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Tandem Cyclopropanation/Cope Rearrangement: A General Method for the Construction of Seven-Membered Rings

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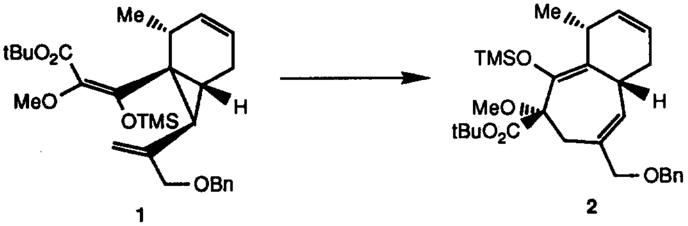
I. Introduction

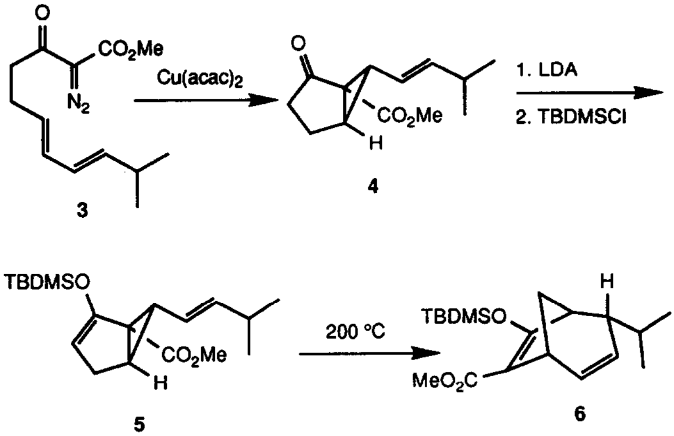
As a number of important natural products contain densely functionalized seven-membered rings, general methods for the construction of these ring systems have been actively pursued.[1] In recent years, annulation processes, such as 4 + 3 annulations between dienes and allyl cations[2] or a nucleophilic vinylcarbene,[3] or 5 + 2 annulations between heterocyclic betaines and alkenes[4] have been shown to be particularly versatile.[5] The most effective method with respect to stereocontrol, however, has been the Cope rearrangement of *cis* divinylcyclopropanes,[6,7,8] as the rearrangement proceeds under mild conditions through a boat transition state with very predictable stereochemistry. An illustration of the efficiency of this chemistry is Wender's recent example directed towards the synthesis of phorbol, in which the Cope rearrangement of **1** proceeded in 87% yield to the bicyclic system **2**.[7]



1 2 (1)

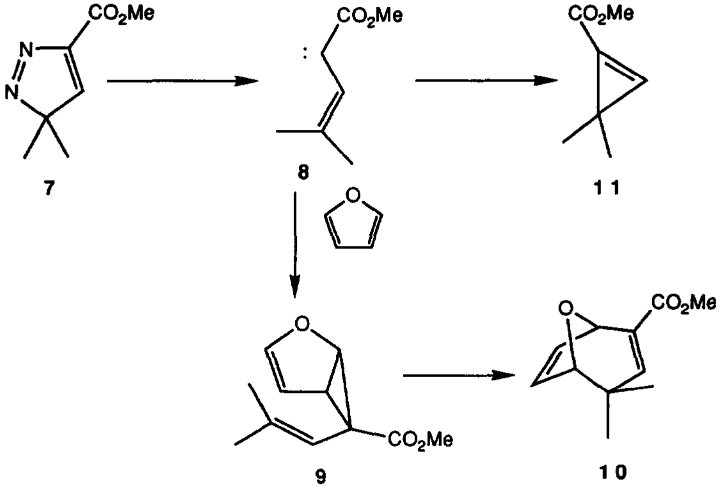
A drawback to the Cope rearrangement procedure is that the stereoselective synthesis of the *cis*-divinylcyclopropanes is still a challenging process, even though a number of elegant methods have been developed to try to overcome this problem.[6] One approach that has been used to prepare divinylcyclopropanes, which is relevant to this report, involves an intramolecular cyclopropanation between a carbenoid and a diene.[8] Copper catalyzed decomposition of the diazo derivative **3** generated the cyclopropane **4**, which was readily elaborated to the *trans*-divinylcyclopropane **5**. The Cope rearrangement of **5** at 200 °C produced the [3.2.1]bicyclic system **6** in essentially quantititative yield. The high temperature for the Cope rearrangement was necessary to isomerize the *trans*-divinylcyclopropane **5** to the *cis*-divinylcyclopropane, and even though the above scheme was successful, competing rearrangement pathways will occur in many instances[6] unless the *cis*-divinylyclopropane is stereoselectively formed.

Scheme 1

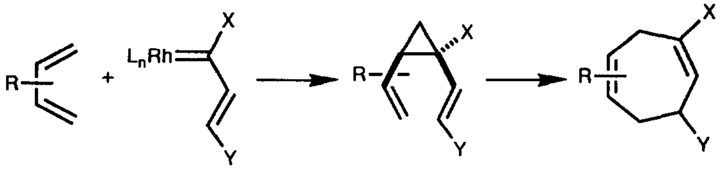


In principle, a simple solution to the problems associated with the synthesis of *cis*-divinylcyclopropanes, would be a stereoselective cyclopropanation between vinylcarbenes and dienes, leading to the possibility of a tandem cyclopropanation/Cope rearrangement process. Franck-Neumann demonstrated that the reaction could be achieved by photolysis of the 3H-pyrazole **7** in the presence of furan.[9] Capture of the vinylcarbene **8** by furan occurred to generate the *cis*-divinylcyclopropane **9**, which was then rearranged to the bicyclic system **10**. The reaction, however, is complicated because vinylcarbenes are very prone to rearrangement, and in this case, a competing reaction was the cyclization of **8** to the cyclopropene **11**, even when furan was used as solvent (**9** : **11** ratio, 2 : 1). Thus, more controllable vinylcarbenes would be required in order to fully develop this synthetic strategy.

Scheme 2



Excellent control of carbene reactivity is often achieved by use of transient metal stabilized carbenoids derived from metal catalyzed decomposition of diazoalkanes.[10] Until quite recently, however, very few examples had been reported of metal catalyzed decomposition of vinyldiazomethanes.[11] Presumably, this is because vinyldiazomethanes themselves have been considered to be unstable, readily cyclizing to 3H-pyrazoles.[12] It is the purpose of this report to illustrate that a wide range of vinyldiazomethanes can indeed be effectively used to generate vinylcarbenoids and that the tandem cyclopropanation/Cope rearrangement (equation 2) is a very general synthetic process.



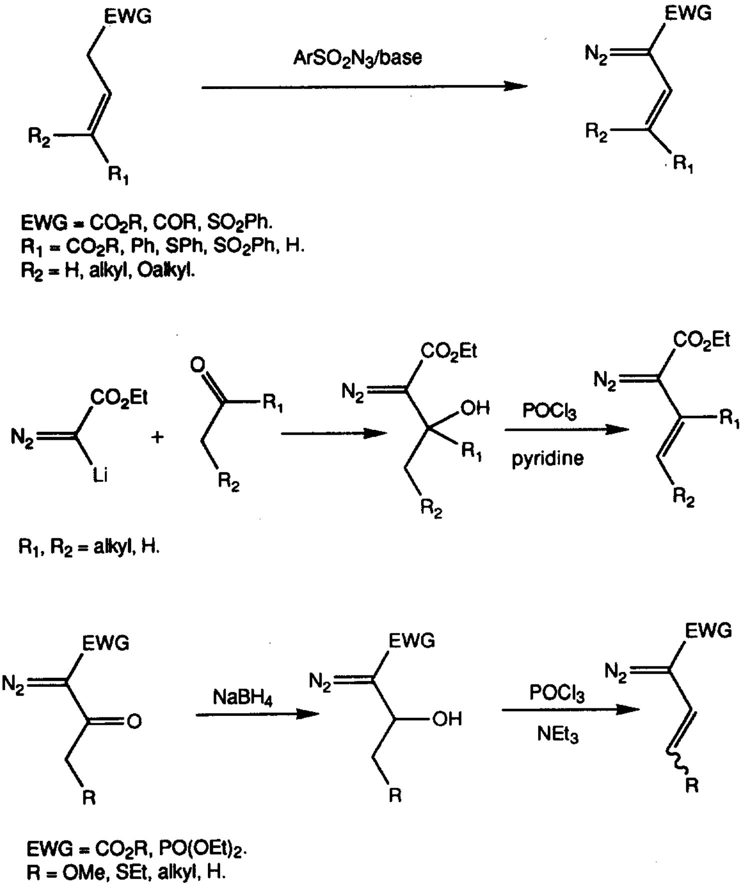
(2)

II. Synthesis of Vinyldiazomethanes

The successful development of the tandem cyclopropanation/Cope rearrangement would require ready access to vinyldiazomethanes of reasonable stability. As kinetic studies indicate that electron withdrawing groups (EWGs) retard the electrocyclization of vinyldiazomethanes to (3H)-pyrazoles,[12a,b] the most promising vinylcarbenoid precursors for the tandem cyclopropanation/Cope rearrangement appeared to be vinyldiazomethanes that contained multiple EWGs. Traditionally, vinyldiazomethanes have been prepared by oxidation of hydrazones,[11d] by base induced elimination of tosylhydrazones[12c,d] or N-acyl-N-nitrosoamines,[11a-

[c,12a] or by photolytic ring opening of 3H-pyrazoles.[9,12b] Davies has found that the diazo-transfer method is very effective for the synthesis of vinyldiazomethanes containing EWGs (Scheme 3).[13,14] By use of triethylamine, DBU, or LDA as base, various vinyldiazomethanes containing one or two EWGs are readily formed. A new, potentially very general approach to vinyldiazomethanes, reported by Padwa,[15] involves condensation of lithium diazoacetate with carbonyl compounds followed by dehydration of the resulting alcohol. A related method, which also employs a dehydration in the last step, begins with sodium borohydride reduction of diazoacetoacetates and related systems.[16] Through these general processes a whole range of different vinyldiazomethanes is now readily available. As expected, the stability of these compounds is strongly dependent on the types of EWGs present. Those with two EWGs appear to be indefinitely stable at 0 °C, while those with a single EWG must be used immediately in subsequent reactions, because they will rearrange within hours to 3H-pyrazoles.[16]

Scheme 3



EWG = CO_2R, COR, SO_2Ph.
R_1 = CO_2R, Ph, SPh, SO_2Ph, H.
R_2 = H, alkyl, Oalkyl.

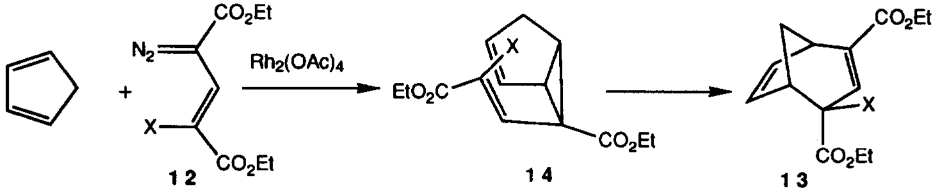
R_1, R_2 = alkyl, H.

EWG = CO_2R, $PO(OEt)_2$.
R = OMe, SEt, alkyl, H.

III. Reaction of Vinylcarbenoids with Dienes

A. Cyclopentadiene

The early attempts at cyclopropanation of alkenes through metal catalyzed decomposition of vinyldiazomethanes had been disappointing. The reported intermolecular reactions had proceeded in very low yields and stereoselectivity,[11a-c] although a few succesful intramolecular examples had been achieved.[11d-g] More recently, however, Davies reported that the rhodium(II) acetate catalyzed decomposition of the vinyldiazomethane **12a** in the presence of cyclopentadiene resulted in the formation of the bicyclo[3.2.1] system **13a** in 98% yield, exclusively as the *endo* product.[17] Efficient formation of the bicyclic system was possible with a variety of vinyldiazomethanes containing two EWGs. The *endo* stereochemistry can be readily rationalized by a tandem cyclopropanation/Cope rearrangement mechanism because divinylcyclopropanes rearrange through a well defined boat transition state with complete and predictable control of stereochemistry.[6] Supporting evidence for this mechanism was seen in the case of bulky vinylcarbenoids because the Cope rearrangement of divinylcyclopropanes is sensitive to steric bulk.[6,18] Thus, decomposition of **12b** in the presence of cyclopentadiene resulted in the formation of the *cis*-divinylcyclopropane **14b** in 89% yield. On standing, **14b** gradually rearranged to **13b** and when heated at 110 °C, **14b** gave an essentially quantitative yield of **13b**. A striking feature of the vinylcarbenoid transformation is that the initial cyclopropanation must be proceeding with a high degree of stereoselectivity. This result is in stark contrast to the generally poor stereoselectivity that occurs in cyclopropanation reactions with the commonly used carbenoids derived from diazoacetates[10] and also from vinyldiazomethanes lacking an EWG α to the diazo group.[11a-c, 19]

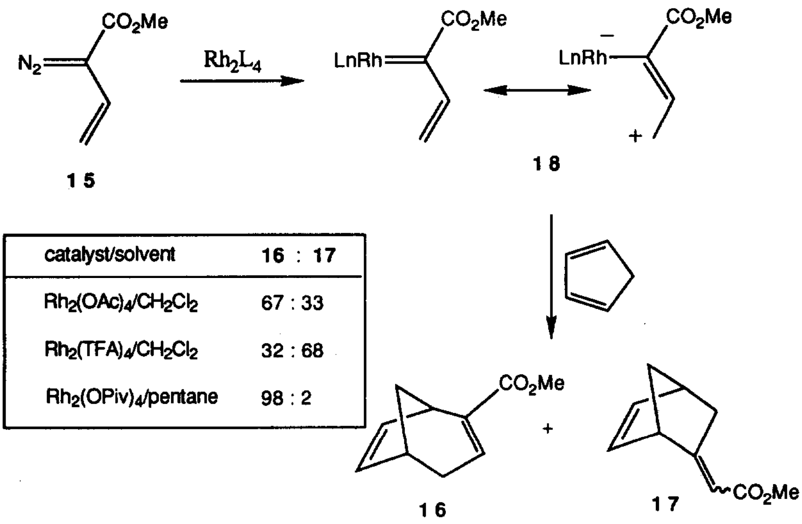


(3)

a: X = H
b: X = OMe

The reaction of vinylcarbenoids containing a single EWG resulted in an unexpected side-reaction.[14] Under the standard conditions of rhodium(II) acetate/dichloromethane, the reaction of the vinyldiazomethane **15** with cyclopentadiene produced a mixture of two bicyclic systems, **16** and **17** in a ratio of 67 : 33. It was considered that the formation of the bicyclo[2.2.1]heptene **17** may have been due to the vinylcarbenoid **18** exhibiting electrophilic character at the vinyl terminus leading to a reaction proceeding though dipolar intermediates. Therefore, the formation of the 3 + 4 annulation product **16**, should be enhanced by use of non polar solvents and electron releasing ligands, and indeed, with rhodium(II) pivalate/pentane the ratio of **16** to **17** was improved to 98 : 2. Side reactions due to reaction at the vinyl terminus were found to be very prevalent with vinylcarbenoids containing a single EWG unless a hydrocarbon solvent is used,[20,21] and it is quite possible that this unexpected reactivity may have been a contributing factor for the poor results obtained in the early studies on metal stabilized vinylcarbenoids.[11a-c]

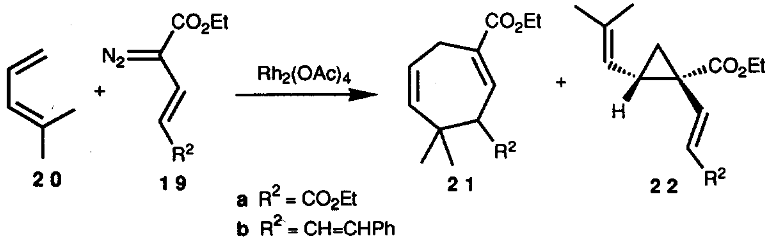
Scheme 4



catalyst/solvent	16 : 17
$Rh_2(OAc)_4/CH_2Cl_2$	67 : 33
$Rh_2(TFA)_4/CH_2Cl_2$	32 : 68
$Rh_2(OPiv)_4$/pentane	98 : 2

B. Acyclic Dienes

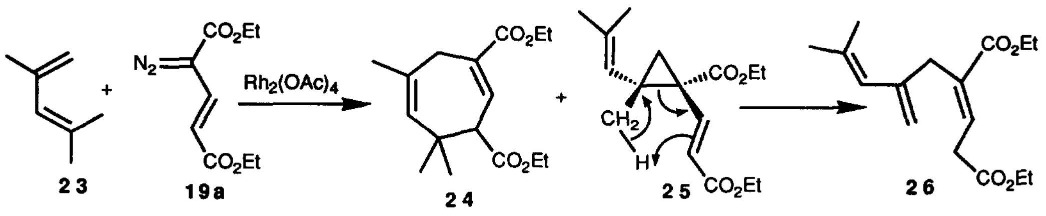
The reaction of vinylcarbenoids with acyclic dienes was somewhat complicated because the stereochemistry of the original cyclopropanation was decreased compared to that in the cyclopentadiene reaction.[22] Rhodium(II) acetate catalyzed decomposition of **19a** in the presence of diene **20** resulted in a 4 : 1 mixture of cycloheptadiene **21a** (presumably derived from the *cis*-divinylcyclopropane) and the *trans*-divinylcyclopropane **22a**. The stereoselectivity, however, is very sensitive to vinylcarbenoid structure, as the reaction with **19b** resulted in the formation of **21b** in 80% yield without any evidence of the formation of **22b**.



(4)

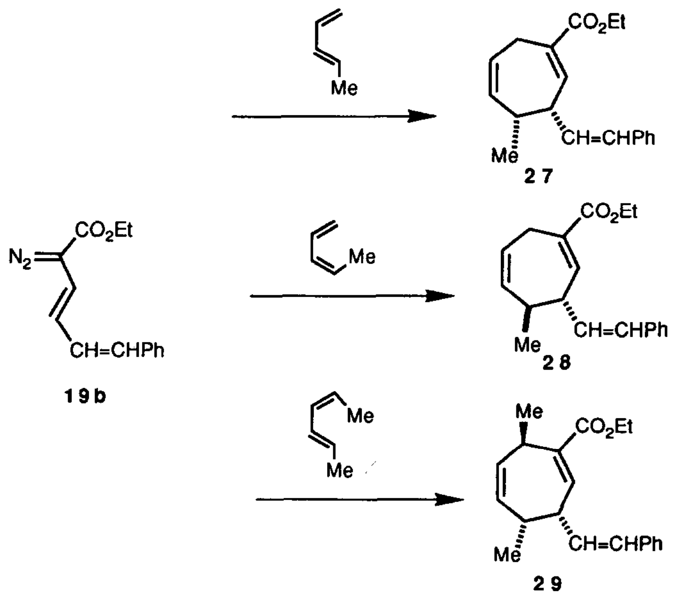
A stereoselective cyclopropanation is extremely advantageous since alternative rearrangements of the *trans*-divinylcyclopropane may occur. For example,[22] rhodium(II) acetate catalyzed decomposition of **19a** in the presence of the diene **23** resulted in the formation of the cycloheptadiene **24** and the *trans*-divinylcyclopropane **25** (4 : 1 ratio), but on attempted purification **25** readily underwent a 1,5-homodienyl rearrangement to the triene **26**.

Scheme 5



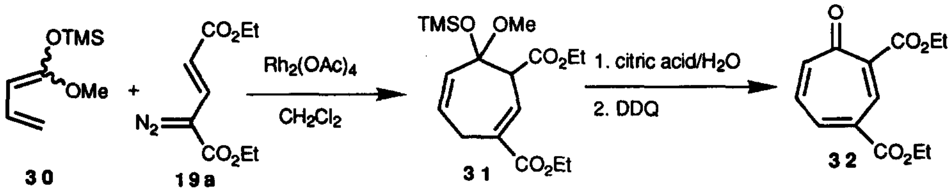
The reaction of **19b** with a series of sterically defined dienes gave a great deal of information about the regioselectivity and stereoselectivity of vinylcarbenoid reactions.[22] In the case of *trans*- and *cis*-1,3-pentadiene, cycloheptadienes **27** (75% yield) and **28** (68% yield) of defined stereochemistry were formed. The cyclopropanation occurs at the most accessible double bond, and the stereochemistry is dictated by the Cope rearrangement. Vinylcarbenoid cyclopropanation is sensitive to steric hindrance on the alkene, and trans alkenes do not lead to effective capture of the carbene. For example, reaction of **19b** with *trans, trans* -2,4-hexadiene failed to generate a cycloheptadiene product, while the reaction with *cis, trans*-2,4-hexadiene proceeded smoothly to generate in 53% yield the cycloheptadiene **29**, whose stereochemistry is consistent with initial cyclopropanation of the cis double bond.

Scheme 6



C. Oxygenated Dienes

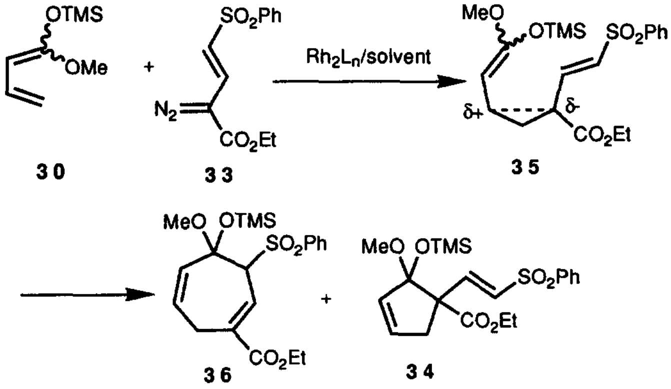
In contrast to the reaction of vinylcarbenoids with alkylated dienes, the reaction of vinylcarbenoids with oxygenated dienes proceeds with excellent stereoselectivity, and offers a very direct approach to tropones and tropolones. This outcome is illustrated in the reaction of **19a** with the diene **30**, as this led to the formation of the cycloheptadiene **31** in 89% yield.[23] Mild hydrolysis of **31** with citric acid followed by DDQ oxidation results in a very short synthesis of the tropone **32** in 92% yield.



(5)

The reaction is applicable to a range of vinylcarbenoids, but an interesting side-reaction was observed in certain systems. For example,[23] rhodium(II) acetate catalyzed decomposition of the vinyldiazomethane **33** in the presence of the diene **30** resulted in predominant formation of the formal 1 + 4 annulation product **34**. The cyclopropanation was considered to proceed in a non-synchronous mode through a dipolar transition state (**35**). As this could allow for the formation of dipolar intermediates if the charges were suitably stabilized, the reaction was repeated with rhodium pivalate/pentane as solvent. By this change in reaction conditions, formation of **34** was completely inhibited and the cycloheptadiene **36** was isolated in 79% yield.

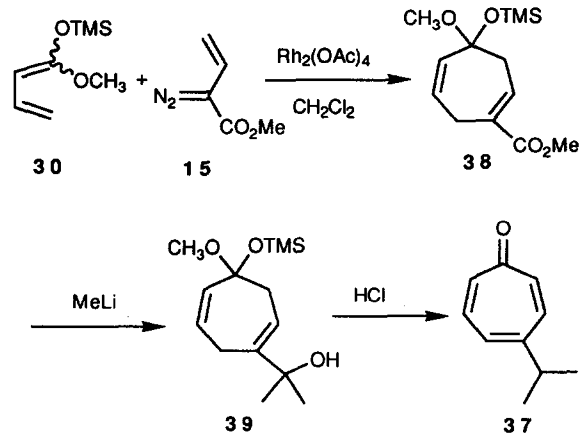
Scheme 7



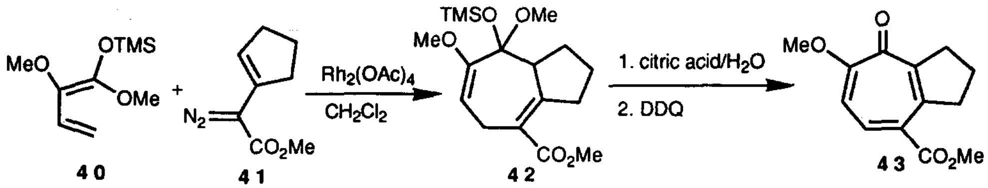
		36,%	34,%
$Rh_2(OAc)_4$	CH_2Cl_2	23	47
$Rh_2(OPiv)_4$	pentane	79	0

An alternative entry to the tropone system would be by elimination of an exocyclic substituent on the cycloheptadiene, and this approach is illustrated in a brief synthesis of nezukone **37**.[23] The cycloheptadiene **38**, generated in 67% yield from the reaction between **15** and **30**, was treated with methyl lithium and the resulting alcohol **39**, on exposure to strong acid, underwent deprotection, dehydration and double bond isomerization to form nezukone **37** in 59% yield.

Scheme 8



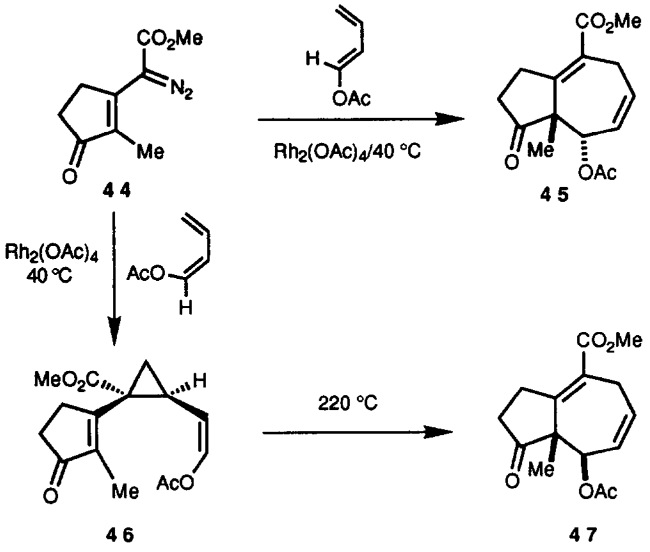
The reaction can be readily extended to more highly oxygenated diene such as **40**, leading into a short synthesis of methyl tropolones.[24] Reaction of the vinyldiazomethane **41** with **40** generated a 68% yield of the fused cycloheptadiene **42**, which was readily converted to the tropolone **43** in 80% yield. Methylation of tropolones usually generates a mixture of regioisomers, and so, a notable feature of this vinylcarbenoid chemistry is that the methyl group is introduced in a defined position.

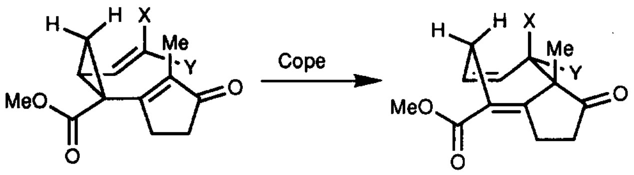


(6)

By use of the more elaborate vinyldiazomethane **44**,[25] the reaction with oxygenated dienes leads to a rapid entry into hydroazulene derivatives. Once again the reaction with a simple diene resulted in only moderate selectivity favoring the *cis*-divinylcyclopropane (2 : 1) but with oxygenated dienes the selectivity was excellent. Highest yields were obtained with silyloxybutadienes, but the reactions with *cis*- and *trans*-1-acetoxy-1,3-butadiene are interesting because they demonstrate the effects of steric hindrance on the Cope rearrangement. The reaction of **44** with *trans*-1-acetoxy-1,3-butadiene led cleanly to the hydroazulene system **45** in 67% yield. In contrast, the product from the reaction of **44** with *cis*-1-acetoxy-1,3-butadiene was the *cis*-divinylcyclopropane **46** (80% yield) and unusually high temperatures (220 °C) were required to convert **46** to the hydroazulene **47**. The effect of alkene geometry on the stereochemistry and the rate of reaction can readily be explained by consideration of the transition state of the Cope rearrangement of divinylcyclopropanes which is believed to involve a boat conformation in which the two vinyl groups point towards the cyclopropane[6] (structure **48**). A trans diene substituent (Y) would generate a trans hydroazulene (**45**), while a cis substituent (X) would lead to a cis product (**47**). Furthermore, a cis substituent (X) would exert a much greater steric crowding[18] than a trans substituent which explains why **46** was isolable.

Scheme 9

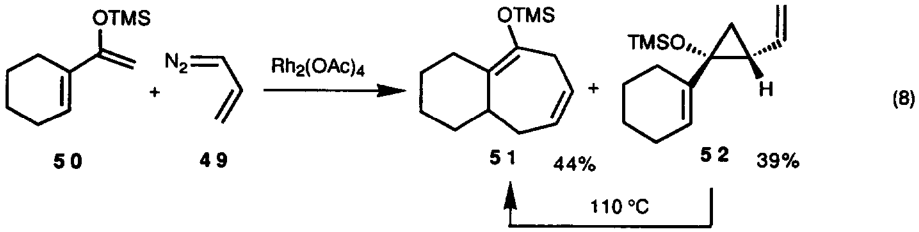




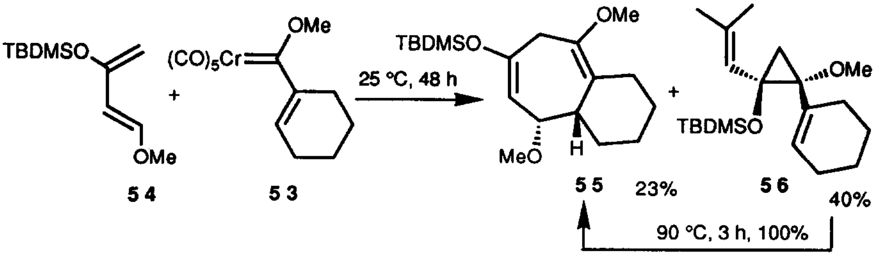
48

(7)

Recently, the reactions of the parent vinyldiazomethane and chlorinated vinyldiazomethanes with oxygenated dienes were reported by de Meijere.[19] Rhodium(II) acetate catalyzed decomposition of **49** in the presence of diene **50** proceeded in good overall yield, but the cyclopropanation showed poor stereoselectivity and a mixture of the cycloheptadiene **51** (44% yield) and *trans*-divinylcyclopropane **52** (39% yield) were generated. A related reaction between the stable chromium vinylcarbene complex **53** and diene **54** has been reported by Wulff.[26] The cycloheptadiene **55** was formed in 23% yield but the major product was the *trans*-divinylcyclopropane **56** (40% yield). In both of these cases, however, respectable yields of cycloheptadienes could be obtained because the *trans*-divinylcyclopropanes underwent an essentially quantitative conversion to cycloheptadienes on heating to 90-110 °C.



(8)

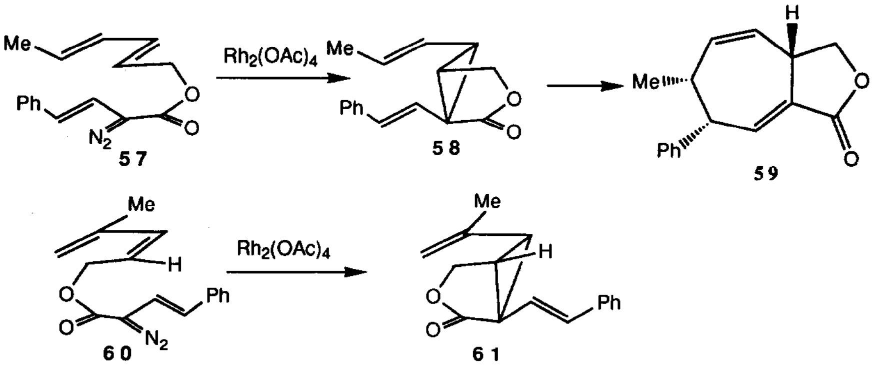


(9)

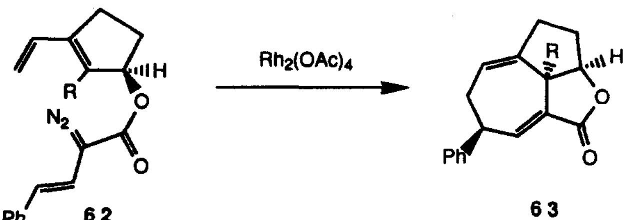
D. Intramolecular Reactions

The formation of isomeric mixtures of cyclopropanes is not an issue in intramolecular reactions between vinylcarbenoids and dienes because the stereochemistry of cyclopropanation is controlled by diene geometry.[27,28] For example,[27] in the case of **57** where the double bond nearest the ester tether is trans, cyclopropanation would be expected to generate a *cis*-divinylcyclopropane **58**, and to lead to the bicyclic system **59**, which was isolated in 76% yield. When the double bond nearest the tether is cis, as is the case with **60**, the *trans*-divinylcyclopropane **61** was formed in 94% yield.

Scheme 10



Other stereogenic centers may be used to control the stereochemistry of the seven-membered ring.[27] Rhodium(II) acetate catalyzed decomposition of **62a** resulted in the formation of the tricyclic system **63a**, whereby the initial cyclopropanation occurred from the same face of the cyclopentene as the ester functionality. The requirement of an open double bond for the initial cyclopropanation was clearly seen in the case of the related methyl derivative **62b**, which failed to form **63b**.

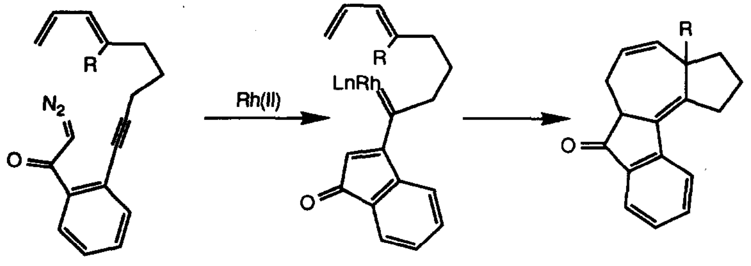


62 **63**

a: R = H; b: R = Me

(10)

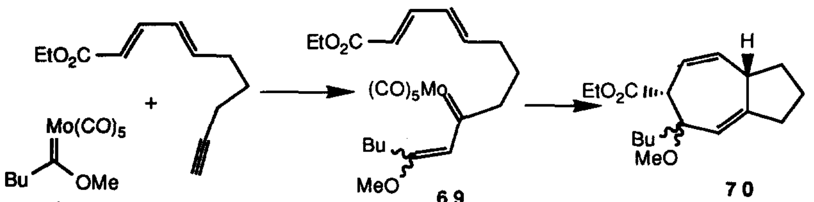
Recently, an alternative strategy has been developed for intramolecular reactions between vinylcarbenoids and dienes. In many instances the reaction of metal-stabilized carbenoids with alkynes can lead to vinylcarbenoids that are then trapped by an appropriately positioned diene to generate cycloheptadienes. Padwa[29] has reported that rhodium(II) mandelate catalyzed decomposition of **64** generated the tetracyclic systems **65** of undefined stereochemistry (50-58% yield), presumably *via* the intermediacy of the vinylcarbenoids **66**. Harvey[30] has reported a similar approach which began with the molybdenum carbene complex **67** and the dienyne **68**, leading to the molybdenum vinylcarbene complex **69**, which then cyclized to a 4.8 : 1 mixture of the hydroazulenes **70** in 87% yield.



64 **66** **65**

R = H, Me

(11)



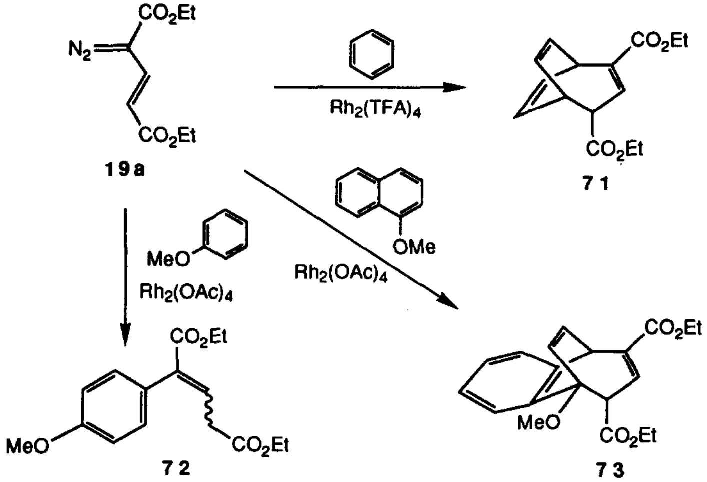
67 **68** **69** **70**

(12)

E. Aromatic Systems

The reaction of vinylcarbenoids is not limited to dienes but may also be extended to a variety of electron rich aromatics.[31,32] Rhodium(II) trifluoroacetate catalyzed decomposition of **19a** in the presence of benzene resulted in a 29% yield of the unstable bicyclo[3.2.2] system **71**.[31] Similar reactions occur with other alkyl benzenes, although the reaction does not appear to be of practical utility because a mixture of unstable isomeric products was formed. In contrast, with methoxybenzenes such as anisole, the alkylation product **72** was produced in 70% yield, whereas with 1-methoxynaphthalene, the 3 + 4 annulation product **73** was cleanly formed. These results may be rationalized by assumption that side reactions due to dipolar intermediates can compete with the cyclopropanation reaction if the aromatic ring is sufficiently electron rich.

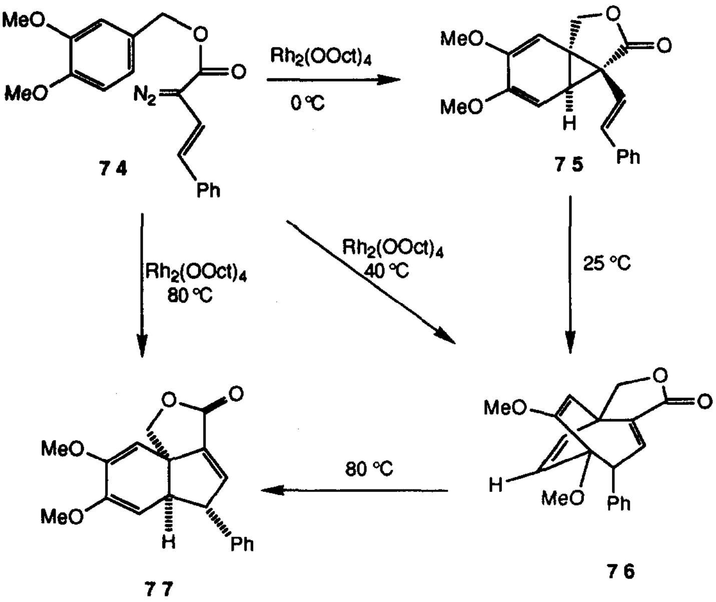
Scheme 11



The intramolecular version of this reaction is interesting because several isomeric structures can be formed and the isolated product is very dependent on the reaction conditions.[31] Rhodium(II) octanoate catalyzed decomposition of **74** at 0 °C, resulted in the formation of the norcaradiene **75** in 48% yield. On standing, in solution, **75** began to undergo a Cope rearrangement to **76** and when the rhodium catalyzed reaction was carried out at 40 °C, the 3 + 4 annulation product **76** was isolated in 72% yield. In solution, **76** was also of limited stability and over several days at room temperature rearrangement to the formal 3 + 2 annulation product **77** occurred, and indeed, if the rhodium catalyzed reaction was carried out at 80 °C, then **77** became the major product (17% isolated yield).

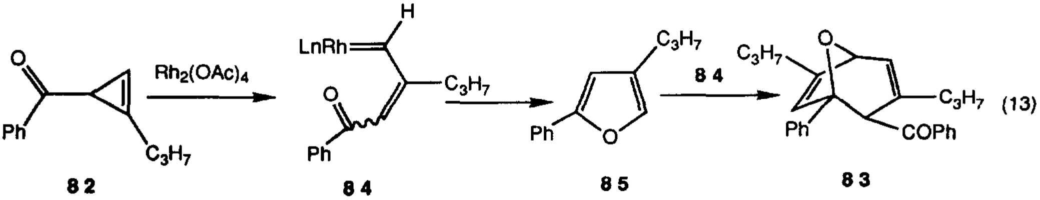
The reaction of vinylcarbenoids with furans can lead to two products, whose distribution is sensitive to the furan substitution pattern.[33,34,35] For example, in the reaction of the vinyldiazomethane **19a** with 2,5-dimethylfuran, the 3 + 4 annulation product **78a** was cleanly formed in 70% yield (Scheme 13). With furan

Scheme 12

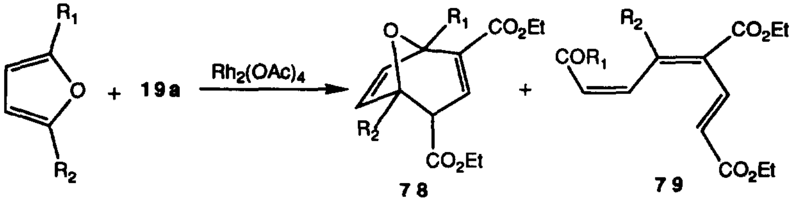


and 2-substituted furans, trienes **79** were also formed, and became the major products as the furans became more electron rich. These results are consistent with a non-synchronous cyclopropanation mechanism leading to two possible dipolar transition states **80** and **81**.[27] In the case of 2,5-disubstituted furans initial bond formation was greatest at the β-position, leading to **80** which proceeded uneventfully to the 3 + 4 annulation products **78**. With furan and 2-substituted furans, however, initial bond formation is greatest at the α-position (structure **81**), and this circumstance can lead either to 3 + 4 annulation products **78**, or to unravelling of the furan ring to trienes **79**.

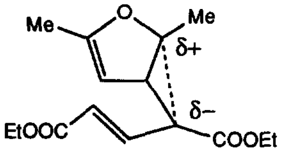
Padwa has recently reported[36] that the rhodium(II) acetate catalyzed ring-opening of the cyclopropene **82** resulted in the formation of the bicyclic system **83** of undefined stereochemistry in 52% yield. The reaction was considered to occur by ring opening of **82** to the vinylcarbenoid **84**. Cyclization of **84** produced the furan **85**, which on reaction with a second equivalent of **84** formed the 3 + 4 annulation product **83**.



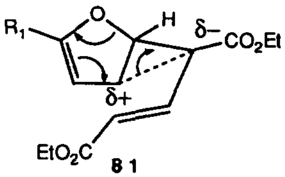
Scheme 13



R_1	R_2	78, % yield	79, % yield
H	H	62	26
Me	H	8	74
OMe	H	0	92
Me	Me	70	0



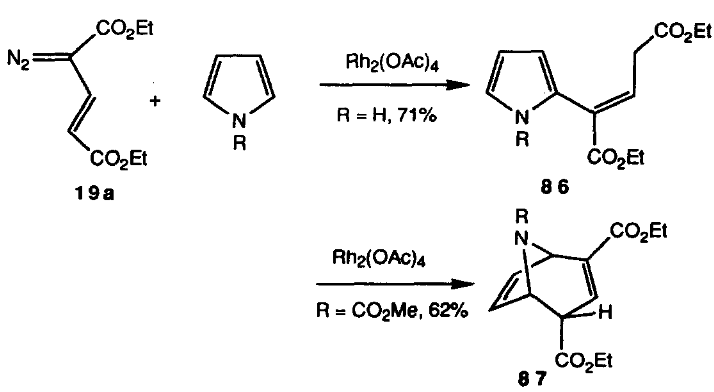
80



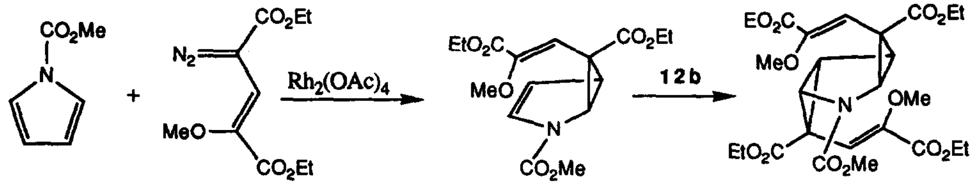
81

The reaction of the vinyldiazomethane **19a** with pyrrole parallels that observed with the methoxybenzenes leading to the alkylation product **86** in 71% yield.[37,38] On change of the substrate to N-(methoxycarbonyl)pyrrole, which decreased the ability of the nitrogen to stabilize a positive charge, a direct entry to the tropane skeleton **87** was achieved in 62% yield.

Scheme 14



An interesting reaction was observed on decomposition of the bulky vinyldiazomethane **12b** in the presence of N-acylated pyrrole.[37] In this case, the initially formed divinylcyclopropane **88** was sterically too constrained to undergo a Cope rearrangement, and instead further reaction of **88** with the vinylcarbenoid occurred to produce the *bis*-cyclopropanated derivative **89** in 33% yield.

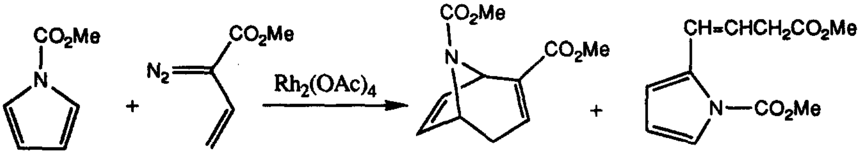


12b **88** **89**

(14)

In the case of vinyldiazomethanes with a single electron withdrawing group, such as **15**, the unsaturated tropane system **90** was not formed cleanly under the traditional reaction conditions of rhodium(II) acetate/dichloromethane. A major side product was the alkylation product **91**, derived from reaction at the vinyl terminus of the vinylcarbeoid.[20] Elimination of the side reaction, however, was readily achieved by use of rhodium(II) hexanoate/hexane, and under these conditions the tropane system **90** was formed in 75% yield.

Scheme 15

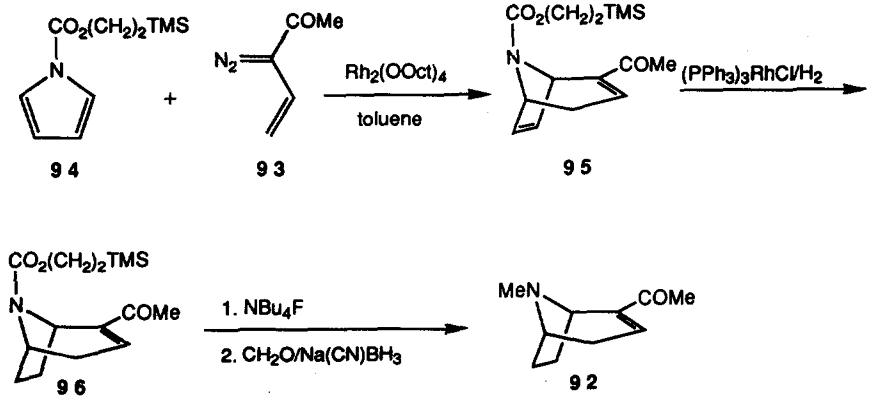


19 **90** **91**

Reaction conditions	ratio **90** : **91**	**90**, % yield
$Rh_2(OAc)_4/CH_2Cl_2$	55 : 45	35
$Rh_2(OHex)_4$/hexane	>95 : 5	75

The potential of this chemistry was highlighted by a short synthesis of ferruginine (**92**).[20] Rhodium(II) octanoate catalyzed decomposition of the vinyldiazomethane **93** in the presence of the protected pyrrole **94** generated the tropane derivative **95** in 73% yield. Selective hydrogenation of **95** produced **96**, which on deprotection and N-methylation was readily converted to **92** (69% overall yield from **95**).

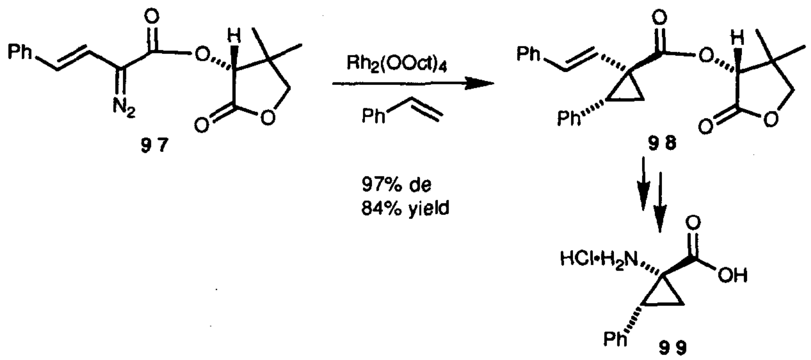
Scheme 16



IV. Asymmetric Reactions of Vinylcarbenoids

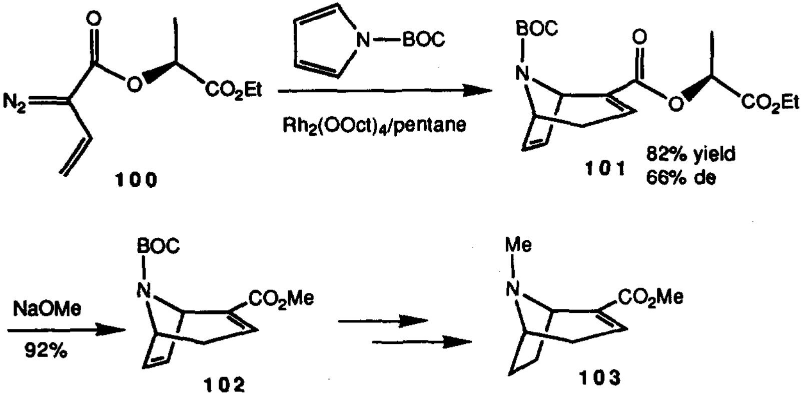
A particularly exciting feature of the tandem cyclopropanation/Cope rearrangement is that an asymmetric synthesis of cycloheptadienes would be possible if the initial cyclopropanation were carried out in an enantioselective mode. Unfortunately, some of the excellent chiral copper and rhodium amide catalysts[39] that have been developed for asymmetric cyclopropanations with diazoacetates were ineffective at decomposition of vinyldiazomethanes.[40] The catalysts were rather sluggish, and rearrangement of the vinyldiazomethanes to 3H-pyrazoles occurred in preference to metal-catalyzed decomposition to vinylcarbenoids. An alternative strategy was undertaken by use of chiral auxiliaries on the vinylcarbenoid, and α-hydroxy esters and particularly (R)-pantolactone were found to lead to excellent levels of stereoselectivity.[41] This approach is illustrated in the rhodium(II) octanoate catalyzed cyclopropanation of styrene by the vinyldiazomethane **97**, which proceeded to form the vinylcyclopropane **98** in 97% diastereomeric excess. Entry into systems with the opposite absolute stereochemistry to **98** was achieved by use of (S)-methyl lactate as the chiral auxiliary. Further conversion of **98** to the cyclopropane amino acid **99** was achieved by oxidative cleavage of the vinyl group followed by a Curtius rearrangement.

Scheme 17



Extension of this approach to the reaction of vinylcarbenoids with dienes would allow the tandem cyclopropanation/Cope rearrangement to be achieved in an asymmetric mode. Decomposition of the vinyldiazomethane **100**, which contains an (S)-ethyl lactate chiral auxiliary, resulted in the formation of the tropane derivative **101** in 66% diastereomeric excess (82% yield).[42] The chiral auxiliary in **101** was readily removed by methanolysis to generate the methyl ester **102**, which was then readily converted to enriched (-)-anhydroecgonine methyl ester (**103**, 43% overall yield from **101**) by a scheme parallel to that used to prepare ferruginine.

Scheme 18



V. Conclusion

The tandem cyclopropanation/Cope rearrangement offers a very general entry to highly functionalized seven-membered rings. A particularly impressive feature of this method is that excellent control of both relative and absolute stereochemistry is possible. The remarkable stereoselectivity of vinylcarbenoid cyclopropanations greatly simplifies the synthesis of *cis*-divinylcyclopropanes and opens up numerous opportunities for the future utilization of *cis*-divinylcyclopropanes in the synthesis of complex natural products.

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