Pergamon

Tetrahedron 58 (2002) 379–471

TETRAHEDRON

Tetrahedron report number 595

Recent advances in synthetic applications of azadienes

S. Jayakumar, M. P. S. Ishar and Mohinder P. Mahajan*

Department of Pharmaceutical Sciences, Guru Nanak Dev University, Amritsar, Punjab 143005, India

Received 28 September 2001

Contents

1. Introduction 379
2. 1-Azabuta-1,3-dienes 382
   2.1. Synthesis of four-membered rings 382
   2.2. Synthesis of five-membered rings 384
      2.2.1. Addition of carbenes to 1-azabuta-1,3-dienes 384
      2.2.2. 1,3-Dipolar cycloadditions to 1-azabuta-1,3-dienes 384
      2.2.3. Miscellaneous reactions for the synthesis of five-membered rings 385
   2.3. Synthesis of six-membered rings 385
      2.3.1. [4+2] Cycloadditions of electron-rich 1-azabuta-1,3-dienes 388
      2.3.2. [4+2] Cycloadditions of electronically-neutral 1-azabuta-1,3-dienes 395
      2.3.3. [4+2] Cycloadditions of electron-deficient 1-azabuta-1,3-dienes 396
   2.4. Miscellaneous reactions of 1-azabuta-1,3-dienes 403
3. 2-Azabuta-1,3-dienes 408
   3.1. Synthesis of 2-azabuta-1,3-dienes 408
      3.1.1. Involving aza-Wittig reactions between *N*-vinylic phoshazenes and carbonyl compounds 408
      3.1.2. Involving imines and related substrates 414
      3.1.3. Miscellaneous reactions 424
   3.2. Cycloaddition reactions of 2-azabuta-1,3-dienes 424
      3.2.1. Synthesis of five-membered rings 424
      3.2.2. Synthesis of six-membered rings 427
         3.2.2.1. Cycloadditions involving alkenes and alkynes 427
         3.2.2.2. Cycloadditions involving enamines 435
         3.2.2.3. Cycloadditions involving carbonyl compounds 436
         3.2.2.4. Cycloadditions involving other hetero dienophiles 443
   3.3. Cycloaddition involving Fischer carbene complexes 449
   3.4. Miscellaneous reactions of 2-azabuta-1,3-dienes 449
4. 1,3-Diazabuta-1,3-dienes 449
   4.1. Synthesis of five-membered rings 450
   4.2. Synthesis of six-membered rings 451
   4.3. Mechanism of 1,3-diazabuta-1,3-diene-ketenes cycloaddition reactions 459

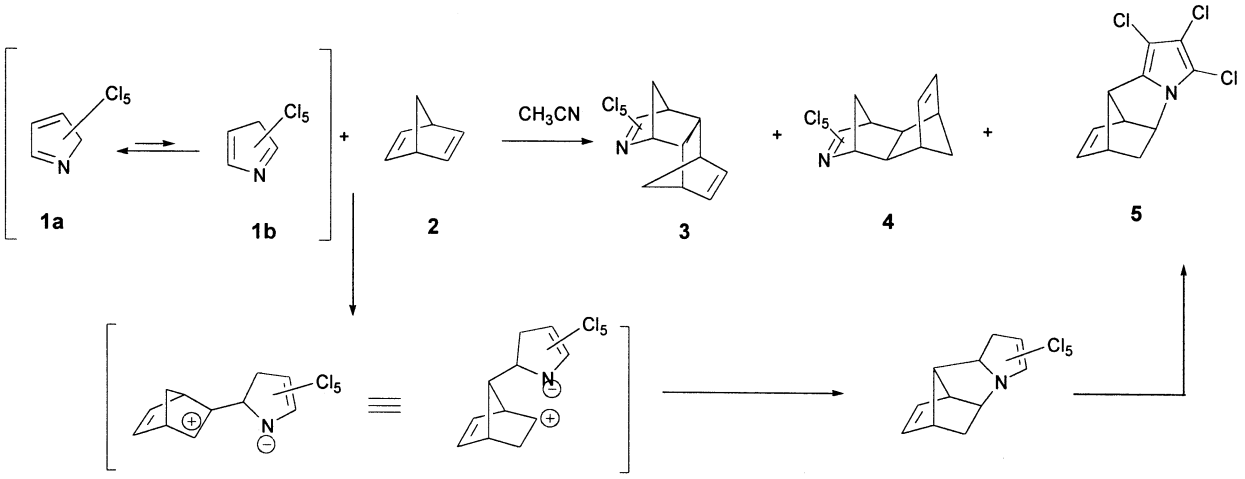
1. Introduction

Nitrogen-containing compounds are widely distributed in nature and include many biologically important molecules. The synthesis of nitrogen-containing heterocycles has attracted considerable attention due largely to their importance as building blocks for many therapeutically useful materials and the wide range of potential biological activity of both the

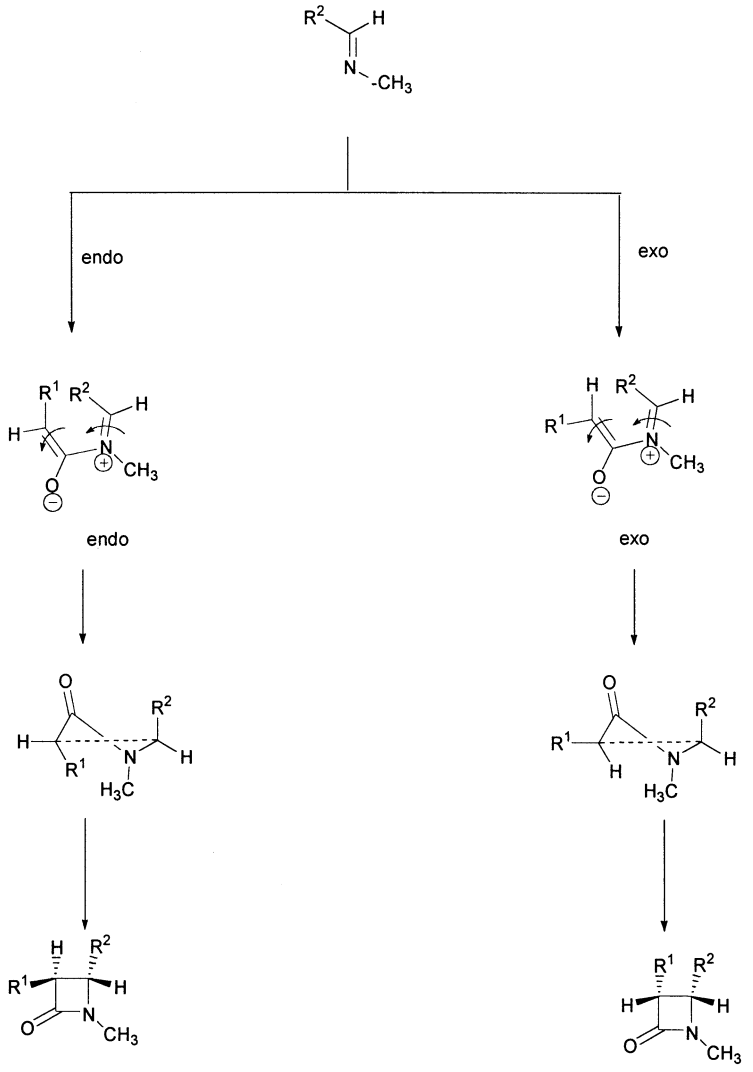
* Corresponding author. Tel.: +91-183-258802-09 ext. 3320; fax: +91-183-258819-20; e-mail: mohinderpmahajan@angelfire.com

0040–4020/02/$ - see front matter
PII: S0040-4020(01)01050-X

synthetic and naturally occurring derivatives. The hetero Diels–Alder methodology employing azadienes represents a straightforward and an efficient approach to nitrogen-containing six-membered heterocycles.[1] Extensive studies have been carried out on this [4+2] cycloaddition process and the rapid rigorous development in this area has led to several reviews highlighting the utility of azadienes as readily available templates in the synthesis of novel

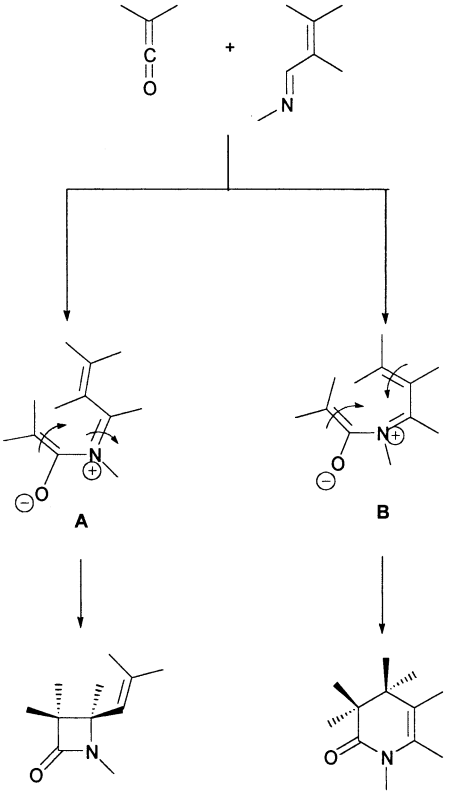


Scheme 1.

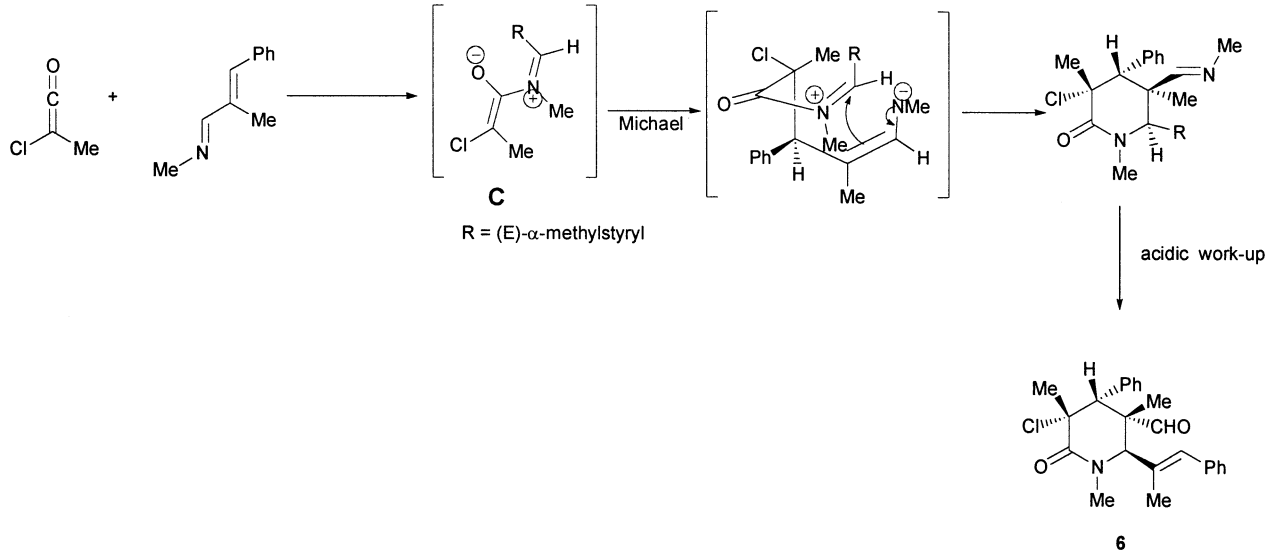


Scheme 2.

heterocycles and complex natural products.[1] This report concerns the chemistry of aza- and 1,3-diazabuta-1,3-dienes and covers the literature published during the last decade including a few references of the late 1980s not covered by the earlier reviews. Other diazadienes have been much less studied and their chemistry is mostly covered by the reviews cited in Ref. 1. Some additional leading papers dealing with the use of 1,2-diazadienes and 1,4-diazadienes have, however been published which are not included in this report. The cycloaddition reactions of heterocyclic azadienes have been reviewed[1i] earlier and are also not included herein. In the past two decades, several papers have additionally appeared on the organometallic complexes derived from azadienes and their utility in organic synthesis. These are considered to be outside the scope of the present report and will be reviewed separately.



Scheme 3.



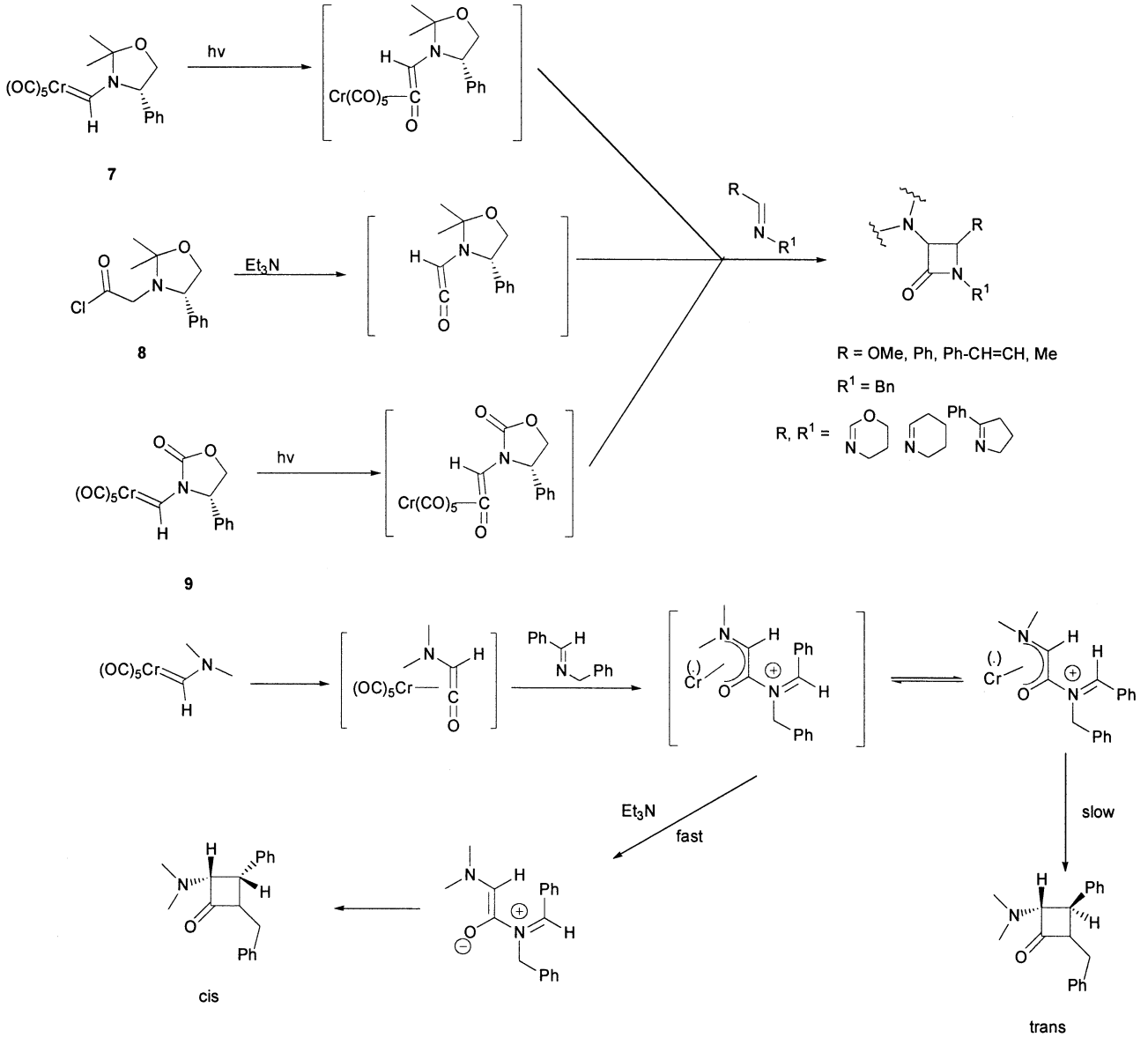
Scheme 4.

2. 1-Azabuta-1,3-dienes

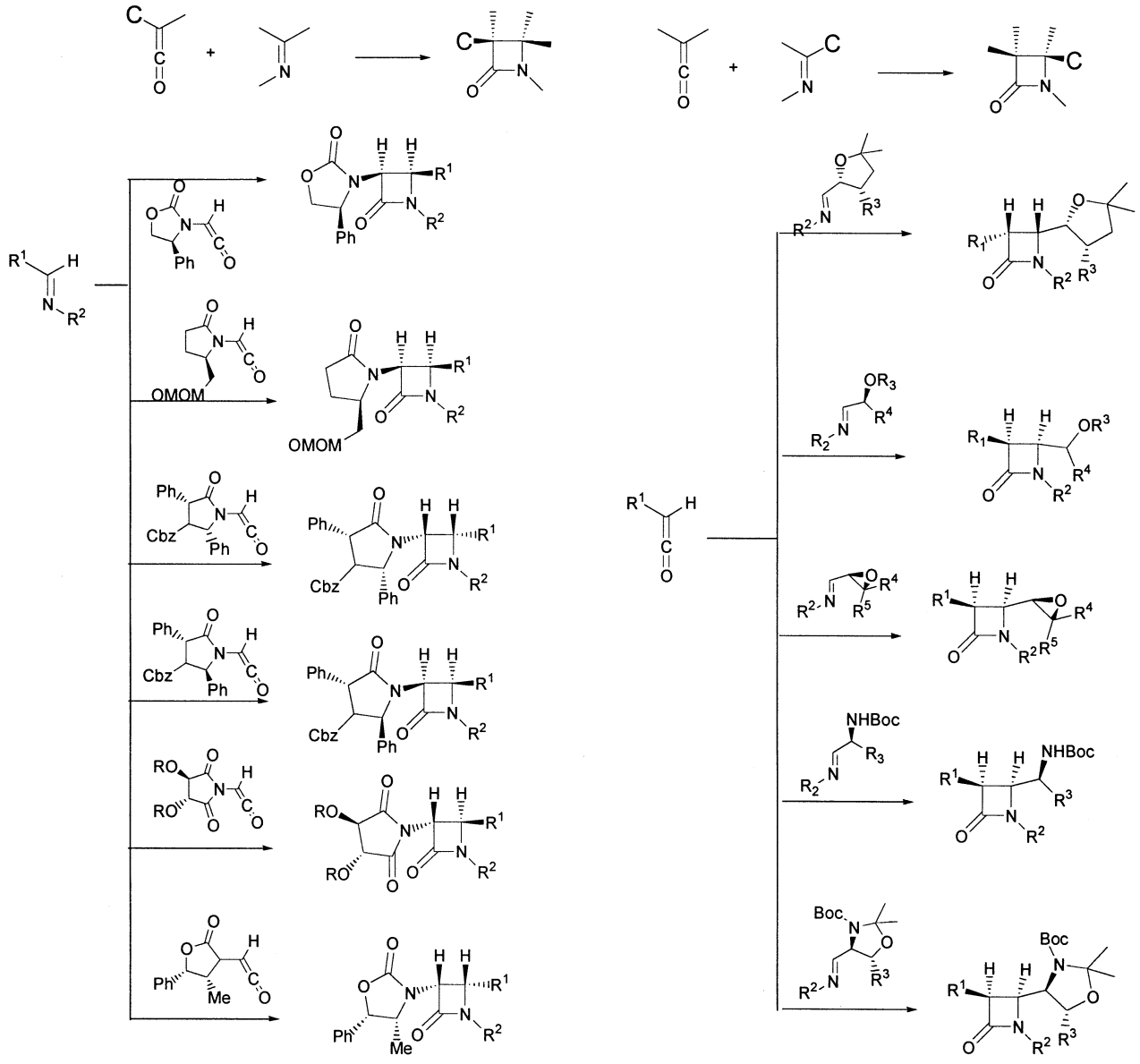
2.1. Synthesis of four-membered rings

1-Azadienes are involved in the synthesis of four-membered rings only through their [2+2] cycloaddition reactions. The major advances in the last decade in [2+2] cycloadditions of 1-azadienes have been in the area of mechanistic and theoretical investigations. Only the C=N double bond of the azadienes is involved in these [2+2] cycloadditions and, where the other addend is a ketene, the reaction is known as the Staudinger reaction;[2] most of the developed mechanistic or theoretical formalisms for these reactions, and [2+2] cycloadditions of imines, in general, remaining the same. Except for the example in which a C=N of a cyclic-1-azadiene (**1a**,**1b**) is involved in a [2+2] addition with norbornadiene (**2**) to yield polycyclic amine **5**, in addition to **3** and **4** (Scheme 1),[3] most of the investigations relate to [2+2] additions with ketenes.

For a rationalisation of the mechanism of the Staudinger reaction, approximate self-consistent-field molecular orbital theory has been employed by Cossio et al.,[4] and these findings corroborated the stepwise mechanism proposed earlier,[5] involving a zwitterionic intermediate (Scheme 2). After formation of the N_1–C_2 β-lactam bond (azadiene/imine nitrogen-central ketene carbon), the second step is the electrocyclic ring closure; the transition state for the electrocyclic ring closure has a significant diradical character. The reported stereoselectivities of the reaction are rationalised in terms of the approach of the addends (*endo*- or *exo*-) and the torquoelectronic effects operating in the transition state.



Scheme 5.

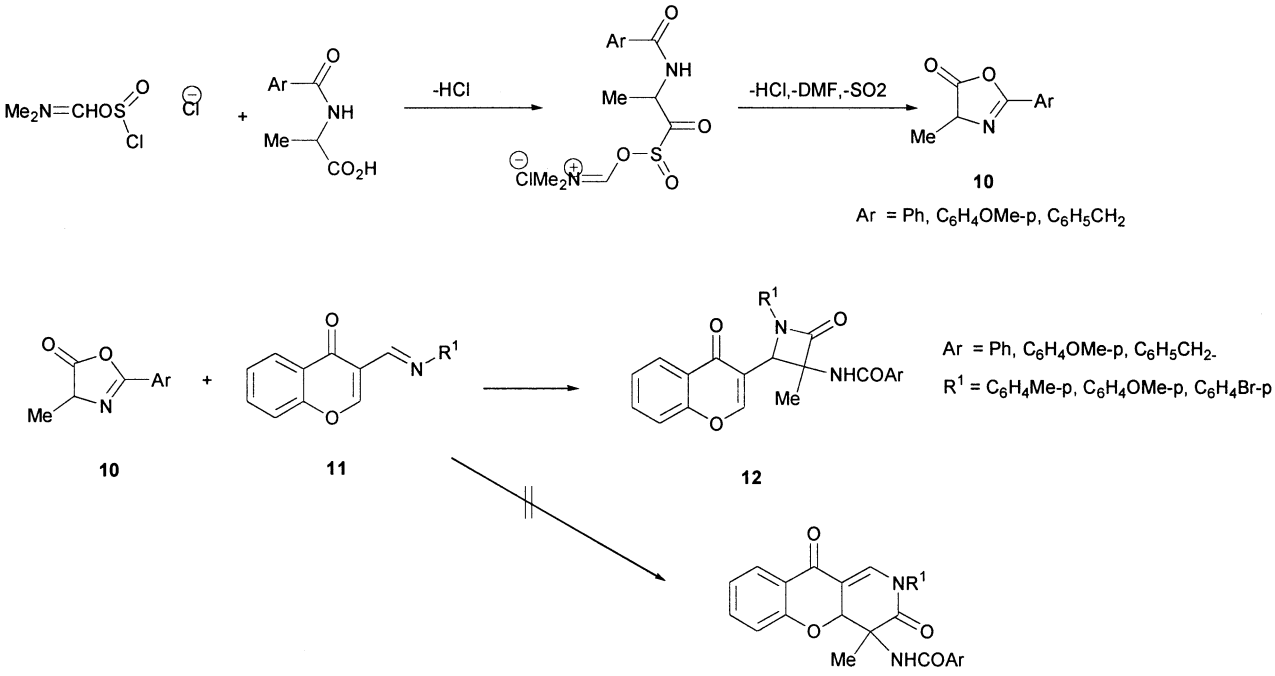


Scheme 6. For precise nature of substituents see citations under Ref. 8.

Recently, Cossio et al.,[6] based on experimental and theoretical investigations, have proposed a detailed account of solvent and substituent effects on the observed periselectivity for the Staudinger reaction between ketenes and 1-azadienes. Although a number of theoretical approaches including semiempirical Hamiltonian AM1, 3 X 3CI-HE/AM1 and CASSCF(2,2)/6-31G* have been evaluated, MP2/6-31G* with incorporation of solvent effects is reported to provide the results which are in best agreement with the experimental observations. On the basis of these investigations[6] it has been concluded that: (i) the Staudinger reaction between ketene and an azadiene leads to preferential formation of [2+2] cycloadducts because solvent, vibrational, thermal and entropic factors favour a conrotatory ring closure in the zwitterionic intermediate (**A**, Scheme 3); (ii) monosubstituted activated ketenes undergo exclusive [2+2] addition on account of the lower energy of the conrotatory ring closure with donor 3-substituents in an outward position and the vinylic moiety at position 4-being inward; (iii) low to high periselectivity is exhibited by disubstituted ketenes and a preference is shown for [4+2] addition due to the low sensitivity of disrotatory ring closure on account of torquoelectronic effects; and (iv) the periselectivity of the reaction is very sensitive to the β-substituent on azadienes due to steric demands of a disrotatory transition state (**B**, Scheme 3).

Formation of another product (**6**) of the reaction between an azadiene and ketene has been rationalised in terms of a zwitterionic intermediate (**C**, Scheme 4).

An earlier investigation[7] comparing the Staudinger reactions of ketenes generated by two different methods, i.e. by photolysis of chromium–carbene complexes (**7**,**9**) and by the reaction of acid chlorides (**8**) with triethylamine (Scheme 5), had led to the



Scheme 7.

establishment of similar mechanistic proposals. The inclusion of triethylamine in the reactions of carbene complexes gave results that closely paralleled the results of ketenes generated from acid chlorides. For ketenes bearing chiral auxiliaries, the difference in stereoselectivities have been attributed to the difference in the nature of the chiral auxiliaries.

The effect on stereoselectivity through chiral control in the Staudinger reaction has also been evaluated both experimentally and theoretically by other workers and the observations have been rationalised in terms of torquoelectronic effects.[8] Based on some involved theoretical investigations, the conrotatory ring closure leading to β-lactams has been shown to be the stereochemistry controlling step and the results were found to be in agreement with the experimental findings involving a number of chiral imines or chiral ketenes (Scheme 6).

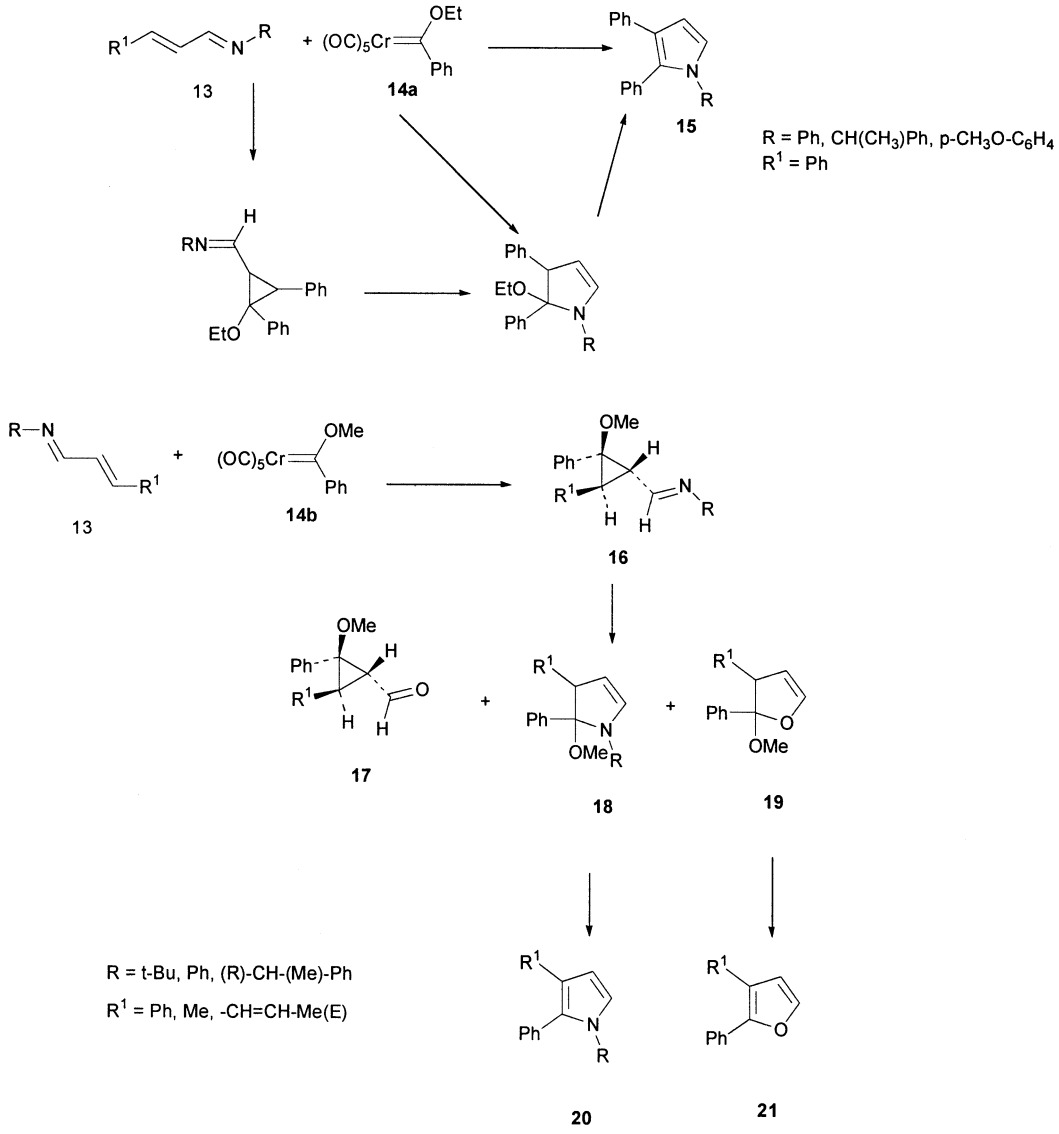
A synthetically useful extension of this reaction has been realised by the use of in situ generated oxazolones (**10**) as *N*-acylaminoketene equivalents, the reaction of which with 3-(*N*-aryliminomethyl)-chromone (**11**) has been utilised to obtain 4-chromone-linked 3-(*N*-acylamino)azetidin-2-ones (**12**, Scheme 7).[9]

2.2. Synthesis of five-membered rings

2.2.1. Addition of carbenes to 1-azabuta-1,3-dienes. Danks and Velo-Rego have reported[10] the thermolysis of the chromium carbene complex (**14**) in the presence of 1-aryl/arylalkyl-4-phenyl-1-aza-1,3-dienes (**13**) leading to the formation of 1,2,3-trisubstituted pyrroles (**15**, Scheme 8).[10] The reaction was postulated to proceed either through initial cyclopropanation followed by rearrangement or by direct [4+1] annulation. Investigations on the same reaction by Barluenga et al.,[11] however, who isolated the cyclopropanated azadienes (**16**), clearly established that the initial reaction is cyclopropanation, followed by tranformation to a mixture of cyclopropane aldehyde (**17**) and five-membered heterocycles (**18**–**21**, Scheme 8). On the contrary, the reactions of arylchlorocarbenes (**23**) generated from arylchlorodiazirines (**22**) with 1-aza-1,3-dienes are reported to proceed through [4+1] annulation (**24**) leading to similarly substituted pyrroles [11b] (**25**, Scheme 9).

2.2.2. 1,3-Dipolar cycloadditions to 1-azabuta-1,3-dienes. The reactions of a number of *N*-arylsulfonyl-4-phenyl-1-aza-1,3-butadienes (**26**) with 2,4-diphenyl-4,5-dihydro-1,3-oxazol-5-one (**27**), which is well known to add both as a nucleophile and a 1,3-dipole, have been investigated.[12] The reaction is reported to be temperature dependent, at room temperature only kinetically controlled nucleophilic addition affords **28**, whereas at 110°C thermodynamically favoured 1,3-dipolar addition leads to various products (**29**–**32**, Scheme 10). The mode of addition of azalactones to *N*-arylsulfonyl-substituted azadienes (**26**) is reported to be markedly different from additions to the corresponding *N*-alkyl/aryl substituted azadienes, in which the formation of β-lactams through [2+2] additions has been observed.[12c,d]

Addition of nitrile oxides (**33**) and munchnones (**40**) to 5-vinyl-isothiazole-1,1-dioxides (**34**) has been reported to occur exclusively at the vinyl group and the cycloadducts (**35**–**38**,**41**) obtained have been found to undergo pyrolytic transformation



Scheme 8.

to the α,β-unsaturated nitriles (**39**,**43**), through the isoxazole (**38**)—or pyrrole-isothiazole-1,1-dioxide (**42**) intermediate[13] (Scheme 11).

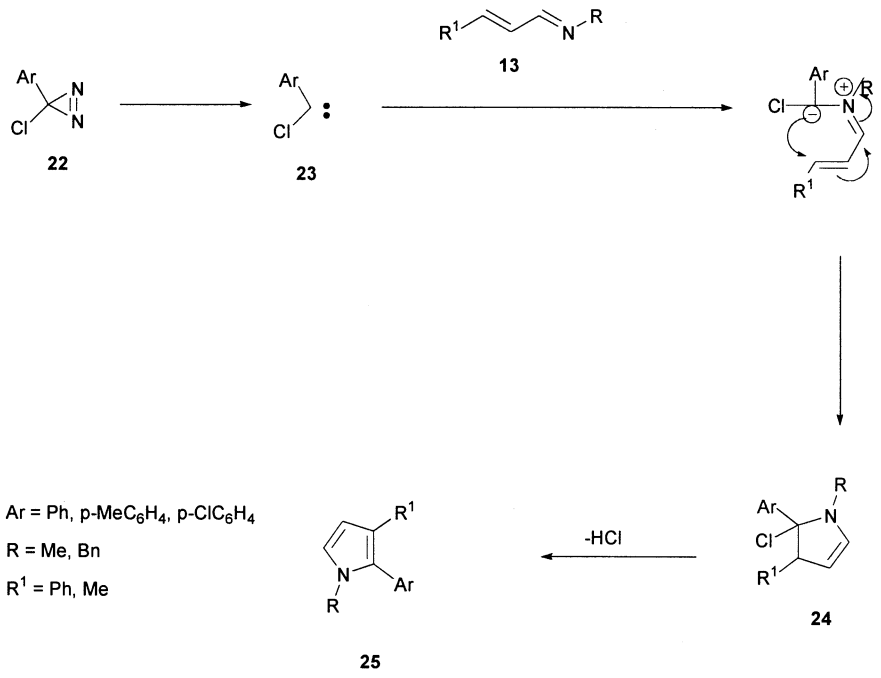
Substituted diazines (**44**) have been found to function preferably as azadienes in inverse electron demand Diels–Alder reactions with electron-rich dienophiles. When reacted with benzonitrile oxide (**45**), these azadienes undergo 1,3-dipolar cycloadditions exclusively across the C=N bond; both mono- and di-nitrile oxide addition products (**46**–**53**) have been isolated[14] (Scheme 12).

Recently, stepwise addition of the all-carbon 1,3-dipole (**55**), derived from catalytic interaction of triphenylphosphine with the allenic ester (**54**), to *N*-(*p*-toluenesulphonyl)-cinnamylideneaniline (**26**) has been reported to selectively involve only the C=N bond; the pyrrolidine (**56**) obtained have been dehydrogenated with DDQ to the substituted pyrroles (**57**, Scheme 13).[15]

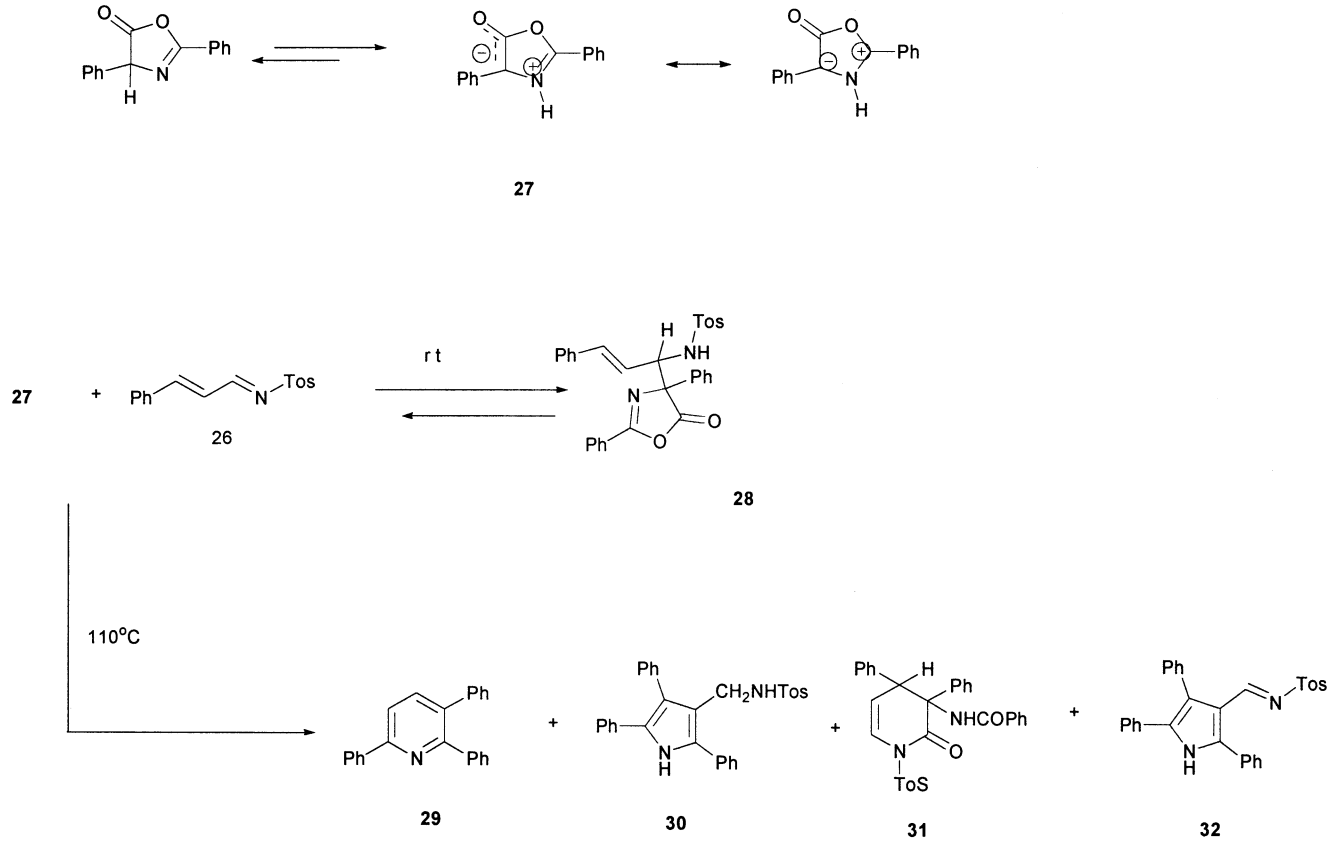
2.2.3. Miscellaneous reactions for the synthesis of five-membered rings. Sequential insertion of CO and ethylene into the C–H bonds of 1-azadienes under $Ru_3(CO)_{12}$ catalysis followed by intramolecular cyclocondensation has been reported to afford 2,3-dihydropyrrol-3-ones (**58**) in moderate to excellent yields (Scheme 14).[16]

2.3. Synthesis of six-membered rings

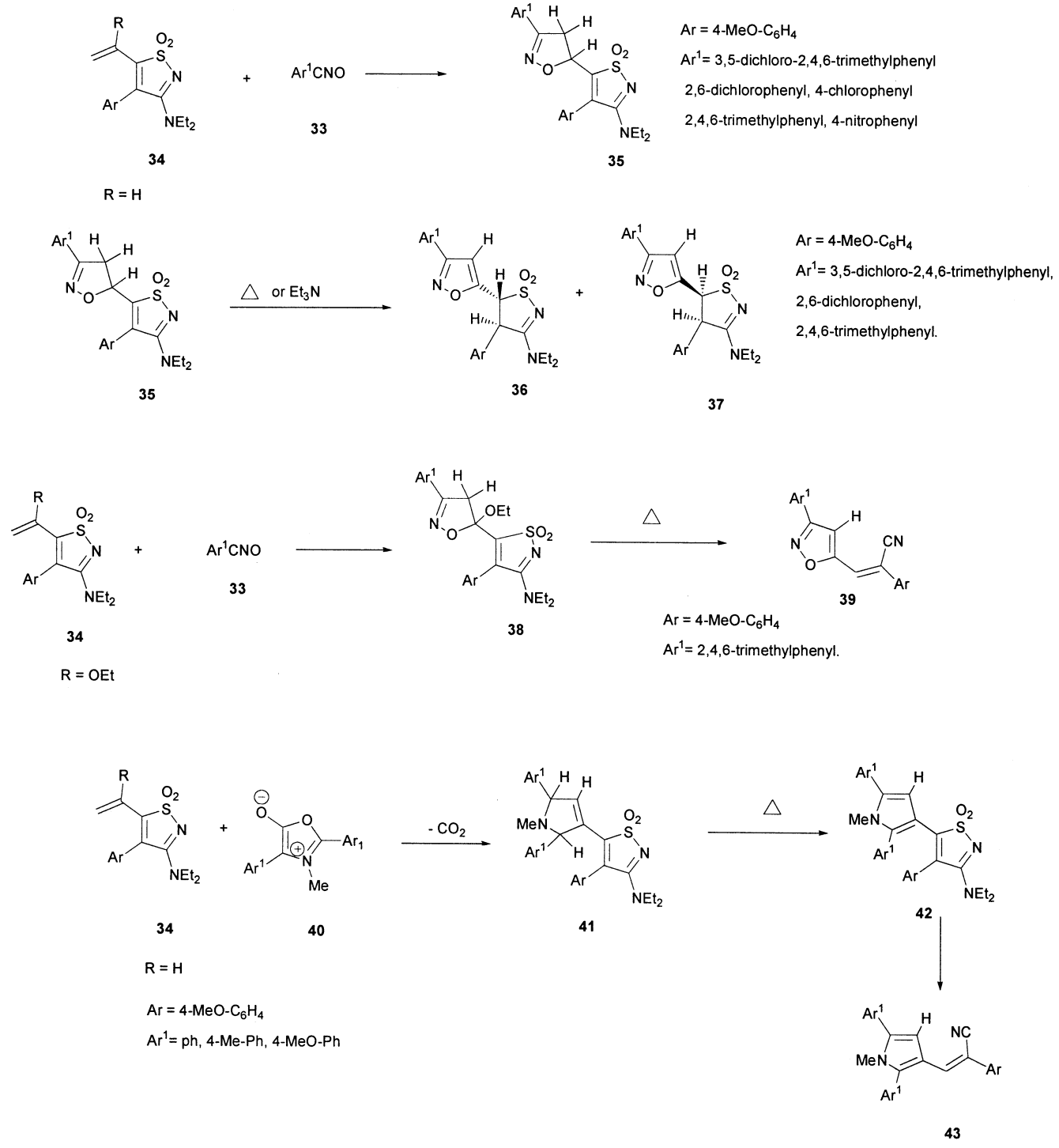
The utilisation of azadienes in the synthesis of six-membered rings is through their involvement in hetero-Diels–Alder reactions, which may be intramolecular or intermolecular. The electron-rich 1-azabutadienes are well known to undergo



Scheme 9.



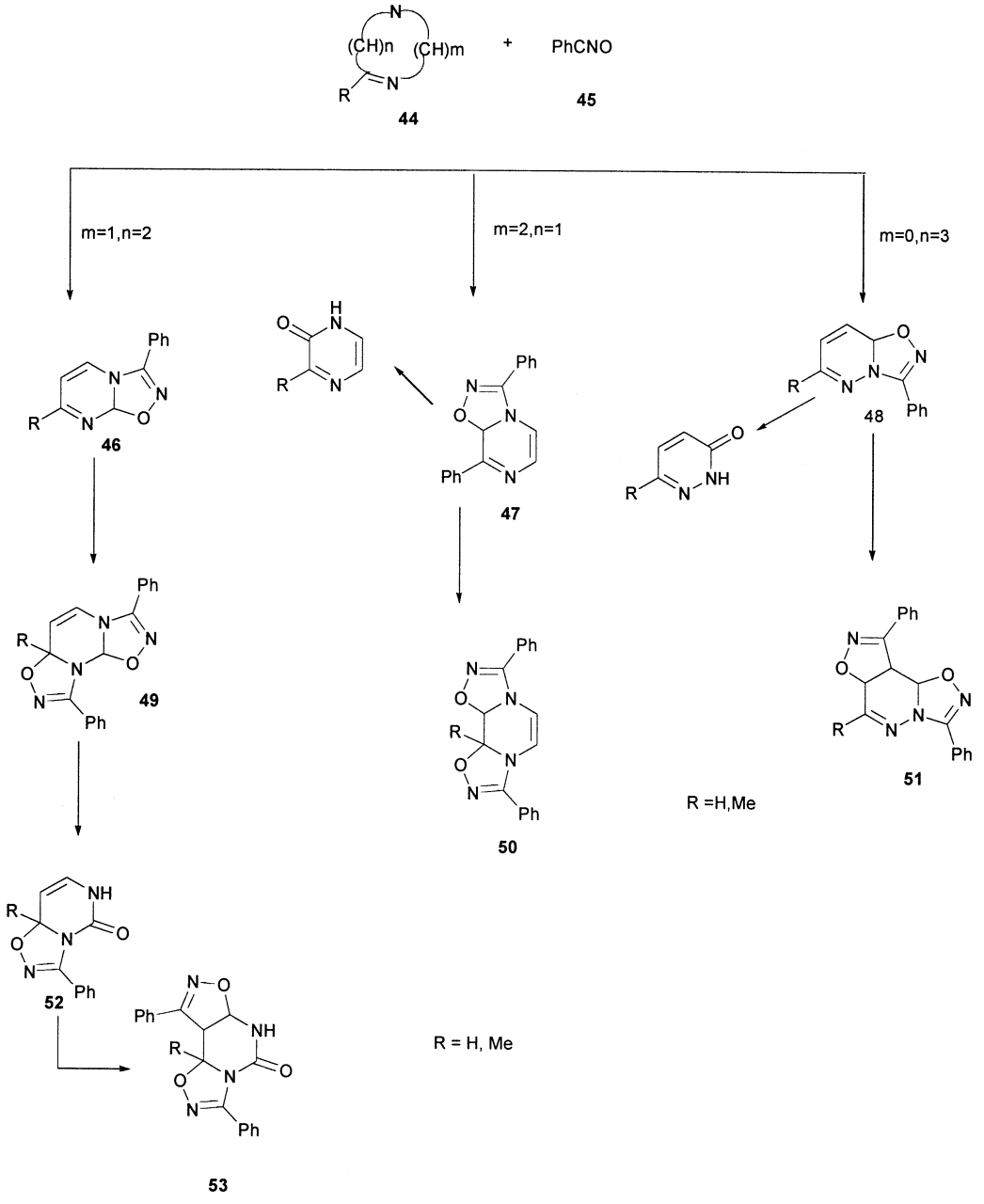
Scheme 10.


Ar = 4-MeO-C6H4
Ar1= 3,5-dichloro-2,4,6-trimethylphenyl
2,6-dichlorophenyl, 4-chlorophenyl
2,4,6-trimethylphenyl, 4-nitrophenyl
34
R = H
33
35
or Et3N
36
37
Ar = 4-MeO-C6H4
Ar1= 3,5-dichloro-2,4,6-trimethylphenyl,
2,6-dichlorophenyl,
2,4,6-trimethylphenyl.
34
R = OEt
38
39
Ar = 4-MeO-C6H4
Ar1= 2,4,6-trimethylphenyl.
34
R = H
40
- CO2
41
42
43
Ar = 4-MeO-C6H4
Ar1= ph, 4-Me-Ph, 4-MeO-Ph

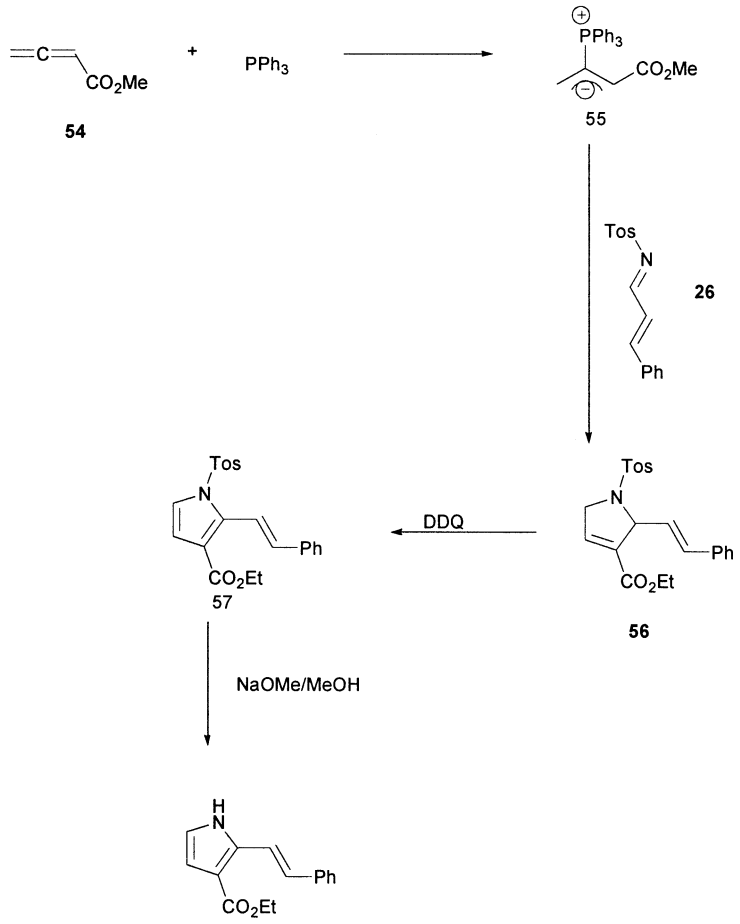
Scheme 11.

facile HOMO-diene controlled [4+2] cycloadditions, but the 4π-participation of the relatively electron-deficient 1-azadienes is reported[1] to suffer from low conversion, competitive [2+2] addition, and low diene reactivity due to an unfavourable *s-cis*/*s-trans* equilibrium, tautomerisation of γ-alkyl-substituted 1-azadienes to enamines precluding [4+2] addition and instability of endocyclic enamine products. In the last decade numerous successful efforts have been made to ensure the 4π-participation of electron-deficient 1-azabutadienes in LUMO-diene controlled hetero-Diels–Alder reactions. At the same time the hetero-Diels–Alder reactions of electron-rich 1-azabutadienes have been extensively exploited for the synthesis of a variety of molecules. A third class of 1-azabutadienes, electron-neutral azadienes, undergo cycloadditions with both electron-rich and electron-deficient addends. Because of the differing reactivity patterns displayed by the different types of 1-azabutadienes, it was considered worthwhile to discuss their [4+2] cycloadditions in separate sections.

2.3.1. [4+2] Cycloadditions of electron-rich 1-azabuta-1,3-dienes. The most prominent amongst the electron-rich 1-azabutadienes are hydrazones of the type (**D**) and the *N*-unsubstituted-4-amino-1-azabutadienes (**E**). The former are derived mainly by condensation of α,β-unsaturated carbonyl systems with *N*,*N*-dialkylhydrazines. The hydrazones of α,β-unsaturated ketones (**60**,**62**) however, have also been obtained efficiently by Wittig reaction of the phosphoranes (**59**), generated in situ

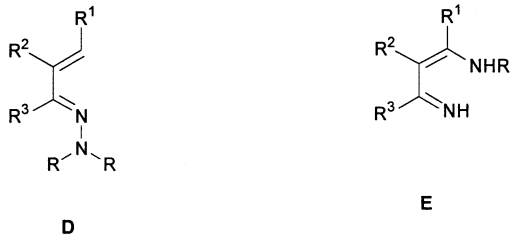


Scheme 12.

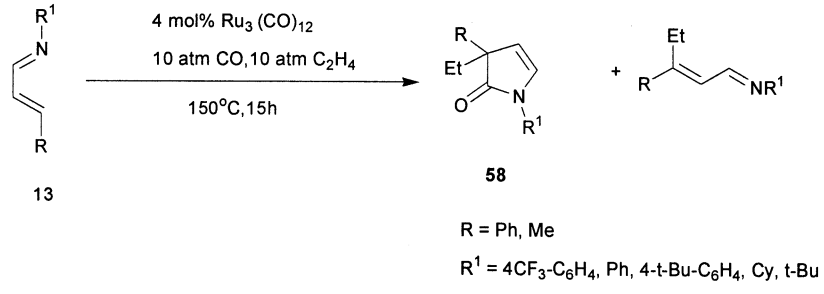


Scheme 13.

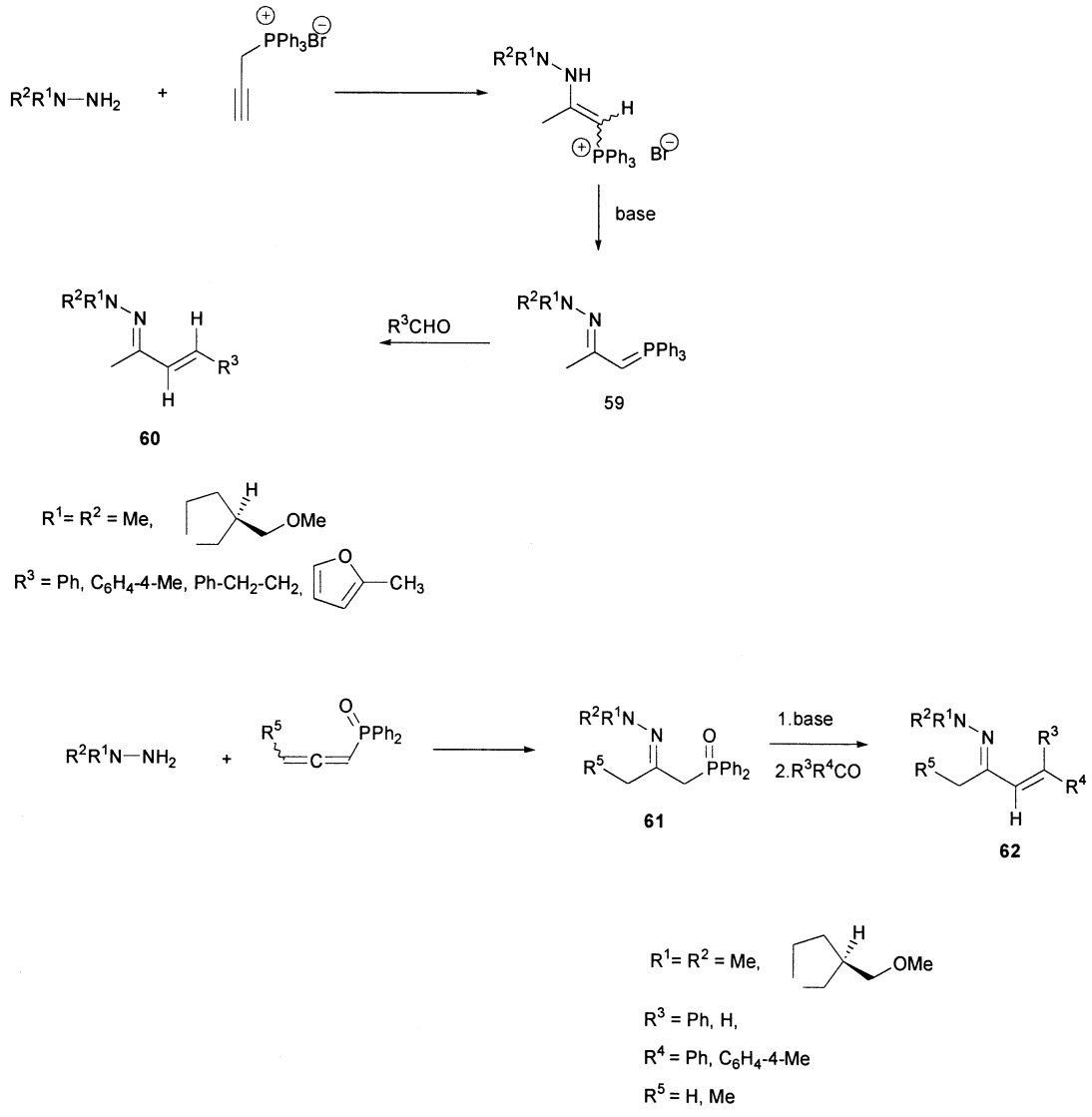
from β-hydrazinophosphonium salts, with aldehydes and olefination of phosphine oxides (**61**) derived from hydrazines (Scheme 15).[17]



The hydrazones (**63**) derived from acrolein, methacrolein and crotonaldehyde have been reported to undergo hetero-Diels–Alder reactions with a number of halogenated quinones (**64**,**66**) to afford, after aromatisation, quinilinequinones[18] (**65**,**67**–**69**).



Scheme 14.



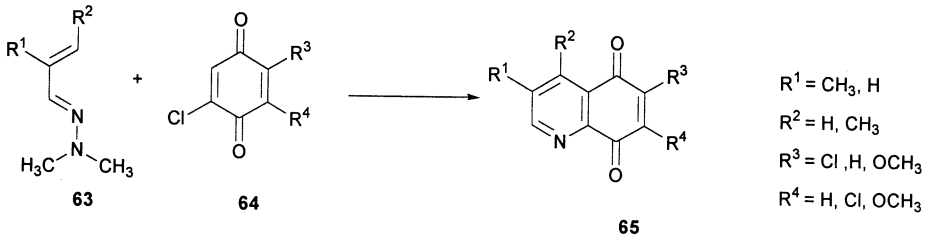
Scheme 15.

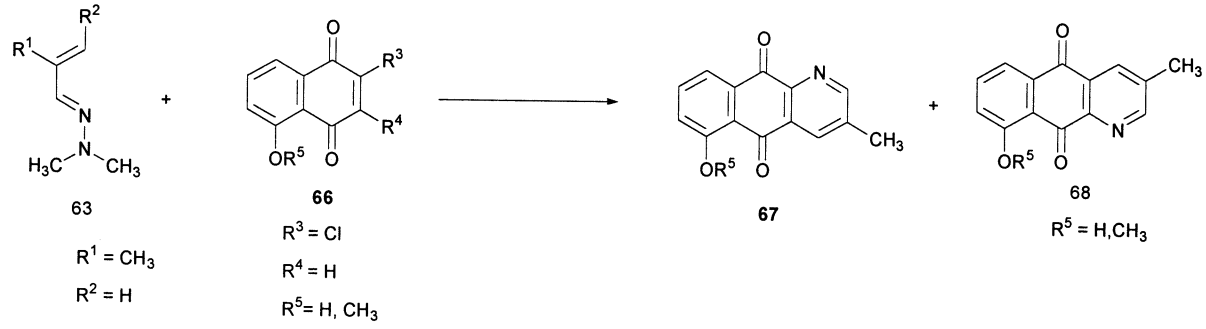
The regiochemistry of addition is reported to be controlled by the substituent on the quinonones (**64**,**66**). By carrying out the reactions of the hydrazones with halogenated quinones (**70**), Perez et al.[18b] have utilised the above reaction to obtain 1,8-diazaanthraquinones (**71**, Scheme 16).

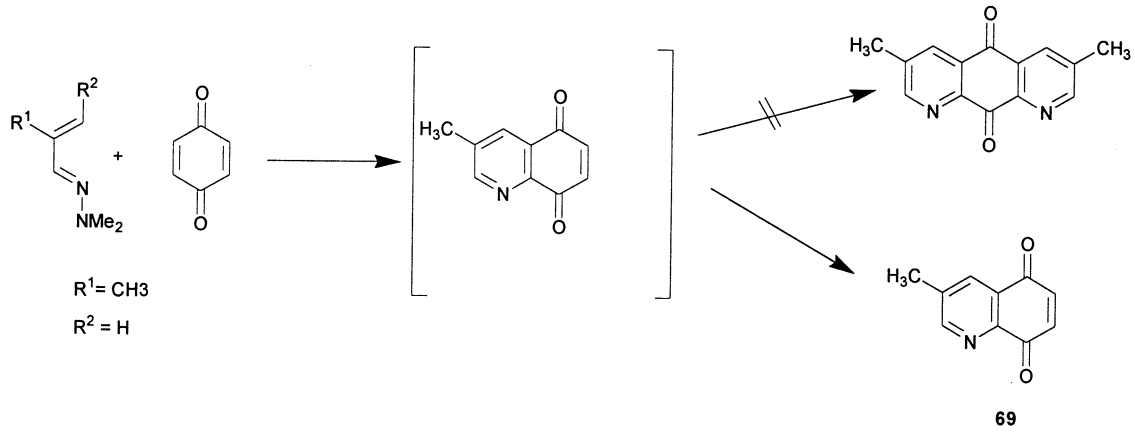
Although regioselective addition of crotonaldehyde *N*,*N*-dimethylhydrazone (**63**) to substituted naphthaquinones (**72**,**74**) has been utilised earlier to obtain 4,5- and 4,8-disubstituted azaanthraquinones (**73**),[19a] the periselectivity of additions involving 2-ethoxybut-2-enal-*N*,*N*-dimethyl-hydrazone and a number of quinoline-5,8-diones (**77**), and 1,4-naphthoquinones (**72**,**74**) has been shown to be dependent on the reaction medium with [4+2] addition leading to **73**, **79** and **80** occurring only in a neutral medium. In an acidic medium (CF_3COOH or BF_3), a [3+2] annulation leads to furoquinolines (**78**)/naphthofurans (**75**,**76**).[19] The latter mode of addition has been exploited[20] to obtain a series of furo[2,3-*f*]quinoline-4,5-diones (**81**), furo[2,3-*g*]quinoline-4,5-diones (**82**) and furo[3,2-*g*]quinoline-4,9-diones (**83**, Scheme 17).

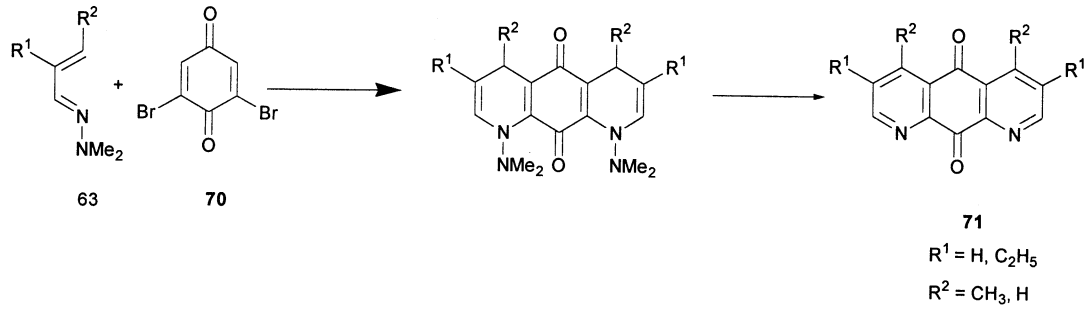
The regiospecific hetero-Diels–Alder reaction of hydrazones with carbazolequinones (**84**), 2- and 3-bromo-carbazolequinones (**87**,**89**) has also been successfully utilised to obtain pyrido[2,3-*b*]- and pyrido[3,2-*b*]carbazol-5,11-diones (**85**,**86**,**88**,**90**, Scheme 18).[21]

Avendano et al. have utilised[22] the addition of 1-azadienes (**63**) with 2,5,8(1*H*)-quinolinetriones (**91**,**95**) for the synthesis of diazanthracenes (**92**–**94**,**97**) related to the antifolate antibiotic diazaquinomycin A. To overcome the formation of by-products arising from conjugate dimethylamine addition to the quinone moiety and competing [3+2] annulated adduct (**96**), it has been reported[22] that the corresponding 1-acylamino-1-azadienes (**98**,**99**) although less reactive, give comparable or better yields of

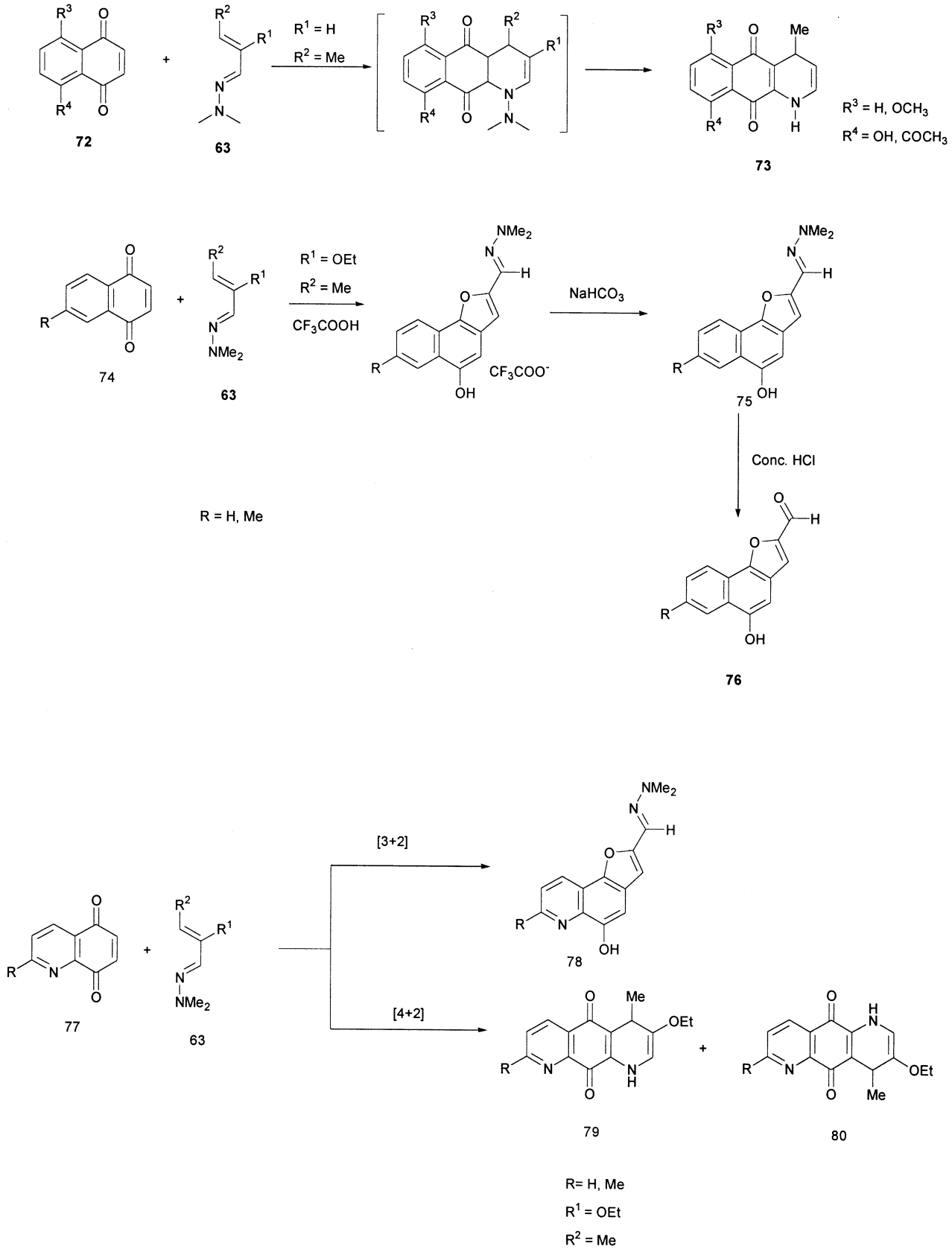

63
64
65
R1 = CH3, H
R2 = H, CH3
R3 = Cl ,H, OCH3
R4 = H, Cl, OCH3


63
R1 = CH3
R2 = H
66
R3 = Cl
R4 = H
R5= H, CH3
67
68
R5 = H,CH3

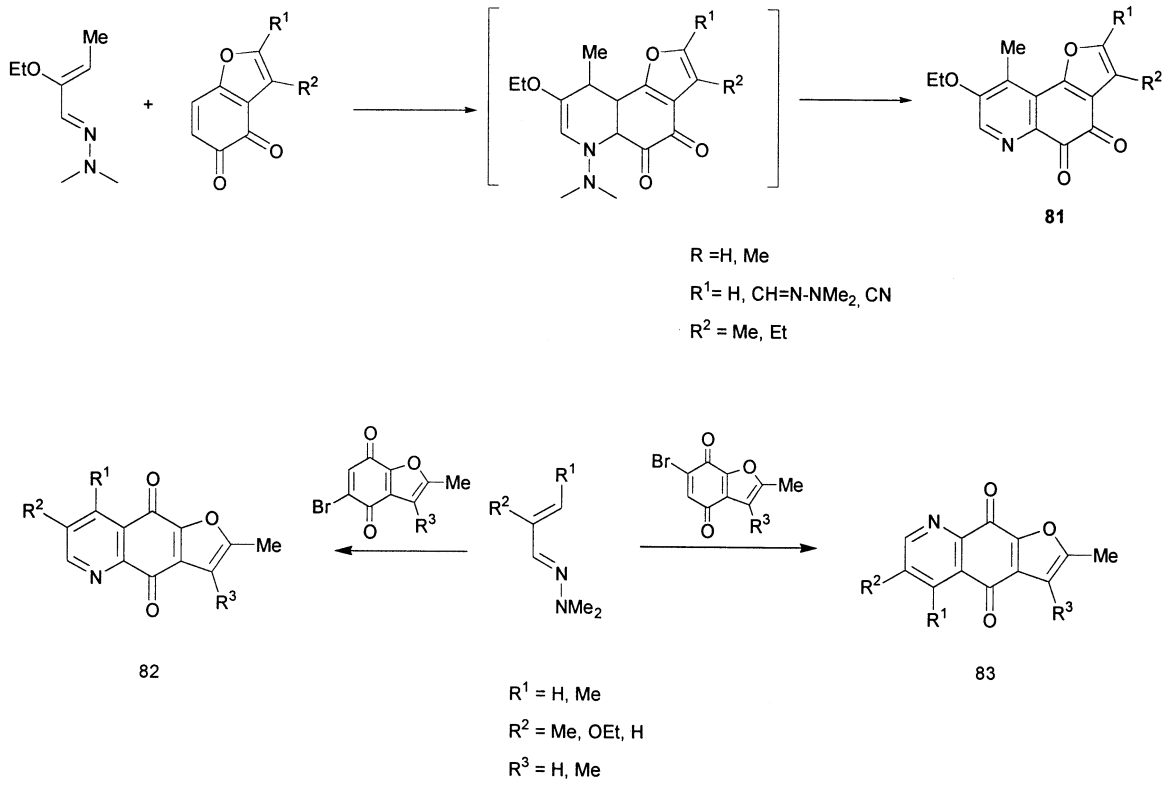

R1= CH3
R2 = H
69


63
70
71
R1 = H, C2H5
R2 = CH3, H

Scheme 16.


R1 = H
R2 = Me
R3 = H, OCH3
R4 = OH, COCH3
72
63
73
74
R1 = OEt
R2 = Me
CF3COOH
NaHCO3
CF3COO-
75
Conc. HCl
R = H, Me
76
77
[3+2]
[4+2]
78
79
80
R= H, Me
R1 = OEt
R2 = Me

Scheme 17.



Scheme 17 (*continued*)

the desired [4+2] adducts (**92**,**94**,**100**). A thorough examination[23] of the reactions of 1-azadienes with a variety of 4-substituted-2,5,8(1*H*)-quinolinetriones (**91**) has revealed that the periselectivity, [4+2]/[3+2], addition, is related to the nature of the 3-substituent. A highly electron-withdrawing 3-substituent favours the [3+2] annulation, which is also aided by the polarity of the solvent (Scheme 19).

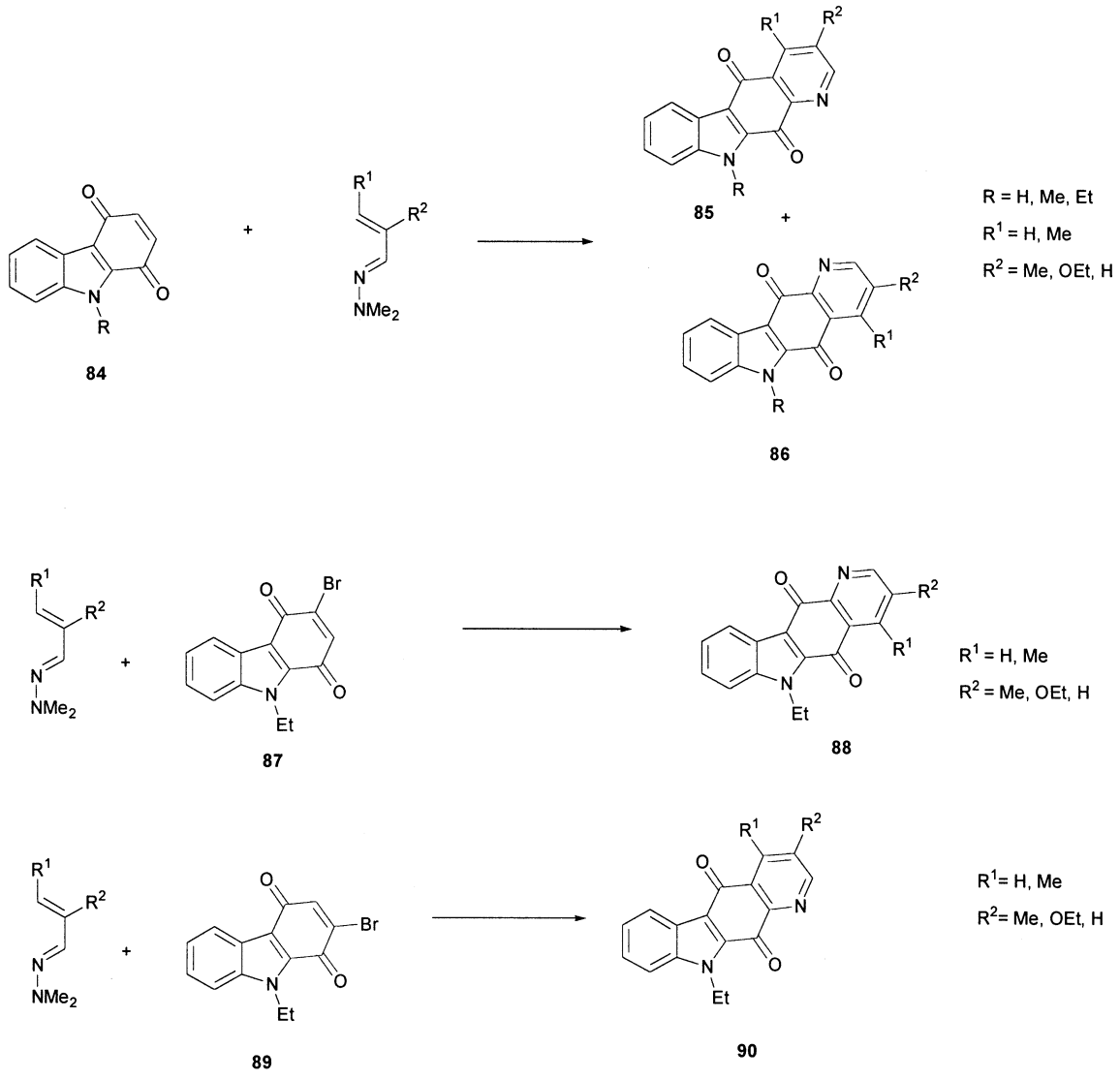
The 4(1*H*)-quinolinone moiety is an essential component of not only the well-known quinolinone antibacterials but also of many marine natural products with broad spectrum antitumor activity. Avenado et al. have utilised[24a] regioselective hetero-Diels–Alder reactions of crotonaldehyde and methacrolein *N*,*N*-dimethylhydrazones (**63**) with a number of quinilinetriones (**101**,**102**) to obtain 1,8-diazaanthracene-2,9,10-triones (**104**,**105**) and 5,8-dihydroxy-quinoline-4-one (**103**,**106**). These workers have also shown that, when the above reactions are carried out in the presence of silica gel, the diazaanthracenes are obtained in excellent yields and the formation of side products is suppressed.[24b] The proposed mechanism for the formation of these products is briefly sketched in Scheme 20.

Avendano et al. have utilised[25] the regiospecific [4+2] cycloadditions of acrolein and crotonaldehyde *N*,*N*-dimethyl-hydrazones (**63**) with 5,6,7,8-tetrahydro-1,4-acridinequinones (**107**), the latter being readily obtained by the reaction of cyclohexanone with 2-amino-3,6-dimethoxybenzaldehydes/acetophenones, with the aim of developing an easy synthetic route to polycyclic aromatic alkaloids of marine origin, possessing a pyrido[*k*]acridine skeleton (**108**–**111**). The regiochemistry of addition could be inverted by the introduction of a bromine atom at C-7 in the acridinequinones (Scheme 21).

Avendano et al. have also reported the application of non-conventional conditions such as ultrasonic irradiation to enhance the yields of cycloadducts under milder reaction conditions with minimisation of side products[26] (Scheme 22).

Prompted by the cytotoxicity of naturally occurring angular tetracyclic quinones, Valderrama et al. have utilised[27] the hetero-Diels–Alder reactions of 1-cyclohexencarboxaldehyde dimethylhydrazone (**112**) with juglone and bromojuglone to 8-hydroxy-1,2,3,4-tetrahydrobenzo[*b*]phenanthridine-7,12-dione (**113**) in 55% yield; **113** has been successfully dehydrogenated to 8-hydroxybenz[*b*]phenanthridine-7,12-dione (**114**, Scheme 23).

The reaction of 1-benzoyl/ethoxycarbonylindole-3-carboxyaldehyde with dimethylhydrazine has been utilised to obtain the hydrazone (**115**) as an indole-based electron-rich 1-azadiene, which has been reacted with DEAD and NMM as dienophiles to obtain [*a*]annellated-γ-carbolines (**116**,**117**, Scheme 24).[28]



Scheme 18.

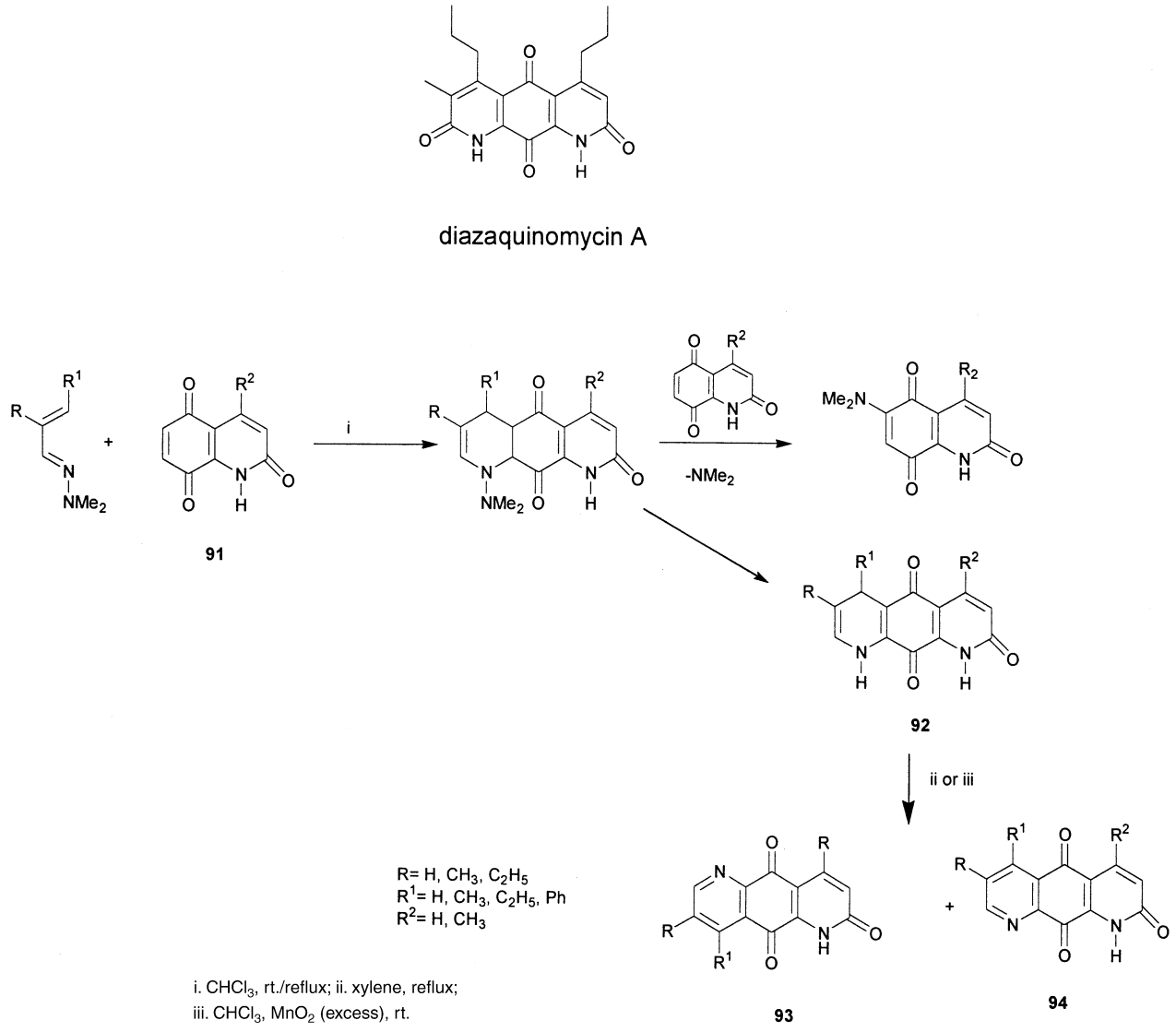
In order to further improve the reactivity of α,β-unsaturated *N*,*N*-dimethylhydrazones as electron-rich dienes, Echavarren et al. have introduced[29] 4-trialkylstannylated/silylated-α,β-unsaturated *N*,*N*-dimethylhydrazones (**118**), obtained by the reaction of *N*,*N*-dimethylhydrazine with β-stannylated/silylated enals, the latter being synthesised by hydrostannylation of propargyl alcohols followed by oxidation with $KMnO_4$. The stannylated/silylated hydrazones (**118**) have been shown to be more efficient in reactions with electron-deficient dienophiles such as quinones and the adducts obtained have been oxidised to obtain benzoquinolinetriones (Scheme 25).

N,*N*-Dimethylhydrazones (**119**,**120**) of α,β-unsaturated carbonyl systems possessing electron-withdrawing substituents (nitrile or methoxycarbonyl) have been shown[30] to be unreactive towards electron-rich dienophiles but they undergo facile hetero-Diels–Alder reactions with electron-deficient dienophiles; the addition responds to the catalytic influence of lithium trifluoromethanesulfonimide (Scheme 26).

Behforouz et al.[31] have prepared novel 1-(*t*-butyldimethylsiloxy)-1-aza-1,3-butadienes (**121**) which have been shown to be highly reactive towards a number of halogenoquinones/quinones and other dienophiles (Scheme 27).

An intramolecular hetero-Diels–Alder reaction involving α,β-unsaturated *N*,*N*-dimethylhydrazones (**122**,**124**,**126**) has been utilised[32] to obtain 2,2′-bipyridines (**123**,**125**,**127**, Scheme 28).

The reaction of 1-dimethylamino-4-(*o*-aminophenyl)-1-aza-1,3-butadiene (**128**) with naphthoquinones and quinolines has been proposed[33] as a route to pyridoacridine alkaloids of marine origin such as ascididemins and amphimedine. The initial addition however, is followed by an intramolecular rearrangement leading to benzo-/pyrido-[*b*]acridine-6,11-dione (Scheme 29).



Scheme 18 (*continued*)

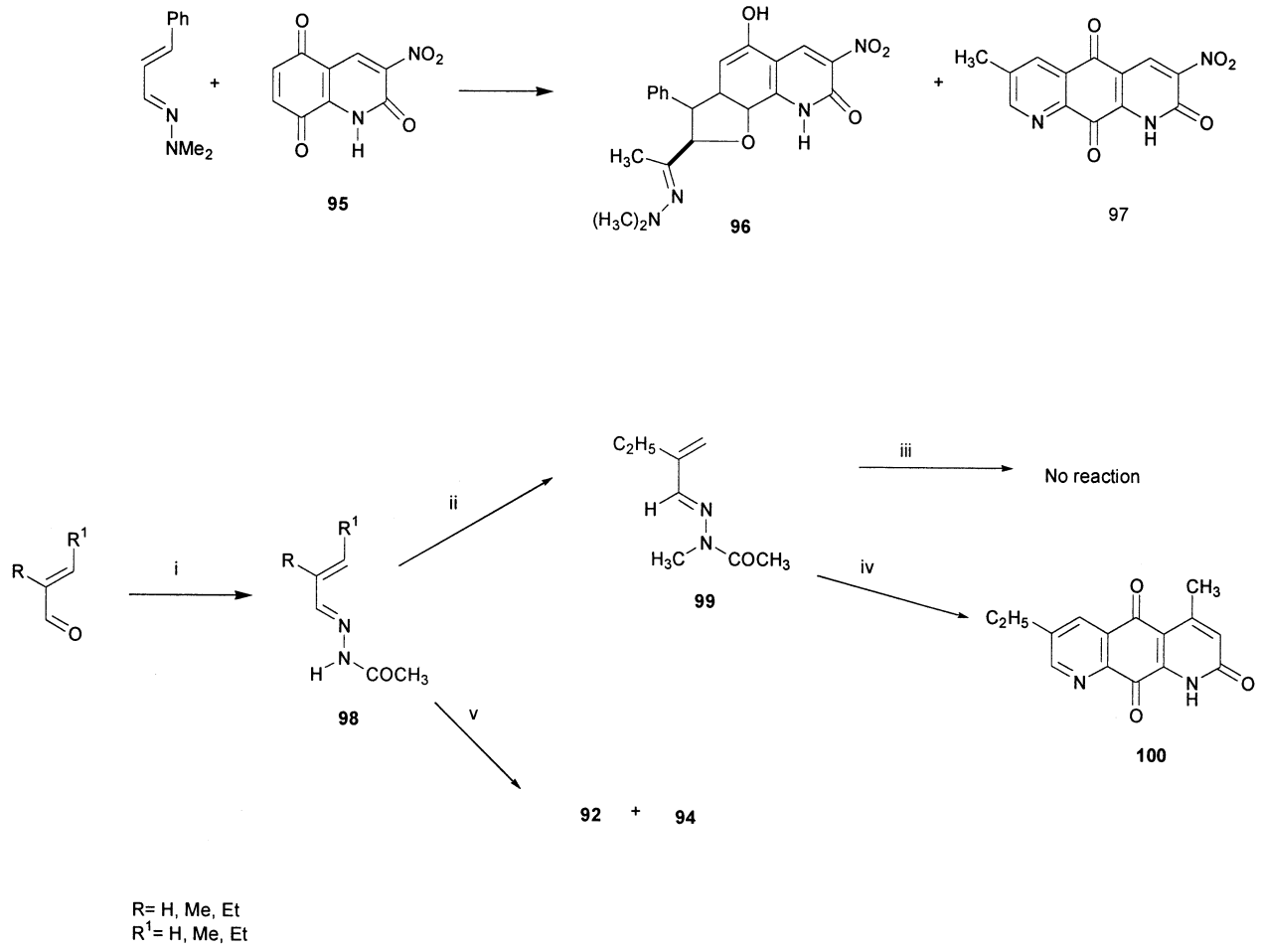
The use of a chiral diene as well as a chiral dienophile has been reported for induction of asymmetry in cycloadditions involving electron-rich 1-azadienes, e.g. the reaction of the homochiral dienophile, 2[(*S*)-1-phenylethyl]-1,2-thiazolin-3-on-(*S*)-oxide, with 1-azadiene yields the cycloadduct (**129**) in good yield and excellent diastereoselectivity.[34] Alternatively, the reaction of the chiral 1-azadiene (**130**) derived from α,β-unsaturated aldehyde and Enders' hydrazine is reported[35] to add to cyclic dienophiles with high facial selectivities and the cycloadducts obtained (**131**,**132**) have been converted to enantiomerically pure substituted piperidines (**133**, Scheme 30).

Highly diastereoselective hetero-Diels–Alder reactions of chiral alkenyldihydroisoxazoles (**134**) with alkenes, and aryl- and arylsulfonyl-isocyanates have been reported to yield novel pyridine (**135**) and pyrimidine derivatives[36] (**136**,**137**, Scheme 31).

The isoxazolopyridine (**139**) has been obtained from the reaction of the hydrazone (**63**) with 4-nitro-3-phenyl-isoxazole[37] (**138**, Scheme 32).

Barluenga et al.[38] have developed simple protocols for the preparation of electron-rich 4-amino-substituted-1-azadienes (**140**) involving ketimines and saturated nitriles. These azadienes are found to be unreactive as heterodienes, but on treatment with dichlorosilanes they are converted to diazasilines (**141**) which have been reported to undergo [4+2] cycloadditions with mono- and di-acetylenecarboxylates, besides undergoing N–Si bond insertion; the initially formed cycloadducts (**142**) are reported to undergo intramolecular rearrangement leading to substituted pyridines[38a,39] (**143**, Scheme 33).

2.3.2. [4+2] Cycloadditions of electronically-neutral 1-azabuta-1,3-dienes. The *N*-aryl- and *N*-alkyl-1-aza-1,3-butadienes are included in this category and are generally obtained by condensation of various amines with conjugated carbonyl



Scheme 19. i. $MeCONHNH_2$, EtOH, reflux, 30 min.; ii. NaH, xylene, reflux, 30 min. and then MeI, reflux, 15h.; iii. quinone, xylene reflux, 7 days; iv. quinone, $CHCl_3$, ultrasound, 45°C, 5 days; v. quinolinietrione, xylene (air), reflux, 12–110h.

compounds, although a method involving pyrolytic fragmentation of 1-methoxycyclopropylamines leading particularly to conjugated ketimines has been recently reported.[40a] Barulenga et al.[40b,c] have also reported a method for the preparation of 2-vinyl-1-aza-1,3-dienes involving an aza-Wittig reaction. The same workers have also introduced[40d] a method for the conversion of allylic amines to 4-substituted-1-aza-1,3-dienes via organozirconium complexes (Scheme 34).

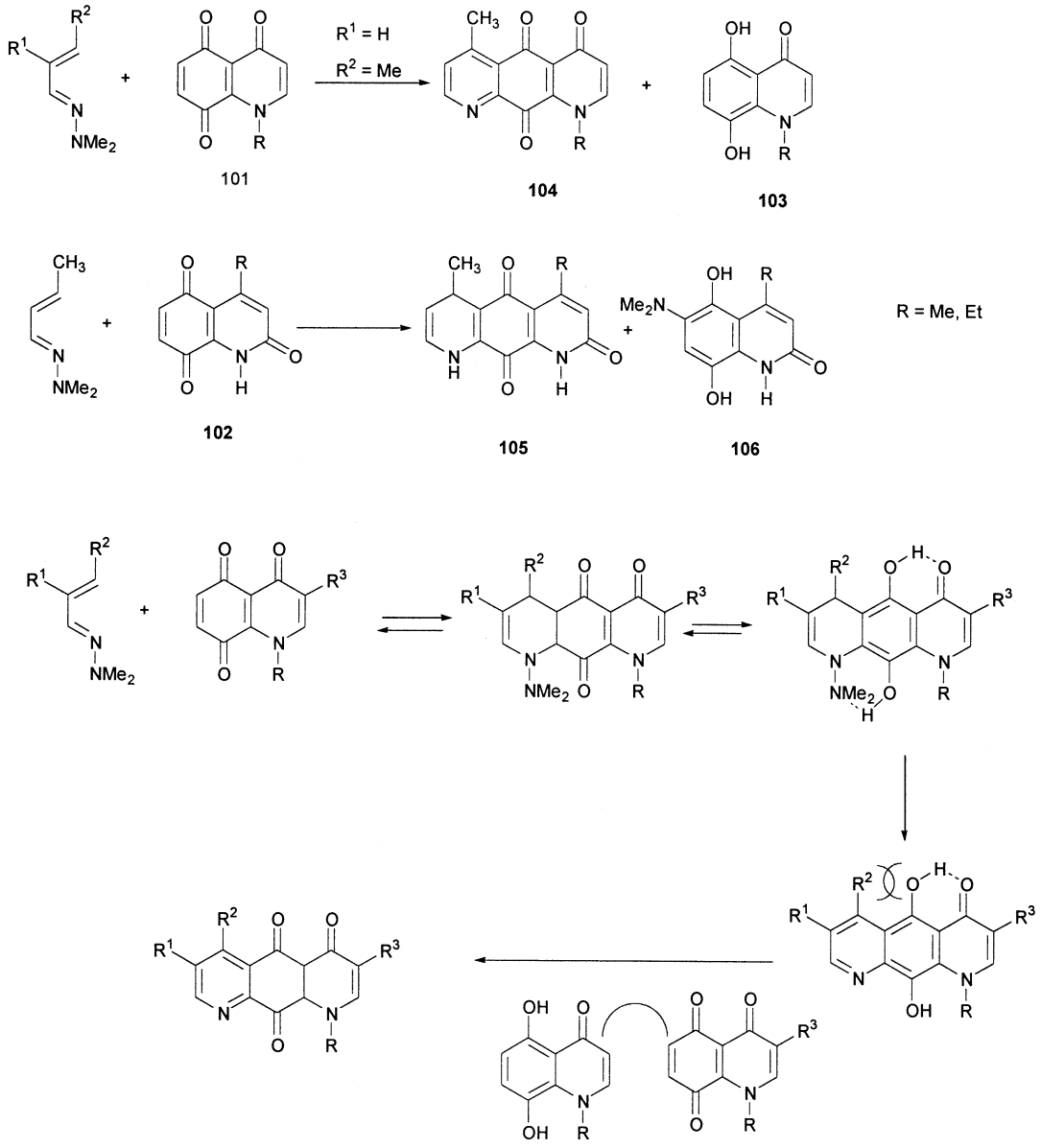
Recently, Eilbracht et al.[41] have reported that hydroformylation and silacarbonylation of acetylenes in the presence of amines leads to the formation, inter alia, of 4-silylated-1-azabutadienes (**144**) which undergo [4+2] cycloadditions with dimethyl-acetylenedicarboxylate to give the substituted 1,4-dihydropyridines (**145**, Scheme 35).

Electrononically neutral but highly reactive 1-azadienes (**147**) have been generated from *o*-*N*-methylamino-α-aryl-benzyl-alcohols (**146**) which undergo, in situ, [4+2] additions with fullerenes[42] (Scheme 36).

Similar reactive 1-azadienes (**149**,**152**,**155**) generated, in situ, from *N*-substituted-*o*-aminobenzyl chlorides (**148**,**151**,**154**) were engaged by Corey et al[43] in intramolecular [4+2] cycloadditions to obtain a number of hydroquinolines (**150**,**153**,**156**, Scheme 37).

Barulenga et al.[44] have reported that neutral 1-azadienes (**157**) undergo [4+2] cycloadditions with alkynyl Fischer complexes (**158**) regioselectively to afford substituted 1,4-dihydropyridines (**159**, Scheme 38).

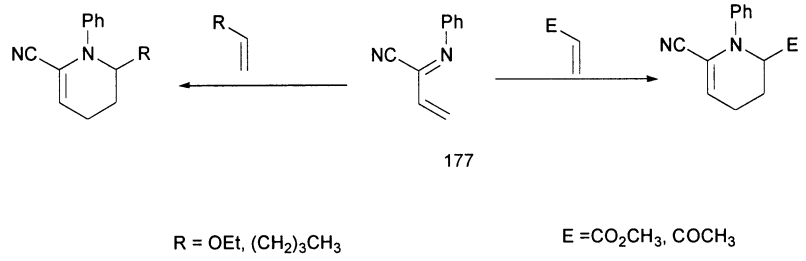
2.3.3. [4+2] Cycloadditions of electron-deficient 1-azabuta-1,3-dienes. Fowler and Teng as a part of their continuing efforts have reported[45] that *N*-acyl-α-cyano-1-azadienes (**160**,**162**) undergo facile intramolecular *exo*-selective hetero-Diels–Alder reactions to afford adducts (**161**,**163**,**164**). They have further reported that azadienes (**165**,**173**) also undergo facile intermolecular *exo*-selective [4+2] cycloadditions with a range of dienophiles to give adducts (**166–172**,**174**).[46] The *N*-arylsulfonyl-1-azadienes are known to undergo highly efficient inverse electron-demand Diels–Alder reactions with electron-rich dienophiles.[47] The reactivity, regiochemistry and stereochemistry of these additions have been



Scheme 20.

interpreted in terms of a concerted mechanism involving a transition state with a high degree of diradical character[46] (Scheme 39).

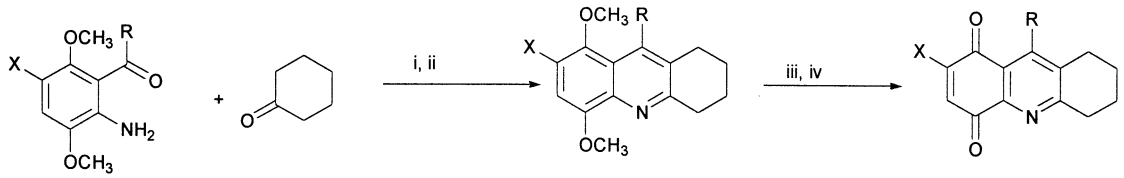
Investigations by Fowler et al.[48] on the influence of the nitrogen substituent on the reactivity of 2-cyano-1-azadienes (**175**,**176a**,**176b**) towards dienophiles with different electronic requirements (styrene, methyl acrylate and ethyl vinyl ether) showed that *N*-phenyl-substituted azadiene was equally reactive towards all three dienophiles; however, *N*-ethoxycarbonyl-substituted azadiene displayed a high electron deficiency by being more reactive with ethyl vinyl ether than styrene and



177

R = OEt, $(CH_2)_3CH_3$

E = CO_2CH_3, $COCH_3$

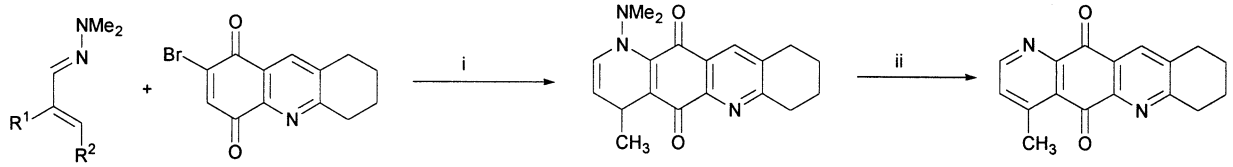


107

X=H,Br
R=H, CH3

i. KOH, EtOH, reflux ii. AcOH, H_2SO_4 (cat), reflux

iii. CAN, $CHCl_3$-H_20, r.t iv. CAN, CH_3CN-H_2O, r.t.

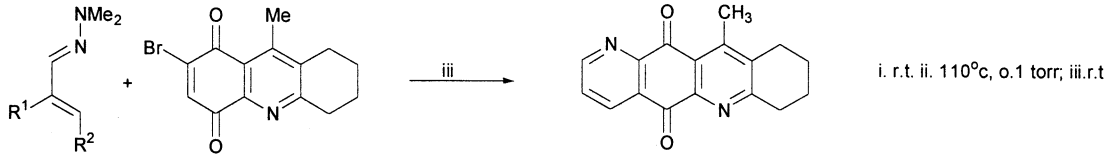


R^1 = H

R^2 = CH_3

108

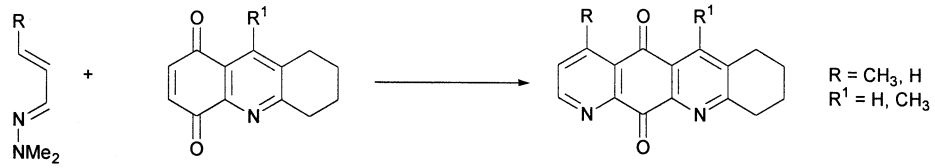
109



R^1 = R^2 = H

110

i. r.t. ii. 110°c, o.1 torr; iii.r.t

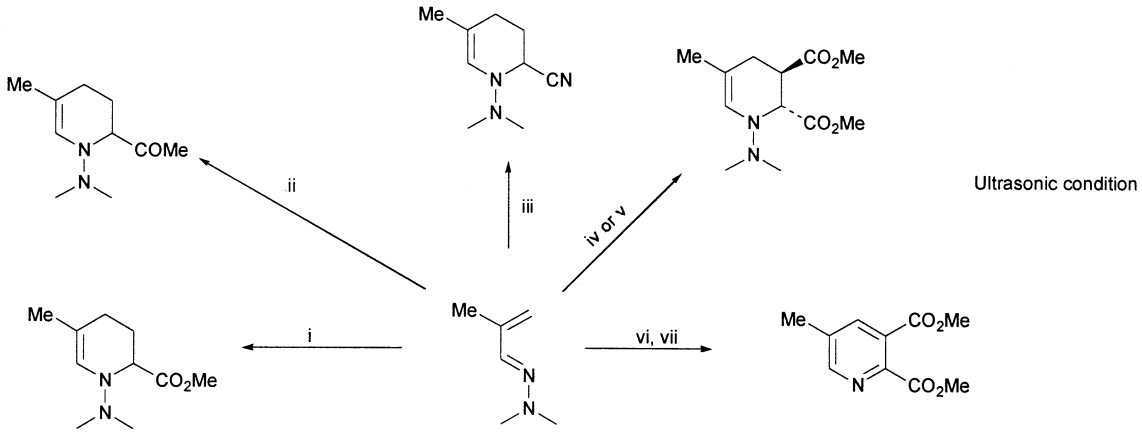


R = CH_3, H

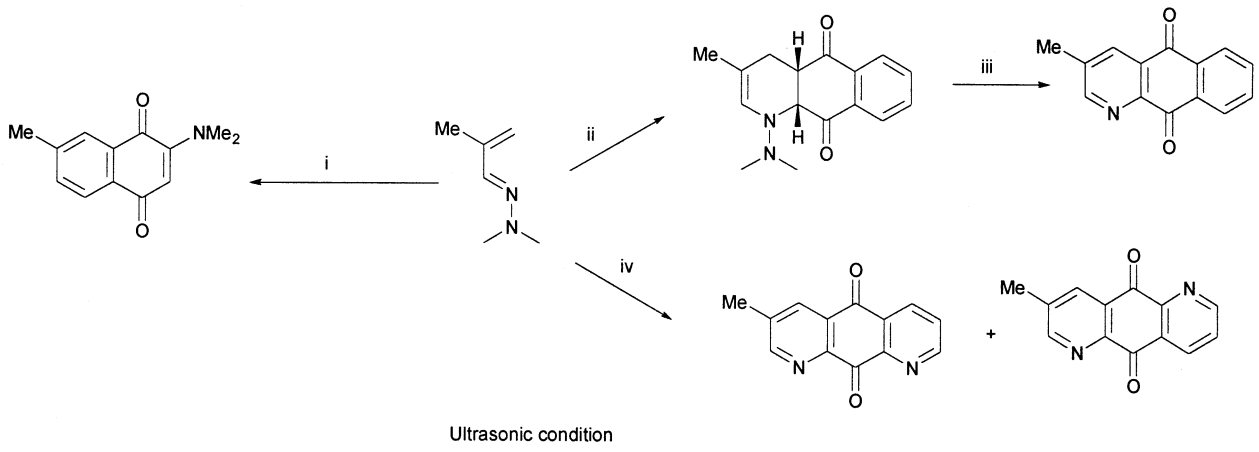
R^1 = H, CH_3

111

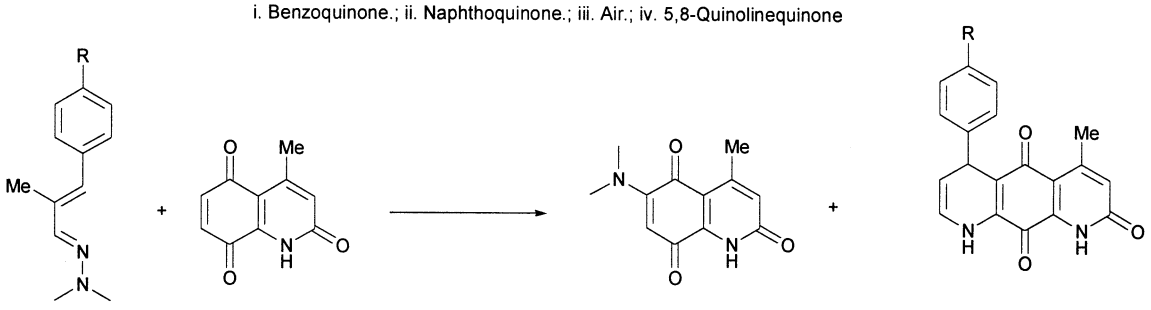
Scheme 21.



i. Methyl acrylate.; ii. Methyl vinyl Ketone.; Acrylonitrile.; Dimethyl fumarate.; Dimethyl maleate.; vi. Dimethyl acetylene dicarboxylate.; vii. Air

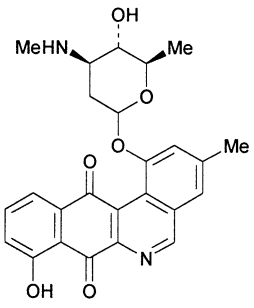


i. Benzoquinone.; ii. Naphthoquinone.; iii. Air.; iv. 5,8-Quinolinequinone

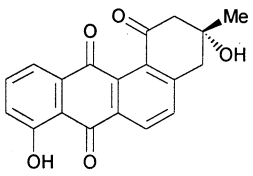


R= H, NMe_2

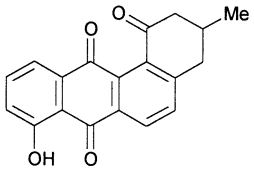
Scheme 22.



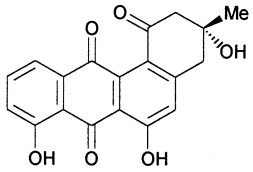
phenantroviridin



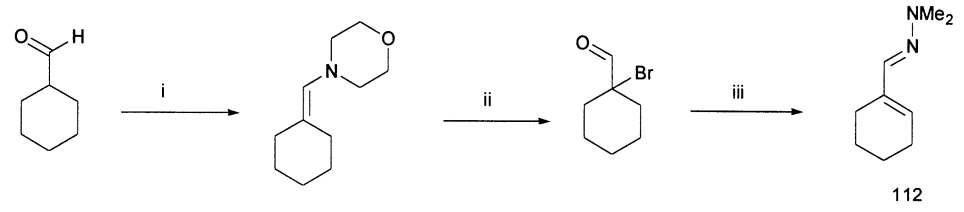
tetrangomycin



ochromicinone

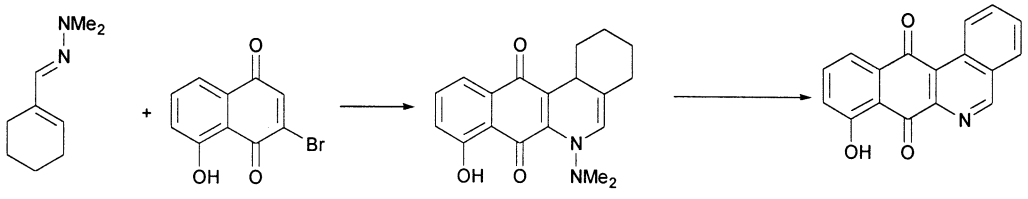


rabelomycin



112

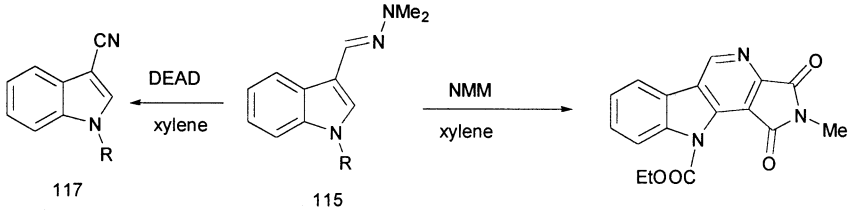
i. morphiline, benzene, reflux; ii. Br_2; iii. N,N′-dimethylhydrazine.



113

114

Scheme 23.



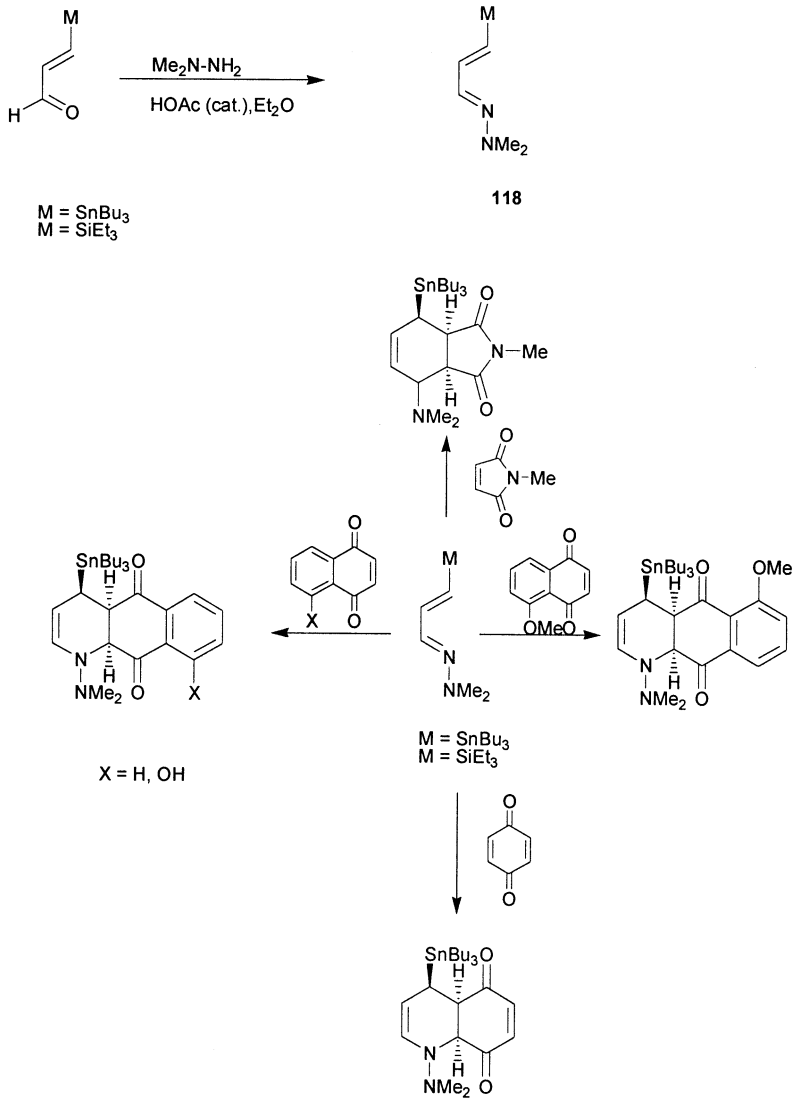
117

115

116

R = COOEt, COPh

Scheme 24.

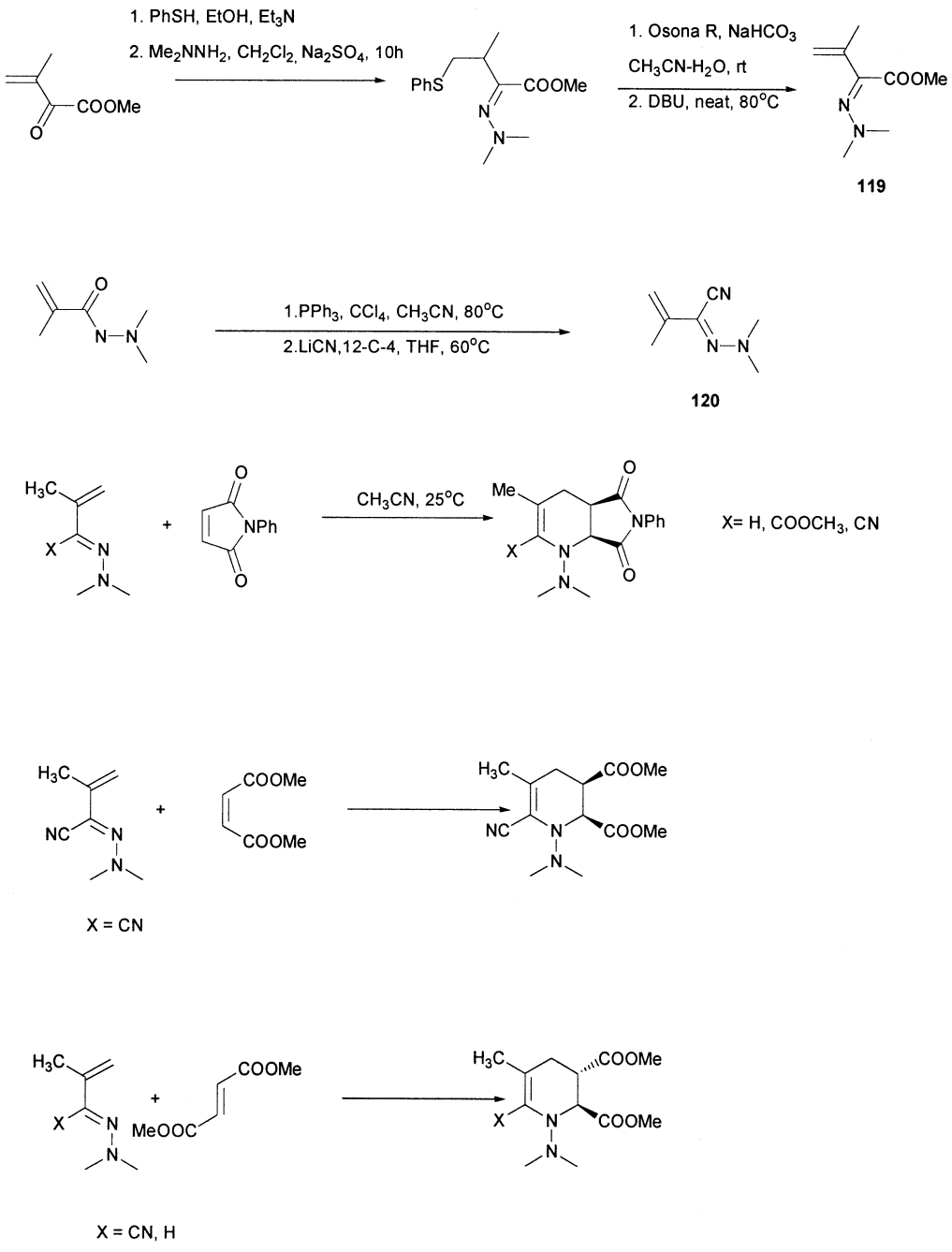


Scheme 25.

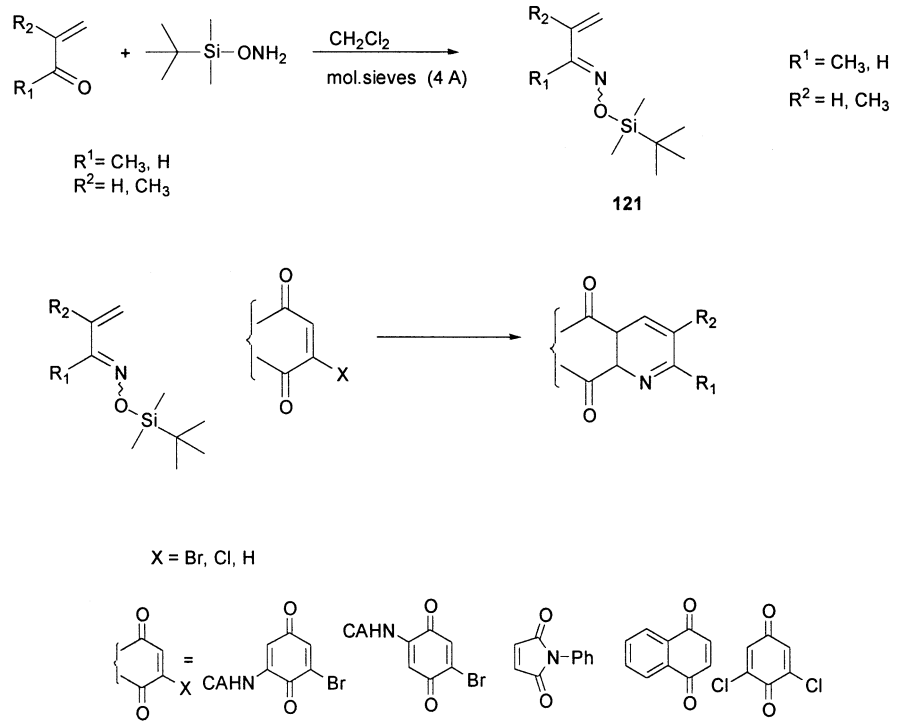
methyl acrylate. The *N*-methoxy-substituted azadiene was found to be relatively unreactive and less regioselective (Scheme 40).

Further studies[49] by the same research group on hetero-Diels–Alder reactions of *N*-phenyl-1-aza-2-cyano-1,3-dienes (**177**) with a number of dienophiles have established that the additions are highly *endo*-selective and proceed with a high degree of synchronicity. These observations have been supported by theoretical calculations [RHF AM1 (MOPAC, version 5.0)] and FMO treatment has indicated that the reactions with electron-rich dienophiles are controlled by the $LUMO_{diene}$ whereas the reaction with electron-deficient dienophiles such as methyl vinyl-ketone is under $HOMO_{diene}$ control. The AM1 level calculations[50] however, predict the *exo*-transition state of the above cycloadditions to be lower in energy than the *endo*-mode which contrasts with experimental observations. On the contrary, earlier calculations on the LUMO-controlled reactions of *N*-phenyl-2-cyano-1-azadiene (**177**) with ethyl vinyl ether had suggested that the secondary orbital interaction between the diene C-2 and the ether oxygen favours the *endo*-transition state;[49,50] a LUMO control has also been envisaged in the highly endospecific, room temperature, hetero-Diels–Alder reactions of *N*-sulfonyl-2-ethoxycarbonyl-1-aza-1,3-butadienes with electron-rich dienophiles.[50b] Theoretical investigations on the transition state structure for the reaction of 1-azadiene with ethylene at STO-3G and 3-21G basis set level have revealed that the addends approach each other in non-parallel planes, and that the transition state of 1-azadiene with ethylene is later than the transition of the butadiene with ethylene[50e] (Scheme 41).

Grierson's group has also developed a protocol for intramolecular cycloadditions of 2-cyano-1-azadienes to obtain fused nitrogen heterocycles[51a] and a convenient and facile route to suitably *N*-substituted-2-cyano-1-aza-dienes (**178**) which readily undergo an intramolecular hetero-Diels–Alder reaction under a variety of conditions including microwave irradiation. The


1. PhSH, EtOH, Et3N
2. Me2NNH2, CH2Cl2, Na2SO4, 10h
COOMe
PhS
COOMe
1. Osona R, NaHCO3
CH3CN-H2O, rt
2. DBU, neat, 80°C
119
1.PPh3, CCl4, CH3CN, 80°C
2.LiCN,12-C-4, THF, 60°C
CN
120
CH3CN, 25°C
X= H, COOCH3, CN
X = CN
X = CN, H

Scheme 26.



Scheme 27.

route to (**179**) involves Eschenmoser-type cycloreversion in *N*-substituted-3-cyano-5,6-dihydro-4*H*-1,2-oxazonium salts.[51b] Motorina and Grierson have described an intramolcular version of 2-cyano-1-azadiene (**180**) cycloadditions leading to fused tetrahydropyridine derivatives (**181**, Scheme 42).[52] The same group has also reported that the hetero Diels–Alder reactions of the 2-cyano-1-azadienes (**178**,**180**) are amenable to Lewis acid catalysis.[53] Copper(II) trifluoromethanesulfonate, its chiral bisoxazoline complex, and bismuth(III) chloride have, for example, been reported to be efficient catalysts for intramolecular cycloadditions of *N*-vinylpropoxy-2-cyano-1-azadienes (**180**).[54]

Intramolecular hetero-Diels–Alder reactions of *N*-phenyl-1-aza-2-cyano-1,3-butadienes (**182**) have also been utilised to obtain 1,4-benzodiazepines[55] (**183**–**185**, Scheme 43).

In reactions of *N*-alkyl-2-cyano-1-azadienes **186** with 2-vinylindoles it has been observed that hetero-Diels–Alder additions of azadienes involve the 2-vinyl group as well as C-2,3 double bond of indole, besides the conjugate addition of indole (C3) to the azadiene (Scheme 44).[55]

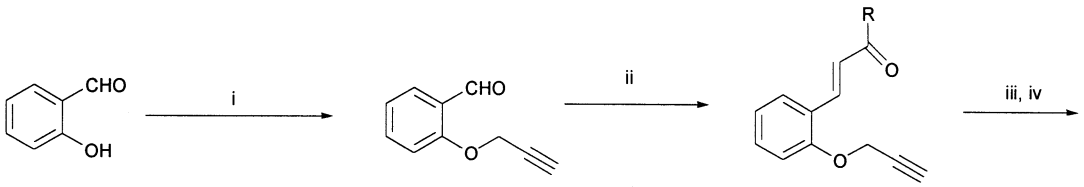
Uyehara et al. have developed protocols for the generation of *N*-acyl-azadienes (**187**) which have been shown to undergo intramolecular [4+2] cycloaddition leading to heterocyclic systems (**188**). This methodology has also been exploited for the synthesis of a piperidine alkaloid (±)-sedridine (**189**, Scheme 45).[56]

The simplest of the 1-azabutadienes has been generated in the gas phase in its N-protonated form and its cycloadditions with a number of dienophiles have been evaluated. Under these conditions the 1-azabutadiene (**190**) has been found to be generally less reactive and unreactive towards ethylene and cyclohexene, undergoing cycloaddition only with alkenes bearing electron-withdrawing substituents. On the contrary the 2-aza analogues has been found to prefer electron-rich dienophiles such as ethyl vinyl ether. The cycloadducts formed have been proposed to be derived via polar (4^++2) cycloadditions which undergo further transformations under the conditions employed[57] (Scheme 46).

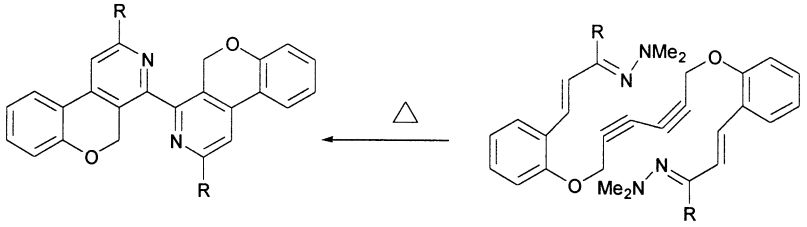
2.4. Miscellaneous reactions of 1-azabuta-1,3-dienes

Although the reactions of metal–carbene complexes have been reported to yield five-membered heterocycles[10,11] Barluenga et al.[58] have reported that the reactions of 1-unsubstituted-4-alkylamino-1-aza-1,3-dienes (**140**) and *N*-hydroxy 1-azabutadienes (**192**) with Fischer carbene complexes [pentacarbonyl (1-methoxyprop-2-enylidene)chromium(0)] leads stereoselectively to 5*H*-6,7-dihydroazepines (**191**,**193**–**196**) in high yields. This apparent [4+3] annulation is shown to proceed through initial [2+1] addition across the electron-rich π-bond of the azadiene followed by a [3,3]sigmatropic shift (Scheme 47).

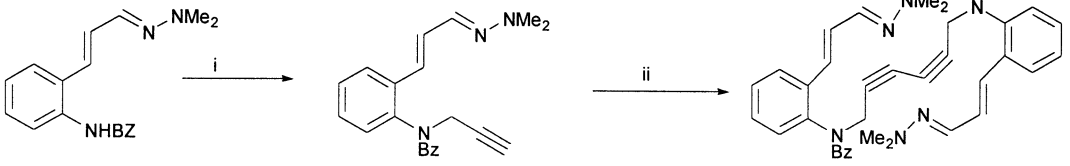
1-Unsubstituted-4-amino-1-azadienes (**140**) have been found to undergo reactions which are highly characteristic of these



i. $HC{\equiv}C\text{-}CH_2Cl$, K_2CO_3, EtOH; ii. (R=H) t-BuN=CH-CH(TMS)$_2$, $ZnBr_2$, THF, followed aq.$ZnCl_2$;iii. Me_2NNH_2, $MgSO_4$, CH_2Cl_2; iv. $Cu(OAc)_2$, Pyridine, MeOH, Ether.



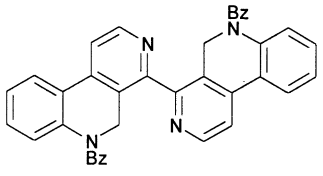
123 **122**



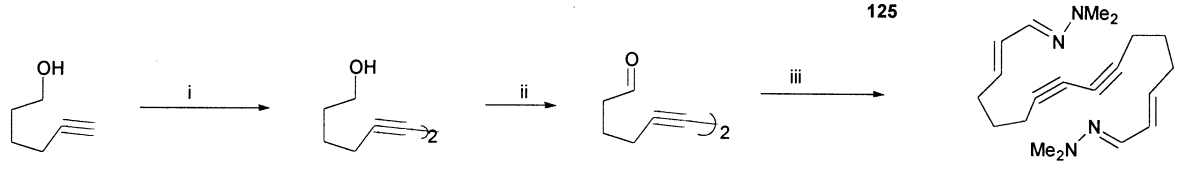
124

heat

$HC{\equiv}C\text{-}CH_2Cl$, KH, DMF; i i. $Cu(OAc)_2$, Pyridine, MeOH, Ether.



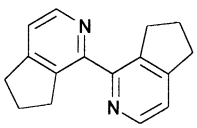
125



126

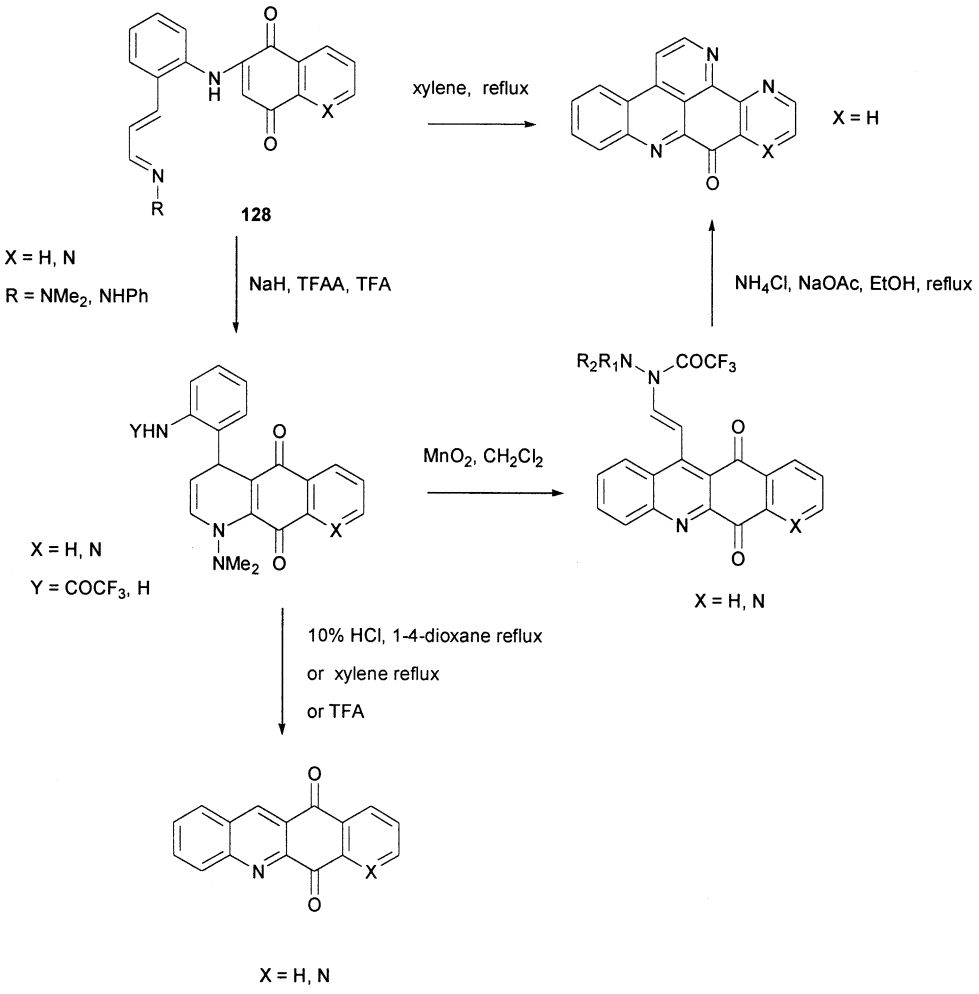
heat

i. $Cu(OAc)_2$, Pyridine, MeOH, Ether. ii.IBX, DMSO; iii. $(EtO)_2CH_2CH{=}NNMe_2$



127

Scheme 28.



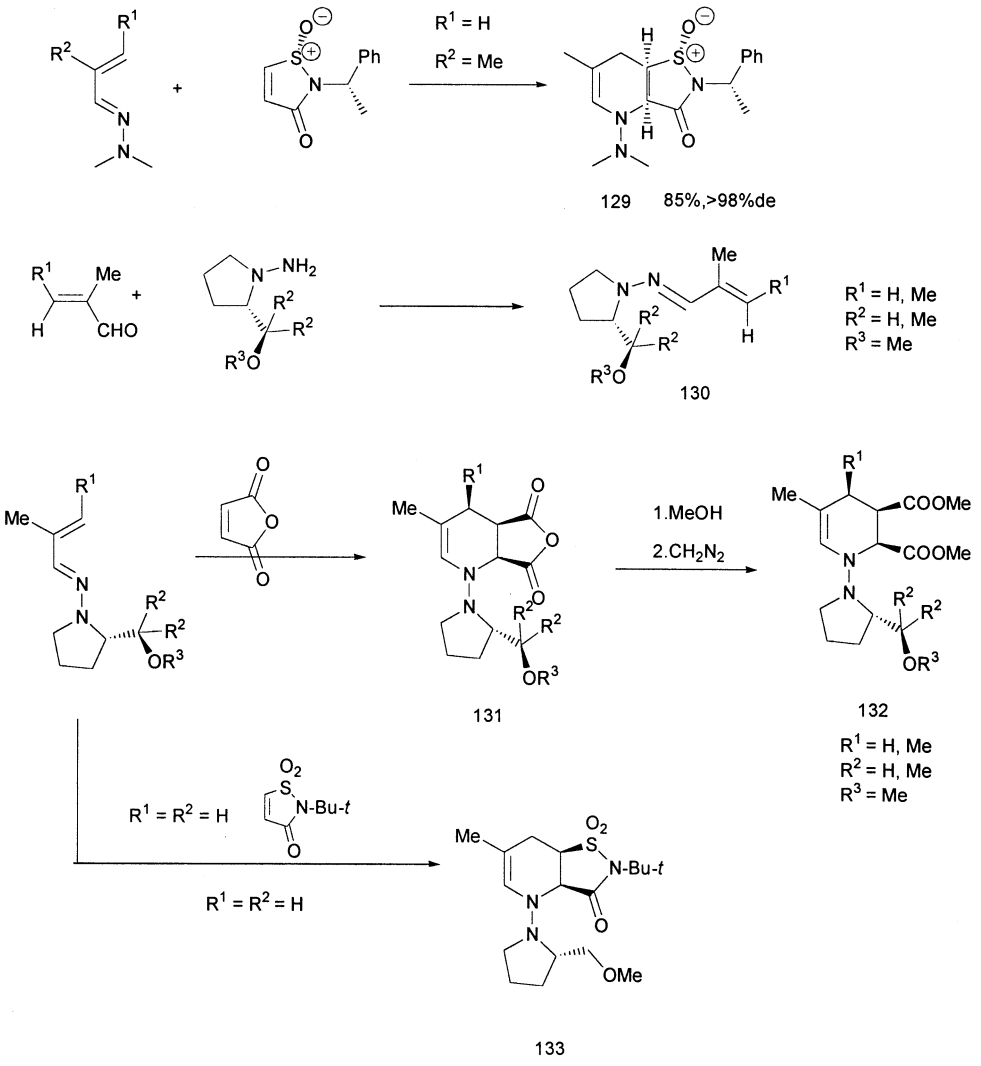
Scheme 29.

compounds. They fail to undergo 4π-addition to common olefinic/acetylenic systems, but when reacted with acetylenes they undergo an initial nucleophilic addition, which is followed by a cyclisation of the intermediate leading to six-membered heterocycles.[38a] On treatment with diphenylsilyldichloride these are converted to diazasilines (**197**) and the latter when reacted with acetylenic dienophiles undergo, besides [4+2] addition, an Si–N bond insertion reaction leading to 1,5-diazocinones (**198**,**199**, Scheme 48).[38] This behaviour has been exploited to obtain the novel diazagermocines (**200**) by reacting the azadiene (**140**) with diethyl- or diphenylgermanium dichloride to obtain 1,3,2-diazagermines followed by germanium–nitrogen bond insertion on treatment with acetylenedicarboxylate.[58] The germocines are reported to rearrange at 70°C to germanium substituted diazocines.[59]

4-Amino-azadienes **140** are well known to react with aldehydes in the presence of $ZnCl_2$ to afford dihydropyrimidine derivatives (**201**,**202**). This reaction has been exploited to obtain substituted polyamines (**203**,**204**) belonging to the biologically active class of polyamines including spermidine, norspermidine and spermine. The reaction of the azadiene with 3-cyanopropionaldehyde and reductive cleavage of the resulting dihydropyrimidines with excess sodium borohydride is reported to yield the nitrile (**203**) in high yield; purification and reduction of the nitrile leads to spermine derivatives[60] (Scheme 49).

The ability of 4-amino-1-azadienes to undergo cyclisation with aldehydes has also been exploited to obtain 1,3-aminoalcohols which have been utilised for the diastereo- and enantio-selective preparation of lactones of the N-terminal amino acid moiety of nikkomycins.[61] By reacting suitably substituted 1-azadienes (**140**) with (*R*)-*O*-benzyllactic aldehyde, via di- and tetrahydropyrimidines (**205**,**206**), β-aminoketones (**207**,**208**, Scheme 50)) have been obtained which have been converted to alcohols and finally to lactones.[61]

The reactions of 4-amino-1-azadienes (**140**) with glyoxalic acid led to the formation of 1,3-oxazines (**209**) which were reduced with sodium cyanoborohydride, resulting in stereoselective preparation of 1,3-aminoalcohols[62] (**210**,**211**, Scheme 51).



Scheme 30.

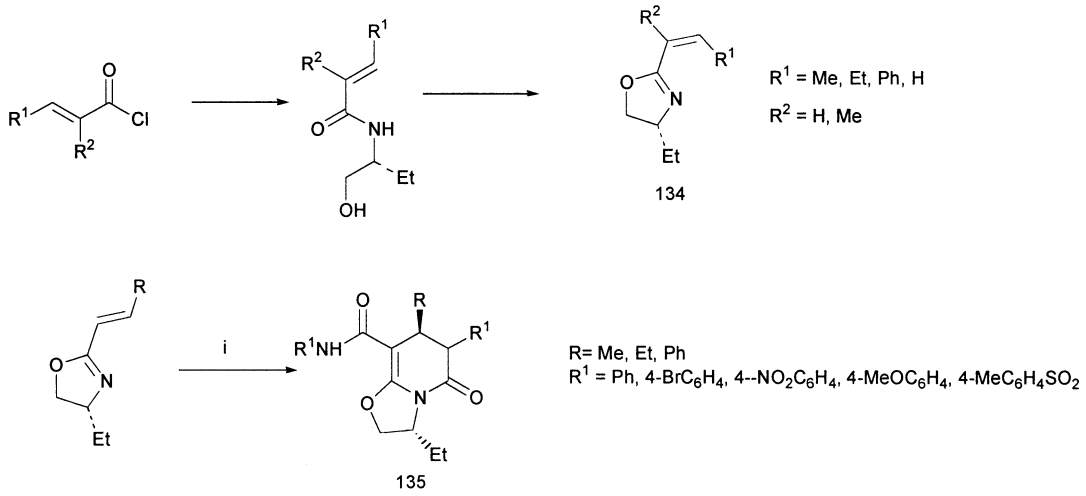
The reactions of 4-amino-1-azadienes (**140**) with dichloro(diisopropylamino)phosphane resulted in the 1,2-dihydro-1,3-2-diazaphosphinines (**212**), which, when reacted with acetylenedicarboxylate, underwent a [5+3] annulation, leading to seven-membered iminophosphoranes (**213**, Scheme 52).[63]

Contrary to the reactions of 4-amino-1-azadienes (**140**) with carbonyl-centred electrophiles wherein nitrogen heterocycles, e.g. pyrimidines (**215**) and dihydropyrimidines (**216**), are obtained, the reactions of these azadienes with alkylating agents and iodobispyridinium tetrafluoroborate resulted in *C*-substituted azadienes which were hydrolysed to 1,3-dicarbonyl compounds[64] (**214**, Scheme 53).

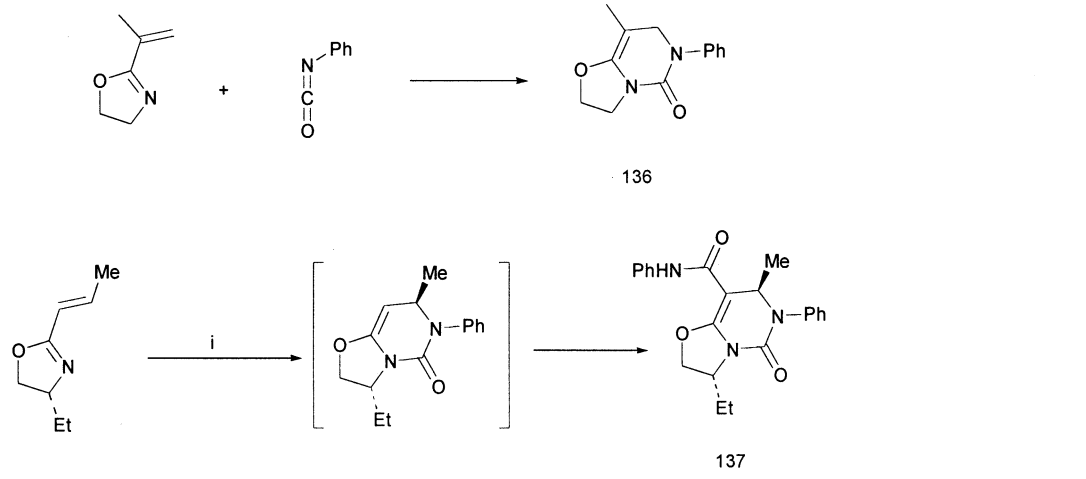
Other interesting synthetic applications of the 4-amino-1-azadienes (**140**) include the conversion of their suitably C-functionalised azadienes to heteropolycyclic compounds having phenanthrene and steroidal skeletons. Thus, 5-allyl-4-phenyl-1,2-dihydropyrimidines and 5-allyl-4-phenylpyrimidin-2(1*H*)-ones derived from 3-allyl-4-phenyl-4-amino-1-azadienes have been converted to dihydrobenzoquinazolines (**217**,**218**).[65] Similarly tetrahydropyrrolo[1,2-*a*]pyrimidines (**219**), prepared in one step from aromatic nitriles and amines derived from 4-aminobutyraldehyde diethyl acetal, were reduced by sodium borohydride, N-allylated and intramolecularly cyclised to novel diazasteroids (**220**, Scheme 54).[66]

1-Azadienes (**222**) derived from 11-formylmethylene-6,11-dihydrobenzo[*b*]oxepin-2-carboxylate (**221**) by reaction with a 2-aminoformanilide derivative has been converted to a novel thromboxane A_2 receptor antagonist (**223**) by elaboration of an imidazole ring involving N-1 of the azadiene (**223**, Scheme 55).[67]

The reactions of 4-alkyl-*N*-bis- and mono(trimethylsilyl)methyl-1-azadienes (**224**) with both dialkyl- and diaryllithium/cyanocuprates in the presence of a Lewis acid (BF_3) have been reported to yield conjugate as well as 1,2-addition products (**225**,**226**, Scheme 56).[68]

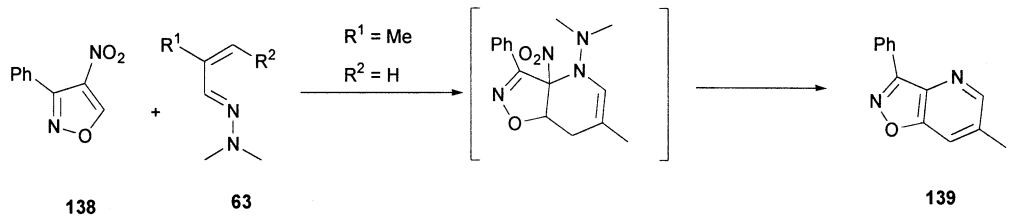


i. (R)-2-aminobutan-1-ol, Na_2CO_3, CH_2Cl_2,. ii. $MeSO_2Cl$, Et_3N, CH_2Cl_2

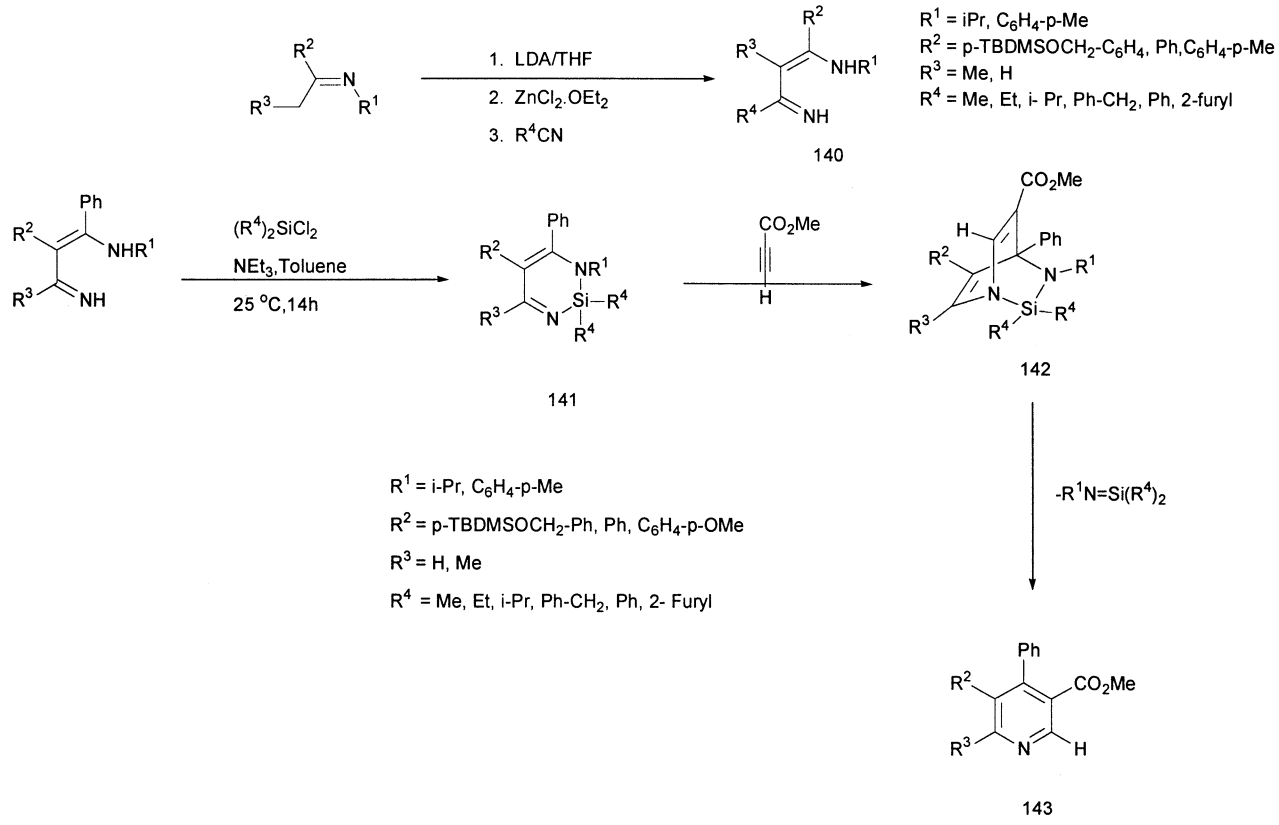


i. 2 equiv. PhNCO, 115°C, 1h or 2 5°C, 24h

Scheme 31.



Scheme 32.



Scheme 33.

1-Aza-1,3-butadienes (**227**–**229**) have been reported to undergo 3,4-, 1,2- and 1,4-cyclocondensation with homophthalic acid anhydride (**230**) to give 3,4-dihydro-1(2*H*)-naphthalenone-4,carboxylic acids (**231a**,**231b**,**231c**,**231d**), 3,4-dihydro-1(2*H*)-isoquinolinone (**232**), 3,4-dihydro-1(2*H*)-pyridinones (**233**) and dienyl derivatives of **230** viz **234a** and **234b**.[69] The product distribution is found to be related to the substituents on the azadiene as well as the reaction conditions (Scheme 57).

Although allene-derived all carbon dipoles (**55**) have been reported to form pyrrolidine derivatives,[70] they are however, when reacted with 3-(*N*-acyliminomethyl)-chromone **235**, observed to undergo [4+3] annulation; the initially-formed adduct **236** undergoing tandem rearrangement to an azepine (**237**, Scheme 58).

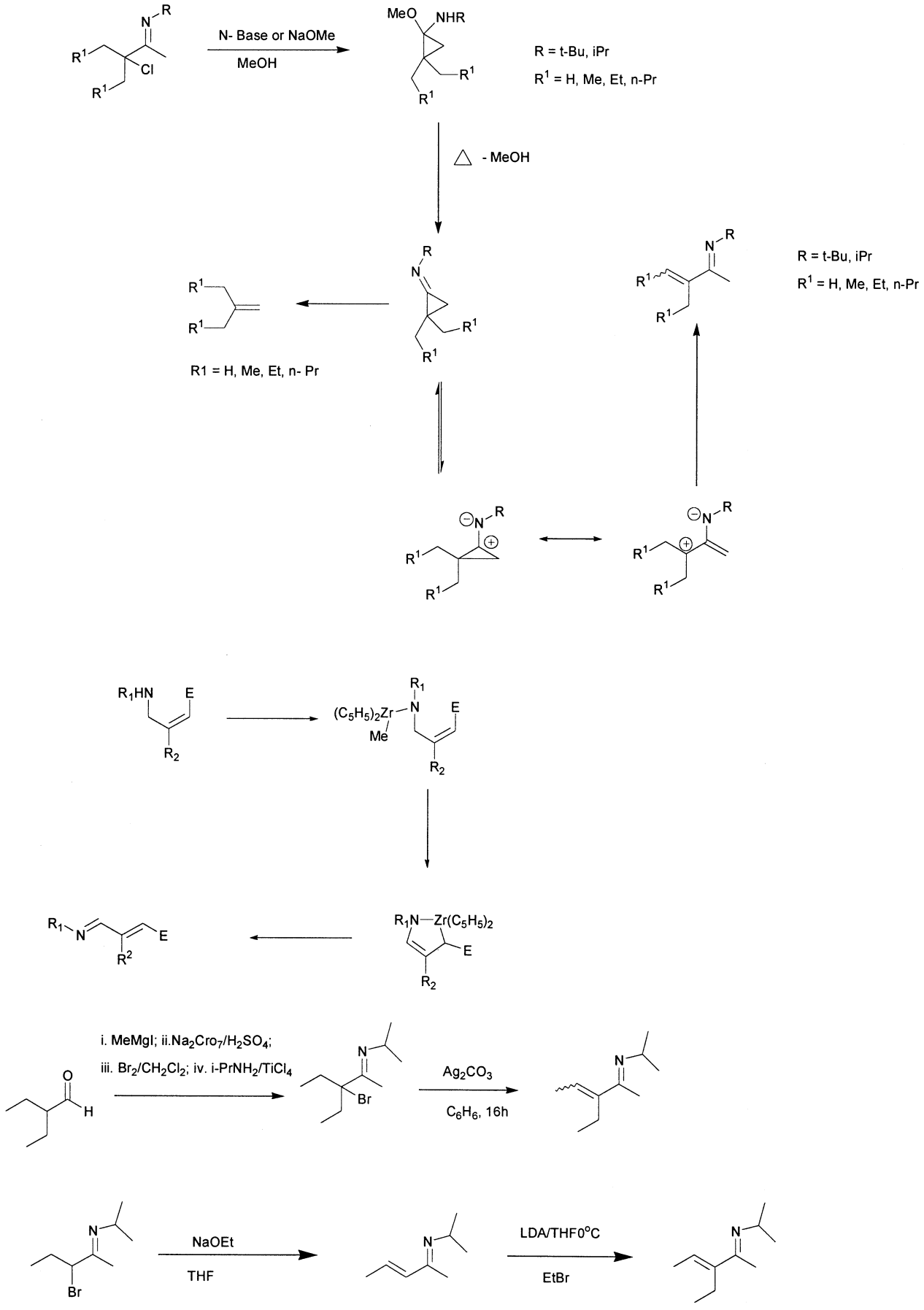
3. 2-Azabuta-1,3-dienes

2-Azadienes represent an important class of compounds and have become useful key intermediates in organic synthesis for the construction of both heterocyclic systems and open-chain polyfunctionalised compounds.[1] The chemistry of 2-azadienes is dominated by [4+2] cycloaddition reactions with alkenes, alkynes, enamines and heterodienophiles including carbonyl-, azo-, and nitroso-compounds, leading to the formation of a great variety of nitrogen-containing six-membered heterocyclic compounds. The literature classification of 2-azadienes is based on their reactivity and, depending upon the substituents, they are classified as: (i) electron-poor 2-azadienes, (ii) electron-rich 2-azadienes and (iii) electronically neutral 2-azadienes.

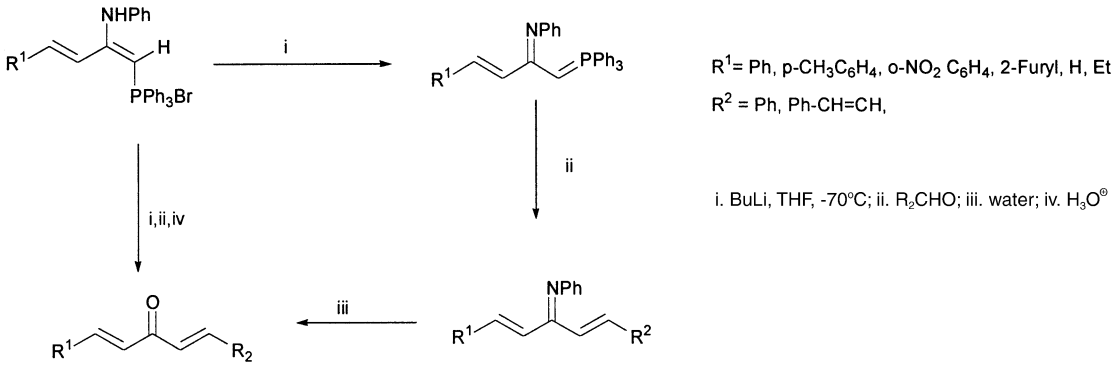
3.1. Synthesis of 2-azabuta-1,3-dienes

The most important and widely employed synthetic routes for the preparation of 2-azadienes employ: (i) aza-Wittig reactions between *N*-vinylic phosphazenes and carbonyl compounds, (ii) imines and related substrates and (iii) miscellaneous substrates.

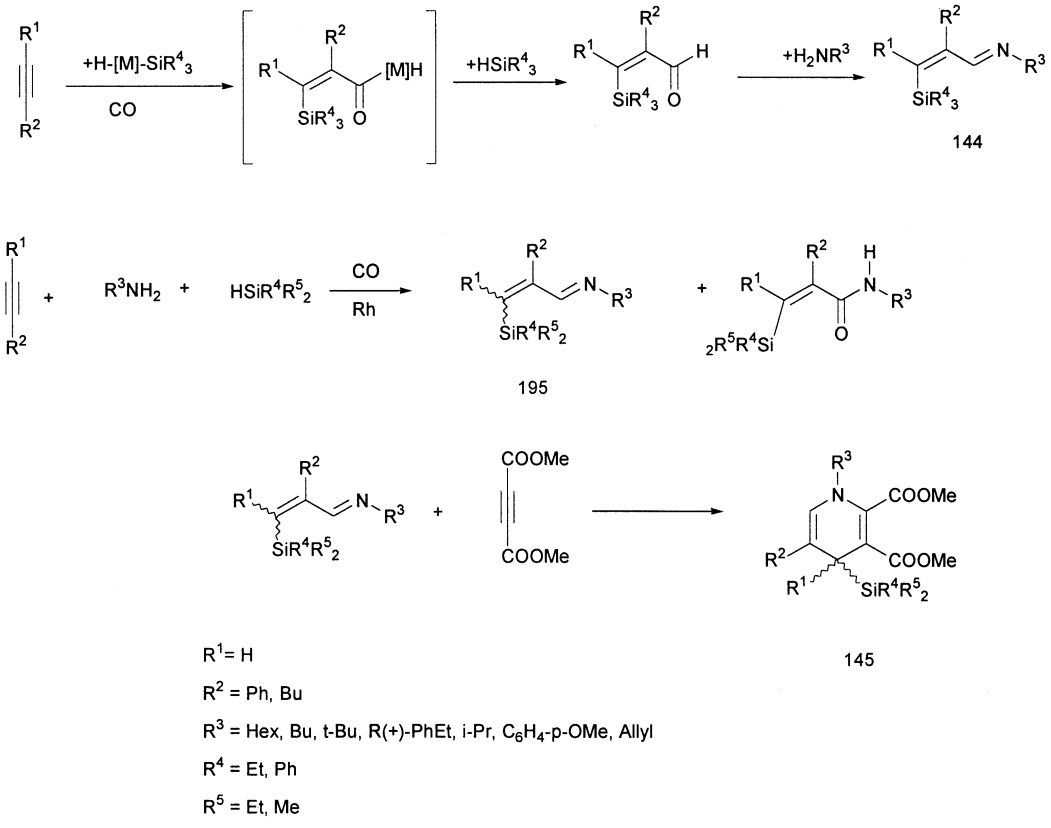
3.1.1. Involving aza-Wittig reactions between *N*-vinylic phoshazenes and carbonyl compounds. *N*-Vinylic phosphazenes represent an important class of compounds having a broad range of applications and they are amongst the most commonly employed precursors for the synthesis of 2-azadienes.[71] Their reactions with carbonyl compounds have been extensively used for the preparation of a large variety of electron-poor and electronically neutral 2-azadienes. It has been reported that, for the *N*-vinylic phosphazenes, an adjacent double bond in conjugation with the phosphazene moiety introduces an interesting problem of site selectivity; reaction at nitrogen (1,2) addition of phosphazene group versus reactions at the γ-carbon atom (1,4) addition. The substituents on the phosphorous atom in *N*-vinylic phosphoranes (**238**) play an important role in the reactivity pattern observed with carbonyl compounds.[72,73] The reactions of phosphazenes derived from triphenylphosphine


N- Base or NaOMe
MeOH
R = t-Bu, iPr
R1 = H, Me, Et, n-Pr
- MeOH
R1 = H, Me, Et, n- Pr
R = t-Bu, iPr
R1 = H, Me, Et, n-Pr
i. MeMgI; ii.Na2Cro7/H2SO4;
iii. Br2/CH2Cl2; iv. i-PrNH2/TiCl4
Ag2CO3
C6H6, 16h
NaOEt
THF
LDA/THF0°C
EtBr

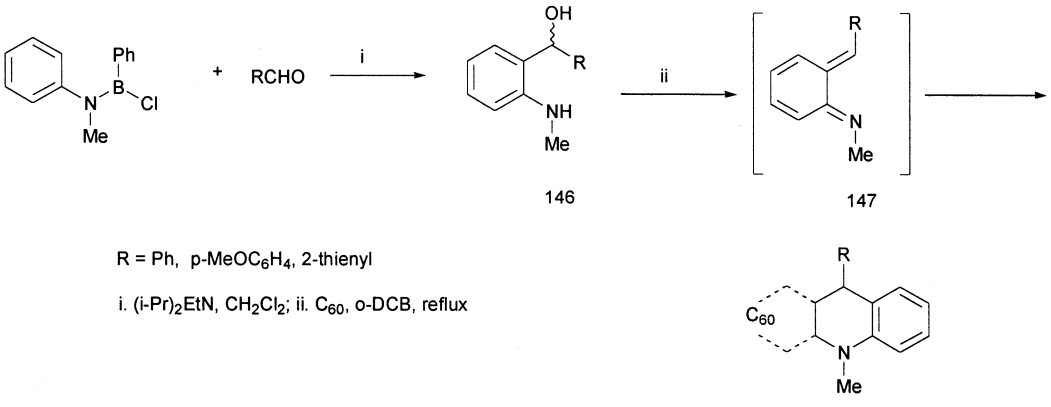
Scheme 34.



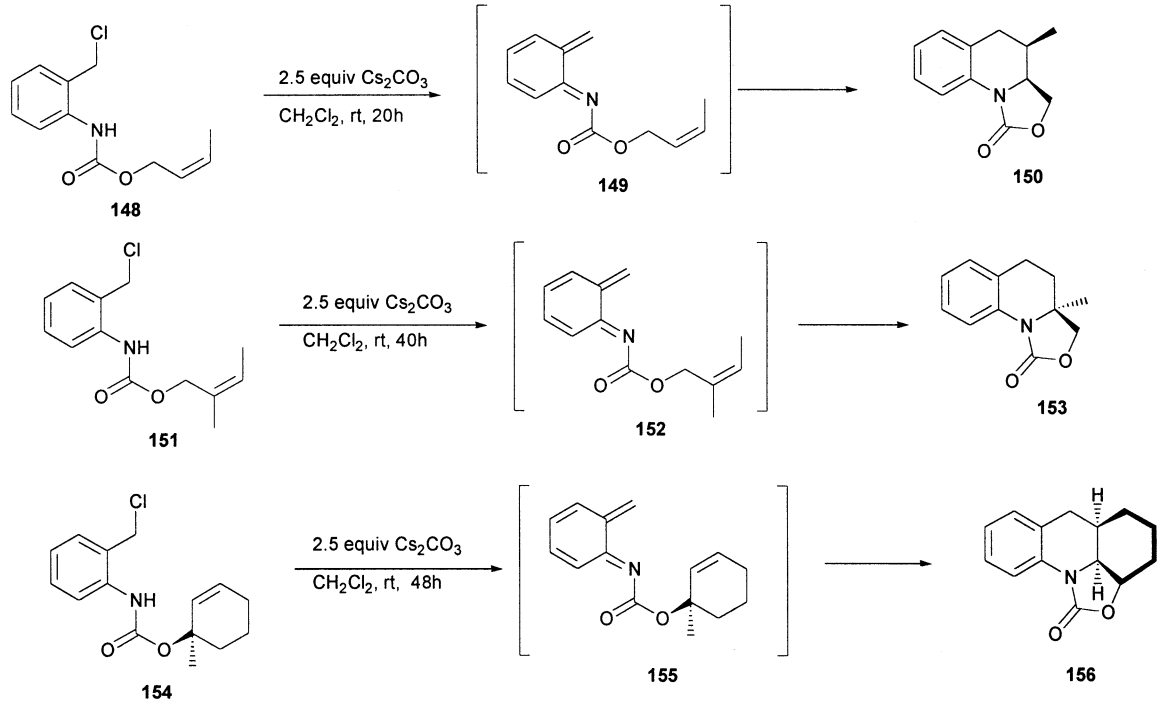
Scheme 34 (*continued*)



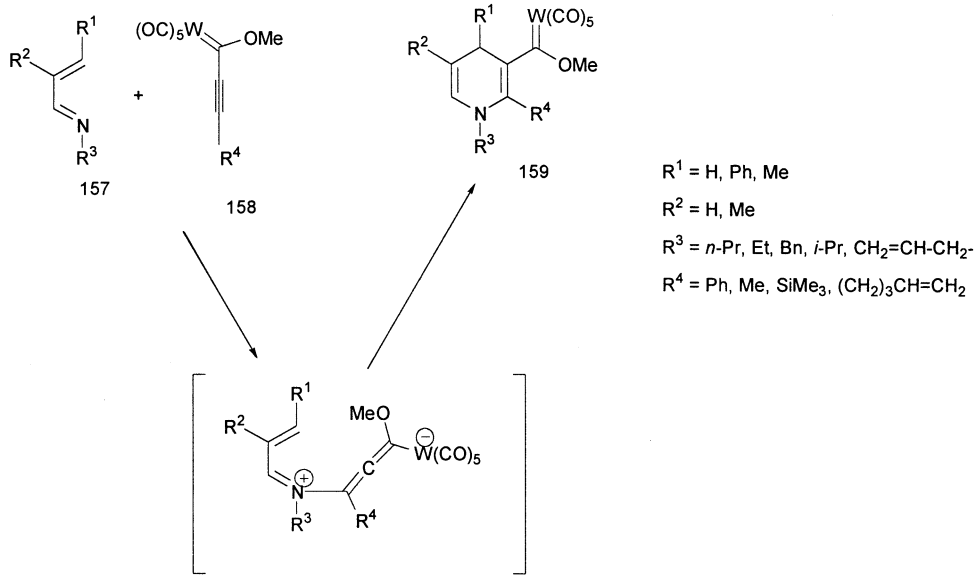
Scheme 35.



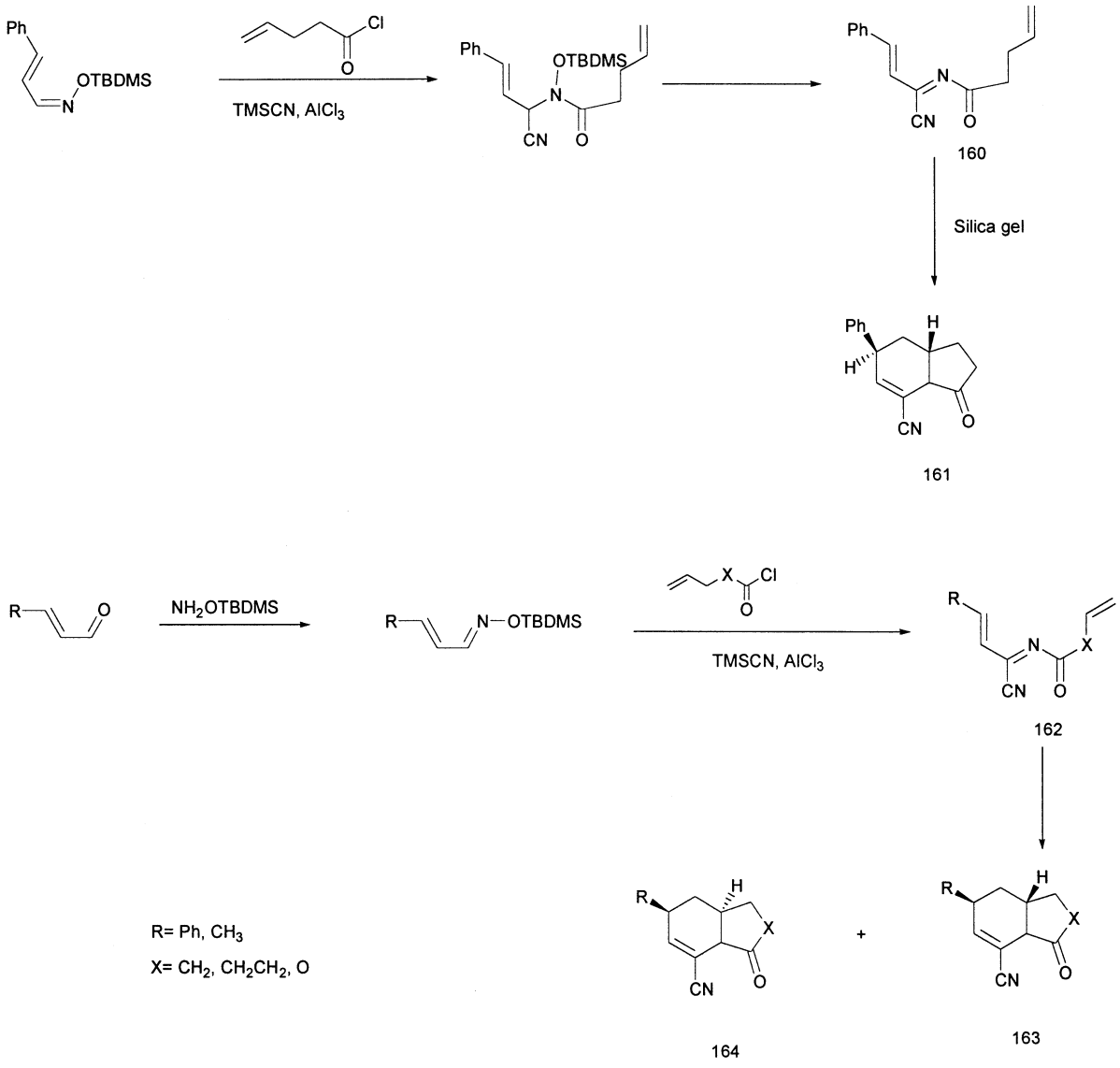
Scheme 36.



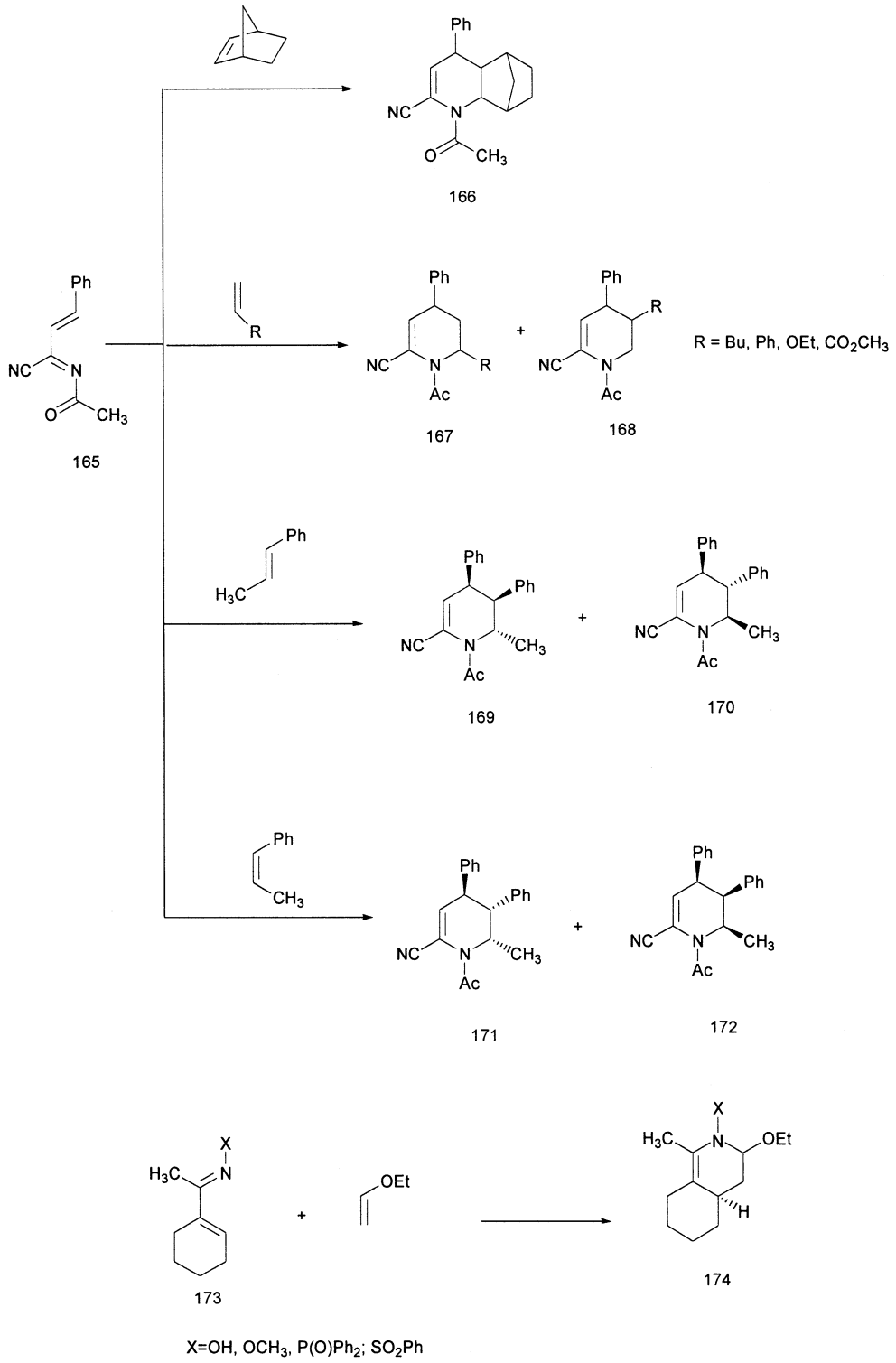
Scheme 37.



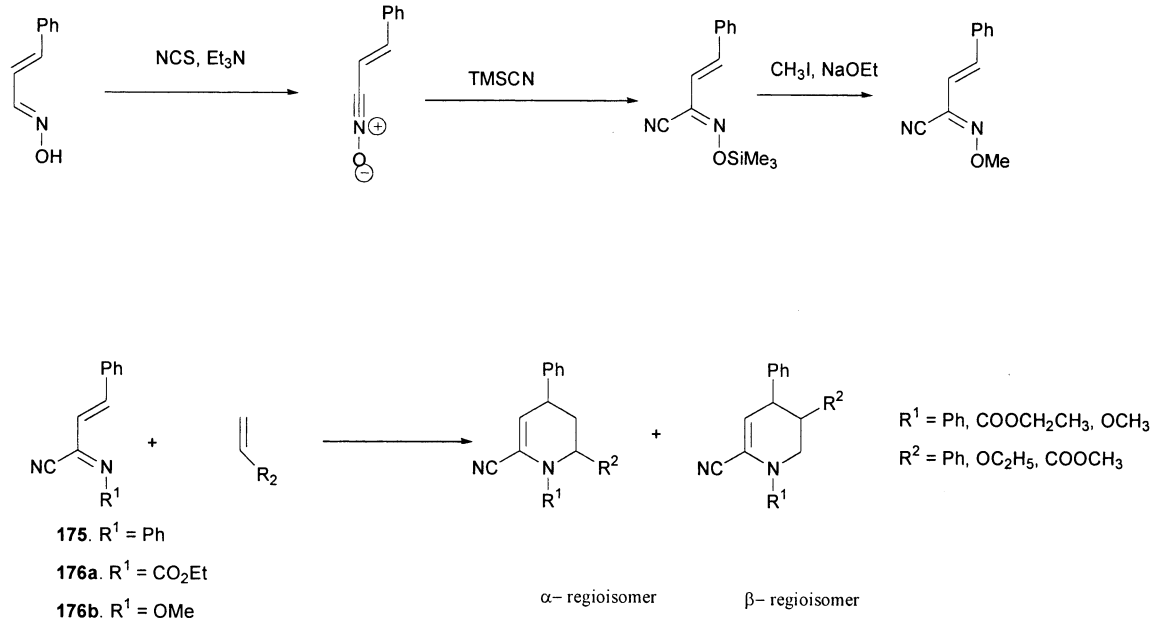
Scheme 38.


Ph
OTBDMS
N
Cl
O
TMSCN, AlCl3
Ph
OTBDMS
N
CN
O
Ph
N
CN
O
160
Silica gel
Ph
H
H
CN
O
161
R
O
NH2OTBDMS
R
N—OTBDMS
X
Cl
O
TMSCN, AlCl3
R
N
X
CN
O
162
R= Ph, CH3
X= CH2, CH2CH2, O
R
H
X
CN
O
+
R
H
X
CN
O
164
163

Scheme 39.



Scheme 39 (*continued*)



Scheme 40.

(R^1=Ph) with carbonyl compounds gave the mono-adduct (**239**), while phosphazenes derived from diphenylmethylphosphine underwent an aza-Wittig (1,2-addition) reaction with carbonyl compounds leading to the formation of the 2-azadiene (**240**, Scheme 59). The use of the more reactive diphenylmethylphosphine led to an enhancement of the nucleophilic character of the phosphazene nitrogen atom.

Palacios et al. have extensively exploited the regioselective aza-Wittig reaction between *N*-vinylic phosphazenes (**241**) and aldehydes to obtain excellent yields of various substituted 2-azadienes (**242**) having an electron-withdrawing alkoxycarbonyl group at the 4-position.[74] The same methodology was extended to the reactions of the phosphazenes (**243**) with ethyl glyoxalate and diethyl ketomalonate to obtain 2-azadienes (**244**); when pyruvonitrile was used as the carbonyl compound, the isolation of the 2-azadiene (**245**) was difficult and the tautomeric diene (**246**) was isolated. Similar strategies have been employed for the construction of some useful 2-azadienes mentioned in Scheme 60.

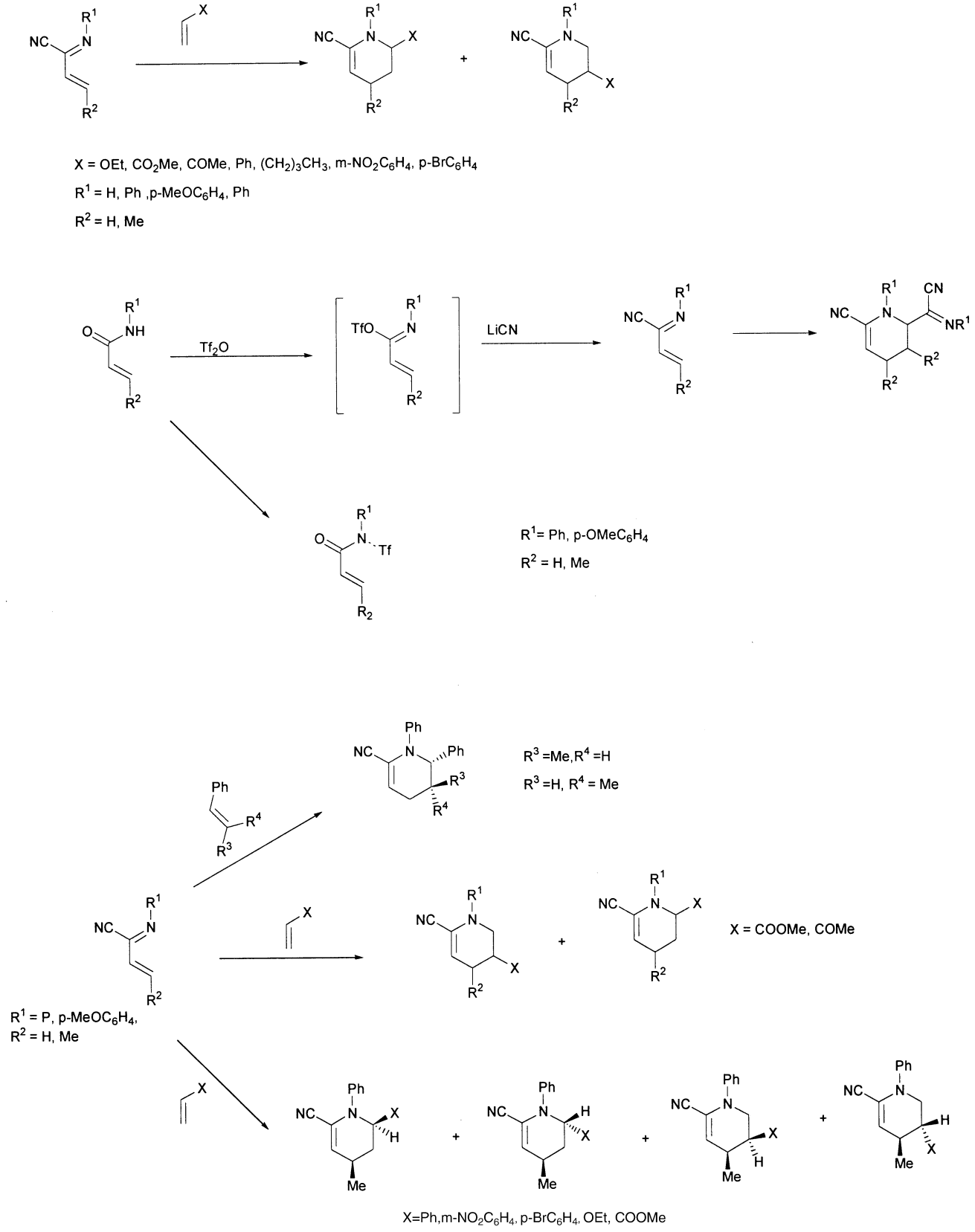
Aza-Wittig reactions of the *N*-vinylic phosphazenes (**249**), obtained from the reaction between the phosphorous ylide (**247**) and the nitrile (**248**), with aromatic and heteroaromatic aldehydes in refluxing chloroform gave the electronically neutral 2-azadiene (**250**), as exclusive *E*,*Z*-isomers.[75] This reactivity was extended to the reactions of phosphazene (**249**) with ethyl glyoxalate and surprisingly these reactions led to the formation of the six-membered ring compounds (**251**) and the expected 2-azadiene could not be isolated (Scheme 61).

Palacios et al. have devised an excellent method for the synthesis of 2-azadienes (**254**) substituted with a phosphonate group in the 3-position.[76] The key step in their strategy involved the olefination of bisphosphonylalkylimino compounds (**253**) with aldehydes in the presence of a base. The required imines (**253**) were easily obtained by a simple condensation of the α-aminomethyl diphosphonate (**252**) with aromatic and heteroaromatic aldehydes (Scheme 62).

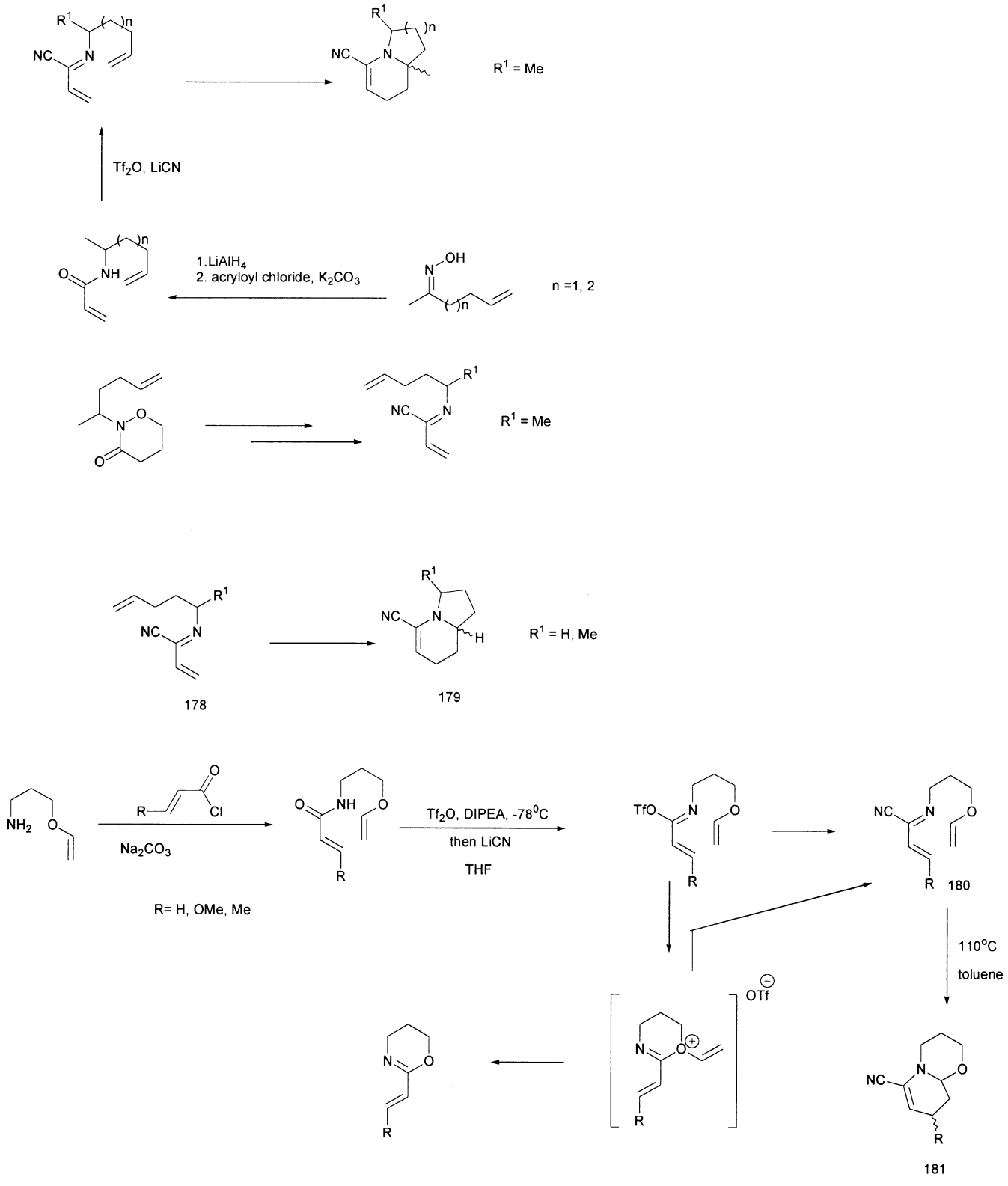
Barluenga et al. have utilised a non-classical aza-Wittig reaction to produce excellent yields of 1-amino-2-azabuta-1,3-dienes (**256**) by reacting *N*-vinylic phoshazene with acetyl chloride and treating the *N*-acylates (**255**) so formed with diethylamine, piperidine or *N*,*N*′-diphenyl-hydrazine in presence of triethylamine[77] (Scheme 63).

3.1.2. Involving imines and related substrates. Ghosez et al. utilised three different routes for the preparation of 2-azadienes having an activating trialkylsilyloxy group at C-3 (**257**–**260**).[78] The first route involves the silylation of *N*-acylimidates, readily available iminoether hydrochlorides and acid chlorides. A more general route involves a convenient single-step conversion of *N*-trialkylsilylimidates and *N*-trialkylsilylimines, derived from non-enolisable aldehydes, into the corresponding azadienes by reaction with an acid chloride in the presence of triethylamine. Finally, cyclic 2-azadienes were prepared by the direct silylation of glutarimide on both oxygen atoms by trialkylsilyl triflate in the presence of triethylamine.[79] Spectroscopic methods were used to confirm the configuration and conformation of the 2-azadienes (Scheme 64).

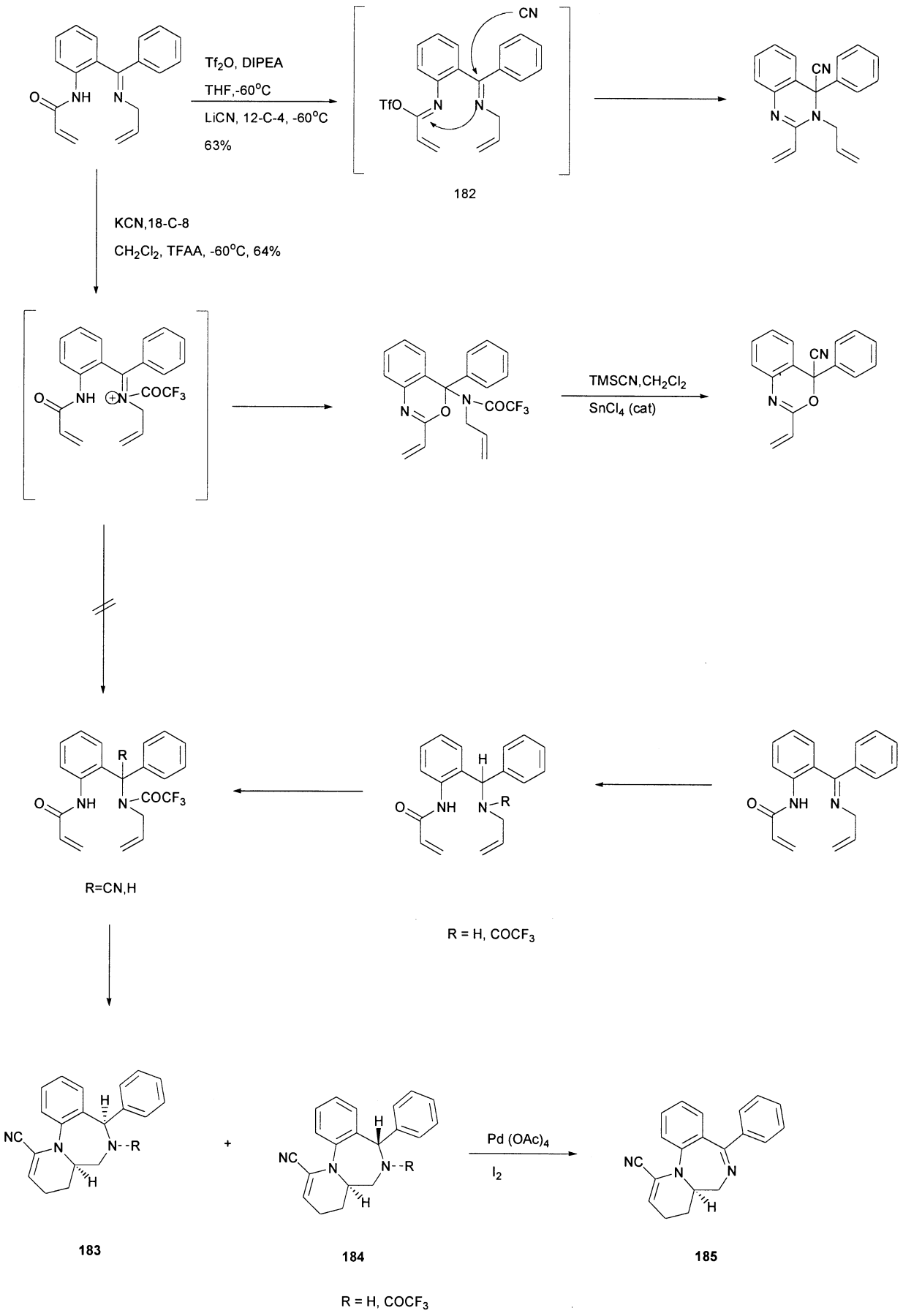
Kascheres et al. reported a nucleophilic-induced transformation of azine-3-methylacrylates (**261**) to 2-azadienes (**262**) having a potential leaving group at the C-1 position[80] (Scheme 65).


X = OEt, CO2Me, COMe, Ph, (CH2)3CH3, m-NO2C6H4, p-BrC6H4
R1 = H, Ph ,p-MeOC6H4, Ph
R2 = H, Me
Tf2O
LiCN
R1= Ph, p-OMeC6H4
R2 = H, Me
R3 =Me,R4 =H
R3 =H, R4 = Me
X = COOMe, COMe
R1 = P, p-MeOC6H4,
R2 = H, Me
X=Ph,m-NO2C6H4, p-BrC6H4, OEt, COOMe

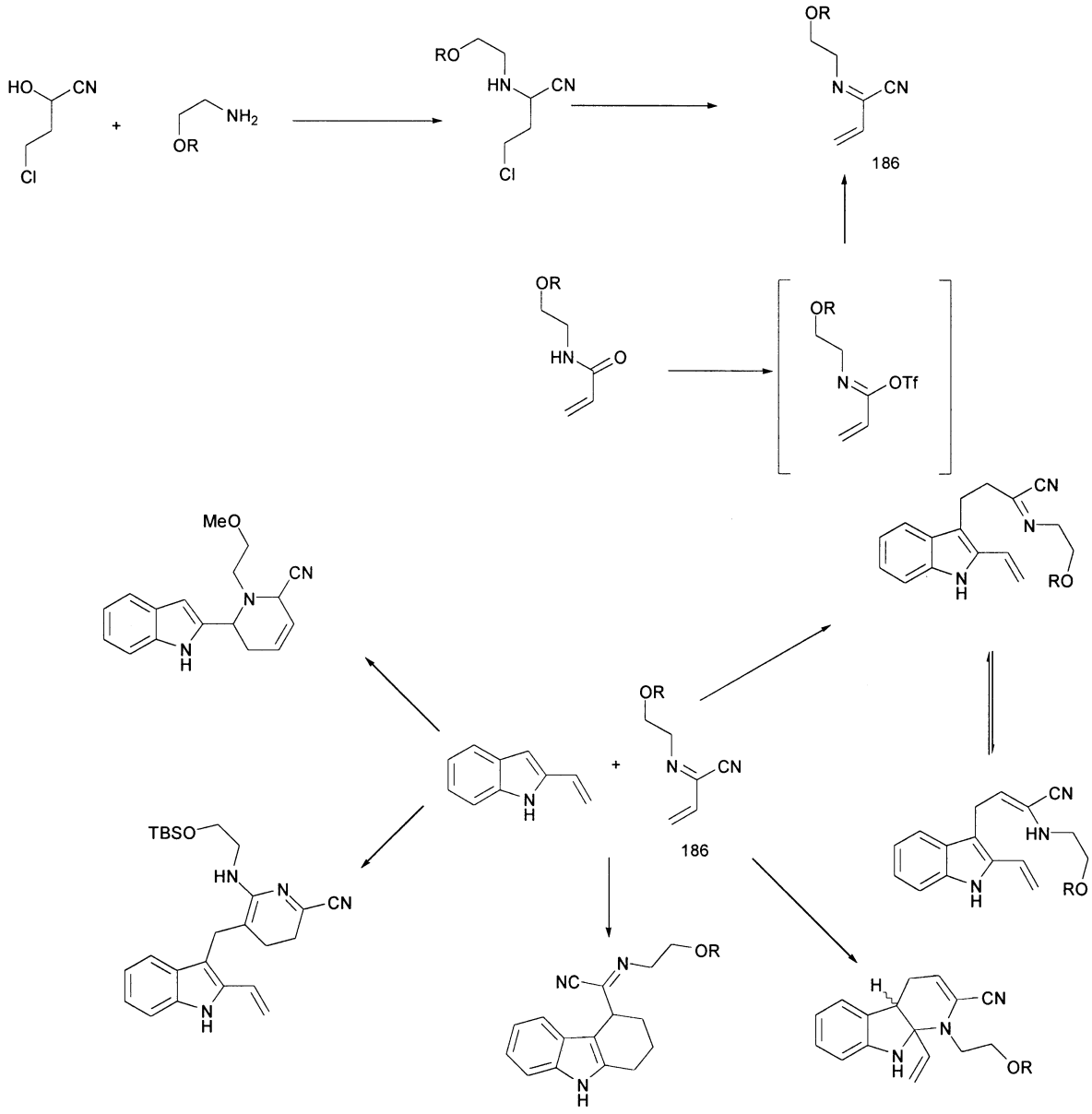
Scheme 41.


R1 = Me
Tf2O, LiCN
1.LiAlH4
2. acryloyl chloride, K2CO3
n =1, 2
R1 = Me
R1 = H, Me
178
179
Na2CO3
R= H, OMe, Me
Tf2O, DIPEA, -78°C
then LiCN
THF
180
110°C
toluene
181

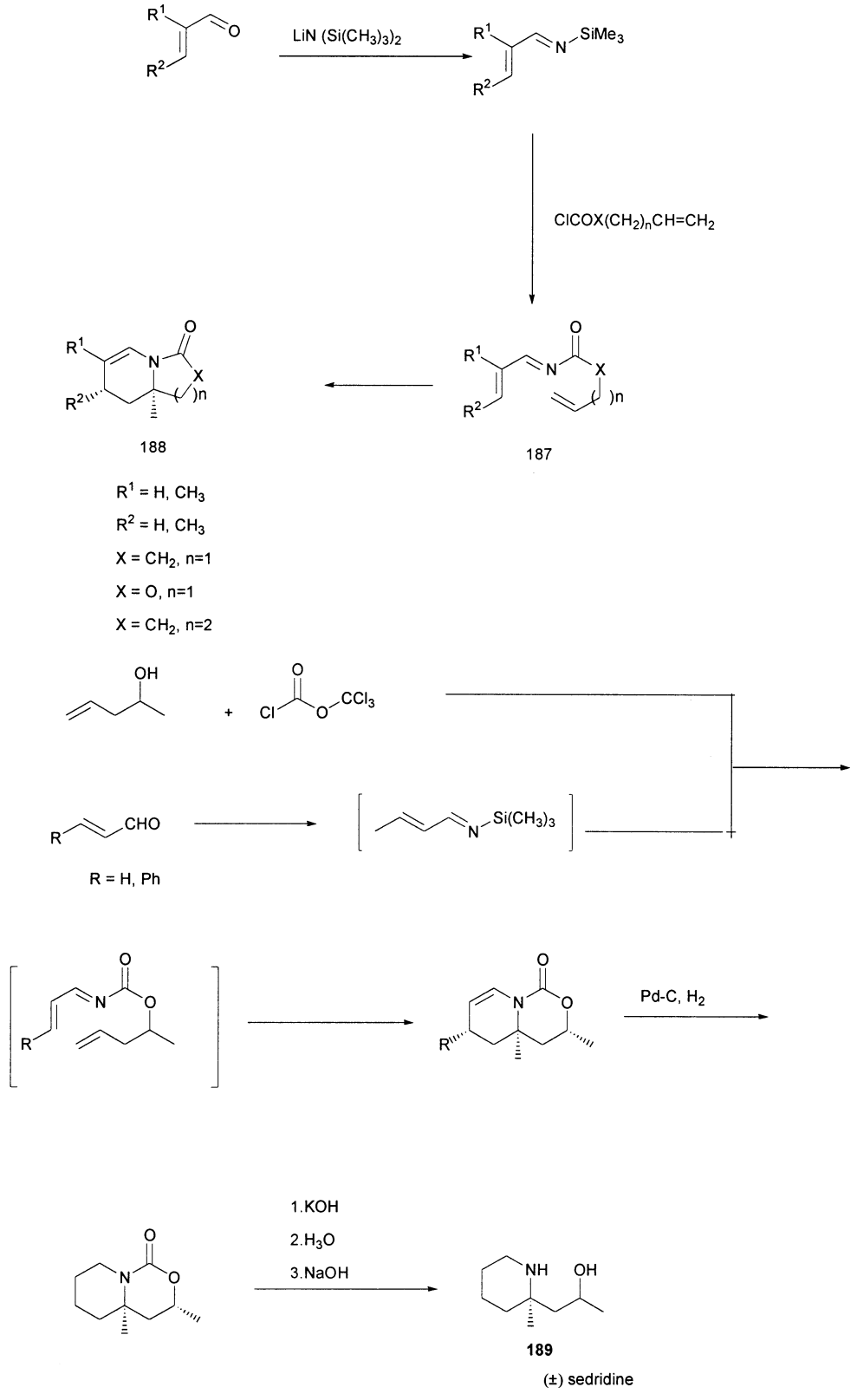
Scheme 42.


Tf2O, DIPEA
THF,-60°C
LiCN, 12-C-4, -60°C
63%
182
KCN,18-C-8
CH2Cl2, TFAA, -60°C, 64%
TMSCN,CH2Cl2
SnCl4 (cat)
R=CN,H
R = H, COCF3
183
184
185
Pd (OAc)4
I2
R = H, COCF3

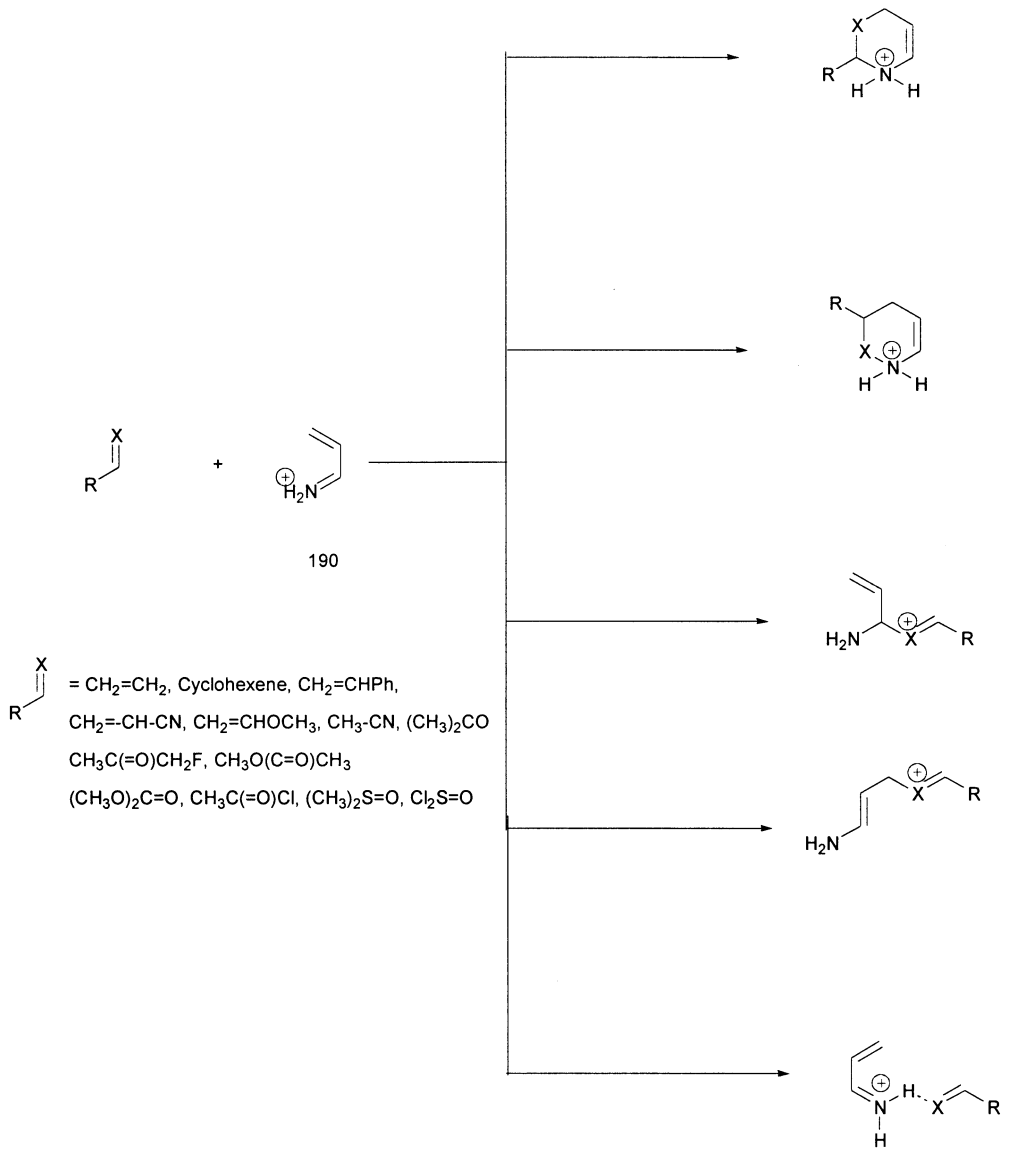
Scheme 43.


HO
CN
Cl
NH2
OR
RO
HN
CN
Cl
OR
N
CN
186
OR
HN
O
OR
N
OTf
MeO
N
CN
N
H
CN
N
RO
N
H
OR
N
CN
186
CN
HN
N
RO
H
TBSO
HN
N
CN
N
H
NC
N
OR
N
H
H
CN
N
N
H
OR

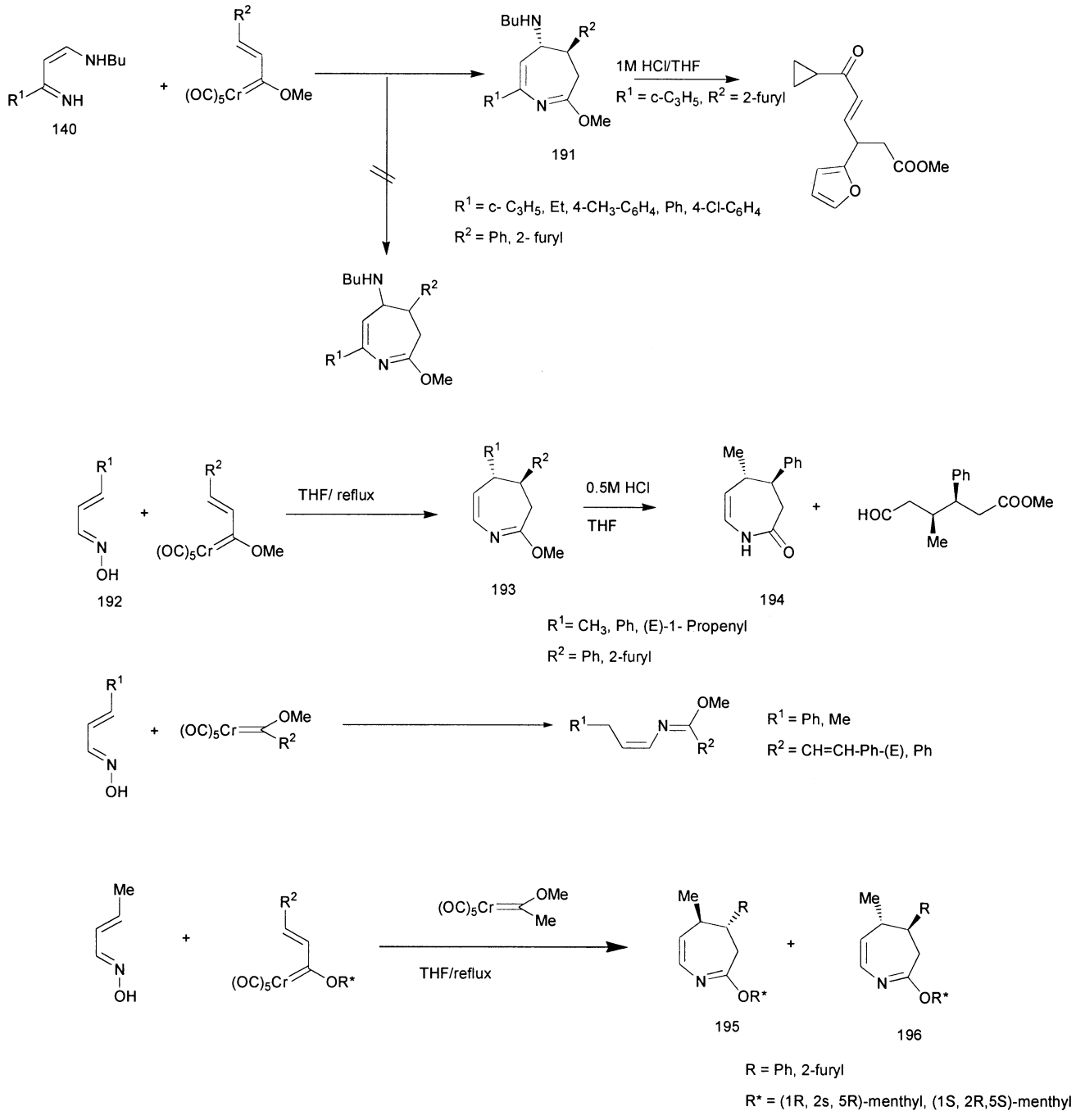
Scheme 44.


LiN (Si(CH3)3)2
SiMe3
ClCOX(CH2)nCH=CH2
188
187
R1 = H, CH3
R2 = H, CH3
X = CH2, n=1
X = O, n=1
X = CH2, n=2
OH
CCl3
CHO
R = H, Ph
Si(CH3)3
Pd-C, H2
1.KOH
2.H3O
3.NaOH
NH
OH
189
(±) sedridine

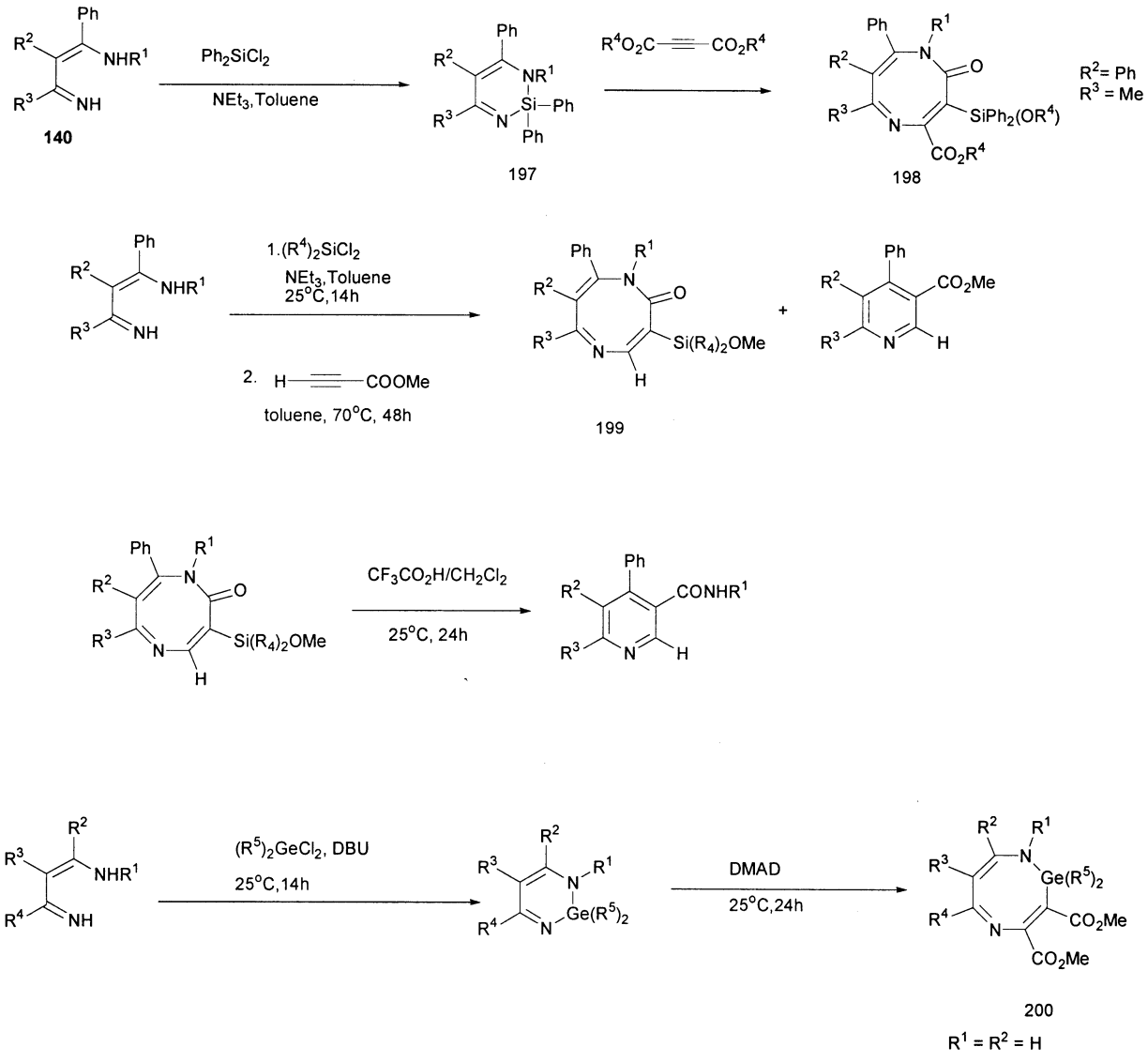
Scheme 45.


X
R
+
H2N
190
= CH2=CH2, Cyclohexene, CH2=CHPh,
CH2=-CH-CN, CH2=CHOCH3, CH3-CN, (CH3)2CO
CH3C(=O)CH2F, CH3O(C=O)CH3
(CH3O)2C=O, CH3C(=O)Cl, (CH3)2S=O, Cl2S=O
N
H
H2N

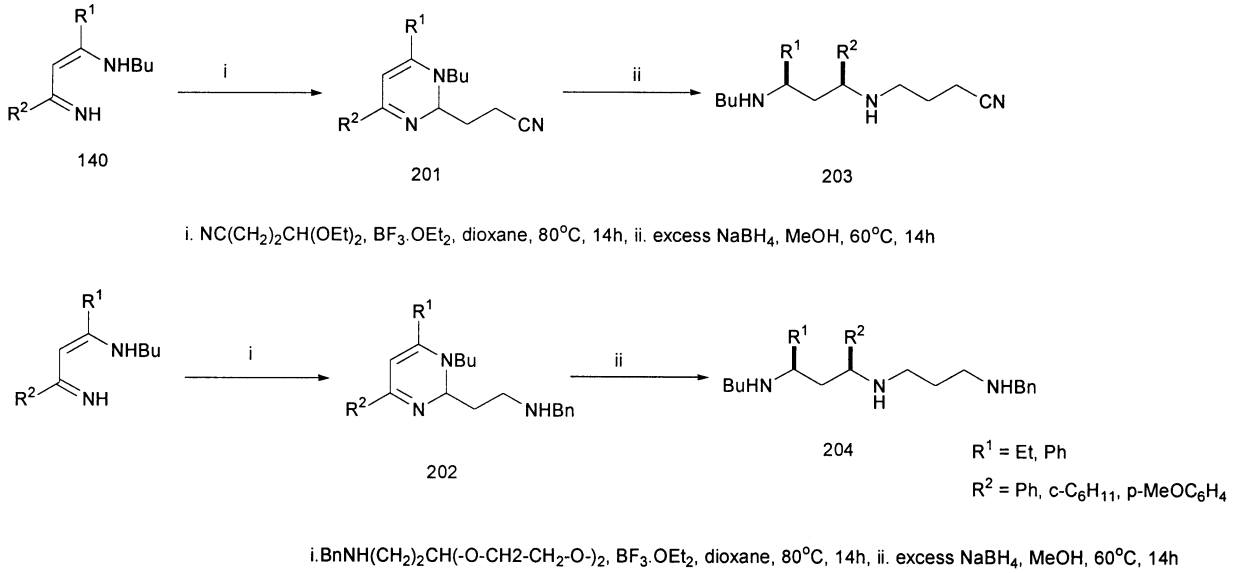
Scheme 46.


NHBu
NH
140
(OC)5Cr
OMe
BuHN
191
1M HCl/THF
R1 = c-C3H5, R2 = 2-furyl
COOMe
R1 = c- C3H5, Et, 4-CH3-C6H4, Ph, 4-Cl-C6H4
R2 = Ph, 2- furyl
THF/ reflux
0.5M HCl
THF
192
193
194
HOC
R1= CH3, Ph, (E)-1- Propenyl
R2 = Ph, 2-furyl
R1 = Ph, Me
R2 = CH=CH-Ph-(E), Ph
THF/reflux
OR*
195
196
R = Ph, 2-furyl
R* = (1R, 2s, 5R)-menthyl, (1S, 2R,5S)-menthyl

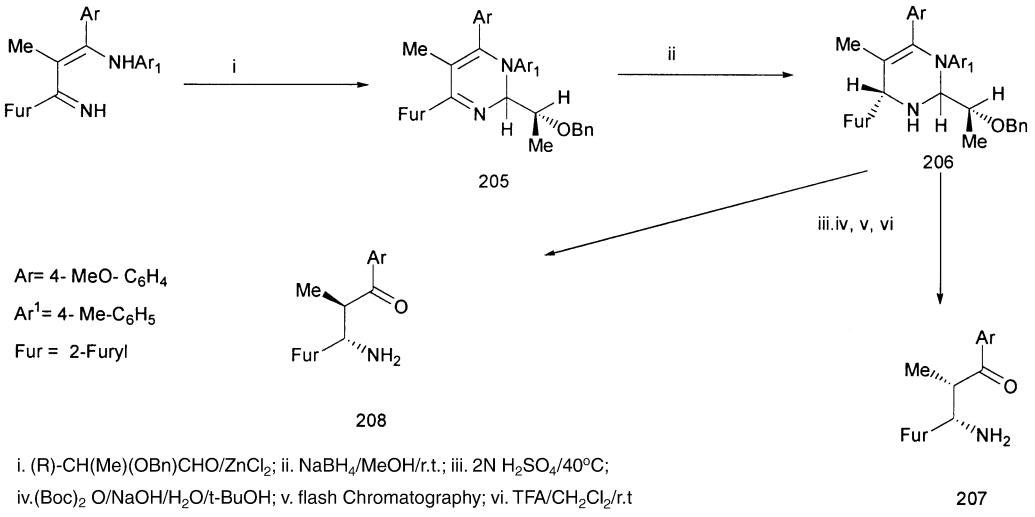
Scheme 47.



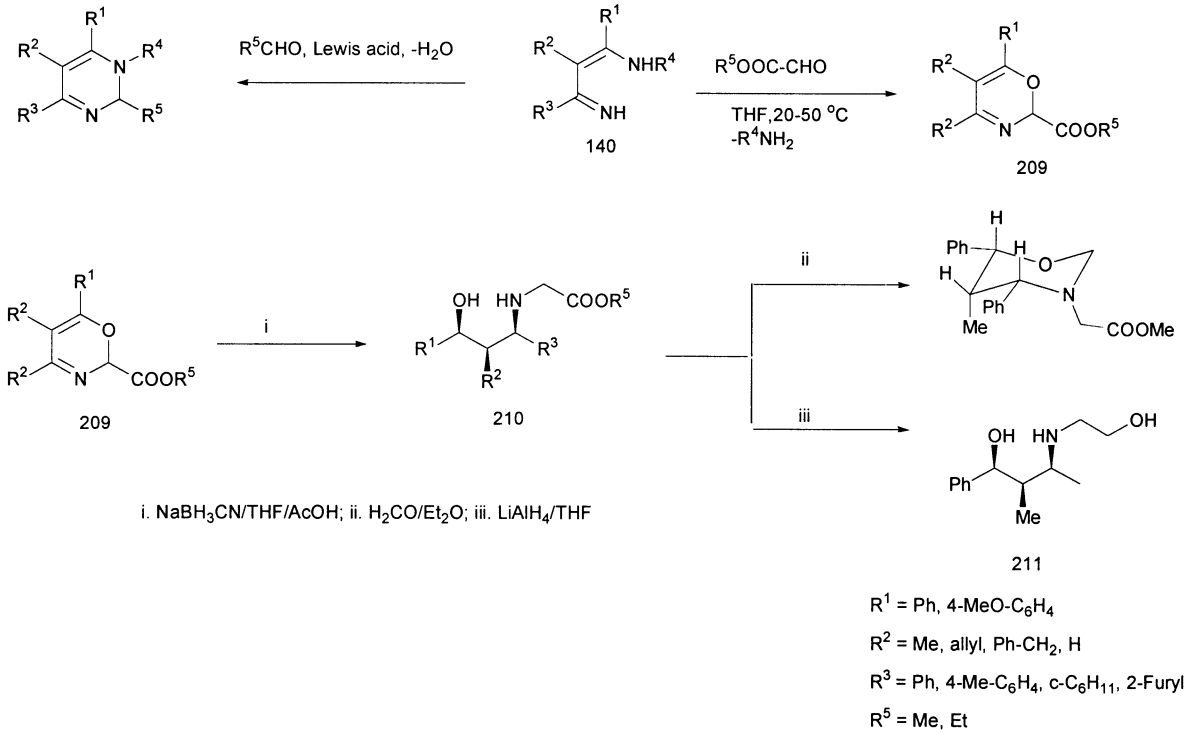
Scheme 48.



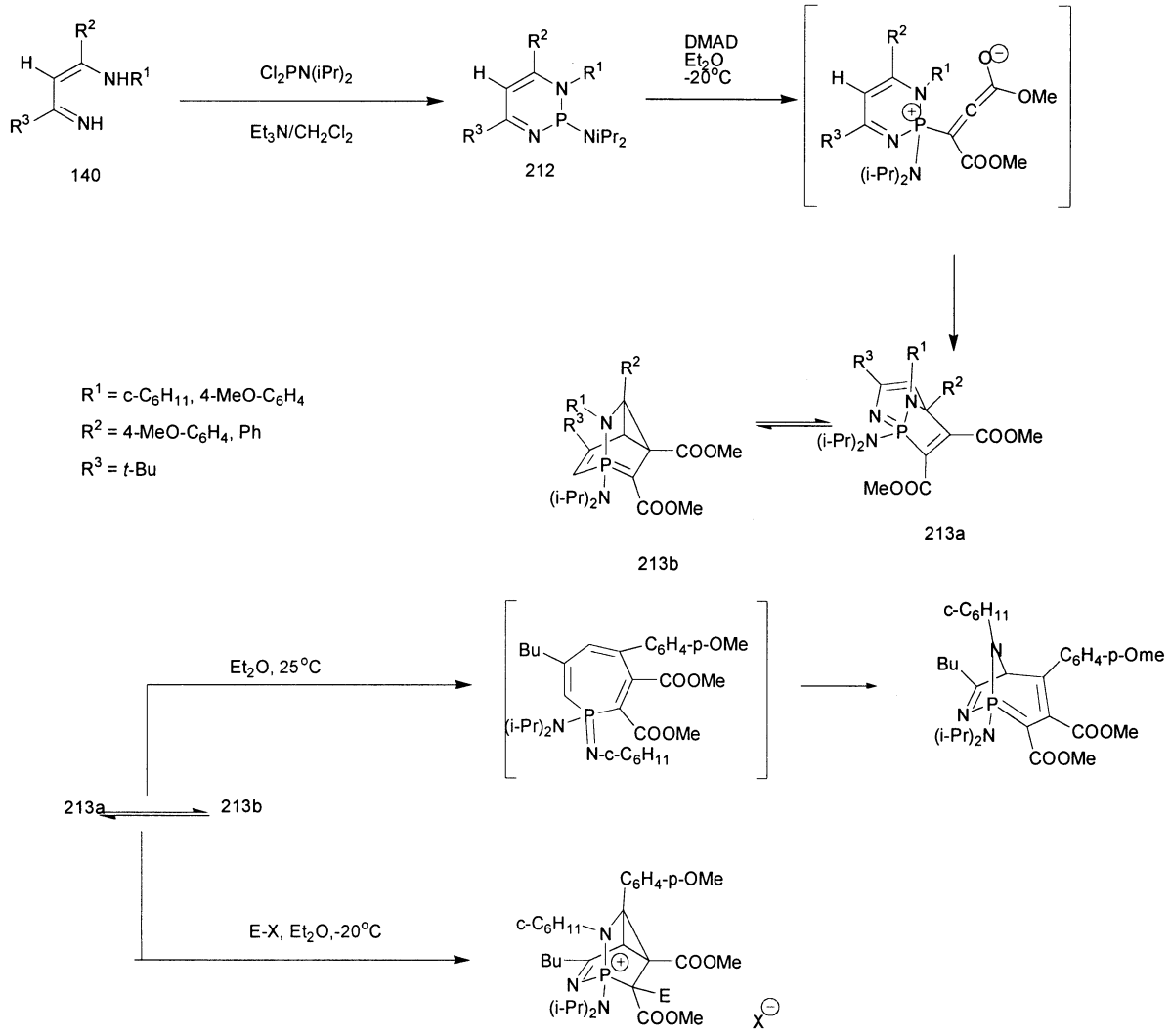
Scheme 49.



Scheme 50.



Scheme 51.



Scheme 52.

Kimpe and co-workers reported the base-induced dehydrochlorination of chloroaldimines (**263**,**265**,**267**) for the preparation of 2-azadienes (**264**,**266**,**268**,**269**) in good yields[81] (Scheme 66).

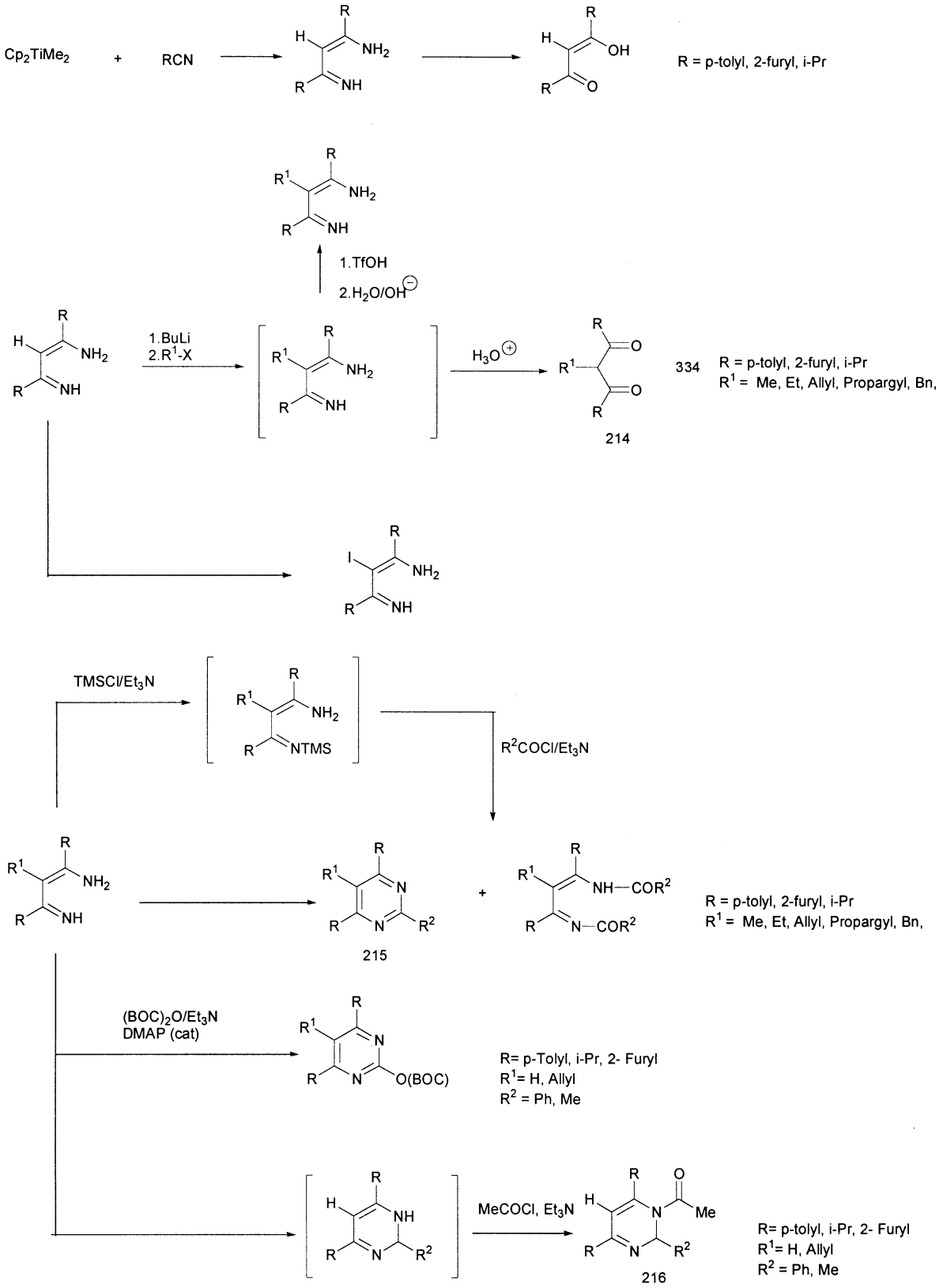
3.1.3. Miscellaneous reactions. Gilchrist et al. have reported that the *N*-arylidenedehydroamino methylester (**270**) can be generated either by reacting thiazolidine methylester with silver carbonate and DBU or by the dehydration of the Schiff base of serine methyl ester with *N*,*N*′-carbonyldiimidazole and triethylamine. These short-lived compounds undergo Diels–Alder reactions with a range of dienophiles.[82] Mariano and co-workers devised methodology to prepare the 2-azadienes **271**, starting from simple starting materials, a powerful synthetic intermediate for the intramolecular Diels–Alder reactions[83] (Scheme 67).

Enamino esters/amide (**272**,**273**) have been reacted with a number of imidoyl halides and *N*,*N*-dimethylformamide dimethylacetal to prepare 2-azadienes (**274**–**281**) in moderate to excellent yields[84] (Scheme 68).

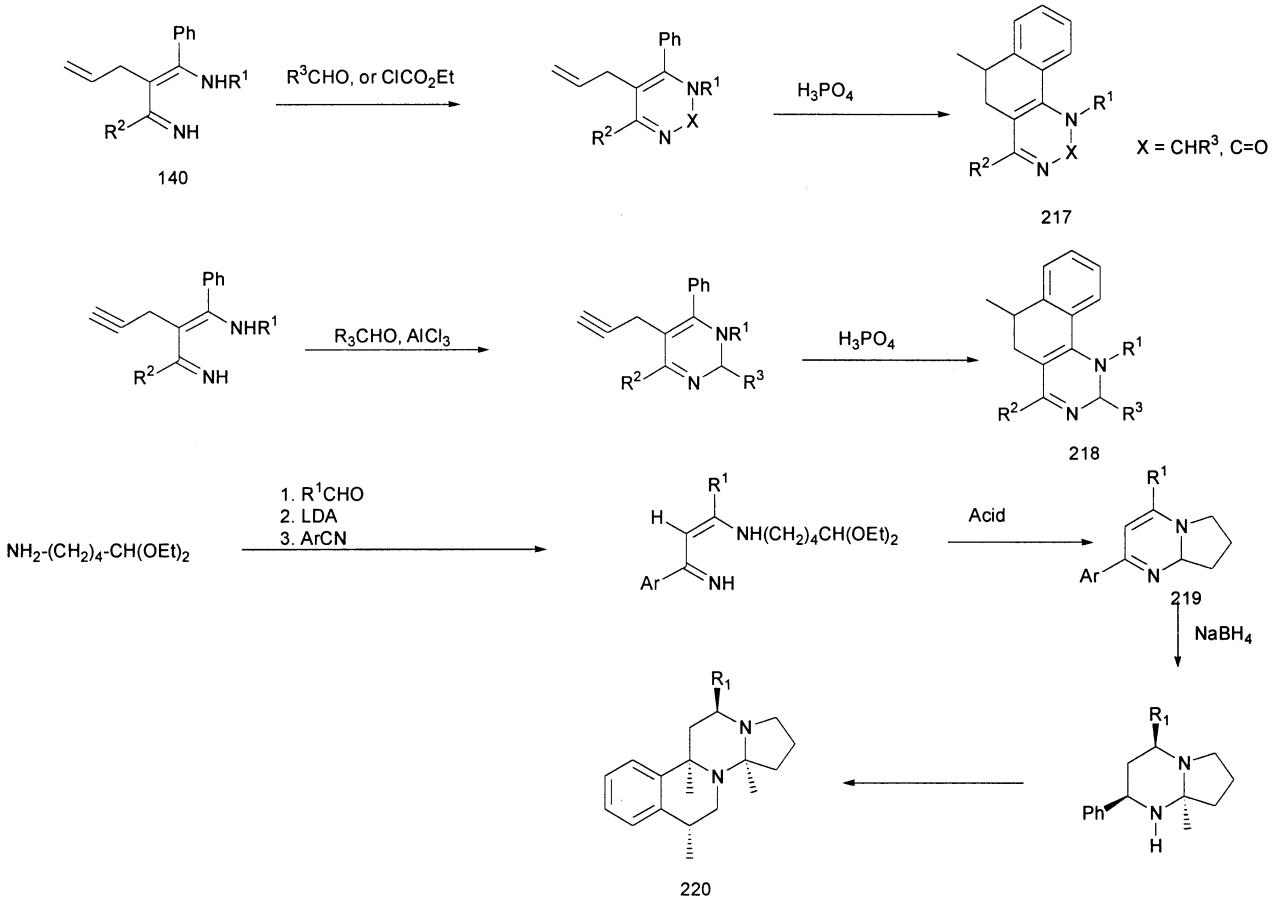
3.2. Cycloaddition reactions of 2-azabuta-1,3-dienes

3.2.1. Synthesis of five-membered rings. Balsamini et al. investigated the effects of the structure and geometry of the substituents on C-4 of 2-azadienes (**282**,**283**) by treating them with 4-nitrobenzonitrileoxide and diazomethane to obtain the 1,3-diolar adducts **284**–**288**. The two 1,3-dipoles behave very differently in terms of steric hindrance and electronic properties. The results of these investigations are summarised in Scheme 69. The role of the 3-carbomethoxy substituent in determining the site selectivity observed in these reactions was examined in relation to the experimental results and to conformational models of some of the tested 2-azadienes dipolarophiles calculated on AM1 bases.[85]

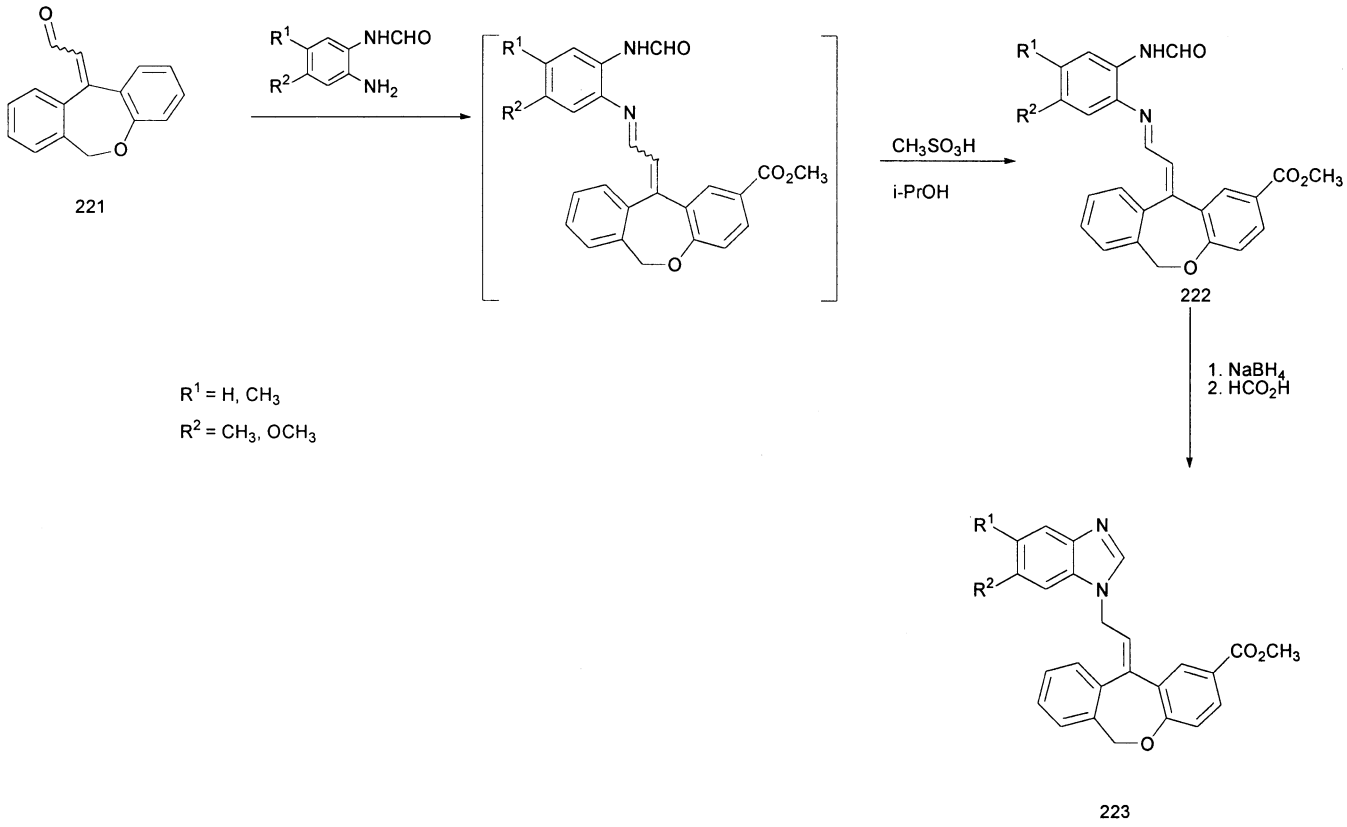
Bongini and Panunzio's group developed a stereoselective route for the conversion of 2-azadienes (**289**) to chiral 3,4,5-trisubstituted-1,5-dihydropyrrol-2-ones (**290**). This four-step transformation involves a stereoselective addition of a, Lewis


Cp2TiMe2
RCN
R = p-tolyl, 2-furyl, i-Pr
1.TfOH
2.H2O/OH
1.BuLi
2.R1-X
H3O
334
R = p-tolyl, 2-furyl, i-Pr
R1 = Me, Et, Allyl, Propargyl, Bn,
214
TMSCl/Et3N
R2COCl/Et3N
215
R = p-tolyl, 2-furyl, i-Pr
R1 = Me, Et, Allyl, Propargyl, Bn,
(BOC)2O/Et3N
DMAP (cat)
O(BOC)
R= p-Tolyl, i-Pr, 2- Furyl
R1= H, Allyl
R2 = Ph, Me
MeCOCl, Et3N
216
R= p-tolyl, i-Pr, 2- Furyl
R1= H, Allyl
R2 = Ph, Me

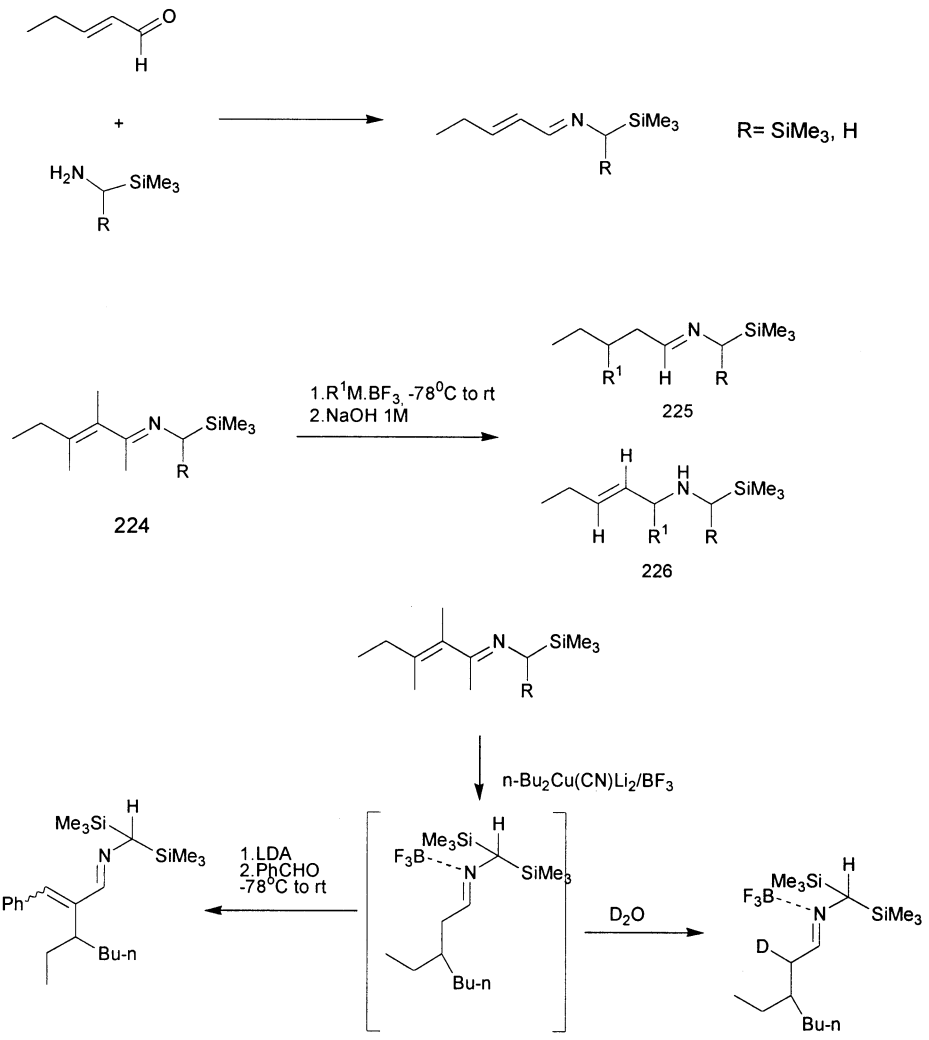
Scheme 53.



Scheme 54.



Scheme 55.



Scheme 56.

acid-catalysed, cyano group to an azadiene followed by intramolecular ring closure to yield the desired pyrrol-2-one (**290**) in satisfactory yields[86,87] (Scheme 70).

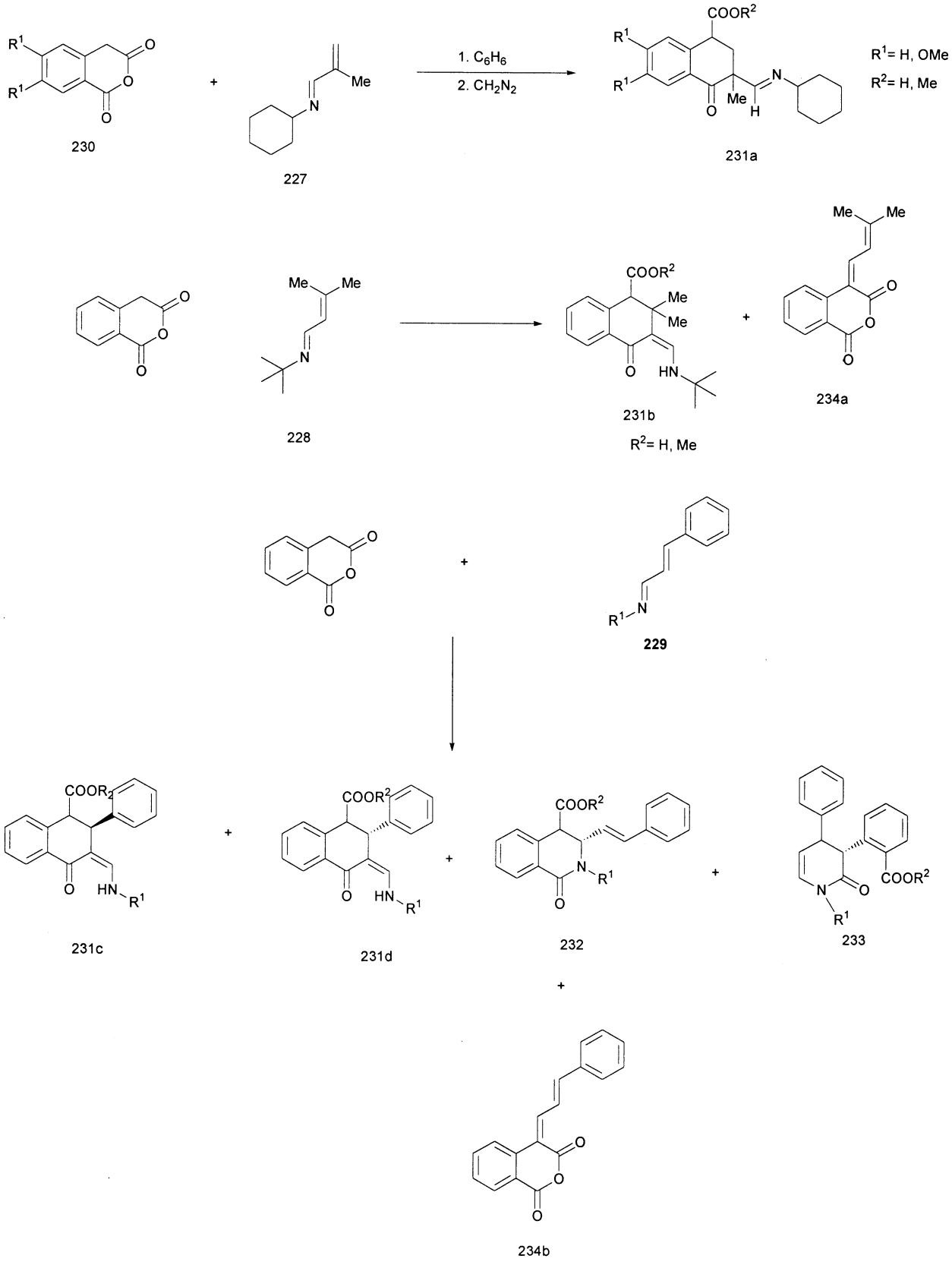
Barluenga et al. observed the formation of a diastereomeric mixture of 3-thiazolines (**292**) in >90% yields on heating (170°C) the 2-azadiene (**291**) with elemental sulfur without any solvent. The isomer ratio was improved using toluene as a solvent at a lower temperature (80°C). The mechanism involves oxidative addition of sulfur at α-position of the imine followed by a [1,5] proton shift and intramolecular attack of the thiol function[88] (Scheme 71).

Fleury and co-workers reported that 4-*sec*-amino-1,1-dicarbonitrile-2-aza-1,3-dienes (**293**–**295**) and their 1-methoxycarbonyl analogues on reaction with various nucleophilic reagents afforded good yields of a large variety of five-membered heterocyclic compounds (**296**–**303**)[89] (Scheme 72).

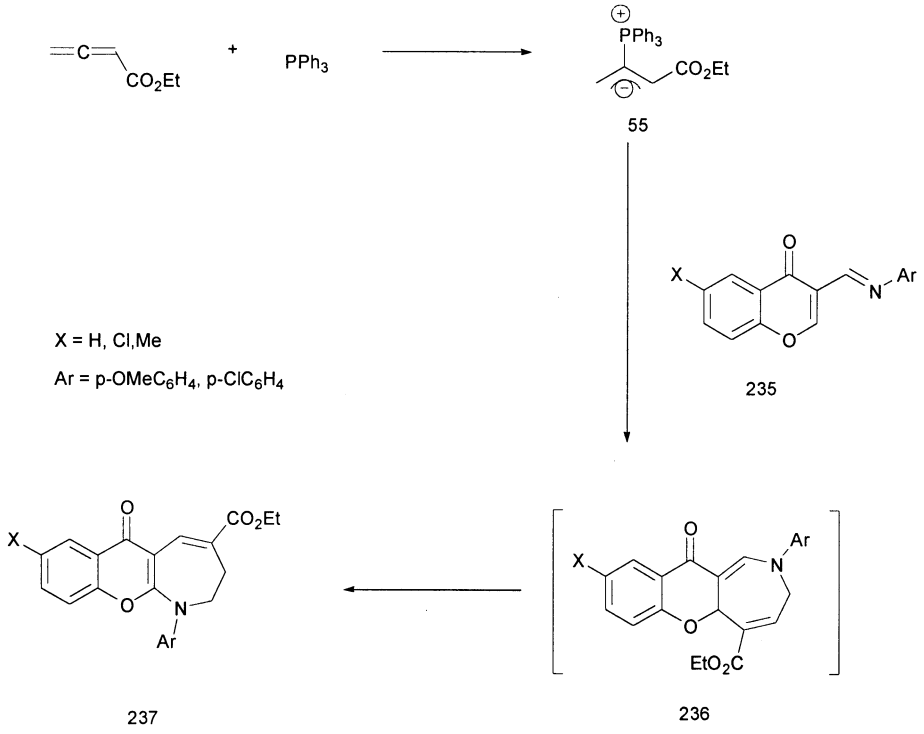
3.2.2. Synthesis of six-membered rings

3.2.2.1. Cycloadditions involving alkenes and alkynes. Palacios and co-workers exploited the inverse electron-demand hetero-Diels–Alder reactions of polysubstituted 2-azadienes (**304**) with strained olefins such as *trans*-cyclooctene and *cis*/*trans*-cyclooctadiene. In these reactions the *trans* ring juncture of the fused bicyclic compounds (**305**,**306**) indicated the maintainance of *E*-configuration of the starting olefins. It was observed that no reaction takes place when azadiene (**307**) is reacted with a less strained olefin such as norbornadiene at 120°C using toluene as solvent. The reported adducts (**308**) were, however obtained when the reactions were performed in a non-aqueous solvent such as diethyl ether ($LiClO_4$–Et_2O)[74] (Scheme 73).

Kascheres et al. investigated the reactions of 2-azadienes (**262**), having a potential leaving agent at the C-1 position, with electron-deficient dienophiles and reported that the 2-azadienes (**262a**, R=H) did not react with DEAD or TCNE. The azadiene


1. C6H6
2. CH2N2
R1= H, OMe
R2= H, Me
230
227
231a
228
231b
234a
229
231c
231d
232
233
234b

Scheme 57.



Scheme 58.

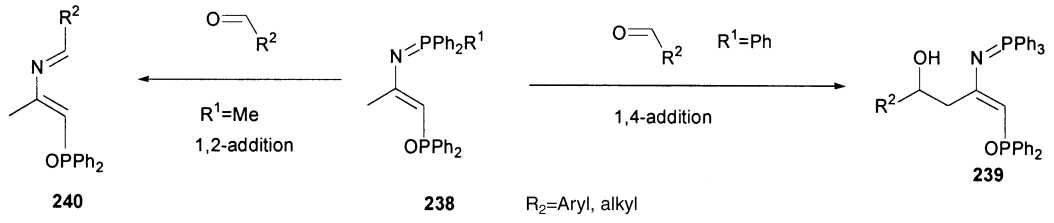
(**262b**, R=Me), however, reacted readily with TCNE at room temperature to afford the hetero-Diels–Alder adducts **309** and **310** in moderate yields[80] (30–80%, Scheme 74).

The cycloaddition reactions of 2-azadienes (**259**) with imide dienophiles[90] (**311**) in the presence of a chiral Lewis-acid catalyst have been reported to yield substituted 2-piperidones (**312**,**313**) via methanolysis of the primary adduct (Scheme 75). The activated 2-azadienes (**257**) have been shown to undergo [4+2] cycloaddition reactions with electron-deficient acetylenes and quinones to form pyridones **314** and fused pyridones (**316**,**317**), respectively.[91] The same group has also reported the cycloaddition of cyclic 2-azadienes (**260**) with various dienophiles.[79] The reaction of 2-azadienes (**260**) with maleic anhydride has been reported to form a mixture (1:1) of *endo* and *exo* Diels–Alder adducts (**318**,**320**) which were hydrolysed to lactams (**319**,**321**). The reactions with other dienophiles resulted in a variable mixture of *endo*/*exo* cycloadducts (**322**,**323**, Scheme 75).

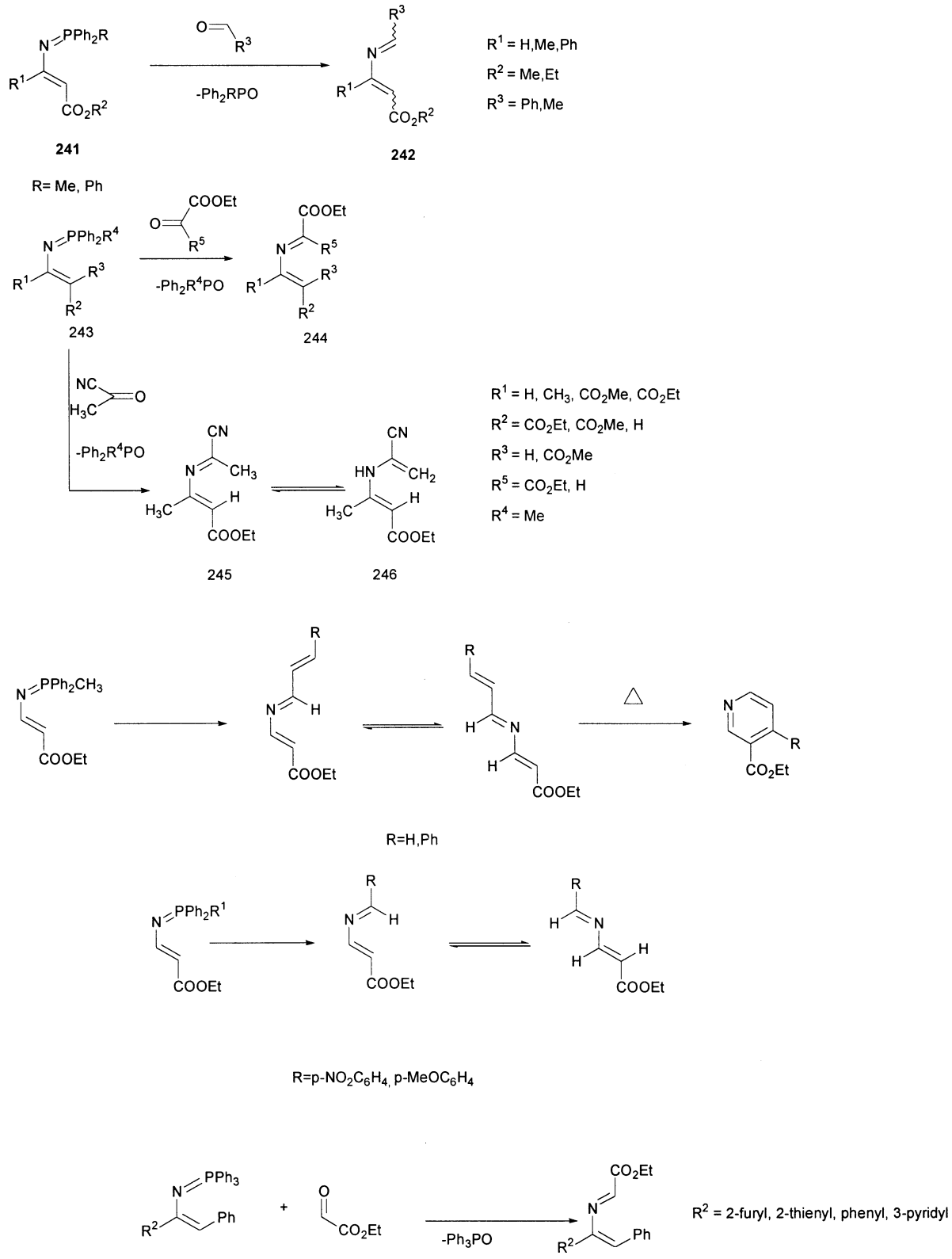
Ghosez et al. investigated the reactions of silyloxy-2-azadienes (**259**) with oxazolines **324** in the presence of methyloxirane and trimethylsilyl triflate and isolated a mixture of *endo*/*exo* [4+2] cycloadducts either as such or in their hydrolysed form **325**[92] (Scheme 76).

Fillion and co-workers reported that the regiospecific Diels–Alder cycloaddition reactions of the 2-azadienes (**326**) with 2-or 3-bromo-5-substituted naphthaquinones (R^3=OH, OMe, OAc) result in the synthesis of the corresponding 2-azaanthraquinon-3-ones (**327**) and (**328**) in moderate to excellent yields. These results indicate that the bromine atom exerts a strong regiochemical control in the cycloadditions compared to the 5-substituent, despite the directing effect of the 5-hydroxy or the 5-methoxy group (Scheme 77).[93]

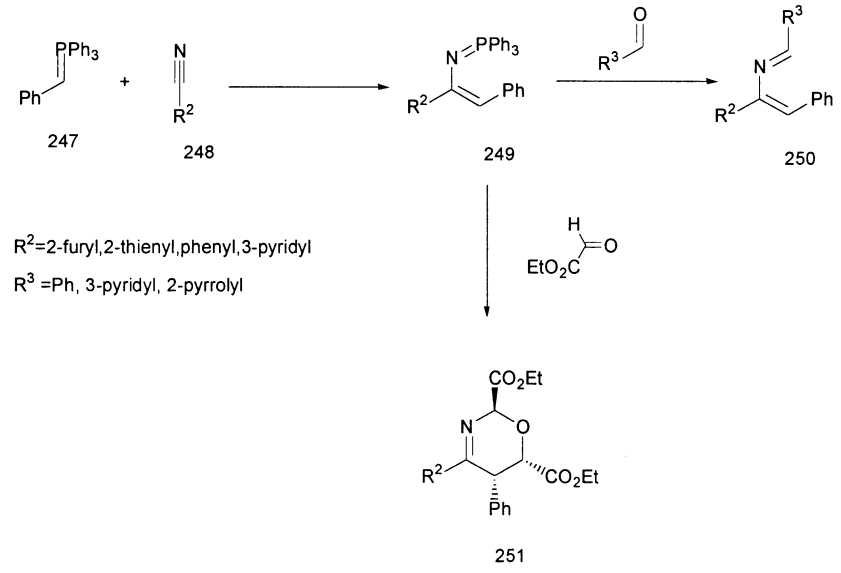
The reactions of 2-aza-4-thia-butadienes (**329**) have been investigated with a variety of dienophiles; with dimethyl acetylene-dicarboxylate, methyl acrylate, (*E*)-β-nitrostyrene, diethyl fumarate, diethyl maleate and NPM moderate to excellent yields of the corresponding [4+2] cycloadducts (**330**–**332**), mostly as single stereo-/regioisomers[94] were obtained (Scheme 78).



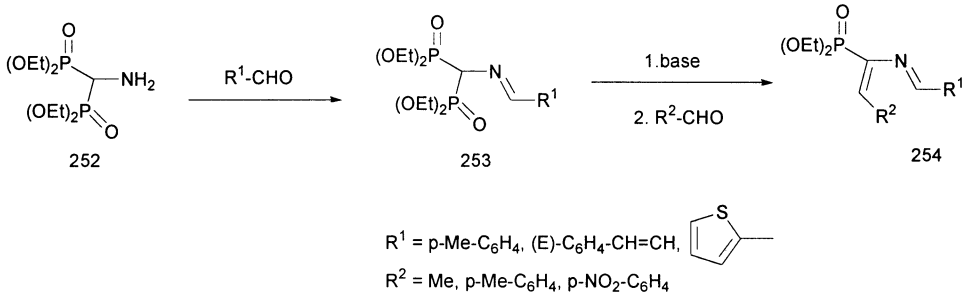
Scheme 59.


R1 = H,Me,Ph
R2 = Me,Et
R3 = Ph,Me
-Ph2RPO
241
242
R= Me, Ph
-Ph2R4PO
243
244
R1 = H, CH3, CO2Me, CO2Et
R2 = CO2Et, CO2Me, H
R3 = H, CO2Me
R5 = CO2Et, H
R4 = Me
245
246
R=H,Ph
R=p-NO2C6H4, p-MeOC6H4
-Ph3PO
R2 = 2-furyl, 2-thienyl, phenyl, 3-pyridyl

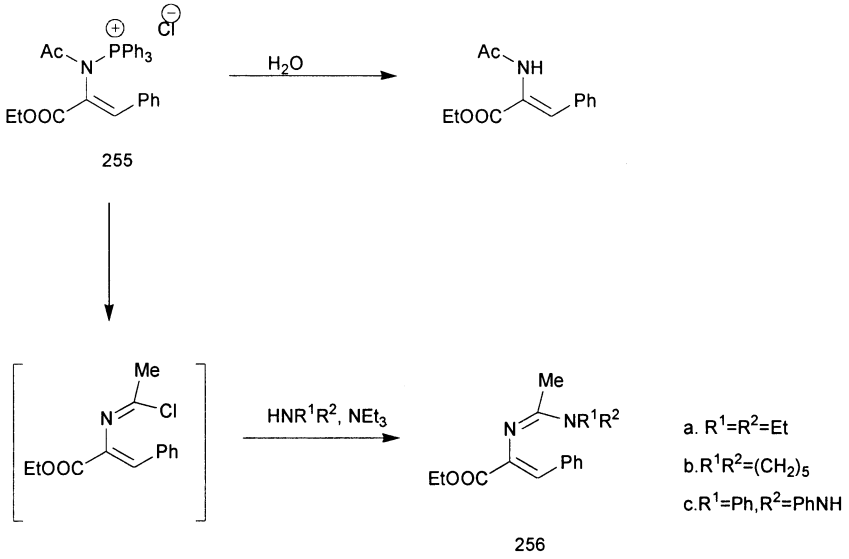
Scheme 60.



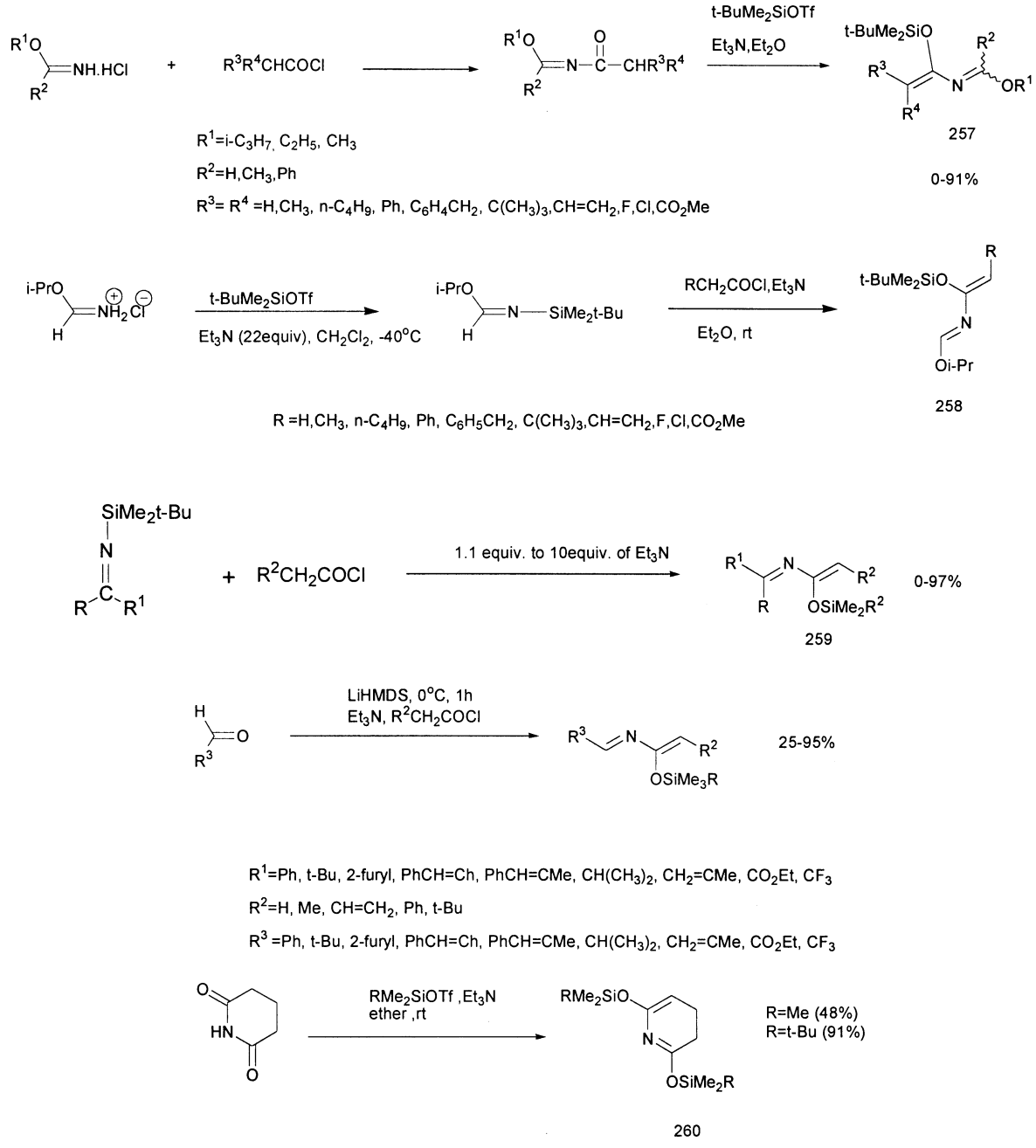
Scheme 61.



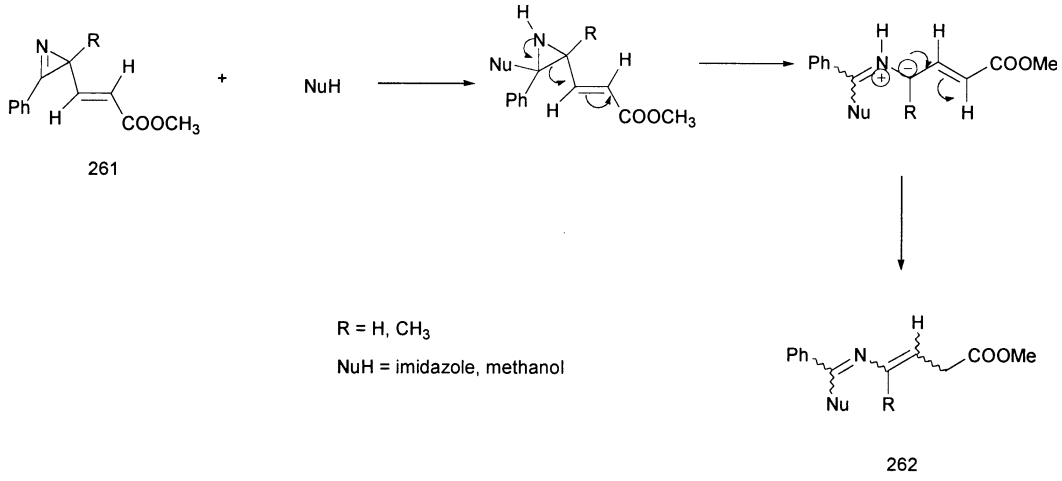
Scheme 62.



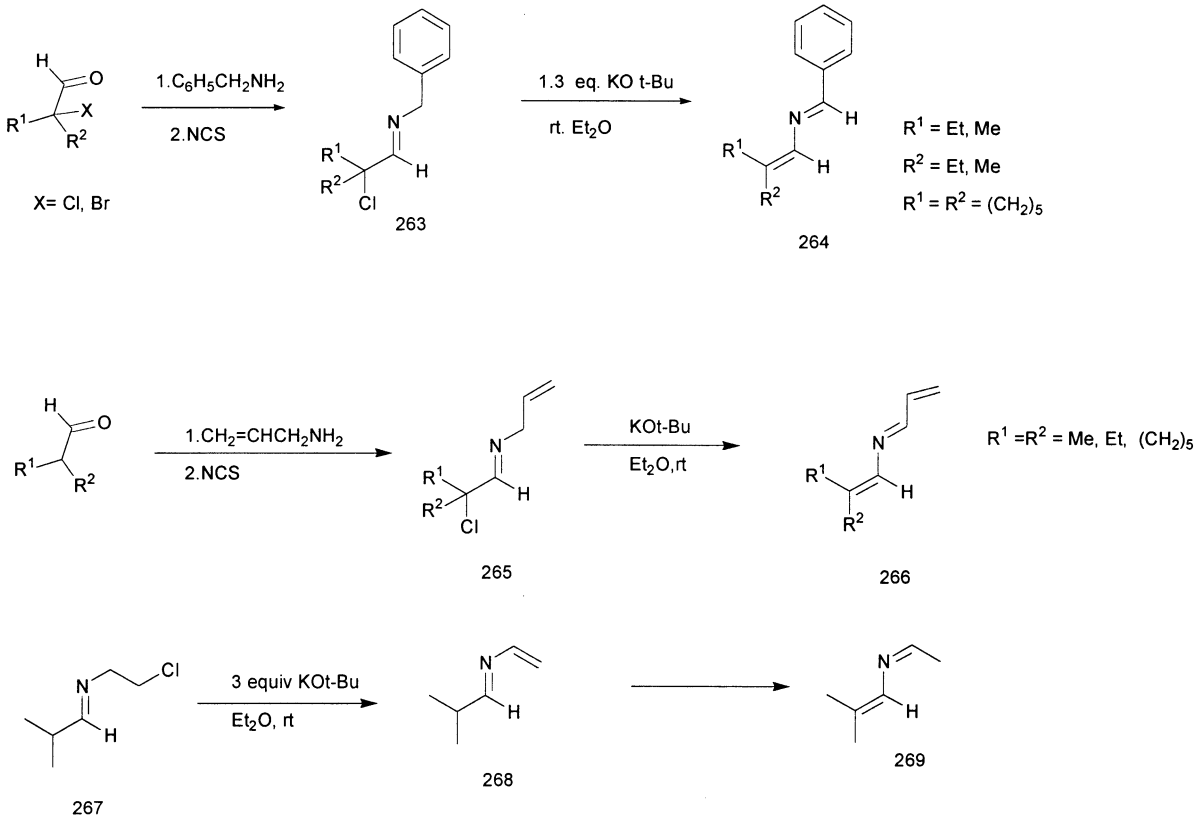
Scheme 63.


t-BuMe2SiOTf
Et3N,Et2O
257
0-91%
R1=i-C3H7, C2H5, CH3
R2=H,CH3,Ph
R3= R4 =H,CH3, n-C4H9, Ph, C6H4CH2, C(CH3)3,CH=CH2,F,Cl,CO2Me
t-BuMe2SiOTf
Et3N (22equiv), CH2Cl2, -40°C
RCH2COCl,Et3N
Et2O, rt
258
R =H,CH3, n-C4H9, Ph, C6H5CH2, C(CH3)3,CH=CH2,F,Cl,CO2Me
1.1 equiv. to 10equiv. of Et3N
259
0-97%
LiHMDS, 0°C, 1h
Et3N, R2CH2COCl
25-95%
R1=Ph, t-Bu, 2-furyl, PhCH=Ch, PhCH=CMe, CH(CH3)2, CH2=CMe, CO2Et, CF3
R2=H, Me, CH=CH2, Ph, t-Bu
R3 =Ph, t-Bu, 2-furyl, PhCH=Ch, PhCH=CMe, CH(CH3)2, CH2=CMe, CO2Et, CF3
RMe2SiOTf ,Et3N
ether ,rt
R=Me (48%)
R=t-Bu (91%)
260

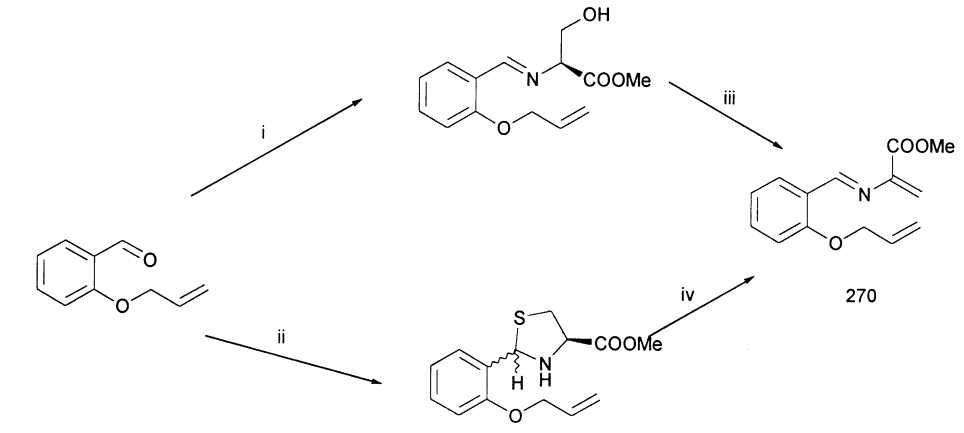
Scheme 64.



Scheme 65.

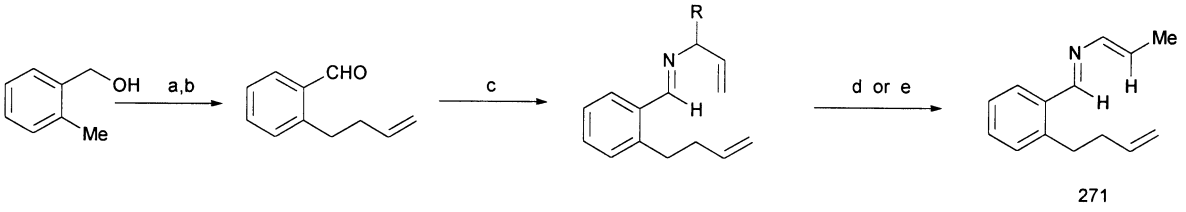


Scheme 66.



i. L-serine methyl ester HCl: ii: + L-cysteine methyl ester HCl, $KHCO_3$;

iii. N,N′-carbonyldiimidazole, Et_3N. iv: Ag_2CO_3, DBU.



a. n-BuLi,THF/CH_2-CH=CH-CH_2Br; b. PCC, CH_2Cl_2; c. C_6H_6, 3A° mol.Sieves;

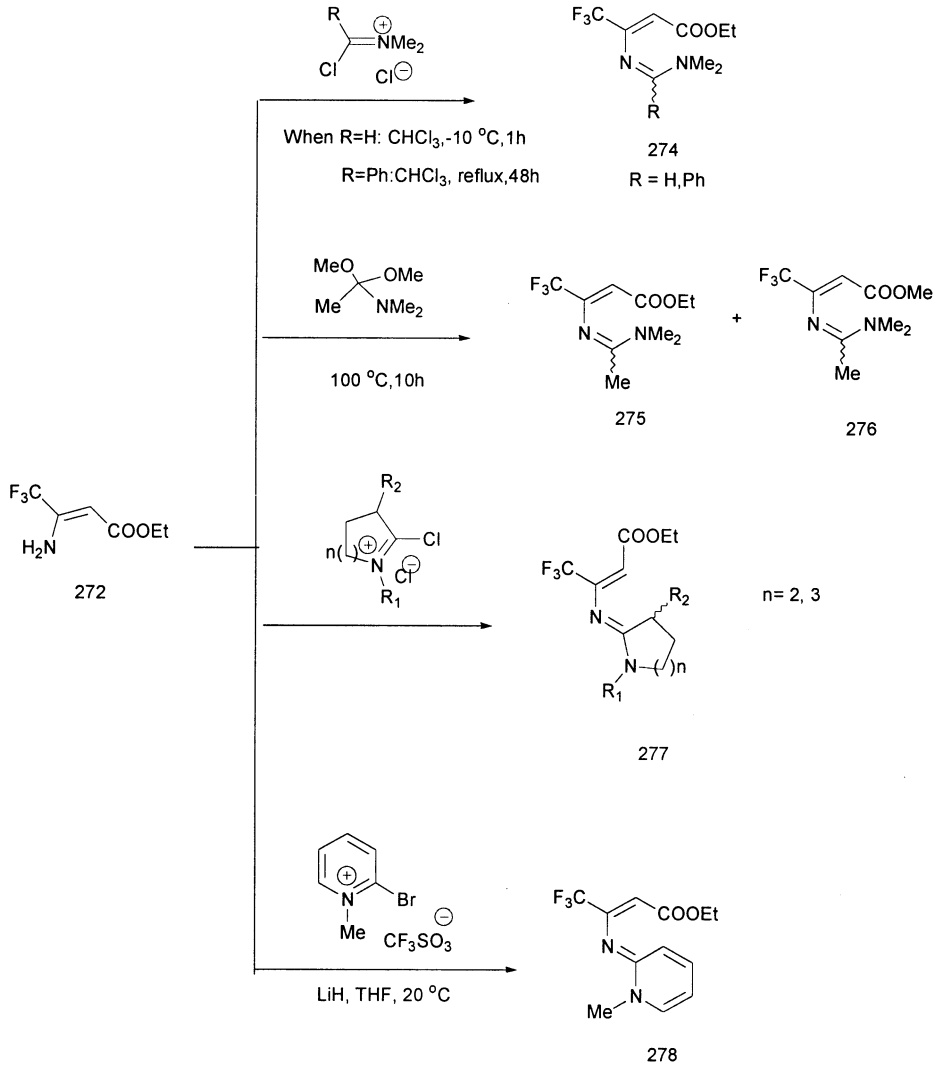
d CsF,THF,0.4equiv.18-crown-6,25°C, 8h;e. KOt-Bu, THF, 18-crown-6,-30 °C, 3min.

Scheme 67.

Balsamini and co-workers reported [4+2] cycloaddition reactions of the electron-poor and electron-neutral 2-azadienes (**282**) with some of the most potent electron-poor dienophiles, such as dimethyl acetylenedicarboxylate (DMAD) and tetracyanoethylene (TCNE) to obtain **333–335**. No reaction was observed, however, with other electron-poor dienophiles, such as methyl *propynonate*, methyl acrylate and acrolein, or with electron-rich dienophiles such as ethyl vinyl ether[95] (Scheme 79). These workers developed a simple methodology for the synthesis of the 1-phenyl-1-ethoxy-2-azadiene (**336**) and carried out its cycloaddition with TCNE, DMAD and ethyl propynoate. Its reaction with 4-PTAD resulted in excellent yields of the [4+2] cycloadduct, whereas with TCNE, the [4+2] cycloadduct **337** initially formed underwent elimination of HCN under chromatographic conditions to yield a tricyano-substituted 1,2-dihydropyridine **338**.[95] The reaction of 2-azadiene (**336**) with 2 equiv. of DMAD resulted in a mixture of products consisting of 2-phenyl-3,4,6-tricarbomethoxypyridine (**339**) and tricarbomethoxy-2-aza-1,3,5-triene (**340**) which on heating at 160°C for 20 h was converted to 6-phenyl-2,3,4-tricarbomethoxypyridine (**341**). A similar reaction was observed on treatment of azadiene (**336**) with ethylpropynoate yielding 2-phenyl-3-carboethoxy-6-carbomethoxypyridine (**342** 20%) and, unexpectedly, the 2-azatriene (**343**) which, on heating at 160°C without solvent, was transformed to 2-phenyl-3,6-dicarbomethoxypyridine (**344**) in 40% yield (Scheme 79).

The generation of the 2-azadiene (**345a**; R=H) from thiazolidines in the presence of a large excess of but-3-en-2-one led to the formation of three compounds (**346–348**) in an overall yield of 76%.[82] Compounds (**347**) and (**348**) are the products which could result from prototropy (imine–enamine tautomerism) of *endo* and *exo* cycloadducts. The origin of compounds (**346**) could not be established. The more electron-rich azadiene (**345b**; R=NMe_2) underwent a Diels–Alder reaction with but-3-en-2-one to form (**349**) and/or (**350**), depending upon the amount of silver carbonate used during the generation of **345b** (Scheme 80).

In an attempt to catalyse the intramolecular Diels–Alder reaction of (**270**), addition of aluminum chloride led to the isolation of the pyridines (**351**) probably formed by dimerisation of **270** followed by aromatisation. The interesting feature of this reaction is that the $AlCl_3$ apparently promotes the dimerisation by the Diels–Alder reaction in which regioselectivity is opposite to that of the uncatalysed process[82] (Scheme 81).



Scheme 68.

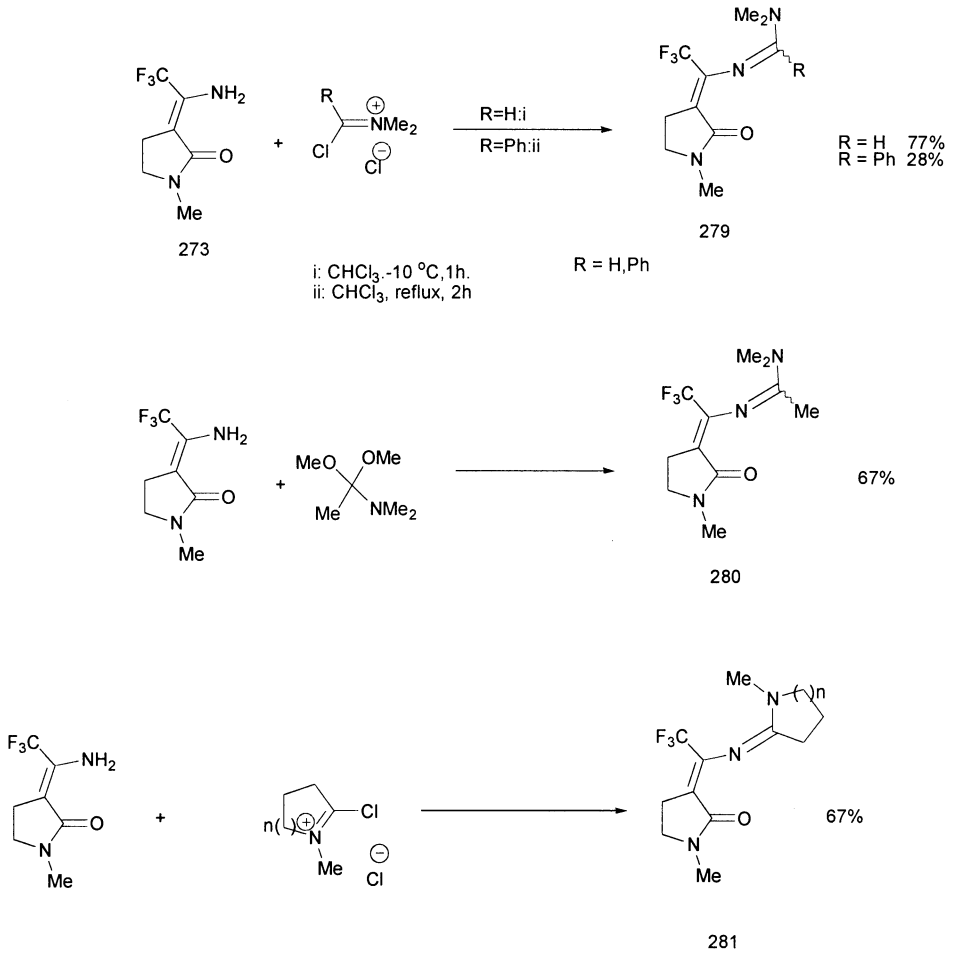
A peculiar characteristic of the 2*H*-1,4-oxazin-2-one skeleton, which contains a 2-azadiene, lactone and chlorimine function, has been described by Hoornaert and co-workers[96] who studied the behaviour of a selection of 3-substituted 5-choloro-6-methyl-2*H*-oxazin-2-ones (**352**) towards different acetylenic compounds and described the formation of the polyfunctionalised pyridines (**353**,**354**) as a mixture of regioisomers (Scheme 82).

Mariano and co-workers developed a simple method for the preparation of the azadienes (**271**) and have successfully utilised these compounds in intramolecular Diels–Alder reactions for synthesis of the fused piperidines (**355**,**356**, Scheme 83) from simple starting materials.[83a]

In order to test the synthetic utility of the 2-azadienes (**250**) formed by aza-Wittig reactions of phosphazenes (**249**) with aldehydes, their electrocyclic ring closures were explored. The 2-azadienes (**250**) which can be isolated under mild conditions on heating afforded high yields of isoquinoline derivatives (**357**, Scheme 84).[75,77]

Bouillon and co-workers have reported that photocyclisation of the 2-azadiene (**273**) resulted in the formation of the heterocycle (**358**) which could be explained by an initial [3,3] electrocyclic rearrangement in a conrotatory fashion, followed by two consecutive [1,3] sigmatropic migrations with retention of configuration[84] (Scheme 85).

3.2.2.2. Cycloadditions involving enamines. In recent years there have been several reports concerning the cycloaddition reactions of electron-deficient 2-azadienes with enamines leading to the simple and elegant methods for the construction of functionalised six-membered heterocycles such as pyridines, dihydropyridines and fused pyridines. The presence of electron-withdrawing groups in the acyclic 2-azadiene has been shown to accelerate its 4π participation in LUMO diene-controlled Diels–Alder reactions. Treatment of 2 equiv. of the phosphazenes (**241**), derived from triphenylphosphine and diphenylmethylphosphine, with 1 equiv. of aromatic aldehydes gave regioselectively good yields of *dihydropyridines*[72]



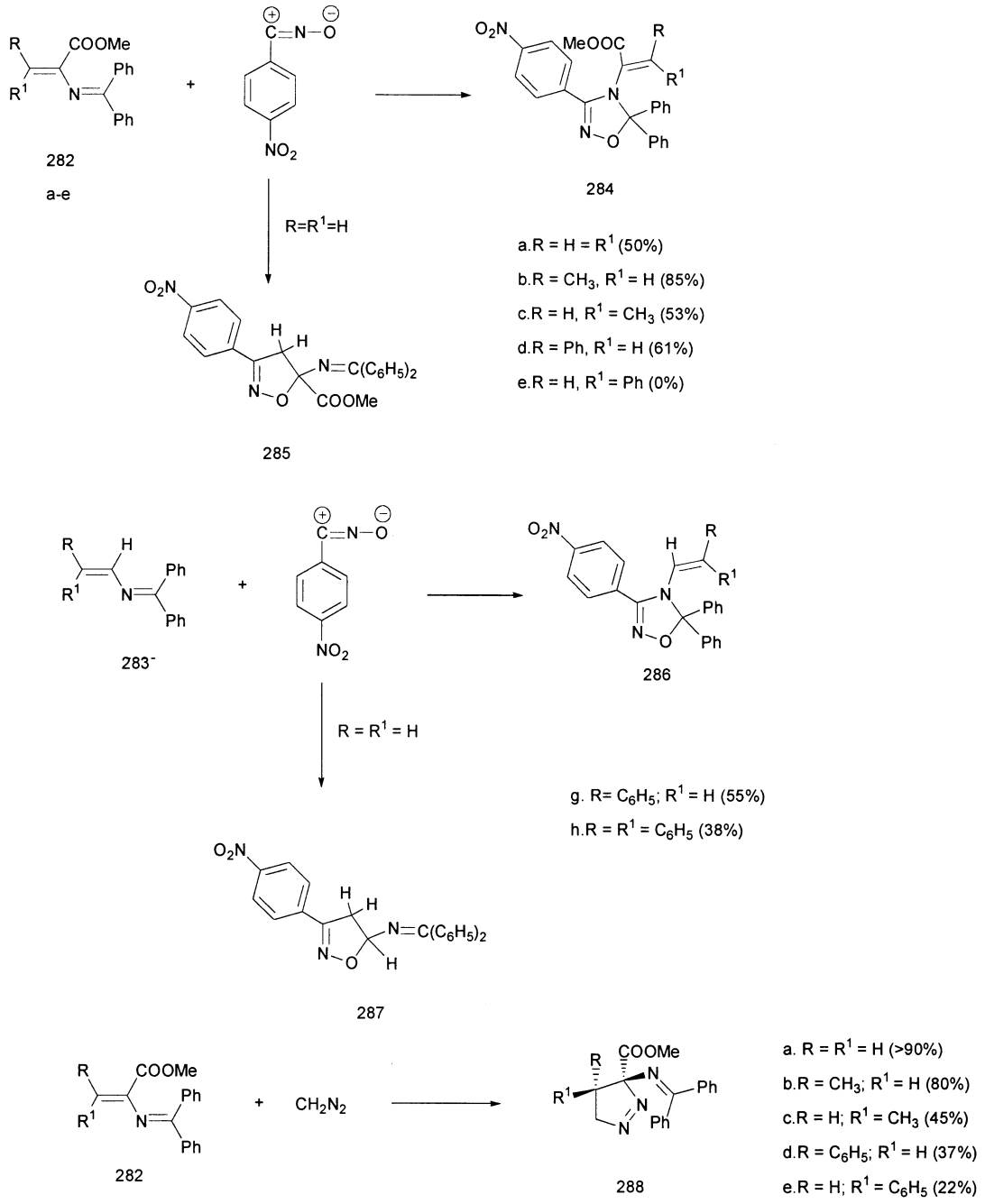
Scheme 68 (*continued*)

(**360**). These dihydropyridines are reportedly formed via the thermal elimination of iminephosphorane from the cycloadduct (**359**) which is in turn obtained by a [4+2] cycloaddition reaction of the 2-azadiene (**242**) with a second molecule of the phosphazene (**241**), a phosphorous-functionalised enamine.[73] The less nucleophilic enamines such as β-enaminoesters, which do not normally react with cyclic heterodienes, have been observed to undergo regioselective Diels–Alder reactions with the electron-deficient 2-azadienes (**242**) to provide the dihydropyridines (**361**) which, on oxidation, yield the functionalised pyridines **362**. The reactions of the azadiene (**242**) with more reactive enamines, pyrrolidinocyclohexanone/pyrrolidinocyclopentanone, at room temperature afforded fused dihydropyridine derivatives (**363**) that were oxidised to bicyclic pyridine compounds (**364**). A similar aza-Wittig reaction was then extended to conjugate phosphazenes (**365**). The reactions of these phosphazene (R^1=Me) with *p*-nitrobenzaldehyde at 45°C initially formed the 2-azadiene (**366**) which was used in situ in a [4+2] cycloaddition reaction with pyrrolidinecyclohexanone to obtain tricyclic phenanthridin-1-one derivatives (**367**). In contrast, a 9-azaanthracene compound (**368**) was obtained in reaction between phosphazene (**365**, R^1=Ph) and aldehydes in *o*-xylene at 160°C in a sealed tube (Scheme 86).

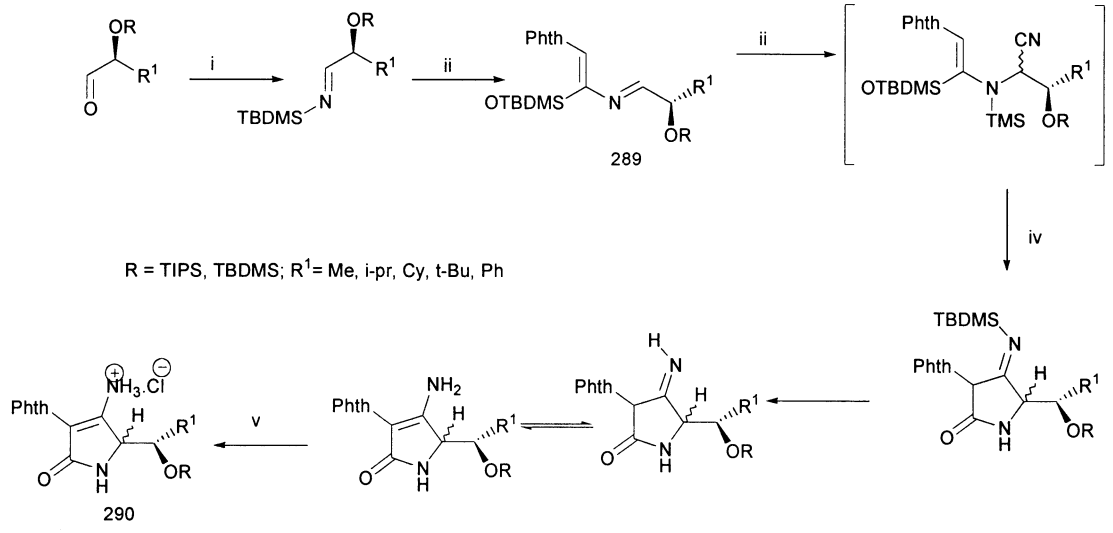
Another communication from the same group described the synthesis and reactivity of phosphazene (**240**), substituted with a phosphorous-containing group, with aldehydes and observed the formation of substituted pyridine (**370**) in [4+2] cycloaddition reactions of 2-azadiene (**369**) with morpholinocyclopentenone (Scheme 87).[97]

Gilchrist et al. have reported highly regioselective cycloaddition reactions of enamines with 2-azadiene[82] (**345**). The products obtained in these reactions were found to be dependent upon the reaction conditions and the substituent present in the 2-azadienes and enamines. Molecular orbital calculations (AM1) have been performed to obtain frontier orbital energies and *polarisation* of a series of acyclic 2-azadienes.[82d] The results of these calculations were used to rationalise the reactivity and regioselectivity observed in Diels–Alder reactions of 2-azadienes with both electron-rich and electron-deficient dienophiles. The unusual reactivity of 2-azadienes in both *normal* and *inverse* Diels–Alder reactions has been attributed to the close HOMO and LUMO energy levels (Scheme 88).

3.2.2.3. Cycloadditions involving carbonyl compounds. Barluenga and co-workers reported the first use of diethyl

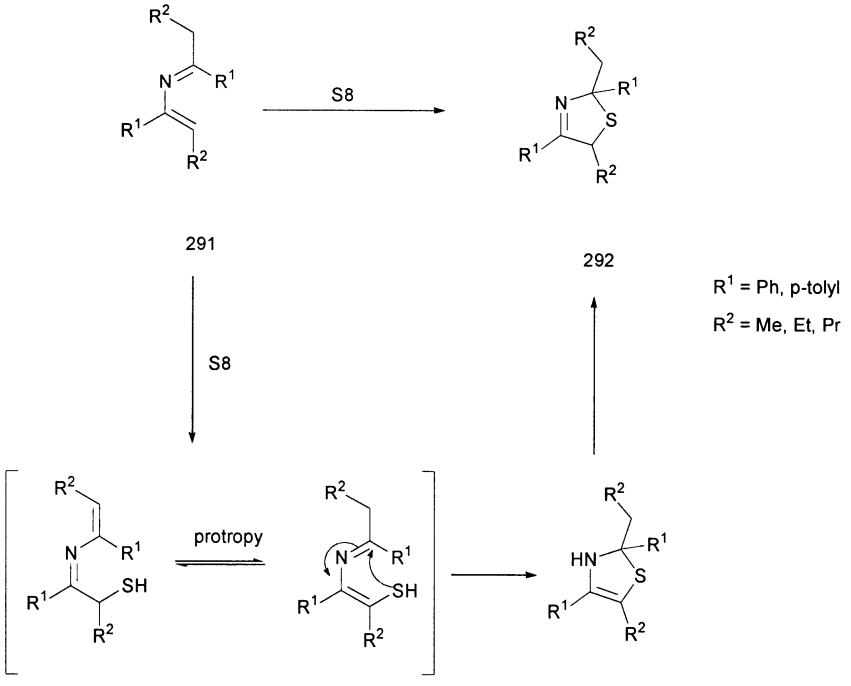

282
a-e
284
a.R = H = R1 (50%)
b.R = CH3, R1 = H (85%)
c.R = H, R1 = CH3 (53%)
d.R = Ph, R1 = H (61%)
e.R = H, R1 = Ph (0%)
R=R1=H
285
283-
286
g. R= C6H5; R1 = H (55%)
h.R = R1 = C6H5 (38%)
R = R1 = H
287
282
CH2N2
288
a. R = R1 = H (>90%)
b.R = CH3; R1 = H (80%)
c.R = H; R1 = CH3 (45%)
d.R = C6H5; R1 = H (37%)
e.R = H; R1 = C6H5 (22%)

Scheme 69.

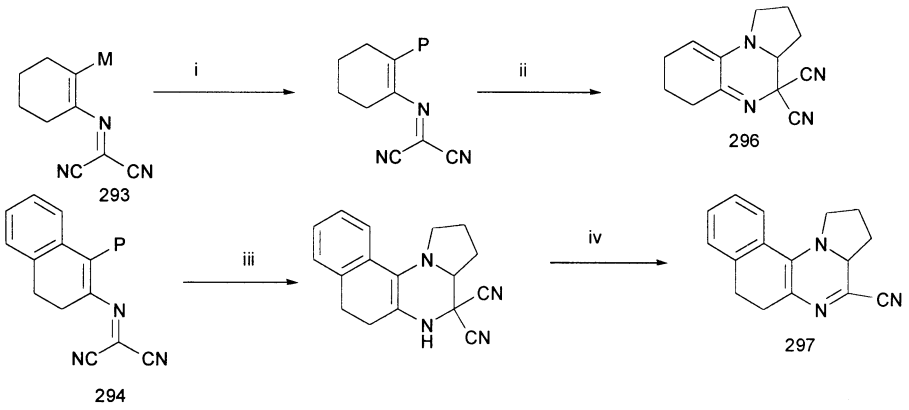


(i) TMS-N(Li)-STBDM, heptane, 0°C; (ii) phthaloylglycine chloride , TEA (iii) TMSCN (iv) $TiCl_4$, (v) HCl, 6N, 24h

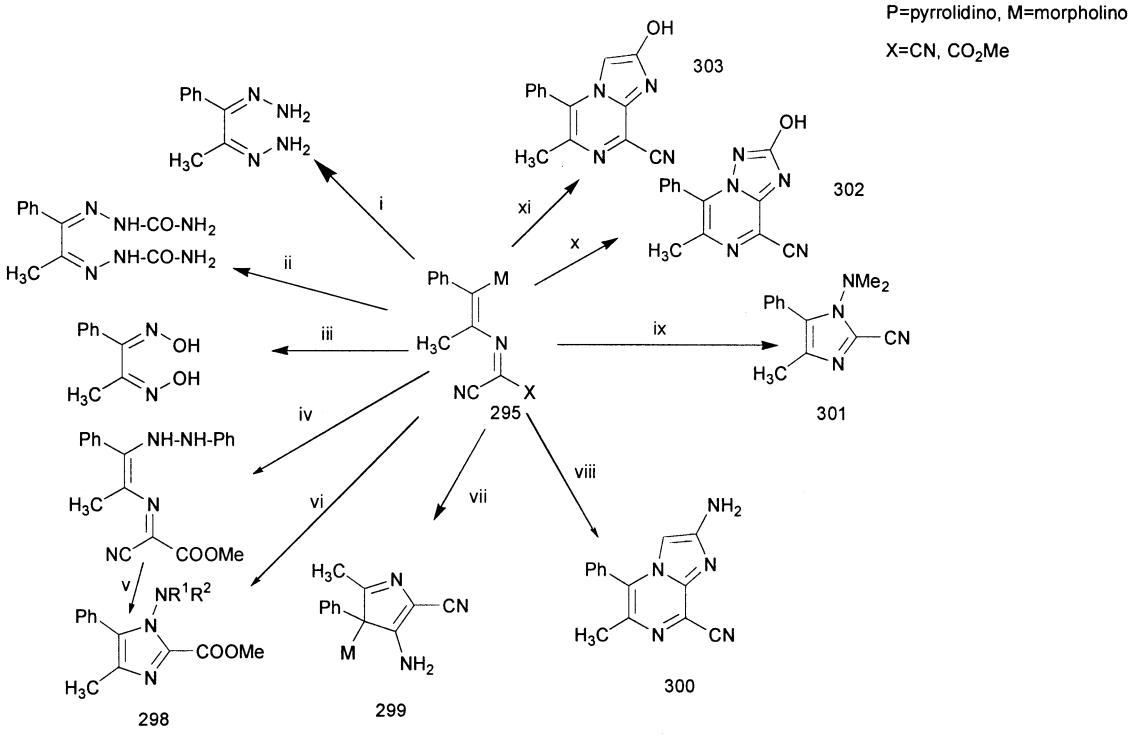
Scheme 70.



Scheme 71.

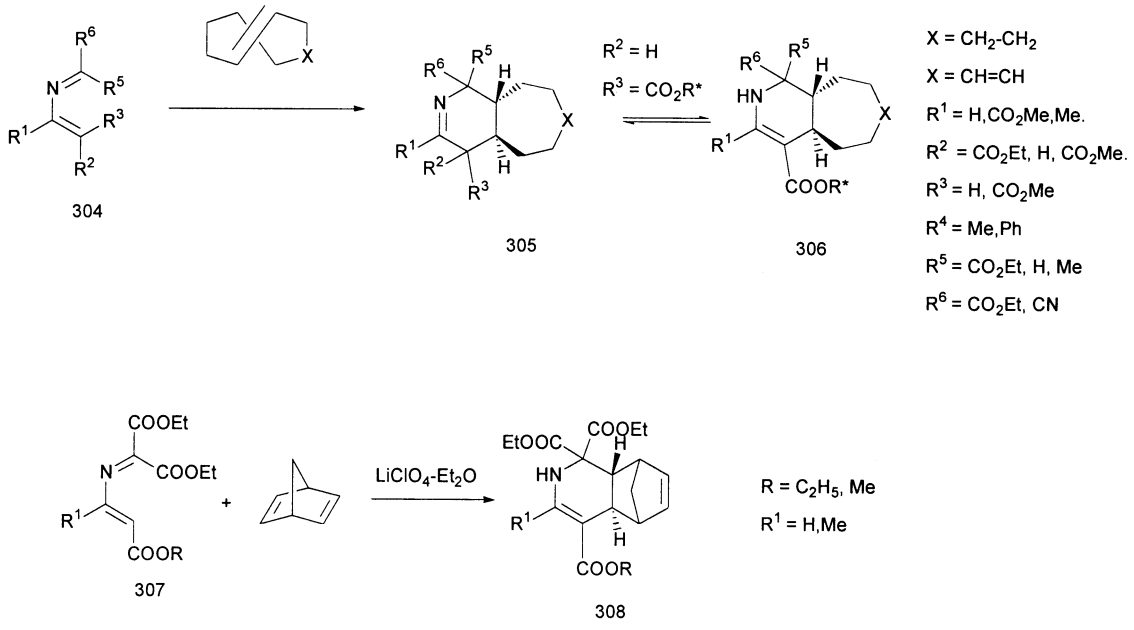


i. pyrrolidine, $CHCl_3$/MeOH, 20 °C, 20h. (ii) CF_3CO_2H/CH_2Cl_2. (iii) CF_3CO_2H/AcOH, 20 °C. (iv) $Bz(Me)_3\overset{\oplus}{N}\overset{\ominus}{O}H$/ AcOEt.



(i). NH_2-NH_2 /MeOH, -20 °C,4h. (ii). $NH_2CONHNH_2$,HCl,Et_3N /MeOH, 25 °C (iii) NH_2OH, HCl/Et_3N/MeOH, -20 °C,4h
(iv). $PhNHNH_2$ /MeOH, -10 °C, 2.5h. (v). MeOH ,reflux, 1h. (vi). PhN(Me)NH_2/$CHCl_3$/MeOH,50 °C, 24h.
(vii). KCN/MeOH,20 °C, 30 min.(viii) $CNCH_2NH_2$,HCl/Et_3N/AcOEt,reflux,30min.(ix). $Me_2NNH_2/CHCl_3$,0 °C, 24h.
(x). $EtOOCNNH_2$/EtOH, reflux. (xi). $EtOOCCH_2NH_2$,HCl/Et_3N/AcOEt, reflux.

Scheme 72.



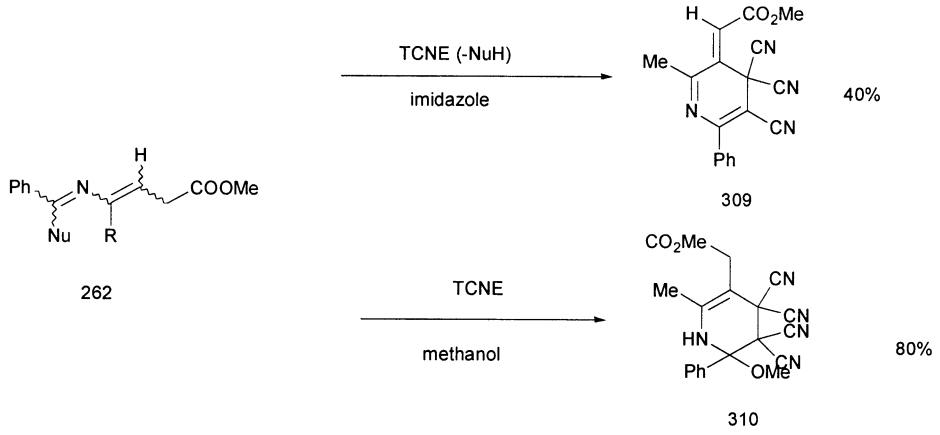
Scheme 73.

ketomalonate and butyl glyoxalate as carbon dioxide equivalents in cycloaddition reactions with 2-azadienes (**371**).[94] The cycloadducts **372/373** obtained in these reactions were further converted to various heterocyclic/acyclic compounds. In another communication these workers reported the formation of the dihydro-1,3-oxazines (**375**) by Lewis acid-catalysed Diels–Alder reactions of the 2-aza-1,3-dienes (**374**) with aldehydes, the oxazines obtained being converted diastereoselectively to 1,3-aminoalcohols (**376**,**377**) having a number of stereocenters[98] (Scheme 89).

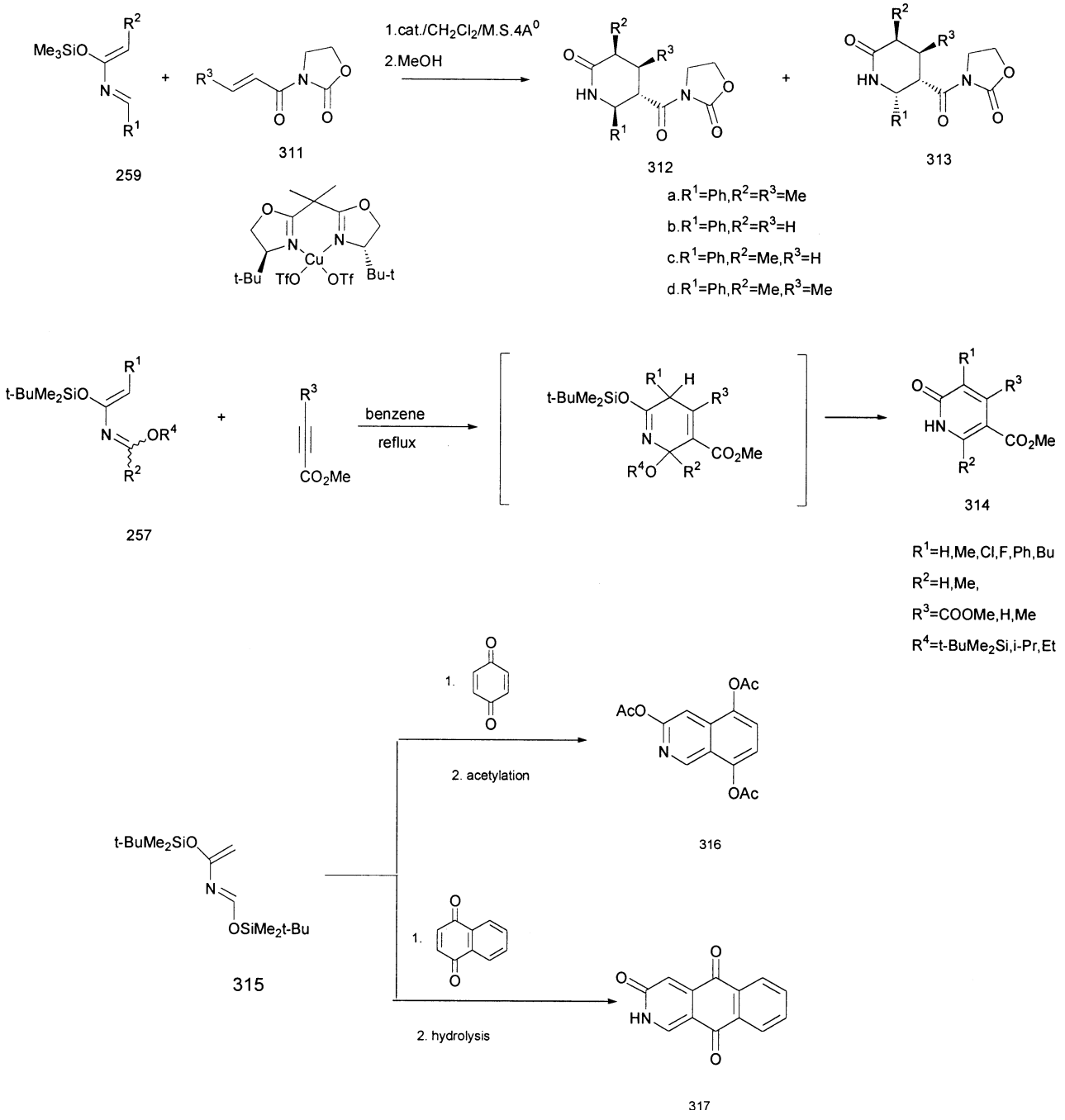
The same workers investigated the halogenation of the 2-azabuta-1,3-dienes (**376**) with *N*-halosuccinimides and the halogenated 2-azadienes were isolated as a mixture of two isomers **378a/378b** in excellent yields, the treatment of (**378a/378b**) with benzaldehyde led to a mixture (83:17) of the two epimers[99] (**379**, Scheme 90).

This group has also reported an interesting cycloaddition mode in the reactions of 2-azadienes (**374**) with *N*,*N*′-carbonyldiimidazole, in the presence of $BF_3{\cdot}OEt_2$, leading to the formation of 4(1*H*)-pyridones (**380**) instead of the expected [4+2] cycloadduct (**381**) or its hydrolysed derivative [100] (**382**, Scheme 91).

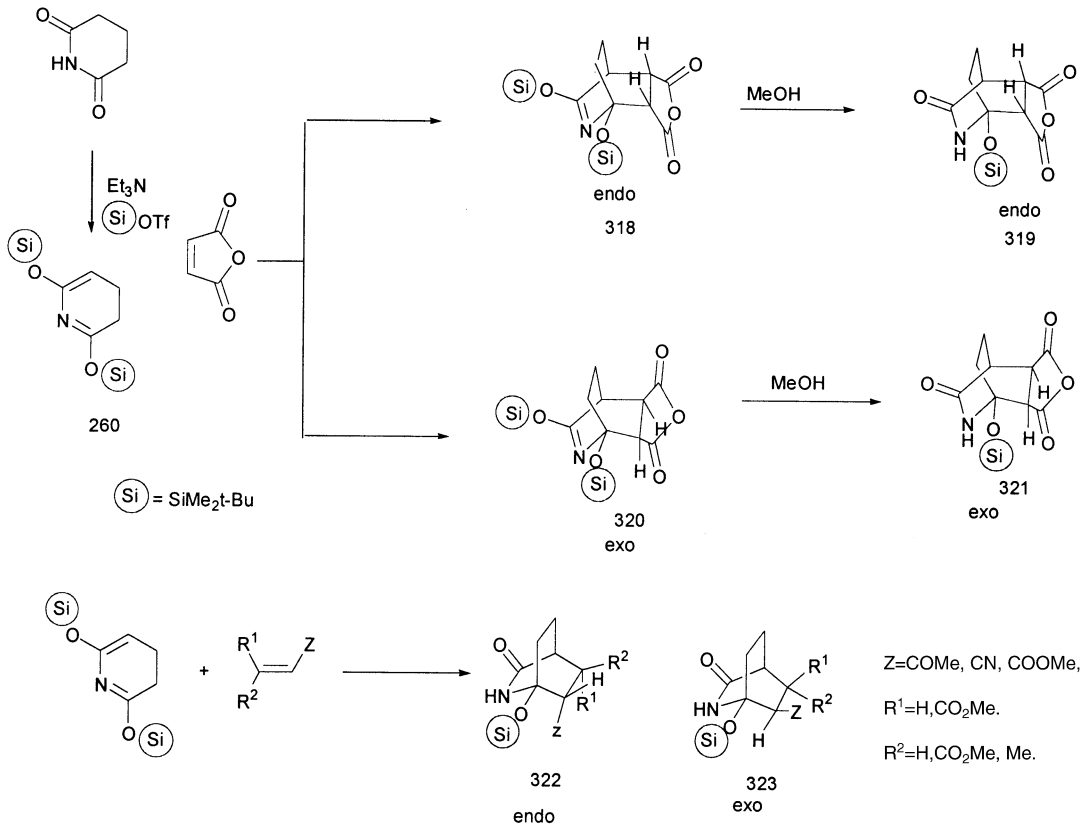
Palacios et al. have reported that the reaction of the conjugated phosphazenes (**249**) with ethyl glyoxalate also resulted in the regio- and stereoselective formation of 5,6-dihydro-2*H*-1,3-oxazines (**251**) as a single stereoisomer. The formation of (**251**) was explained by an initial aza-Wittig reaction followed by a [4+2] cycloaddition reaction of the 2-azadiene (**250**) with another molecule of aldehyde. The formation of the oxazine (**251**) as a single stereoisomer suggests that the [4+2] cycloaddition follows an *exo* selectivity. All attempts to isolate the intermediate azadiene were unsuccessful but this could be detected by spectroscopic techniques. Better yields of (**251**) were obtained in the presence of $LiClO_4$–Et_2O. Diethyl



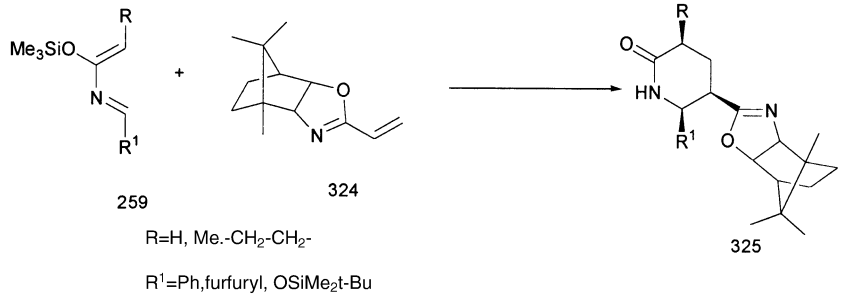
Scheme 74.


1.cat./CH2Cl2/M.S.4A0
2.MeOH
259
311
312
313
a.R1=Ph,R2=R3=Me
b.R1=Ph,R2=R3=H
c.R1=Ph,R2=Me,R3=H
d.R1=Ph,R2=Me,R3=Me
benzene
reflux
257
314
R1=H,Me,Cl,F,Ph,Bu
R2=H,Me,
R3=COOMe,H,Me
R4=t-BuMe2Si,i-Pr,Et
1.
2. acetylation
316
315
2. hydrolysis
317

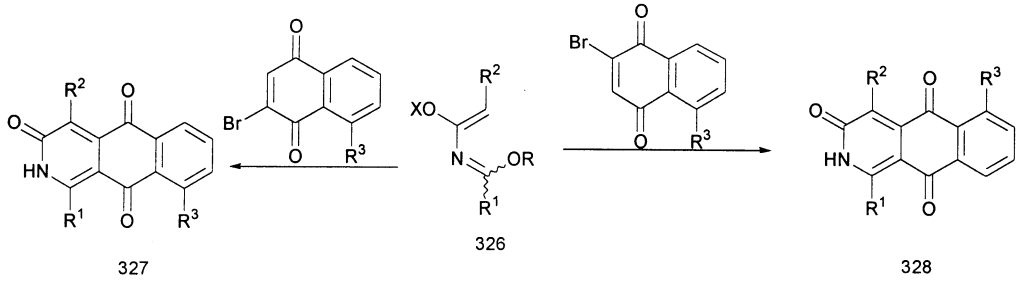
Scheme 75.



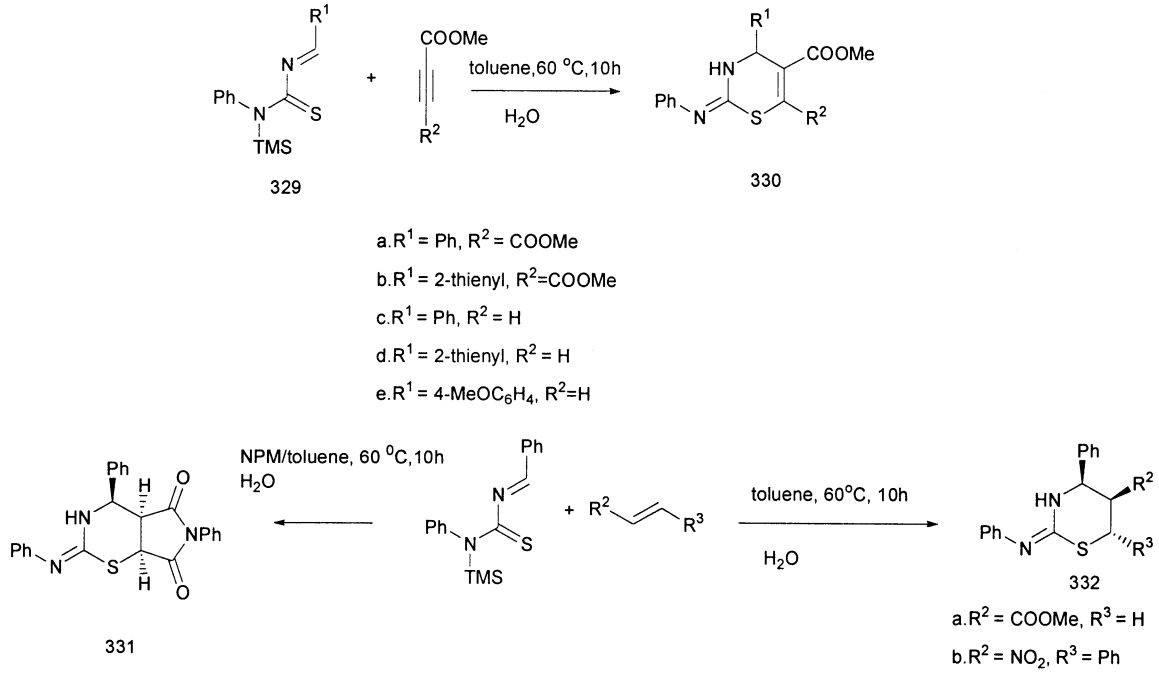
Scheme 75 (*continued*)



Scheme 76.



Scheme 77.



Scheme 78.

ketomalonate also reacted with azadiene (**250**) in the presence of $LiClO_4$–Et_2O to give a mixture of stereoisomers **383**,**384** (Scheme 92).[75]

Bongini et al. have reported an interesting observation that the 2-azadiene (**385**) undergoes [4+2] cycloaddition reaction with acetaldehyde in the presence of $BF_3{\cdot}Et_2O$, leading to oxazines (**386**). In absence of a Lewis acid catalyst, however, the azadiene (**385**) underwent electrocyclisation to β-lactams[86] (**387**, Scheme 93).

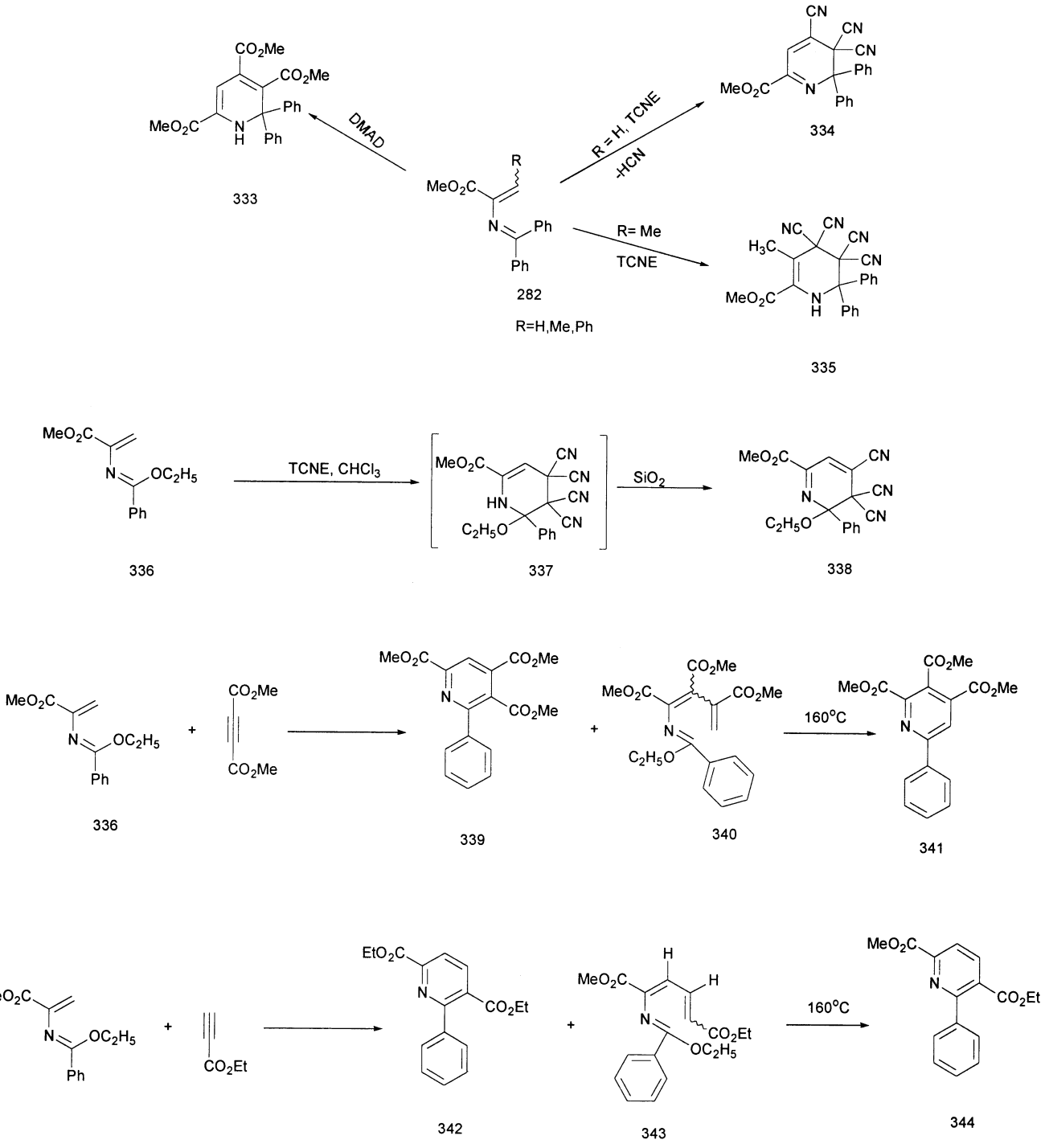
3.2.2.4. Cycloadditions involving other hetero dienophiles. There have been a few reports concerning the participation of 2-azadienes in [4+2] cycloaddition reactions with azodienophiles leading to moderate yields of the triazene derivatives. The simplest 2-azadiene (**388**) has been generated in the gas phase in its N-protonated form and its cycloadditions with a number of dienophiles have been evaluated. The 2-azadiene has been found to prefer eletron-rich dienophiles such as ethyl vinyl ether. The formation of the cycloadducts is explained via a polar [4^++2] cycloaddition as observed for 1-azadienes (Scheme 94).[101]

Kascheres et al. observed that the electronically neutral and somewhat electron-donating 2-azadiene (**262**), having a potential leaving group at the C-1 position, smoothly participated in a Diels–Alder reaction with diethyl azodicarboxylate to yield [4+2] adduct **389** (Scheme 95).[80]

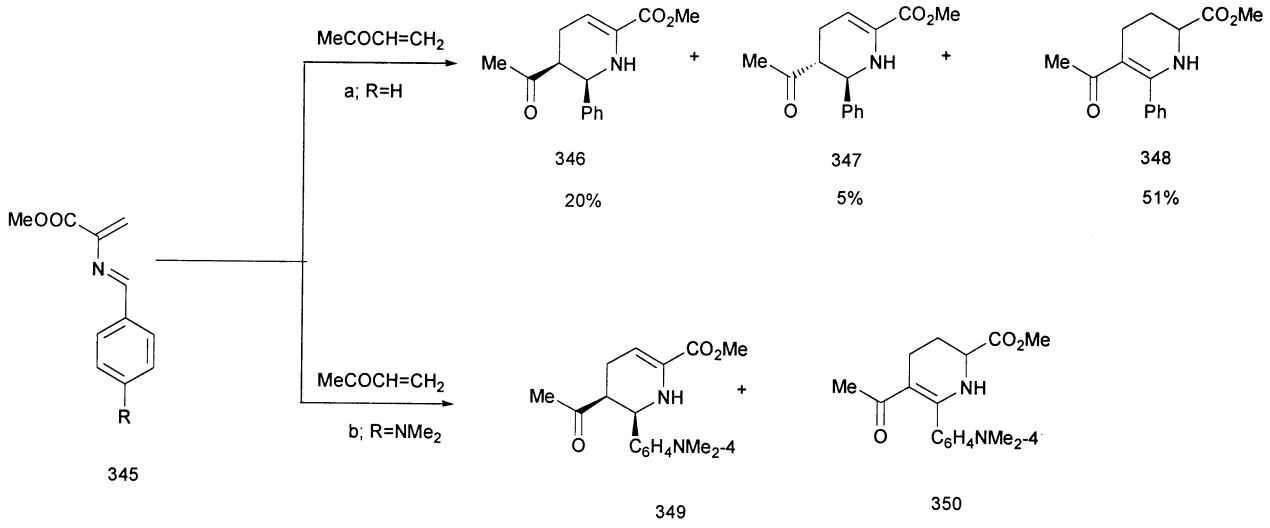
Participation of the 2-azadiene (**378**) in Diels–Alder reactions was tested by using different types of dienophiles. The reactions of (**378**, X=Cl) with dialkyl azodicarboxylates afforded the epimeric Diels–Alder mixture of adducts (**390**) in yields above 70%. In all cases, the reaction was found to occur through the more reactive trisubstituted tautomer (**378a**).[99] The experimental results of the above reactions revealed that the cycloaddition takes place through the face bearing the alkyl group (Fig. 1). In order to explain the diastereofacial selectivity in the Diels–Alder reactions of heterodienes (**378**) with dialkyl azodicarboxylates, theoretical studies using the AM1[99c] method were carried out. The same group has also reported tandem cycloaddition rearrangement in reactions of neutral-2-azadiene **378** (X=Cl) with trimethylsilylisothiocyanate leading to a simple and efficient synthesis of 1*H*-1,4-diazapine-7(6*H*)-thiones (**392**) via the 1,2-dihydropyrimidine-4(3*H*)-thione **391** (Scheme 96).[102]

3-Carbomethoxy-1,1-diphenyl-2-aza-1,3-dienes (**282**) and their 1-phenyl-1-ethoxy-analogues (**336**), which have good thermal stability compared to the 1-phenyl-3-carbomethoxy derivatives, have been utilised in cycloaddition reactions with some of the most potent electron-poor dienophiles. Their reactions with 4-PTAD have been found to result in good yields (70–90%) of the corresponding [4+2] cycloadducts (**393**,**394**, Scheme 97).[95]

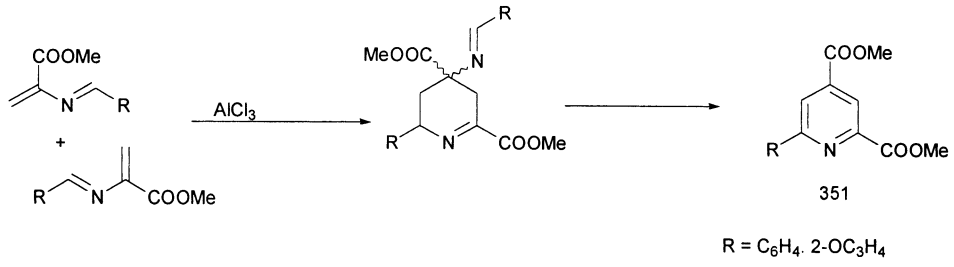
Barluenga et al., in order to prepare the previously unknown 1,3,5-triazene skeleton, studied the reactions of 1-thia-3-aza dienes (**329**) with azodienophiles such as dialkyl azodicarboxylates. The room temperature reactions of the thiazadienes with



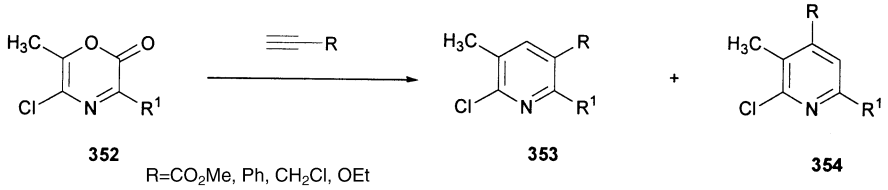
Scheme 79.



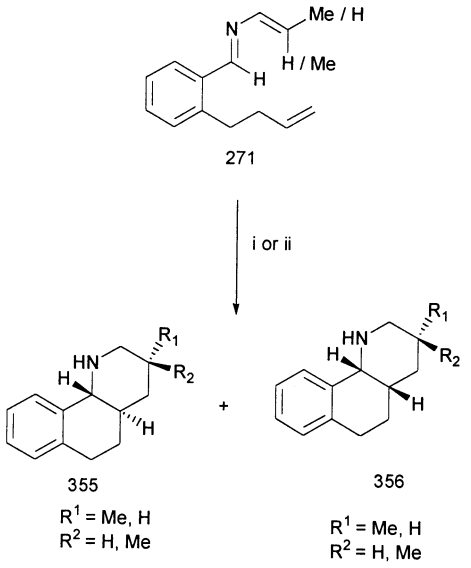
Scheme 80.



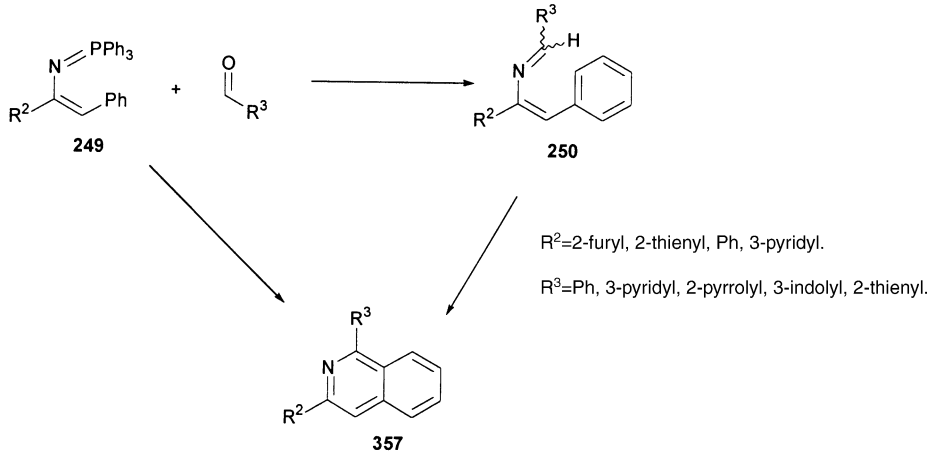
Scheme 81.



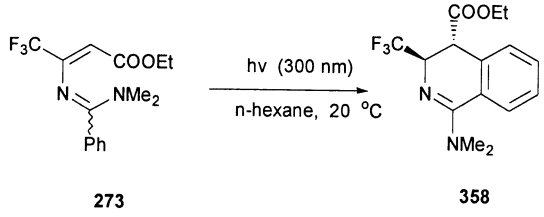
Scheme 82.



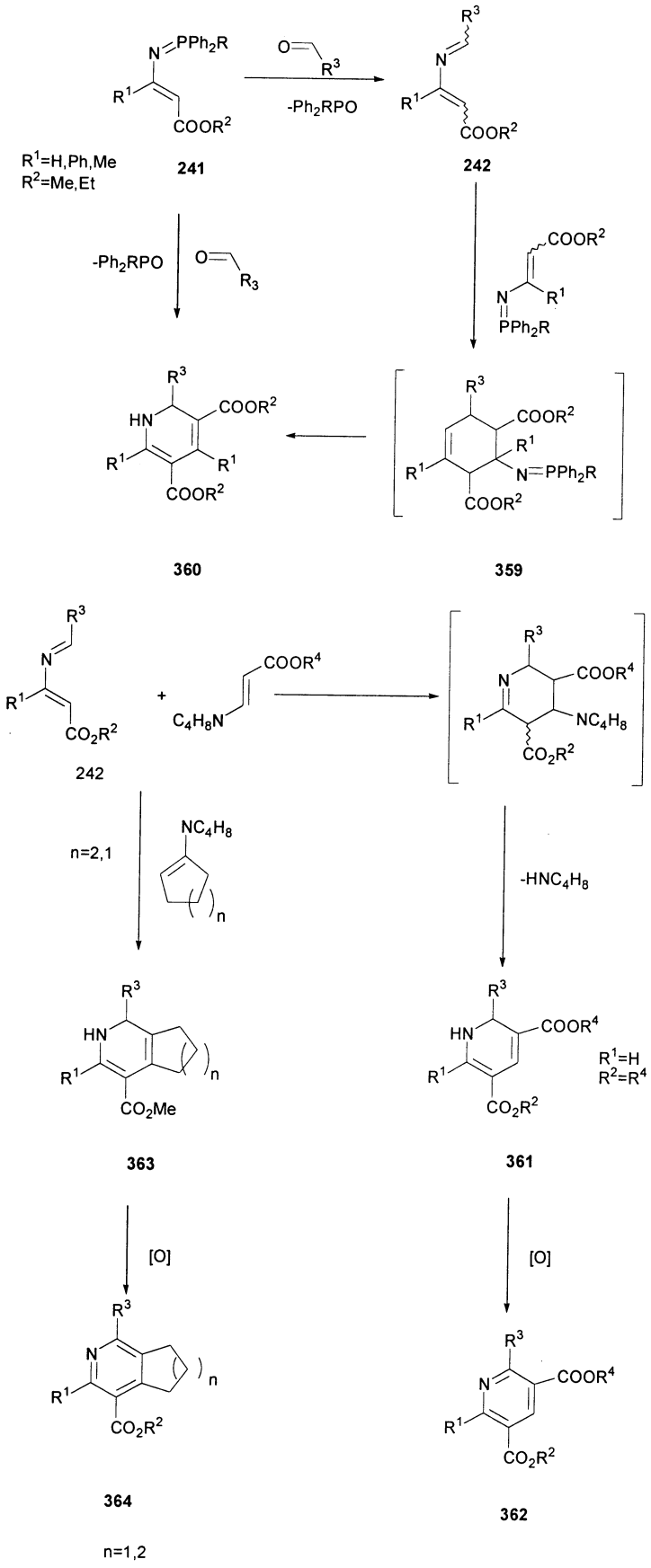
Scheme 83.



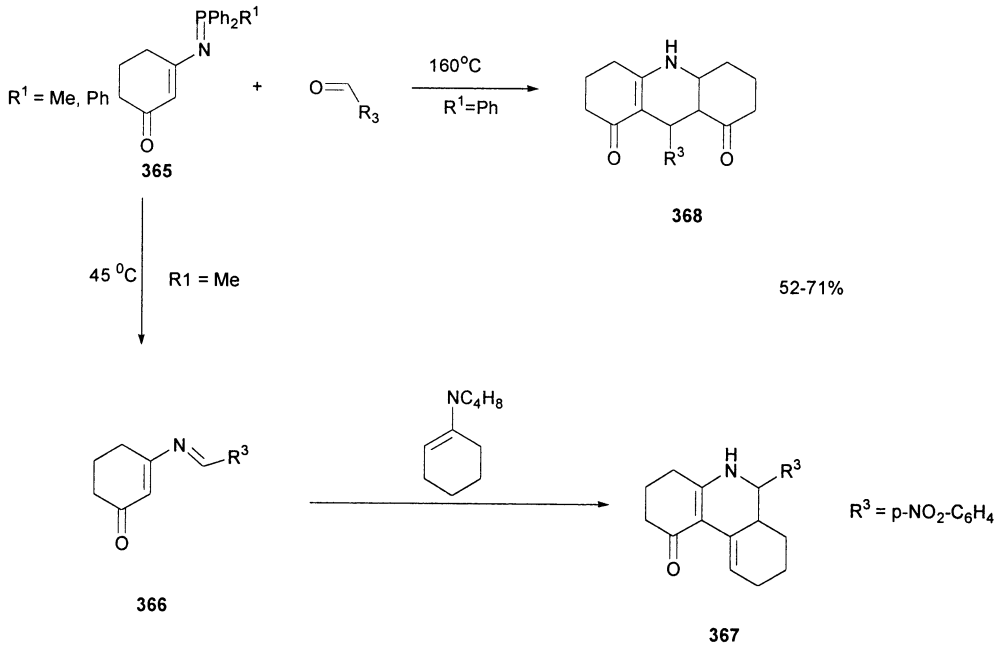
Scheme 84.



Scheme 85.


R1=H,Ph,Me
R2=Me,Et
241
242
-Ph2RPO
-Ph2RPO
360
359
n=2,1
n=1,2
-HNC4H8
R1=H
R2=R4
363
361
364
362
[O]
[O]

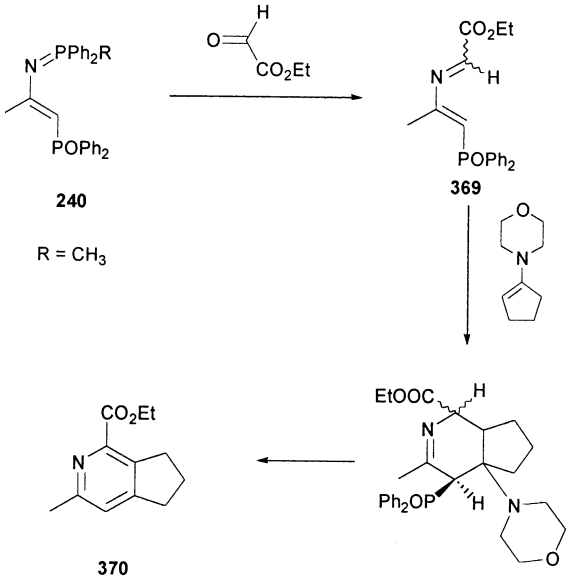
Scheme 86.



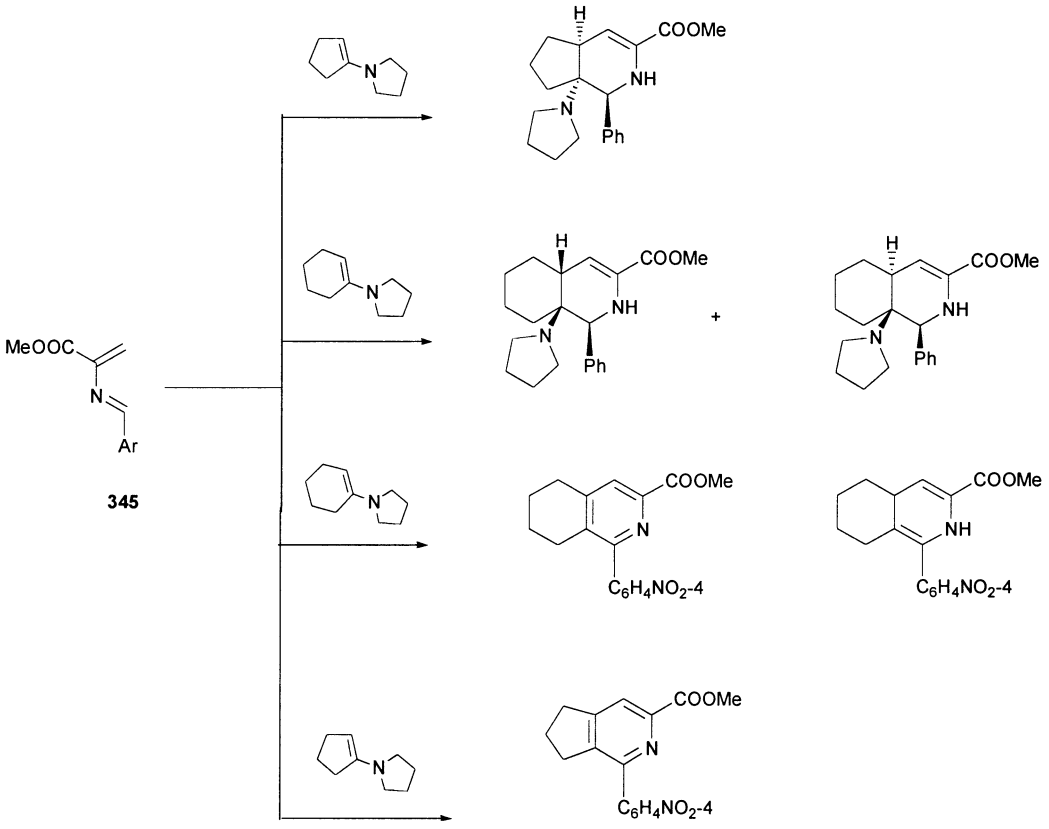
Scheme 86 (*continued*)

the dialkyl azodicarboxylate resulted in the formation of the thiatriazenes (**395**) in excellent yields, which on heating at 130°C in a sealed tube, underwent sulfur extrusion and carbon–nitrogen bond formation giving the thiazoline (**396**) in moderate yields. The cyclic azo derivative (PTAD) underwent smooth cycloaddition at room temperature to form fused thiatriazenes (**397**, Scheme 98).[94]

Ghosez at al. have employed the Diels–Alder methodology for the preparation of six-membered aza-aromatic compounds by reactions of various 2-azadienes (**257**) bearing activating trialkylsilyloxy and alkoxy groups with activated nitriles.[91] The primary adducts formed (**398**) in these reactions spontaneously aromatised to give the pyrimidinone derivatives (**399**) after methanolysis. They have also reported a systematic study on the Diels–Alder reactions of substituted 2-azadienes (**259**) with several classes of nitroso compounds, the adducts formed being converted to α-aminoacids (**400**,**401**, Scheme 99).[103]



Scheme 87.



Scheme 88.

3.3. Cycloaddition involving Fischer carbene complexes

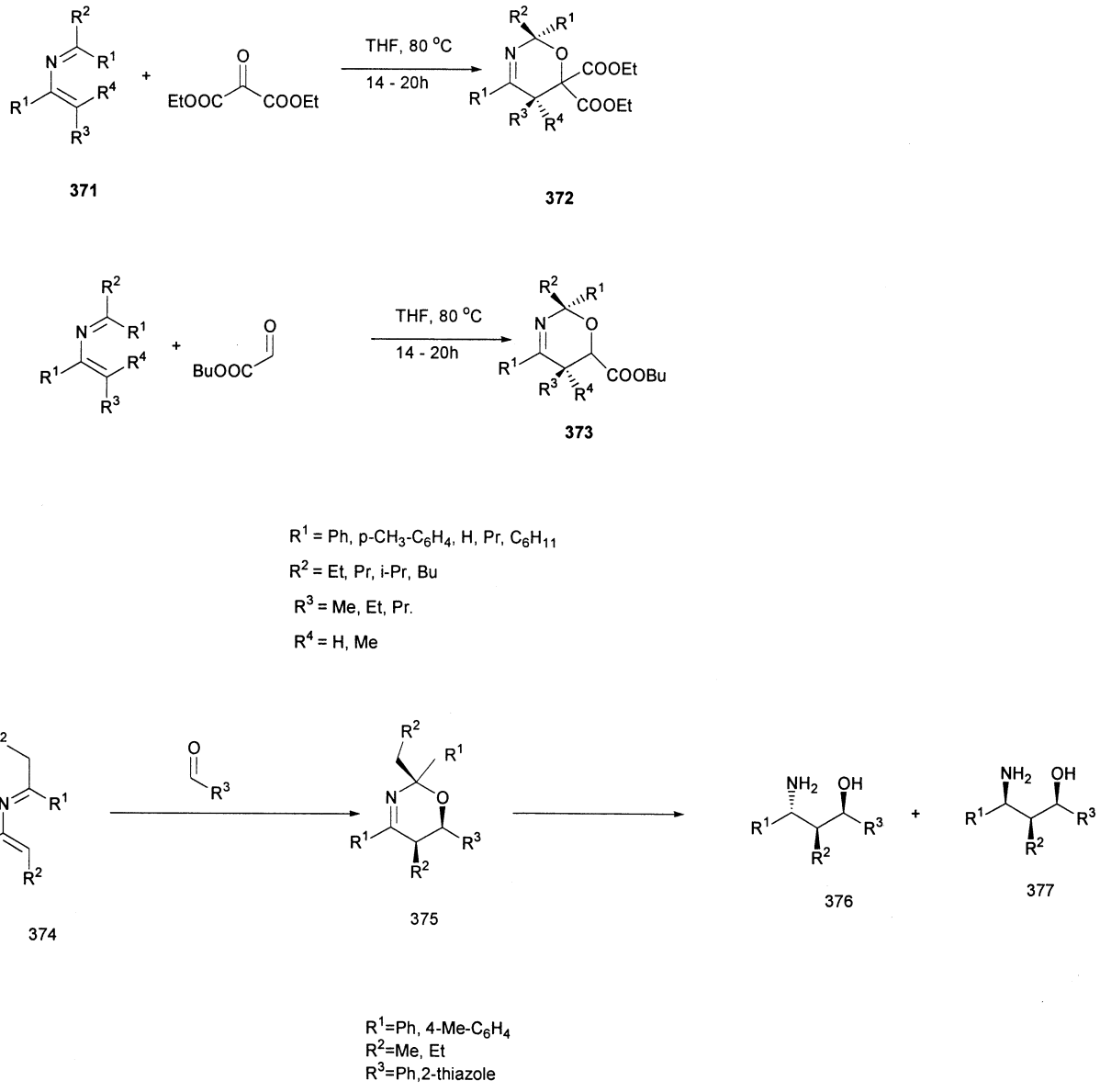
Barluenga et al. studied the synthetic utility of structurally diverse Fischer carbene complexes towards substituted 3-[trimethylsilyloxy]-2-azadienes (**259**). Each class of carbene complex showed a different behaviour, giving five- to seven-membered nitrogen heterocycles in good to excellent yields. Aryl-and heteroaryl–metal carbenes undergo [4+1] cycloadditions with the dienes (**259**) leading to the pyrrolidinone derivatives (**402**,**403**,**404**) depending upon the C-1 substituent of the dienes (**259**). The [(trimethylsilyl)ethynyl]tungsten complexes behave as activated dienophiles, affording the regioselective metal-containing and metal-free [4+2] cycloadducts (**405**,**406**), respectively, whereas the [phenylethynyl]-tungsten metal-containing complexes furnish the azofluorenones (**407**) by a tandem [4+2] cycloaddition/pentaannulation process. Regioselective [4+3] cycloaddition is the only transformation observed in the reactions of alkenyl carbene tungsten complexes. Their reaction with phenyl substituted azadienes resulted in a 1:1 mixture of the diastereoisomers **408** and **409**, while the *cis*-diastereoisomers (**408**) are formed selectively in the case of *tert*-butyl-substituted azadienes. This heptaannulation is proposed to occur via a cyclopropanation followed by an aza-Cope rearrangement (Scheme 100).[104]

3.4. Miscellaneous reactions of 2-azabuta-1,3-dienes

Armesto et al. reported the formation of the 4-alkoxy-2-azabuta-1,3-dienes (**411**) in the reactions of **410** with MeI or Me_2SO_4 as the *O*-alkylating agents. If a large excess of dimethyl sulfate is used the azadiene (**412**) formed by a second alkylation and cyclisation led to the formation of the *N*-methyl-2,3,5-triphenyl pyrrrole (**413**). *O*-Methylated and *O*-benzylated 2-azadienes (**414**) in the presence of perchloric acid followed a photo-Mannich reaction leading to isoquinoline derivatives (**415**, Scheme 101).[105]

4. 1,3-Diazabuta-1,3-dienes

Since 1976, there has been sporadic interest in the synthesis and reactions, especially the cycloaddition reactions of 1,3-diazabuta-1,3-dienes.[106] These azadienes have been shown to undergo [4+1] cycloaddition with isocyanides,[107] [4+2] cycloaddition with acetylenic esters,[108] enamines,[109] electrocyclic ring closure involving aromatic ring leading to the formation of dihydroquinazolenes/quinazolenes,[110] [2+2] and [4+2] cycloaddition with ketenes.[111,106] Reactions with oxazolines as



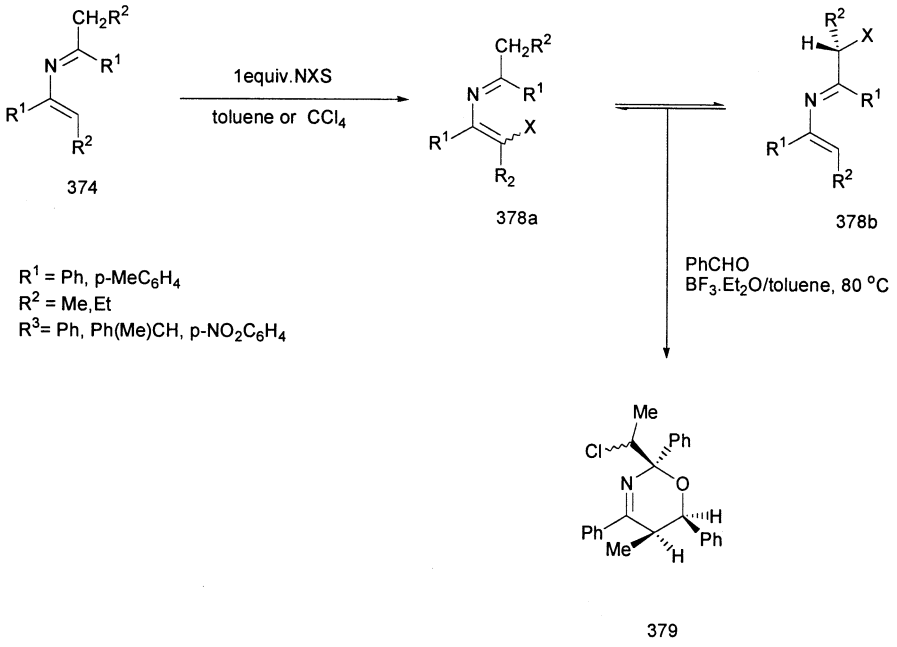
Scheme 89.

masked amidoketene,[112] and Reformatsky reagents derived from ethyl bromoacetate as unsubstituted ketene equivalents.[113] Some of these developments have been reviewed by Barulenga and Tomas.[1] Presently emphasis has been placed on the synthesis and cycloaddition reactions of 1,3-diazabuta-1,3-dienes, especially with ketenes, which has been one of our major areas of research interests in the past few years.

4.1. Synthesis of five-membered rings

In recent years, a few examples of unusual cycloaddition reactions involving 1,3-diazabuta-1,3-dienes have been described, including an unusual 1,4-methylene transfer from the Simmons–Smith reagent[114] to 1,3-diazabuta-1,3-dienes (**416**,**418**) which has been shown to yield 4-*sec*-amino substituted imidazoles (**417**,**420**). The formation of imidazoles was explained by the complexation-induced proximity effects depicted in Scheme 102. The formation of imidazoles (**420**) in the reactions of 1,3-diazabuta-1,3-dienes (**418**) with the Simmons–Smith reagent, however, is believed to proceed through the initial formation of aziridines (**419**).[115]

The α-nitrosostyrenes (**422**), which act as the 4π-component in hetero Diels–Alder reactions with a variety of alkenes, have been observed to undergo regioselective and unusual [3+2] cycloaddition reactions with imines (**421**) and 1,3-diazabuta-1,3-dienes (**416**,**418**,**425**) leading to the formation of imidazoles (**427**) and imidazole oxides (**423**,**424**,**426**, Scheme 103).[116]



Scheme 90.

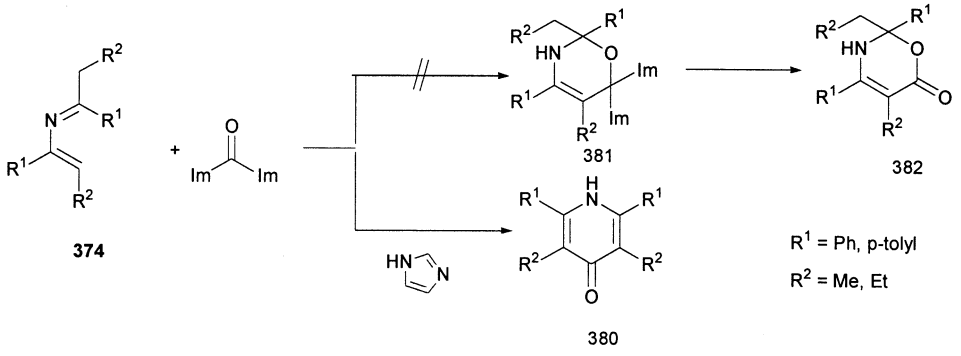
4.2. Synthesis of six-membered rings

Rossi et al.[110] in their attempts to synthesise 1,3-diazabuta-1,3-dienes (**429**), reacted *N*-imidoyl-iminophosphoranes (**428**) with aliphatic and aromatic aldehydes in boiling xylene and isolated quinazolines (**431**) and/or dihydroquinazolines (**430**) in 46–90% yields. The formation of quinazolines was rationalised in terms of a thermal six-electron electrocyclic ring closure of the initially-formed 1-aryl-1,3-diazabutadienes (**429**), which could not be isolated. Subsequently, they reported the successful synthesis of the 1,3-diazadienes (**433**) by the reactions of the dibutylphosphoramidate (**432**) with benzaldehyde under milder reaction conditions[117] (Scheme 104).

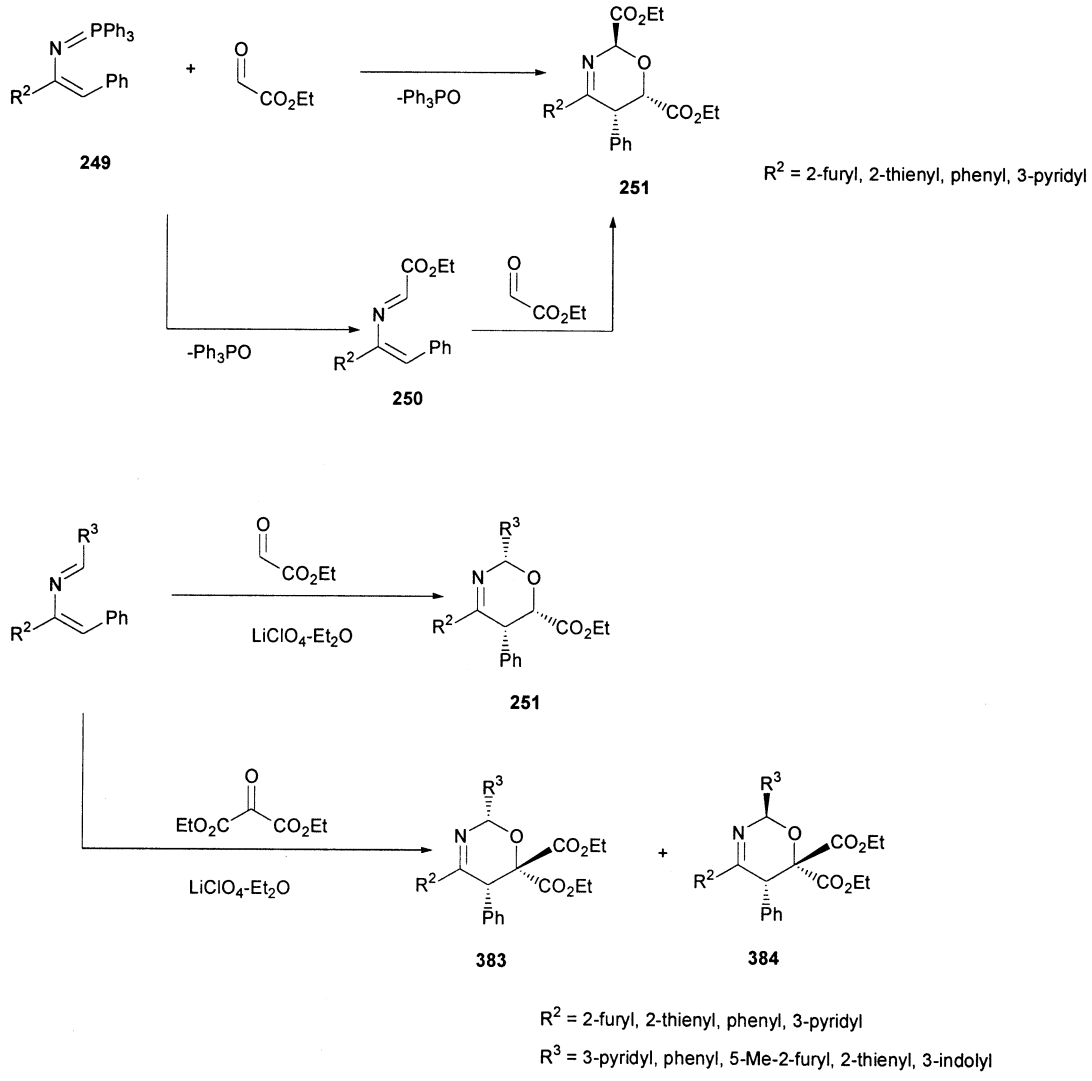
Similarly, *S*,*S*-dimethyl-*N*-(*N*-arylbenzimidoyl)sulfimides (**434**) on reactions with enamines in refluxing tetralin furnished quinazolines (**435**, 30–80%) and (**436**, 10–15%).[118] A similar reactions with enamines derived from ketones resulted in quinazolines (**437**, 45–57%) and **438** (0–3% Scheme 105).

Recently Muchowski and co-workers have devised methods for the preparation of stable acyclic 1-unsubstituted-1,3-diazabuta-1,3-dienes bearing a leaving group at the 4-position in latent (**439**), masked (**442**) and unprotected (**440**,**444**,**445**,**446**) forms.[119] The compounds **442** and **444** are relatively stable and isolable 1*H*-1,3-diazabuta-1,3-dienes. The [4+2] cylcoaddition reactions of these diazabuta-1,3-dienes with various alkynes led to the formation of the six-membered heterocylic compounds (**441**,**443**,**447**,**448**) in moderate to excellent yields (Scheme 106).

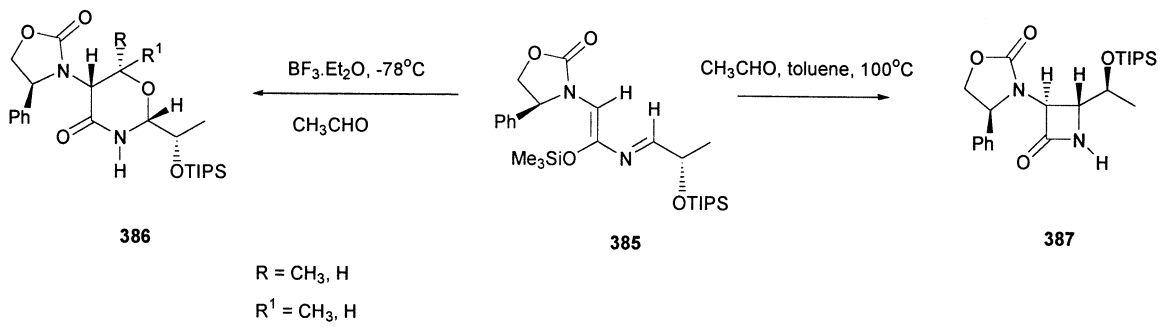
We have devised simple and convenient methods for the synthesis of stable acylic 1,3-diazadienes



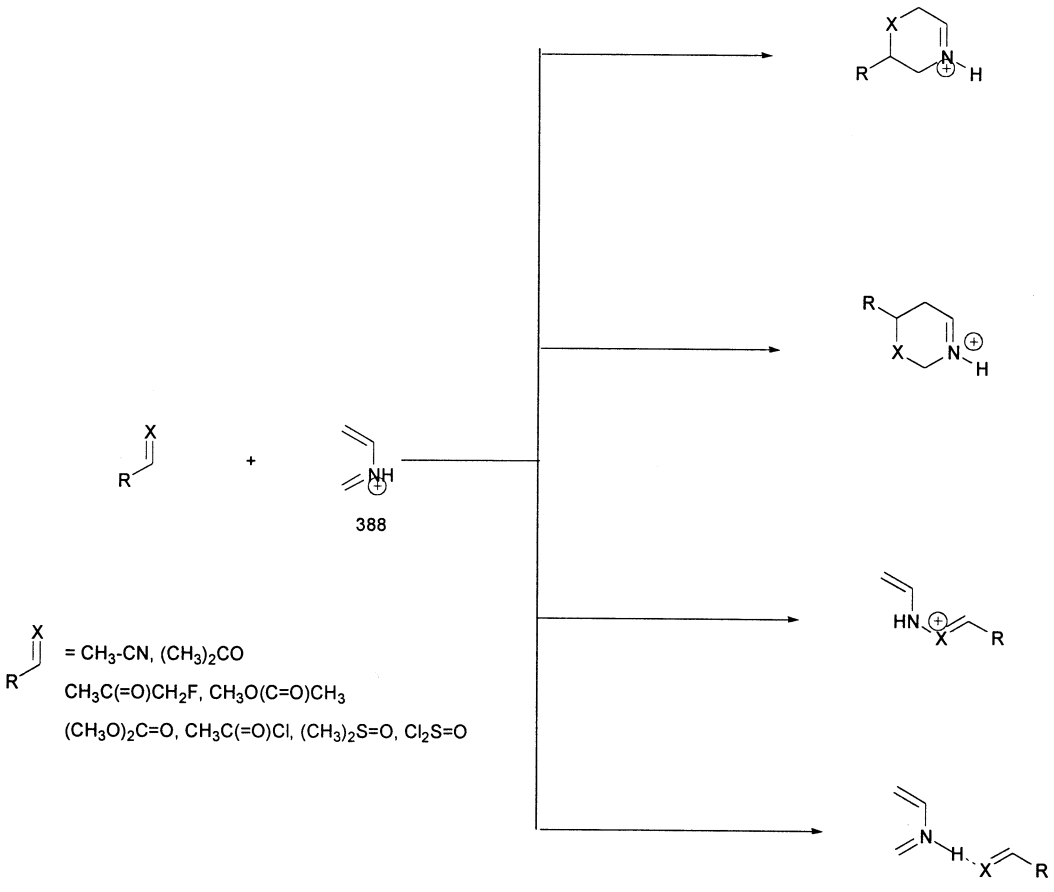
Scheme 91.



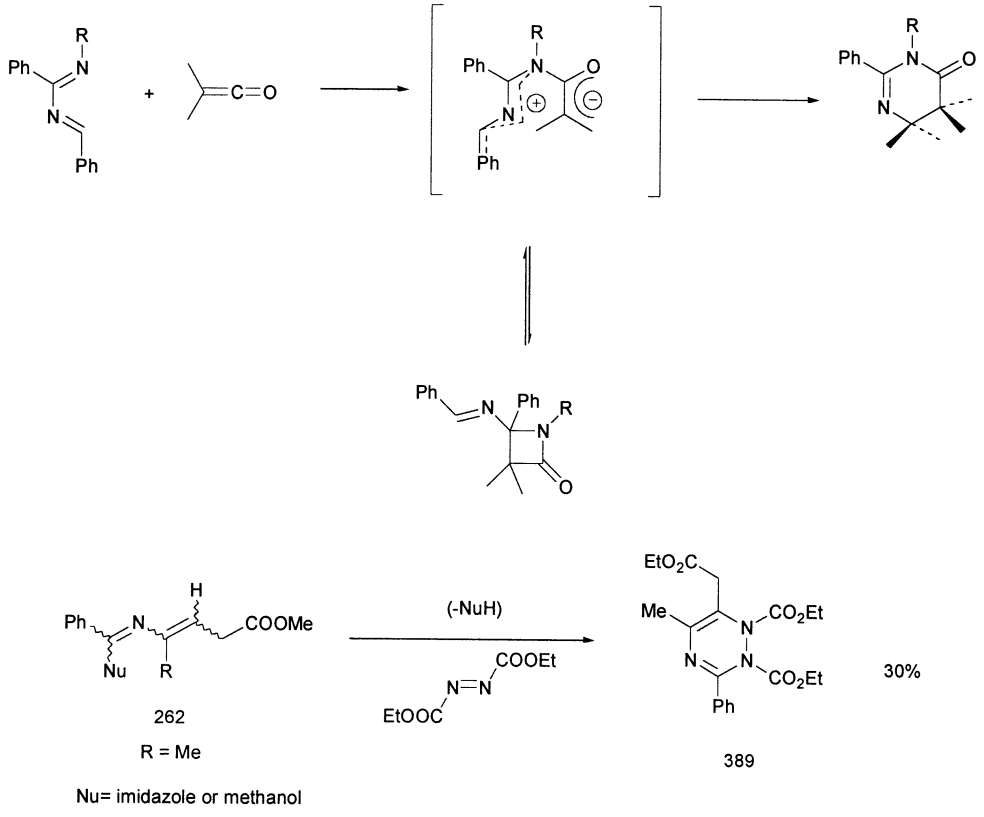
Scheme 92.



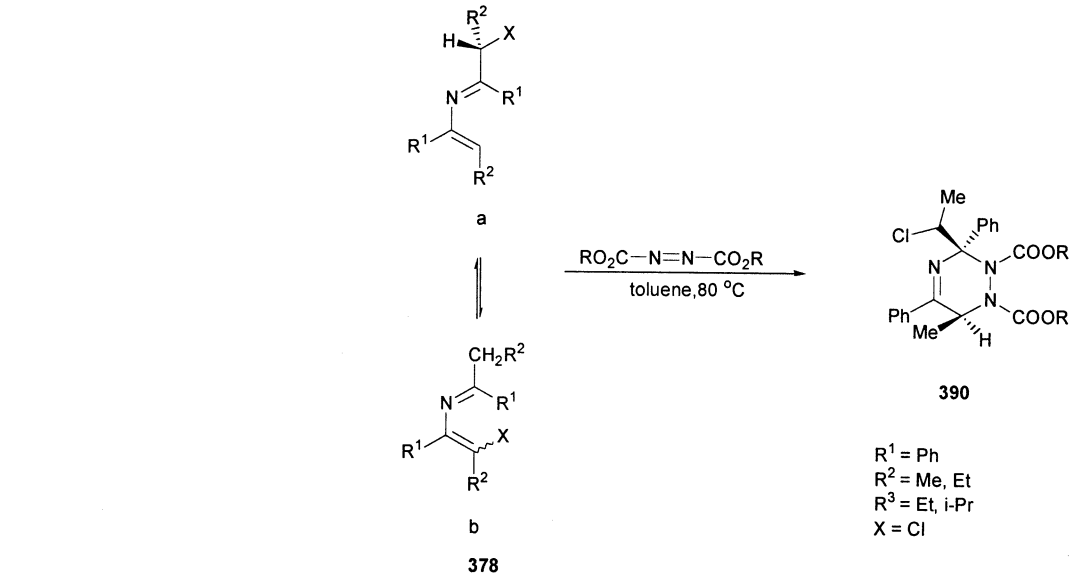
Scheme 93.



Scheme 94.



Scheme 95.



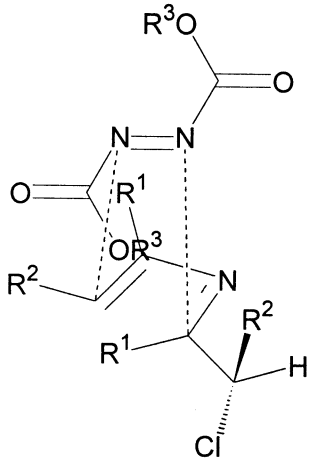
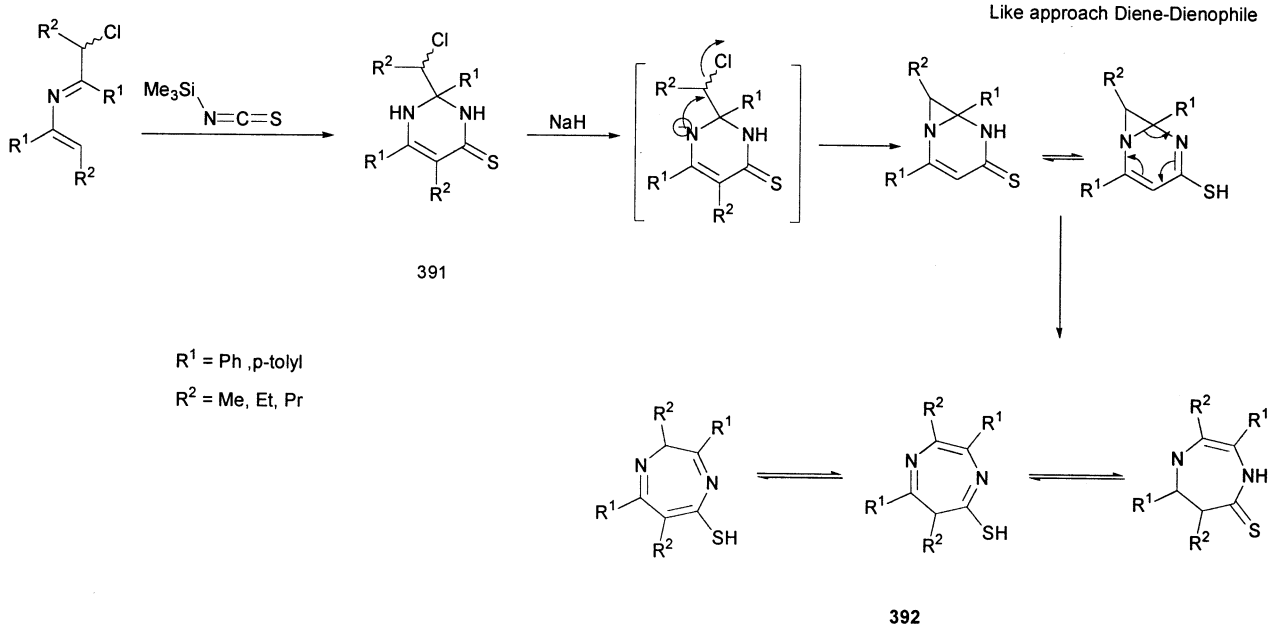
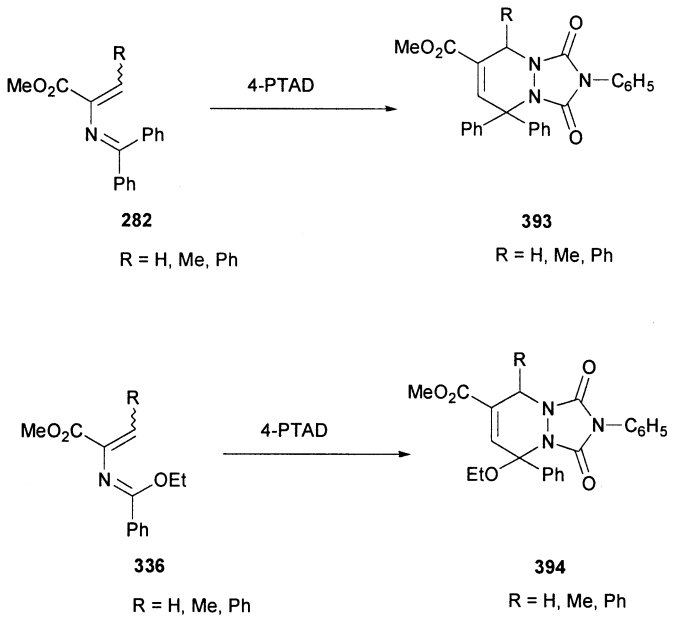


Fig. 1

Like approach Diene-Dienophile



Scheme 96.

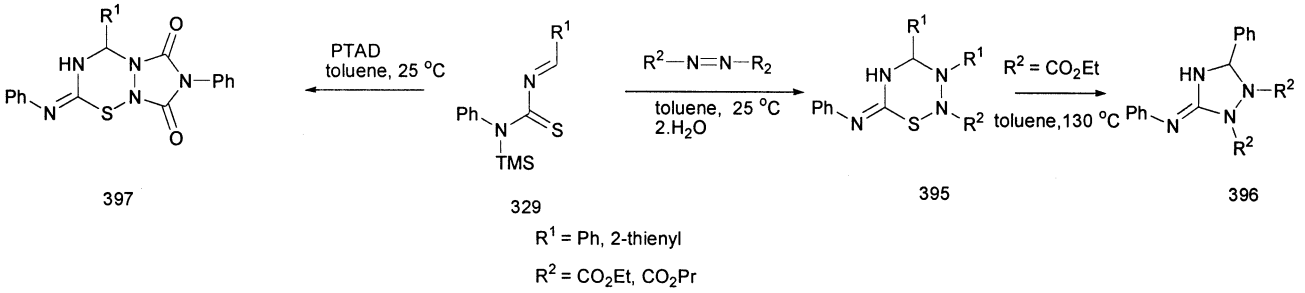


Scheme 97.

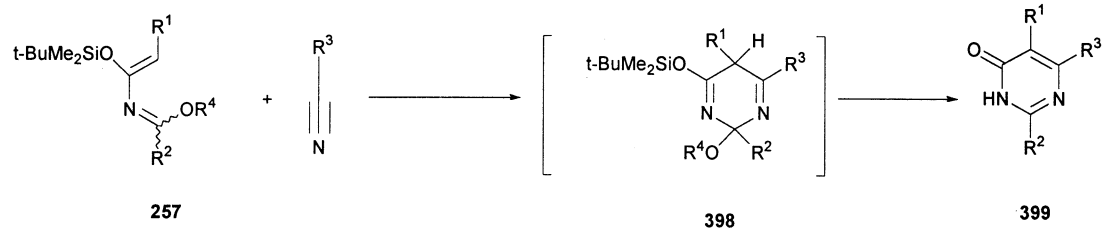
(**416**,**418**,**425**,**449**,**450**,**451**,**452**)[120] and successfully utilised them in [4+2] cycloaddition reactions with monosubstituted ketenes[120,121] viz phenyl-, vinyl-, isopropenyl-, chloro-, bromo-, iodo-, phthalimido-, succinimido- and cyanaoketenes. All of these reactions are believed to proceed through the stereoselective formation of [4+2] cycloadducts (**F**,**G**,**H**, Scheme 107) as intermediates and furnished good yields of variety of functionalised pyrimidinone derivatives **453**,**454**,**455**. Semi-empirical AM1 calculations on the azadienes (**425**) and (**452**) have been performed to explain the mechanisum for the formation of pyrimidinones, in regioselective reactions of the 1,3-diazabuta-1,3-dienes (**425**) and (**452**) with monosubstiututed ketenes[120b,121f] (Scheme 107). Some interesting observations have been made on the reactions of a number of 1,3-diazabuta-1,3-dienes **416**,**418**,**425**,**452** with haloketenes[120c,121c] (Scheme 108). In the reactions of 1,3-diazabuta-1,3-dienes **416**,**418**,**425**,**452** the nature of the pyrimidinone **456**,**457**,**458**,**460**,**461**,**462**,**464** formed has been found to vary with the nature of the halogen (Cl, Br, I) on the haloketene. An interesting rearrangement involving an episulphonium intermediate (**459a**,**459b**) has been shown to accompany the [4+2] cycloaddition reactions of 1,3-diazabuta-1,3-dienes (**418**) with chloro-, bromo-, iodo-, chloromethyl- and dichloroketenes[121a] (Scheme 108). A similar rearrangement, involving the aziridinium intermediate (**463**) leading to pyrimidinones (**464**), was observed in the reactions of 1,3-diazabuta-1,3-dienes (**425**,**452**) with haloketenes (Scheme 108).[121]

Recently, we have described unusual and interesting tandem [1,5] H and SMe shifts accompanying [4+2] cycloaddition reactions of 1,3-diazabuta-1,3-dienes (**418**) with butadienylketene.[122a] These reactions led to the isolation of the pyrimidinones (**465**) and (**466**). Similar tandem sigmatropic shifts have been noticed in the reactions of *N*-arylamino-1,3-diazabuta-1,3-dienes (**425**) with butadienylketene[122b] resulting in the formation of pyrimidinones **467**,**468**,**469** (Scheme 109).

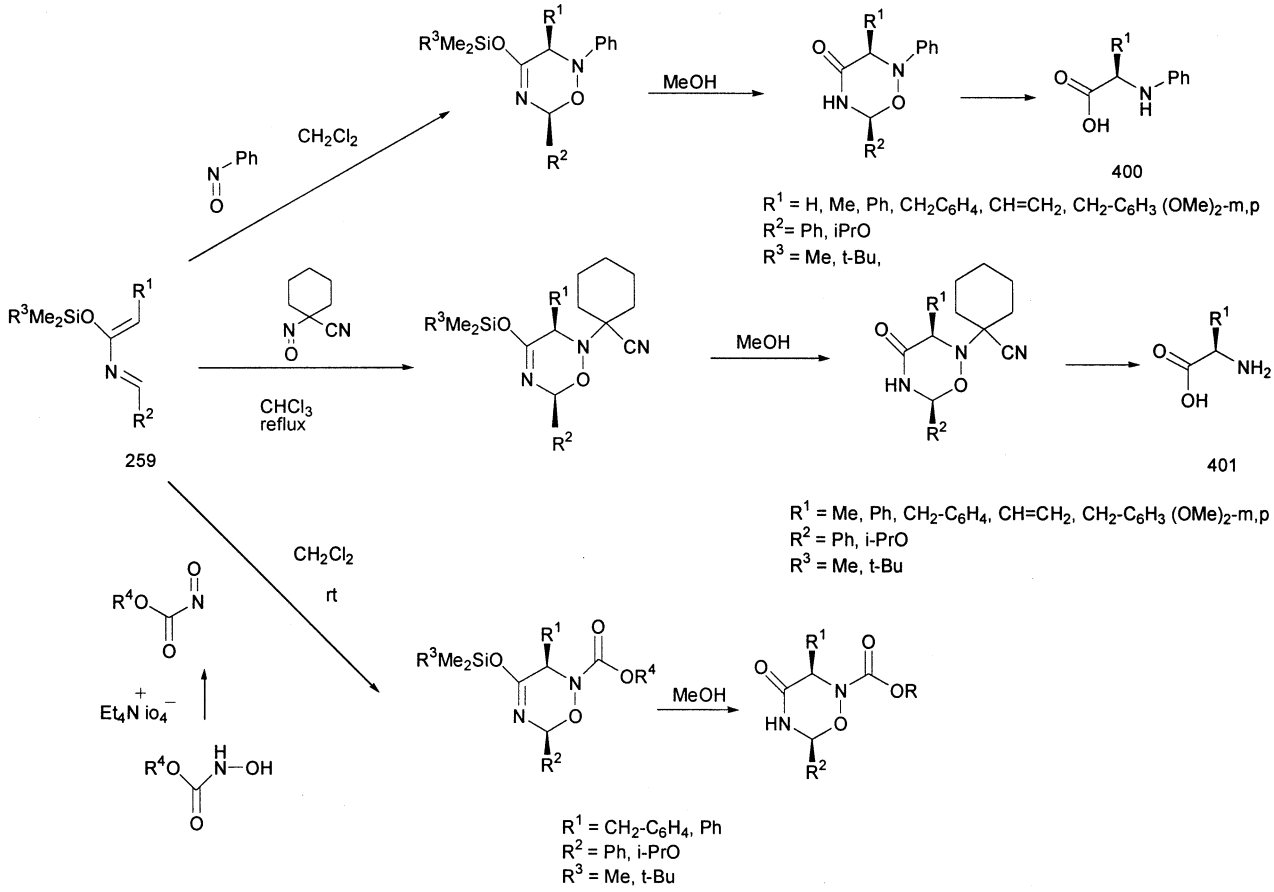
Rossi et al. have described the formation of the dihydropyrimidinone (**470**) in the reactions of the diazabutadiene (**433**) with ketenes and reported the first example of a [4+2] cycloaddition between a fully aryl substituted diazadiene and



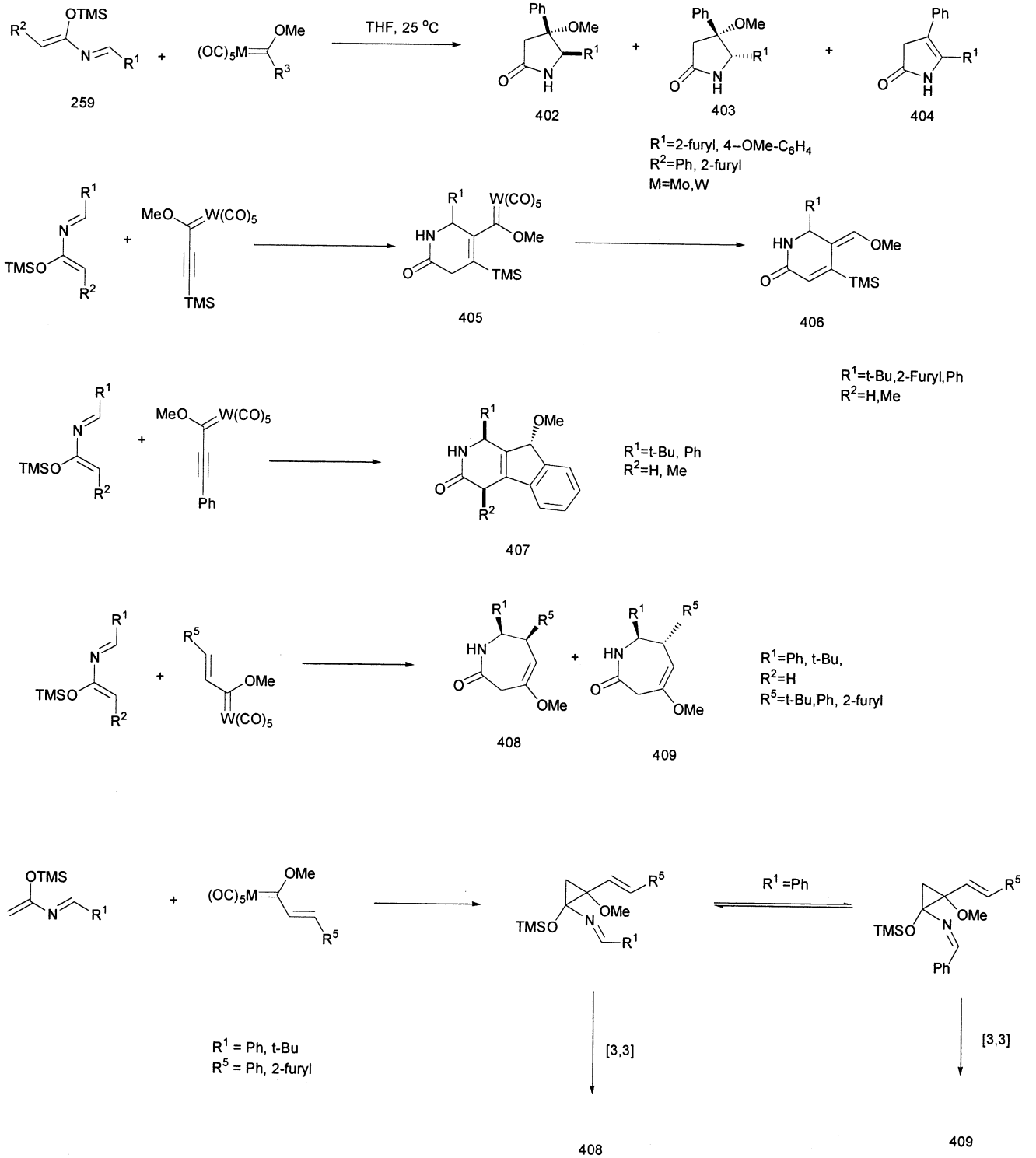
Scheme 98.



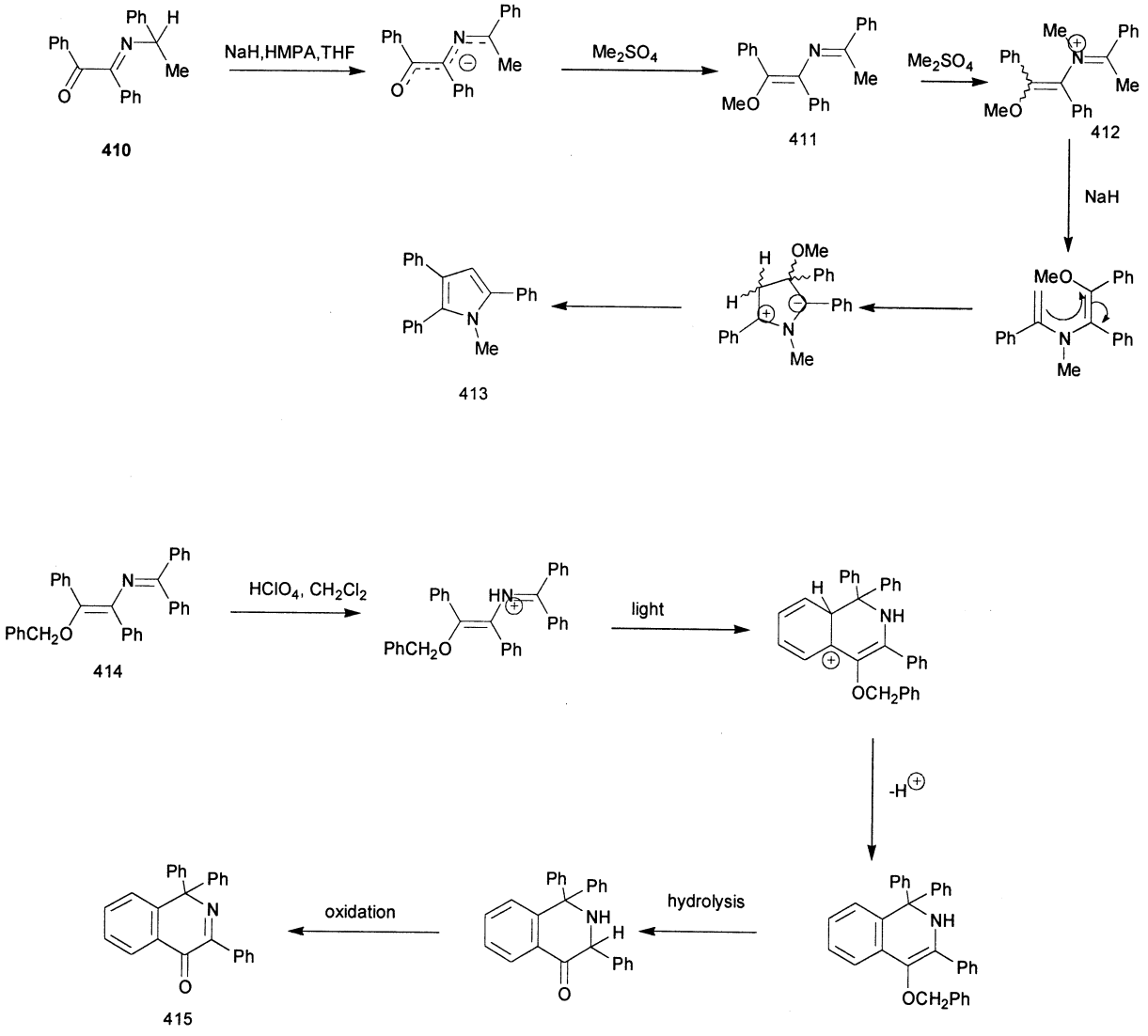
R^1=H, Me, F, Cl, Bu.
R^2=H, Me.
R^3=p-Tos, Cl_3C, CO_2Et
R^4=i-Pr, Et



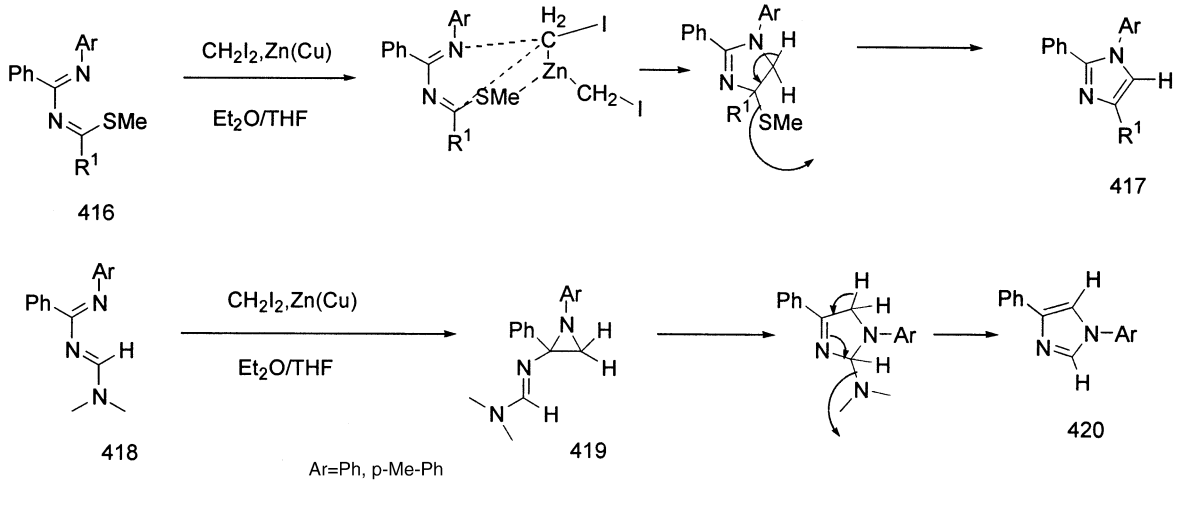
Scheme 99.


THF, 25 °C
259
402
403
404
R1=2-furyl, 4--OMe-C6H4
R2=Ph, 2-furyl
M=Mo,W
405
406
R1=t-Bu,2-Furyl,Ph
R2=H,Me
407
R1=t-Bu, Ph
R2=H, Me
408
409
R1=Ph, t-Bu,
R2=H
R5=t-Bu,Ph, 2-furyl
R1 =Ph
[3,3]
R1 = Ph, t-Bu
R5 = Ph, 2-furyl

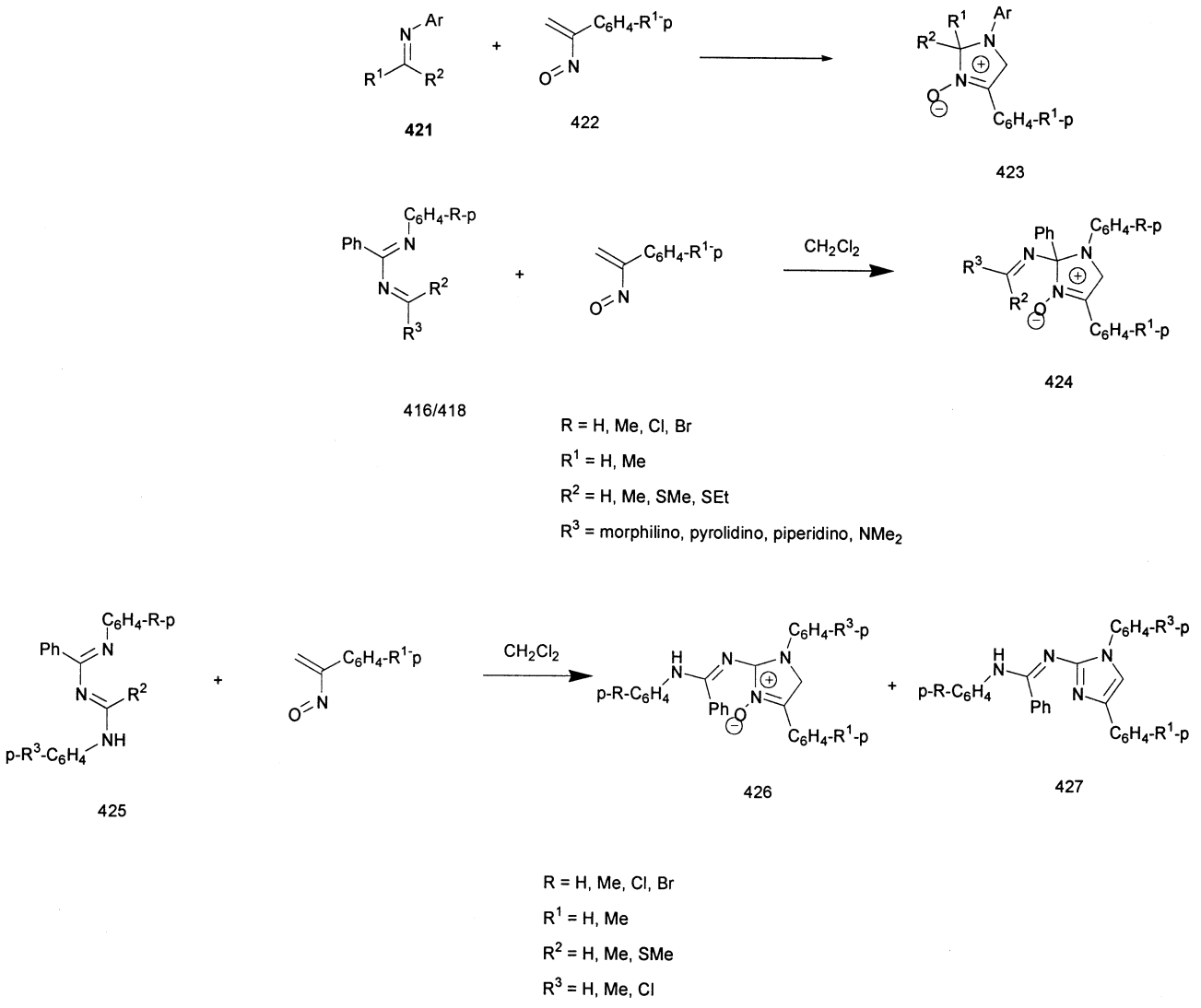
Scheme 100.



Scheme 101.



Scheme 102.



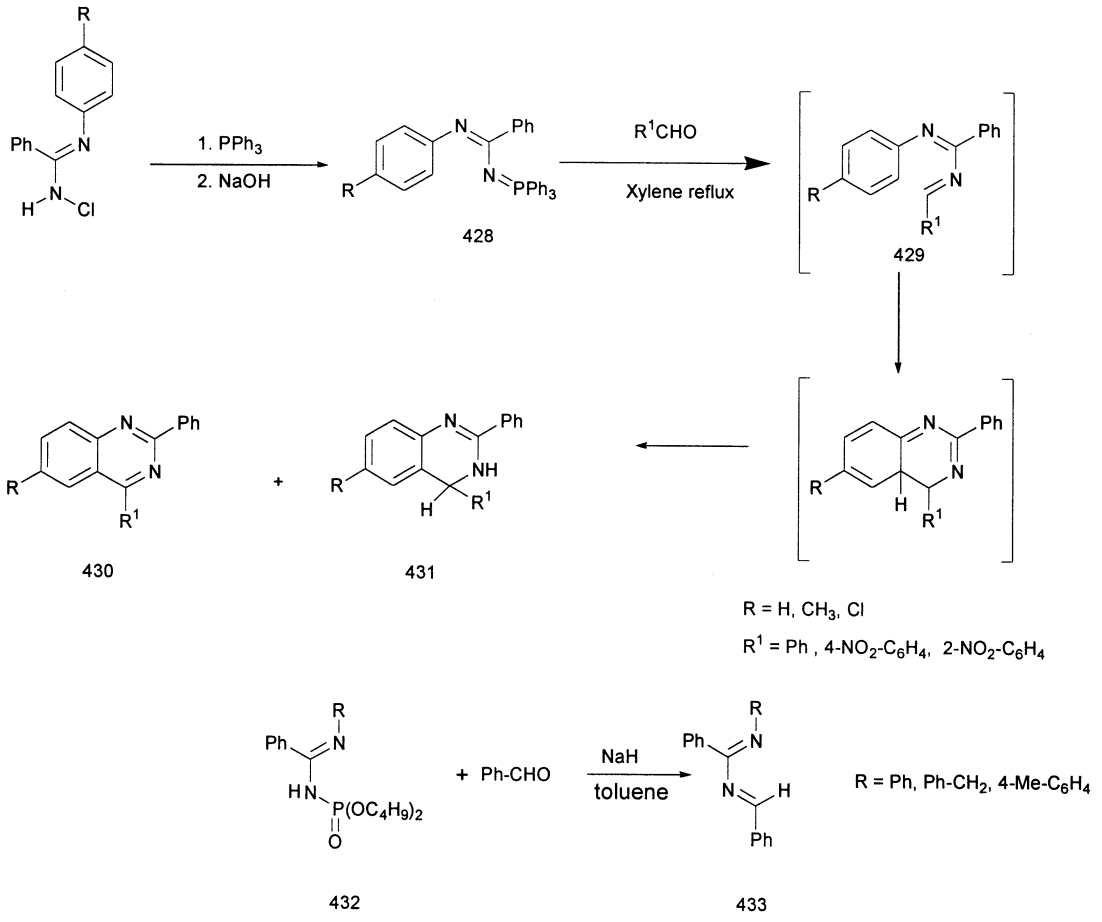
Scheme 103.

diphenylketene.[123] In addition, the replacement of an *N*-aryl by a benzyl group (**471**) led to the initial formation and isolation of azetidinones (**472**, Scheme 110).

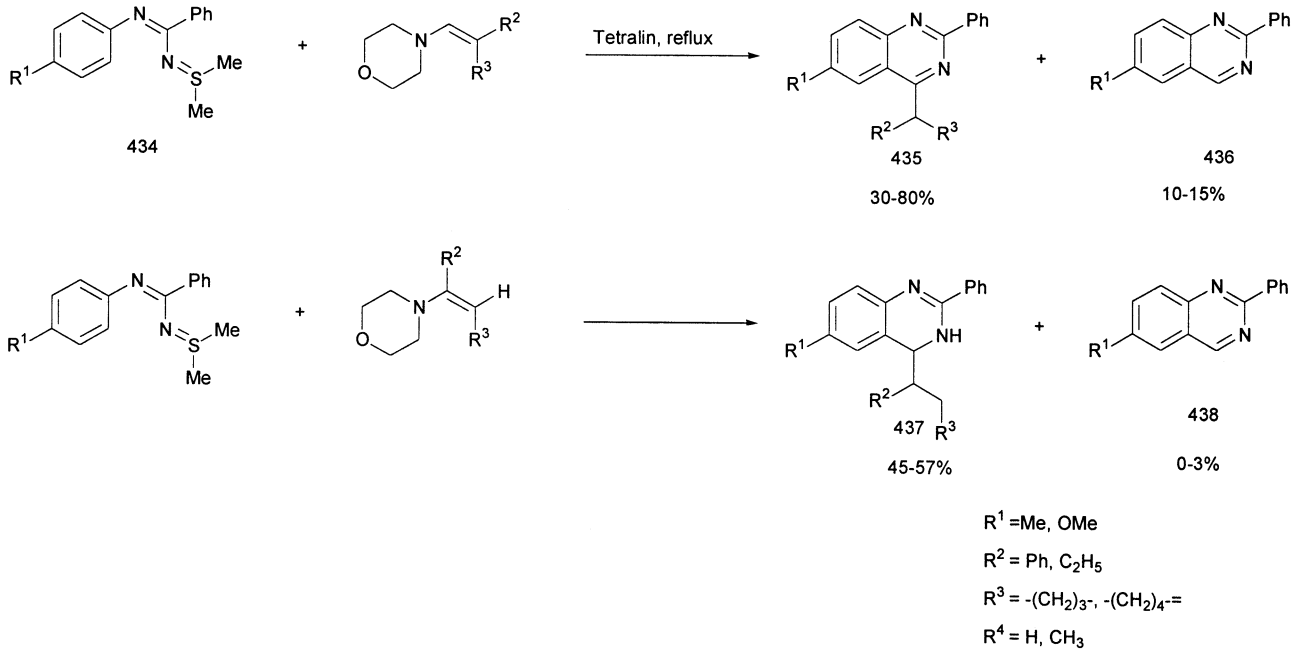
4.3. Mechanism of 1,3-diazabuta-1,3-diene-ketenes cycloaddition reactions

The reactions of 1,3-diazabuta-1,3-dienes with ketenes have been observed to follow either a [2+2] or [4+2] cycloaddition mode, resulting in the formation of azetidinones or pyrimidinones, respectively. In recent years, a number of research groups have made contributions towards explaining the observed selectivity in these cycloadditions. Wurthwein et al.[111] investigated these cycloaddition reactions by varying the size of the substituent at the 1-, 2- and 4-position of the 1,3-diazabuta-1,3-dienes and supported the earlier findings of Matsuda et al.[124] that the observed selectivity is determined by steric factors. Recently, Rossi et al.[123] reported that the mode of cycloaddition is governed more by the size of the substituent at the N-1 and C-2 positions of the 1,3-diazabuta-1,3-dienes. A polar stepwise mechanism for reversible formation of β-lactams by a kinetically-governed process, tending towards the more stable pyrimidinone has been proposed.[123] On the other hand, pyrimidinones are thermodynamically controlled products and their formation is irreversible. It was suggested that, apart from steric factors, electronic factors also play a dominant role in influencing the observed selectivity.[121a]

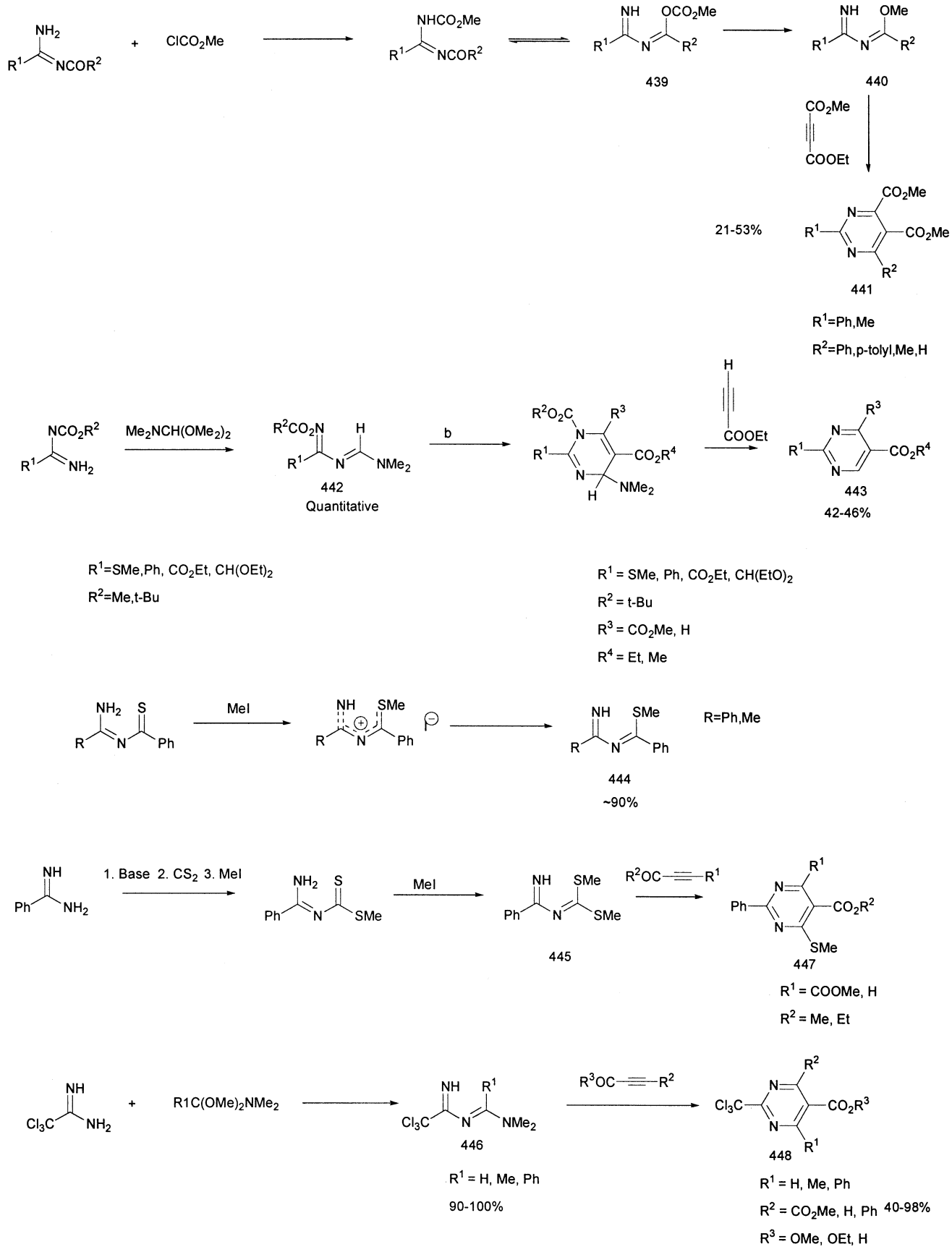
Recently, we have performed theoretical calculations on conformational preferences for substituted 1,3-diazabuta-1,3-dienes and their reactions with ketenes.[125] It has been suggested that the formation of a pyrimidinone in these reactions occurs through a concerted but asynchronous [4+2] cycloaddition. The formation of an azetidinone occurs either via an oxadiazine followed by a Claisen rearrangement or a zwitterionic intermediate obtained from the *Z*-isomers of the diazadienes. The azetidinone can also transform to the pyrimidinone via a [3,3] sigmatropic shift to give back the oxadiazine, followed by retero-Diels–Alder



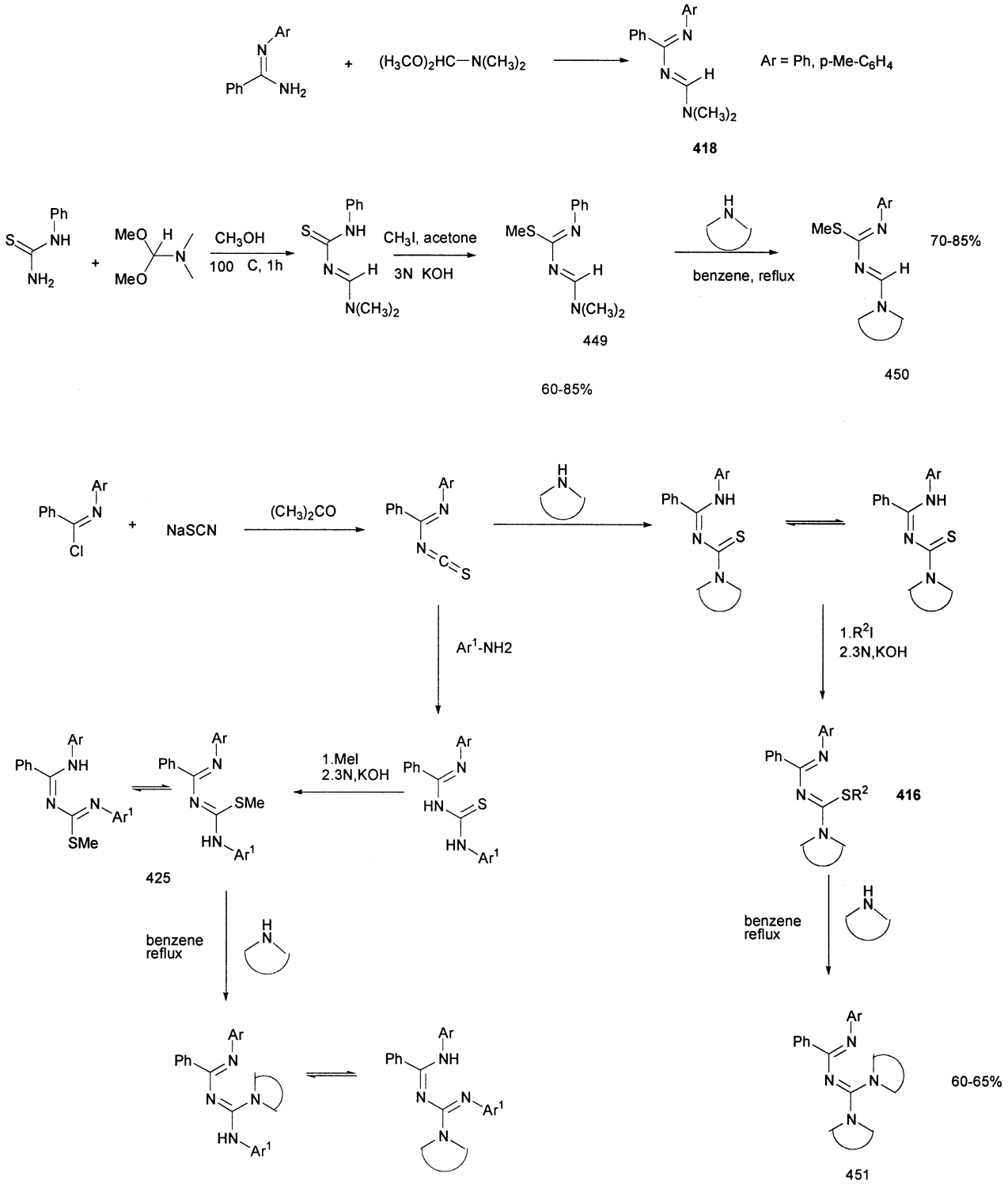
Scheme 104.



Scheme 105.


ClCO2Me
439
440
COOEt
21-53%
441
R1=Ph,Me
R2=Ph,p-tolyl,Me,H
Me2NCH(OMe)2
442
Quantitative
b
COOEt
443
42-46%
R1=SMe,Ph, CO2Et, CH(OEt)2
R2=Me,t-Bu
R1 = SMe, Ph, CO2Et, CH(EtO)2
R2 = t-Bu
R3 = CO2Me, H
R4 = Et, Me
MeI
R=Ph,Me
444
~90%
1. Base 2. CS2 3. MeI
MeI
445
447
R1 = COOMe, H
R2 = Me, Et
R1C(OMe)2NMe2
446
R1 = H, Me, Ph
90-100%
448
R1 = H, Me, Ph
R2 = CO2Me, H, Ph 40-98%
R3 = OMe, OEt, H

Scheme 106.

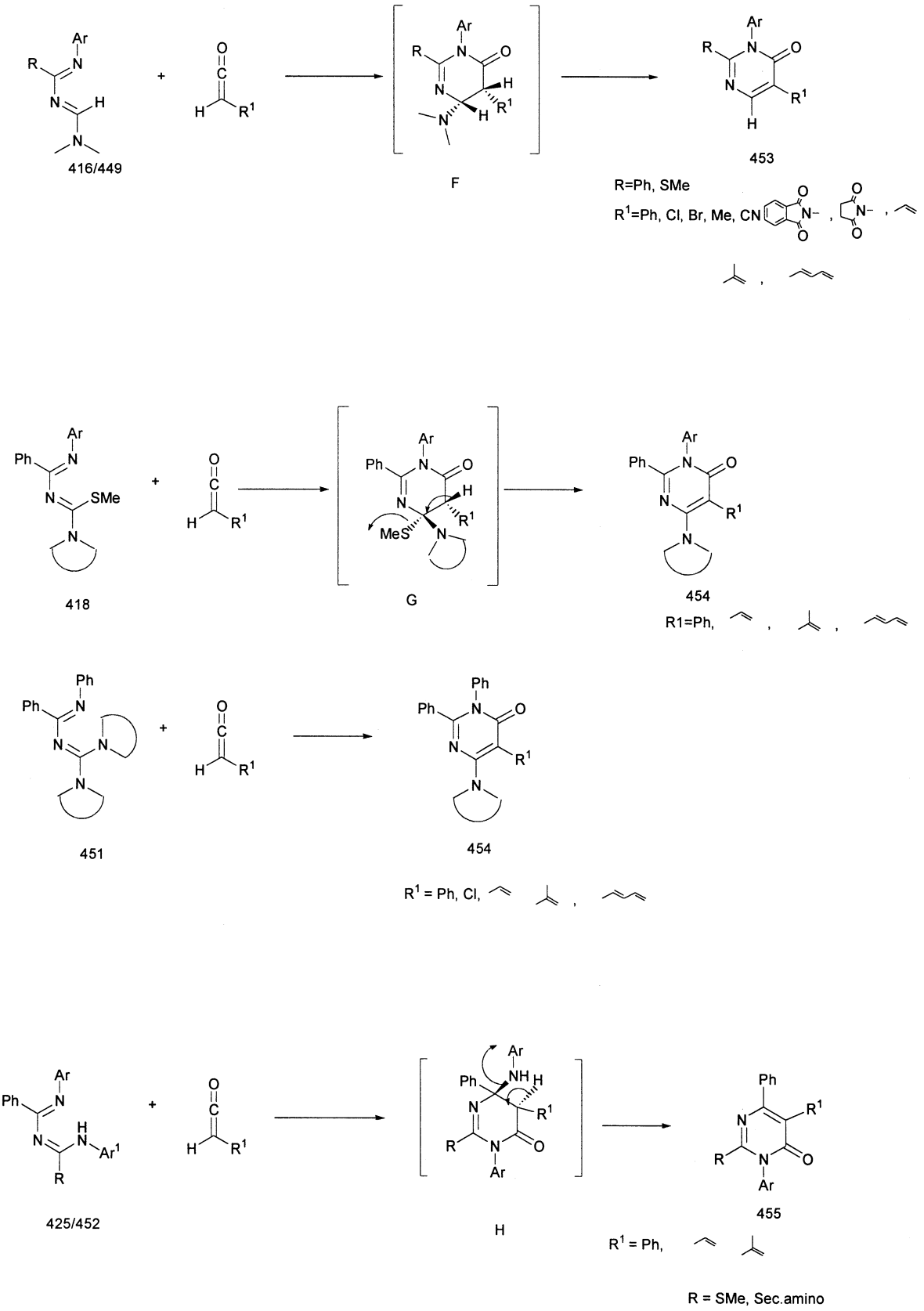


Ar=Ph, *p*-Me-C_6H_4, *p*-MeO-C_6H_4, *p*-Cl-C_6H_4, *p*-Br-C_6H_4

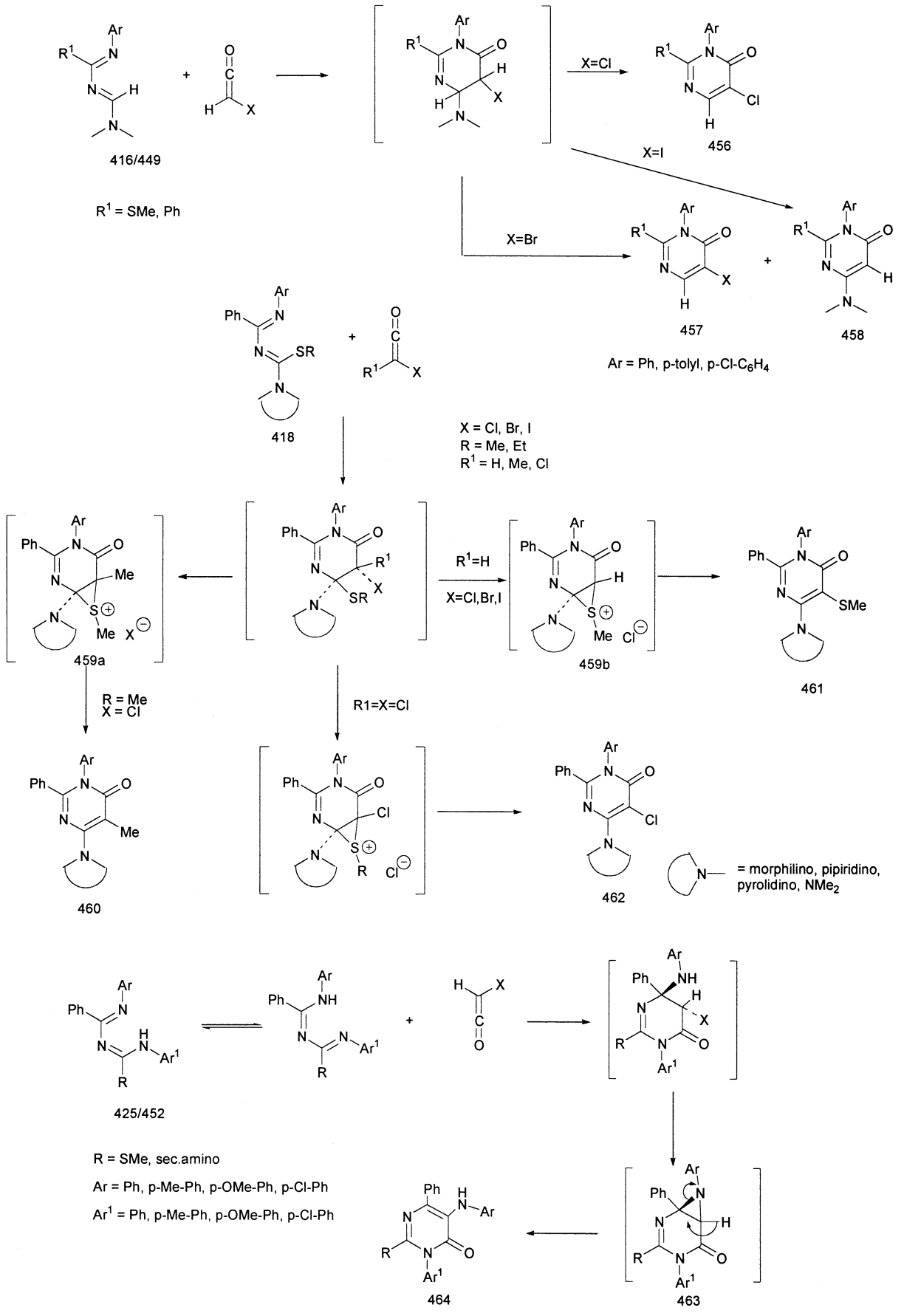
Ar^1=Ph, *p*-Me-C_6H_4, *p*-OMe-C_6H_4, *p*-Cl-C_6H_4, *p*-Br-C_6H_4

R=R^1=morpholino, pypiridino, pyrrolidino, dimethylamino, diethylamino

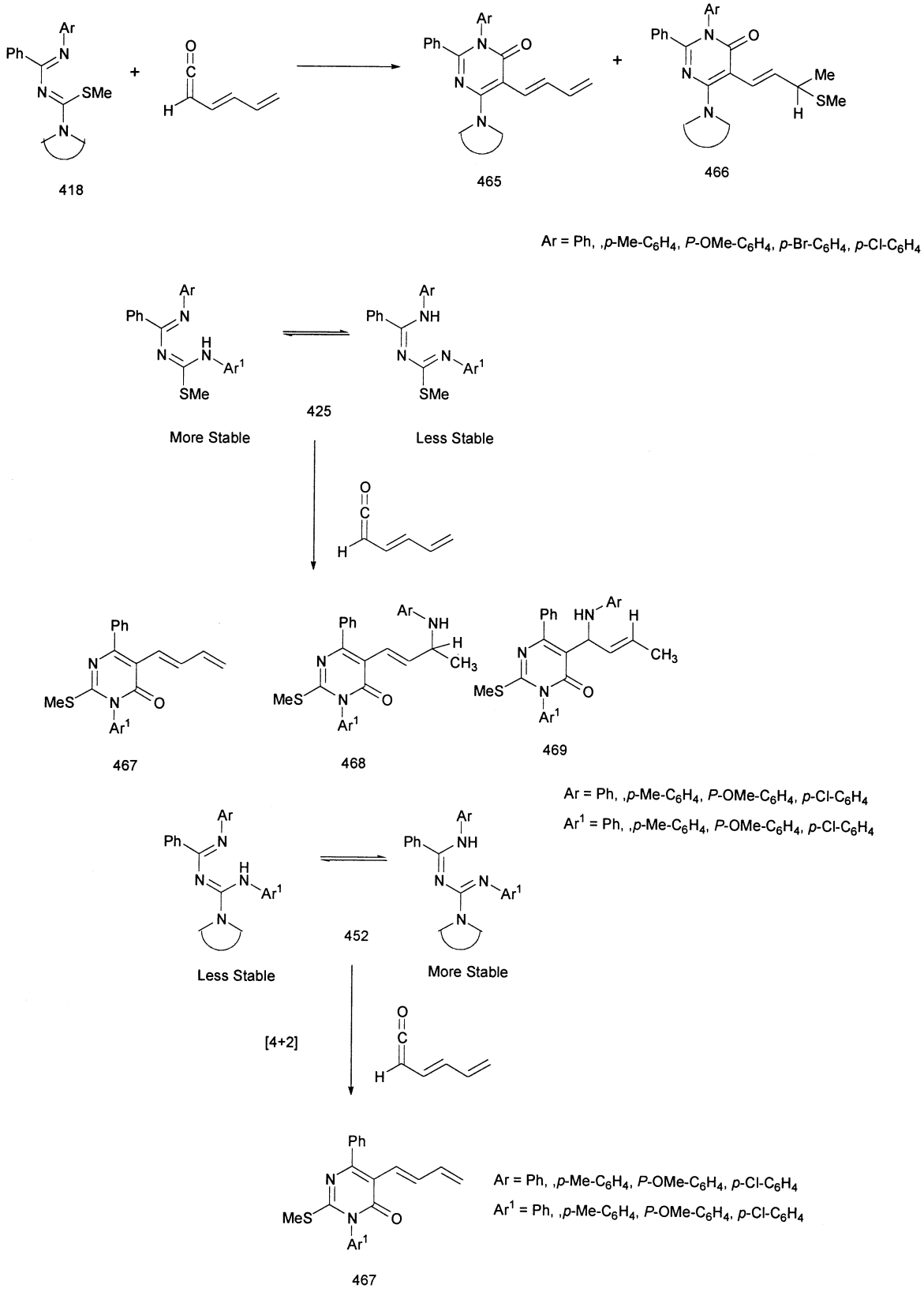
Scheme 106 (*continued*)


416/449
F
453
R=Ph, SMe
R1=Ph, Cl, Br, Me, CN
418
G
454
R1=Ph,
451
454
R1 = Ph, Cl,
425/452
H
455
R1 = Ph,
R = SMe, Sec.amino

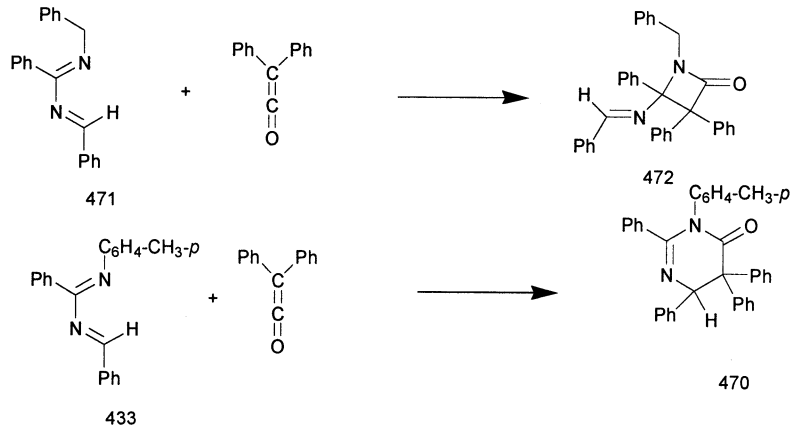
Scheme 107.


416/449
R1 = SMe, Ph
X=Cl
456
X=I
X=Br
457
458
Ar = Ph, p-tolyl, p-Cl-C6H4
418
X = Cl, Br, I
R = Me, Et
R1 = H, Me, Cl
459a
R = Me
X = Cl
R1=H
X=Cl,Br,I
459b
461
R1=X=Cl
460
462
= morphilino, pipiridino, pyrolidino, NMe2
425/452
R = SMe, sec.amino
Ar = Ph, p-Me-Ph, p-OMe-Ph, p-Cl-Ph
Ar1 = Ph, p-Me-Ph, p-OMe-Ph, p-Cl-Ph
464
463

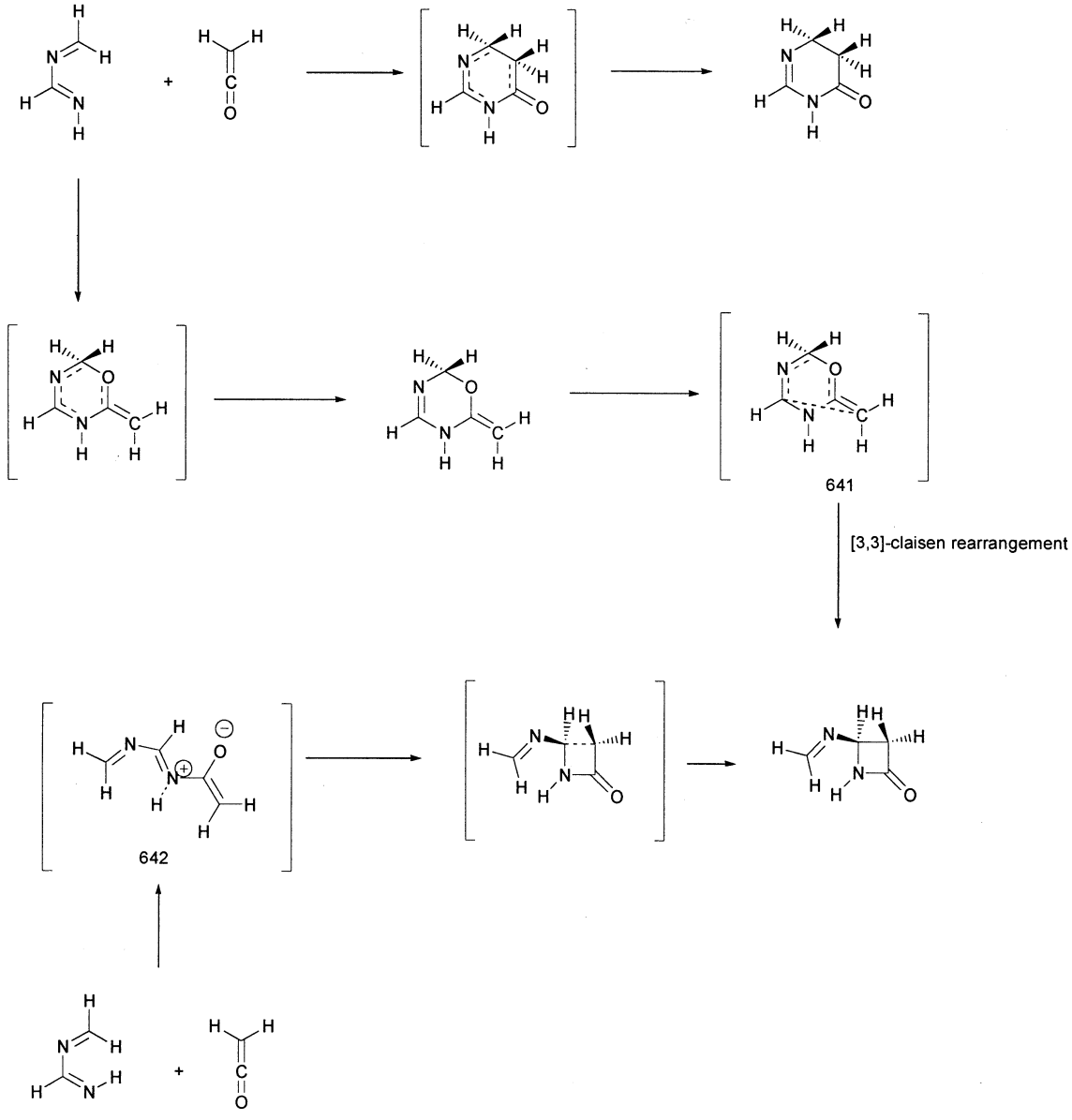
Scheme 108.


418
465
466
Ar = Ph, ,p-Me-C6H4, P-OMe-C6H4, p-Br-C6H4, p-Cl-C6H4
425
More Stable
Less Stable
467
468
469
Ar = Ph, ,p-Me-C6H4, P-OMe-C6H4, p-Cl-C6H4
Ar1 = Ph, ,p-Me-C6H4, P-OMe-C6H4, p-Cl-C6H4
452
Less Stable
More Stable
[4+2]
467
Ar = Ph, ,p-Me-C6H4, P-OMe-C6H4, p-Cl-C6H4
Ar1 = Ph, ,p-Me-C6H4, P-OMe-C6H4, p-Cl-C6H4

Scheme 109.



Scheme 110.



Scheme 111.

cleavage to the *E*-isomer and its [4+2] cycloaddition reaction with the carbon–carbon double bond of the ketene (Scheme 111). This mechanism has been able to successfully explain the observed stereoselective formation of [4+2] cycloadducts which are unlikely to evolve through the zwitterionic intermediate, proposed in earlier mechanisms.

Acknowledgements

Authors gratefully acknowledge the financial support from CSIR, New Delhi and S. J. is grateful to CSIR, New Delhi for a Senior Research Fellowship.

References

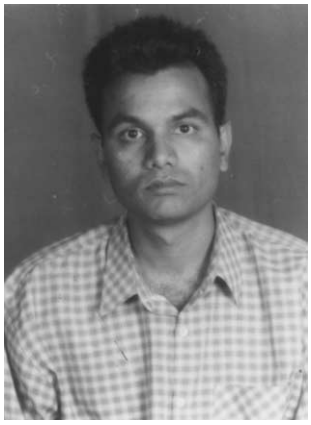
1. For recent reviews on azadienes see: (a) Boger, D. L. *Tetrahedron* **1983**, *39*, 2869. (b) Boger, D. L. *Chem. Tract-Org. Chem.* **1996**, *9*, 149. (c) Barluenga, J.; Tomas, M. *Adv. Heterocycl. Chem.* **1993**, *57*, 1. (d) Boger, D. L. *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 5 Chapter 4.3. (e) Ghosez, L. *Stereocontrolled Organic Synthesis*; Blackwell: London, 1994; p 193. (f) Boger, D. L.; Weinreb, S. M. *Hetero Diels–Alder Methodology in Organic Synthesis*; Academic: San Diego, 1987. (g) Boger, D. L.; Patel, M. *Progress in Heterocyclic Chemistry*; Suschizky, H., Scriven, E. F. V., Eds.; Pergamon: London, 1989; Vol. 1, p 30. (h) Boger, D. L. *Chem. Rev.* **1986**, *86*, 781. (i) Radl, S. *Aldrichim. Acta* **1997**, *30*, 97. (j) Attanasi, O. A.; Filippone, P. *Synlett* **1997**, 1128. (k) Sandhu, J. S.; Sain, B. *Heterocycles* **1987**, *26*, 777. (l) Ghosez, L.; Serckx-Ponchin, B.; Rivera, M.; Bayard, P.; Sainte, F.; Demoulin, A.; Frisque-Hesbain, A. M.; Mockel, A.; Munoz, L.; Bernard-Henriet, C. *J. Heterocycl. Chem.* **1985**, *22*, 69. (m) Boger, D. L. *Bull. Soc. Chim. Belg.* **1990**, *99*, 599. (n) Behforonz, M.; Ahmadian, M. *Tetrahedron* **2000**, *56*, 5259.
2. Staudinger, H. *Liebigs Ann. Chem.* **1907**, *356*, 51.
3. Rammash, B. Kh.; Atwood, J. L.; Weeks, J. A.; Wong, J. L. *J. Org. Chem.* **1987**, *52*, 2712.
4. Cossio, F. P.; Ugalde, J. M.; Lopez, X.; Lecea, B.; Palomo, C. *J. Am. Chem. Soc.* **1993**, *115*, 995.
5. Brady, W. T.; Shieh, C. H. *J. Org. Chem.* **1983**, *48*, 2499 and references therein.
6. Lecea, B.; Arrastia, I.; Arrieta, A.; Roa, G.; Lopez, X.; Arriortua, M. I.; Ugalde, J. M.; Cossio, F. P. *J. Org. Chem.* **1996**, *61*, 3070.
7. Hegedus, L. S.; Montgomery, J.; Narukawa, Y.; Snustad, D. C. *J. Am. Chem. Soc.* **1991**, *113*, 5784.
8. (a) Lopez, R.; Sordo, T. L.; Sordo, J. A.; Gonzalez, J. *J. Org. Chem.* **1993**, *58*, 7036. (b) Cossio, F. P.; Arrieta, A.; Lecea, B.; Ugalde, J. M. *J. Am. Chem. Soc.* **1994**, *116*, 2093. (c) Hubschwerlen, C.; Schmid, G. *Helv. Chim. Acta* **1983**, *66*, 2206. (d) Kabayashi, Y.; Takemoto, Y.; Ito, Y.; Terashima, S. *Tetrahedron Lett.* **1990**, *31*, 3031. (e) Kobayashi, Y.; Takemoto, Y.; Kamiyo, T.; Haradala, H.; Ito, Y.; Terashima, S. *Tetrahedron* **1992**, *48*, 1853. (f) Palomo, C.; Cossio, F. R.; Ontoria, J. M.; Odriozola, J. M. *Tetrahedron Lett.* **1991**, *32*, 3105. (g) Terashima, S. *Synlett* **1992**, 691. (h) Evans, D. A.; Williams, J. M. *Tetrahedron Lett.* **1988**, *29*, 5065. (i) Frazier, J. M.; Staszak, M. A.; Weigel, L. O. *Tetrahedron Lett.* **1992**, *33*, 857. (j) Palomo, C.; Cossio, F. P.; Cuevar, C.; Lecea, B.; Mielgo, A.; Roman, P.; Lugiv, A.; Martinez-Ripoll, M. *J. Am. Chem. Soc.* **1992**, *114*, 9340. (k) Ikota, N.; Hamaki, A. *Heterocycles* **1984**, *21*, 418. (l) Ikota, N.; Shibata, H.; Koga, K. *Chem. Pharm. Bull.* **1985**, *33*, 3299.
9. Prajapati, D.; Mahajan, A. R.; Sandhu, J. S. *J. Chem. Soc., Perkin Trans. 1* **1992**, 1821.
10. Danks, T. N.; Velo-Rego, D. *Tetrahedron Lett.* **1994**, *35*, 9443.
11. (a) Barluenga, J.; Tomas, M.; Lopez-Pelegrin, J. A.; Rubio, E. *J. Chem. Soc., Chem. Commun.* **1995**, 665. (b) Romashin, Y. N.; Liu, M. T. H.; Bonneau, R. *J. Chem. Soc., Chem. Commun.* **1999**, 447.
12. (a) Croce, P. D.; Ferraccioli, R.; Rosa, C. L. *J. Chem. Soc., Perkin Trans. 1* **1994**, 2499. (b) Consonni, R.; Croce, P. D.; Ferraccioli, R.; Rosa, C. L. *J. Chem. Res. (S)* **1991**, 188. (c) Croce, P. D.; Ferrraccioli, R.; Rosa, C.; Pilat, T. *J. Chem. Soc., Perkin Trans. 2* **1993**, 1511. (d) Funke, E.; Huisgen, R. *Chem. Ber.* **1971**, *104*, 3222.
13. Clerici, F.; Gelmi, M. L.; Soave, R.; Valle, M. *Tetrahedron* **1998**, *54*, 11285.
14. Grassi, G.; Risitano, F.; Foti, F. *Tetrahedron* **1995**, *51*, 11885.
15. Xu, Z.; Lu, X. *Tetrahedron Lett.* **1997**, *38*, 3461.
16. Berger, D.; Imhof, W. *J. Chem. Soc., Chem. Commun.* **1999**, 1457.
17. Palacios, F.; Aparicio, D.; Santos, J. M. *Tetrahedron Lett.* **1993**, *34*, 3481.
18. (a) Chagr, M.; Fillion, H.; Pougny, A. *Tetrahedron Lett.* **1988**, *29*, 5913. (b) Nebois, P.; Fillion, H.; Benameur, L.; Fenet, B.; Luche, J.-L. *Tetrahedron* **1993**, *49*, 9767.
19. (a) Levesque, S.; Brassard, P. *Heterocycles* **1994**, *38*, 2205. (b) Perez, J. M.; Avendano, C.; Menendez, J. C. *Tetrahedron Lett.* **1997**, *38*, 4717.
20. (a) Nebois, P.; Cherkaoui, O.; Benameur, L.; Fillion, H.; Fenet, B. *Tetrahedron* **1994**, *50*, 8457. (b) Cherkaoui, O.; Nebois, P.; Fillion, H.; Domard, M.; Fenet, B. *Tetrahedron* **1996**, *52*, 9499.
21. Poumaroux, A.; Bouaziz, Z.; Domard, M.; Fillion, H. *Heterocycles* **1997**, *45*, 585.
22. Perez, J. M.; Avendano, C.; Menendez, J. C. *Tetrahedron* **1995**, *51*, 6573.
23. Blanco, M. M.; Alonso, M. A.; Avendano, C.; Menendez, J. C. *Tetrahedron* **1996**, *52*, 5933.
24. (a) Blanco, M. M.; Avendano, C.; Menendez, J. C. *Tetrahedron* **1997**, *53*, 11465. (b) Perez, J. M.; Alvarado, P. L.; Alonso, M. A.; Avendano, C.; Menendez, J. C. *Tetrahedron Lett.* **1996**, *37*, 6955.
25. Blanco, M. M.; Avedano, C.; Menendez, J. C. *Tetrahedron* **1999**, *55*, 12637.
26. Vilfacampa, M.; Perez, J. M.; Avendano, C.; Menendez, J. C. *Tetrahedron* **1994**, *50*, 10047.
27. Valderrama, J. A.; Gonzalez, M. F.; Valderrama, C. *Tetrahedron* **1999**, *55*, 6039.
28. Biswas, G. K.; Nath, A. C.; Mukherjee, B.; Patra, A.; Chakrabarty, M. *Tetrahedron Lett.* **1992**, *33*, 117.

29. Cuerva, J. M.; Echavarren, A. M. *Synlett* **1997**, 173.
30. Tamion, R.; Mineur, C.; Ghosez, L. *Tetrahedron Lett.* **1995**, *36*, 8977.
31. Behforouz, M.; Gu, Z.; Stelzer, L. S.; Ahmadian, M.; Hadad, J.; Scherschel, J. A. *Tetrahedron Lett.* **1997**, *38*, 2211.
32. Bushby, N.; Moody, C. J.; Riddick, D. A.; Waldon, I. R. *J. Chem. Soc., Chem. Commun.* **1999**, 793.
33. Cuerva, J. M.; Cardenas, D. J.; Echavarren, A. M. *J. Chem. Soc., Chem. Commun.* **1999**, 1721.
34. Waldner, A. *Tetrahedron Lett.* **1989**, 3061.
35. Beaudegnies, R.; Ghosez, L. *Tetrahedron: Asymmetry* **1994**, *5*, 557.
36. Elliott, M. C.; Kruiswijk, E. *J. Chem. Soc., Chem. Commun.* **1997**, 2311.
37. Turchi, S.; Giomi, D.; Nesi, R. *Tetrahedron* **1995**, *51*, 7085.
38. (a) Barluenga, J.; Aznar, F.; Fustero, S.; Tomas, M. *Pure Appl. Chem.* **1990**, *62*, 1957. (b) Barluenga, J.; Losada, C. P.; Olano, P. *Tetrahedron Lett.* **1993**, *34*, 5497.
39. (a) Barluenga, J.; Tomas, M.; Ballesteros, A.; Kong, J.-S. *Afinidad* **1993**, *448*, 366. (b) Barluenga, J.; Tomas, M.; Ballesteros, A.; Kong, J.-S. *Synthesis* **1992**, 106.
40. (a) Kimpe, N.; Buck, K.; Booten, K. *Tetrahedron Lett.* **1992**, *33*, 393. (b) Barluenga, J.; Merino, I.; Palacios, S. *J. Chem. Soc. Perkin Trans. 1* **1991**, 341. (c) Barluenga, J.; Merino, I.; Palacios, S. *Tetrahedron Lett.* **1989**, *30*, 5493. (d) Barluenga, J.; Sanz, R.; Gonzalez, R.; Fananas, F. J. *J. Chem. Soc., Chem. Commun.* **1994**, 989.
41. Barfacker, L.; Hollmann, C.; Eilbracht, E. *Tetrahedron* **1998**, *54*, 4493.
42. Martin, N.; Grau, A. M.; Sanchez, L.; Seoane, C.; Torres, M. *J. Org. Chem.* **1998**, *63*, 8074.
43. Steinhagen, H.; Corey, E. J. *Angew. Chem., Int. Ed. Engl.* **1999**, *38*, 1928.
44. Barluenga, J.; Tomas, M.; Lopez-Pelegrin, J. A.; Rubio, E. *Tetrahedron Lett.* **1997**, *38*, 3981.
45. Teng, M.; Fowler, F. W. *Tetrahedron Lett.* **1989**, *30*, 2481.
46. Teng, M.; Fowler, F. W. *J. Org. Chem.* **1990**, *55*, 5646.
47. Boger, D. L.; Corbett, W. L.; Curran, T. T.; Kasper, A. M. *J. Am. Chem. Soc.* **1991**, *113*, 1713.
48. Trione, C.; Toledo, L. M.; Kuduk, S. D.; Fowler, F. W.; Grieson, D. S. *J. Org. Chem.* **1993**, *58*, 2075.
49. Sisti, N. J.; Motorina, I. A.; Dau, M.-E. T. H.; Riche, C.; Fowler, W. F.; Grieson, D. S. *J. Org. Chem.* **1996**, *61*, 3715.
50. (a) Boger, D. L.; Kasper, A. M. *J. Am. Chem. Soc.* **1989**, *111*, 1517. (b) Boger, D. L.; Corbett, W. L.; Wiggins, J. M. *J. Org. Chem.* **1990**, *55*, 2999. (c) Boger, D. L.; Curran, T. T. *J. Org. Chem.* **1990**, *55*, 5439. (d) Boger, D. L.; Nakahara, S. *J. Org. Chem.* **1991**, *56*, 880. (e) Dau, M. E. T. H.; Flament, J.-P.; Lefour, J.-M.; Riche, C.; Grierson, D. S. *Tetrahedron Lett.* **1992**, *33*, 2343.
51. (a) Sisti, N. Z.; Zeller, E.; Grierson, D. S.; Fowler, F. W. *J. Org. Chem.* **1997**, *62*, 2093. (b) Motorina, I. A.; Fowler, F. W.; Grierson, D. S. *J. Org. Chem.* **1997**, *62*, 2098.
52. Motorina, I. A.; Grierson, D. S. *Tetrahedron Lett.* **1999**, *40*, 7211.
53. Motorina, I. A.; Grierson, D. S. *Tetrahedron Lett.* **1999**, *40*, 7215.
54. Dubois, C. G.; Adams, D. R.; Sisti, N. J.; Fowler, F. W.; Grierson, D. S. *Tetrahedron Lett.* **1998**, *39*, 4283.
55. Dufour, B.; Motorina, I. A.; Fowler, F. W.; Grierson, D. S. *Heterocycles* **1994**, *37*, 1455.
56. (a) Uyehara, T.; Suzuki, I.; Yamamoto, Y. *Tetrahedron Lett.* **1990**, *33*, 3753. (b) Uyehara, T.; Chiba, N.; Suzuki, I.; Yamamoto, Y. *Tetrahedron Lett.* **1991**, *34*, 4371.
57. Augusti, R.; Gozzo, F. C.; Mpraes, L. A. B.; Sparrapan, R.; Eberlin, M. N. *J. Org. Chem.* **1998**, *63*, 4889.
58. (a) Barluenga, J.; Tomas, M.; Ballesteros, A.; Santamaria, J.; Lopez-Ortiz, F. *J. Chem. Soc., Chem. Commun.* **1994**, 321. (b) Barluenga, J.; Tomas, M.; Ballesteros, A.; Santamaria, J.; Carbajo, R. J.; Lopez-Ortiz, F.; Garcia-Granda, S.; Pertierra, P. *Chem. Eur. J.* **1996**, *2*, 88.
59. Barluenga, J.; Tomas, M.; Ballesteros, A.; Kong, J.-S.; Granda, S. G.; Peritierra, P. *Organometallics* **1992**, *11*, 2348.
60. Barluenga, J.; Kouznestov, V.; Rubio, E.; Tomas, M. *Tetrahedron Lett.* **1993**, *34*, 1981.
61. Barluenga, J.; Viado, A. L.; Aguilar, E.; Fustero, S.; Olano, B. *J. Org. Chem.* **1993**, *58*, 5972.
62. Barluenga, J.; Tomas, M.; Ballestros, A.; King, J.-S. *Tetrahedron* **1996**, *52*, 3095.
63. (a) Barluenga, J.; Tomas, M.; Bieger, K.; Granda, S. G.; Garcia, R. S. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 896. (b) Barluenga, J.; Tomas, M.; Bieger, K.; Granda, S. G.; Garcia, R. S. *J. Organomet. Chem.* **1997**, *529*, 233.
64. Barluenga, J.; Pozo, C.; Olano, B. *Synthesis* **1996**, 133.
65. Barluenga, J.; Tomas, M.; Sobrino, A. S.; Rubio, E. *Tetrahedron Lett.* **1990**, *31*, 2189.
66. Barluenga, J.; Tomas, M.; Jardon, J.; Rubio, E.; Gotor, V. *Synthesis* **1989**, 230.
67. (a) Sugaya, T.; Kato, N.; Tomioka, S.; Tamaki, K. *Chem. Lett.* **1990**, 2181. (b) Sugaya, T.; Kato, N.; Sakaguchi, A.; Tomioka, S. *Synthesis* **1995**, 1257.
68. (a) Bonini, M. F.; Fochi, M.; Franchini, M. C.; Mazzanti, G.; Ricci, A.; Picard, J. P.; Cargues, J.; Aizpurua, J. M.; Palomo, C. *Synlett* **1997**, 1321.
69. Georgieva, A.; Stanoeva, E.; Spassov, S.; Haimova, M.; De Kimpe, N.; Boelens, M.; Keppens, M.; Kemme, A.; Mishnev, A. *Tetrahedron* **1995**, *51*, 6099.
70. Kumar, K.; Kapoor, R.; Kapur, A.; Ishar, M. P. S. *Org. Lett.* **2000**, *2*, 2023.
71. For recent reviews on the aza-Wittig reactions of phosphazenes see: (a) Barluenga, J.; Palacios, F. *Org. Prep. Proced. Int.* **1991**, *23*, 1. (b) Eguchi, S.; Matsushita, Y.; Yamashita, K. *Org. Prep. Proced. Int.* **1992**, *24*, 209. (c) Gololubov, Y. G.; Kaskhin, L. F. *Tetrahedron* **1992**, *48*, 1353. (d) Molina, P.; Vilaplana, M. J. *Synthesis* **1994**, 1197.
72. (a) Molina, P.; Aller, E.; Lopez-Lazaro, A.; Alajarin, M.; Lorenzo, A. *Tetrahedron Lett.* **1994**, *35*, 3817. (b) Molina, P.; Pastor, A.; Vilaplana, M. J. *J. Org. Chem.* **1996**, *61*, 8094.
73. (a) Palacios, F.; Rubiales, G. *Tetrahedron Lett.* **1996**, *37*, 6379. (b) Palacios, F.; Herran, E.; Rubiales, G. *J. Org. Chem.* **1999**, *64*, 6239.

74. (a) Palacios, F.; Heredia, I. P.; Rubiales, G. *Tetrahedron Lett.* **1993**, *34*, 4377. (b) Palacios, F.; Heredia, I. P.; Rubiales, G. *J. Org. Chem.* **1995**, *60*, 2384.
75. Palacios, F.; Alonso, C.; Rubiales, G. *J. Org. Chem.* **1997**, *62*, 1146.
76. Palacios, F.; Gil, M. J.; Marigorta, E. M.; Rodriguez, M. *Tetrahedron Lett.* **1999**, *40*, 2411.
77. (a) Barluenga, J.; Ferrero, M.; Palacios, F. *J. Chem. Soc., Perkin Trans. 1* **1990**, 2193. (b) Barluenga, J.; Ferrero, M.; Palacios, F. *Tetrahedron Lett.* **1988**, *29*, 4863.
78. Ghosez, L.; Bayard, Ph.; Nshimyumukiza, P.; Gouverneur, V.; Sainte, F.; Beaudegnies, R.; Rivera, M.; Hesbain, A. M. F.; Wynants, C. *Tetrahedron* **1995**, *51*, 11021.
79. Rivera, M.; Shelkens, H.; Sainte, F.; Mbiya, K.; Ghosez, L. *Tetrahedron Lett.* **1988**, *29*, 4573.
80. Barroso, M. T.; Kascheres, A. *J. Org. Chem.* **1999**, *64*, 49.
81. (a) Kimpe, N. D.; Stanoeva, E.; Verhe, R.; Schamp, N. *Synthesis* **1988**, 587. (b) Kimpe, N. D.; Sulmon, P.; Moens, L.; Schamp, N.; Decercq, J-P.; Van Meerssche, M. *J. Org. Chem.* **1986**, *51*, 3839. (c) Kimpe, N. D.; Yao, Z-P.; Boyeykens, M.; Nagy, M. *Tetrahedron Lett.* **1990**, *31*, 2771. (d) Kimpe, D. N.; Nagy, M.; Boeykenes, M.; Shueren, D. A. *J. Org. Chem.* **1992**, *57*, 5761.
82. (a) Gilchrist, T. L.; Gonsalves, A. M. R.; Teresa, M. D. V. P. *Tetrahedron Lett.* **1993**, 4097. (b) Gilchrist, T. L.; Gonsalves, A. M. R.; Teresa, M. V. D. P. *Tetrahedron* **1994**, *50*, 13709. (c) Barkley, J. V.; Gilchrist, T. L.; Gonsalves, A. M. D. R.; Teresa, M. V. D. *Tetrahedron* **1995**, *51*, 13455. (d) Teresa, M. V. D.; Fausto, R.; Gonsalves, A.; Gildhrist, P. L. *J. Org. Chem.* **1998**, *63*, 5350.
83. (a) Ho, E.; Cheng, Y. S.; Mariano, P. S. *Tetrahedron Lett.* **1988**, *29*, 4799. (b) Cheng, F. S.; Ho, E.; Mariano, P. S. *Tetrahedron* **1988**, *44*, 7013.
84. Bouillon, J. P.; Maliverney, C.; Janousek, Z.; Viehe, H. G. *Bull. Soc. Chim. Fr.* **1997**, *134*, 47.
85. Balsamini, C.; Bedini, A.; Spadoni, G.; Burdisso, M.; Capelli, A. M. *Tetrahedron* **1994**, *50*, 3773.
86. Bongini, A.; Panunzio, M.; Bandini, E.; Martelli, G.; Spunta, G. *J. Org. Chem.* **1997**, *62*, 8911.
87. Bongini, E.; Martelli, G.; Spunta, G.; Bongini, A.; Panunzio, M.; Piersanti, G. *Tetrahedron: Asymmetry* **1999**, *10*, 1445.
88. Barluenga, J.; Carlon, R. P.; Pelaez, E.; Joglar, J.; Lopez, F.; Fustero, S. *Tetrahedron* **1992**, *46*, 9745.
89. (a) Legroux, D.; Schoeni, J. P.; Pont, C. P.; Fleury, J. P. *Helv. Chim. Acta* **1987**, *70*, 187. (b) Legroux, D.; Brom, J.; Fleury, J. P. *Helv. Chim. Acta* **1990**, *73*, 1210.
90. Jnoff, E.; Ghosez, L. *J. Am. Chem. Soc.* **1999**, *121*, 2617.
91. Ghosez, L.; Jnoff, E.; Bayard, P.; Sainte, F.; Beaudegnies, R. *Tetrahedron* **1999**, *55*, 3387.
92. Pouilhes, A.; Langlois, Y.; Nshimyumukiza, P.; Mbiya, A.; Ghosez, L. *Bull. Soc. Chim. Fr.* **1993**, *130*, 304.
93. Bouammali, B.; Pautet, F.; Fillion, H. *Tetrahedron* **1993**, *49*, 3125.
94. (a) Barluenga, J.; Tomas, M.; Ballesteros, A.; Lopez, L. A. *Tetrahedron Lett.* **1989**, *30*, 6923. (b) Barluenga, J.; Tomas, M.; Ballesteros, A.; Lopez, L. A. *Synthesis* **1995**, 985.
95. (a) Balsamini, C.; Bedini, A.; Spadoni, G.; Burdisso, M.; Capelli, A. M. *Tetrahedron* **1994**, *50*, 3773. (b) Balsamini, C.; Spadoni, G.; Bedini, A.; Tarzia, G.; Lanfranchi, M.; Pellinghelli, M. A. *J. Heterocycl. Chem.* **1992**, *29*, 1593.
96. (a) Van Aken, K. J.; Lux, G. M.; Deroover, G. G.; Meerpoel, L.; Hoornaert, G. J. *Tetrahedron* **1994**, *50*, 5211. (b) Meerpoel, L.; Hoornaert, G. *Tetrahedron Lett.* **1989**, *30*, 3183. (c) Meerpoel, L.; Hoornaert, G. *Synthesis* **1990**, 905. (d) Meerpoel, L.; Deroover, G.; Van Aken, K.; Lux, G.; Hoornaert, G. *Synthesis* **1991**, 765. (e) Fannes, C.; Meerpoel, L.; Toppet, S.; Hoornaert, G. *Synthesis* **1992**, 705. (f) Van Aken, K.; Meerpoel, L.; Hoornaert, G. *Tetrahedron Lett.* **1992**, *33*, 2713. (g) Van Aken, K.; Hoornaert, G. *J. Chem. Soc., Chem. Commun.* **1992**, 895. (h) Loosen, P. K.; Tutonda, M. G.; Khorasani, M. F.; Compernolle, F.; Hoorneert, G. J. *Tetrahedron* **1991**, *47*, 9259. (i) Meerpoel, L.; Joly, G. J.; Hoornaert, G. J. *Tetrahedron* **1993**, *49*, 4085.
97. Palacios, F.; Aparcio, D.; Santos, J. M. *Tetrahedron* **1996**, *52*, 4857.
98. Barluenga, J.; Joglar, J.; Gonzalez, F. J.; Fustero, S.; Kruger, C.; Tsay, Y-H. *Synthesis* **1991**, 381.
99. (a) Barluenga, J.; Gonzalez, F. J.; Fustero, S. *Tetrahedron Lett.* **1990**, 397. (b) Barluenga, J.; Aznar, F.; Fustero, S.; Tomas, M. *Pure Appl. Chem.* **1990**, *62*, 1957. (c) Barluenga, J.; Sordo, T. L.; Sordo, J. A.; Fustero, S.; Gonzalez, J. *J. Mol. Struct. (Theochem)* **1994**, *315*, 63. (d) Barluenga, J.; Gonzalez, F. J. *J. Org. Chem.* **1991**, *56*, 4459.
100. (a) Barluenga, J.; Carlon, R. P.; Gonzalez, F. J.; Fustero, S. *Tetrahedron Lett.* **1990**, *31*, 3793. (b) Barluenga, J.; Carlon, R. P.; Gonzalez, F. J.; Fustero, S. *J. Org. Chem.* **1991**, *56*, 6751.
101. Augusti, R.; Gozzo, F. C.; Moraes, L. A. B.; Sparrapan, R.; Eberlin, M. N. *J. Org. Chem.* **1998**, *63*, 4889.
102. Barluenga, J.; Carlon, R. P.; Gonzalez, F. J.; Lopez, F.; Fustero, S. *J. Chem. Soc., Chem. Chemmun.* **1991**, 1704.
103. Gouverneur, V.; Ghosez, L. *Tetrahedron* **1996**, *52*, 7585.
104. Barluenga, J.; Tomas, M.; Ballesteros, A.; Santamaria, J.; Sobrino, S. A. *J. Org. Chem.* **1997**, *62*, 9229.
105. (a) Armesto, D.; Ortiz, M. J.; Perez-Ossorio, R. *J. Chem. Soc., Perkin Trans. 1* **1986**, 2021. (b) Armesto, D.; Gallego, M. G.; Horspool, W. M.; Ortiz, M. J.; Perez-Ossorio, R. *Synthesis* **1987**, 657. (c) Armesto, D.; Horspool, W. M.; Ortiz, M. J.; Romano, S. *J. Chem. Soc., Perkin Trans. 1* **1992**, 171.
106. (a) Crooks, S.; Sykes, P. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1791. (b) Mazumdar, S. N.; Ibnusaud, I.; Mahajan, M. P. *Tetrahedron Lett.* **1987**, *28*, 2641. (c) Mazumdar, S. N.; Sharma, M.; Mahajan, M. P. *Tetrahedron Lett.* **1986**, *27*, 5875(c). (d) Barluenga, J.; Tomas, M.; Bellesteros, A.; Lopez, L. A. *Tetrahedron Lett.* **1989**, *30*, 4573.
107. Gorel, G.; Marchand, E.; Toupet, L.; Foucaud, A. *J. Org. Chem.* **1989**, *54*, 1185.
108. Ibnusaud, I.; Malar, E. P. J.; Sundaram, N. *Tetrahedron Lett.* **1990**, *47*, 1473.
109. Barluenga, J.; Tomas, M.; Bellesteros, A.; Lopez, L. A. *Heterocycles* **1994**, *37*, 1109.
110. Rossi, E.; Celentano, G.; Stradi, R.; Strada, A. *Tetrahedron Lett.* **1990**, *31*, 903.
111. (a) Wurthwein, E. U.; Luthadart, P. *Tetrahedron Lett.* **1988**, *29*, 921. (b) Luthardt, P.; Moller, M. H.; Rodewald, U.; Wurthwein, E. U. *Chem. Ber.* **1989**, *122*, 1705.

112. (a) Sain, B.; Singh, S. P.; Sandhu, J. S. *Tetrahedron Lett.* **1991**, *32*, 5151. (b) Sain, B.; Singh, S. P.; Sandhu, J. S. *Tetrahedron* **1992**, *48*, 4567.
113. Mazumdar, S. N.; Mahajan, M. P. *Tetrahedron Lett.* **1990**, *31*, 4215.
114. Jayakumar, S.; Ishar, M. P. S.; Mahajan, M. P. *Tetrahedron Lett.* **1998**, *39*, 6557.
115. Jayakumar, S.; Mahajan, M. P. Unpublished results.
116. (a) Sharma, A. K.; Mazumdar, S. N.; Mahajan, M. P. *Tetrahedron Lett.* **1993**, *34*, 7961. (b) Sharma, A. K.; Mazumdar, S. N.; Mahajan, M. P. *J. Chem. Soc., Perkin Trans. 1* **1997**, 3065. (c) Sharma, A. K.; Hundal, G.; Obrai, S.; Mahajan, M. P. *J. Chem. Soc., Perkin Trans. 1* **1999**, 615.
117. (a) Rossi, E.; Calabrese, D.; Farma, F. *Tetrahedron* **1991**, *47*, 5819. (b) Rossi, E.; Pini, E. *Tetrahedron* **1996**, *52*, 7939.
118. Rossi, E.; Stradi, R.; Visentin, P. *Tetrahedron* **1990**, *46*, 3581.
119. (a) Guzman, A.; Romero, F.; Talamus, F. X.; Villena, R.; Greenhouse, R.; Muchowski, J. M. *J. Org. Chem.* **1996**, *61*, 2470. (b) Guzman, A.; Romero, F.; Talamus, F. X.; Villena, R.; Greenhouse, R.; Muchowski, J. M. *Tetrahedron Lett.* **1992**, *33*, 3449.
120. (a) Mazumdar, S. N.; Mahajan, M. P. *Synthesis* **1990**, 417. (b) Dey, P. D.; Sharma, A. K.; Rai, S. N.; Mahajan, M. P. *Tetrahedron* **1995**, *51*, 7459. (c) Sharma, A. K.; Mahajan, M. P. *Tetrahedron* **1997**, *53*, 13841.
121. (a) Mukherjee, S.; Mazumdar, S. N.; Sharma, A. K.; Mahajan, M. P. *Heterocycles* **1998**, *47*, 933. (b) Mazumdar, S. N.; Mahajan, M. P. *Tetrahedron* **1991**, *47*, 1473. (c) Mazumdar, S. N.; Sharma, A. K.; Mukherjee, S.; Gupta, D. S.; Mahajn, M. P. *Tetrahedron* **1994**, *50*, 7579. (d) Sharma, A. K.; Mahajan, M. P. *Heterocycles* **1995**, *40*, 787. (e) Dey, P. D.; Sharma, A. K.; Mahajan, M. P. *Tetrahedron* **1995**, *51*, 7459. (f) Dey, P. D.; Sharma, A. K.; Bhartam, P. V.; Mahajan, M. P. *Tetrahedron* **1997**, *53*, 13829.
122. (a) Sharma, A. K.; Jayakumar, S.; Mahajan, M. P. *Tetrahedron Lett.* **1998**, *39*, 7205. (b) Sharma, A. K.; Jayakumar, S.; Mahajan, M. P. Unpublished results.
123. Rossi, E.; Abbiati, G.; Pini, E. *Tetrahedron* **1997**, *53*, 14107.
124. Mastuda, I.; Yamamoto, S.; Ishii, Y. *J. Chem. Soc., Perkin Trans. 1* **1976**, 1528.
125. Bhartam, P. V.; Kumar, R. S.; Mahajan, M. P. *Org. Lett.* **2000**, *2*, 2725.

Biographical sketch



S. Jayakumar: Born in 1973 at Paravur, Kerala, India. He received his B.Sc. and M.Sc. in chemistry from Mahatma Gandhi University and Nagarjuna University. He then joined Professor Mahajan's research group in 1996 for his doctoral studies. His research is focussed on the studies on the synthetic application of azadienes and imines, directed towards the synthesis of various novel heterocylic compounds. His research interests include total synthesis of natural products, synthesis of biologically interesting molecules using cycloaddition reactions, transition metal induced transformations in organic synthesis and reaction mechanisms.

M. P. S. Ishar: Born in 1956 at Kathua, Jammu and Kashmir, India, obtained his masters degree in Organic Chemistry from Jammu University and PhD in 1986 from Indian Institute of Technology Delhi, India. After serving as Senior Scientific Officer (1986–1987) in Photochemical Laboratory at Indian Institute of Technology Delhi (1987–1990). In 1991, he joined as Reader in Guru Nanak Dev University, Amritsar, where he is presently Professor in the Department of Pharmaceutical Sciences. His research interest lies in Organic Photochemistry, application of cycloaddition reactions in organic synthesis and in the synthesis of medicinally important molecules, and steroid chemistry.

Mohinder P Mahajan: Born in 1947 at Gurdaspur, Punjab (India), and obtained his PhD in 1975 from Punjabi University, Patiala, under the supervision of Professor N. K. Ralthan. He was a post-doctoral associate with Professor M. V. George at the Indian Institute of Technology, Kanpur, Alexander-Von-Humboldt Fellow with Professor Rolf Huisgen at Munich. He was later associated with Professor Gordon Kirby at Glasgow University, United Kingdom. He started his independent academic carrier in 1979 as lecturer at North-Eastern Hill University, Shillong, where he was promoted to full Professor in 1991. In 1996 he shifted to Guru Nanak Dev University, Amritsar as Chairman of the Department of Pharmaceutical Sciences. His research interests include Chemistry of heterodienes, the applications of cycloaddition reactions in synthesis important heterocyclic compounds, synthesis of biologically potent molecules and studies of reaction mechanism.