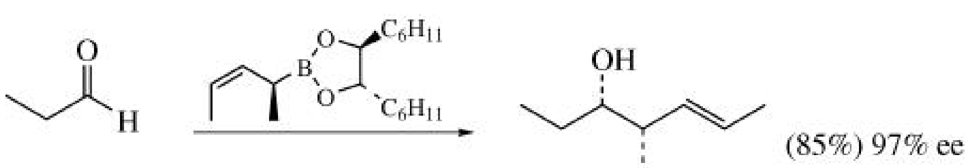


(125)



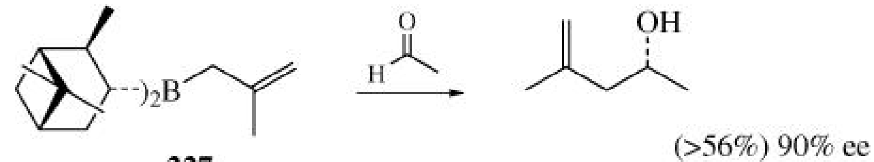
(126)

reagents are the most commonly used, while other chiral reagents are also available (Eq. 127). (205, 255)



(127)

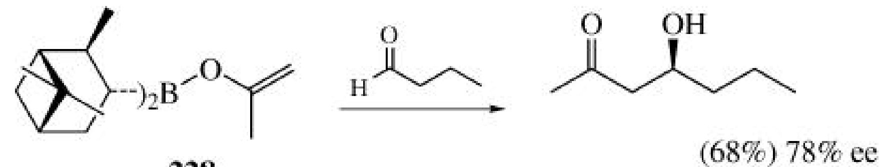
In certain cases, these reactions are more selective than the corresponding boron-mediated aldol reactions. Allylation reagent **227** (256) affords products of higher enantiomeric excess than the corresponding methyl ketone aldol reaction. (121) Surprisingly, the aldehyde facial selectivity is opposite in these two reactions and this is explained by the allylation (Eq. 128) proceeding through a chair



227

(128)

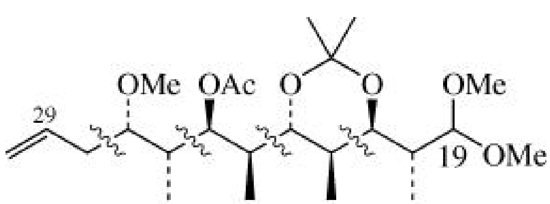
transition state, (257) whereas the unsubstituted enolate **228** (Eq. 129) reacts via a boat transition state. (146)



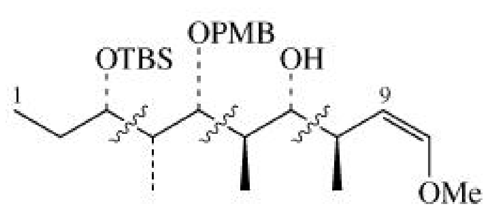
228

(129)

Allylations and crotylations are especially well suited to an iterative synthetic strategy. For example, the C(19)–C(29) fragment **229** of rifamycin S was prepared by three successive crotylation reactions and one allylation reaction. (253) Similarly, the C(1)–C(9) segment **230** of denticulatins A and B was prepared in such a manner. (205,206) This highlights one difference between boron-mediated crotylations/allylations and the aldol reaction. The latter reaction is especially well suited to the joining of two large fragments, as desired in convergent natural product synthesis. The use of allylation/crotylation reactions in such convergent syntheses is limited by the availability of the necessary reagents.



229



230

6. Experimental Conditions

The most common method for the generation of boron enolates requires the use of a tertiary amine base in conjunction with a dialkylboron triflate or chloride reagent. Both of these boron reagents are strongly Lewis acidic and moisture-sensitive. Hence, like most water-sensitive reactions, a boron-mediated aldol reaction requires care in experimental technique. The reactions must be carried out under an inert atmosphere using anhydrous solvents and reagents. So long as the ketone and aldehyde are not overly volatile, they can be dried via azeotropic removal of water under reduced pressure. Sensitive aldehydes can be used without chromatographic purification, and residual impurities often do not hinder the reaction. A readily available aldehyde is frequently used in large excess compared with the enolate, but it is often better to use just a slight excess of the aldehyde.

Boron enolates are normally geometrically stable over the temperature range in which most reactions are conducted (–78° to room temperature). However, they do not store and need to be freshly prepared for best results.

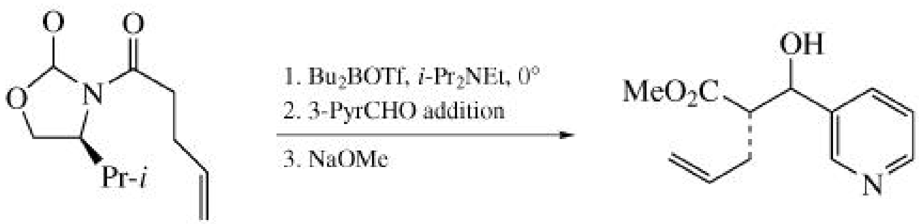
While Bu_2BOTf and 9-BBNOTf are commercially available, most problems encountered in the boron-mediated aldol reaction result from the use of impure triflate reagents. If a given reaction is not performing well, freshly prepared boron reagent should be used. (258-260) While the choice of amine base between Et_3N and *i*-Pr_2NEt is normally arbitrary, Et_3N may be beneficial in that it more strongly coordinates excess Bu_2BOTf which may otherwise be detrimental, especially when sensitive aldehydes are used. (58,76,261,262) Other workers have noted that *i*-Pr_2NEt is superior to Et_3N (263) and hence experimentation may decide which of these two bases is better for a given reaction. Dichloromethane is normally the solvent of choice, although nonpolar solvents such as toluene or pentane can also be used. (57)

When using dialkylboron chlorides, diethyl ether is the favored solvent though dichloromethane and pentane are adequate. Dicyclohexylboron chloride is commercially available, but it is easily synthesized and can be stored at –20° for several months without noticeable deterioration. Both enantiomers of the boron chloride reagent Ipc_2BCl are commercially available, and this material is suitable for most purposes.

The enolizing ability of the various reagents is important, especially when the enolization of carbonyl compounds other than ketones or imides is required. The enolization of esters can be achieved using boron triflate reagents such as Bu_2BOTf. (264,265) However, the selective enolization of an ethyl ketone in the presence of a potentially enolizable ester is possible using triflate reagents,

(21) and such an example is included in the Experimental Procedures section. Dialkylboron chlorides will not enolize esters and will only slowly enolize thioesters. Use of the corresponding dialkylboron bromides is often preferred for the latter reaction. Dicyclohexylboron iodide has been introduced as a reagent capable of the enolization of esters and amides. (266-268)

The boron-mediated syn aldol reaction of Evans auxiliaries operates well on a large scale (an experimental procedure for a 560-g reaction has been reported (269)) with the enolization carried out at 0°, then addition of the aldehyde at –78°. Certain reactions may not need to be performed at –78°; for example, in Eq. 130 the aldehyde was added at 5° with no deterioration in the reaction selectivity. (270)



Aldehyde addition (°)	% ee
–78°	>99
–40°	>98
–5°	>99

(130)

In a small number of cases, removal of the boron atom after an aldol reaction can be problematic, and a useful check for residual boron is ^{11}B NMR spectroscopy. Normally, an oxidative workup with aqueous H_2O_2/pH 7 buffer is employed, which oxidizes boron and leads to clean breakdown of the boron chelate, thus affording the aldol adduct. [**CAUTION**: H_2O_2 may generate organic peroxides.] Occasionally an oxidative workup is inappropriate, owing to sensitive functionality, and alternative procedures are available (see the Experimental Procedures section for such an example). Even after an oxidative workup, removal of the boron atom may occasionally be difficult, and azeotropic removal with methanol or addition of diethanolamine may be appropriate. The use of IRA-743 resin to sequester boron has also been reported. (129)

7. Experimental Procedures

7.1.1. Di-n-butylboron Triflate (Bu_2BOTf) (8d,8h,269)

To a well-stirred solution of Bu_3B (711 mL, 531 g, 2.92 mol) was added CF_3SO_3H (15 mL, 25.4 g, 0.17 mol). The reaction mixture was warmed to 40° and stirred until gas evolution commenced (usually <10 minutes) [**CAUTION**: venting of the evolved butane is necessary] . The remainder of the CF_3SO_3H (258 mL, 439 g, 2.92 mol) was then added dropwise via a dropping funnel such that the internal temperature remained at 40–45°. At the end of the addition, the temperature was raised to 50° and the flask was placed under vacuum (20 mm Hg). Subsequent distillation (64–65°/2.5 mm Hg) provided the title product (682 g, 85%) as a yellow oil. ^{13}C NMR ($CDCl_3$) δ 118.1, 25.1, 21.5, 13.6 (one signal not observed).

7.1.2. Dicyclohexylboron Chloride [($C_6H_{11})_2BCl$] (14, 271)

To a solution of dried cyclohexene (21.2 mL, 210 mmol) in anhydrous Et_2O (90 mL) under an argon atmosphere at 0° was slowly added monochloroborane·dimethyl sulfide (11.6 mL, 8.62 M, 100 mmol). The mixture was stirred at 0° for 2 hours and then the solvent was removed by distillation. The resulting crude product was distilled under reduced pressure (104–105°/0.5 mm Hg) to afford the title compound (16.65 g, 80%, d ~ 0.97) as a colorless oil. ^{11}B NMR ($CDCl_3$) δ 76.2. ^{13}C NMR ($CDCl_3$) δ 36.3, 27.7, 27.2, 26.6.

7.1.3. (–)-Diisopinocampheylborane [(–)-Ipc_2BH] of >99.5% ee (272)

To a solution of (+)- α -pinene (40 mL, 250 mmol, 91% ee) in THF (30 mL) maintained at 20–25° was added $BH_3{\cdot}Me_2S$ (10 mL, 100 mmol) slowly to control the mildly exothermic reaction. Precipitation may occur at this stage; if so, the reaction was warmed to 50° until dissolution occurred. The clear solution was then allowed to stand at room temperature for 18 hours after which it was cooled to 0° for 2 hours. The supernatant was removed and the crystalline Ipc_2BH was washed with pentane (20 mL), then dried under reduced pressure to afford the title compound (25.9 g, 91%).

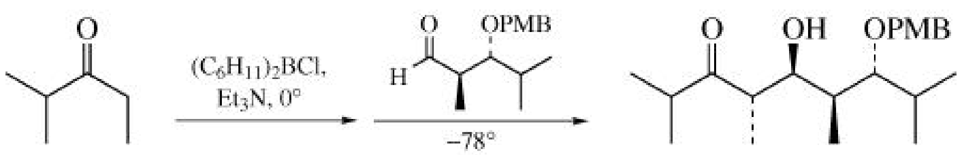
7.1.4. (–)-Diisopinocampheylboron Chloride [(–)-Ipc_2BCl] (139, 142, 273)

To a cooled (–78°) suspension of (–)-Ipc_2BH (23.2 g, 81.2 mmol) in Et_2O (40 mL) was added a solution of anhydrous HCl (90 mL of a 1 M solution in Et_2O, 90 mmol). The reaction mixture was then allowed to warm to 0° and stirred at this temperature until a solution resulted (2 hours) [**CAUTION**: venting of the evolved hydrogen gas is necessary] . The reaction was then concentrated under reduced pressure taking care to maintain anhydrous conditions. The residue was then crystallized from anhydrous pentane to afford the title compound (18.6 g, 71%) as colorless crystals, mp 54–56°. ^{11}B

NMR ($CDCl_3$) δ 74.0. ^{13}C NMR ($CDCl_3$) δ 47.7, 41.0, 39.0, 37.5, 34.2, 32.7, 28.3, 28.1, 23.2, 22.7.

7.1.5. (–)-Diisopinocampheylboron Triflate [(–)-Ipc$_2$BOTf] (119, 121, 140, 143)

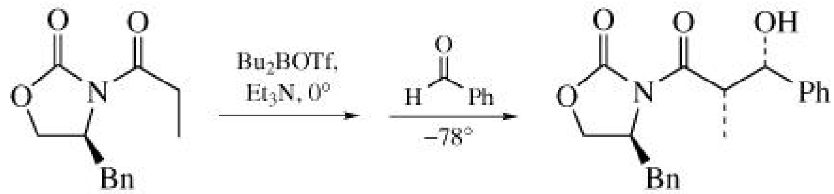
TfOH (1.44 mL, 16.3 mmol) was added slowly to a gently stirred, cooled (0°) suspension of (–)-Ipc_2BH (4.66 g, 16.3 mmol) in anhydrous hexane. After 15 minutes, the mixture was warmed to 20° (hydrogen evolution) and the colorless solution of the reagent was cannulated from the orange residue. Addition of hexane (6 mL) provided a reagent solution (ca. 1 M) which can be used in aldol reactions, or concentration followed by distillation (oven 130°, 0.05 mm Hg) affords the title compound. $[\alpha]_D^{22} - 43.5$(*c* 30.4, hexane). ^{13}C NMR ($CDCl_3$) δ 118.9 (q, *J* = 318 Hz), 48.3, 41.5, 39.3, 37.3, 33.9, 28.6, 28.3, 23.4, 22.7.



7.1.6. (4S,5S,6S,7R)-5-Hydroxy-7-[4-(methoxybenzyl)oxy]-2,4,6,8-tetramethylnonan-3-one (Anti Aldol Reaction of an Achiral Ketone with a Chiral Aldehyde) (38)

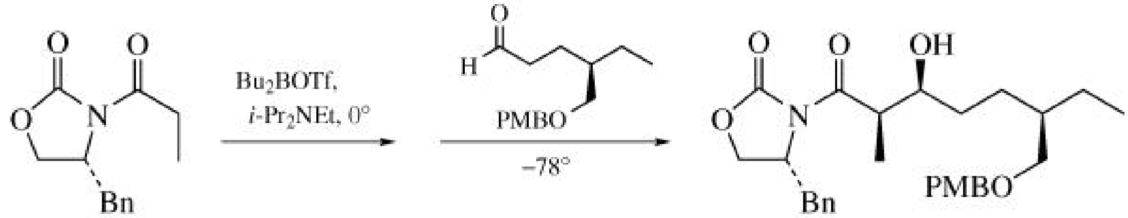
Dicyclohexylboron chloride (262 μL, 1.22 mmol) was added to a cooled (0°) solution of 2-methylpentan-3-one (137 μL, 1.11 mmol) in Et_2O (6 mL), followed by dropwise addition of Et_3N (186 μL, 1.33 mmol). The resulting white mixture was stirred at 0° for 1 hour, then cooled to –78° and a solution of the aldehyde (250 mg, 1.00 mmol) in Et_2O (0.25 mL) was added dropwise and the resulting mixture stirred for 2 hours. The reaction was quenched by addition of pH 7 buffer (ca. 10 mL) and diluted with methanol (~5 mL). After the mixture was warmed to 0°, 30% aq. H_2O_2 (1.2 mL) was added and the mixture was stirred at room temperature for 1 hour. The volatiles were removed under reduced pressure and the residue extracted with Et_2O, then washed with $NaHCO_3$ and brine, dried ($MgSO_4$), and purified by MPLC (Michel–Miller column size C, 10% EtOAc/hexanes) to afford the title compound (294 mg, 84%). Silylation of crude material with 1-(trimethylsilyl)imidazole and subsequent GLC analysis indicated an initial 93:7 ratio of aldol isomers. $[\alpha]_D^{21} - 41.5$(*c* 1.20, $CHCl_3$). IR (thin film) 3483, 2967, 2935, 2875, 1711, 1613, 1587, 1515, 1464, 1382, 1302, 1250, 1036 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.27–7.22 (m, 2 H), 6.87–6.83 (m, 2 H), 4.54 (ABq, *J* = 10.5 Hz, 2 H), 4.13 (dt, *J* = 9.7, 1.3 Hz, 1 H), 3.79 (s, 3 H), 3.36

(d, J = 1.4 Hz, 1 H), 3.36 (dd, J = 8.2, 3.3 Hz, 1 H), 2.86 (dq, J = 9.8, 7.0 Hz, 1 H), 2.74 (septet, J = 6.9 Hz, 1 H), 2.05 (m, 1 H), 1.86 (ddq, J = 7.1, 3.3, 1.5 Hz, 1 H), 1.09 (d, J = 7.0 Hz, 3 H), 1.05 (d, J = 6.8 Hz, 3 H), 1.05 (d, J = 6.8 Hz, 3 H), 1.04 (d, J = 6.6 Hz, 3 H), 0.92 (d, J = 6.8 Hz, 3 H), 0.91 (d, J = 7.0 Hz, 3 H).



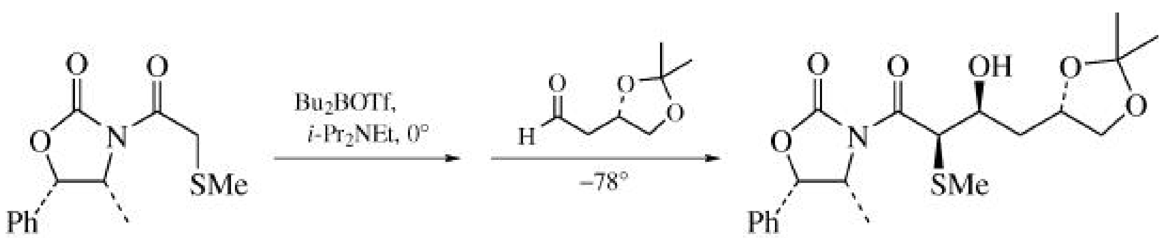
7.1.7. [3-(2S,3S)-4S]-3-(3-Hydroxy-3-phenyl-2-methyl-1-oxopropyl)-4-(phenylmethyl)oxazolidin-2-one (Auxiliary Controlled Syn Aldol Reaction with an Achiral Aldehyde) (42)

Dibutylboron triflate (27 mL, 0.107 mol), followed by Et_3N (16.7 mL, 0.120 mol) were added dropwise to an ice-cooled solution of the imide (21.2 g, 0.091 mol) in CH_2Cl_2 (200 mL) so that the internal temperature of the reaction did not exceed 3°. The reaction mixture was then cooled to –78° and freshly distilled benzaldehyde (10.3 mL, 0.101 mol) was added via a syringe pump. The reaction mixture was stirred at –78° for 20 minutes and then warmed to 0° for a further 1 hour, after which pH 7 buffer (100 mL) and methanol (300 mL) were added. A solution of methanol–30% aqueous H_2O_2 (300 mL of a 2:1 solution) was then added cautiously at such a rate as to maintain the internal reaction temperature below 10°. After stirring at room temperature for 1 hour, the resulting mixture was concentrated to a slurry which was extracted with Et_2O (3 × 500 mL) and the combined organic extracts were washed with 5% aq. $NaHCO_3$ (500 mL), brine (500 mL), then dried ($MgSO_4$) and concentrated in vacuo to afford the crude aldol adduct. Recrystallization of this material (EtOAc/hexane) afforded the diastereomerically pure product (28.6 g, 93%), mp 92–93°. GC analysis of the crude aldol product indicated >97% diastereomeric purity; $[\alpha]_D$ + 75.7° (*c* 1.00, CH_2Cl_2). IR (CH_2Cl_2) 3520, 3040, 2980, 1695, 1455, 1385, 1212, 1110 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.2 (d, J = 7.0 Hz, 1 H), 2.8 (dd, J = 13.4, 9.5 Hz, 1 H), 3.1 (d, J = 2.7 Hz, 1 H), 3.3 (dd, J = 13.4, 3.4 Hz, 1 H), 4.1 (m, 3 H), 4.6 (m, 1 H), 5.1 (m, 1 H), 7.1–7.5 (m, 10 H).



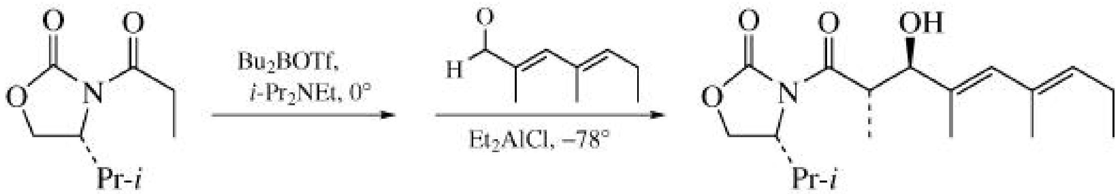
7.1.8. (R)-3-{(2R,3S,6R)-3-Hydroxy-6-([(4-methoxyphenyl)methoxy]methyl)2-methyl-1-oxo-octyl}-4-(phenylmethyl)-1,3-oxazolidin-2-one (Auxiliary Controlled Syn Aldol Reaction with a Chiral Aldehyde) (274)

Dibutylboron triflate was added to a cooled (0°) solution of the imide (13.4 g, 57.7 mmol) in CH_2Cl_2 (105 mL) under nitrogen at such a rate as to maintain the internal temperature below 5°. Diisopropylethylamine (8.9 g, 69.1 mmol) was then added, giving a yellow solution which was cooled to –78°, and a solution of the aldehyde (13.1 g, 52.4 mmol) in CH_2Cl_2 (26 mL) was added dropwise. After 20 minutes, the solution was warmed to 0° and stirred at that temperature for 1 hour before being recooled to –10° and quenched by addition of pH 7 buffer (50 mL), methanol (250 mL), and 30% aq. H_2O_2 (50 mL). The resulting mixture was stirred at 0° for 1 hour and then concentrated in vacuo to remove the volatiles. The aqueous residue was extracted with Et_2O (3 × 150 mL) and the combined organic extracts were washed with aq. $NaHCO_3$ (100 mL), and brine (100 mL), then dried ($MgSO_4$) and purified by flash chromatography (55% EtOAc/hexanes) to afford the title compound (25.30 g, 100%) as a colorless oil (ds > 99% by analytical HPLC). $[\alpha]_D^{28} - 40.9$(*c* 0.35, $CHCl_3$). IR (neat) 3530, 2940, 1785, 1700, 1515, 1385, 1245, 1210 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.27 (m, 7 H), 6.87 (m, 2 H), 4.69 (m, 1 H), 4.42 (s, 2 H), 4.20 (m, 2 H), 3.91 (m, 1 H), 3.80 (s, 3 H), 3.74 (qd, *J* = 7.1, 2.6 Hz, 1 H), 3.33 (d, *J* = 5.5 Hz, 2 H), 3.01 (m, 2 H), 2.89 (d, *J* = 3.0 Hz, 1 H), 1.66–1.29 (m, 7 H), 1.25 (d, *J* = 7.0 Hz, 3 H), 0.87 (t, *J* = 7.4 Hz, 3 H).



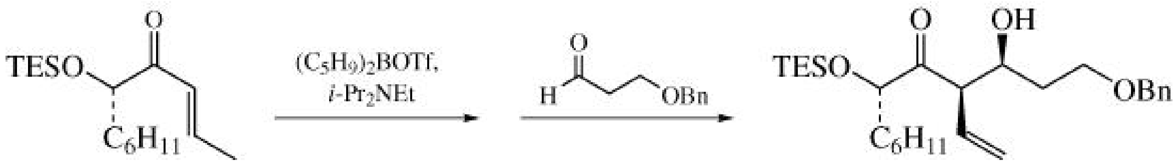
7.1.9. (2¢R,3¢S,5¢S,4R,5S)-3-(3¢-Hydroxy-5',6'-(isopropylidene-dioxy)-2¢-(methylthio)hexanoyl)-4-methyl-5-phenyloxazolidin-2-one (Auxiliary Controlled Syn Aldol Reaction of a Thiomethyl Imide) (56)

A solution of the imide (4.06 g, 15.3 mmol) in CH_2Cl_2 (32 mL) cooled to 0° was treated with freshly prepared Bu_2BOTf (4.74 g, 17.3 mmol), and then *i*-Pr_2NEt (2.45 g, 24.1 mmol) was added and the mixture stirred at 0° for 70 minutes. The mixture was cooled to –70° and a solution of the aldehyde (2.00 g, 13.9 mmol) in CH_2Cl_2 (10 mL) was added over 5 minutes. The reaction mixture was then stirred for 14 hours while being allowed to warm to room temperature. After addition of pH 7 buffer (50 mL), the resulting mixture was stirred for 90 minutes and then extracted with CH_2Cl_2 (2 × 20 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash chromatography (20% EtOAc/hexanes) afforded the title compound (5.06 g, 89%) as a yellow oil. $[\alpha]_D^{23} + 12.3$(*c* 0.42, $CHCl_3$). IR (neat) 3482, 2985, 1773, 1701, 1687, 1654 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.48–7.29 (m, 5 H), 5.70 (d, *J* = 7.5 Hz, 1 H), 4.84 (m, 1 H), 4.70 (d, *J* = 7.1 Hz, 1 H), 4.38 (m, 1 H), 4.23 (m, 1 H), 4.14 (dd, *J* = 8.2, 6.8 Hz, 1 H), 3.63 (dd, *J* = 8.2, 6.5 Hz, 1 H), 3.18 (d, *J* = 1.6 Hz, 1 H), 2.17 (s, 3 H), 1.84 (apparent t, *J* = 6.2 Hz, 2 H), 1.44 (s, 3 H), 1.37 (s, 3 H), 0.92 (d, *J* = 6.6 Hz, 3 H).



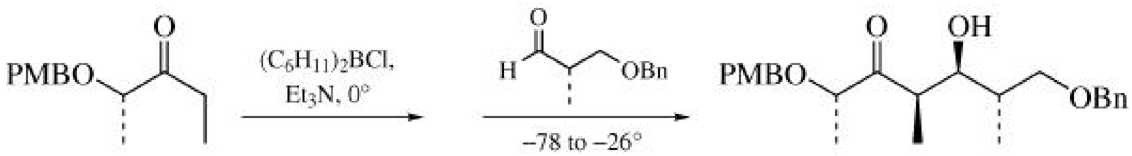
7.1.10. (4R)-3-[(2S,3S,4E,6E)-3-Hydroxy-2,4,6-trimethyl-1-oxa-4,6-nonadienyl]-4-isopropyloxazolidin-2-one (Auxiliary Controlled Anti Aldol Reaction of an Imide Auxiliary with an Achiral Aldehyde Precomplexed with a Lewis Acid) (47)

To a cooled (0°) solution of the imide (370 mg, 2.0 mmol) in CH_2Cl_2 (4 mL) was added *i*-Pr_2NEt (390 µL, 2.3 mmol) followed by a solution of Bu_2BOTf (2.2 mL of a 1 M solution in CH_2Cl_2) and stirring was continued for 1 hour. Separately, CH_2Cl_2 (4 mL) was added to a solution of Et_2AlCl (3.3 mL of a 1.8 M solution in toluene) and after cooling to –78°, a solution of the aldehyde (415 mg, 3.0 mmol) was added. After the mixture was stirred for 5 minutes, the boron enolate was added dropwise and the reaction mixture was slowly warmed to room temperature over a 12-hour period. After the mixture was recooled to –78°, methanol (10 mL) and 35% aq. H_2O_2 (2 mL) were added and after warming to 0°, water (20 mL) was added and the aqueous phase was extracted with Et_2O(4 × 50 mL). The combined organic fractions were washed with sat. aq. $NaHCO_3$ and brine (20 mL), then dried ($MgSO_4$), and concentrated. Column chromatography of the residue afforded an inseparable mixture of minor aldol isomers (15%) and the title compound (476 mg, 74%) as colorless crystals, mp 88° (hexanes). $[\alpha]_D^{20} - 96.0$(*c* 4.00, CH_2Cl_2). ^1H NMR($CDCl_3$) δ 5.88 (s, 1 H), 5.32 (br. t, *J* = 7.2 Hz, 1 H), 4.48–4.42 (m, 1 H), 4.31–4.00 (m, 1 H), 2.66 (d, *J* = 6.9 Hz, 1 H), 1.06 (d, *J* = 6.6 Hz, 3 H), 0.98 (t, *J* = 7.5 Hz, 3 H), 0.91 (d, *J* = 7 Hz, 3 H), 0.88 (d, *J* = 7 Hz, 3 H).



7.1.11. (1S,3R,4S)-4-Hydroxy-1-triethylsilyloxy-6-benzyloxy-1-cyclohexyl-3-vinylhexan-2-one (Auxiliary Controlled Syn Aldol Reaction of an α -Oxygenated Crotyl Ketone with an Achiral Aldehyde) (275)

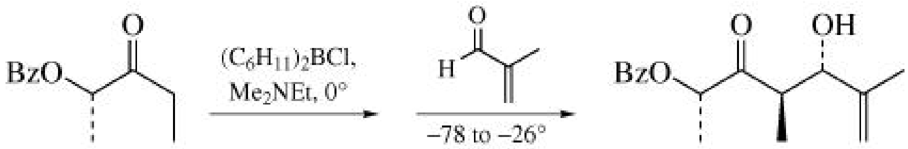
To a cooled (–78°) solution of the ketone (150 mg, 0.506 mmol) in CH_2Cl_2 (10 mL) was added *i*-Pr_2NEt (224 μL, 1.29 mmol) followed by $(C_5H_9)_2BOTf$ (256 μL, 1.03 mmol). The reaction was stirred at 0° for 2.5 hours and then cooled to –78° and a solution of the aldehyde (2.5 equiv.) in CH_2Cl_2 was added and the reaction mixture warmed to 0° and stirred for 2.5 hours. Methanol (3 mL), pH 7 buffer (3 mL), and 30% aq. H_2O_2 (0.5 mL) were added and stirring was continued for 1 hour. Usual workup (see other experimental procedures for examples) followed by column chromatography (15% Et_2O/hexane) afforded the title compound (215 mg, 93%). $[\alpha]_D^{25} + 118.3$7.32 (m, 5 H), 5.84 (ddd, *J* = 18, 10, 9 Hz, 1 H), 5.32 (d, *J* = 10 Hz, 1 H), 5.26 (d, *J* = 18 Hz, 1 H), 4.51 (s, 2 H), 4.15 (m, 1 H), 3.96 (d, *J* = 5 Hz, 1 H), 3.72–3.52 (complex m, 4 H), 1.97–1.41 (complex m, 8 H), 1.30–0.83 (complex m, 5 H), 0.94 (t, *J* = 8 Hz, 9 H), 0.58 (q, *J* = 8 Hz, 6 H).



7.1.12. (2R,4R,5S,6S)-7-Benzyloxy-5-hydroxy-2-(p-methoxybenzyloxy)-4, 6-dimethylheptan-3-one (Auxiliary Controlled Syn Aldol Reaction of a Lactate-Derived Chiral Ketone with a Chiral Aldehyde) (276)

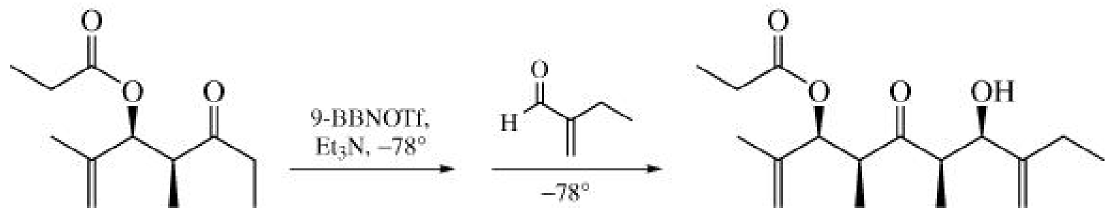
To a cooled (–78°) stirred solution of dicyclohexylboron chloride (2.67 mL, 13 mmol) in dry Et_2O (40 mL) under argon was added triethylamine (2.1 mL, 15 mmol) followed by a solution of the ketone (2.22 g, 10 mmol) in Et_2O (40 mL). After the reaction was stirred at –78° for 1 hour and then 0° for 3 hours, then recooled to –78°, a solution of the freshly prepared aldehyde (2.85 g, 16 mmol) in Et_2O (20 mL) was added. After stirring for 1 hour, the reaction mixture was transferred to the freezer (–25°) for 16 hours and then quenched at 0° by the addition of methanol (40 mL), pH 7 buffer (40 mL), and

30% aq. H_2O_2 (40 mL). Stirring continued for 1 hour, after which time the reaction mixture was partitioned between water (100 mL) and CH_2Cl_2(3 × 100 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (10% EtOAc/hexanes) afforded a minor isomer (240 mg, 6%) and the title compound (2.96 g, 86%) as a colorless oil. $[\alpha]_D^{20} - 10.7$(*c* 0.69, $CHCl_3$). IR (thin film) 3491, 2975, 2935, 2873, 1715, 1612, 1514 cm^{-1}. ^1H NMR($CDCl_3$) δ 7.34–7.24 (m, 7 H), 6.87 (d, ABq, *J* = 8.6 Hz, 2 H), 4.50–4.40 (m, 4 H), 4.09 (q, *J* = 6.5 Hz, 1 H), 3.96–3.92 (m, 1 H), 3.80 (s, 3 H), 3.48 (dd, *J* = 9.2, 4.2 Hz, 1 H), 3.41 (dd, *J* = 9.2, 4.9 Hz, 1 H), 3.17–3.11 (m, 1 H), 3.00 (d, *J* = 2.0 Hz, 1 H), 1.84–1.76 (m, 1 H), 1.33 (d, *J* = 6.9 Hz, 3 H), 1.17 (d, *J* = 7.0 Hz, 3 H), 1.00 (d, *J* = 7.0 Hz, 3 H).



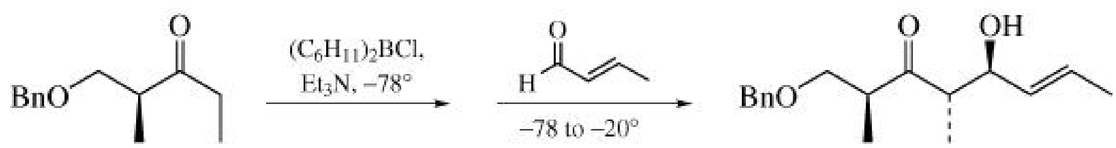
7.1.13. (2S,4R,5S)-2-Benzoyloxy-5-hydroxy-4,6-dimethyl-6-hepten-3-one (Auxiliary Controlled Anti Aldol Reaction of a Lactate-Derived Chiral Ketone with an Achiral Aldehyde) (110, 277)

To a cooled (–78°), stirred solution of freshly prepared dicyclohexylboron chloride (140 µL, 0.778 mmol) in anhydrous Et_2O (2 mL) under argon was added Me_2NEt (84 µL, 0.78 mmol) followed by a solution of the ketone (89.0 mg, 0.432 mmol) in Et_2O (2 mL). The reaction mixture was then warmed to 0° and stirred at this temperature for 3 hours before recooling to –78°, after which freshly distilled methacrolein (143 µL, 1.73 mmol) was added and stirring at –78° was continued for 2 hours before the mixture was transferred to a freezer (–26°) for a further 16 hours. The reaction mixture was quenched at 0° by addition of methanol (2 mL) and pH 7 buffer (2 mL); 30% aq. H_2O_2 (2 mL) was then added cautiously and stirring was continued for 1 hour. The resulting mixture was partitioned between water (30 mL) and CH_2Cl_2(3 × 30 mL) and the combined organic phases were dried ($MgSO_4$) and concentrated in vacuo and the crude material was subjected to flash chromatography (50% Et_2O/hexane), thus affording the title compound (116 mg, 97%, 99% ds by HPLC analysis) as a white solid, mp 59–60°. $[\alpha]_D^{20} + 29.0$(*c* 0.60, $CHCl_3$). IR ($CHCl_3$) 3509, 1718, 1601 cm^{-1}. ^1H NMR($CDCl_3$) δ 8.07 (d, *J* = 7.4 Hz, 2 H), 7.56 (t, *J* = 7.4 Hz, 2 H), 7.44 (t, *J* = 7.4 Hz, 2 H), 5.44 (q, *J* = 7.0 Hz, 1 H), 4.95 (s, 1 H), 4.92 (s, 1 H), 4.25 (d, *J* = 8.8 Hz, 1 H), 3.01 (dq, *J* = 8.8, 7.2 Hz, 1 H), 2.28 (s, 1 H), 1.71 (s, 3 H), 1.56 (d, *J* = 7.0 Hz, 3 H), 1.03 (d, *J* = 7.2 Hz, 3 H).



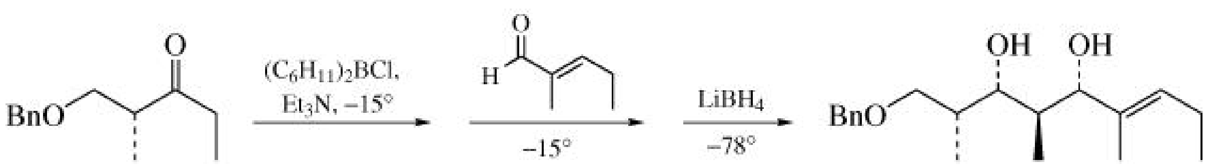
7.1.14. (3SR,4SR,6RS,7RS)-2-Ethyl-3-hydroxy-4,6,8-trimethyl-7-propanoyl oxy-1,8-nonadien-5-one (Syn Aldol Reaction of a Chiral Ketone with an Achiral Aldehyde) (21)

To a cooled (–78°) stirred solution of 9-BBN triflate (1.30 mL, 0.66 mmol, 0.5 M in hexanes) in Et_2O (2.0 mL) was added Et_3N (124 µL, 0.89 mmol), then a solution of the ketone (95 mg, 0.44 mmol) in ether (1.5 mL). The reaction mixture was stirred at –78° for 4 hours, then freshly distilled 2-ethylacrolein was added (215 µL, 2.20 mmol) followed by stirring for a further 1.5 hours at –78°. The reaction mixture was partitioned between pH 7 buffer (5 mL) and CH_2Cl_2(3 × 10 mL) and the combined organic extracts were washed with brine (5 mL), dried ($MgSO_4$), and concentrated in vacuo. The resulting oil was dissolved in a methanol-pH 7 buffer mixture (5:1, 6 mL overall), cooled to 0°, and 30% aq. H_2O_2 (1 mL) was added, dropwise. The resulting mixture was stirred for 1 hour at 0°, then water (10 mL) was added followed by extraction with CH_2Cl_2(3 × 10 mL). The combined organic extracts were washed with sat. aq. $NaHCO_3$ (10 mL) and brine (10 mL), then dried ($MgSO_4$), and concentrated in vacuo to give the crude aldol product. HPLC separation (20% EtOAc in hexane) showed a ratio of 91:7:2 SS:SA:AS diastereomeric aldol products, which were isolated as a series of colorless oils (100 mg, 76% overall yield). The title compound was the major diastereomer: IR (thin film) 3500, 3100, 1735, 1710, 1645 cm^{-1}.^{1}H NMR($CDCl_3$) δ 5.44 (d, *J* = 5.9 Hz, 1 H), 5.13 (br s, 1 H), 4.94 (m, 2 H), 4.93 (br s, 1 H), 4.36 (br s, 1 H), 3.13 (d, *J* = 2.1 Hz, 1 H), 3.09 (dq, *J* = 6.7, 6.7 Hz, 1 H), 2.80 (qd, *J* = 7.3, 1.8 Hz, 1 H), 2.32 (q, *J* = 7.6 Hz, 2 H), 2.00–1.82 (m, 2 H), 1.74 (s, 3 H), 1.11 (t, *J* = 7.6 Hz, 3 H), 1.07 (d, *J* = 6.7 Hz, 3 H), 1.05 (t, *J* = 7.4 Hz, 3 H), 1.04 (d, *J* = 7.3 Hz, 3 H).



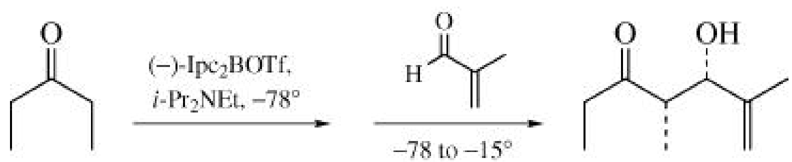
7.1.15. (2S,4S,5S,6E)-1-Benzyloxy-5-hydroxy-2,4-dimethyl-6-octen-3-one (Anti Aldol Reaction of a Chiral Ketone with an Achiral Aldehyde) (122)

To a cooled (–78°), stirred solution of ($C_6H_{11})_2BCl$ (5.00 mL, 23.0 mmol) in Et_2O (30 mL) was added dropwise Et_3N (4.22 mL, 30.3 mmol) followed by addition of a solution of the ketone (3.90 g, 18.9 mmol) in Et_2O (20 mL), whereupon a white precipitate formed. After 3 hours at –78°, freshly distilled crotonaldehyde (3.13 mL, 37.8 mmol) was added dropwise and the reaction mixture was stirred at –78° for a further 3 hours, before being left in the freezer (–20°) for 16 hours. The reaction mixture was then partitioned between Et_2O(3 × 200 mL) and pH 7 buffer (200 mL) and the combined organic extracts were concentrated in vacuo; the residue was resuspended in methanol (50 mL) and pH 7 buffer (10 mL) and cooled to 0°. Hydrogen peroxide (20 mL, 30% aq.) was added dropwise and stirring was continued at room temperature for 1 hour. The mixture was then poured into distilled water (200 mL) and extracted with CH_2Cl_2(3 × 200 mL). The combined organic extracts were washed in turn with 5% aq. $NaHCO_3$ (150 mL) and brine (150 mL), dried ($MgSO_4$), and concentrated in vacuo to afford a yellow oil. Flash chromatography (10% Et_2O/ CH_2Cl_2) provided 4.86 g (93%) of the desired anti-anti aldol product as a colorless oil. HPLC analysis indicated > 98:2 selectivity. $[\alpha]_D^{20} + 17.1$(*c* 4.3, $CHCl_3$). IR (thin film) 3440, 1700 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.33–7.25 (m, 5 H), 5.71 (dqd, *J* = 15.3, 6.4, 0.9 Hz, 1 H), 5.43 (ddq, *J* = 15.3, 7.7, 1.6 Hz, 1 H), 4.49 and 4.47 (ABq, *J* = 12.0 Hz, 2 H), 4.16 (apparent t, *J* = 7.7 Hz, 1 H), 3.67 (dd, *J* = 8.8, 8.7 Hz, 1 H), 3.44 (dd, *J* = 8.8, 5.0 Hz, 1 H), 3.07 (dqd, *J* = 8.7, 7.0, 5.0 Hz, 1 H), 2.81 (br s, 1 H), 2.75 (dq, *J* = 7.7, 7.1 Hz, 1 H), 1.70 (br d, *J* = 6.4 Hz, 3 H), 1.05 (d, *J* = 7.0 Hz, 3 H), 1.04 (d, *J* = 7.1 Hz, 3 H).



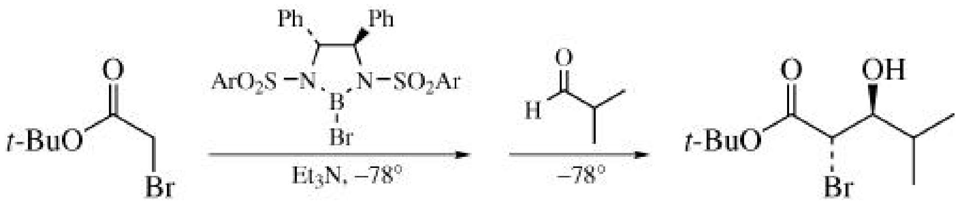
7.1.16. (2R,3S,4S,5S,6E)-2,4,6-Trimethyl-1-phenylmethoxy-6-nonene-3,5-diol (Anti Aldol Reaction of a Chiral Ketone and an Achiral Aldehyde Followed by in situ LiBH₄ Reduction) (123, 124)

To a stirred solution of dicyclohexylboron chloride (2.4 mL, 11 mmol) in dry Et_2O (20 mL) was added Et_3N (1.6 mL, 11 mmol) and the mixture was cooled to –15°. A solution of the ketone (1.54 g, 7.5 mmol) in Et_2O (5 mL) was added and the mixture was stirred for 2 hours at –15°. A solution of (*E*)-2-methyl-2-pentenal (1.5 mL, 13.1 mmol) in Et_2O (5 mL) was added and stirring was continued at this temperature for 2 hours. The reaction mixture was then cooled to –78° and $LiBH_4$ (19.2 mL, 2 M solution in THF, 38 mmol) was added. After 2 hours, the reaction mixture was partitioned between Et_2O(3 × 100 mL) and sat. aq. NH_4Cl (60 mL), the organic extracts were combined and washed with brine, then concentrated in vacuo to give an oil. Purification by flash chromatography (CH_2Cl_2) gave the semipure boronate (4.3 g). This residue was suspended in cold (0°) MeOH (30 mL) and 10% aq. NaOH (10 mL) and 30% aq. H_2O_2 (15 mL) were added and stirring was continued at room temperature for 2 hours. The resulting mixture was then poured into water (150 mL) and extracted with CH_2Cl_2(3 × 150 mL). The combined organic extracts were washed with sat. aq. $NaHCO_3$ (50 mL), sat. aq. $NaHSO_3$ (50 mL), and brine (50 mL), then dried ($MgSO_4$) and concentrated in vacuo to give a yellow oil. Purification by flash chromatography (10% Et_2O/ CH_2Cl_2) gave the title compound (1.85 g, 81%) as a colorless solid, mp 64–65° (pentane). $[\alpha]_D^{20} + 15.6$(*c* 1.4, $CHCl_3$). IR ($CHCl_3$) 3440, 2970, 2930, 2870 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.37 – 7.27 (m, 5 H), 5.33 (t, *J* = 6.9 Hz, 1 H), 4.52 (s, 2 H), 4.16 (s, 1 H), 4.08 (s, 1 H), 3.90 (d, *J* = 9.2 Hz, 1 H), 3.84 (d, *J* = 9.2 Hz, 1 H), 3.60 – 3.55 (m, 2 H), 2.02 (qd, *J* = 7.5, 6.9 Hz, 2 H), 1.97 – 1.92 (m, 1 H), 1.79 – 1.72 (m, 1 H), 1.60 (s, 3 H), 0.99 (d, *J* = 7.0 Hz, 3 H), 0.95 (t, *J* = 7.5 Hz, 3 H), 0.59 (d, *J* = 6.8 Hz, 3 H).



7.1.17. (4S,5S)-5-Hydroxy-4,6-dimethyl-6-hepten-3-one (Aldol Reaction of an Achiral Ketone with an Achiral Aldehyde Using a Chiral Boron Reagent) (121)

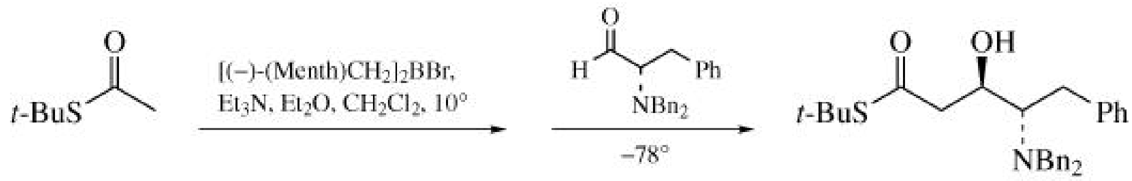
A freshly prepared stock solution (see above) of (–)-Ipc_2BOTf (2.05 mL, 3.9 mmol, ca. 1.9 M in hexane) was diluted with CH_2Cl_2 (16 mL) and cooled to –78°. Diisopropylethylamine (1.04 mL, 6.0 mmol) was added, followed by diethyl ketone (300 μL, 3.0 mmol). After 3 hours, freshly distilled methacrolein (330 μL, 4 mmol) was added and stirring was continued at –78° for 1 hour and then the reaction was transferred to the refrigerator (–15°) for 12 hours. The reaction mixture was then partitioned between Et_2O(3 × 20 mL) and pH 7 buffer (20 mL). The combined organic extracts were concentrated in vacuo, then dissolved in methanol (15 mL), and pH 7 buffer (3 mL) and 30% aq. H_2O_2 (4 mL) were added and stirring was continued at 0° for 1 hour. The reaction mixture was then poured into water and extracted with CH_2Cl_2(3 × 30 mL). The combined organic extracts were washed with sat. aq. $NaHCO_3$ and brine, then dried ($MgSO_4$) and concentrated in vacuo. The resulting oil was purified by flash chromatography (10% Et_2O/ CH_2Cl_2) to afford the title compound (365 mg, 78%) as a colorless oil. The syn/anti ratio was determined by 400-MHz ^1H NMR analysis to be 98:2 and a chiral shift experiment indicated 91% ee. $[\alpha]_D^{20} - 33.8$(*c* 3.7, $CHCl_3$). IR (thin film) 3460, 1700, 1650 cm^{-1}. ^1H NMR ($CDCl_3$) δ 5.04 (m, 1 H), 4.92 (m, 1 H), 4.37 (d, *J* = 3.6 Hz, 1 H), 2.72 (qd, *J* = 7.2, 3.6 Hz, 1 H), 2.57 (dq, *J* = 18.1, 7.3 Hz, 1 H), 2.49 (dq, *J* = 18.1, 7.3 Hz, 1 H), 1.68 (s, 3 H), 1.06 (d, *J* = 7.2 Hz, 3 H), 1.04 (t, *J* = 7.3 Hz, 3 H).



7.1.18. tert-Butyl (2S,3S)-(–)-2-Bromo-3-hydroxy-4-methylpentanoate (Aldol Reaction of an Achiral Ester with an Achiral Aldehyde Using a Chiral Boron Reagent) (167)

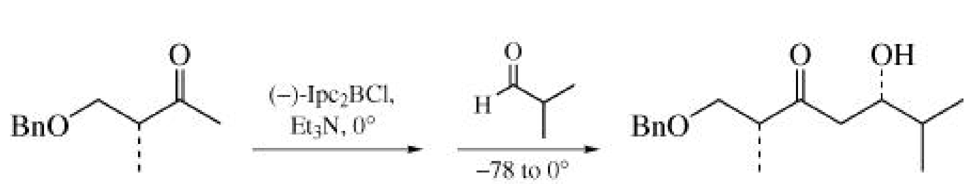
(*R,R*)-Bis[3,5-di(trifluoromethyl)benzenesulfonyl]-1,2-diamino-1,2-diphenylethane (10.0 g, 13.1 mmol) was heated at 65° under reduced pressure (ca. 1 mm Hg) and the flask was then filled with nitrogen and cooled to 23°. Anhydrous CH_2Cl_2 (150 mL) was added and the resulting solution was cooled to –78°, then treated with BBr_3 (10 mL of a 2.0 M sol. in CH_2Cl_2, 20 mmol). The reaction mixture was slowly returned to ambient temperature and stirred for 18 hours. The solvent was removed in vacuo while maintaining an anhydrous atmosphere, then CH_2Cl_2 (30 mL) was added and the solvent was removed as before. High vacuum was then applied (ca 1 mm Hg) for 10 minutes while heating at 40° and then the flask was opened to nitrogen, then replaced under vacuum, and this cycle was repeated five times. Toluene (300 mL) was added and the resulting mixture was warmed until a solution resulted, which was then cooled to –78°, and Et_3N (2.01 mL, 14.4 mmol) was added dropwise and the mixture was stirred at –78° for 5 minutes. *tert*-Butyl bromoacetate (2.01 mL, 12.4 mmol) was added and the mixture was stirred at –78° for 5 hours, after which a solution of isobutyraldehyde (1.01 mL, 11.8 mmol) in toluene (13 mL) was added and stirring was continued for 5 hours. While the mixture was held at –78°, methanol (5 mL) was added to quench the reaction, which was then diluted with Et_2O (300 mL). The organic layer was washed with brine (150 mL), dried ($MgSO_4$), and concentrated in vacuo, after which the crude product was treated with CH_2Cl_2 (5 mL) and hexanes (100 mL). After the mixture was stirred at room temperature for 1 hour, the white precipitate was filtered and washed with hexanes (100 mL) to afford recovered diamine (8.9 g, 89%

recovery). The filtrate was evaporated and the residue was purified by column chromatography (20% Et_2O/hexanes) to yield the title compound (2.83 g, 90%). Analysis indicated anti:syn = 98:2, 92% ee for anti). $[\alpha]_D^{20} - 10.9$ (*c* 2.62, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 4.12 (d, *J* = 7.9, 1 H), 3.78 (m, 1 H), 2.66 (d, *J* = 6.6 Hz, 1 H), 2.13 – 2.07 (m, 1 H), 1.50 (s, 9 H), 1.01 (d, *J* = 6.8 Hz, 3 H), 0.92 (d, *J* = 6.8 Hz, 3 H).



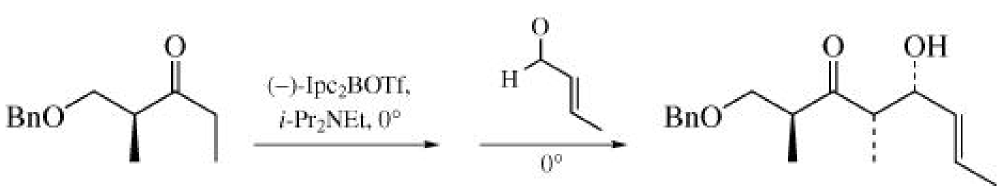
7.1.19. tert-Butyl (3R,4S)-4-[N,N]-Dibenzylamino-3-hydroxy-5-phenylpentanthioate (Aldol Reaction of an Achiral Thioester with a Chiral Aldehyde Using a Chiral Boron Reagent) (165)

To a cooled solution of *tert*-butyl thioacetate (31 mg, 0.23 mmol) in Et_2O(950 µL) was added a solution of [(–)-(Menth)CH_2]$_2$BBr (880 µL of a 0.4 M solution in CH_2Cl_2, 0.34 mmol) followed by Et_3N (52 µL, 0.37 mmol). The reaction mixture was stirred at 10° for 2.5 hours, then cooled to –78° and dibenzyl phenylalaninal (99 mg, 0.30 mmol) was added dropwise and stirring was continued for a further 18 hours. The reaction was quenched by addition of pH 7 buffer (1 mL) and then the solvent was removed in vacuo. The residue was dissolved in methanol (5 mL) then treated with pH 7 buffer (1 mL) and 30% aq. H_2O_2 (1 mL) and stirred at room temperature for 45 minutes. The reaction mixture was concentrated in vacuo, then extracted twice with CH_2Cl_2. The organic extracts were washed with water then brine, dried (Na_2SO_4), and concentrated under reduced pressure. Column chromatography (15% EtOAc/hexanes) afforded the title compound (79 mg, 75%) as a colorless oil. $[\alpha]_{365(Hg)}^{20} - 84.6$ (*c* 1.42, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 7.40 – 7.10 (m, 15 H), 4.40 – 4.25 (m, 1 H), 3.78 – 3.58 (2 × ABq, *J* = 13.8 Hz, 4 H), 3.20 – 2.70 (m, 5 H), 2.45 – 2.30 (m, 1 H), 1.48 (s, 9 H).



7.1.20. (2R,5S)-1-Benzyloxy-5-hydroxy-2,6-dimethylheptan-3-one (Double Stereodifferentiating Aldol Reaction between a Chiral Ketone, an Achiral Aldehyde, and a Chiral Boron Reagent) (151)

To a cooled (0°) solution of (+)-Ipc_2BCl (2.07 g, 6.45 mmol) in anhydrous Et_2O (25 mL) was added Et_3N (0.90 mL, 6.45 mmol) followed by a solution of (*R*)-1-benzyloxy-2-methylbutan-3-one (0.793 g, 4.1 mmol) in Et_2O (15 mL). The white suspension was stirred for 3 hours at 0° before cooling to –78°, and isobutyraldehyde (1.24 g, 17.2 mmol) was added dropwise. The reaction mixture was allowed to warm to –50° over 2 hours and then stirred at 0° for 1 hour. The reaction was quenched by sequential addition of methanol (140 mL), pH 7 buffer (56 mL), and 30% aq. H_2O_2 (14 mL) and the biphasic system was stirred vigorously at 0° for 10 minutes and then at room temperature for 1 hour. The mixture was poured into water (100 mL) and extracted with EtOAc/hexanes (1:1 v/v) (5 × 100 mL). The combined organic extracts were washed with H_2O (100 mL), dried ($MgSO_4$), and concentrated in vacuo. The resulting oil was subjected to column chromatography (EtOAc/hexanes, 15:85) to afford the title compound (980 mg, 91%) as a colorless oil. ^{1}H NMR analysis (500 MHz) indicated a diastereoselectivity of 95:5. $[\alpha]_D^{20} - 50.4$(*c* 0.27, $CHCl_3$). IR 3462, 1707 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 7.25–7.36 (m, 5 H), 4.50 (d, *J* = 12 Hz, 1 H), 4.46 (d, *J* = 12 Hz, 1 H), 3.82 (ddd, *J* = 9.7, 5.8, 2.2 Hz, 1 H), 3.57 (dd, *J* = 8.8, 8.4 Hz, 1 H), 3.48 (dd, *J* = 8.8, 4.2 Hz, 1 H), 2.92 (m, 1 H) 2.68 (dd, *J* = 17.4, 9.8, 1 H), 2.54 (dd, *J* = 17.4, 2.3 Hz, 1 H), 1.67 (m, 1 H), 1.06 (d, *J* = 7 Hz, 3 H), 0.91 (d, *J* = 6.8 Hz, 3 H), 0.89 (d, *J* = 6.8 Hz, 3 H).



7.1.21. (2S,4S,5R,6E)-1-Benzyloxy-5-hydroxy-2,4-dimethyl-6-octen-3-one (Double Stereodifferentiating Aldol Reaction between a Chiral Ketone, an Achiral Aldehyde, and a Chiral Boron Reagent) (119, 122, 278)

To a stirred solution of (–)-Ipc_2BOTf (1.09 mL, 0.65 mmol, ~0.6 M in hexane) in CH_2Cl_2 (2 mL) at room temperature was added *i*-Pr_2NEt (228 µL, 1.31 mmol) followed by the ketone (90 mg, 0.44 mmol) in CH_2Cl_2 (2 mL). After 3 hours at room temperature, the reaction mixture was cooled to 0° and freshly distilled crotonaldehyde (108 µL, 1.31 mmol) was added. After stirring at 0° for 1 hour, the reaction mixture was transferred to the refrigerator (–4°) for 16 hours, then partitioned between Et_2O(3 × 20 mL) and pH 7 buffer (20 mL) and the combined organic extracts were concentrated in vacuo. The residue was resuspended in methanol (4 mL) and pH 7 buffer (1 mL) and cooled to 0° C, then 30% aq. H_2O_2 (2 mL) was added dropwise and stirring was continued at room temperature for 1 hour. The mixture was then poured into water (20 mL) and extracted with CH_2Cl_2(3 × 20 mL). The combined organic extracts were washed in turn with 5% aq. $NaHCO_3$ (15 mL) and brine (10 mL), dried ($MgSO_4$), and concentrated in vacuo to afford a yellow oil. Flash chromatography (10% Et_2O/ CH_2Cl_2) allowed separation of the aldol products from isopinocampheol; HPLC purification (10% Et_2O/ CH_2Cl_2) provided minor aldol products (11 mg, 8%) along with the title compound (78.1 mg, 65%). $[\alpha]_D^{20}$ + 26.2 (*c* 5.0, $CHCl_3$). IR (thin film) 3450, 1690, 1600 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.36 – 7.23 (m, 5 H), 5.68 (dqd, *J* = 15.3, 6.3, 1.1 Hz, 1 H), 5.44 (ddq, *J* = 15.3, 6.2, 1.3 Hz, 1 H), 4.47 (ABq, *J* = 12.1 Hz, 2 H), 4.33 (ddd, *J* = 6.2, 4.0, 1.1 Hz, 1 H), 3.64 (app. t, *J* = 8.7 Hz, 1 H), 3.43 (dd, *J* = 8.7, 5.2 Hz, 1 H), 3.08 (dqd, *J* = 8.7, 7.1, 5.2 Hz, 1 H), 2.78 (qd, *J* = 7.1, 4.0 Hz, 1 H), 1.68 (dd, *J* = 6.3, 1.3 Hz, 3 H), 1.12 (d, *J* = 7.1 Hz, 3 H), 1.04 (d, *J* = 7.1 Hz, 3 H).

8. Tabular Survey

An effort has been made to tabulate all reported examples of asymmetric boron-mediated aldol reactions from mid-1981 until the end of 1995. Tables I–IIIB are listed in order of increasing carbon count of the enolate precursor and then the aldehyde. Tables IVA–VB are arranged in order of increasing carbon count of the chiral ligands, enolate precursor, and aldehyde. Table VI lists the reported examples of chiral boron enolates adding to ketones. Protecting groups are not included in the carbon count. When two compounds have the same carbon count, the compounds are ordered by increasing hydrogen number.

Isolated yields of the combined aldol products are included in parentheses and a dash indicates that no yield was reported. Where an enantiomeric excess is reported, it relates to the major product of a reaction. The solvent used in the reaction is dichloromethane unless otherwise indicated.

The following abbreviations have been used in the tables:

Bn	benzyl
Boc	*tert*-butoxycarbonyl
BOM	benzyloxymethyl
Bz	benzoyl
C_5H_9	cyclopentyl
C_6H_{11}	cyclohexyl
Cbz	benzyloxycarbonyl
DEIPS	diethylisopropylsilyl
DMIPS	dimethylisopropylsilyl
LDA	lithium diisopropylamide
MEM	methoxyethoxymethyl
MOM	methoxymethyl
Np	2-naphthyl
PMB	*p*-methoxybenzyl
PMP	*p*-methoxyphenyl
TBS	*tert*-butyldimethylsilyl
TBDPS	*tert*-butyldiphenylsilyl
TCE	2,2,2-trichloroethyl
TES	triethylsilyl
TFA	trifluoroacetic acid

THP	2-tetrahydropyranyl
TIPS	triisopropylsilyl
TMS	trimethylsilyl
Ts	*p*-toluenesulfonyl

Table I. Achiral Enolates with Chiral Aldehydes

View PDF

Table IIA. Chiral Enolates (Auxiliary Control) with Achiral Aldehydes

View PDF

Table IIB. Chiral Enolates (Auxiliary Control) with Chiral Aldehydes

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Table IIIA. Chiral Enolates (Substrate Control) with Achiral Aldehydes

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Table IIIB. Chiral Enolates (Substrate Control) with Chiral Aldehydes

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Table IVA. Chiral Enolates (Ligand Control) with Achiral Aldehydes

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Table IVB. Chiral Enolates (Ligand Control) with Chiral Aldehydes

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Table VA. Chiral Enolates (Ligand and Substrate Control) with Achiral Aldehydes

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Table VB. Chiral Enolates (Ligand and Substrate Control) with Chiral Aldehydes

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Table VI. Chiral Enolates (Auxiliary Control) with Ketones

View PDF

TABLE I. ACHIRAL ENOLATES WITH CHIRAL ALDEHYDES

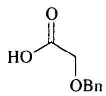
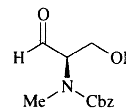
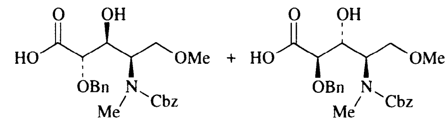
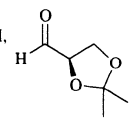
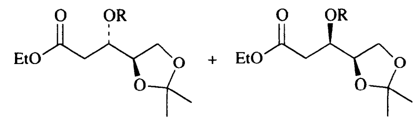
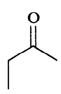
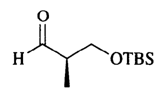
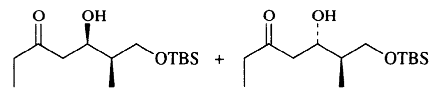
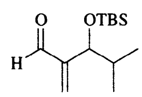
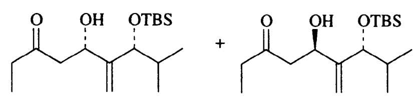
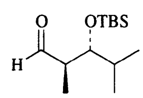
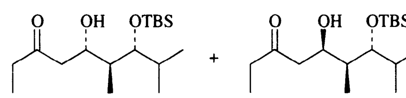
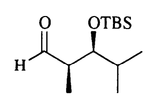
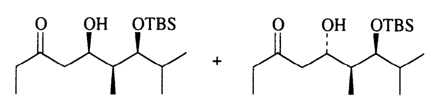
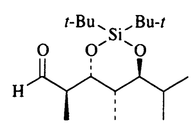
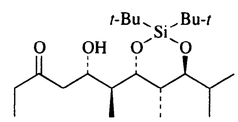
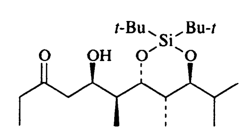
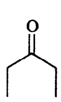
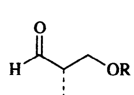
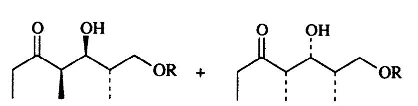
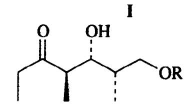
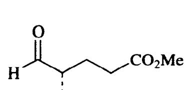
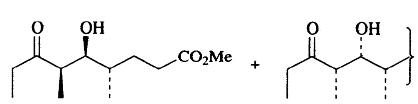
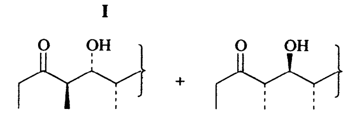
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
C_2				
	Bu_2BOTf, *i*-Pr_2NEt, Et_2O		 I (67) I:II = 72:28 II	239
C_4				
EtO—≡	1. $Hg(OAc)_2$, Ph_2BOH, Aldehyde 2. Alkyne		 I II R = H or Ac, (55) I:II = 92:8	279
	$(C_6H_{11})_2BCl$, Et_3N, Et_2O		 I (71) I:II = 50:50 II	32
	$(C_6H_{11})_2BCl$, Et_3N, Et_2O	 racemic	 I (89) I:II = 76:24 II	33
	$(C_6H_{11})_2BCl$, Et_3N, Et_2O		 I (74) I:II = 52:48 II	34
	$(C_6H_{11})_2BCl$, Et_3N, Et_2O		 I (83) I:II = 76:24 II	34
	$(C_6H_{11})_2BCl$, Et_3N, Et_2O		 I + (81) I:II = 70:30  II	34, 35
C_5				
	Bu_2BOTf, *i*-Pr_2NEt		 I II  III R = Bn, (—) I:II:III = 56:30:14 R = TBS, (—) I:II:III = 50:43:7	29
	1. Bu_2BOTf, *i*-Pr_2NEt 2. CF_3CO_2H		 I II  III IV (—) I:II:III:IV = 42:28:25:5[a]	29

TABLE I. ACHIRAL ENOLATES WITH CHIRAL ALDEHYDES (*Continued*)

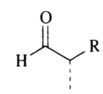
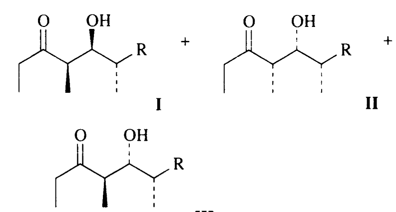
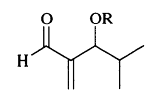
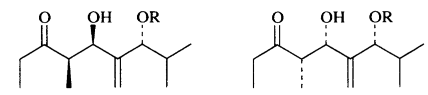
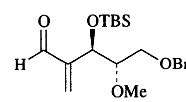
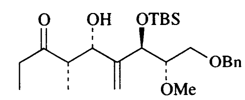
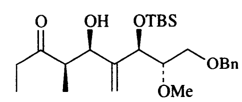
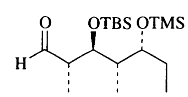
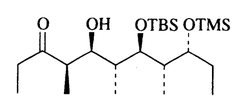
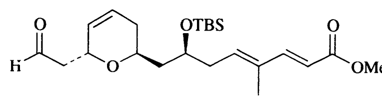
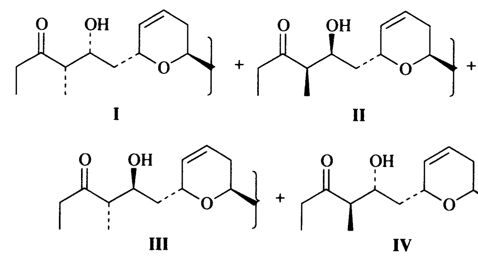
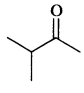
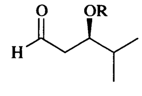
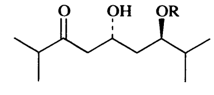
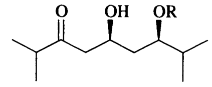
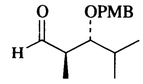
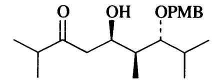
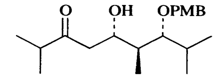
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
	Bu_2BOTf, i-Pr_2NEt		 I + II + III R = CH_2OBn, (—) I:II:III = 57:31:12 R = CH_2OTBS, (—) I:II:III = 50:43:7 R = Ph, (—) I:II:III = 13:83:4 R = C_6H_{11}, (—) I:II:III = 78:13:9	29
	Bu_2BOTf, i-Pr_2NEt	 racemic	 I, II R = Bn, (>62) I:II = 69:31 R = TBS, (>62) I:II = 75:25 R = TBDPS, (26) I:II = 93:7	33
	Bu_2BOTf, i-Pr_2NEt Et_2O		 I + (60) I:II = 79:21  II	36
	9-BBNOTf, i-Pr_2NEt		 (85)	22
			 I + II + III + IV	
	Bu_2BOTf, i-Pr_2NEt		(81) I:II = 84:16	34, 35
	$(C_6H_{11})_2BCl$, Et_3N, Et_2O		(58) III:IV = 56:45	35
	Bu_2BOTf, i-Pr_2NEt		 I + R = PMB, (82) I:II = 42:58 R = TBS, (79) I:II = 52:48  II	37
	9-BBNOTf, i-Pr_2NEt		 I + (91) I:II = 69:31  II	39

TABLE I. ACHIRAL ENOLATES WITH CHIRAL ALDEHYDES (*Continued*)

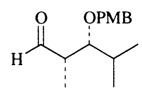
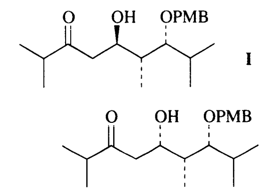
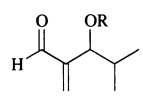
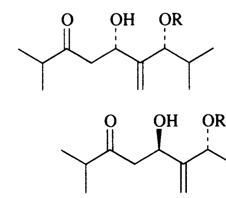
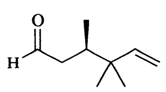
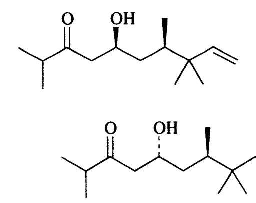
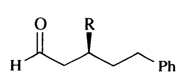
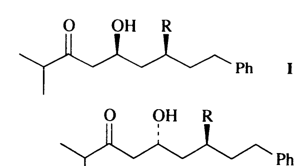
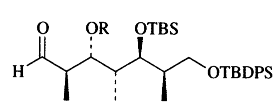
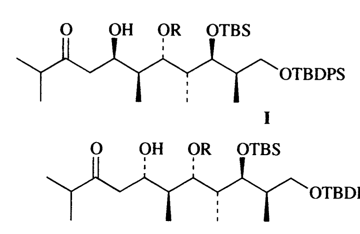
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
	9-BBNOTf, *i*-Pr_2NEt		 I + II (85) I:II = 77:23	39
	$(C_6H_{11})_2BCl$, Et_3N, Et_2O	 racemic	 I + II	
			R = TBS, (89) I:II = 71:29	280
			R = TBDPS, (60) I:II = 89:11	33
	9-BBNOTf, *i*-Pr_2NEt		 I + II (92) I:II = 66:34	37
	9-BBNOTf, *i*-Pr_2NEt		 I + II	37
			R = OPMB, (77) I:II = 56:44	
			R = OTBS, (82) I:II = 48:52	
			R = OAc, (77) I:II = 73:27	
			R = Cl, (68) I:II = 77:23	
			 I + II	20
	9-BBNOTf, Et_3N		R = MOM, (80) I:II = 75:25	
	Bu_2BOTf, Et_3N		R = MOM, (84) I:II = 62:38	
	$(C_5H_9)_2BOTf$, Et_3N		R = MOM, (72) I:II = 52:48	
	9-BBNOTf, Et_3N		R = TMS, (86) I:II = 59:41	
	Bu_2BOTf, Et_3N		R = TMS, (82) I:II = 10:90	
	$(C_5H_9)_2BOTf$, Et_3N		R = TMS, (49) I:II = 20:80	
	9-BBNOTf, Et_3N		R = TES, (92) I:II = 40:60	
	Bu_2BOTf, Et_3N		R = TES, (74) I:II = 5:95	
	$(C_5H_9)_2BOTf$, Et_3N		R = TES, (78) I:II = 14:86	

TABLE I. ACHIRAL ENOLATES WITH CHIRAL ALDEHYDES (*Continued*)

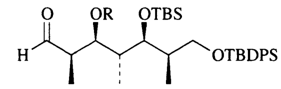
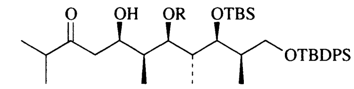
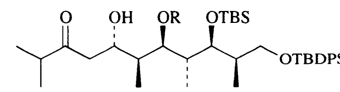
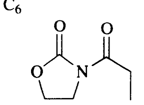
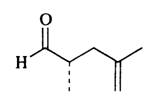
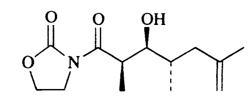
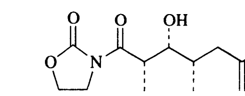
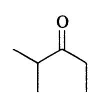
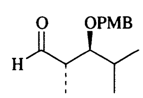
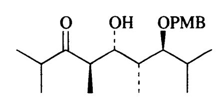
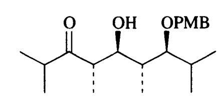
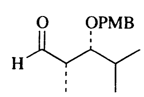
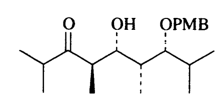
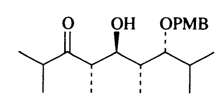
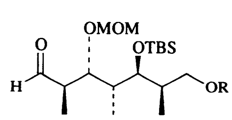
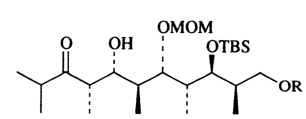
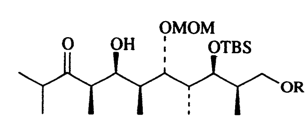
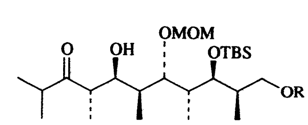
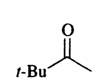
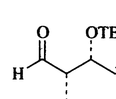
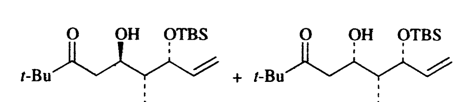
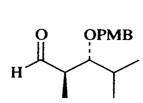
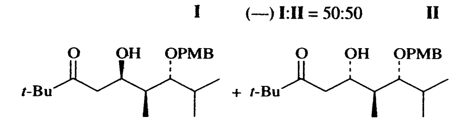
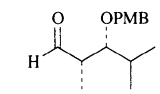
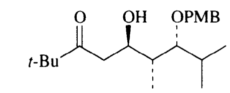
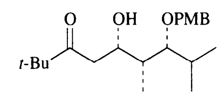
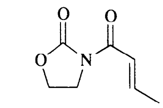
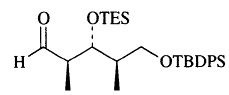
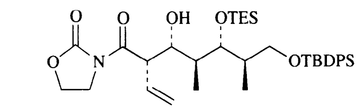
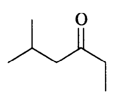
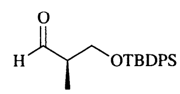
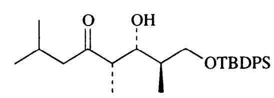
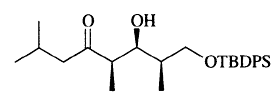
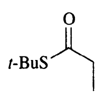
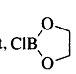
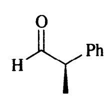
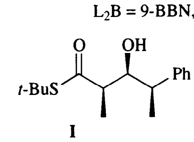
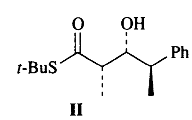
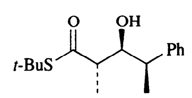
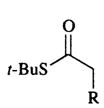
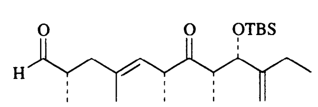
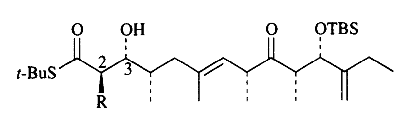
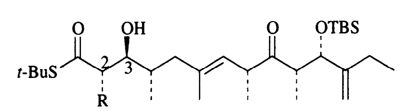
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
	9-BBNOTf, Et_3N Bu_2BOTf, Et_3N $(C_5H_9)_2BOTf$, Et_3N 9-BBNOTf, Et_3N Bu_2BOTf, Et_3N $(C_5H_9)_2BOTf$, Et_3N		 I +  II R = MOM, (82) I:II = 41:59 R = MOM, (69) I:II = 61:39 R = MOM, (86) I:II = 50:50 R = TES, (36) I:II = 50:50 R = TES, (94) I:II = 45:55 R = TES, (77) I:II = 52:48	20
C_6 	Bu_2BOTf, Et_3N		 I + (—) I:II = 64:36  II	27
	$(C_6H_{11})_2BCl$, Et_3N, Et_2O		 I + (84) I:II = 93:7  II	38
	$(C_6H_{11})_2BCl$, Et_3N, Et_2O		 I + (82) I:II = 74:26  II	38
	9-BBNOTf, Et_3N		 I +  II +  III R = TBDPS, (53) I:II:III = 75:15:10	281
	9-BBNOTf[b]		 I (—) I:II = 50:50 II	40
	9-BBNOTf, i-Pr_2NEt		 I (—) I:II = 73:27 II	39

TABLE I. ACHIRAL ENOLATES WITH CHIRAL ALDEHYDES (*Continued*)

Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
	9-BBNOTf, *i*-Pr_2NEt		 I +  II (79) I:II = 80:20	39
C_7 	Bu_2BOTf, Et_3N		 (84) 95:5	23
	L_2BOTf, *i*-Pr_2NEt, Et_2O		 I +  II $L_2B = Bu_2B$, (59) I:II = 70:30; L_2B = 9-BBN, (93) I:II = 55:45	180
	*i*-Pr_2NEt, ClB		 I +  II +  III (68) I:II:III = 90.6:7.5:1.9	231
	$(C_6H_{11})_2BCl$, Et_3N, solvent (see table)		 I +  II	

	Solvent	Yield	Ratio of I:II:2,3-Syn	Refs.
R = Me	CH_2Cl_2	(76)[c]	71:29:—	282
R = Me	Pentane	(77)[c]	45:55:—	26
R = Me	Et_2O	(71)	52:44:4	21
R = Et	Et_2O	(75)	61:37:2	21

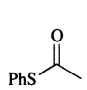
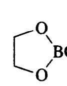
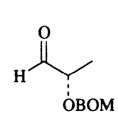
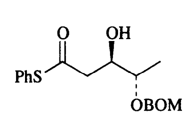
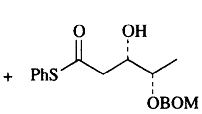
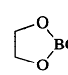
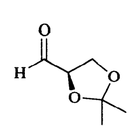
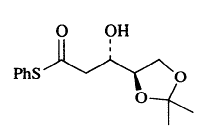
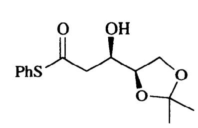
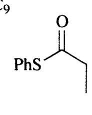
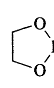
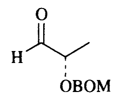
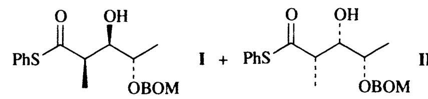
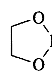
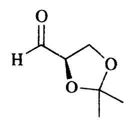
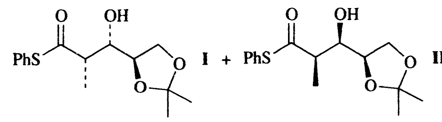
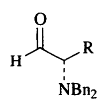
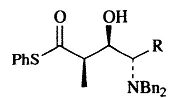
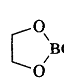
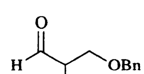
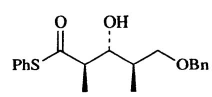
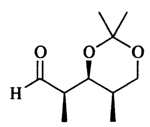
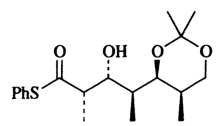
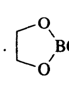
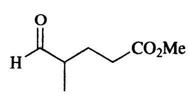
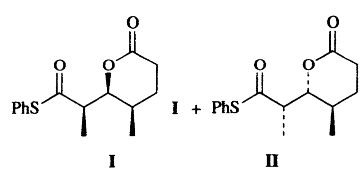
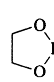
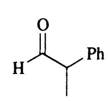
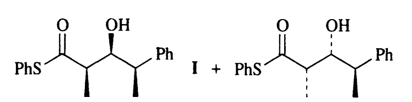
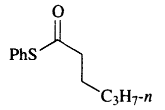
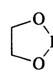
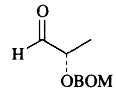
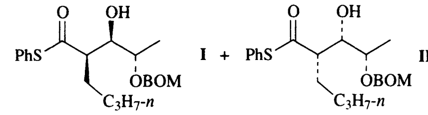
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
C_8 	 BCl, *i*-Pr_2NEt		 I +  II (50-60) I:II = 52:48	31
	 BCl, *i*-Pr_2NEt		 I +  II (50-60) I:II = 80:20	31

TABLE I. ACHIRAL ENOLATES WITH CHIRAL ALDEHYDES (*Continued*)

Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
C_9 	 BCl, i-Pr_2NEt		 (50-60) I:II = 67:33[d]	31
	 BCl, i-Pr_2NEt		 (50-60) I:II = 88:12[d]	31
	9-BBNOTf, i-Pr_2NEt		 R = Me, (—) >97:3; R = Bn, (—) >97:3; R = i-Pr, (—) 76:24; R = i-Bu, (—) 76:24	30[g]
	 BCl, i-Pr_2NEt	 racemic	 (50-60) 55:45[e]	31
	9-BBNOTf, i-Pr_2NEt Et_2O		 (69)	283, 284
	1.  BCl, i-Pr_2NEt 2. CF_3CO_2H	 racemic	 (50-60) I:II = 50:50[d]	31
	 BCl, i-Pr_2NEt	 racemic	 (50-60) I:II = 90:10[d]	31
C_{12} 	 BCl, i-Pr_2NEt		 (50-60) I:II = 70:30[f]	31

[a] The products shown in this equation are not the actual isolated products. Compounds **I** and **IV** cyclized to δ-lactones, while compounds **II** and **III** were transesterified to n-butyl esters.

[b] The amine base used in this reaction was not specified.

[c] The aldehyde used in this reaction was racemic.

[d] The syn:anti ratios ranged from 20:1 to 30:1.

[e] The structure of the minor isomer was not assigned.

[f] The syn:anti ratios were 30:1.

[g] For a related reaction, see reference 401.

TABLE IIA. CHIRAL ENOLATES (AUXILIARY CONTROL) WITH ACHIRAL ALDEHYDES

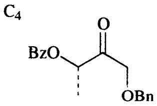
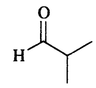
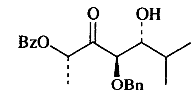
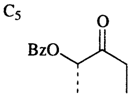
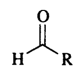
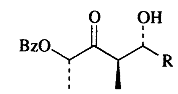
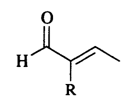
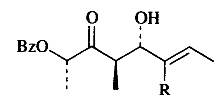
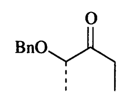
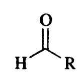
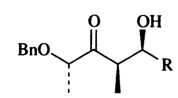
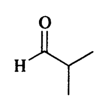
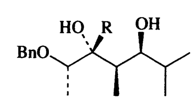
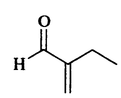
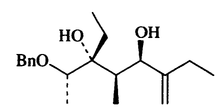
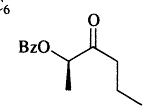
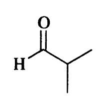
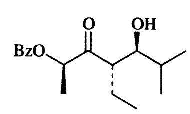
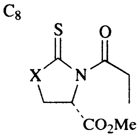
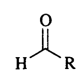
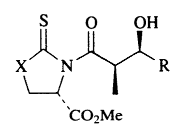
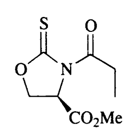
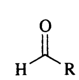
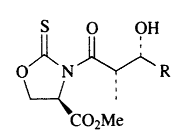
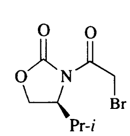
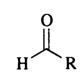
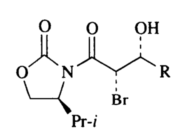
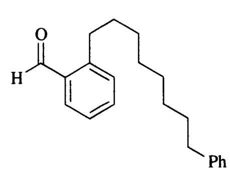
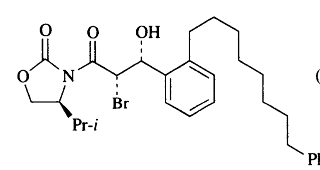
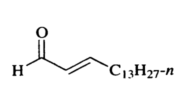
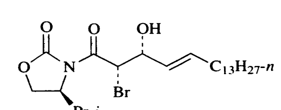
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
C_4 	$(C_6H_{11})_2BCl$, Me_2NEt, Et_2O		 (77) 99:1	110
C_5 	$(C_6H_{11})_2BCl$, Me_2NEt, Et_2O		 R = Et, (93) >99:1	110
			R = C(Me)=CH_2, (97) 98:2	110
			R = *i*-Pr, (95) 97:3	110, 36
			R = Ph, (85) >99:1	110
	$(C_6H_{11})_2BCl$, Me_2NEt, Et_2O		 R = H, (95) 93:7	285
			R = Me, (86) >99:1	118
	$(C_6H_{11})_2BCl$, Et_3N, Et_2O		 R = *i*-Pr, (81) 92:8	110
			R = Pr, (89) 90:10	110
			R = C(Me)=CH_2, (87) 90:10	110
			R = C(Et)=CH_2, (85) 90:10	117
	1. $(C_6H_{11})_2BCl$, Et_3N, Et_2O 2. RMgBr		 R = Me, (80) 90:10	117
			R = CH_2=C(Me), (66) 90:10	
	1. $(C_6H_{11})_2BCl$, Et_3N, Et_2O 2. EtMgBr		 (92) 90:10	117
C_6 	$(C_6H_{11})_2BCl$, Me_2NEt, Et_2O		 (95) 93:7	110
C_8 	Bu_2BOTf, *i*-Pr_2NEt		 X, R: S, *i*-Pr (87); S, Ph (76); O, *i*-Pr (81); O, Ph (89)	76
	Bu_2BOTf, *i*-Pr_2NEt		 R = *i*-Pr, (83)	76, 87-89
			R = Ph, (78)	76
				
	Bu_2BOTf, *i*-Pr_2NEt		R = *i*-Pr, (51), >98:2	59, 60
	Bu_2BOTf, *i*-Pr_2NEt		R = *i*-Bu, (48), >98:2	60
	Bu_2BOTf, *i*-Pr_2NEt		R = *n*-C_5H_{11}, (62) >98:2	60
	Et_2BOTf, *i*-Pr_2NEt		R = Ph, (63) 98:2	286, 287
	Bu_2BOTf, *i*-Pr_2NEt		 (60) 93:7	286, 287
	Bu_2BOTf, Et_3N		 (77) 94:6	288

TABLE IIA. CHIRAL ENOLATES (AUXILIARY CONTROL) WITH ACHIRAL ALDEHYDES (*Continued*)

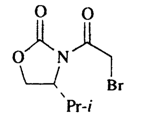
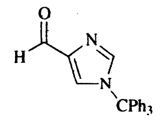
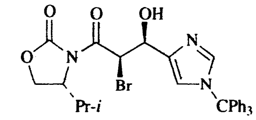
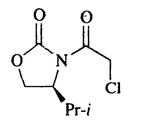
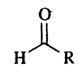
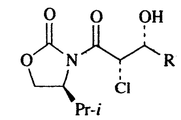
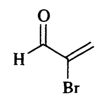
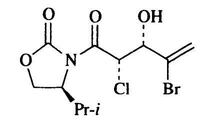
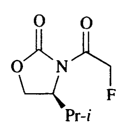
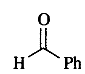
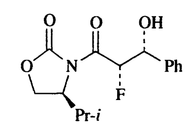
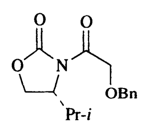
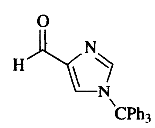
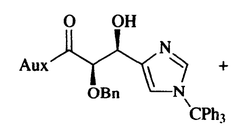
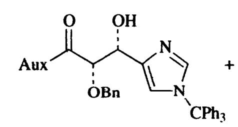
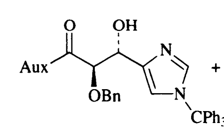
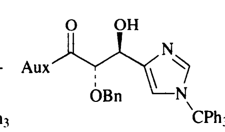
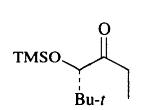
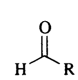
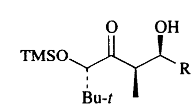
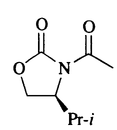
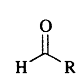
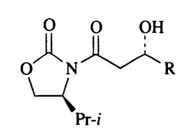
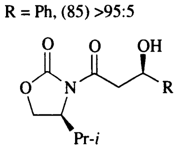
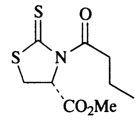
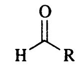
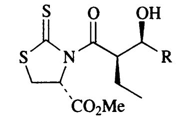
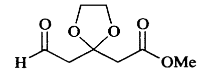
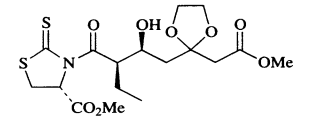
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
	Bu_2BOTf, Et_3N		 (72)	289, 49, 50
				
	Bu_2BOTf, i-Pr_2NEt		R = i-Pr, (52) >98:2	59, 60
	Bu_2BOTf, i-Pr_2NEt		R = i-Bu, (55) >98:2	59, 60
	Bu_2BOTf, i-Pr_2NEt		R = n-C_5H_{11}, (62) >98:2	59, 60
	Et_2BOTf, i-Pr_2NEt		R = Ph, (68) >99:1	286, 287
	Bu_2BOTf, i-Pr_2NEt		 (71)	290, 291
	Bu_2BOTf, i-Pr_2NEt		 (60) 65:35	287
			 I +  II +  III +  IV	
	9-BBNOTf, i-Pr_2NEt		(89) **I**:**II**:**III**:**IV** = 26.4:4.2:67.4:2.0	261
	$(C_5H_9)_2BOTf$, i-Pr_2NEt		(98) **I**:**II**:**III**:**IV** = —:30:—:70	261
	Bu_2BOTf, i-Pr_2NEt		 R = $(CH_2)_2OBn$, (85) >95:5; R = i-Pr, (70) >95:5; R = t-Bu, (80)[a] >95:5; R = Ph, (85) >95:5	109
	Bu_2BOTf, i-Pr_2NEt		 I +  II	
			R = Me, (—) **I**:**II** = 72:28	41
			R = i-Pr, (—) **I**:**II** = 52:48	41, 44
C_9 	Bu_2BOTf, i-Pr_2NEt		 R = i-Pr, (85); R = Ph, (90)	76
	Bu_2BOTf, i-Pr_2NEt		 (77)	86

TABLE IIA. CHIRAL ENOLATES (AUXILIARY CONTROL) WITH ACHIRAL ALDEHYDES (*Continued*)

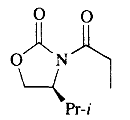
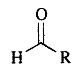
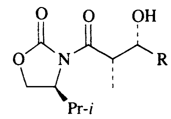
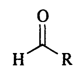
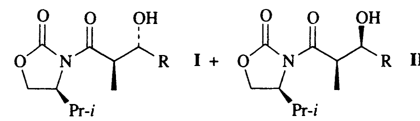
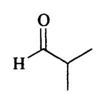
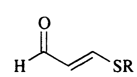
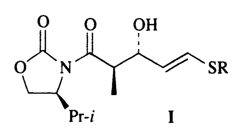
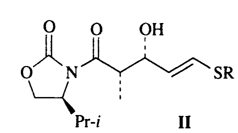
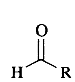
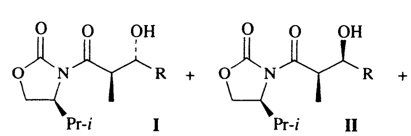
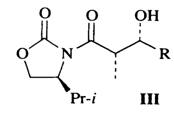
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
				
	Bu_2BOTf, i-Pr_2NEt		R = Me, (—)	143
	Bu_2BOTf, i-Pr_2NEt		R = CH=CH_2, (98) >98:2	102,292, 293
	Bu_2BOTf, i-Pr_2NEt		R = CH_2NHBOC, (83)	50
	Bu_2BOTf, Et_3N		R = Et, (84)	258,294
	Bu_2BOTf, i-Pr_2NEt		R = i-Pr, (78) 99.8:0.2	41,43,295
	Bu_2BOTf, i-Pr_2NEt		R = n-Bu, (75) >99:1	41
	Bu_2BOTf, i-Pr_2NEt		R = Ph, (88) >99.8:0.2	41,44, 71,82
	1. Bu_2BOTf, i-Pr_2NEt 2. Aldehyde, Et_2AlCl		 R = Et, (81) **I**:**II** = 88:12 R = C(Me)=CH_2, (67) **I**:**II** = 90:10 R = i-Bu, (86) **I**:**II** = 86:14 R = t-Bu, (65) **I**:**II** = 95:5 R = Ph, (62) **I**:**II** = 74:26	103
	1. Bu_2BOTf, i-Pr_2NEt 2. Aldehyde, additive		**I** + **II**, R = i-Pr Additive $TiCl_4$ (2 eq), (83) **I**:**II** = 16:84 $SnCl_4$ (0.5 eq), (51) **I**:**II** = 95:5 $SnCl_4$ (2 eq), (60) **I**:**II** = 13:87 Et_2AlCl (2 eq), (63) **I**:**II** = 95:5	103
	Bu_2BOTf (1.9 eq)		 **I**  **II**	102
	i-Pr_2NEt (2.2 eq)		R = t-Bu, (74) **I**:**II** = 25:75	
	i-Pr_2NEt (2.2 eq)		R = Ph, (90) **I**:**II** = 92:8	
	i-Pr_2NEt (2.2 eq)		R = 2-naphthyl, (76) **I**:**II** = 93:7[b]	
	Et_3N (2.4 eq)		R = " , (87) **I**:**II** = <2:98[b]	
	i-Pr_2NEt (2.2 eq)		R = 2,4,6-$(Me)_3C_6H_2$, (85) **I**:**II** = 91:9	
	Et_3N (2.4 eq)		R = " , (83) **I**:**II** = <2:98	
	i-Pr_2NEt (2.2 eq)		R = 2,4,6-$(i\text{-}Pr)_3C_6H_2$, (85) **I**:**II** = 89:11	
	Et_3N (2.4 eq)		R = " , (92) **I**:**II** = <2:98	
	Bu_2BOTf, Et_3N		  **III** R = CF_3, (62) **I**:**II**:**III** = 85:15:— R = $CF_3/TiCl_4$, (83) **I**:**II**:**III** = 46:54:— R = CO_2Et, (50) **I**:**II**:**III** = 44:35:20 R = COPh, (55) **I**:**II**:**III** = 54:42:4 R = $CF_2(CH_2)_3Ph$, (33) **I**:**II**:**III** = 82:12:6	107

TABLE IIA. CHIRAL ENOLATES (AUXILIARY CONTROL) WITH ACHIRAL ALDEHYDES (*Continued*)

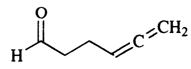
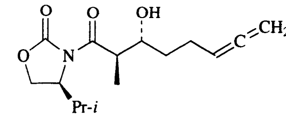
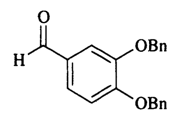
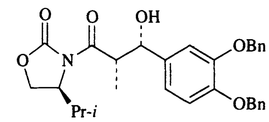
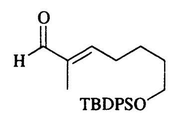
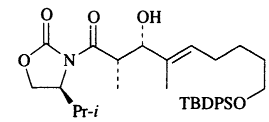
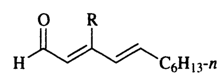
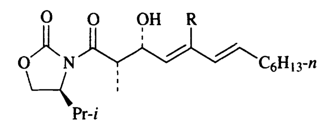
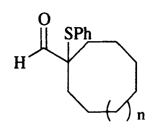
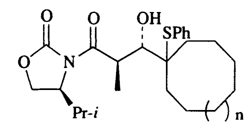
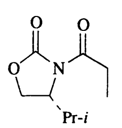
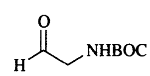
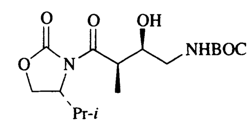
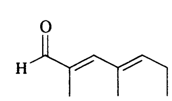
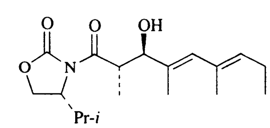
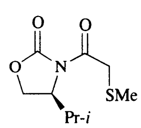
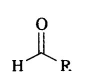
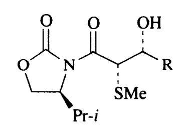
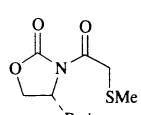
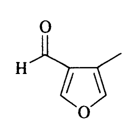
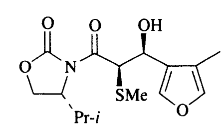
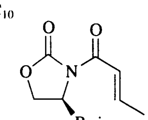
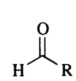
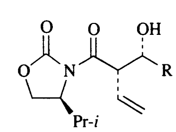
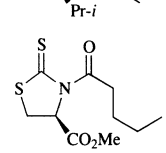
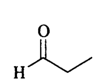
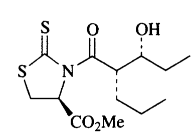
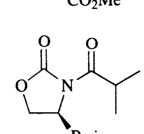
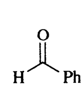
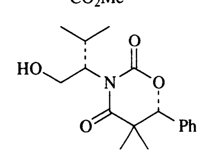
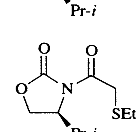
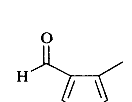
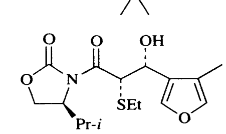
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
	1. Bu_2BOTf, i-Pr_2NEt 2. Aldehyde, Et_2AlCl		 (85) 75:25	65
	Bu_2BOTf, i-Pr_2NEt		 (90) >95:5	296
	Bu_2BOTf, i-Pr_2NEt		 (69)	297
	Bu_2BOTf, Et_3N		 R = H, (84) >97:3; R = Me, (74) >97:3	298
	1. Bu_2BOTf, i-Pr_2NEt 2. Aldehyde, Et_2AlCl		 n = 1, (63) 51:49; n = 4, (69) 84:16	299, 300
	Bu_2BOTf, i-Pr_2NEt		 (65)	50
	1. Bu_2BOTf, i-Pr_2NEt 2. Aldehyde, Et_2AlCl		 (89) 83:17	47
	Bu_2BOTf, i-Pr_2NEt		 R = Me, (—) 99.6:0.4; R = Pr, (—) 98.9:1.1; R = i-Pr, (—) 98.4:1.6; R = Ph, (—) 92.4:7.6	41; 41; 41, 44; 41
	Bu_2BOTf, Et_3N		 (80)	301, 302
C_{10} 	Bu_2BOTf, Et_3N		 R = Me, (82) >98:2; R = Et, (94) >98:2; R = i-Pr, (90) >98:2; R = Ph, (92) >98:2	51
	Bu_2BOTf, i-Pr_2NEt		 (81)	303
	Bu_2BOTf, i-Pr_2NEt		 (23) 96:4	106
	Bu_2BOTf, Et_3N		 (72)	302

TABLE IIA. CHIRAL ENOLATES (AUXILIARY CONTROL) WITH ACHIRAL ALDEHYDES (*Continued*)

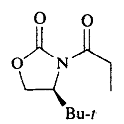
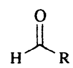
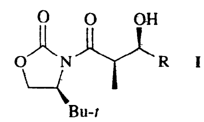
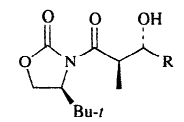
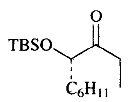
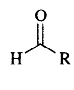
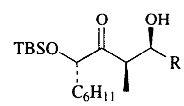
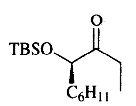
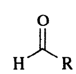
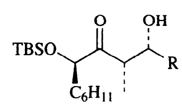
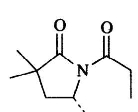
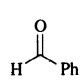
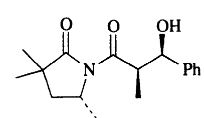
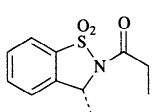
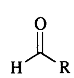
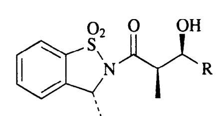
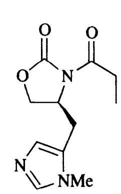
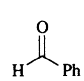
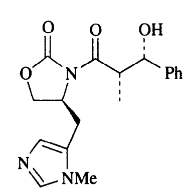
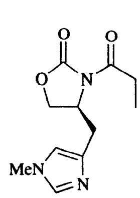
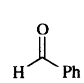
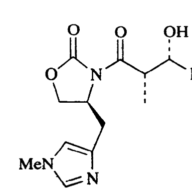
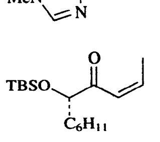
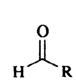
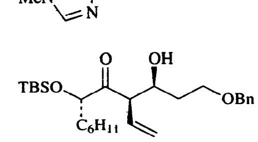
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
	1. Bu_2BOTf, i-Pr_2NEt 2. Aldehyde, $TiCl_4$ (2 eq)		 I +  II R = Et, (72) I:II = 88:12 R = i-Pr, (70) I:II = 94:6 R = C(Me)=CH_2, (65) I:II = 87:13 R = i-Bu, (68) I:II = 87:13 R = t-Bu, (50) I:II = 89:11 R = Ph, (65) I:II = 92:8	103
	i-Pr_2NEt			
	$(C_5H_9)_2BOTf$		R = H, (90) >99:1	112
	$(C_5H_9)_2BOTf$		R = Et, (70-85) >99:1	108
	$(C_5H_9)_2BOTf$		R = $(CH_2)_2OBn$, (70-85) >99:1	108, 114
	9-BBNOTf		R = $(CH_2)_2OBn$, (—) 94:6	304
	Bu_2BOTf		R = $(CH_2)_2OBn$, (—) 94:6	304
	Bu_2BOTf		R = C(Me)=CH_2, (85) >96:4	115
	Bu_2BOTf		R = i-Pr, (70-85) >99:1	108
	9-BBNOTf		R = i-Pr, (—) >99:1	304
	$(C_5H_9)_2BOTf$		R = Ph, (70-85) >98:2	108
	$(C_5H_9)_2BOTf$, i-Pr_2NEt		 R = H, (90) >99:1 R = Et, (85) 99:1	112 116
	Bu_2BOTf, i-Pr_2NEt		 (84) >97:3	77
C_{11} 	Et_2BOTf, i-Pr_2NEt		 R = Me, (71) >99:1 R = Et, (85) R = i-Pr, (95) >99:1 R = i-Bu, (78) >99:1 R = Ph, (84) >99:1	97 98 97 97 97
	Bu_2BOTf[c]		 (80)	85
	Bu_2BOTf[c]		 (86)	85
	$(C_5H_9)_2BOTf$, i-Pr_2NEt		 R = Me, (70) 93:7 R = Et, (78) 93:7 R = i-Pr, (21) >98:2 R = Ph, (82) 93:7	275

TABLE IIA. CHIRAL ENOLATES (AUXILIARY CONTROL) WITH ACHIRAL ALDEHYDES (*Continued*)

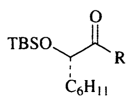
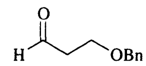
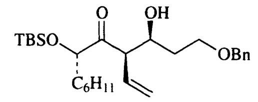
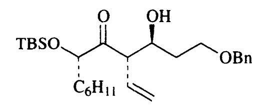
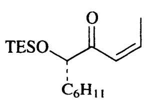
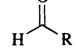
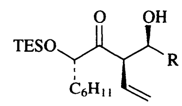
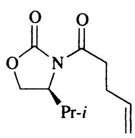
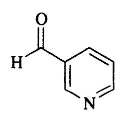
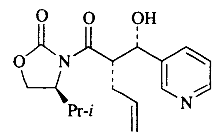
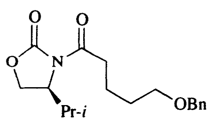
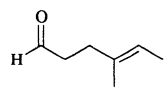
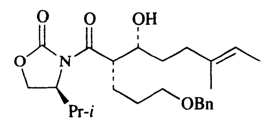
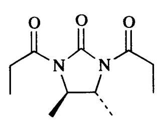
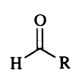
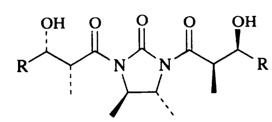
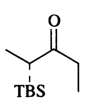
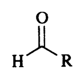
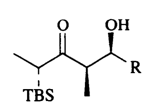
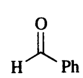
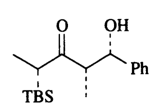
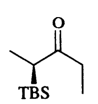
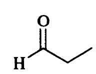
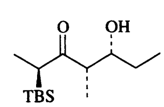
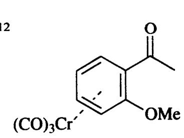
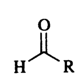
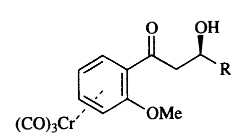
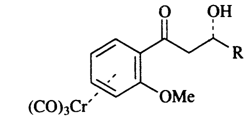
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
			 I +  II	275
	R = (*E*)-CH=CHMe, $(C_5H_9)_2BOTf$, *i*-Pr_2NEt		(89) **I**:**II** = 22:78	
	R = " , Bu_2BOTf, *i*-Pr_2NEt		(70) **I**:**II** = 38:62	
	R = " , 9-BBNOTf, *i*-Pr_2NEt		(96) **I**:**II** = 33:67	
	R = (*Z*)-CH=CHMe, $(C_5H_9)_2BOTf$, *i*-Pr_2NEt		(80) **I**:**II** = 91:9	
	R = " , Bu_2BOTf, *i*-Pr_2NEt		(47) **I**:**II** = 80:20	
	R = " , 9-BBNOTf, *i*-Pr_2NEt		(89) **I**:**II** = 75:25	
	R = $CH_2CH=CH_2$, $(C_5H_9)_2BOTf$, *i*-Pr_2NEt		(71) **I**:**II** = 95:5	
	$(C_5H_9)_2BOTf$, *i*-Pr_2NEt		 R = Me, (85) >99:1 R = $(CH_2)_2OBn$, (93) >99:1 R = Et, (81) >99:1 R = *i*-Pr, (77) >99:1 R = Ph, (83) >99:1	275
	Bu_2BOTf, *i*-Pr_2NEt		 (68)	270
	Bu_2BOTf, Et_3N		 (68) 97:3	53
	Bu_2BOTf, *N*-ethylpiperidine		 R = Me, (54) R = Et, (24) R = Ph, (51)	305
	Bu_2BOTf, *i*-Pr_2NEt		 R = Me, (>55) ~90:10 R = Et, (>62) ~90:10 R = *i*-Pr, (>62) ~90:10 R = $(CH_2)_2Ph$, (>55) ~90:10	111
	Bu_2BOTf, *i*-Pr_2NEt		 (>68) ~90:10	111
	Bu_2BOTf, *i*-Pr_2NEt		 (>58) ~90:10	111
C_{12} 	Bu_2BOTf, *i*-Pr_2NEt, Et_2O		 I +  II R = Et, (80) **I**:**II** = 90:10[d] R = (*E*)-CH=CH(Me), (77) **I**:**II** = 88:12 R = *i*-Pr, (81) **I**:**II** = 95:5[d] R = Ph, (75) **I**:**II** = 92:8[d] R = (*E*)-CH=CH(Ph), (78) **I**:**II** = 89:11[d]	306

TABLE IIA. CHIRAL ENOLATES (AUXILIARY CONTROL) WITH ACHIRAL ALDEHYDES (*Continued*)

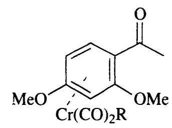
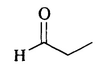
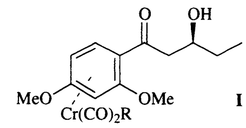
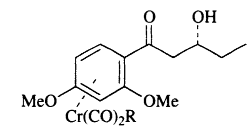
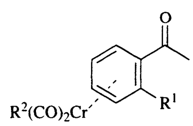
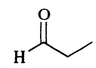
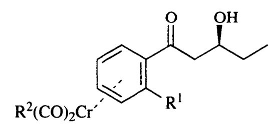
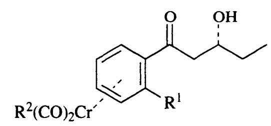
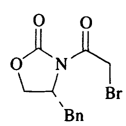
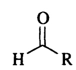
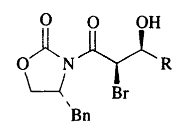
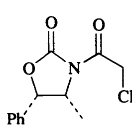
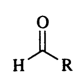
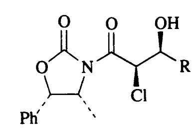
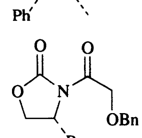
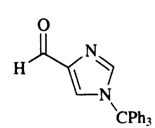
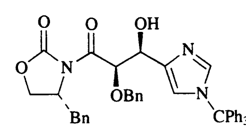
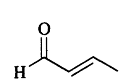
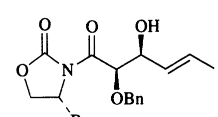
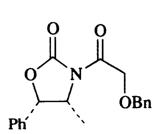
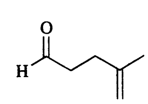
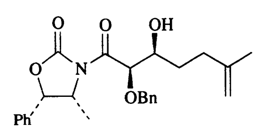
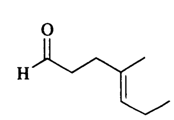
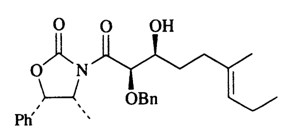
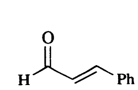
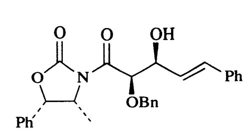
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
 racemic	Bu_2BOTf, i-Pr_2NEt, Et_2O		 I +  II R = CO, (85) I:II = 90:10 R = PPh_3, (30) I:II = 50:50 R = $P(OPh)_3$, (80) I:II = 50:50 R = $P(OMe)_3$, (55) I:II = 80:20	306
 racemic	Bu_2BOTf, i-Pr_2NEt, Et_2O		 I +  II R^1 = OMe, R^2 = CO, (80) I:II = 90:10 R^1 = OPr-i, R^2 = CO, (75) I:II = 85:15 R^1 = Me, R^2 = CO, (45) I:II (or II:I) = 40:60 R^1 = OMe, R^2 = PPh_3, (50) I:II = 88:12 R^1 = OPr-i, R^2 = PPh_3, (30) I:II = 70:30 R^1 = Me, R^2 = PPh_3, (40) I:II = 50:50 R^1 = OMe, R^2 = $P(OPh)_3$, (85) I:II = 88:12 R^1 = OMe, R^2 = $P(OMe)_3$, (60) I:II = 86:14	306
	Bu_2BOTf, Et_3N		 R = C(Me)=CH_2, (50) 97:3 R = i-Pr, (63) 98:2	307 58
	Bu_2BOTf, Et_3N, Et_2O		 R = Me, (67) 95:5 R = i-Pr, (75) 96:4 R = Ph, (79) 97:3	58
	$(C_5H_9)_2BOTf$, i-Pr_2NEt		 (97) 94:6	261
	Bu_2BOTf, Et_3N		 (92)	308, 260
	Bu_2BOTf, Et_3N		 (78) >98:2	68
	Bu_2BOTf, Et_3N		 (84)	309
	Bu_2BOTf, Et_3N		 (96)	310

TABLE IIA. CHIRAL ENOLATES (AUXILIARY CONTROL) WITH ACHIRAL ALDEHYDES (*Continued*)

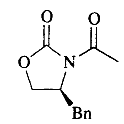
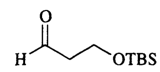
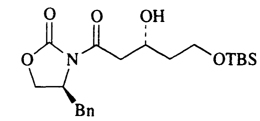
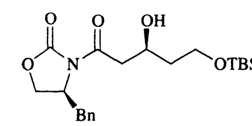
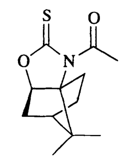
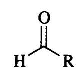
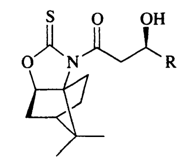
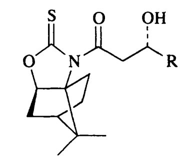
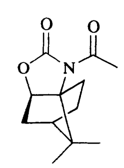
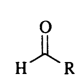
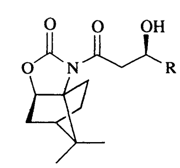
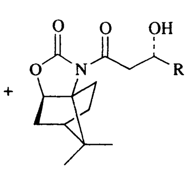
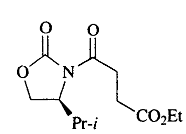
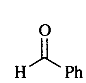
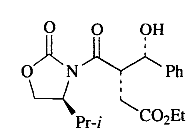
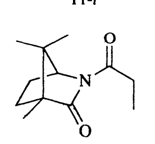
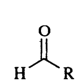
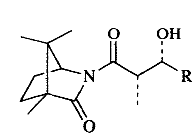
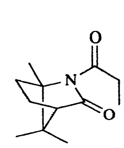
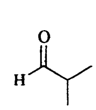
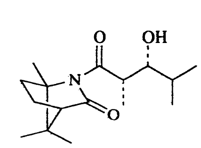
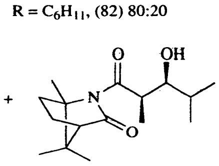
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
	Bu_2BOTf, Et_3N		 I +  II (61) I:II = 62:38	311
			 I +  II	
	9-BBNOTf, *i*-Pr_2NEt		R = Pr, (88) I:II = 87:13	93, 94
	Bu_2BOTf, *i*-Pr_2NEt		R = Pr, (83) I:II = 75:25	93, 94
	9-BBNOTf, *i*-Pr_2NEt		R = *i*-Pr, (84) I:II = 86:14	93, 94
	Bu_2BOTf, *i*-Pr_2NEt		R = *i*-Pr, (69) I:II = 76:24	93, 94
	9-BBNOTf, *i*-Pr_2NEt		R = Ph, (86) I:II = 96:4	93, 94
	Bu_2BOTf, *i*-Pr_2NEt		R = Ph, (74) I:II = 75:25	93, 94
	9-BBNOTf, *i*-Pr_2NEt		R = (*E*)-CH=CHMe, (84) I:II = >99:1	93, 94
	Bu_2BOTf, *i*-Pr_2NEt		R = (*E*)-CH=CHMe, (69) I:II = 92:8	93, 94
	9-BBNOTf, *i*-Pr_2NEt		R = (*E*)-CH=CHEt, (65) I:II = >99:1	93
	9-BBNOTf, *i*-Pr_2NEt		R = (*E*)-CH=CHPr, (63) I:II = >99:1	93
	9-BBNOTf, *i*-Pr_2NEt		R = (*E*)-CH=CHTMS, (59) I:II = 93:7	93
	9-BBNOTf, *i*-Pr_2NEt		R = (*E*)-CH=CHPh, (61) I:II = 95:5	93
	9-BBNOTf, *i*-Pr_2NEt		R = (*E*)-CH=CHSPh, (78) I:II = 97:3	93
			 I +  II	94
	9-BBNOTf, *i*-Pr_2NEt		R = (*E*)-CH=CHMe, (58) I:II = 67:33	
	Bu_2BOTf, *i*-Pr_2NEt		R = (*E*)-CH=CHMe, (62) I:II = 35:65	
	9-BBNOTf, *i*-Pr_2NEt		R = Pr, (61) I:II = 71:29	
	Bu_2BOTf, *i*-Pr_2NEt		R = Pr, (71) I:II = 27:73	
	9-BBNOTf, *i*-Pr_2NEt		R = *i*-Pr, (67) I:II = 60:40	
	Bu_2BOTf, *i*-Pr_2NEt		R = *i*-Pr, (61) I:II = 30:70	
	9-BBNOTf, *i*-Pr_2NEt		R = Ph, (60) I:II = 64:36	
	Bu_2BOTf, *i*-Pr_2NEt		R = Ph, (82) I:II = 44:56	
	Bu_2BOTf, *i*-Pr_2NEt		 (69)	41
	Et_2BOTf, *i*-Pr_2NEt		 R = (*E*)-CH=CHMe, (69) 91:9 R = Pr, (62) 80:20 R = *i*-Pr, (87) 92:8 R = *t*-Bu, (43) 86:14 R = Ph, (83) 92:8 R = C_6H_{11}, (82) 80:20	312
	Et_2BOTf, *i*-Pr_2NEt		 I +  II (35) I:II = 69:31	312

TABLE IIA. CHIRAL ENOLATES (AUXILIARY CONTROL) WITH ACHIRAL ALDEHYDES (*Continued*)

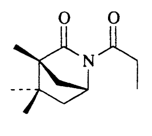
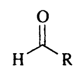
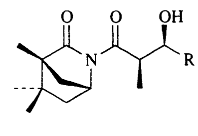
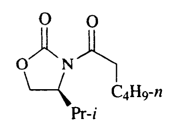
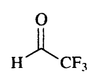
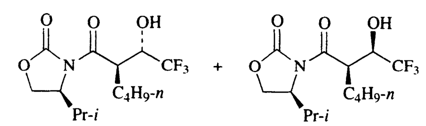
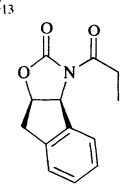
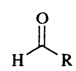
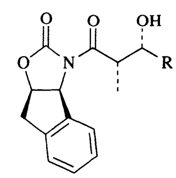
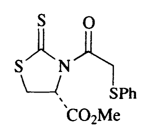
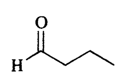
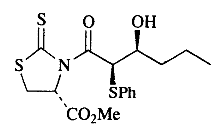
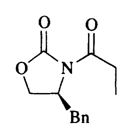
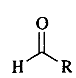
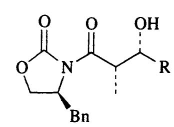
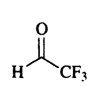
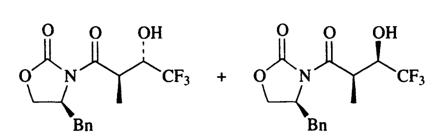
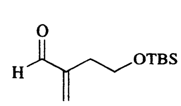
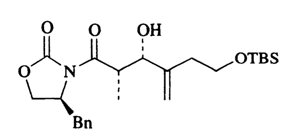
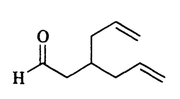
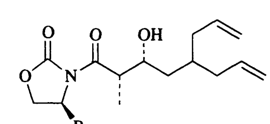
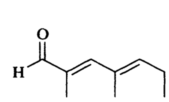
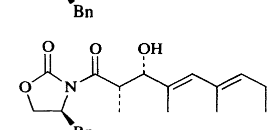
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
	Et_2BOTf, i-Pr_2NEt		 R = (*E*)-CH=CHMe, (76) >98:2 R = Pr, (64) >98:2 R = *i*-Pr, (68) >98:2 R = *t*-Bu, (36) >98:2 R = Ph, (95) >98:2 R = C_6H_{11}, (67) >98:2	79
	Bu_2BOTf, i-Pr_2NEt		 I (60) I:II = 81:19 II	107
C_{13} 	Bu_2BOTf, Et_3N		 R = Me, (71) >99:1 R = *i*-Pr, (73) >99:1 R = Ph, (64) >99:1 R = (*E*)-CH=CHPh, (62) >99:1	80
	Bu_2BOTf, i-Pr_2NEt		 (87)	76
				
	Bu_2BOTf, Et_3N		R = CH_2OBn, (74) 98:2	313
	Bu_2BOTf, Et_3N		R = Me, (85)	314, 315
	Bu_2BOTf, i-Pr_2NEt		R = $CH{=}CH_2$, (83)	239
	Bu_2BOTf, i-Pr_2NEt		R = Et, (91)	316, 317
	Bu_2BOTf, Et_3N		R = *i*-Pr, (83) >99:1	220
	Bu_2BOTf, Et_3N		R = $(CH_2)_3OTBS$, (70) >99:1	318
	Bu_2BOTf, Et_3N		R = $(CH_2)_2CH{=}CH_2$, (90)	319
	9-BBNOTf, i-Pr_2NEt		R = $(CH_2)_4OBn$, (84) 97:3	320
	Bu_2BOTf, Et_3N		R = Ph, (93) >97:3	321
	Bu_2BOTf, Et_3N		R = (*E*)-CH=CHPh, (93)	309
	Bu_2BOTf, Et_3N		 I (80) I:II = 78:22 II	107
	Bu_2BOTf, i-Pr_2NEt		 (77) 88:12	322
	Bu_2BOTf, Et_3N		 (>72)	323
	Bu_2BOTf, i-Pr_2NEt		 (93)	47

TABLE IIA. CHIRAL ENOLATES (AUXILIARY CONTROL) WITH ACHIRAL ALDEHYDES (*Continued*)

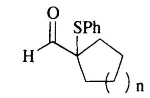
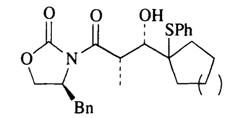
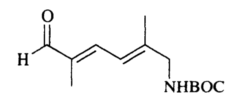
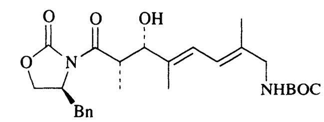
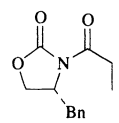
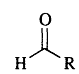
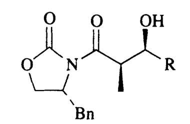
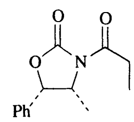
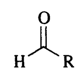
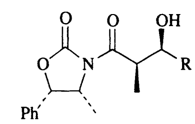
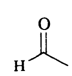
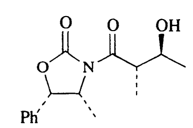
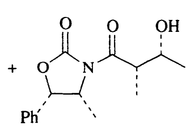
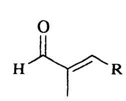
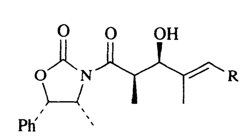
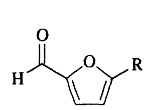
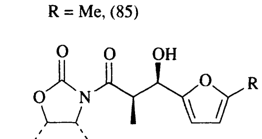
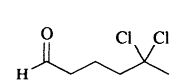
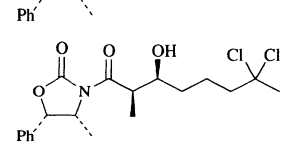
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
	Bu_2BOTf, *i*-Pr_2NEt		 n = 1, (88) >95:5; n = 2, (76) >90:10	324, 300
	Bu_2BOTf, Et_3N		 (93) 88:12	298
	Bu_2BOTf, Et_3N		 R = Et, (80) 98.5:1.5	269, 325
			R = (*E*)-CH=CHMe, (99) >99:1	274, 222
			R = *i*-Pr, (80)	326, 327
				
	Bu_2BOTf, Et_3N		R = Me, (93) >98:2	328, 53
	Bu_2BOTf, Et_3N		R = CH_2OBn, (83) >99:1	61
	Bu_2BOTf, *i*-Pr_2NEt		R = Et, (>80)	329
	Bu_2BOTf, *i*-Pr_2NEt		R = $CH=CH_2$, (80)	292, 330
	Bu_2BOTf, Et_3N		R = $(CH_2)_2OBn$, (85)	331
	Bu_2BOTf, Et_3N		R = $(CH_2)_2OPMB$, (87)	61, 332
	Bu_2BOTf, *i*-Pr_2NEt		R = $(CH_2)_2OBz$, (—)	35
	Bu_2BOTf, *i*-Pr_2NEt		R = *i*-Pr, (91) >99.8:0.2	41,333,334
	Bu_2BOTf, *i*-Pr_2NEt		R = Bu, (95) >99.8:0.2	41
	Bu_2BOTf, Et_3N		R = (*E*)-CH=CHEt, (92)	61
	Bu_2BOTf, Et_3N		R = *n*-C_5H_{11}, (71) 98:2	335
	Bu_2BOTf, *i*-Pr_2NEt		R = Ph, (89) >99.8:0.2	41, 48
	Bu_2BOTf, Et_3N		R = (*E*)-CH=CHPh, (70) >95:5	185, 186
			 I +  II	104
	1. Bu_2BOTf (1.1 eq), *i*-Pr_2NEt 2. MeCHO, Et_2AlCl		(84) I:II = 71:29	
	1. Bu_2BOTf (2.0 eq), *i*-Pr_2NEt 2. MeCHO		(90) I:II = 88:12	
				
	Bu_2BOTf, *i*-Pr_2NEt		R = H, (80)	336
	9-BBNOTf, *i*-Pr_2NEt		R = I, (65)	184, 181
	Bu_2BOTf, Et_3N		R = Me, (85)	337, 338
	Bu_2BOTf, Et_3N		 R = H, (92) >99:1	45, 46
			R = Et, (81)	339, 258
	Bu_2BOTf, Et_3N		 (92)	335

TABLE IIA. CHIRAL ENOLATES (AUXILIARY CONTROL) WITH ACHIRAL ALDEHYDES (*Continued*)

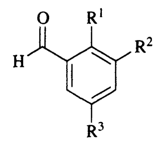
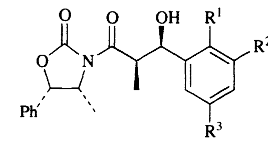
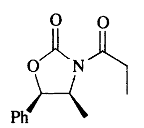
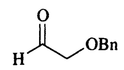
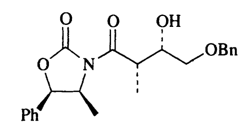
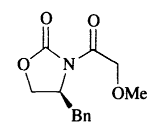
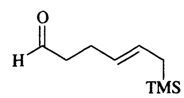
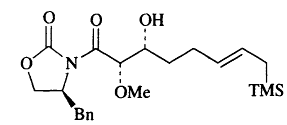
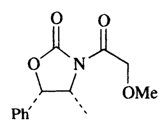
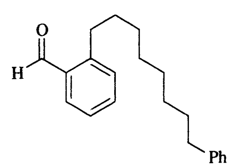
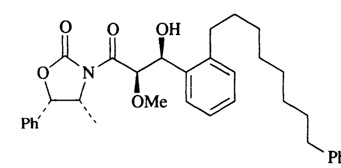
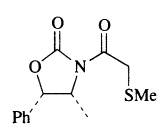
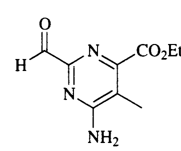
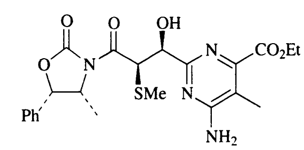
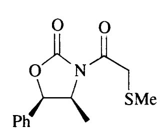
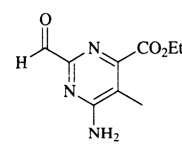
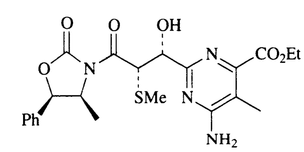
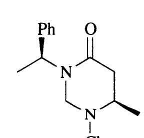
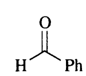
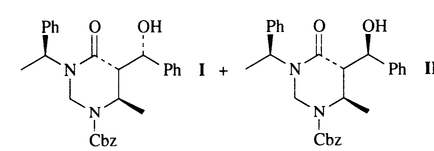
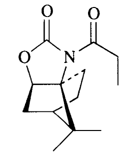
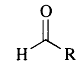
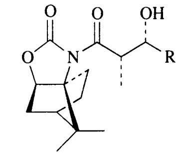
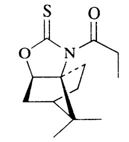
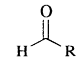
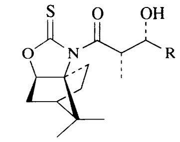
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
				
	Bu_2BOTf, i-Pr_2NEt		$R^2 = NO_2$, $R^1 = R^3 = H$, (82) >98:2	182
	Bu_2BOTf, Et_3N		$R^1 = OMe$, $R^2 = R^3 = H$, (83) >98:2	182
	Bu_2BOTf, Et_3N		$R^1 = OMe$, $R^2 = NO_2$, $R^3 = H$, (88) >98:2	182
	Bu_2BOTf, i-Pr_2NEt		$R^1 = R^2 = OMe$, $R^3 = H$, (80) >98:2	182
	Bu_2BOTf, i-Pr_2NEt		$R^1 = R^3 = OMe$, $R^2 = H$, (64) >98:2	182
	Et_2BOTf, Et_3N		$R^1 = R^3 = OMe$, $R^2 = NO_2$, (88) >98:2	182-184
	Bu_2BOTf, Et_3N		$R^1 = R^3 = OMe$, $R^2 = NO_2$, (80) >97:3	185,186
	Bu_2BOTf, Et_3N		 (79)	331
	Bu_2BOTf, Et_3N		 (89) >96:4	192
	Bu_2BOTf, i-Pr_2NEt		 (99) >96:4	340
	Bu_2BOTf, i-Pr_2NEt		 (67) >95:5	341
	Bu_2BOTf, i-Pr_2NEt		 (59) >95:5	341
	1. LiHMDS 2. $(RO)_2BCl$ 3. Aldehyde		 R = Me, (80) **I**:**II** = 80:20 R = i-Pr, (80) **I**:**II** = 80:20 R = n-Bu, (80) **I**:**II** = 80:20	342
	Bu_2BOTf, i-Pr_2NEt		 R = Pr, (69) >99:1 R = i-Pr, (68) >99:1 R = (E)-CH=CHMe, (73) >99:1 R = Ph, (72) >99:1	84, 83
	Bu_2BOTf, i-Pr_2NEt		 R = Pr, (78) >99:1 R = i-Pr, (79) >99:1 R = (E)-CH=CHMe, (81) >99:1 R = Ph, (86) >99:1	84

TABLE IIA. CHIRAL ENOLATES (AUXILIARY CONTROL) WITH ACHIRAL ALDEHYDES (*Continued*)

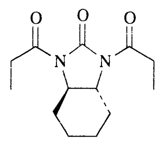
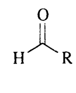
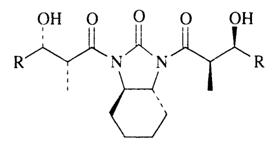
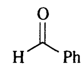
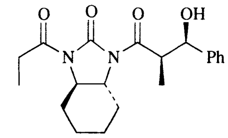
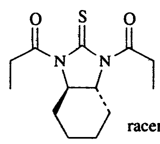
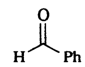
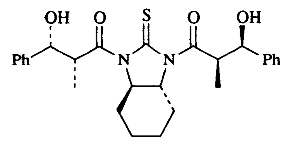
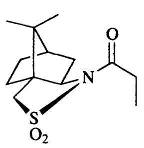
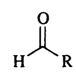
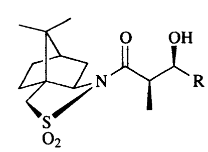
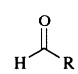
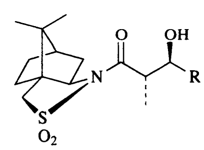
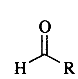
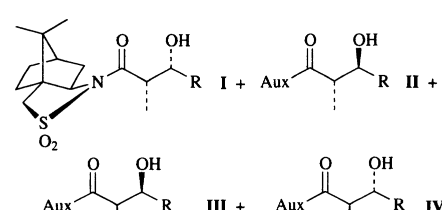
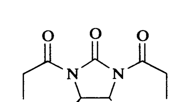
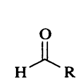
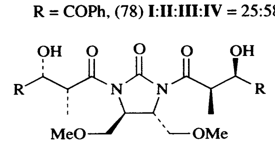
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
	Bu_2BOTf, *N*-ethylpiperidine		 R = Me, (67) >96:4[d]	82, 81
			R = Et, (78) >96:4[d]	82, 81
			R = Pr, (71) >96:4[d]	82, 81
			R = *i*-Pr, (82) >96:4[d]	82, 81
			R = *t*-Bu, (66)[d]	82
			R = Ph, (69) >96:4	82, 81
	Bu_2BOTf, *N*-ethylpiperidine		 (61)[e]	82
 racemic	Bu_2BOTf, *N*-ethylpiperidine		 (59)	82
				
	Bu_2BOTf, *i*-Pr_2NEt		R = Me, (78) >99:1	95, 96
	Et_2BOTf, *i*-Pr_2NEt		R = Et, (83) 98:2	95, 96
	Et_2BOTf, *i*-Pr_2NEt		R = *i*-Pr, (82) 97:3	95, 96
	Bu_2BOTf, *i*-Pr_2NEt		R = (*E*)-CH=CHMe, (59) >98:2	95
	Bu_2BOTf, *i*-Pr_2NEt		R = Ph, (80) 99:1	95, 96
	Bu_2BOTf, *i*-Pr_2NEt		R = *p*-$MeOC_6H_4$, (48) 97.5:2.5	95
	1. Et_2BOTf, *i*-Pr_2NEt 2. Aldehyde, $TiCl_4$		 R = Me, (76) 96:4	343
			R = Et, (79) 98:2	
			R = *i*-Pr, (75) 99:1	
			R = (*E*)-CH=CHMe, (64) 94:6	
			R = C(Me)=CH_2, (61) 98:2	
			R = *i*-Bu, (76) 98:2	
			R = *t*-Bu, (76) 98:2	
			R = 2-furyl, (53) 94:6	
			R = Ph, (80) 99:1	
			R = C_6H_{11}, (75) 98:2	
			R = *p*-$O_2NC_6H_4$, (72) 96:4	
			R = *p*-$MeOC_6H_4$, (70) 89:11	
				100
	Et_2BOTf, *i*-Pr_2NEt		R = CF_3, (96) **I**:**II**:**III**:**IV** = 19:7:73:1	
	1. Et_2BOTf, *i*-Pr_2NEt 2. Aldehyde, $TiCl_4$		R = CF_3, (89) **I**:**II**:**III**:**IV** = 1:99:—:—	
	Et_2BOTf, *i*-Pr_2NEt		R = CO_2Et, (66) **I**:**II**:**III**:**IV** = 49:30:21:—	
	Et_2BOTf, *i*-Pr_2NEt		R = $CF_2(CH_2)_3Ph$, (86) **I**:**II**:**III**:**IV** = 49:30:21:—	
	Et_2BOTf, *i*-Pr_2NEt		R = COPh, (78) **I**:**II**:**III**:**IV** = 25:58:17:—	
	Bu_2BOTf, *N*-ethylpiperidine		 R = Me, (35)	305
			R = Et, (53)	
			R = *t*-Bu, (59)	
			R = Ph, (90)	

TABLE IIA. CHIRAL ENOLATES (AUXILIARY CONTROL) WITH ACHIRAL ALDEHYDES (*Continued*)

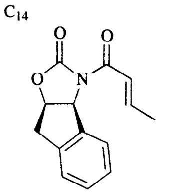
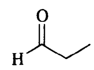
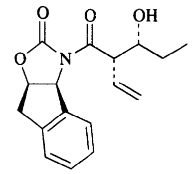
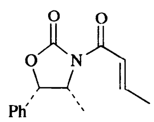
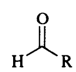
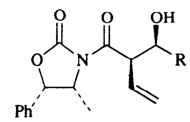
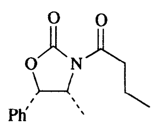
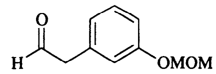
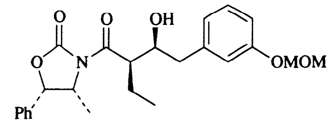
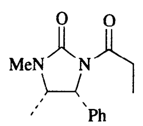
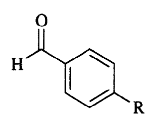
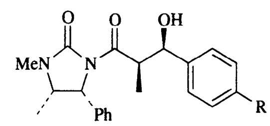
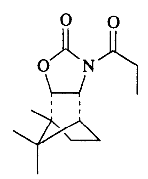
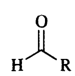
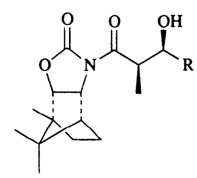
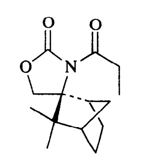
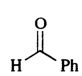
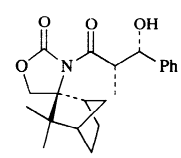
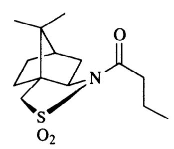
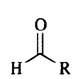
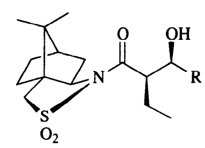
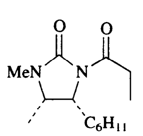
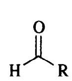
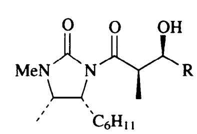
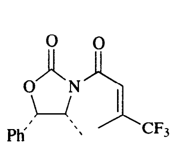
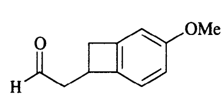
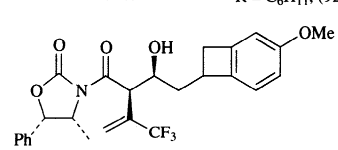
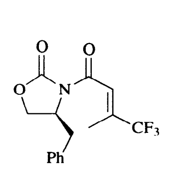
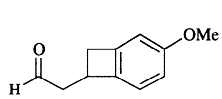
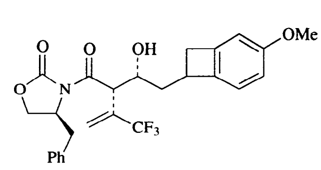
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
C_{14}				
	Bu_2BOTf, Et_3N		 (51) >99:1	80
	Bu_2BOTf, Et_3N		 R = Et, (93) >98:2 R = *i*-Pr, (93) >98:2 R = Ph, (88) >98:2	51
	Bu_2BOTf, *i*-Pr_2NEt		 (83)	263
	Bu_2BOTf, Et_3N		 R = H, (88) 98:2 R = OMe, (92) 96:4 R = NO_2, (85) 96:4	344, 345[f]
	1. Bu_2BOTf, *i*-Pr_2NEt 2. Aldehyde, THF		 R = *i*-Pr, (86) >99:1 R = Ph, (52) >99:1	346
	Bu_2BOTf, *i*-Pr_2NEt		 (—) 95:5	78
				95, 96
	Et_2BOTf, *i*-Pr_2NEt		R = Me, (87) 96:4	
	Bu_2BOTf, *i*-Pr_2NEt		R = *i*-Pr, (80) 99:1	
	Bu_2BOTf, *i*-Pr_2NEt		R = Ph, (70) 97.5:2.5	
	Bu_2BOTf, Et_3N		 R = Me, (80) 96:4 R = *i*-Pr, (82) >99:1 R = Ph, (75) 98:2 R = C_6H_{11}, (92) >99:1	347, 345
C_{15}				
	Bu_2BOTf, Et_3N		 (65)	348
	Bu_2BOTf, Et_3N		 (77)	348

TABLE IIA. CHIRAL ENOLATES (AUXILIARY CONTROL) WITH ACHIRAL ALDEHYDES (*Continued*)

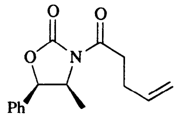
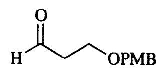
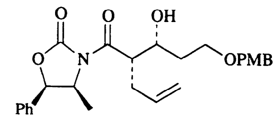
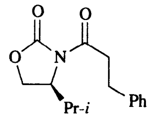
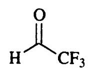
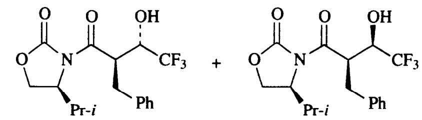
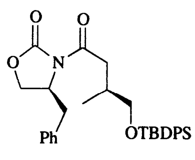
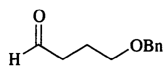
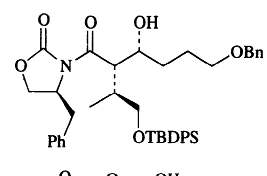
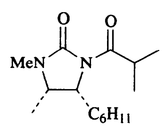
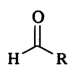
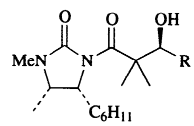
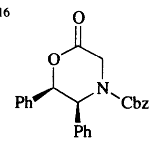
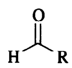
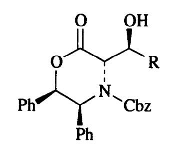
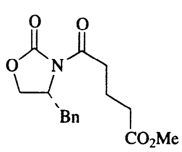
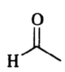
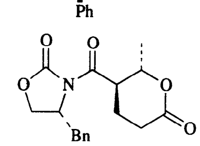
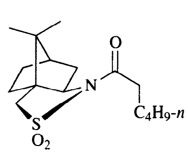
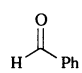
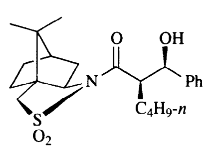
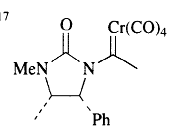
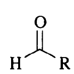
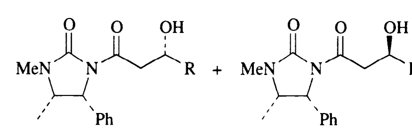
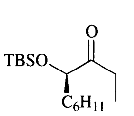
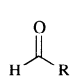
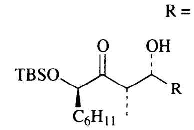
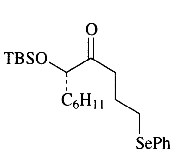
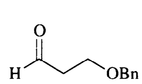
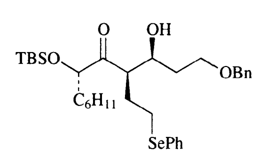
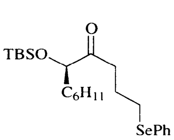
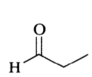
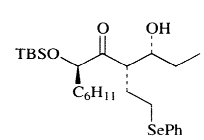
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
	$(C_5H_9)_2BOTf$, i-Pr_2NEt		 (95)	190
	Bu_2BOTf, Et_3N		 I (64) I:II = 70:30 II	107
	Bu_2BOTf, Et_3N		 (88)	259
	Bu_2BOTf, Et_3N		 R = Ph, (80) >99:1 R = C_6H_{11}, (40) >99:1	345
C_{16} 	Bu_2BOTf, i-Pr_2NEt		 R = Me, (70) 81:19 R = Pr, (46) 83:17 R = i-Pr, (50) 83:17	349
	1. Bu_2BOTf, Et_3N 2. Aldehyde 3. PPTS		 (79)	319
	Bu_2BOTf, i-Pr_2NEt		 (64) >98:2	95
C_{17} 	1. BuLi 2. Bu_2BOTf 3. Aldehyde 4. AcOH, $(NH_4)_2Ce(NO_2)_6$		 I II R = Pr, (76) I:II = 86:14 R = i-Pr, (55) I:II = 75:25 R = Ph, (76) I:II = 86:14	91
	$(C_5H_9)_2BOTf$, i-Pr_2NEt		 R = H, (90) >99:1 R = Et, (85) 99:1	112 116
	$(C_5H_9)_2BOTf$, i-Pr_2NEt		 (—)	350
	$(C_5H_9)_2BOTf$, i-Pr_2NEt		 (97) >99:1	350

TABLE IIA. CHIRAL ENOLATES (AUXILIARY CONTROL) WITH ACHIRAL ALDEHYDES (*Continued*)

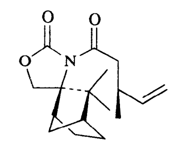
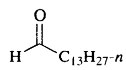
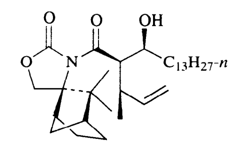
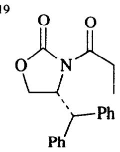
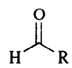
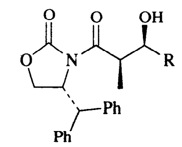
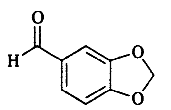
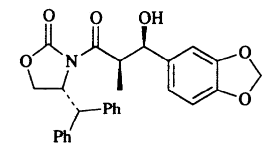
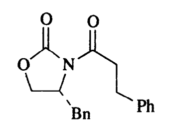
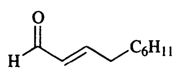
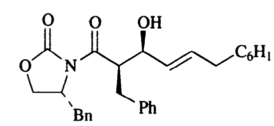
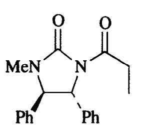
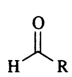
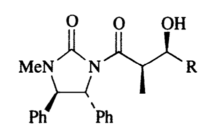
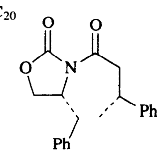
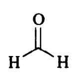
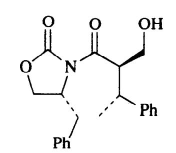
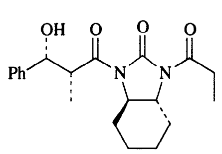
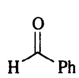
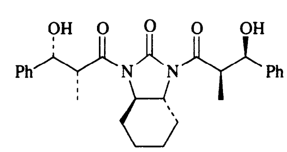
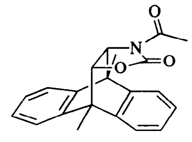
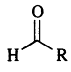
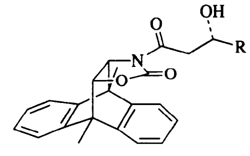
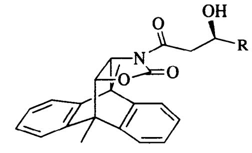
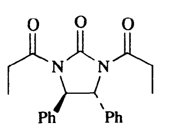
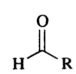
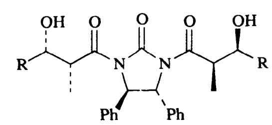
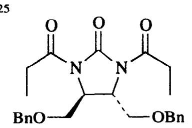
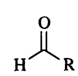
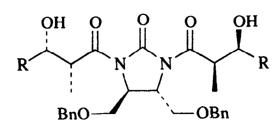
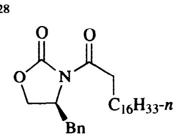
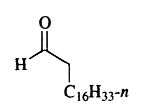
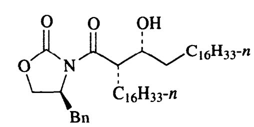
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
	Bu_2BOTf, i-Pr_2NEt		 (82)	351
C_{19} 	Bu_2BOTf, i-Pr_2NEt		 R = n-C_5H_{11}, (84) >98:2 R = Ph, (83) >99:1	352
	Bu_2BOTf, i-Pr_2NEt		 (82) >98:2	352
	Bu_2BOTf, i-Pr_2NEt		 (84) >90:10	353
	Bu_2BOTf, i-Pr_2NEt		 R = Me, (48) >99:1 R = CH=CH$_2$, (23) >99:1 R = Et, (38) >99:1 R = Ph, (66) >99:1 R = 2-naphthyl, (72) >99:1	354
C_{20} 	Bu_2BOTf, i-Pr_2NEt		 (75)	355
	Bu_2BOTf, N-ethylpiperidine		 (72)	82
C_{21} 			 I +  II	92
	Bu_2BOTf, i-Pr_2NEt		R = i-Pr, (93) I:II = 90:10	
	1. Bu_2BOTf, i-Pr_2NEt 2. Aldehyde, $TiCl_4$		R = i-Pr, (56) I:II = 93:7	
	Bu_2BOTf, i-Pr_2NEt		R = Ph, (93) I:II = 86:14	
	1. Bu_2BOTf, i-Pr_2NEt 2. Aldehyde, $TiCl_4$		R = Ph, (69) I:II = 23:77	

TABLE IIA. CHIRAL ENOLATES (AUXILIARY CONTROL) WITH ACHIRAL ALDEHYDES (*Continued*)

Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio		Refs.
	Bu_2BOTf, *N*-ethylpiperidine			R = Me, (74) >96:4[d] R = *i*-Pr, (67) >96:4[d] R = Ph, (72) >96:4	71, 82
C_{25} 	Bu_2BOTf, *N*-ethylpiperidine			R = Me, (35) R = Et, (66) R = Ph, (71)	305
C_{28} 	9-BBNOTf, *i*-Pr_2NEt			(82)	356

[a] Concomitant loss of the trimethylsilyl group occurred upon workup.

[b] This reaction was repeated several times varying the amounts of Bu_2BOTf and base and also in solvents other than CH_2Cl_2.

[c] No base was required in this reaction.

[d] This reaction was performed on racemic enolate precursor.

[e] "Mono" adducts of this bifunctional reagent were also obtained with other aldehydes.

[f] Reactions of this auxiliary with five nonaromatic aldehydes were also performed, but selectivity was poor.

TABLE IIB. CHIRAL ENOLATES (AUXILIARY CONTROL) WITH CHIRAL ALDEHYDES

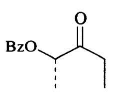
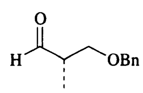
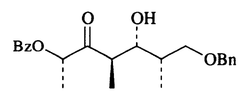
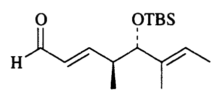
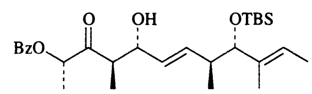
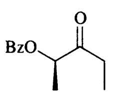
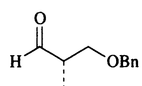
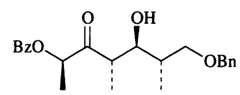
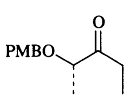
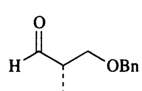
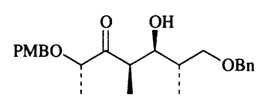
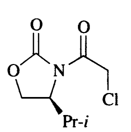
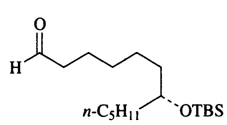
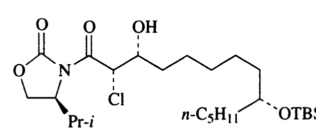
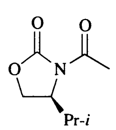
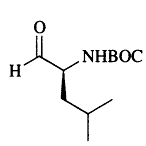
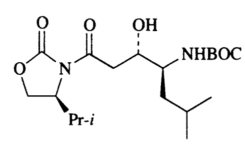
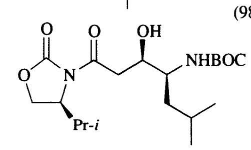
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
C_5 	$(C_6H_{11})_2BCl$, Me_2NEt, Et_2O		 (80) >97:3	110
	$(C_6H_{11})_2BCl$, Me_2NEt, Et_2O		 (95) >99:1	118
	$(C_6H_{11})_2BCl$, Me_2NEt, Et_2O		 (61) 95:5	110
	$(C_6H_{11})_2BCl$, Et_3N, Et_2O		 (86) 94:6	276
C_8 	Bu_2BOTf, Et_3N		 (87)	357
	Bu_2BOTf, i-Pr_2NEt		 **I** +  **II** (98) **I**:**II** = 78:22	92

TABLE IIB. CHIRAL ENOLATES (AUXILIARY CONTROL) WITH CHIRAL ALDEHYDES (*Continued*)

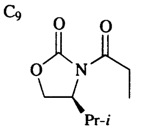
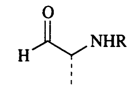
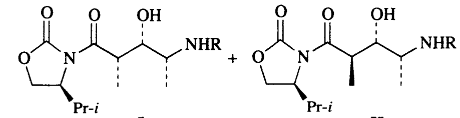
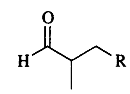
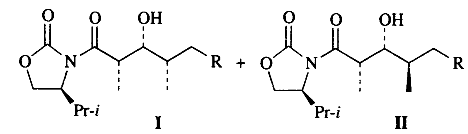
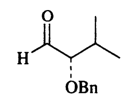
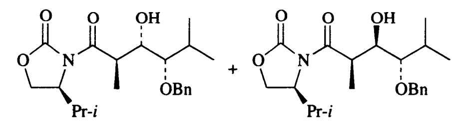
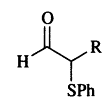
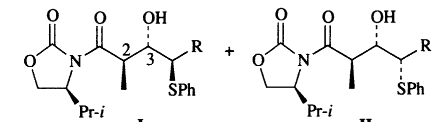
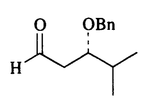
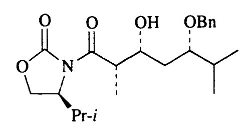
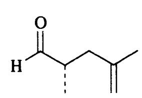
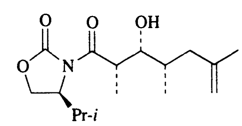
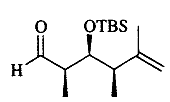
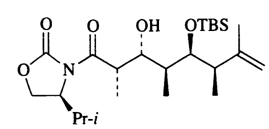
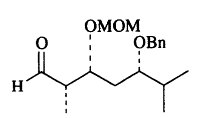
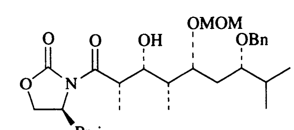
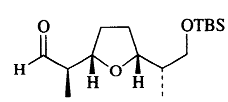
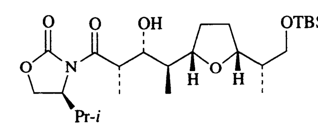
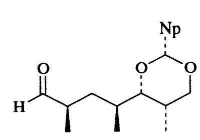
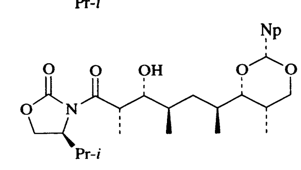
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
C_9 			 I + II	
	Bu_2BOTf (1.0 eq), Et_3N (1.1 eq)		R = BOC, (100) I:II = 100:0	48-50
	Bu_2BOTf (1.5 eq), Et_3N (1.4 eq)		R = BOC, (25) I:II = 38:62	48
	Bu_2BOTf (1.0 eq), Et_3N (1.1 eq)		R = Cbz, (53) I:II = 100:0	48
	Bu_2BOTf (1.5 eq), Et_3N (1.4 eq)		R = Cbz, (36) I:II = 18:82	48
		 racemic	 I + II	
	Bu_2BOTf, i-Pr_2NEt		R = SPh, (70) I:II = 50:50	63
	Bu_2BOTf, i-Pr_2NEt		R = OBn, (85) I:II = 54:46	62
	Bu_2BOTf, i-Pr_2NEt		 I + II (—) I:II = 67:33[a]	358
	1. Bu_2BOTf, i-Pr_2NEt 2. Aldehyde, Et_2AlCl	 racemic	 I + II R = Et, (79) I:II = 75:25 R = Pr, (81) I:II:2,3-syn = 85:14:<1 R = i-Pr, (—) I:II:2,3-syn = 89:7:4	64
	Bu_2BOTf, Et_3N		 (95)	74, 75
	Bu_2BOTf, i-Pr_2NEt		 (—) 99.8:0.2	27
	Bu_2BOTf, i-Pr_2NEt		 (68)	295
	Bu_2BOTf, Et_3N		 (95)	74, 75
	Bu_2BOTf, i-Pr_2NEt		 (75)	65
	Bu_2BOTf, Et_3N		 (85) >98:2	359, 360

TABLE IIB. CHIRAL ENOLATES (AUXILIARY CONTROL) WITH CHIRAL ALDEHYDES (*Continued*)

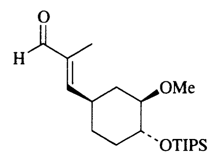
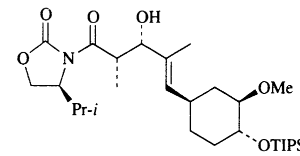
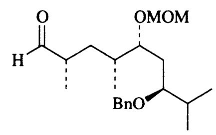
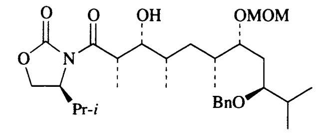
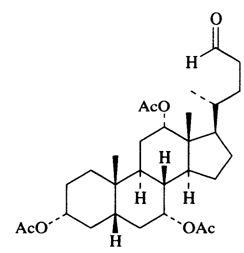
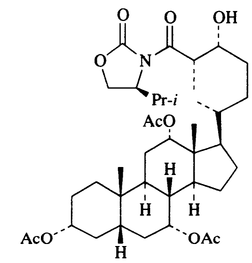
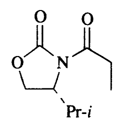
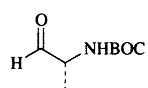
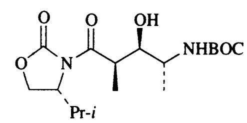
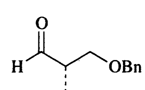
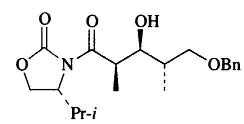
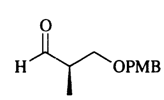
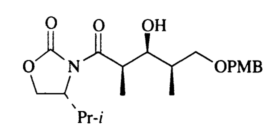
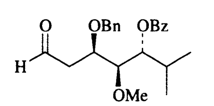
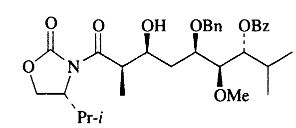
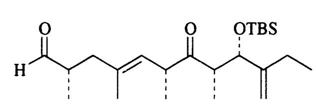
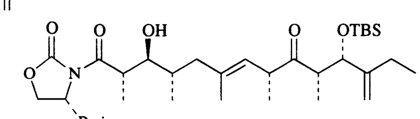
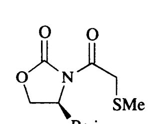
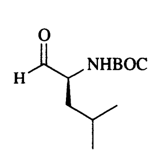
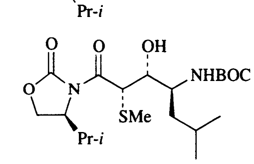
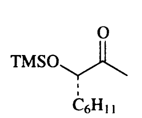
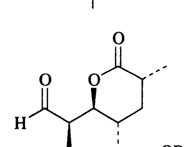
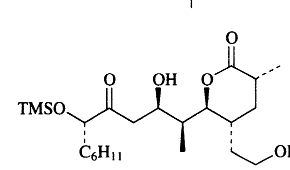
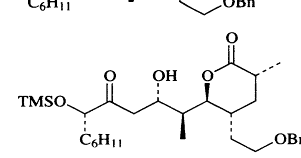
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
	Bu_2BOTf, i-Pr_2NEt		 (>88) >99:1	187
	Bu_2BOTf, i-Pr_2NEt		 (88)	74, 75
	Bu_2BOTf, i-Pr_2NEt		 (83)	361
	Bu_2BOTf, i-Pr_2NEt		 (79)	50
	Bu_2BOTf, i-Pr_2NEt		 (78) >97:3	201, 202
	Bu_2BOTf, Et_3N		 (94) 89:11	362
	Bu_2BOTf, Et_3N		 (90)	362
	1. Bu_2BOTf, i-Pr_2NEt 2. Aldehyde, Et_2AlCl		 (40)	21
	Bu_2BOTf, i-Pr_2NEt		 (—)	363
	9-BBNOTf, i-Pr_2NEt		 **I** + (88) **I**:**II** = 80:20  **II**	113

TABLE IIB. CHIRAL ENOLATES (AUXILIARY CONTROL) WITH CHIRAL ALDEHYDES (*Continued*)

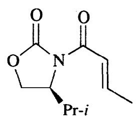
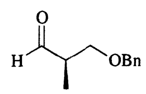
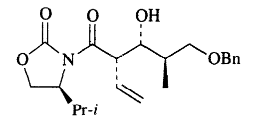
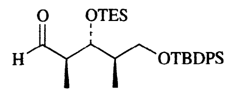
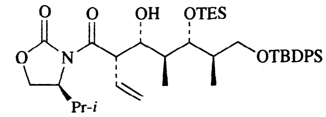
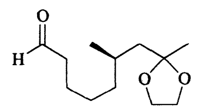
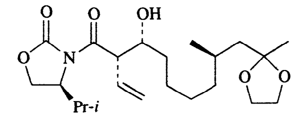
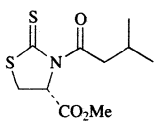
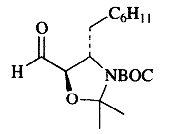
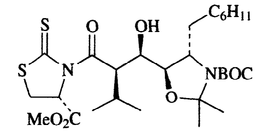
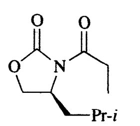
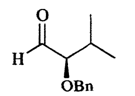
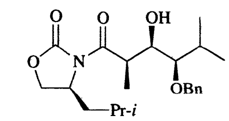
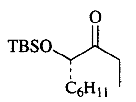
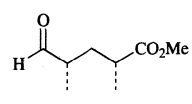
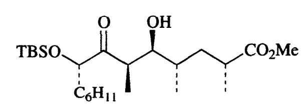
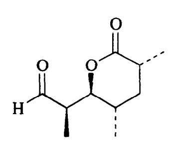
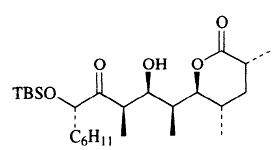
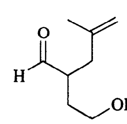
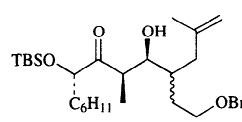
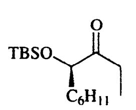
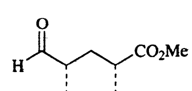
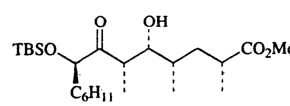
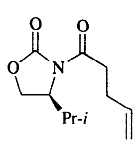
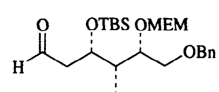
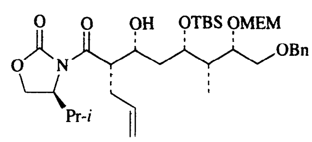
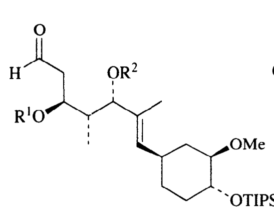
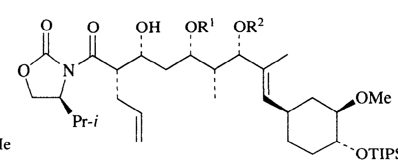
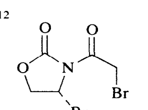
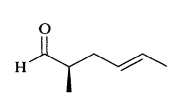
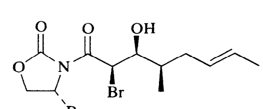
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
C_{10} 	Bu_2BOTf, Et_3N		 (58)	51
	Bu_2BOTf, Et_3N		 (84-90)	23
	Bu_2BOTf, Et_3N		 (66) 94:6	54
	Bu_2BOTf, i-Pr_2NEt		 (73)	364
	Bu_2BOTf, i-Pr_2NEt		 (89) 94:6[a]	358, 365
	$(C_5H_9)_2BOTf$, i-Pr_2NEt		 (85) 97.5:2.5	116, 304
	$(C_5H_9)_2BOTf$, i-Pr_2NEt		 (71) 93:7	116
	Bu_2BOTf, i-Pr_2NEt	 racemic	 (80)	113
	$(C_5H_9)_2BOTf$, i-Pr_2NEt		 (—) 94:6	116, 304
C_{11} 	Bu_2BOTf, i-Pr_2NEt		 (75)	189
	Bu_2BOTf, i-Pr_2NEt		 R^1 = TIPS, R^2 = TES, (95) R^1–R^2 = PMP, (>90)	187 191
C_{12} 	Bu_2BOTf, Et_3N		 (63) 94:6	58

TABLE IIB. CHIRAL ENOLATES (AUXILIARY CONTROL) WITH CHIRAL ALDEHYDES (*Continued*)

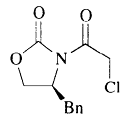
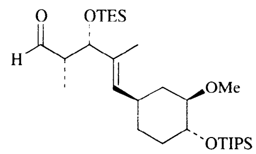
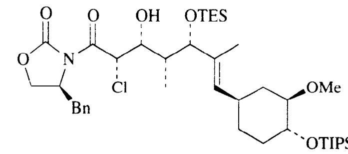
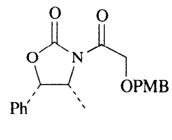
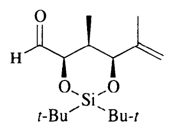
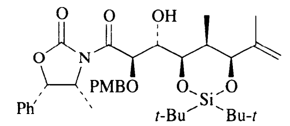
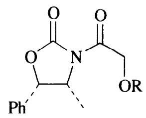
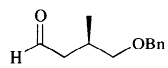
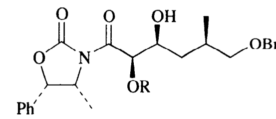
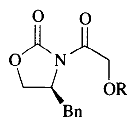
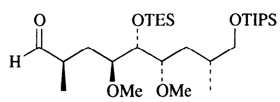
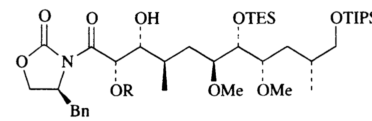
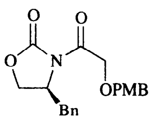
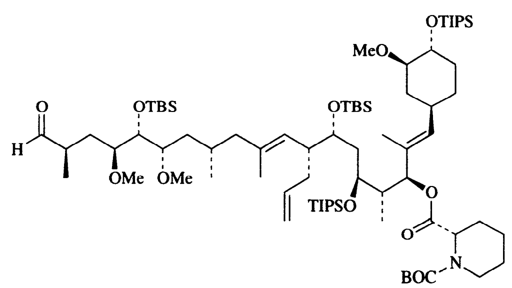
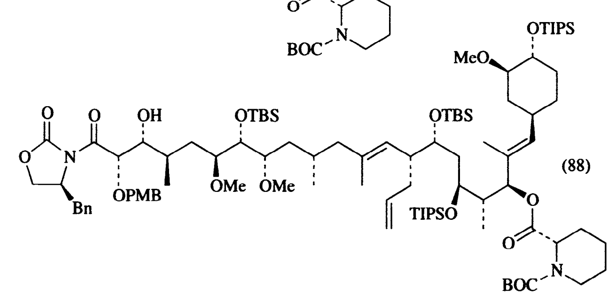
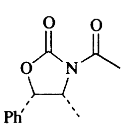
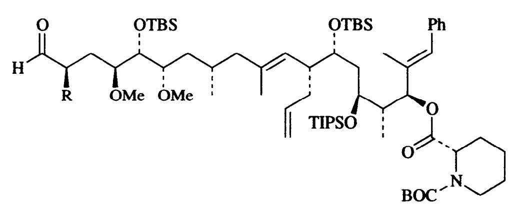
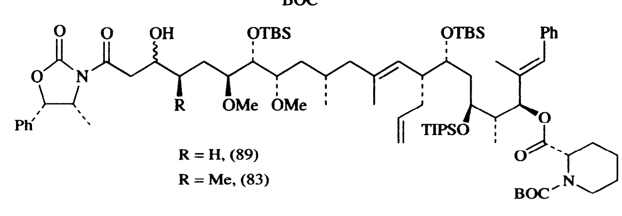
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
	Bu_2BOTf, Et_3N		 (92)	57
	Bu_2BOTf, Et_3N		 (78)[a]	61
	Bu_2BOTf, Et_3N		 R = Bn, (75) R = PMB, (84)	194 57
	Bu_2BOTf, Et_3N		 R = PMB, (90) R = TCE, (>50)	57 57
	Bu_2BOTf, Et_3N, toluene		 (88)	57, 188
	Bu_2BOTf, Et_3N		 R = H, (89) R = Me, (83)	194

TABLE IIB. CHIRAL ENOLATES (AUXILIARY CONTROL) WITH CHIRAL ALDEHYDES (*Continued*)

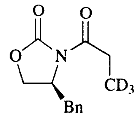
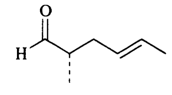
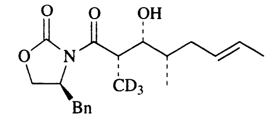
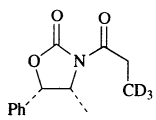
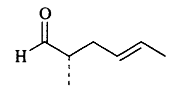
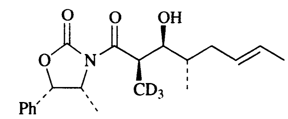
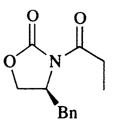
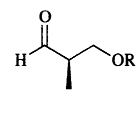
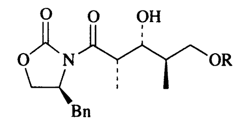
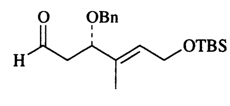
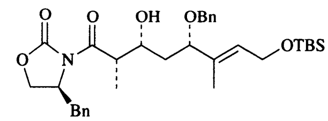
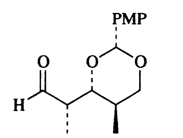
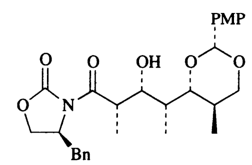
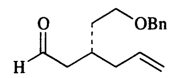
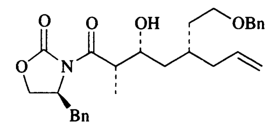
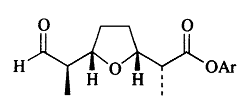
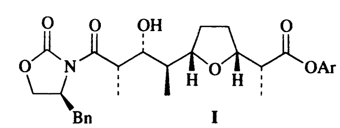
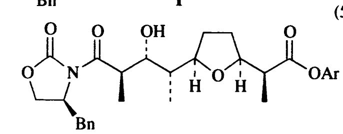
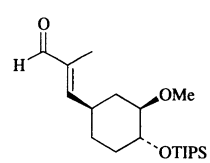
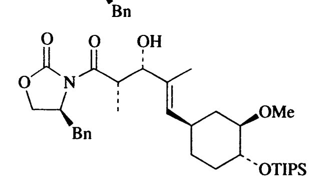
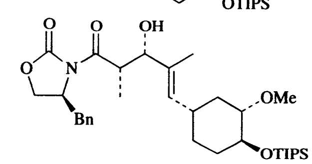
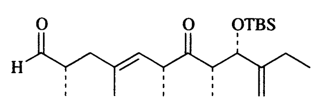
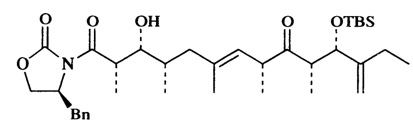
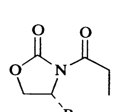
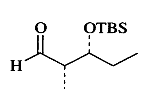
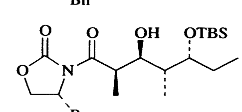
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
C_{13} 	Bu_2BOTf, *i*-Pr_2NEt		 (65)	366
	Bu_2BOTf, *i*-Pr_2NEt		 (65)	366
	Bu_2BOTf, Et_3N		 R = Bn, (94) R = PMB, (>89)	198 196
	Bu_2BOTf, *i*-Pr_2NEt		 (80)	367
	Bu_2BOTf, Et_3N		 (80)	196
	Bu_2BOTf, Et_3N		 (100)	368
	Bu_2BOTf, *i*-Pr_2NEt	 racemic Ar = 2,6-di-*t*-Bu-4-methoxyphenyl	 I + I (55) I:II = 75:25  II	65
	Bu_2BOTf, Et_3N	 racemic	 +  (88)	57
	Bu_2BOTf, *i*-Pr_2NEt		 (52)	21
	Bu_2BOTf, *i*-Pr_2NEt		 (87)	369

TABLE IIB. CHIRAL ENOLATES (AUXILIARY CONTROL) WITH CHIRAL ALDEHYDES (*Continued*)

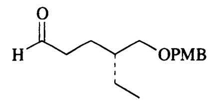
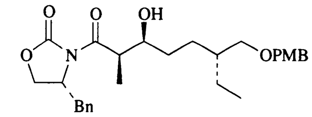
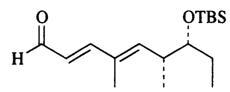
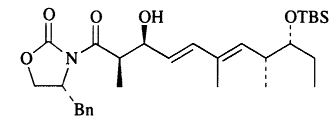
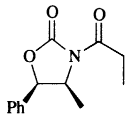
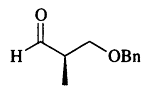
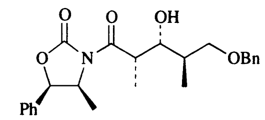
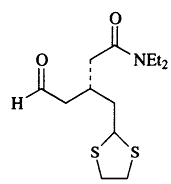
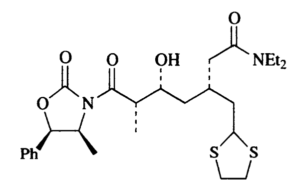
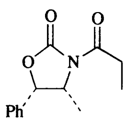
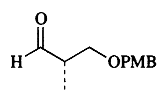
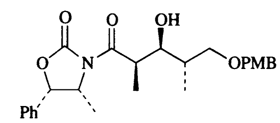
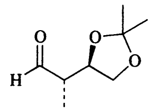
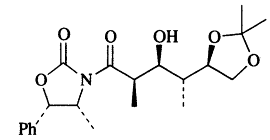
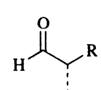
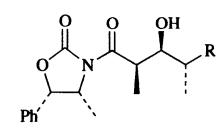
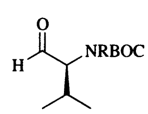
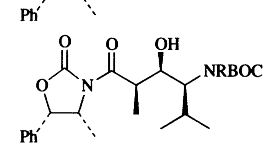
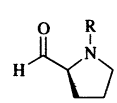
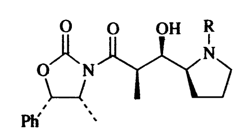
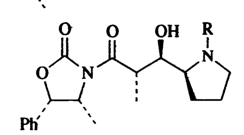
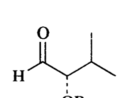
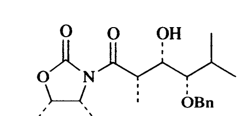
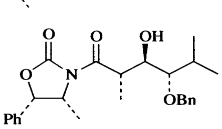
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
	Bu_2BOTf, Et_3N		 (100) >99:1	274
	Bu_2BOTf, Et_3N		 (>63)	370
	Bu_2BOTf, Et_3N		 (>85)	371
	Bu_2BOTf, i-Pr_2NEt		 (92)	372
			 (54)	373
	Bu_2BOTf, i-Pr_2NEt		 (72) 92:8	374
	Bu_2BOTf, i-Pr_2NEt		 R = Me, (63); R = Et, (63)	375
	Bu_2BOTf, Et_3N		 R = H, (100) >99:1; R = Me, (96) >99:1	48
			 I +  II	
	Bu_2BOTf (1.1 eq), Et_3N (1.3 eq)		R = BOC, (92) I:II = >99:1	48,376, 377
	Bu_2BOTf (1.5 eq), Et_3N (1.4 eq)		R = BOC, (83) I:II = 5:95	48,376, 377
	Bu_2BOTf (1.0 eq), Et_3N (1.1 eq)		R = Cbz, (82) I:II = >99:1	48
	Bu_2BOTf (1.5 eq), Et_3N (1.4 eq)		R = Cbz, (74) I:II = 2:98	48
	Bu_2BOTf, i-Pr_2NEt		 I + (—) I:II = 83:17[a]  II	358

TABLE IIB. CHIRAL ENOLATES (AUXILIARY CONTROL) WITH CHIRAL ALDEHYDES (*Continued*)

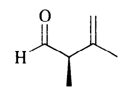
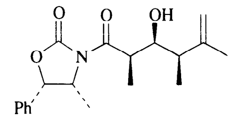
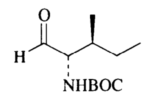
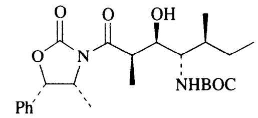
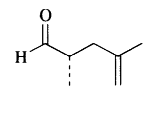
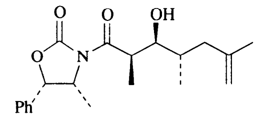
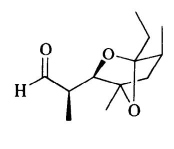
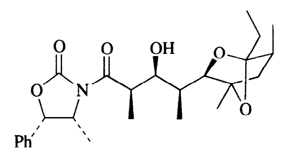
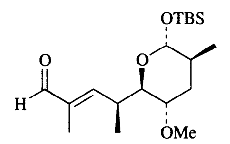
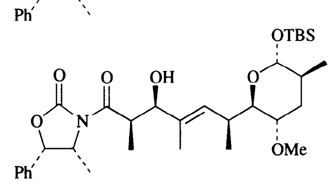
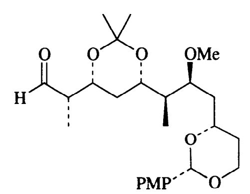
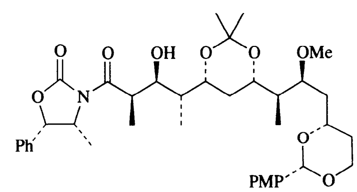
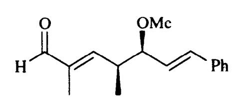
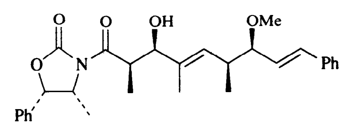
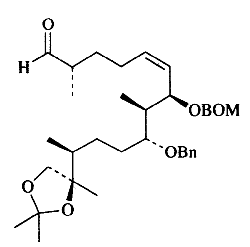
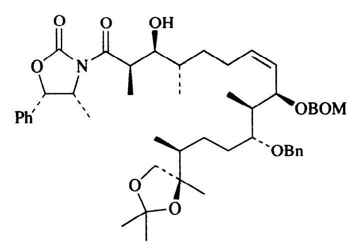
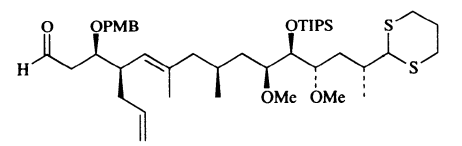
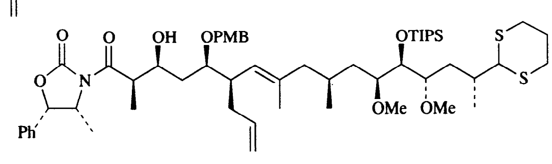
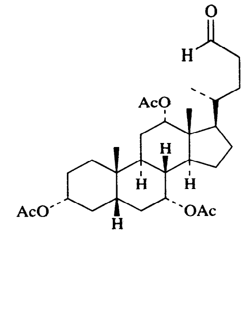
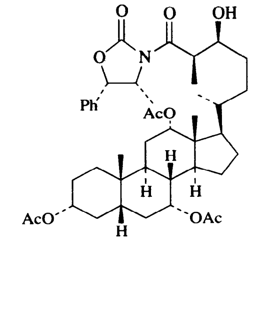
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
	Bu_2BOTf, $i\text{-}Pr_2NEt$		 (>77)	295
	Bu_2BOTf, Et_3N		 (100) >99:1	48
	Bu_2BOTf, $i\text{-}Pr_2NEt$		 (86) 99.8:0.2	27, 359
	Bu_2BOTf, Et_3N		 (62)	258
	Bu_2BOTf, Et_3N		 (>82)	46
	Bu_2BOTf, $i\text{-}Pr_2NEt$		 (88)	212
	Bu_2BOTf, Et_3N		 (77) >95:5	185, 186
	Bu_2BOTf, Et_3N		 (97)	309
	Bu_2BOTf, Et_3N		 (87)	193
	Bu_2BOTf, $i\text{-}Pr_2NEt$		 (94) 91:9	361

TABLE IIB. CHIRAL ENOLATES (AUXILIARY CONTROL) WITH CHIRAL ALDEHYDES (*Continued*)

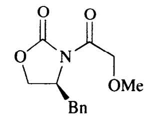
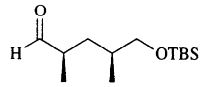
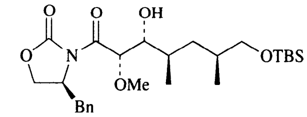
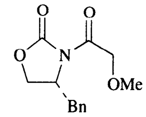
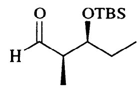
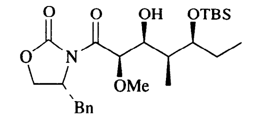
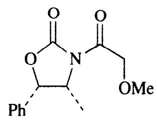
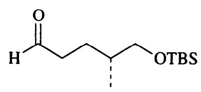
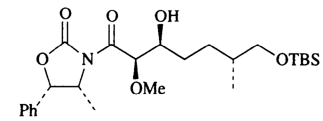
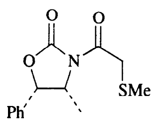
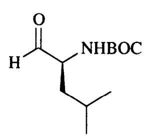
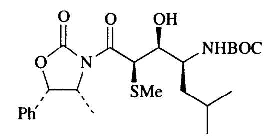
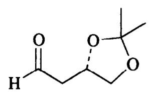
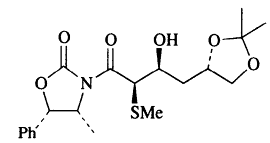
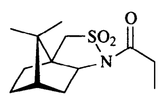
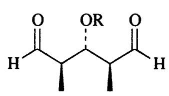
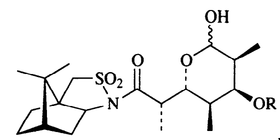
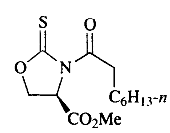
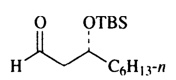
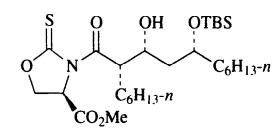
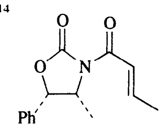
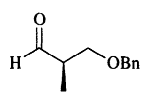
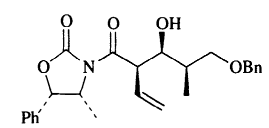
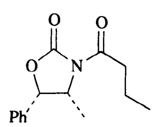
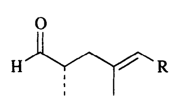
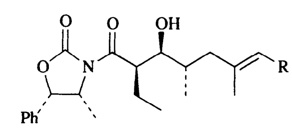
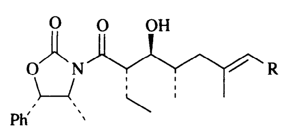
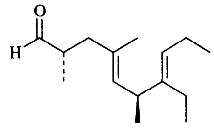
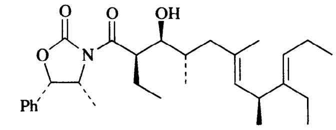
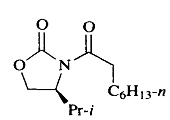
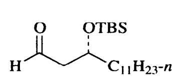
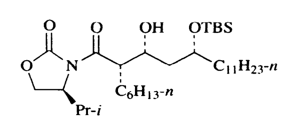
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
	Bu_2BOTf, i-Pr_2NEt		 (>50)	378, 379
	Bu_2BOTf, Et_3N		 (82)	325
	Bu_2BOTf, i-Pr_2NEt		 (96) 94:6	380, 379
	Bu_2BOTf, i-Pr_2NEt		 (14)	381
	Bu_2BOTf, i-Pr_2NEt		 (86) >96:4	56
	Et_2BOTf, i-Pr_2NEt		 R = TBS, (~80) >92:8; R = TIPS, (95) >95:5	207
	Bu_2BOTf, i-Pr_2NEt		 (73)	90
C_{14} 	Bu_2BOTf, Et_3N		 (58)	53
			 **I** +  **II**	
	Bu_2BOTf, i-Pr_2NEt		R = H, (64) **I**:**II** = 60:40	382, 383
	Bu_2BOTf, Et_3N		R = H, (—) **I**:**II** = 75:25	382, 383
	Bu_2BOTf, Et_3N		R = Me, (84) **I**:**II** = >99:1	360
	Bu_2BOTf, Et_3N		 (82) >96:4	360
	Bu_2BOTf, i-Pr_2NEt		 (74)	90

TABLE IIB. CHIRAL ENOLATES (AUXILIARY CONTROL) WITH CHIRAL ALDEHYDES (*Continued*)

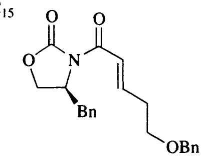
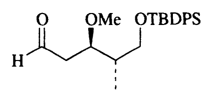
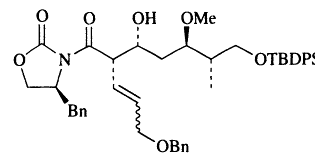
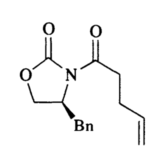
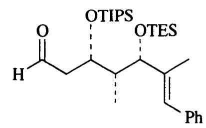
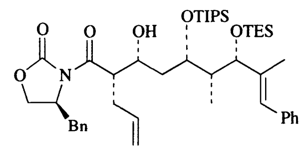
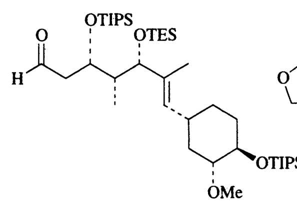
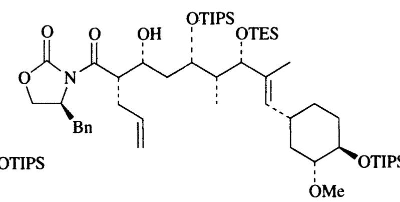
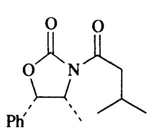
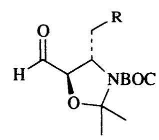
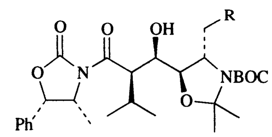
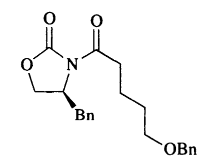
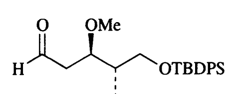
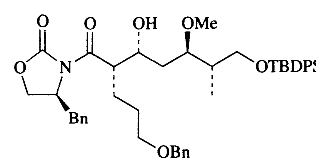
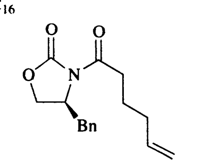
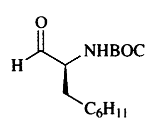
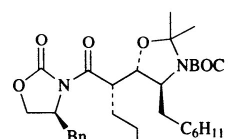
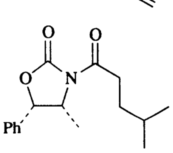
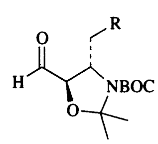
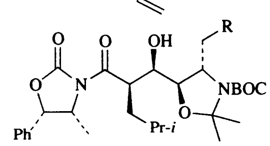
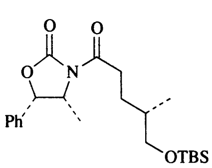
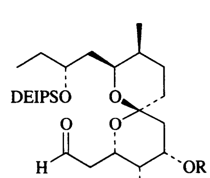
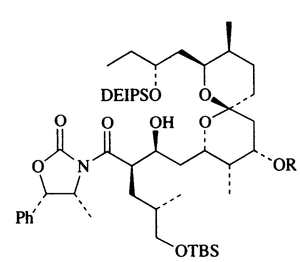
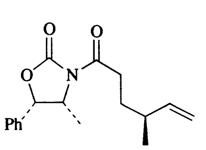
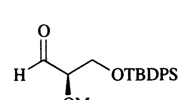
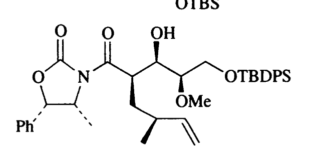
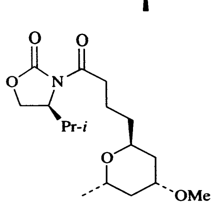
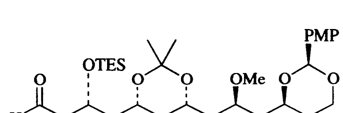
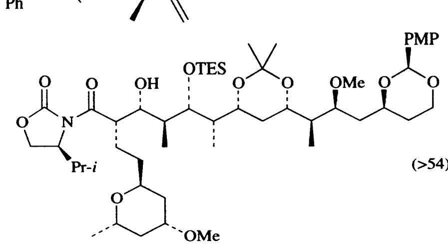
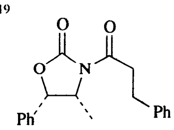
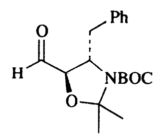
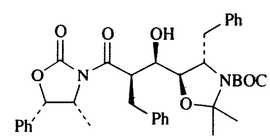
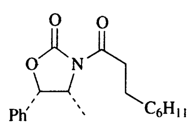
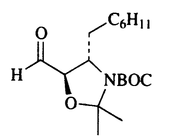
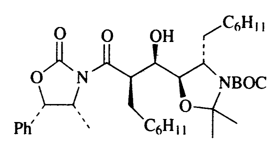
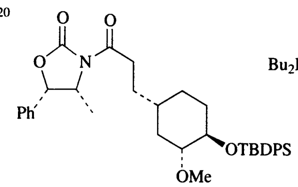
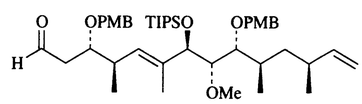
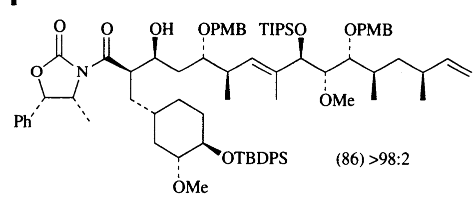
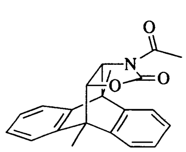
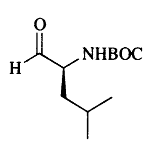
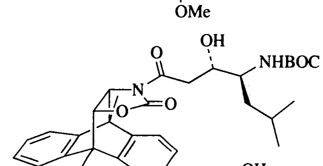
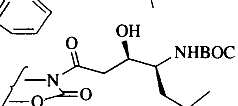
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
C_{15} 	—		 (70) >95:5 E:Z = 50:50	384
	Bu_2BOTf, Et_3N		 (86)	194
	Bu_2BOTf, Et_3N		 (95)	57
	Bu_2BOTf, i-Pr_2NEt		 R = i-Pr, (77) R = C_6H_{11}, (90)	69 70, 364
	Bu_2BOTf, Et_3N		 (58)	72
C_{16} 	1. 9-BBNOTf, Et_3N 2. $(MeO)_2CMe_2$, TsOH		 (63)	262
	Bu_2BOTf, i-Pr_2NEt		 R = i-Pr, (—) R = C_6H_{11}, (73)	70
	Bu_2BOTf, Et_3N	 R = $CH_2OCH_2CCl_3$	 (87)	61
C_{17} 	Bu_2BOTf, Et_3N		 (73) >98:2	73
	Bu_2BOTf, i-Pr_2NEt		 (>54)	211

TABLE IIB. CHIRAL ENOLATES (AUXILIARY CONTROL) WITH CHIRAL ALDEHYDES (*Continued*)

Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
C_{19}				
	Bu_2BOTf, i-Pr_2NEt		 (—)	70
	Bu_2BOTf, i-Pr_2NEt		 (—)	70
C_{20}				
	Bu_2BOTf, Et_3N		 (86) >98:2	73
C_{21}				
	Bu_2BOTf, i-Pr_2NEt		 **I** +  **II** (96) **I**:**II** = 95.5:4.5	92

[a] The major product from this reaction is not the anticipated result.

TABLE IIIA. CHIRAL ENOLATES (SUBSTRATE CONTROL) WITH ACHIRAL ALDEHYDES

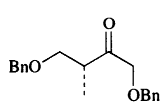
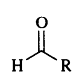
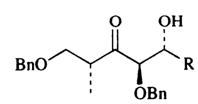
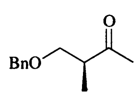
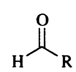
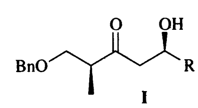
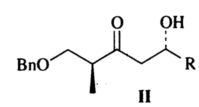
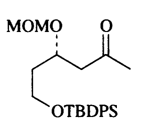
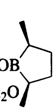
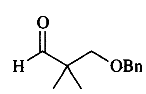
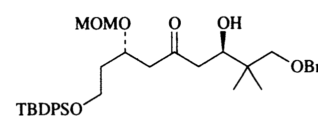
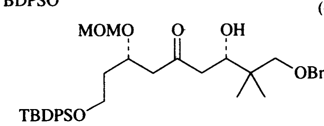
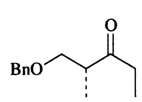
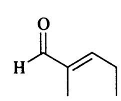
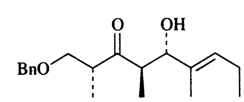
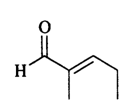
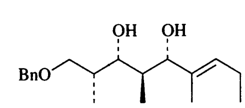
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
C_5 	$(C_6H_{11})_2BCl$, Et_3N, Et_2O		 R = *i*-Pr, (95) 95:5; R = C(Me)=CH_2, (88) 95:5	128
			 **I** +  **II**	120
	Bu_2BOTf, *i*-Pr_2NEt		R = C(Me)=CH_2, (45) **I**:**II** = 84:16	
	$(C_6H_{11})_2BOTf$, *i*-Pr_2NEt		R = C(Me)=CH_2, (40) **I**:**II** = 86:14	
	$(C_6H_{11})_2BCl$, Et_3N, Et_2O		R = Pr, (84) **I**:**II** = 88:12	
C_6 	*i*-Pr_2NEt, TfOB  pentane, Et_2O		 **I** +  **II** (—) **I**:**II** = 52:48	159
	$(C_6H_{11})_2BCl$, Et_3N, Et_2O		 (—) 97:3	123
	1. $(C_6H_{11})_2BCl$, Et_3N, Et_2O 2. $LiBH_4$		 (81) 96:4	123

TABLE IIIA. CHIRAL ENOLATES (SUBSTRATE CONTROL) WITH ACHIRAL ALDEHYDES (*Continued*)

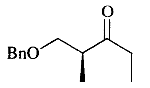
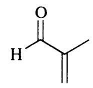
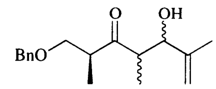
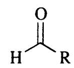
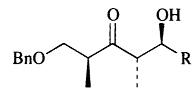
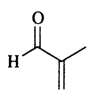
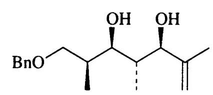
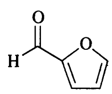
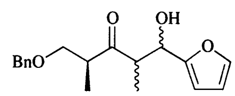
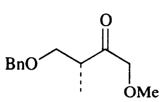
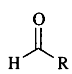
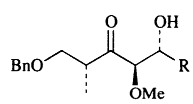
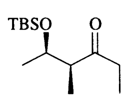
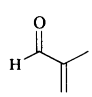
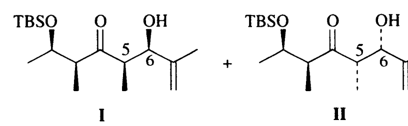
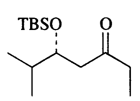
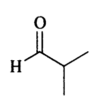
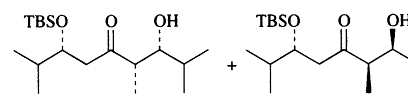
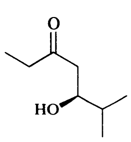
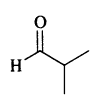
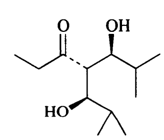
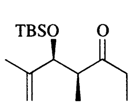
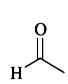
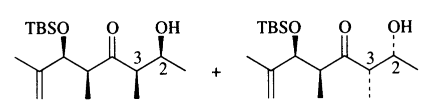
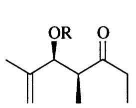
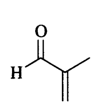
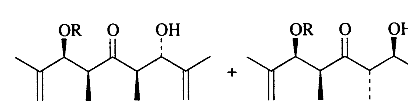
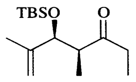
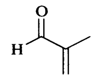
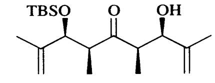
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
				
	Bu_2BOTf, Et_3N, 0°		(57) anti:syn 94:6	119
	Bu_2BOTf, *i*-Pr_2NEt, −78°		(76) anti:syn 11:89[a]	119, 122
	$(C_6H_{11})_2BCl$, Et_3N, Et_2O			
			R = Pr, (72) 95:5	120
			R = (*E*)-CH=CHMe, (93) 97:3	122, 120, 125, 133
			R = *i*-Pr, (89) >94:6	120
			R = C(Me)=CH_2, 0° (72) 92:8	120
			R = C(Me)=CH_2, −78° (93) 97:3	122, 120, 128, 385
	1. $(C_6H_{11})_2BCl$, Et_3N, Et_2O 2. $LiBH_4$		 (83) 94:6	386
				119
	Bu_2BOTf, Et_3N		(66) anti:syn = 84:16	
	9-BBNOTf, Et_3N		(66) anti:syn = 75:25	
	$(C_6H_{11})_2BCl$, Et_3N, Et_2O		 R = Et, (97) 95:5; R = (*E*)-CH=CHMe, (83) 96:4	128
C_7 				130
	Bu_2BOTf, *i*-Pr_2NEt		(90) **I:II:5,6-anti** = 84:5:11	
	9-BBNOTf, *i*-Pr_2NEt		(70) **I:II:5,6-anti** = 85:5:10	
C_8 	$PhBCl_2$, *i*-Pr_2NEt		 (68) **I:II** = 87:13	136
	BCl_3, *i*-Pr_2NEt		 (41)	387
C_9 				130
	Bu_2BOTf, Et_3N		(85) **I:II:2,3-anti** = 63:3:34	
	9-BBNOTf, Et_3N		(97) **I:II:2,3-anti** = 83:7:10	
 racemic	$(C_6H_{11})_2BCl$, Et_3N, Et_2O		 R = TBS, (81) **I:II** = 82:18; R = TIPS, (90) **I:II** = 87:13	132
 racemic	9-BBNOTf, Et_3N		 (>70)	132

TABLE IIIA. CHIRAL ENOLATES (SUBSTRATE CONTROL) WITH ACHIRAL ALDEHYDES (*Continued*)

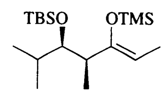
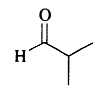
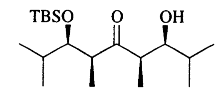
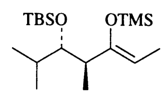
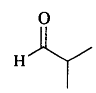
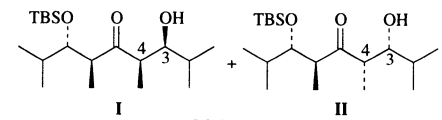
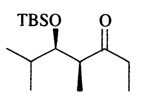
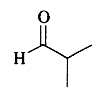
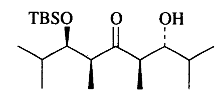
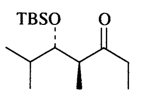
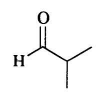
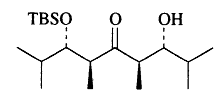
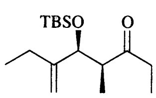
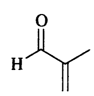
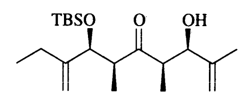
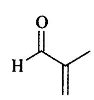
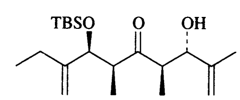
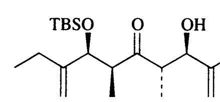
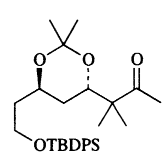
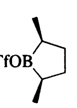
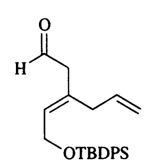
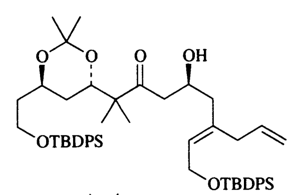
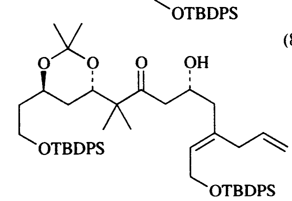
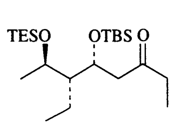
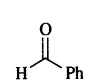
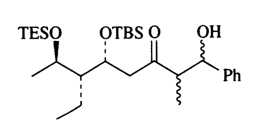
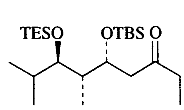
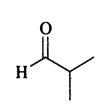
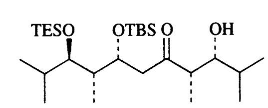
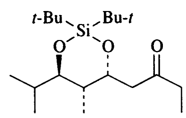
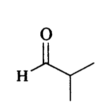
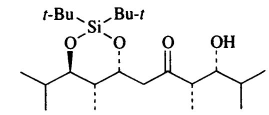
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
	9-BBNBr		 (66) 92:8	135
	9-BBNBr		 (68) **I**:**II**:**3,4-anti** = 89:3:8	135
	$(C_6H_{11})_2BCl$, Et_3N, Et_2O		 (90) 94:6	129
	$(C_6H_{11})_2BCl$, Et_3N, Et_2O		 (75) 96:4	129
C_{10} 	9-BBNOTf, Et_3N		 (87) 95:5	21, 26
	$(C_6H_{11})_2BCl$, Et_3N, Et_2O		 **I** +  **II** (93) **I**:**II** = 79:21[b]	132
	*i*-Pr_2NEt, TfOB  pentane, Et_2O		 **I** +  **II** (80-90) **I**:**II** = 75:25	178
	Bu_2BOTf, *i*-Pr_2NEt		 (51)[c]	203
C_{11} 	$PhBCl_2$, *i*-Pr_2NEt		 (—) 62:38[d]	136
	$PhBCl_2$, *i*-Pr_2NEt		 (72) >99:1	136

TABLE IIIA. CHIRAL ENOLATES (SUBSTRATE CONTROL) WITH ACHIRAL ALDEHYDES (*Continued*)

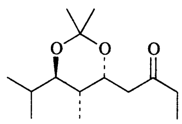
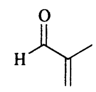
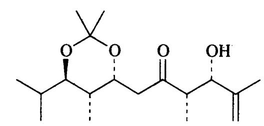
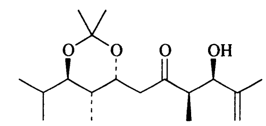
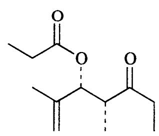
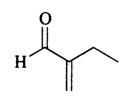
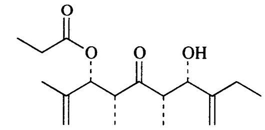
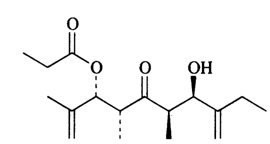
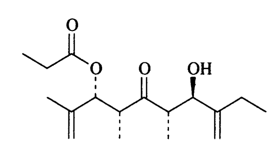
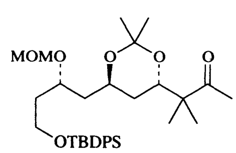
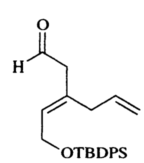
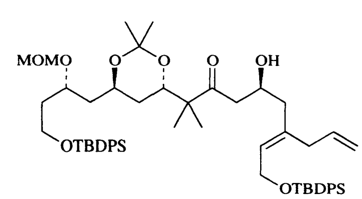
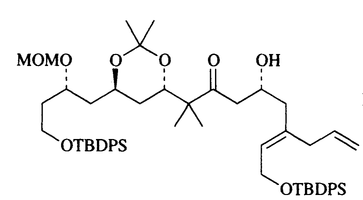
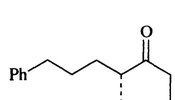
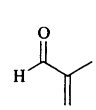
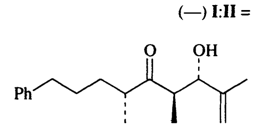
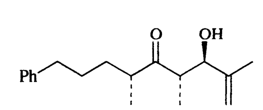
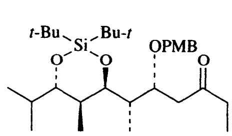
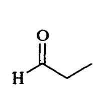
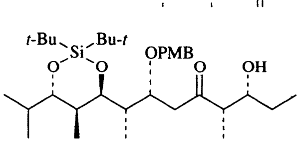
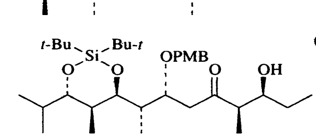
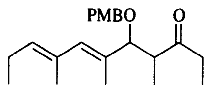
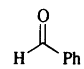
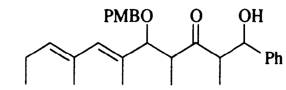
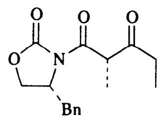
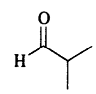
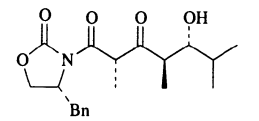
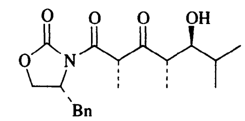
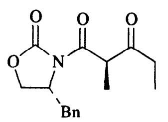
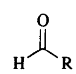
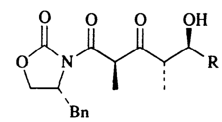
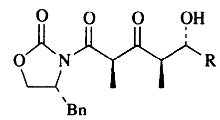
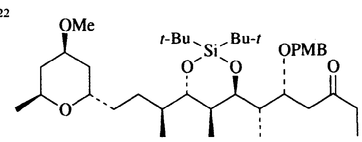
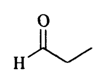
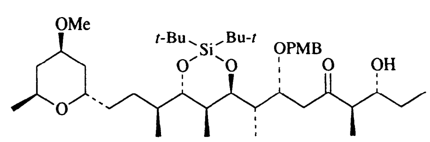
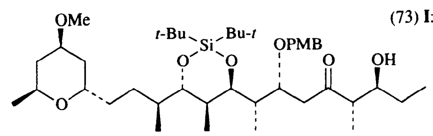
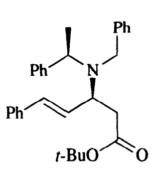
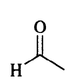
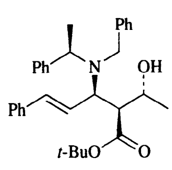
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
			 I +  II	36
	Bu_2BOTf, *i*-Pr_2NEt, CH_2Cl_2		(78) I:II = 78:22	
	Bu_2BOTf, *i*-Pr_2NEt, Et_2O		(76) I:II = 84:16	
C_{12} 	9-BBNOTf, Et_3N		 I +  II +  III (76) I:II:III = 91:7:2	21
	Et_2BOTf, *i*-Pr_2NEt		 I +  II (—) I:II = 67:33	159, 153
C_{14} 	$(C_6H_{11})_2BCl$, Et_3N, Et_2O		 I +  II (—) I:II (or II:I) = 72:28	128
	Bu_2BOTf, *i*-Pr_2NEt		 I +  II (75) I:II = 67:33	34

TABLE IIIA. CHIRAL ENOLATES (SUBSTRATE CONTROL) WITH ACHIRAL ALDEHYDES (*Continued*)

Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
	9-BBNOTf, i-Pr_2NEt, Et_2O		 (88)[e]	47
C_{16} 	$(C_6H_{11})_2BCl$, $EtNMe_2$, Et_2O		 I +  II (89) I:II = 83:17	129
	$(C_6H_{11})_2BCl$, $EtNMe_2$, Et_2O		 I +  II	129
		R = Pr, (70) I:II = 80:20 R = i-Pr, (93) I:II = 84:16 R = C(Me)=CH_2, (78) I:II = 92:8 R = $(CH_2)_2Ph$, (84) I:II = 88:12		
C_{22} 	$(C_6H_{11})_2BCl$, Et_3N, Et_2O		 I +  II (73) I:II = 50:50	35
C_{26} 	1. LDA, THF 2. $B(OR)_3$ 3. Aldehyde		 R = Me, (82) 76:25 R = Bu, (89) 91:9	388

[a] The syn isomers have been assigned as syn-syn:syn-anti = 54:46.

[b] This reaction was performed using racemic ketone.

[c] The product was reported as a mixture of syn stereoisomers.

[d] The stereochemistry of the minor adduct was not determined.

[e] The stereochemistry of this product was not depicted.

TABLE IIIB. CHIRAL ENOLATES (SUBSTRATE CONTROL) WITH CHIRAL ALDEHYDES

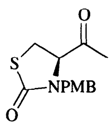
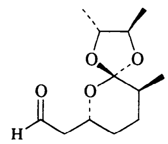
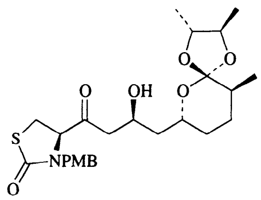
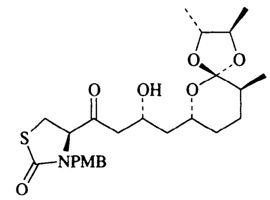
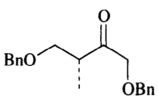
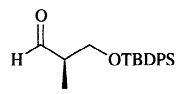
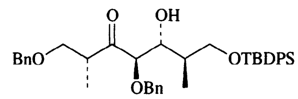
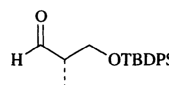
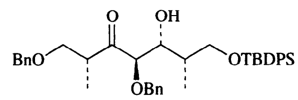
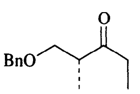
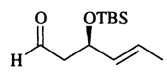
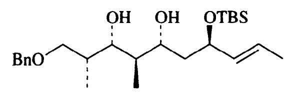
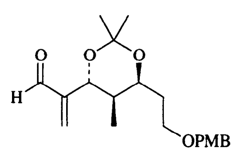
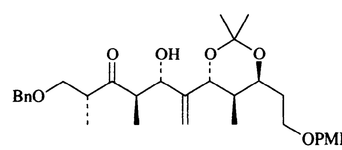
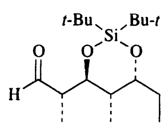
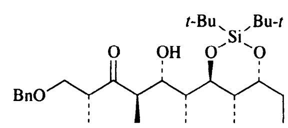
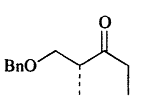
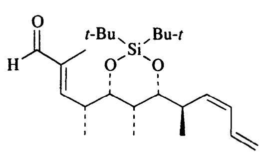
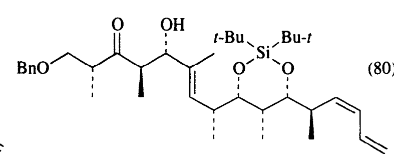
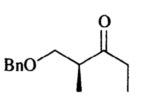
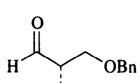
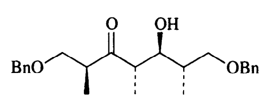
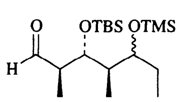
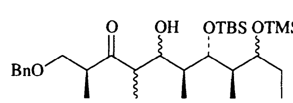
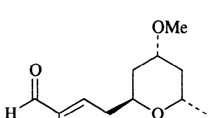
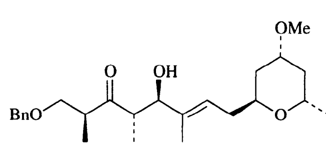
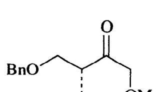
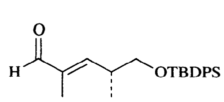
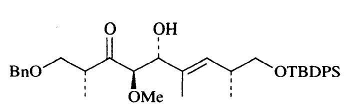
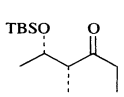
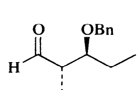
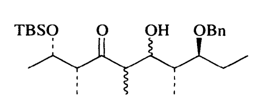
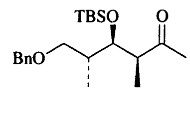
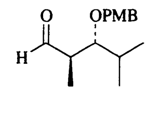
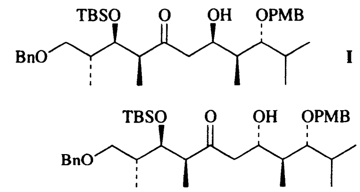
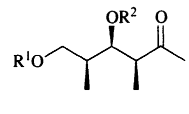
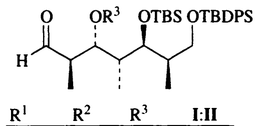
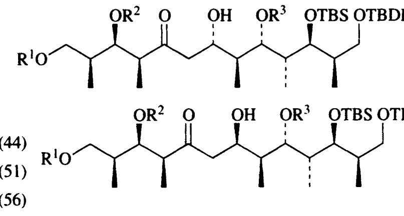
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
C_5 	Bu_2BOTf, i-Pr_2NEt		 **I** +  **II** (87) **I**:**II** = 80:20	389, 390
	$(C_6H_{11})_2BCl$, Et_3N, Et_2O		 (83) 80:20	128
	$(C_6H_{11})_2BCl$, Et_3N, Et_2O		 (90) 95:5	128
C_6 	1. $(C_6H_{11})_2BCl$, Et_3N, Et_2O 2. $LiBH_4$		 (91) 97:3	127
	$(C_6H_{11})_2BCl$, Et_3N, Et_2O		 (75) >95:5	332
	$(C_6H_{11})_2BCl$, Et_3N, Et_2O		 (91) >98:2	126
	$(C_6H_{11})_2BCl$, Et_3N, Et_2O		 (80) 97:3	197
	$(C_6H_{11})_2BCl$, Et_3N, Et_2O		 (81) 98:2	385
	9-BBNOTf, i-Pr_2NEt		 (>61)[a]	391
	$(C_6H_{11})_2BCl$, Et_3N, Et_2O		 (84) 97:3	213, 208
	$(C_6H_{11})_2BCl$, Et_3N, Et_2O		 (94) 97:3	127
C_7 	Bu_2BOTf, i-Pr_2NEt		 (>43)[a]	392

TABLE IIIB. CHIRAL ENOLATES (SUBSTRATE CONTROL) WITH CHIRAL ALDEHYDES (*Continued*)

Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
C_8 	Bu_2BOTf, Et_3N		 I + (65) I:II = 55:45 II	179
	Bu_2BOTf, *i*-Pr_2NEt, Et_2O		 I + II	20

R^1	R^2	R^3	I:II	
TBS	Bn	MOM	75:25	(44)
TBS	Bn	TES	97:3	(51)
TBS	TBS	MOM	69:31	(56)
TBS	TBS	TES	97:3	(40)
PMB	TBS	TES	91:9	(59)

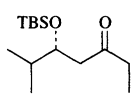
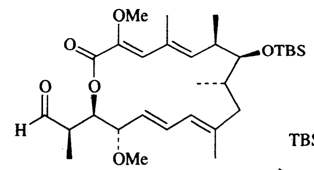
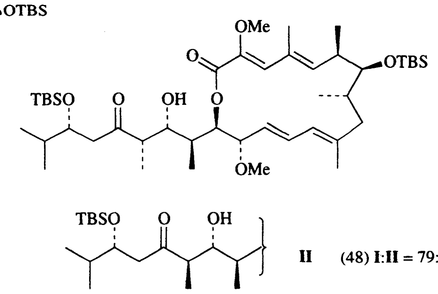
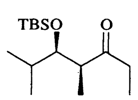
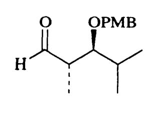
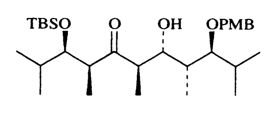
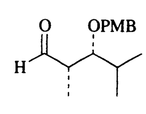
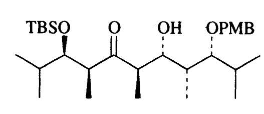
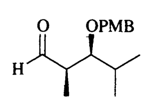
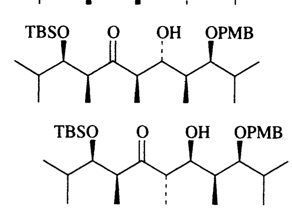
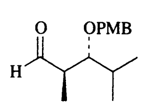
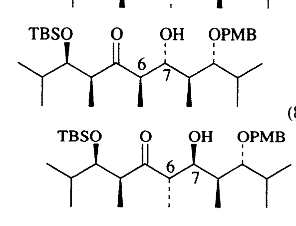
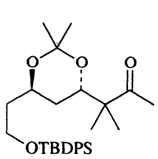
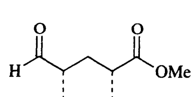
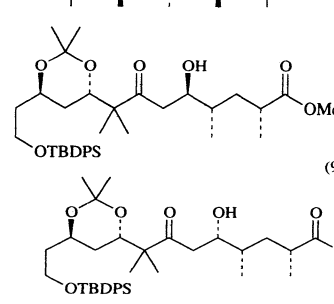
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
	$PhBCl_2$, *i*-Pr_2NEt		 I + II (48) I:II = 79:21	136
C_9 	$(C_6H_{11})_2BCl$, Et_3N, Et_2O		 (85) >99:1	38
	$(C_6H_{11})_2BCl$, Et_3N, Et_2O		 (84) >99:1	38
	$(C_6H_{11})_2BCl$, Et_3N, Et_2O		 I + (79) I:II = 81:19 II	38
	$(C_6H_{11})_2BCl$, Et_3N, Et_2O		 I + (83) I:II:6,7-syn = 65:25:10 II	38
C_{10} 	Et_2BOTf, *i*-Pr_2NEt, Et_2O		 I + (90) I:II = 88:12 II	178

TABLE IIIB. CHIRAL ENOLATES (SUBSTRATE CONTROL) WITH CHIRAL ALDEHYDES (*Continued*)

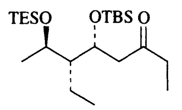
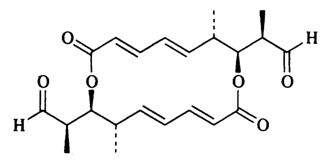
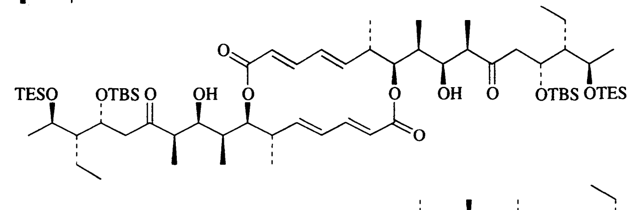
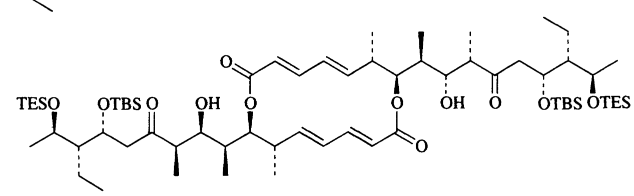
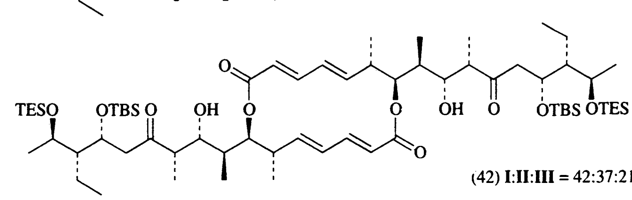
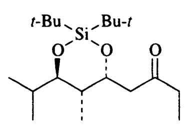
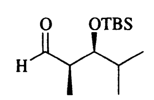
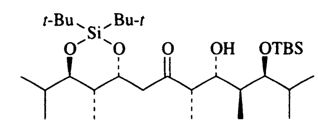
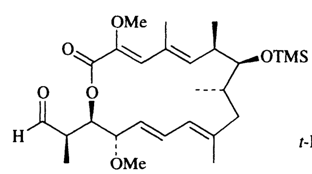
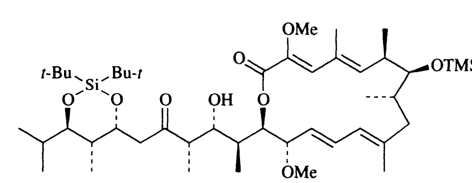
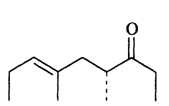
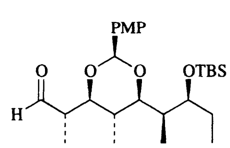
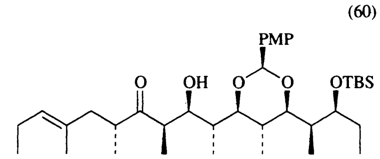
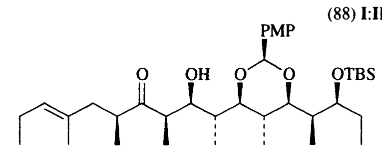
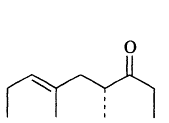
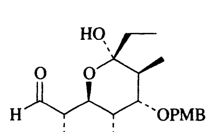
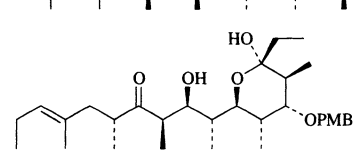
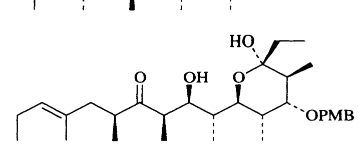
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
	Bu_2BOTf, *i*-Pr_2NEt		 I +  II +  III (42) **I**:**II**:**III** = 42:37:21	202, 203
C_{11}				
	$PhBCl_2$, *i*-Pr_2NEt		 (56) >99:1	136
	$PhBCl_2$, *i*-Pr_2NEt		 (60) >95:5	136
 70-85% ee	9-BBNOTf, *i*-Pr_2NEt, Et_2O, hexane		 I + (88) **I**:**II** = 75:25  II	205
	9-BBNOTf, *i*-Pr_2NEt, Et_2O, hexane		 I +  II ketone (ca. 80% ee), (89) **I**:**II** = 78:22 ketone (racemic), (62) **I**:**II** = 25:75	205, 206

TABLE IIIB. CHIRAL ENOLATES (SUBSTRATE CONTROL) WITH CHIRAL ALDEHYDES (*Continued*)

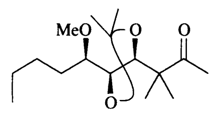
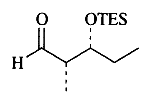
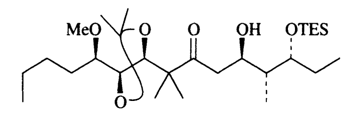
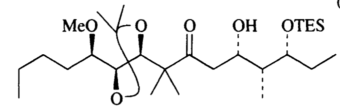
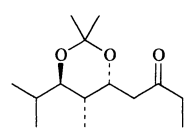
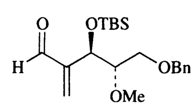
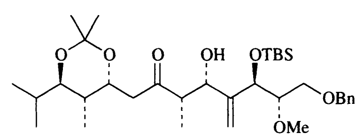
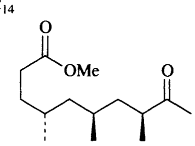
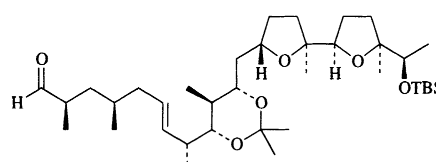
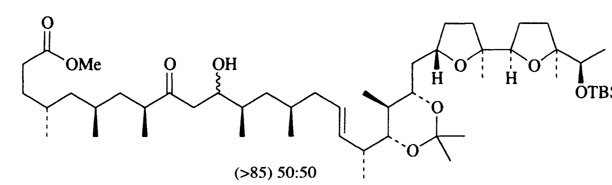
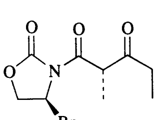
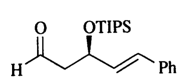
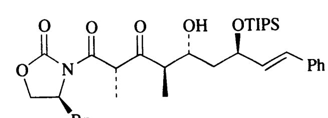
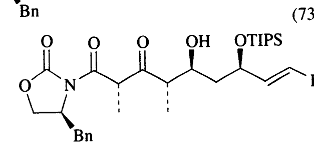
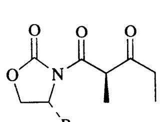
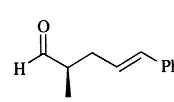
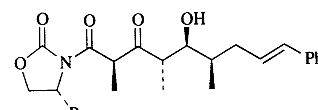
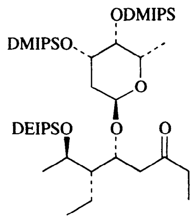
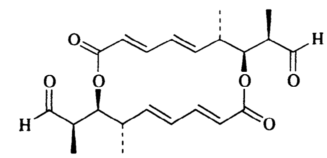
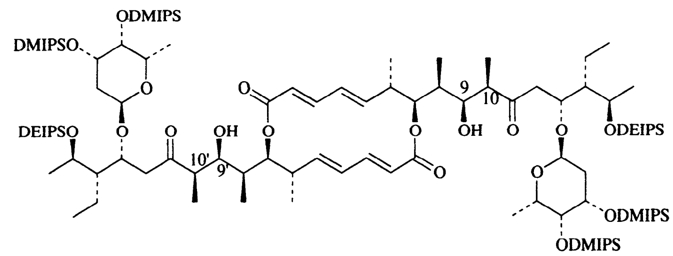
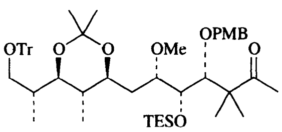
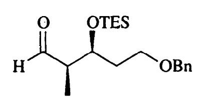
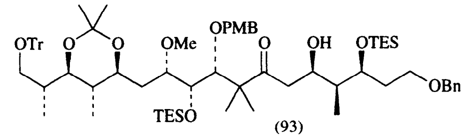
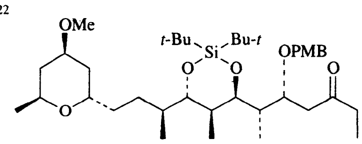
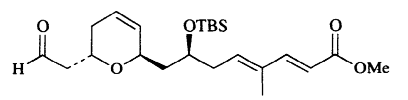
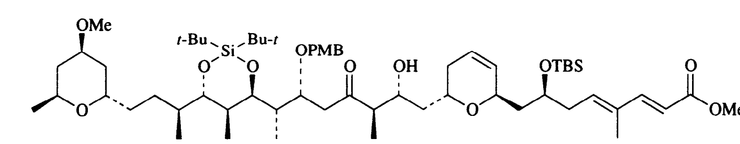
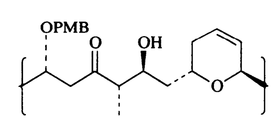
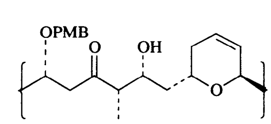
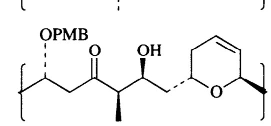
Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
	Et_2BOTf, *i*-Pr_2NEt		 **I** +  **II** (86) **I**:**II** = 89:11	178
	Bu_2BOTf, *i*-Pr_2NEt, Et_2O		 (69) 82:18	36
C_{14} 	Bu_2BOTf, *i*-Pr_2NEt		 (>85) 50:50	53, 393
C_{16} 	$(C_6H_{11})_2BCl$, Et_2NMe, Et_2O		 **I** +  **II** (73) **I**:**II** = 82:18	199
	$(C_6H_{11})_2BCl$, $EtNMe_2$, Et_2O		 (87) 97:3	129, 222, 223

TABLE IIIB. CHIRAL ENOLATES (SUBSTRATE CONTROL) WITH CHIRAL ALDEHYDES (*Continued*)

Enolate Precursor	Reaction Conditions	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
	L_2BOTf, i-Pr_2NEt, Et_2O, THF		**I** = (9*S*,9'*S*,10*R*,10'*R*) [as shown] **II** = (9*R*,9'*S*,10*S*,10'*R*) **III** = (9*R*,9'*R*,10*S*,10'*S*)	
			L_2B = Bu_2B, (63) **I**:**II**:**III** = 41:38:21	200, 180
			L_2B = $(n$-$C_5H_{11})_2B$, (57) **I**:**II**:**III** = 34:45:21	180
			L_2B = 9-BBN, (61) **I**:**II**:**III** = 65:27:8	180
				
C_{17} 	$(C_6H_{11})_2BCl$, Et_3N		 (93)	240
C_{22} 			 **I** +  **II** +  **III** +  **IV**	
	$(C_6H_{11})_2BCl$, Et_3N, Et_2O		(83) **I**:**II**:**III**/**IV** = 52:35:13	215,35
	Bu_2BOTf, i-Pr_2NEt		(82) **III**:**IV** = 77:23	35

[a] The stereochemistry of this product was not reported.

TABLE IVA. CHIRAL ENOLATES (LIGAND CONTROL) WITH ACHIRAL ALDEHYDES

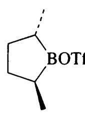
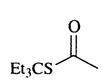
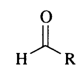
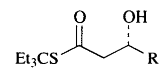
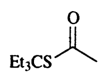
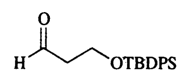
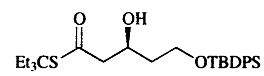
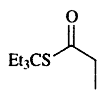
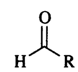
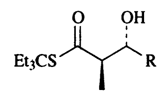
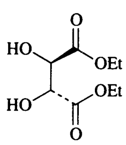
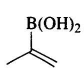
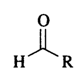
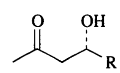
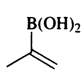
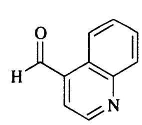
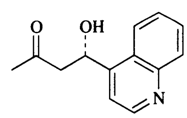
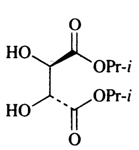
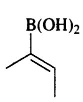
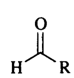
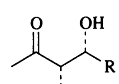
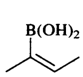
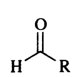
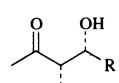
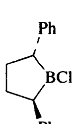
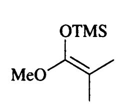
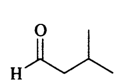
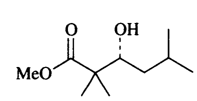
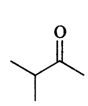
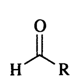
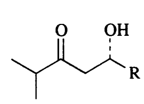
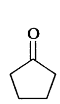
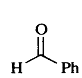
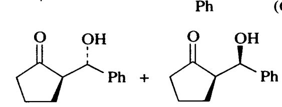
Reaction Conditions	Enolate Precursor	Aldehyde	Product(s) and Yield(s) (%), Isomer Ratio, % ee	Refs.
C_6  (*S*,*S*)-reagent				
L_2BOTf, *i*-Pr_2NEt pentane			 R / % ee $(CH_2)_2OBn$ (93) 84.9 Pr (82) 86.6 *i*-Pr (81) 86.9 *t*-Bu (71) 94.4 Ph (78) 89.0 C_6H_{11} (95) 85.6	152
L_2BOTf, *i*-Pr_2NEt pentane			 (79) 89% ee	159, 153
L_2BOTf, *i*-Pr_2NEt pentane			 R / ratio / % ee $(CH_2)_2OBn$ (93) 97:3 92.2 Pr (91) >97:3 93.0 *i*-Pr (85) >97:3 95.4 *t*-Bu (95) >97:3 95.8 Ph (71) >97:3 95.7 C_6H_{11} (82) >97:3 93.1	152
C_8 				
1. Boronic acid, diol 2. Me_3NO 3. Aldehyde			 R / % ee (*E*)-C(Me)=CHMe (64) 57 Ph (62) 65 C_6H_{11} (61) 60 $(CH_2)_2Ph$ (59) 41	171
1. Boronic acid, diol 2. Me_3NO 3. Aldehyde			 (55) 48% ee	171
C_{10} 				
1. Boronic acid, diol 2. Me_3NO 3. Aldehyde			 R / ratio / % ee *n*-C_5H_{11} (74) >95:5 72 $CHEt_2$ (47) >95:5 58 Ph (75) >95:5 65	177
1. Boronic acid, diol 2. Me_3NO 3. Aldehyde			 R / ratio / % ee *n*-C_5H_{11} (45) >95:5 30 Ph (43) >95:5 25	177
C_{16} 				
L_2BCl, *i*-Pr_2NEt			 (57) 90% ee	154
L_2BCl, *i*-Pr_2NEt			 R / % ee *n*-C_5H_{11} (67) 81 *t*-Bu (55) 84 Ph (60) 32	154
L_2BCl, *i*-Pr_2NEt			 I + II (65) I:II = 87:13 92% ee	154

TABLE IVA. CHIRAL ENOLATES (LIGAND CONTROL) WITH ACHIRAL ALDEHYDES (*Continued*)

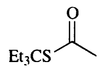
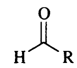
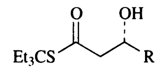
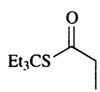
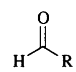
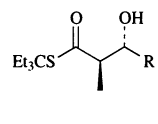
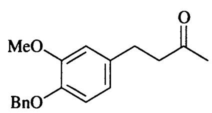
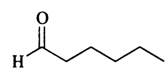
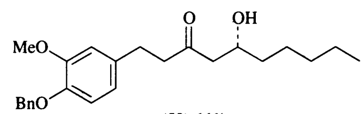
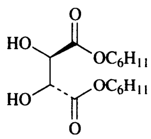
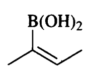
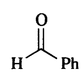
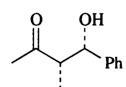
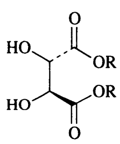
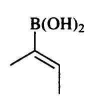
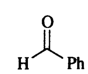
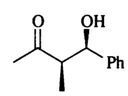
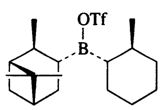
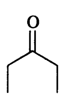
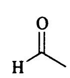
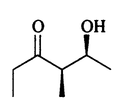
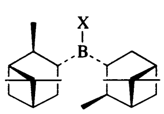
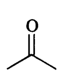
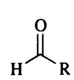
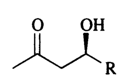
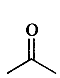
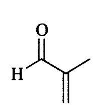
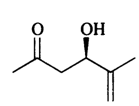
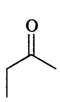
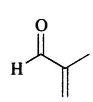
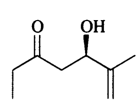
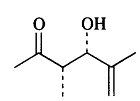
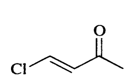
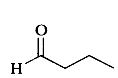
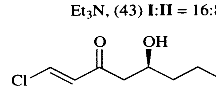
Reaction Conditions	Enolate Precursor	Aldehyde	Product(s) and Yield(s) (%), Isomer Ratio, % ee	Refs.
L_2BCl, *i*-Pr_2NEt			 R / % ee *i*-Pr (72) 92 *i*-Bu (92) >95 *n*-C_6H_{13} (78) 95 C_6H_{11} (87) 95	 155 155, 156 155, 156 155
L_2BCl, *i*-Pr_2NEt			 R / % ee *i*-Pr (82) 99 *t*-Bu (68) 94.3 *n*-C_6H_{13} (36) 100 C_6H_{11} (58) 98.7	155
L_2BCl, *i*-Pr_2NEt			 (58) 66% ee	154
 1. Boronic acid, diol 2. Me_3NO 3. Aldehyde			 (65) >95:5, 66% ee	177
 1. Boronic acid, diol 2. Me_3NO 3. Aldehyde			 R = Ph, (45) >95:5, 4% ee R = Ts, (55) >95:5, 30% ee	177
C_{17}  L_2BOTf, *i*-Pr_2NEt			 (26) 33% ee	143, 121
C_{20}  (−)-Ipc_2BX (−)-Ipc_2BOTf, *i*-Pr_2NEt			 R / Solvent / % ee C(Me)=CH_2 CH_2Cl_2 (59) 73 C(Me)=CH_2 toluene (20) 67 C(Me)=CH_2 hexane (34) 65 Pr — (68) 78 Ph — (78) 57	145, 121
(−)-Ipc_2BCl, Et_3N			 (67) 62% ee	121
(−)-Ipc_2BOTf, base			 I +  II *i*-Pr_2NEt, (71) I:II = 62:38 (62% ee of I) Et_3N, (43) I:II = 16:84 (93% ee of II)	145, 121
(−)-Ipc_2BOTf, *i*-Pr_2NEt			 (55) 67% ee	394

TABLE IVA. CHIRAL ENOLATES (LIGAND CONTROL) WITH ACHIRAL ALDEHYDES (*Continued*)

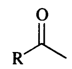
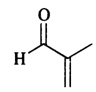
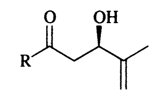
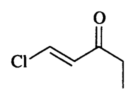
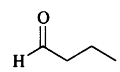
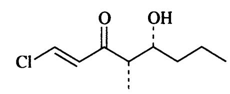
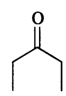
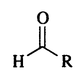
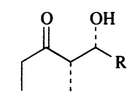
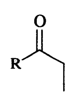
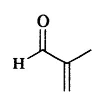
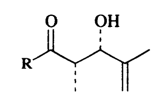
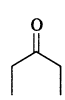
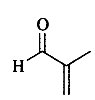
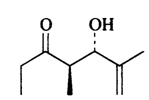
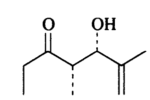
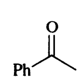
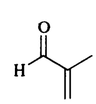
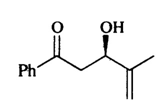
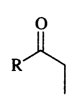
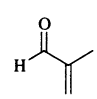
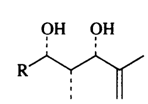
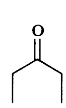
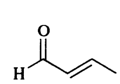
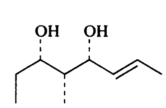
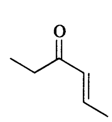
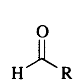
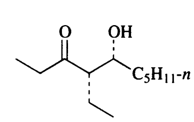
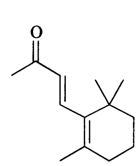
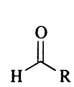
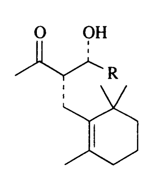
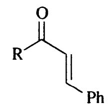
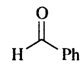
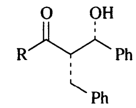
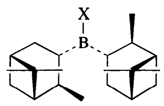
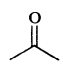
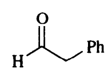
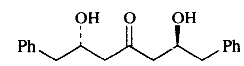
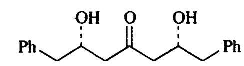
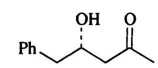
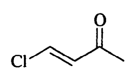
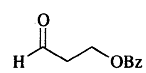
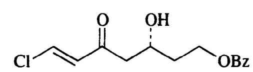
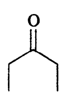
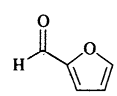
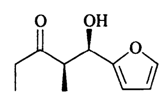
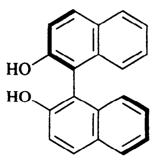
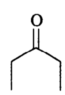
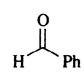
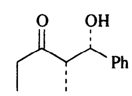
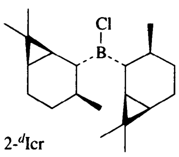
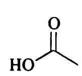
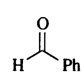
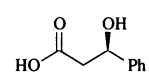
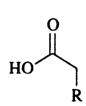
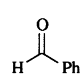
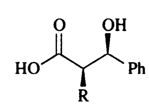
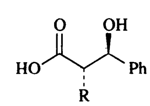
Reaction Conditions	Enolate Precursor	Aldehyde	Product(s) and Yield(s) (%), Isomer Ratio, % ee	Refs.
(−)-Ipc_2BOTf, i-Pr_2NEt			 R / ratio / % ee	145, 121
			i-Pr (56) 92:8 65[a]	
			i-Bu (62) >97:3 53	
			Ph (48) — 61	
(−)-Ipc_2BOTf, i-Pr_2NEt			 (40) >97:3, 80% ee	394
(−)-Ipc_2BOTf, i-Pr_2NEt			 R / ratio / % ee	
			Me (CH_2Cl_2) (91) 97:3 82	121,143
			Me (Et_2O) (—) — 51	143
			Me (hexane) (—) — 56	143
			C(Me)=CH_2 (78) 98:2 91	121,143
			(E)-CH=CHMe (75) 98:2 86	121,143
			Pr (92) 97:3 80	121,143
			i-Pr (45) 96:4 66	121,143
			2-furyl (84) 96:4 80	121,143
			C(Et)=CH_2 (77) 97:3 86	21
(−)-Ipc_2BOTf, i-Pr_2NEt			 R / ratio / % ee	121
			i-Pr (99) 95:5 88	
			i-Bu (79) 97:3 86	
			Ph (97) 98:2 91	
(−)-Ipc_2BCl, Et_3N			 **I** +  **II** (80) **I**:**II** = 80 (<20% ee):20 (80% ee)	121
(−)-Ipc_2BOTf, i-Pr_2NEt			 (48) 61% ee	145, 121
1. (−)-Ipc_2BOTf, i-Pr_2NEt 2. Aldehyde 3. $NaBH_4$			 R / ratio / % ee	144
			Et (56) 94:6 92	
			i-Pr (48) 85:15 90	
			i-Bu (59) 88.5:11.5 91	
			Ph (43) 96.5:3.5 96	
1. (−)-Ipc_2BOTf, i-Pr_2NEt 2. Aldehyde 3. $NaBH_4$			 (52) 87.5:12.5, 88% ee	144
				
(−)-Ipc_2BH, THF			R = C_5H_{11}-n, (54) 65% ee	147,148
(−)-Ipc_2BH, $CHCl_3$			R = Ph, (65) 64% ee	148
				
(−)-Ipc_2BH, THF			R = Me, (60) 75% ee	148,147
(−)-Ipc_2BH, THF			R = Ph, (77) 75% ee	148,147
(−)-Ipc_2BH, CH_2Cl_2			R = Ph, (70) 62% ee	148
(−)-Ipc_2BH, THF			R = t-Bu, (30) 50% ee	148

TABLE IVA. CHIRAL ENOLATES (LIGAND CONTROL) WITH ACHIRAL ALDEHYDES (*Continued*)

Reaction Conditions	Enolate Precursor	Aldehyde	Product(s) and Yield(s) (%), Isomer Ratio, % ee	Refs.
(–)-Ipc_2BH, THF			 R = Me, (91) 90% ee R = Ph, (80) 60% ee	148,147
 (+)-Ipc_2BX				
1. Ketone, (+)-Ipc_2BCl, Et_3N, Et_2O 2. Aldehyde 3. repeat steps 1 and 2			 I +  II +  III (73) I:II:III = 48:15:37	395[b]
(+)-Ipc_2BCl, i-Pr_2NEt, toluene			 (56) 80% ee	214, 209
(+)-Ipc_2BOTf, i-Pr_2NEt			 (86) 96:4 80% ee	121
				
(–)-Binaphthol, BCl_3, i-Pr_2NEt			 (24) 46% ee[c]	396
 2-[d]Icr				
1. Acid, LDA, THF 2. (2-[d]Icr)$_2$BCl 3. Aldehyde			 (53) 72% ee	397
1. Acid, LDA, THF 2. (2-[d]Icr)$_2$BCl 3. Aldehyde			 I +  II	397

R		I:II
Me	(90)	90 (90% ee):10 (20% ee)
Ph	(68)	95 (>99% ee):5 (—)
SMe	(85)	90 (>99% ee):10 (—)
OPh	(68)	80 (98% ee):20 (50% ee)

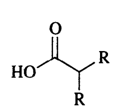
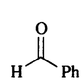
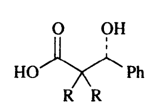
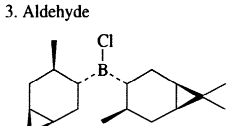
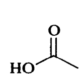
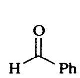
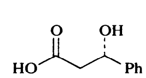
Reaction Conditions	Enolate Precursor	Aldehyde	Product(s) and Yield(s) (%), Isomer Ratio, % ee	Refs.
1. Acid, LDA, THF 2. (2-[d]Icr)$_2$BCl 3. Aldehyde			 R = Me, (90) >99% ee R = Et, (60) >99% ee	397
 4-[d]Icr				
1. Acid, LDA, THF 2. (4-[d]Icr)$_2$BCl 3. Aldehyde			 (50) 42% ee	397

TABLE IVA. CHIRAL ENOLATES (LIGAND CONTROL) WITH ACHIRAL ALDEHYDES (*Continued*)

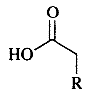
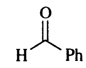
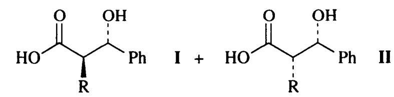
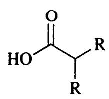
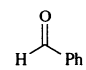
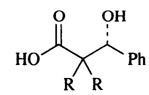
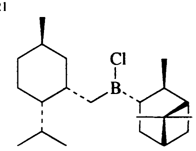
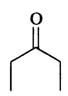
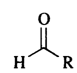
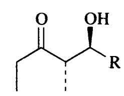
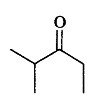
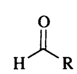
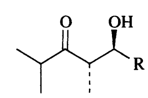
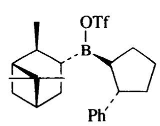
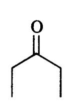
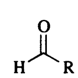
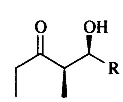
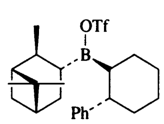
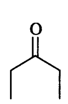
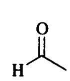
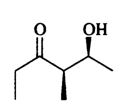
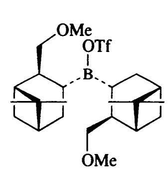
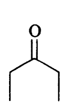
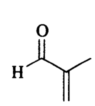
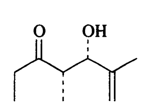
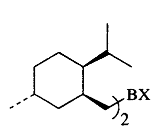
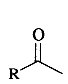
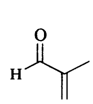
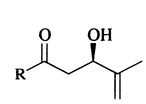
Reaction Conditions	Enolate Precursor	Aldehyde	Product(s) and Yield(s) (%), Isomer Ratio, % ee	Refs.
1. Acid, LDA, THF 2. (4-^{d}Icr)$_2$BCl 3. Aldehyde			 R / I:II Me (90) 87 (22% ee):13 (92% ee) Ph (68) 57 (52% ee):43 (>99% ee) SMe (82) 92 (61% ee):8 (>99% ee) OPh (70) 80 (80% ee):20 (96% ee)	397
1. Acid, LDA, THF 2. (4-^{d}Icr)$_2$BCl 3. Aldehyde			 R = Me, (90) 94% ee R = Et, (56) >99% ee	397
C_{21}  (+)-IpcB[(−)-(Menth)CH$_2$]Cl, Et$_3$N, Et$_2$O			 R = C(Me)=CH$_2$, (25-38) 70:30, 30% ee R = Ph, (25-38) 70:30, 18% ee	398
(+)-IpcB[(−)-(Menth)CH$_2$]Cl, Et$_3$N, Et$_2$O			 R = C(Me)=CH$_2$, (25-38) >98:2, 33% ee R = Ph, (25-38) >98:2, 41% ee	398
 (−)-IpcLBOTf, *i*-Pr$_2$NEt			 R / ratio / % ee Me (60) 97:3 52 C(Me)=CH$_2$ (52) 96:4 28 Pr (65) 97:3 46 *i*-Pr (36) 96:4 32	121
C_{22}  (−)-IpcLBOTf, *i*-Pr$_2$NEt			 (17) 97:3, 33% ee	121
 L$_2$BOTf, *i*-Pr$_2$NEt			 (45) 90% ee	121
 [(−)-(Menth)CH$_2$]$_2$BX [(−)-(Menth)CH$_2$]$_2$BCl, Et$_3$N, Et$_2$O			 R / %ee Me (65) 58 Et (51) 63^d *i*-Pr (66) 76 *i*-Bu (80) 55 *t*-Bu (62) 75 Ph (81) 69	161

TABLE IVA. CHIRAL ENOLATES (LIGAND CONTROL) WITH ACHIRAL ALDEHYDES (*Continued*)

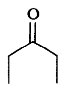
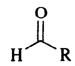
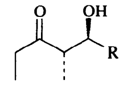
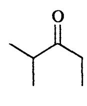
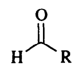
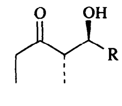
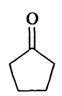
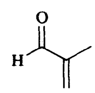
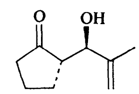
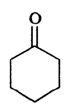
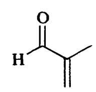
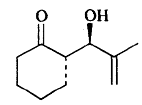
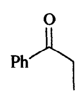
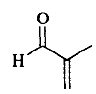
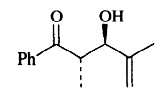
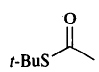
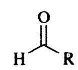
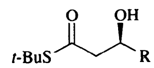
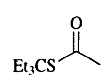
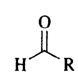
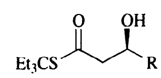
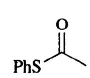
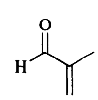
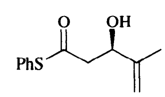
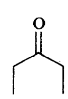
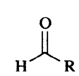
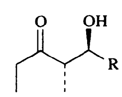
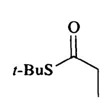
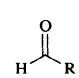
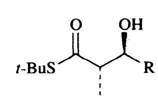
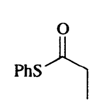
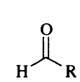
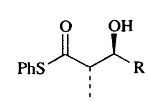
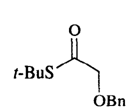
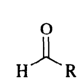
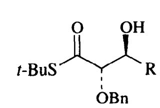
Reaction Conditions	Enolate Precursor	Aldehyde	Product(s) and Yield(s) (%), Isomer Ratio, % ee	Refs.
[(−)-(Menth)CH$_2$]$_2$BCl, Et$_3$N, Et$_2$O			 R = Et, (50) 92:8, 80% ee R = C(Me)=CH$_2$, (62) 93:7, 75% ee	161
[(−)-(Menth)CH$_2$]$_2$BCl, Et$_3$N, Et$_2$O			 R, ratio, % ee Et (50) 97:3 85 C(Me)=CH$_2$ (51) >99:1 88 C_6H_{11} (54) >99:1 74	161
[(−)-(Menth)CH$_2$]$_2$BCl, Et$_3$N, Et$_2$O			 (60) >99:1, 74% ee	161
[(−)-(Menth)CH$_2$]$_2$BCl, Et$_3$N, Et$_2$O			 (59) >99:1, 56% ee	161
[(−)-(Menth)CH$_2$]$_2$BCl, Et$_3$N, Et$_2$O			 (60) >99:1, 86% ee	161
[(−)-(Menth)CH$_2$]$_2$BBr, Et$_3$N, Et$_2$O, CH$_2$Cl$_2$			 R, % ee Pr (85) 94.0 *i*-Pr (75) 95.2 C(Me)=CH$_2$ (71) 87.2 Ph (68) 89.4 C_6H_{11} (88) 93.4 (CH$_2$)$_2$Ph (90) 96.6	162
[(−)-(Menth)CH$_2$]$_2$BBr, Et$_3$N, Et$_2$O, CH$_2$Cl$_2$			 R, % ee *i*-Pr (85) 94.8 C(Me)=CH$_2$ (60) 85.0 Ph (64) 86.0	162
[(−)-(Menth)CH$_2$]$_2$BBr, Et$_3$N, Et$_2$O, CH$_2$Cl$_2$			 (60) 60% ee	162
[(−)-(Menth)CH$_2$]$_2$BBr, Et$_3$N, Et$_2$O, CH$_2$Cl$_2$			 R, ratio, % ee C(Me)=CH$_2$ (55) 97.5:2.5 75 Ph (70) 90:10 72	162
[(−)-(Menth)CH$_2$]$_2$BBr, Et$_3$N, Et$_2$O, CH$_2$Cl$_2$			 R, ratio, % ee Pr (64) 97:3 98 *i*-Pr (61) 96:4 98 C(Me)=CH$_2$ (43) 94:6 98 Ph (69) 95:5 98 (*E*)-CH=CHPh (66) 97:3 98 (CH$_2$)$_2$Ph (57) 97:3 98	162
[(−)-(Menth)CH$_2$]$_2$BBr, Et$_3$N, Et$_2$O, CH$_2$Cl$_2$			 R, ratio, % ee C(Me)=CH$_2$ (68) 80:20 98 Ph (65) 74:26 98	162
[(−)-(Menth)CH$_2$]$_2$BBr, Et$_3$N, Et$_2$O, CH$_2$Cl$_2$			 R, ratio, % ee Pr (57) 97:3 95.2 *i*-Pr (50-60) 97:3 95.4 C(Me)=CH$_2$ (78) 98:2 95.6 Ph (65) 97:3 94	163

TABLE IVA. CHIRAL ENOLATES (LIGAND CONTROL) WITH ACHIRAL ALDEHYDES (*Continued*)

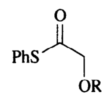
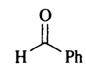
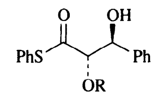
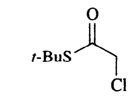
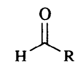
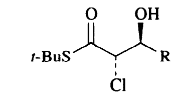
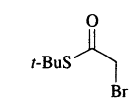
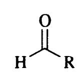
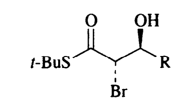
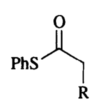
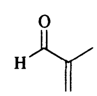
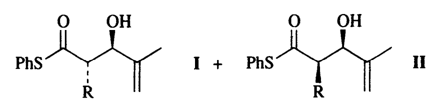
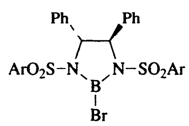
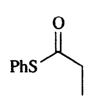
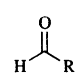
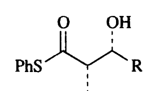
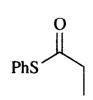
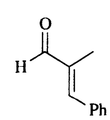
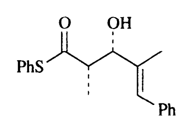
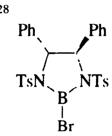
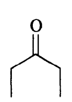
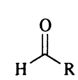
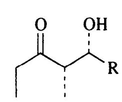
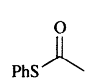
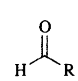
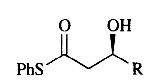
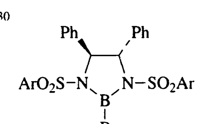
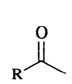
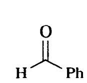
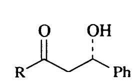
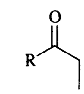
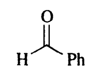
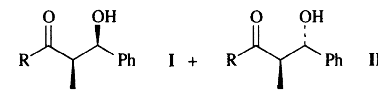
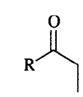
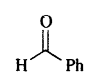
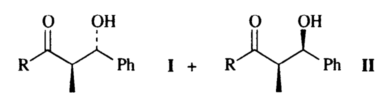
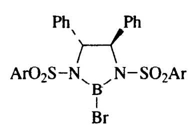
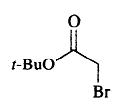
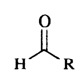
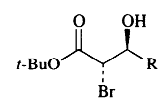
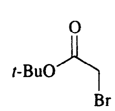
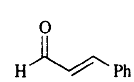
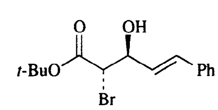
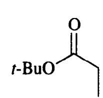
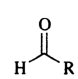
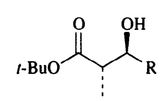
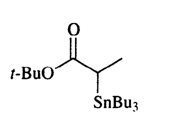
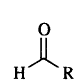
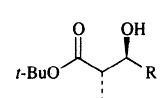
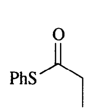
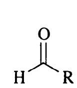
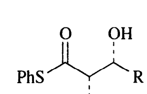
Reaction Conditions	Enolate Precursor	Aldehyde	Product(s) and Yield(s) (%), Isomer Ratio, % ee	Refs.
[(−)-(Menth)CH_2]$_2$BBr, Et_3N, Et_2O, CH_2Cl_2			 R / ratio / % ee Bn (40-50) >99:1 96 TBS (79) >99:1 97	163
[(−)-(Menth)CH_2]$_2$BBr, Et_3N, Et_2O, CH_2Cl_2			 R / ratio / % ee Pr (73) 96:4 94.6 *i*-Pr (70) 96:4 94 Ph (65) 91:9 >98	163
[(−)-(Menth)CH_2]$_2$BBr, Et_3N, Et_2O, CH_2Cl_2			 R / ratio / % ee Pr (45) >99:1 >98 *i*-Pr (55) 97:3 >98 Ph (40-50) 97:3 >98	163
[(−)-(Menth)CH_2]$_2$BBr, Et_3N, Et_2O, CH_2Cl_2			 I + II R = Cl, (55) I:II = 52 (92.6% ee):48 (90% ee) R = Br, (55) I:II = 80 (92% ee):20 (86% ee)	163 163
C_{26}  Ar = *p*-$O_2NC_6H_4$				
L_2BBr, *i*-Pr_2NEt			 R / ratio / % ee *i*-Pr (72) 95:5 97 Ph (70) 98:2 95	170, 169
L_2BBr, *i*-Pr_2NEt			 (54)[g]	194
C_{28} 				
L_2BBr, *i*-Pr_2NEt			 R = Et, (91) >98% ee R = *i*-Pr, (85) 95% ee R = Ph, (95) 97% ee	170, 169
L_2BBr, *i*-Pr_2NEt			 R = *i*-Pr, (82) 83% ee R = Ph, (84) 91% ee	170
C_{30}  Ar = 3,5-$(CF_3)_2C_6H_3$				
L_2BBr, *i*-Pr_2NEt			 R = OBu-*t*, (73) 80% ee R = SBu-*t*, (82) 73% ee R = SBu-*t*, (94) 52% ee[e] R = SPh, (82) 64% ee	168

TABLE IVA. CHIRAL ENOLATES (LIGAND CONTROL) WITH ACHIRAL ALDEHYDES (*Continued*)

Reaction Conditions	Enolate Precursor	Aldehyde	Product(s) and Yield(s) (%), Isomer Ratio, % ee	Refs.
L_2BBr, *i*-Pr_2NEt				168
			R / (yield) / I:II / % ee OBu-*t* (89) 4:96 94 SBu-*t* (73) 71:29 50 SPh (90) 99:1 97 OBn (73) 84:16 97 SBn (79) 70:30 81	
L_2BBr, Et_3N, toluene, hexane				168
			R / (yield) / I:II / % ee OBu-*t* (64) 98:2 94 SBu-*t* (86) 94:6 46 SPh (78) 6:94 95 OBn (78) 85:15 97 SBn (84) 91:9 94	
 Ar = 3,5-$(CF_3)_2C_6H_3$				
				
			R / (yield) / I:II / % ee	
L_2BBr, Et_3N, toluene			*i*-Pr (90) 98:2 92	167
L_2BBr, Et_3N, CH_2Cl_2			Ph (86) 98:2 96	166
L_2BBr, Et_3N, toluene			Ph (94) 99:1 98	166
L_2BBr, Et_3N, toluene			C_6H_{11} (65) 98:2 91	166
L_2BBr, Et_3N, CH_2Cl_2			$(CH_2)_2Ph$ (70) 92:8 74	166
L_2BBr, Et_3N, toluene			$(CH_2)_2Ph$ (72) 95:5 91	166
L_2BBr, Et_3N, toluene			 (96) 99:1, 98% ee	166
L_2BBr, Et_3N, toluene, hexane			 R / (yield) / ratio / % ee Ph (93) 98:2 94[f] C_6H_{11} (82) 94:6 75 (*E*)-CH=CHPh (81) 99:1 98[f]	19, 169 19 19
L_2BBr, Et_3N, toluene, hexane			 R / (yield) / ratio / % ee Ph (80) 97:3 93 C_6H_{11} (72) 92:8 71 (*E*)-CH=CHPh (89) 96:4 96	399
L_2BBr, *i*-Pr_2NEt			 R / (yield) / ratio / % ee Ph (93) 99:1 97 C_6H_{11} (86) 98:2 91 $(CH_2)_2Ph$ (79) 98:2 83	19, 169 19 19

[a] This reaction was performed in toluene.

[b] The configuration of the product from this reaction would suggest that the enantiomeric reagent (–)-Ipc_2BCl was used.

[c] Arbitrary assignment of the syn-configuration was made.

[d] This reaction was performed in CH_2Cl_2.

[e] This reaction was performed in toluene/hexane and using Et_3N as base.

[f] This reaction was also performed in CH_2Cl_2 as solvent giving similar results.

[g] The enantiomeric excess of this product was not reported.

TABLE IVB. CHIRAL ENOLATES (LIGAND CONTROL) WITH CHIRAL ALDEHYDES

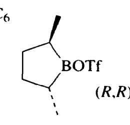
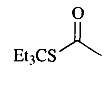
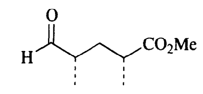
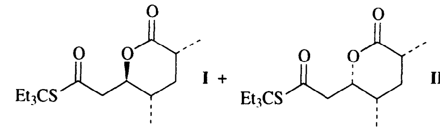
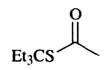
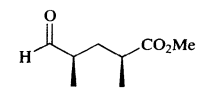
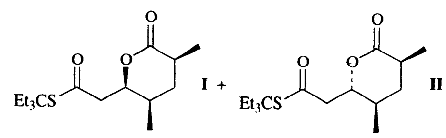
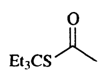
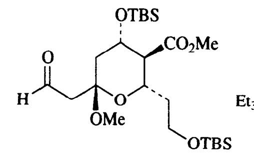
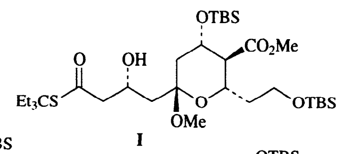
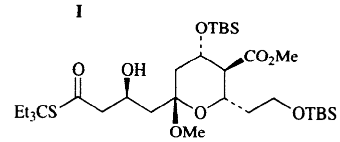
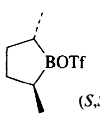
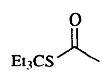
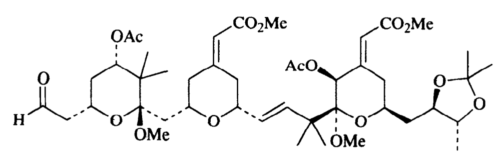
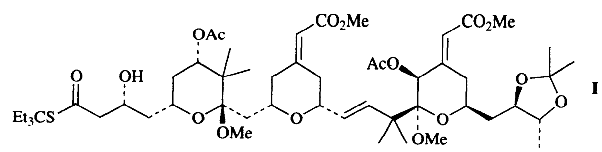
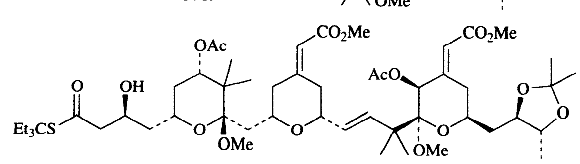
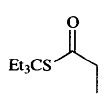
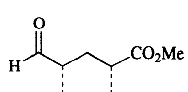
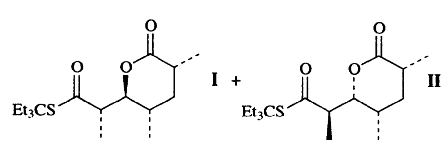
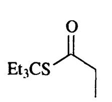
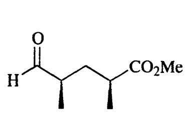
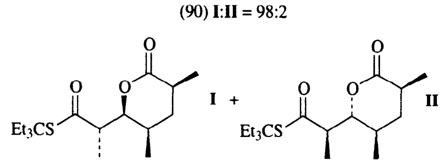
Reaction Conditions	Enolate Precursor	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
C_6  (R,R)-L_2BOTf				
1. (R,R)-L_2BOTf, i-Pr_2NEt, Et_2O 2. CF_3CO_2H			 (81) I:II = 91:9	157, 153
1. (R,R)-L_2BOTf, i-Pr_2NEt, Et_2O 2. CF_3CO_2H			 (83) I:II = 86:14	157, 153
			 I +  II	158
(S,S)-L_2BOTf, i-Pr_2NEt, Et_2O			(88-93) I:II = 91:9	
(R,R)-L_2BOTf, i-Pr_2NEt, Et_2O			(88-93) I:II = 11:89	
 (S,S)-L_2BOTf				
(S,S)-L_2BOTf, i-Pr_2NEt, Et_2O			 I +  II (>83) I:II = 75:25	160
1. (R,R)-L_2BOTf, i-Pr_2NEt, Et_2O 2. CF_3CO_2H			 (90) I:II = 98:2	157, 153
1. (R,R)-L_2BOTf, i-Pr_2NEt, Et_2O 2. CF_3CO_2H			 (83) I:II = 96:4	157, 153

TABLE IVB. CHIRAL ENOLATES (LIGAND CONTROL) WITH CHIRAL ALDEHYDES (*Continued*)

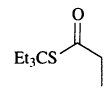
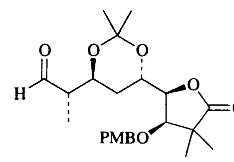
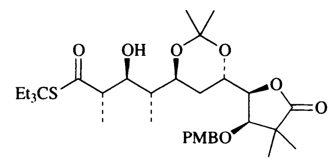
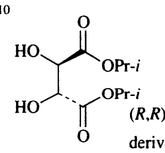
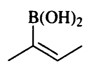
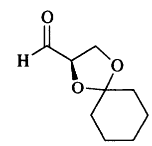
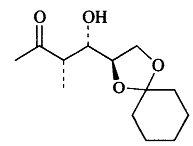
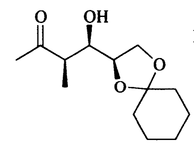
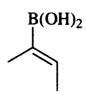
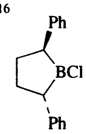
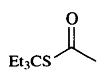
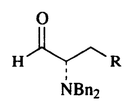
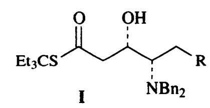
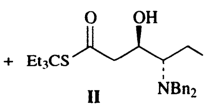
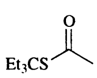
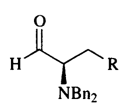
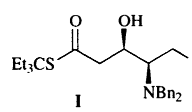
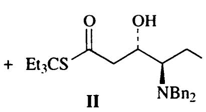
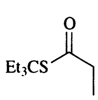
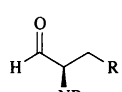
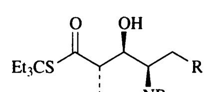
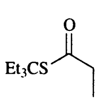
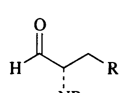
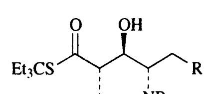
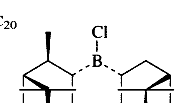
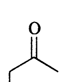
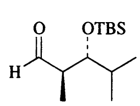
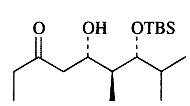
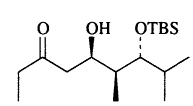
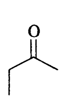
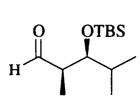
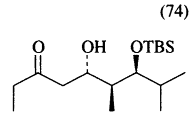
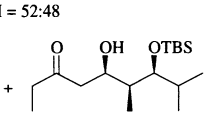
Reaction Conditions	Enolate Precursor	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
(*R,R*)-L_2BOTf, *i*-Pr_2NEt, Et_2O			 (82) 92:8	240
C_{10}  (*R,R*)-tartrate derived				
1. Boronic acid, diol 2. Me_3NO 3. Aldehyde			 I +  II (*R,R*)-tartrate, (55) I:II = 99:1 (*S,S*)-tartrate, (46) I:II = 80:20	177
		"	I + II (*R,R*)-tartrate, (54) I:II = 99:1 (*S,S*)-tartrate, (48) I:II = 68:32	177
C_{16}  (*S,S*)-L_2BCl				
(*S,S*)-L_2BCl, *i*-Pr_2NEt (*R,R*)-L_2BCl, *i*-Pr_2NEt			 I +  II R = *i*-Pr, (85) I:II = 6:94 R = Ph, (50) I:II = 97:3	155
(*S,S*)-L_2BCl, *i*-Pr_2NEt (*R,R*)-L_2BCl, *i*-Pr_2NEt			 I +  II R = *i*-Pr, (80) I:II = 7:93 R = Ph, (65) I:II = 96:4	155
(*S,S*)-L_2BCl, *i*-Pr_2NEt			 R = *i*-Pr, (—) 95:5 R = Ph, (—) 93:7	155
(*S,S*)-L_2BCl, *i*-Pr_2NEt			 R = *i*-Pr, (—) >99:1 R = Ph, (—) 98:2	155
C_{20}  (–)-$(Ipc)_2BCl$				
(+)-$(Ipc)_2BCl$, Et_3N, Et_2O (–)-$(Ipc)_2BCl$, Et_3N, Et_2O $(C_6H_{11})_2BCl$, Et_3N, Et_2O			 I +  II (43) I:II = 95:5 (33) I:II = 29:71 (74) I:II = 52:48	34
(+)-$(Ipc)_2BCl$, Et_3N, Et_2O (–)-$(Ipc)_2BCl$, Et_3N, Et_2O $(C_6H_{11})_2BCl$, Et_3N, Et_2O			 I +  II (44) I:II = 73:21 (70) I:II = 5:95 (83) I:II = 24:76	34

TABLE IVB. CHIRAL ENOLATES (LIGAND CONTROL) WITH CHIRAL ALDEHYDES (*Continued*)

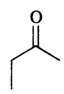
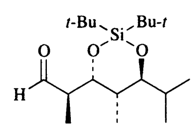
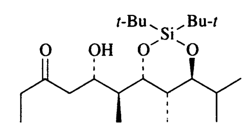
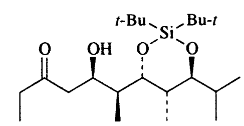
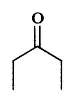
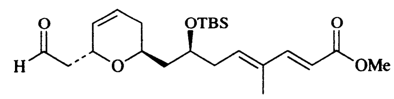
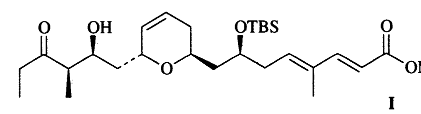
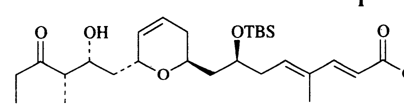
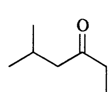
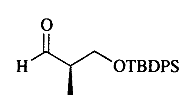
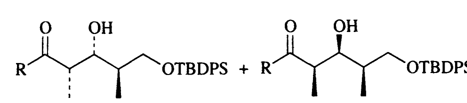
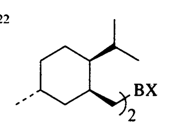
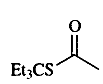
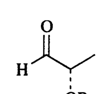
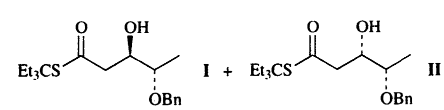
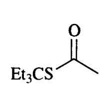
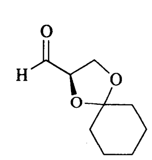
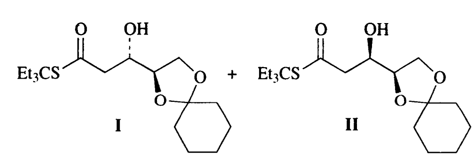
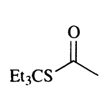
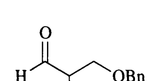
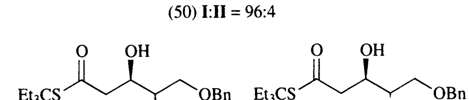
Reaction Conditions	Enolate Precursor	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
			 I +  II	34, 35
(+)-(Ipc)$_2$BCl, Et$_3$N, Et$_2$O			(75) I:II = >95:5	
(–)-(Ipc)$_2$BCl, Et$_3$N, Et$_2$O			(40) I:II = 77:23	
(C$_6$H$_{11}$)$_2$BCl, Et$_3$N, Et$_2$O			(81) I:II = 70:30	
(+)-(Ipc)$_2$BOTf, *i*-Pr$_2$NEt			 I + I  II (37) I:II = 75:25	34, 35
(–)-(Ipc)$_2$BOTf, *i*-Pr$_2$NEt			 I + II R = *i*-Bu (30), I:II = 67:33	180
C$_{22}$  [(–)-(Menth)CH$_2$]$_2$BX				
			 I + II	164
[(–)-(Menth)CH$_2$]$_2$BBr, Et$_3$N, Et$_2$O			(75) I:II = 93:7	
[(+)-(Menth)CH$_2$]$_2$BBr, Et$_3$N, Et$_2$O			(65) I:II = 6:94	
			 I + II	164
[(–)-(Menth)CH$_2$]$_2$BBr, Et$_3$N, Et$_2$O			(45) I:II = 3:97	
[(+)-(Menth)CH$_2$]$_2$BBr, Et$_3$N, Et$_2$O			(50) I:II = 96:4	
[(–)-(Menth)CH$_2$]$_2$BBr, Et$_3$N, Et$_2$O		 racemic	 I II (70) I:II = 50:50[a]	164

TABLE IVB. CHIRAL ENOLATES (LIGAND CONTROL) WITH CHIRAL ALDEHYDES (*Continued*)

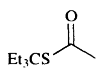
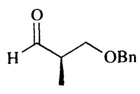
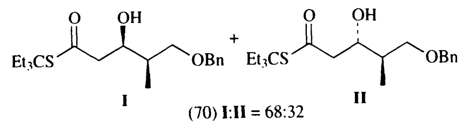
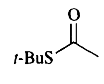
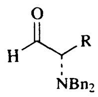
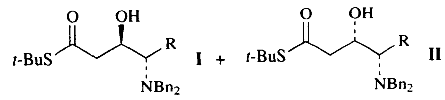
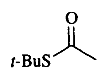
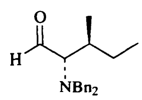
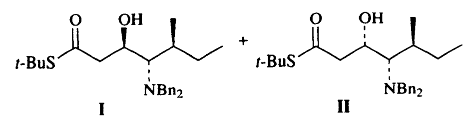
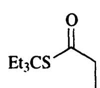
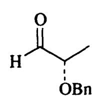
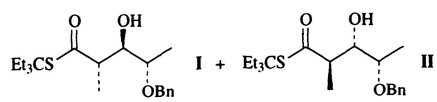
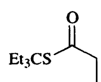
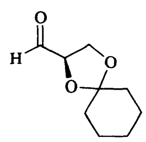
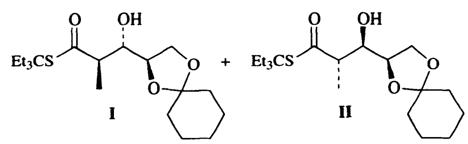
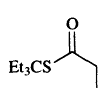
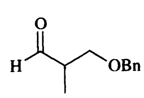
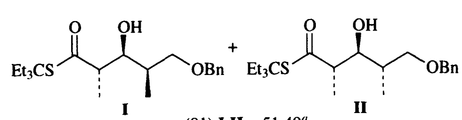
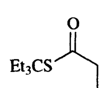
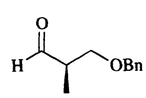
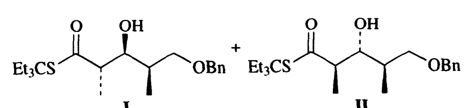
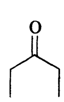
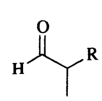
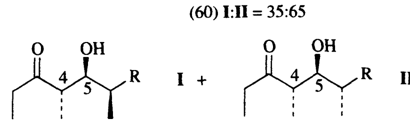
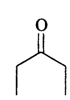
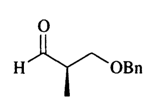
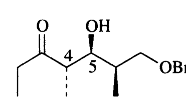
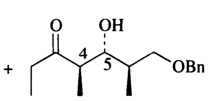
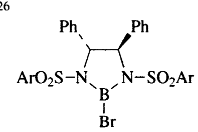
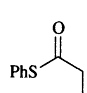
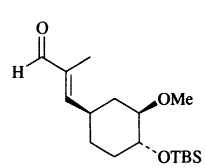
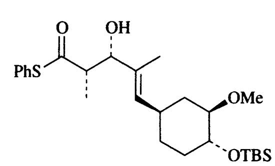
Reaction Conditions	Enolate Precursor	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
				164
[(−)-(Menth)CH_2]$_2$BBr, Et_3N, Et_2O			(70) I:II = 68:32	
[(+)-(Menth)CH_2]$_2$BBr, Et_3N, Et_2O			(60) I:II = 4:96	
				165
			R (yield) I:II	
[(−)-(Menth)CH_2]$_2$BBr, Et_3N, Et_2O			Me (80) 98.5:1.5	
[(+)-(Menth)CH_2]$_2$BBr, Et_3N, Et_2O			Me (75) 3.7:96.3	
[(−)-(Menth)CH_2]$_2$BBr, Et_3N, Et_2O			*i*-Pr (80) >99:1	
[(+)-(Menth)CH_2]$_2$BBr, Et_3N, Et_2O			*i*-Pr (72) 3.5:96.5	
[(−)-(Menth)CH_2]$_2$BBr, Et_3N, Et_2O			*i*-Bu (78) >99:1	
[(+)-(Menth)CH_2]$_2$BBr, Et_3N, Et_2O			*i*-Bu (71) 2.5:97.5	
[(−)-(Menth)CH_2]$_2$BBr, Et_3N, Et_2O			Bn (75) 98.6:1.4	
[(+)-(Menth)CH_2]$_2$BBr, Et_3N, Et_2O			Bn (70) 3.2:96.8	
				165
[(−)-(Menth)CH_2]$_2$BBr, Et_3N, Et_2O			(75) I:II = 98.2:1.8	
[(+)-(Menth)CH_2]$_2$BBr, Et_3N, Et_2O			(71) I:II = 4.6:95.4	
				164
[(−)-(Menth)CH_2]$_2$BBr, Et_3N, Et_2O			(65) I:II = 99:1	
[(+)-(Menth)CH_2]$_2$BBr, Et_3N, Et_2O			(60) I:II = 1:99	
				164
[(−)-(Menth)CH_2]$_2$BBr, Et_3N, Et_2O			(45) I:II = 5:95	
[(+)-(Menth)CH_2]$_2$BBr, Et_3N, Et_2O			(50) I:II = 99:1	
[(−)-(Menth)CH_2]$_2$BBr, Et_3N, Et_2O		 racemic	 (81) I:II = 51:49[a]	164
				164
[(−)-(Menth)CH_2]$_2$BBr, Et_3N, Et_2O			(60) I:II = 95:5	
[(+)-(Menth)CH_2]$_2$BBr, Et_3N, Et_2O			(60) I:II = 35:65	
[(−)-(Menth)CH_2]$_2$BBr, Et_3N, Et_2O		 racemic	 R = CH_2OBn (68), I:II:4,5-*syn* = 62:33:5[a]; R = Ph, (75) I:II:4,5-*syn* = 86:4:10, 25% ee	164

TABLE IVB. CHIRAL ENOLATES (LIGAND CONTROL) WITH CHIRAL ALDEHYDES (*Continued*)

Reaction Conditions	Enolate Precursor	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
			 I +  II	164
[(−)-(Menth)CH_2]$_2$BBr, Et_3N, Et_2O			(72) **I:II:4,5-syn** = 71:24:5	
[(+)-(Menth)CH_2]$_2$BBr, Et_3N, Et_2O			(64) **I:II:4,5-syn** = 37:55:8	
C_{26}				
 Ar = 3,5-$(O_2N)_2C_6H_3$				
(*S,S*)-L_2BBr, *i*-Pr_2NEt			 (85) 96:4	195

[a] No assessment of the enantiomeric purity of these products was given.

TABLE VA. CHIRAL ENOLATES (LIGAND AND SUBSTRATE CONTROL) WITH ACHIRAL ALDEHYDES

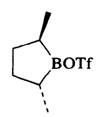
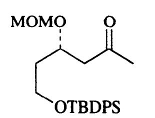
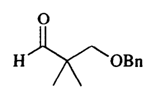
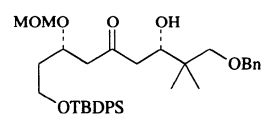
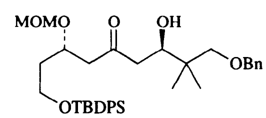
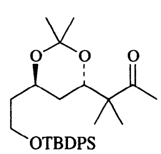
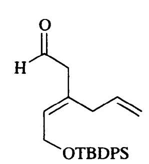
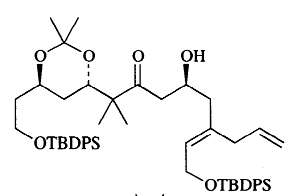
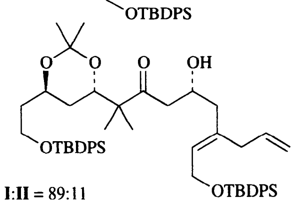
Reaction Conditions	Enolate Precursor	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
C_6 			 I +  II	159, 153
(*S*,*S*)-L_2BOTf, *i*-Pr_2NEt, pentane, Et_2O			(87) I:II = 80:20	
(*R*,*R*)-L_2BOTf, *i*-Pr_2NEt, pentane, Et_2O			(—) I:II = 20:80	
			 I +  II	178, 160
(*R*,*R*)-L_2BOTf, *i*-Pr_2NEt, pentane, Et_2O			(86) I:II = 89:11	
(*S*,*S*)-L_2BOTf, *i*-Pr_2NEt, pentane, Et_2O			(80-90) I:II = 33:67	

TABLE VA. CHIRAL ENOLATES (LIGAND AND SUBSTRATE CONTROL) WITH ACHIRAL ALDEHYDES (*Continued*)

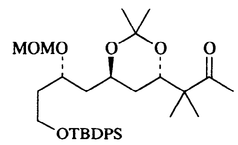
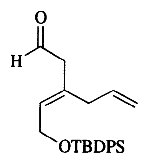
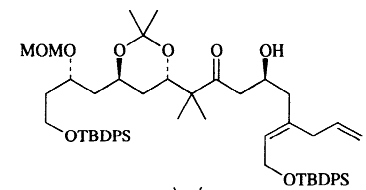
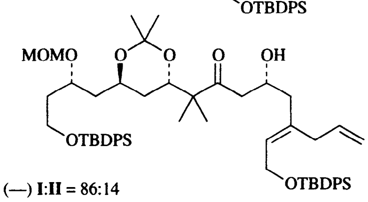
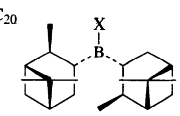
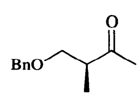
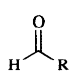
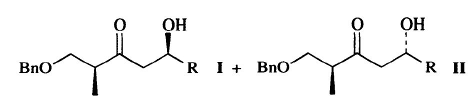
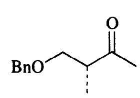
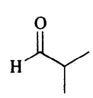
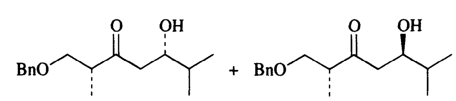
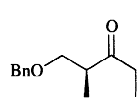
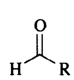
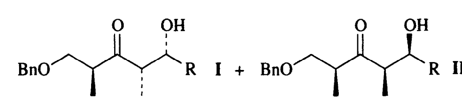
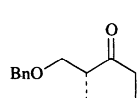
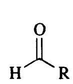
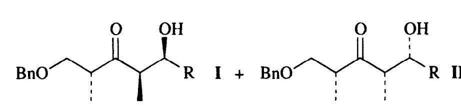
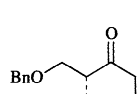
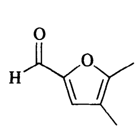
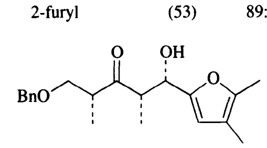
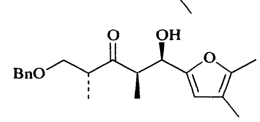
Reaction Conditions	Enolate Precursor	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
			 I +  II	159, 153
(R,R)-L_2BOTf, i-Pr_2NEt, pentane, Et_2O			(—) I:II = 86:14	
(S,S)-L_2BOTf, i-Pr_2NEt, pentane, Et_2O			(86) I:II = 33:67	
C_{20}  (−)-$(Ipc)_2BX$				
(−)-$(Ipc)_2BOTf$, i-Pr_2NEt				120
			R: $C(Me{=}CH_2$ (84) I:II 93:7	
			R: Pr (74) I:II 92:8	
			R: Ph (77) I:II 84:16	
(+)-$(Ipc)_2BCl$, Et_3N Et_2O			 I (91) I:II = 95:5 II	151
	 97% ee			
(−)-Ipc_2BOTf, i-Pr_2NEt			R: Me (65) I:II 92:8	119
(−)-Ipc_2BOTf, i-Pr_2NEt			R: (E)-CH=CHMe (73) I:II 89:11	278, 119, 122
(−)-Ipc_2BOTf, i-Pr_2NEt			R: $C(Me)=CH_2$ (62) I:II 93 (>99% ee):7 (64% ee)	119
(+)-Ipc_2BOTf, i-Pr_2NEt			R: $C(Me)=CH_2$ (74) I:II 7 (64% ee):93 (>99% ee)	119, 278, 122
(−)-Ipc_2BOTf, i-Pr_2NEt			R: 2-furyl (60) I:II 92:8	119
(+)-Ipc_2BOTf, i-Pr_2NEt			R: 2-furyl (64) I:II 10:90	119
	 84% ee			119
(−)-Ipc_2BOTf, i-Pr_2NEt			R: $C(Me)=CH_2$ (74) I:II 13 (9% ee): 87 (99% ee)	
(−)-Ipc_2BOTf, i-Pr_2NEt			R: 2-furyl (81) I:II 14:86	
(+)-Ipc_2BOTf, i-Pr_2NEt			R: 2-furyl (53) I:II 89:11	
(−)-Ipc_2BOTf, Et_3N			 I + (63) I:II = 89:11  II	400

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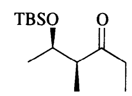
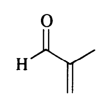
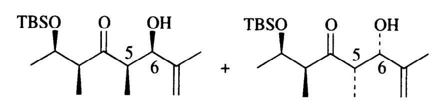
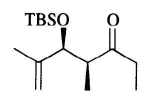
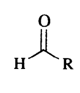
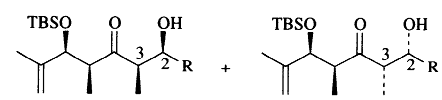
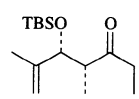
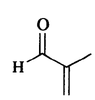
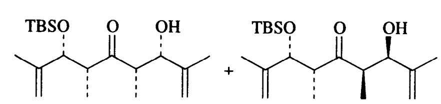
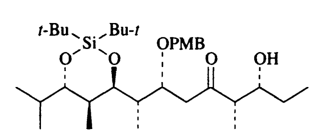
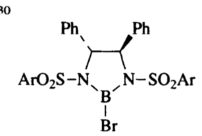
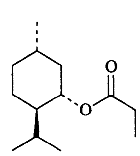
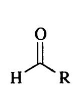
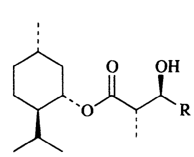
TABLE VA. CHIRAL ENOLATES (LIGAND AND SUBSTRATE CONTROL) WITH ACHIRAL ALDEHYDES (*Continued*)

Reaction Conditions	Enolate Precursor	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
	 82% ee		 I + II	130
(+)-Ipc_2BOTf, Et_3N			(62) **I:II:5,6-anti** = 91:3:6	
(−)-Ipc_2BOTf, Et_3N			(67) **I:II:5,6-anti** = 72:21:7	
	 90% ee		 I + II	
(+)-Ipc_2BOTf, Et_3N			R = Me, (65) **I:II:2,3-anti** = 94:2:4	130
(−)-Ipc_2BOTf, Et_3N			R = Me, (67) **I:II:2,3-anti** = 72:24:4	130
(+)-Ipc_2BOTf, Et_3N			R = C(Me)=CH_2, (79) **I:II** = 98:2	131
(−)-Ipc_2BOTf, Et_3N			R = C(Me)=CH_2, (—) **I:II** = 69:31	131
	 racemic	 0.5 equiv	 I + II	131, 132
(−)-Ipc_2BOTf, Et_3N			(34) **I:II** = 97:3, 89% ee	
(+)-Ipc_2BOTf, Et_3N			(36) **ent-I:ent-II** = 98:2, 95% ee	
			 II	
(+)-Ipc_2BOTf, i-Pr_2NEt			(42) **I:II** = 88:12	
(−)-Ipc_2BOTf, i-Pr_2NEt			(49) **I:II** = 8:92	
C_{30}  Ar = 3,5-$(CF_3)_2C_6H_3$				
L_2BBr, Et_3N, toluene, hexane			 R = C_6H_{11}, (91) 93:7[a]; R = $(CH_2)_2Ph$, (83) 97:3[a]	19

[a] This reaction was also repeated in CH_2Cl_2 with similar results.

TABLE VB. CHIRAL ENOLATES (LIGAND AND SUBSTRATE CONTROL) WITH CHIRAL ALDEHYDES

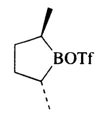
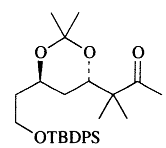
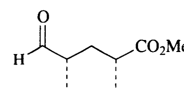
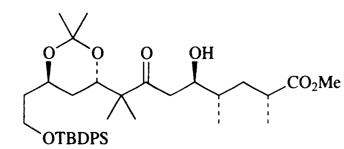
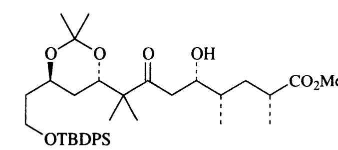
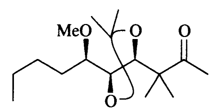
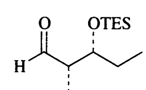
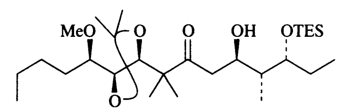
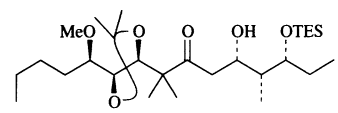
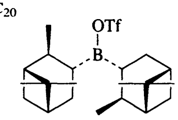
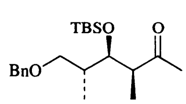
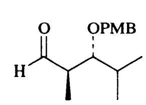
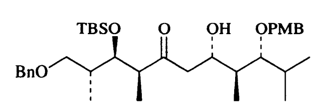
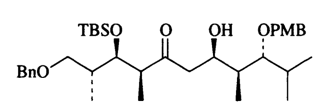
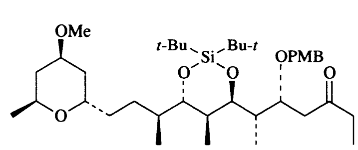
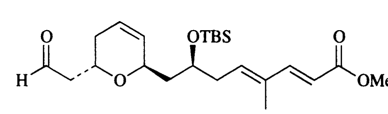
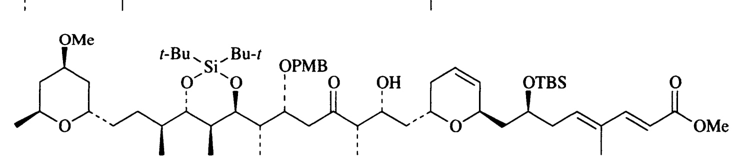
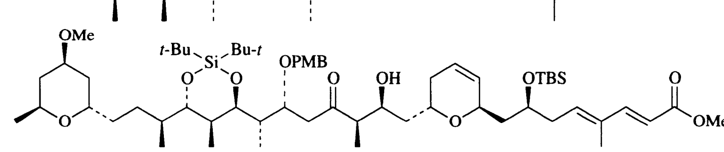
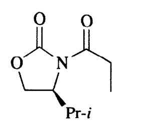
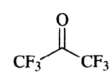
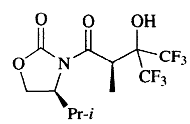
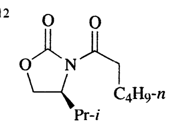
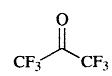
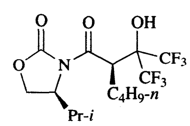
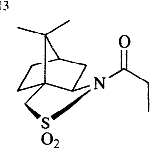
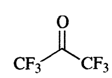
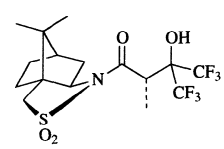
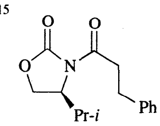
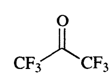
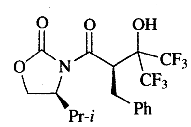
Reaction Conditions	Enolate Precursor	Aldehyde	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
C_6				
 (*R*,*R*)-L_2BOTf			 **I** +  **II**	178
(*R*,*R*)-L_2BOTf, *i*-Pr_2NEt			(94) **I**:**II** = 96:4	
(*S*,*S*)-L_2BOTf, *i*-Pr_2NEt			(92) **I**:**II** = 50:50	
			 **I** +  **II**	178
(*R*,*R*)-L_2BOTf, *i*-Pr_2NEt			(84) **I**:**II** = 95:5	
(*S*,*S*)-L_2BOTf, *i*-Pr_2NEt			(81) **I**:**II** = 67:33	
C_{20}				
 (−)-$(Ipc)_2$BOTf				
(−)-$(Ipc)_2$BOTf, Et_3N			 **I** +  **II**	179
			(72) **I**:**II** = 67:33	
			 **I** +  **II**	
(+)-$(Ipc)_2$BOTf, *i*-Pr_2NEt			(16) **I**:**II** = 50:50	35

TABLE VI. CHIRAL ENOLATES (AUXILIARY CONTROL) WITH KETONES

Enolate Precursor	Reaction Conditions	Ketone	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
C_6 	Bu_2BOTf, Et_3N		 (90) >99:1	107
C_{12} 	Bu_2BOTf, Et_3N		 (88) 95:5	107
C_{13} 	Bu_2BOTf, Et_3N		 (93)	100
C_{15} 	Bu_2BOTf, Et_3N		 (86) >99:1	107

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End Notes

To simplify discussion, (*Z*)- and (*E*)- enolates are assigned whereby the oxygen–metal substituent is designated a higher priority than R^1 (see Eqs. 3 and 4).

*

* The yield and selectivity of this reaction are improvements over the published procedure (see Experimental Procedures for details). (120,151)

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The Catalyzed α -Hydroxyalkylation and α -Aminoalkylation of Activated Olefins (The Morita—Baylis—Hillman Reaction)

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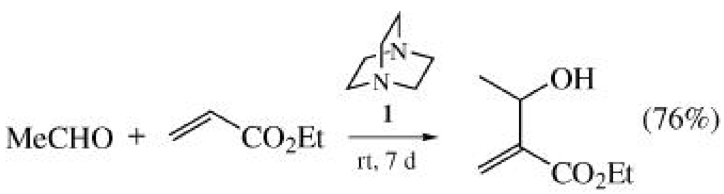
1. Introduction

In a patent application published in 1972, Baylis and Hillman reported the reaction of acetaldehyde with ethyl acrylate and acrylonitrile in the presence of catalytic amounts of 1,4-diazabicyclo[2.2.2]octane (DABCO; **1**) to give the α -hydroxyethylated products in good yields (Eq. 1). (1) No structure proof was

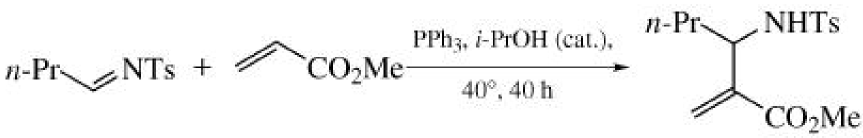


(1)

given. (2) The assignment eventually was shown to be correct, but since the initial disclosure was not followed by a journal publication, this remarkably simple, atom-efficient, and useful reaction was ignored for a number of years, (3-5) and it has been only fairly recently that its potential has begun to be explored. The transformation is now commonly referred to as the Baylis—Hillman reaction. This is unfortunate because credit for its invention clearly belongs to Morita, (6) who five years earlier, in patents (7-16) and a brief paper (17) reported the same reaction with the exception that tertiary phosphines were used as the catalysts; he also proposed the currently accepted mechanism. Baylis and Hillman made reference to Morita's work in their patent application. (1) It is true that tertiary amines in general are cheaper, less toxic, and more readily removed than tertiary phosphines. However, the latter sometimes give higher yields in shorter reaction times, and there are a number of examples where they are the only useful catalysts (see Tables VIII and XII).

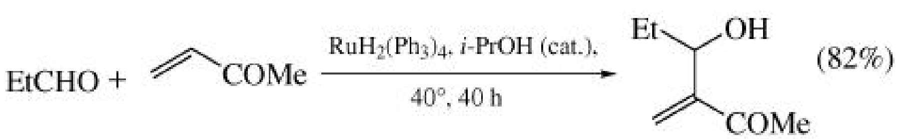
The DABCO-catalyzed reaction is slow, and reaction times at room temperature of days or even weeks are common. Attempts to remedy this situation by use of other amine catalysts, change of reaction temperature, high pressure, or microwave irradiation have been partially successful. Activated olefins other than acrylonitrile and acrylic esters that have now been shown to undergo the reaction include α , β -unsaturated aldehydes and ketones, vinyl sulfoxides, vinyl sulfones, vinylsulfonates, and vinylphosphonates. β

-Substituted activated olefins do not normally react. Among electrophiles other than aldehydes, unactivated ketones undergo the Morita— Baylis— Hillman reaction only under high pressure, but activation such as in α -halo ketones, α -keto esters, α -keto lactones, and nonenolizable α -diketones often produces very reactive substrates. Imines also can be employed, provided they carry a sufficiently electronegative group on nitrogen (Eq. 2). (18)



(2)

This review covers *catalyzed* α -hydroxyalkylations and α-aminoalkylations of activated olefins. Transition metal catalyzed reactions of this type, such as the



(3)

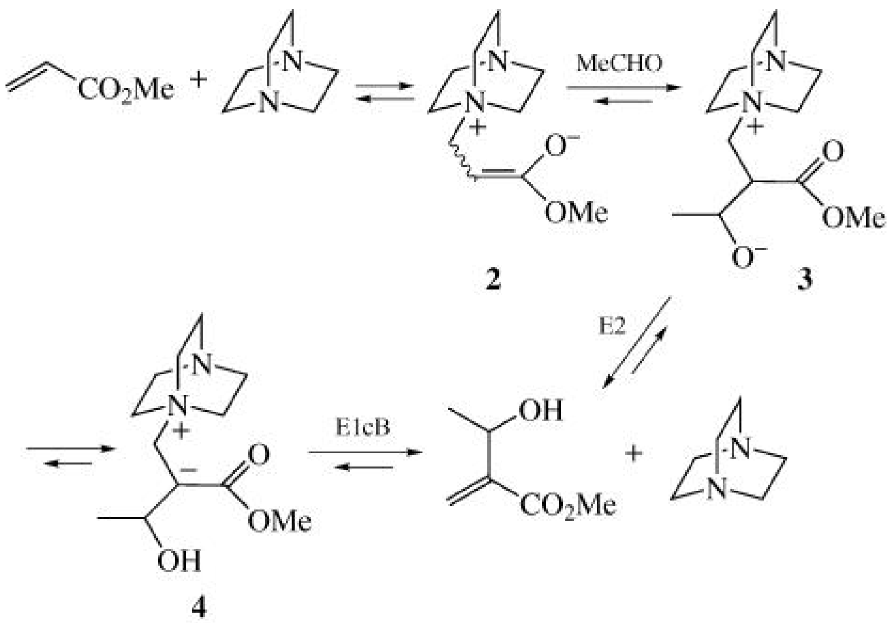
one illustrated in Eq. 3, (19) are also included even though they proceed by a different mechanism. Transformations that require stoichiometric amounts of reagents or more than one step are summarized in the section on Comparison With Other Methods but are not included in the Tabular Survey. The Morita–Baylis–Hillman reaction has been reviewed before. (20-22)

1.1.1. Warning
Development of severe contact dermatitis has been reported after exposure to the reaction products of formaldehyde with methyl acrylate (23) and of aldehydes with aryl acrylates. (24) Until the scope of this problem is determined, special precautions should be taken in handling all products of this type.

2. Mechanism and Catalysts

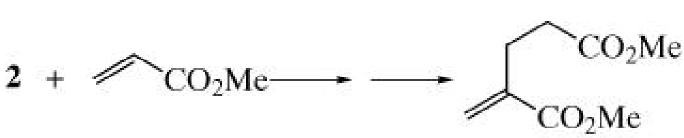
2.1. Amine-catalyzed Reactions

The generally accepted mechanism (5, 20, 25-28) is illustrated for the DABCO-catalyzed reaction of acetaldehyde with methyl acrylate in Eq. 4. Addition of the



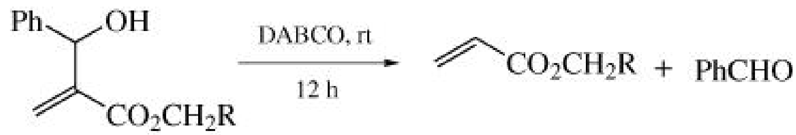
(4)

catalyst to the activated olefin furnishes zwitterion **2**, which reacts with the electrophile to give zwitterion **3**. Base-assisted *anti* E2 elimination (5) of the catalyst followed by protonation completes the reaction. Alternatively, internal proton transfer to give zwitterion **4** may precede E1cB elimination. Indications that both paths may operate stem from a study of the pressure and solvent dependence of the reaction of benzaldehyde with crotononitrile. (28) Protonation of zwitterion **3** by an external proton donor is yet another possible path, evidence for which is presented below. Addition of the activated olefin to zwitterion **2** to give the head-to-tail dimer (Eq. 5) is a problem only with very reactive activated olefins such as



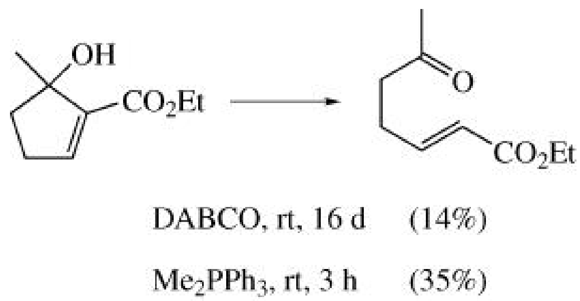
(5)

aryl vinyl ketones (see the section on Side Reactions in Scope and Limitations). The Morita–Baylis–Hillman reaction has been shown to be reversible in a number of cases (Eqs. 6, (27, 29) 7, (29) and 8 (30)). All involve acrylates, which are among the

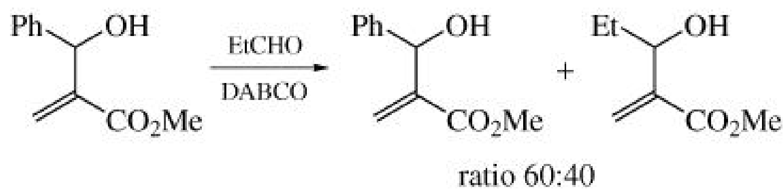


R	Time	I (%)
Et	6 d	(13)
$CHCl_2$	12 h	(19)
CF_3	12 h	(25)
CCl_3	12 h	(20)

(6)



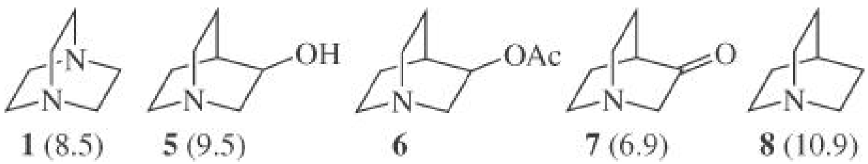
(7)



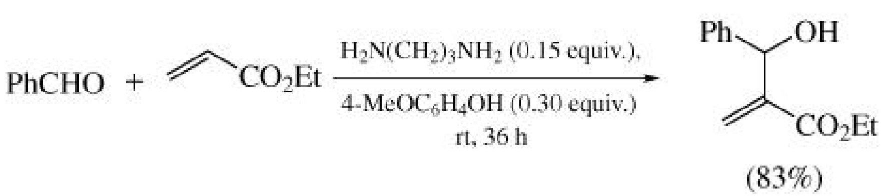
(8)

least reactive substrates in the forward reaction; whether additions to the more reactive activated olefins such as acrylonitrile or α , β -unsaturated ketones are also reversible remains to be established. The adduct of benzaldehyde to crotononitrile is stable for at least two days in the presence of DABCO at ambient or elevated pressure, but this may be due to steric hindrance of the reverse reaction. (28) The reaction is first order each in substrates and catalyst. (26, 31) There is no difference in the rates of the reactions of acetaldehyde with α -protio and α -deuterioacrylonitrile. (26) The third step, proton transfer in zwitterion **3**, thus occurs after the rate-determining step; the absence of an isotope effect also excludes the remote possibility, (30) at least in this case, that the first step is formation of a vinyl anion by abstraction of the α proton by the catalyst. The second step, attack of the electrophile on zwitterion **2**, is thus considered to be rate determining. None of the intermediates in Eq. 4 has been detected spectroscopically, (30) but indirect evidence for zwitterion **4** has been reported (Eq. 74). (32) No radical species indicative of an electron-transfer mechanism were detected by esr spectroscopy in the reaction of 4-pyridinecarboxaldehyde with methyl acrylate catalyzed by 3-hydroxyquinuclidine. (31)

In an effort to find more efficient catalysts, a number of other tertiary amines have been investigated. In the series of bicyclic amines **1** and **5–8**, only 3-hydroxyquinuclidine (**5**) is more effective than DABCO (**1**). Four- to tenfold reductions in half-lives are achieved, (33, 34) and catalyst **5** is now routinely used in Morita–Baylis–Hillman reactions. The bicyclic bases 3-acetoxyquinuclidine (**6**), (33) 3-quinuclidone (**7**), (35) and quinuclidine (**8**) (36) are all poorer catalysts than



DABCO. The relative effectiveness in this series roughly follows the pK_a values (37, 38) (given in parentheses) which to a first approximation can be taken as a measure of the nucleophilicity of the catalyst. Quinuclidine (**8**) is the exception, perhaps because with only one nitrogen it has half the effective concentration of DABCO. The activity of 3-hydroxyquinuclidine has been attributed to stabilization of zwitterion **2** (Eq. 4) by intramolecular hydrogen bonding between the 3-hydroxy group and the negatively charged oxygen. (34) However, modeling studies indicate that such an intermediate suffers from unfavorable nonbonded interactions, and the rate-enhancing effect of 3-hydroxyquinuclidine is now attributed to its ability to protonate zwitterion **3** intermolecularly. (36-36a) Protonation is also achieved by addition of catalytic amounts of methanol, (34, 39, 40) 2-propanol, (41) 1,1,1,3,3,3-hexafluoro-2-propanol, (42) or acetic acid. (40, 43) The same effect may operate in the acceleration of Morita–Baylis–Hillman reactions catalyzed by 1,3-diaminopropane in the presence of phenols (Eq. 9); (44) in the absence of the phenol,

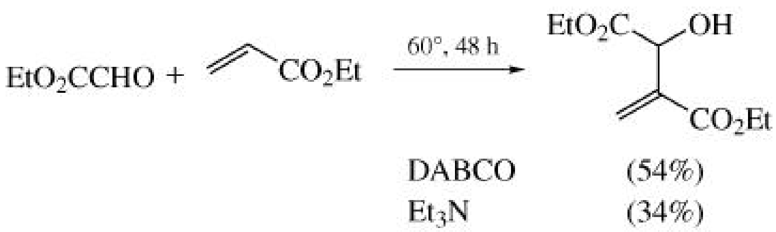


(9)

the reaction required nine days to go to completion. No explanation was given and an extension of this effect to DABCO and similar amines was not reported. (44)

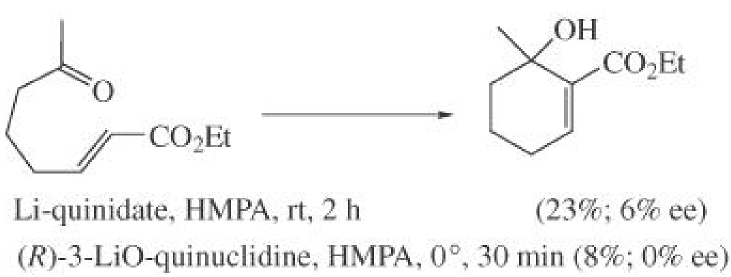
Chiral disubstituted derivatives of DABCO have also been used as catalysts;

they are discussed in the section on Stereochemistry. The nitrogen in simple tertiary amines is more hindered than in the bicyclic amines mentioned above, but a number have been employed successfully. Thus triethylamine is only slightly less effective than DABCO in the reaction of ethyl glyoxylate with ethyl acrylate (Eq. 10). (45) Similar results are obtained in the reaction of methyl acrylate



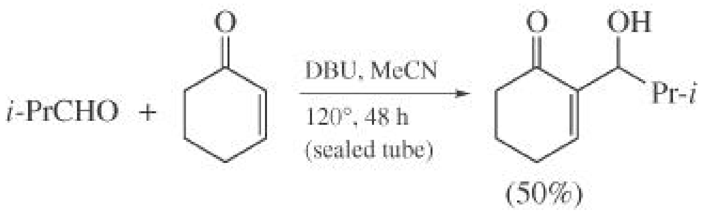
(10)

with aqueous formaldehyde. (46) In the reaction of the same aldehyde with ethyl acrylate, catalyst efficacy decreases in the expected order trimethylamine > dimethylethylamine > methyldiethylamine > triethylamine. (47) Tripropylamine fails to catalyze the addition of benzaldehyde to acrylonitrile at ambient pressure and temperature. (41) Methyldiethylamine or triethylamine is used extensively in pressure-induced Morita–Baylis–Hillman reactions where attenuation of the catalyst activity is often required. (28, 48-50) Branching α to the nitrogen greatly reduces or eliminates catalytic activity. (41) Thus diisopropylethylamine, 2-dipropylaminobutanol, and *N,N*-dipropyl- α -methylbenzylamine all fail to catalyze the addition of acrylonitrile to benzaldehyde even under 15 kbar pressure. (41) This is attributed to steric effects and to lower nucleophilicity of the nitrogen as a consequence of a more sp^2-like configuration. (41) In view of the success with 3-quinuclidinol, it is surprising that simple amino alcohols such as dimethylaminoethanol apparently have not been investigated as potential catalysts. Other amines that were tried but found to be less active than DABCO or inactive are retronecine, (51, 52) brucine, (52) cinchonidine, (52) quinidine, (29, 52) quinine, (52, 53) *N*-methylprolinol, (52, 53) nicotine, (53) *N*-methylephedrine, (53) 1,8-bis(dimethylamino)naphthalene, (54) and macrocyclic diamine “receptors.” (41) The lithium salts of quinidine and (*R*)-3-quinuclidinol have been employed in the intramolecular reaction shown in Eq. 11 (29) in which DABCO



(11)

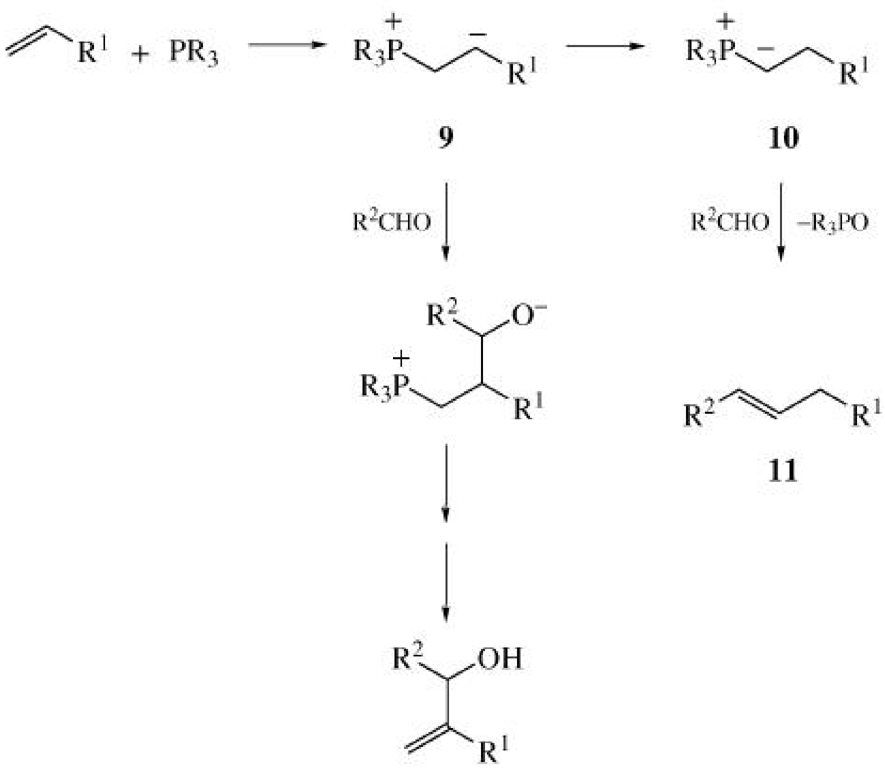
is ineffective. DBU (1,8-diazabicylo[5.4.0]undec-7-ene) and 4-dimethylaminopyridine are as effective as 1,3-diaminopropane in the reaction of benzaldehyde with ethyl acrylate in the presence of a phenol (Eq. 9). (44) Other authors, on the other hand, report that DBU alone gives less satisfactory results than DABCO or is inactive. (55-57) DBU catalyzes the addition of isobutyraldehyde to cyclohexen-3-one (Eq. 12), (57, 58) but this reaction proceeds via the dienolate since methyl vinyl ketone fails to react under these conditions.



(12)

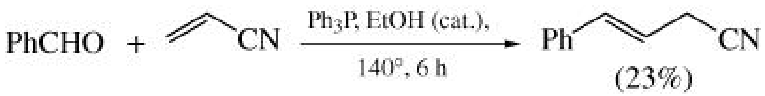
2.2. Phosphine-catalyzed Reactions

The most likely mechanism of the α -hydroxyalkylation reaction catalyzed by tertiary phosphines (Eq. 13) (17) is identical to that of the amine-catalyzed reaction



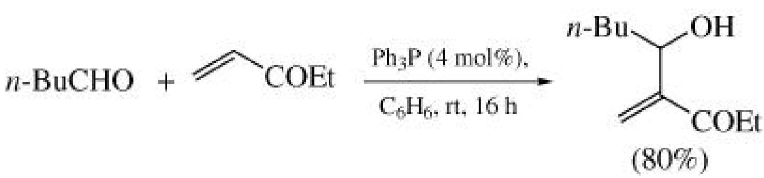
(13)

except that the initially formed zwitterion **9** can isomerize to phosphorus ylide **10**, which can then undergo a Wittig reaction to give olefin **11**. The latter process may require elevated temperatures (59, 60) (Eq. 14), (60) since it is not observed in reactions



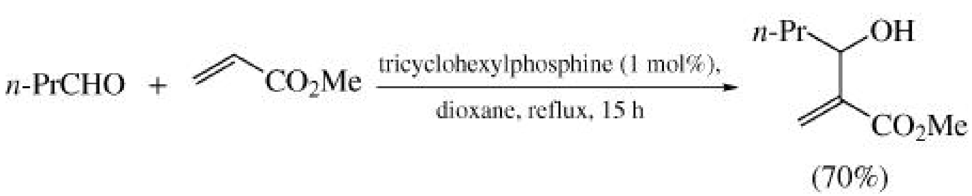
(14)

that proceed under mild conditions such as the α -aminoalkylation reaction shown in Eq. 2 (18) or the α -hydroxyalkylation involving the more reactive α , β -unsaturated ketones (61, 62) (Eq. 15). (62)



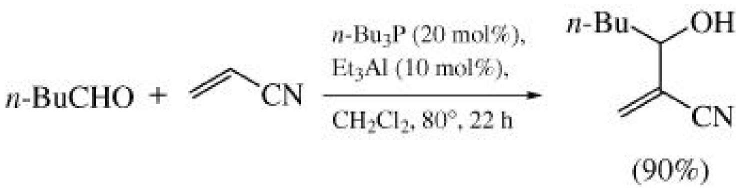
(15)

With tertiary alkyl or mixed arylalkylphosphines, products of Wittig reactions have not been reported, and acrylates and acrylonitrile can be employed; the reactions also proceed considerably faster than with triphenylphosphine. Phosphines of this type that have been used successfully in the Morita–Baylis–Hillman reaction include tricyclohexylphosphine, (7, 8, 17, 63) tricyclooctylphosphine, (14) diethylcyclohexylphosphine, (14) *n*-butyldicyclohexylphosphine, (14) dimethylphenylphosphine, (29) di-(*n*-butyl)phenylphosphine, (14) (isobutyl)(methyl)phenylphosphine, (29) methyldiphenylphosphine, (29) ("chlorohexyl")diphenylphosphine, (7) and (4-hydroxybutyl)diphenylphosphine. (7, 8, 14) An example is given in Eq. 16. (7) Tributylphosphine



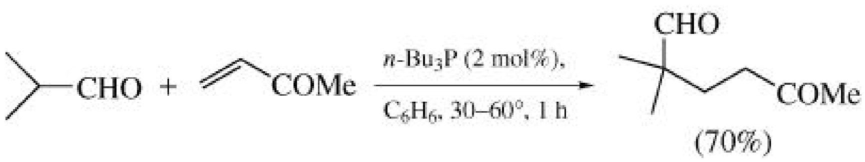
(16)

has been recommended as the consistently most efficacious phosphine catalyst in Morita–Baylis–Hillman reactions. (63) It has been employed also in conjunction with triethylaluminum in the addition of aldehydes to acrylonitrile (Eq. 17). (64)



(17)

The Lewis acid is believed to activate the aldehyde by coordination to the carbonyl oxygen. (64) The effect of Lewis acids on amine-catalyzed reactions does not appear to have been investigated. With α-branched aldehydes, tributylphosphine gives Michael adducts (62, 65) (Eq. 18). (65) On the other hand, use of this catalyst is reported (63)

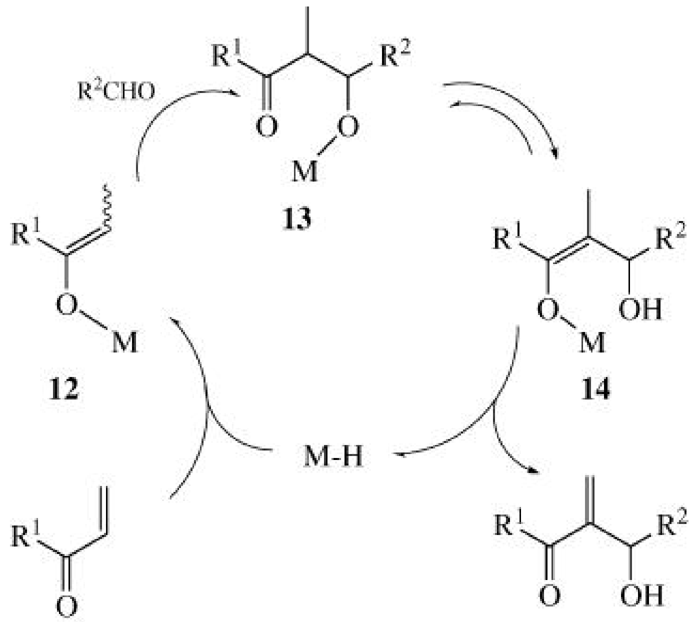


(18)

to eliminate aldol condensations, which may be a problem when amines are used as catalysts. (66) Head-to-tail dimers (Eq. 5) are formed in many phosphine-catalyzed Morita–Baylis–Hillman reactions, but the amounts are usually small. Trimethylphosphine and 1,4-diphosphabicyclo[2.2.2]octane, the phosphorus analog of DABCO, do not catalyze the addition of propionaldehyde to methyl acrylate. (63)

2.3. Transition Metal Complex Catalyzed Reactions

Aldehydes add to α , β -unsaturated ketones under the influence of rhodium and ruthenium hydride complexes. (19, 67-69) The tentative mechanism (Eq. 19) (19) involves



(19)

initial formation of metal enolate species **12**, which reacts with the aldehyde to give intermediate **13**; reversible metal migration to give enolate **14** followed by elimination of metal hydride completes the cycle. Catalysts effective in this transformation are $RhH(PPh_3)_4$, (19, 67) $RuH_2(PPh_3)_4$, (19, 68) $[Rh(cyclooctadiene)\ (Ph_2PCH_2CH_2PPh_2)]^+PF_6^-$ in the presence of hydrogen, (19) and $[RhH_m(P\text{-}P)S_n]^+BF_4^-$ where P-P are various chiral diphosphines and S are solvent molecules. (69) $RhH(Ph_2PMe)$ and $RhH(Ph_2PCH_2CH_2PPh_2)_2$ are ineffective. (19) Addition of small amounts of alcohols is beneficial in rhodium hydride catalyzed reactions, but other solvents reduce the yields drastically. (19) This has been taken as evidence against the possibility that the phosphines in the metal complexes are the true catalysts since phosphine-catalyzed Morita–Baylis–Hillman reactions proceed well in solution. Head-to-tail dimerization of the α, β -unsaturated ketone again is only a minor side reaction except for hindered aldehydes such as 2-ethylhexanal or activated enones such as phenyl vinyl ketone where dimerization becomes the predominant reaction. The rhodium hydride catalyzed α -hydroxyalkylation reaction has been extended to acrylonitrile, (69) but experimental details have not yet been published. Acrylates are inactive. (69)

3. Reaction Parameters

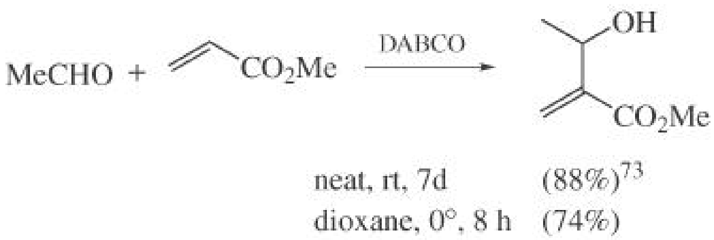
3.1. Solvents

As a third-order process, the Morita–Baylis–Hillman reaction as a rule is slowed by dilution with solvents. Reactions are usually carried out neat, preferably with either the activated olefin or the electrophile in excess. There are, however, exceptions. The beneficial effect of adding small amounts of proton donors such as alcohols or acetic acid has already been mentioned. Solvents have been used to overcome poor solubilities of either or both substrates. For amine-catalyzed reactions, tetrahydrofuran, dioxane, dimethoxymethane, glycol ethers, diethyl ether, acetonitrile, chloroform, methylene chloride, methanol, ethanol, *n*-butanol, and *tert*-butanol have been used. Tetrahydrofuran is routinely employed to attenuate the high reactivity of α , β -unsaturated ketones. Phosphine-catalyzed reactions have been carried out in benzene or dioxane. In the DABCO-catalyzed reaction of benzaldehyde with acrylonitrile, the relative rates in a series of solvents decrease in the order water ≌ formamide ≌ ethylene glycol > methanol ≌*N*-methylacetamide > dimethyl sulfoxide ≌ dimethylformamide ≌ neat > tetrahydrofuran ≌ toluene. (70) The beneficial effect of polar solvents (see also ref. 41) has been attributed to an increase in the equilibrium constant for the formation of zwitterion **2** (Eq. 4). The effect of water is particularly noteworthy since the substrates are only poorly water soluble and the reaction is zero order in this solvent. A hydrophobic effect has been invoked as a possible explanation, (70) but the evidence derived from salt effects is ambiguous: addition of lithium iodide or sodium iodide accelerates the reaction in water, potassium iodide has no effect, and cesium iodide and lithium chloride inhibit it. (70) The last slightly accelerates the reaction of *m*- and *p*-phthalaldehyde with methyl acrylate in the absence of a solvent. (71)

3.2. Temperature and Microwave Irradiation

Most amine-catalyzed Morita–Baylis–Hillman reactions have been carried out at room temperature where reaction rates are often low. This may be a consequence of reports that elevated temperatures cause side reactions. However, there are a number of examples in the Tabular Survey where satisfactory yields at shorter reaction times are obtained by use of elevated temperatures. In the DABCO-catalyzed reaction of acetaldehyde with methyl acrylate, the half-life is reduced from 50 hours at 22° to 1.5 hours at 43°. With other aldehydes the temperature effect is less pronounced but still significant. (72) Polymerization of the activated olefin, one of the more serious side reactions at elevated temperatures, can be minimized in most cases by addition of a radical inhibitor.

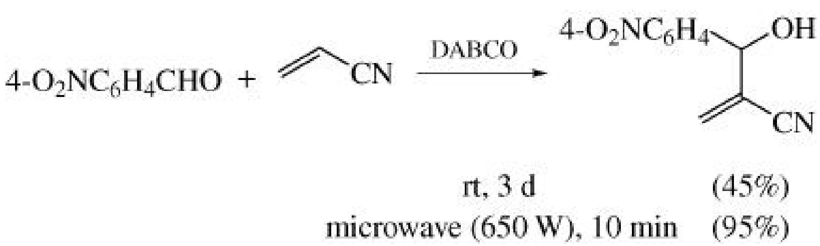
Remarkably, lowering the reaction temperature also increases the rates of amine- and phosphine-catalyzed reactions involving acrylates (Eq. 20). (63) The effect



(20)

is particularly dramatic in view of the fact that these reactions were carried out in rather low concentration in dioxane or methylene chloride as the solvent. Differences in equilibrium and rate constants for the formation and reaction of the *E* and *Z* forms of zwitterion **2** (Eq. 4) at different temperatures are believed to be a possible rationale for the rate acceleration at low temperatures. It remains to be determined whether this phenomenon is general for all Morita–Baylis–Hillman reactions. Of relevance in this regard are the reports that the DABCO-catalyzed reactions of *p*-tolualdehyde with acrylonitrile (49) and of benzaldehyde with phenyl acrylate (24) proceed more slowly at low temperature.

Rapid attainment of elevated reaction temperatures is possible with microwave irradiation, and this method has been applied successfully to the Morita–Baylis–Hillman reaction. (74-76) An example is given in Eq. 21. (76) However, use of commercial

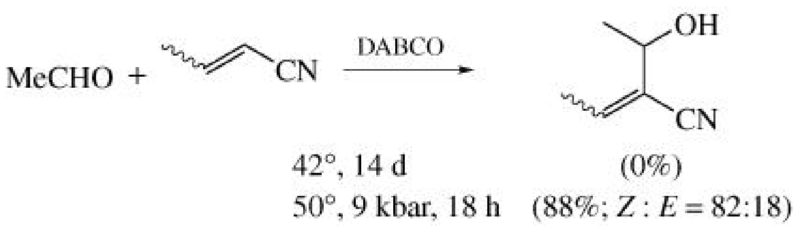


(21)

microwave ovens (77, 78) requires sealed-tube techniques, which limits the scale and introduces an explosion hazard. (78) These problems are overcome with a continuous microwave reactor; (74, 75) for instance, the DABCO-catalyzed reaction of aqueous formaldehyde with methyl acrylate at 160° proceeds in a yield of 30% with a reaction time of 1.5 minutes. (75)

3.3. Pressure and Sonication

The Morita–Baylis–Hillman reaction is expected to have a large negative volume of activation because of bond formation and charge development prior to and in the rate-determining step, and thus be subject to rate acceleration by increased pressure. Indeed the volume of activation for the DABCO-catalyzed reaction of acetaldehyde with acrylonitrile is – 79 mL/mole, which is considered to be the sum of the activation volumes for the first two steps of the reaction (Eq. 4), formation of zwitterion **2** and its rate-determining reaction with the aldehyde. (26) The rate of the reaction increases eightfold between ambient pressure and 0.74 kbar, and a million-fold rate increase is extrapolated for a pressure of 5 kbar. (26) In a study of solvent effects in this reaction (at unspecified pressures) equimolar amounts of ethylene glycol increased the rate fourfold in spite of the dilution effect. Monohydric alcohols are not as effective and other solvents even less so. (26) Application of elevated pressures is used to force reactions that fail at ambient pressure, such as addition of ketones to acrylonitrile (but not acrylic esters) (79) or addition of aldehydes to crotononitrile (Eq. 22). (49) The effect of solvents and pressure



(22)

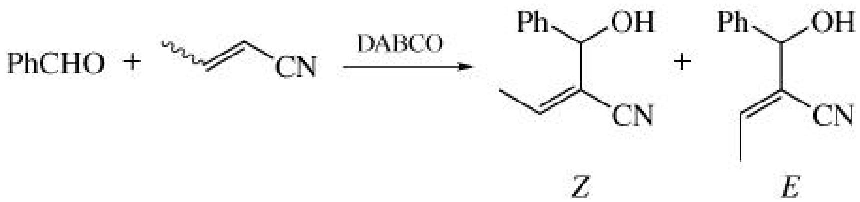
on the product *E/Z* ratio in a closely related reaction (28) is discussed in the section on Stereochemistry. The DABCO-catalyzed addition of propionaldehyde to phenyl vinyl sulfone proceeds in 33% yield at ambient or 0.2 kbar pressure but fails at 7 kbar. (80) This has been attributed to decreasing solubility with increasing pressure although other workers report (with no experimental details) that they did not encounter this problem. (81) In pressure-induced Morita–Baylis–Hillman reactions, polymerization of the activated olefin can be minimized by using an excess of the electrophile; (53) increasing the amount of catalyst or dilution with a solvent is also beneficial. (41)

Exposure of reaction mixtures to ultrasound locally produces the same effect as high pressure. However, in the DABCO-catalyzed addition of a series of aliphatic, alicyclic, and aromatic aldehydes to methyl acrylate, only small rate increases are observed on sonication. (72)

4. Stereochemistry

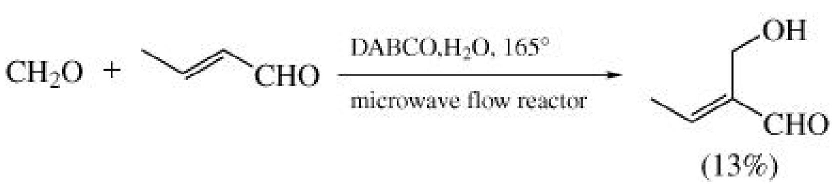
4.1. *E-Z* Selectivity

Since β -substituted activated olefins do not undergo the Morita–Baylis–Hillman reaction at ambient pressure, little is known about the *E-Z* selectivity. Polar solvents favor formation of the *E* isomer in the pressure-induced reaction of benzaldehyde with crotononitrile (Eq. 23). (28) *E/Z* ratios at 8 kbar range from about 1



(23)

without solvent or in tetrahydrofuran to 4 in methanol. Increased pressure also leads to higher *E/Z* ratios but this effect is solvent dependent. In chloroform, the *E/Z* ratio goes from about 1 at 6 kbar to ca. 23 at 15 kbar whereas no change in ratio is observed when methanol is used as the solvent. The *E/Z* ratios for different catalysts at a constant 8 kbar pressure range from 1 for DABCO to 2 for 3-hydroxyquinuclidine and 4 for triethylamine. These results, as well as those of a similar study with methyl crotonate, (82) have been interpreted in terms of E2 or E1cB mechanisms (Eq. 4) predominating depending on the reaction conditions. (28) In the pressure-induced reaction of the less bulky acetaldehyde with crotononitrile, the *Z* isomer predominates by a ratio of 4.5:1 (Eq. 22). (49) Addition of formaldehyde to (*E*)-crotonaldehyde in a microwave flow-reactor gives the *E* isomer exclusively in low yield (Eq. 24). (74)



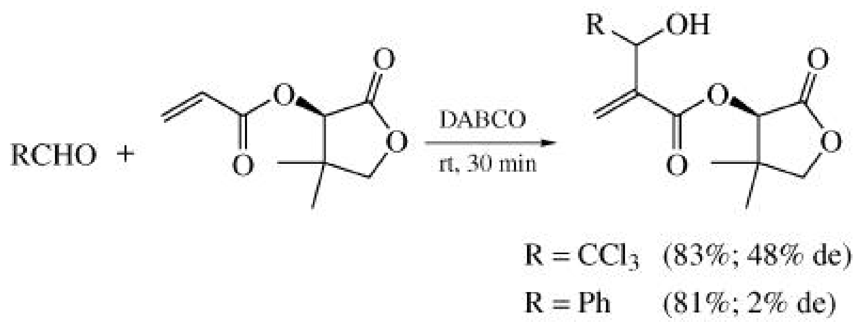
(24)

4.2. Diastereoselectivity

Two or more diastereomers are formed in reactions where either or both the activated olefin or the electrophile contain asymmetric centers. Considerable effort has been expended to understand and optimize the observed selectivities but so far with only limited success.

4.2.1. Asymmetric Center in the Activated Olefin

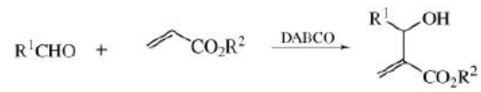
The generally low selectivity observed in this situation is usually attributed to the large distance between the chiral and the reacting centers. Most examples reported so far involve esters of acrylic acid. The results in Table A (30, 53, 83-86) show that the diastereoselectivity in most cases is poor except for the reaction of menthyl esters 17 with aromatic aldehydes under high pressure where de values up to 100% have been reported. (53) Less bulky aldehydes add to esters 17 with much lower diastereoselectivity, even under pressure. The results have been interpreted in terms of attack by the aldehyde on the *si* face of zwitterion **2** (Eq. 4) to produce the *S* configuration at the newly created chiral center, (53) but the absolute configuration has not been determined. Additions to 8-phenylmenthyl esters 18 (83) in general are more diastereoselective than additions to menthyl esters 17; this has been attributed (83) to a π -stacking effect. (87) It has been argued that in additions to esters 18, it is the reactivity of the aldehyde rather than its bulk that determines the degree of diastereoselectivity; reactive aldehydes give higher de values since the opportunity for equilibration by reverse reaction is diminished. However, the very rapid reactions depicted in Eq. 25 (88) show moderate and no diastereoselectivity, respectively.

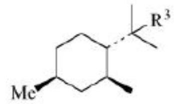


(25)

A study of diastereoselectivity as a function of reaction time has not yet been reported. The large spread of de values for the reaction of propionaldehyde with camphorsulfonamide 20 is unexplained, as is the similarly large difference in de values for the reactions of benzaldehyde and *p*-tolualdehyde with menthyl ester 17 at ambient pressure. (53)

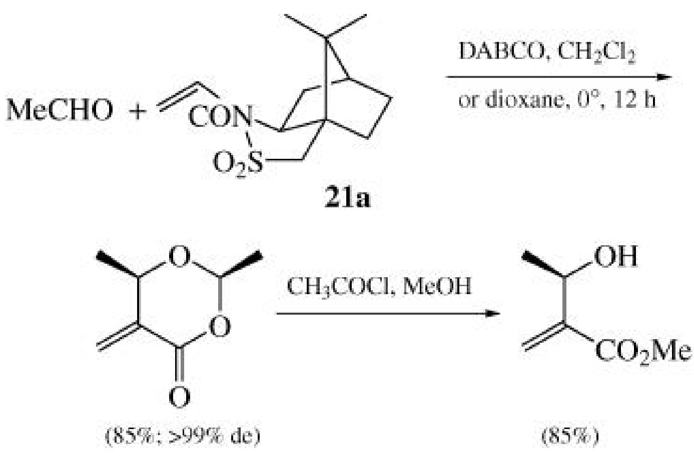
Table A. Diastereomeric Excess in Reactions of Aldehydes with Chiral Acrylates



R² / R¹	MeCHCO$_2$Me	PhCHCO$_2$Et	 R³ = H	R³ = Ph	 R⁴ = *i*-Pr	R⁴ = C$_6$H$_{11}$	R⁴ = Bn
	15	**16**	**17**	**18**	**19**	**20**	**21**
Cl$_3$C				70		25	
Me			6–16, 16[a]	2	30		
Et			16	65	42	7, 9, 70	6
i-Pr			7	42		20	
MeOCH$_2$CHMe	38	38	30			NR[b]	
C$_6$H$_{11}$				31		26	
Ph			10–22, 100[a]	35, 86[a]	15	10–25	18
4-MeC$_6$H$_4$			100, 87[a]				
4-EtC$_6$H$_4$			94[a]				
4-O$_2$NC$_6$H$_4$				60		9	
Naphthyl			23				
2-Furyl			17–20	30			

[a]The reaction was carried out at 6–8.5 kbar. [b]There was no reaction.

The most impressive results reported to date involve reactions of aliphatic aldehydes with camphor sultam acrylate **21a** to give 2,4-dialkyl-5-methylene-1,3-dioxan-4-ones in high diastereoselectivity (Eq. 25a). (88a) The products are



(25a)

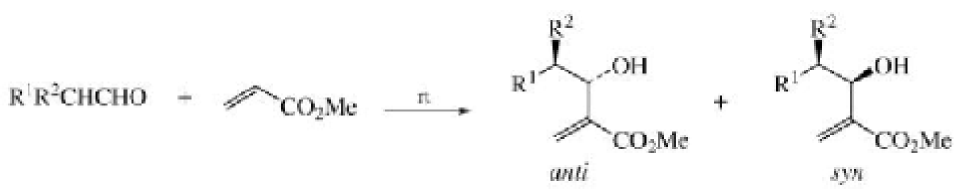
readily converted into α -hydroxyalkyl acrylates, and the chiral auxiliary is easily recovered. This type of reaction involving two molecules of the aldehyde has been also observed with esters of acrylic acid in which the alcohol moiety is a good leaving group (Eqs. 29, 30).

In the single α -hydroxyalkylation of a vinyl sulfoxide, DABCO-catalyzed addition of phenyl vinyl sulfoxide to benzaldehyde at 19 kbar pressure gives the two diastereomers in equal amounts (Eq. 41). (81)

4.3. Asymmetric Center in the Electrophile

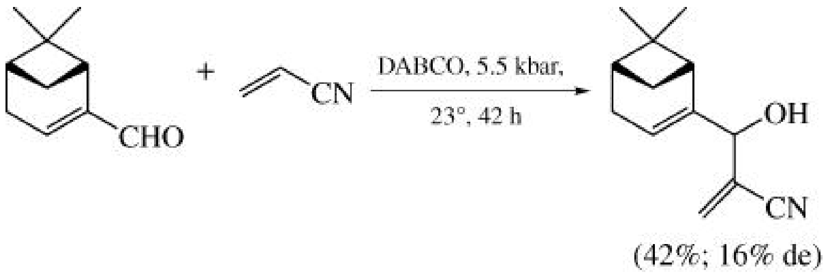
The most extensive study involves addition of single enantiomers of α-branched aldehydes to acrylates and methyl vinyl ketone. (30, 89-92) *Syn/anti* (93) ratios were determined by X-ray crystallography or NMR spectroscopy of the trichloroacetylurethane derivatives. (94-96) A selection of results (30) is presented in Table B. A change of catalyst has an effect only on the rate but not on the *syn/anti* ratio (entries 1 and 2). Similarly, the amount of catalyst affects only the rate. Substitution of the carbomethoxy group in the activated olefin by a *tert*-butoxycarbonyl or acetyl group has little effect on the *syn/anti* ratios. In the majority of additions in this series, the *anti* isomers (93) are formed predominantly in agreement with the Felkin— Anh model. Values of de are modest; the best (78%) is achieved with the heterocyclic aldehyde in entry 9. Bulky substituents do not necessarily lead to high selectivity (entries 4 and 8). The selectivity reversal in entry 7 has been rationalized in terms of hydrogen bonding involving the amino nitrogen in the transition state. Attempts at double diastereodifferentiation in this series (Table A, line 5) have been disappointing.

Table B.



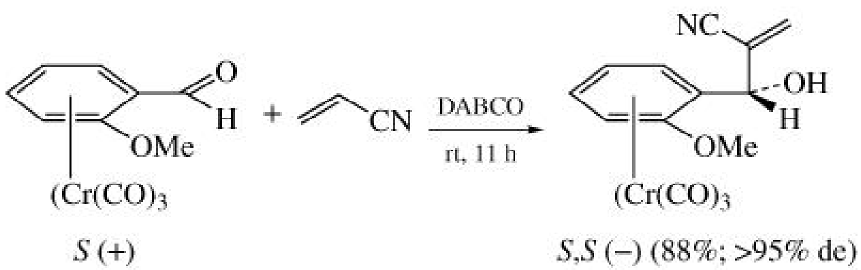
Entry	R^1	R^2	Conditions	Yield (%)	*anti:syn*
1	Me	$MeOCH_2O$	DABCO, 4 d	(55)	70:30
2	Me	$MeOCH_2O$	3-Quinuclidinol, 1.5 d	(60)	72:28
3	Me	$BnOCH_2O$	DABCO, 6 d	(42)	70:30
4	Ph	$MeOCH_2O$	DABCO, >10 d	(42)	37:63
5	*n*-Pr	Me	3-Quinuclidinol, 60 d	(30)	35:65
6	—$CH_2OC(Me)_2O$—		DABCO, 55 d	(62)	69:31
7	Me	$NHCO_2Bu$-*t*	DABCO, 7 d	(80)	26:74
8	Me	*N*-Phthalimidyl	DABCO, 3.5 d	(28)	46:54
9	—$CH_2OC(Me)_2N(CO_2Bu$-*t*)—		DABCO, <11 d	(43)	89:11

In the two examples investigated so far, (53) application of high pressure does not enhance diastereoselectivity appreciably. The first example involves (*R*)-myrtenal (Eq. 26). In the second example, reaction of isopropylidene (*R*)-glyceraldehyde with acrylonitrile under 4 kbar pressure, the diastereomeric excess is 23%. In both reactions, ambient pressure gives equimolar mixtures of the two diastereomers.



(26)

Excellent diastereoselectivities, often approaching 100%, are achieved in reactions involving tricarbonylchromium complexes of *ortho*-substituted aromatic benzaldehydes (Eq. 27). (97) Similar results are obtained with methyl acrylate and



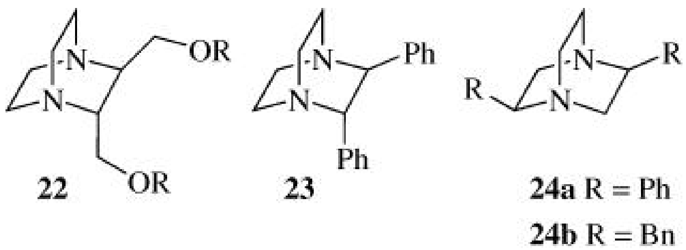
(27)

with complexes of *o*-chlorobenzaldehyde. In the reactions of methyl acrylate with tricarbonylchromium complexes of *o*-fluorobenzaldehyde and *o*-tolualdehyde, the de values are lower (84 and 68%, respectively). The dependence of diastereoselectivity on the nature of the *ortho* substituent is also observed in additions of tricarbonylchromium complexes of *ortho*-substituted benzaldehyde tosylimines to methyl acrylate and acrylonitrile. (98) The products are easily decomplexed by exposure to air and sunlight.

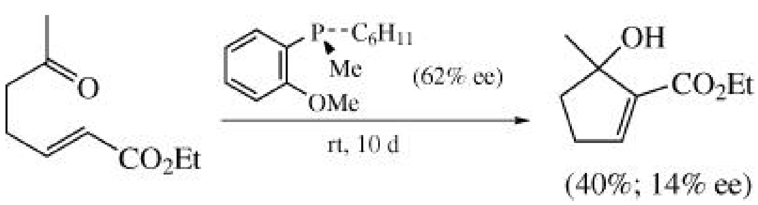
4.4. Enantioselectivity

Attempts to achieve high enantioselectivity in the Morita— Baylis— Hillman reaction by use of chiral catalysts have met with only limited success so far. Low values of ee are often obtained even when the chiral center is close to the nitrogen atom. The problem is further complicated by the fact that many chiral catalysts suffer from low efficacy, and application of high pressure is usually required. In the reaction of acetaldehyde with methyl vinyl ketone, 8–12% enantiomeric excesses are obtained with brucine, cinchonidine, quinidine, and quinine, and none with (*S*)-(–)- prolinol. (52) Retronecine catalyzes the reaction of *p*-nitrobenzaldehyde with methyl acrylate and methyl vinyl ketone, but the ee values are 11 and 0%, respectively. (52) Similarly low ee values (10–17%) are obtained in the reaction of acetaldehyde with acrylonitrile at

9 kbar pressure catalyzed by (1*R*,2*S*)-*N*-methylephedrine, (*S*)-(–)- nicotine, and (*S*)-(–)- prolinol; quinine fails to catalyze this reaction. (53) The most promising results have been obtained with chiral, 2,3-disubstituted derivatives **22** of DABCO. (39) The addition of 4-nitrobenzaldehyde to methyl vinyl ketone catalyzed by amine **22** (R = CH_2Ph) proceeds with 47% ee at 5 kbar and 12% ee at ambient pressure. Catalysts with other groups R (*t*-$BuPh_2Si$,*i*-Pr_3Si, Ph, mesityl, 1-naphthyl, 1-naphthoyl, 1-anthryl, and Cbz-gly) are less effective. Reaction of benzaldehyde with acrylonitrile at 12 kbar catalyzed by chiral *trans*-2,3-diphenyl-1,4-diazabicyclo[2.2.2]octane (**23**) (99) proceeds with only 11% ee; similar results are obtained with (–)-3-hydroxyquinuclidine, brucine, strychnine, cinchonidine, cinchonine, quinine, and quinidine. (82) The chiral 2,5-diphenyl (**24a**) (100) and 2,5-dibenzyl (**24b**) (101) derivatives of DABCO have been synthesized; the former is ineffective in Morita— Baylis— Hillman reactions, (102) and results with the latter have not been reported as yet.



There appear to be only two attempts to catalyze a Morita— Baylis— Hillman reaction with a chiral phosphine. The intramolecular reaction depicted in Eq. 28



(28)

proceeds with only low asymmetric induction. (29) In the reaction of benzaldehyde tosylimine with methyl acrylate catalyzed by chiral 2,3 bis(diphenylphosphino)butane, the two enantiomers are formed in equal amounts. (18) A two-step α -hydroxyalkylation of acrylates and methyl vinyl ketone, which proceeds with high enantioselectivity, (103) is described in the section on Comparison with Other Methods.

The reaction of acetaldehyde with acrylonitrile in L-ethyl lactate under 5 kbar pressure catalyzed by racemic 3-hydroxyquinuclidine proceeds with essentially no enantioselectivity (3% ee). (53) α -Hydroxyalkylacrylates have been resolved by fractional crystallization of diastereomeric salt mixtures of the corresponding acids (104) and by kinetic resolution involving hydrogenation with rhodium biphosphine (105) and other chiral catalysts (see references given in the section on Synthetic Utility). Additional methods include acetylation with vinyl acetate catalyzed by *Pseudomonas AK*, (106) and selective hydrolysis of the acetates by pigliver esterase. (107) Kinetic resolution of 3-methylene-4-(4-nitrophenyl)-4-hydroxy-2-butanone is achieved by Katsuki— Sharpless epoxidation, (39) that of ethyl 2-(1-acetoxyethyl)acrylate by the action of esterases. (108) α -Aminoalkylacrylates have been subjected to kinetic resolution by hydrogenation with rhodium and ruthenium biphosphine catalysts. (109)

5. Scope and Limitations

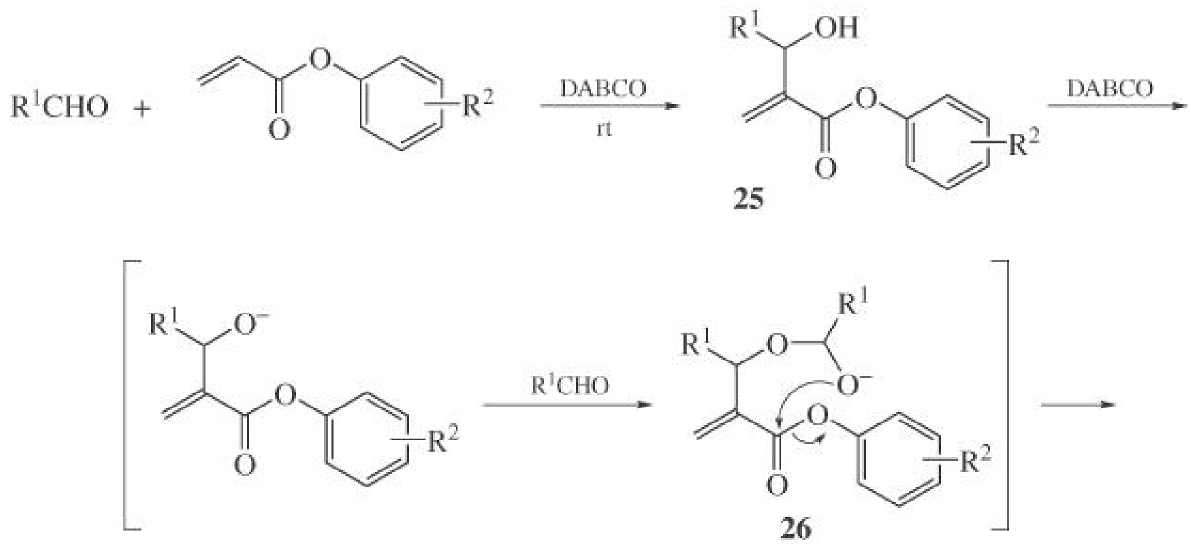
Kinetic data that would provide an accurate reactivity order among activated olefins and electrophiles are almost nonexistent. The statements made in this section with regard to relative reactivities are therefore only a rough guide and may not hold true in a specific case.

5.1. The Activated Olefin

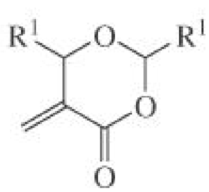
The reactivity of activated olefins appears to decrease in the order acrolein ≌ phenyl vinylsulfonate > α , β -unsaturated ketones > acrylonitrile > acrylic esters ≌ ethyl vinylphosphonate > phenyl vinyl sulfone > phenyl vinyl sulfoxide ≌acrylamides. With the exception of the unusually high reactivity of phenyl vinylsulfonate, for which only one example exists, the reactivity increases with the electronegativity of the activating group, as would be expected based on the mechanism of the Morita— Baylis— Hillman reaction. The nature of the amine catalyst does not appear to have any influence on the reactivity order. (33)

5.1.1. Acrylates (Tables I-A to I-E, VIII, X, XI)

Esters of acrylic acid constitute by far the largest group of activated olefins employed in the Morita— Baylis— Hillman reaction, probably because of the versatility of the ester group in further reactions. In a series of additions of benzaldehyde to alkyl acrylates (Table C), (27) the time required after which no more product is formed increases with steric bulk and with chain length of the alcohol. The latter effect may also be steric in nature if the chain folds back on itself, or it could be a consequence of a less polar reaction medium since the reactions were carried with a 30% excess of acrylate and without a solvent. Esters with electronegative groups in the alcohol such as in 2-fluoroethyl, 2-chloroethyl, 2-hydroxyethyl, 2-thiocyanoethyl, 2-phenethyl, and acetylmethyl acrylates react somewhat faster (2–4 days) under the same conditions, 2,2,2-trifluoroethyl acrylate (15 hours) and 2,2,2-trichloroethyl acrylate (36 hours) even more so. 2-Dimethylaminoethyl acrylate requires 8 days. Oddly, 2-bromoethyl acrylate, 3-chloropropyl acrylate, and 6-bromohexyl acrylate fail to react. As a rule, aromatic esters of acrylic acid react more rapidly than aliphatic ones. (24, 27) The results in Table D, (27) obtained under the same conditions as those in Table C, show that there is no simple correlation of substituent σ values with rate. Esters of acrylic acid with 4-trifluoromethylphenol (σ 0.53), 3-cyanophenol (σ 0.62), 4-cyanophenol (σ 0.70), and 4-nitrophenol (σ 0.81) fail to react altogether. This has been attributed to reduced nucleophilicity of intermediate zwitterion **2** (Eq. 4). Aliphatic aldehydes also react with aryl acrylates more rapidly than with alkyl acrylates, but 5-methylene-1,3-dioxan-4-ones (**27**) are isolated exclusively or in admixture with the normal products **25** (Eq. 29). (24) Formation of heterocycles **27** is also observed in the addition of aliphatic aldehydes to pantolactone acrylate. (88, 110) The more stable *cis* isomers are formed predominantly, and mixed products can be isolated by sequential addition of two different aldehydes (Eq. 30). (110) The rate-enhancing effect of the pantolactone and aryloxy moieties in these reactions is considered to be electronic in nature; (36) both are also good leaving groups, which explains the subsequent cyclization. This presumes that small amounts of adducts **26** (Eq. 29) are usually formed in α -hydroxyalkylation reactions. Esters of acrylic acid with lactic and mandelic acids also show enhanced reactivity relative to aliphatic acrylates, but these reactions stop at the α -hydroxyalkylation stage. (36, 110)

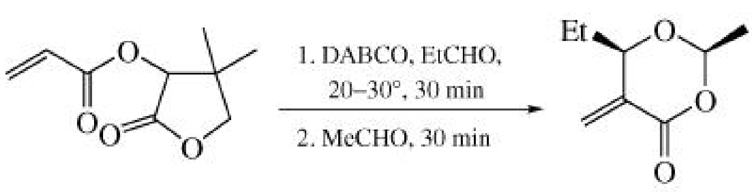


(29)



27

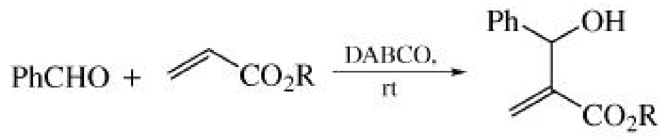
R^1	R^2	Conditions	% **25**	% **27**
Me	H	rt, 2 h	0	57
Me	4-MeO	rt, 8 h	0	69
i-Pr	H	rt, 14 h	25	25
Me	2,4,6-Me_3	rt, 14 h	43	5



(83%; 86% de)

(30)

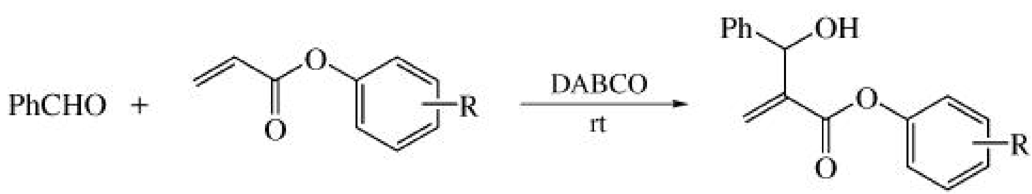
Table C.



R	time (d)	yield (%)
Me	6	(89)
Et	7	(79)
n-Bu	4	(85)
i-Bu	16	(85)
t-Bu	28	(65)
n-C_6H_{13}	9	(82)
n-C_8H_{17}	12	(78)
n-$C_{10}H_{21}$	14	(75)
2-Adamantyl[a]	62	(40)

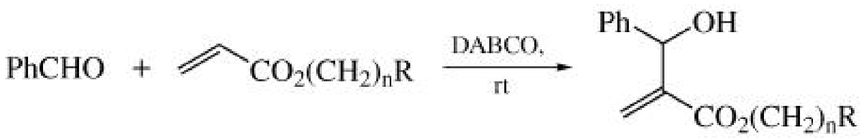
[a]The reaction was carried out in dioxane

Table D.



R	σ	time (h)	yield (%)
4-Me_2N	−0.63	84	(62)
4-MeO	−0.28	8	(54)
4-Me	−0.14	36	(55)
3-Me_2N	−0.10	20	(61)
H	0	5	(55)
3-MeO	0.10	24	(43)
4-F	0.15	72	(39)
3-F	0.34	5	(43)
3-CF_3	0.46	24	(22)

Only small rate enhancements are observed in the reaction of aliphatic and aromatic aldehydes with a series of ω -hydroxyalkyl acrylates (Eq. 31) (111) even



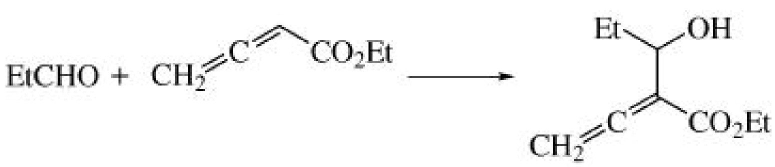
n	R	Timd (d)	Yield (%)
2	H	7	(79)[27]
2	OH	5	(50)
3	OH	3	(66)
4	OH	3	(85)
6	OH	4	(80)
10	OH	6	(78)

(31)

though addition of small amounts of an alcohol increases the rates of Morita–Baylis–Hillman reactions.

5.1.2. Allenic Esters (Table I-F)

Ethyl allenecarboxylate reacts with propionaldehyde (Eq. 32) or heptanal in the presence of DABCO more rapidly than does ethyl acrylate,



(32)

DABCO, ether, rt, 16 h (41%)
n-BuLi, –100°, THF, 5 h (58%)

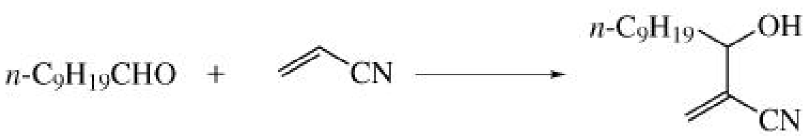
even though the reaction is carried out in solution. (112) Since β -substituted acrylates normally do not undergo the Morita–Baylis–Hillman reaction (see below), it is possible that a change of mechanism involving direct formation of the anion by abstraction of the α proton has taken place; such a mechanism presumably operates when a stoichiometric amount of butyllithium is employed to effect the same net reaction.

5.1.3. Acrylamides (Tables II-A, II-B, VIII)

No additions of aldehydes to acrylamides under ambient conditions have been reported. Even the very reactive 2-pyridinecarboxaldehyde fails to react with either acrylamide or *N,N*-dimethylacrylamide. (113) The diethylmethylamine-catalyzed reaction of acetaldehyde with acrylamide under 5 kbar pressure is reported to give the α -hydroxyalkylation product in 83% yield after three hours at 20°. (48) Similarly, DABCO-catalyzed addition of acetone to acrylamide under 5 kbar pressure is reported to produce the Morita–Baylis–Hillman product in 5% yield after 17 hours. (25) However, no experimental details or structure proofs have been published for either reaction. The same applies to the report (76) that microwave irradiation of a mixture of 3,4,5-trimethoxybenzaldehyde, acrylamide, and DABCO in methanol for 25 minutes produces the α -hydroxyalkylation product in 40% yield. The poor reactivity of acrylamides is not surprising since they are less electrophilic than most of the other activated olefins discussed in this chapter. However, sultam **21a** (Eq. 25a), which carries a second electron-withdrawing group on nitrogen, reacts readily with aldehydes. (88a) Other amides of this type, such as *N*-acylacrylamides, may behave similarly.

5.1.4. Acrylonitrile (Table III-A–D, VIII–XI)

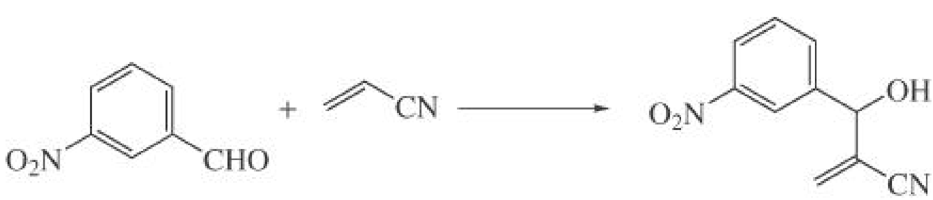
Acrylonitrile appears to be somewhat more reactive toward aldehydes than alkyl acrylates, but the evidence is not conclusive. Phosphine catalysts appear to be well suited for these reactions (Eq. 33, 34).



(33)

DABCO, rt, 7 d (84%)[55]

n-Bu_3P, Et_3Al, CH_2Cl_2, sealed tube, 80°, 22 h (74%)[64]



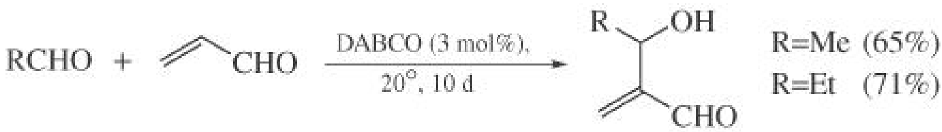
(34)

DABCO, rt, 24 h (22%)[49]

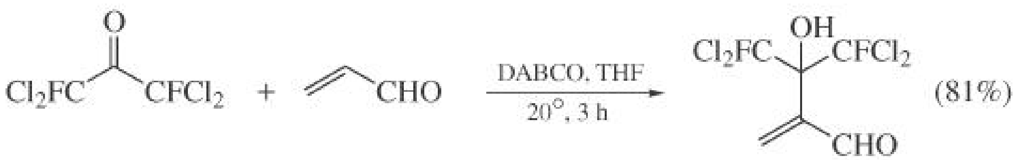
$(C_6H_{11})_3P$, dioxane, 30°, 6 h (74%)[7]

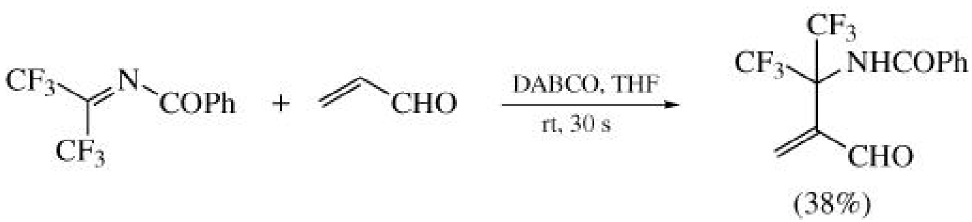
5.1.5. Acrolein (Tables IV, VIII–XI)

The DABCO-catalyzed addition of acetaldehyde and propionaldehyde proceeds in good yields (Eq. 35). (49) The catalyst concentration


(35)

was kept low, perhaps to minimize polymerization of acrolein. The latter is the exclusive path in the attempted addition of 2-pyridinecarboxaldehyde (113) and α -diketones (114) to acrolein. Halo ketones (Eq. 36) (115) and activated imines (Eq. 37) (116) react very rapidly with acrolein.

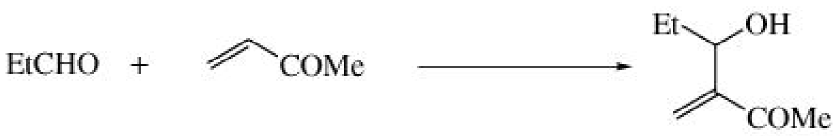

(36)


(37)

Acrolein has been reported to add to itself in the Morita–Baylis–Hillman fashion, (25) but experimental data and a structure proof of the product have not yet been published.

5.1.6. α , β -Unsaturated Ketones (Tables V-A–D, VIII, X, XI)

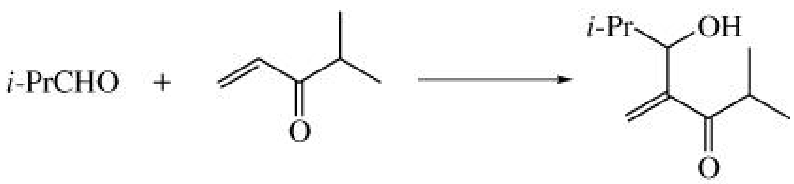
Additions of aldehydes to alkyl vinyl ketones proceed well with tertiary amine, tertiary phosphine, and rhodium or ruthenium complex catalysts (Eq. 38). Amine-catalyzed additions are often cleaner when carried out in a solvent, usually tetrahydrofuran.



DABCO, rt, 24 h	(84%; ref. 117)
3-Quinuclidinol, rt, 15 h	(85%; ref. 33)
Ph_3P, benzene, 30°, 18 h	(63%; ref. 61)
$RuH_2(Ph_3P)_4$, *i*-PrOH (cat.), 40°, 40 h	(82%; ref. 19)

(38)

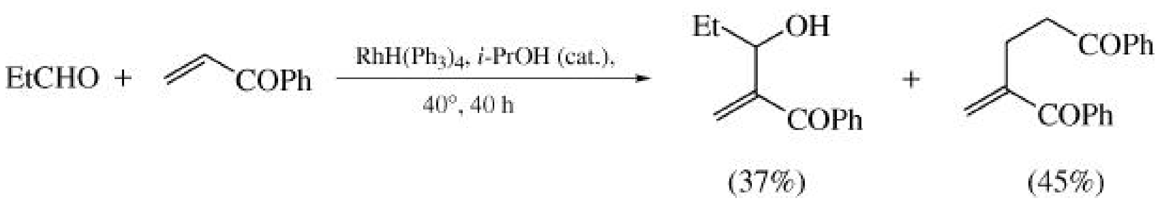
α -Branched alkyl vinyl ketones react more slowly with DABCO catalysis, but with no reduction in rate when catalyzed with tertiary phosphines (Eq. 39) or



DABCO, rt, 6 d	(21%; ref. 118)
Ph_3P, benzene, rt, 16 h	(68%; ref. 62)

(39)

with the rhodium or ruthenium complex system. (19) There is only one report of an aryl vinyl ketone undergoing the Morita–Baylis–Hillman reaction (Eq. 40), (19)

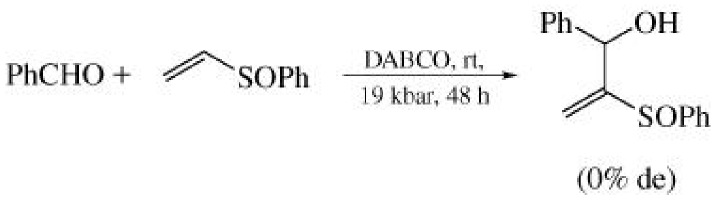


(40)

possibly because such ketones dimerize rapidly, especially in the presence of DABCO (see Table XIII-D and the section on Side Reactions). Cyclic enones have not yet been employed in the Morita–Baylis–Hillman reaction. They may be less sterically encumbered than acyclic β -substituted activated olefins, which do not react except under high pressure (see below).

5.1.7. Vinyl Sulfoxides, Vinyl Sulfones, and Vinylsulfonates (Table VI)

Only additions of aldehydes to these substrates have been reported so far, and in all cases the activating substituent carries a phenyl group. In the single example involving a vinyl sulfoxide, drastic reaction conditions are required to achieve a “satisfactory” yield (Eq. 41). (81) No reaction is observed at ambient pressure. (56)



(41)

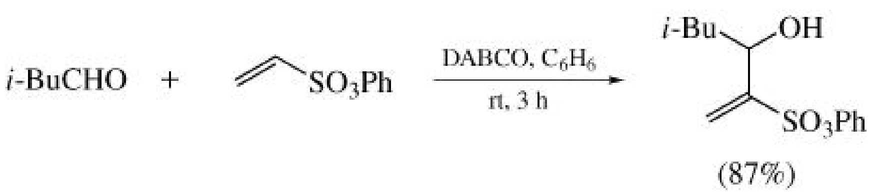
Phenyl vinyl sulfone reacts at ambient pressure and temperature, but reaction times of weeks are common, especially with less reactive aldehydes (Eq. 42). (56) In

R	time	Yield (%)
3-pyridyl	1 d	(46)[80]
Me	2 wk	(84)
Ph	3 wk	(57)
t-Bu	21 wk	(10)

(42)

view of the poor reactivity, it is surprising that neither 3-quinuclidinol nor any of the nonamine catalysts appear to have been employed in these reactions. Vinyl phenyl sulfone is expected to react with some of the more reactive electrophiles such as α -keto esters, halo ketones, and imines, but there are no reports on these variations to date.

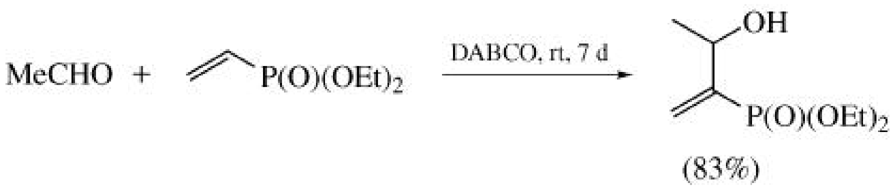
Phenyl vinylsulfonate is surprisingly reactive (Eq. 43), (119) but only one example of this class of compounds has been reported.



(43)

5.1.8. Vinylphosphonates (Table VII)

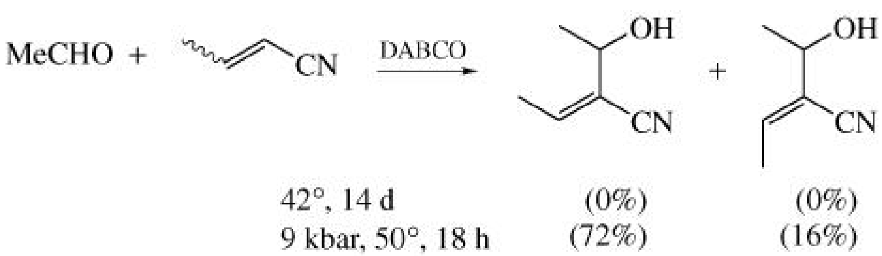
Only reactions of diethyl vinylphosphonate have been reported so far. (120) They appear to resemble alkyl acrylates in reactivity (Eq. 44).



(44)

5.1.9. β -Substituted Activated Olefins

The only successful examples reported to date involve methyl crotonate, crotononitrile, and crotonaldehyde. The DABCO-catalyzed reaction of acetaldehyde with methyl crotonate under 10 kbar pressure at 55° is reported to produce the α -hydroxyalkylation product in “low” yield after 20 hours; the product was characterized only by mass spectroscopy. (49) No structure proof has been published yet for the reaction product of 4-nitrobenzaldehyde with methyl crotonate under microwave irradition (40 minutes, 10% yield). (76) Crotononitrile (Eq. 45) (49) is more reactive than methyl crotonate. (49) Propionaldehyde is reported to react with crotononitrile under the same conditions; the yield is “low” and the product was characterized by mass spectroscopy only. The same applies to the pressure-induced reaction of acetone with crotononitrile. (49)



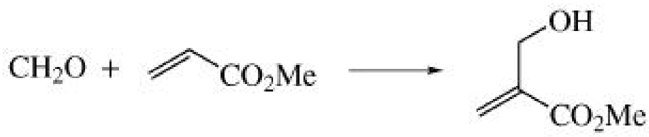
(45)

The reaction of benzaldehyde with crotononitrile under high pressure (Eq. 23) and that of formaldehyde with crotonaldehyde under microwave irradiation (Eq. 24) have been mentioned in the section on *E/Z* selectivity. Benzaldehyde fails to react with dimethyl fumarate or phenyl styryl ketone even under 15 kbar pressure. (82) Clearly, more effective catalysts will have to be developed for β -substituted activated olefins to be amenable to the Morita–Baylis–Hillman reaction.

5.2. The Electrophile

5.2.1. Aldehydes

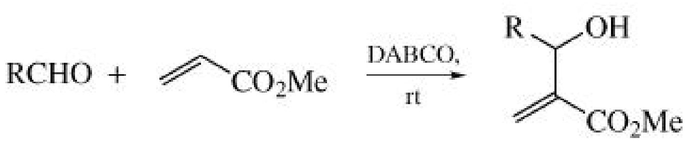
Aldehydes are the most commonly used electrophiles. As expected on the basis of both electronic and steric considerations, they are much more reactive than simple ketones. Formaldehyde can be employed as an aqueous solution (formalin), the polymer (paraformaldehyde), as a solution of the monomer in an organic solvent, or as a hemiacetal (Eq. 46). (46) Similar results are



(46)

Formalin	DABCO, H_2O, MeOH, rt, 48 h	(75%)
Paraformaldehyde	Me_3N, H_2O, 60°, 3 h	(80%; ref. 47)
Monomer	DABCO, EtOH, rt, 72 h	(59%)
Cyclohexanol hemiacetal	DABCO, cyclohexanol, rt, 70 h	(45%)

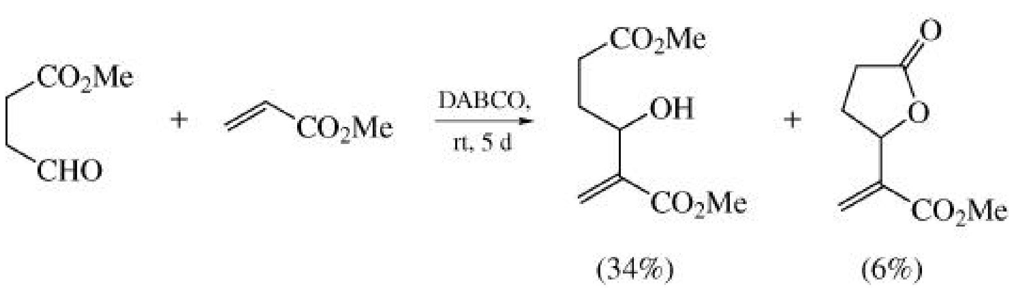
obtained in additions to acrylonitrile, methyl vinyl ketone, and phenyl vinyl sulfone . Aqueous formaldehyde is reported not to react with diethyl vinylphosphonate. (120) Other aliphatic aldehydes with chains of about six carbons or less appear to be only slightly less reactive than formaldehyde. Longer chain and especially α -branched aldehydes react rather slowly (Eq. 47). With DABCO catalysis, pivalaldehyde (2,2-dimethylpropanal)



R	time	yield (%)
Me	7 d	(88)[73]
n-$C_{14}H_{29}$	9 d	(72)[122]
i-Pr	13 wk	(68)[123]
Cl_3C	20 h	(>55)[5]
CO_2Me	48 h	(74)[45]

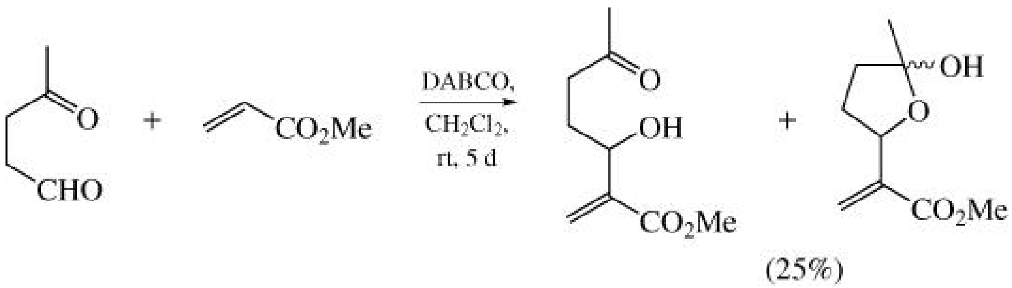
(47)

does not react with methyl acrylate (121) and only very slowly with phenyl vinyl sulfone (Eq. 42). Electron-withdrawing groups on the α carbon enhance reactivity (Eq. 47). Partial lactonization occurs when the aldehyde contains an ester group at a favorable distance in the chain (124, 125) (Eq. 48). (125) The formyl group reacts exclusively in keto aldehydes but

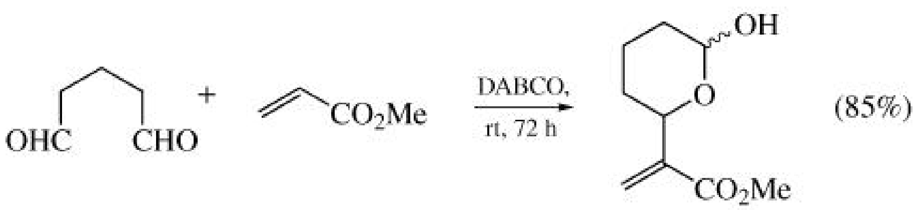


(48)

some hemiketalization takes place in the product (Eq. 49). (124) Glutaraldehyde reacts with methyl acrylate to give a cyclic hemiacetal (Eq. 50). (126)

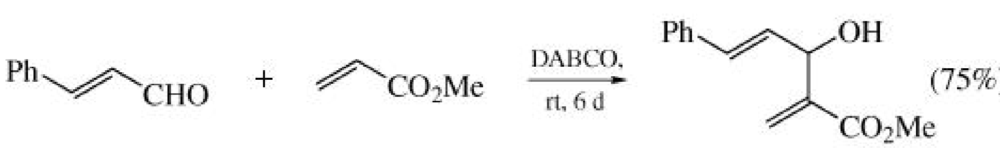


(49)



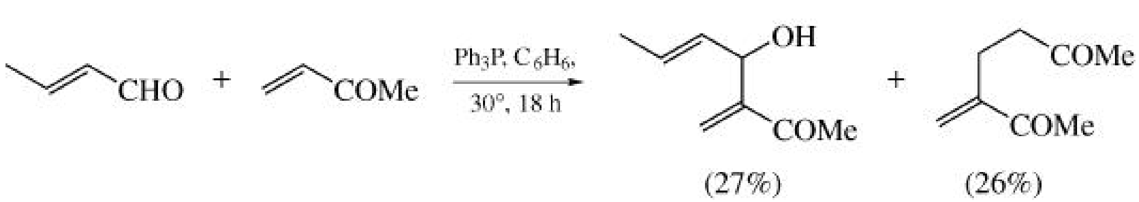
(50)

Attempts to add acrolein to activated olefins lead to polymerization instead, (127) but methacrolein, crotonaldehyde, β , β -dimethylacrolein, and cinnamaldehyde react normally with acrylates (Eq. 51) (127) and acrylonitrile. Dimerization of the activated



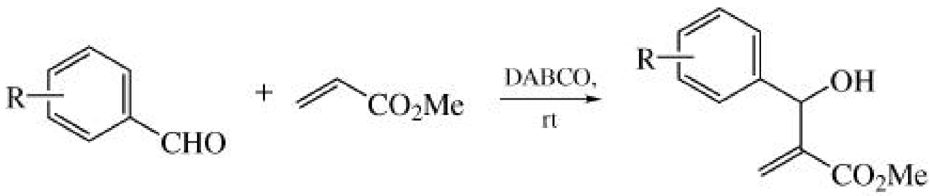
(51)

olefin occurs exclusively in the attempted DABCO-catalyzed addition of methacrolein and crotonaldehyde to methyl vinyl ketone; (127) some α -hydroxyalkylation product is isolated with phosphine catalysis (Eq. 52). (61) Crotonaldehyde does not add to phenyl vinyl sulfone . (56)



(52)

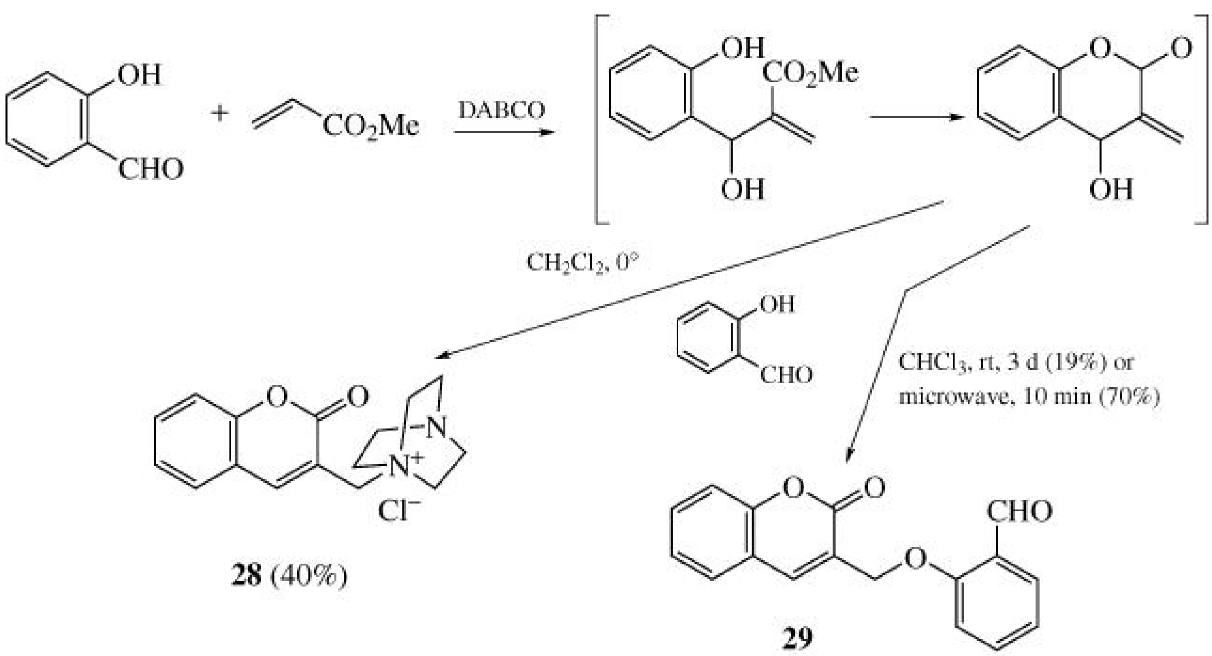
Aromatic aldehydes, especially those containing electron-withdrawing groups, add to activated olefins in high yield (Eq. 53). The exceptional reactivity



R	Time	Yield (%)
H	2 d	(92)[126]
2-Cl	4 d	(90)[97]
4-NO_2	18 h	(95)[128]
4-MeO	20 d	(90)[129]

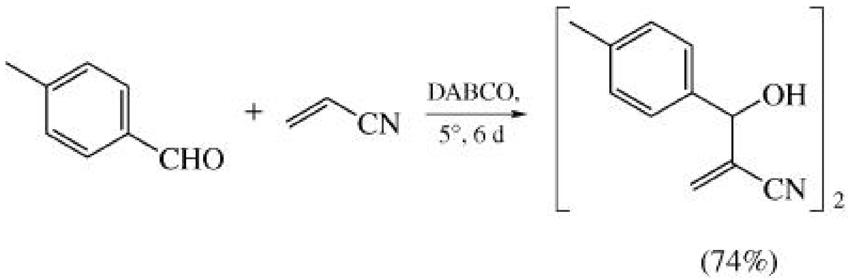
(53)

of tricarbonylchromium complexes of benzaldehyde and *ortho*-substituted benzaldehydes (97) has been mentioned in the section on Diastereoselectivity (Eq. 27). Yields are low when aromatic aldehydes are used in combination with rhodium and ruthenium complexes. (19) The DABCO-catalyzed reaction of 2-hydroxybenzaldehyde with methyl acrylate in chloroform leads to diadduct **29**, (54) which is also obtained on microwave irradiation (76) (Eq. 54). With methylene chloride as the



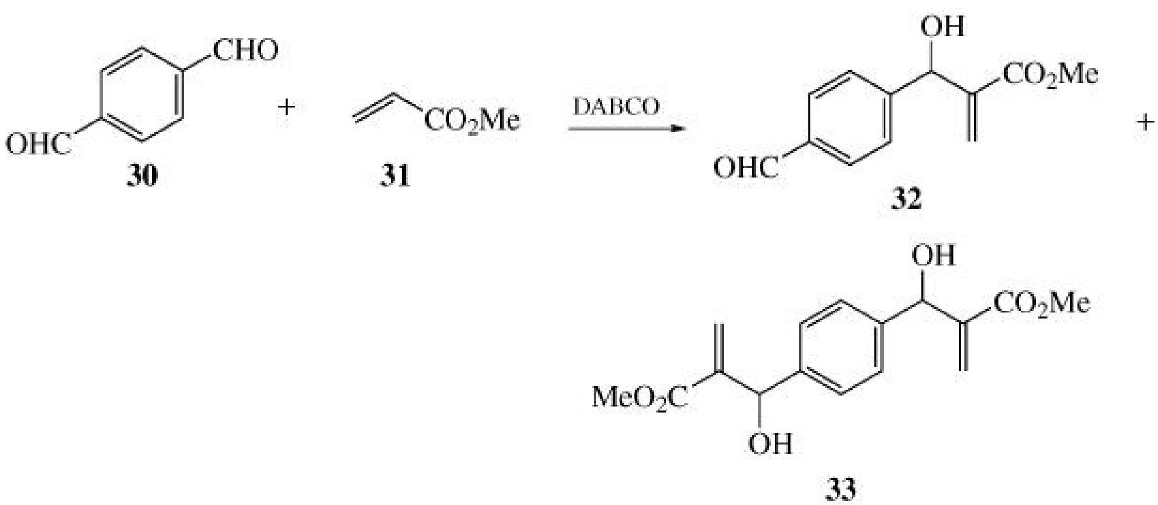
(54)

solvent, formation of quaternary salt **28** is reported; the chloride ion is presumably derived from the solvent. (32) In the reaction of aromatic aldehydes with acrylonitrile, 2:1 complexes with DABCO are sometimes formed (49, 130) (Eq. 55). (49)



(55)

They are readily decomposed by treatment with acid. (130) Mono- or diadducts may be obtained in the DABCO-catalyzed reaction of aromatic or heteroaromatic dialdehydes with methyl acrylate (Table I-E) (71, 126, 131) (Eq. 56). (71) With *ortho*-phthalaldehyde, a cyclic hemiacetal is the sole product (Eq. 57). (126) The reactivity



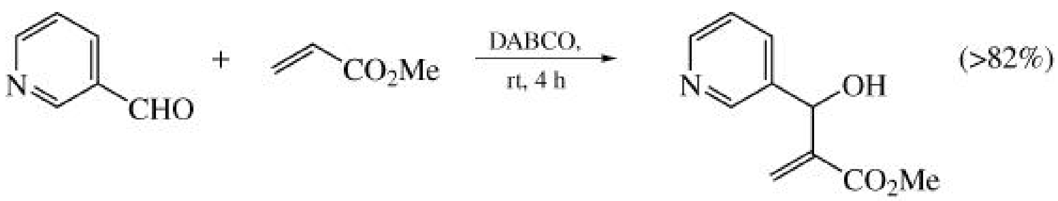
(56)

Ratio **30:31**	catalyst (mol %)	time	**32**	**33**
1:2	50	2.5 h	(94%)	(4%)
1:10	100	96 h	(2%)	(90%)

(86%) (57)

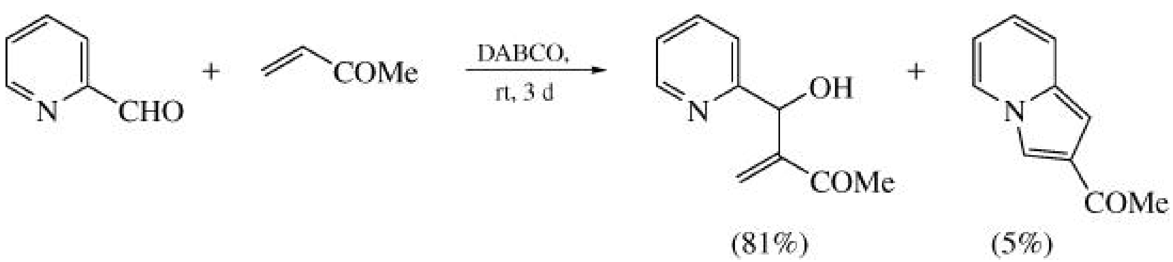
of polynuclear aromatic aldehydes decreases in the order benzaldehyde > 1-naphthaldehyde > 9-anthraldehyde. The last does not add to methyl acrylate with DABCO catalysis at room temperature. (132)

Heteroaromatic aldehydes are excellent electrophiles in the Morita–Baylis–Hillman reaction because of their increased electrophilicity (Eq. 58). (5) The heteroatom



(58)

is also believed to facilitate the proton transfers that are involved in the reaction. (5) A small amount of a cyclization product is formed in addition to the normal product in the reaction of 2-pyridinecarboxaldehyde with methyl vinyl ketone (Eq. 59). (113)



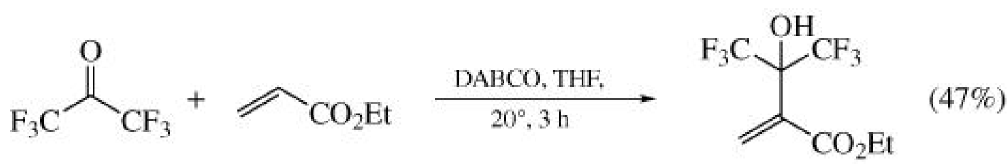
(59)

5.2.2. Ketones (Table VIII)

Unactivated ketones do not undergo the Morita–Baylis–Hillman reaction under ambient conditions. Acetone adds to *n*-butyl acrylate under the influence of DABCO at 120°, but the conversion is only 7% after 4–6 days. (74) Acetone (Eq. 60), (49) methyl ethyl ketone, and cyclohexanone react under

(60)

high pressure with acrylonitrile (25, 48, 49) but not with methyl acrylate. (79) Hindered ketones, such as diisopropyl ketone and aryl alkyl ketones, fail to react even under high pressure. (49) On the other hand, halogenated ketones, even hindered ones, add readily to acrolein (Eq. 36), acrylonitrile, ethyl acrylate (Eq. 61), (115) and presumably also to α , β -unsaturated ketones. The reluctance of

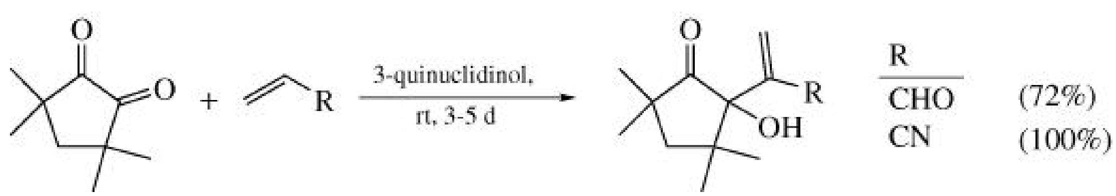


(61)

ketones to undergo α -hydroxyalkylation thus appears to be electronic rather than steric in nature.

5.2.3. α -Diketones (Table IX)

Reaction of 3,3,5,5-tetramethyl-1,2-cyclopentanedione with acrolein and acrylonitrile (Eq. 62), but not methyl acrylate, gives the

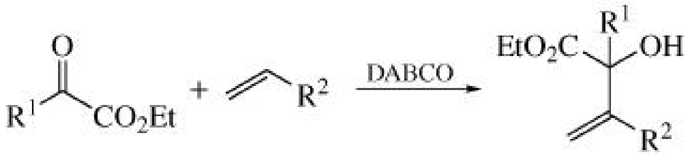


(62)

mono- α -hydroxyalkylation products in high yields. (114) Other nonenolizable α -diketones, such as 2,3-bornanedione or 2,3-norbornanedione, react only with acrylonitrile. No reaction is observed with 3,3,6,6-tetramethylcyclohexane-1,2-dione.

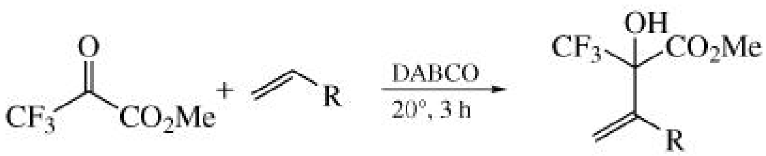
5.2.4. α -Keto Esters and α -Keto Lactones (Table X)

α -Keto esters are very reactive electrophiles in the Morita–Baylis–Hillman reaction (Eqs. 63, (133, 134) 64 (115)).



R^1	R^2	Conditions	Yield
Ph	CO_2Me	rt, 7 d	(49%)
EtO_2C	COMe	rt, 30 min	(74%)

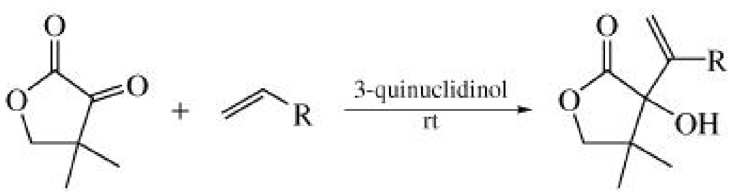
(63)



R	Time	Yield
CHO	1 h	(57%)
CN	2 h	(30%)
CO_2Et	3 h	(72%)
COMe	1 h	(80%)

(64)

The keto lactone **34** is less reactive (Eq. 65); (114) the reaction fails with methyl acrylate, probably for steric reasons. (114)



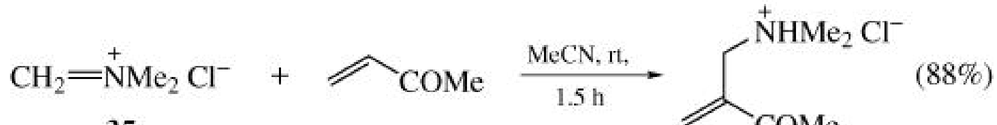
34

R		
CHO	3 d	(31 %)
CN	24 h	(81 %)

(65)

5.2.5. Imines and Iminium Salts (Table XI)

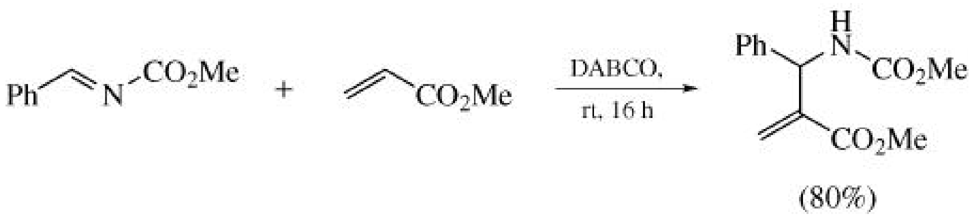
The iminium salt **35**, generated in situ from bis(dimethylamino)methane and acetyl chloride, reacts with methyl vinyl ketone in the absence of a catalyst to give the α -aminoalkylation product in high yield (Eq. 66). (135) The mechanism is believed to be similar to that of



35

(66)

the Morita–Baylis–Hillman reaction with chloride ion or a small amount of bis(dimethylamino)methane acting as the catalyst. Imines are excellent electrophiles provided that they carry a sufficiently electronegative substituent on nitrogen. Activating groups that have been employed include methoxycarbonyl (Eq. 67), (136) *tert*-butylcarbonyl, carbobenzoxy, and *p*-toluenesulfonyl (Eq. 68). (18)



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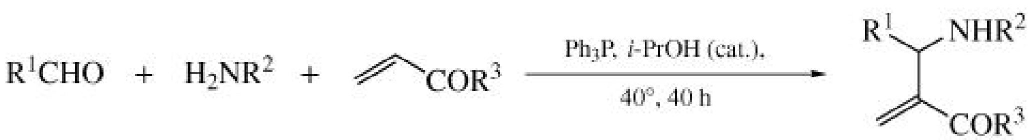
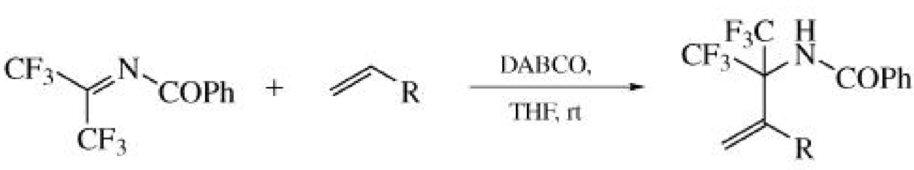


(68)

R^1	R^2	R^3	Yield
n-Pr	Ts	OMe	(80%)
Ph	CO_2Bu-*t*	Me	(50%)

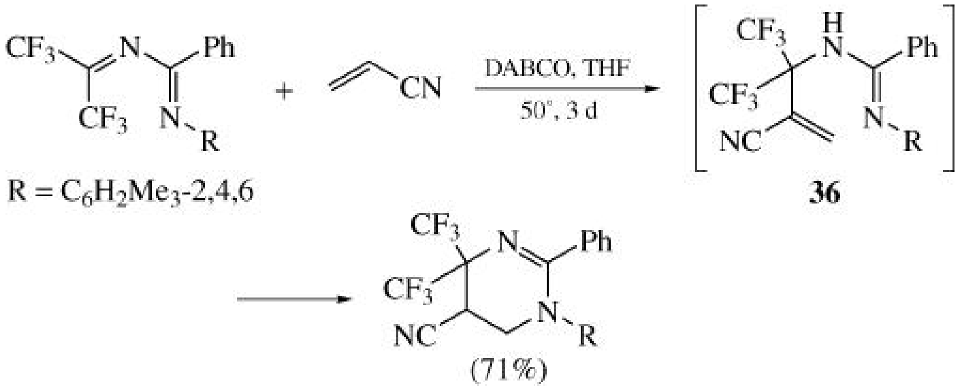
In the last example, the imine is prepared in situ from the aldehyde and amine. Hexafluoroacetone imines are among the most reactive electrophiles employed in the Morita–Baylis–Hillman reaction (Eq. 69). (116) When the imine is part of a 1,3-diazabutadiene



R	time	
CHO	30 s	(38%)
COMe	6 min	(51%)
CN	2 h	(68%)
CO_2Et	24 h	(69%)

(69)

system, the initial adduct **36**, which can be observed by (19)F NMR spectroscopy, cyclizes to give a tetrahydropyrimidine (Eq. 70). (137) This occurs even when the diazabutadiene is part of an aromatic system (Eq. 71). (137) Like the



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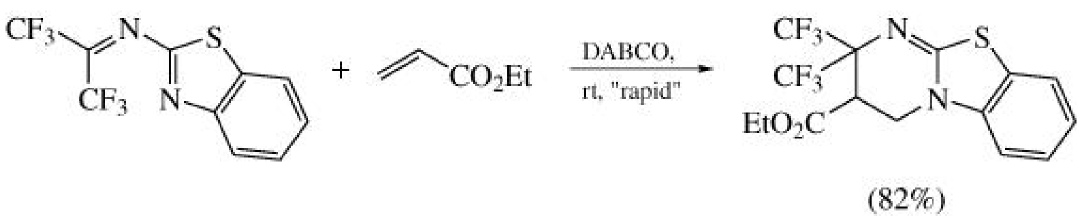
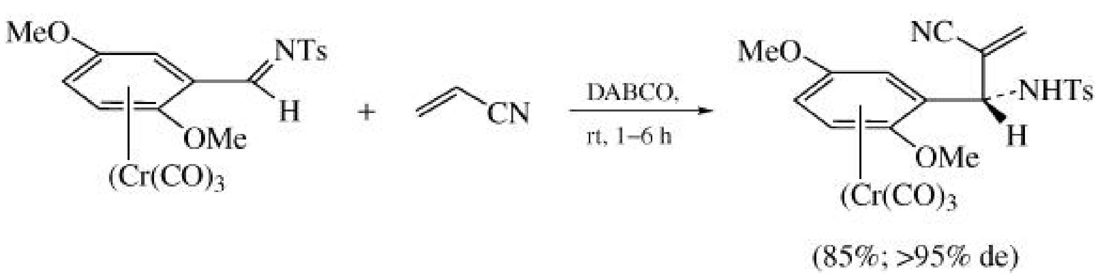


(71)

corresponding benzaldehyde derivatives (Eq. 27), tricarbonylchromium complexes of benzaldimines add rapidly and with excellent diastereoselectivity to activated olefins (Eq. 72). (98) The products are readily decomplexed in high yield and



(72)

without epimerization by treatment with air and sunlight. The failure of imines derived from aliphatic aldehydes to add to activated olefins has been attributed to enolization. (138)

5.2.6. Other Electrophiles

Esters, alkyl halides, vinyl ethers, acetic anhydride, and epoxides either do not react under Morita–Baylis–Hillman reaction conditions or give intractable mixtures. (49)

5.3. Intramolecular Reactions

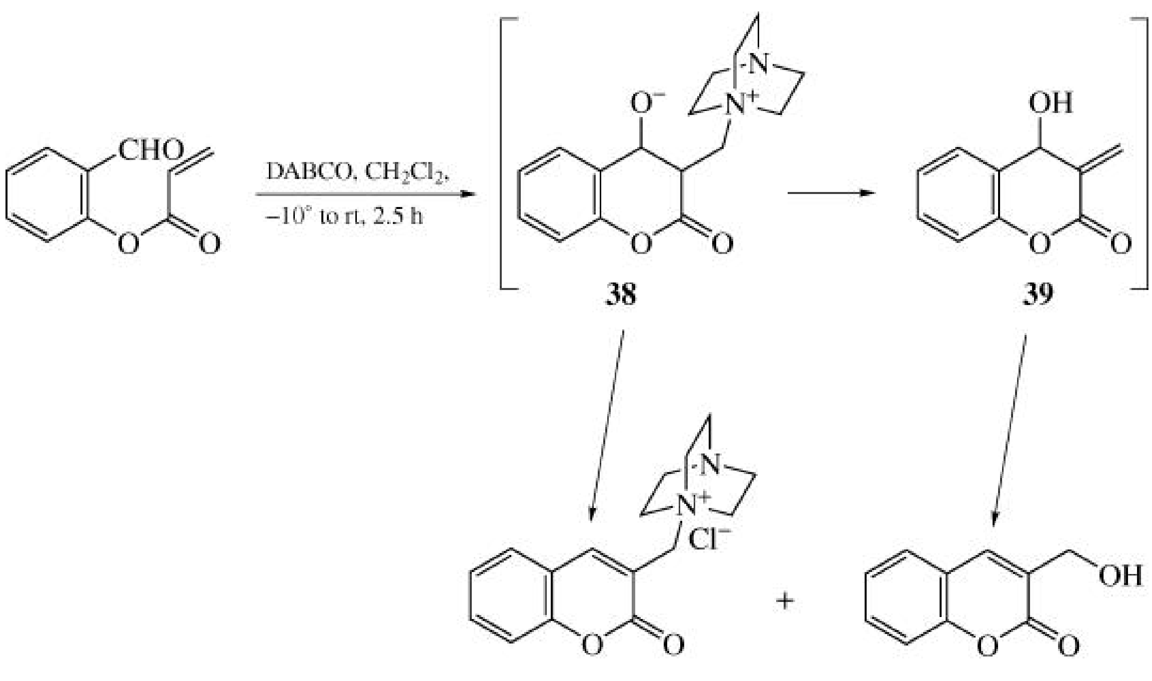
The literature abounds with examples of dramatically increased rates and stereoselectivities of intramolecular reactions as compared to their intermolecular counterparts. Nevertheless, this aspect of the Morita–Baylis–Hillman reaction has received little attention. The cyclization of ketones **37** (Eq. 73) (29) is not

37

(73)

n	Conditions	Yield (%)
0	PhPMeBu-*i*, rt, 30 d	(50)
1	$PhPMe_2$, rt, 6 d	(17)

particularly efficient, but it has to be kept in mind that the corresponding intermolecular reaction, addition of acetone to methyl crotonate, fails even under high pressure. The only other reported example of an intramolecular α -hydroxyalkylation is shown in Eq. 74. (32) The source of the chloride ion in salt **40** must be the



(74)

solvent. Isolation of salt **40** has been taken as evidence for the intermediacy of zwitterion **38**, although salt **40** could in principle also arise from intermediate **39** (cf. Eq. 54).

5.4. Side Reactions

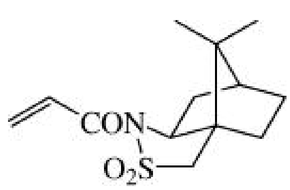
5.4.1. Dimerization and Polymerization of the Activated Olefin (Tables XIII-A–D)

Head-to-tail dimers are formed when the activated olefin acts as the electrophile in Morita–Baylis–Hillman reactions (Eq. 75). This side reaction does

(75)

not occur with methyl and ethyl acrylate, which do not dimerize at room temperature even with equimolar amounts of DABCO. (49, 139) Under 4-kbar pressure at 36°, methyl acrylate gives 25% of the dimer and 8% of a mixture of trimer, tetramer, and pentamer after 23 hours. (49) Acrylates with electronegative groups in the alcohol moiety dimerize under the influence of 20–40 mole percent of DABCO (CO_2**R**; time, yield): 4-nitrophenyl, 9 hours, 99%; pantolactone, 10 hours, 100%; phenyl and *p*-tolyl, 10 hours, 98%; ethyl mandelate, 8 days, 95%; ethyl lactate, 14 days, 89%. (139) Successful additions to all of these esters have been reported, although the yield from the 4-nitrophenyl ester is low. Whether dimerization is reversible in the presence of DABCO does not appear to have been established, nor has the influence of amine structure on the rate of dimerization been investigated. Tertiary phosphines appear to produce more acrylate dimers than DABCO (see Table XIII-A).

Only dimer formation (17–22%) is observed when acrylamide **41** is treated with aliphatic or aromatic aldehydes in the presence of DABCO at room temperature (84)

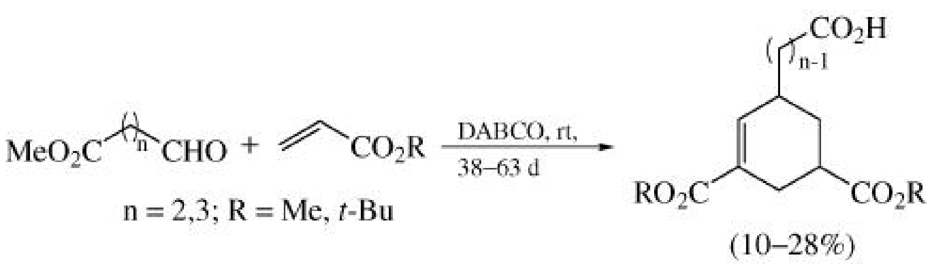


41

(but not at 0°; Eq. 25a). With 50 mol % of DABCO, acrylonitrile dimerizes to the extent of 40% after 10 days at room temperature; (140) with 1 mol % of the catalyst 65% of the dimer is formed after 23 hours at 36° and 4 kbar pressure. (49) With phosphines, dimerization appears to be somewhat more prominent (see Table XIII-C). α , β -Unsaturated ketones dimerize more rapidly than either acrylates or acrylonitrile (Table XIII-D), but their reactivity in α -hydroxyalkylation reactions is also higher. Substrates containing electronegative groups, such as aryl vinyl ketones and acetylmethyl vinyl ketone, (140) are particularly prone to dimerization with both DABCO and tertiary phosphine catalysis. (61, 62) Polymerization appears to be a significant problem only with acrolein and with some of the other activated olefins at elevated temperatures. The more hindered 2-pentyl acrylate, (50) and presumably also *tert*-butyl acrylate, are less prone to polymerize than methyl acrylate.

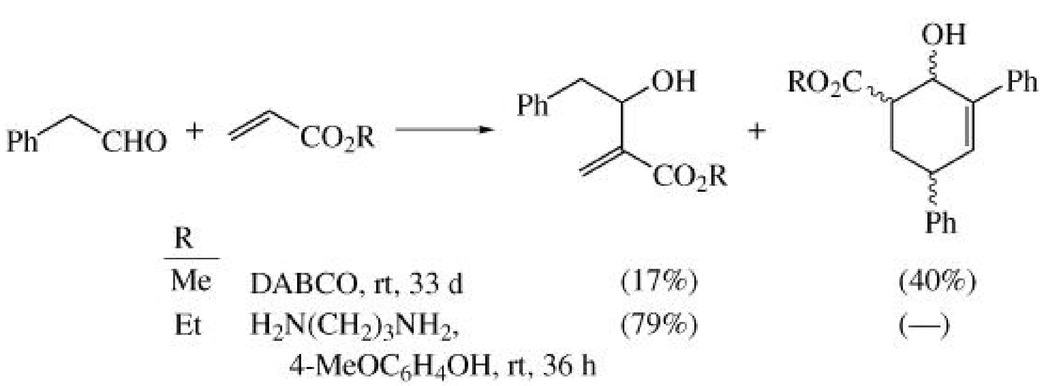
5.4.2. Aldol and Michael Additions

Even though DABCO is capable of abstracting the α hydrogen from aldehydes, (37, 141) products arising from these two reactions have been reported only rarely. The products shown in Eq. 76 are believed to



(76)

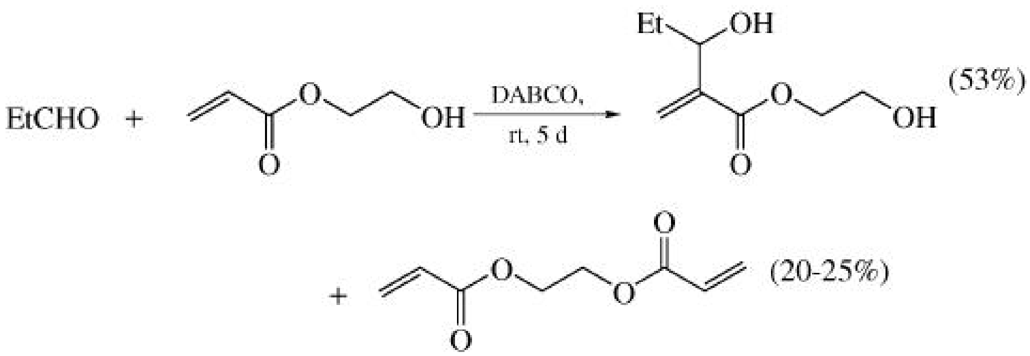
arise by initial Michael addition of the aldehyde to the acrylate; the normal α -hydroxyalkylation products are formed in only small amounts. (124) The Michael addition of 2-methylpropanal to methyl vinyl ketone (Eq. 18) and acrylonitrile in the presence of tributylphosphine has been reported. (65) DABCO-induced aldol condensation of phenylacetaldehyde with itself is postulated to be the first step in the formation of the main product in Eq. 77, (124) but this side reaction can be avoided by use of the 1,3-diaminopropane/4-methoxyphenol catalyst system. (44)



(77)

5.4.3. Miscellaneous Side Reactions

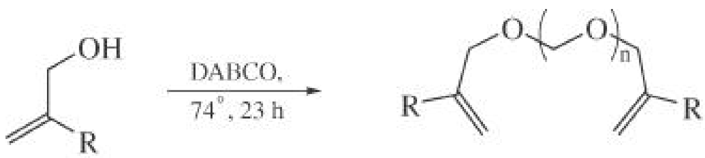
In the reaction of 4-chlorobutanal with methyl acrylate, the yield of α-hydroxyalkylation product is reduced as a consequence of quaternization of DABCO by the chloroaldehyde. (5) Solvolysis of methyl acrylate is observed when ethylene glycol or water is used as the solvent. (42) Some 1,2-ethanediol diacrylate is formed in the reaction of propionaldehyde with 2-hydroxyethyl acrylate (Eq. 78). (111)



(78)

5.4.4. Further Reactions of Initial Products under Morita–Baylis–Hillman Conditions

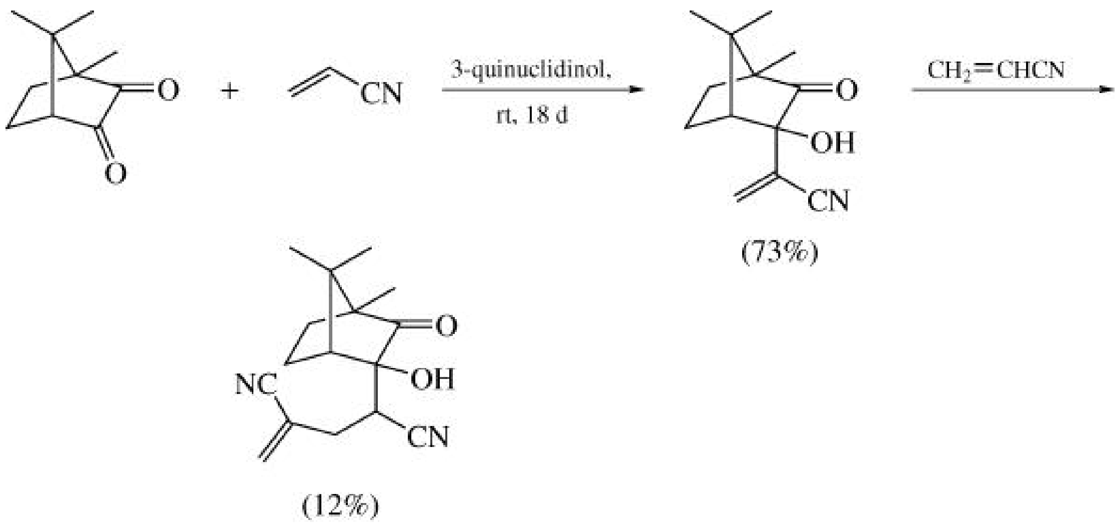
Methyl α -hydroxymethylacrylate is converted into its ether **42** ($R = CO_2Et; n = 0$) under the influence of DABCO (Eq. 79). (142) This and higher



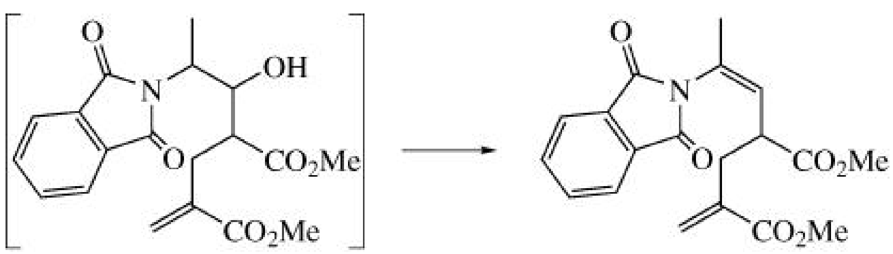
42; $R = CO_2Et$, n = 0 (54%)

(79)

ethers (**42**; $R = CO_2R; n = 1,2$) are thus formed as side products in the reaction of formaldehyde with acrylates, (142, 143) and presumably also with other activated olefins. α -Hydroxymethylacrylonitrile is converted into its ether (**42**; R = CN; n = 0) on attempted distillation. (74) Ether formation does not appear to be a problem with α-hydroxyalkylation products derived from other aldehydes. The formation of 4-oxo-5-methylene-1,3-dioxanes in the addition of aldehydes to the pantolactone ester of acrylic acid (Eq. 30) and of aliphatic aldehydes to aryl acrylates (Eq. 29) has been mentioned previously. Similarly, the formation of lactones (Eq. 48), acetals (Eqs. 49, 57), or ketals (Eq. 49) in products having ester, aldehyde, or keto groups at appropriate distances has already been mentioned, as has been the formation of cyclization products resulting from intramolecular Michael additions (Eqs. 59, 70, and 71). The formation of small amounts of 2:1 adducts of activated olefin and aldehyde is sometimes observed (76, 114) (Eq. 80). (114) In one reaction, loss of water from the diadduct occurred (Eq. 81). (144)



(80)

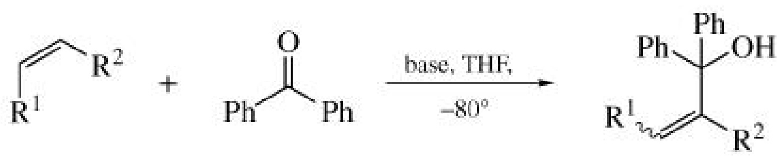


(81)

6. Comparison with Other Methods

When yields are reasonable, the catalyzed α-hydroxyalkylation and α-aminoalkylation reactions discussed in this chapter are unsurpassed in their simplicity, economy, and atom efficiency. However, they do have serious limitations, such as the lack of reactivity of most ketones and β-substituted activated olefins, and often poor diastereo- and enantioselectivty. The following is a survey of alternative methods for preparing Morita–Baylis–Hillman products from either the same or different starting materials.

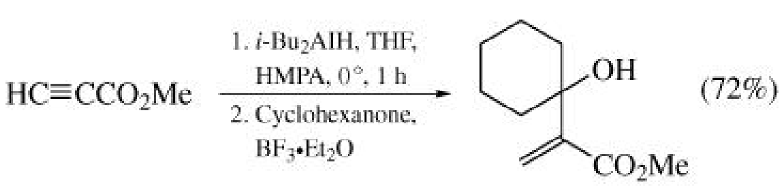
The direct formation of anions from activated olefins with strong bases is feasible, but interception of these intermediates with electrophiles has to compete against their great propensity to polymerize. (145) Furthermore, the strongly basic conditions may induce aldol and/or Michael additions when enolizable aldehydes or ketones are employed. The anions of acrylonitrile and methyl acrylate add to benzophenone (Eq. 82); (146) addition of the former to protected sugar aldehydes has



R^1	R^2	base	
D	CN	LiN(Pr-*i*)$_2$	(31%)
D	CO_2Me	Li tetramethylpiperidide	(27%)
Ph	CN	$LiNEt_2$	(83%)

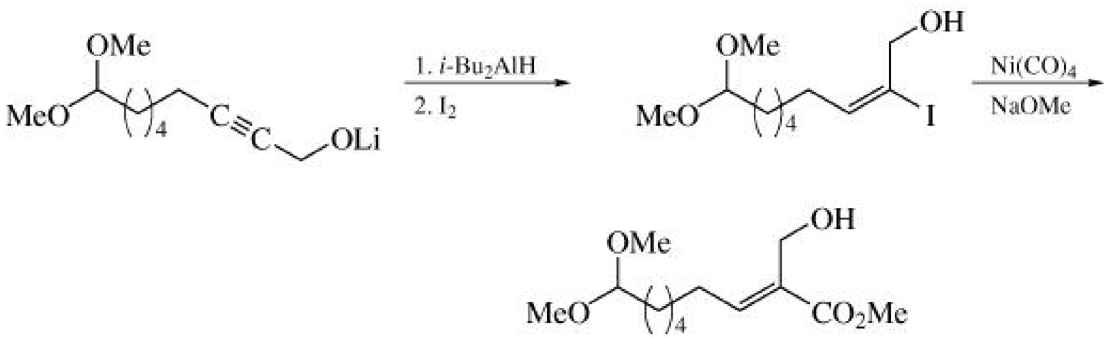
(82)

also been reported. (147) Higher yields are often obtained from β -substituted vinyl anions (146, 148-153) (Eq. 82), (146) since they are less prone to polymerization. The formation and reaction of the anion of ethyl allenecarboxylate was mentioned previously (Eq. 32). Aluminum species obtained by addition of diisobutylaluminum hydride to methyl propiolate react with aldehydes to give α -hydroxyalkylacrylates. (154) Addition to ketones requires Lewis acid catalysis (154, 155) (Eq. 83); (154) alkyl



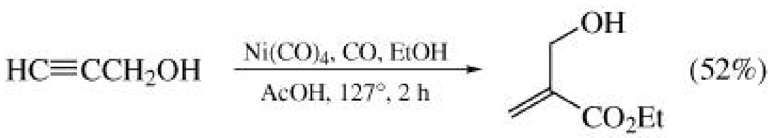
(83)

ethynyl ketones perform poorly in this reaction. A variation of this approach is shown in Eq. 84. (156) α -Hydroxyalkylacrylates are produced by reaction of



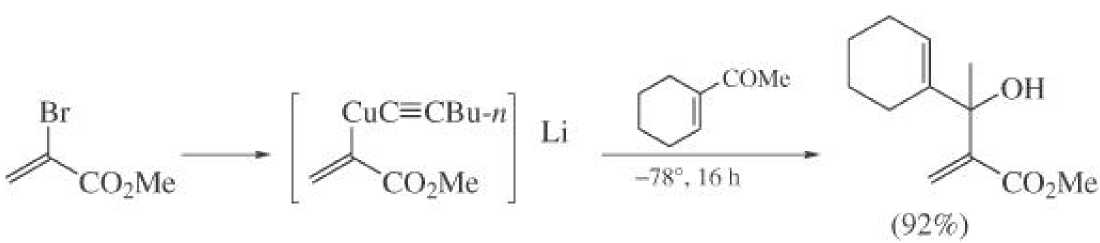
(84)

acetylenic alcohols (Eq. 85) (157) or acetates (158) with nickel carbonyl in ethanol. The cuprate derived from methyl α -bromoacrylate reacts readily with ketones and



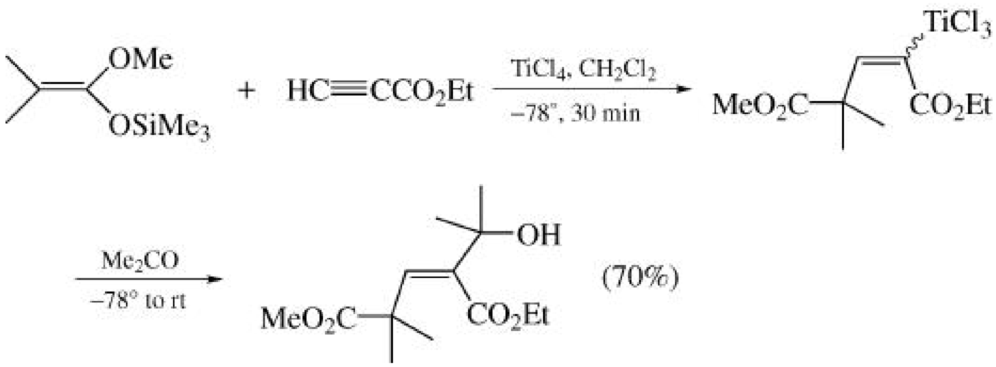
(85)

aldehydes, including α , β -unsaturated ones (Eq. 86). (159) For references on the generation and reactivity of other α -metal derivatives of acrylic esters, see ref. 160.



(86)

The titanium species generated by the reaction of ketene (alkyl)(trimethylsilyl) acetals with ethyl propiolate react with aldehydes or ketones to give β -substituted α -hydroxyalkylacrylates (Eq. 87). (160) α -Anions of acrylates, acrylonitrile, and

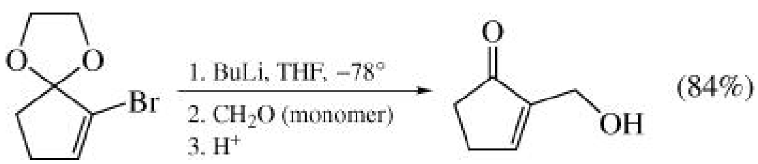


(87)

α , β -unsaturated ketones can be generated from the corresponding α -trimethylsilyl derivatives with fluoride ion; (161-163) both β -substituted activated olefins and ketones can be employed (Eq. 88). (161)

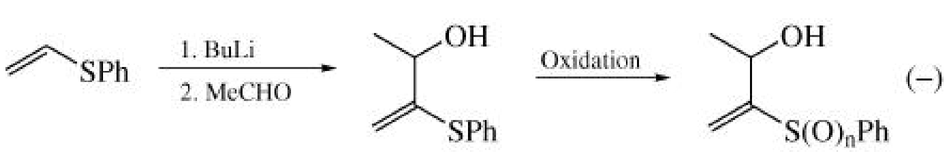
(88)

Temporary protection of the activating group in α , β -unsaturated aldehydes, (164) ketones, (165, 166) and esters (167) as the acetal, ketal, or orthoester, respectively, permits generation of the vinyl anion from the corresponding bromo compound. After addition of an electrophile, the activating group is liberated by acid treatment (Eq. 89). (165) α-Hydroxyalkylation products of phenyl vinyl sulfone and phenyl



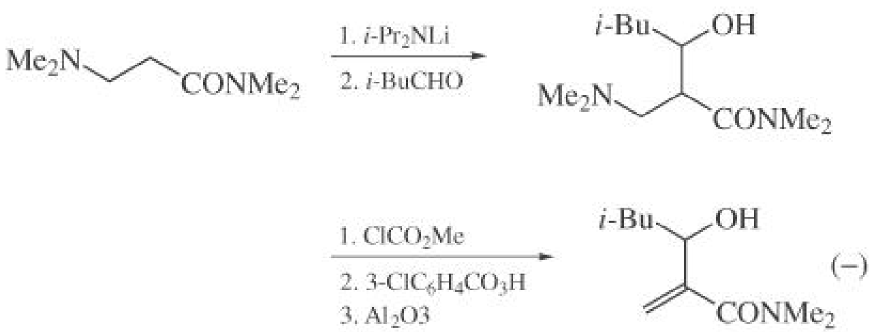
(89)

vinyl sulfoxide are accessible by a related approach involving lithiation of phenyl vinyl sulfide followed by addition of an aldehyde and oxidation (Eq. 90). (81) Alternatively,



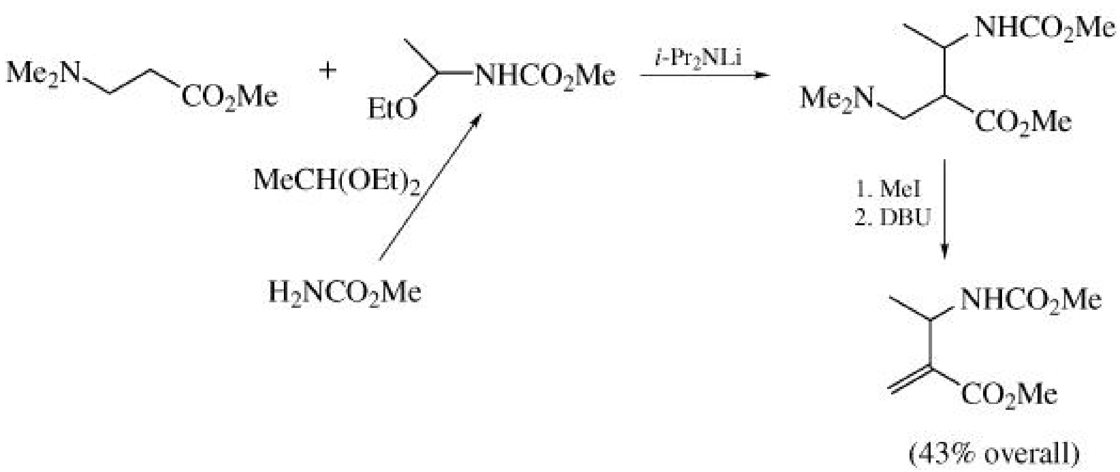
(90)

the double bond in an activated olefin is temporarily protected, for instance, by addition of a secondary amine. The resulting β -amino compound is then subjected to an aldol condensation, (119, 168-174) and the protecting group is removed by Hofmann elimination of the quaternary iodide, usually by use of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), or by Cope elimination. (119, 171) The hydroxy group usually needs to be protected to avoid retroaldol reactions. The example of Eq. 91 (119) shows the preparation of an α -hydroxyalkylation product of dimethylacrylamide



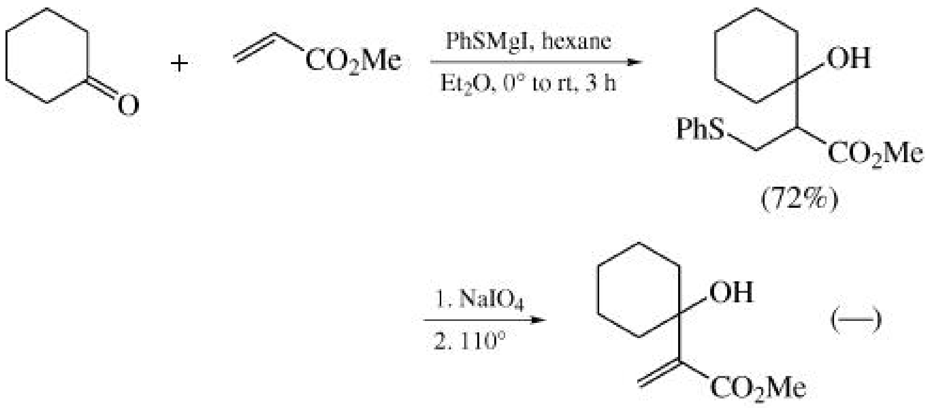
(91)

which is not accessible by a Morita–Baylis–Hillman reaction. The method can also be applied to the synthesis of β-substituted olefins. (173, 175) Use of prolinol as a temporary protecting group and chiral auxiliary leads to products with fair diastereoselectivity. (173, 175) An analogous approach permits access to α-aminoalkylation products (Eq. 92). (136) The thiophenyl group has also been

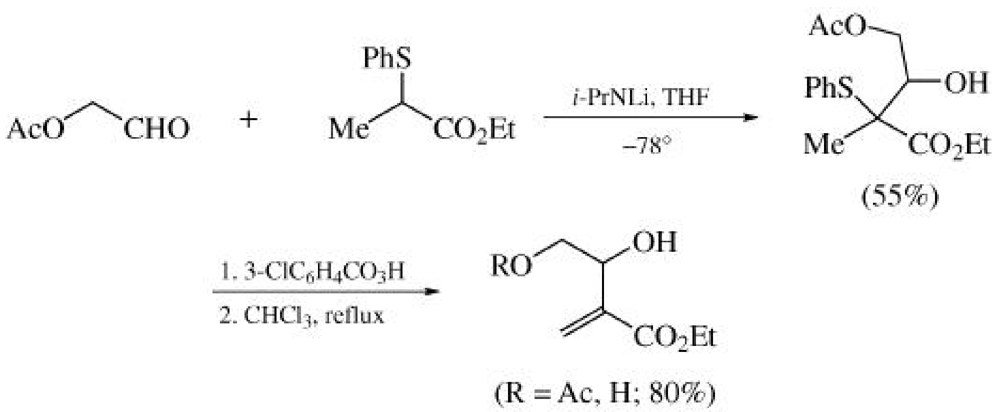


(92)

employed as a temporary protecting group (Eq. 93). (176) A variation of this approach (177, 178) is shown in Eq. 94. (177) A chiral tolylsulfoxide group can be



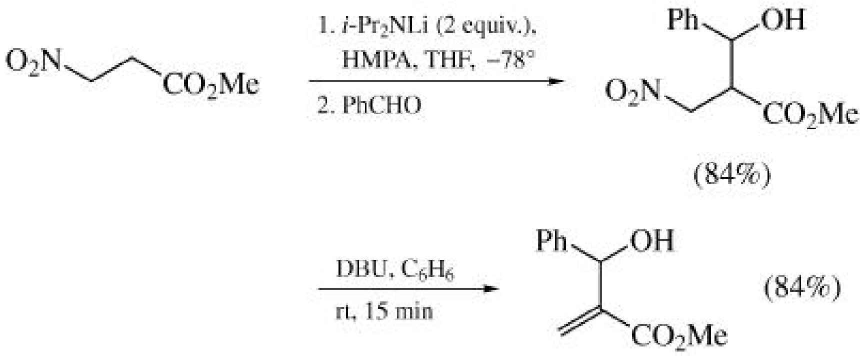
(93)



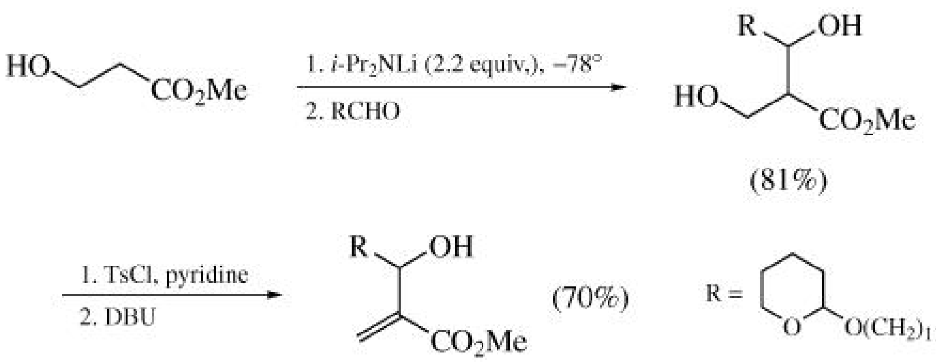
(94)

employed in place of the phenylthio group in this sequence; (179) in this case a Grignard reagent is used as the base, and elimination of sulfoxide is accomplished by thermolysis. In another variation, (180) a preformed enolate in the form of a (methylthio) (methyl)ketene acetal is employed in a Lewis acid catalyzed aldol reaction.

A nitro group (Eq. 95) (181) or a hydroxy group (182-184) (Eq. 96) (182) can serve as a temporary protecting group of the double bond as well. The latter approach takes

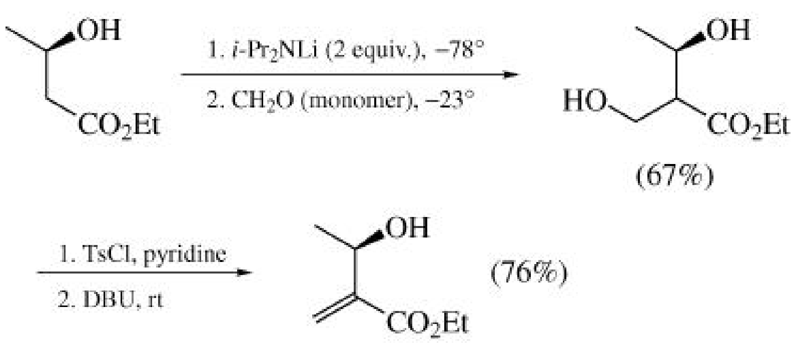


(95)



(96)

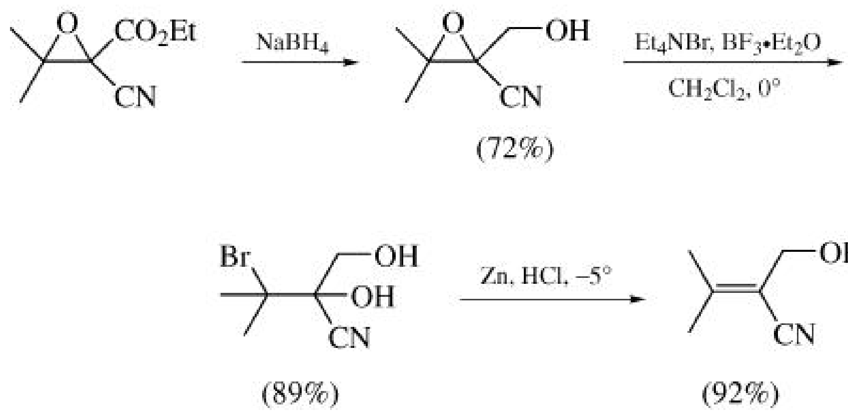
advantages of the different reactivities of the primary and secondary hydroxy groups in the intermediate. This is also used in a variation shown in Eq. 97, (185) which leads to enantiomerically pure α-hydroxyalkylacrylates.



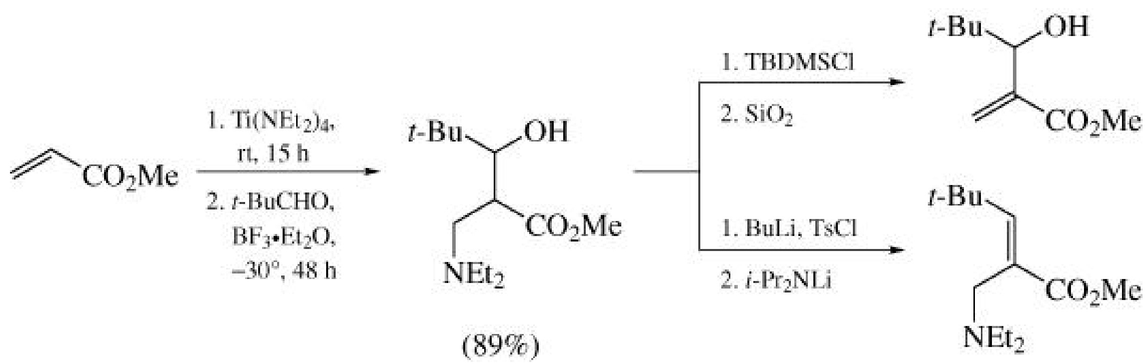
(97)

An approach to 2-hydroxyalkylacrylonitriles employs glycidic esters as starting materials (Eq. 98). (186)

The tandem β -addition/ α -functionalization strategy (187) has been applied to the preparation of α -hydroxyalkylation and α -aminoalkylation products of activated olefins (Eq. 99). (188) With α, β -unsaturated ketones, trimethylsilylamines give higher yields than the titanium reagents. (188) Organoaluminum reagents of type R_2AlX (X = PhS, PhSe, and I) have also been used in this type of reaction. (189)

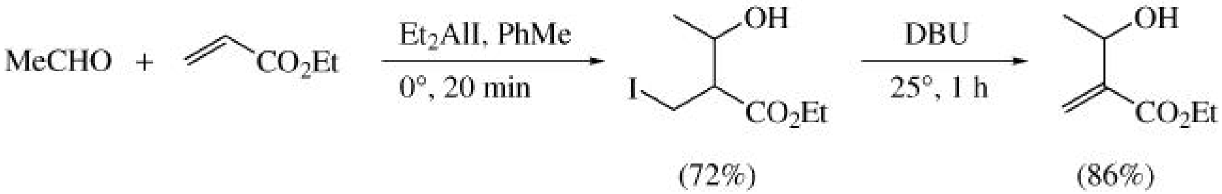


(98)



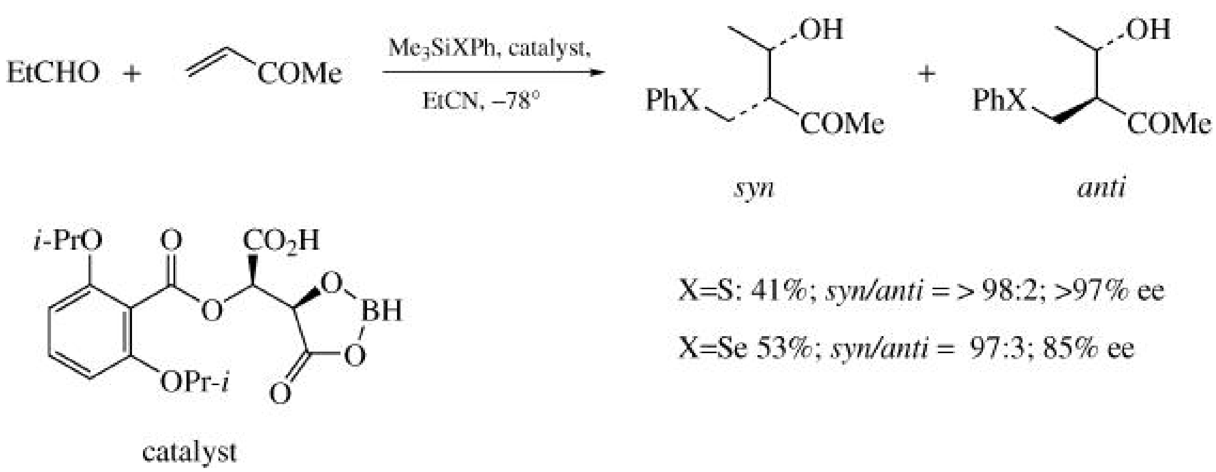
(99)

Conditions are mild enough to permit use of butenolide as a substrate. Diethylaluminum iodide appears to be the reagent of choice because of the ease of hydrogen iodide removal in the second step (Eq. 100). (189) The second step proceeds spontaneously



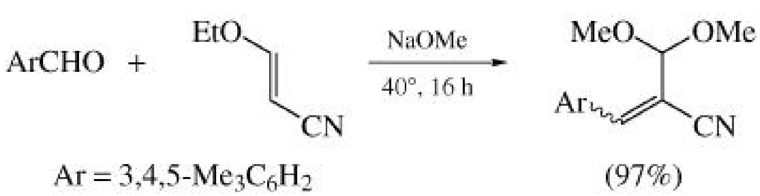
(100)

without the addition of a base with α , β -unsaturated ketones. (189-191) Other reagents that are used in the α -hydroxyalkylation of α , β -unsaturated ketones include trimethylsilyl triflate with dimethyl sulfide (192) or with pyridine, (193) (phenylseleno)dialkylboranes, (194) and (trimethylsilyl)(phenyl)selenide catalyzed by trimethylsilyl triflate. (195) Catalysis of the last reaction by a chiral borane provides α -hydroxyalkylated α , β -unsaturated ketones in high enantiomeric excess. Trimethylsilyl phenyl sulfide gives somewhat lower yields but higher enantioselectivities (Eq. 101). (103) Elimination of the benzenethiol is achieved by oxidation with *m*-chloroperoxybenzoic acid followed by heating to 130–150°; in the selenium series this is achieved by treatment with hydrogen peroxide at room temperature. Little or no recemization occurs in either variant.



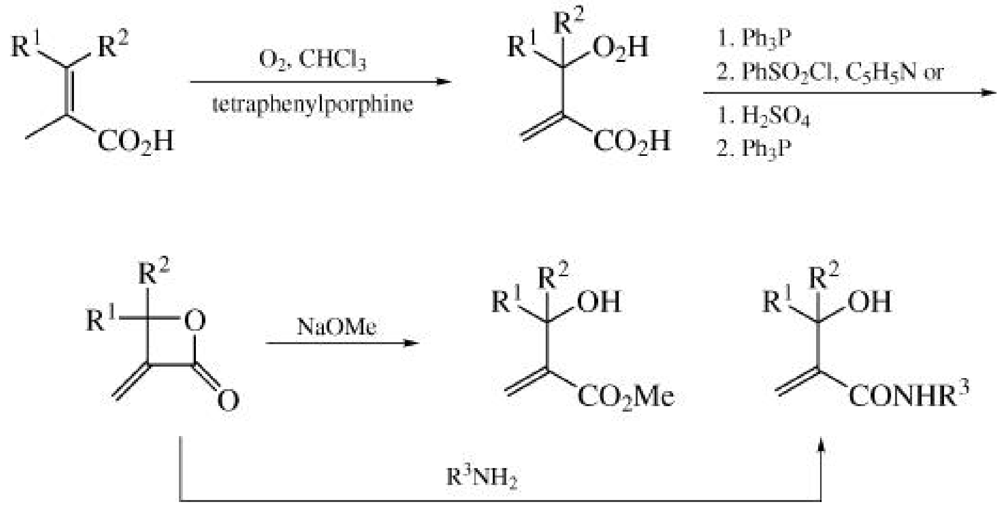
(101)

Acetals of α -formylcrotononitrile derivatives are obtained by addition of sodium methoxide and aromatic aldehydes to β -ethoxyacrylonitrile (Eq. 102). (196)



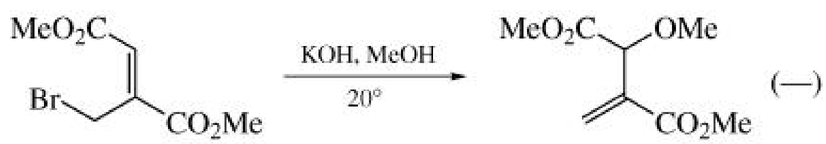
(102)

The approach depicted in Eq. 103 involves an ene reaction of singlet oxygen and permits access to both esters and amides of α -hydroxyalkylacrylic acids. (197-202)

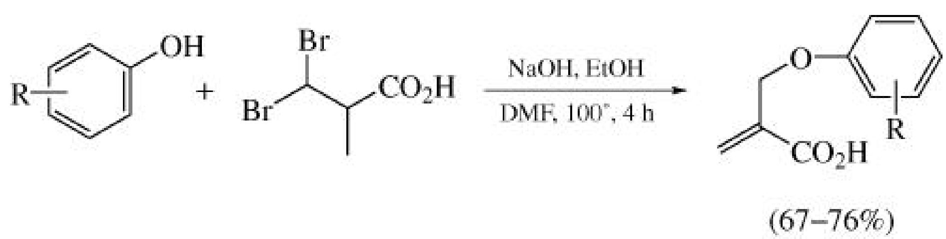


(103)

Derivatives of α -hydroxymethylacrylic acid can be obtained according to Eqs. 104 (203) and 105. (204, 205)

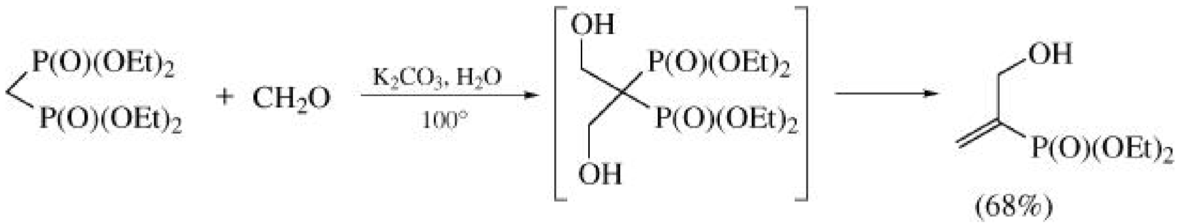


(104)



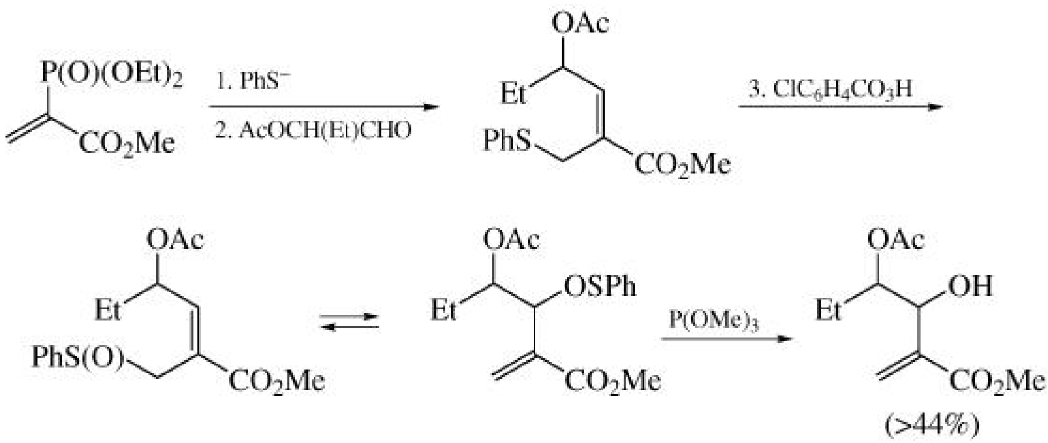
(105)

Ethyl 2-hydroxymethylacrylate is also prepared by a Wittig–Horner reaction of triethyl phosphonoacetate with formaldehyde. (206, 207) The corresponding acid is obtained by heating diethyl bis(hydroxymethyl)malonate with sulfuric acid. (208) Diethyl 2-(hydroxymethyl)vinylphosphonate, which is not accessible by the Morita–Baylis–Hillman reaction (Table VII), is formed in the reaction of tetraethyl methylenediphosphonate with formaldehyde (Eq. 106). (209) The Wittig–Horner reagent



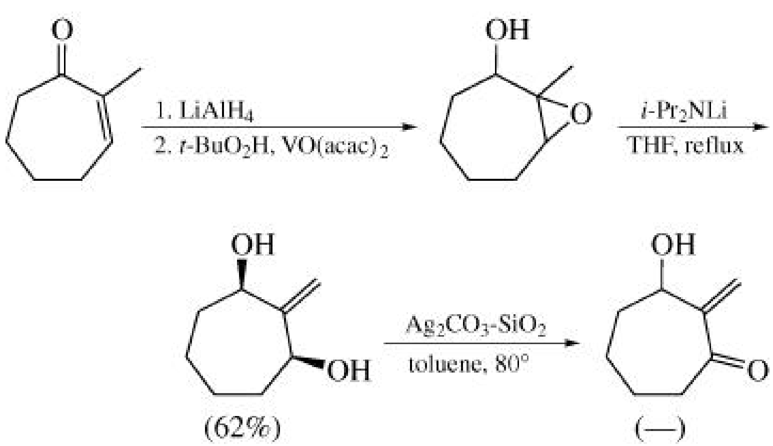
(106)

obtained by addition of thiophenoxide to triethyl methylenephosphonoacetate reacts with aldehydes to give an intermediate that can be converted into α -hydroxyalkylacrylates in two steps (Eq. 107). (210)



(107)

Products of formal intramolecular Morita–Baylis–Hillman reactions are obtained by an apparently general method depicted in Eq. 108. (211)

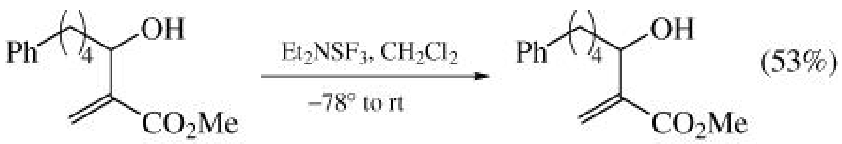


7. Synthetic Utility

Products of the Morita–Baylis–Hillman reaction contain three functionalities amenable to further manipulation: the hydroxy or amino group, the double bond, and the olefin-activating group. The following is a nonexhaustive overview of reactions of these functional groups. A more extensive treatment of this subject is found in a recent review. (22)

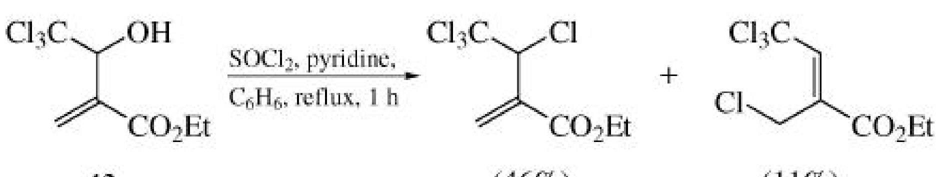
7.1. Reactions of the Hydroxy Group

Reaction of 2-hydroxyalkylacrylates with diethyl (212) or dimethylaminosulfur trifluoride (213) produces the fluorides without allylic rearrangement (Eq. 109). (212)



(109)

Ethyl 2-fluoromethylacrylate has also been prepared from the corresponding bromide with tetrabutylammonium fluoride in hexamethylphosphoric triamide. (206) With aluminum trichloride (from the acetate), (214) thionyl chloride, (11, 206) phosgene, (215) and *N*-chlorosuccinimide/dimethyl sulfide, (182, 216) the rearranged chlorides are obtained by an S_N2' mechanism. With thionyl chloride in the presence of pyridine, adduct **43** gives predominantly the unrearranged chloride (Eq. 110). (215)

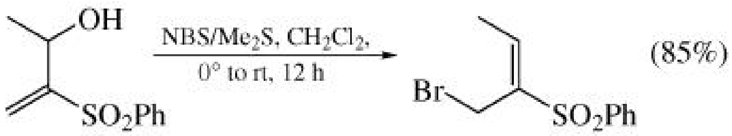


43

(110)

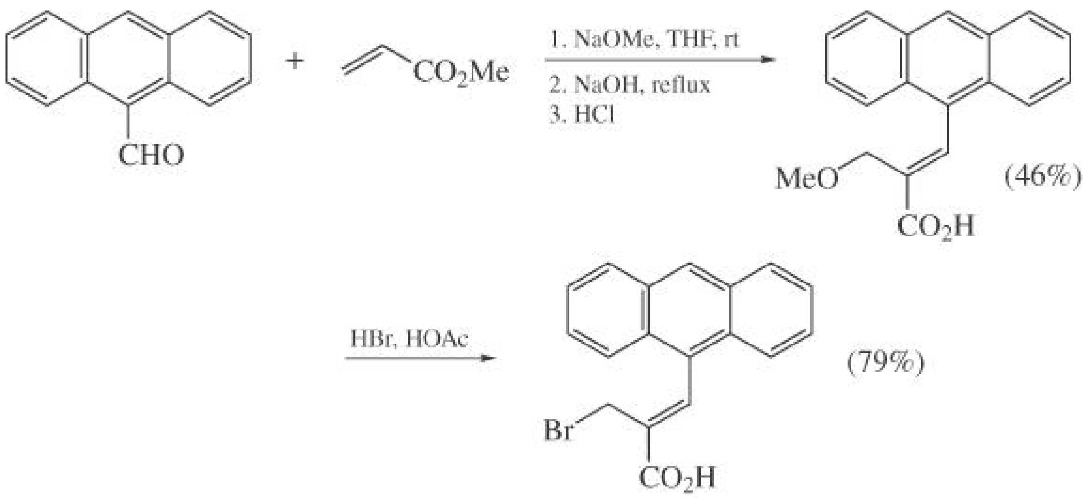
Equimolar mixtures of rearranged and unrearranged chlorides are obtained from ethyl 2-(1-hydroxyethyl)acrylate and ethyl 2-(1-hydroxybutyl)acrylate with hexachloroacetone/triphenylphosphine; from ethyl 2-hydroxybenzylacrylate only the rearranged chloride is formed. (217) The rearranged bromides are formed by treatment of 2-hydroxyalkylacrylates with hydrogen bromide, with (40, 143, 218-223) or without (224) addition of concentrated sulfuric acid. Other reagents that accomplish this transformation are *N*-bromosuccinimide/dimethyl sulfide, (4, 5, 73, 182, 216, 225-228) cupric bromide on silica, (229) and phosphorus tribromide. (207, 230-232) *N*-Bromosuccinimide/dimethyl sulfide is also used to convert

2-hydroxyalkylvinyl phenyl sulfones into the rearranged bromides (56, 233, 234) (Eq. 111). (56) Rearranged iodides are formed from



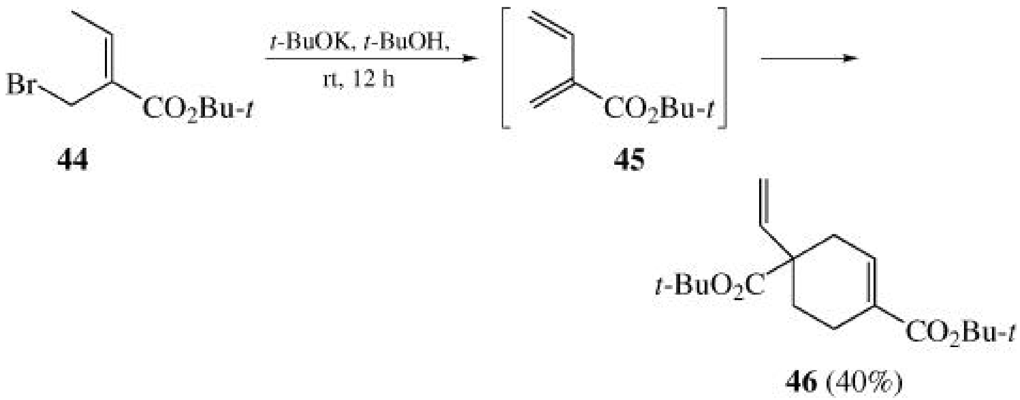
(111)

2-hydroxyalkylacrylates with hydrogen iodide in phosphoric acid (217) or from the corresponding bromides with sodium iodide in acetone. (206, 230) The synthesis of those 2-bromomethyl-3-arylacrylic acids that are not accessible by the above routes because the Morita–Baylis–Hillman reaction fails can be accomplished by the sequence of Eq. 112. (132)



(112)

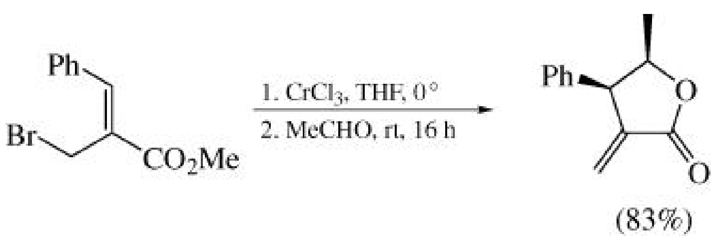
The 2-haloalkyl derivatives of activated olefins are versatile intermediates. (235) Base-induced elimination of rearranged bromide **44** gives the cyclohexene diester **46** by Diels–Alder dimerization of the very reactive intermediate diene **45** (Eq. 113). (236) Reduction of the rearranged bromides with lithium triethylborohydride proceeds with allylic rearrangement to give 2-alkylacrylates (Eq. 114). (216) Reactions with anions of β -ketoesters, (4, 217, 220) phenylacetylide, (237) lithium enolates, (56) and organocuprates (56) have been described. Conversion of the allylic bromides into organometallic species and reactions of the latter with aldehydes or ketones have been described involving the following metals: zinc, (238-241) chromium, (223, 242) tin, (223, 243, 244) indium, (245) bismuth, (243) and palladium/tin (from



(113)

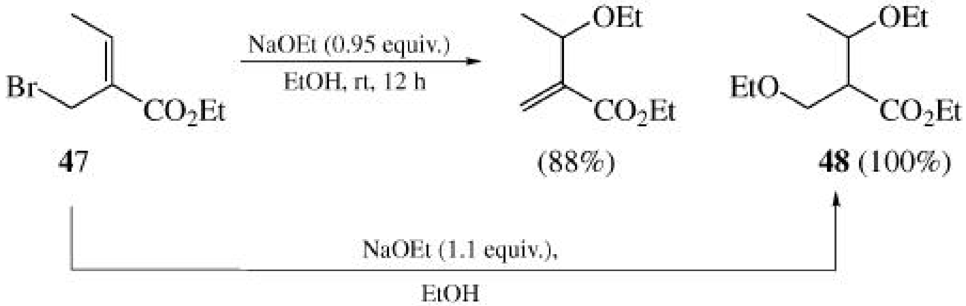
(114)

the alcohols). (246) Some of these reactions lead directly to α-methylene- γ -butyrolactones (223, 246) (Eq. 115). (223) Reaction of methyl 2-chloromethylbutenoate



(115)

with the salt $CpMo(CO)_3Na$ is the first step in the preparation of a molybdenum complex of trimethylenemethane. (247) Reaction of the rearranged bromides with alkoxides (203, 231, 237, 248) gives the ethers of the original Morita–Baylis–Hillman adducts; with more than one equivalent of the alkoxide the Michael adduct **48** is formed (Eq. 116). (237) Reaction of bromide **47** with sodium acetate in refluxing



(116)

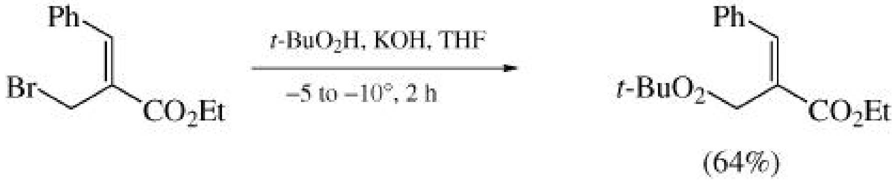
methanol, (228) on the other hand, proceeds without allylic rearrangement as does the reaction of the sodium salt **49** with oxygen, sulfur, and carbon nucleophiles (Eq. 117). (237) Unrearranged products are often obtained from 2-bromomethylcinnamates;

49

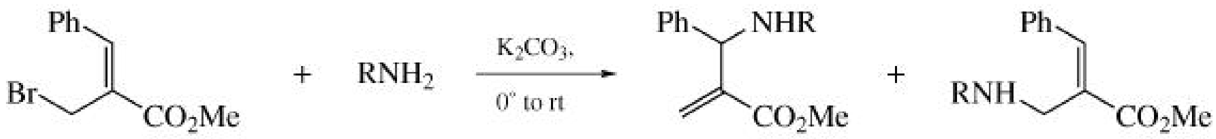
Conditions	X	Yield (%)
NaOMe, MeOH, rt, 16 h	MeO	(100)
PhONa, MeOH, rt, 16 h	PhO	(83)
PhSNa, MeOH, rt, 16 h	Phs	(94)
n-BuLi, THF, –78°, 5 h	*n*-Bu	(70)
t-BuLi, Et_2O, –78° to rt, 1 h	*t*-Bu	(—)
$(PhC{\equiv}C)_2Mg$, THF, 0° to rt, 1 h	PhC≡C	(66)

(117)

examples are the reactions with sodium sulfite (40) and the potassium salt of *tert*-butylhydroperoxide (Eq. 118). (230) Amines add to give S_N2 and/or S_N2' products depending on the amine (218, 249) and solvent (Eq. 119). (218) Amines **50** are



(118)

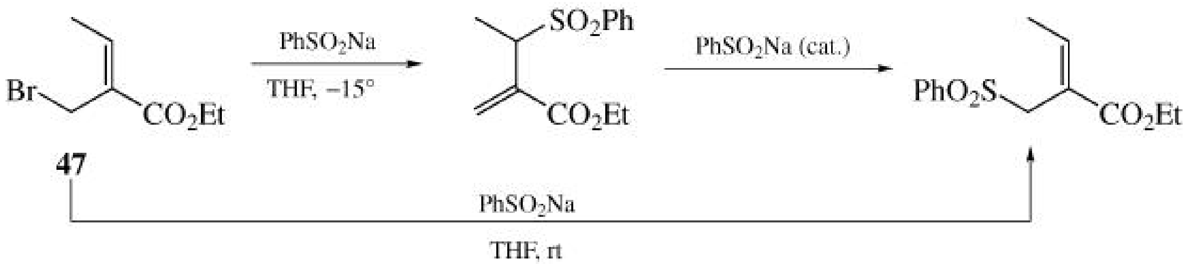


50 **51**

(119)

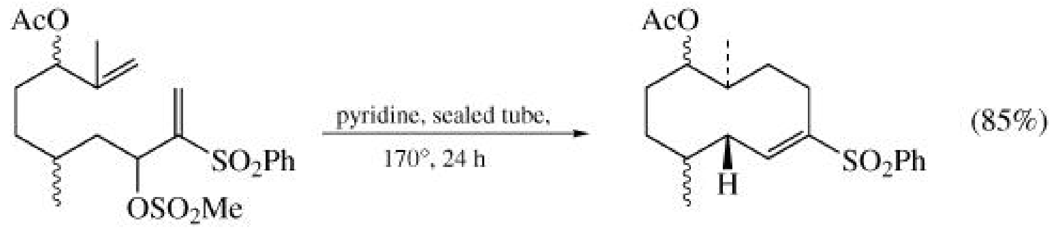
R	Solvent	**50**	**51**
i-Pr	pet, ether, 4 d	(73%)	(0%)
	MeCN, 30 min	(0%)	(69%)
4-$MeOC_6H_4$	pet, ether, 24 h	(21%)	(47%)
	MeCN, 1 h	(0%)	(59%)

slowly converted into the more stable isomers **51**, (56, 249) especially in polar solvents or in the presence of excess amine. (249) Amines of type **50** are also accessible via phenylselenium species. (225) Amines **51** where R is phenyl can also be prepared from the alcohols by treatment with phenyl isocyanate followed by cesium fluoride induced decarboxylation. (129) Amines **50** and **51** can be converted into methylene- and alkylidene- β -lactams, respectively. (218) Reaction of bromide **47** with sodium benzenesulfinate at low temperature gives the S_N2' product which rapidly isomerizes at room temperature (230, 250) (Eq. 120). (250) With thiolates, only the S_N2 products are isolated from bromides of type **47**. (56, 230) Wittig reagents can be prepared from the allylic bromides and triphenylphosphine; (251) the chlorides and trialkyl phosphites give either S_N2 or S_N2' products. (11, 215) The bromine can be replaced by a trimethylsilyl group with trimethylsilane in the presence of cuprous iodide. (216)



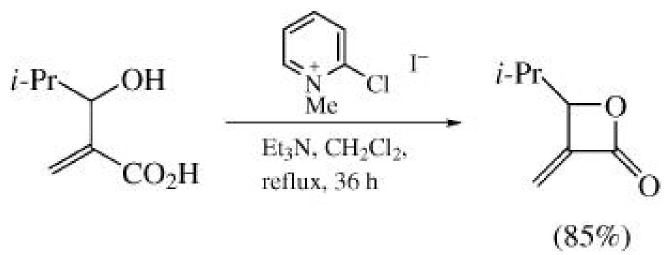
(120)

Elimination of the hydroxy group from Morita–Baylis–Hillman products is accomplished with acetic anhydride and pyridine at reflux (17) or by treatment of a derivative, such as the methanesulfonate, with a base. The very reactive dienes so obtained often dimerize in a Diels–Alder fashion (124, 252, 253) (Eq. 113), but can be isolated (234, 254) or trapped with an external diene or dienophile (124, 255) or internal dienophile (Eq. 121) (256)



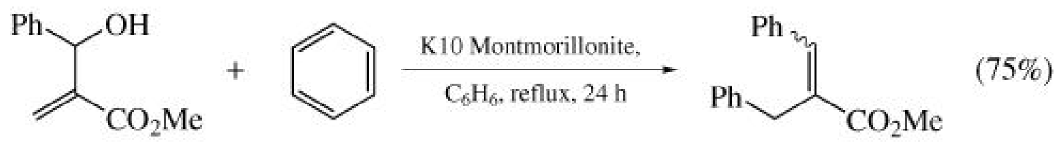
(121)

α -Hydroxyalkylacrylic acids can be cyclized to methylenepropiolactones (Eq. 122). (199, 257) The intermediate formation of acetals from α -hydroxyalkylacrylates



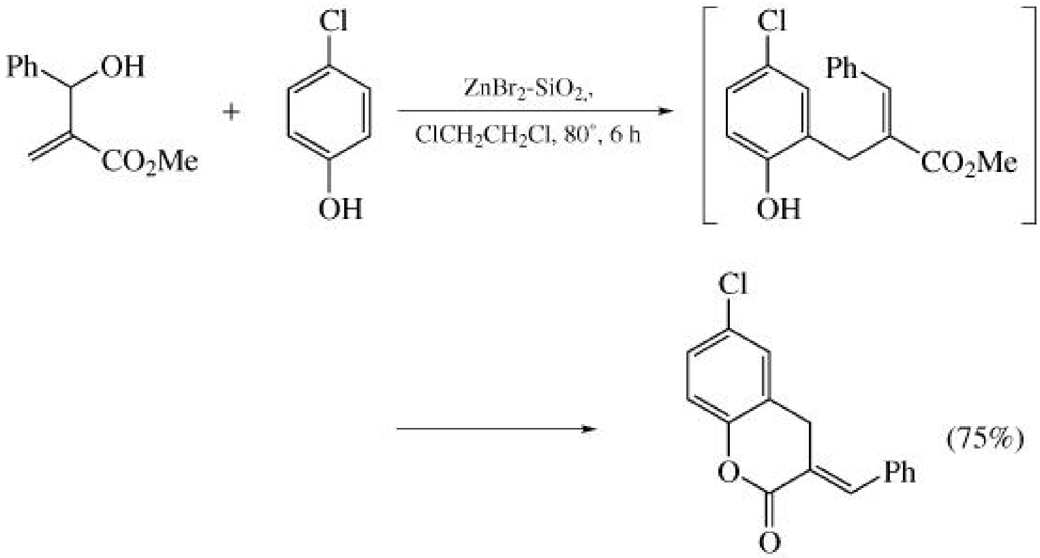
(122)

and aldehydes has been mentioned previously (Eq. 29). Friedel–Crafts reaction of α -hydroxyalkylacrylates or their acetates with benzene proceeds with allylic rearrangement (214, 258) (Eq. 123). (258) With phenols, coumarin derivatives are

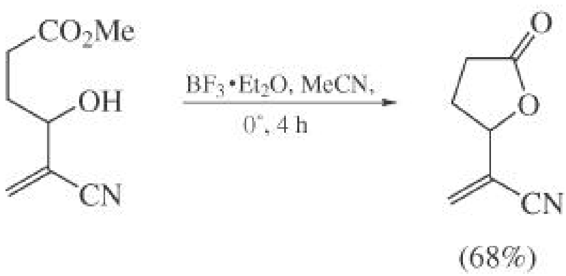


(123)

formed (Eq. 124). (259) Substrates with ester groups in the side chain can be cyclized to give lactones (Eq. 125). (125)

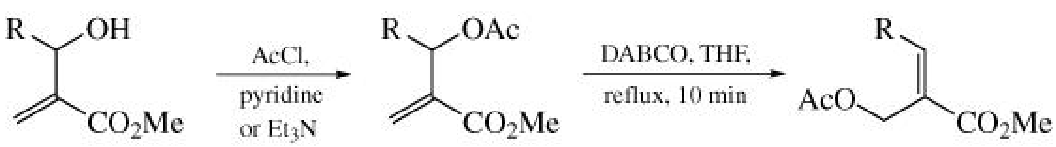


(124)



(125)

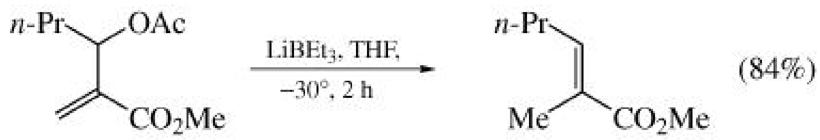
Unrearranged acetates of α -hydroxyalkylated activated olefins can be prepared by the action of acetyl chloride in the presence of a base. Acetates derived from aromatic aldehydes (R = Ar) are rearranged to the isomeric acetates by DABCO (129, 260) (Eq. 126) or a number of other reagents such as benzyltriethylammonium chloride



(126)

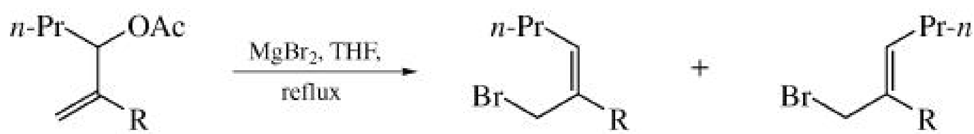
52

with cesium fluoride, potassium fluoride on alumina, or potassium carbonate at 80° (129) Acetates **52** are reactive intermediates which can be used in S_N2' substitution reactions such as the reduction (50, 216, 227, 261) shown in Eq. 127 (216) to give olefins that are isomeric to those obtained in Eq. 114. Other



(127)

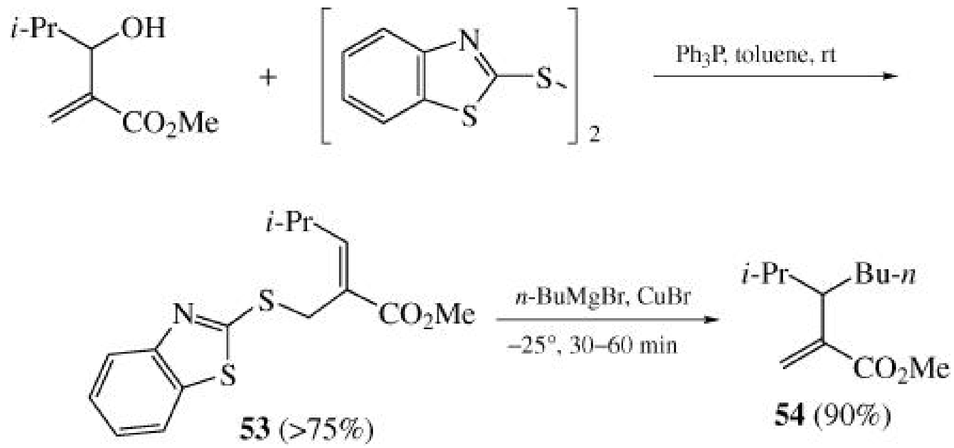
nucleophiles employed in S_N2' reactions with acetates **52** include anions of β-diketones, (262, 263) cyanoacetic ester, (262) nitroalkanes, (262) Grignard reagents, (122, 264-266) ammonia, (129, 231) primary (129, 131) and secondary amines, (129) sodium azide, (129) triethyl phosphite, (267) and the complex $Bu_3SnCuLiBr·Me_2S$. (268) The stereochemical outcome of the reaction with magnesium bromide depends on the olefin-activating group (Eq. 128). (269)



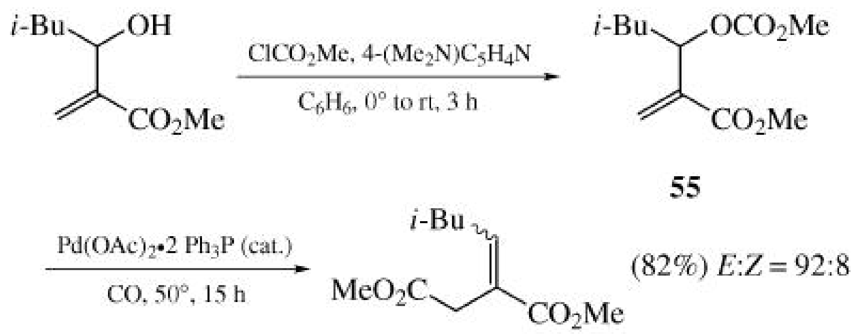
(128)

R	time (h)	% *Z*	% *E*
CO_2Me	3	64	0
CN	10	6	64

Treatment of 2-hydroxyalkylacrylates with carboxylic acids under Mitsunobu conditions gives almost exclusively the S_N2' products. (226, 228) In a transformation involving two S_N2' reactions, the α-substituted acrylates **54** are obtained via thioether **53** (Eq. 129). (270) The mixed carbonates **55** are used in palladium-catalyzed carbonylation reactions (Eq. 130). (119, 271) Phenyl ethers (272) and vinyl

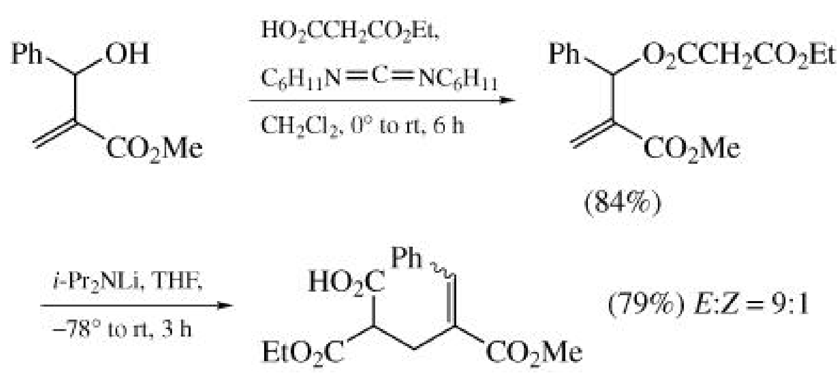


(129)

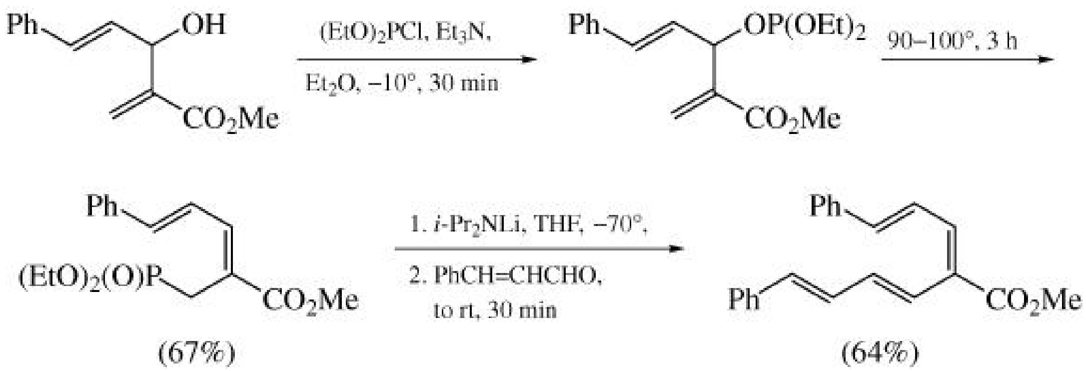


(130)

ethers (272-274a) have been subjected to the Claisen rearrangement (Eq. 131). (274) α -Hydroxyalkylacrylates and α-hydroxyalkylacrylonitriles react with dialkyl chlorophosphites to give phosphonates by an Arbuzov rearrangement. (12, 275) The latter can be used in Wittig–Horner reactions (Eq. 132). (275)

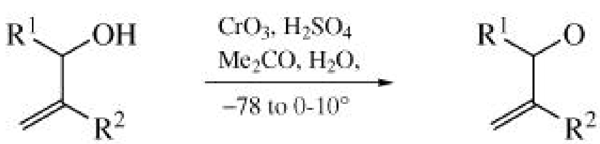


(131)



(132)

Oxidation of the hydroxy group to give highly reactive doubly activated olefins has been accomplished with Jones reagent (Eq. 133). (43, 80) Pyridinium chlorochromate



(81%)

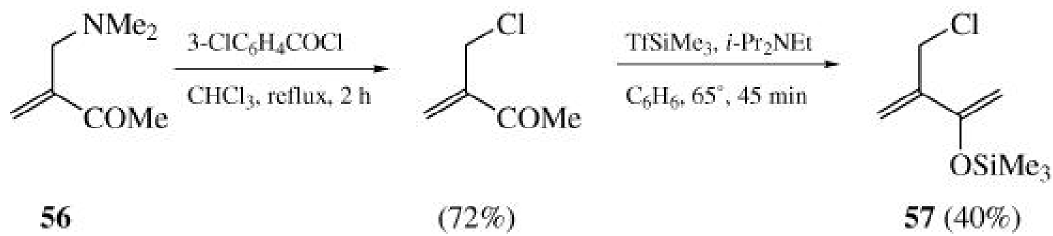
R^1	R^2	Yield (%)
Ph	SO_2Ph	(71)
Ph	CO_2Bu-*t*	(38)
n-Pr	SO_2Ph	(81)
n-Pr	CO_2Bu-*t*	(51)

(133)

on silica is much less effective. (43) Methyl 2-hydroxyalkylacrylates have also been converted into the corresponding keto compounds by temporarily protecting the double bond as the Diels–Alder adduct with anthracene. (9) The adduct of acetaldehyde with acrylonitrile could not be oxidized with a number of powerful oxidizing agents, (49) but its Michael adduct with methanol can be oxidized with Jones reagent. Elimination of methanol is then accomplished by thermolysis with phosphorus pentoxide to give 2-acetylacrylonitrile, which polymerizes on exposure to air or moisture. (276)

7.2. Reactions of the Amino Group

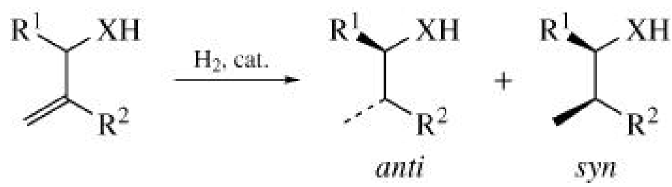
Aminoketone **56** is converted into diene **57** by the sequence of reactions shown in Eq. 134. (135) α -Aminoalkylacrylates can be cyclized to give methylene- β -lactams. (218)



(134)

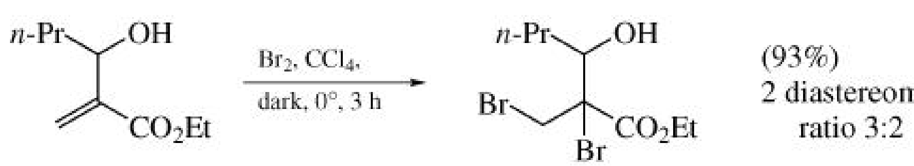
7.3. Reactions of the Double Bond

Additions to the double bond in Morita–Baylis–Hillman adducts give rise to products that are formally those of an aldol reaction. Catalytic hydrogenation and other methods of saturating the double bond have been studied extensively (Eq. 135). (277, 278) The substrates investigated include esters ($R^2 = CO_2R^3$, X = O), (85, 105, 203, 279-285)



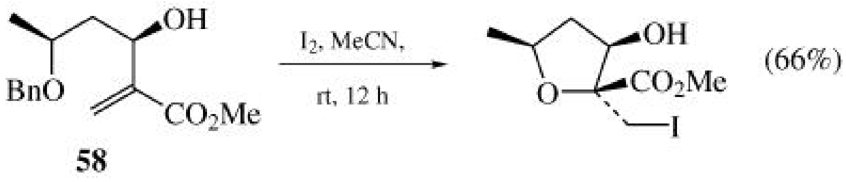
(135)

α , β -unsaturated ketones (R^2 = COMe, X = O), (19, 286) phenylsulfoxides [R^2 = PhS(O); X = O], (81) and phenyl sulfones [$R^2 = PhS(O)_2$; X = O], (81) as well as α -aminoalkylation products ($R^2 = CO_2R^3$, X = NR^4). (109, 136, 138) Addition of bromine to the double bond of 2-hydroxyalkylacrylates (178, 287) or their acetates (287) proceeds readily in high yield (Eq. 136). (178) Reaction of the dibromides

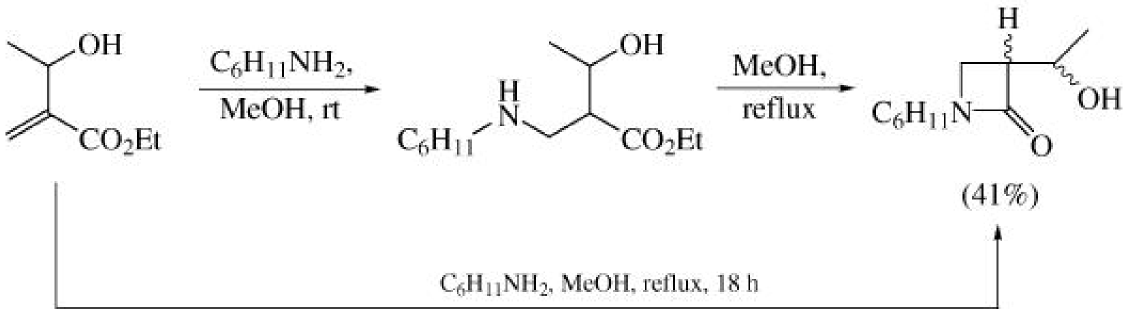


(136)

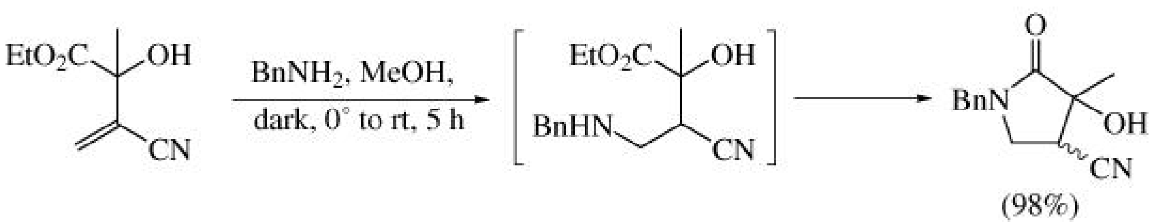
with a variety of bases gives bromoepoxy esters, (287) or, with prior protection of the hydroxy group, β -bromoacrylates. (178, 287) A tetrahydrofuran derivative is obtained on treatment of ester **58** with iodine (Eq. 137). (90) Michael additions of

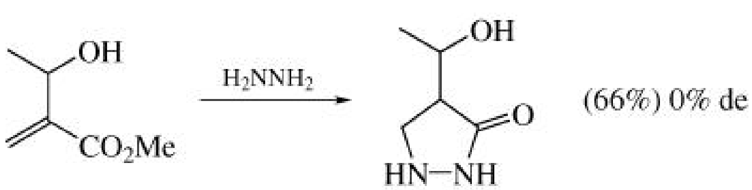
 (137)

the anions of dialkyl malonate, (127, 288) thiophenol, (185) and organocuprates (288a) to the double bond of Morita–Baylis–Hillman products have been reported. Reaction with ammonia leads to secondary or tertiary amines; (289) with primary amines, (108, 123, 290-292) precursors to β -lactams are obtained (Eq. 138). (291) Secondary

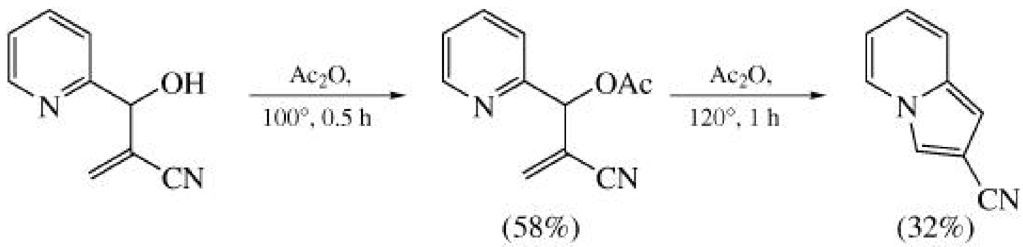
 (138)

amines can also be added. (32) Addition of secondary amines or hydrazines to 2-hydroxyalkylacrylonitriles derived from α -ketoesters leads directly to heterocycles (Eq. 139), (293) as does the reaction of 2-hydroxyalkylacrylates with hydrazine (Eq. 140). (294) Addition of hydrazine and mono- and disubstituted hydrazines to

 (139)

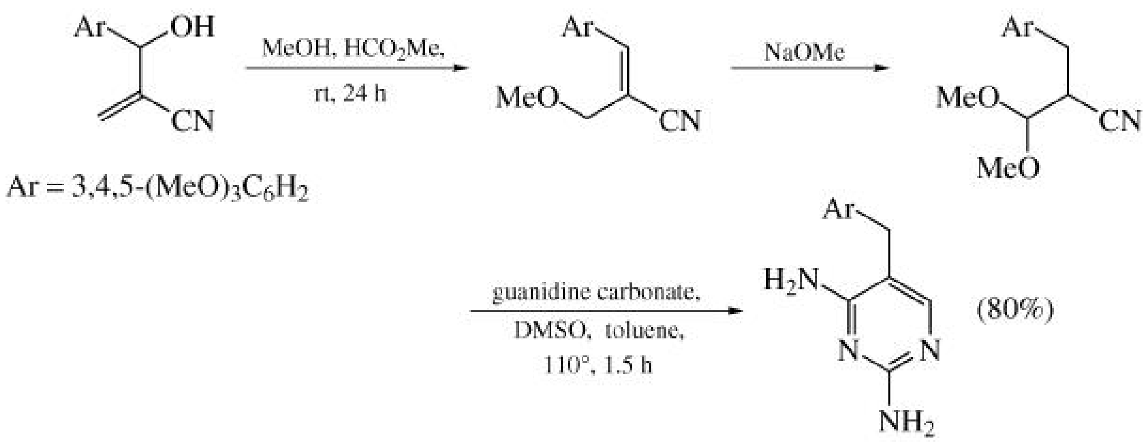
 (140)

simple 2-hydroxyalkylacrylonitriles also leads to heterocycles. (292, 293) Morita–Baylis–Hillman adducts of 2-pyridinecarboxaldehyde can be cyclized to indolizines (Eq. 141); (113) the adduct of 2-pyridinecarboxaldehyde to methyl vinyl ketone



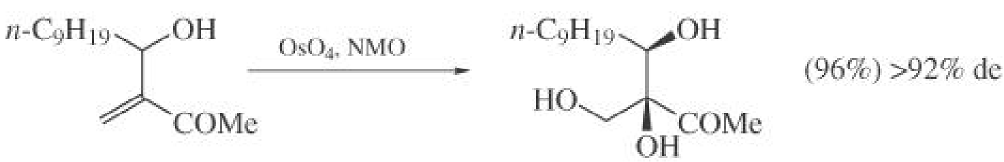
(141)

cyclizes slowly at room temperature (Eq. 59). The reaction sequence shown in Eq. 142 leads to the antibacterial trimethoprim. (130) Vicinal dihydroxylation



(142)

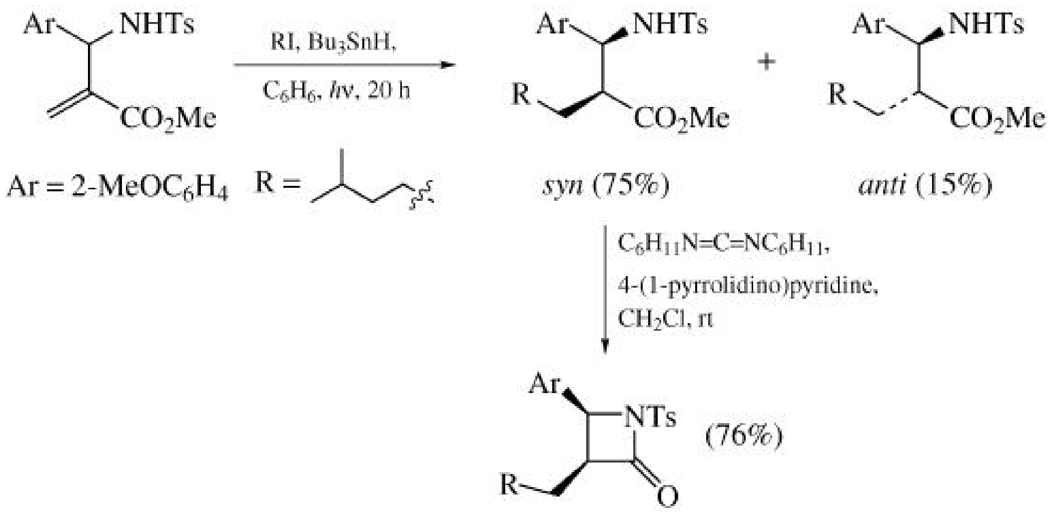
of the double bond has been carried out with catalytic osmium tetroxide in conjunction with *N*-methylmorpholine *N*-oxide (NMO) (164, 295) (Eq. 143) (295) or



(143)

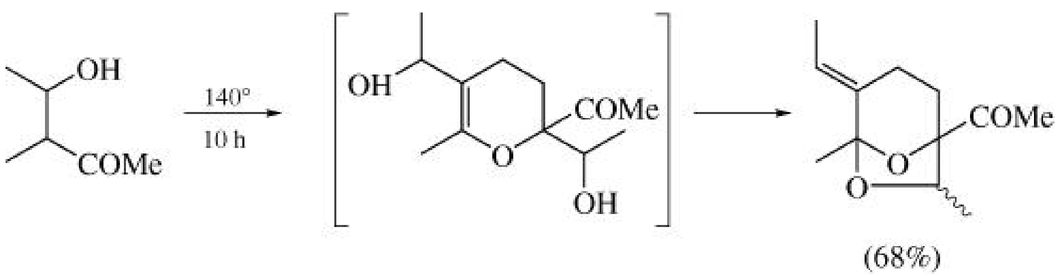
hydrogen peroxide. (294a) Epoxidation is achieved with a variety of reagents, including *m*-chloroperoxybenzoic acid, (212) sodium hypochlorite, (128) hydrogen peroxide in base, (190) lithium *tert*-butylhydroperoxide, (152) and Katsuki–Sharpless reagents. (39, 190) The last fail to epoxidize 2-hydroxyalkylacrylonitriles. (190) Aziridination of the activated double bond has also been reported. (296) Radical additions have been carried out to the double bonds of 2-hydroxyalkylacrylates or the corresponding acids, (297-304)

2-hydroxyalkylacrylonitriles, (305) and 2-hydroxyalkylenones. (302) A synthesis of β -lactams is based on radical additions to 2-aminoalkylacrylates (Eq. 144). (306) Additions of benzonitrile oxide, (307, 308) diazomethane, (308) and nitrilimines (307)



(144)

appear to be the only 1,3-dipolar cycloadditions to the double bond of Morita–Baylis–Hillman products reported so far. The only known Diels–Alder reactions involving these substrates appear to be the dimerization of 2-hydroxyalkylenones (Eq. 145) (309) and the previously mentioned addition to anthracene. (9)

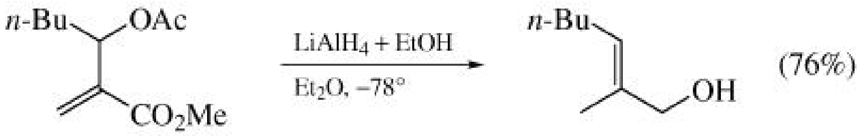


(145)

The homo or copolymerization (310) of 2-hydroxyalkylacrylates, (3, 10, 23, 213, 311-314) 2-hydroxyalkylacrylonitriles, (3, 10, 15, 213, 313, 315-317) and 2-hydroxyalkylenones (213) have been reported.

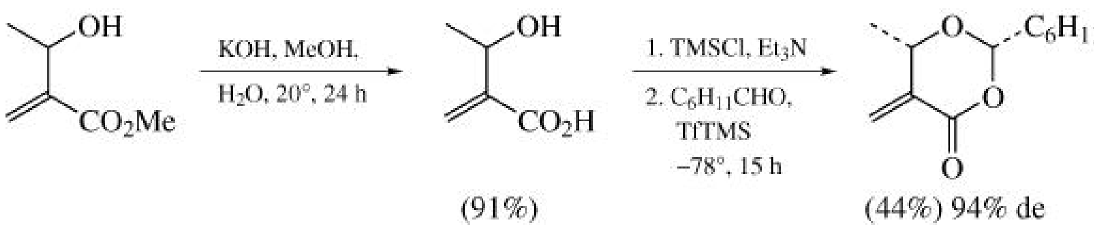
7.4. Reactions of the Activating Group

Reduction of the ester group in 2-hydroxyalkylacrylates to give the diol is carried out with aluminum hydride followed by sodium borohydride (235) or by di-isobutylaluminum hydride with (318-321) or without (322) protection of the hydroxy group. Direct reduction of the ester to the aldehyde does not appear to have been reported. It is achieved by oxidation of the monoprotected diol. (319, 320) Acetates of 2-hydroxyalkylacrylates are reduced by lithium ethoxyaluminum hydride with loss of the acetoxy group (261, 323) (Eq. 146). (261) Addition of Grignard reagents



(146)

to 2-hydroxyalkylacrylates gives ketones and/or tertiary carbinols. (288a) α -Hydroxyalkylacrylic acid are readily made by base hydrolysis; they can be converted into methylenedioxanones (Eq. 147), (303, 324) which on radical additions and



(147)

treatment with an alcohol give *threo* aldol products. Methods exist for the reductive removal of a phenylsulfonyl group attached to a double bond, (325, 326) but it remains to be determined whether they can be applied successfully to addition products of electrophiles to phenyl vinyl sulfone .

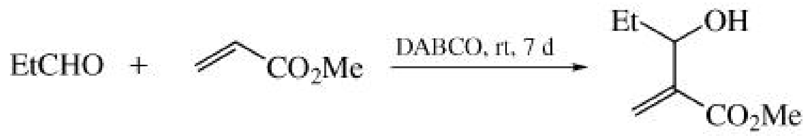
8. Experimental Conditions

The principal experimental hurdle to overcome in amine-catalyzed Morita–Baylis–Hillman reactions is the low rate. The simplest remedy appears to be the use of stoichiometric amounts of DABCO or the more reactive 3-hydroxyquinuclidine. Employing an excess of either the activated olefin or the electrophile is also beneficial; the choice will depend on the cost and ease of removal of the reagent used in excess. A more than sixfold excess should be avoided since the dilution effect leads to a reduction of the rate. (42) Ease of dimerization of the activated olefin by the catalyst system used is another consideration. Tables XIII-A–D list conditions and yields of dimerizations with catalysts commonly used in the Morita–Baylis–Hillman reaction. Addition of small amounts of a proton source such as methanol, 1,1,1,3,3,3-hexafluoro-2-propanol, or acetic acid increases rates, as do certain salts. Solvents usually reduce rates but they may be necessary with poorly soluble substrates (see discussion of solvents in the section on Reaction Parameters). Use of tetrahydrofuran leads to cleaner products in additions to α , β -unsaturated ketones and acrylonitrile . (41) Carrying out the reaction at low temperatures (63) (Eq. 20) should be considered. Elevated temperatures also increase reaction rates, but polymerization of the activated olefin may become a problem. Addition of small amounts (1 mol % or less) of a polymerization inhibitor such as hydroquinone, 4-methoxyphenol, 5-*tert*-butyl-4-hydroxy-2-methylphenyl sulfide, (41) or phenothiazine is essential in that case, especially if the inhibitor added to commercial samples of activated olefins has been removed by prior distillation or other purification methods. Phosphine catalysts such as tributylphosphine may provide higher reaction rates than tertiary amines. If the equipment is available, application of high pressure should be considered. Larger scale (>1.5 mL) experiments involving acrylonitrile (and possibly of other activated olefins) under high pressure require special precautions because polymerization of this monomer is highly exothermic. (41) Microwave irradiation also appears to increase rates considerably, but the reactions have to be carried out in sealed vessels, and provisions (77) should be made to guard against the possibility of explosions. (78) The order of addition can be important in special cases. Thus slow addition of α -keto esters to the catalyst mixed with an excess of acrylonitrile (134) leads to much improved yields as compared to mixing all reactants at the outset. Similar improvements are observed when α , β -unsaturated ketones are added slowly to tetrahydrofuran solutions of the electrophile and catalyst, (37, 117) although other workers report satisfactory yields without this precaution. (140)

The catalyst should be removed during the isolation procedure to reduce the amount of product that needs to be purified and to prevent the reverse reaction when purification is effected by distillation or sublimation at elevated temperatures. For amine catalysts all that is needed is an acid wash. Excess aldehydes or aldol side products can be removed as the water-soluble bisulfite complexes. (49)

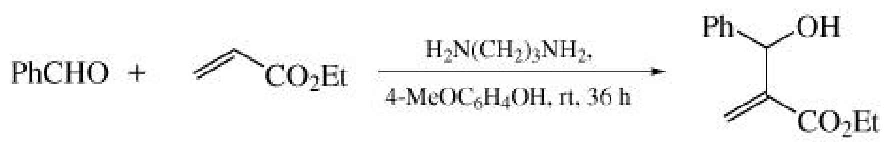
The cautionary note in the Introduction should be heeded.

9. Experimental Procedures



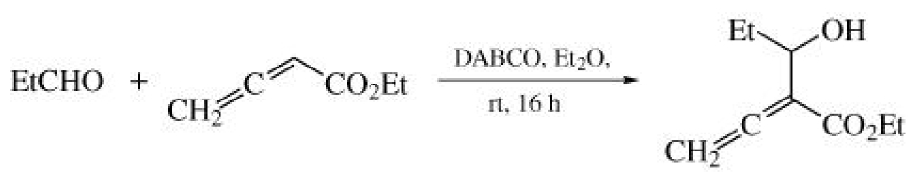
9.1.1. Methyl 3-Hydroxy-2-methylenepentanoate (DABCO-Catalyzed Reaction of an Aliphatic Aldehyde with Methyl Acrylate)

This preparation is described in *Organic Syntheses*. (281)



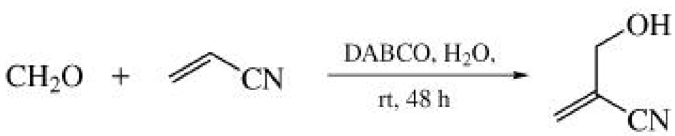
9.1.2. Ethyl 3-Hydroxy-2-methylene-3-phenylpropionate (Addition of an Aromatic Aldehyde To Ethyl Acrylate Catalyzed by 1,3-Diaminopropane/4-Methoxyphenol) (44)

A mixture of 20 g (0.2 mol) of ethyl acrylate, 29.7 g (0.28 mol) of freshly purified benzaldehyde, 2.2 g (0.03 mol) of 1,3-propanediamine, and 7.4 g (0.06 mol) of 4-methoxyphenol was stirred at room temperature for 36 hours, at which time gas chromatography verified the absence of ethyl acrylate. The mixture was chromatographed directly on silica (elution with hexane/ethyl acetate) to give 34.2 g (83%) of the title product. ^{1}H NMR δ 1.2 (t, *J* = 7 Hz, 3 H); 3.0 (br, 1 H); 4.13 (q, *J* = 7 Hz, 2 H); 5.40 (br, 1 H); 5.7 (s, 1 H); 6.2 (s, 1 H); 7.25 (s, 5 H). IR 3450, 1710, 1270, 1150, 1040, 700 cm^{-1}. In the absence of 4-methoxyphenol, the reaction required 216 hours to go to completion.



9.1.3. Ethyl 3-Hydroxy-2-vinylidenepentanoate (DABCO-Catalyzed Reaction of an Aliphatic Aldehyde with an Allenic Ester) (112)

To a solution of 44 mg (0.39 mmol) of DABCO in 1 mL of dry ether under argon at – 6° was added 0.32 g (2.82 mmol) of ethyl 2,3-butadienoate followed by 0.16 g (2.76 mmol) of propionaldehyde. The bath was removed, the mixture was stirred for 16 hours at room temperature and poured into water. The product was extracted into ether, the extracts were washed with dilute hydrochloric acid and water and dried with magnesium sulfate. Removal of the solvent gave 194 mg (42%) of the title compound. ^{1}H NMR ($CDCl_3$) δ 5.11 (s, 1 H), 5.08 (s, 1 H), 4.16 (m, 3 H), 2.78 (s, 1 H), 0.93 (q, J = 7 Hz, 3 H); ^{13}C NMR (CCl_4) δ 10.1, 14.1, 28.3, 61.1, 70.7, 80.5, 102.9, 167.0, 212.3; IR (neat) 3500, 1965, 1941, 1710, 1260 cm^{-1}. Anal. Calcd. for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.25; H, 8.16.

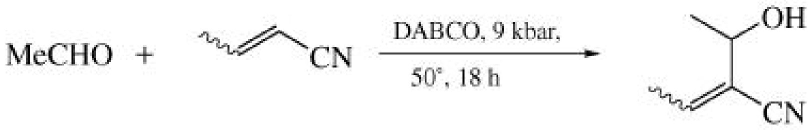


9.1.4. 2-Hydroxymethylacrylonitrile (DABCO-Catalyzed Reaction of Aqueous Formaldehyde with Acrylonitrile) (46)

A mixture of 159 g (3.0 mol) of acrylonitrile , 225 g (3.0 mol) of 40% aqueous formaldehyde solution, and 12.5 g (0.11 mol) of DABCO was stirred at room temperature for 48 hours. The volatile components were removed under 10 mm vacuum and the residue was dissolved in 400 mL of ether. The solution was washed with 70 mL of 8% hydrochloric acid and 70 mL of brine and dried with sodium sulfate. Removal of the solvent and fractional distillation of the residue gave 164 g (66%) of the title compound, bp 84–86° (0.2 mm).

9.1.5. 2-Methylene-3-Hydroxypentanenitrile (Reaction of an Aliphatic Aldehyde with Acrylonitrile Catalyzed by a Phosphine) (7)

To a refluxing solution of 5.3 g (0.1 mol) of acrylonitrile and 11.6 g (0.2 mole) of propionaldehyde in 20 mL of dioxane was added under nitrogen during 15 minutes a solution of 0.3 g (1.1 mmol) of tricyclohexylphosphine in 10 mL of dioxane. Reflux was continued for 12 hours, the solvent was removed and the residue was distilled to give 3.88 g (35%) of the title compound, bp 60–61° (0.4 mm). ^{1}H NMR δ 5.98 (s, 2 H), 4.12 (d, *J* = 6.5 Hz, 1 H), among others; IR 2229, 1623 cm^{-1}. Anal. Calcd. for C_6H_9NO : C, 64.84; H, 8.16; N, 12.60. Found: C, 64.65; H, 8.19; N, 12.52.

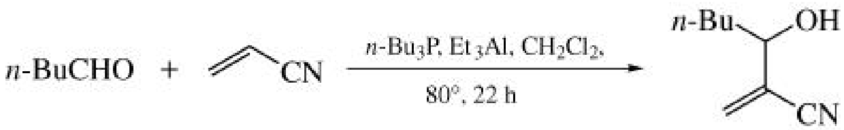


9.1.6. (E)- and (Z)-2-(1-Hydroxyethyl)-2-butenenitrile (DABCO-Catalyzed Reaction of an Aliphatic Aldehyde with Crotononitrile Under Pressure) (49)

A mixtutre of (*E*)- and (*Z*)-crotononitrile (5 mL, 61.4 mmol), acetaldehyde (3.45 mL, 61.4 mmol), and DABCO (0.34 g; 3 mmol) was placed in a poly(tetrafluoroethylene) cylinder and pressurized to 9 kbar at 50° for 18 hours. Ether (20 mL) was added, and the solution was washed with 10 mL of 10% hydrochloric acid and dried with magnesium sulfate, and the volatiles were removed under vacuum. Flash chromatography of the residue and elution with ether/petroleum ether (2:1) gave 5.1 g (72%) of the *Z* isomer of the title compound followed by 1.1 g (16%) of the *E* isomer. *Z* isomer: ^{1}H NMR(C_6D_6) δ 1.26 (d, *J* = 3.3 Hz, 3 H), 1.63 (d, *J* = 3.5 Hz, 3 H), 3.34 (br s, 1 H), 4.17 (q, *J* = 3.3 Hz, 1 H), 6.09 (q, *J* = 3.5 Hz, 1 H); IR 3440, 2225, 1650 cm^{-1}; HRMS calculated for C_6H_9NO : 111.06841; found: 111.0675. *E* isomer: ^{1}H NMR(C_6D_6) δ 1.25 (d, *J* = 3.3 Hz), 1.37 (d, *J* = 3.5 Hz), 3.34 (br s, 1 H), 4.49 (q, *J* = 3.3 Hz, 1 H), 5.99 (q, *J* = 3.5 Hz, 1 H); IR 3440, 2225, 1650 cm^{-1}; HRMS calculated for C_6H_9NO : 111.06841; found: 111.0675.

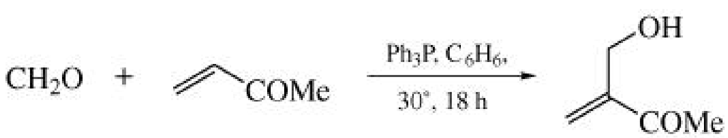
9.1.7. 3-Hydroxy-4-methyl-2-methylene-4-pentenenitrile (DABCO-Catalyzed Reaction of an Olefinic Aldehyde with Acrylonitrile) (127)

A mixture of 0.70 g (10 mmol) of methacrolein, 0.53 g (10 mmol) of acrylonitrile , and 0.17 g (1.5 mmol) of DABCO was stirred under nitrogen in the dark for 4 days. Methylene chloride (20 mL) was added, and the solution was washed with two 20-mL portions of 1 N hydrochloric acid. The organic phase was dried with sodium sulfate, the solvent was removed, and the residue was chromatographed on silica. Elution with hexane/ethyl acetate (4:1) gave 0.82 g (67%) of the title compound as an oil. ^{1}H NMR($CDCl_3$) δ 6.06 (s, 1 H), 6.02 (s, 1 H), 5.14 (s, 1 H), 5.04 (s, 1 H), 4.65 (s, 1 H), 2.40 (br, 1 H), 1.69 (s, 3 H); ^{13}C NMR($CDCl_3$) δ 142.5, 130.4, 124.8, 116.7, 114.8, 75.7, 17.2; MS *m/z* 123 (9%), 108 (35%).



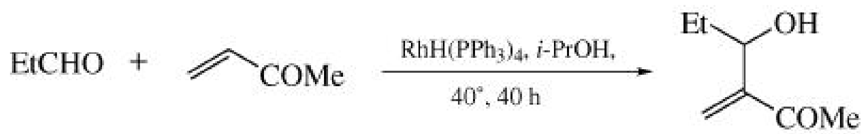
9.1.8. 2-Methylene-3-hydroxyheptanenitrile (Reaction of an Aliphatic Aldehyde with Acrylonitrile Catalyzed by Tributylphosphine/Triethylaluminum) (64)

To a solution of 203 mg (1 mmol) of tributylphosphine, 0.26 mL (0.5 mmol) of a 1.9 M solution of triethylaluminum in hexane, and 1 mL of methylene chloride in a pressure bottle was added under nitrogen a solution of 266 mg (5 mmol) of acrylonitrile and 859 mg (10 mmol) of pentanal in 10 mL of methylene chloride. The bottle was closed and heated to 80° for 22 hours. The solution was washed with 3 N hydrochloric acid and brine, and the solvent was removed. Chromatography of the residue on silica gel and elution with benzene/ethyl acetate (20:1) gave 0.19 g of the aldol product, 2-propyl-2-heptenal, followed by 628 mg (90%) of the title compound. ^{1}H NMR δ 6.09 (br, 2 H), 4.27 (br, 1 H), 1.1–2.0 (m, 6 H), 0.7–1.1 (m, 3 H); ^{13}C NMR δ 13.9, 22.4, 27.2, 35.5, 72.2, 117.1, 127.1, 129.8; IR 3670–3100, 2240, 1628 cm^{-1}. Anal. Calcd. for $C_8H_{13}NO$: C, 69.03; H, 9.41. Found: C, 68.96; H, 9.63.



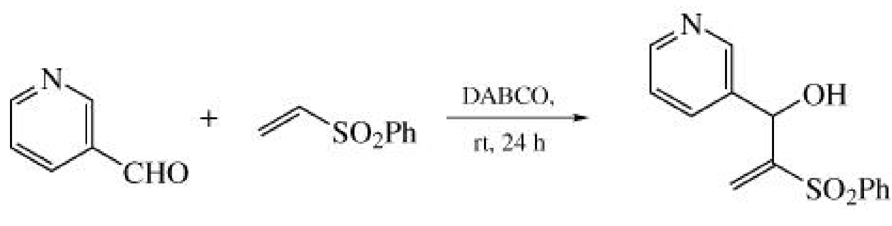
9.1.9. 4-Hydroxy-3-methylene-2-butanone (Reaction of Formaldehyde with 3-Buten-2-one Catalyzed by Triphenylphosphine) (61)

A mixture of 7.0 g (0.1 mol) of 3-buten-2-one, 6.0 g (0.2 mol) of formaldehyde (of unspecified type), 1.0 g (4 mmol) of triphenylphosphine, and 10 mL of benzene was stirred under nitrogen at 30° for 18 hours and poured into dilute hydrochloric acid. The product was extracted into ether, and the extracts were washed successively with brine, dilute sodium bicarbonate solution, and brine, and then dried with sodium sulfate. Removal of the solvent and distillation of the residue gave 3.4 g (34%) of the title product, bp 70–71° (8 mm). IR 3400, 1675 cm^{-1}; ^1H NMR δ2.30 (s, 3 H), 4.16 (s, 2 H), 5.96 (s, 1 H), 6.01 (s, 1 H); MS *m/z* 100.



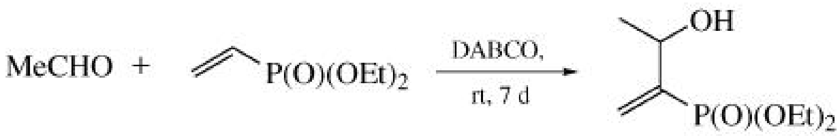
9.1.10. 4-Hydroxy-3-methylene-2-hexanone (Reaction of an Aliphatic Aldehyde with 3-Buten-2-one Catalyzed by a Rhodium Complex) (19)

A mixture of 264 mg (3.8 mmol) of 3-buten-2-one, 484 mg (7.4 mmol) of propanal, 53 mg (0.89 mmol) of 2-propanol, and 36 mg (0.032 mmol) of $RhH(PPh_3)_4$ was placed under argon in a Carius tube which was cooled, evacuated, sealed under vacuum, and heated in a 40° bath for 40 hours. The product was concentrated under reduced pressure, bulb-to-bulb distilled, and the crude product was purified further by chromatography on silica gel. Elution with hexane/ethyl acetate (4:1) gave 376 mg (78%) of the title product as a colorless oil. ^1HNMR δ 5.97 (s, 1 H), 5.90 (s, 1 H), 4.29 (t, J = 5.3 Hz, 1 H), among others; IR 3525, 1665 cm^{-1}; MS *m/z* 128, 99 (base peak), among others.



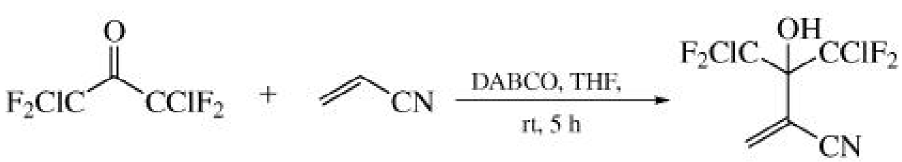
9.1.11. 2-(Benzenesulfonyl)-1-(3-pyridyl)-2-propenol (DABCO-catalyzed Reaction of a Heterocyclic Aldehyde with a Sulfone) (80)

DABCO (60 mg, 0.5 mmol) was added to a mixture of 840 mg (5 mmol) of phenyl vinyl sulfone and 1.6 g (15 mmol) of 3-pyridinecarboxaldehyde and the mixture was left at room temperature for 24 hours. Excess aldehyde was removed under vacuum and the residue was purified by flash chromatography on silica gel. Elution with ethyl acetate/ether (1:1) and crystallization from ether gave 630 mg (46%) of the title compound, mp 121°. ^1H NMR[$(CD_3)_2SO$] δ 8.53–8.52 (m, 2 H), 7.74–7.40 (m, 6 H), 7.18 (m, 1 H), 6.59 (s, 1 H), 6.42 (s, 1 H), 6.36 (br s, 1 H), 5.50 (br s, 1 H); ^{13}C NMR[$(CD_3)_2SO$] δ 152.8, 148.7, 148.6, 139.4, 136.4, 134.5, 133.5, 129.2, 127.6, 126.4, 123.1, 66.1; IR $(CHCl)_3$ 1320, 1310, 1165, 1145, 690 cm^{-1}; HRMS calculated for $C_{14}H_{13}NO_3S$: 275.0616; found: 275.0614.



9.1.12. Diethyl (2-Hydroxy-1-methylenepropane)phosphonate (DABCO-Catalyzed Reaction of an Aliphatic Aldehyde with Diethyl Vinylphosphonate) (120)

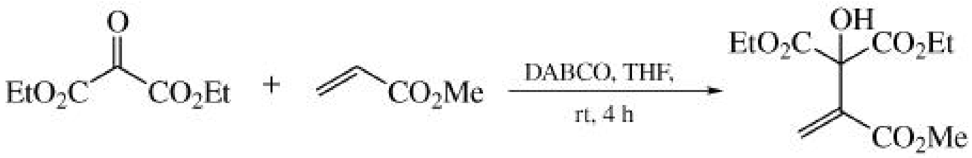
To 3.28 g (20 mmol) of diethyl vinylphosphonate was added 0.97 g (22 mmol) of ethanal and 0.45 g (4 mmol) of DABCO and the mixture was stirred at room temperature for 7 days. Methylene chloride (50 mL) was added and the solution was washed with 20 mL of 1.5 M hydrochloric acid and saturated aqueous sodium bicarbonate solution. The solvent was removed and the residue was distilled to give 3.19 g (83%) of the title compound as an oil, bp 64° (0.65 mm). ^{1}H NMR δ 6.4 (m, 1 H), 5.9 (m, 1 H), 5.05 (d/q, J = 34.5/6.5 Hz, 1 H), 4.15 (two q, J = 7 Hz, 4 H), 1.3 (d, J = 6.5 Hz, 3 H), 1.28 (t, J = 7 Hz, 6 H).



9.1.13. 4-Chloro-4,4-difluoro-3-(chlorodifluoromethyl)-3-hydroxy-2-methy lene Butanenitrile (DABCO-Catalyzed Reaction of a Halo Ketone with Acrylonitrile) (115)

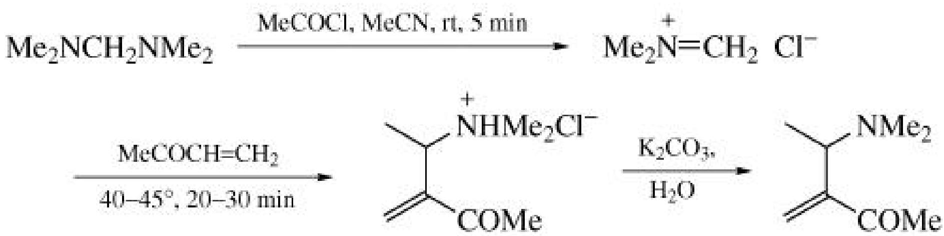
To a stirred mixture of 1.06 g (0.02 mol) of acrylonitrile and 0.22 g (2 mmol) of DABCO in 15 mL of dry tetrahydrofuran was added at 20° 4.0 g (0.02 mol) of 1,3-dichloro-1,1,3,3-tetrafluoropropan-2-one. The mixture was stirred for 5 hours, poured into 100 mL of 5% hydrochloric acid, and extracted with three 20-mL portions of methylene chloride. The extracts were washed with water to pH 7, and dried with magnesium sulfate. Removal of the solvent and crystallization of the residue from hexane gave 1.76 g (35%) of the title compound, mp 53–54°. ^{1}H NMR[$(CD_3)_2CO$)] δ 6.68 (s, 1 H), 6.82 (s, 1 H), 4.47 (s, 1 H); ^{19}F NMR[$(CD_3)_2CO$)] δ -18.59 ppm (from external CF_3CO_2H);

^{13}C NMR[$(CD_3)_2CO$)] δ92.2, 112.7, 115.1 126.1, 139.2. Anal. Calcd. for $C_6H_4Cl_2F_4NO$: C, 28.57; H, 1.19; N, 5.56. Found: C, 28.57; H, 1.21; N, 5.56.



9.1.14. Methyl 3,3-Dicarboethoxy-3-hydroxy-2-methylenepropanoate (DABCO-Catalyzed Reaction of a Keto Ester with Methyl Acrylate) (133)

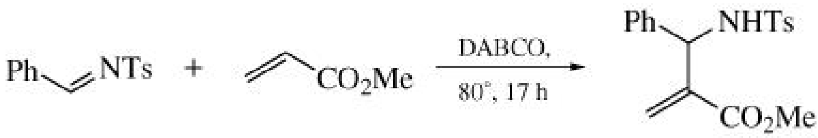
A solution of 0.87 g (5 mmol) of diethyl ketomalonate, 0.43 g (5 mmol) of methyl acrylate, and 56 mg (0.5 mmol) of DABCO in 3.7 mL of tetrahydrofuran was allowed to stand at room temperature for 4 hours. Methylene chloride (25 mL) was added, and the solution was washed sequentially with dilute hydrochloric acid and aqueous sodium bicarbonate solution, and dried with sodium sulfate. Removal of the solvent and chromatography of the residue (hexane/ethyl acetate 4:1) gave 1.0 g (77%) of the title compound. ^{1}H NMR δ 6.42 (s, 1 H), 6.02 (s, 1 H), 4.56 (br, 1 H), 4.3 (q, J = 6 Hz, 4 H), 3.78 (s, 3 H), 1.32 (t, J = 6 Hz, 6 H); ^{13}C NMR 13.35, 51.76, 62.41, 78.71, 127.59, 137.36, 162.39, 168.77; IR (neat) 3460, 1730, 1630 cm^{-1}.



9.1.15. 4-Dimethylamino-3-methylene-2-pentanone (Uncatalyzed Reaction of an Iminium Salt with 3-Buten-2-one) (135)

To a stirred solution of 10.5 g (103 mmol) of bis(dimethylamino)methane in 70 mL of acetonitrile was added dropwise with ice cooling 7.9 g (101 mmol) of acetyl chloride. The suspension was stirred at room temperature for 5 minutes, 8.5 g (125 mmol) of 3-buten-2-one was added, and stirring was continued at 40–45° until the mixture became homogeneous (20–30 minutes). The solvent was removed under vacuum at 20°, dry, cold ether (100 mL) was added, and the hydrochloride of the title compound was collected by filtration and washed with ether. The salt was further purified by dissolution in methylene chloride, filtration, and removal of the solvent to give 14.4 g (88%) of the hydrochloride of the title compound, mp 135°. ^{1}H NMR($CDCl_3$) δ 2.40 (s, 3 H), 2.78 (s, 6 H), 4.02 (s, 2 H), 6.71 (s, 1 H), 6.99 (s, 1 H), 9.0 (br, 1 H). Anal. Calcd. for $C_7H_{14}ClNO$: C, 51.38; H, 8.56; Cl, 21.71; N, 8.56. Found: C, 51.35; H, 8.66; Cl, 21.75; N, 8.55.

A solution of the salt (12 g) in 15 mL of water was added to a solution of 30 g of potassium carbonate in 30 mL of water, the mixture was extracted with four 20-mL portions of ether, and the solvent was removed from the dried ($MgSO_4$) ether extracts. Distillation of the residue gave 7.7 g (83%) of the title compound, bp 59–60° (15 mm), n^{20}_D 1.4485. ^{1}H NMR δ 2.15 (s, 6 H); 2.24 (s, 3 H), 3.12 (s, 2 H), 5.95 (s, 1 H), 6.07 (s, 1 H); ^{13}C NMR δ 24.4, 43.6, 57.3, 124.6, 143.9, 197.6; IR 1640, 1690 cm^{-1}.



9.1.16. Methyl 2-Methylene-3-phenyl-3-(4-toluenesulfonylamino)propanoate (DABCO-Catalyzed Reaction of an Imine with Methyl Acrylate) (138)

A mixture of 337 mg (1.3 mmol) of benzaldehyde *N*-(4-toluenesulfonyl)imine, 112 mg (1.3 mmol) of methyl acrylate, and 15 mg (0.13 mmol) of DABCO was heated in a sealed tube to 80° for 17 hours. Unreacted methyl acrylate was removed under vacuum and the residue was taken up in chloroform (20 mL). The solution was washed with two 2-mL portions of 2 M hydrochloric acid and two 5-mL portions of water, and dried with sodium sulfate. Removal of the solvent and chromatography of the residue on silica gel (elution with ether/petroleum ether 1 : 1) gave 202 mg (45%) of the title compound, mp 80–81°. ^{1}H NMR δ 2.39 (s, 3 H), 3.58 (s, 3 H), 5.32 (d, J = 8.9 Hz, 1 H), 5.82 (d, J = 8.8 Hz, 1 H), 5.83 (s, 1 H), 6.21 (s, 1 H), 7.1–7.3 (m, 7 H), 7.66 (d, J = 8.3 Hz, 2 H). IR (film) 3250, 1720 cm^{-1} Anal. Calcd. for $C_{18}H_{19}NO_4S$: C, 62.6; H, 5.5; N, 4.0. Found: C, 62.7; H, 5.6; N, 4.0.

10. Tabular Survey

An effort has been made to cover catalyzed α -hydroxyalkylation and α -aminoalkylation reactions of activated olefins completely through the middle of 1996, but omissions are probably inevitable. Tables I–VII list reactions of aldehydes with acrylates, acrylamides, acrylonitriles, acrolein, α , β -unsaturated ketones, vinyl sulfoxides, vinyl sulfones, vinylsulfonates, and diethyl vinylphosphonate. Some of these tables are subdivided further according to aldehyde type; the criterion is the group that the formyl function is *directly* attached to. Esters of glyoxylic acid are listed as aldehydes rather than α -ketoesters. Formylferrocene is treated as an olefinic aldehyde. Tables VIII–XI list additions of various electrophiles other than aldehydes to activated olefins. Table XII is devoted to intramolecular Morita–Baylis–Hillman reactions. Tables XIII-A–D, which are not exhaustive, list the dimerizations of the activated olefins discussed in this chapter under the conditions of the Morita–Baylis–Hillman reaction.

Within each table, entries are arranged according to increasing carbon count of the electrophile. In transition metal complexes, ligands are not included in the carbon count. Within groups with identical carbon count, entries are arranged in the order of increasing hydrogen count. For each electrophile, activated olefins are listed in the same order as that specified for the electrophiles. The symbols (+) and (–) next to ester substrates are the signs of rotations of the alcohols from which the esters were made.

The amounts listed in the conditions column in parentheses after the catalyst and other addends are in mole equivalents relative to the limiting substrate. A dash in this column indicates that no conditions have been reported. A dash in the yield column signifies that the product was isolated but no yield was given. A zero (0) in the yield column means that the reaction did not proceed under the conditions listed. When a reaction has been reported in more than one publication, the conditions producing the highest yield are given and the reference to that paper is given first. The following abbreviations are used:

Bn	benzyl
t-BOC	*tert*-butoxycarbonyl
Bz	benzoyl
CBZ	carbobenzyloxy
C_6H_{11}	cyclohexyl
DIOP	2,3-*O*-isopropylidene-2,3-dihydroxy-1,4-bis-(diphenylphosphino)butane
DB	1,4-diazabicyclo[2.2.2]octane (DABCO)
HFI	1,1,1,3,3,3-hexafluoro-2-propanol

HMPA	hexamethylphosphoric triamide
HQ	3-hydroxyquinuclidine
TBDMS	*tert*-butyldimethylsilyl
TBDPS	*tert*-butyldiphenylsilyl
Tf	trifluoromethanesulfonyl (triflyl)
THP	2-tetrahydropyranyl
TMS	trimethylsilyl
Ts	*p*-toluenesulfonyl

Table I-A. Reactions of Acrylates with Aliphatic and Alicyclic Aldehydes

View PDF

Table I-B. Reactions of Acrylates with Olefinic Aldehydes

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Table I-C. Reactions of Acrylates with Aromatic Aldehydes

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Table I-D. Reactions of Acrylates with Heterocyclic Aldehydes

View PDF

Table I-E. Reactions of Methyl Acrylate with Dialdehydes

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Table I-F. Reactions of Allenic Esters with Aldehydes

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Table II-A. Reactions of Acrylamides with Aldehydes

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Table II-B. Reactions of Camphor Sultam Acrylate with Aldehydes

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Table III-A. Reactions of Acrylonitriles with Aliphatic and Alicyclic Aldehydes

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Table III-B. Reactions of Acrylonitrile with Olefinic Aldehydes

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Table III-C. Reactions of Acrylonitriles with Aromatic Aldehydes

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Table III-D. Reactions of Acrylonitrile with Heterocyclic Aldehydes

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Table IV. Reactions of α , β -Unsaturated Aldehydes with Aldehydes

View PDF

Table V-A. Reactions of α , β -Unsaturated Ketones with Aliphatic and Alicyclic Aldehydes

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Table V-B. Reactions of α , β -Unsaturated Ketones with Olefinic Aldehydes

View PDF

Table V-C. Reactions of α , β -Unsaturated Ketones with Aromatic Aldehydes

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Table V-D. Reactions of α , β -Unsaturated Ketones with Heterocyclic Aldehydes

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Table VI. Reactions of Vinyl Sulfoxides, Vinyl Sulfones, and Vinylsulfonates with Aldehydes

View PDF

Table VII. Reactions of Diethyl Vinylphosphonate with Aldehydes

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Table VIII. Reactions of Activated Olefins with Monoketones

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Table IX. Reactions of Activated Olefins with Polyketones

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Table X. Reactions of Activated Olefins with α -Ketoesters and α -Ketolactones

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Table XI. Reactions of Activated Olefins with Imines and Iminium Salts

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Table XII. Intramolecular Reactions

View PDF

Table XIII-A. Dimerization of Acrylates

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Table XIII-B. Dimerization of Acrylamides

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Table XIII-C. Dimerization of Acrylonitrile

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Table XIII-D. Dimerization of α , β -Unsaturated Ketones

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TABLE I-A. REACTIONS OF ACRYLATES WITH ALIPHATIC AND ALICYCLIC ALDEHYDES

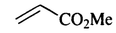
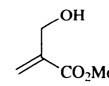
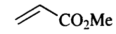
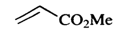
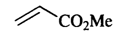
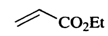
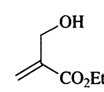
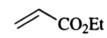
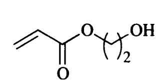
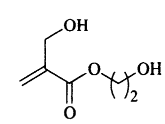
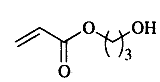
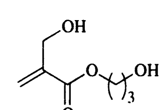
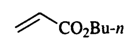
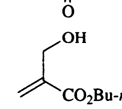
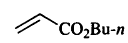
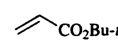
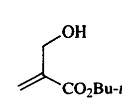
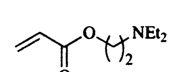
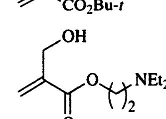
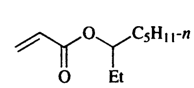
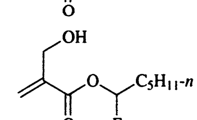
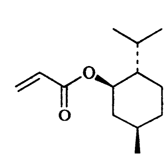
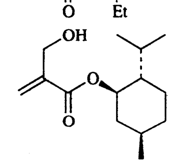
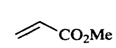
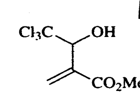
Aldehyde	Acrylate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_1				
HCHO (paraformaldehyde)		DB (0.05), 95°, 4 h, or 45°, 14 h	 I (23)[a]	143
	"	DB (0.03), rt, 10 d	I (66)[b]	142, 268
	"	Me_3N (0.5), H_2O, 60°, 3 h	I (80)	47
	"	$P(C_6H_{11})_3$ (0.01), dioxane, sealed tube, 80-90°, 15 h	I (36)	8
HCHO (gas)		DB (0.07), EtOH, rt, 72 h	I (59)	46
HCHO (formalin)		DB (0.06), H_2O, MeOH, rt, 48 h	I (75)	46, 23, 142, 311
	"	Me_3N (0.5), H_2O, air, 4-$MeOC_6H_4OH$ (0.001), 40°, 6 h	I (72)	47
	"	DB (0.11), microwave flow reactor, 158-164°, 90 s	I (30)	74, 75
HCHO (cyclohexanol hemiacetal)		DB (0.07), cyclohexanol, rt, 70 h	I (45)	46
HCHO (formalin)		DB (0.1), H_2O, THF, rt, 36 h	 I (80)	235, 46, 327
	"	DB (0.11), microwave flow reactor, 150-175°	I (32)	74
	"	Me_3N (0.4), H_2O, air, 4-$MeOC_6H_4OH$ (0.001), 80°, 2 h	I (89)	47
HCHO (paraformaldehyde)		Me_3N (0.5), H_2O, 4-$MeOC_6H_4OH$ (0.001), 50°, 6 h	I (90)	47
HCHO (formalin)		1. Me_3N (0.5), *i*-Pr_2O, H_2O, <40°, 2. 50°, 8 h	 (35)	47
HCHO (formalin)		DB (0.09), EtOH, rt, 72 h	 (81)	46
HCHO (paraformaldehyde)		DB (0.07), rt, 10 d	 I (20)[c]	142
HCHO (formalin)		Me_3N (0.5), H_2O, air 4-$MeOC_6H_4OH$ (0.001), 60°, 3 h	I (69)	47
		DB (0.11), microwave flow reactor, 170-180°	I (45)	74
HCHO (formalin)		—	 (—)	231
HCHO (formalin)		DB (0.09), rt, 50 h	 (75)	46
HCHO (formalin)		DB (0.1), EtOH, 50°, 36 h	 (71)	46
HCHO (formalin)		—	 (—)	231
C_2				
Cl_3CCHO		DB (0.15), rt, 20 h	 (>55)	5

TABLE I-A. REACTIONS OF ACRYLATES WITH ALIPHATIC AND ALICYCLIC ALDEHYDES (*Continued*)

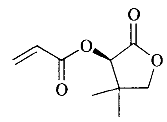
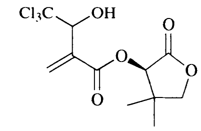
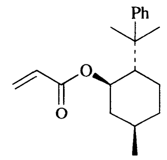
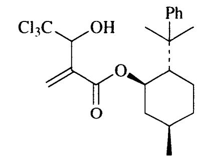
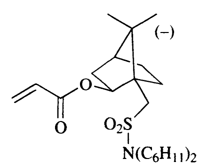
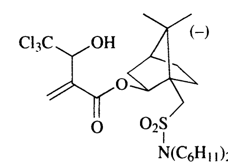
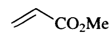
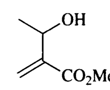
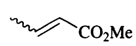
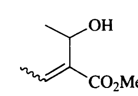
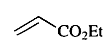
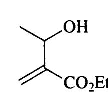
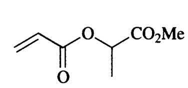
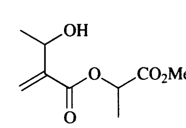
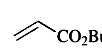
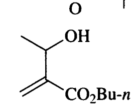
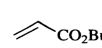
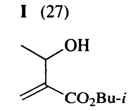
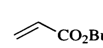
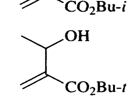
Aldehyde	Acrylate	Conditions	Product(s) and Yield(s) (%)	Refs.
		DB (0.2), rt, 30 min	 (83) 48% de	88
		DB (1.0), rt, 14 d	 (58) 70% de	83
		DB (0.1), rt, 2 d	 (68) 25% ee	84, 328
MeCHO		DB (0.11), rt, 7 d	 I (88)	73, 49, 123, 223, 270, 294, 300, 308
		DB (0.09), dioxane, 0°, 8 h	I (74)	63
		HQ (0.05), rt, $t_{1/2}$ <15 h	I (90)	33
		$(C_6H_{11})_3P$ (0.01), dioxane, 120-130°, 2 h	I (23)	17, 7, 8
		DB (0.5), microwave, 10 min	I (40)	76
		Et_2NMe, (0.05), 9 kbar, 20°, 10 min	I (86)	49
		DB (0.08), 10 kbar, 55°, 20	 (—)[d]	49
		DB (0.05), rt, 7 d	 I (94)	4, 1, 222, 322
	"	DB (0.05), 120-124°, 8 h	I (59)	1
	"	Me_3N (0.5), air, 4-$MeOC_6H_4OH$ (0.001), 60°, 3 h	I (35)	47
	"	$H_2N(CH_2)_3NH_2$ (0.15), 4-$MeOC_6H_4OH$ (0.3), rt, 36 h	I (93)	44
	"	$(C_6H_{11})_3P$ (0.01), dioxane, reflux, 9 h	I (25)	7
	"	Et_2NMe (0.08), THF, 12 kbar, 20°, 10 min	I (98)	48
		DB (0.4), rt, 100 min	 (95)	36, 110
		$H_2N(CH_2)_3NH_2$ (0.15), 4-$MeOC_6H_4OH$ (0.3), rt, 24 h	 I (90)	44
	"	$(C_6H_{11})_3P$ (0.01), dioxane, 120-130°, 2 h	I (—)	7
	"	DB (0.04), microwave flow reactor, 120°	I (27)	74
		DB (0.1), rt, 14 d	 (—)	222
		DB (0.11), rt, 7 d	 (92)	236, 5, 123, 222, 300

TABLE I-A. REACTIONS OF ACRYLATES WITH ALIPHATIC AND ALICYCLIC ALDEHYDES (*Continued*)

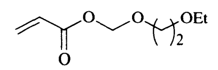
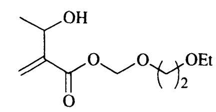
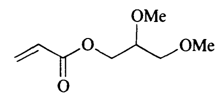
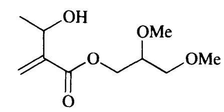
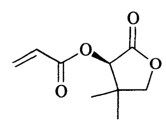
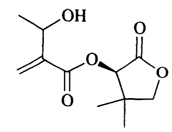
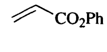
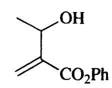
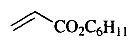
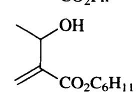
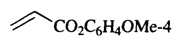
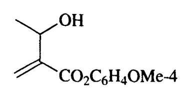
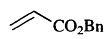
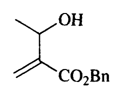
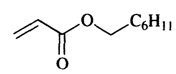
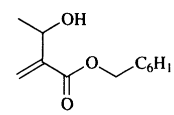
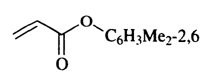
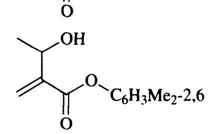
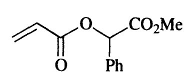
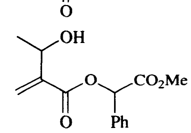
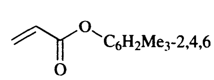
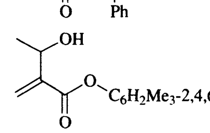
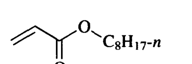
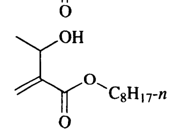
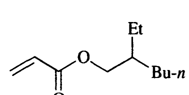
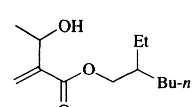
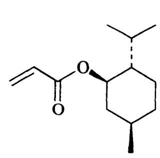
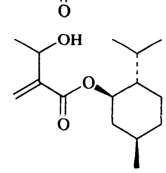
Aldehyde	Acrylate	Conditions	Product(s) and Yield(s) (%)	Refs.
		DB (0.1), rt, 14 d	 (—)	222
		DB (0.1), rt, 14 d	 (—)	222
		DB (0.2), rt, 30 min	 I (0)[e]	88, 110
		1. DB (0.2), 20-30°, 20 min 2. EtCHO	I (0)[f]	110
		DB (0.1), rt, 2 h	 (0)[g]	24
		DB (0.1), rt, 14 d	 (—)	222
		DB (0.1), rt, 8 h	 (0)[h]	24
		$(C_6H_{11})_3P$ (0.007), dioxane, 120-130°, 2 h	 (—)	7
		DB (0.1), rt, 14 d	 (—)	222
		DB (0.1), 0°, 6 h	 (36)[i]	24
		DB (0.4), rt, 90 min	 (98)	36. 110
		DB (0.1), rt, 14 h	 (43)[i]	24
		$(C_6H_{11})_3P$ (0.007), dioxane, 120-130°, 2 h	 (40)	7
		DB (0.1), rt, 14 d	 (—)	222
	 (–)	DB (—), 16°, 18 d	 I (95) 14% de	53, 85, 86
		DB (—), 7 kbar, 30°, 113 h	I (36) 16% de	53

TABLE I-A. REACTIONS OF ACRYLATES WITH ALIPHATIC AND ALICYCLIC ALDEHYDES (*Continued*)

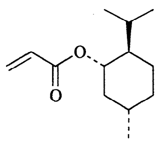
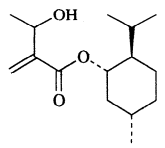
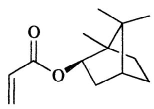
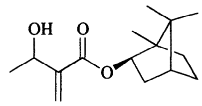
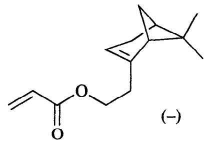
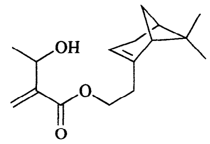
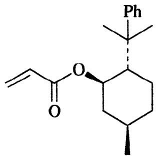
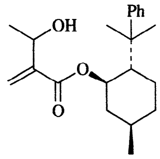
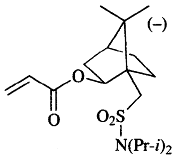
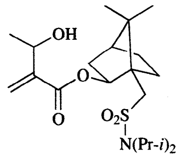
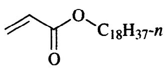
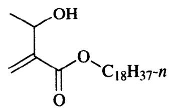
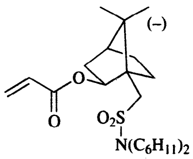
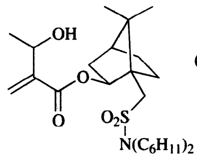
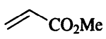
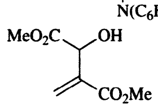
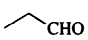
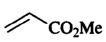
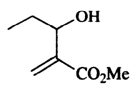
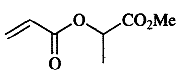
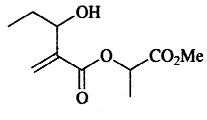
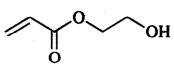
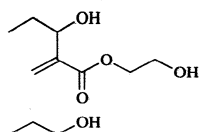
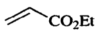
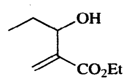
Aldehyde	Acrylate	Conditions	Product(s) and Yield(s) (%)	Refs.
	 (+)	DB (0.05)	 (—) 6% de	85, 253
	 (–)	DB (—), 5.5 kbar, 26°, 21 h	 (48)	53
	 (–)	DB (—), 5.5 kbar, 26°, 21 h	 (30) 36% de	53
		DB (1.0), rt, 14 d	 (73) 2% de	83
	 (–)	DB (0.1), rt, 2 d	 (70) 30% de	86, 253
		$H_2N(CH_2)_3NH_2$ (0.15), 4-$MeOC_6H_4OH$ (0.3), rt, 5 d	 (89)	44
	 (–)	DB (1.0), rt, 4 d	 (76) >74% ee	253
C_3				
MeO_2CCHO		DB (0.07), 25°, 48 h	 (74)	45
		DB (0.05), rt, 7 d	 I (71)	281, 123, 226, 228, 268
	"	DB (0.09), dioxane, 0°, 8 h	I (71)	63
	"	HQ (0.05), rt, $t_{1/2}$ = 5 h	I (61)	33
	"	*n*-Bu_3P, (—), rt, 2 h	I (80)	63, 50
	"	$(C_6H_{11})_3P$ (0.014), dioxane, reflux, 15 h	I (32)	7, 8, 17, 63
	"	DB (0.5), microwave, 10 min	I (70)	76
	"	DB (0.15), 4.9 kbar, 25°, 4 h	I (56)	50
		DB (0.4), rt, 100 min	 (86)	36, 110
		DB (0.15), rt, 5 d	 (53)[j]	111
		DB (—), rt, 4.5 d	 I (50)	128, 222
	"	$H_2N(CH_2)_3NH_2$ (0.15), 4-$MeOC_6H_4OH$ (0.3), rt, 48 h	I (75)	44

TABLE I-A. REACTIONS OF ACRYLATES WITH ALIPHATIC AND ALICYCLIC ALDEHYDES (*Continued*)

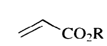
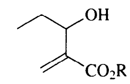
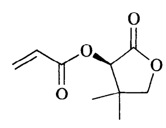
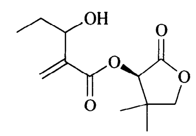
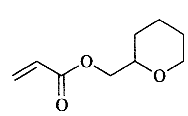
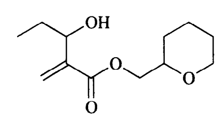
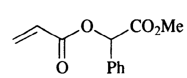
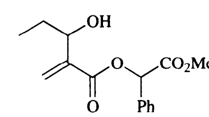
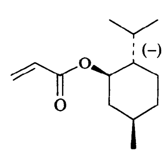
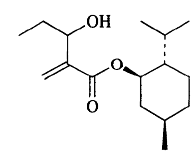
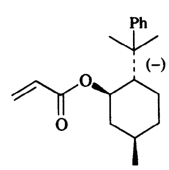
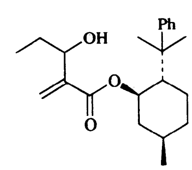
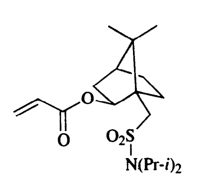
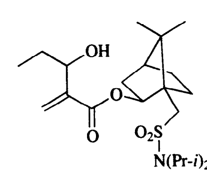
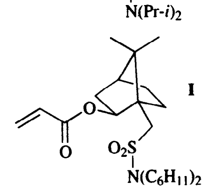
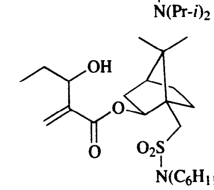
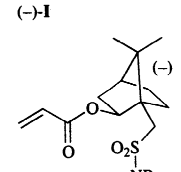
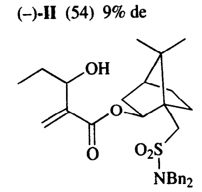
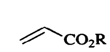
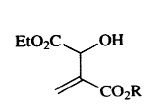
Aldehyde	Acrylate	Conditions	Product(s) and Yield(s) (%)	Refs.
				
	R			
	n-Bu	$H_2N(CH_2)_3NH_2$ (0.15), 4-$MeOC_6H_4OH$ (0.3), rt, 48 h	(69)	44
	i-Bu	DB (0.1), rt, 14 d	(—)	222
	t-Bu	[k], rt, 12 d	(62)	119, 43
	CH(Me)Pr-*n*	DB (0.15), 4.9 kbar, 50°, 4 h	(72)	50
	$CH(Et)_2$	DB (0.15), 4.9 kbar, 50°, 4 h	(72)	280
	4-THP	DB (0.1), rt, 14 d	(—)	222
		DB (0.2), rt, 30 min	 I (0)[l]	88
	"	1. DB (0.2), 20-30°, 30 min 2. MeCHO, 30 min	I (0)[m]	110
		DB (0.1), rt, 14 d	 (—)	222
		DB (0.4), rt, 90 min	 (89)	36, 110
		DB (0.1), rt, 7 d	 I (78) 16% de	86
		DB (1.0), rt, 14 d	 I (81) 65% de	83
		DB (0.1), rt, 7 d	 (70) 42% de	86
	 I	DB (0.1), rt, 10 d	 II (45) 70% de	86
	(+)-I	DB (0.1), rt, 21 d	(+)-II (60) 7% de[n]	84, 328
	(−)-I	DB (0.1), rt, 24 d	(−)-II (54) 9% de	84, 328
		DB (0.1), rt, 7 d	 (74) 6% de	84, 328
C_4				
EtO_2CCHO				
	R			
	Me	DB (0.2), 50°, 12 h	(80)	282, 45
	Et	DB (0.09), 60°, 48 h	(54)	45
	Et	Et_3N (—), 60°, 48 h	(34)	45

TABLE I-A. REACTIONS OF ACRYLATES WITH ALIPHATIC AND ALICYCLIC ALDEHYDES (*Continued*)

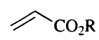
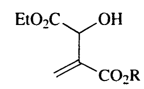
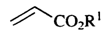
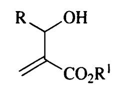
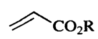
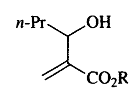
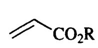
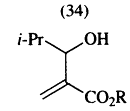
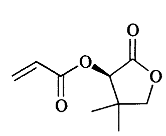
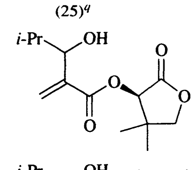
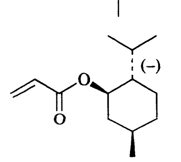
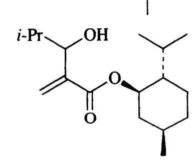
Aldehyde	Acrylate	Conditions	Product(s) and Yield(s) (%)	Refs.
				45
	R			
	$(CH_2)_2OH$	DB (0.09), MeCN, 25°, 70 h	(58)	
	$(CH_2)_2NMe_2$	DB (0.13), dioxane, 25°, 70 h	(54)	
RCHO				
R	R^1			
$Cl(CH_2)_2CCl_2$	Me	HQ (0.2), HFI (0.06), rt, 2.2 h	(13)	42
$Cl(CH_2)_3$	Me	DB (0.15), rt, 7d	(60)[o]	5, 216
$MeO(CH_2)_2$	Me	DB (0.15), rt	(36)	124
$MeS(CH_2)_2$	Me	HQ (0.2), HFI (0.06), rt, 6 h	(0)	42
$(MeO)_2CH$	Et	DB (0.1), MeOH (0.36), 4-$MeOC_6H_4OH$ (0.0002), rt, 9 d	(—)	330
$(MeO)_2CH$	$(CH_2)_2OH$	DB (0.1), MeOH (0.36), 4-$MeOC_6H_4OH$ (0.0001), 70°, 5 h	(—)	330
$(MeO)_2CH$	$(CH_2)_2NMe_2$	DB (0.1), MeOH (0.36), 4-$MeOC_6H_4OH$ (0.0001), 70°, 5 d	(—)	330
n-PrCHO				
	R			
	Me	DB (0.15), rt, 7 d	(85)	216, 49, 227, 308, 319
	Me	$(C_6H_{11})_3P$ (0.012), dioxane, reflux, 15 h	(70)	7, 8
	Et	$H_2N(CH_2)_3NH_2$ (0.15), 4-$MeOC_6H_4OH$ (0.3), rt, 60 h	(79)	44
	Et	DB (—)	(85)	178
	Et	$Ph_2P(CH_2)_4OH$ (0.05), neat, reflux, 10 h	(23)	8, 7
	$(CH_2)_2OH$	DB (0.15), rt, 5 d	(55)	111
	$CH_2CH{=}CH_2$	$(C_6H_{11})_3P$ (0.05), reflux, 3 h	(33)	7
	t-Bu	DB (0.15), HOAc (0.03), 35°, 14 d	(20)	43
	t-Bu	DB (0.1), 6 kbar, 7 d	(34)	43
i-PrCHO				
	R			
	Me	DB (0.05), rt, 13 weeks	(68)	123, 270, 271, 300, 308, 319, 331
	Me	DB (0.09), 0°, 12 h	(69)	63
	Me	DB (0.05), 50°, 5 weeks	(57)	123
	Me	Ph_3P (0.006), dioxane, 120-130°, 2 h	(—)[p]	17
	Et	$H_2N(CH_2)_3NH_2$ (0.15), 4-$MeOC_6H_4OH$ (0.3), rt, 60 h	(67)	44
	CH(Me)Pr-*n*	DB (0.15), 4.9 kbar, 50°, 4 h	(72)	50
	Ph	DB (0.1), rt, 14 h	(25)[q]	24
		DB (0.2), rt, 30 min	 (0)[r]	88
		DB (0.1), rt, 14 d	 (77) 7% de	86

TABLE I-A. REACTIONS OF ACRYLATES WITH ALIPHATIC AND ALICYCLIC ALDEHYDES (*Continued*)

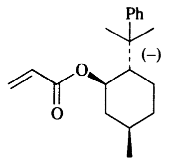
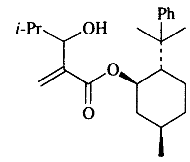
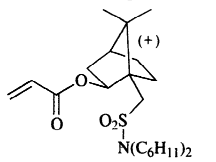
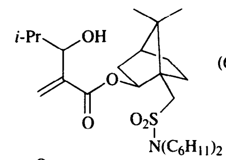
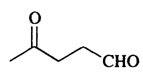
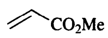
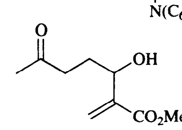
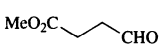
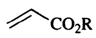
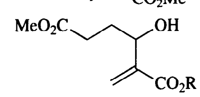
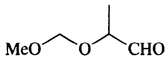
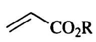
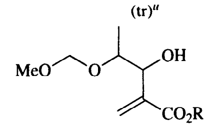
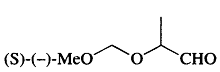
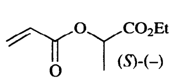
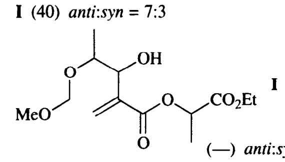
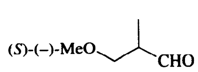
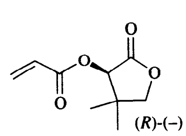
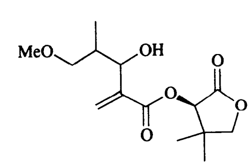
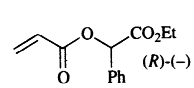
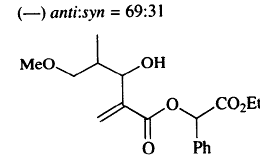
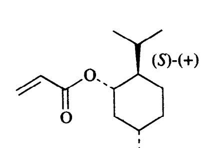
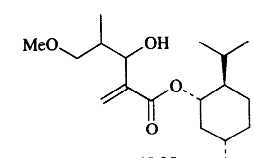
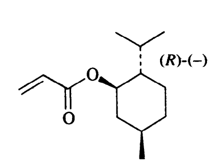
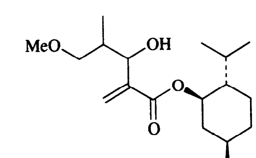
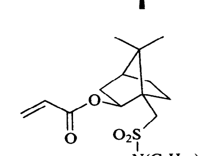
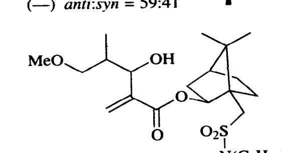
Aldehyde	Acrylate	Conditions	Product(s) and Yield(s) (%)	Refs.
		DB (1.0), rt, 14 d	 (76) 42% de	83
		DB (0.1), rt, 15 d	 (63) 20% de	84, 324
C_5 		DB (0.15), CH_2Cl_2, rt, 5 d	 (25)[e]	124
	 R			
	Me	DB (0.1), rt, 5 d	(40)[f]	125, 124
	t-Bu	DB (0.15), HOAc (0.03), rt, 38 d	(tr)[a]	124
	 R		 I	
	Me	DB (0.1), rt, 4 d	I (55) *anti*:*syn* = 7:3	30, 89
	Me	HQ (0.1), rt, 36 h	I (60) *anti*:*syn* = 72:28	30, 89
	Bu-*t*	DB (0.1), rt, 30 d	I (40) *anti*:*syn* = 7:3	30
		DB (0.2), rt, 2 d	 I (—) *anti*:*syn* = 69:31	30
	"	HQ (0.1), 4 d	I (—) *anti*:*syn* = 68:32	30
		DB (0.1), rt, 9 d	 (—) *anti*:*syn* = 69:31	30
		DB (0.1), rt, 4 d	 (—) *anti*:*syn* = 69:31	30
		DB (1.0), rt, 3.5 d	 (—) *anti*:*syn* = 65:35	30
		DB (0.4), rt, 16 d	 (—) *anti*:*syn* = 59:41	30
		DB (1.0), rt, >14 d	 (0)	30

TABLE I-A. REACTIONS OF ACRYLATES WITH ALIPHATIC AND ALICYCLIC ALDEHYDES (*Continued*)

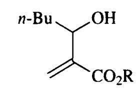
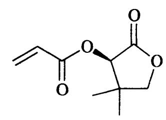
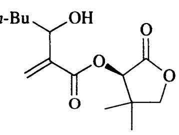
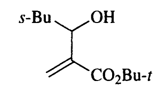
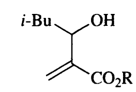
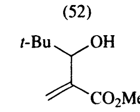
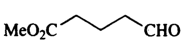
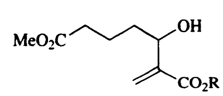
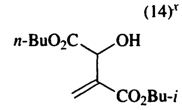
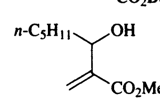
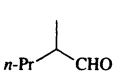
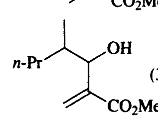
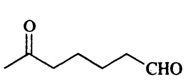
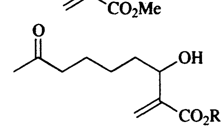
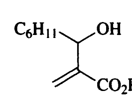
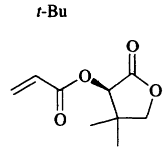
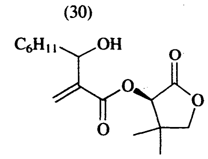
Aldehyde	Acrylate	Conditions	Product(s) and Yield(s) (%)	Refs.
n-BuCHO	CO_2R			
	R			
	Me	DB (0.3), rt, 6 d	(87)	261, 332
	Et	*n*-Bu$(C_6H_{11})_2$P, (0.02), 40°, 20 h	(68)	14
		DB (0.2), rt, 30 min	 (0)[v]	88
s-BuCHO	CO_2Bu-*t*	HQ (0.15), rt, 18 d	 (17)	43
i-BuCHO	CO_2R			
	R			
	Me	HQ (0.2), HFI (0.06), 45°, 36 h	(91)	42
	Me	DB (0.2), rt, 5 d	(56)	318, 271
	Me	DB (0.09), 0°, 12 h	(68)	63
	Et	$H_2N(CH_2)_3NH_2$ (0.15), 4-$MeOC_6H_4OH$ (0.3), rt, 60 h	(70)	44
	i-Pr	DB (0.2), rt, several d	(62)	271
	t-Bu	[k], rt, 19 d	(95)	119, 43
	t-Bu	DB (0.1), 6 kbar, rt, 7 d	(52)	43
t-BuCHO	CO_2Me	DB (—), rt, 10 d	 (0)	121
C_6				
	CO_2R			
	R			
	Me	DB (0.15), HOAc (0.03), rt	(46)[w]	124
	t-Bu	DB (0.15), HOAc (0.03), rt, 63 d	(14)[x]	124
n-BuO_2CCHO	CO_2Bu-*i*	DB (0.09), 50°, 27 h	 (66)	45
n-$C_5H_{11}CHO$	CO_2Me	DB (0.2), rt, 6 d	 (85)	122, 261
	CO_2Me	HQ (0.4), rt, 60 d	 (30) *anti*:*syn* = 35:65	30
C_7				
	CO_2R	DB (—)	 (—)	333
$C_6H_{11}CHO$	CO_2R			
	R			
	Me	HQ (0.25), HFI (0.1), 45°, 2 d	(66)	42, 72
	t-Bu	HQ (0.15), rt, 18 d	(30)	43
		DB (0.2), rt, 30 min	 **I** (0)[v]	88
	"	1. DB (0.2), 20-30°, 30 min 2. MeCHO, 30 min	**I** (0)[z]	88
	"	1. DB (0.2), 20-30°, 30 min 2. *i*-PrCHO, 30 min	**I** (0)[aa]	88

TABLE I-A. REACTIONS OF ACRYLATES WITH ALIPHATIC AND ALICYCLIC ALDEHYDES (*Continued*)

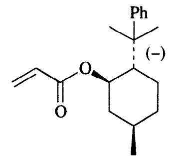
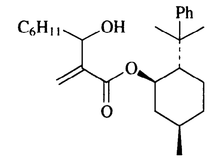
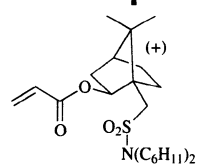
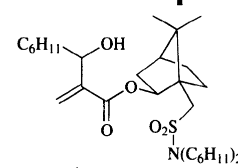
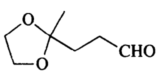
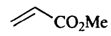
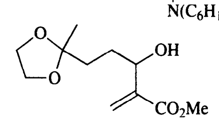
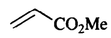
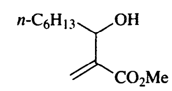
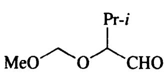
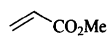
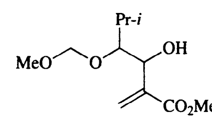
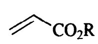
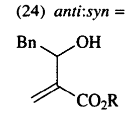
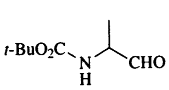
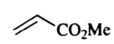
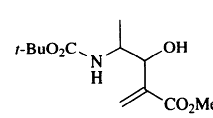
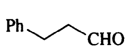
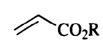
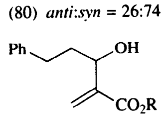
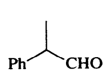
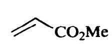
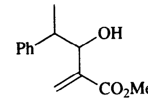
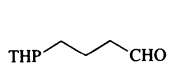
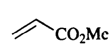
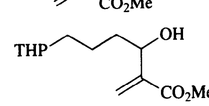
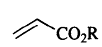
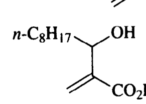
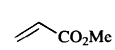
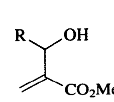
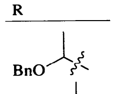
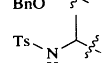
Aldehyde	Acrylate	Conditions	Product(s) and Yield(s) (%)	Refs.
		DB (1.0), rt, 14 d	 (67) 31% de	83
		DB (0.1), rt, 24 d	 (56) 26% de	84, 328
		DB (0.15), rt, 10 d	 (63)	216
n-$C_6H_{13}CHO$		DB (0.3), rt, 6 d	 I (83)	261, 332
	"	$H_2N(CH_2)_3NH_2$ (0.15), 4-$MeOC_6H_4OH$ (0.3), rt, 48 h	I (74)	44
		DB (1.0), rt, 34 d	 (24) *anti*:*syn* = 51:49	30
C_8				
BnCHO				
	R			
	Me	DB (0.15), HOAc (0.03), rt, 33 d	(17)[bb]	124
	Et	$H_2N(CH_2)_3NH_2$ (0.15), 4-$MeOC_6H_4OH$ (0.3), rt, 36 h	(79)	44
		DB (0.1), rt, 7 d	 (80) *anti*:*syn* = 26:74	30, 92
C_9				
				
	R			
	Me	DB (0.15), rt, 18 d	(72)	124
	Me	DB (0.09), 0°, 8 h	(67)	63
	Me	HQ (0.2), HFI (0.06), 45°, 24 h	(67)	42
	t-Bu	HQ (0.15), rt, 18 d	(35)	43
		HQ (0.2), HFI (0.06), 45°, 26 h	 (47) 58% de	42
		DB (0.15), rt, 7 d	 (87)	216
n-$C_8H_{17}CHO$				
	R			
	Me	DB (—)	(70-85)	270
	Et	$H_2N(CH_2)_3NH_2$ (0.15), 4-$MeOC_6H_4OH$ (0.3), rt, 48 h	(72)	44
C_{10}				
RCHO				
R				
		DB (0.1), rt, 14 d	(68) *anti*:*syn* = 3:2	30, 89
		DB (1.0), rt, <6 d	(68) *anti*:*syn* = 44:56	30

TABLE I-A. REACTIONS OF ACRYLATES WITH ALIPHATIC AND ALICYCLIC ALDEHYDES (*Continued*)

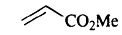
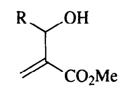
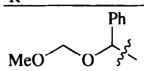
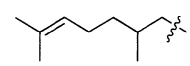
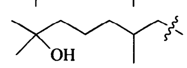
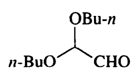
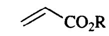
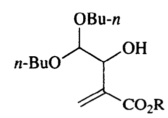
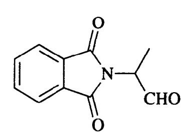
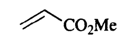
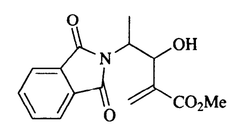
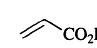
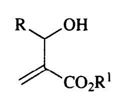
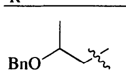
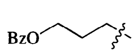
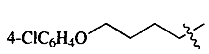
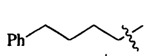
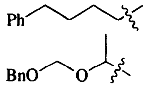
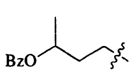
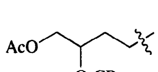
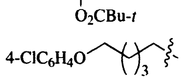
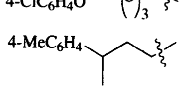
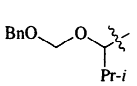
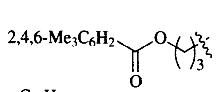
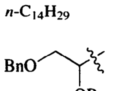
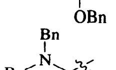
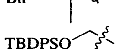
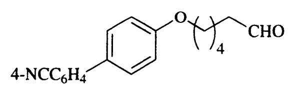
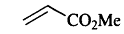
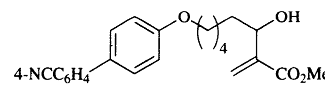
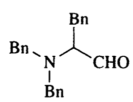
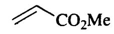
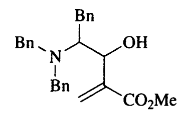
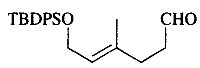
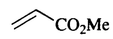
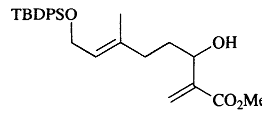
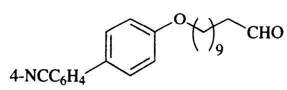
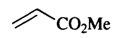
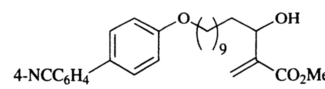
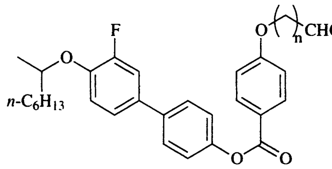
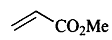
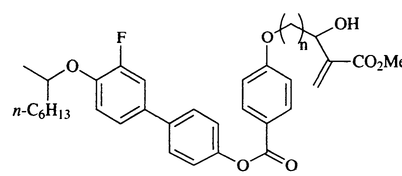
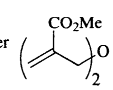
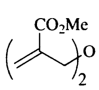
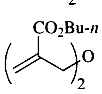
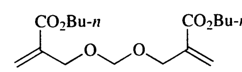
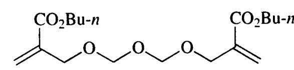
Aldehyde	Acrylate	Conditions	Product(s) and Yield(s) (%)	Refs.
RCHO				
R				
		DB (0.1), rt, >10 d	(42) *anti*:*syn* = 37:63	30
		DB (0.15), rt, 20 d	(77)	331
		HQ (0.2), HFI (0.06), 45°, 36 h	(93) 0% de	42
				
	R			
	Et	DB (0.1), n-BuOH (0.01), 4-$MeOC_6H_4OH$ (0.0002), rt, 9 d	(—)	330
	n-Bu	"	(—)	330
C_{11} 		DB (1.0), rt, 3.5 d	 (28) *anti*:*syn* = 46:54[cc]	30, 92, 144
RCHO				
R	R^1			
 (3*S*)	Me	DB (0.08), rt, 7 d	(70) 51% de	90
	Me	DB (0.15), rt, 7 d	(95)	216, 5, 227
	Me	DB (0.12), rt, 139 h	(39)	212
	Me	DB (0.03), rt, 5 d	(24)	212
	Me	DB (1.0), rt, 6 d	(42) *anti*:*syn* = 7:3	30
	t-Bu	HQ (0.1), rt, 40 d	(30) *anti*:*syn* = 81:19	30
C_{12} 	Me	DB (0.15), rt, 8 d	(92)	216, 227
	Me	DB (0.15), rt, 7 d	(89)	216
	Me	DB (0.16), rt, 113 h	(10)	212
	Me	DB (0.3), rt, 14 d	(55)	261, 332
C_{13} 	Me	DB (1.0), rt, 23 d	(68) *anti*:*syn* = 41:59	30
	t-Bu	DB (1.0), rt, 30 d	(53) *anti*:*syn* = 33:67	30
C_{14} 	Me	DB (0.15), rt, 7 d	(87)	216, 5
C_{15} *n*-$C_{14}H_{29}$	Me	DB (0.3), rt, 9 d	(72)	122
C_{17} 	Me	DB (0.5), rt, 20 d	(48) *anti*:*syn* = 65:35	30
	Me	HQ (1.0), rt, 20 d	(71) *anti*:*syn* = 72:28	30, 92
C_{18} 	Me	DB (—)	(40)	320, 298

TABLE I-A. REACTIONS OF ACRYLATES WITH ALIPHATIC AND ALICYCLIC ALDEHYDES (*Continued*)

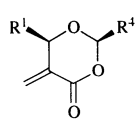
	Aldehyde	Acrylate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{19}			HQ (0.32), rt, 7 d	 (80)	213
C_{23}			DB (1.0), rt, 31 d	 (80) *anti:syn* = 67:33	30, 92
			DB (—)	 (—)	301
C_{24}			HQ (0.32), rt, 7 d	 (82)	213
			HQ (0.36), rt, 14 d		313
	n				
C_{34}	6			(65)	
C_{38}	10			(55)	

[a] The ether  was formed in 60% yield.

[b] The ether  was formed in 3% yield.

[c] The ethers  (19%),  (21%), and  (5%) were also formed.

[d] A single product, characterized by mass spectroscopy only, was formed in low yield.

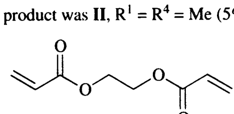
[e] The product was  **II**, $R^1 = R^4$ = Me, (84%), 87% de, 10% ee

[f] The product was **II**, R^1 = Me, R^4 = Et, (86%), 88% de, low ee.

[g] The product was **II**, $R^1 = R^4$ = Me (57%).

[h] The product was **II**, $R^1 = R^4$ = Me (69%).

[i] The second product was **II**, $R^1 = R^4$ = Me (5%).

[j] The diester  was formed in 20-25% yield.

[k] The catalyst was not specified but was probably DABCO (0.2).

[l] The product was **II**, $R^1 = R^4$ = Et (89%), 78% de.

[m] The product was **II**, R^1 = Et, R^4 = Me, (83%), 86% de.

[n] The de was enriched to 70% by crystallization from hexanes.

[o] The catalyst was partially quaternized by the chloroaldehyde.

[p] The conversion was 70-90%.

[q] The second product was II, $R^1 = R^4$ = *i*-Pr (25%).

[r] The second product was II, $R^1 = R^4$ = *i*-Pr (78%), 81% de, 22% ee.

[s] Some hemiketal is included in the yield.

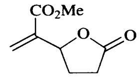
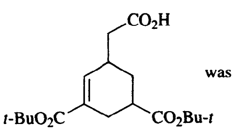
[t] The lactone  was formed in 6% yield.

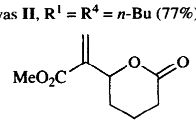
TABLE I-A. REACTIONS OF ACRYLATES WITH ALIPHATIC AND ALICYCLIC ALDEHYDES (*Continued*)

Aldehyde	Acrylate	Conditions	Product(s) and Yield(s) (%)	Refs.

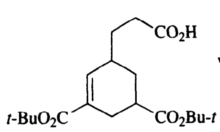
[u] The acid 

was formed in 28% yield.

[v] The product was **II**, $R^1 = R^4 = n$-Bu (77%) 78% de.

[w] Some lactone 

is included in the yield.

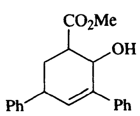
[x] The acid 

was formed in 20% yield.

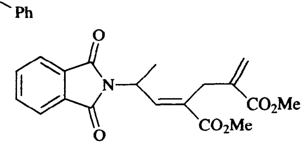
[y] The product was **II**, $R^1 = R^4 = C_6H_{11}$ (61%), 86% de, 39% ee.

[z] The product was **II**, $R^1 = C_6H_{11}$, R^4 = Me (52%).

[aa] The product was **II**, $R^1 = C_6H_{11}$, $R^4 = i$-Pr (50%).

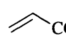
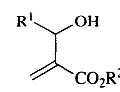
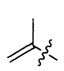
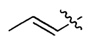
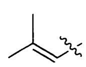
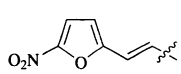
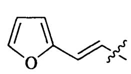
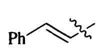
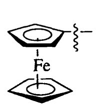
[bb] The ester 

was formed in 40% yield.

[cc] The formation of diester 

was reported in ref. 144.

TABLE I-B. REACTIONS OF ACRYLATES WITH OLEFINIC ALDEHYDES

	Aldehyde	Acrylate	Conditions	Product(s) and Yield(s) (%)	Refs.
	R^1CHO	 CO_2R^2			
	R^1	R^2			
C_3	$CH_2{=}CH$	Me	DB (0.15), rt	(0)[a]	127
C_4		Me	DB (0.15), rt, 20 d	(33)	5, 127
		Me	DB (0.15), MeOH (0.01), rt, 20 d	(31)	275, 127, 334
		Et	$H_2N(CH_2)_3NH_2$ (0.15), 4-$MeOC_6H_4OH$ (0.3), rt, 60 h	(66)	44
		n-Bu	$H_2N(CH_2)_3NH_2$ (0.15), 4-$MeOC_6H_4OH$ (0.3), rt, 72 h	(66)	44
C_5		Me	DB (0.15), 4-MeOH (0.01), rt, 25 d	(35)	275
C_7		Me	HQ (0.2), HFI (0.06), rt, 9 h	(0)	42
		Me	HQ (0.1), $CHCl_3$, rt, 14 d	(38)	334
C_9		Me	DB (0.15), rt, 6 d	(75)	127, 76, 275, 334
		Me	DB (0.5), microwave, 45 min	(15)	76
C_{11}		Me	HQ (0.2), HFI (0.06), 65°, 2 d	(0)	42

[a] The product was a polymer.

TABLE I-C. REACTIONS OF ACRYLATES WITH AROMATIC ALDEHYDES

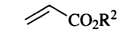
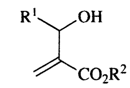
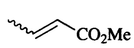
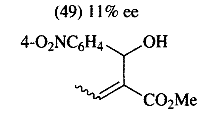
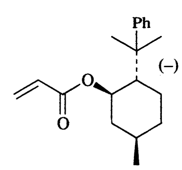
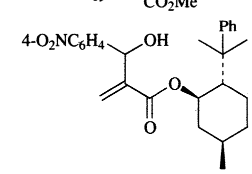
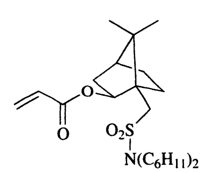
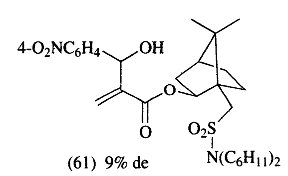
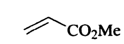
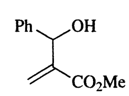
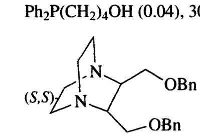
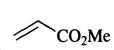
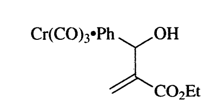
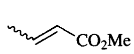
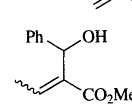
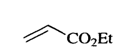
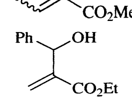
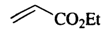
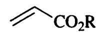
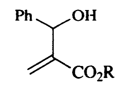
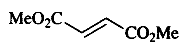
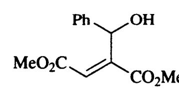
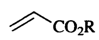
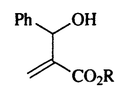
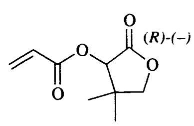
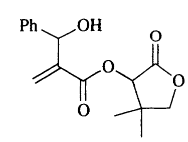
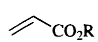
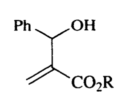
Aldehyde	Acrylate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7				
R^1CHO				
R^1	R^2			
3,4-$F_2C_6H_3$	Me	HQ (0.2), HFI (0.06), rt, 5 h	(93)	42
3,5-$Cl_2C_6H_3$	Me	HQ (0.2), HFI (0.06), 45°, 1 h	(87)	42
2-FC_6H_4•$Cr(CO)_3$ (±)	Me	DB (0.5), rt, 7 h	(92) 84% de	97
2-ClC_6H_4	Me	DB (0.5), rt, 2 d	(>90)	97
	Et	$H_2N(CH_2)_3NH_2$ (0.15), 4-$MeOC_6H_4OH$ (0.3), rt, 36 h	(91)	44
2-ClC_6H_4•$Cr(CO)_3$ (±)	Me	DB, (0.5), rt, 6 h	(89) >95% de	97
2-ClC_6H_4•$Cr(CO)_3$ (*S*)-(+)	Me	DB (0.5), rt, 8 h	(97) >95% de[a]	97
4-ClC_6H_4	Me	DB (—), rt, 72 h	(95)	128, 107
	Et	$H_2N(CH_2)_3NH_2$ (0.15), 4-$MeOC_6H_4OH$ (0.3), rt, 24 h	(95)	44
4-BrC_6H_4	*t*-Bu	DB (0.15), HOAc (0.03), 35°, 21 d	(81)	43
3-$O_2NC_6H_4$	Me	HQ (0.1), HFI (0.06), rt, 90 min	(97)	42
4-$O_2NC_6H_4$	Me	DB (—), rt, 18 h	(95)	128
	Me	HQ (0.1), HFI (0.06), 25°, 42 min	(95)	42
	Me	(*S*)-(–)-retronecine (0.05), rt, 2 weeks	(49) 11% ee	51, 52
4-$O_2NC_6H_4CHO$		DB (0.5), microwave, 40 min	 (10)[b]	76
		DB (1.0), $CHCl_3$, rt, 14 d	 (65) 60% de	83
		DB (0.1), rt, 30 d	 (61) 9% de	84, 328
PhCHO		DB (0.5), rt, 4 d	 **I** (92)	126, 5, 24, 27, 76, 104, 123, 129, 221, 261, 300, 308
	"	DB (0.9), dioxane, 0°, 4 h	**I** (68)	63
	"	HQ (0.2), HFI (0.075), 37°, 23 h	**I** (85)	42
	"	DB (0.5), microwave, 10 min	**I** (34)	76
	"	PPh_3, (0.006), dioxane, 120-130°, 2 h	**I** (—)[c]	17
	"	$Ph_2P(CH_2)_4OH$ (0.04), 30-35°, 20 h	**I** (19)	7, 8
		 (0.15), hydroquinone (0.01), THF/MeOH (5:1),[d] 10 kbar, 30°, 23 h	**I** (72) 10% ee[e]	39
PhCHO•$Cr(CO)_3$		DB (0.5), rt, 6 h	 (94)	97
PhCHO		DB (0.1), 15 kbar, 50°, 45 h	 (—) *E*:*Z* = 1	82
		DB (0.13), rt, 7 d	 **I** (79)	27, 222, 284, 335
	"	$H_2N(CH_2)_3NH_2$ (0.15), 4-$MeOC_6H_4OH$ (0.3), rt, 36 h	**I** (83)	44

TABLE I-C. REACTIONS OF ACRYLATES WITH AROMATIC ALDEHYDES (*Continued*)

Aldehyde	Acrylate	Conditions	Product(s) and Yield(s) (%)	Refs.
		$4\text{-}Me_2NC_5H_4N$ (0.15), $4\text{-}MeOC_6H_4OH$ (0.3), rt, 36 h	I (79)	44
	"	DBU (0.15), $4\text{-}MeOC_6H_4OH$ (0.3), rt, 36 h	I (81)	44
				
	R			
	$(CH_2)_2F$	DB (0.13), rt, 3 d	(81)	27
	$(CH_2)_2Cl$	DB (0.13), rt, 3 d	(61)	27
	$(CH_2)_2Br$	DB (0.13), rt, 2 d	(0)	27
	$(CH_2)_2OH$	DB (0.15), rt, 5 d	(50)[f]	111, 27
	CH_2CF_3	DB (0.13), rt, 15 h	(58)	27
	CH_2CCl_3	DB (0.13), rt, 36 h	(64)	27
		DB (—), 15 kbar, 50°, 250 h	 (0)	82
				
	R			
	$CH_2CH{=}CH_2$	DB (0.13), rt, 3 d	(75)	27
	CH_2COMe	DB (0.13), rt, 2 d	(65)	27
	$(CH_2)_3OH$	DB (0.15), rt, 3 d	(66)	111
	$(CH_2)_2OMe$	DB (0.13), rt, 4 d	(89)	27
	$(CH_2)_2SCN$	DB (0.13), rt, 2 d	(66)	27
	n-Bu	DB (0.13), rt, 4 d	(85)	27
	"	$H_2N(CH_2)_3NH_2$ (0.15), $4\text{-}MeOC_6H_4OH$ (0.3), rt, 36 h	(89)	44
	"	DB (0.11), microwave flow reactor, 120°	(23)	74
	i-Bu	DB (0.13), rt, 16 d	(85)	27
	t-Bu	DB (0.15), HOAc (0.03), 35°, 21 d	(77)	43, 27
	$(CH_2)_4OH$	DB (0.15), rt, 3 d	(85)	111
	$(CH_2)_2NMe_2$	DB (0.13), rt, 8 d	(82)	27
	(*S*)-(–)-EtO_2CCHMe	DB (1.0), rt, 12 d	(—), 4% de	30
	$3\text{-}FC_6H_4$	DB (0.13), rt, 5 h	(43)	27
	$4\text{-}FC_6H_4$	DB (0.13), rt, 3 d	(39)	27
	$4\text{-}ClC_6H_4$	DB (0.13), rt, 3 d	(42)	27
	$4\text{-}O_2NC_6H_4$	DB (1.5), $CHCl_3$, rt, 72 h	(16)	24, 27
	Ph	DB (0.1), rt, 3 h	(78)	24, 27
		DB (—)	 (81) 2% de	88, 30
				
	R			
	n-C_6H_{13}	DB (0.13), rt, 9 d	(82)	27
	$(CH_2)_6OH$	DB (0.15), rt, 4 d	(80)	111
	$3\text{-}CF_3C_6H_4$	DB (0.13), rt, 124 h	(22)	27
	$4\text{-}CF_3C_6H_4$	DB (0.13), rt, 10 d	(0)	27
	$3\text{-}NCC_6H_4$	DB (0.13), rt, 10 d	(0)	27
	$4\text{-}NCC_6H_4$	DB (0.13), rt, 10 d	(0)	27
	$3\text{-}FC_6H_4CH_2$	DB (0.13), rt, 90 h	(77)	27
	$4\text{-}FC_6H_4CH_2$	DB (0.13), rt, 92 h	(85)	27
	$3\text{-}MeC_6H_4$	DB (0.13), rt, 36 h	(54)	27
	$4\text{-}MeC_6H_4$	DB (0.13), rt, 36 h	(55)	27
	$3\text{-}MeOC_6H_4$	DB (0.13), rt, 24 h	(43)	27
	$4\text{-}MeOC_6H_4$	DB (0.13), rt, 8 h	(54)	27, 24
	$(CH_2)_6SCN$	DB (0.13), rt, 6 d	(68)	27
	$3\text{-}F_3CC_6H_4CH_2$	DB (0.13), rt, 67 h	(83)	27
	$4\text{-}F_3CC_6H_4CH_2$	DB (0.13), rt, 67 h	(88)	27

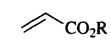
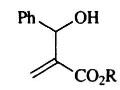
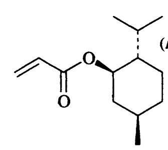
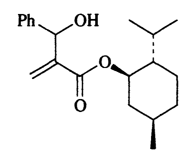
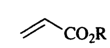
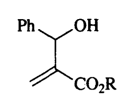
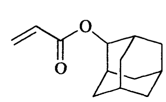
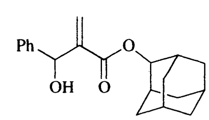
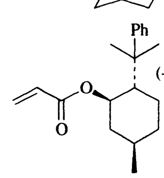
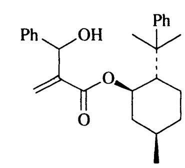
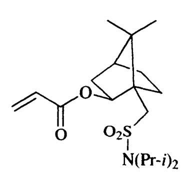
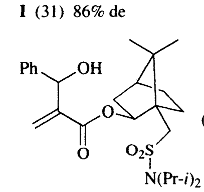
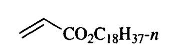
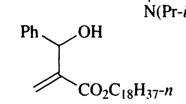
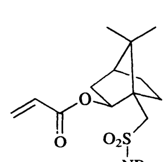
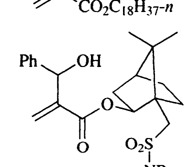
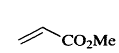
Aldehyde	Acrylate	Conditions	Product(s) and Yield(s) (%)	Refs.
	 R			
	4-$MeO_2CC_6H_4$	DB (0.13), rt, 20 h	(37)	27
	3-$MeC_6H_4CH_2$	DB (0.13), rt, 120 h	(83)	27
	4-$MeC_6H_4CH_2$	DB (0.13), rt, 120 h	(76)	27
	3-$MeOC_6H_4CH_2$	DB (0.13), rt, 120 h	(86)	27
	4-$MeOC_6H_4CH_2$	DB (0.13), rt, 192 h	(86)	27
	2,6-$Me_2C_6H_3$	DB (1.5), $CHCl_3$, rt, 72 h	(49)	24
	$Ph(CH_2)_2$	DB (0.13), rt, 4 d	(84)	27
	3-$Me_2NC_6H_4$	DB (0.13), rt, 20 h	(61)	27
	4-$Me_2NC_6H_4$	DB (0.13), rt, 84 h	(62)	27
	n-C_8H_{17}	DB (0.13), rt, 12 d	(78)	27
	n-BuCH(Et)CH_2	DB (0.13), rt, 20 d	(54)	27
	(*R*)-(−)-MeO_2CCHPh	DB (1.0), rt, 10 d	(—) 34% de	30
	$(CH_2)_9OH$	DB (0.15), rt, 12 d	(60)	111
	 (*R*)-(−)	DB (—), 17°, 48 d	 I (93) 22% de	53, 30, 86
	"	DB (—), 7.5 Kbar, 30°, 21 h	I (42) 100% de	53
	 R			
	n-$C_{10}H_{21}$	DB (0.13), rt, 14 d	(75)	27
	$(CH_2)_{10}OH$	DB (0.15), rt, 6 d	(78)	111
		DB (0.13), dioxane, rt, 62 d	 (40)	27
	 (−)	DB (1.0), rt, 14 d	 I (82) 35% de	83
	"	DB (—), 8 kbar, 35°, 70 h	I (31) 86% de	53
		DB (0.1), rt, 10 d	 (84) 15% de	86
		$H_2N(CH_2)_3NH_2$ (0.15), 4-$MeOC_6H_4OH$ (0.3), rt, 10 d	 (81)	44
	 R			
	C_6H_{11}	DB (0.1), rt, 15 d	(80) 25% de	86, 30, 84
	Bn	DB (0.1), rt, 5 d	(71) 18% de	84, 328
2-HOC_6H_4CHO		DB (0.05), $CHCl_3$, rt, 3 d	[g] (19)	54, 76
	"	DB (0.1), CH_2Cl_2, 0°	[h] (40)	32
	"	DB (0.5), microwave, 10 min	[g] (70)	76

TABLE I-C. REACTIONS OF ACRYLATES WITH AROMATIC ALDEHYDES (*Continued*)

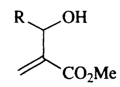
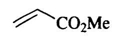
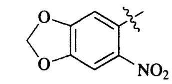
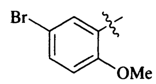
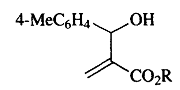
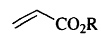
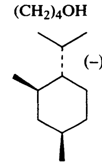
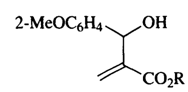
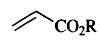
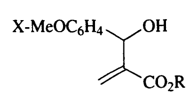
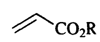
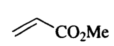
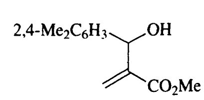
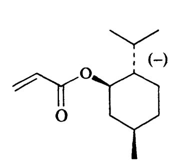
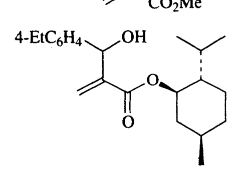
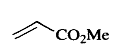
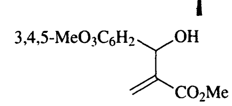
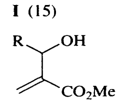
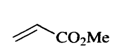
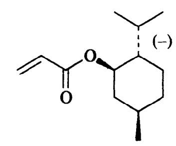
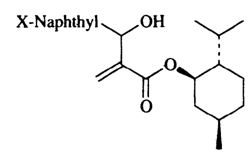
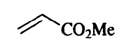
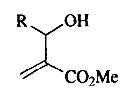
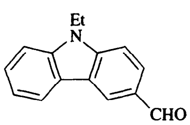
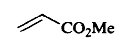
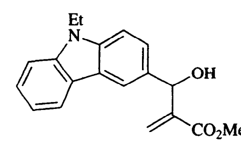
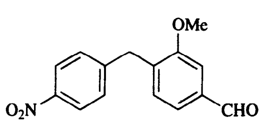
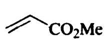
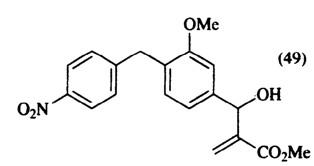
Aldehyde	Acrylate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
RCHO				
R				
2-$F_3CC_6H_4$		HQ (0.2), HFI (0.06), 45°, 26 h	(93)	42
4-NCC_6H_4		HQ (0.1), HFI (0.03), rt, 2.3 h	(91)	42
		HQ (0.2), HFI (0.06), rt, 5.5 h	(88)	42
		HQ (0.2), HFI (0.06), 45°, 10 h	(93)	42
4-$H_2NCOC_6H_4$		HQ (0.2), HFI (0.06), 45°, 29 h	(46)	42
2-MeC_6H_4•$Cr(CO)_3$ (±)		DB (0.5), rt, 48 h	(90) 68% de	97
				
4-MeC_6H_4CHO				
	R			
	Me	DB (—), rt, 30 d	(95)	128, 107, 261
	$(CH_2)_3OH$	DB (0.15), rt, 5 d	(68)	111
	$(CH_2)_4OH$	DB (0.15), rt, 6 d	(60)	111
		DB (—), 17°, 48 d	(30) 100% de	53
	"	DB (—), 8.5 Kbar, 31°, 46 h	(31) 87% de	53
				
2-$MeOC_6H_4CHO$				
	R			
	Me	DB (0.15), rt, 20 d	(90)	129, 97
2-$MeOC_6H_4CHO$•$Cr(CO)_3$ (±)	Me	DB (0.5), rt, 93 h	(87) >95% de	97
(*S*)-(+)	Me	DB (0.5), rt, 93 h	(85) >95% de[a]	97
2-$MeOC_6H_4CHO$	$(CH_2)_3OH$	DB (0.15), rt, 6 d	(54)	111
	$(CH_2)_4OH$	DB (0.15), rt, 6 d	(56)	111
				
X-$MeOC_6H_4CHO$				
X	R			
3	Me	HQ (—)	(91)	224
4	Me	DB (0.15), rt, 20 d	(90)	129
	Me	HQ (0.3), HFI (0.1), 37°, 26 h	(41)	42
?	Et	$H_2N(CH_2)_3NH_2$ (0.15), 4-$MeOC_6H_4OH$ (0.3), rt, 96 h	(72)	44
?	*n*-Bu	$H_2N(CH_2)_3NH_2$ (0.15), 4-$MeOC_6H_4OH$ (0.3), rt, 96 h	(74)	44
C_9				
2,4-$Me_2C_6H_3CHO$		HQ (0.3), HFI (0.12), 45°, 30 h	 (45)	42
4-EtC_6H_4CHO		DB (—), 8.5 kbar, 31°, 46 h	 (32) 94% de	53
C_{10}				
3,4,5-$MeO_3C_6H_2CHO$		DB (0.5), rt, 4 d	 **I** (5)	76
	"	HQ (0.2), HFI (0.06), 45°, 27 h	**I** (48)	42
	"	DB (0.5), microwave, 30 min	**I** (15)	76
C_{11}				
RCHO				
R				
1-Naphthyl		DB (—), rt, $t_{1/2}$ = 12 d	(—)	132, 107, 300
2-Naphthyl		HQ (0.2), HFI (0.075), 37°, 14 h	(83)	42

TABLE I-C. REACTIONS OF ACRYLATES WITH AROMATIC ALDEHYDES (*Continued*)

	Aldehyde	Acrylate	Conditions	Product(s) and Yield(s) (%)	Refs.
	X-Naphthyl		DB (—), 6 kbar, 27°, 140 h	 (57) 23% de	53
	RCHO				
	R				
	i-BuC_6H_4		HQ (0.2), HFI (0.06), 45°, 36 h	(60)	42
C_{13}	4-PhC_6H_4		HQ (0.2), HFI (0.06), Ar, rt, 12 h	(83)	42
	3-PhOC_6H_4		HQ (0.3), HFI (0.1), 37°, 5 h	(92)	42
C_{14}	2-BnOC_6H_4		DB (1.0), rt, 12 d	(90)[i]	32
C_{15}	9-Anthryl		DB (—). rt, 12 d	(0)	132
			HQ (0.2), HFI (0.06), 45°, 210 h	 (21)	42
			HQ (0.2), HFI (0.06), 70°, 24 h	 (49)	42

[a] The product has the *S,S* (–) configuration.

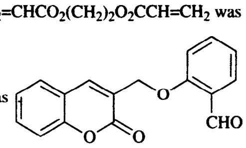
[b] The product was a mixture of *cis* and *trans* isomers.

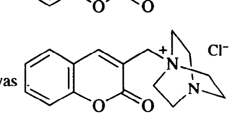
[c] The conversion was 70-90%.

[d] In pure THF, the yield was 14%.

[e] The product has the *S* configuration.

[f] The diester $CH_2{=}CHCO_2(CH_2)_2O_2CCH{=}CH_2$ was formed in 20-35% yield.

[g] The product was 

[h] The product was 

[i] The number refers to the crude yield.

TABLE I-D. REACTIONS OF ACRYLATES WITH HETEROCYCLIC ALDEHYDES

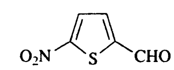
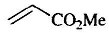
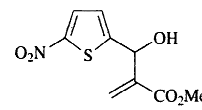
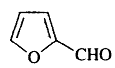
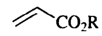
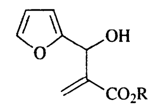
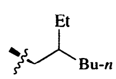
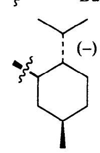
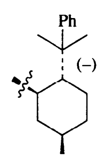
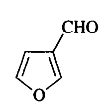
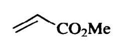
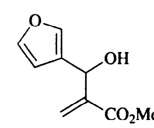
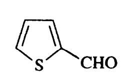
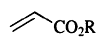
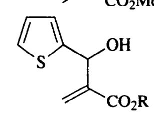
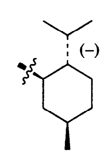
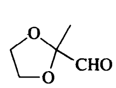
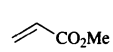
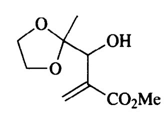
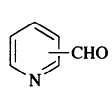
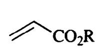
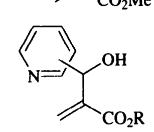
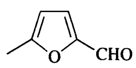
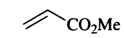
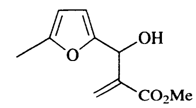
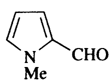
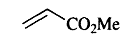
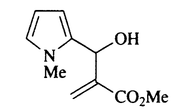
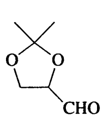
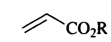
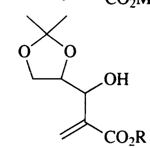
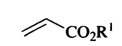
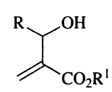
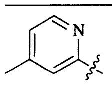
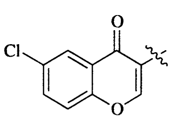
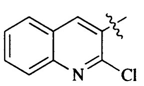
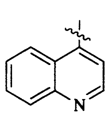
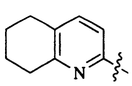
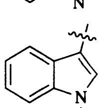
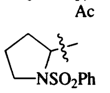
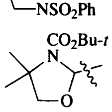
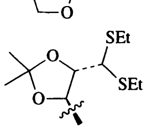
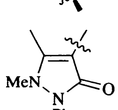
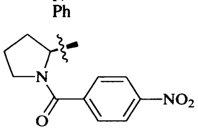
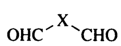
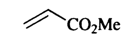
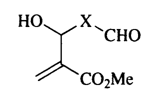
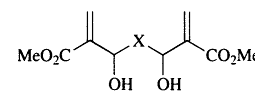
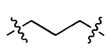
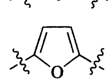
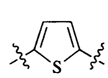
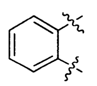
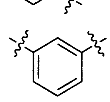
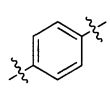
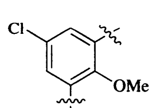
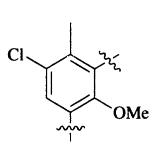
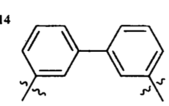
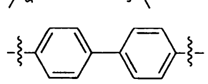
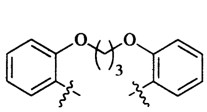
Aldehyde	Acrylate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5				
		HQ (0.1), HFI (0.1), Ar, rt, 30 min	 (56)	42
				
	R			
	CH_2CF_3	DB (0.13), rt, 2 h	(54)	27
	Me	DB (0.13), rt, 24 h	(76)	27, 5, 123, 129
	$(CH_2)_2Cl$	DB (0.13), rt, 17 h	(70)	27
	$(CH_2)_2OMe$	DB (0.13), rt, 36 h	(90)	27
	n-Bu	DB (0.13), rt, 3 d	(88)	27
	$(CH_2)_2NMe_2$	DB (0.13), rt, 3 d	(86)	27
	Ph	DB (0.1), rt, 8 h	(21)	24
		DB (0.13), rt, 154 h	(86)	27
		DB (0.1), rt, 18 h	(85) 20% de	86, 53
		DB (1.0), rt, 14 d	(59) 30% de	83
		HQ (0.2), HFI (0.06), Ar, 45°, 6 h	 (35)	42
				
	R			
	Me	DB (0.15), rt, 3 d	(92)	129
	Me	HQ (0.2), HFI (0.06), Ar, 45°, 7 h	(54)	42
	Et	$H_2N(CH_2)_3NH_2$ (0.15), 4-$MeOC_6H_4OH$ (0.30), rt, 36 h	(94)	44
		DB (—), 6 kbar, 27°, 6 d	(52)	53
		DB (—), rt	 (63)	227
C_6				
				
Position	R			
2	Me	DB (0.05), $CHCl_3$, rt, 3 d	(94)	113, 129
2	Et	DB (0.05), rt	(96)	113
2	*i*-Pr	DB (0.05), rt, 3 d	(51)	113
3	Me	DB (—), $CHCl_3$, rt, 16 h	(94)	34, 5
3	Et	$H_2N(CH_2)_3NH_2$ (0.15), 4-$MeOC_6H_4OH$ (0.3), rt, 24 h	(85)	44
3	Ph	DB (0.1), 0°, 10 min	(54)	24
4	Me	DB (0.1), 0°, 10 min	(83)	34, 336
4	Me	HQ (0.05), HFI (0.03), rt, 3.5 h	(88)	42, 33

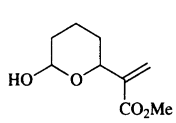
TABLE I-D. REACTIONS OF ACRYLATES WITH HETEROCYCLIC ALDEHYDES (*Continued*)

Aldehyde	Acrylate	Conditions	Product(s) and Yield(s) (%)	Refs.
		HQ (0.1), $CHCl_3$, rt, 14 d	 (33)	334
		HQ (0.2), HFI (0.06), 65°, 2 d	 (0)	42
	 R			
	Me	DB (0.1), rt, 55 d	(62) *anti*:*syn* = 69:31	30
	Me	HQ (0.1), rt, 45 d	(40) *anti*:*syn* = 75:25	30
	t-Bu	DB (0.1), rt, 90 d	(61) *anti*:*syn* = 66:34	30
RCHO R	 R^1			
C_7 	Me	DB (0.05), rt	(94)	113
	Me	HQ (0.2), HFI (0.08), 25°, 4.5 h	(95)	42
C_{10} 	Me	HQ (0.2), HFI (0.06), rt, 18 h	(0)	42
	Me	HQ (0.2), HFI (0.06), 45°, 2.2 h	(98)	42
	Me	DB (—), $CHCl_3$, rt, 16 h	(100)	34
	Me	HQ (0.05), HFI (0.03), rt, 5 h	(99)	42
	Me	DB (0.05), rt	(83)	113
C_{11} 	Me	HQ (0.2), HFI (0.06), 65°, 2 d	(0)	42
	Me	DB (1.0), rt, 12 h	(55) *anti*:*syn* = 87:13	30, 92
	Me	DB (1.0), rt, 7 d	(85) *anti*:*syn* = 86:14	91, 30
	Et	PPh_3 (1.1), 100°, 22 h	(17)[a]	59
C_{12} 	Me	HQ (0.2), HFI (0.06), 65°, 2 d	(0)	42
	Me	DB (1.0), rt, 7 d	(75) *anti*:*syn* = 75:25	91

[a] The product was a mixture of diastereomers; also formed were $R^1CH{=}CHCH_2CO_2Et$ (34%) and $R^1CHOHCH{=}CHCO_2Et$ (18%).

TABLE I-E. REACTIONS OF METHYL ACRYLATE WITH DIALDEHYDES

Aldehyde	Acrylate	Conditions	Product(s) and Yield(s) (%)	Refs.
 I X	 II I:II		 A  B	
C_5 	1:2	DB (0.5), rt, 72 h	A (0)[a]	126, 71
C_6 	1:2	DB (0.5), THF, rt, 4 h	A (50)	126, 71, 131
	1:5	DB (1.0), rt, 27 h	B (60)	
	1:2	DB (0.5), rt, 2 h	A (67)	126, 71
	1:5	DB (1.0), rt, 48 h	B (67)	126, 71
C_8 	1:2	DB (0.5), rt, 8 h	A (0)[b]	126
	1:5	DB (0.5), rt, 5 h	A (85) + B (10)	71, 126
	1:5	DB (0.5), LiCl, (0.1), rt, 2 h	A (82) + B (18)	71
	1:10	DB (1.0), rt,72 h	A (2) + B (96)	71, 126, 131
	1:2	DB (0.5), 20°, 2.5 h	A (94) + B (4)	71, 126, 131, 336a
	1:10	DB (1.0), 20°, 96 h	A (2) + B (96)	71, 126, 128, 131, 336a
C_9 	1:3	HQ (0.3), rt, 12 d	B (86)	131
C_{10} 	1:3	HQ (0.3), rt, 22 d	B (10)	131
C_{14} 	1:2	DB (0.5), THF, rt, 72 h	A (55)	126, 71
	1:5	DB (1.0), rt, 84 h	B (94)	126, 71
	1:2	DB (0.5), THF, rt, 20 d	A (56)	126, 71
	1:5	DB (1.0), rt, 96 h	B (86)	126, 71
C_{17} 	1:3	HQ (0.3), rt, 21 d	B (94)	131

[a] The product was  (85%).

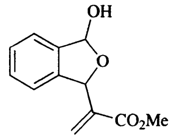
[b] The product was  (86%).

TABLE I-F. REACTIONS OF ALLENIC ESTERS WITH ALDEHYDES

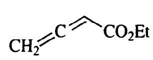
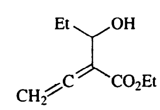
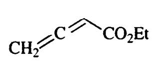
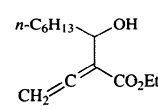
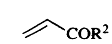
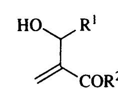
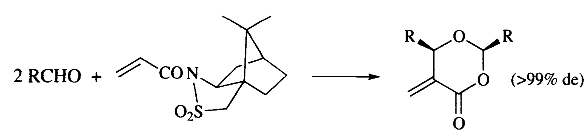
Aldehyde	Allenic Ester	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3				
EtCHO		DB (0.14), Et_2O, –6 to 23°, 16 h	 (41)	112, 337
C_7				
n-$C_6H_{13}CHO$		DB (0.14), Et_2O, 0 to 25°, 34 h	 (54)	112, 337

TABLE II-A. REACTIONS OF ACRYLAMIDES WITH ALDEHYDES

	Aldehyde	Acrylamide	Conditions	Product(s) and Yield(s) (%)	Refs.
	R^1CHO				
	R^1	R^2			
C_2	Me	NH_2	Et_2NMe (0.08), 5 kbar, 20°, 3 h	(83)[a]	48
C_5	*i*-Bu	NMe_2	—	(0)	119
C_6	2-Pyridyl	NH_2	DB (0.05), rt, 3d	(0)	113
		NMe_2	DB (0.05), rt, 3d	(0)	113
C_{10}	3,4,5-$(MeO)_3C_6H_2$	NH_2	DB (0.5), MeOH, microwave, 25 min	(40)[a]	76
		NH_2	DB (0.5), MeOH, rt, 3 d	(0)	75

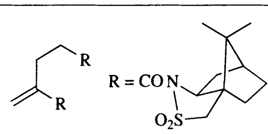
[a] No analytical or spectral data were reported.

TABLE II-B. REACTIONS OF CAMPHOR SULTAM ACRYLATE WITH ALDEHYDES



	R	Conditions	Yield (%)	Refs.
C_2	Me	DB (0.1), CH_2Cl_2 or dioxane, 0°, 12 h	(85)	88a
C_3	Et	DB (0.1), CH_2Cl_2 or dioxane, 0°, 12 h	(98)	88a
		DB (0.1), rt, 10 d	(0)[a]	84
C_4	$MeCO_2CH_2$	DB (0.1), CH_2Cl_2 or dioxane, 0°, 12 h	(68)	88a
	n-Pr	DB (0.1), CH_2Cl_2 or dioxane, 0°, 12 h	(70)	88a
	i-Pr	DB (0.1), CH_2Cl_2 or dioxane, 0°, 12 h	(33)	88a
		DB (0.1), rt, 5 d	(0)[b]	84
C_5	*i*-Bu	DB (0.1), CH_2Cl_2 or dioxane, 0°, 12 h	(67)	88a
C_7	Ph	DB (0.1), rt, 7 d	(0)[c]	84, 88a
C_9	$PhCH_2CH_2$	DB (0.1), CH_2Cl_2 or dioxane, 0°, 12 h	(68)	88a
C_{19}	$TBDPSOCH_2$	DB (0.1), CH_2Cl_2 or dioxane, 0°, 12 h	(40)	88a

[a] Dimer **I**

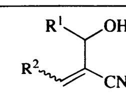


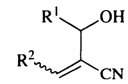
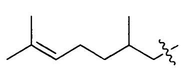
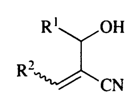
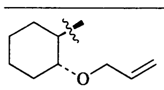
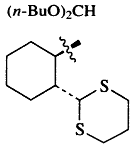
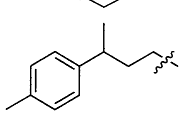
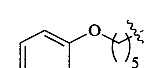
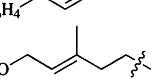
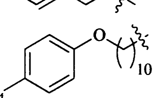
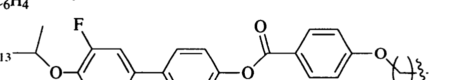
was formed in 19% yield.

[b] Dimer **I** was formed in 22% yield.

[c] Dimer **I** was formed in 17% yield.

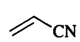
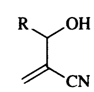
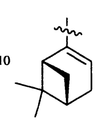
TABLE III-A. REACTIONS OF ACRYLONITRILES WITH ALIPHATIC AND ALICYCLIC ALDEHYDES

	Aldehyde	Acrylonitrile	Conditions	Product(s) and Yield(s) (%)	Refs.
	R^1CHO				
	R^1	R^2			
C_1	H (formalin)	H	DB (0.04), H_2O, rt, 48 h	(66)	46
			DB (0.05), microwave flow reactor, 125-135°	(76)[a,b]	74
			Me_3N (0.5), H_2O, 4-$MeOC_6H_4OH$ (0.001), 60°, 3 h	(68)	47
	H	H	DB (—), 2-5 kbar, 5 min	(90)	25, 48
	H (formalin)	Me	DB (0.11), microwave flow reactor, 160-170°	(2)[c]	74
C_2	Me	H	DB (0.1), rt, 8 d	(87)	338, 1, 49, 117
			Et_2NMe (0.02). 8 kbar, 20°, 5 min	(96)[a]	49, 25, 48
			HQ (—), (+) $MeCHOHCO_2Et$, 5 kbar, rt, 24 h	(81) 3% ee	53
			(1*R*,2*S*)-*N*-Methylephedrine (—), 9 kbar, 36°, 100 h	(18) 10% ee	53
			(*S*)-(–)-Nicotine (—), 9 kbar, 35°, 45 h	(15) 11% ee	53
			(*S*)-1-Methylprolinol (—), 9 kbar, 40°, 74 h	(28) 17% ee	53
			(–)-Quinine, 9 kbar, 60°, 48 h	(0)	53
			$P(C_6H_{11})_3$ (0.004), dioxane, pyridine, 120°, 2 h	(25)	13, 7, 14, 17
	Me	Me	DB (0.05), 42°, 14 d	(0)	49
			DB (0.05), 9 kbar, 50°, 18 h	(88) *Z*:*E* = 4.5	49
C_3	Et	H	DB (0.15), rt, 40 h	(81)	55, 49, 338
			$H_2N(CH_2)_3NH_2$ (0.15), 4-$MeOC_6H_4OH$ (0.3), rt, 24 h	(92)	44
			Et_2NMe (0.06), 8 kbar, 30°, 5 min	(70)[a]	49, 25
			$P(C_6H_{11})_3$ (0.012), dioxane, reflux, 12 h	(35)	1, 17
			$\{RhH_n[(–)DIOP]\ Me_2CO\}^+\ BF_4^-$ (—)	(—)	69
	Et	Me	DB (0.08), 10 kbar, 55°, 20 h	(—)[c]	49
C_4	EtO_2C	H	DB (0.09), 25°, 70 h	(51)	45
	n-Pr	H	DB (0.1), rt, 9 d	(81)	338, 49
			Et_2NMe (0.03), 8 kbar, 45°, 45 min	(70)[a]	49
			$P(C_6H_{11})_3$ (0.02), dioxane, reflux, 16 h	(49)	16
			P("chlorohexyl")$_3$ (0.02), dioxane, reflux, 16 h	(67)	7

Aldehyde		Acrylonitrile	Conditions	Product(s) and Yield(s) (%)	Refs.
	R^1CHO				
	R^1	R^2			
	i-Pr	H	DB (0.1), rt, 10 d	(87)	338, 49, 55
			Et_2NMe (0.03), 8 kbar, 40°, 1h	(85)[a]	49
			$P(C_6H_{11})_3$ (0.006), dioxane, N_2, 120-130°, 2 h	(—)[d]	17
	$(MeO)_2CH$	H	DB (0.1), MeOH (0.35), 4-$MeOC_6H_4OH$ (0.0002), rt, 9 d	(52)	330
C_5	$MeO_2C(CH_2)_2$	H	DB (0.1), rt, 5 d	(38)	125
	n-Bu	H	DB (—)	(—)	261
			n-Bu_3P (0.2), Et_3Al (0.1), C_6H_{14}, CH_2Cl_2, 80°, 22 h	(90)[e]	64
			$P(C_6H_{11})_3$ (0.012), pyridine, cyclohexane, 40°, 20 h	(88)[f]	14
	s-Bu	H	DB (0.1), rt, 14 d	(66)[g]	338
	i-Bu	H	DB (0.15), rt, 40 h	(69)	55, 271
C_6	*n*-C_5H_{11}	H	DB (0.3), rt, 3 d	(87)	55, 261
			$P(C_6H_{11})_3$•CS_2 (0.016), dioxane, 120°, 12 h	(—)	7
C_7	3-Cyclohexenyl	H	DB (0.1), rt, 12 d	(77)	338, 49, 117
			Et_2NMe (0.1), 9 kbar, 20°, 1 h	(63)	49
	Cyclohexyl	H	DB (0.1), rt, 21 d	(81)	338
			n-Bu_3P (0.2), Et_3Al (0.1), C_6H_{14}, CH_2Cl_2, 80°, 22 h	(70)	64
			$P(C_6H_{11})_3$•CS_2 (0.016), dioxane, 120°, 12 h	(—)	7
	n-C_6H_{13}	H	DB (0.15), rt, 4 d	(74)	261, 332
C_8	Bn	H	$P(C_6H_{11})_3$•CS_2 (0.016), dioxane, 120°, 12 h	(—)	7
	n-C_7H_{15}	H	$P(C_6H_{11})_3$ •CS_2 (0.016), dioxane, 120°, 12 h	(45)	7, 17
C_9	$PhCH_2CH_2$	H	DB (0.15), rt, 50 h	(76)	55
	Cyclooctyl	H	$P(C_6H_{11})_3$•CS_2 (0.016), dioxane, 120°, 12 h	(—)	7
C_{10}		H	DB (0.15), rt, 7 d	(85)	331
	R^1CHO				
	R^1	R^2			
		H	DB (0.05), hexane, hydroquinone (—), 8 kbar, rt, 18 h	(70)	82
	n-C_9H_{19}	H	DB (0.3), rt, 7 d	(84)	55
		H	*n*-Bu_3P (0.2), Et_3Al (0.1), hexanes, CH_2Cl_2, 80°, 22 h	(74)	64
	(*n*-BuO)$_2$CH	H	DB (0.1), *n*-BuOH (0.01), 4-$MeOC_6H_4OH$ (0.0002), rt, 9 d	(57)	330
C_{11}		H	DB (0.2), hydroquinone (—), THF, 12 kbar, rt, 18 h	(90)	82
C_{12}		H	DB (0.15), rt, 10 d	(54)	261, 332
C_{19}	 4-NCC_6H_4	H	HQ (0.32), rt, 48 h	(80)	213, 316
C_{23}	 TBDPSO	H	DB (—), rt	(—)	305
C_{24}	 4-NCC_6H_4	H	HQ (0.32), rt, 48 h	(80)	213
	 *n*-C_6H_{13}				
C_{34}	n = 6	H	HQ (0.34), rt, 48 h	(70)	313
C_{38}	n = 10	H	HQ (0.34), rt, 48 h	(79)	313

[a] The number refers to the yield of crude product.
[b] The product formed the ether on attempted distillation.
[c] The product was characterized by mass spectroscopy only.
[d] The yield was 70-90% based on unrecovered aldehyde.
[e] The aldol product was formed in small amounts.
[f] The number refers to the conversion.
[g] The product was a 62:38 mixture of the two diastereomers.

TABLE III-B. REACTIONS OF ACRYLONITRILE WITH OLEFINIC ALDEHYDES

Aldehyde	Acrylonitrile	Conditions	Product(s) and Yield(s) (%)	Refs.
RCHO R				
C_3 CH_2=CH		DB (0.15), rt	(0)[a]	127
C_4 CH_2=C(Me)		DB (0.15), rt, 4 d	(67)	127
MeCH=CH		DB (0.1), rt, 2 d	(59)	117, 127, 338
C_9 PhCH=CH (*trans*)		DB (0.15), rt, 3 d	(20)	127, 76
		DB (0,5), microwave, 25 min	(44)	76
C_{10} 		DB (—), 23°	(—)	53
		DB (—), 5.5 kbar, 23°, 42 h	(42) 16% de	53

[a] The product was a polymer.

TABLE III-C. REACTIONS OF ACRYLONITRILES WITH AROMATIC ALDEHYDES

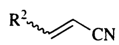
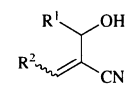
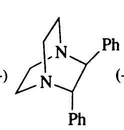
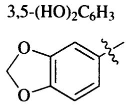
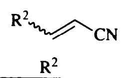
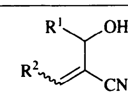
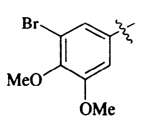
Aldehyde	Acrylonitrile	Conditions	Product(s) and Yield(s) (%)	Refs.
R^1CHO				
R^1	R^2			
C_7 2-ClC_6H_4	H	DB (0.11), rt, 6 h	(55)	117
4-ClC_6H_4	H	DB (—), rt, 100 h	(91)	128, 127
		$(C_6H_{11})_3P$ (0.05), dioxane, sealed tube, 30°, 6 h	(79)	7, 17
3-$O_2NC_6H_4$	H	DB (0.27), rt, 24 h	(22)	49
		$(C_6H_{11})_3P$ (0.05), dioxane, sealed tube, 30°, 6 h	(74)	7
4-$O_2NC_6H_4$	H	DB (0.5), rt, 3 d	(45)	76
		DB (0.5), microwave, rt, 10 min	(95)	76
Ph	H	DB (0.11), rt, 40 h	(79)	117, 49, 55, 127, 261
		DB (0.15), H_2O, LiI or NaI, rt, 2-3 h	(93)	70
		DB (0.04), 5 kbar, 20°, 5 min	(92)	48, 49
		$Ph_2P(CH_2)_4OH$ (0.04), rt, 20 h	(15)	7, 17
		n-Bu_3P (0.2), Et_3Al (0.1), hexanes, CH_2Cl_2, 80°, 22 h	(27)	64
		(+)  (—), 12 kbar, 15 h	(53)[a] 11% ee	82
Ph	Me	DB (0.1), $CHCl_3$, 8 kbar, 17 h	(—) E:Z = 1:1	28, 82
		DB (0.1), $CHCl_3$, 15 kbar, 17 h	(—) E:Z = 23:1	28, 82
3,5-$(HO)_2C_6H_3$	H	Et_3N (0.19), THF/$CHCl_3$ (1:1), 15 kbar, 50°, 19 h	(75)	41
C_8 	H	DB (0.56), rt, 48 h	(95)[b]	130
4-MeC_6H_4	H	DB (0.08), 5°, 6 d	(74)[c]	49, 127, 130
		DB (0.08), 42°, 75 h	(78)	49, 261

TABLE III-C. REACTIONS OF ACRYLONITRILES WITH AROMATIC ALDEHYDES (*Continued*)

Aldehyde	Acrylonitrile	Conditions	Product(s) and Yield(s) (%)	Refs.
R^1CHO				
R^1	R^2			
4-MeC_6H_4	H	DB (0.08), 10 kbar, 40°, 2 h	(64)[d]	49
		$(C_6H_{11})_3P$ (0.05), dioxane, sealed tube, 30°, 6 h	(58)	7, 17
2-$MeOC_6H_4$	H	DB (—)	(—)	127
(*S*)-(+)-2-$MeOC_6H_4$•$Cr(CO)_3$	H	DB (0.5), rt, 11 h	(88) >95% de[e]	97
4-$MeOC_6H_4$	H	DB (0.5), rt, 3d	(13)	76, 49
		DB (0.06), 5°, 7 d	(43)[c]	49
		DB (0.1), 5.6 kbar, 42°, 21 h	(25)[d]	49, 25
		DB (0.5), microwave, 10 min	(25)	76
		$(C_6H_{11})_3P$ (0.05), dioxane, sealed tube, 30°, 6 h	(80)	7
C_9 	H	DB (0.5), rt	(—)[b]	130
4,5-$(MeO)_2C_6H_3$	H	DB (0.5), rt, 48	(95)[b]	130
C_{10} 4-*i*-PrC_6H_4	H	DB (—)	(—)	127
3,4,5-$(MeO)_3C_6H_2$	H	DB (0.5), $MeOCH_2OMe$, H_2NCHO, rt, 20-36 h	(>90)[b]	130, 76
		DB (0.5), microwave, 10 min	(0)[f]	76
C_{11} 1-Naphthyl	H	DB (—)	(—)	127
C_{13} 4-PhC_6H_4	H	DB (0.11), rt, 6 d	(80)	49
		DB (0.02), 5 kbar, 20°, 2 h	(86)	48, 49

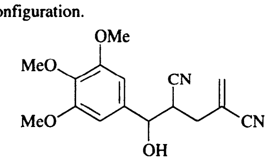
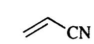
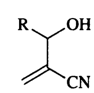
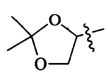
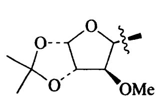
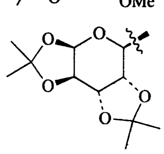
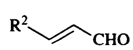
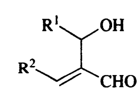
[a] The number refers to the conversion.
[b] The product was a 2:1 complex with DABCO from which the normal adduct could be obtained by treatment with acid; the latter was obtained directly when the isolation procedure included an acid wash.
[c] The product was a 2:1 complex with DABCO.
[d] The number is the yield of crude product.
[e] The product has the *S,S* (–) configuration.
[f] The product was the diadduct  (55% yield).

TABLE III-D. REACTIONS OF ACRYLONITRILE WITH HETEROCYCLIC ALDEHYDES

Aldehyde	Acrylonitrile	Conditions	Product(s) and Yield(s) (%)	Refs.
RCHO				
R				
C_6 2-Pyridyl		DB (0.05), rt, 3 d	(92)	113
		DB (—), rt	(—) 0% de	53
		DB (—), 4 kbar, rt, 21 h	(47) 23% de	53
C_9 		DB (1.1), rt, 20 h	(37)[a]	339
C_{12} 		DB (1.1), rt, 20 h	(57)[a]	339

[a] Two diastereomers were formed but only the major isomer was isolated.

TABLE IV. REACTIONS OF α,β-UNSATURATED ALDEHYDES WITH ALDEHYDES

	Aldehyde	Unsaturated Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.
	R^1CHO				
	R^1	R^2			
C_1	H (formalin)	Me	DB (0.0.3), microwave (flow reactor), 165°	(13)	74
C_2	Me	H	DB (0.03), 20°, 10 d	(65)	49
			Et_2NMe (0.08), 15 kbar, 20°, 25 min	(95)	48, 49
C_3	CH_2=CH	H	DB (—), 30 min	(20[a]	25
	Et	H	DB (0.03), 20°, 10 d	(71)	49
C_6	2-Pyridyl	H	DB (0.05). rt, 3d	(0)[b]	113

[a] No analytical or spectroscopic data were given and the reaction was not mentioned in the full paper (ref. 49).

[b] The acrolein polymerized even in the presence of hydroquinone as radical inhibitor.

TABLE V-A. REACTIONS OF α,β-UNSATURATED KETONES WITH ALIPHATIC AND ALICYCLIC ALDEHYDES

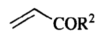
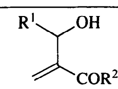
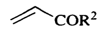
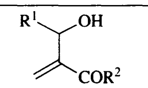
	Aldehyde	Ketone	Conditions	Product(s) and Yield(s) (%)	Refs.
	R^1CHO				
	R^1	R^2			
C_1	H (paraformaldehyde)	Me	DB (—), THF, 80°	(—)	309
	H (formalin)	Me	DB (—), H_2O, <80°	(—)	309
			DB (0.11), microwave flow reactor, 99-101°	(17)	74
	H	Me	PPh_3 (0.04), benzene, 30°, 18 h	(34)	61
C_2	Me	Me	DB (0.03), rt, 3.3 d	(90)	49, 117, 252, 309, 338
			HQ (0.1), CH_2Cl_2, rt, 20 h[a,b]	(72)	340, 33, 341
			$H_2N(CH_2)_3NH_2$ (0.15), 4-$MeOC_6H_4OH$ (0.3), rt, 26 h	(55)	44
			Et_2NMe (0.03), 4 kbar, 20°, 30 min	(55)	49, 48
			Quinidine (—), rt, 7 d	(—) 12% ee	52
			Cinchonidine (—), rt, 4.5 d	(—) 10% ee	52
			Brucine (—), rt, 4.75 d	(—) 8% ee	52
			Quinine (—), rt, 4.5 d	(—) 8% ee	52
			(*S*)-(-)-*N*-Methylprolinol (—), rt, 4 d	(—) 0% ee	52
			PPh_3 (0.04), benzene, 30°, 18 h	(61)	61
	Me	Et	PPh_3 (0.04), benzene, rt, 16 h	(65)	62
C_3	Et	Me	DB (0.11), rt, 24 h	(84)	117, 49, 252, 309, 338
			HQ (0.05), $CHCl_3$, 21°, 15 h	(85)	33, 340, 341
			Et_2NMe (0.22), 2 kbar, 20°, 2 h	(56)	49
			Ph_3P, (0.04), benzene, 30°, 18 h	(63)	61
			$RuH_2(PPh_3)_4$ (0.01), *i*-PrOH (0.2), 40°, 40 h	(82)	19, 68
			$\{RhH_n[(-)DIOP]\ Me_2CO\}^+\ BF_4^-$ (0.01), 105°, 5.5 h	(—) 23% ee[c]	69
	Et	Et	DB (0.15), rt, 2 d	(61)	118
			PPh_3 (0.04), benzene, rt, 16 h	(68)	62
			$RuH_2(PPh_3)_4$ (0.01), *i*-PrOH (0.2), 40°, 40 h	(87)	19, 68
	Et	*i*-Pr	DB (0.20), rt, 6 d	(22)	118

TABLE V-A. REACTIONS OF α,β-UNSATURATED KETONES WITH ALIPHATIC AND ALICYCLIC ALDEHYDES (*Continued*)

	Aldehyde	Ketone	Conditions	Product(s) and Yield(s) (%)	Refs.
	R^1CHO				
	R^1	R^2			
	Et	*n*-Bu	PPh_3 (0.04), benzene, rt, 16 h	(79)	62
	Et	*i*-Bu	DB (0.15), rt, 4 d	(31)	118
			$RuH_2(PPh_3)_4$ (0.01), *i*-PrOH (0.2), 40°, 40 h	(53)	19
	Et	*n*-C_5H_{11}	PPh_3 (0.04), benzene, rt, 16 h	(70)	62
	Et		$RuH_2(PPh_3)_4$ (0.01), *i*-PrOH (0.2), 40°, 40 h	(64)	19
	Et	Ph	$RhH(PPh_3)_4$ (0.01), *i*-PrOH (0.2), 40°, 40 h	(37)[d]	19
	Et	C_6H_{11}	$RhH(PPh_3)_4$ (0.01), *i*-PrOH (0.2), 40°, 40 h	(79)	19
	Et	*n*-C_6H_{13}	PPh_3 (0.04), benzene, rt, 16 h	(74)	62
	Et	*n*-BuCHEt	$RhH(PPh_3)_4$ (0.01), *i*-PrOH (0.2), 40°, 40 h	(58)	19, 67
	Et	$Ph(CH_2)_2$	$RuH_2(PPh_3)_4$ (0.01), *i*-PrOH (0.2), 40°, 40 h	(54)	19
	Et	*n*-C_8H_{17}	$RhH(PPh_3)_4$ (0.01), *i*-PrOH (0.2), 40°, 40 h	(70)	19
C_4	CO_2Et	Me	DB (0.09), rt, overnight	(55)	343
	n-Pr	Me	DB (0.15), rt, 7 d	(—)	252
			PPh_3 (0.04), benzene, 30°, 16 h	(63)	61
			$RhH(PPh_3)_4$ (0.01), *i*-PrOH (0.2), 40°, 40 h	(61)	19, 67, 68
	n-Pr	Et	DB (0.15), rt, 2 d	(59)	118
			PPh_3 (0.04), benzene, rt, 16 h	(66)	62
	n-Pr	*i*-Pr	DB (0.20), rt, 6 d	(21)	118
			PPh_3 (0.04), benzene, rt, 16 h	(68)	62
	n-Pr	*i*-Bu	DB (0.15), rt, 3 d	(35)	118
	i-Pr	Me	DB (0.1), THF, rt, 11 d	(63)	338
			HQ (0.1), CH_2Cl_2, rt, 20 h[a]	(62)	340, 341
			PPh_3 (0.04), benzene, 30°, 16 h	(70)	61
			$RuH_2(PPh_3)_4$ (0.01), *i*-PrOH (0.2), 40°, 40 h	(72)	19, 68
	i-Pr	Et	DB (0.20), rt, 2 d	(60)	118
			PPh_3 (0.04), benzene, rt, 16 h	(78)	62
	i-Pr	*n*-Pr	PPh_3 (0.04), benzene, rt, 16 h	(77)	62

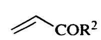
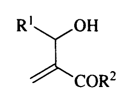
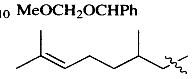
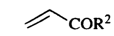
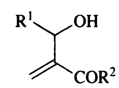
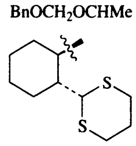
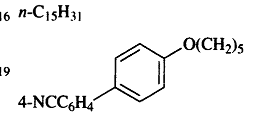
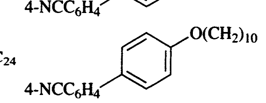
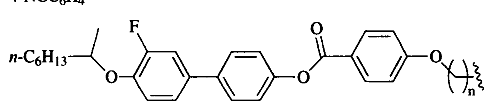
	Aldehyde	Ketone	Conditions	Product(s) and Yield(s) (%)	Refs.
	R^1CHO				
	R^1	R^2			
	i-Pr	*i*-Pr	DB (0.20), rt, 6 d	(20)	118
	i-Pr	*i*-Bu	DB (0.15), rt, 4 d	(30)	118
	$MeO(CH_2)_2$	Me	DB (0.15), THF, 7 d	(—)	252
C_5	$MeO_2C(CH_2)_2$	Me	DB (0.1), rt, 4 d	(48)	125, 252
	n-Bu	Me	PPh_3 (0.04), benzene, rt, 16 h	(90)	61
	n-Bu	Et	PPh_3 (0.04), benzene, rt, 16 h	(80)	62
	s-Bu	Me	DB (0.1), THF, rt, 12 d	(64)	338
	s-Bu	Et	PPh_3 (0.04), benzene, rt, 16 h	(75)	62
	i-Bu	Me	DB (0.15), THF, 7 d	(—)	252, 309
			$RhH(PPh_3)_4$ (0.01), *i*-PrOH (0.2), 40°, 40 h	(76)	19, 67
	$MeOCH_2OCHMe$	Me	DB (0.1), rt, 2.5 h	(54) *anti*:*syn* = 71:29	30, 89
			HQ (0.1), rt, 20 min	(80) *anti*:*syn* = 71:29	30, 89
C_6	$MeO_2C(CH_2)_3$	Me	DB (0.15), THF, 7 d	(—)	252
	n-C_5H_{11}	Me	DB (0.15), THF, 3 d	(65)	140, 342
	t-$BuCH_2$	Me	DB (0.15), THF, 7 d	(—)	252
C_7	Cyclohexyl	Me	DB (0.1), THF, rt, 18 d	(80)	338
			HQ (0.1), CH_2Cl_2, rt, 20 h[a]	(51)	190, 340
	n-C_6H_{13}	Me	DB (0.15), THF, rt, 80 h	(73)	140, 342
			PPh_3 (0.04), benzene, 30°, 16 h	(43)	61
C_8	Bn	Me	DB (0.1), THF, rt, 7 d	(64)	338
	n-C_7H_{15}	Me	DB (0.15), THF, rt, 100 h	(63)	140, 117, 342
	n-BuCHEt	Me	$RuH_2(PPh_3)_4$ (0.01), *i*-PrOH (0.2), 40°, 40 h	(14)[e]	19, 67, 68
C_9	$Ph(CH_2)_2$	Me	DB (0.15), THF, rt, 85 h	(65)	140, 252, 309, 342
C_{10}	$MeOCH_2OCHPh$	Me	DB (0.1), rt, 6 d	(70) *anti*:*syn* = 38:62	30, 89
		Me	PPh_3 (0.04), benzene, 30°, 16 h	(56)	61
	n-C_9H_{19}	Me	DB (0.15), THF, rt, 10 d	(62)	140, 342

TABLE V-A. REACTIONS OF α,β-UNSATURATED KETONES WITH ALIPHATIC AND ALICYCLIC ALDEHYDES (*Continued*)

	Aldehyde	Ketone	Conditions	Product(s) and Yield(s) (%)	Refs.
	R^1CHO				
	R^1	R^2			
C_{11}	$BnOCH_2OCHMe$	Me	HQ (0.1), rt, <1 h	(80) *anti*:*syn* = 77:23	30
		Me	DB (0.2), rt, 4 d	(10)[f]	82
C_{16}	n-$C_{15}H_{31}$	Me	DB (0.15), THF, rt, 15 d	(36)	140, 342
C_{19}		Me	HQ (0.15), THF, rt, 36 h	(64)	213
C_{24}		Me	HQ (0.15), THF, rt, 36 h	(70)	213
					
C_{34}	n = 6	Me	HQ (0.36), THF, rt, 36 h	(76)	313
C_{38}	n = 10	Me	HQ (0.36), THF, rt, 36 h	(66)	313

[a] The α,β-unsaturated ketone was added to the aldehyde during 8 hours followed by 12 hours at room temperature (refs. 340, 341).

[b] The half-life for a catalyst concentration of 0.05 was 20 minutes (ref. 33).

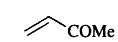
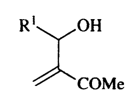
[c] The ee value for this experiment was the best in a series using different chiral catalysts.

[d] The dimer $R_2CO(CH_2)_2C(=CH_2)COR_2$ was formed in 45% yield.

[e] The dimer $R_2CO(CH_2)_2C(=CH_2)COR_2$ was formed in 42% yield.

[f] The dimer $R_2CO(CH_2)_2C(=CH_2)COR_2$ was formed exclusively when the reaction was carried out under 12 kbar pressure.

TABLE V-B. REACTIONS OF α,β-UNSATURATED KETONES WITH OLEFINIC ALDEHYDES

	Aldehyde	Ketone	Conditions	Product(s) and Yield(s) (%)	Refs.
	R^1CHO				
	R^1				
C_3	CH_2=CH		DB (0.15), rt	(0)[a]	127
C_4	MeCH=CH		DB (0.15), rt	(0)[b]	127
			PPh_3 (0.04), benzene, 30°, 18 h	(27)[c]	61
	CH_2=C(Me)		DB (0.15), rt	(0)[b]	127
C_6	*n*-PrCH=CH		PPh_3 (0.04), benzene, 30°, 18 h	(19)[d]	61
C_9	PhCH=CH		DB (0.15), rt	(0)[a]	127

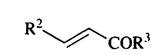
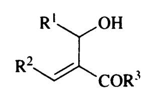
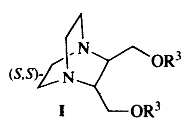
[a] The product was a polymer.

[b] The only product isolated was the dimer $MeCO(CH_2)_2C(=CH_2)COMe$.

[c] The dimer $MeCO(CH_2)_2C(=CH_2)COMe$ was formed in 26% yield.

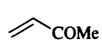
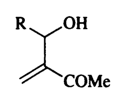
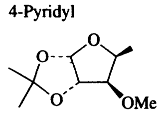
[d] The dimer $MeCO(CH_2)_2C(=CH_2)COMe$ was formed in 49% yield.

TABLE V-C. REACTIONS OF α,β-UNSATURATED KETONES WITH AROMATIC ALDEHYDES

Aldehyde	Ketone		Conditions	Product(s) and Yield(s) (%)	Refs.
R^1CHO					
R^1	R^2	R^3			
C_7 2,4-$Cl_2C_6H_3$	H	Me	DB (0.15), THF, 8 d	(65)	140
4-ClC_6H_4	H	Me	DB (0.15), THF, 8 d	(61)	140
4-$O_2NC_6H_4$	H	Me	 I R^3 = Bn (0.15), hydroquinone (0.01), THF, 5 kbar, 30°, 12 h	(45) 47% ee[a,b]	39
			I, R^3 = TBDPS (0.15), hydroquinine (0.01), THF, rt, 21 d	(42) 15% ee[b,c]	39
			Retronecine (—), rt, 30 d	(—) 0% ee	52
Ph	H	Me	DB (0.11), rt, 30 h	(72)	117, 140, 342
			PPh_3 (0.04), benzene, 30°, 18 h	(57)[d]	61
			$RuH_2(PPh_3)_4$ (0.01), *i*-PrOH (0.2), 40°, 40 h	(33)	19, 68
Ph	Ph	Me	DB (—), 15 kbar, 50°, 250 h	(0)	82
Ph	H	Et	DB (0.15), rt, 2 d	(58)	118
			PPh_3 (0.04), rt, 16 h	(55)[e]	62
C_8 4-MeC_6H_4	H	Me	DB (0.15), THF, rt, 9 d	(56)	140

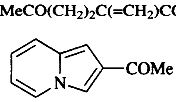
[a] The major product has the *S* configuration.
[b] These conditions gave the highest ee values for the formation of the *R* or *S* isomer, respectively in experiments with a series of catalysts of type **I** under 5 kbar or ambient pressure.
[c] The major product has the *R* configuration.
[d] The dimer $MeCO(CH_2)_2C(=CH_2)COMe$ was formed in 29% yield.
[e] The dimer $EtCO(CH_2)_2C(=CH_2)COEt$ was formed in 32% yield.

TABLE V-D. REACTIONS OF α,β-UNSATURATED KETONES WITH HETEROCYCLIC ALDEHYDES

Aldehyde	Ketone	Conditions	Product(s) and Yield(s) (%)	Refs.
RCHO				
R				
C_5 2-Furyl		DB (0.03), THF, rt	(—)[a]	342
		PPh_3 (0.04), benzene, 30°, 18 h	(45)[b]	61
C_6 2-Pyridyl		DB (0.05), rt, 3 d	(81)[c]	113
4-Pyridyl		HQ (0.05), rt, $t_{1/2}$<0.37 min	(85)	33
C_9 		DB (0.1), rt, 20 h	(45)[d]	339

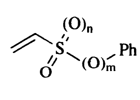
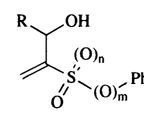
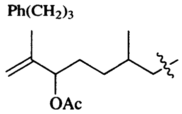
[a] The reaction "was not clean."

[b] The dimer $MeCO(CH_2)_2C(=CH_2)COMe$ was formed in 24% yield.

[c] The ketone  was formed in 5% yield.

[d] A mixture of diastereomers was formed, but only the major isomer of unknown stereochemistry was isolated.

TABLE VI. REACTIONS OF VINYL SULFOXIDES, VINYL SULFONES, AND VINYLSULFONATES WITH ALDEHYDES

	Aldehyde	Vinyl Reactant		Conditions	Product(s) and Yield(s) (%)	Refs.
	RCHO					
	R	m	n			
C_1	H (paraformaldehyde)	0	1	DB (0.1), THF, reflux, 2 d	(33)	80
C_2	Me	0	0	DB (—), rt	(0)	56
	Me	0	1	DB (0.1), rt, 2 wks	(84)	56, 80, 152, 233, 234
		0	1	DB (—), "high pressure, fast"	(—)	81
C_3	Et	0	1	DB (0.1), rt, 11 d	(33)	234, 56, 80
		0	1	DB (—), 0.2 kbar,[a] 8 d	(33)	80, 344
C_4	MeCH=CH	0	1	DB (0.1), rt	(0)	56
	n-Pr	0	1	DB (0.1), rt, 4 wks	(75)	56, 80, 152, 233, 234
	i-Pr	0	1	DB (0.1), THF, rt, 50 d	(24)	152, 56
C_5	2-Furyl	0	1	DB (0.1), rt, 3 wks	(20)	56
	n-Bu	0	1	DB (0.1), rt, 10 wks	(79)	56, 233
	i-Bu	0	1	DB (0.1), rt, 11 wks	(81)	56, 80, 233, 234
	i-Bu	1	1	DB (0.1), benzene, rt, 3 h	(87)	119
	t-Bu	0	1	DB (0.1), rt, 21 wks	(10)	56
C_6	3-Pyridyl	0	1	DB (0.1), rt, 1 d	(46)	80
C_7	Ph	0	0	DB (0.1), 19 kbar, rt, 48 h	("satisfactory")[b]	81
	Ph	0	1	DB (0.1), rt, 3 wks	(57)	56, 80, 233, 234
C_9	$Ph(CH_2)_2$	0	1	DB (0.1), rt, 21 d	(36)	80, 234
C_{10}	$Ph(CH_2)_3$	0	1	DB (0.1), rt, 15 d	(67)	80
C_{12}		0	1	DB (0.1), rt, 8 wks	(47)	234, 256

[a] At 6 kbar, the yield was reported to be 0%; other workers, however, did not experience this problem (ref. 81).

[b] A 1:1 mixture of diastereomers was formed.

TABLE VII. REACTIONS OF DIETHYL VINYLPHOSPHONATE WITH ALDEHYDES

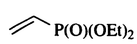
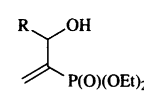
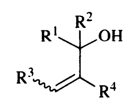
	Aldehyde	Vinylphosphonate	Conditions	Product(s) and Yield(s) (%)	Refs.
	RCHO				
	R				
C_1	H (formalin)		DB (—), H_2O	(0)	120
C_2	Me		DB (0.2), rt, 7 d	(83)	120
C_3	Et		DB (0.2), rt, 10 d	(78)	120
C_4	*n*-Pr		DB (0.2), rt, 10 d	(73)	120
	i-Pr		DB (0.2), rt, 14 d	(74)	120
C_5	*n*-Bu		DB (0.3), rt, 21 d	(68)	120
	i-Bu		DB (0.3), rt, 29 d	(54)	120

TABLE VIII. REACTIONS OF ACTIVATED OLEFINS WITH MONOKETONES

	Ketone		Olefin		Conditions	Product(s) and Yield(s) (%)	Refs.
	R^1COR^2						
	R^1	R^2	R^3	R^4			
C_3	Cl_2FC	CCl_2F	H	CN	DB (0.1), THF, 20°, 5 h	(35)	115
	Cl_2FC	CCl_2F	H	CHO	DB (0.1), THF, 20°, 3 h	(81)	115
	Cl_2FC	CCl_2F	H	CO_2Et	DB (0.1), THF, 20°, 16 h	(84)	115
	F_3C	CF_2Br	H	CO_2Et	DB (0.1), THF, 20°, 16 h	(39)	115
	F_3C	CF_3	H	CHO	DB (0.1), THF, 20°	(—)[a]	115
	F_3C	CF_3	H	CO_2Me	HQ (0.2), HFI (0.06), 20°, 6.5 h	(57)	42
	F_3C	CF_3	H	CO_2Et	DB (0.1), THF, 20°, 3 h	(47)	115
	Me	Me	H	CN	DB (0.1), 40°, 14 d	(0)	25, 49
					Et_2NMe (0.08), THF, 12 kbar, 20°, 1 h	(92)	48, 25, 49
	Me	Me	H	CO_2Bu-*n*	DB (0.41), sealed tube, 120°, 4.6 d	(7)[b]	74
	Me	Me	Me	CN	DB (0.08), 10 kbar, 55°, 20 h	("low")[c]	49
	Me	Me	H	$CONH_2$	DB (—), 5 kbar, 17 h	(5)[d]	25
	Me	Me	H	CO_2Me	DB (—), 5 kbar, 2 h	(0)[e]	25
C_4	Me	Et	H	CN	DB (0.06), 40°, 14 d	(0)	49
					DB (0.06), 10 kbar, 26°, 20 h	(14)	49, 48
	Me	Et	H	CO_2Me	DB (—), 5 kbar, 2 h	(0)[e]	25
C_6	$-(CH_2)_5-$		H	CN	DB (0.02), 40°, 14 d	(0)	49
					DB (0.01), 9 kbar, 26°, 1 h	(42)	49, 25
C_9	$-(CH_2)_2N(Pr\text{-}i)(CH_2)_2-$		H	CO_2Me	HQ (0.2), HFI (0.06), 65°, 2d	(0)	42

[a] The product could not be separated from the solvent.

[b] The number is the conversion. The product was characterized by mass spectroscopy only.

[c] Two products were formed in a ratio of 40:1; they were characterized by mass spectroscopy only.

[d] No analytical or spectral data were reported.

[e] The reports (ref. 25) that acetone and methyl ethyl ketone react with methyl acrylate under pressure are in error (ref. 79).

TABLE IX. REACTIONS OF ACTIVATED OLEFINS WITH POLYKETONES

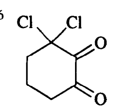
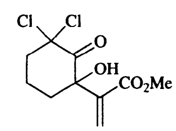
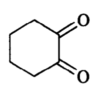
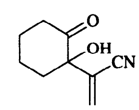
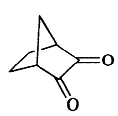
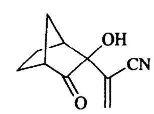
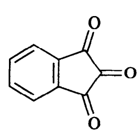
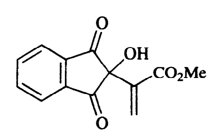
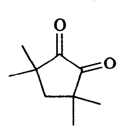
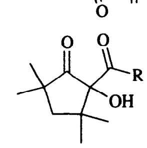
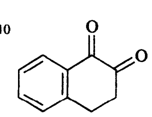
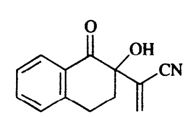
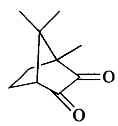
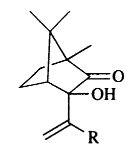
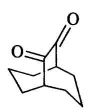
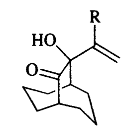
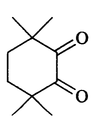
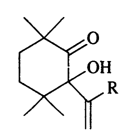
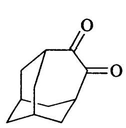
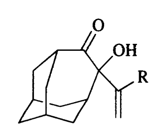
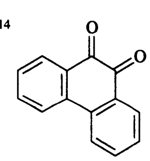
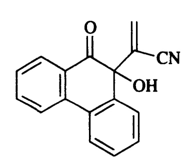
Diketone	R (CH2=CH–R)	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6 	CO_2Me	HQ (0.2), HFI (0.06), 20°, 24 h	 (0)[a]	42
	CN	DB (—)	 (—)[b]	345
C_7 	CN	HQ (0.13), rt, 24 h	 (8)	114
C_9 	CO_2Me	HQ (0.05), HFI (0.0015), rt, 36 h	 (88)	42
				
	CN	HQ (0.1), rt, 3 d	(100)	114
	CHO	HQ (0.1), THF, rt, 5 d	(72)	114
	CO_2Me	HQ (—)	(0)[a]	114
C_{10} 	CN	DB (—)	 (—)[c]	345

TABLE IX. REACTIONS OF ACTIVATED OLEFINS WITH POLYKETONES (*Continued*)

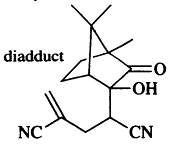
Diketone	R	Conditions	Product(s) and Yield(s) (%)	Refs.
	R			
	CN	HQ (0.1), rt, 18 d	(73)[d,e]	114
	CHO	[f]	(0)[g]	114
	CO_2Me	HQ (0.1), rt, 17 d	(0)[b]	114
				
	CN	HQ (0.27), rt, 24 h	(68)	114
	CHO	HQ (0.27), rt, 24 h	(0)[g]	114
	CO_2Me	HQ (0.27), rt, 24 h	(0)[b]	114
	CN, CHO, CO_2Me	—	 (0)[h]	114
C_{11} 				
	CN	HQ (0.02), rt, 24 h	(70)	114
	CHO	HQ (—)	(0)[g]	114
	CO_2Me	HQ (0.02), rt, 24 h	(0)[b]	114
C_{14} 	R CN	DB (—)	 (—)[c]	345

[a] There was no reaction.

[b] The product was a complex mixture.

[c] The yield was "unsatisfactory."

[d] The regio- and stereochemistry are tentative.

[e] In some experiments, the diadduct  was obtained in 12% yield.

[f] The reaction was tried with DABCO, 3-hydroxyquinuclidine, Ph_3P, or Et_3N, neat or in THF or benzene, at −78° to room temperature, with or without sonication.

[g] The acrolein polymerized.

[h] No reaction occurred with acrylonitrile or methyl acrylate; with acrolein, polymerization took place.

TABLE X. REACTIONS OF ACTIVATED OLEFINS WITH α-KETOESTERS AND α-KETOLACTONES

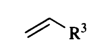
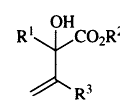
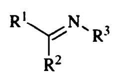
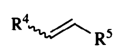
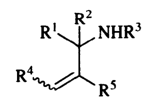
	Ketone		Olefin	Conditions	Product(s) and Yield(s) (%)	Refs.
	$R^1COCO_2R^2$					
	R^1	R^2	R^3			
C_4	F_3C	Me	CN	DB (0.1), 20°, 2 h	(30)	115
	F_3C	Me	CHO	DB (0.1), 20°, 1 h	(57)	115
	F_3C	Me	COMe	DB (0.1), 20°, 1 h	(80)	115
	Me	Me	CN	DB (0.15), rt, 24 h	(38)	134
	Me	Me	CO_2Me	DB (0.15), rt, 14 d	(78)	254
C_5	F_3C	Me	CO_2Et	DB (0.1), 20°, 3 h	(72)	115
	Me	Et	CN	DB (0.15), rt, 24 h	(41)	134
C_6	$-CH_2C(Me)_2-$		CN	HQ (0.2), rt, 24 h	(81)	114
	$-CH_2C(Me)_2-$		CHO	HQ (0.2), rt, 3 d	(31)	114
	$-CH_2C(Me)_2-$		CO_2Me	HQ (—)	(0)	114
C_7	EtO_2C	Et	CN	DB (0.1), THF, rt, 3 h	(80)	133
	EtO_2C	Et	COMe	DB (0.05), rt, 30 min	(74)	133
	EtO_2C	Et	CO_2Me	DB (0.1), THF, rt, 4 h	(77)	133
	EtO_2C	Et	CO_2Et	DB (0.1), THF, rt, 6 h	(73)	133
	EtO_2C	Et	CO_2Bu-*t*	DB (0.1), THF, rt, 36 h	(67)	133
C_{10}	Ph	Et	CN	DB (0.3), rt, 5 d	(65)	134
	Ph	Et	CO_2Me	DB (0.3), rt, 7 d	(49)	134
C_{11}	$4\text{-}MeC_6H_4$	Et	CN	DB (0.3), rt, 7 d	(74)	134
	$4\text{-}MeC_6H_4$	Et	CO_2Me	DB (0.3), rt, 9 d	(41)	134

TABLE XI. REACTIONS OF ACTIVATED OLEFINS WITH IMINES AND IMINIUM SALTS







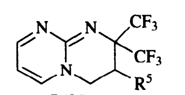
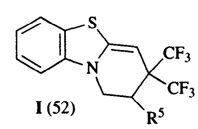
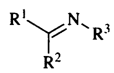
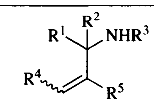
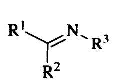
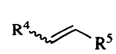
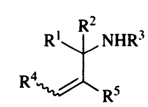
	Imine			Olefin		Conditions	Product(s) and Yield(s) (%)	Refs.
	R^1	R^2	R^3	R^4	R^5			
C_3	H	H	Me_2[a]	H	COMe	MeCN, rt, 1.5 h	(88)[b]	135
C_6	*n*-Pr	H	Ts[c]	H	CO_2Me	PPh_3 (0.008), *i*-PrOH (cat.), 40°, 40 h	(80)	18
C_7	CF_3	CF_3	2-Pyrimidyl	H	CN	DB ("pinch"), THF, rt, "rapid"	 I (85)	137
	CF_3	CF_3	2-Pyrimidyl	H	CHO	DB ("pinch"), THF, rt, "rapid"	I (52)	137
	CF_3	CF_3	2-Pyrimidyl	H	COMe	DB ("pinch"), THF, rt, "rapid"	I (87)	137
	CF_3	CF_3	2-Pyrimidyl	H	COEt	DB ("pinch"), THF, rt, "rapid"	I (93)	137
	CF_3	CF_3	2-Pyrimidyl	H	CO_2Et	DB ("pinch"), THF, rt, "rapid"	I (55)	137
	CF_3	CF_3	2-Pyrimidyl	H	CO_2Bu-*t*	DB ("pinch"), THF, rt, "rapid"	I (80)	137
C_8	Ph	H	CO_2Me	H	CO_2Me	DB (0.2), rt, 16 h	(80)[d]	136
C_{10}	CF_3	CF_3	2-Benzothiazolyl	H	CN	DB ("pinch"), THF, rt, "rapid"	 I (52)	137
	CF_3	CF_3	2-Benzothiazolyl	H	CHO	DB ("pinch"), THF, rt, "rapid"	I (29)	137
	CF_3	CF_3	2-Benzothiazolyl	H	COMe	DB ("pinch"), THF, rt, "rapid"	I (95)	137
	CF_3	CF_3	2-Benzothiazolyl	H	COEt	DB ("pinch"), THF, rt, "rapid"	I (93)	137
	CF_3	CF_3	2-Benzothiazolyl	H	CO_2Et	DB ("pinch"), THF, rt, "rapid"	I (82)	137
	CF_3	CF_3	2-Benzothiazolyl	H	CO_2Bu-*t*	DB ("pinch"), THF, rt, "rapid"	I (86)	137

TABLE XI. REACTIONS OF ACTIVATED OLEFINS WITH IMINES AND IMINIUM SALTS (*Continued*)

	Imine			Olefin		Conditions	Product(s) and Yield(s) (%)	Refs.

	R^1	R^2	R^3	R^4	R^5	Conditions	Product(s) and Yield(s) (%)	Refs.
	CF_3	CF_3	COPh	H	CN	DB ("pinch"), THF, rt, 2 h	(68)	116
	CF_3	CF_3	COPh	H	CHO	DB ("pinch"), THF, rt, 36 s	(38)	116
	CF_3	CF_3	COPh	H	COMe	DB ("pinch"), THF, rt, 6 min	(51)	116
	CF_3	CF_3	COPh	H	COEt	DB ("pinch"), THF, rt, 6 min	(91)	116
	CF_3	CF_3	COPh	H	CO_2Et	DB ("pinch"), THF, rt, 24 h	(69)	116
	CF_3	CF_3	COPh	H	CO_2Bu-*t*	DB ("pinch"), THF, rt, 24 h	(67)	116
C_{11}	CF_3	CF_3	COC_6H_4Me-4	H	CN	DB ("pinch"), THF, rt, 2.5 h	(52)[e]	116
	CF_3	CF_3	COC_6H_4Me-4	H	CHO	DB ("pinch"), THF, rt, 36 s	(27)	116
	CF_3	CF_3	COC_6H_4Me-4	H	COMe	DB ("pinch"), THF, rt, 6 min	(89)[f]	116
	CF_3	CF_3	COC_6H_4Me-4	H	COEt	DB ("pinch"), THF, rt, 6 min	(88)[g]	116
	CF_3	CF_3	COC_6H_4Me-4	H	CO_2Et	DB ("pinch"), THF, rt, 36 h	(62)[h]	116
	CF_3	CF_3	COC_6H_4Me-4	H	CO_2Bu-*t*	DB ("pinch"), THF, rt, 42 h	(88)[i]	116
	Ph	H	Boc	H	COMe	PPh_3 (0.008), *i*-PrOH (cat.), 40°, 40 h	(50)	18
C_{12}	2-ClC_6H_4•$Cr(CO)_3$	H	C_6H_{11}	H	CN	DB (0.5), 20°, 6 h	(0)	97, 98
C_{13}	2-MeC_6H_4•$Cr(CO)_3$	H	C_6H_{11}	H	CN	DB (0.5), 20°, 6 h	(0)	97, 98
	2-$MeOC_6H_4$•$Cr(CO)_3$	H	C_6H_{11}	H	CN	DB (0.5), 20°, 6 h	(0)	97, 98
	2-FC_6H_4	H	Ts	H	CO_2Me	DB (—)	(—)	306
	2-ClC_6H_4	H	Ts	H	CO_2Me	DB (—)	(—)	306
	(±)-2-ClC_6H_4•$Cr(CO)_3$	H	Ts	H	CN	DB (0.5), rt, 1-6 h	(55) >95% de	98
	3-$O_2NC_6H_4$	H	Ts	H	CO_2Et	DB (0.1), 80°, 17 h	(53)	138, 346
	Ph	H	Ts	H	CO_2Me	DB (0.1), 80°, 17 h	(45)	138
	Ph	H	Ts[c]	H	CO_2Me	PPh_3 (0.008), *i*-PrOH (cat.), 40°, 40 h	(98)[j]	18
	Ph	H	Ts[c]	Me	CO_2Me	PPh_3 (0.008), *i*-PrOH (cat.), 40°, 40 h	(0)	18
	Ph	H	Ts	H	CO_2Et	DB (0.1), 80°, 17 h	(80)	138, 346
	Ph	H	Ts	H	CO_2Bu-*t*	DB (0.1), 80°, 17 h	(60)	138

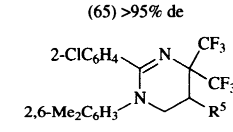
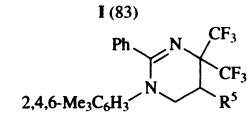
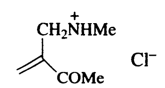
	R^1	R^2	R^3	R^4	R^5	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14}	Ph	H	CBz[c]	H	CO_2Me	PPh_3 (0.008), *i*-PrOH (cat.), 40°, 40 h	(53)	18
	2-MeC_6H_4	H	Ts	H	CO_2Me	DB (—)	(—)	306
	(±)-2-MeC_6H_4•$Cr(CO)_3$	H	Ts	H	CN	DB (0.5), rt, 1- 6 h	(82) 68% de	98
	4-MeC_6H_4	H	Ts	H	CO_2Me	DB (0.1), 80°, 17 h	(72)	138, 346
	2-MeO	H	Ts	H	CO_2Me	DB (—)	(—)	306
	(±)-2-$MeOC_6H_4$•$Cr(CO)_3$	H	Ts	H	CN	DB (0.5), rt, 1- 6 h	(87) >95% de	98, 97
	(+)-2-$MeOC_6H_4$•$Cr(CO)_3$	H	Ts	H	CN	DB (0.5), rt, 1- 6 h	(88) >95% de	98
	(±)-2-$MeOC_6H_4$•$Cr(CO)_3$	H	Ts	H	CO_2Me	DB (0.5), rt, 1- 6 h	(93) >95% de	98
	(−)-2-$MeOC_6H_4$•$Cr(CO)_3$	H	Ts	H	CO_2Me	DB (0.5), rt, 1- 6 h	(88) >95% de	98
	4-$MeOC_6H_4$	H	Ts	H	CO_2Et	DB (0.1), 80°, 17 h	(72)	138, 346
C_{15}	2,5-$(MeO)_2C_6H_3$•$Cr(CO)_3$	H	Ts	H	CN	DB (0.5), rt, 1- 6 h	(85) >95% de	98
	2,5-$(MeO)_2C_6H_3$•$Cr(CO)_3$	H	Ts	H	CO_2Me	DB (0.5), rt, 1- 6 h	(65) >95% de	98
C_{18}	CF_3	CF_3	$C(C_6H_4Cl$-2$)=NC_6H_3Me_2$-2,6	H	CN	DB ("pinch"), THF, 50°, 3 d	 I (67)	137
	CF_3	CF_3	$C(C_6H_4Cl$-2$)=NC_6H_3Me_2$-2,6	H	CHO	DB ("pinch"), THF, 50°, 3 d	I (32)	137
	CF_3	CF_3	$C(C_6H_4Cl$-2$)=NC_6H_3Me_2$-2,6	H	COMe	DB ("pinch"), THF, 50°, 3 d	I (70)	137
	CF_3	CF_3	$C(C_6H_4Cl$-2$)=NC_6H_3Me_2$-2,6	H	COEt	DB ("pinch"), THF, 50°, 3 d	I (83)	137
	CF_3	CF_3	$C(Ph)=NC_6H_2Me_3$-2,4,6	H	CN	DB ("pinch"), THF, 50°, 3 d	 I (71)	137
	CF_3	CF_3	$C(Ph)=NC_6H_2Me_3$-2,4,6	H	CHO	DB ("pinch"), THF, 50°, 3 d	I (28)	137
	CF_3	CF_3	$C(Ph)=NC_6H_2Me_3$-2,4,6	H	COMe	DB ("pinch"), THF, 50°, 3 d	I (67)	137
	CF_3	CF_3	$C(Ph)=NC_6H_2Me_3$-2,4,6	H	COEt	DB ("pinch"), THF, 50°, 3 d	I (74)	137

TABLE XI. REACTIONS OF ACTIVATED OLEFINS WITH IMINES AND IMINIUM SALTS (*Continued*)

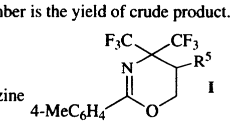
Imine	Olefin	Conditions	Product(s) and Yield(s) (%)	Refs.

[a] The substrate was $CH_2{=}NMe_2^+\ Cl^-$.

[b] The product was  Cl^- .

[c] The imine was prepared in situ from the aldehyde R^1CHO and the amide R^3NH_2.

[d] The number is the yield of crude product.

[e] The oxazine  **I** was formed in 7% yield (ref. 137).

[f] The oxazine I was formed in 5% yield (ref. 137).

[g] The oxazine I was formed in 4% yield (ref. 137).

[h] The oxazine I was formed in 5% yield (ref. 137).

[i] The oxazine I was formed in 4% yield (ref. 137).

[j] There was no asymmetric induction when chiraphos was used in place of triphenylphosphine.

TABLE XII. INTRAMOLECULAR REACTIONS

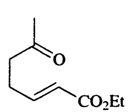
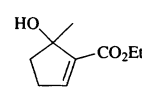
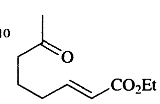
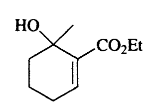
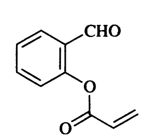
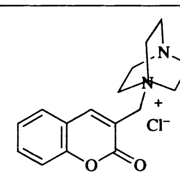
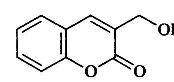
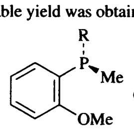
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9 			
	DB (0.15), rt, 32 d	(0)[a]	29
	$P(Bu\text{-}n)_3$	(39)[b]	29
	(0.25), rt, 1 d	(50)	29
	PPhMeBu-*i*	(40) 14% ee	29
	(0.25), rt, 30 d	(0)[d]	29
	(–)-CAMP,[c]		
C_{10} 	(0.18), rt, 10 d		
	NaOEt (1.0), EtOH, -30° to rt, 2 h		
	DB (0.25), rt, 1 d	(0)	29
	$PPhMe_2$ (0.25), rt, 6 d	(17)	29
	Lithium quinidate (0.25), HMPA, rt, 2 h	(23) 6% ee[e]	29
	HQ (lithium salt of *R* isomer) (0.25), HMPA, 0°, 30 min	(8) 0% ee	29

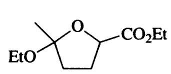
TABLE XII. INTRAMOLECULAR REACTIONS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
		 (70) +  (10)	32

[a] The product was an 81:19 mixture of the *trans* and *cis* isomers of the substrate.

[b] A comparable yield was obtained with $PPhMe_2$ as the catalyst.

[c] CAMP is  (I, R = C_6H_{11}) . With (–)-PAMP (I; R = Ph), no reaction occurred.

[d] The product was the cyclic ether  (40%) in addition to 10% of unreacted substrate.

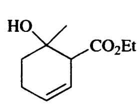
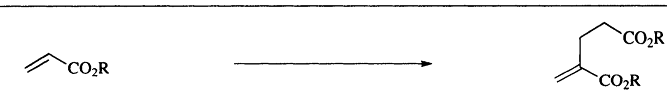
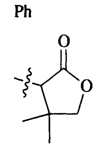
[e] The isomerized ester  was formed in 6% yield.

TABLE XIII-A. DIMERIZATION OF ACRYLATES

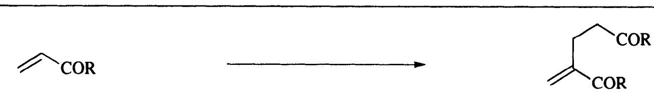


	R	Conditions	Yield (%)	Refs.
C_4	Me	DB (0.2-1.0), rt, 30 d	(0)	139
		DB (0.05), 4 kbar, 36°, 23 h	(25)[a]	49
		$P(Bu\text{-}n)_3$ (0.1), 0°, 1 h	(62)	50, 347
		$Ph_2PCH_2PPh_2$ (0.001), 80°, 18 h	(64)	348
		PPh_3 (0.1), 4.9 kbar, 50°, 4 h	(50)	50
C_5	Et	DB (0.05), 20°, 4 d	(0)	49
		DB (0.02), 4 kbar, 36°, 23 h	(9)[b]	40
		$P(NMe_2)_3$ (0.2), 60°, 2 h	(61)	349
		$P(Bu\text{-}n)_3$ (0.09), MeCN, 40-45°, 3 h	(46)	350
		$Ph_2PCH_2PPh_2$ (0.002), 100°, 18 h	(12)	348, 351
C_7	*t*-Bu	$P(NMe_2)_3$ (0.1), 20°, 16 h	(72)	349
C_8	$CHMeCO_2Et$	DB (0.4), rt, 14 d	(89)	139
C_9	$4\text{-}O_2NC_6H_4$	DB (0.2), THF, rt, 9 h	(99)	139
	Ph	DB (0.2), rt, 15 h	(98)	139
		DB (0.2), rt, 10 h	(100)	139
C_{10}	$4\text{-}MeC_6H_4$	DB (0.2), rt, 15 h	(98)	130
C_{13}	$CH(Ph)CO_2Et$	DB (0.4), rt, 8 d	(95)	139

[a] The trimer (6%), tetramer (1.5%), and pentamer (0.4%) were also formed.

[b] The trimer was formed in 2.5% yield.

TABLE XIII-B. DIMERIZATION OF ACRYLAMIDES



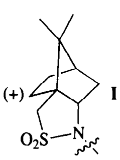
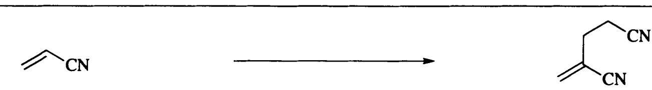
R	Conditions	Yield (%)	Refs.
C_{13}			
(+)  I	DB (1.0), Me_2CHCHO, 5 d	(22)	84
(−)-I	DB (1.0), Me_2CHCHO, 5 d	(23)	84

TABLE XIII-C. DIMERIZATION OF ACRYLONITRILE



Conditions	Yield (%)	Refs.
DB (0.5), rt, 10 d	(40)	140. 352
DB (0.01), 4 kbar, 36°, 23 h	(65)[a,b]	49
$P(Bu\text{-}n)_3$ (0.016), MeCN, *t*-BuOH, 45-50°, 2 h	(11)	351
$P(C_6H_4Me\text{-}4)_3$ (0.004), Et_3SiOH, 160°, 11 h	(21)[c]	353
$P(Bu\text{-}n)_3$ (0.01), $CH_2{=}CHCO_2Et$, *t*-BuOH, 102°, 7 h	(9)[d]	353

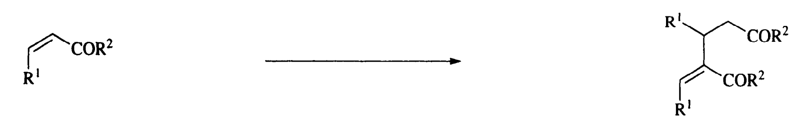
[a] The trimer was formed in 12% yield.

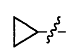
[b] A polymer was formed in the presence of pyridine (ref. 357).

[c] The β-addition product $NC(CH_2)_2CH{=}CHCN$ was formed in 5% yield.

[d] The ethyl acrylate dimer $CH_2{=}C(CO_2Et)(CH_2)_2CO_2Et$ (5%) and the mixed dimer $CH_2{=}C(CO_2Et)(CH_2)_2CN$ (10%) were also formed.

TABLE XIII-D. DIMERIZATION OF α,β-UNSATURATED KETONES



	R^1	R^2	Conditions	Yield (%)	Refs.
C_4	H	Me	DB (0.11), rt, 7 d	(80)	117
			DB (0.15), THF, rt, 4 d	(59)	140, 352
			$P(C_6H_{11})_3$-CS_2 (0.02), dioxane, rt, 24 h	(82)	354
			PPh_3 (0,02), *t*-BuOH, 25°, 24 h	(72)	355, 353
			$RhCl(PMe_3)_3$ (0.005), Me_2CO, 80°, 5 h	(24)	356
C_5	H		$RhCl(PMe_3)_3$ (0.005), Me_2CO, 80°, 5 h	(5)	356
	H	Et	DB (0.15), rt, 40 h	(60)	352, 140
			PPh_3 (0.04), benzene, 25-30°, 12 h	(62)	358
C_6	H	CH_2OAc	DB (0.15), THF, rt, 1 h	(63)	140
	H	*n*-Pr	PPh_3 (0.04), benzene, 25-30°, 12 h	(68)	358
	H	*i*-Pr	PPh_3 (0.04), benzene, 25-30°, 12 h	(78)	358
C_7	H	*t*-Bu	PPh_3 (0.04), benzene, 25-30°, 12 h	(59)	358
			$RhCl(PMe_3)_3$ (0.005), Me_2CO, 80°, 5 h	(32)	356
	–$(CH_2)_3$–		DBU (—), 1,3-dimethyl-2-imidazolidinone, 185°, 24 h	(85)[a]	57
C_8	H	5-Me-2-furyl	$RhCl(PMe_3)_3$ (0.005), Me_2CO, 80°, 5 h	(91)	356
	H	*n*-C_5H_{11}	PPh_3 (0.04), benzene, 25-30°, 12 h	(77)	358
C_9	H	4-ClC_6H_4	DB (0.15), rt, THF, 4 h	(70)	140
	H	Ph	DB (0.15), 35°, 15 min	(62)	140, 352
			PPh_3 (0.04), benzene, 25-30°, 12 h	(42)	358
			$RhCl(PMe_3)_3$ (0.005), Me_2CO, 80°, 5 h	(99)	356
	H	*n*-C_6H_{13}	PPh_3 (0.04), benzene, 25-30°, 12 h	(85)	358
C_{10}	H	4-MeC_6H_4	DB (0.15), 35°, 1 h	(49)	140, 352
			$RhCl(PMe_3)_3$ (0.005), Me_2CO, 80°, 5 h	(99)	356
	H	4-$MeOC_6H_4$	DB (0.15), THF, rt, 24 h	(73)	140
C_{13}	H	1-Naphthyl	$RhCl(PMe_3)_3$ (0.005), Me_2CO, 80°, 5 h	(92)	356

[a] In the presence of ethyl acrylate, acrylonitrile, or phenyl vinyl sulfone, α-substituted 2-cyclohexen-1-ones are formed, probably via the dienolate.

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[4 + 3] Cycloaddition Reactions

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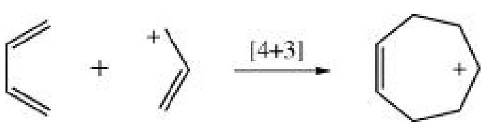
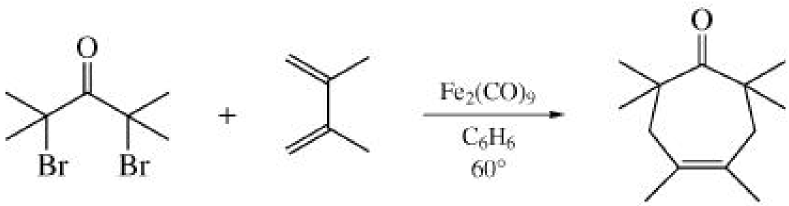
1. Introduction

Cycloaddition in its many manifestations represents one of the most powerful methods in organic chemistry for making cyclic structures. The high levels of convergency and stereoselectivity that frequently characterize these processes are particularly attractive from a preparative point of view. Five- and six-membered rings are typically made by the well-known 1,3-dipolar and Diels–Alder cycloaddition reactions, respectively, and so-called higher-order cycloaddition processes have emerged recently as useful methodology for the construction of medium-sized carbocycles. (1)

Seven-membered ring systems, owing primarily to their broad occurrence as substructures in many classes of natural products, are particularly important targets for synthesis, but there are relatively few ways currently available for *de novo* synthesis of these ring systems. As a general solution to this problem, [4 + 3] cycloaddition between a 1,3-diene and an allyl, or more frequently an oxyallyl, cation offers rapid access to functionalized seven-membered carbocycles with many of the attendant virtues of other cycloaddition processes. Considerable

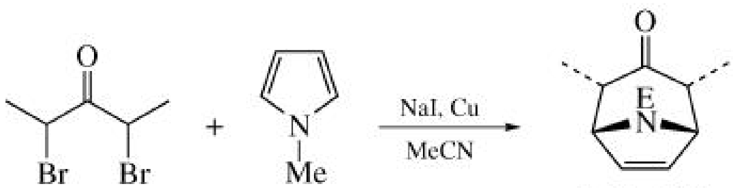


effort has been expended recently to exploit the synthetic utility of these reactions, and several informative reviews of the subject are currently available. (2-7) Electronically, the process is quite similar to the Diels–Alder reaction and can be viewed as a [4 π (4C) + 2 π (3C)] combination in which the allyl cation participates as the reactive 2 π component. Much of the developmental work associated with [4 + 3] cycloaddition has focused on approaches to the generation of the allyl or oxyallyl cation reaction partner, and a number of useful methods have emerged. Typical examples are depicted in Eqs. 1, (8) 2, (9) and 3. (10)



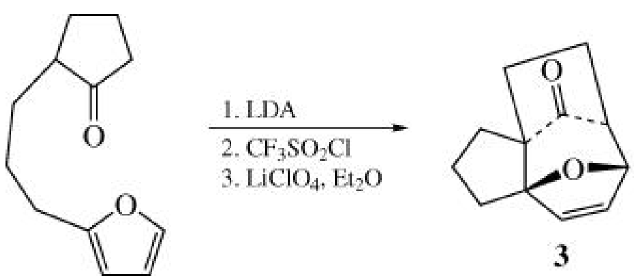
1

(71%) (1)



2 (E = Me)

(76%) (2)



3

(55%) (3)

While a wide range of 1,3-diene partners have been employed in these reactions, π -excessive heterocycles such as furan and pyrrole have been shown to be particularly useful participants and, recently, intramolecular versions of the [4 + 3] process have been effectively applied to natural product synthesis. (11)

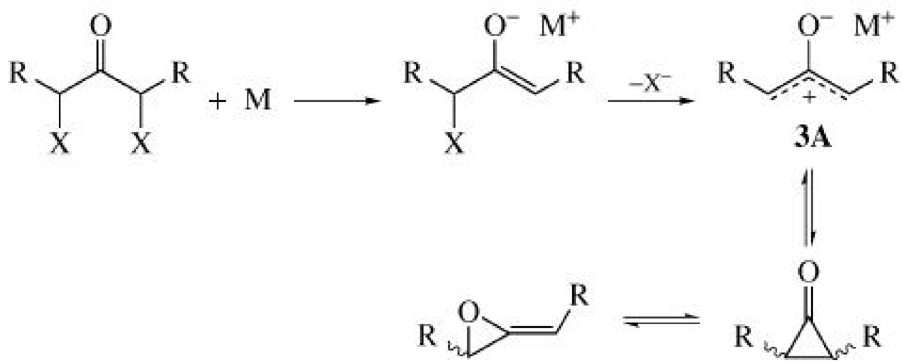
This chapter reviews the literature of [4 + 3] cycloadditions that involve allyl and oxyallyl cations and closely related 2 π (3C) reactants to mid-1996. Those [4 + 3] cycloadditions previously compiled by Noyori and Hayakawa in their 1983 review of reductive dehalogenations of polyhaloketones (5) are also included in the current review so that all relevant examples are located in one document. Other 4 + 3 annulation processes that afford seven-membered carbocycles but that employ other types of reactive intermediates are not covered in this survey.

2. Mechanisms and Stereochemistry

The precise mechanistic characteristics of a given [4 + 3] cycloaddition reaction depend critically on a subtle interplay of several factors, including the nucleophilicity of the diene and the electrophilicity of the allyl cation, as well as the electronic properties of substituents located on the 2 π (3C) partner.

A common method for producing oxyallyl cation intermediates involves a two-electron reduction of an appropriate α , α ′-dihaloketone that initially affords a metal enolate (Scheme I). Zinc(0) and iron(0) reagents are frequently employed for this purpose. This species can then undergo S_N1-type ionization (possibly metal-assisted) to afford the corresponding oxyallyl-metal intermediate **3A**, which can, and frequently does, interconvert among the cyclopropanone and allene oxide structural isomers (Eq. 3a).

Scheme 1.

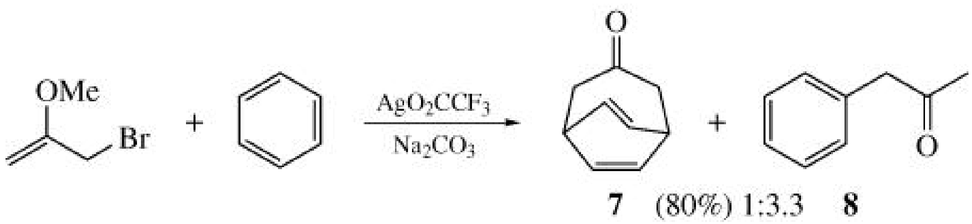


(Eq. 3a)

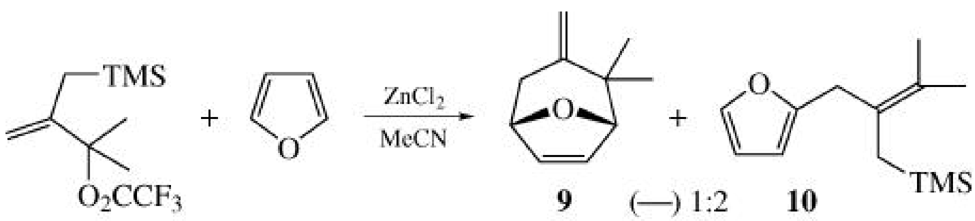
The relative importance of these species is a function of several factors, and the parent cation (R = H) is thought to isomerize rapidly to the other two forms. (12, 13) In practice, most preparatively useful cations have one or more nonhydrogen substituents at the 1 and 3 positions, since the oxyallyl cation intermediate is known to be stabilized by the presence of electron-donating groups at these locations. Indeed, α ,α ′-dibromoacetone itself is not an acceptable participant in [4 + 3] cycloaddition because of the absence of appropriate substitution. Increasing the covalent character of the M - O bond also enhances the stability of species **3A**. For instance, employing $Fe_2(CO)_9$ as the reducing agent affords well-behaved allyl cations, owing in part to the highly covalent nature of the iron–oxygen bond. These species are among the most electrophilic 2 π(3C) reactants available and often give different reaction profiles than the more ionic (and less electrophilic) sodium-based cations.

In an effort to focus attention on the key issues controlling the course of [4 + 3] cycloadditions, Hoffmann has divided these reactions into two principal mechanistic categories, reflecting whether a particular reactant combination proceeds via a concerted bond-formation (A) or via a stepwise process (B) (Fig.

1). (4) A third category (C) is reserved for stepwise reactions in which subsequent ring formation is thwarted, and products of diene electrophilic substitution prevail. In those instances involving a stepwise process, the extent of cyclization (pathway B) relative to substitution (pathway C) is dependent to a large measure on the life-time of the allyl cation intermediate **5** (Eq. 3b). Examples of typical reactions in the class (B)/(C) manifold are presented in Eqs. 4 and 5. (14, 15) It is noteworthy that substantial amounts of substitution products are formed in these reactions.

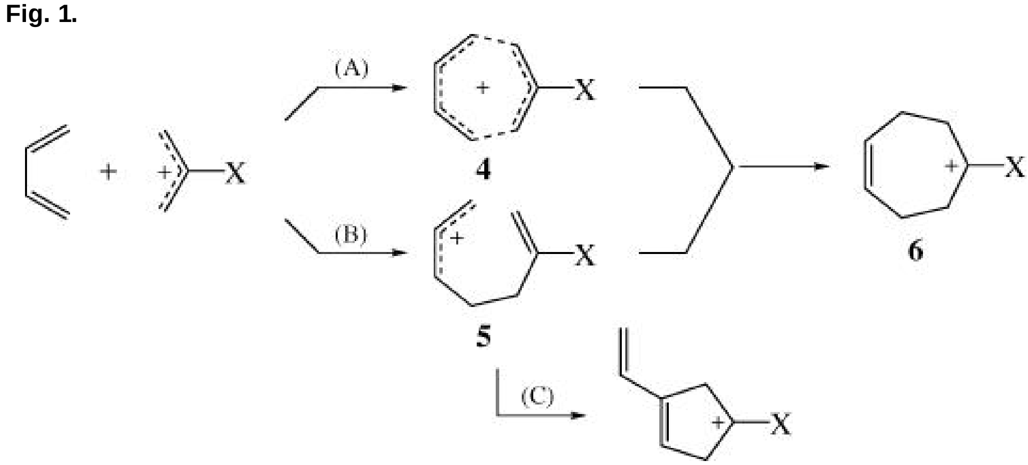


(4)

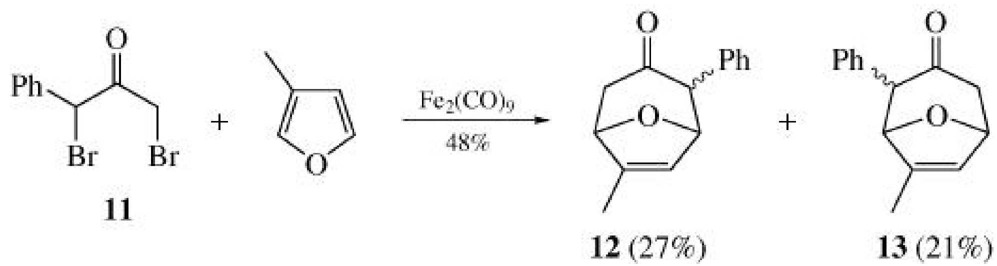


(5)

Fig. 1.

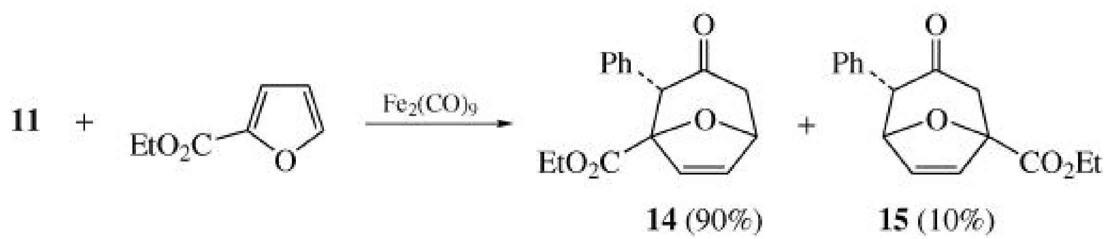


On the other hand, some [4 + 3] cycloadditions involving oxyallyliron(II) cation intermediates, as well as others derived from reductive processes, appear to be concerted in nature, (16) and involve a symmetry-allowed [4 π + 2 π] reaction. Interestingly, the metal center appears not to participate directly in the actual bond-forming event, an observation that is in contrast to most other known transition metal mediated cycloadditions. An informative example of this type of reaction can be seen in the combination of dibromoketone **11** with 3-methylfuran in the presence of $Fe_2(CO)_9$ (Eq. 6).



(6)

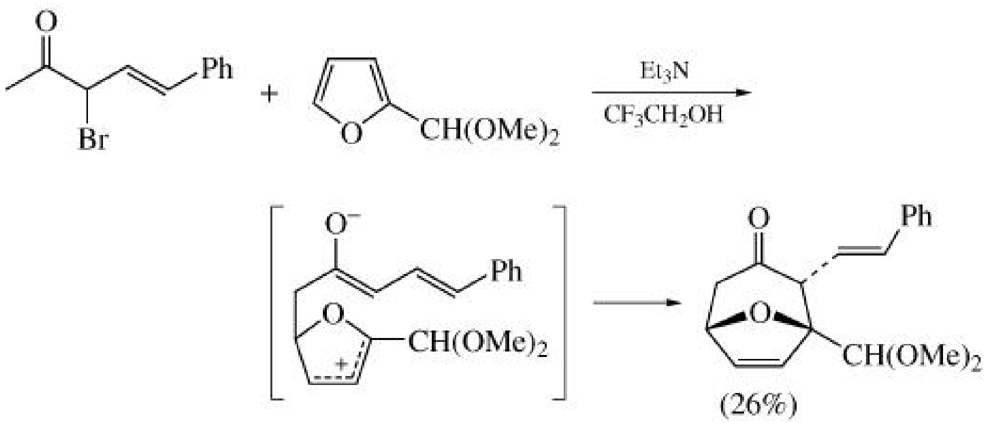
The rather indiscriminate regioselectivity exhibited by many of these [4 + 3] reactions is consistent with FMO control of the process. The HOMOs of various 3-substituted furans are known to be nearly symmetrical and do not vary significantly with changes in the electronic nature of the substituents. For example, 3-carboethoxyfuran affords a regiochemical mix similar to that found with 3-methylfuran in reaction with the oxyallyl species derived from **11**. In contrast, high syn-regioselectivity is observed with 2-carboethoxyfuran as the 4 π partner (Eq. 7). Secondary MO interactions between the phenyl group on the oxyallyl



(7)

iron reactant and the ester group on the furan have been invoked to explain this result. While a number of regioselective [4 + 3] cycloadditions are known, the extent of regioselection is normally less pronounced than in the Diels–Alder process.

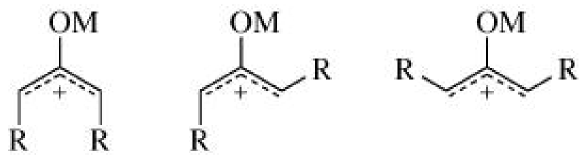
It is noteworthy that high levels of regioselection are observed in cycloadditions between unsymmetrically substituted reactants under basic conditions, and frequently the more hindered adduct prevails. (17) This selectivity has been rationalized by invoking a nonsynchronous process where the less-substituted centers bond first (Eq. 7a).



(7a)

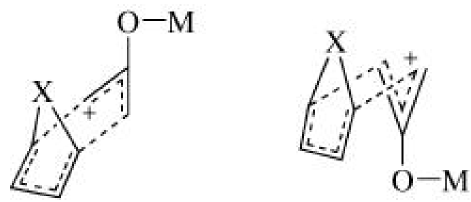
The stereochemical course of [4 + 3] cycloaddition reactions is also a complex issue and is intimately associated with the position of the particular reaction on the mechanistic continuum. As a result these reactions, as a class, tend to be somewhat less stereoselective than Diels–Alder cycloadditions, although some examples are known to display impressive selectivity patterns. Furthermore, the phenomenological basis for stereoselection in these reactions is quite subtle and seems to depend to a larger extent on the conditions of a particular reaction than is typical for most pericyclic processes. Issues such as the electrophilicity of the allyl cation intermediate, reaction solvent polarity, and nucleophilicity of the diene partner all can have a profound influence on the steric course of [4 + 3] cycloadditions. Although the factors affecting the stereochemical course of these transformations can be subtle, several useful trends have been discerned that can allow reasonable predictions to be made in many instances.

Two topologically distinct transition states can be envisioned for the [4 + 3] cycloaddition reaction, an extended (chair-like) TS and a compact (boat-like) arrangement (Fig. 2). These designations correspond to the *exo* and *endo* orientations, respectively, in the Diels–Alder reaction. The steric analysis of these reactions, however, can become more complex than in the Diels–Alder reaction, since the configurational identity of the transient allyl cation intermediate may be unclear. For acyclic cations three possibilities can exist, the U form **(16)**, the sickle form **(17)**, and the W configuration **(18)**. In many cases, the W form seems to prevail, at least as the initially formed reactive species. (4)



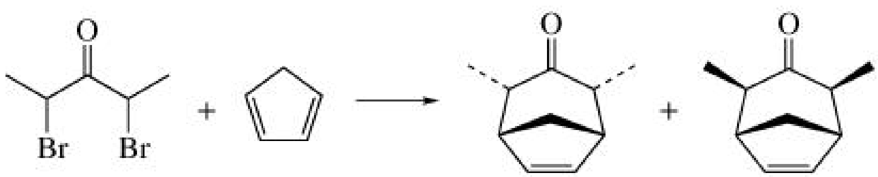
16 **17** **18**

Fig. 2.



Extended TS (chair-like) Compact TS (boat-like)

Several interesting studies reveal many of the salient stereochemical features of the [4 + 3] cycloaddition process. For example, the propensity for a reaction to follow an extended pathway has been linked to the electrophilicity of the intermediate oxyallyl cation. (8, 18) Exposing 2,4-dibromopentan-3-one to three different reducing conditions affords cycloadducts **19** (from a compact TS) and **20** (from an extended TS) in differing ratios (Eq. 8). Each of the reactions is assumed to

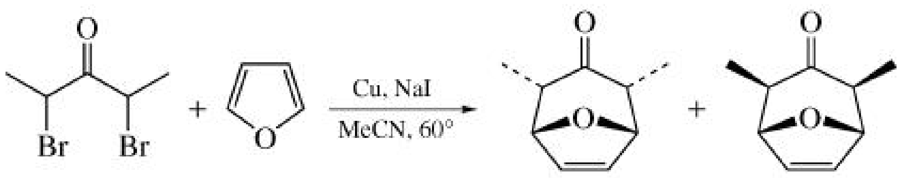


19 **20** (8)

Conditions	19	20
Cu, NaI, MeCN	6.4	1 (91%)
Zn/Cu, DME	1.7	1 (—)
$Fe_2(CO)_9$, C_6H_6	0.89	1 (86%)

follow a concerted (A) pathway as evidenced by an absence of any configurational “leakage” during the course of the reaction. The putative sodium oxyallyl cation (weakly electrophilic) most strongly favors the compact reaction pathway, while the more electrophilic iron species begins to favor the extended transition state. Several rationales have been forwarded to explain this trend, including secondary orbital interactions and conformational control. (4, 7, 19-21)

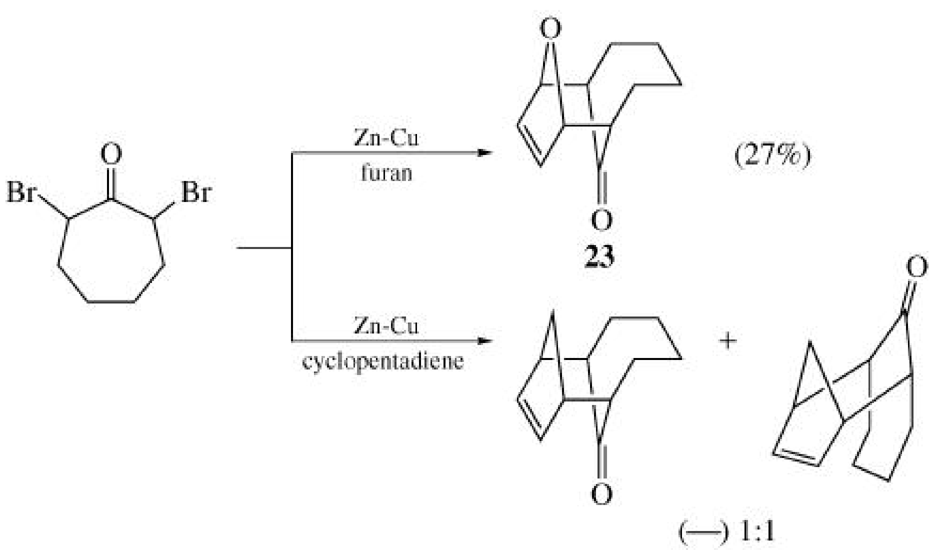
In the presence of furan as the 4 π partner, the oxyallyl cation derived from 2,4-dibromopentan-3-one affords mixtures of products that arise from the compact and extended transition states as well as considerable quantities of a third adduct exhibiting a trans relationship between the two methyl groups, indicating a loss of oxyallyl configurational integrity. This observation has been taken as evidence for a change to a Class B (stepwise) mechanism. Furthermore, a greater preference for the compact mode of cycloaddition is noted in this case relative to the previous study. In general, furan is known to favor the compact TS to a greater extent than does cyclopentadiene. (4) A typical preparative scale example is shown in Eq. 9. (22) The predominant stereoisomer is from the compact TS, and only a trace of the product possessing trans methyl groups is obtained.



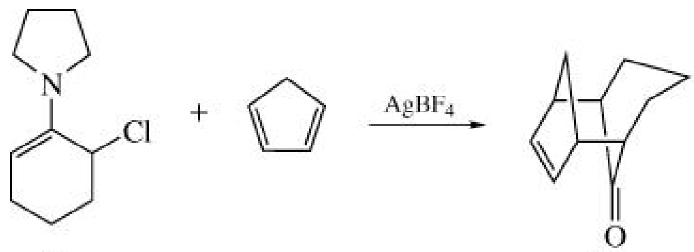
21 (48%) **22** (5%)

(9)

The stereochemistry of cycloaddition employing cyclic oxyallyl cations has also been examined in some detail, although the chemical yields of products are frequently low. (23, 24) The reaction profile of the oxyallyl cation derived from 2,7-dibromocycloheptanone is typical. With furan, cyclic cations again prefer to react via the compact transition state to afford adduct **23**, while no selectivity is observed when cyclopentadiene serves as the 4 π partner (Eq. 10). In contrast, chloroenamine **24**, when treated with cyclopentadiene in the presence of $AgBF_4$, affords adduct **25** as a 93:7 mixture favoring the compact isomer (Eq. 11). (25)



(10)



24 **25** (76%) (11)

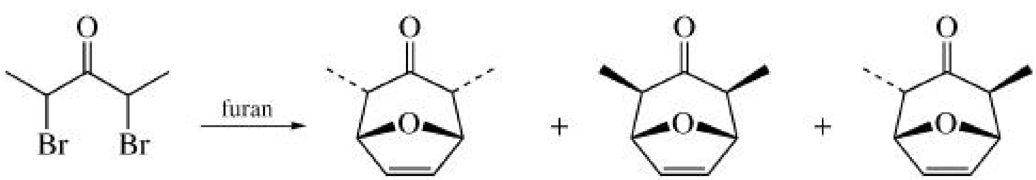
In summary, although the sense and extent of stereoselectivity in [4 + 3] cycloadditions is somewhat variable relative to other cycloaddition reactions, careful choice of reactants and reaction conditions can lead to reasonably effective control of the steric course of these reactions.

3. Scope and Limitations

Rapid access to functionalized seven-membered carbocycles from readily available starting materials remains one of the principal synthetic virtues of [4 + 3] cycloaddition. Successful implementation of this methodology in a given situation, however, depends critically on the choice of oxyallyl cation precursor and on the conditions employed to produce this transient three-carbon species. Over the years numerous methods for producing allyl cations have been reported, and the reactivity characteristics of these species with diene partners span a range from highly organized, concerted processes to stepwise, dipolar reactions that frequently give rise to uncyclized products. The stereochemical features of these transformations are equally variable. However, judicious choice of reactants and reaction conditions can lead to the rapid production of useful seven-membered ring systems with good efficiency and predictable stereocontrol.

3.1. Reductive Conditions

Reduction of α , α′-dihaloketones has emerged as one of the principal methods for preparing oxyallyl cation intermediates for cycloaddition. (5) The character of the subsequent cycloaddition, however, is critically dependent on the specific reducing agent employed. Examination of the cycloaddition between furan and the oxyallyl cation derived from 2,4-dibromopentan-3-one under several conditions illustrates some of these issues (Eq. 12). (8, 22, 26)

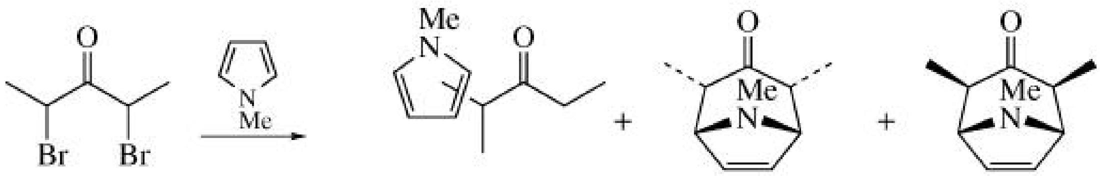


21 **22** **26** (12)

Conditions	21	22	26
Cu, NaI	(48%)	(5%)	—
Zn, Cu	(69%)	(8%)	(7%)
$Fe_2(CO)_9$	(40%)	—	(50%)

As mentioned previously, furan tends to strongly favor a compact transition state during cycloaddition, and in most instances these reactions proceed in a concerted (Class A) fashion. (3) The Cu/NaI reduction conditions are known to provide one of the least electrophilic oxyallyl cation species because of the ionic nature of the Na–O bond. As a consequence, the product mixture obtained under these conditions is consistent with a concerted, compact *endo*-selective reaction pathway. The zinc-based oxyallyl cation (from Zn/Cu) is of intermediate electrophilicity, and a small amount of stereochemical “leakage” is noted with the formation of *trans* adduct **26**. Hoffmann has argued that loss of allyl cation configuration is a sufficient criterion for the intervention of a Class B (stepwise) mechanistic pathway. (4) Finally, the iron(II)-based allyl cation, known to be the most electrophilic metal-based cation, gives rise to a substantial quantity of adduct **26**, further indicating the appearance of a stepwise process.

A striking example of the influence of cation electrophilicity on the course of a reaction can be seen with *N*-methylpyrrole serving as the diene partner (Eq. 13). (8, 9, 27) Only the least electrophilic 2 π (3C) partner (from Cu/NaI) affords

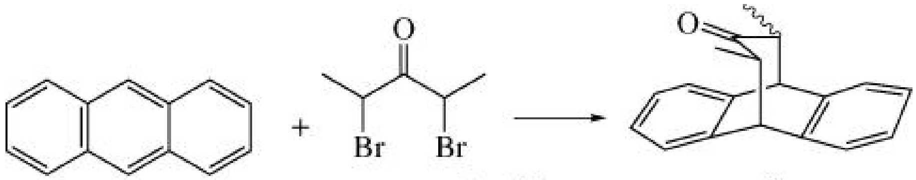


27 **28** **29** (13)

Conditions	27	28	29
Zn/Cu	(60%)	—	—
$Fe_2(CO)_9$	(81%)	—	—
Cu, NaI	—	(76%)	(13%)

[4 + 3] cycloadducts. Even a slightly more electrophilic species (from Zn/Cu) gives rise to regioisomeric mixtures of electrophilic substitution (Class C) products, and the strongly electrophilic oxyallyliron species gives only Class C products as well. *N*-Acyl and *N*-carboalkoxypyrroles however, afford [4 + 3] cycloadducts with both Zn–Cu couple and $Fe_2(CO)_9$-based oxyallyl cations, and these transformations have been exploited for tropane alkaloid synthesis. (8, 28)

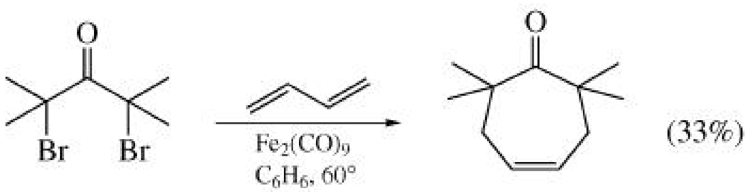
It is noteworthy that the cycloaddition of oxyallyl zinc cations derived from Zn–Cu couples can be dramatically improved by performing the reaction in the presence of trimethylsilyl chloride. In an impressive example, the yield of adduct **30** improves from 22 to 93% using this technique (Eq. 14). (29, 30) The transformation presumably proceeds through a more electrophilic silyloxy cation intermediate.



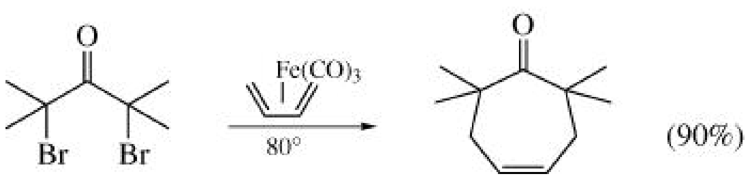
Conditions	30
Zn/Cu	(22%)
Zn/Cu, TMSCl	(93%)

(14)

A significant distinction that separates the Diels–Alder reaction from the [4 + 3] cycloaddition process is the relative paucity of viable examples of the later employing acyclic dienes as 4 π partners. This situation is normally ascribed to a strict requirement for the diene to exist principally or exclusively in the s-*cis* conformation for efficient [4 + 3] cycloaddition to occur. Although the Diels–Alder reaction also occurs via the diene s-*cis* conformation, the transient nature of the allyl cation intermediates exacerbates this requirement in [4 + 3] processes. Examples listed in Eqs. 15 and 16 dramatically illustrate the veracity



(15)

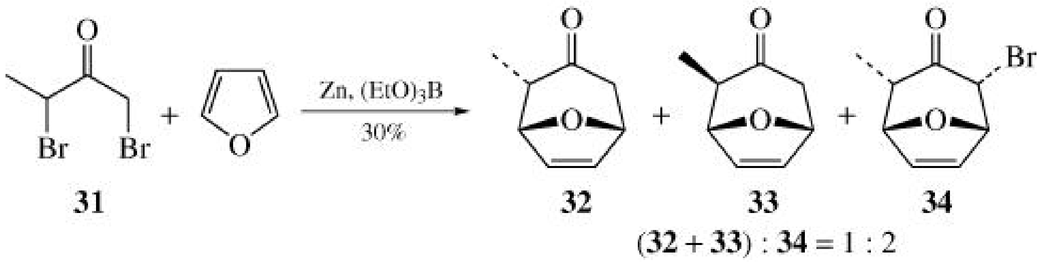


(16)

of this rationale. (8) While 1,3-butadiene itself affords the corresponding cycloadduct in only modest yield, the corresponding reaction with (η^4-butadiene) tricarbonyliron(0), wherein the diene is locked in an s-*cis* arrangement, affords the same product with much greater efficiency.

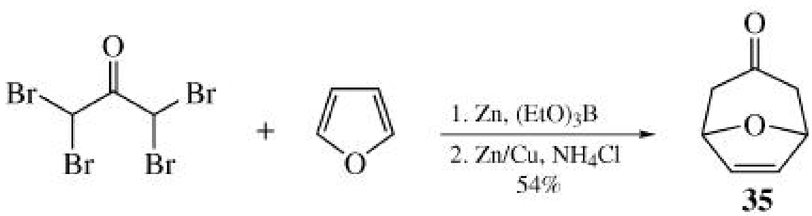
The reduction of polyhaloketones using Zn and $(EtO)_3B$ offers an interesting alternative means of preparing oxyallyl cations. (31) A notable feature of these conditions is their compatibility with minimally substituted α , α

′-dibromoketones such as **31** (Eq. 17). Indeed, it appears that at least one α -hydrogen must be



(17)

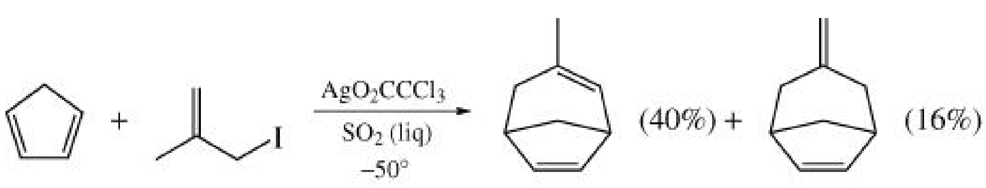
present in the dibromide substrate for reactions to occur under these conditions. The unexpected isolation of bromide **34** from this reaction provides some insight into the mechanism of oxyallyl cation production, which appears to involve initial formation of an enolborate intermediate. An appealing feature of this methodology is that it is suitable for large-scale reactions, as evidenced by the preparation of adduct **35** on a 1-mole scale using the two-step sequence shown in Eq. 18. (32)



(18)

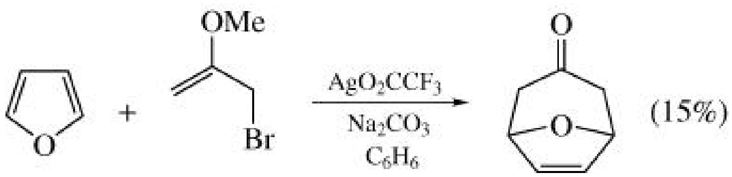
3.2. Solvolysis Conditions

Lewis-acid promoted cleavage of allyl halides is a particularly direct route into allyl cations. (33, 34) Cycloadditions involving simple allyl cation reactants can be problematic, however, and frequently require reaction conditions that are not amenable to scaleup (Eq. 19). (35) It is noteworthy that a closely related reaction with furan affords only products derived from Class C pathways.



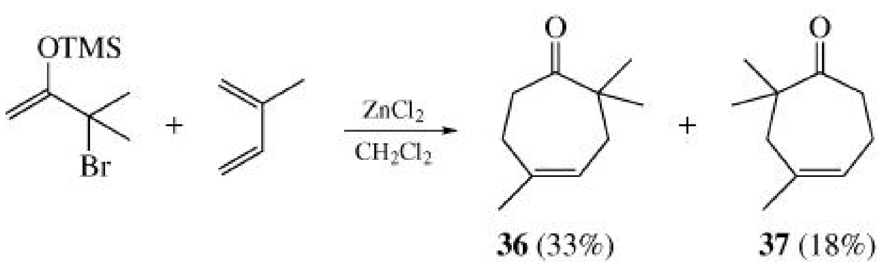
(19)

The 2-methoxyallyl system has also been examined as a 2 π(3C) component in [4 + 3] cycloaddition. (34) Carefully controlled conditions are necessary for the isolation of cyclic products from these reactions and the yields are frequently low (Eq. 20).



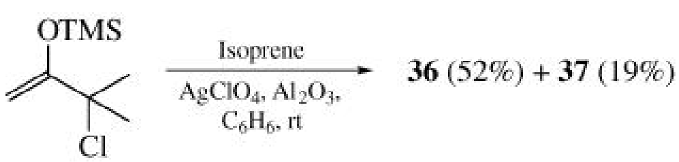
(20)

The closely related 2-silyloxyallyl cations have been explored with modest success in cycloaddition. The cation in these cases is prepared in situ by ZnX_2^- or AgX^- promoted heterolysis, and the presence of several terminal alkyl or aryl substituents is usually required for efficient ionization to occur in these substrates (Eq. 21). (36)



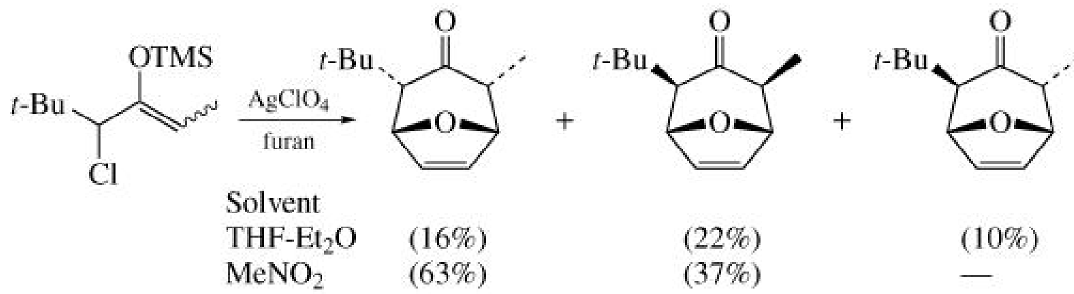
(21)

It is of interest to note that only a modest change in the conditions of the cycloaddition depicted in Eq. 21 results in improvement in the efficiency and regioselectivity of the reaction (Eq. 22). (19)



(22)

The choice of solvent frequently can have a profound effect on the course of the silyloxyallyl cation cycloaddition reactions. The results in Eq. 23 reveal the

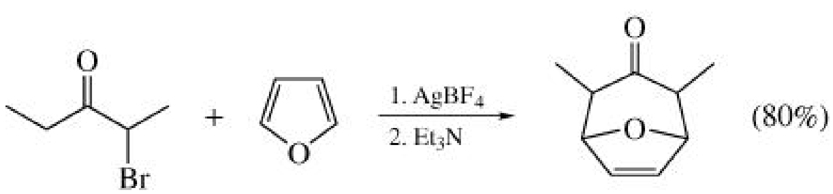


(23)

effect of changing solvent from a THF/Et_2O mixture to nitromethane. (19) It has been suggested that the reaction performed in nitromethane is concerted while the ether solvent mix favors a stepwise pathway.

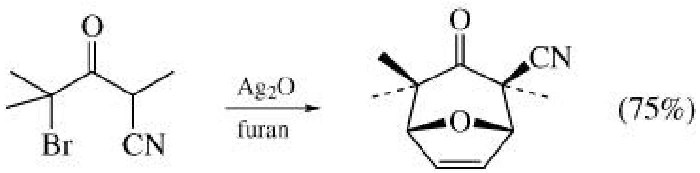
3.3. Base-Mediated Conditions

Exposure of α -haloketones to various basic conditions is also a popular method for generating oxyallyl cations for use in [4 + 3] cycloadditions. Access to the halocarbon substrates is frequently more convenient and economical than to their dihalo counterparts. On the other hand, the requirement in some cases for stoichiometric quantities of a silver salt renders the overall process quite expensive. As a consequence, a number of less expensive and more convenient procedures have been developed. In a typical example of a silver-promoted reaction, a monobromoketone was treated with a stoichiometric quantity of silver tetrafluoroborate at room temperature. Subsequent addition of the diene partner and triethylamine afforded serviceable yields of cycloadducts (Eq. 24). (37, 38)



(24)

A number of related silver salt-mediated processes have also been employed successfully in cycloaddition reactions; however, effective ring formation has been recorded only for substrates with considerable substitution on the 1 and 3 positions of the allylic system. (39-41) Reactions mediated by Ag_2O are typical in this regard (Eq. 25). A less costly version of this process using $LiClO_4$/Et_3N to generate the

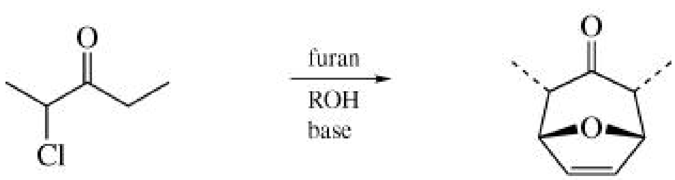


(25)

corresponding lithium oxyallyl intermediate has been developed, and in some instances a modest level of regiocontrol is observed with substituted furans. (42, 43)

From a large-scale preparative perspective, the observation that useful oxyallyl cations can be generated directly with base in appropriate solvents is particularly attractive. The choice of alcohol solvent is important for the success of these reactions, and 2,2,2-trifluoroethanol and 2,2,3,3-tetrafluoro-1-propanol have emerged as solvents of choice. (43-45) In many cases optimum yields of cycloadducts can be obtained by employing $NaOCH_2CF_3$ in CF_3CH_2OH , as illustrated in Eq. 26. A limitation to this method is the need to employ a large excess of the allyl cation trapping agent. (46, 47) This is, in fact, a drawback to most intermolecular oxyallyl cation-based [4 + 3] cycloadditions presented in this chapter.

Cyclic precursors have recently been the subject of considerable study as 2 π (3C) components in [4 + 3] cycloaddition. In many instances superior results



Conditions	
Et_3N, MeOH	(39%)
NaOMe, MeOH	(53%)
Et_3N, CF_3CH_2OH	(77%)
$NaOCH_2CF_3$,CF_3CH_2OH	(80%)

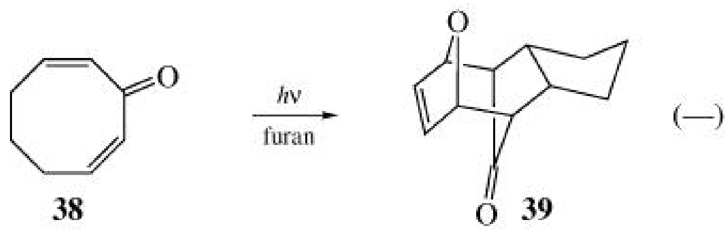
(26)

are obtained by employing basic conditions for the generation of the oxyallyl cation intermediates (Eq. 27). (43) It is noteworthy that considerably lower yields of adducts are realized using various reductive conditions in related processes. (48)

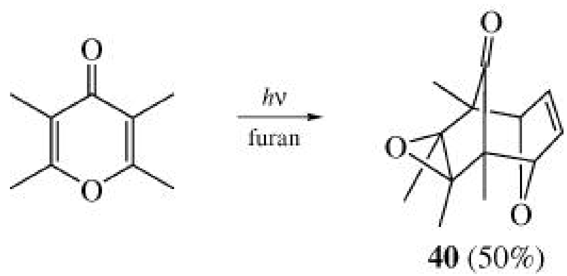
(27)

3.4. Photochemical Conditions

Photochemical routes for generating oxyallyl cations represent an intriguing possibility for mild [4 + 3] cycloaddition. Interesting and informative examples are depicted in Eqs. 28 and 29.



(28)

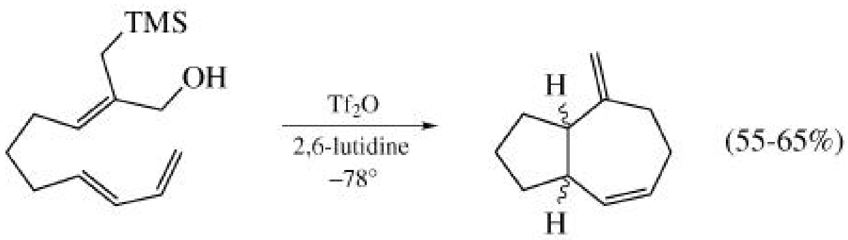


(29)

Irradiation of dienone **38** in the presence of furan gives cycloadduct **39** exclusively as the compact (*endo*) adduct. (49) Pyrone photochemistry has also yielded a rich array of [4 + 3] cycloaddition opportunities. (50-52) The efficiencies of these reactions are quite variable, but in certain circumstances preparatively significant yields can be obtained as shown in Eq. 29. Once again good stereoselectivity appears to prevail in these transformations.

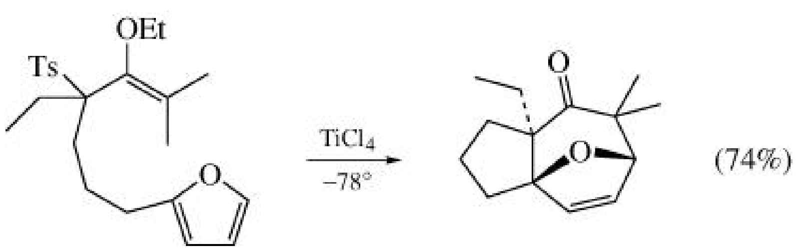
3.5. Intramolecular Cycloadditions

Recently, intramolecular [4 + 3] cycloadditions have been employed for the rapid buildup of molecular complexity in the construction of polycyclic systems. In some cases the allylic cation moiety is generated by an ionization process promoted by a Lewis acid. For example, hydroazulene systems can be constructed in good yields via heterolysis of an allylic triflate at low temperatures (Eq. 30). (53) A



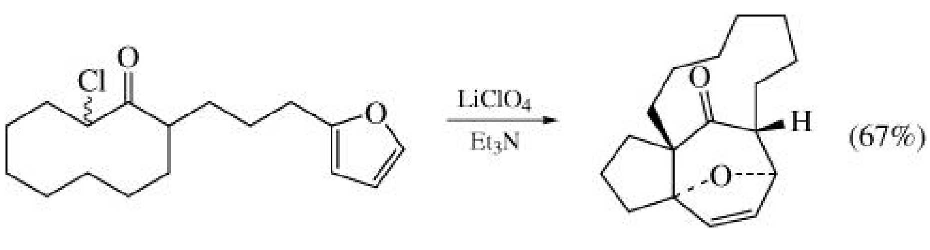
(30)

mixture of the *cis* and *trans* isomers was isolated from this process. Relatively efficient trapping of oxyallyl cations with a tethered furan moiety also affords functionalized hydroazulenes, primarily as single stereoisomers (Eq. 30a). (54) A



(30a)

fascinating cycloaddition occurs between an oxyallyl cation generated within a 10-membered carbocycle and a tethered furan to yield a rare *trans*-bridged tetracyclic product (Eq. 31). (55) This result provides important insight into the configurational character of the oxyallyl cation intermediate involved in the reaction.

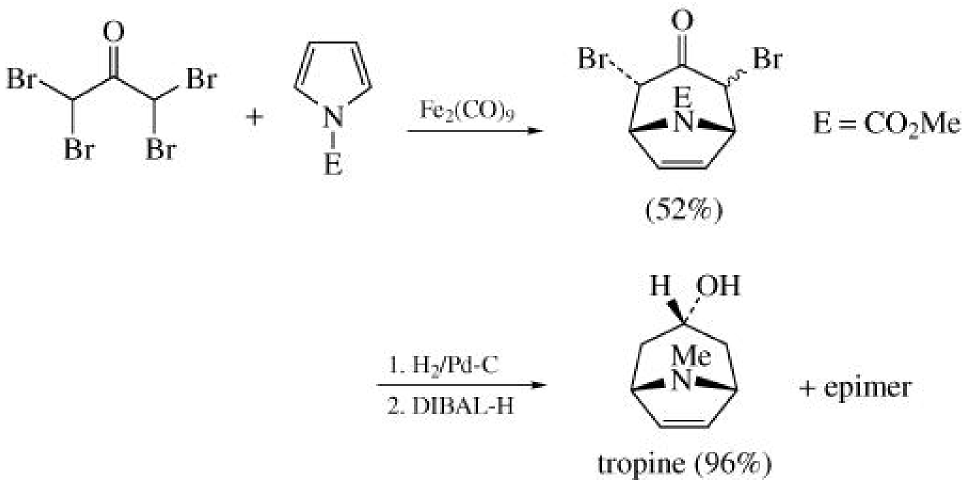


(31)

3.6. Applications to Synthesis

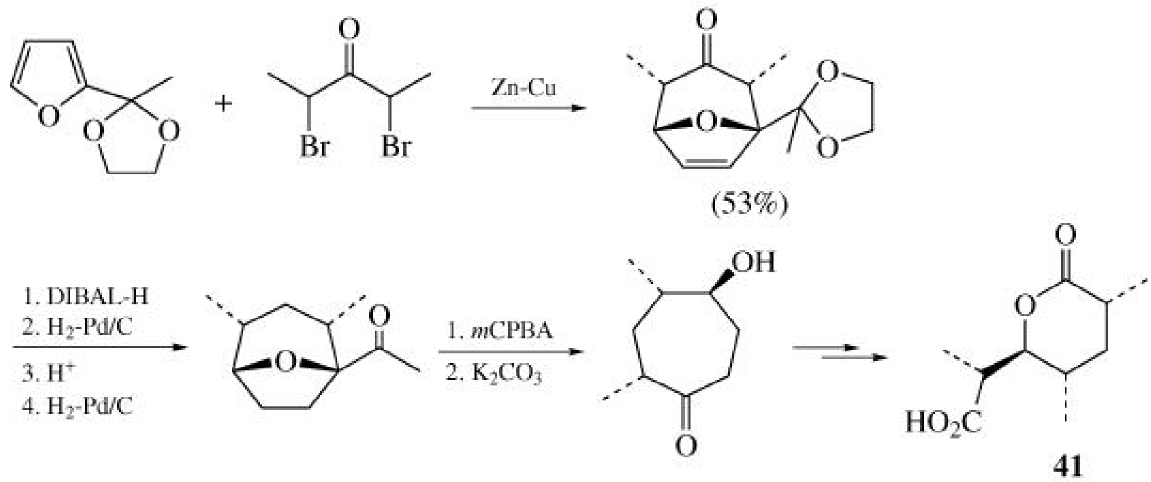
One of the principal virtues of [4 + 3] cycloaddition in which a heterocyclic diene participates as the 4 π reaction partner is the rapid construction of functionalized and conformationally rigid seven-membered carbocycles. Flexible cycloheptane ring systems are notorious for their conformational ambiguities, and the production of rigid bicyclic intermediates via these cycloadditions permits stereoselective post-cycloaddition manipulations to be performed. This feature of these reactions has been exploited to good advantage in a number of natural product syntheses.

An obvious set of targets for these cycloadditions are the tropane alkaloids. Noyori and co-workers have reported an efficient synthesis of tropine using a cycloaddition between an oxyallyliron intermediate and *N*-carbomethoxypyrrole as the key entry into the characteristic azabicyclo [3.2.1]octane ring system (Eq. 32). (28) Related approaches have also been reported by Mann and co-workers. (27, 56)



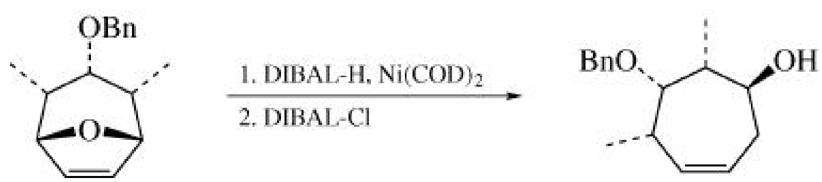
(32)

A synthesis of racemic Prelog–Djerassi lactone **(41)** featuring a stereoselective [4 + 3] cycloaddition (via a compact TS) between a substituted furan and a zinc-based oxyallyl cation nicely illustrates how the rigid oxabicyclo[3.2.1]octane system produced in these reactions can be exploited for stereocontrolled post-cycloaddition manipulation (Eq. 33). (57)



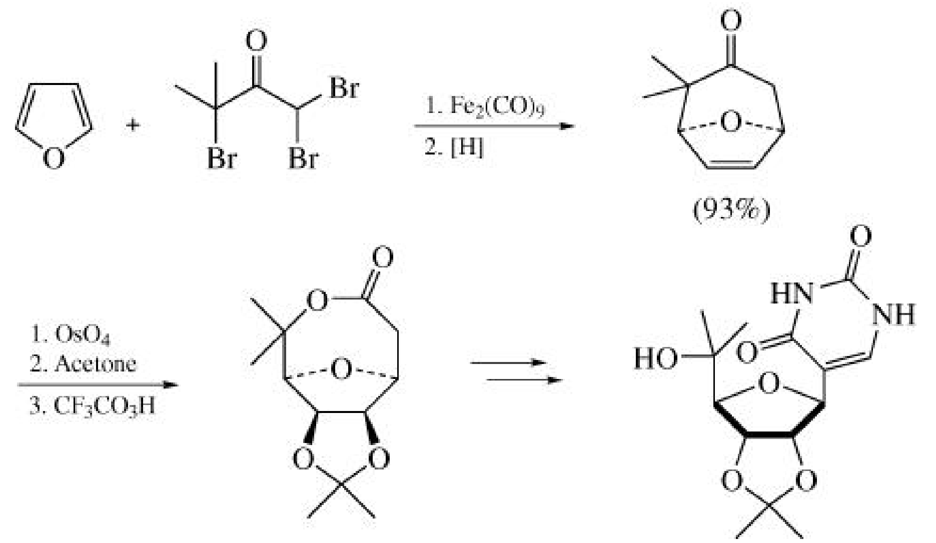
(33)

A number of methods have been developed for ring-opening of the oxabicyclo [3.2.1]octane system that greatly expands the utility of [4 + 3] cycloaddition in stereoselective synthesis, allowing access to stereochemically elaborate cycloheptane rings (Eq. 34). (58-60)



(34)

The stereocontrolled preparation of nucleosides represents another example of how the stereochemical information contained in the oxabicyclo[3.2.1]octane ring system can be exploited to synthetic advantage. Routine [4 + 3] cycloaddition constructs a platform from which the ribofuranosyl skeleton can be elaborated employing straightforward chemistry (Eq. 35). (61)

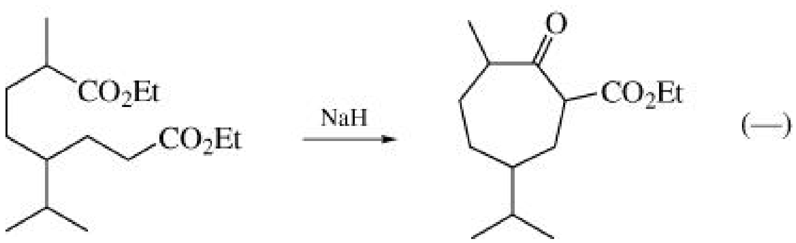


(35)

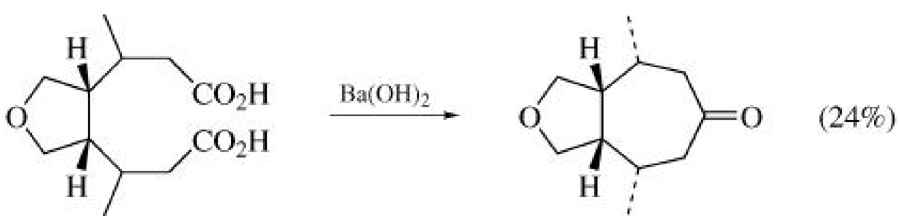
4. Comparison with Other Methods

From a synthetic perspective the principal virtue of [4 + 3] cycloaddition is the ease with which seven-membered carbocycles can be assembled. In many cases the precursors are readily available and reasonable chemical yields are common. When cyclic diene partners are employed, conformationally rigid and facially biased products emerge, which are well suited for stereoselective post-cycloaddition manipulations. While there exists a multitude of methods for making six-membered ring systems, the synthetic repertoire remains relatively limited for the next higher homolog. A liability that many of these methods share is the lack of stereocontrol during the ring-forming event. Often this is an advantage of the [4 + 3] process. Classical methods for ring closure of functionalized acyclic precursors have had some success when applied to seven-membered rings, but stereocontrol can still be problematic.

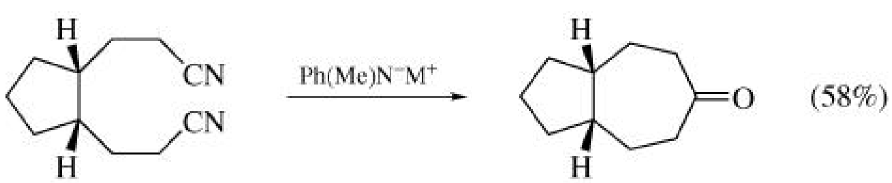
The Dieckmann condensation (Eq. 36), (62) the Ruzicka cyclization (Eq. 37), (63) the Thorpe–Ziegler reaction (Eq. 38), (64) and acid-mediated olefin cyclizations (Eq. 39) (65) have all been successfully applied to seven-membered ring construction. In many cases fusion to a second ring enhances cyclization efficiency.



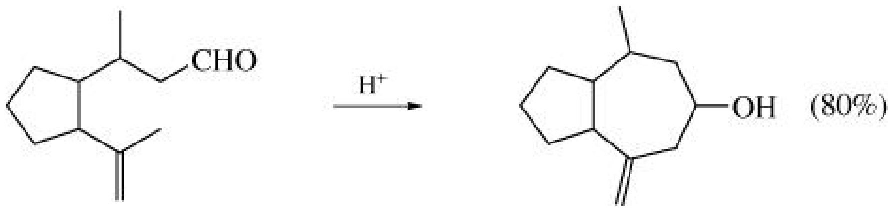
(36)



(37)

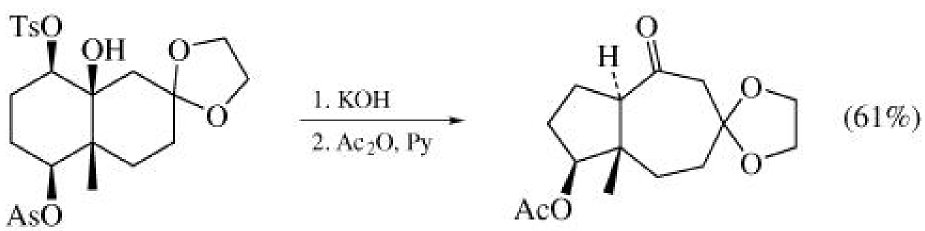


(38)



(39)

Ring expansion of readily available six-membered ring precursors has been used frequently for making seven-membered rings in natural product synthesis. An important feature of this strategy is the ability to exploit the stereocontrol afforded by the conformationally well behaved six-membered ring system as well as the stereoelectronic requirements of the ring-expansion process itself (Eq. 40). (66)

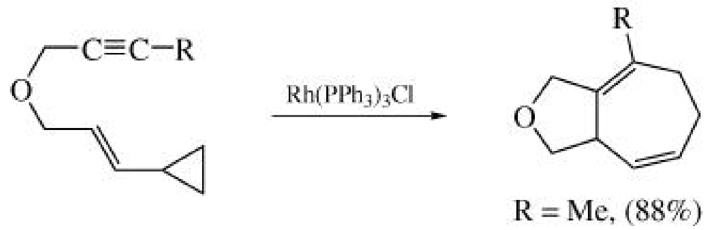


(40)

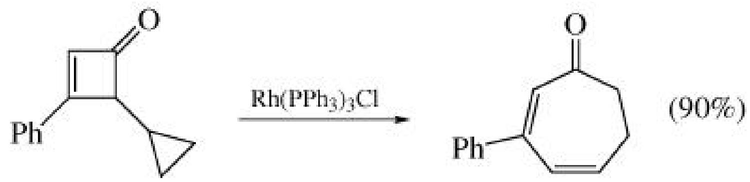
In spite of its successes for the preparation of other ring sizes, olefin metathesis chemistry has been applied to the synthesis of seven-membered rings only rarely (Eq. 41). Consequently, comparison with [4 + 3] cycloaddition is difficult at this time. (67)

(41)

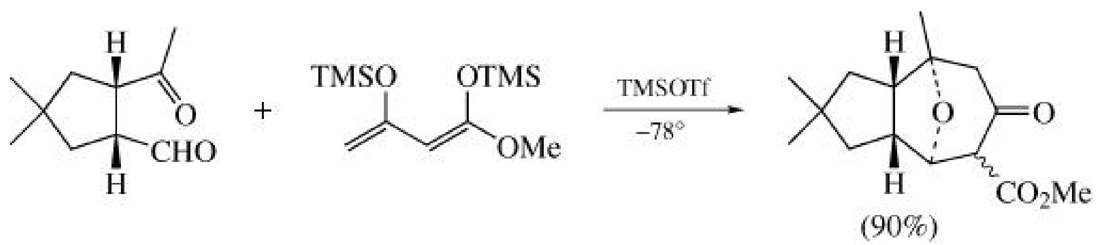
Recently, intramolecular metal-promoted cycloaddition chemistry has been successfully applied to the synthesis of seven-membered rings (Eq. 42). (68) A related

 (42)

metal-mediated rearrangement of a cyclopropyl–cyclobutenone substrate affords seven-membered rings in good yields (Eq. 43). (69)

 (43)

Lewis acid-promoted annulations of 1,4-dicarbonyl compounds with bis-(trimethylsilyl)enol ethers has been developed as an efficient and versatile entry into seven-membered carbocycles that frequently exhibit an oxygen bridge. (70) As such, the products of this process are reminiscent of those formed in the [4 + 3] cycloaddition pathway and possess many of the same advantages that stem from the rigidity of the seven-membered ring (Eq. 44).

 (44)

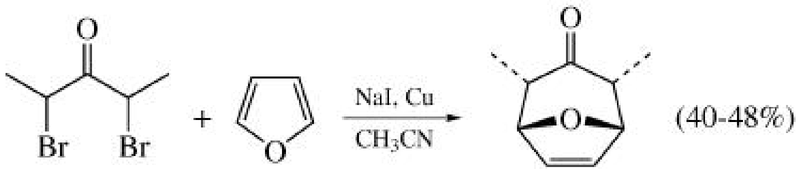
For certain applications, [4 + 3] cycloaddition holds significant advantages over many of these methods. For example, when Class A (concerted) reaction conditions are employed with a cyclic diene partner such as furan, the resultant high level of stereoselectivity is often difficult to match in other cycloheptannulation approaches.

5. Experimental Conditions

For haloketone cycloadditions involving reductive conditions, commercially available reducing agents are satisfactory in most cases, although some agents require preparation such as Zn/Cu and Zn/Ag couples. These are normally prepared under standard conditions from zinc metal and various copper or silver salts, respectively. (29) In several cases employing Zn/Cu as the reducing agent, enhanced reaction efficiency can be achieved by the addition of trimethylsilyl chloride to the reaction mixture. A mixture of copper and dry sodium iodide has also emerged as a convenient set of reducing conditions for [4 + 3] cycloadditions. (22) [**Caution:** Reactions involving $Fe_2(CO)_9$ and $Fe(CO)_5$ should be carried out in a well-ventilated hood since carbon monoxide gas may be produced during the reaction.]

Optimum conditions for effecting base-mediated cycloadditions of α -haloketones vary considerably. However, the best results are frequently obtained by employing fluorinated solvents such as CF_3CH_2OH or $CF_2HCF_2CH_2OH$ in conjunction with triethylamine or alkoxide bases. Nonfluorinated alcohols of lower polarity are generally less effective solvents for cycloaddition. In certain cases, triethylamine in conjunction with an ethereal solution of $LiClO_4$ is effective as well.

6. Experimental Procedures



6.1.1. 2 α ,4 α -Dimethyl-8-oxabicyclo[3.2.1]oct-6-en-3-one (Reduction of an α , α '-Dihaloketone with NaI/Cu) (22)

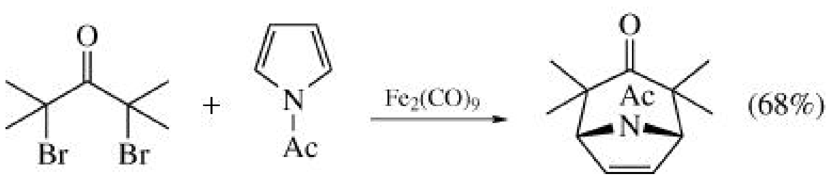
A 1-L, three-necked, round-bottomed flask was fitted with a 100-mL dropping funnel having a nitrogen inlet tube, a magnetic stirrer, a thermometer, and an efficient double-surface condenser carrying a nitrogen outlet tube connected to a bubbler, and placed on a combined hot plate–magnetic stirring unit in a heat-resistant glass dish acting as a water bath. Dry acetonitrile (200 mL) was introduced into the flask, followed by 90 g (0.60 mol) of dried, powdered sodium iodide, with vigorous stirring under a slow stream of nitrogen. When the stirring bar rotated steadily, 20 g (0.31 g-atom) of powdered copper-bronze was added, followed by 28 g (30 mL, 0.41 mol) of freshly distilled furan. The dropping funnel was then charged with a solution of 24.4 g (0.100 mol) of 2,4-dibromopentan-3-one in 50 mL of dry acetonitrile, which was rapidly added to the stirred reaction mixture. The temperature rose to 45–50°, and a characteristic oatmeal-colored precipitate formed. After about 2 hours the temperature began to drop, and the reaction was maintained at 50–60° with the water bath for a total reaction time of 4 hours.

The flask was cooled to 0° with crushed ice, and 150 mL of dichloromethane was added with stirring. The reaction mixture was poured into a 2-L beaker containing 500 mL of water and 500 mL of crushed ice; material remaining in the flask was rinsed into the beaker with 10 mL of dichloromethane. The mixture was stirred thoroughly, further salts being precipitated, until the ice melted, and filtered into a cooled filter flask under reduced pressure through a sintered or Büchner funnel and a kieselguhr filter-aid cake. The beaker and filter cake were washed with 50 mL of dichloromethane, and the clear combined filtrates were transferred to a 2-L separatory funnel while still cold.

The mixture was shaken vigorously, the lower layer was separated and stored in ice, and the aqueous layer was extracted with two 50-mL portions of dichloromethane. The combined organic extracts were shaken with 100 mL of ice-cold, concentrated aqueous ammonia (35% w/w), filtered through a filter-aid cake, and separated. The extraction and filtration were repeated with fresh ammonia solution using the same filter. The filter was washed with 50 mL of dichloromethane, and the organic layer was separated and dried over $MgSO_4$. The dried solution was filtered, the filter was washed with 50 mL of dichloromethane, and the solvent was removed on a rotary evaporator at 30°. The flask containing the residual oil was cooled to 0° before exposure to air.

The light-yellow oil was dissolved in 60 mL of 30% anhydrous diethyl ether in pentane and treated with 2 g of Na_2SO_4 and 0.5 g of decolorizing carbon. The mixture was swirled for a few minutes, allowed to settle, and filtered by gravity through three sheets of fine filter paper into a 100-mL round-bottomed flask with a 14/20 joint. The filter was washed with 10 mL of pentane, and the flask was sealed by wiring on a 14-mm serum cap. The flask was placed on a cork ring, lowered into an insulated container (large Dewar bottle, Styrofoam box, etc.) half filled with dry ice, and cooled slowly to –78°. When crystallization was complete, a nitrogen supply was connected to the flask *via* a syringe needle; the supernatant liquid was then withdrawn by syringe and replaced with 50 mL of pentane, previously cooled to –78°.

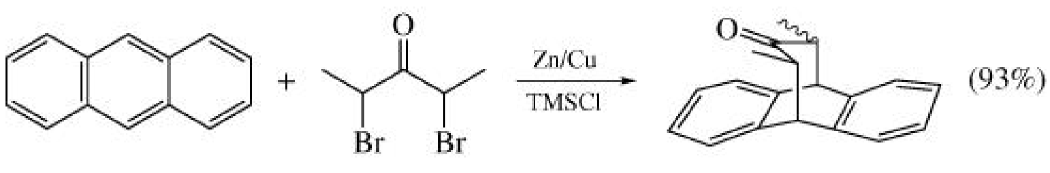
The flask was swirled, washing the crystals, and the pentane was withdrawn. The flask was connected to a vacuum (water pump) via the nitrogen inlet and warmed to room temperature. The crude cycloadduct (6.1–7.3 g, 40–48%) was isolated as colorless needles, mp 43.5–45°, from the first recrystallization. Pure 2 α ,4 α -dimethyl-8-oxabicyclo[3.2.1]oct-6-en-3-one can be obtained by crystallization from pentane at –78° with minimal loss, mp 45–46°.



6.1.2. 8-Acetyl-2,2,4,4,-tetramethyl-8-azabicyclo[3.2.1]oct-6-en-3-one(Reduction of an α , α'-Dibromoketone with Diiron nonacarbonyl) (8, 5)

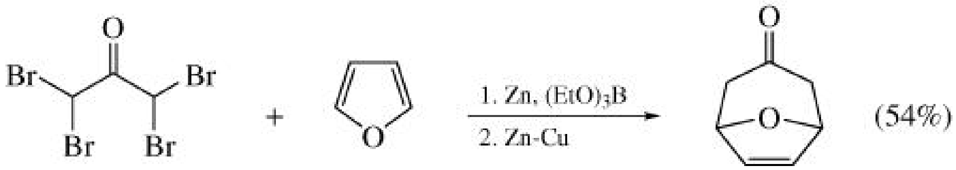
Into a 50-mL, two-necked flask equipped with a serum cap and a nitrogen balloon was placed 1.10 g (3.02 mmol) of diiron nonacarbonyl. After the system was flushed with nitrogen, 10 mL of dry benzene, 1.62 g (5.96 mmol) of 2,4-dibromo-2,4-dimethylpentan-3-one, and 218 mg (2.00 mmol) of *N*-acetylpyrrole, freshly distilled from sodium hydride, were successively added through the rubber septum by a syringe. The mixture was stirred at 40–50° for 18.5 hours. The reaction mixture was diluted with 15 mL of ethyl acetate, washed with three 10-mL portions of saturated aqueous $NaHCO_3$

solution followed by 5 mL of brine, and dried over Na_2SO_4. Concentration of the organic layer gave 1.2 g of an orange oil, which was subjected to column chromatography (25 g of silica gel). Elution with 1:3 ethyl acetate-*n*-hexane followed by evaporation of the solvents gave some unreacted starting dibromoketone. The fractions eluted with ethyl acetate afforded 302 mg (68%) of the title compound as pale yellow crystals. Recrystallization from hexane gave an analytical sample: IR (CCl_4)cm^{-1}: 1720, 1660; ^1H NMR(CCl_4) δ : 1.02 (s, 6 H), 1.23 (s, 3 H), 1.30 (s, 3 H), 2.08 (s, 3 H), 4.32 (bs, 1 H), 4.92 (bs, 1 H), 6.42 (bs, 2 H).



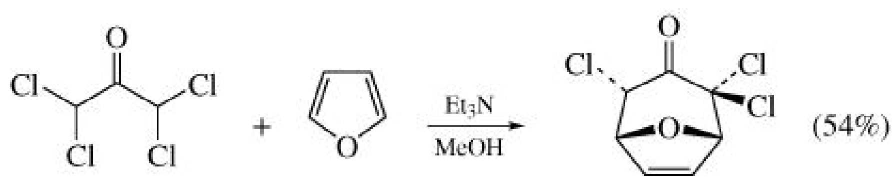
6.1.3. 11,13-Dimethyl-12-oxo-9,10-dihydro-9,10-propanoanthracene(Reduction with Zinc–Copper Couple in the Presence of Chlorotrimethylsilane) (29)

Anthracene (3 g, 16.9 mmol) was dissolved in benzene (30 mL) at 80°. Zinc dust (2 g, 32 mg-atom) and copper(I) chloride (0.32 g, 3.2 mmol) were added through a powder funnel, and the mixture was stirred for several minutes. Chlorotrimethylsilane (4.9 g, 36 mmol) was added, followed by 2,4-dibromopentan-3-one (7.45 g, 30 mmol) in benzene (5 mL). A second portion of zinc (2 g, 32 mg-atom) and copper(I) chloride (0.32 g, 3.2 mmol) was added and the mixture maintained at 80° for 4 hours. The hot reaction mixture was filtered to remove the Zn/Cu couple and the flask was rinsed with several portions of dichloromethane. On cooling, a solid mass precipitated and additional dichloromethane was added. The resulting solution was washed twice with saturated aqueous ammonium chloride solution, once with water, and once with saturated sodium chloride solution. The aqueous layers were washed with dichloromethane and the combined organic phase was dried over $MgSO_4$. The solvent was removed in vacuo and the crude product was chromatographed on silica gel (CH_2Cl_2 as eluent). This afforded 4.1 g (93%) of product as a mixture of epimers: ^1H NMR($CDCl_3$) δ 1.14 (d, *J* = 7 Hz, 6 H), 2.74 (d, q, *J* = 2.3, 7 Hz, 2 H), 3.80 (d, *J* = 7.3 Hz, 2 H), 7.22 (m, 8 H).



6.1.4. 8-Oxabicyclo[3.2.1]oct-6-en-3-one(Reduction of an α , α '-Haloketone Using the Zn/(EtO)$_3$B Method) (32)

A solution of 1,1,3,3-tetrabromopropanone (374 g, 1.0 mol) and triethyl borate (200 mL, 172 g, 1.2 mol) in dry THF (200 mL) was added during 1.5 hours to a mixture of zinc powder (68.6 g, 1.05 g-atom) and dry furan (136 g, 2.0 mol) in dry THF (200 mL) stirred under nitrogen and protected from light. The ensuing reaction heated the mixture to reflux, and the mixture was stirred overnight (19 hours) at room temperature. The mixture was then cooled to –15°, treated with water (200 mL), and stirred at 0° for 0.3 hour. Insoluble material was removed by filtration and washed with ether (500 mL), and the combined filtrates were diluted with water (800 mL). The heavy organic layer was separated, and the aqueous layer was extracted with ether (2 × 350 mL) which had first been used to wash further insoluble material. The combined organic layers were washed with saturated aqueous sodium chloride, dried, and concentrated at ca. 30°. The residue was treated with methanol (200 mL) and immediately added to a stirred and cooled (dry ice/acetone bath) mixture of powdered zinc-copper couple [from Zn, 230 g, 3.5 g-atom)] and ammonium chloride (250 g) in methanol (1 g/L) at a rate such that the internal temperature was maintained at 15–25°. The mixture was stirred overnight at room temperature under nitrogen and protected from light, and was then filtered. The solid was washed with dichloromethane (900 mL) and the combined filtrates were diluted with water (1.6 g/L), the organic layer was separated, and the aqueous layer was extracted with dichloromethane (300 mL + 4 × 150 mL). The combined organic layers were dried and the solvent was removed by distillation, initially at atmospheric pressure and then under reduced pressure; direct distillation (no condenser) in vacuo of the magnetically stirred residue (from a flask heated in a hot-water bath up to 100°) into a cooled (dry ice acetone) flask gave the ketone (67.1 g, 54%) (distillation temperature ca. 40–80° at 0.3 mmHg) as a white crystalline solid, mp 38–39° (lit., (34) 38°). The product was stored in the dark at –20° under argon.

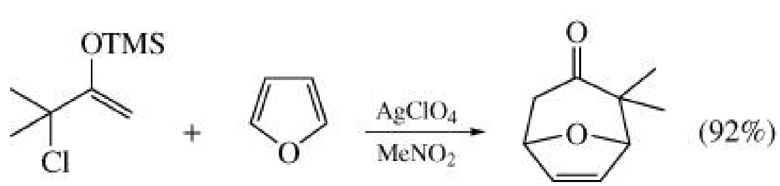


6.1.5. 2,2,4-endo-Trichloro-8-oxabicyclo[3.2.1]oct-6-en-3-one (Base-Promoted Cycloaddition Between a Haloketone and a Diene) (71)

1,1,3,3-Tetrachloro-propan-2-one (1.96 g, 10 mmol) was added with stirring to a mixture of furan (10 mL), methanol (10 mL), and triethylamine (1.11 g, 11 mmol); stirring was continued at room temperature for 3 days. At this time, the yellow-brown solution was poured into water (100 mL) and extracted with diethyl ether (5 × 40 mL). The combined ether extracts were washed with saturated aqueous sodium chloride solution (40 mL) and dried over $MgSO_4$. The solvent was removed in vacuo and the solid residue was dissolved in a few mL of diethyl ether. Cooling (+5°) afforded colorless crystals (640 mg). Distillation of the mother liquor (Kugelrohr at 90–100°/0.002 Torr) gave a second crop. Total yield of product 1.232 g (54%) mp 88–89°, ^{1}H NMR(C_6D_6 δ 4.26 (dd, *J* = 4.6, 1.6 Hz, 1 H), 4.46 (d, *J* = 4.6 Hz, 1 H), 4.54 (d, *J* = 1.6 Hz, 1 H).

6.1.6. endo-2,endo-4- and exo-2,exo-4-Dimethylbicyclo[3.2.1]oct-6-en-3-one (Base-Mediated Cycloaddition Between a Monohaloketone and a Diene) (72)

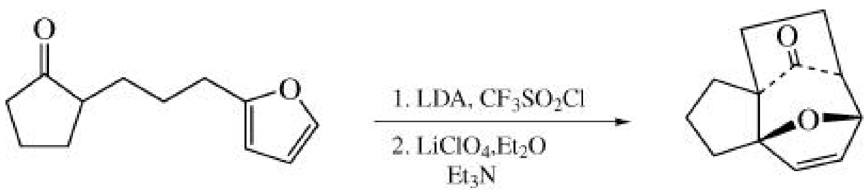
To a mixture of 2-bromopentan-3-one (1.65 g, 10 mmol) and freshly distilled cyclopentadiene (10 mL) was added dropwise at room temperature a solution of sodium 2,2,3,3-tetrafluoropropoxide in 2,2,3,3-tetrafluoro-1-propanol (1 M, 10 mL). The resulting mixture was allowed to stir for 20 hours at which time diethyl ether (20 mL) was added and the mixture filtered. The solvent was removed in vacuo and the residue was distilled (Kugelrohr, 100–120° at 11 Torr) to afford 1.07 g (71%) of an oil consisting of an epimeric mixture of cycloadducts.



6.1.7. 2,2-Dimethyl-8-oxabicyclo[3.2.1]oct-6-en-3-one(Silver Salt-Promoted Cycloaddition Between a Silyloxyallyl Chloride and a Diene) (19)

To a well-stirred mixture of silver perchlorate (2.25 g, 10 mmol), calcium carbonate (2 g), and furan (1.7 g, 25 mmol) in nitromethane (20 mL) at 0° was added a solution of 1,1-dimethyl-2-(trimethylsilyloxy)allyl chloride (1 g, 5.2 mmol) in nitromethane (5 mL) over a period of 15 minutes. The resulting mixture was stirred for 15 minutes at 0° and then diluted with ether (40 mL). Sodium chloride solution was added until the inorganic materials aggregated. The organic layer was separated, washed with Na_2CO_3 solution, dried, and the solvent removed in vacuo to afford crude product. The product was isolated by chromatography on alumina to yield 727 mg (92%) of product as colorless crystals: mp 46–47°.

CAUTION: Silver perchlorate is a fire and explosion hazard. It should be kept away from open flames and from sources of heat or sparks; contact with combustible materials can cause fires. Silver perchlorate forms solvent complexes with many common solvents, including benzene, pyridine, and ethanol. These complexes, as well as silver perchlorate itself, can explode when subjected to impact or friction.



6.1.8. (±)-(3a α ,6 α ,7 β ,9a β)-2,3,6,7,8,9-Hexahydro-3a,b-epoxy-7,9a-methano-1H-cyclopentacyclocten-10-one (Intramolecular Cycloaddition) (55)

To a solution of diisopropylamine (290 mg, 2.85 mmol) in freshly distilled THF (6.55 mL) was added *n*-BuLi (1.04 mL of a 2.5 M solution) at –78°. After stirring for 15 minutes at this temperature, 2-[3-(2-furanyl)propyl]cyclopentanone (500 mg, 2.6 mmol) in THF (6.5 mL) was added dropwise via syringe with stirring over a 10-minute period. The reaction mixture was then stirred for an additional 30 minutes, at which time trifluoromethanesulfonyl chloride (526 mg, 3.1 mmol) was added. The reaction mixture was stirred for 5–10 minutes and then removed from the cold bath and quenched with water. The reaction mixture was diluted with ether (12 mL) and worked up. The crude chloroketone was dissolved in freshly distilled ether (26 mL). Anhydrous $LiClO_4$ (8.3 g, 78 mmol) and freshly distilled triethylamine (790 mg, 7.8 mmol) were added. The mixture was allowed to stir at room temperature for 12–48 hours. Column chromatography (silica gel, 12% ethyl acetate/hexanes) of the crude reaction mixture gave the cycloadduct as a mixture favoring the *endo* isomer in 53% yield. Recrystallization (hexanes) gave the major isomer: mp 83°, ^1H NMR($CDCl_3$) δ 6.28 (bd, *J* = 5.7 Hz, 1 H), 6.09 (d, *J* = 5.8 Hz, 1 H), 4.69 (dd, *J* = 1.5, 3.4 Hz, 1 H), 2.41 (dd, *J* = 4.0, 5.6 Hz, 1 H), 2.17–2.12 (m, 1 H), 2.08–1.99 (m, 3 H), 1.94–1.69 (m, 4 H), 1.5–1.4 (m, 2 H). [**CAUTION:** Lithium perchlorate should be handled with the same precautions as silver perchlorate (see above).]

7. Tabular Survey

[4 + 3] Cycloaddition reactions are grouped in Tables I–VI according to the reaction conditions employed to generate the allyl cation reaction partner and follow the order of topics discussed in the Scope and Limitations section [Table I (Reductive Conditions); Table II (Solvolysis Conditions); Table III (Base Conditions); Table IV (Photochemical); Table V (Intramolecular); and Table VI (Miscellaneous Examples)]. Tables I–III are further divided into subcategories related to the types of 4 π reaction partners involved. Table I (Reductive Conditions) includes all of the entries surveyed in Noyori and Hayakawa's *Organic Reactions* chapter on "Reductive Dehalogenations" (1983, Vol. 29, pp. 163–344) as well as all subsequent examples published until mid-1996. Miscellaneous reaction conditions, such as metal-promoted cycloadditions, that could not be placed in Tables I–V are collected in Table VI.

Within each table, the reactions are listed according to increasing carbon number in the oxyallyl cation precursor, and the count is based on the total number of carbon atoms in these reactants that also appear in the final product. For example, spectator ligands around a metal center or carbons in a leaving group are not included in the count.

Yields are given in parentheses, and a dash indicates that no yields or experimental conditions were provided in the original reference.

The following abbreviations are used in the tables:

Ac	acetyl
C_3H_5	cyclopropyl
Et_2O	diethyl ether
DME	1,2-dimethoxyethane
THF	tetrahydrofuran
TBDMS	*tert*-butyldimethylsilyl

Table I. [4 + 3] Cycloaddition of Haloketones (Reductive Conditions) A. With Open-Chain 1,3-Dienes

View PDF

Table I. [4 + 3] Cycloaddition of Haloketones (Reductive Conditions) B. With Carbocyclic Dienes

View PDF

Table I. [4 + 3] Cycloaddition of Haloketones (Reductive Conditions) C. With Pyrrole Derivatives

View PDF

Table I. [4 + 3] Cycloaddition of Haloketones (Reductive Conditions) D. With Furan Derivatives

View PDF

Table I. [4 + p3] Cycloaddition of Haloketones (Reductive Conditions) E. With Anthracene

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Table II. [4 + 3] Cycloaddition of Allyl Cations (Solvolytic Conditions) A. With Open-Chain 1,3-Dienes

View PDF

Table II. [4 + 3] Cycloaddition of Allyl Cations (Solvolytic Conditions) B. With Carbocyclic Dienes

View PDF

Table II. [4 + 3] Cycloaddition of Allyl Cations (Solvolytic Conditions) C. With Pyrrole Derivatives

View PDF

Table II. [4 + 3] Cycloaddition of Allyl Cations (Solvolytic Conditions) D. With Furan Derivatives

View PDF

Table III. [4 + 3] Cycloaddition of Haloketones (Base Conditions) A. With Open-Chain 1,3-Dienes

View PDF

Table III. [4 + 3] Cycloaddition of Haloketones (Base Conditions) B. With Carbocyclic Dienes

View PDF

Table III. [4 + 3] Cycloaddition of Haloketones (Base Conditions) C. With Pyrrole Derivatives

View PDF

Table III. [4 + 3] Cycloaddition of Haloketones (Base Conditions) D. With Furan Derivatives

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Table IV. Photoinitiated [4 + 3] Cycloadditions A. With Carbocyclic Dienes

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Table IV. Photoinitiated [4 + 3] Cycloadditions B. With Furan

View PDF

Table V. Intramolecular [4 + 3] Cycloadditions

View PDF

Table VI. Miscellaneous [4 + 3] Cycloadditions

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TABLE I. [4+3] CYCLOADDITION OF HALOKETONES (REDUCTIVE CONDITIONS)

A. With Open-Chain 1,3-Dienes

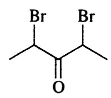
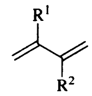
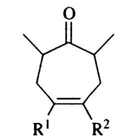
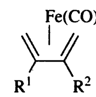
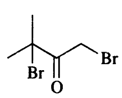
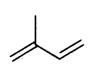
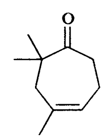
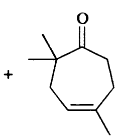
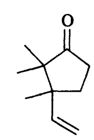
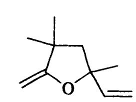
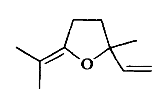
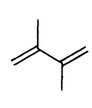
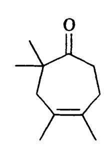
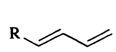
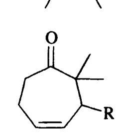
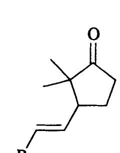
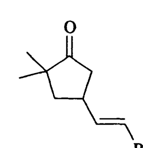
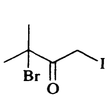
Haloketone	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5 				
	R^1 / R^2			
	$Fe_2(CO)_9$ H / H	C_6H_6, 80°, 16 h	(30)	8,73
	H / Me	*hv*, C_6H_6, 25°, 36 h	(36)	8,73
	$CeCl_3$-$SnCl_2$ H / Me	THF, 0° to rt, 5 h	(37)	74
	Me / Me	C_6H_6, 60°, 34 h	(46)	8,73
	$CeCl_3$-$SnCl_2$ Me / Me	THF, 0° to rt, 5 h	(48)	74
	$(CH_2)_4$	C_6H_6, 63°, 46 h	(80)	8
	$C(Me)(CN)CH_2$	C_6H_6, 60°, 1.5 h	(65)	75
				
	R^1 / R^2			
	H / H	C_6H_6, 80°, 16 h	(40)	8,73
	H / Me	C_6H_6, 120°, 12 h	(51)	8
	Me / Me	C_6H_6, 120°, 4 h	(33)	8
			 A +  B +  C +  D +  E	
	CuI, LiI	MeCN, <30°, 9 h	(—) (A/B/C):(D/E) = 2:26	76
	CuI, NaI	MeCN, <30°, 9 h	(—) (A/B/C):(D/E) = 2:43	76
	CuI, NaI	DME, <30°, 9 h	(—) (A/B/C):(D/E) = 2:33	76
	Cu, *n*-Bu_4NI	MeCN, <30°, 9 h	(—) (A/B/C):(D/E) = 2:16	76
	$CeCl_3$, $SnCl_2$, 	THF, 0° to rt	 (37)	74
	Zn/Cu, 		 A +  B +  C	
	R = H	MeCN, DME	(1) A:B = 93:7	77
	R = Me	1. MeCN, DME, 10°, 1.5 h 2. 25°, 24 h	(8) A:B = 62:38	77
	R = Me	Isopentane	(20) A:B:C = 26:65:9	77

TABLE I. [4+3] CYCLOADDITION OF HALOKETONES (REDUCTIVE CONDITIONS) (*Continued*)

A. With Open-Chain 1,3-Dienes (*Continued*)

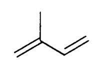
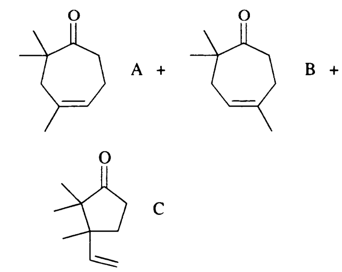
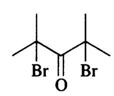
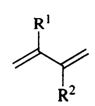
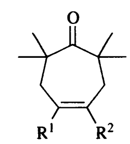
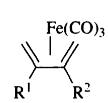
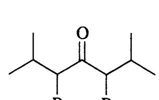
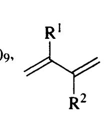
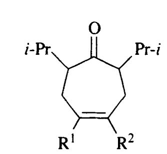
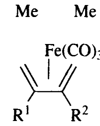
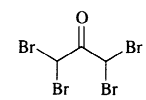
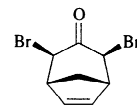
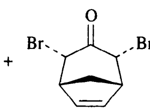
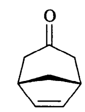
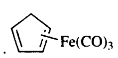
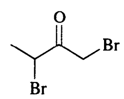
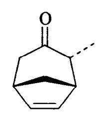
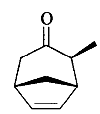
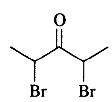
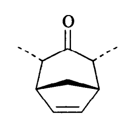
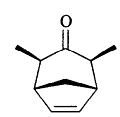
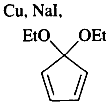
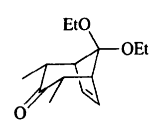
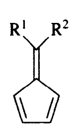
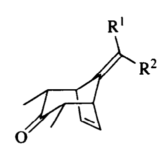
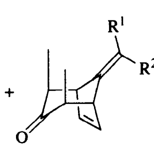
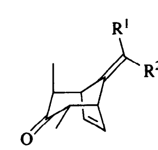
Haloketone	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
			 A + B + C	
	Zn/Cu	C_6H_6, isopentane or DME	A/B/C (23 : 54: 23) (12)	78,77
	Zn/Cu	MeCN, DME, 10°, 24 h	A/B/C (48 : 43 : 9) (5)	78
	Hg, NaI	MeCN	(—)	73
	$Fe_2(CO)_9$	C_6H_6, 57°, 10 h	A/B/C (26 : 46 : 30) (—)	78
	$Fe_2(CO)_9$	C_6H_6, 57°, 20 h	A/B/C (22 : 43 : 30) (—)	78
	$Fe_2(CO)_9$	C_6H_6, 60 to 80°, 12 h	A/B/C (11 : 28 : 61) (—)	78
	$Fe_2(CO)_9$	C_6H_6, reflux, 4.5 h	A/B/C (— : 1 : 3.6) (—)	78
C_7 				
	R^1 / R^2			
	$Fe_2(CO)_9$ H / H	C_6H_6, 60°, 38 h	(33)	8,73
	H / Me	C_6H_6, 65°, 38 h	(47)	8,73
	Me / Me	C_6H_6, 60°, 38 h	(71)	8,73
	$CeCl_3$-$SnCl_2$ Me / Me	THF, 0°	(30)	74
	$Fe_2(CO)_9$ $CH_2CH(COMe)(CH_2)_2$	C_6H_6, 65°	(71)	79
	$CH_2C(CO_2Et)_2OCH_2$	C_6H_6, 65°	(47)	79
				
	R^1 / R^2			
	H / H	C_6H_6, 80°, 4 h	(90)	8,73
	H / Me	C_6H_6, 87°, 12 h	(70)	8,73
	Me / Me	C_6H_6, 80°, 12 h	(100)	8
C_9 	$Fe_2(CO)_9$, 			
	R^1 / R^2			
	H / H	C_6H_6, 90°, 12 h	(44)	8,73
	H / Me	*h*ν, C_6H_6, 25°, 36 h	(31)	8,73
	Me / Me	C_6H_6, 60°, 38 h	(36)	8
				
	R^1 / R^2			
	H / H	C_6H_6, 70°, 40 h	(77)	8,73
	Me / Me	C_6H_6, 120°, 20 h	(55)	8,73

TABLE I. [4+3] CYCLOADDITION OF HALOKETONES (REDUCTIVE CONDITIONS) (*Continued*)

B. With Carbocyclic Dienes

Haloketone	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3 	Zn, cyclopentadiene, $(EtO)_3B$	THF, 15 h	 (12) +  (25) + A B  C (8)	31
	1. $Fe(CO)_5$, cyclopentadiene 2. Zn/Cu, NH_4Cl	THF/C_6H_6, 80°, 30-40 min MeOH, 15 min	C (60, 47)	8,80,81
	1.  2. Zn/Cu, NH_4Cl	Ether, 14 h MeOH, 18 h	C (60, 47)	82
C_4 	Zn, cyclopentadiene, $(EtO)_3B$	THF, 15 h	 (8) +  (6)	31
C_5 	Cyclopentadiene		 A +  B	
	Cu, NaI	MeCN, 4.5 h	A/B (6.4 : 1) (91)	18
	Cu, NaI	MeCN, 50°, 2 h	A/B (6.4 : 1) (82)	83
	Zn/Cu	DME, –10°	A/B (1.67 : 1) (—)	26,84
	$Fe_2(CO)_9$	C_6H_6, 60°, 25 h	A/B (47 : 53) (86)	8,73
	$CeCl_3$-$SnCl_2$	THF, 0°	A/B (72 : 73) (88)	74
	Zn/CuCl, TMSCl	dioxane, sonication, 3 h	(90)	85
	Zn/Cu, TMSCl	dioxane, 20°, 24 h	(65)	85
	$Fe_2(CO)_9$	C_6H_6, 40-90°, 12-80 h	(81)	85
	Cu, NaI, 	MeCN, 20°, 18 h	 (11)	18
			 A +  B +  C	

	R^1	R^2	Conditions	Product(s) and Yield(s) (%)	Refs.
Cu, NaI	Me	Me	MeCN, 20°, 24.5 h	A/B (4.6 : 1) (80)	18
	H	OAc	MeCN, 20°, 18 h	A/C (5.2 : 1) (70, 33)	18
Zn/Cu	Me	Me	DME, –15°, 2 h	A/B/C (12.2 : 10 : 1) (—)	18
	Me	Me	—	A/C (ca. 5 : 1) (60)	86
	Me	*t*-Bu	—	A/B/C (20 : 1 : 1) (60)	86
	Me	Ph	—	A/B/C (5 : 1 : trace) (60)	86

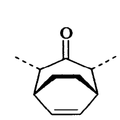
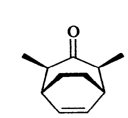
Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
$Fe_2(CO)_9$, 1,3-cyclohexadiene	C_6H_6, 30°, 24 h	 (52) +  (34)	87

TABLE I. [4+3] CYCLOADDITION OF HALOKETONES (REDUCTIVE CONDITIONS) (*Continued*)

B. With Carbocyclic Dienes (*Continued*)

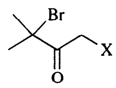
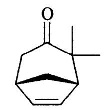
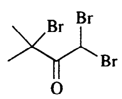
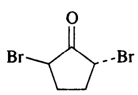
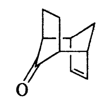
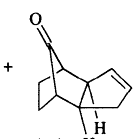
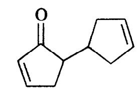
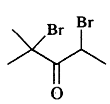
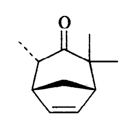
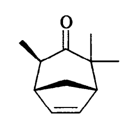
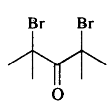
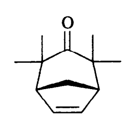
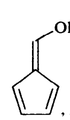
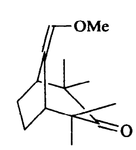
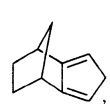
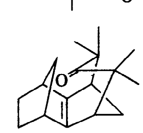
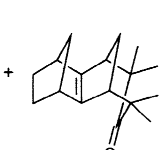
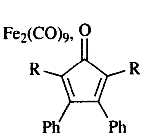
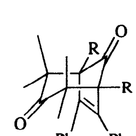
Haloketone	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
	Cyclopentadiene		 I	
X = Br	Zn, $(EtO)_3B$	THF, overnight	(55)	31
	Zn/Cu	—	(30)	26,84
	$CeCl_3$-$SnCl_2$	THF, 0° to rt	(71)	74
	Zn-Cu	dioxane, sonication	(81)	85
X = I	Zn, $(EtO)_3B$	THF, overnight	(76)	31
	1. $Fe_2(CO)_9$, cyclopentadiene 2. Zn/Cu, NH_4Cl	1. THF, C_6H_6, 80°, 70 min 2. MeOH, 20 min	I (83, 66)	88,8
	$Fe_2(CO)_9$, cyclopentadiene	—	 (—) +  (—) +  (—)	89
	Cyclopentadiene		 A +  B	
	Zn, $(EtO)_3B$	THF, overnight	A/B (2.2 : 1) (78)	31
	Zn/Cu	DME, –5 to 0°	A/B (3.8 : 1) (60)	26,84
C_7 				
	Zn/Cu, cyclopentadiene	DME, –5° to rt	(65)	26, 84
	$Fe_2(CO)_9$	C_6H_6, 60°, 38 h	(82, 71)	8, 73
	Zn/CuCl, TMSCl	dioxane, 5 °, 12 h	(55)	30
	$CeCl_3$-$SnCl_2$	THF, 0°	(70)	74
	Zn/Cu	dioxane, sonication	(88)	85
	, $Fe_2(CO)_9$	—	 (56)	90
	, $Fe_2(CO)_9$	C_6H_6, 60°, 36 h	 (29) +  (7)	20
	$Fe_2(CO)_9$, 			
	R			
	Me	C_6H_6, 50°, 35 h	(35)	91
	Et	C_6H_6, 60°, 16 h	(29)	91
	n-Pr	C_6H_6, 50°, 34 h	(26)	91
	n-Bu	C_6H_6, 60°, 32 h	(22)	91
	Ph	—	(0)	91

TABLE I. [4+3] CYCLOADDITION OF HALOKETONES (REDUCTIVE CONDITIONS) (*Continued*)

B. With Carbocyclic Dienes (*Continued*)

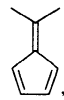
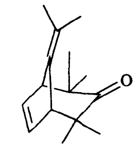
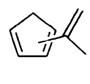
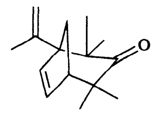
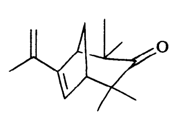
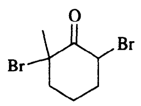
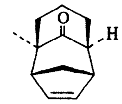
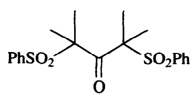
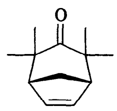
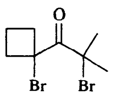
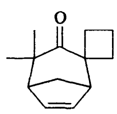
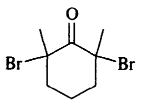
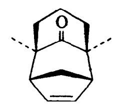
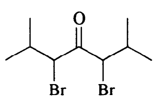
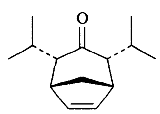
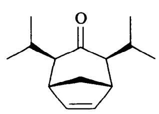
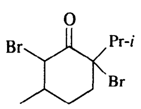
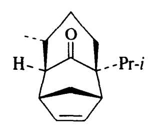
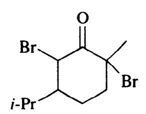
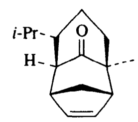
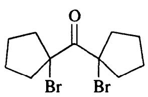
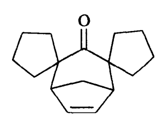
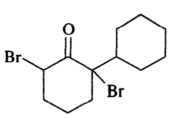
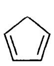
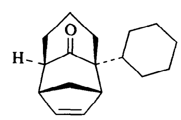
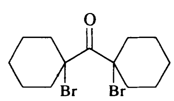
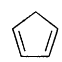
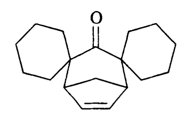
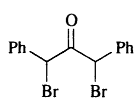
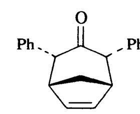
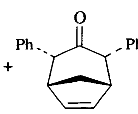
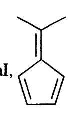
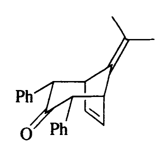
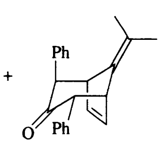
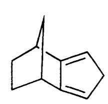
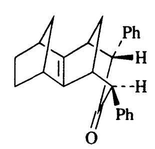
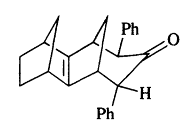
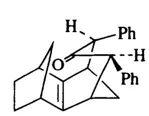
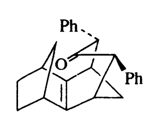
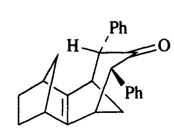
Haloketone	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
	, Zn/CuCl, TMSCl	DME, 0° to rt	 (3)	92
	, Zn/CuCl, TMSCl	DME, 0° to rt	 (12) +  (—)	92
	, NaI/Cu	MeCN, rt, 6 h	 (25)	93
	, $Fe_2(CO)_9$, $TiCl_4$	CH_2Cl_2, 0°	 (32)	94
	, Zn/Cu	Dioxane, sonication	 (84)	85
	, NaI, Cu	MeCN, rt, 6 h	 (18)	93
C_9 	$Fe_2(CO)_9$, cyclopentadiene	C_6H_6, 90°, 12 h	 (47) +  (43)	8, 73
C_{10} 	, NaI/Cu	MeCN, rt, 6 h	 I (30)	93
	, $Zn/(EtO)_3B$	THF, 5 h	I (5)	93
	, NaI/Cu	MeCN, rt, 6 h	 (41)	93
C_{11} 	, Zn/Cu	Dioxane, sonication	 (71)	85
C_{12} 	, NaI/Cu	MeCN, rt, 6 h	 (13)	93

TABLE I. [4+3] CYCLOADDITION OF HALOKETONES (REDUCTIVE CONDITIONS) (*Continued*)

B. With Carbocyclic Dienes (*Continued*)

Haloketone	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{13} 	, Zn/Cu	Dioxane, sonication	 I (71)	85
	, Zn/Cu	Dioxane, rt	I (26)	85
C_{15} 	NaI, cyclopentadiene	MeCN, reflux, 15 min	 (40) +  (60)	96
	NaI/Cu	Acetone	No reaction	97
	NaI, 	Acetone	 +  (total 90)	86
	, X		 A +  B +  C +  D +  E	20, 21

X		A	B	C	D	E
NaI, Cu	MeCN, acetone, rt, 5 h	1.6	2.8	0.3	5.3	11.8
NaI	MeCN, acetone, reflux, 1 h	—	3	—	18	6
Zn-Cu	Glyme, rt, 15 h	—	0.5	1.7	2.1	1.7
$Fe_2(CO)_9$	THF, rt, 6 h	—	2.5	0.3	22.6	10.3
$Fe_2(CO)_9$	C_6H_6, rt, 6 h	—	0.3	6	9	2.3

TABLE I. [4+3] CYCLOADDITION OF HALOKETONES (REDUCTIVE CONDITIONS) (*Continued*)

C. With Pyrrole Derivatives

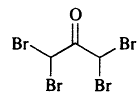
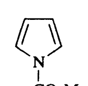
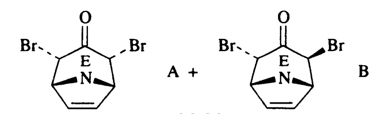
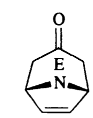
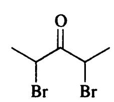
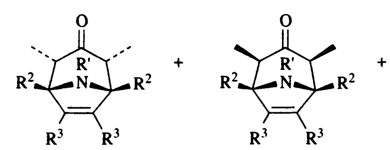
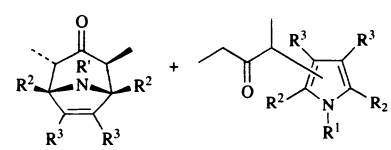
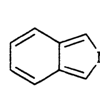
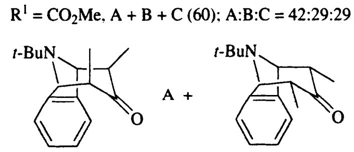
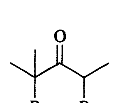
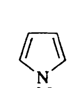
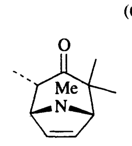
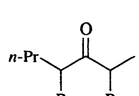
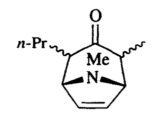
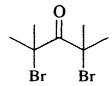
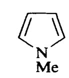
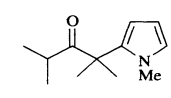
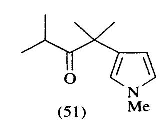
Haloketone	Reactants	R^1	R^2	R^3	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3 						 E = CO_2Me	
	Zn/Cu				DME, –5°, 2.5 h	A (30)	28
	$Fe_2(CO)_9$				C_6H_6, 50°, 72 h	A/B (2 : 1) (70, 52)	28, 98
	1. Zn/Cu 2. Zn/Cu, NH_4Cl				1. DME, –5 to 10°, 1 h 2. 25°, 2 h 3. MeOH, 5 min	 I (25) E = CO_2Me	28
	1. $Fe_2(CO)_9$ 2. Zn/Cu, NH_4Cl				C_6H_6, 50°, 72 h MeOH, 3 h	I (57)	28
C_5 						 	
	Cu, NaI	H	H	H	MeCN, 3-4 h	A + B (65) A:B = 6:1	9
	Cu, NaI	Me	H	H	MeCN, 3-4 h	A (89)	9
	Cu, NaI	Me	H	H	MeCN, 8 h	B (52)	27, 99
	Cu, NaI	Ph	H	H	MeCN, 20°, 4 h	A (—)	18
	Cu, NaI	H	Me	H	MeCN, 3-4 h	A (66)	9
	Cu, NaI	H	Me	Me	MeCN, 3-4 h	A (50)	9
	Cu, NaI	Me	Me	H	MeCN, 3-4 h	A (74)	9
	Zn/Cu	Me	H	H	—	α-D (60)	27, 99
	$Fe_2(CO)_9$	Me	H	H	C_6H_6, 40°, 70 h	α-D (48), β-D (60)	8, 100, 101
	$Fe_2(CO)_9$	Et	H	H	*hν*, C_6H_6, 10 h	R^1 = CO_2Me, A + B + C (60); A:B:C = 42:29:29	8
	 NBu-*t*, NaI/Cu				MeCN	 (60) A:B = 1:24	102
C_6 	 , Cu, NaI				MeCN, 3-4 h	 (70)	9
C_7 	Cu, NaI				MeCN	 (57)	27, 99
	 , $Fe_2(CO)_9$				C_6H_6, 40°, 18 h	 (31) +  (51)	8, 101

TABLE I. [4+3] CYCLOADDITION OF HALOKETONES (REDUCTIVE CONDITIONS) (*Continued*)

C. With Pyrrole Derivatives (*Continued*)

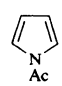
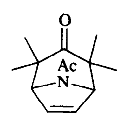
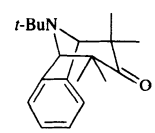
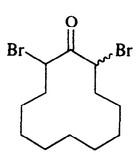
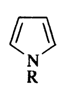
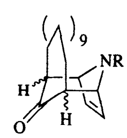
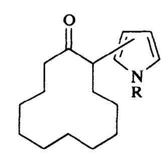
Haloketone	Reactants		Conditions	Product(s) and Yield(s) (%)	Refs.
	, $Fe_2(CO)_9$		C_6H_6, 40 - 50°, 18.5 h	 (68)	8, 100
	Zn/CuCl, ultrasound		Dioxane	 (43)	102
C_{12}  I				 A +  B	5
		R			
cis-I	Cu, NaI	Me	MeCN, C_6H_6, 50°, 48 h	α-B (34)	
	Cu, NaI	TMS	MeCN, C_6H_6,, 24 h	α-B, R = H (—); β-B, R = H (—)	
	$Fe_2(CO)_9$	Et	C_6H_6, 50°, 48 h	A, R = CO_2Me (77)	
	$Fe_2(CO)_9$	$CO_2CH_2CCl_3$	C_6H_6, 64°, 2 h	A (58), α-B (19)	
	$Fe_2(CO)_9$	CO_2Bu-*t*	C_6H_6, 50°, 21 h	A (5); α-B, R = H (2)	
	$Fe_2(CO)_9$	CO_2Bn	C_6H_6, 91°, 2 h	A (58); α-B (14)	
trans-I	Cu, NaI	Me	MeCN, C_6H_6, 50°, 48 h	α-B (5)	

TABLE I. [4+3] CYCLOADDITION OF HALOKETONES (REDUCTIVE CONDITIONS) (*Continued*)

D. With Furan Derivatives

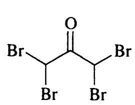
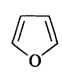
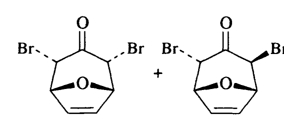
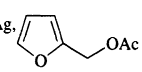
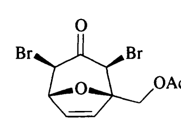
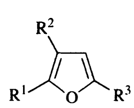
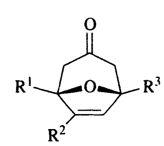
Haloketone	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3 			 A B	
	Zn, $(EtO)_3B$	THF, 15 h	A (30)	31, 27, 99, 103, 104, 32
	Zn/Ag	1. THF, –10°, 2 h 2. 25°, 12 h	A (65)	105, 106
	$Fe_2(CO)_9$	Reflux, 48 h	A + B (63), A:B = 9:1	8, 81, 107, 107a
	Zn, Ag, 	1. THF, –10°, 10 min 2. 20°, 12 h	 (52)	5
				
	R^1 / R^2 / R^3			
	1. Zn/Ag — H, H, H 2. Zn/Cu, NH_4Cl	1. THF, –10°, 2 h 2. 25°, 12 h MeOH, 15 min	(55)	105
	1. Zn/Ag — H, OBn, H 2. Zn/Cu, NH_4Cl	1. THF, 0°, 1 h 2. 20°, 48 h MeOH, 25°, 1 h	(14)	108
	1. Zn/Ag — H, OTHP, H 2. Zn/Cu, NH_4Cl	1. THF, 0°, 1 h 2. 20°, 60 h MeOH, 20°, 2 h	(31)	5, 109

TABLE I. [4+3] CYCLOADDITION OF HALOKETONES (REDUCTIVE CONDITIONS) (*Continued*)

D. With Furan Derivatives (*Continued*)

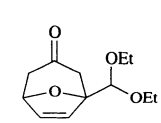
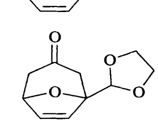
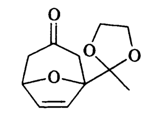
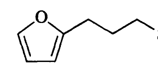
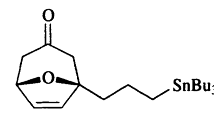
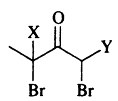
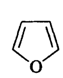
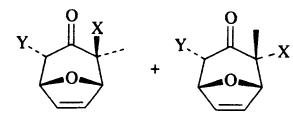
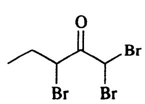
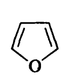
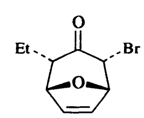
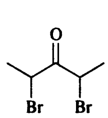
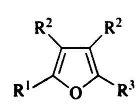
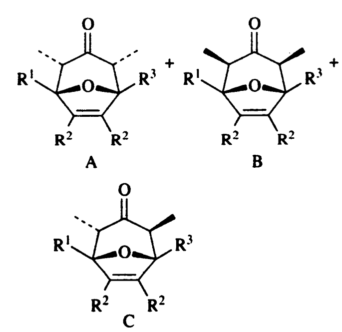
Haloketone	Reactants	R^1	R^2	R^3	Conditions	Product(s) and Yield(s) (%)	Refs.
	1. Zn/Ag	H	OBn	H	1. THF, –10°, 1 h	(35)	5
					2. 30°, 49 h		
	2. Zn/Cu, NH_4Cl				3. MeOH, 0°, 2 h		
					4. 25°, 1 h		
	1. Zn/Ag	H	OAc	H	THF, 20°, 12 h	(46)	110
	2. Zn/Cu, NH_4Cl				MeOH, 20°, 1 h		
	1. Zn/Ag	H	Me	H	THF, 20°	(60)	111
	2. Zn/Cu, NH_4Cl				MeOH, 20°		
	1. Zn/Ag	H	Me	H	THF, 20°, 14 h	(86)	112
	2. Zn/Cu, NH_4Cl				MeOH, 20°, 1 h		
	1. Zn/Ag	Me	H	Me	THF, 20°, 12 h	(66)	113, 114
	2. Zn/Cu, NH_4Cl				1. MeOH, 0°, 2 h		
					2. 20°, 1 h		
	1. Zn/Ag	H	Bu-*t*	H	1. THF, 0°, 2 h	(23)	5, 108
					2. 20°, 6 h		
	2. Zn/Cu, NH_4Cl				MeOH, 20°, 1 h		
	1. Zn/Ag	H	C_5H_{11}-*n*	H	1. THF, 0°, 1 h	(20)	5, 108
					2. 30°, 48 h		
	2. Zn/Cu, NH_4Cl				MeOH, 15°, 2 h		
	1. Zn/Ag	H	H	C_5H_{11}-*n*	1. THF, –10°, 1 h	(50)	5
					2. 25°, 12 h		
	2. Zn/Cu, NH_4Cl				MeOH, 1 h		
	1. Zn/Ag	H	H	Ph	1. THF, –10 to 25°, 1 h	(62)	5
					2. 25°, 40 h		
	2. Zn/Cu, NH_4Cl				MeOH, 2 h		
	1. Zn/Ag	H	Ph	H	1. THF, –10°, 30 min	(22)	5
					2. 20°, 48 h		
	2. Zn/Cu, NH_4Cl				MeOH, 2 h		
		R^1	R^2	R^3			
	1. Zn/Ag	Me	H	Me	1. THF, –10°, 30 min	(66)	5
					2. 20°, 48 h		
	2. Zn/Cu, NH_4Cl				MeOH, 2 h		
	1. Zn/Ag	C_5H_{11}-*n*	H	C_5H_{11}-*n*	1. THF, –10°, 1 h	(41)	5, 113
					2. 20°, 24 h		
	2. Zn/Cu, NH_4Cl				MeOH, 0°, 4 h		
	1. Zn/Ag	Ph	H	Ph	1. THF, –10°, 10 min	(53)	5
					2. 20°, 12 h		
	2. Zn/Cu, NH_4Cl				MeOH, 20°, 1 h		
	1. $Fe_2(CO)_9$	H	H	H	Reflux, 48 h	(63)	8
	2. Zn/Cu, NH_4Cl				MeOH, 15 min		
	1. $Fe_2(CO)_9$	H	H	Br	C_6H_6, 60°, 3 h	(44)	5
	2. Zn/Cu, NH_4Cl				MeOH, 15 min		
	1. $Fe_2(CO)_9$	H	H	Me	C_6H_6, 60°, 5 h	(70)	111, 107
	2. Zn/Cu, NH_4Cl				MeOH, 25°, 1 h		
	1. $Fe_2(CO)_9$	H	H	Pr-*i*	C_6H_6, 60°, 2 h	(47)	115, 81
	2. Zn/Cu, NH_4Cl				MeOH, 30 h		
	1. $Fe_2(CO)_9$	H	Pr-*i*	H	C_6H_6, 60°, 2.5 h	(71)	115, 116
	2. Zn/Cu, NH_4Cl				MeOH, 20 min		
	1. $Fe_2(CO)_9$	H	H	C_5H_{11}-*n*	C_6H_6, 60°, 5 h	(67)	5, 111
	2. Zn/Cu, NH_4Cl				MeOH, 25°, 1 h		
	1. $Fe_2(CO)_9$	H	H	Ph	C_6H_6, 60°, 5 h	(63)	117
	2. Zn/Cu, NH_4Cl				MeOH, 25°, 1 h		
	$Fe_2(CO)_9$, $R^1 = R^2 = H$, $R^3 = CH(OEt)_2$				C_6H_6, 65°, 2 d	 (30)	118
	$Fe_2(CO)_9$, $R^1 = R^2 = H$, $R^3 = \underline{CHOCH_2CH_2O}$				C_6H_6, 65°, 2 d	 (15)	118

TABLE I. [4+3] CYCLOADDITION OF HALOKETONES (REDUCTIVE CONDITIONS) *(Continued)*

D. With Furan Derivatives *(Continued)*

Haloketone	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
	$Fe_2(CO)_9$, $R^1 = R^2 = H$, $R^3 = C(Me)OCH_2CH_2O$	C_6H_6, 65°, 2 d	 (16)	119
	 SnBu3, Zn-Ag	THF, rt, 22 h	 (13)	119
C_4 			 A + B	
X = Y = H	Zn, $(EtO)_3B$	THF, 15 h	X = Y = H, A/B (total 10)	31
X, Y = H, Br	Zn, $(EtO)_3B$	THF, 15 h	X = Y = H, A/B (total 9) X = H, Y = Br (23), A and/or B, X = Br, Y = H (14)	31
X = Y = Br	Zn/Ag	1. THF, −10°, 2.5 h 2. 25°, 17 h	A and/or B, X = Y = Br (61)	105, 61, 120
	1. Zn/Ag 2. Zn/Cu, NH_4Cl	1. THF, −10°, 2.5 h 2. 25°, 17 h MeOH, 1 h	A, X = Y= H (53)	105
	1. $Fe_2(CO)_9$ 2. Zn/Cu, NH_4Cl	24 h MeOH, 15 min	X = Y = H, A/B (55 : 45) (63)	8
C_5 	, Zn/Cu	—	 (30)	27, 99
			 A + B + C	

Reactants	R^1	R^2	R^3	Conditions	Product(s) and Yield(s) (%)	Refs.
Cu, NaI	H	H	H	MeCN, 45 to 60°, 4 h	A (48)	22, 27, 99, 121-123
Cu, NaI	H	H	H	MeCN	A + B + C (—); A:B:C = 91:3:6	18
Zn/Cu	H	H	H	—	A + B + C (70)	27, 99
Zn/Cu	H	H	H	DME, −10°, 1.5 h	A + B + C (85); A:B:C = 81:10:9	26, 57, 124
Zn/Cu	H	H	H	DME	A + B + C (—); A:B:C = 74:9:7	18
Zn/Cu	H	H	H	MeCN	A + B + C (—); A:B:C = 75:10:15	18
Zn/Cu, *n*-BuNClO$_4$	H	H	H	DME	A + B + C (—); A:B:C = 79:8:13	18
$CeCl_3$, $SnCl_2$	H	H	H	THF	A + B + C (90); A:B:C = 62:28:10	74
ZnCu, $LiClO_4$	H	H	H	DME	A + B + C (—); A:B:C = 92:4:4	18
$CeCl_3$, $SnCl_2$	H	H	Me	THF, 0° to rt	A + B (90); A:B = 70:30	74
Zn/Cu	H	H	$C(Me)O(CH_2)_2O$	DME, 0 to 25°, 16 h	A (53)	57
Zn/Cu	H	Me	H	DME	A + B + C (—); A:B:C = 45:34:21	18
Zn/Ag	H	H	H	1. THF, −10°, 1 h 2. 25°, 12 h	A (80)	105
$Fe_2(CO)_9$	H	H	H	C_6H_6, 40°, 53 h	A + C (90); A:C = 44:56	8
$Fe_2(CO)_9$	Me	H	Me	C_6H_6, 80°, 16 h	A (78)	8, 114, 125
$CeCl_3$, $SnCl_2$	Me	H	Me	THF, 0° to rt	A + B (91); A:B = 63:37	74

TABLE I. [4+3] CYCLOADDITION OF HALOKETONES (REDUCTIVE CONDITIONS) *(Continued)*

D. With Furan Derivatives *(Continued)*

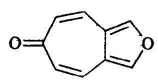
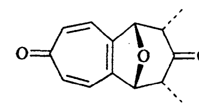
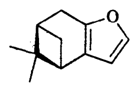
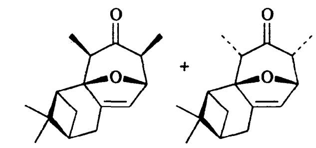
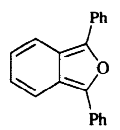
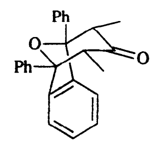
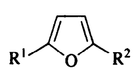
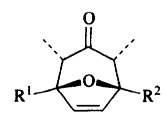
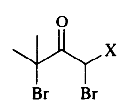
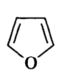
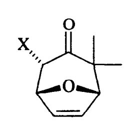
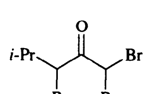
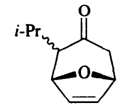
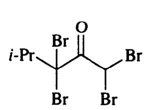
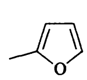
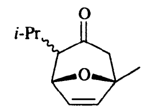
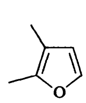
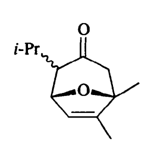
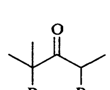
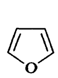
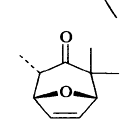
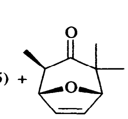
Haloketone	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
	 , Cu/KI	MeCN, 60°	 (30)	126
	 , Cu/NaI	MeCN	 A B A + B (50), A:B = 3:2	127
	 , Cu/NaI	MeCN	 (81)	102
	 , Zn/Ag	THF, –10°		119
	R^1 / R^2			
	H / $(CH_2)_3OTHP$		(35)	
	Me / $(CH_2)_3SnBu_3$		(—)	
	H / $CH_2N(CO_2Me)CH_2SnBu_3$		(55)	
	H / $CH_2OCH_2SnBu_3$		(22)	
	H / $CH_2SCH_2SnBu_3$		(24)	
	H / $(CH_2)_4SnBu_3$		(43)	
				
X = H	Zn/Cu	Acetone	X = H (20)	26
X = Br	Zn/Ag	1. THF, –10°, 1.5 h 2. 25°, 16 h	X = Br (55)	105, 61, 120
	1. Zn/Ag 2. Zn/Cu, NH_4Cl	1. THF, –10°, 1.5 h 2. 25°, 19 h MeOH, 1 h	X = H (50)	105
	1. $Fe_2(CO)_9$ 2. Zn/Cu, NH_4Cl	Reflux, 40 h MeOH, 15 min	X = H (93)	8
	$CeCl_3$-$SnCl_2$	THF, 0° to rt	X = H (78)	74
	1. $Fe_2(CO)_9$, furan 2. Zn/Cu, NH_4Cl	Reflux, 16 h MeOH, 1.5 h	 (35)	8, 81
	 , Zn-Ag	THF	 (7)	128
	 , Zn-Ag	THF	 (7)	128
	 , Zn-Cu	Acetone, –5° to rt	 (35) +  (<5) A B	26

TABLE I. [4+3] CYCLOADDITION OF HALOKETONES (REDUCTIVE CONDITIONS) (*Continued*)

D. With Furan Derivatives (*Continued*)

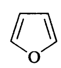
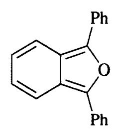
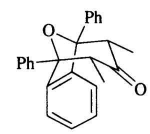
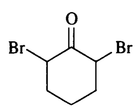
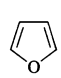
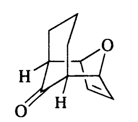
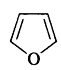
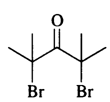
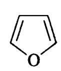
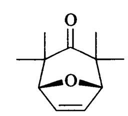
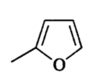
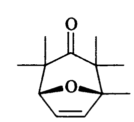
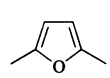
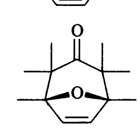
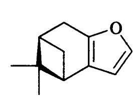
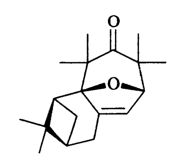
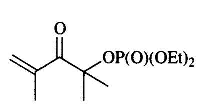
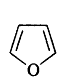
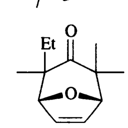
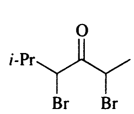
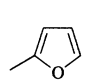
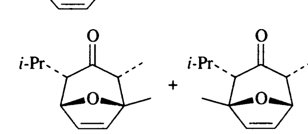
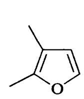
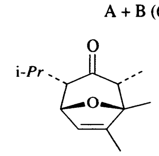
Haloketone	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
	 , $Fe_2(CO)_9$	40°, 45 h	A and/or B (84)	8
	 , Zn/CuCl	Ultrasound	 (50)	102
	 , $Fe_2(CO)_9$	Reflux, 30 h	 I (35)	8, 101
	 , Cu, NaI	MeCN, rt, 6 h	I (9)	93
C_7 				
	Zn/Cu	Acetone, –5° to rt	(43)	26
	$Fe_2(CO)_9$	40°, 38 h	(96)	8
	$Fe_2(CO)_9$	C_6H_6, 40°, 38 h	(89)	8
	$2e^-$, n-Bu_4NBF_4	MeCN, 14°	(—)	129
	$Fe(CO)_5$, $TiCl_4$	CH_2Cl_2, 0°	(77)	94
	Me_2CuLi	Et_2O, –78°, 0.5 h	(6)	130
	Fe-graphite	40°, 15 h	(88)	131
	$CeCl_3$, $SnCl_2$	THF, 0° to rt	(77)	74
	Zn/Cu	dioxane, sonication	(91)	85
	 , $Fe_2(CO)_9$, $TiCl_4$	CH_2Cl_2, 0°	 (—)	94
	 , $Fe_2(CO)_9$, $TiCl_4$	CH_2Cl_2, 0°	 (38)	94
	 , Zn/Cu	Ultrasound, dioxane	 (38)	127
	 , Me_2CuLi	Et_2O, –78°	 (5)	130
	 , Cu, NaI	MeCN, rt	 A B A + B (60), A:B = 3:1	128
	 , Cu, NaI	MeCN, rt	 (73)	128, 132

TABLE I. [4+3] CYCLOADDITION OF HALOKETONES (REDUCTIVE CONDITIONS) *(Continued)*

D. With Furan Derivatives *(Continued)*

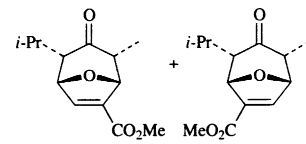
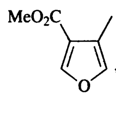
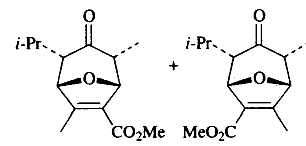
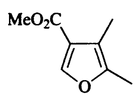
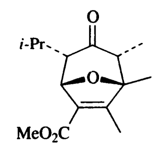
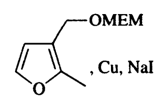
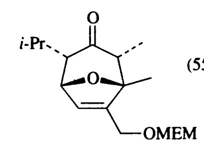
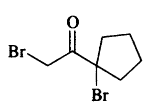
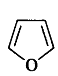
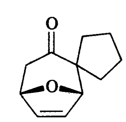
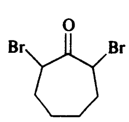
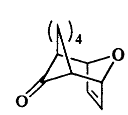
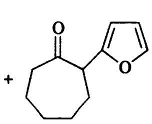
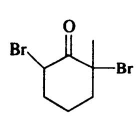
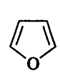
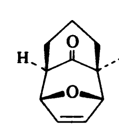
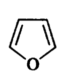
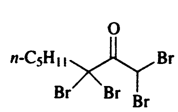
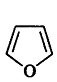
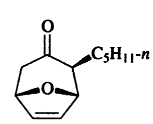
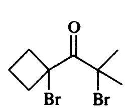
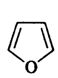
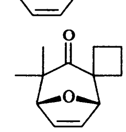
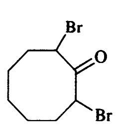
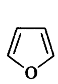
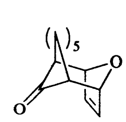
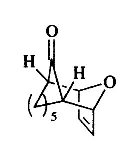
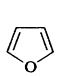
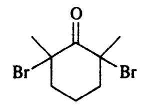
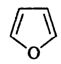
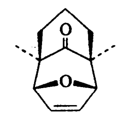
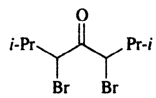
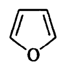
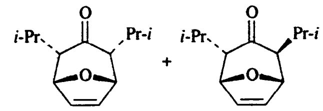
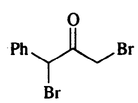
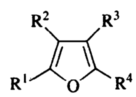
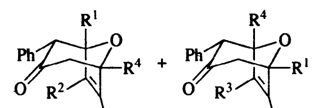
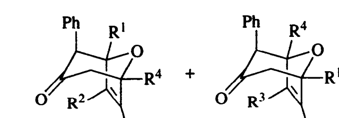
Haloketone	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
		MeCN, rt	 A B A + B (52), A:B = 1:1	128
	, Cu, NaI	MeCN, rt	 A B A + B (35), A:B = 1:1	128
	, Cu, NaI	MeCN, rt	 (42)	128
	, Cu, NaI	MeCN, rt	 (55	128
	, Zn, CuI, TMSCl	1. THF, 0°, 3 h, 2. rt, 3 h	 (42)	133, 134
	, $Fe_2(CO)_9$	Reflux, 62 h	 +  (54) (21)	8, 101
	, Cu, NaI	MeCN, rt, 6 h	 I (25)	93
	, Zn, $B(OEt)_3$	MeCN, rt, 6 h	I (15)	93
	1. Zn/Ag,  2. Zn/Cu, NH_4Cl	1. THF, –10°, 2 h 2. 25°, 39 h MeOH	 (47)	5, 61, 120
	, Zn/Cu	Dioxane, sonication	 (88)	85
	, $Fe_2(CO)_9$	Reflux, 48 h	 +  A (27) B (10)	8, 101
	, Zn/Cu	C_6H_6, rt	A (—) + B (—)	135

TABLE I. [4+3] CYCLOADDITION OF HALOKETONES (REDUCTIVE CONDITIONS) (*Continued*)

D. With Furan Derivatives (*Continued*)

Haloketone	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
	, Cu, NaI	MeCN, rt, 6 h	 (22)	93
C_9 	, $Fe_2(CO)_9$		 A + B	
		40°, 80 h	A/B (77:23) (96)	8
		C_6H_6, 40°, 80 h	A/B (75:25) (89)	8
		DMF, 22 h	A (20)	136
			 A + B +  C + D	

	R^1	R^2	R^3	R^4	Conditions	A + B	A:B	C + D	C:D	Refs.
Zn/Cu	H	Me	H	H	DME, −10°	(36)	65:35	(18)	64:36	5
Zn/Cu	H	CO_2Et	H	H	DME, −10°	(41)	67:33	(—)	—	5
Zn/Cu	CO_2Et	H	H	H	DME, −10°	(40)	88:12	(—)	—	5
Zn/Cu	CO_2Me	Me	H	H	DME, −10°	(20)	95:5	(—)	—	5

	R^1	R^2	R^3	R^4	Conditions	A + B	A:B	C + D	C:D	Refs.
Zn/Cu	CO_2Me	H	H	Me	DME, −10°	(23)	79:21	—	—	5
Zn/Cu	CO_2Me	H	Me	H	DME, −10°	(20)	80:20	—	—	5
Zn/Ag	H	H	H	H	1. THF, −10°, 1.5 h 2. 25°, 19	(77)	100:0	—	—	5
$Fe_2(CO)_9$	H	Br	H	H	C_6H_6, 30°	(44)	65:35	(29)	66:34	16
$Fe_2(CO)_9$	H	Me	H	H	C_6H_6, 30°	(29)	56:44	(19)	56:44	16
$Fe_2(CO)_9$	H	CO_2Me	H	H	C_6H_6, 30°	(52)	55:45	—	—	16
$Fe_2(CO)_9$	CO_2Me	H	H	H	C_6H_6, 30°	(56)	90:10	—	—	16
$Fe_2(CO)_9$	CO_2Me	Me	H	H	C_6H_6, 30°	(63)	92:8	—	—	16
$Fe_2(CO)_9$	CO_2Me	H	H	Me	C_6H_6, 30°	(65)	65:35	—	—	16
$Fe_2(CO)_9$	CO_2Me	H	Me	H	C_6H_6, 30°	(85)	76:24	—	—	16

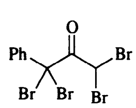
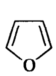
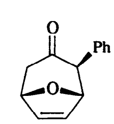
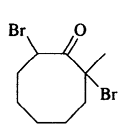
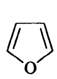
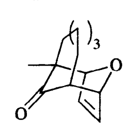
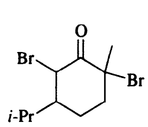
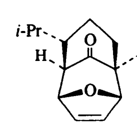
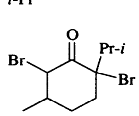
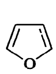
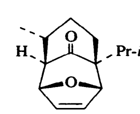
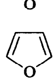
Haloketone	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
	1. , Zn/Ag 2. Zn/Cu, NH_4Cl	1. THF, −10°, 2 h 2. 25°, 12 h MeOH, 1 h	 (48)	61, 120
	, Cu, NaI	MeCN, 15 h	 (13)	133
C_{10} 	, Cu, NaI	MeCN, rt, 6 h	 (27)	93
	, Cu, NaI	MeCN, rt, 6 h	 I (22)	93
	, Zn, $(EtO)_3B$	THF, 5 h	I (35)	93

TABLE I. [4+3] CYCLOADDITION OF HALOKETONES (REDUCTIVE CONDITIONS) (*Continued*)

D. With Furan Derivatives (*Continued*)

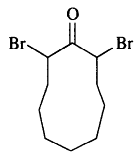
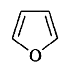
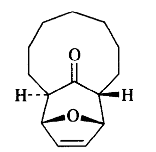
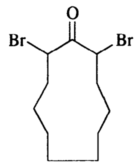
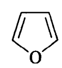
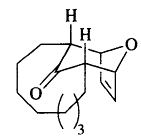
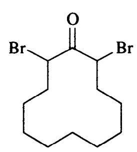
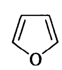
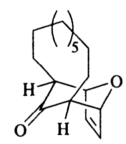
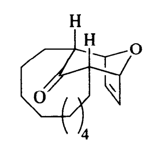
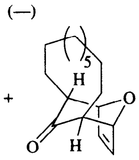
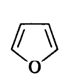
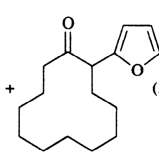
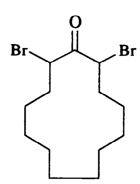
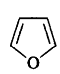
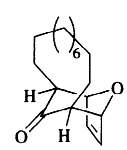
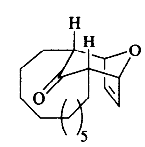
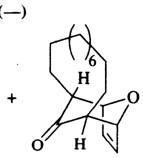
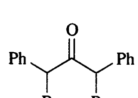
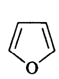
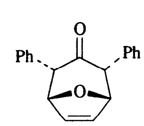
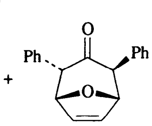
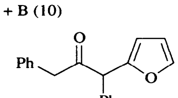
Haloketone	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
	, Zn/Cu	C_6H_6, rt	 (—)	135
C_{11} 	, Zn/Cu	—	 (—)	
C_{12} 	, Zn/Cu		 A (—) +  B (—) +  C (—)	137, 135
	, $Fe_2(CO)_9$	Reflux, 40 h	A (7) + C (45) +  (34)	8, 101
	, Zn/Cu	—	 (—) +  (—) +  (—)	137, 135
C_{15} 			 A +  B	
	Cu, NaI	MeCN, 80°	A and/or B (80)	27, 99
	Zn/Cu	MeCN, reflux, 2 days	A (29) + $PhCH_2COCHPh_2$ (49)	96
	Hg	—	A (35)	96
	$Fe_2(CO)_9$	25°, 6 h	A (45) + B (45)	8
	$Fe_2(CO)_9$	C_6H_6, 25°, 21 h	A + B (1 : 1) (90)	138, 139
	Me_2CuLi	−78°	A and/or B (20)	140
	NaI	—	A (65)	97
	NaI	MeCN, reflux	A (30) + B (10) +  (45)	96

TABLE I. [4+3] CYCLOADDITION OF HALOKETONES (REDUCTIVE CONDITIONS) (*Continued*)

E. With Anthracene

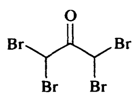
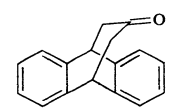
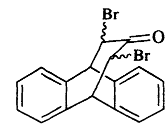
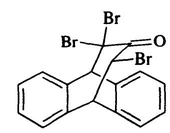
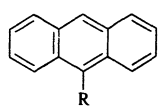
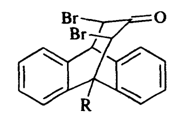
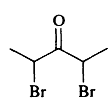
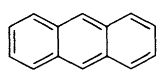
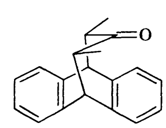
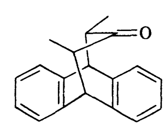
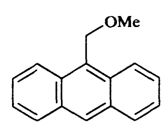
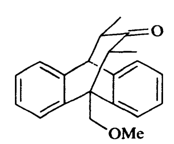
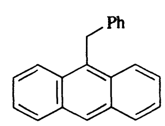
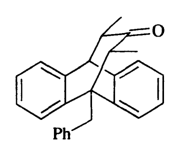
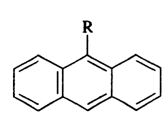
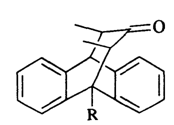
Haloketone	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3 	Anthracene, Zn/Cu	Dioxane, 80°	 (22)	141
	Anthracene, Zn/Cu, TMSCl	Dioxane, 80°, 2 h	 **I** (15)	142
	Anthracene, Zn/Cu, ultrasound	Dioxane, 8 h	**I** (28)	142
	Anthracene, Zn/Cu, *N,O*-bis(TMS)acetamide, ultrasound	C_6H_6	 (42)	142
	, Zn/Cu	Dioxane, ultrasound		
	R			
	Me		(71)	141
	OMe		(64)	141
	$CH=CH_2$		(71)	141, 143
	$CH_2CH=CH_2$		(67)	141, 143
	$(CH_2)_2CH=CH_2$		(70)	141
C_5 			 A +  B	
	Zn, CuCl	Dioxane, 80-85°, 5 h	A/B (ca. 90 : 10) (22)	29, 29a
	Zn, CuCl, TMSCl	C_6H_6	A/B (ca. 1 : 1) (93)	29, 29a
	Zn-Cu, ultrasound	Dioxane	A/B (76 : 24) (29)	142
	Zn-Cu, *N,O*-bis(TMS)acetamide	C_6H_6	A/B (82 : 18) (44)	142
	, Zn-Cu, *N,O*-bis(TMS)acetamide	C_6H_6	 (24)	142
	, Zn-Cu, *N,O*-bis(TMS)acetamide	C_6H_6	 (30)	142
	, Zn-Cu	Dioxane, ultrasound		141
	R			
	Br		(40)	
	$CH_2CH=CH_2$		(65)	
	OTMS		(37)	

TABLE I. [4+3] CYCLOADDITION OF HALOKETONES (REDUCTIVE CONDITIONS) (*Continued*)

E. With Anthracene (*Continued*)

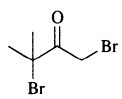
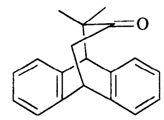
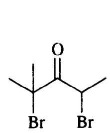
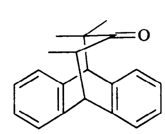
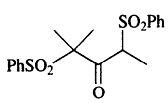
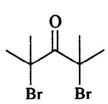
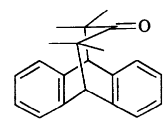
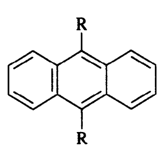
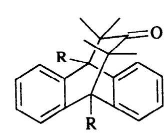
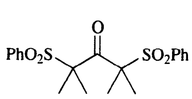
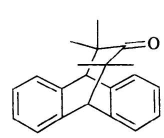
Haloketone	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
	Anthracene, Zn, CuCl	Dioxane, 80-85°, 5 h	 **I** (12)	29, 29a
	Anthracene, Zn, CuCl, TMSCl	C_6H_6	**I** (76)	29, 29a
C_6 	Anthracene, Zn, CuCl	Dioxane, 80-85°, 5 h	 **I** (25)	29, 29a
	Anthracene, Zn, CuCl, TMSCl	C_6H_6	**I** (97)	29, 29a
	Anthracene, $Fe(CO)_5$, $TiCl_4$	CH_2Cl_2, 0°	**I** (12)	94
C_7 	Anthracene, Zn, CuCl	Dioxane, 80-85°, 5 h	 **I** (3)	29, 29a
	Anthracene, Zn, CuCl, TMSCl	C_6H_6	**I** (71)	29, 29a
		C_6H_6		
	R			
	Zn-Cu, TMSCl — Me		(40)	29a
	OMe		(30)	29a
	Zn-Cu — H, OTMS	Dioxane, ultrasound	(26)	141
	Anthracene, $Fe(CO)_5$, $TiCl_4$	CH_2Cl_2, 0°	 (86)	94

TABLE II. [4+3] CYCLOADDITION OF ALLYL CATIONS (SOLVOLYTIC CONDITIONS)

A. With Open-Chain 1,3-Dienes

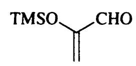
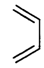
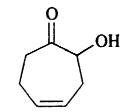
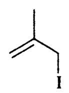
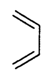
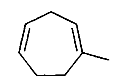
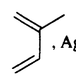
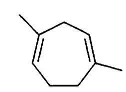
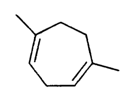
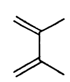
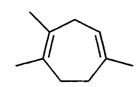
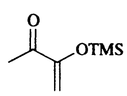
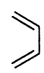
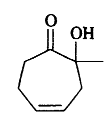
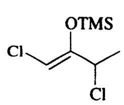
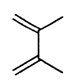
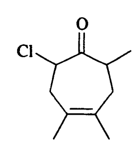
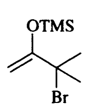
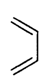
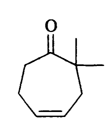
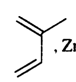
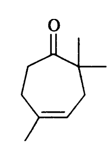
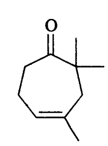
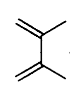
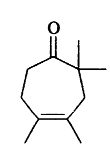
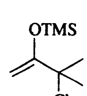
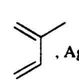
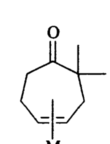
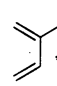
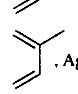
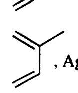
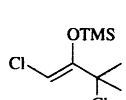
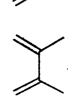
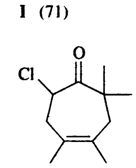
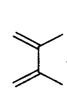
Cation Precursor	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3				
	, $SnCl_4$	CH_2Cl_2, –78°, 0.6 h	 (32)	144
C_4				
	, AgO_2CCF_3	Isopentane, –78°, 6 h	 (6)	145
	, AgO_2CCF_3	Isopentane, –78°, 1 h	 +  (total 47)	145
	, AgO_2CCF_3	Isopentane, –78°, 1 h	 (4)	145
	, $TiCl_4$	CH_2Cl_2, –78°, 1 h	 (—)	146
	, AgO_2CCF_3	$MeNO_2$, –15°	 (10)	19
C_5				
	, $ZnCl_2$	CH_2Cl_2, –78°, 2 h	 (26)	36
	, $ZnCl_2$	CH_2Cl_2, –78°, 50 min	 (33) +  (18)	36
	, $ZnCl_2$	CH_2Cl_2, –78°, 2 h	 (60)	36
	, $AgClO_4$, $CaCO_3$	Et_2O, THF, 0°, 45 min	 I (64)	147
	, $AgClO_4$	$MeNO_2$, 0°	I (58)	19
	, $AgClO_4$	THF, Et_2O, 0°	I (65)	19
	, $AgClO_4$, Al_2O_3	C_6H_6, rt	I (71)	19
	, $ZnCl_2$	$MeNO_2$, 0°, 1.5 h	 I (32)	19
	, $ZnCl_2$	THF, Et_2O, 0°, 1.5 h	I (10)	19

TABLE II. [4+3] CYCLOADDITION OF ALLYL CATIONS (SOLVOLYTIC CONDITIONS) (*Continued*)

A. With Open-Chain 1,3-Dienes (*Continued*)

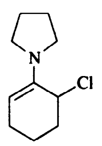
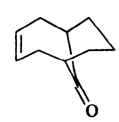
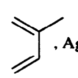
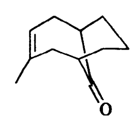
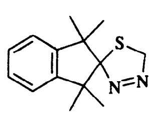
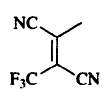
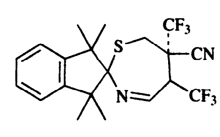
Cation Precursor	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10} 	 , $AgBF_4$	CH_2Cl_2, –60°	 (27)	25
	 , $AgBF_4$	CH_2Cl_2, –60°	 (30)	25
C_{14} 		Cyclohexane, 50°, 7.5 h	 (86)	148

TABLE II. [4+3] CYCLOADDITION OF ALLYL CATIONS (SOLVOLYTIC CONDITIONS) (*Continued*)

B. With Carbocyclic Dienes

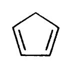
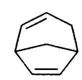
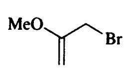
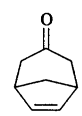
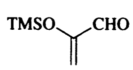
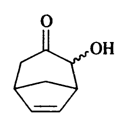
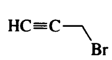
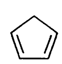
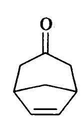
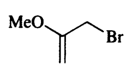
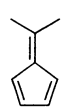
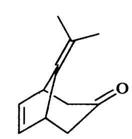
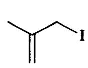
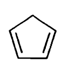
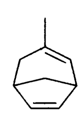
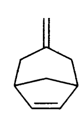
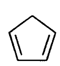
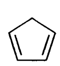
Cation Precursor	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3 	, AgO_2CCF_3	Isopentane, −78°, 6 h	 (6)	145
	, AgO_2CCF_3, Na_2CO_3	C_6H_6, isopentane, rt, 30 h	 (17)	34
	, $SnCl_4$	CH_2Cl_2, −78°, 5 h	 (72) α : β = 73 : 27	144
	, AgO_2CCF_3	Pentane, 0°	 (13)	149, 150
	, AgO_2CCF_3, Na_2CO_3	C_6H_6, isopentane, rt, 30 h	 (1)	34
C_4 	, AgO_2CCF_3, Na_2CO_3	SO_2, −50°, 1.5 h	 **I** (40) +  **II** (16)	35, 151
	, AgO_2CCF_3, Na_2CO_3	C_6H_6, 0°, 1 h	**I** (42) + **II** (18)	151
	, AgO_2CCF_3, Na_2CO_3	Isopentane, −78°, 6 h	**I** (50) + **II** (20)	145

TABLE II. [4+3] CYCLOADDITION OF ALLYL CATIONS (SOLVOLYTIC CONDITIONS) (*Continued*)

B. With Carbocyclic Dienes (*Continued*)

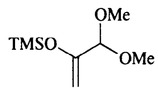
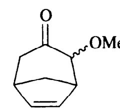
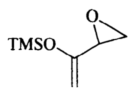
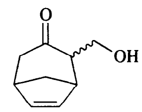
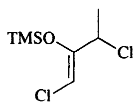
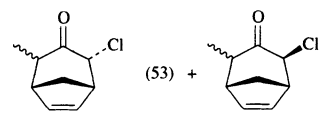
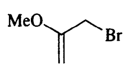
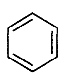
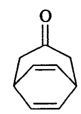
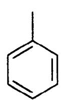
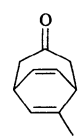
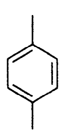
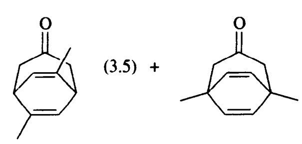
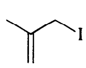
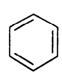
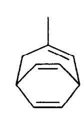
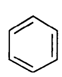
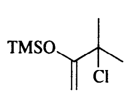
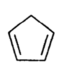
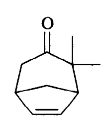
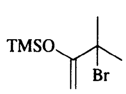
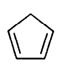
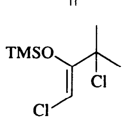
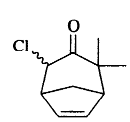
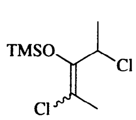
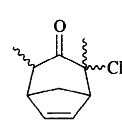
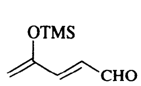
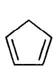
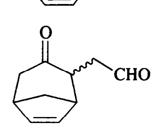
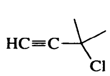
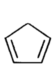
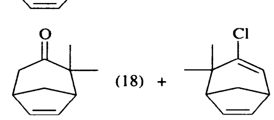
Cation Precursor	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
	, TMSOTf	CH_2Cl_2, –78°, 3 h	 (50)	152
	, TMSOTf	CH_2Cl_2, –50°, 3 h	 (47)	153
	, $AgClO_4$	$MeNO_2$, 0°	 (53) + (23)	19
	, AgO_2CCCl_3, Na_2CO_3	Isopentane, rt, 25 h	 (20)	14, 154, 155
	, AgO_2CCCl_3, Na_2CO_3	Isopentane, rt, 25 h	 (0.5)	154
	, AgO_2CCCl_3, Na_2CO_3	Isopentane, rt, 25 h	 (3.5) + (0.5)	154
	, AgO_2CCCl_3, Na_2CO_3	SO_2, –50°, 1.5 h	 I (20)	35
	, AgO_2CCCl_3, Na_2CO_3	Isopentane, –78°, 6 h	I (30)	145
	, $AgClO_4$, $CaCO_3$	Et_2O, THF, 0°, 45 min	 I (91)	147, 19
	, $ZnCl_2$	CH_2Cl_2, –78°, 2 h	I (54)	36
	, $AgClO_4$	$MeNO_2$, 0°, 1 h	 I (80)	19
	, $AgClO_4$	Et_2O, THF, 0°, 1 h	I (8)	19
	, $AgClO_4$	$MeNO_2$, 0°, 1 h	 (64)	19
	, $SnCl_4$	CH_2Cl_2, –78°, 0.5 h	 (76)	153
	, AgO_2CCF_3	Pentane	 (18) + (19)	150, 149

TABLE II. [4+3] CYCLOADDITION OF ALLYL CATIONS (SOLVOLYTIC CONDITIONS) (*Continued*)

B. With Carbocyclic Dienes (*Continued*)

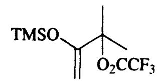
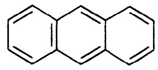
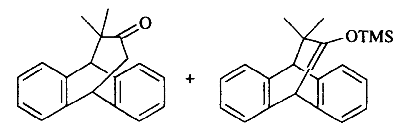
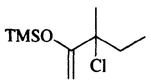
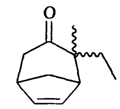
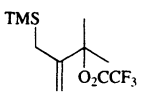
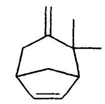
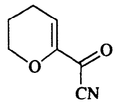
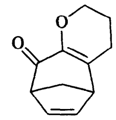
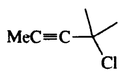
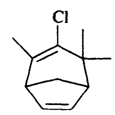
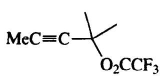
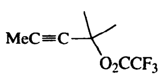
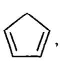
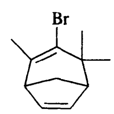
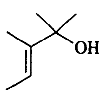
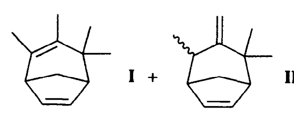
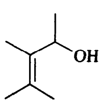
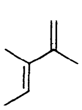
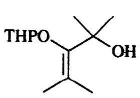
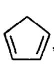
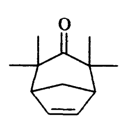
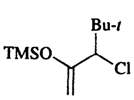
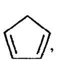
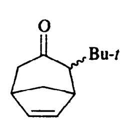
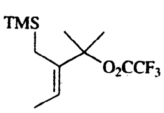
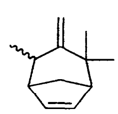
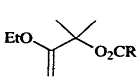
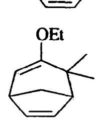
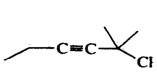
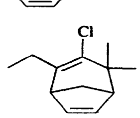
Cation Precursor	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
	, $ZnCl_2$	CH_2Cl_2, DIEA reflux, 7 h	 (total 95)	156
C_6				
	, $AgClO_4$	THF, Et_2O, 0°, 1 h	 (71)	19
	, $ZnCl_2$	MeCN, DIEA, 0°	 (45)	15
	, $AlCl_3$	PhMe, −78 to 0°, 12 h	 (70)	157
	, $ZnCl_2$	CH_2Cl_2, −40°, 1 h	 **I** (36)	158, 149
	, $ZnCl_2$	CH_2Cl_2, DIEA, rt	**I** (42)	156
	, $ZnBr_2$	CH_2Cl_2, DIEA, rt	 (39)	156
C_7				
		TsOH, pentane, 0° to rt	 total (37)	159
		TsOH, pentane, 0° to rt	**I** + **II** (—)	159
		TsOH, pentane, 0° to rt	**I** + **II** (—)	159
	, $TiCl_4$	PhNHMe, CH_2Cl_2, −20°	 (44)	92
	, $AgClO_4$	$MeNO_2$, 0°, 1 h	 (60)	19
	, $ZnCl_2$	MeCN, DIEA, 0°	 (60)	15
	, $ZnCl_2$	MeCN, DIEA, rt	 R: Me (76); CF_3 (76)	156
	, $ZnCl_2$	CH_2Cl_2, −40°, 1 h	 (28)	158, 149

TABLE II. [4+3] CYCLOADDITION OF ALLYL CATIONS (SOLVOLYTIC CONDITIONS) (*Continued*)

B. With Carbocyclic Dienes (*Continued*)

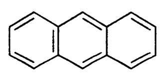
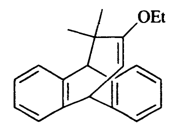
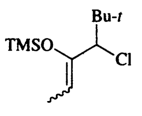
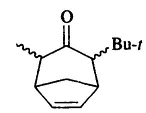
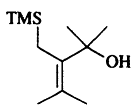
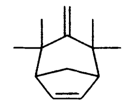
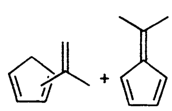
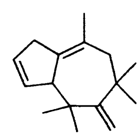
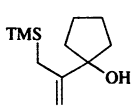
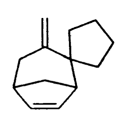
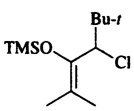
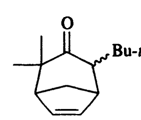
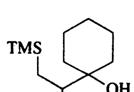
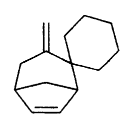
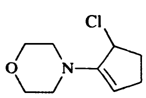
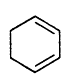
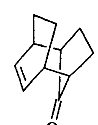
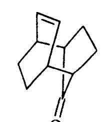
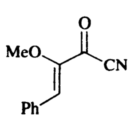
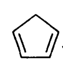
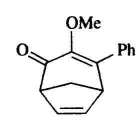
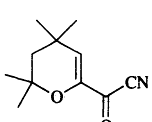
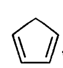
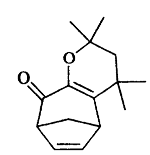
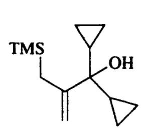
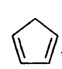
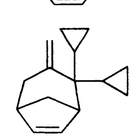
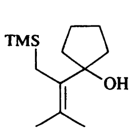
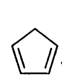
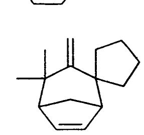
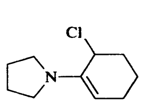
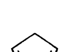
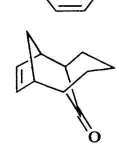
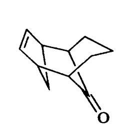
Cation Precursor	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
	, $ZnCl_2$	CH_2Cl_2, DIEA, reflux	 (96)	156
C_8 	, $AgClO_4$	$MeNO_2$, 0°, 1 h	 (60)	19
	, $TiCl_4$	PhNHMe, CH_2Cl_2, –20°	 (38)	30
	, $TiCl_4$	PhNHMe, CH_2Cl_2, –20°	 (20)	92
	, $TiCl_4$	PhNHMe, CH_2Cl_2, –20°	 (43)	92
C_9 	, $AgClO_4$	$MeNO_2$, 0°, 1 h	 (82)	19
	, $TiCl_4$	PhNHMe, CH_2Cl_2, –20°	 (15)	92
		—	 +  (—)	160
C_{10} 	, $AlCl_3$	PhMe, –78 to 0°	 (10)	157
	, $AlCl_3$	PhMe, –78 to 0°	 (36)	157
	, $TiCl_4$	PhNHMe, CH_2Cl_2, –20°	 (20)	92
	, $TiCl_4$	PhNHMe, CH_2Cl_2, –20°	 (58)	92
	, $AgBF_4$	CH_2Cl_2, –60°	 +  (76) 97:3	25, 161

TABLE II. [4+3] CYCLOADDITION OF ALLYL CATIONS (SOLVOLYTIC CONDITIONS) (*Continued*)

B. With Carbocyclic Dienes (*Continued*)

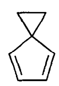
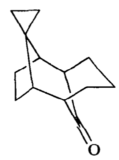
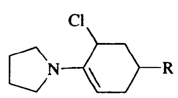
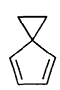
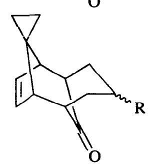
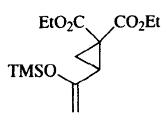
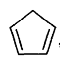
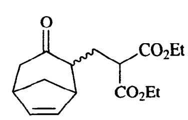
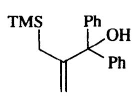
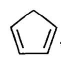
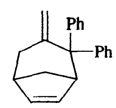
Cation Precursor	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
	 , $AgBF_4$	CH_2Cl_2, -60°	 (42)	162, 162a
 R = TBS, TIPS, BOM	 , $AgBF_4$	CH_2Cl_2, -60°	 (38-44)	162a, 161, 163
C_{11} 	 , $TiCl_4$	CH_2Cl_2, 0°, 3 h	 (55)	153
C_{16} 	 , $TiCl_4$	CH_2Cl_2, PhNHMe, −20°	 (21)	92

TABLE II. [4+3] CYCLOADDITION OF ALLYL CATIONS (SOLVOLYTIC CONDITIONS) (*Continued*)

C. With Pyrrole Derivatives

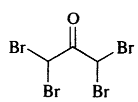
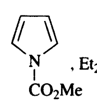
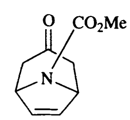
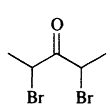
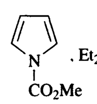
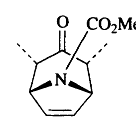
Cation Precursor	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3 	 , Et_2Zn	C_6H_6, 0° to rt, 23 h	 (59)	56
C_5 	 , Et_2Zn	C_6H_6, 0° to rt, 20 h	 (55)	56

TABLE II. [4+3] CYCLOADDITION OF ALLYL CATIONS (SOLVOLYTIC CONDITIONS) *(Continued)*

D. With Furan Derivatives

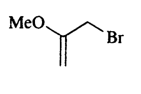
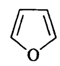
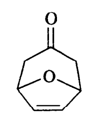
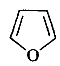
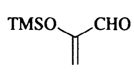
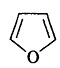
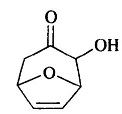
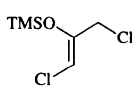
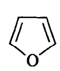
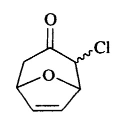
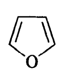
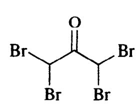
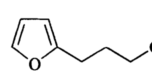
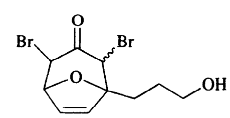
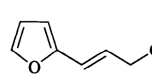
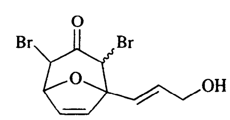
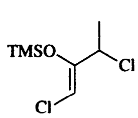
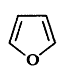
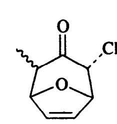
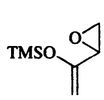
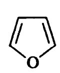
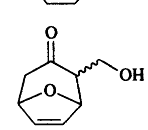
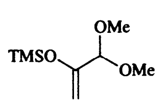
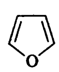
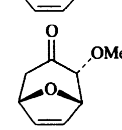
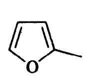
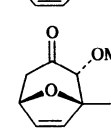
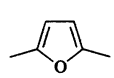
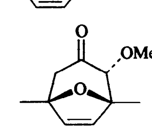
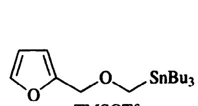
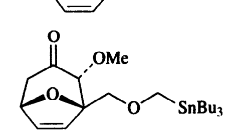
Cation Precursor	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3				
	 , AgO_2CCF_3, Na_2CO_3	C_6H_6, isopentane rt, 30 h	 I (15)	34
	 , AgO_2CCF_3, Na_2CO_3	CCl_4, –10°, 1 h	I (31)	164
	 , $SnCl_4$	CH_2Cl_2, –78°, 10 min	 (43)	144
	 , $AgClO_4$	$MeNO_2$, 0°, 7 h	 I (80) α : β = 89 : 11	19
	 , $AgClO_4$	DME, Et_2O, 40°	I (45) α : β = 80 : 20	19
	 OH, Et_2Zn	C_6H_6, 0° to rt, 2 h	 (51)	165
	 OH, Et_2Zn	C_6H_6, 0° to rt, 2 h	 (55)	165
C_4				
	 , $AgClO_4$	$MeNO_2$, 0°, 0.5 h	 (87) α : β = 1 : 1	19
	 , TMSOTf	CH_2Cl_2, –50°, 3 h	 (12)	153
	 , TMSOTf	CH_2Cl_2, –78°, 3 h	 (67)	152
	 , TMSOTf	CH_2Cl_2, –78°, 3 h	 (54)	152
	 , TMSOTf	CH_2Cl_2, –78°, 3 h	 (78)	152
	 TMSOTf	$EtNO_2$, –78°, 2.5 h	 (33)	119

TABLE II. [4+3] CYCLOADDITION OF ALLYL CATIONS (SOLVOLYTIC CONDITIONS) (*Continued*)

D. With Furan Derivatives (*Continued*)

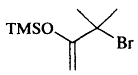
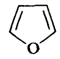
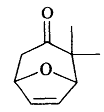
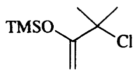
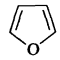
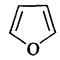
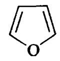
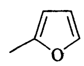
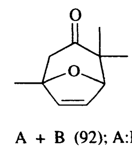
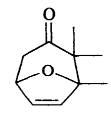
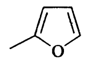
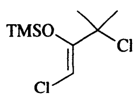
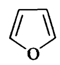
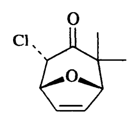
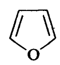
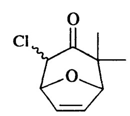
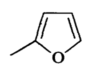
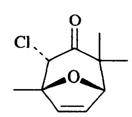
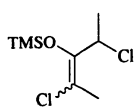
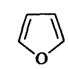
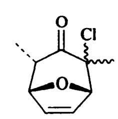
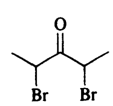
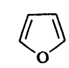
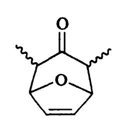
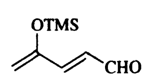
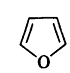
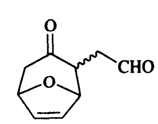
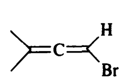
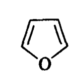
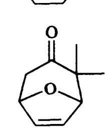
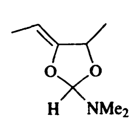
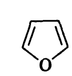
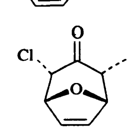
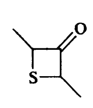
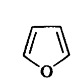
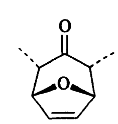
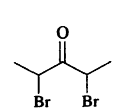
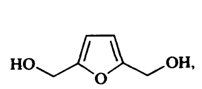
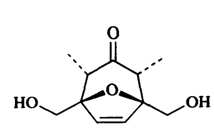
Cation Precursor	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5				
	, $ZnCl_2$	CH_2Cl_2, −78°, 1.5 h	 I (97)	36
	, $AgClO_4$	Et_2O, THF, 0°	I (85)	147, 19
	, $AgClO_4$	$MeNO_2$, 0°, 0.5 h	I (92)	19
	, $AgClO_4$, Al_2O_3	C_6H_6, rt, 3 h	I (91)	19
	, $AgClO_4$	Et_2O, THF, 0°, 45 min	 A (33) +  B (2)	147, 19
	, $AgClO_4$	$MeNO_2$, 0°, 0.5 h	A + B (92); A:B = 65:35	19
	, $AgClO_4$	$MeNO_2$, 0°, 0.5 h	 (89)	147, 19
	, $AgClO_4$	Et_2O, THF, 0°, 1 h	 (3)	19
	, $AgClO_4$	$MeNO_2$, 0°, 0.5 h	 (57)	19
	, $AgClO_4$	$MeNO_2$, 0°, 1 h	 (78)	19
	, Et_2Zn	0° to rt, 22 h	 (53) $\alpha:\beta = 9:1$	56
	, $SnCl_4$	CH_2Cl_2, −78°, 2 h	 (36)	153
	, KOBu-*t*	Hexanes, −10° to rt, 12 h	 (10)	166
		H^+, rt	 (—)	167
	, PR_3	Furan, MeOH	 (—)	168
	, Et_2Zn	C_6H_6, rt	 (8)	165

TABLE II. [4+3] CYCLOADDITION OF ALLYL CATIONS (SOLVOLYTIC CONDITIONS) (*Continued*)

D. With Furan Derivatives (*Continued*)

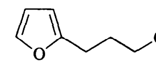
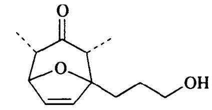
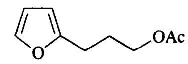
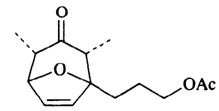
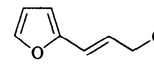
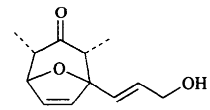
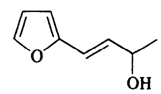
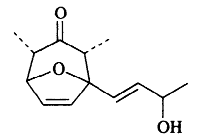
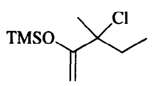
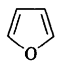
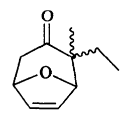
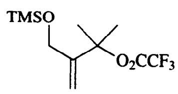
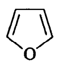
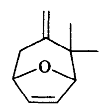
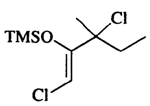
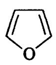
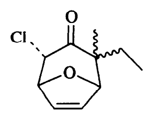
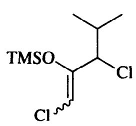
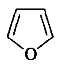
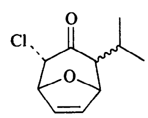
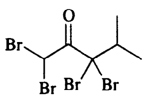
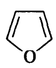
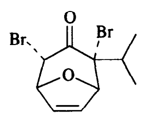
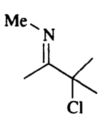
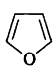
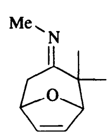
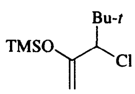
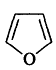
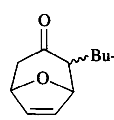
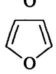
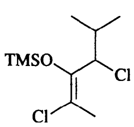
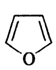
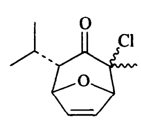
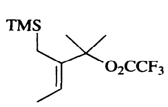
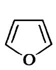
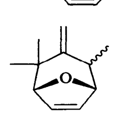
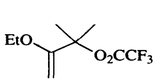
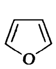
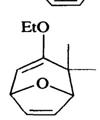
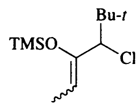
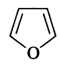
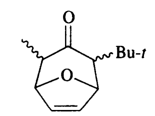
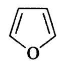
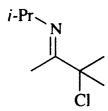
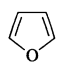
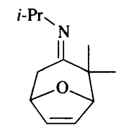
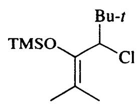
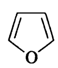
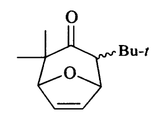
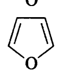
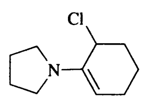
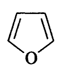
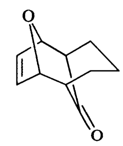
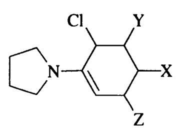
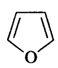
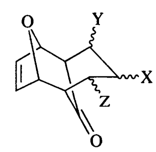
Cation Precursor	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
	, Et_2Zn	C_6H_6, rt	 (56)	165
		C_6H_6, rt	 (55)	165
	, Et_2Zn	C_6H_6, rt	 (46)	165
	, Et_2Zn	C_6H_6, rt	 (29)	165
C_6				
	, $AgClO_4$	$MeNO_2$, 0°, 0.5 h	 (81)	19
	, $ZnCl_2$	CH_2Cl_2, DIEA, 0°	 (—)	15
	, $AgClO_4$	$MeNO_2$, 0°, 0.4 h	 (89)	19
	, $AgClO_4$		 (76)	19
	, Et_2Zn	C_6H_6, 0° to rt, 6 h	 (52)	56
	, $AgBF_4$	CH_2Cl_2, reflux, 1-3 h	 (60)	169
C_7				
	, $AgClO_4$	$MeNO_2$, 0°, 1 h	 **I** (49)	19
	, $AgClO_4$	THF, Et_2O, 0°, 1 h	**I** (8)	19
	, $AgClO_4$	$MeNO_2$, 0°, 0.5 h	 (66)	19
	, $ZnCl_2$	CH_2Cl_2, DIEA, 0°	 (—)	15
	, $ZnCl_2$	MeCN, DIEA, rt	 (72)	156

TABLE II. [4+3] CYCLOADDITION OF ALLYL CATIONS (SOLVOLYTIC CONDITIONS) (*Continued*)

D. With Furan Derivatives (*Continued*)

Cation Precursor	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
	, $AgClO_4$	$MeNO_2$, 0°, 1 h	 I (84)	19
	, $AgClO_4$	THF, Et_2O, 0°, 1 h	I (35)	19
	, $AgBF_4$	CH_2Cl_2, reflux, 1-3 h	 (95)	169
	, $AgClO_4$	$MeNO_2$, 0°, 0.5 h	 I (86)	19
	, $AgClO_4$	THF, Et_2O, 0°, 0.5 h	I (34)	19
C_{10}				
	, $AgBF_4$	CH_2Cl_2, –60°	 (68)	25, 170
	, $AgBF_4$	CH_2Cl_2, –78°, 4 h		48

X	Y	Z	Yield (%)
OTIPS	H	H	(65)
Me	H	H	(78)
H	OTIPS	H	(9)
H	H	Me	(70)

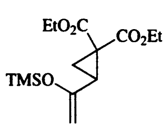
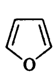
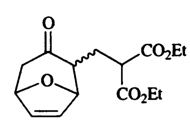
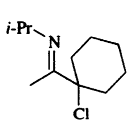
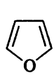
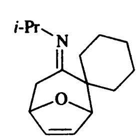
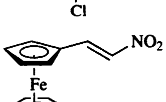
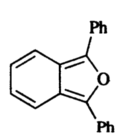
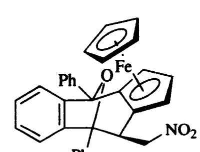
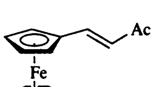
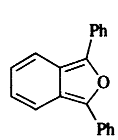
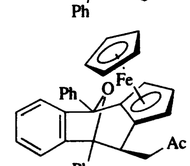
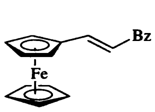
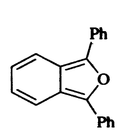
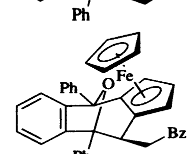
Cation Precursor	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11}				
	, $TiCl_4$	CH_2Cl_2, 0°, 3 h	 (15)	153
	, $AgBF_4$	CH_2Cl_2, reflux, 1-3 h	 (40)	169
C_{12}				
	, $AlCl_3$	CH_2Cl_2, 30 h	 (20)	171
C_{14}				
	, $AlCl_3$	CH_2Cl_2, 24 h	 (61)	171
C_{19}				
	, $AlCl_3$	CH_2Cl_2, 29 h	 (32)	171

TABLE III. [4+3] CYCLOADDITION OF HALOKETONES (BASE CONDITIONS)

A. With Open-Chain 1,3-Dienes

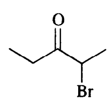
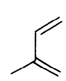
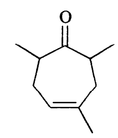
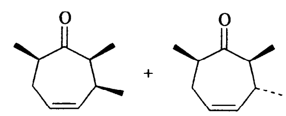
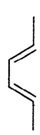
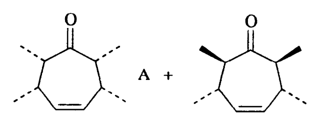
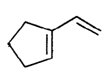
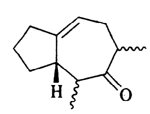
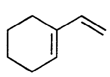
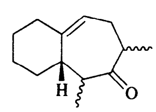
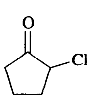
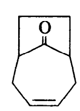
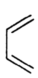
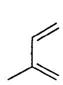
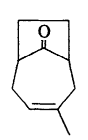
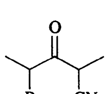
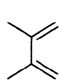
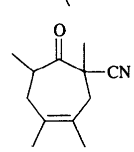
Haloketone	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5 	 , Et_3N	CF_3CH_2OH, rt, 15 h	 (45)	44
	 , $NaOCH_2CF_3$	CH_3CH_2OH, rt	 (—)	44
	 , $NaOCH_2CF_2CHF_2$	$CF_2HCF_2CH_2OH$, 15 h	 A + B A:B (42:58) (15)	72
	 $NaOCH_2CF_2CHF_2$	$CF_2HCF_2CH_2OH$, 15 h	 (33)	72
	 $NaOCH_2CF_2CHF_2$	$CF_2HCF_2CH_2OH$, 15 h	 (13)	72
	 , $NaOCH_3$	MeOH, −20°, 4 h	 **I** (5)	172
	 , $NaOCH_2CF_3$	CF_3CH_2OH, 1.5 h	**I** (44)	172
	 , $NaOCH_2CF_3$	CF_3CH_2OH, 0°, 30 min	 (52)	172
C_6 	 , Ag_2O	—	 (10)	172a

TABLE III. [4+3] CYCLOADDITION OF HALOKETONES (BASE CONDITIONS) (*Continued*)

B. With Carbocyclic Dienes

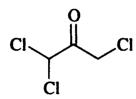
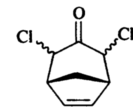
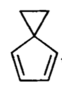
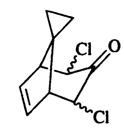
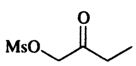
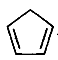
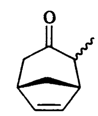
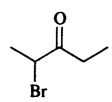
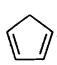
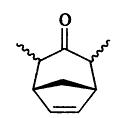
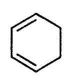
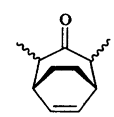
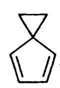
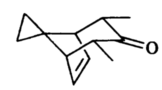
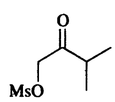
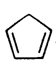
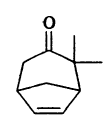
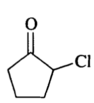
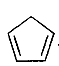
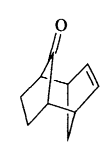
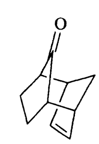
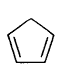
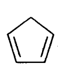
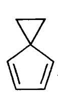
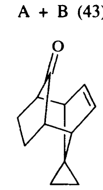
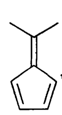
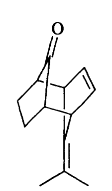
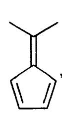
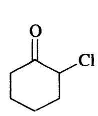
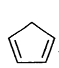
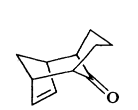
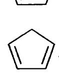
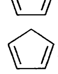
Haloketone	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3 	, $NaOCH_2CF_2CHF_2$	$F_2CHCF_2CH_2OH$, 0°	 (91)	172b
	, $NaOCH_2CF_2CHF_2$	$F_2CHCF_2CH_2OH$, 0°	 (69)	172b
C_4 	, Et_3N, $LiClO_4$	Et_2O	 (38)	173
C_5 	, $NaOCH_2CF_2CHF_2$	$CF_2HCF_2CH_2OH$, 20 h	 (71)	72
	, $NaOCH_2CF_2CHF_2$	$CF_2HCF_2CH_2OH$, 20 h	 (14)	72
	, $NaOCH_2CF_2CHF_2$	$CF_2HCF_2CH_2OH$, 20 h	 (74)	72
	, Et_3N, $LiClO_4$	Et_2O	 (52)	173
	, NaOMe	MeOH, 0°, 30 min	 A +  B (—)	172
	, $NaOCH_2CF_3$	CF_3CH_2OH, 0°, 15 min	A + B (79), A:B = 70:30	172
	, Et_3N, $LiClO_4$	Et_2O, 3.5 h	A + B (43), A:B = 71:29	172
	, $NaOCH_2CF_3$	CF_3CH_2OH, 0°, 30 min	 (58)	172
	, Et_3N	CF_3CH_2OH, 53 h	 **I** (49)	172
	, Et_3N, $LiClO_4$	Et_2O, 76 h	**I** (73)	172
C_6 	, $NaOCH_2CF_3$	CF_3CH_2OH, 0°	 **I** (—)	174
	, Et_3N	CF_3CH_2OH, 3 d	**I** (51)	48
	, Et_3N	$CHF_2CF_2CH_2OH$, 3 d	**I** (65)	48

TABLE III. [4+3] CYCLOADDITION OF HALOKETONES (BASE CONDITIONS) (*Continued*)

B. With Carbocyclic Dienes (*Continued*)

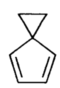
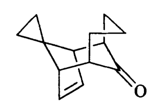
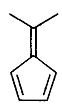
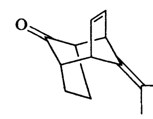
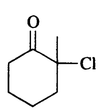
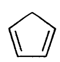
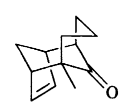
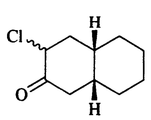
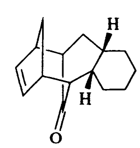
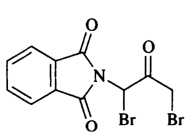
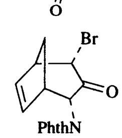
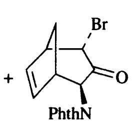
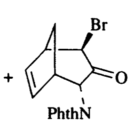
Haloketone	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
	, Et_3N	CF_3CH_2OH, rt	 (13)	48
	, Et_3N, $LiClO_4$	Et_2O	 (—)	174
C_7 	, Et_3N	CF_3CH_2OH, 3 d	 **I** (17)	48
	, Et_3N	$CF_3CF_2CH_2OH$, 1 d	**I** (43)	48
C_{10} 	, Et_3N	CF_3CH_2OH, rt, 3 d	 (38)	48
C_{11} 	, Et_3N	CF_3CH_2OH, 0°	 A +  B +  C A + B + C (75), A:B:C = 2:1:0	95, 175
	, Et_3N, $LiClO_4$	Et_2O	A + B + C (46), A:B:C = 3.7:1:2.8	175

TABLE III. [4+3] CYCLOADDITION OF HALOKETONES (BASE CONDITIONS) (*Continued*)

C. With Pyrrole Derivatives

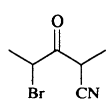
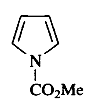
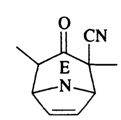
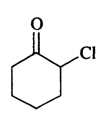
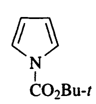
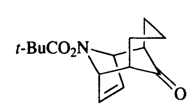
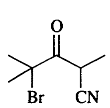
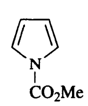
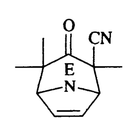
Haloketone	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6 	, Ag_2O	—	 $E = CO_2Me$ (—)	172a
	, Et_3N	CF_3CH_2OH, rt	 (13)	48
C_7 	, Ag_2O	—	 $E = CO_2CH_3$ (—)	172a

TABLE III. [4+3] CYCLOADDITION OF HALOKETONES (BASE CONDITIONS) (*Continued*)

D. With Furan Derivatives

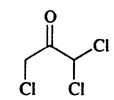
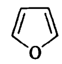
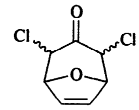
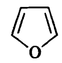
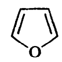
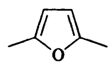
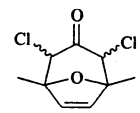
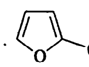
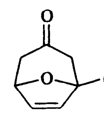
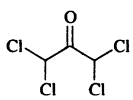
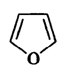
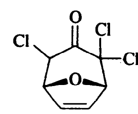
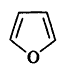
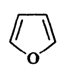
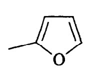
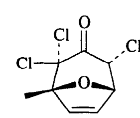
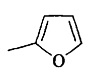
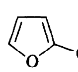
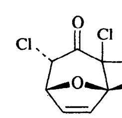
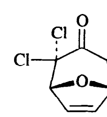
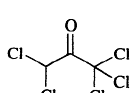
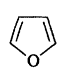
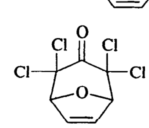
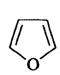
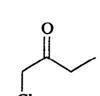
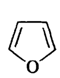
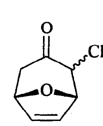
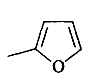
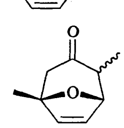
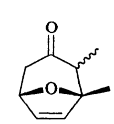
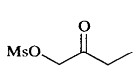
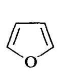
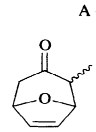
Haloketone	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3 	 , $NaOCH_2CF_3$	CF_3CH_2OH, 20 min	 I (51)	172b
	 , Et_3N, $LiClO_4$	Et_2O, 2.5 h	I (12)	172b
	 , $NaOCH_2CF_2CHF_2$	$F_2HCCF_2CH_2OH$, 0° to rt, 20 min	I (70)	172b
	 , $NaOCH_2CF_2CHF_2$	$F_2HCCF_2CH_2OH$, 0°	 (95)	172b
	1.  $(CH_2)_nCO_2Me$, $NaOCH_2CF_2CF_2H$ 2. Zn/CuCl	$F_2HCCF_2CH_2OH$, 4 h MeOH, 15 h	 $(CH_2)_nCO_2Me$, n: 2 (34), 3 (32), 4 (30)	72
	 , Et_3N, $LiClO_4$	Et_2O, rt, 2.5 h	 I (34)	42, 43, 45
	 , Et_3N	CF_3CH_2OH	I (—)	176, 38
	 , Et_3N	MeOH, rt, 3 d	I (54)	71, 177
	 , Et_3N	CF_3CH_2OH, rt, 3.5 h	 I (52)	128
	 , Et_3N	MeOH	I (45)	168
	 $CH(OMe)_2$, Et_3N	CF_3CH_2OH, rt, 90 min	 $CH(OMe)_2$, +  $CH(OMe)_2$, (63)	176, 177
	 , Et_3N, $LiClO_4$	Et_2O, rt, 2.5 h	 I (51)	42, 45
	 , Et_3N	CF_3CH_2OH, rt, 75 min	I (52)	43
C_4 	 , Et_3N, $LiClO_4$	Et_2O, rt	 (5) A:B (4 : 1) (68)	42
	 , Et_3N, $LiClO_4$	Et_2O, rt	 A +  B A + B (68), A:B = 4:1	40
	 , Et_3N	CF_3CH_2OH, rt, 11 d	 (13)	173

TABLE III. [4+3] CYCLOADDITION OF HALOKETONES (BASE CONDITIONS) (*Continued*)

D. With Furan Derivatives (*Continued*)

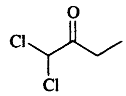
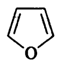
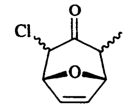
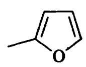
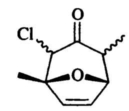
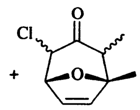
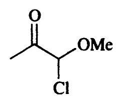
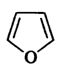
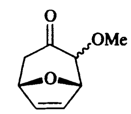
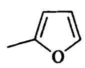
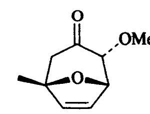
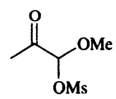
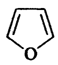
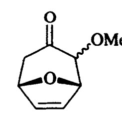
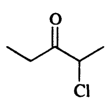
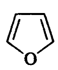
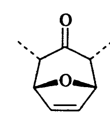
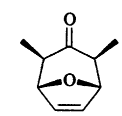
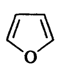
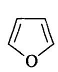
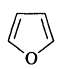
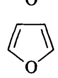
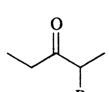
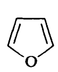
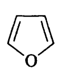
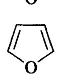
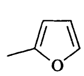
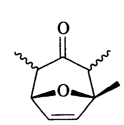
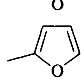
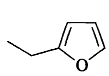
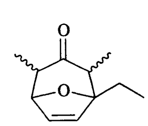
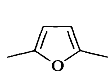
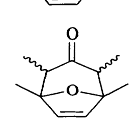
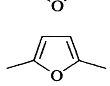
Haloketone	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
	, Et_3N, $LiClO_4$	Et_2O, rt, 2 h	 (72)	42
	, Et_3N, $LiClO_4$	Et_2O, rt	 A +  B A + B (68), A:B = 4:1	40
	, Et_3N, $LiClO_4$	Et_2O, rt, 24 h	 (44)	172b
	, Et_3N, $LiClO_4$	Et_2O, rt	 (38)	172b
	, $NaOCH_2CF_3$	CF_3CH_2OH, 24 h	 (—)	172b
C_5 	, Et_3N, $LiClO_4$	Et_2O, rt, 6 h	 A +  B A + B (78), A:B = 81:19	42, 178
	, $NaOCH_2CF_3$	CF_3CH_2OH, rt, 1 d	A + B (93)	43, 45
	, Et_3N	MeOH, 60 d	A + B (39)	44, 47
	, NaOMe	MeOH, 48 h	A + B (53)	44
	, Et_3N	CF_3CH_2OH, rt, 5 d	A + B (77)	45
	, Et_3N	MeOH, rt, 3 d	A + B (52)	47, 44
	, $NaOCH_2CF_3$	CF_3CH_2OH, 1 d	A + B (93)	43, 45
	, Et_3N, $AgBF_4$	MeCN, rt, 16 h	A + B (80)	37
	, Et_3N	MeOH, rt, 4 d	 I (77)	44
	, Et_3N, $AgBF_4$	MeCN, 16 h	I (53)	37
	, Et_3N, $AgBF_4$	MeCN, 16 h	 (65)	37
	, Et_3N, $AgBF_4$	MeCN, 16 h	 I (83)	37
	, $NaOCH_2CF_2CF_2H$	$F_2HCCF_2CH_2OH$	I (87)	72

TABLE III. [4+3] CYCLOADDITION OF HALOKETONES (BASE CONDITIONS) (*Continued*)

D. With Furan Derivatives (*Continued*)

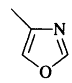
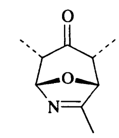
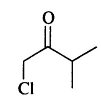
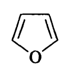
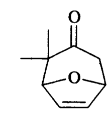
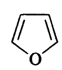
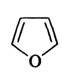
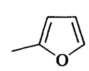
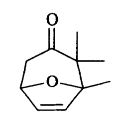
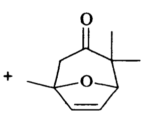
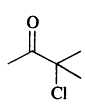
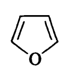
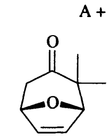
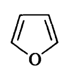
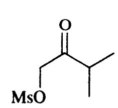
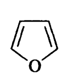
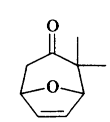
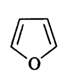
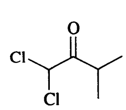
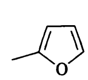
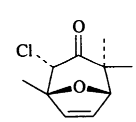
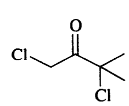
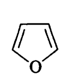
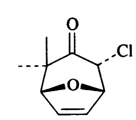
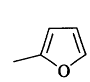
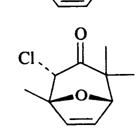
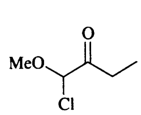
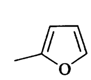
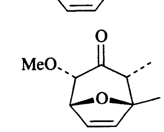
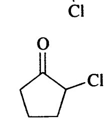
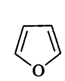
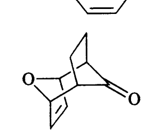
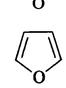
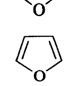
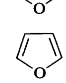
Haloketone	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
	 , $NaOCH_2CF_2CF_2H$	$F_2HCCF_2CH_2OH$	 (13)	72
	 , Et_3N, $LiClO_4$	Et_2O, rt, 43 h	 I (66)	42
	 , Et_3N	CF_3CH_2OH, rt, 25 d	I (45)	45, 43
	 , $NaOCH_2CF_3$	CF_3CH_2OH, rt, 29 d	I (56)	45, 43
	 , Et_3N, $LiClO_4$	Et_2O	 A +  B A + B (49), A:B = 1:1	40
	 , Et_3N, $LiClO_4$	Et_2O, 117 d	 I (68)	39
	 , $NaOCH_2CF_3$	CF_3CH_2OH	I (56)	178
	 , Et_3N	CF_3CH_2OH, 48 h	 I (47)	173
	 , Et_3N, $LiClO_4$	Et_2O, 0.5 h	I (68)	173
	 , Et_3N, $LiClO_4$	Et_2O, rt	 (48)	40
	 , Et_3N, $LiClO_4$	Et_2O, 2 h	 (52)	39
	 , Et_3N, $LiClO_4$	Et_2O, rt	 (68)	40
	 , Et_3N, $LiClO_4$	Et_2O, rt	 (49)	40
	 , Et_3N, $LiClO_4$	Et_2O, 4 h	 I (64)	42
	 , NaOMe	CF_3OH, 30 min	I (73)	172
	 , Et_3N	MeOH, rt, 3 d	I (37)	172
	 , $NaOCH_2CF_3$	CF_3CH_2OH, rt, 20 min	I (80)	172

TABLE III. [4+3] CYCLOADDITION OF HALOKETONES (BASE CONDITIONS) (*Continued*)

D. With Furan Derivatives (*Continued*)

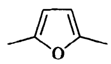
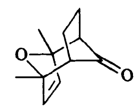
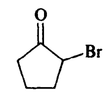
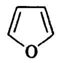
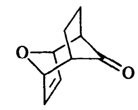
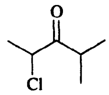
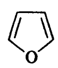
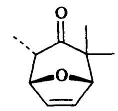
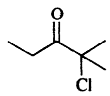
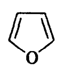
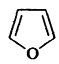
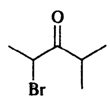
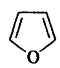
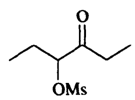
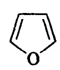
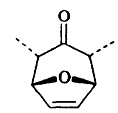
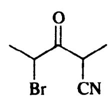
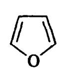
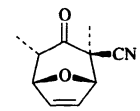
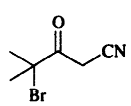
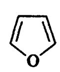
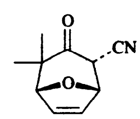
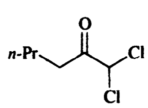
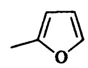
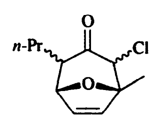
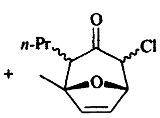
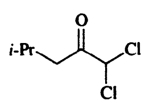
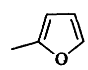
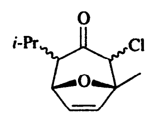
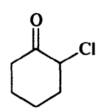
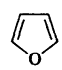
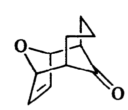
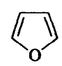
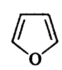
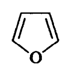
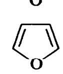
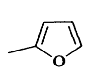
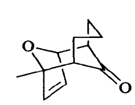
Haloketone	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
	, $NaOCH_2CF_3$	CF_3CH_2OH, 0°, 45 min	 (82)	172
	, Et_3N, $LiClO_4$	Et_2O, 5 h	 (63)	42
C_6 	, Et_3N	CF_3CH_2OH, rt, 10 d	 I (68)	43, 45
	, Et_3N	CF_3CH_2OH, rt, 4 d	I (73)	43
	, $NaOCH_2CF_3$	CF_3CH_2OH, rt, 3 d	I (91)	43
	, Et_3N	MeOH, 2 d	I (30)	47
	, Et_3N	CF_3CH_2OH, rt, 2 h	 (78)	173
	, Ag_2O	rt, 20 h	 (22)	39, 46
	, Ag_2O	rt, 4 d	 (31)	39
	, Et_3N, $LiClO_4$	Et_2O, rt	 A +  B A + B (78), A:B = 5:1	40
	, Et_3N, $LiClO_4$	Et_2O, rt	 (54)	40
	, $NaOCH_2CF_3$	CF_3CH_2OH, rt	 I (—)	174
	, Et_3N, $LiClO_4$	Et_2O, 45 h	I (81)	42
	, Et_3N	CF_3CH_2OH, rt, 3 d	I (70)	48
	, $(i\text{-}Pr)_2NEt$	CF_3CH_2OH, rt, 3 d	I (63)	48
	, proton sponge	CF_3CH_2OH, rt, 3 d	I (32)	48
	, Et_3N	CF_3CH_2OH, rt, 3 d	 (66)	48

TABLE III. [4+3] CYCLOADDITION OF HALOKETONES (BASE CONDITIONS) (*Continued*)

D. With Furan Derivatives (*Continued*)

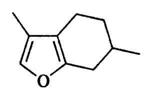
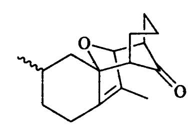
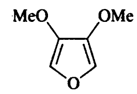
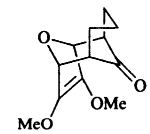
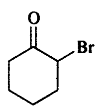
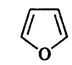
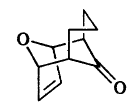
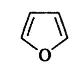
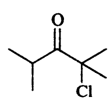
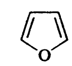
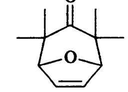
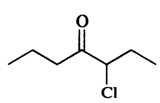
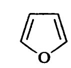
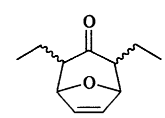
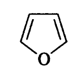
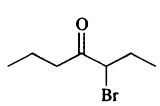
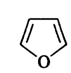
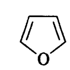
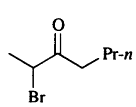
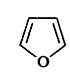
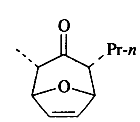
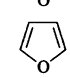
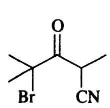
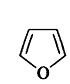
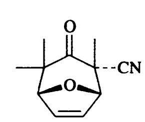
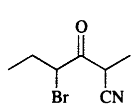
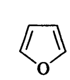
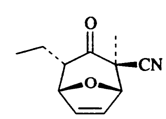
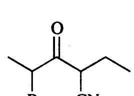
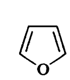
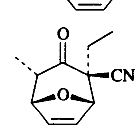
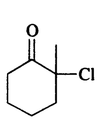
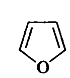
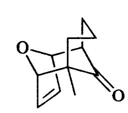
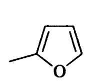
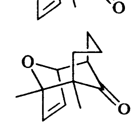
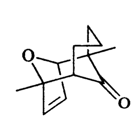
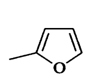
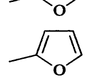
Haloketone	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
	 , Et_3N	CF_3CH_2OH, rt, 2 d	 (25)	48
	 , NaH	Et_2O, 15 h	 (—)	179
	 , Et_3N	CF_3CH_2OH, rt, 3 d	 I (84)	43, 45
	 , Et_3N, $LiClO_4$	Et_2O, 4.5 h	I (68)	42
C_7 	 , base	CF_3CH_2OH, rt, 19 months	 (21)	178
	 , base	CF_3CH_2OH, rt	 I (—)	178
	 , Et_3N, $LiClO_4$	Et_2O, 24 h	I (83)	42
	 , Et_3N, $LiClO_4$	Et_2O, 5 h	I (79)	42
	 , Et_3N, $LiClO_4$	MeOH, 2 d	I (—)	47
	 , Et_3N, $AgBF_4$	MeCN, rt, 6 h	 I (75)	37
	 , Et_3N, $AgBF_4$	MeOH, 2 d	I (—)	47
	 , Ag_2O	rt, 18 h	 (75)	39
	 , Ag_2O	rt, 14 h	 (45)	39
	 , Ag_2O	rt, 19 h	 (50)	39
	 , Et_3N	CF_3CH_2OH, 12 h	 (56)	48
	 , Et_3N	CF_3CH_2OH, rt, 3 h	 A +  B A + B (60), A:B = 7:1	48
	 , $(i\text{-}Pr)_2NEt$	CF_3CH_2OH, 1.5 h	A + B (47), A:B = 20:1	48
	 , DBU	CF_3CH_2OH, 1.5 h	A + B (33), A:B = 7:1	48

TABLE III. [4+3] CYCLOADDITION OF HALOKETONES (BASE CONDITIONS) (*Continued*)

D. With Furan Derivatives (*Continued*)

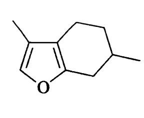
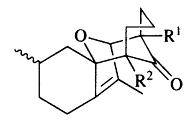
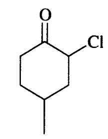
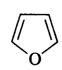
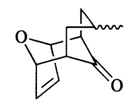
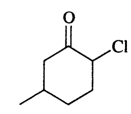
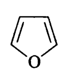
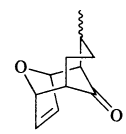
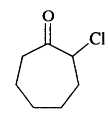
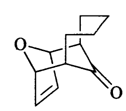
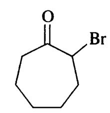
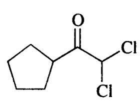
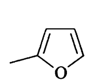
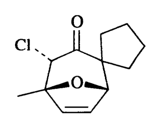
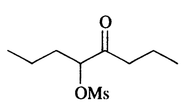
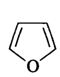
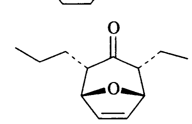
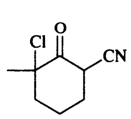
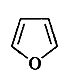
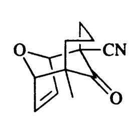
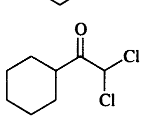
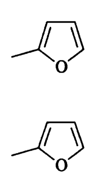
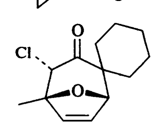
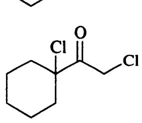
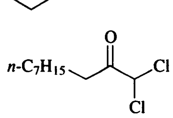
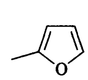
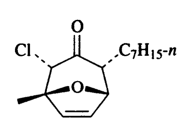
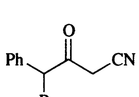
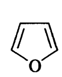
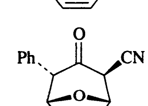
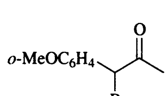
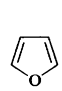
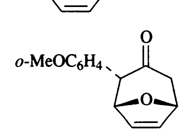
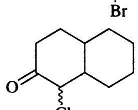
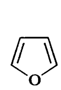
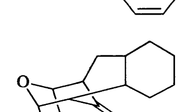
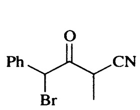
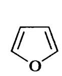
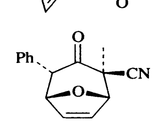
Haloketone	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
	 , Et_3N	CF_3CH_2OH, 2 h	 A: R^1 = Me, R^2 = H; B: R^1 = H, R^2 = Me; A + B (23), A:B = 5:3	48
	 , Et_3N	CF_3CH_2OH, rt, 3 d	 (49)	48
	 , Et_3N	CF_3CH_2OH, rt, 3 d	 (63)	48
	 , Et_3N, $LiClO_4$	Et_2O, 34 d	 **I** (11)	42
	, Et_3N, $LiClO_4$	Et_2O, 11 d	**I** (16)	42
	 , Et_3N, $LiClO_4$	Et_2O, rt	 (48)	40
C_8 	 , Et_3N	CF_3CH_2OH, rt, 3.5 h	 (75)	173
	 , Ag_2O	64 h	 (10)	39
	 , Et_3N, $LiClO_4$	Et_2O	 **I** (83)	40
	, Et_3N, $LiClO_4$	Et_2O	**I** (75)	40
C_{10} 	 , Et_3N, $LiClO_4$	Et_2O	 (59)	40
	 , Ag_2O	—	 (—)	41
	 , Et_3N	CF_3CH_2OH, rt, 24 h	 (73)	180
	 , Et_3N	CF_3CH_2OH, rt, 3 d	 (61)	48
C_{11} 	 , Ag_2O	—	 (—)	41

TABLE III. [4+3] CYCLOADDITION OF HALOKETONES (BASE CONDITIONS) (*Continued*)

D. With Furan Derivatives (*Continued*)

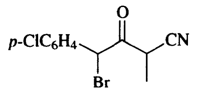
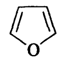
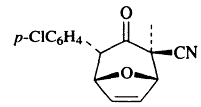
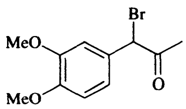
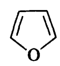
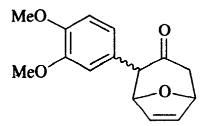
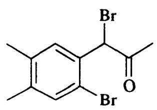
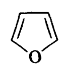
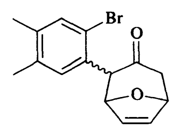
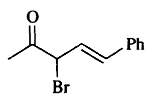
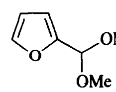
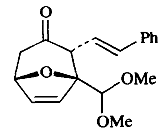
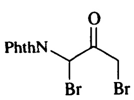
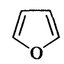
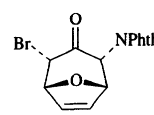
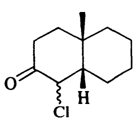
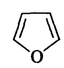
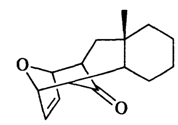
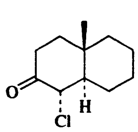
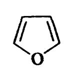
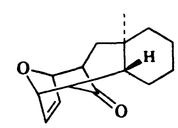
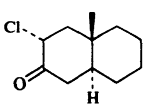
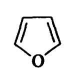
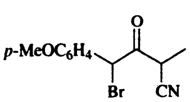
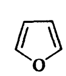
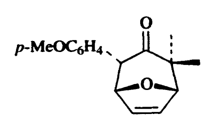
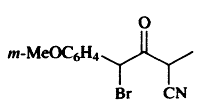
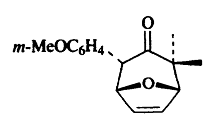
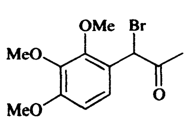
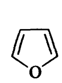
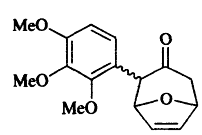
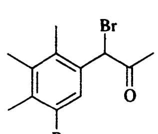
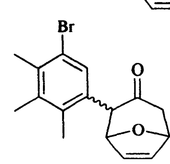
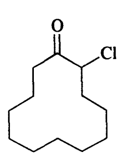
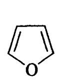
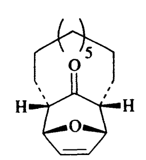
Haloketone	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
	 , Ag_2O	—	 (—)	41
	 , Et_3N	CF_3CH_2OH, rt, 24 h	 (28)	41
	 , Et_3N	CF_3CH_2OH, rt, 24 h	 (54)	41
	 , Et_3N	CF_3CH_2OH	 (26)	17, 177
	 , Et_3N	CH_3CH_2OH, 0 to 45°, 4 h	 (60)	175
	 , Et_3N	CF_3CH_2OH, rt, 3 d	 (71)	48
	 , Et_3N	CF_3CH_2OH, rt, 3 d	 **I** (66)	48
	 , Et_3N	CF_3CH_2OH, rt, 10 d	**I** (66)	48
C_{12}				
	 , Ag_2O	—	 (—)	41
	 , Ag_2O	—	 (—)	41
	 , Et_3N	CF_3CH_2OH, rt,	 (10)	180
	 , Et_3N	CF_3CH_2OH, rt,	 (10)	180
	 , Et_3N, $LiClO_4$	Et_2O, 30 h	 (56)	42

TABLE III. [4+3] CYCLOADDITION OF HALOKETONES (BASE CONDITIONS) (*Continued*)

D. With Furan Derivatives (*Continued*)

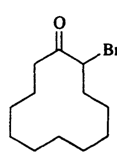
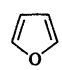
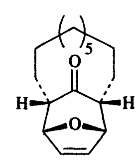
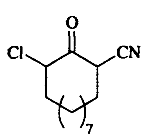
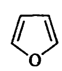
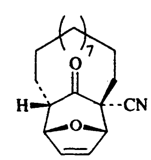
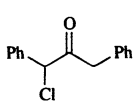
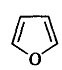
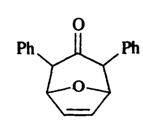
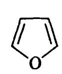
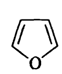
Haloketone	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
	, Et_3N, $LiClO_4$	Et_2O, 23 h	 (58)	42
C_{13} 	, Ag_2O	rt, 20 h	 (20)	39
C_{15} 	, 2,6-lutidine	DMF, 96 h	 I (18)	181
	, Et_3N	MeOH	I (—)	47
	, Al_2O_3	—	I (—)	96

TABLE IV. PHOTOINITIATED [4+3] CYCLOADDITIONS

A. With Carbocyclic Dienes

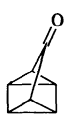
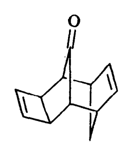
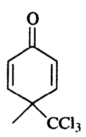
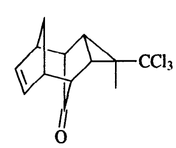
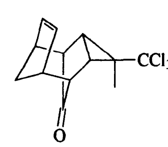
Substrate	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7 		n-C_5H_{12}, $h\nu$, 11 h	 (37)	182
C_8 		C_6H_6, $h\nu$, 25 h	 (—) +  (—)	183, 184

TABLE IV. PHOTOINITIATED [4+3] CYCLOADDITIONS (*Continued*)

B. With Furan

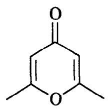
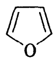
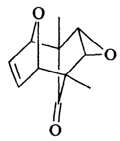
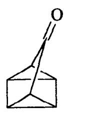
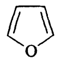
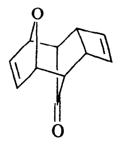
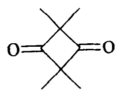
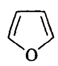
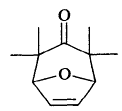
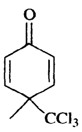
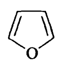
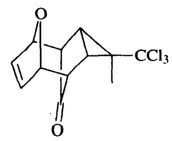
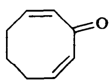
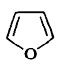
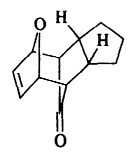
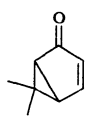
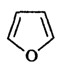
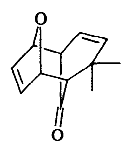
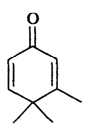
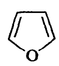
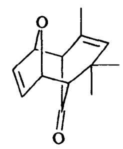
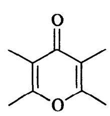
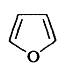
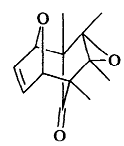
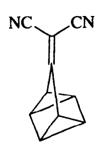
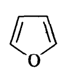
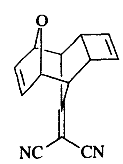
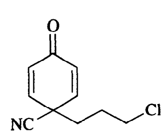
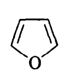
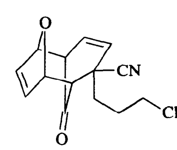
Substrate	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7 		CF_3CH_2OH, *hv*, 35 h	 (37)	50, 51
		*hv*, 20 h	 (50)	182
C_8 		67°, *hv*	 (35)	185, 186
	, Et_3N	*hv*	 (—)	184
		*hv*	 (—)	49
		Et_2O, *hv*	 (—)	187
C_9 		Et_2O, *hv*	 (—)	187
		CF_3CH_2OH, *hv*	 (39)	52
C_{10} 		*hv*, 20 min	 (9)	188
		C_6H_6, *hv*, 18 h	 (20)	189

TABLE IV. PHOTOINITIATED [4+3] CYCLOADDITIONS (*Continued*)

B. With Furan (*Continued*)

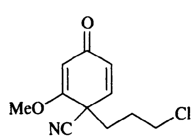
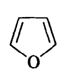
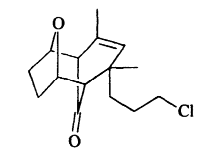
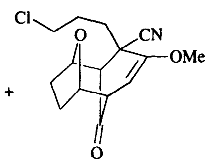
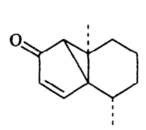
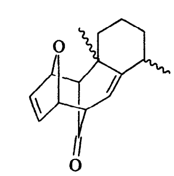
Substrate	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
		C_6H_6, *hν*, 16 h	 (21) +  (32)	189
C_{12} 		*hν*	 (—)	190

TABLE V. INTRAMOLECULAR [4+3] CYCLOADDITIONS

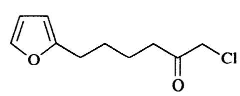
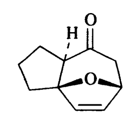
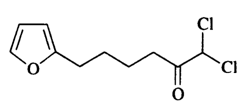
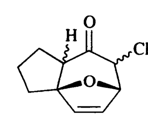
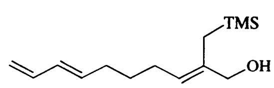
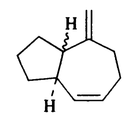
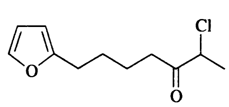
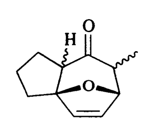
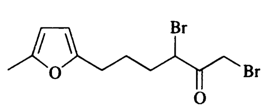
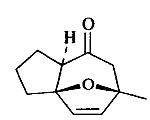
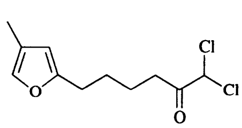
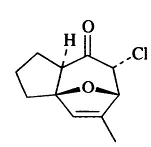
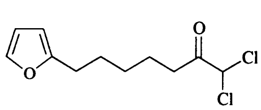
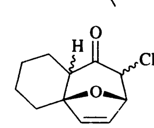
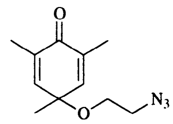
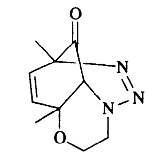
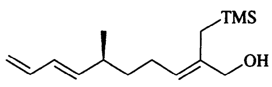
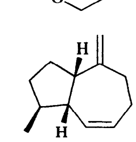
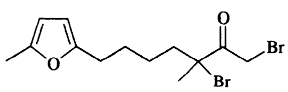
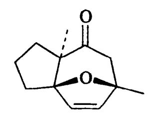
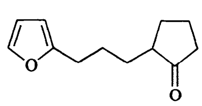
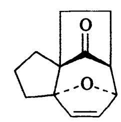
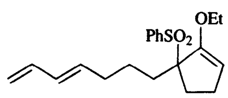
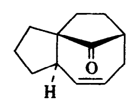
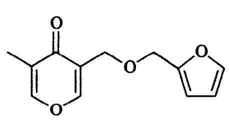
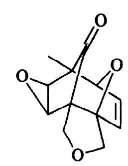
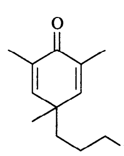
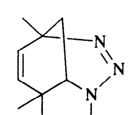
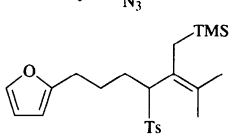
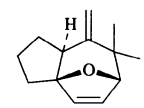
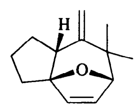
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10}			
	Et_3N, $LiClO_4$, Et_2O, rt, 4 d	 (10)	191
	Et_3N, $LiClO_4$, Et_2O, rt, 22 h	 (76)	191
C_{11}			
	Tf_2O, 2,6-lutidine, CH_2Cl_2, −78°	 (65)	53
	Et_3N, $LiClO_4$, Et_2O, rt, 12 h	 (84)	191
	$Fe_2(CO)_9$, C_6H_6, 80°, 3 h	 (41)	192
	Et_3N, $LiClO_4$, Et_2O, 53 h	 (70)	193
	Et_3N, $LiClO_4$, Et_2O, rt, 19 h	 (30)	191

TABLE V. INTRAMOLECULAR [4+3] CYCLOADDITIONS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	*hv*, THF, 2 h	 (75)	194, 195
C_{12}			
	Tf_2O, 2,6-lutidine, CH_2Cl_2, –78°	 (82)	196
	$Fe_2(CO)_9$, C_6H_6, 80°, 3 h	 (38)	192
	1. LDA, CF_3SO_2Cl 2. $LiClO_4$, Et_3N, Et_2O	 (55)	10, 55, 197
	$TiCl_4$, CH_2Cl_2, –78°	 (81)	10
	*hv*, CF_3CH_2OH, 0.5 h	 (10)	52
	*hv*, THF, 2 h	 (64)	194, 195
C_{13}			
		 A +  B	

Conditions	A + B	A:B	Refs.
hv, MeCN, 35°, 2.5 h	(13)	1:6.5	198
hv, MeCN, 52°, 17.3 h	(34)	1:8.1	198
hv, MeCN, 52°, 2.2 h	(20)	1:8.7	198
hv, MeCN, 52°, 2.4 h	(30)	1:8.4	198
hv, MeCN, 52°, 3.5 h	(27)	1:9	198
hv, MeCN, 52°, 5 h	(22)	0:1	198
hv, acetone, 43°, 3.5 h	(26)	1:5.2	198
hv, C_6H_6, 45°, 2.5 h	(—)	1:3.8	198
hv, MeOH, 47°, 9.5 h	(30)	1:7.8	198
hv, CH_2Cl_2, 35°, 2.5 h	(20)	1:1.5	198
hv, Et_2O, 43°, 7.5 h, $LiClO_4$	(8)	1:7.7	198
hv, Et_2O, 34°, 2.5 h, $LiClO_4$	(24)	1:8.8	198
hv, Et_2O, 34°, 2.5 h, $LiClO_4$	(8)	1:7.1	198
hv, Et_2O, 32°, 2.5 h, $LiClO_4$	(12)	—	198
hv, MeCN, 10°, 2.5 h	(19)	1:5.6	198
hv, MeCN, 35°, 2.5 h	(35)	1:7.8	198
hv, MeCN, 35°, 2.5 h	(23)	1:7.5	198
$TiCl_4$, –78°, 0.3 h	(14)	—	199
$ZnCl_2$, –78°, 1 h	(41)	1:3.9	199
BF_3•Et_2O, –78 to –22°, 4.6 h	(18)	1;3.8	199
$AlCl_3$, –78°, 0.8 h	(37)	1.3:1	199
$AlCl_3$, –78°, 0.8 h	(40)	1:2.3	199

TABLE V. INTRAMOLECULAR [4+3] CYCLOADDITIONS (*Continued*)

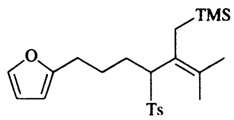
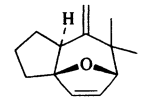
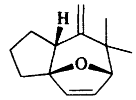
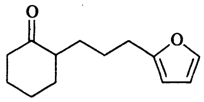
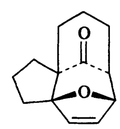
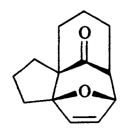
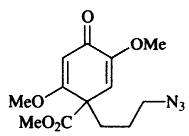
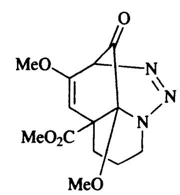
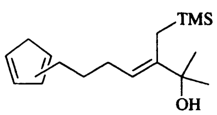
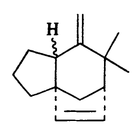
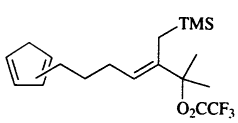
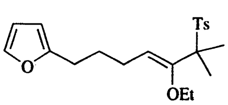
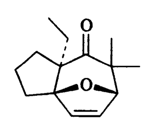
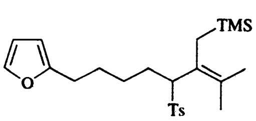
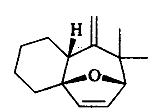
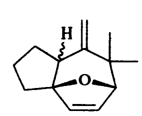
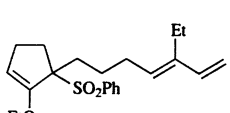
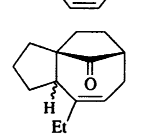
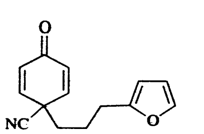
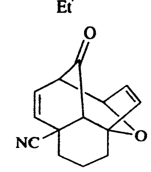
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
		 A +  B	
		A + B A:B	
	$AlClEt_2$, –78 to –22°, 4.5 h	(47) 1.2:1	199
	$AlClMe_2$, –78 to –22°, 17.5 h	(62) 1.1:1	199
	$AlMe_3$ (0.01 M), –78 to –22°, 16.4 h	(71) 1.7:1	199
	$AlMe_3$ (0.005 M), –78 to –22°, 16.4 h	(63) 1:2.5	199
	1. LDA, CF_3SO_2Cl 2. $LiClO_4$, Et_2O	 A +  B A + B (54), A:B = 1:2.5	55
	*hv*, C_6H_6, 28 h	 (10)	195
C_{14} 	$TiCl_4$, PhNHMe, CH_2Cl_2, –60°	 I (6)	200, 201
	$ZnCl_2$, MeCN, 0°	I (9)	201
	$ZnCl_2$, C_5H_{12}, Al_2O_3, –30°	I (16)	201
	ZnI_2, C_5H_{12}, Al_2O_3, –30°	I (—)	201
	$TiCl_4$, CH_2Cl_2, –78°	 (74)	54, 202, 203
	$AlMe_3$, CH_2Cl_2, 22.25 h, –78°	 (39)	199
	hv, MeCN	 (16)	199
	$TiCl_4$, CH_2Cl_2, –78°	 (57)	10
	*hv*, C_6H_6, 5 h	 (—)	189

TABLE V. INTRAMOLECULAR [4+3] CYCLOADDITIONS (*Continued*)

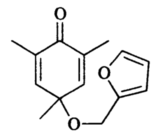
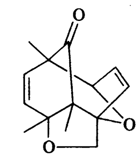
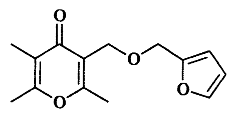
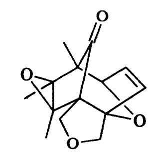
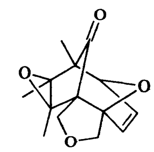
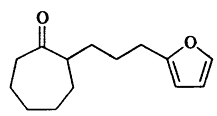
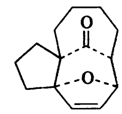
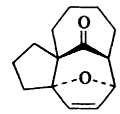
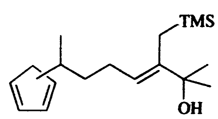
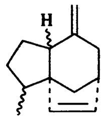
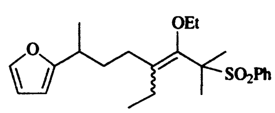
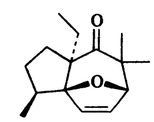
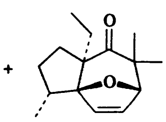
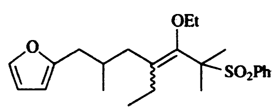
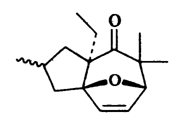
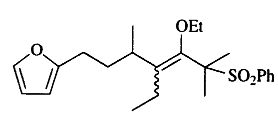
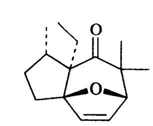
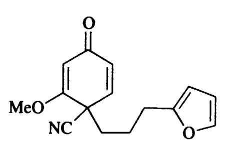
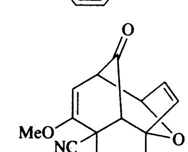
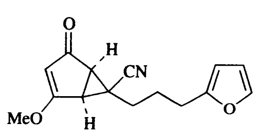
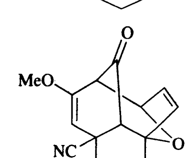
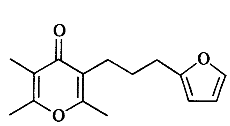
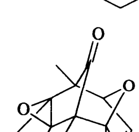
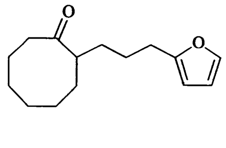
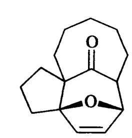
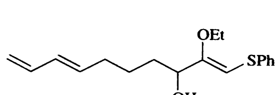
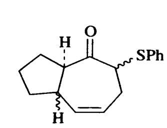
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	*hν*, C_6H_6	 (80)	195
	*hν*, CF_3CH_2OH, 2 h	 (30) +  (20)	52
	1. LDA, CF_3SO_2Cl 2. $LiClO_4$, Et_3N	 (49) +  (7)	11, 55
C_{15} 	1. $(CF_3CO)_2O$, $EtN(Pr\text{-}i)_2$ 2. $ZnCl_2$, Al_2O_3, –60°	 (16)	92
	$TiCl_4$, CH_2Cl_2, –78°	 A +  B A + B (58), A:B = 60:40	202, 203a
	$TiCl_4$, CH_2Cl_2, –78°	 (54)	202, 203a
	$TiCl_4$, CH_2Cl_2, –78°	 (58)	202, 203a
	*hν*, C_6H_6, 7.5 h	 (40)	189
	*hν*, (Pyrex)	 (43)	189
	*hν*, CF_3CH_2OH	 (10)	52
	1. LDA, CF_3SO_2Cl 2. $LiClO_4$, Et_2O	 I (17)	55
	1. LDA, CF_3SO_2Cl 2. $NaOCH_2CF_3$, CF_3CH_2OH	I (69)	55
C_{16} 	$(CF_3SO_2)_2O$, CH_2Cl_2, 2,6-lutidine, –78°	 (63)	204

TABLE V. INTRAMOLECULAR [4+3] CYCLOADDITIONS (*Continued*)

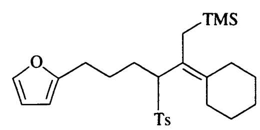
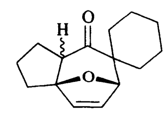
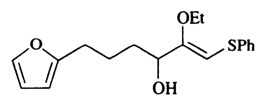
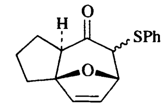
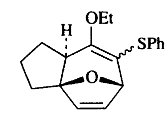
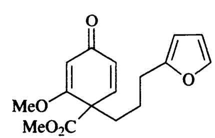
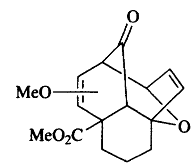
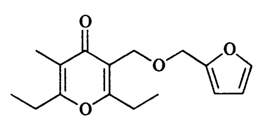
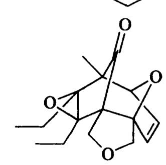
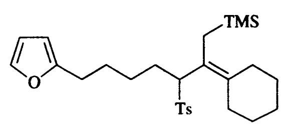
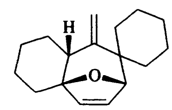
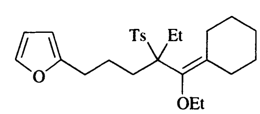
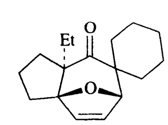
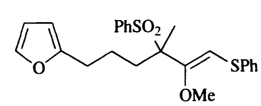
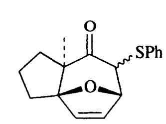
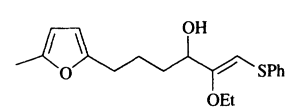
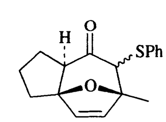
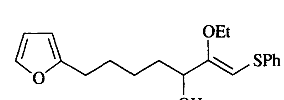
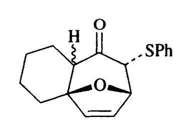
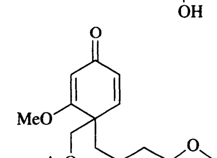
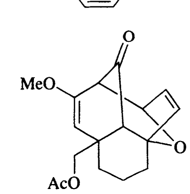
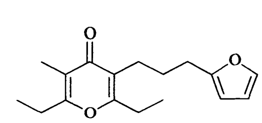
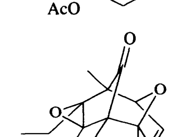
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
		 I (11)	198
	$AlMe_3$, CH_2Cl_2, −78°	I (71)	199
	$(CF_3SO_2)_2O$, CH_2Cl_2, 2,6-lutidine, −78°	 (49) +  (37)	204
	*hv*	 (19)	189
	*hv*, CF_3CH_2OH	 (19)	52
C_{17} 	$AlMe_3$, CH_2Cl_2, −78°	 I (50)	199
	hv, MeCN	I (22)	198
	$TiCl_4$, CH_2Cl_2, −78°	 (66)	54, 202
	$TiCl_4$, CH_2Cl_2, −78°	 (12)	205
	$(CF_3SO_2)_2O$, CH_2Cl_2, 2,6-lutidine, −78°	 (48)	204
	$(CF_3SO_2)_2O$, CH_2Cl_2, 2,6-lutidine, −78°	 (59)	204
	*hv*, C_6H_6, 30 h	 (27)	195
	*hv*, CF_3CH_2OH	 (19)	52

TABLE V. INTRAMOLECULAR [4+3] CYCLOADDITIONS (*Continued*)

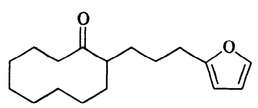
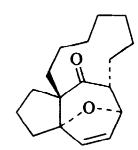
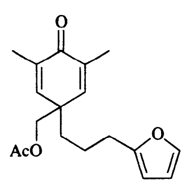
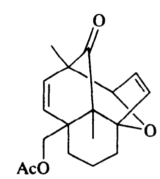
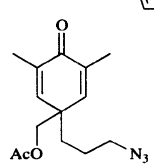
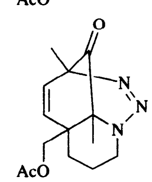
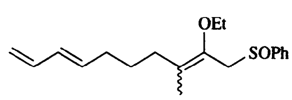
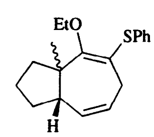
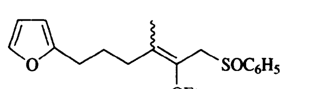
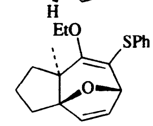
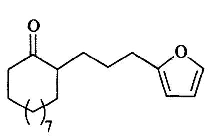
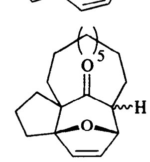
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	1. LDA, CF_3SO_2Cl 2. $LiClO_4$, Et_3N	 (63)	11, 55
C_{18} 	$h\nu$, C_6H_6, 3.5 h	 (100)	195
	$h\nu$, C_6H_6, 1.5 h	 (17)	195
C_{19} 	$(CF_3SO_2)_2O$, CH_2Cl_2, 2,6-di-*tert*-butylpyridine	 (53)	205
	$(CF_3SO_2)_2O$, CH_2Cl_2, 2,6-lutidine, rt	 (86)	204
	1. LDA, $(CF_3SO_2)_2O$ 2. $LiClO_4$, Et_2O	 (69)	11, 55

TABLE VI. MISCELLANEOUS [4+3] CYCLOADDITIONS

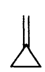
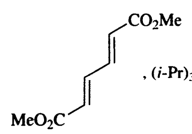
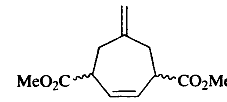
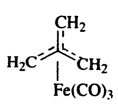
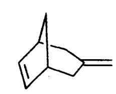
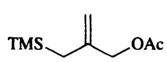
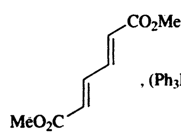
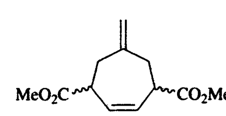
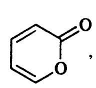
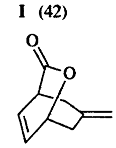
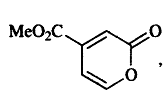
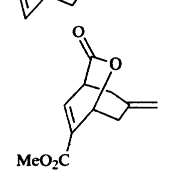
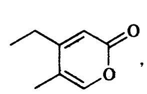
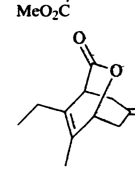
3C Partner	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4				
	, $(i\text{-}Pr)_3P$, Pd^0	—	 (67)	206
		*hv*, $n\text{-}C_5H_{12}$	 (23)	207
	, $(Ph_3P)_4Pd$	THF, dppe	 **I** (18)	208
	Dimethyl muconate, $(Ph_3P)_4Pd$	Dioxane, dppe	**I** (20)	208, 209
	Dimethyl muconate, $[(i\text{-}PrO)_3P]_4Pd$	THF	**I** (42)	208
	, $[(i\text{-}PrO)_3P]_4Pd$	C_6H_6, 80°	 (70)	210
	, $[(i\text{-}PrO)_3P]_4Pd$	C_6H_6, 80°	 (—)	210
	, $[(i\text{-}PrO)_3P]_4Pd$	C_6H_6, 80°	 (84)	210

TABLE VI. MISCELLANEOUS [4+3] CYCLOADDITIONS (*Continued*)

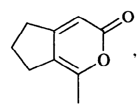
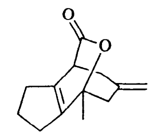
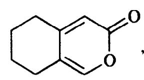
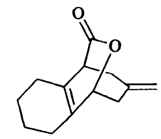
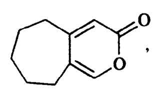
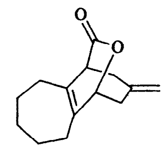
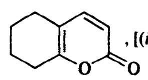
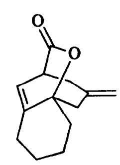
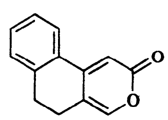
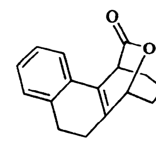
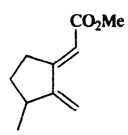
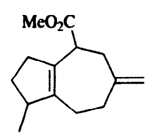
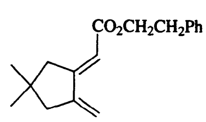
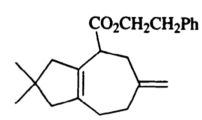
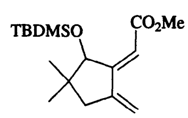
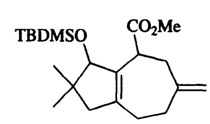
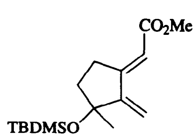
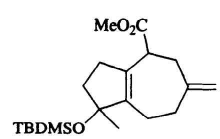
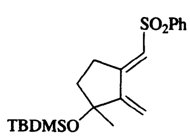
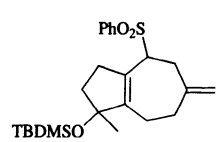
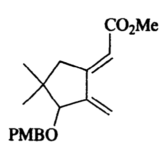
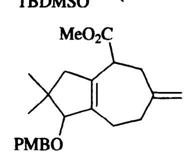
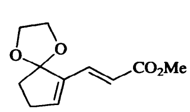
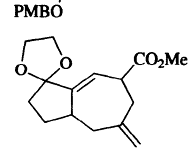
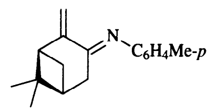
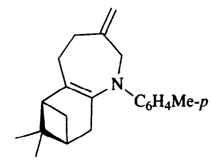
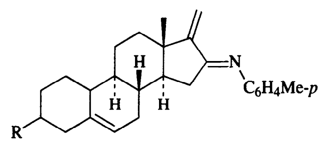
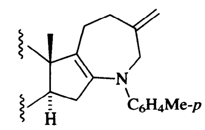
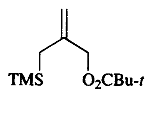
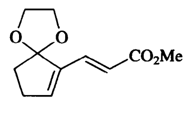
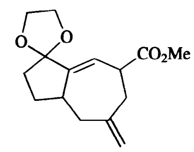
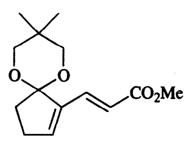
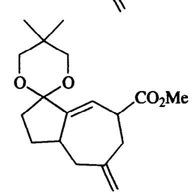
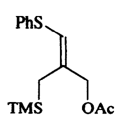
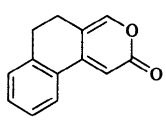
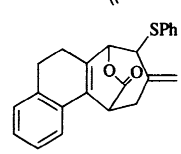
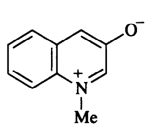
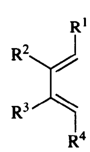
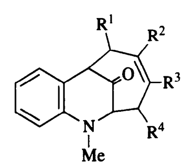
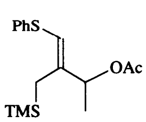
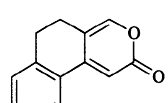
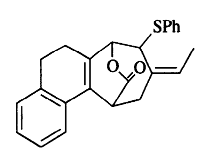
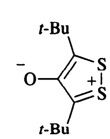
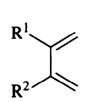
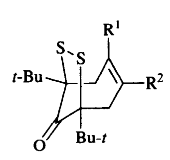
3C Partner	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
	, $[(i\text{-PrO})_3P]_4Pd$	C_6H_6, 80°	 (86)	210
	, $[(i\text{-PrO})_3P]_4Pd$	C_6H_6, 80°	 (90)	210
	, $[(i\text{-PrO})_3P]_4Pd$	C_6H_6, 80°	 (92)	210
	, $[(i\text{-PrO})_3P]_4Pd$	C_6H_6, 80°	 (23)	210
	, $[(i\text{-PrO})_3P]_4Pd$	C_6H_6, 80°	 (90)	210
		$[(i\text{-PrO})_3P]_4Pd$, THF, reflux	 (76)	211
		$[(i\text{-PrO})_3P]_4Pd$, THF, reflux	 (88)	211
		$[(i\text{-PrO})_3P]_4Pd$, THF, reflux	 (87)	211
		$[(i\text{-PrO})_3P]_4Pd$, THF, reflux	 (65)	211
		$[(i\text{-PrO})_3P]_4Pd$, THF, reflux	 (73)	211
		$[(i\text{-PrO})_3P]_4Pd$, THF, reflux	 (80)	211
		$Pd(OAc)_2$, $(i\text{-PrO})_3P$, BuLi, PhMe	 **I** (22)	212
		$Pd(OAc)_2$, dppe, THF, 60°	**I** (37)	212

TABLE VI. MISCELLANEOUS [4+3] CYCLOADDITIONS (*Continued*)

3C Partner	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
		$Pd(OAc)_2$, $(i\text{-}PrO)_3P$, PhMe, 100°	 (100)	213
	 R = TBDMSO	$Pd(OAc)_2$, $(i\text{-}PrO)_3P$, dioxane, 100°	 (100)	213
		$Pd(OAc)_2$, dppe, THF, 60°	 (39)	212
		$Pd(OAc)_2$, $(i\text{-}PrO)_3P$, THF, 60°	 (40)	212
C_{10}				
		$Pd(OAc)_2$, $(i\text{-}PrO)_3P$, dioxane, dppp	 (76)	214
		Et_3N		215

R^1	R^2	R^3	R^4	Yield (%)
H	H	H	H	(40)
Me	H	H	H	(25)
H	H	H	Me	(45)
H	Me	H	H	(20)
H	H	Me	H	(62)
H	Me	Me	H	(57)

3C Partner	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11}				
		$Pd(OAc)_2$, PH_3, dioxane, 100°	 (75)	214
		PhMe, 110 °		216

R^1	R^2	Yield (%)
Me	Me	(72)
Ph	H	(47)
$(CH_2)_4$		(81)

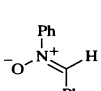
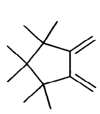
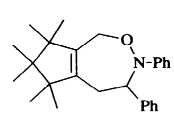
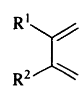
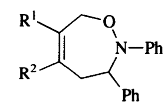
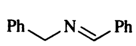
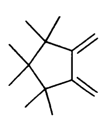
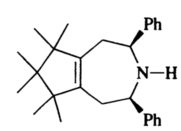
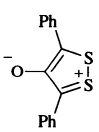
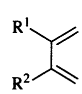
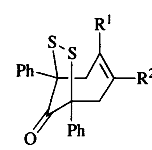
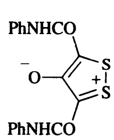
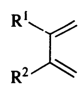
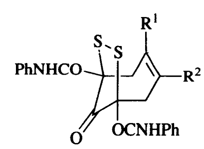
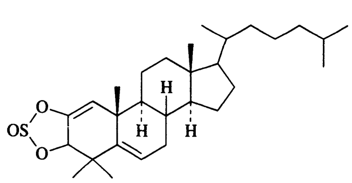
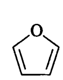
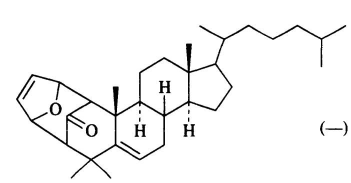
3C Partner	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
		C_6H_6, 80°	 (18)	217, 218

TABLE VI. MISCELLANEOUS [4+3] CYCLOADDITIONS (*Continued*)

3C Partner	Reactants	Conditions	Product(s) and Yield(s) (%)	Refs.
		PhMe, 110 °		218
	R¹ R²			
	Me Me		(3)	
	Ph H		(3)	
	$(CH_2)_3$		(9)	
C_{14}				
		LDA, THF, rt, 4 d	 (52)	219
C_{15}				
		PhMe, 110 °		216
	R¹ R²			
	Me Me		(71)	
	Me H		(34)	
	$(CH_2)_4$		(66)	
C_{17}				
		PhMe, 110 °		216
	R¹ R²			
	Me Me		(76)	
	$(CH_2)_4$		(80)	
C_{29}				
		48 h	 (—)	220

8. Acknowledgments

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