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CYCLOALKENES BY INTRAMOLECULAR WITTIG REACTION

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CONTENTS

1. INTRODUCTION

The Wittig reaction

The condensation of a carbonyl compound with an alkylidenetriphenylphosphorane (1) to give an olefin and triphenylphosphine oxide, the so-called Wittig carbonyl olefination reaction or simply Wittig reaction[1] (Scheme 1), has become one of the favorites among the numerous methods of olefin

1

Scheme 1.

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syntheses.[2] The Wittig reaction has several advantages: As a rule, no double bond isomerization occurs under the reaction conditions, i.e. the new C=C double bond appears exclusively at the site of the former CO function. The starting materials, aldehydes or ketones and phosphonium salts derived from alkyl halides and triphenylphosphine, are readily available. The geometry of the double bond (*E*/*Z*) may be influenced to a considerable extent by the choice of the reaction conditions.[3] The main drawback of the Wittig reaction is its susceptibility to steric hindrance. Whereas aldehydes normally give olefins in high yields, ketones often react less satisfactorily. The Wittig reaction usually fails in the synthesis of a tetrasubstituted olefin.

Stability and reactivity of phosphoranes **1** are influenced to a great extent by the substituents at the ylid C atom. So-called non-stabilized phosphoranes prepared from primary and secondary alkyltriphenylphosphonium salts (**1**, R^3 or $R^4 = H$, alkyl) are highly reactive. Stabilized phosphoranes bearing an electron-withdrawing group, which allows delocalization of the negative charge α to phosphorus by resonance (**1**, $R^3 = COR$, COOR, CN, SO_2R), are less reactive and only weakly basic. The reactivity of benzylidenephosphorane and related aromatic phosphoranes (**1**, $R^3 = aryl$) lies somewhere in between, these ylids are called moderate or semi-stabilized.

For the preparation of olefins bearing electron-withdrawing, conjugating functional groups, it is advantageous to use the Horner or Wadsworth–Emmons modification of the Wittig reaction[4] (Scheme 2).

2

Scheme 2.

Owing to their increased nucleophilicity, anions of phosphonates (**2**, $R^3 = COR$, COOR, CN, ...) often give higher yields of olefins than the corresponding stabilized phosphoranes. The work-up is also more convenient than in the classic Wittig reaction, however, simple alkyl phosphonate carbanions (**2**, $R^3/R^4 = H$, alkyl) fail to give olefins. Other modifications with carbanions of diphenylphosphine oxides, thiophosphonates or phosphonic acid amides have not found widespread application.

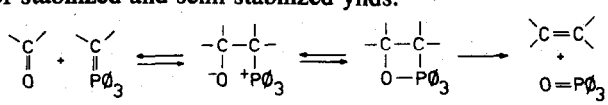
Scope of the review

The scope of this review is a survey of intramolecular Wittig reactions, in which a C=C double bond is formed by condensation of a CO function with an alkylidenephosphorane group incorporated in the same molecule (**3**). Many examples of intramolecular Wittig reactions are cited in the review of Zbiral on the synthesis of heterocycles with prosphorus-containing reagents[5] and in the review of Vollhardt on bis-Wittig reactions in the synthesis of nonbenzenoid aromatic ring systems.[6] These older examples will be discussed only when needed to understand more recent results. Intramolecular alkylations of alkylidenephosphoranes[7] will not be treated, however, cycloalkene-forming reactions of carbonyl compounds **4** bearing a phosphonate group[4] will be included.

3 **4**

Ring size and ring strain

It is commonly assumed that the first step of the Wittig reaction is the formation of a single bond between the ylid carbon α to phosphorus and the carbonyl carbon leading to an intermediate phosphorus betaine **5** (Scheme 3).[1] However, ^{31}PNMR studies on the reaction of non-stabilized ylids and carbonyl compounds in salt-free solutions indicate the presence of oxaphosphetane **6** as the only intermediate. To account for these and other observations, a ($\pi_{2a} + \pi_{2s}$) cycloaddition mechanism without the intermediacy of betaine **5** was postulated.[8] Although **5** cannot be observed directly, it can be trapped. Further experiments with isotopically labelled compounds proved a fast equilibrium between a zwitterionic intermediate like **5** and the oxaphosphetane **6** even at −80°.[9] Scheme 3 represents one possible mechanistic interpretation which is in accord with the experimental facts. Formation of the intermediates is reversible in the case of stabilized and semi-stabilized ylids.



5 **6**

Scheme 3.

In an intramolecular Wittig reaction, a bicyclic oxaphosphetane **6** must be formed. It is therefore no surprise that cyclopropenes and cyclobutenes are not accessible by this reaction. The corresponding oxaphosphabicyclo[2.1.0]pentanes and [2.2.0]hexanes would be excessively strained, although the P-O bond is much longer than a C–C single bond.[10] The β-carbonyl alkylidenephosphoranes **7**, hypothetical precursors of cyclopropenes, are hard to come by, because the corresponding acylethyl-triphenylphosphonium salts undergo Hofmann type elimination of triphenylphosphine on base treatment.[11,12] γ-Carbonyl alkylidenephosphoranes **8** rather give cyclooctadienes by double condensation than cyclobutenes.[13] Triphenylphosphine elimination and formation of a cyclopropyl ketone can also occur.[12]

7 **8**

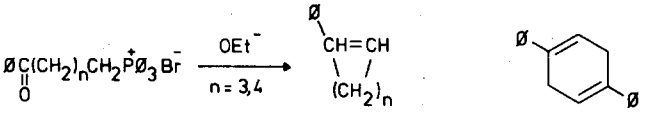
As expected on the basis of the mechanistic interpretation shown in Scheme 3, the common 5-, 6- and also 7-membered rings are produced fairly easily by intramolecular Wittig reaction. The formation of medium- and large-ring cycloalkenes requires high dilution techniques, but can be readily accomplished.

The oxaphosphetane **6** undergoes irreversible cleavage to the C=C double bond and triphenylphosphine oxide (Scheme 3). This last step is fairly exothermic. The Wittig reaction may therefore be used for the synthesis of highly strained cyclic olefins. As long as the carbonyl carbon and the phosphorus ylid carbon can come within reasonable distance from each other and react to give a single bond in a ring with five or more atoms, there are good chances that finally the strained cycloalkene is formed.

2. CYCLIZATION OF PREFORMED CARBONYL ALKYLTRIPHENYLPHOSPHONIUM SALTS AND CARBONYL PHOSPHONATES

Carbocylic rings

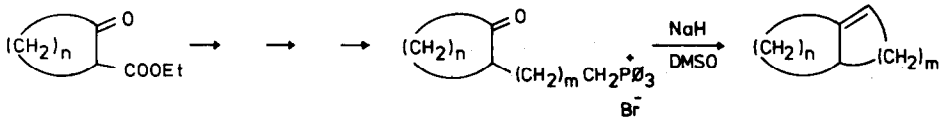
The first example of an intramolecular Wittig reaction with a carbonyl alkyltriphenylphosphonium salt was reported in 1962 by two independent groups.[12,14] The alkylidenephosphoranes prepared from 5-benzoylpentyl- and 4-benzoylbutyl-triphenylphosphonium bromide[9] with sodium ethoxide or butyllithium underwent ring closure to 1-phenylcyclohexene (**10**, n = 4) and 1-phenylcyclopentene (**10**, n = 3), respectively. The next lower homologue, 1-phenylcyclobutene (**10**, n = 2) could not be obtained, and elimination of triphenylphosphine was observed. Benzoylethyl-triphenylphosphonium bromide (**9**, n = 1) gave a low yield of the bis-Wittig product, 1,4-diphenylcyclohexa-1,4-diene (**11**).



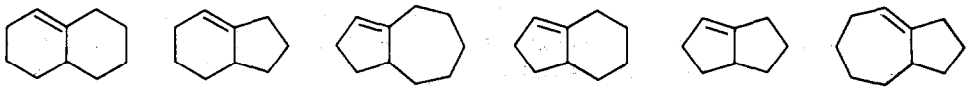
9 **10** **11**

The intramolecular Wittig reaction is the method of choice for the synthesis of annulated bridgehead olefins **14** free of double bond isomers. The corresponding phosphonium salts **13** are readily accessible by alkylation of ketoesters **12** with α,ω-dibromoalkanes followed by hydrolysis, decarboxylation and treatment with triphenylphosphine. With sodium hydride in dimethylsulfoxide, olefins **15–19** incorporating cyclopentene or cyclohexene rings are then obtained in yields of 50–66%. The cycloheptene ring in hydrazulene **20** was formed in 19% yield.[15]

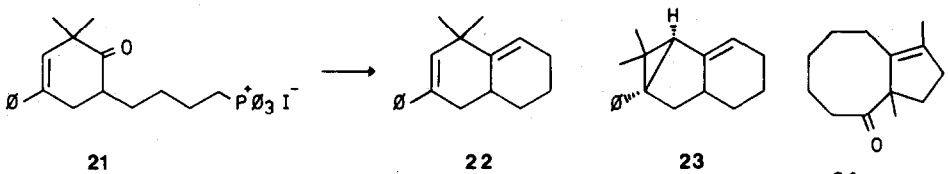
The Wittig reaction usually fails on attempted condensation of highly substituted ketones with alkylidenephosphoranes other than methylidenephosphorane. It is therefore interesting to note that phosphonium iodide **21** yields 73% of the cycloalkene **22** on base treatment. The cyclopropyl olefin **23** was prepared similarly.[16] The remarkable synthesis of a tetrasubstituted double bond in compound **24** by intramolecular Wittig reaction was reported recently.[17]



12 **13** **14**



15 16 17 18 19 20

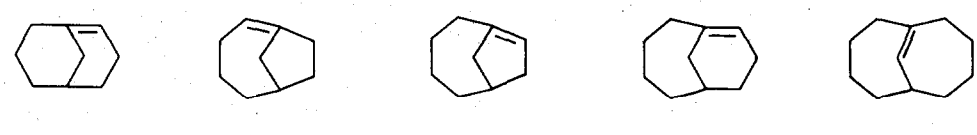


21 22 23 24

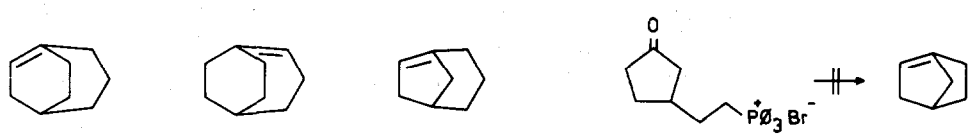
Strained cycloalkenes

A number of "real" bridgehead olefins, which are of interest in connection with Bredt's rule,[18] have been successfully prepared by intramolecular Wittig reaction from the corresponding ketophosphonium bromides.

Olefins **25**, **26**, and **27** belong to the class of bridged (*E*)-cyclooctenes. Like (*E*)-cyclooctene itself, they are stable and can be isolated at room temperature, but their double bond is highly strained and reactive. If during the Wittig reaction and the work-up oxygen and traces of acid are rigorously excluded, high yields of pure bridgehead olefins (e.g. 57% of **27**) may be obtained.[19] Bicyclo[3.3.1]non-1-ene **25** has also been prepared in the (−)(5*S*)-configuration starting with optically active bromoketone.[20] The homologous bridgehead olefin bicyclo[4.3.1]dec-1(9)-ene **28** is less strained and less reactive, it has been prepared similarly.[21] Olefins **29–32**, formally bridged (*E*)-cycloheptenes, cannot be isolated in the intramolecular Wittig reaction. They dimerize rapidly, but may be trapped, e.g. by 2,5-diphenylbenzo[c]furan.[22,23] Base treatment of ketophosphonium bromide **33** gave none of the expected dimers or trapping products from 1-norbornene **34**, formally a bridged (*E*)-cyclohexene, thereby demonstrating the limits of the intramolecular Wittig reaction in the synthesis of strained bridgehead olefins.[23]

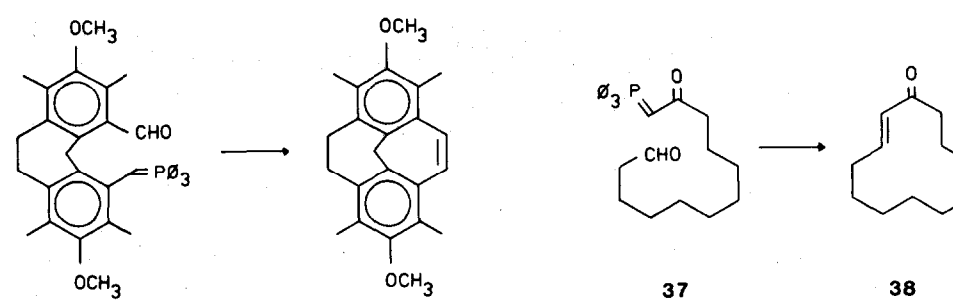


25 26 27 28 29



30 31 32 33 34

Another example for the synthesis of a strained cycloalkene is reported in cyclophane chemistry. The double bond in the [2.1.2](1,2,3)cyclophane **36** was obtained by cyclization of the corresponding benzaldehyde-benzylidenephosphorane **35**.[24]

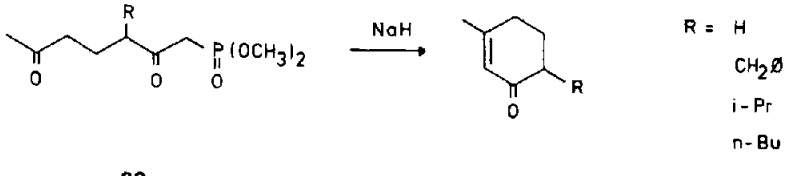


35 36 37 38

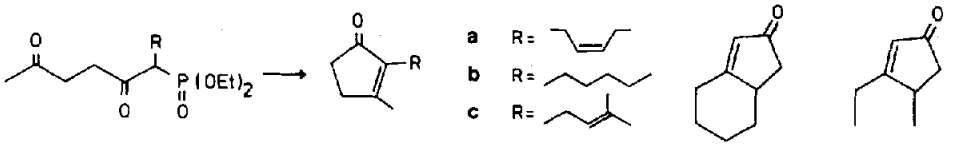
α,β-Unsaturated ketones

Phosphoranes stabilized by an α-CO group may undergo intramolecular condensations with reactive aldehyde functions. Cyclododecene-3-one **38** was obtained by cyclization of the preformed stabilized phosphorane-aldehyde **37** under almost neutral conditions.[25]

Substituted α,β-unsaturated ketones are better prepared by a Horner or Wadsworth–Emmons reaction, taking advantage of the increased nucleophilicity of carbanions of conjugated ketophosphonates compared with the corresponding stabilized phosphoranes. 2,6-Diketophosphonates such as **39** give high yields of cyclohexenones **40** on treatment with sodium hydride in dimethoxyethane.[26] 2,5-Diketophosphonates lead to cyclopentenones: *cis*-Jasmon **42a** and the related compounds **42b** and **c** were prepared from phosphonates **41**.[27] Cyclopenten-3-ones substituted in 1- and 5-position such as **43** and **44** are also accessible by this reaction.[28]



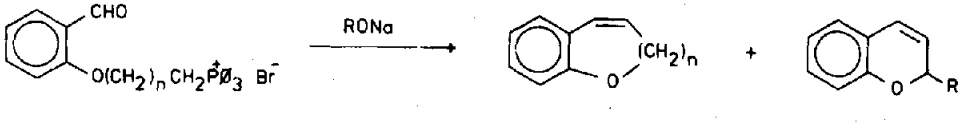
39 **40**



41 **42** **43** **44**

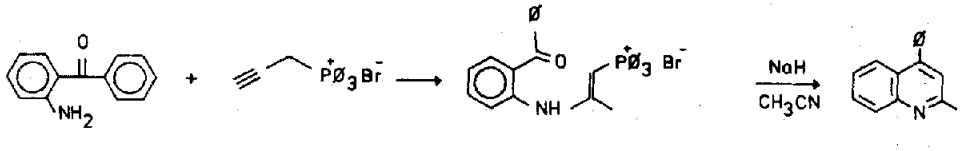
Heterocyclic rings

Many examples are known in which a heterocyclic alkene is formed from a phosphorane connected with a CO group by a chain containing a heteroatom. The *o*-hydroxybenzaldehyde derivatives **45** cyclize to dihydrobenzoxepin (**46**, n = 2)[29] and to the 8-membered ring in dihydrobenzoxocin (**46**, n = 3) on treatment with sodium alkoxide.[30] Rearrangements under ring contraction yielding 2-methyl- and 2-ethyl-2H-chromene **47** are observed, but can be suppressed by suitable reaction conditions. The analogous phosphonium bromide **45**, n = 1 yields 2H-chromene (**46**, n = 1); **45** is not isolated, but prepared in situ by addition of the anion of *o*-hydroxybenzaldehyde to vinyltriphenylphosphonium bromide (*vide infra*).[31]



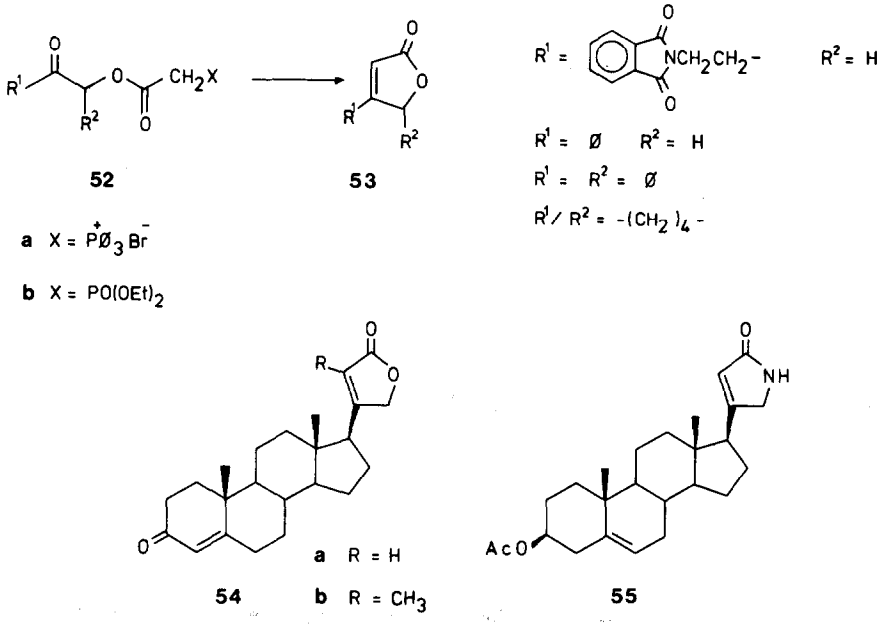
45 **46** **47**

o-Aminobenzophenone (**48**) reacts with propargyltriphenylphosphonium bromide (**49**) to give, after a proton shift, the aminovinylphosphonium salt **50**. On reaction with sodium hydride in acetonitrile, **50** cyclizes to 2-methyl-4-phenylquinoline (**51**). A number of related syntheses of substituted quinolines have also been reported.[32]



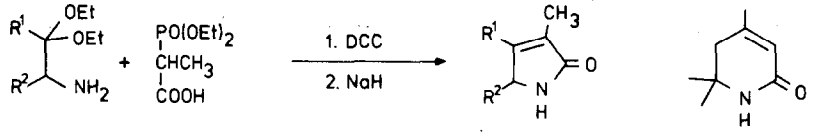
48 **49** **50** **51**

Triphenylphosphonioacetates of α-hydroxyketones (**52a**) condense to butenolides **53** already with triethylamine in methylene chloride. A related diethylphosphonoacetate **52b** was made directly from α-bromocyclohexanone and potassium diethylphosphonoacetate, however, the cyclization to **53** seemed to be less satisfactory.[33] When 21-hydroxy-20-keto-steroids are treated with the mixed anhydride of trifluoroacetic and diethylphosphonoacetic acid followed by potassium carbonate, cardenolides such as **54a** are formed in high yield.[34] The corresponding 22-methyl-cardenolide **54b** and related cardenolides had been synthesized before by intramolecular Wittig reaction.[35] The synthesis of cardenolide glycosides with halogen, alkyl, and alkoxy substituents in the butenolide ring has also been achieved by intramolecular condensation of the corresponding substituted diethylphosphonoacetates.[36] An analogous unsaturated lactam, the steroid pyrrolinone **55**, was obtained from a 20-keto-21-chloracetamide via the corresponding phosphonium chloride.[37]



52 **53** **54** **55**

The pyrrolinone synthesis exemplified with **55** is fairly general. α-Aminoketones protected as their diethylketals **56** are condensed with α-diethylphosphonopropionic acid **57** and then treated with sodium hydride in dimethoxyethane to give pyrrolinones **58**. Diacetoneamine, a β-aminoketone, and diethylphosphonoacetic acid give rise to the dihydropyridone **59**.[38]

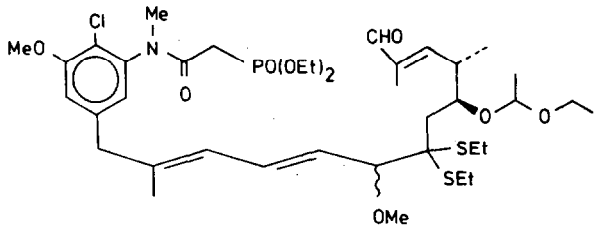


56 **57** **58** **59**

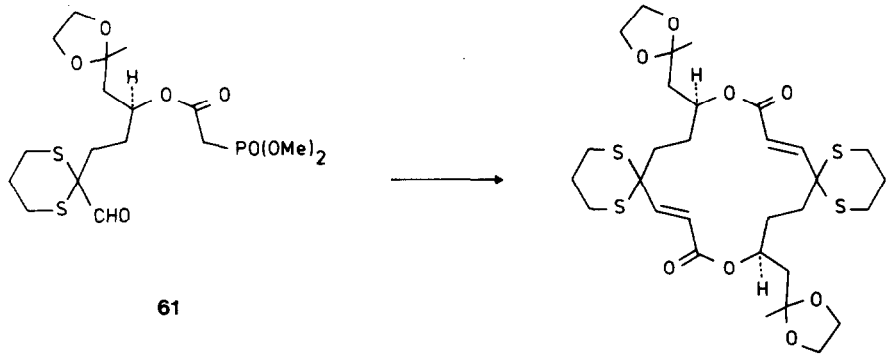
R^1 = Et, R^2 = H
R^1 = R^2 = Me

In a recent synthesis of (±)-N-methylmaysenine, ring closure of the 19-membered lactam was accomplished by an intramolecular condensation of compound **60** with a diethylphosphonoacetamide and an α,β-unsaturated aldehyde function.[39] A double condensation (a bis-Wittig reaction) was used in the synthesis of the 16-membered dilactide **62** with C_2-symmetry, an intermediate which is readily converted to (−)vermiculine. When the aldehyde phosphonate **61** with *S*-configuration is treated with sodium hydride in tetrahydrofuran under high dilution conditions, the dilactide **62** is formed in 49% yield, along with some larger cyclic oligomers. No normal intramolecular ring closure to the corresponding 8-membered lactone occurred. A stepwise condensation, which was shown to be feasible with a racemic model compound, proved therefore to be unnecessary.[40]

Much work on intramolecular Wittig reactions has been done in the field of penemic and cephemic acids. The 2,2-dimethyl-3cephem-4-carboxylic ester **64** is obtained on cyclization of the stabilized

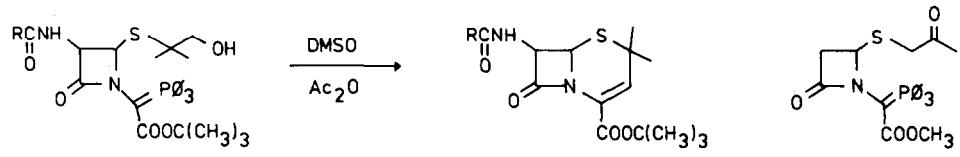


60

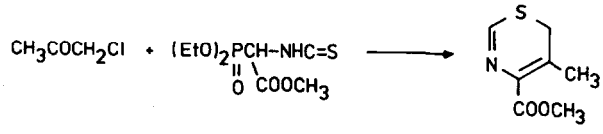


61 62

phosphorane **63**. The aldehyde function is generated *in situ* by Kornblum oxidation of the OH group.[41] A mixture of 3-methyl-2- and 3-cephem-4-carboxylic esters is formed from α-thioketone **65**.[42] Several examples of intramolecular Wittig reactions of keto-phosphoranes and keto-phosphonates have been reported for oxygen and carbon analogs of **65** and related azetidinones.[43] In a different approach, the 1,3-thiazine ring system (**67**) is constructed from chloroacetone and methyl α-thioformamido-diethylphosphonoacetate **66**. Cycloaddition of azidoketene to **67** eventually leads to a cephemic ester.[44]

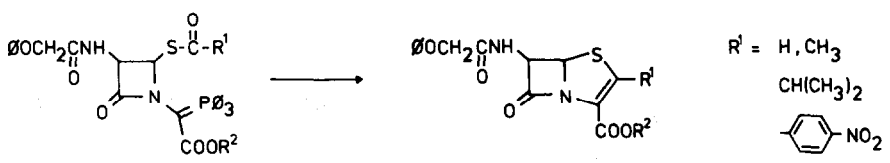


63 R = $\emptyset CH_2$, $\emptyset OCH_2$ **64** **65**



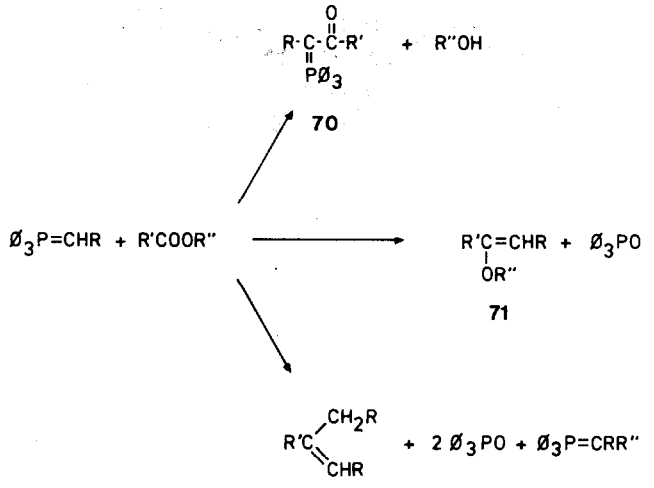
66 **67**

Construction of the penemic acid skeleton in **69** requires condensation of a stabilized phosphorane with the CO function of a thioester. In spite of the fact that thioesters and phosphoranes usually give α-ketophosphoranes with loss of a thiol,[45] this cyclization has been accomplished with a number of substituted thioazetidinones.[46] Related Wittig reactions leading to carbapenemic esters (7-oxo-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylates) have also been reported.[47]



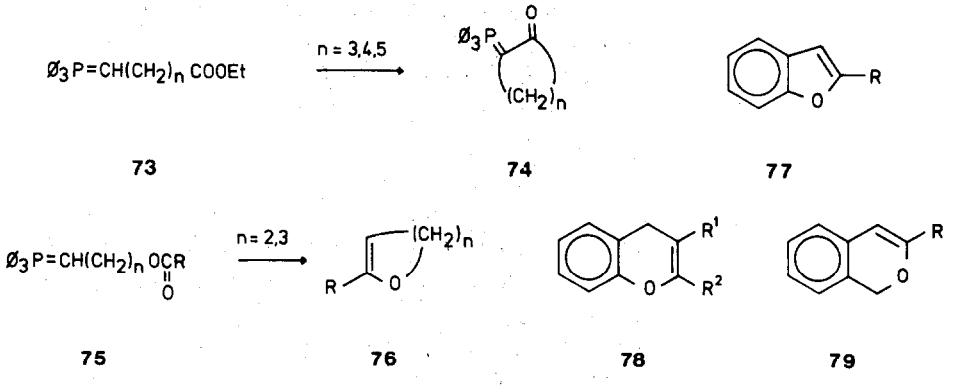
68 **69**

The CO group of an ester function is much less reactive in the Wittig reaction than an aldehyde or a ketone. Normally, the formation of a stabilized phosphorane **70** with loss of the alcohol portion of the ester, i.e. acylation of the phosphorane, is observed (Scheme 4).[45,48] In the case of formic, oxalic, and diethoxy-, fluoro- and trifluoroacetic esters, enolether **71**, the product of a "normal" Wittig reaction, may be found on reaction with semi-stabilized and stabilized phosphoranes.[49] With a large excess of phosphorane in a dipolar aprotic solvent, a double condensation to yield the alkylated olefin **72** can be accomplished.[50]



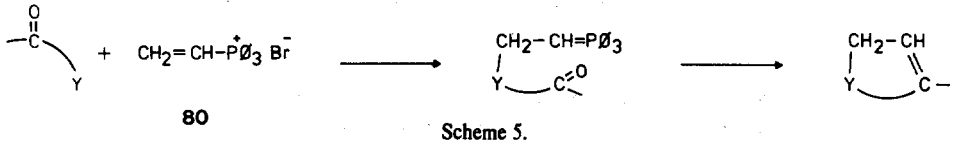
Scheme 4.

As expected, phosphoranes **73** (n = 3,4,5) derived from ω-iodocarboxylic esters yield cyclic α-ketophosphoranes **74** by intramolecular acylation.[51] However, phosphoranes **75** (n = 2,3) derived from ω-bromoalkanols cyclize fairly readily to the corresponding enolether dihydrofuran and dihydropyran **76**, respectively, if a non-polar solvent such as toluene is used.[52] A series of benzofurans **77**, chromenes **78**, and isochromenes **79** was prepared similarly.[53]



3. ADDITION OF FUNCTIONALIZED CARBONYL COMPOUNDS TO VINYLPHOSPHONIUM SALTS AND VINYLPHOSPHONATES

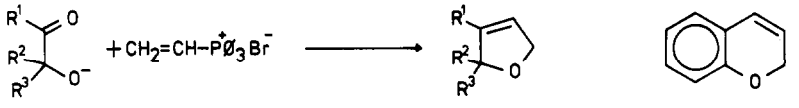
Substituted alkylidenephosphoranes are accessible not only by base treatment of the corresponding alkylphosphonium salts, but also by addition of nucleophiles to vinylphosphonium salts. If the nucleophile contains a CO group, addition leads to a carbonyl alkylidenephosphorane suitable for cyclization (Scheme 5).



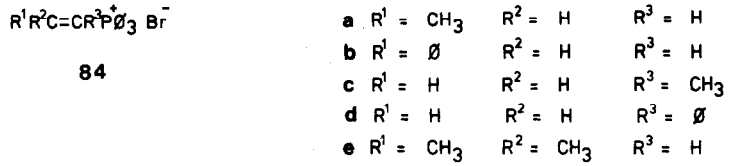
Scheme 5.

Heterocyclic rings

A number of heterocyclic compounds have been synthesized according to this scheme, and a concise and well-presented compilation may be found in the review of Zbiral.[5] For instance, the addition of the anion of an α-hydroxyketone **81** to vinyltriphenylphosphonium bromide **80** eventually leads to a 2,5-dihydrofuran **82**.[54,55] The anion of *o*-hydroxybenzaldehyde and **80** give 2H-chromene **83**.[31,54] Such addition-cyclization reactions can also be accomplished with substituted vinyltriphenylphosphonium salts **84**. Addition of the anion of benzoin (**81**, $R^1 = R^2 = \emptyset$, $R^3 = H$) to the methyl- and phenyl-substituted vinyltriphenylphosphonium bromides **84a-c** leads to 2,5-dihydro-2,3-diphenylfurans **85**. However, considerable amounts of the corresponding phosphoranes **86** are also obtained by an alternative addition reaction. α-Phenylvinyltriphenylphosphonium bromide (**84d**) does not undergo intramolecular Wittig reactions, probably because the intermediate semi-stabilized carbonyl benzylidenephosphorane is not reactive enough to undergo cyclization.[56]

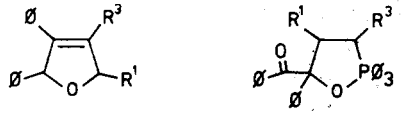


81 **80** **82** **83**



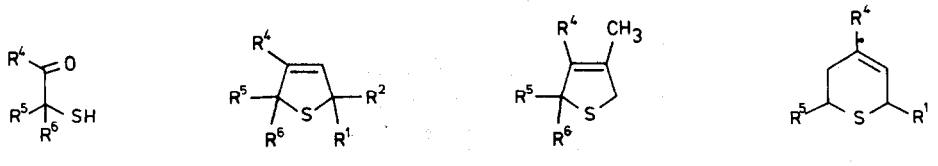
84

a	$R^1 = CH_3$	$R^2 = H$	$R^3 = H$
b	$R^1 = \emptyset$	$R^2 = H$	$R^3 = H$
c	$R^1 = H$	$R^2 = H$	$R^3 = CH_3$
d	$R^1 = H$	$R^2 = H$	$R^3 = \emptyset$
e	$R^1 = CH_3$	$R^2 = CH_3$	$R^3 = H$



85 **86**

Anions of α-mercaptoketones **87** add to unsubstituted (**80**) or β-substituted (**84a**, **84e**) vinylphosphonium salts to give 2,5-dihydrothiophenes **88**.[57] It was also possible to form 2,5-dihydrothiophenes **89** with a tetrasubstituted double bond in acceptable yields from α-methylvinyltriphenylphosphonium bromide (**84c**) and the anions of some unhindered α-mercaptoketones, but other α-substituted vinylphosphonium salts react only with the less hindered α-mercaptoaldehydes (**87**, $R^4 = H$).[58] These variously substituted dihydrothiophenes **88** and **89** are potential precursors for substituted butadienes by oxidation and pyrolysis of the resulting sulfones. β-Mercaptoketones and aldehydes react with vinylphosphonium salts **80** and **84a** to produce dihydrothiopyrans **90**.[59]



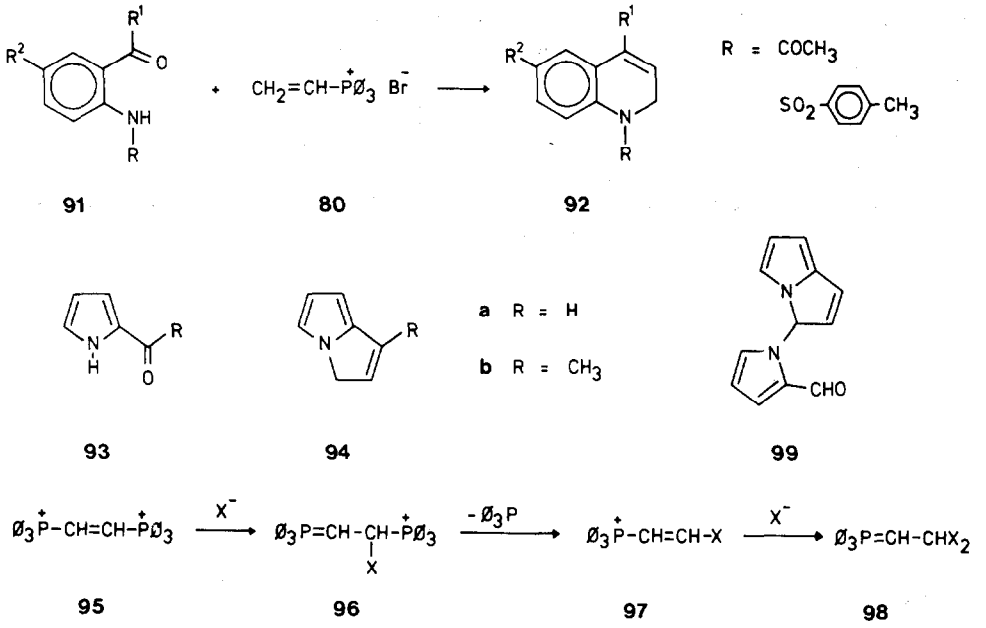
87 **88** **89** **90**

$R^1, R^2 = H, CH_3$ $R^1 = H, CH_3$

A great number of N-containing heterocycles have been prepared by addition reactions of nucleophiles to vinylphosphonium salts. Dihydroquinolines **92** are formed from *o*-acetamido- or *o*-tosyl-

amidophenones **91** and vinyltriphenylphosphonium bromide **80**.[60] 3H-Pyrrolizine (**94a**) and 1-methyl-3H-pyrrolizine (**94b**) are obtained from 2-formyl- and 2-acetylpyrrole (**93a,b**), respectively.[61]

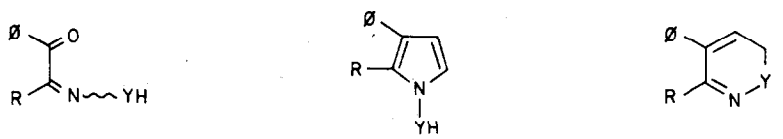
Ethene-1,2-bistriphenylphosphonium bromide **95** also adds nucleophiles (Scheme 6). The intermediate phosphorane **96** loses triphenylphosphine, and the newly formed substituted vinylphosphonium salt **97** can add an additional molecule of the nucleophile and give the disubstituted phosphorane **98**. Such a sequence of reactions has been observed with 2-formylpyrrole (**93a**), which, after cyclization, produces pyrrolizine **99** and other compounds derived thereof.[62]



91 80 92 93 94 99 95 96 97 98

Scheme 6.

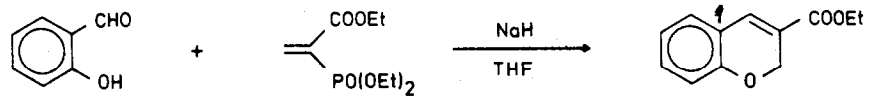
Surprisingly, monooximes of α-dicarbonyl compounds (**100**, Y = O) and vinyltriphenylphosphonium bromide **80** yield 1-hydroxypyrroles **101** (Y = O), and none of the expected 6H-oxazines **102** (Y = O). Monohydrazones of benzil (**100**, R = Ø, Y = NØ, NCH_3, NCOOEt) were found to give 2,3-dihydropyridazines (**102**, Y = NØ, NCH_3, NCOOEt) except the benzoylhydrazone (**100**, R = Ø, Y = NCO Ø), which gave the corresponding 1-benzamidopyrrole (**101**, R = Ø, Y = NCOØ), A reasonable explanation for this differing behaviour is, that only compounds with (*Z*)-configuration at the C=N bond can give 6-membered heterocycles, but this suggestion needs further experimental verification.[63]



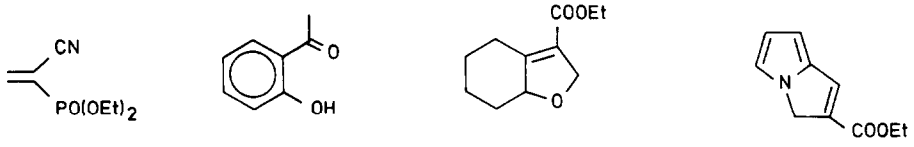
100 101 102

Vinylphosphonates add nucleophiles to give phosphonate carbanions ready to undergo Horner–Wadsworth–Emmons reactions, if the α-position is stabilized by an electron-withdrawing functional group such as a carboxylic ester or a nitrile. When the nucleophile contains a suitable CO group, intramolecular cyclizations comparable to those of vinylphosphonium salts (Scheme 5) can be accomplished.

The anion of *o*-hydroxybenzaldehyde **103** adds to ethyl α-(diethylphosphono)acrylate (**104**). Cyclization leads to 3-ethoxycarbonyl-2H-chromene **105** in a reaction related to the formation of unsubstituted chromene **83** from **103** and vinylphosphonium salt **80** mentioned above.[64] α-(Diethylphosphono)acrylonitrile (**106**) reacts analogously.[65] Similar condensations have been accomplished with 2-hydroxybenzaldehydes substituted with Cl, Br or OMe, but failed with the corresponding ketone, *o*-hydroxyacetophenone (**107**).[64-66] That the reaction is not restricted to aldehydes is demonstrated by the formation of dihydrofuran **108** from 2-hydroxycyclohexanone and vinylphosphonate **104**.[64]

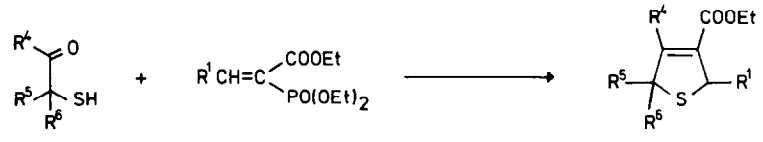


103 104 105



106 107 108 109

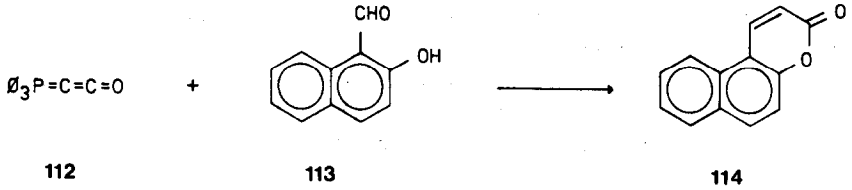
Pyrrole-2-carbaldehyde **93a** reacts not only with vinyltriphenylphosphonium bromide **80** (*vide supra*), but also with ethyl α-(diethylphosphono)acrylate **104**. Ethyl 3H-pyrrolizine-2-carboxylate **109** is thereby formed.[65] 2,5-Dihydrothiophene-3-carboxylic esters **111** are obtained from α-mercaptocarbonyl compounds **87** and phosphonate **104** or β-phenyl-, β-cyclohexyl-, and β-n-propyl-vinylphosphonates **110**.[67]



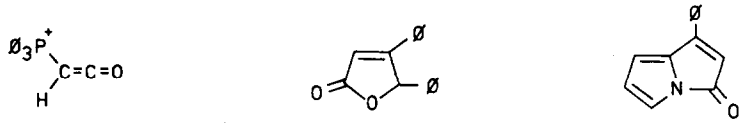
87 104 R^1 = H 111

110 R^1 = Ø, ⬡, $CH_3CH_2CH_2$-

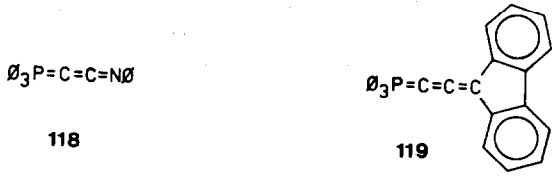
Phosphorus ylids with cumulated double bonds undergo a variety of unusual reactions. When the ketene-phosphorane **112** is treated with 2-hydroxynaphthaldehyde (**113**), proton transfer to the ylid carbon in **112** generates triphenylphosphonioketene ((**115**). This highly reactive intermediate incorporates a vinylphosphonium salt partial structure capable of undergoing an intramolecular Wittig reaction with the anion of **113**. The product finally obtained is the benzocoumarone **114**. Benzoin and phosphorus ylid **112** give 3,4-diphenylbutenolide **116**, and 2-benzoylpyrrole leads to the bicyclic lactam 1-phenylpyrrolizin-3-one **117**. Related cyclizations are observed with the keteneimine-phosphorane **118** and the cumulene-phosphorane **119**.[68]



112 113 114



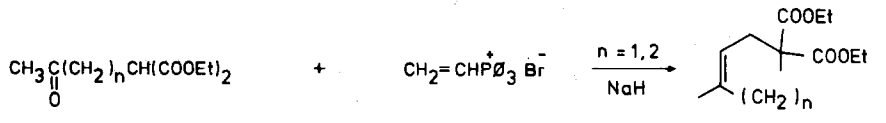
115 116 117



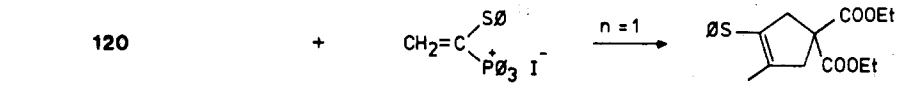
118 119

Carbocyclic rings

Anions of ketoalkylmalonic esters (**120**) add to vinyltriphenylphosphonium bromide **80** to give the cyclic 5- and 6-membered (but no 7-membered) unsaturated malonic esters **121**.[69] When α-phenylthiovinylphosphonium iodide **122** is condensed with diethyl (2-oxopropyl)malonate (**120**, n = 1), vinyl thioether **123** is obtained, which can easily be hydrolysed to the corresponding cyclopentanone.[70]

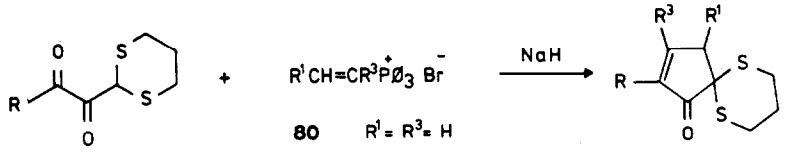


120 + **80** → (n = 1,2; NaH) → **121**



120 + **122** → (n = 1) → **123**

Carbanions obtained on base treatment of 2-(α-oxoacyl)-1,3-dithianes **124** react with vinyltriphenylphosphonium bromide **80** or the analogous methylated phosphonium salts **84a** and **84c**. Cyclopentenedione-monothioketals **125** are thereby formed.[71]



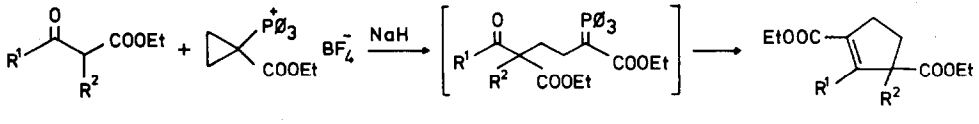
124 + **80** ($R^1 = R^3 = H$) + **84a** ($R^1 = CH_3$, $R^3 = H$) + **84c** ($R^1 = H$, $R^3 = CH_3$) → (NaH) → **125**

4. ADDITION OF ENOLATES TO CYCLOPROPYL- AND BUTADIENYLPHOSPHONIUM SALTS

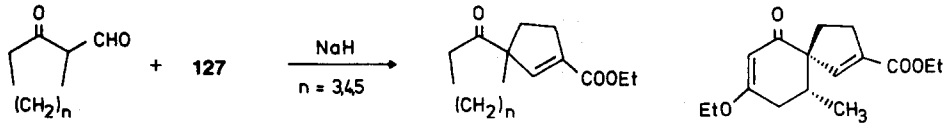
Cyclopropylphosphonium salts

As was shown in the preceding chapter, a carbonyl compound containing a nucleophilic functional group in suitable position may be elaborated to a cycloalkene containing *two* more C atoms by reaction with vinylphosphonium salt **80** (Scheme 5). *Three* C atoms can be introduced by reaction with a cyclopropylphosphonium salt.[72] To assist the ring-opening of the cyclopropane by nucleophiles, an additional carbanion-stabilizing functional group geminal to the triphenylphosphonium group is necessary in general for a successful intramolecular Wittig reaction.

1-Ethoxycarbonylcyclopropylphosphonium tetrafluoroborate **127** reacts with anions of β-keto-esters **126** to give carbonyl alkylidenephosphoranes **128**, which cyclize to cyclopentene-1,3-dicarboxylic esters **129**.[73] α-Formylcyclanones **130** yield the corresponding spiro-cyclopentenecarboxylic esters **131**. Application of this reaction to 3-ethoxy-6-formyl-5-methylcyclohex-2-en-1-one leads to the spiro[4.5]decane **132**, an intermediate in a synthesis of β-vetivone.[74]



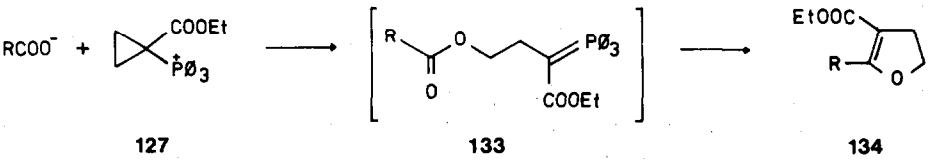
126 + **127** → (NaH) → **128** → **129**



130 + **127** → (NaH; n = 3,4,5) → **131** → **132**

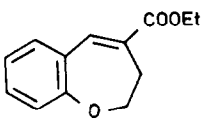
1-Ethoxycarbonylcyclopropylphosphonium tetrafluoroborate **127** is opened by a variety of carboxylic acid anions. The intermediate stabilized phosphorane-esters **133** cyclize to 4,5-dihydrofuran-3-carboxylic esters **134**.[75] This enolether formation corresponds to the cyclization of the non-stabilized phosphorane-ester **75** (*vide supra*).

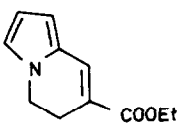
The analogy of vinylphosphonium salt **80** and cyclopropylphosphonium salt **127** is further demonstrated by the formation of 4-carbethoxy-2,3-dihydro-1-benzoxepin **135** from the sodium salt of *o*-hydroxybenzaldehyde, and of 5,6-dihydroindolizine-7-carboxylic ester **136** from the anion of pyrrole-2-carbaldehyde **93a**.[73]



127 **133** **134**

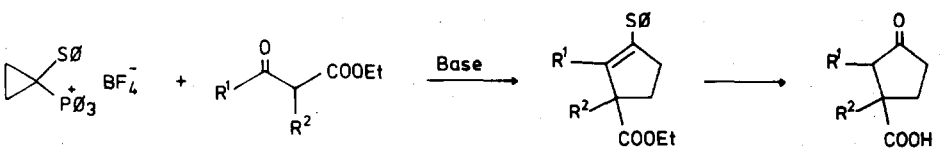
R = H, CH_3, FCH_2, Ø, ØCH=CH





135 **136**

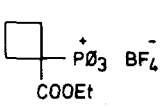
The ring-opening of a cyclopropylphosphonium salt is also assisted by the phenylthio group. 1-Phenylthiocyclopropylphosphonium tetrafluoroborate **137** reacts with the anion of β-keto-esters **126** to yield cyclopentenyl thioethers **138**, which are hydrolysed to cyclopentan-3-onecarboxylic acids **139**.[76]



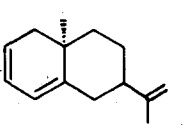
137 **126** **138** **139**

Butadienylphosphonium salts

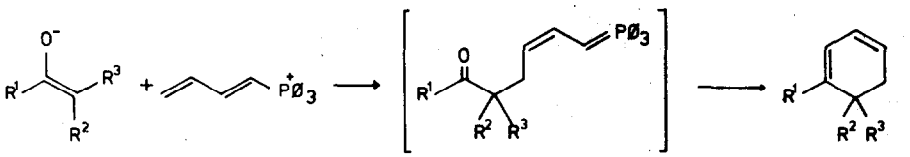
1-Ethoxycarbonylcyclobutylphosphonium tetrafluoroborate **140** does not undergo clean ring-opening with nucleophiles.[73] However, incorporation of *four* C atoms into a cycloalkene may be accomplished by reaction of a suitable nucleophile with 1,3-butadien-1-yltriphenylphosphonium bromide **142**, the "vinylogue" of vinylphosphonium salt **80**. Addition of an enolate **141** to **142** occurs at the δ-position and leads to a propenylidenephosphorane **143**, which cyclizes to a 1,6,6-trisubstituted 1,3-cyclohexadiene **144**.[77] The reaction is fairly versatile and allows also the formation of annulated cyclohexadienes such as **145** from readily available ketones.[78]



140

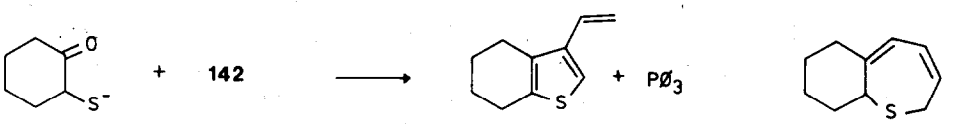


145



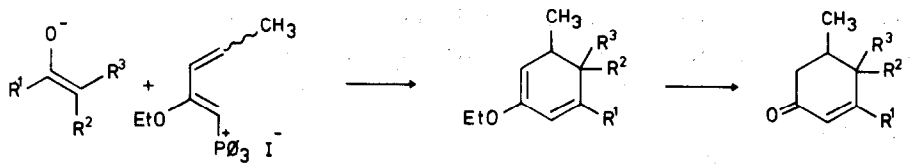
141 **142** **143** **144**

The reaction seems to be restricted to the formation of 6-membered rings. The anion of 2-mercaptocyclohexanone **146** and butadienylphosphonium salt **142** gave none of the anticipated 7-membered heterocycle **148**. An alternative cyclization reaction yielding 3-vinyl-4,5,6,7-tetrahydrobenzo[b]thiophene **147** and triphenylphosphine occurred.[79]

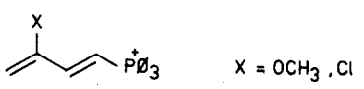


146 **147** **148**

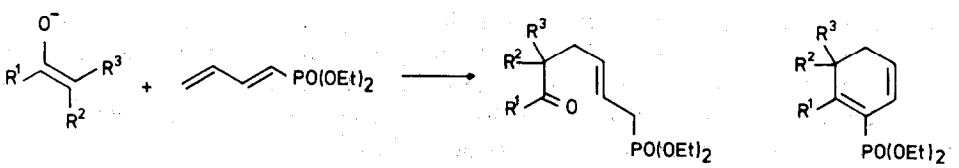
Intramolecular Wittig reaction of an enolate **141** and 2-ethoxy-1,3-pentadienyltriphenylphosphonium iodide **149** yields 3-ethoxy-5-methyl-1,3-cyclohexadienes **150**. Subsequent hydrolysis leads to a number of interesting substituted cyclohexenones **151**. Attempts to condensate the corresponding 3-methoxy- or 3-chloro-1,3-butadienyltriphenylphosphonium salt **152** with enolates were unsuccessful.[80]



141 **149** **150** **151**



152



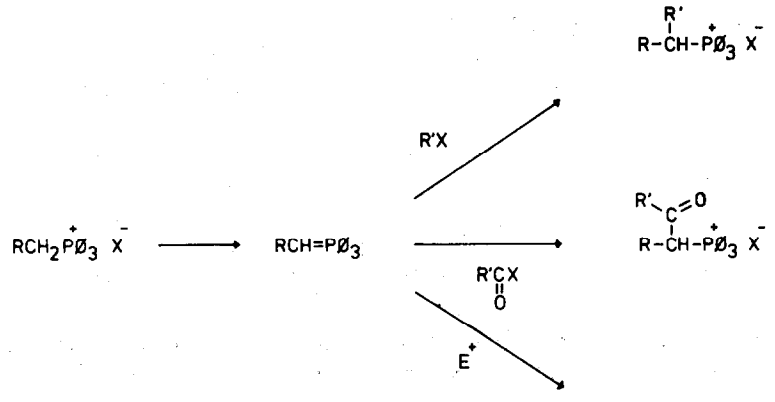
141 **153** **154** **155**

As expected, enolates **141** add to diethyl 1,3-butadienylphosphonate **153** in the δ-position. However, no intramolecular Wittig reaction is observed,[78] and the simple product of a Michael addition, the substituted ketoallylphosphonate **154**, is isolated. Lithium enolates of aldehydes (**141**, $R^1 = H$) give rise to 1,3-cyclohexadien-2-ylphosphonates **155**, probably by an aldol type cyclization followed by dehydration of an intermediate allylphosphonate **154** ($R^1 = H$).[81] The failure of butadienylphosphonate **153** to undergo cyclizations analogous to those of butadienylphosphonium bromide **142** is not surprising when taking into consideration, that phosphonates require an additional electron-withdrawing substituent at the α-C atom, if a Wittig-type reaction should occur.[4]

5. ADDITION OF ALKYLIDENEPHOSPHORANES AND PHOSPHONATE CARBANIONS TO FUNCTIONALIZED CARBONYL COMPOUNDS

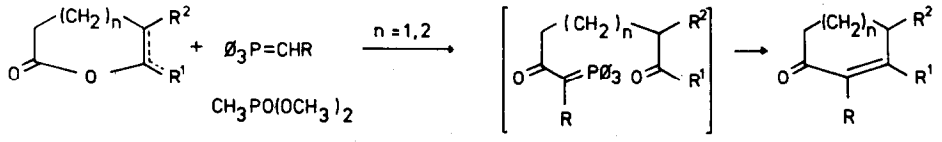
In the preceding two chapters, formation of carbonyl alkylidenephosphoranes by addition of nucleophiles to electrophilic phosphonium salts was discussed. When phosphonium salts are deprotonated, nucleophilic phosphoranes are formed. Their nucleophilicity may be exploited by alkylation with alkyl halides, acylation with acyl chlorides or thioesters, and related reactions with suitable electrophiles (Scheme 7).[1,7] The newly formed phosphonium salt is deprotonated by the starting phosphorane, if the electrophile introduced acidifies the α-C atom. In this case, either two moles of starting phosphorane are consumed or an additional base must be added.

When the electrophile contains a suitable CO group, carbonyl alkylidenephosphoranes and hence cycloalkenes are formed. For instance, alkylidenephosphoranes add to the CO group of γ- or δ-enollactones **156** to give, after a proton shift, stabilized carbonyl phosphoranes **157** bearing an additonal CO group. These cyclize readily to cyclopentenones and cyclohexenones **158**, respectively. The reaction



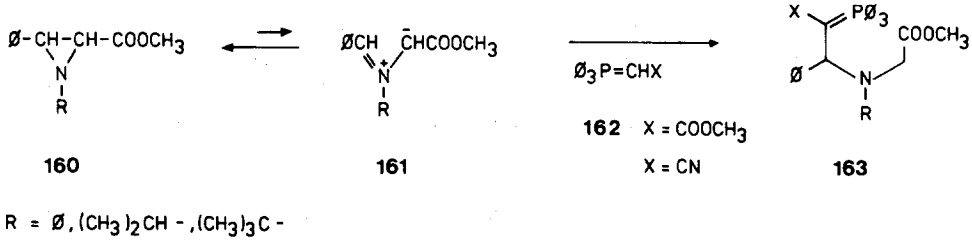
Scheme 7.

has been applied to some steroidal enollactones.[82] Similar or even better yields of **158** are obtained, when enollactones **156** are treated with the anion of dimethyl methylphosphonate **159**.[82,83]



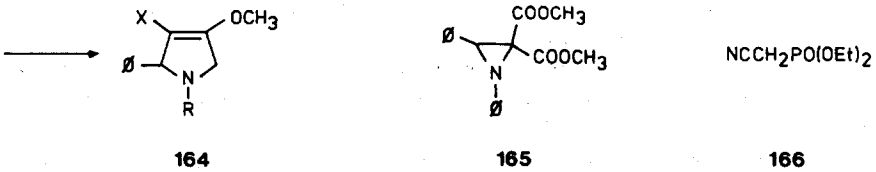
156 **159** **157** **158**

3-Phenylaziridine-2-carboxylates **160** are in equilibrium with a small amount of the corresponding azomethine ylids **181**. These ylids are trapped by addition of methoxycarbonyl- or cyano-methyl-idenetriphenylphosphorane **162**, which combine with the electrophilic C atom to give the intermediate phosphorane-esters **163** after a proton shift. The stabilized phosphorane function in **163** now undergoes an intramolecular Wittig reaction with the ester CO group, and the enolether 3-methoxy-3-pyrroline **164** is formed. The doubly activated aziridine **165** and the stabilized phosphoranes **162** react analogously and give a mixture of stereoisomers of the corresponding 3-pyrroline-2-carboxylates related to **164**. It is noteworthy that the same transformation can be accomplished also with **165** and the anion of diethyl cyanomethylphosphonate **166**, albeit in lower yield.[84] This is one of the rare examples reported in the literature of a Wittig-type reaction between a phosphonate carbanion and the CO group of an ester.[49]



160 **161** **162** **163**

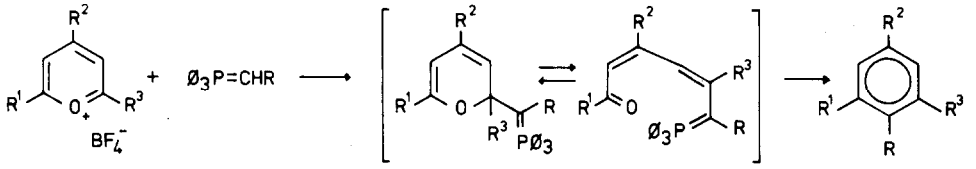
R = Ø, $(CH_3)_2CH$-, $(CH_3)_3C$-



164 **165** **166**

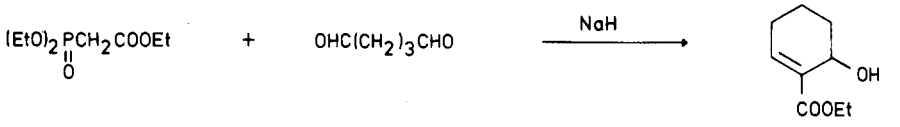
Alkylidenephosphoranes add to pyrylium tetrafluoroborates **167**. The resulting phosphonium salt is deprotonated by the starting phosphorane to a new phosphorane **168**, which is in equilibrium with its

open-chain form **169**. Cyclization of **169** gives the substituted benzene **170**.[85]



167 **168** **169** **170**

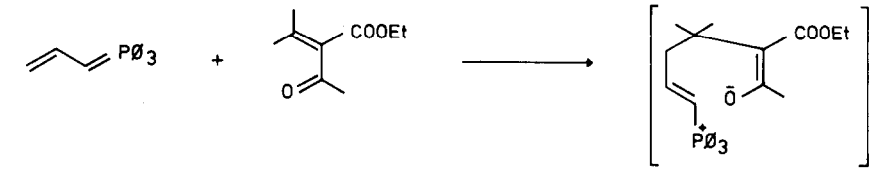
A double condensation of ethyl diethylphosphonoacetate **171** with glutaraldehyde **172** gives ethyl 6-hydroxy-1-cyclohexenecarboxylate **173**.[86] It is reasonable to assume that the β-oxyphosphonate obtained from **171** and one aldehyde group does not undergo the usual cleavage into olefin and diethylphosphonate, but is deprotonated at the α-C atom and then reacts with the other aldehyde function in an intramolecular Wittig reaction.



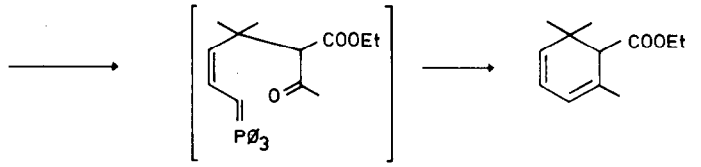
171 **172** **173**

6. ADDITION OF PROPENYLIDENEPHOSPHORANES TO α,β-UNSATURATED CARBONYL COMPOUNDS

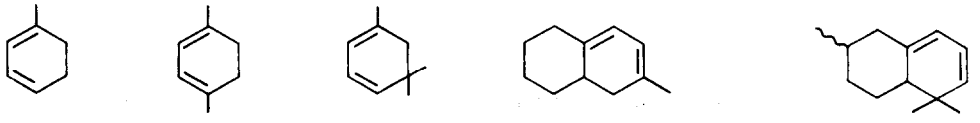
The nucleophilic properties of propenylidenephosphoranes, i.e. phosphorus ylids conjugated with a C=C double bond, have also been exploited. On deprotonation of allyltriphenylphosphonium chloride, the propenylidenephosphorane **174** is formed. Compound **174** adds to α,β-unsaturated carbonyl compounds, e.g. to ethyl α-isopropylideneacetoacetate **175**, in a Michael fashion. A proton shift in the intermediate vinylphosphonium enolate **176** then gives the carbonyl propenylidenephosphorane **177**, which undergoes cyclization to ethyl 2,6,6 trimethyl-2,4-cyclohexadienecarboxylate **178**. A "normal" Wittig reaction between **174** and **175** followed by electrocyclic ring closure of the intermediate hexatriene would give another cyclohexadiene isomer. This reaction path can therefore be excluded.[87] The ester function is not crucial: A number of substituted (including bicyclic) cyclohexadienes **179–185** have been prepared from the appropriate α,β-unsaturated ketone and propenylidenetriphenylphosphorane **174** and 2-butenylidenetriphenylphosphorane **186**, respectively. 3-Methyl-2-butenylidenetriphenylphosphorane **187** does not react at the γ-position due to steric congestion.[88]



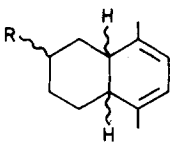
174 **175** **176**



177 **178**

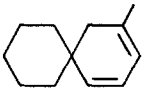


179 **180** **181** **182** **183**



184

R = H, $COOCH_3$



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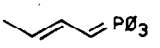

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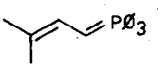
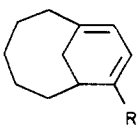


187

Condensation of endocyclic α,β-unsaturated ketones with unsubstituted or substituted propenylidenephosphoranes gives rise to bridged bicyclic cyclohexadienes. For instance, bicyclo[5.3.1]undeca-7,9-dienes **188** (R = H, CH_3, Ø) and bicyclo [4.3.1]deca-6,8-diene **189** were obtained from 2-cycloocten-1-one and 2-cyclohepten-1-one, respectively. This type of intramolecular Wittig reaction is also capable of producing highly strained dienes: 2-Cyclohexen-1-one and propenylidenephosphorane **174** gave rise to bicyclo[3.3.1]nona-1,3-diene **190**, and 4-methylbicyclo[3.2.1]octa-1,3-diene **191** was generated from 2-cyclopenten-1-one and 2-butenylidenephosphorane **186**. Bridgehead olefins **190** and **191** are too strained to be isolated. They may be trapped as a mixture of Diels-Alder adducts with 1,5-diphenylbenzo[c]furan, otherwise, only dimerization products are found.[89]



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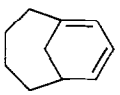

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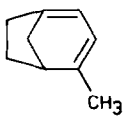
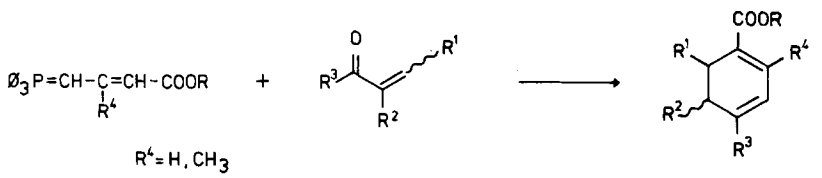
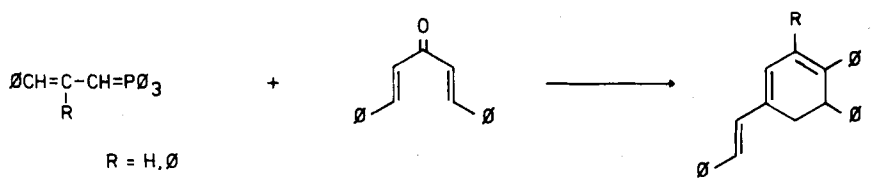


191

Similar cyclization reactions have been realized with other substituted propenylidenephosphoranes. Acrylic esters **192** and a variety of α,β-unsaturated ketones were condensed to give 2,3-dihydrobenzoic esters **193**. The corresponding acrylonitrile or acrylamide react alike.[90] 3-Phenyl- or 2,3-diphenylpropenylidenetriphenylphosphorane **194** and 1,5-diphenylpentadien-3-one **195** afforded cyclohexadienes **196**.[91]

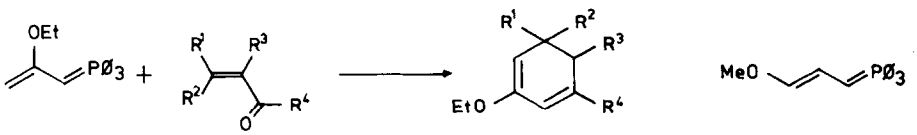


192 193



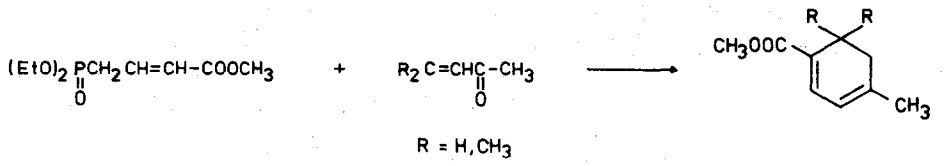
194 195 196

2-Ethoxypropenylidenetriphenylphosphorane **197** reacts smoothly with a variety of structurally different α,β-unsaturated ketones. The 2-ethoxycyclohexadienes **198** formed are suitable precursors for the corresponding cyclohexenones.[92] 3-Methoxypropenylidenetriphenylphosphorane **199** failed to undergo a Michael addition to α,β-unsaturated ketones. A normal Wittig reaction yielding the open-chain trienes was observed instead.[93]

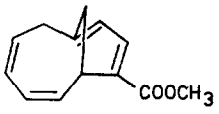


197 198 199

Because of the relationship of phosphonium salts and phosphonates, one would expect that anions of allylphosphonates undergo Michael additions like the corresponding propenylidenephosphoranes. Indeed, the anion of methyl 4-diethylphosphono-2-butenoate **200** and methyl vinyl ketone or mesityl oxide combine to 2,3-dihydrobenzoic ester **201**.[94] The ester group in γ obviously suffices to stabilize the carbanion α to the phosphonate so that an intramolecular Wittig-type reaction can take place. Phosphonate **200** and cycloocta-2,4,6-trienone afford the bridged dihydrobenzoic ester **202** which underwent base-catalyzed isomerisation to **203**, an intermediate on the way to 1,5-methanol[10]annulene.[95]



200 201



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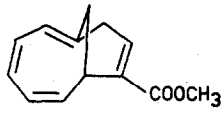
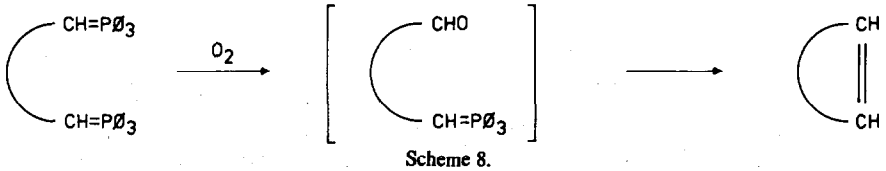


203

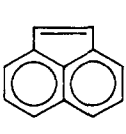
7. OXIDATION OF BISALKYLIDENEPHOSPHORANES

Oxidation of non-stabilized alkylidenetriphenylphosphoranes with molecular oxygen leads to aldehydes (or ketones) and triphenylphosphine oxide. These aldehydes react with unoxidized phosphoranes to give olefins in a Wittig reaction.[96] Ring closure with formation of cycloalkenes is observed with bisalkylidenephosphoranes (Scheme 8).



Scheme 8.

Cyclopentene, cyclohexene, cycloheptene, and some policyclic olefins with 5- to 8-membered rings such as acenaphthene **204**, phenanthrene **205**, *cis*-octahydronaphthalene **206**, or dibenzocycloheptatriene **207** were readily formed from the corresponding bis-ylids and molecular oxygen in dimethyl sulfoxide. Oxidation of the bisalkylidenephosphorane **208** derived from butane-1,4-bistriphenylphosphonium bromide lead to the dimerization product, 1,5-cyclooctadiene **209**. No cyclobutene was formed. Medium-sized cycloolefins cannot be obtained by autoxidation of the corresponding bis-ylids. For instance, oxidation of the bis-ylid **210** prepared from decane-1,10-bistriphenylphosphonium bromide gave no cyclodecene, but the dimeric (Z,Z)-1,11-cycloeicosadiene. Higher oligomers up to cyclohexacontahexaene were also isolated.[97] However, the synthesis of 9,9-dichlorobicyclo[6.1.0]non-4-ene **212**, a formal derivative of (*E*,*Z*)-1,5-cyclooctadiene, was accomplished by oxidation of bis-ylid **211** under conditions of high dilution.[98]



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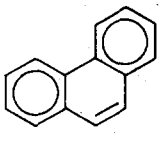

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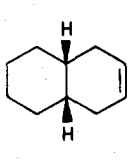

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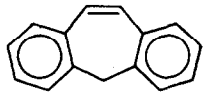

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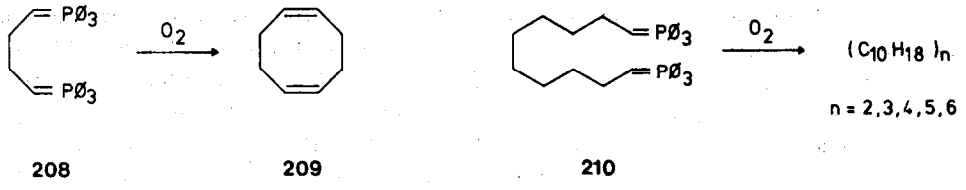
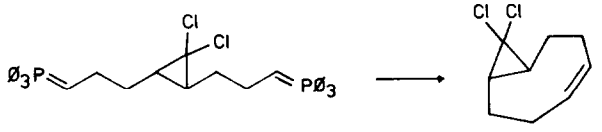


208 209 210

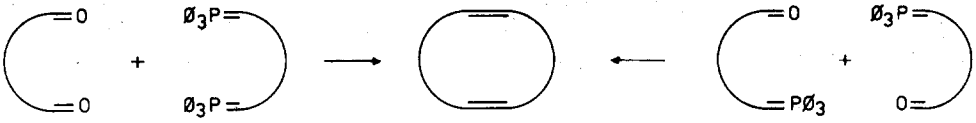


211 212

Stabilized phosphoranes are stable against air oxidation, but can be oxidized to the corresponding carbonyl compound with aqueous sodium periodate. Semi-stabilized phosphoranes undergo dimerization to olefins: The benzylic triphenylphosphonium periodates are precipitated from an aqueous solution of the phosphonium halide and sodium periodate and then treated with a base. Application of this reaction to bis-phosphonium salts leads to good yields of aromatic cycloalkenes such as **204**, **205**, and **207**.[99]

8. BIS-WITTIG REACTIONS

A double intermolecular Wittig reaction of a dicarbonyl compound with a bisalkylidenephosphorane, termed bis-Wittig reaction,[6] may lead to a cyclic diene (Scheme 9). Cyclic dienes are also formed on dimerization of a carbonyl phosphorane, if for some reason simple intramolecular cyclization cannot occur. In principle, either type of dimerization reaction can also be accomplished with suitable phosphonate carbanions.

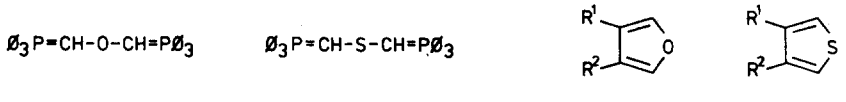


Scheme 9.

It is reasonable to assume that such double condensations occur stepwise, the second step being an intramolecular Wittig reaction of an olefin bearing a carbonyl and a phosphorane (or phosphonate) functional group. However, little is known about the exact course of the bis-Wittig reaction. Usually the bis-ylid is preformed from the corresponding bistriphenylphosphonium salt and base, and the dicarbonyl compound added in the second step. In some cases higher yields are obtained when the bis-ylid is generated in presence of the dicarbonyl compound.

A recent review of bis-Wittig reactions in the synthesis of nonbenzenoid aromatic ring systems by K. P. C. Vollhardt contains all the relevant examples in the literature up to 1974.[6] Only the principle reaction types will therefore be illustrated and newer examples cited. The classification according to ring size will be adopted as in Vollhardt's review. Dimerizations of carbonyl phosphoranes have been treated in part under earlier headings (see, e.g. **9** (n = 1),[14] **61**,[40] **208** and **210**[97]).

Bis-ylids **213** and **214** prepared *in situ* from dimethyl ether and dimethyl sulfide α,α'-bistriphenylphosphonium bromide or chloride have been condensed with α-diketones to furans **215** and thiophenes **216**, respectively.[100] When the α-diketone is 1,2-cyclobutanedione or a derivative thereof, interesting strained oxa- or thiabicyclo[3.2.0]heptadienes may be obtained.[101]

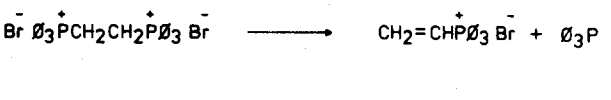


213 214 215 216

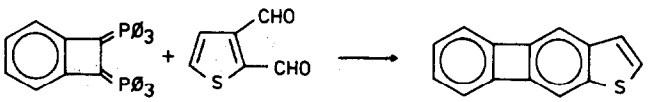
In principle, 6-membered rings could be formed from a 1,2-bisalkylidenephosphorane and a 1,4-dicarbonyl compound, from two 3-carbon units, or from a 1,4-bis-ylid and an α-dicarbonyl compound.

1,2-Bisalkylidenephosphoranes are not readily accessible. Ethane-1,2-bistriphenylphosphonium

bromide **217** and strong base give vinyltriphenylphosphonium bromide **80** and one equivalent of triphenylphosphine: The intermediate mono-ylid contains a nucleofugal triphenylphosphonio group β to the negatively charged ylid C atom and therefore suffers elimination.[102] However, bis-ylid **218** can be prepared from benzocyclobutene-1,2-bistriphenylphosphonium bromide and base and is reasonably stable, because triphenylphosphine elimination would generate a benzocyclobutadiene system.[103] Condensation of bis-ylid **218** with thiophene-2,3-dicarbaldehyde **219** leads to a benzene ring: Biphenylene[2,3-b]thiophene **220** is formed, albeit in a yield of 0.9% only.[104]



217 **80**

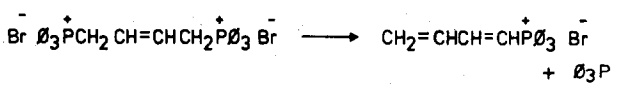


218 **219** **220**

The 3-carbon bisalkylidenephosphorane **221** can be generated from propane-1,3-bistriphenylphosphonium bromide and base and shows normal reactivity and stability.[102] Keto-bis-ylid **222** formally containing one stabilized and one non-stabilized prosphorane functional group is obtained from acetone-1,3-bistriphenylphosphonium chloride,[105] but neither **221** nor **222** have been condensed with 1,3-dicarbonyl compounds to build a 6-membered ring.

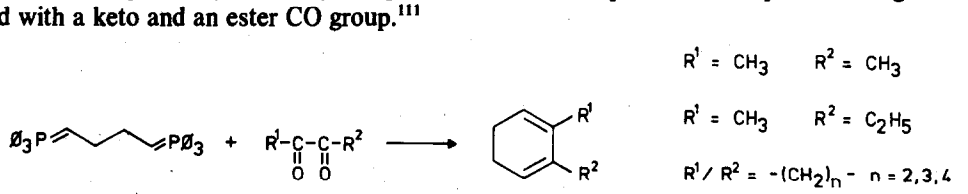
An elimination reaction occurs with (*E*)- or (*Z*)-2-butene-1,4-bistriphenylphosphonium bromide **223**, which gives butadienyltriphenylphosphonium bromide **142** and triphenylphosphine.[78,79,106] In spite of the high propensity to undergo elimination, some intermolecular Wittig reactions with (*Z*)-**223** and aldehydes have been accomplished by *in situ* generation of the 1,4-bis-ylid,[107] but successful examples of bis-Wittig reactions with **223** are not known. The corresponding saturated bis-ylid **224**, obtained e.g. from

221 **222**

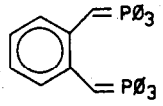


223 **142**

butane-1,4-bistriphenylphosphonium bromide and potassium t-butoxide, is fairly stable. Compound **224** and α-diketones **225** give 2,3-dialkyl-1,3-cyclohexadienes **226**, which are difficult to prepare free of isomers by other methods. Phenylglyoxal (**225**, $R^1 = \emptyset$, $R^2 = H$) yields 2-phenyl-1,3-cyclohexadiene, but aliphatic α-ketoaldehydes fail to give the expected bis-Wittig products.[108] Substituted naphtalenes may be formed from suitable α-dicarbonyl compounds and bis-ylid **227**.[109] Compound **227** is best prepared *in situ*, because base treatment of *o*-xylylenebistriphenylphosphonium bromide still leads to a high proportion of triphenylphosphine by 1,4-elimination.[110] Bis-alkylidenephosphorane **227** and diethyl ketomalonate **228** gave ethyl 3-ethoxy-2-naphthoate **229**. This represents a unique bis-Wittig reaction of a bis-ylid with a keto and an ester CO group.[111]



224 **225** **226**



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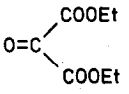

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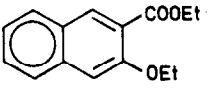
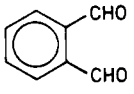


229

The oldest reported example of a bis-Wittig reaction (and of any kind of intramolecular Wittig reaction) is the formation of benzocycloheptatriene **231** from phthalaldehyde **230** and the bis-ylid **221**.[102] Isomerization of **231** to its double bond isomer can be suppressed, when the bis-ylid is prepared with sodium amide in liquid ammonia and the Wittig reaction is conducted in diethyl ether and tetrahydrofuran. In an analogous reaction, cyclobutadiene-1,2-dicarbaldehyde iron tricarbonyl **232** and bis-alkylidenephosphorane **221** generated *in situ* gave a mixture of two isomeric annulated cycloheptatrienes **233**, and with bis-ylid **222**, annulated cycloheptatrienone **234** was formed.[112]



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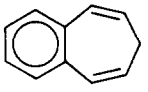

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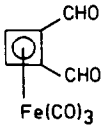

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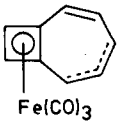

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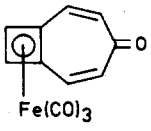

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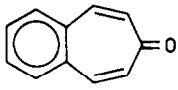

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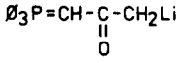
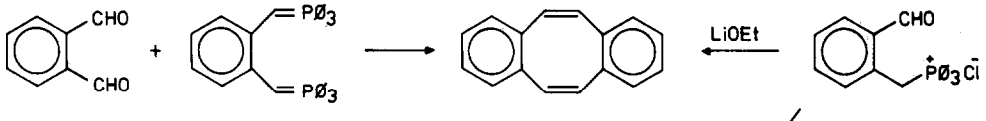


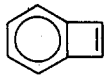
236

Phthalaldehyde **230** and bis-ylid **222** should give benzocycloheptatrienone **235**. The same transformation can be accomplished in good yield by the lithium enolate **236** of acetonylidenetriphenylphosphorane in a combined aldol-type and intramolecular Wittig reaction.[113]

The 8-membered ring in benzocyclooctatriene **237** is formed in a bis-Wittig reaction between phthalaldehyde **230** and bis-ylid **224**.[102] With bis-ylid **227**, the corresponding dibenzocyclooctatetraene **238** is obtained.[114] Dimerization of the phosphorane prepared from *o*-formylbenzyltriphenylphosphonium chloride **239** and lithium ethoxide yields the same dibenzocyclooctatetraene **238**; no benzocyclobutadiene **240** or products derived thereof are found.[113] As expected, thiophene-2,3-dicarbaldehyde **219** and bis-ylid **224** give the thiophenocyclooctatriene **241**, and the analogous reaction with bis-ylid **227** prepared *in situ* from *o*-xylylene-bistriphenylphosphonium bromide leads to cyclooctatetraene **242** with annulated benzene and thiophene rings.[104]



230 227 238 239



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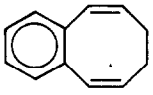

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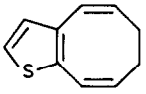

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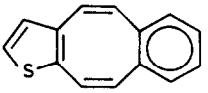
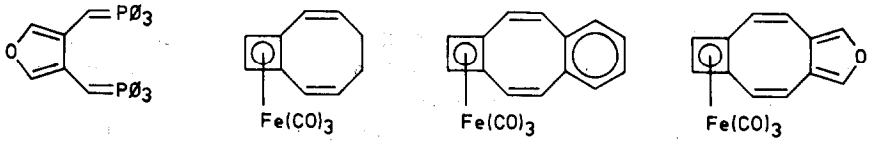
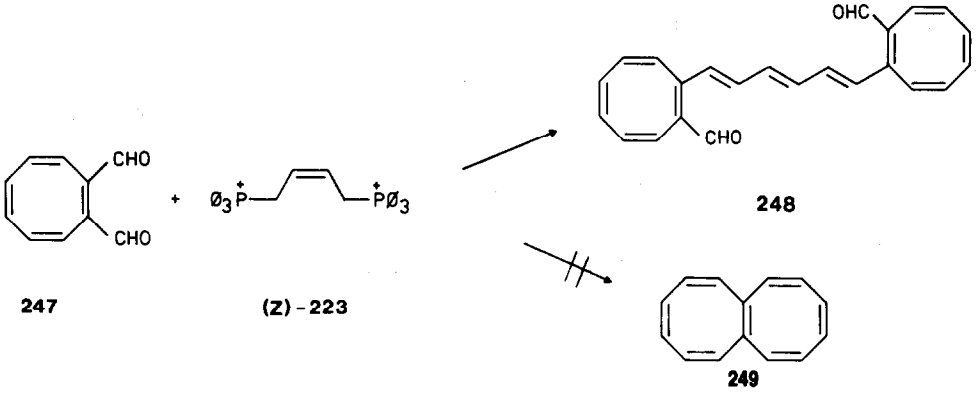


242

Cyclobutadiene-1,2-dicarbaldehyde iron tricarbonyl **232** reacts with bis-ylid **224**, **227** and **243** to give the corresponding cyclobutadiene iron tricarbonyls **224**, **245** and **246** with annulated 8-membered rings. As expected, no adduct was obtained from dialdehyde **232**, (*Z*)-2-butene-1,4-bistriphenylphosphonium bromide **223**, and base.[115] Cyclooctatetraene-1,2-dicarbaldehyde **247** and **223** gave also none of the anticipated octalene **249**, however, an open chain 2 : 1 adduct **248** was isolated in 5% yield.[116]



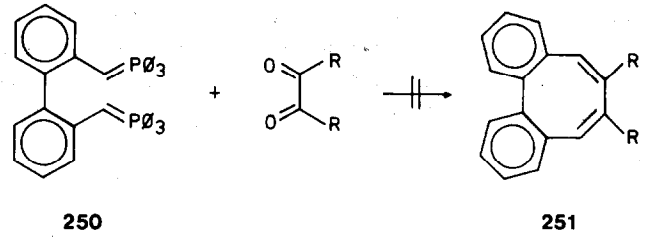
243 **244** **245** **246**



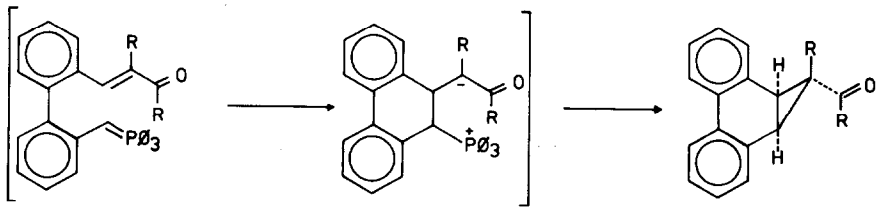
247 **(Z)-223** **248**

249

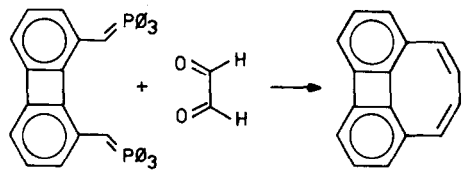
In analogy to the reactions cited above, one would expect the formation of cyclooctatetraenes **251** from biphenyl-2,2'-bismethylidenetriphenylphosphorane **250** and α-dicarbonyl compounds. However, dibenzonorcaradienes **253** are formed by an alternative reaction pathway. The intermediate carbonyl benzylidenephosphorane **252** undergoes an intramolecular Michael addition in place of a Wittig reaction. Loss of triphenylphosphine then generates the 3-membered ring.[117] In the related biphenylene-1,8-bismethylidenetriphenylphosphorane **254**, the two phosphorane functional groups are further apart. Condensation with glyoxal therefore leads to the expected cyclooctatetraene **255**.[118]



250 **251**

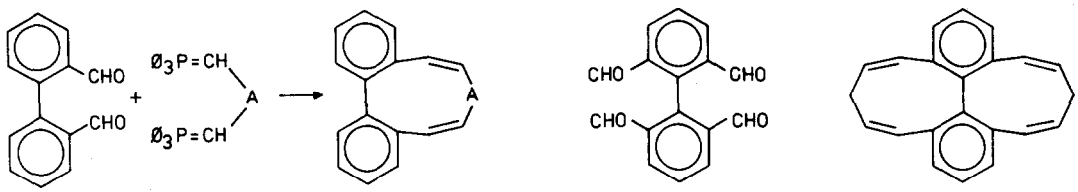


252 **253**

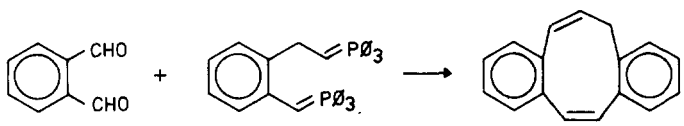


254 255

9-Membered rings as in **257** are available from biphenyl-2,2′-dicarbaldehyde **256** and bis-ylids **213**, **214** and **221**.[119,120] Two consecutive bis-Wittig reactions of biphenyl-2,2′-6,6′-tetracarbaldehyde **258** and propane-bisylidenetriphenylphosphorane **221** were used in the synthesis of the dihydrodibenzononalene **259**.[121] Phthalaldehyde **230** and the unsymmetrical bis-alkylidenephosphorane **260** give 1,2:5,6-dibenzocyclononatetraene **261**.[120,122] Both **257** (A = CH_2) and **261** have been deprotonated to the aromatic 10π anion, and **259** and butyllithium produced the presumably planar 18π dibenzononalenide dianion.



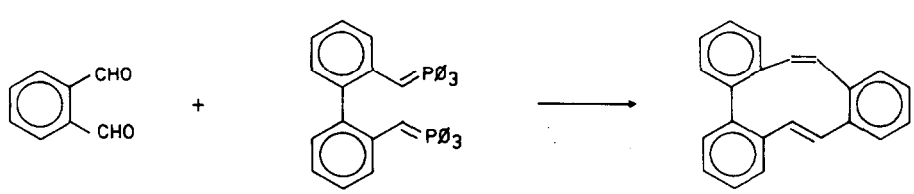
256 **213** A = O; **214** A = S; **221** A = CH_2 **257** **258** **259**



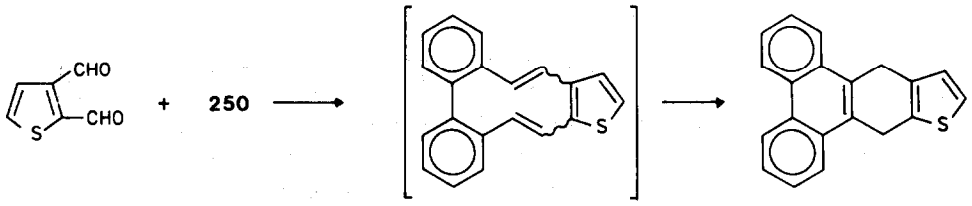
230 **260** **261**

Numerous examples are known for the formation of 10-membered and larger rings by the bis-Wittig reaction.[6] Phthalaldehyde **230** and biphenyl-2,2′-bismethylidenetriphenylphosphorane **250** give (*E,Z*)-1,2:3,4:7,8-tribenzocyclodecapentaene **262**, which undergoes transannular ring closure on heating.[123] Thiophene-2,3-dicarbaldehyde **219** and bis-ylid **250** are expected to yield the [10]annulene **263**, but this primary product proved to be too unstable to be isolated. A 18% yield of the corresponding phenanthrene **264** formed by electrocyclic ring closure followed by a hydrogen shift was found instead.[124]

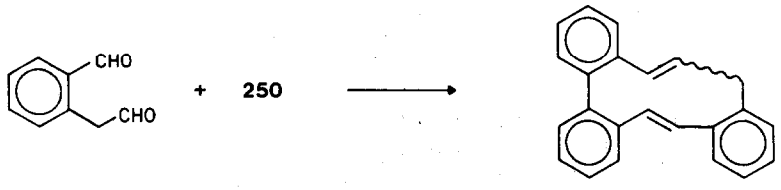
The synthesis of (*E,E*)- and (*E,Z*)-1,2:5,6:7,8-tribenzocycloundecapentaene **266** from homophthalaldehyde **265** and bis-ylid **250** has been reported. Experiments to prepare an aromatic [11]annulenium cation from **266** failed, but both the (*E,E*)- and the (*E,Z*)-isomer gave a blue "homoaromatic" anion with sodium methylsulfinylmethylid.[125] (*E,E*)- and (*E,Z*)-1,2:5,6:7,8:11,12-tetrabenzocyclotridecahexaene **268** is formed from biphenyl-2,2′-dicarbaldehyde **256** and diphenylmethane-2,2′-bismethylidenetriphenylphosphorane **267**. The anion of (*E,E*)-**268**, a 14π system, shows some diatropic, i.e. aromatic character.[120,126]



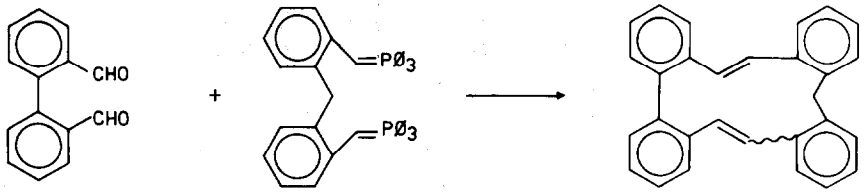
230 **250** **262**



219 263 264

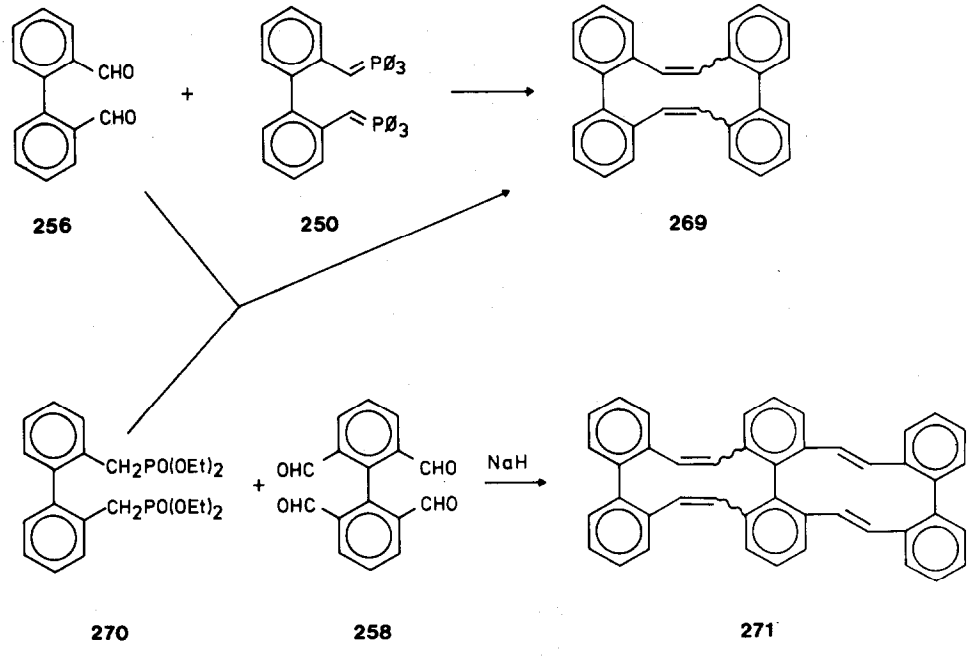


265 266



256 267 268

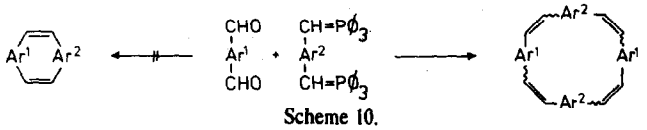
Tetrabenzo[12]annulene **269** has been synthesized from biphenyl-2,2'-dicarbaldehyde **256** and biphenyl-2,2'-bismethylidenetriphenylphosphorane **250** (performed or generated *in situ*) by several groups.[127] Recently it has been found that the highest yield (8%) of (*E,E*)-**269** can be obtained from dialdehyde **256** and the dianion of biphenyl-2,2'-bis(diethyl methylphosphonate) **270**. Compound **271** with two fused [12]annulene rings was obtained from biphenyl-2,2',6,6'-tetracarbaldehyde **258** and two equivalents of bis-phosphonate **270** as a mixture of the (*E,E,E,E*)-and the (*E,Z,Z,E*)-isomer in 4.2 and 0.4% yield, respectively.[128] 15-Membered macrocycles were synthesized recently by bis-Wittig reaction of the bis-phosphonate corresponding to **222**.[138] A bis-phosphonate containing to formyl groups was used in the preparation of bridged annulenes by consecutive bis-Wittig reactions.[139]



256 250 269

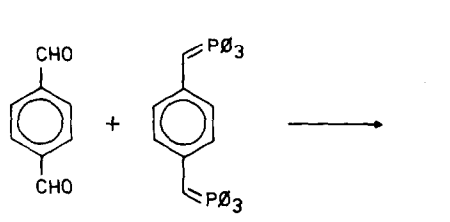
270 258 271

If bis-Wittig reactions would lead to strained cyclophanes, fourfold Wittig reactions involving two molecules each of dialdehyde and bis-alkylidenephosphorane are observed instead (Scheme 10). This does not contradict the statement made earlier that the Wittig reaction allows the formation of strained double bonds. Because of the stepwise nature of the bis-Wittig reaction, one double bond is formed before the second CO and phosphorane group react with each other. Once the double bond is in place, CO and phosphorane group are too far away from each other for a successive interaction, and then react with another molecule.

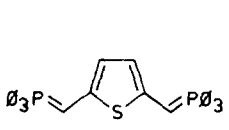


Scheme 10.

Condensation of terephthalaldehyde **272** and the *p*-xylene-bisylidenetriphenylphosphorane **273** prepared *in situ* with lithium ethoxide in dimethylformamide at −40° leads to a 15% yield of [2.2.2.2]paracyclophane-1,9,17,25-tetraene **274**.[129] The reaction has been extended to bis-alkylidenephosphoranes substituted by iodine or bromine in the aromatic nucleus, to thiophene-2,5-bismethylidenetriphenylphosphorane **275** and the naphthalene-derived phosphoranes **276**, **277**, **278**, and 4,4′-biphenyldicarbaldehyde **279**, 4,4′-bibenzyldicarbaldehyde **280**, naphthalene-2,6-dicarbaldehyde **281**, thiophene-2,5-dicarbaldehyde **282**, and furan-2,5-dicarbaldehyde **283**.[130] In some reactions, small amounts of larger cyclophanes incorporating three molecules of dialdehydes and three molecules of bis-ylid were also found. Benzene-1,4-dipropenal **284** and anthracene-9,10-dipropenal **285** react with bis-ylid **273** to give [4.4.4.4]cyclophanes incorporating butadiene bridges, albeit in low yield.[131]



272 **273** **274**



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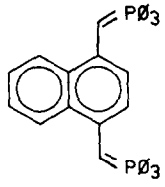

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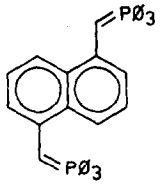

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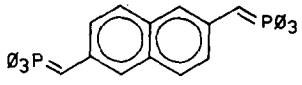

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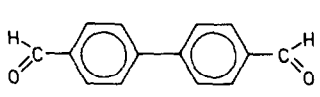

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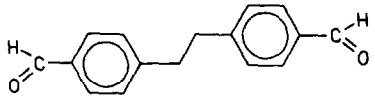

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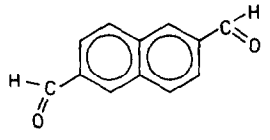

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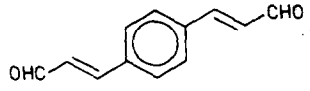

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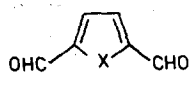
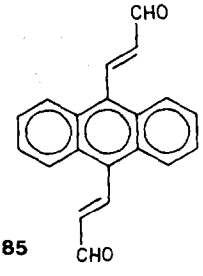


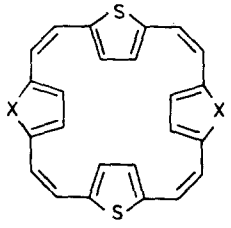
282 X = S

283 X = O

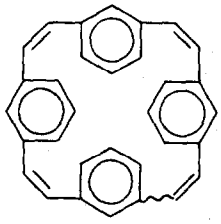


285

Condensation of thiophene-2,5-bismethylidenetriphenylphosphorane **275** with thiophene-2,5-dicarbaldehyde **282** or furan-2,5-dicarbaldehyde **283** leads to the [24]annulene tetrasulfide **286** and its dioxygen analogue **287**, respectively.[132] [2.2.2.2]Metacyclophanetetraene **288** (all-(*Z*) and (*E,Z,Z,Z*)) and mixed meta/para- and ortho/paracyclophanes **289** (all-(*Z*)) and **290** (all-(*Z*) and (*E,Z,Z,Z*)) have also been prepared by 4-fold Wittig reaction. Again some larger cyclophanes from a 6-fold Wittig reaction were isolated.[133] Reaction of biphenyl-3,3'-dicarbaldehyde with biphenyl-3,3'-bismethylidenetriphenylphosphorane gave [2.0.2.0]metacyclophanediene **291** in a normal bis-Wittig reaction.[134]



286 X = S
287 X = O



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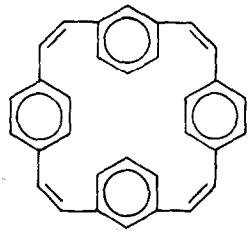

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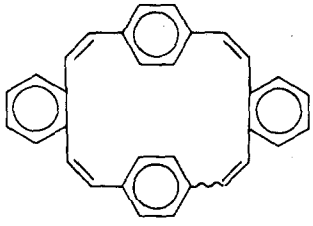

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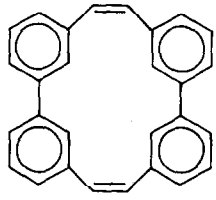
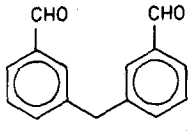


291

4-Fold Wittig reactions are not restricted to aromatic bis-alkylidenephosphoranes only. Diphenylmethane-3,3'-dicarbaldehyde **292** and propane-bisylidenetriphenylphosphorane **221** prepared *in situ* gave none of the expected [1.5]metacyclophanediene **293**, but, after hydrogenation, [5.1.5.1]metacyclophane **294** with a 24-membered ring.[135] [5.5]Paracyclophanetetraene **295** was prepared from bis-ylid **221** and terephtalaldehyde **272**, albeit in low yield.[136]



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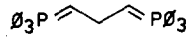
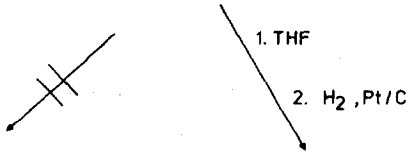
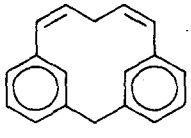
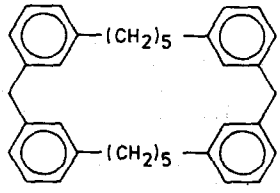


221

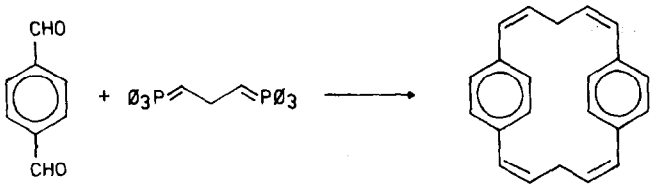




293

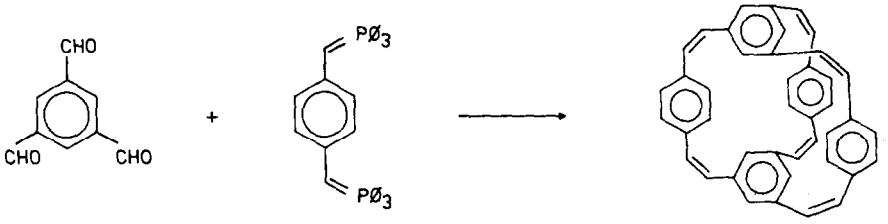


294



272 221 295

A 6-fold Wittig reaction has been accomplished with 1,3,5-benzene-tricarbaldehyde **296** and *p*-xylene-bisylidenetriphenylphosphorane **273** prepared *in situ* with lithium ethoxide in dimethylformamide at −40°. The cage compound **297** was isolated in 1.7% yield.[137] Meanwhile, 6-fold Wittig reactions have been performed with trialdehyde **296** and a number of other aromatic bis-ylids.[136]



296 273 297

REFERENCES

[1]A. Maercker, *Org. React.* **14**, 270 (1965); A. W. Johnson, *Ylid Chemistry*. Academic Press, New York (1966); H. J. Bestmann and R. Zimmermann, *Fortschr. Chem. Forsch.* **20**, 1 (1971); H. J. Bestmann and O. Klein, Houben-Weyl, *Methoden der organischen Chemie* (Edited by E. Müller), Vol. **5/1b**, p. 383. Georg Thieme Verlag, Stuttgart (1972); M. Schlosser, *Methodicum Chimicum* (Edited by F. Korte, H. Zimmer and K. Niedenzu), Vol. **7**, p. 529. Georg Thieme Verlag, Stuttgart (1976).

[2]J. Reucroft and P. G. Sammes, *Quart. Rev. Chem. Soc.* **25**, 135 (1971); Houben-Weyl, *Methoden der organischen Chemie* (Edited by E. Müller), Vols. **5/1b**, **1c** and **1d**. Georg Thieme Verlag, Stuttgart (1970/72).

[3]M. Schlosser, *Topics in Stereochemistry* **5**, 1 (1970).

[4]J. S. Boutagy and R. E. Thomas, *Chem. Rev.* **74**, 87 (1974); W. S. Wadsworth, Jr., *Org. React.* **25**, 73 (1977).

[5]E. Zbiral, *Synthesis* 775 (1974).

[6]K. P. C. Vollhardt, *Ibid.* 765 (1975).

[7]H. J. Bestmann and R. Zimmermann, *Chem. Ztg.* **96**, 649 (1972); H. J. Bestmann and R. Zimmermann, *Carbon-Carbon Bond Formation* (Edited by R. L. Augustine), Vol. **1**, p. 353. Dekker, New York (1979).

[8]E. Vedejs and K. A. J. Snoble, *J. Am. Chem. Soc.* **95**, 5778 (1973); D. W. Allen and H. Ward, *Tetrahedron Letters* 2707 (1979).

[9]M. Schlosser and Huynh Ba Tuong, *Angew. Chem.* **91**, 675 (1979); *Ibid.* Int. Ed. Engl. **18**, 633 (1979); M. Schlosser, A. Pickala, C. Tarchini and Huynh Ba Tuong, *Chimia* **29**, 341 (1975).

[10]G. Chioccola and J. J. Daly, *J. Chem. Soc.* A 568 (1968).

[11]H. J. Bestmann, F. Seng and H. Schulz, *Chem. Ber.* **96**, 465 (1963); H. J. Christau, J. P. Vors and H. Christol, *Synthesis* 538 (1979); see however M. I. Schevchuk, I. V. Megera, N. A. Burachenko and A. V. Dombrovskii, *J. Org. Chem. USSR* **10**, 169 (1974).

[12]C. E. Griffin and G. Witschard, *J. Org. Chem.* **29**, 1001 (1964).

[13]M. J. Berenguer, J. Castells, R. M. Galard and M. Moreno-Mañas, *Tetrahedron Letters* 495 (1971); C. Brown and M. V. Sargent, *J. Chem. Soc.* C, 1818 (1969).

[14]T. I. Bieber and E. H. Eisman, *J. Org. Chem.* **27**, 678 (1962); C. E. Griffin and G. Witschard, *Ibid.* **27**, 3334 (1962).

[15]K. B. Becker, A. F. Boschung and C. A. Grob, *Helv. Chim. Acta* **56**, 2733 (1973); K. B. Becker, *Ibid.* **60**, 68 (1977).

[16]H. E. Zimmermann and L. M. Tolbert, *J. Am. Chem. Soc.* **97**, 5497 (1975).

[17]S. Chatterjee, *Chem. Commun.* 620 (1979).

[18]G. Köbrich, *Angew. Chem.* **85**, 494 (1973); *Ibid.* Int. Ed. Engl. **12**, 464 (1973); G. L. Buchanan, *Chem. Soc. Rev.* **3**, 41 (1974); R. Keese, *Angew. Chem.* **87**, 568 (1975); *Ibid.* Int. Ed. Engl. **14**, 528 (1975).

[19]K. B. Becker, *Chimia* **28**, 726 (1974); K. B. Becker, *Tetrahedron Letters* 2207 (1975); K. B. Becker, *Helv. Chim. Acta* **60**, 81 (1977).

[20]M. Nakazaki, K. Naemura and S. Nakahara, *Chem. Commun.* 82 (1979); *J. Org. Chem.* **44**, 2438 (1979).

[21]R. Keese, personal communication (1979).

[22]K. B. Becker and J. L. Chappuis, *Helv. Chim. Acta* **62**, 34 (1979) and unpublished results.

[23]W. G. Dauben and J. D. Robbins, *Tetrahedron Letters* 151 (1975).

[24]H. B. Renfroe, J. A. Gurney and L. A. R. Hall, *J. Am. Chem. Soc.* **89**, 5304 (1967).

[25]K. E. Wilson, Ph.D. Thesis, University of Alberta (1973), cited in S. Masamune, G. S. Bates and J. W. Corcoran, *Angew. Chem.* **89**, 602 (1977); *Ibid.* Int. Ed. Engl. **16**, 585 (1977).

[26]P. A. Grieco and C. S. Pogonowski, *Synthesis* 425 (1973).

[27]R. D. Clark, L. G. Kozar and C. H. Heathcock, *Synth. Commun.* **5**, 1 (1975).

[28]E. Piers, B. Abeysekera and J. R. Scheffer, *Tetrahedron Letters* 3279 (1979); see also H.-J. Altenbach, *Angew. Chem.* **91**, 1005 (1979); *Ibid.* Int. Ed. Engl. **18**, 940 (1979); M. R. Roberts and R. H. Schlessinger, *J. Am. Chem. Soc.* **101**, 7626 (1979); G. Stork and E. Nakamura, *J. Org. Chem.* **44**, 4010 (1979); K. C. Nicolaou, S. P. Seitz, M. R. Pavia, N. A. Petasis, *Ibid.* **44**, 4011 (1979).

[29]E. E. Schweizer, C. J. Berninger, D. M. Crouse, R. A. Davis and R. S. Logothetis, *Ibid.* **34**, 207 (1969); E. E. Schweizer, T. Minami and D. M. Crouse, *Ibid.* **36**, 4028 (1971).

[30]E. E. Schweizer, T. Minami and S. E. Anderson, *Ibid.* **39**, 3038 (1974).

[31]E. E. Schweizer, J. G. Liehr and D. J. Monaco, *Ibid.* **33**, 2416 (1968).

[32]E. E. Schweizer, C. S. Kim, C. S. Labaw and W. P. Murray, *Chem. Commun.* 7 (1973); E. E. Schweizer, S. DeVoe Goff and W. P. Murray, *J. Org. Chem.* **42**, 200 (1977).

[33]S. F. Krauser and A. C. Watterson, Jr., *Ibid.* **43**, 3400 (1978).
[34]S. F. Donovan, M. A. Avery and J. E. McMurray, *Tetrahedron Letters* 3287 (1979).
[35]H. G. Lehmann and R. Wiechert, *Angew. Chem.* **80**, 317 (1968); *Ibid.* Int. Ed. Engl. **7**, 300 (1968); see also W. Fritsch, U. Stache and H. Ruschig, *Liebigs Ann.* **699**, 195 (1966); W. Fritsch, U. Stache, W. Haede, K. Radscheit and H. Ruschig, *Ibid.* **721**, 168 (1969).
[36]W. Eberlein, J. Nickl, J. Heider, G. Dahms and H. Machleidt, *Chem. Ber.* **105**, 3686 (1972).
[37]T. W. Güntert, H. H. A. Linde, M. S. Ragab and S. Spengel, *Helv. Chim. Acta* **60**, 334 (1977); S. El-Dine, K. Faust, T. W. Güntert, E. Hauser, H. H. A. Linde and S. Spengel, *Ibid.* **62**, 1283 (1979).
[38]G. Stork and R. Matthews, *Chem. Commun.* 445 (1970). For related examples see T. Sato, R. Ito, Y. Hayakawa and R. Noyori, *Tetrahedron Letters* 1829 (1978).
[39]A. I. Meyers, D. M. Roland, D. L. Comins, R. Henning, M. P. Fleming and K. Shimizu, *J. Am. Chem. Soc.* **101**, 4732 (1979); A. I. Meyers, D. L. Comins, D. M. Roland, R. Henning and K. Shimizu, *Ibid.* **101**, 7104 (1979).
[40]K. F. Burri, R. A. Cardone, Wen Yean Chen and P. Rosen, *Ibid.* **100**, 7069 (1978).
[41]R. Scartazzini, H. Peter, H. Bickel, K. Heusler and R. B. Woodward, *Helv. Chim. Acta* **55**, 408 (1972).
[42]D. Bormann, *Liebigs Ann.* 1391 (1974).
[43]C. L. Branch, J. H. C. Nayler and M. J. Pearson, *J. Chem. Soc.* Perkin Trans. I 1450 (1978); C. L. Branch and M. J. Pearson, *Ibid.* 2268 (1979); M. Narisada, H. Onoue and W. Nagata, *Heterocycles* **7**, 839 (1977); R. N. Guthikonda, L. D. Cama and B. G. Christensen, *J. Am. Chem. Soc.* **96**, 7584 (1974); M. Narisada, T. Yoshida, H. Onoue, M. Ohtani, T. Okada, T. Tsuji, I. Kikkawa, N. Haga, H. Satoh, H. Itani and W. Nagata, *J. Med. Chem.* **22**, 757 (1979); I. Ernest, *Helv. Chim. Acta* **62**, 2681 (1979); *Ibid.* **63**, 201 (1980).
[44]R. W. Ratcliffe and B. G. Christensen, *Tetrahedron Letters* 4649 (1973).
[45]H. J. Bestmann and B. Arnason, *Ibid.* 455 (1961); *Chem. Ber.* **95**, 1513 (1962).
[46]I. Ernest, J. Gosteli, C. W. Greengrass, W. Holick, D. E. Jackman, H. R. Pfaendler and R. B. Woodward, *J. Am. Chem. Soc.* **100**, 8214 (1978); M. Lang, K. Prasad, W. Holick, J. Gosteli, I. Ernest and R. B. Woodward, *Ibid.* **101**, 6296 (1979); P. Lombardi, G. Franceschi and F. Arcamore, *Tetrahedron Letters* 3777 (1979).
[47]H. Onoue, M. Narisada, S. Uyeo, H. Matsumura, K. Okada, T. Yano and W. Nagata, *Ibid.* 3867 (1979); A. J. G. Baxter, K. H. Dickinson, P. M. Roberts, T. C. Smale and R. Southgate, *Chem. Commun.* 236 (1979); R. J. Ponsford, P. M. Roberts and R. Southgate, *Ibid.* 847 (1979).
[48]G. Wittig and U. Schöllkopf, *Chem. Ber.* **87**, 1318 (1954); S. Trippett and D. M. Walker, *J. Chem. Soc.* 1266 (1961).
[49]W. Grell and H. Machleidt, *Liebigs Ann.* **693**, 134 (1966); H. J. Bestmann, K. Rostock and H. Dornauer, *Angew. Chem.* **78**, 335 (1966); *Ibid.* Int. Ed. Engl. **5**, 308 (1966); H. J. Bestmann, H. Dornauer and K. Rostock, *Chem. Ber.* **103**, 2011 (1970); M. LeCorre, *C. R. Hebd. Séances Acad. Sci. Ser.* C, **276**, 963 (1973); *Bull. Soc. Chim. Fr.* 2005 (1974); V. Subramanyam, E. H. Silver and A. H. Soloway, *J. Org. Chem.* **41**, 1272 (1976).
[50]A. P. Uijttewaal, F. L. Jonkers and A. van der Gen, *Ibid.* **44**, 3157 (1979).
[51]H. O. House and H. Babad, *Ibid.* **28**, 90 (1973); L. D. Bergel'son, V. A. Vaver, L. I. Barsukov and N. M. Shemyakin, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk* 1134 (1963); *Chem. Abstr.* **59**, 8607 (1963).
[52]A. Hercouet and M. LeCorre, *Tetrahedron Letters* 5 (1979).
[53]A. Hercouet and M. LeCorre, *Ibid.* 2145 (1979); B. Begasse, A. Hercouet and M. LeCorre, *Ibid.* 2149 (1979); A. Hercouet and M. LeCorre, *Ibid.* 2995 (1979).
[54]E. E. Schweizer, *J. Am. Chem. Soc.* **86**, 2744 (1964).
[55]E. E. Schweizer and J. G. Liehr, *J. Org. Chem.* **33**, 583 (1968); E. E. Schweizer, W. S. Creasy, J. G. Liehr, M. E. Jenkins and D. L. Dalrymple, *Ibid.* **35**, 601 (1970).
[56]E. E. Schweizer and W. S. Creasy, *Ibid.* **36**, 2244 (1971); E. E. Schweizer, A. T. Wehman and D. M. Nycz, *Ibid.* **38**, 1583 (1973).
[57]J. M. McIntosh, H. B. Goodbrand and G. M. Masse, *Ibid.* **39**, 202 (1974); J. M. McIntosh and G. M. Masse, *Ibid.* **40**, 1294 (1975).
[58]J. M. McIntosh and R. S. Steevensz, *Can. J. Chem.* **55**, 2442 (1977).
[59]J. M. McIntosh and H. Khalil, *Ibid.* **54**, 1923 (1976).
[60]E. E. Schweizer and L. D. Smucker, *J. Org. Chem.* **31**, 3146 (1966).
[61]E. E. Schweizer and K. K. Light, *J. Am. Chem. Soc.* **86**, 963 (1964); *J. Org. Chem.* **31**, 870 (1966).
[62]W. Flitsch and E. R. Gesing, *Tetrahedron Letters* 1997 (1976); *Chem. Ber.* **113**, 614 (1980).
[63]E. E. Schweizer and C. M. Kopay, *J. Org. Chem.* **37**, 1561 (1972).
[64]W. A. Kleschick and C. H. Heathcock, *Ibid.* **43**, 1256 (1978).
[65]T. Minami, H. Suganuma and T. Agawa, *Chem. Lett.* 285 (1978).
[66]J. Ide, R. Endo and S. Muramatsu, *Ibid.* 401 (1978).
[67]J. M. McIntosh and R. A. Sieler, *Can. J. Chem.* **56**, 226 (1978); *J. Org. Chem.* **43**, 4431 (1978).
[68]H. J. Bestmann, G. Schmid and D. Sandmeier, *Angew. Chem.* **88**, 92 (1976); *Ibid.* Int. Ed. Engl. **15**, 115 (1976); see also J. Motoyoshiya, J. Enda, Y. Ohshiro and T. Agawa, *Chem. Commun.* 900 (1979).
[69]E. E. Schweizer and G. J. O'Neill, *J. Org. Chem.* **30**, 2082 (1965); M. E. Kuehne and R. E. Damon, *Ibid.* **42**, 1825 (1977).
[70]A. T. Hewson, *Tetrahedron Letters* 3267 (1978).
[71]I. Kawamoto, S. Muramatsu and Y. Yura, *Ibid.* 4223 (1974).
[72]E. E. Schweizer, C. J. Berninger and J. C. Thompson, *J. Org. Chem.* **33**, 336 (1968).
[73]P. L. Fuchs, *J. Am. Chem. Soc.* **96**, 1607 (1974).
[74]W. G. Dauben and D. J. Hart, *Ibid.* **97**, 1622 (1975); *Ibid.* **99**, 7307 (1977).
[75]W. G. Dauben and D. J. Hart, *Tetrahedron Letters* 4353 (1975).
[76]J. P. Marino and R. C. Landick, *Ibid.* 4531 (1975).
[77]P. L. Fuchs, *Ibid.* 4055 (1974).
[78]G. Büchi and M. Pawlak, *J. Org. Chem.* **40**, 100 (1975).
[79]J. M. McIntosh and F. P. Seguin, *Can. J. Chem.* **53**, 3526 (1975).
[80]S. F. Martin and S. R. Desai, *J. Org. Chem.* **43**, 4673 (1978).
[81]S. D. Darling, F. N. Muralidharan and V. B. Muralidharan, *Tetrahedron Letters* 2757 (1979); *Ibid.* 2761 (1979).
[82]C. A. Henrick, E. Böhme, J. A. Edwards and J. H. Fried, *J. Am. Chem. Soc.* **90**, 5926 (1968).
[83]E. J. Corey and D. L. Boger, *Tetrahedron Letters* 4597 (1978).
[84]F. Texier and R. Carrié, *Ibid.* 4163 (1971); R. Danion-Bougot, D. Danion, J. Hamelin and R. Carrié, *C. R. Hebd. Séances Acad. Sci.* Ser. C, **277**, 1041 (1973); M. Vaultier, R. Danion-Bougot, D. Danion, J. Hamelin and R. Carrié, *Bull. Soc. Chim. Fr.* 1537 (1976).
[85]G. Märkl, *Angew. Chem.* **74**, 696 (1962); see also K. Dimroth, K. H. Wolf and H. Wache, *Ibid.* **75**, 860 (1963).
[86]B. G. Kovalev and N. P. Dormidontova, *J. Gen. Chem. USSR* **40**, 910 (1970).

[87]G. Büchi and H. Wüest, *Helv. Chim. Acta* **54**, 1767 (1971).
[88]W. G. Dauben, D. J. Hart, J. Ipaktschi and A. P. Kozikowski, *Tetrahedron Letters* 4425 (1973); C. A. Grob, Th. Schweizer, P. Wenk and R. S. Wild, *Helv. Chim. Acta* **60**, 482 (1977).
[89]W. G. Dauben and J. Ipaktschi, *J. Am. Chem. Soc.* **95**, 5088 (1973).
[90]F. Bohlmann and Ch. Zdero, *Chem. Ber.* **106**, 3779 (1973).
[91]A. Padwa and L. Brodsky, *J. Org. Chem.* **39**, 1318 (1974).
[92]S. F. Martin and S. R. Desai, *Ibid.* **42**, 1664 (1977).
[93]S. F. Martin and P. J. Garrison, *Tetrahedron Letters* 3875 (1977).
[94]J. Castells, J. Font, T. Ibara, A. Llitjos and M. Moreno-Mañas, *An. Quim.* **74**, 773 (1978).
[95]S. Masamune, D. W. Brooks, K. Morio and R. L. Sobczak, *J. Am. Chem. Soc.* **98**, 8277 (1976).
[96]H. J. Bestmann and O. Kratzer, *Chem. Ber.* **96**, 1899 (1963).
[97]H. J. Bestmann, H. Häberlein and O. Kratzer, *Angew. Chem.* **76**, 226 (1964); H. J. Bestmann, H. Häberlein, H. Wagner and O. Kratzer, *Chem. Ber.* **99**, 2848 (1966); H. J. Bestmann and H. Pfüller, *Angew. Chem.* **84**, 528 (1972); *Ibid.* Int. Ed. Engl. **11**, 508 (1972).
[98]J. A. Deyrup and M. F. Betkousi, *J. Org. Chem.* **40**, 284 (1975).
[99]H. J. Bestmann, R. Armsen and H. Wagner, *Chem. Ber.* **102**, 2259 (1969).
[100]K. Dimroth, G. Pohl and H. Follmann, *Ibid.* **99**, 634 (1966); K. Dimroth, H. Follmann and G. Pohl, *Ibid.* **99**, 642 (1966).
[101]P. J. Garratt and K. P. C. Vollhardt, *J. Am. Chem. Soc.* **94**, 1022 (1972); *Ibid.* **94**, 7087 (1972); P. J. Garratt and D. N. Nicolaides, *J. Org. Chem.* **39**, 2222 (1974).
[102]G. Wittig, H. Eggers and P. Duffner, *Chem. Ber.* **619**, 10 (1958).
[103]A. T. Blomquist and V. J. Hruby, *J. Am. Chem. Soc.* **89**, 4996 (1967).
[104]D. N. Nicolaides, *Synthesis* 127 (1977).
[105]D. B. Denney and J. Song, *J. Org. Chem.* **29**, 495 (1964).
[106]J. A. Ford, Jr. and C. V. Wilson, *Ibid.* **26**, 1433 (1961); R. N. McDonald and T. W. Campbell, *Ibid.* **24**, 1969 (1959).
[107]H. Heitmann, J. H. Sperna Weiland and H. O. Huisman, *Koninkl. Ned. Akad. Wetenschap.*, Proc. Ser. B **64**, 165 (1961); *Chem. Abstr.* **55**, 17562f (1961); see also H. Pommer, *Angew. Chem.* **72**, 911 (1960).
[108]K. Becker, *Synthesis* 238 (1980).
[109]A. Schönberg, E. Singer and H. Schulze-Pannier, *Ibid.* 723 (1974); M. P. Cava, H. Firouzabadi and M. Krieger, *J. Org. Chem.* **39**, 480 (1974).
[110]J. A. Elix and M. V. Sargent, *J. Am. Chem. Soc.* **90**, 1631 (1968).
[111]W. H. Ploder and D. F. Tavares, *Can. J. Chem.* **48**, 2446 (1970).
[112]M. B. Stringer and D. Wege, *Tetrahedron Letters* 65 (1977); *Aust. J. Chem.* **31**, 1607 (1978).
[113]E. A. Sancaktar, J. D. Taylor, J. V. Hay and J. F. Wolfe, *J. Org. Chem.* **41**, 509 (1976).
[114]C. E. Griffin and J. A. Peters, *Ibid.* **28**, 1715 (1963).
[115]F. A. Kaplan and B. W. Roberts, *J. Am. Chem. Soc.* **99**, 513 (1977).
[116]H. Alper and R. A. Partis, *Gazz. Chim. Ital.* **107**, 201 (1977).
[117]H. J. Bestmann and H. Morper, *Angew. Chem.* **79**, 578 (1967); *Ibid.* Int. Ed. Engl. **6**, 561 (1917); H. J. Bestmann, H. Morper and W. Distler, unpublished (cited in Ref.[7]).
[118]C. F. Wilcox, Jr., J. P. Uetrecht and K. K. Grohmann, *J. Am. Chem. Soc.* **94**, 2532 (1972); C. F. Wilcox, Jr., J. P. Uetrecht, G. D. Grantham and K. G. Grohmann, *Ibid.* **97**, 1914 (1975).
[119]A. P. Bindra, J. A. Elix, P. J. Garratt and R. H. Mitchell, *Ibid.* **90**, 7372 (1968); P. J. Garratt and K. A. Knapp, *Chem. Commun.* 1215 (1970); M. Rabinovitz, A. Gazit and E. D. Bergman, *Ibid.* 1430 (1970).
[120]M. Rabinovitz, I. Willner, A. Gamliel and A. Gazit, *Tetrahedron* **35**, 667 (1979).
[121]I. Willner and M. Rabinovitz, *J. Am. Chem. Soc.* **99**, 4507 (1977).
[122]M. Rabinovitz and I. Willner, *Tetrahedron Letters* 4447 (1974).
[123]K. Grohmann and F. Sondheimer, *J. Am. Chem. Soc.* **89**, 7119 (1967).
[124]D. N. Nicolaides, *Synthesis* 675 (1976).
[125]A. Dagan and M. Rabinovitz, *Tetrahedron Letters* 4529 (1976).
[126]A. Gamliel, I. Willner and M. Rabinovitz, *Synthesis* 410 (1977).
[127]H. A. Staab, E. Wehinger and W. Thorwart, *Chem. Ber.* **105**, 2290 (1972); K. Grohmann, P. D. Howes, R. H. Mitchell, A. Monahan and F. Sondheimer, *J. Org. Chem.* **38**, 808 (1973); I. Agranat, M. A. Kraus, E. D. Bergmann, P. J. Roberts and O. Kennard, *Tetrahedron Letters* 1265 (1973).
[128]I. Agranat, B. Rabinovitz and Wu-Chang Shaw, *J. Org. Chem.* **44**, 1936 (1979).
[129]B. Thulin, O. Wennerström and H. E. Högberg, *Acta Chem. Scand.* B **29**, 138 (1975).
[130]B. Thulin and O. Wennerström, *Ibid.* B **30**, 369 (1976); *Ibid.* B **30**, 688 (1976); B. Thulin, O. Wennerström, I. Somfai and B. Chmielarz, *Ibid.* B **31**, 135 (1977); D. Tanner, B. Thulin and O. Wennerström, *Ibid.* B **33**, 443 (1979).
[131]D. Tanner, B. Thulin and O. Wennerström, *Acta Chem. Scand.* B **33**, 464 (1979).
[132]A. Strand, B. Thulin and O. Wennerström, *Ibid.* B **31**, 521 (1977).
[133]B. Thulin, O. Wennerström and I. Somaai, *Ibid.* B **32**, 109 (1978).
[134]B. Thulin and O. Wennerström, *Tetrahedron Letters* 929 (1977).
[135]N. Finch and C. W. Gemenden, *J. Org. Chem.* **44**, 2804 (1979).
[136]O. Wennerström, personal communication.
[137]H. E. Högberg, B. Thulin and O. Wennerström, *Tetrahedron Letters* 931 (1977).
[138]G. Büchi and H. Wüest, *Helv. Chim. Acta* **62**, 2661 (1979).
[139]E. Vogel, H. M. Deger, J. Sombroek, J. Palm, A. Wagner and J. Lex, *Angew. Chem.* **92**, 43 (1980); *Ibid.* Int. Ed. Engl. **19**, 41 (1980).