Reactive Intermediates from *N*-Aziridinylimines

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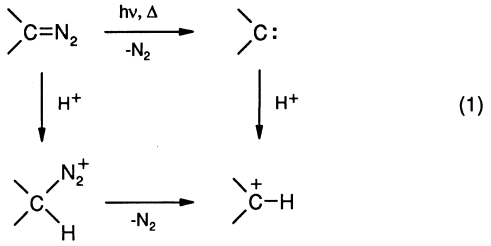
N-Aziridinylimines are readily obtained from carbonyl compounds and 1-aminoaziridines, of which the 2-phenyl and *trans*-2,3-diphenylaziridine derivatives are the most popular. Diazo compounds are formed upon thermolysis or photolysis of *N*-aziridinylimines, with elimination of alkenes. The diazo compounds can be trapped by intramolecular addition to alkenes, but otherwise decompose as they are formed, giving rise to carbenes and products derived therefrom. The transformation $R_2CO \rightarrow R_2CN_2 \rightarrow R_2C$ is most often achieved with the anions (salts) of arenesulfonylhydrazones. However, the non-ionic and weakly basic *N*-aziridinylimines have the advantage that they are compatible with nonpolar solvents and with a wide range of substituents. These properties were exploited in the fragmentations of α,β-epoxyketones (→ alkynones) and α,β-epoxyaldehydes (→ β-hydroxyvinylidenes → cyclopentenols) as well as in the syntheses of unsaturated nitriles, silanes, and ethers. Laser flash photolysis of *N*-aziridinylimines in fluorinated alcohols was used to demonstrate the protonation of carbenes and to measure absolute reaction rates of carbocations. The Shapiro reaction of *N*-aziridinylimines, performed with catalytic amounts of R_2NLi, was found to produce alkenes with excellent regio- and stereoselectivity. As radical acceptors, *N*-aziridinylimines are superior to alkenes. On this basis, selective (tandem) cyclizations were designed for the synthesis of natural products.

Diazo compounds give rise to a variety of reactive intermediates[1]. Carbenes, diazonium ions, and carbocations can be formed, depending on the reaction conditions (eq. 1). Labile diazo compounds must be generated in situ from more stable precursors, such as sulfonylhydrazones. Heat or light induce the elimination of arenesulfinates from the anions (salts) of arenesulfonylhydrazones, with formation of diazo compounds (Bamford-Stevens reaction (eq. 2)[1][2].



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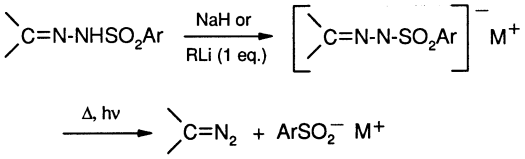

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The Bamford-Stevens reaction has been applied widely, for good reasons: (a) Arenesulfonyl-hydrazones are obtained in acceptable yields even from moderately reactive carbonyl compounds. As a rule, the sulfonylhydrazones are readily purified by crystallization. (b) Conditions and rates for the Bamford-Stevens reaction can be influenced by the proper choice of aryl substituents (although tosylhydrazones are used most often). (c) Extraction with water conveniently removes $ArSO_2M$ from the product mixture. However, some limitations are obvious, particularly for substrates that are base-sensitive. Moreover, the salts of arenesulfonylhydrazones are incompatible with acidic media and difficult to apply in nonpolar solvents, owing to solubility problems[3]. Consequently, there is a need for *covalent*, *neutral* diazo precursors. *N*-Aziridinylimines fill this need remarkably well and also show a rich chemistry of their own.

1. Preparation of *N*-Aziridinylimines

The first *N*-aziridinylimine was obtained by König et al.[4] from the reaction of benzalazine with dimethylsulfoxonium methylide (eq. 3). The authors noted that the novel compound decomposed at ca. 100°C to give styrene and, presumably, phenyldiazomethane. Huisgen et al.[5] succeeded in trapping the diazo compound with acrylonitrile. Soon thereafter, 1-aminoaziridines were developed as reagents that convert carbonyl compounds into *N*-aziridinylimines[6]. The method of choice for 2,3-disubstituted species is the oxidative addition of *N*-aminophthalimide to alkenes,

MICROREVIEWS: This feature introduces the readers to the authors' research through a concise overview of the selected topic. Reference to important work from others in the field is included.

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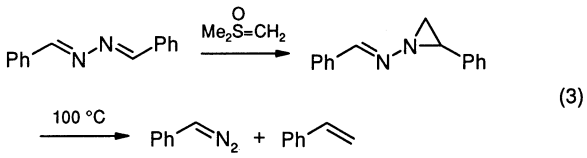

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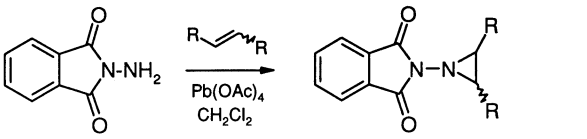

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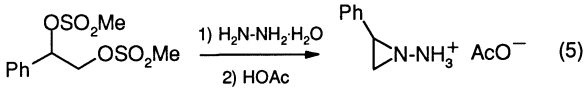

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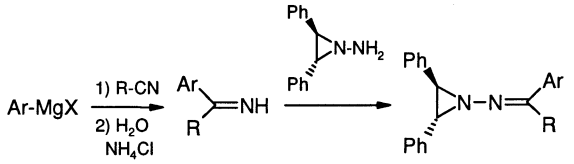

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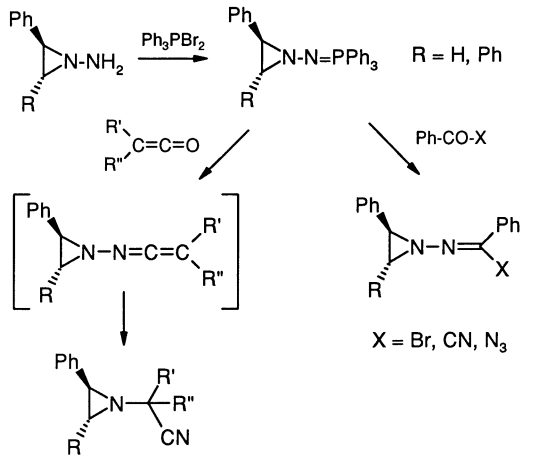

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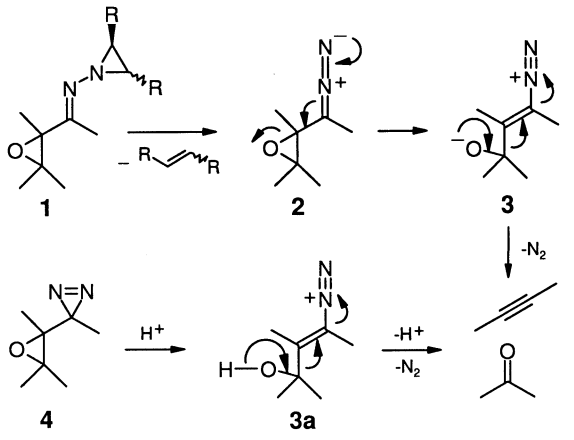
followed by hydrazinolysis (eq. 4). Except for mechanistic studies[7], 1-amino-*trans*-2,3-diphenylaziridine[8] has been employed almost exclusively. The preferred route to 1-amino-2-phenylaziridine is the hydrazinolysis of 1-phenylethane-1,2-diol dimesylate (eq. 5)[8]. (**CAUTION!** 1-Amino-2-phenyl-aziridinium *acetate* is explosive, and proper precautions should be taken whenever it is used).

Practical aspects dictate the choice between 2-phenyl and 2,3-diphenylaziridinylimines. As a rule, the diphenyl compounds decompose at lower temperatures and undergo photolysis more readily, owing to stronger absorption. On the other hand, styrene may be more convenient to remove from the resulting mixture than stilbene, depending on the volatility of the desired products.

A disadvantage of *N*-aminoaziridines is that mild conditions ($\leq 40\,^{\circ}C$) are required to form the *N*-aziridinylimines, and less reactive carbonyl compounds (such as aryl ketones) do not react under these conditions. This problem can often be solved by replacing carbonyl compounds with the analogous imines, which are readily accessible from nitriles and Grignard reagents (eq. 6)[9]. The treatment of *N*-aminoaziridines with Ph_3PBr_2 affords phosphine imides which convert acyl derivatives into *N*-aziridinylimines (eq. 7)[10]. With ketenes, however, rearrangement of the intervening imines was observed (eq. 7)[11].

2. Fragmentation of α,β-Epoxyketones

The conversion of α,β-epoxyketones into diazo compounds is followed by fragmentation into carbonyl compounds, alkynes, and nitrogen (eq. 8). This reaction was discovered by Eschenmoser et al.[12] and, almost simultaneously, by Tanabe et al.[13], using tosylhydrazones. It became apparent, however, that many α,β-epoxyketones, particularly those bearing β-H, do not tolerate Bamford-Stevens conditions. In most of these cases, application of the aziridinylimine method gave good results[6]. Details of a prototype reaction, 2,3-epoxycyclohexan-1-one (**5**) → 5-hexynal (**6**)[14] (eq. 9), and a comprehensive report[15] have been published by the Eschenmoser group. With regard to the reaction mechanism, the following findings are relevant: (a) The extrusion of alkenes from *N*-ariridinylimines was studied with two pairs of *cis*/*trans* isomers (R = Ph, Me)[7]. Stereospecificity suggests a concerted, cheletropic reaction. (b) The fragmentation appears to proceed from α,β-epoxy-



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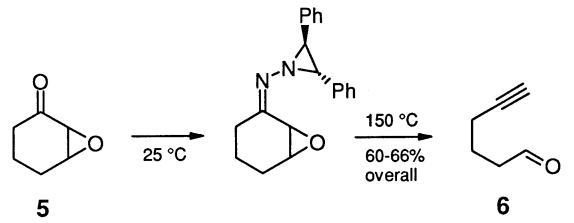

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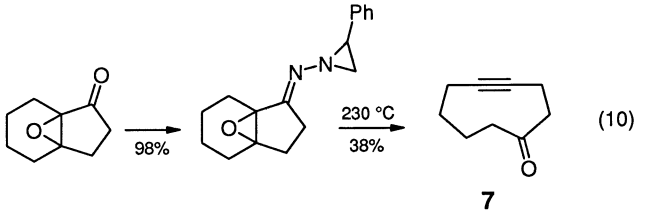
diazoalkanes (**2**) rather than from carbenes. Although this point is not clear for the thermolysis of *N*-ariridinylimines (**1**), the *acid-catalyzed* fragmentation of α,β-epoxydiazirines (**4**) is uniquely consistent with the intervention of alkenediazonium ions (**3, 3a**)[16].

The oxides of bicyclic enones undergo fragmentation to give cycloalkynones[15][17] (eq. 10). Substrates derived from 4-cyclonynone (**7**) were used to study transannular p-π interactions[17]. The fragmentation of α,β-epoxyketones was applied in the syntheses of the insect pheromone propylure (**8**)[18] (eq. 11), of *A*-norsteroids[15][16] (eq. 12), and of racemic[19] as well as nonracemic building blocks for vitamin B_{12}[20] (eqs. 13 and 14).



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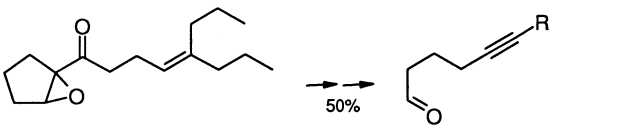

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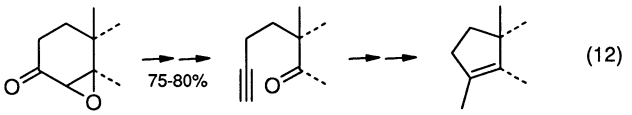

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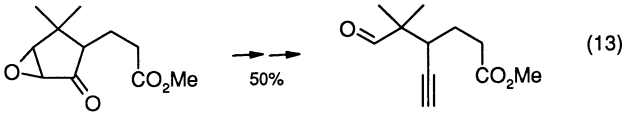

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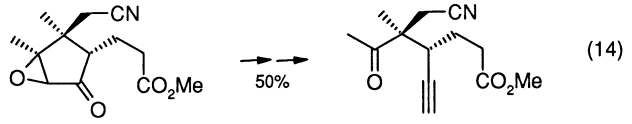

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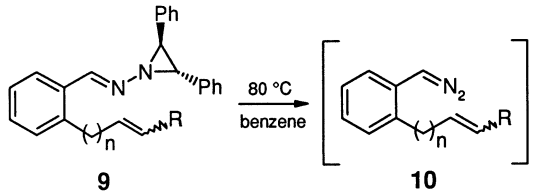
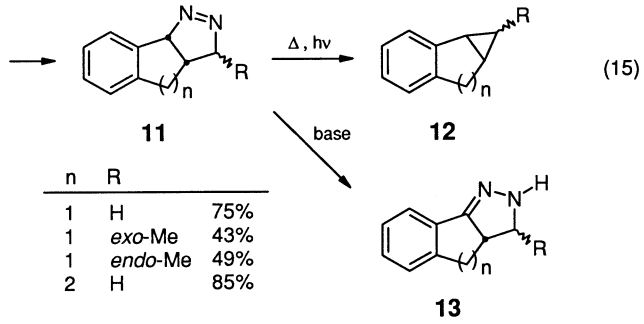
3. Formation of Dihydropyrazoles

The diazo compounds **10** are scavenged by stereospecific intramolecular addition, to form the 4,5-dihydro-3*H*-pyrazoles (Δ^1-pyrazolines) **11**[21] (eq. 15). Thermolysis or photolysis of **11** affords the cyclopropanes **12** with partial inversion of configuration. The *N*-aziridinylimines **9** are the preferred diazo precursors since the basic conditions associated with tosylhydrazone salts cause isomerization of **11** into 3,5-dihydro-1*H*-pyrazoles (Δ^2-pyrazolines) **13**[21] which cannot be converted into **12**. The analogously annelated indole **15** was prepared from the aziridinylimine **14**[22] (eq. 16). Thermally labile dihydropyrazoles may decompose as they are formed, as was observed with **17**[23]. The tricyclic ketones **18** were obtained on heating of the aziridinylimines **16** in benzene at 80°C (eq. 17). Light-induced vinylcyclopropane rearrangement of **18** provided a series of tricyclo[4.3.0.$0^{3,7}$]non-4-en-2-ones (brex-4-en-2-ones) **19**[23]. At somewhat higher temperatures, the aziridinylimine **20** underwent a reaction sequence (4 steps) leading to **21** (eq. 18). This procedure was applied to nonracemic **20** in a synthesis of (−)-longifolene (**22**)[24].





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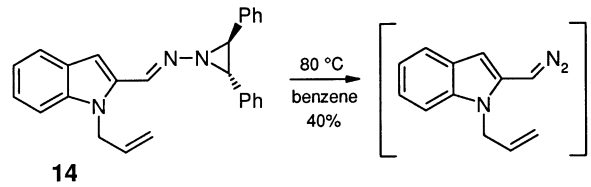

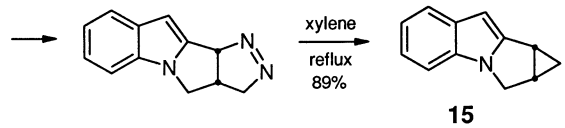

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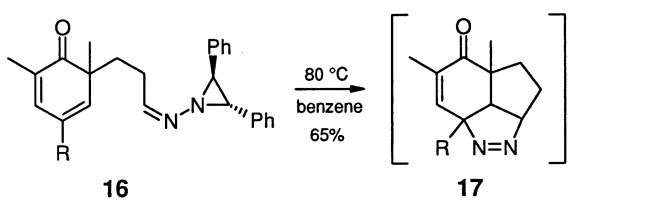
4. Generation of Carbenes and Carbenoids

As a rule, thermal or photochemical excitation of diazo compounds generates carbenes[1]. It is known, however, that (excited) diazo compounds can "mimic" the reactions of carbenes, to undergo rearrangements accompanied by the extrusion of nitrogen[25]. *N*-Aziridinylimines are afflicted by this mechanistic ambiguity as are other diazo precursors. Thermolysis of **23** and of 1-diazopropylbenzene (**24**) afforded 1-propenylbenzene with the same *E*:*Z* ratio (ca. 75:25)[26]. A different *E*:*Z* ratio ca. 64:36) was obtained on pyrolysis of **26** (which involves the carbene−



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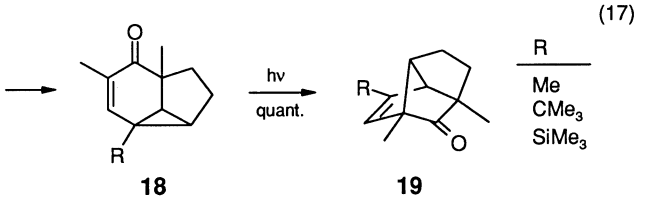

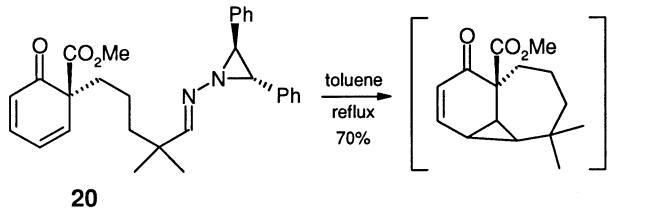

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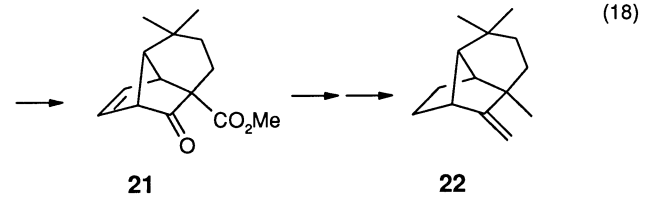

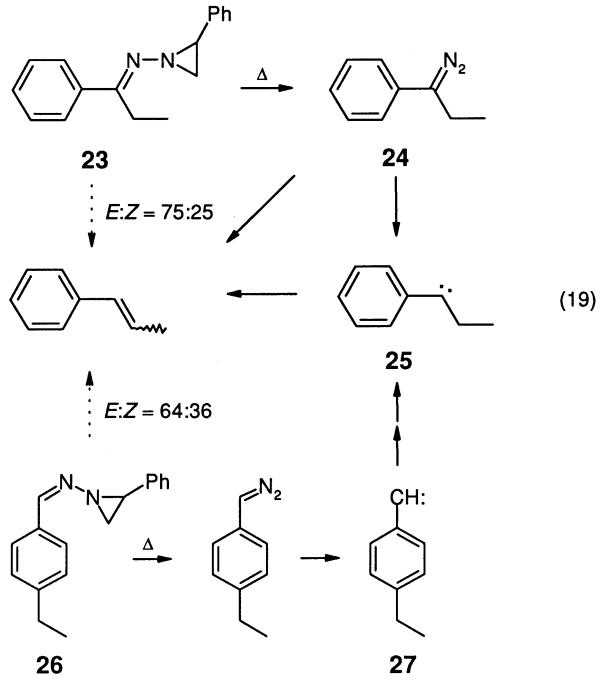

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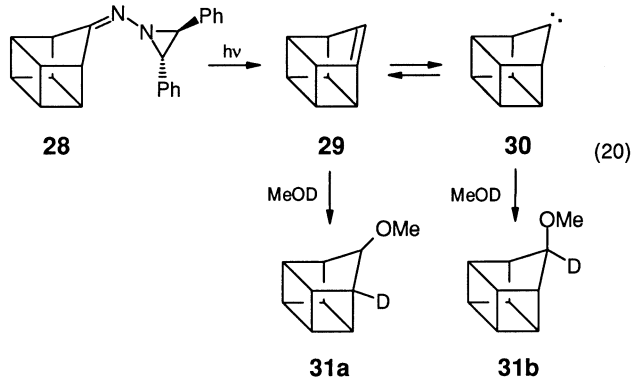

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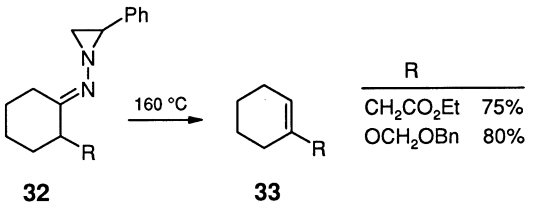
carbene rearrangement **27** → **25**) and with other "non-diazo" routes to **25**. The contribution of carbene **25** to the reactions of **23** and **24** can be no more than 75%. An extreme situation was encountered for homocub-1(9)-ene (**29**) and homocub-9-ylidene (**30**) which appear to be in equilibrium, with K close to unity[27][28]. Trapping of **29** and **30** with MeOD leads to the isotopomeric ethers **31a** and **31b**, respectively. When **28** was photolyzed in benzene−MeOD, the ratio of **31a**:**31b** was found to increase with [MeOD][27]. This result implies that **29** is the first intermediate generated from **28**.

Aziridinylimines can be useful for the synthesis of alkenes as a variety of functional groups are tolerated. Carbenic 1,2-H shifts are regioselective, with methine hydrogens (R_2CH-) strongly preferred to methylene hydrogens (RCH_2-). Thus, 2-R-cyclohexanones were converted into 1-R-cyclohexenes **33** by way of the aziridinylimines **32**[29] (eq. 21). The unsaturated nitrile **35** was obtained in 92% yield from the aziridinylimine **34** (eq. 22), whereas the analogous tosylhydrazone provided none of the desired alkene[29]. The competition of two CH_2 groups, normally ca. 1:1, is strongly affected by β-trimethylsilyl groups. The aziridinylimines **36** were found to give allylsilanes (**37**) in preference to homoallylsilanes (**38**)[30] (eq. 23). The effect of additional alkyl groups R′ is in accordance with expectation: the **37**:**38** ratio is not influenced by 1-R′, increased by 2-R′, and lowered by 4-R′. The regioselectivity in favor of **37** is further enhanced by addition of rhodium(II) acetate while the stereoselectivity changes from $E>Z$ for the thermal reaction to $E<Z$ in the presence of catalyst[30].

Aziridinylimines appear to be the only diazo precursors that are compatible with transition metal catalysts. However, aside from eq. 23, few examples of the generation of carbenoids from aziridinylimines have been reported. Carbenoid−thioamide interaction is involved in the rhodium(II)-catalyzed formation of the enamide **40** from **39**[31]. The ring closure (eq. 24), was key to a new synthesis of functionalized benzazepine substructures. Indene (**44**) was obtained on thermolysis (cyclohexane, reflux, 52%) or photolysis (diethyl ether, 38%) of the aziridinylimine **41** in the presence of cuprous chloride[32]. The intervening carbenoid undergoes electrocyclization to give isoindene (**42**) which is trapped with dimethyl fumarate (→ **43**) or proceeds to **44** by way of a 1,5-H shift (eq. 25).

A reaction sequence similar to eq. 25 starts from the aziridinylimine **45** and leads eventually to 1-ethynylindene (**46**)[33]. Isomerization of the primary propargylene, **47a** → **47b**, occurs prior to cyclization, **47b** → **48** → **46** (eq. 26).



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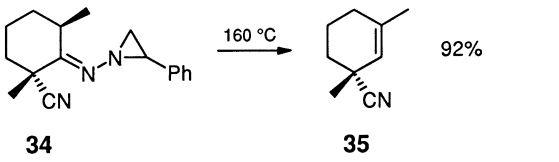

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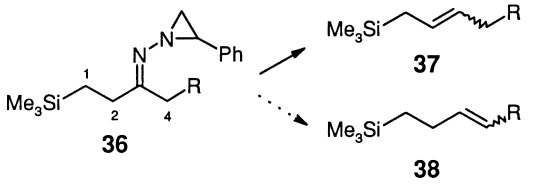

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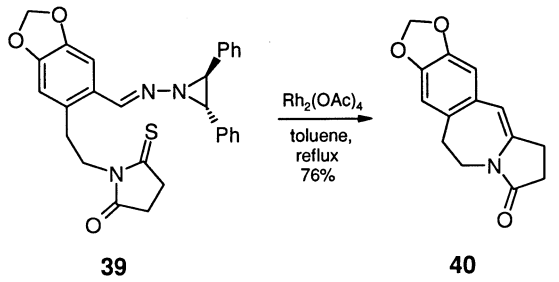
R	Conditions	37:38	*E*:*Z*-37	Yield (%)
n-C_6H_{13}	toluene, 145 °C	74:26	80:20	68
	+ 2% $Rh_2(OAc)_4$	98:2	14:86	72
n-$C_{11}H_{23}$	toluene, 145 °C	76:24	80:20	69
	+ 2% $Rh_2(OAc)_4$	98:2	17:83	72
CH_2Ph	toluene, 145 °C	92:8	80:20	66
	+ 2% $Rh_2(OAc)_4$	99:1	14:86	71



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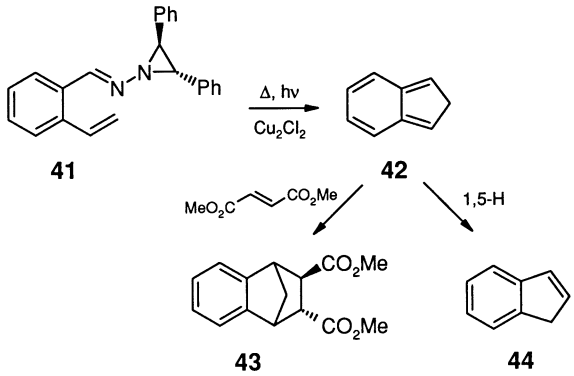

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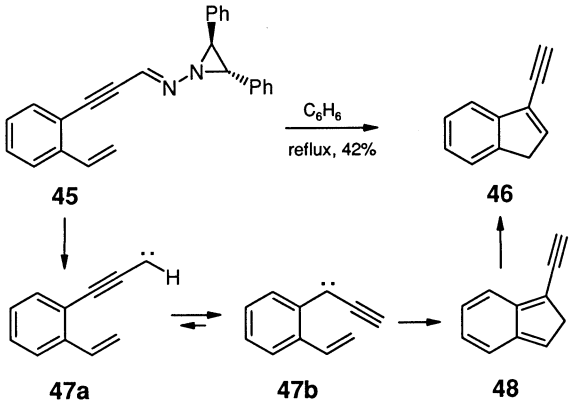
With the homologous compound **49**, isomerization of the carbene precedes intramolecular addition to the double bond (eq. 27). Hence the formation of **50** cannot proceed



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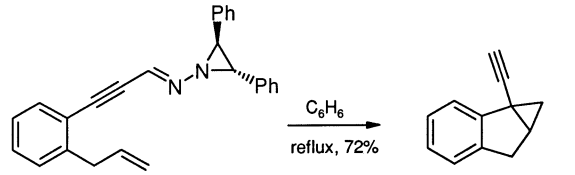

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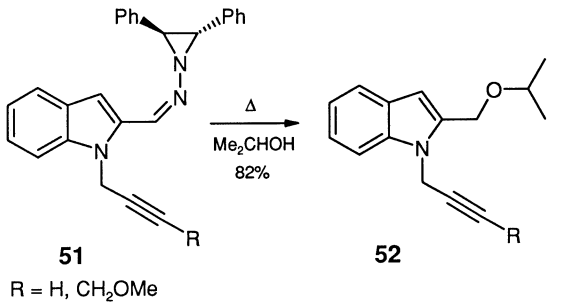

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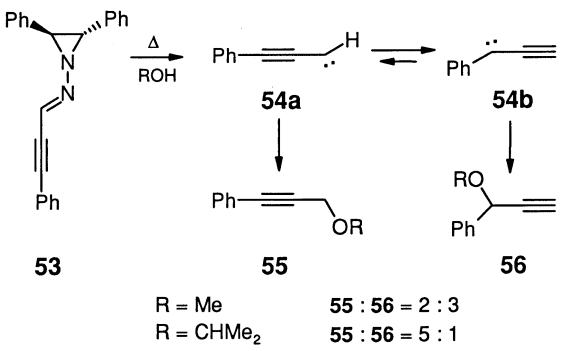
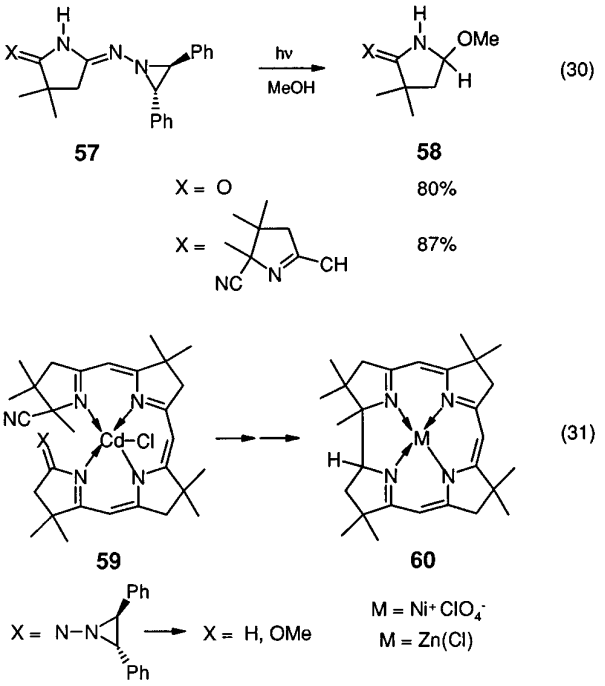


(29)

by way of a pyrazoline (Section 2). In contrast, no intramolecular addition of the 2-indolylcarbene generated from **51** was observed. Heating of **51** in toluene produced a solvent adduct (cycloheptatriene, 78%) while heating in 2-propanol afforded the ether **52** (eq. 28)[34].

The intermediate(s) generated from **53** were scavenged by alcohols to give mixtures of the ethers **55** and **56**, thus demonstrating the isomerism of phenylpropargylene (**54**) (eq. 29)[33]. The carbenic O−H insertion reaction has been utilized for the "partial reduction" of cyclic carboxamides (eq.



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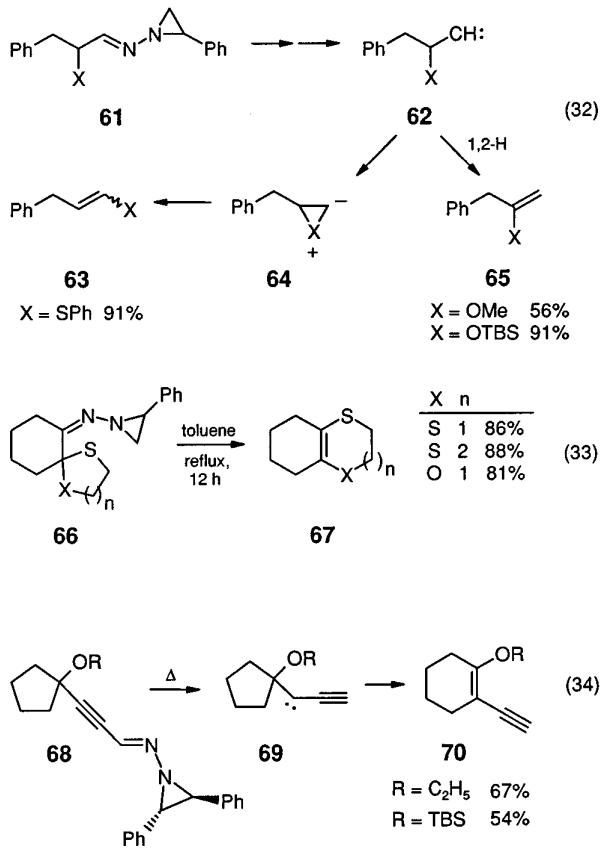
(31)

30). The carboxamides were alkylated with $Et_3O^+BF_4^-$, and the resulting imino esters were treated with *N*-amino-*trans*-2,3-diphenylaziridine to give the aziridinylimines **57** (60−70%). Photolysis of **57** in methanol afforded the amino ethers **58**[35]. This procedure was applied in a synthesis of the corrin complexes **60** (eq. 31). The conversion of aziridinylimine into ether (49−63%) was performed with the cadmium complex **59**. The coupling of rings A and D was achieved electrochemically, after exchange of cadmium for nickel[35].

The intramolecular participation of hetero atoms was examined with 2-X-3-phenylpropylidenes (**62**) which were generated from the aziridinylimines **61**[36]. With X = SPh, 1-phenylthio-3-phenyl-propene (**63**, $E{:}Z \approx 1$) was formed, presumably by way of the ylide **64** (eq. 32). Analogous 1,2-shifts of sulfur, leading to **67**, were found with the thioacetals and dithioacetals **66** (eq. 33)[36]. In contrast, the migration of alkoxy groups does not compete with 1,2-H shifts, **62** → **65**. However, alkoxy groups appear to promote 1,2-alkyl shifts which are otherwise reluctant to occur. This effect was uncovered with the aziridinylimines **68** whose thermolysis generated the alkynylcarbenes **69** and eventually afforded 1-alkoxy-2-ethinylcyclohexenes (**70**) (eq. 34)[33]. The analogous reactivity of the aziridinylimines **71**, derived from 2-R-tetrahydrofuran- and tetrahydropyran-2-carboxyldehydes, was utilized for the ring expansion of cyclic ethers (**71** → **72** → **73**) (eq. 35)[37]. The bicyclic carbene **75** rearranges with exclusive migration of bond a since a bridgehead alkene would result from migration of bond b (eq. 36). Hence the ring size of the cyclic ether does not change whereas the adjacent carbocycle is expanded, **74** →



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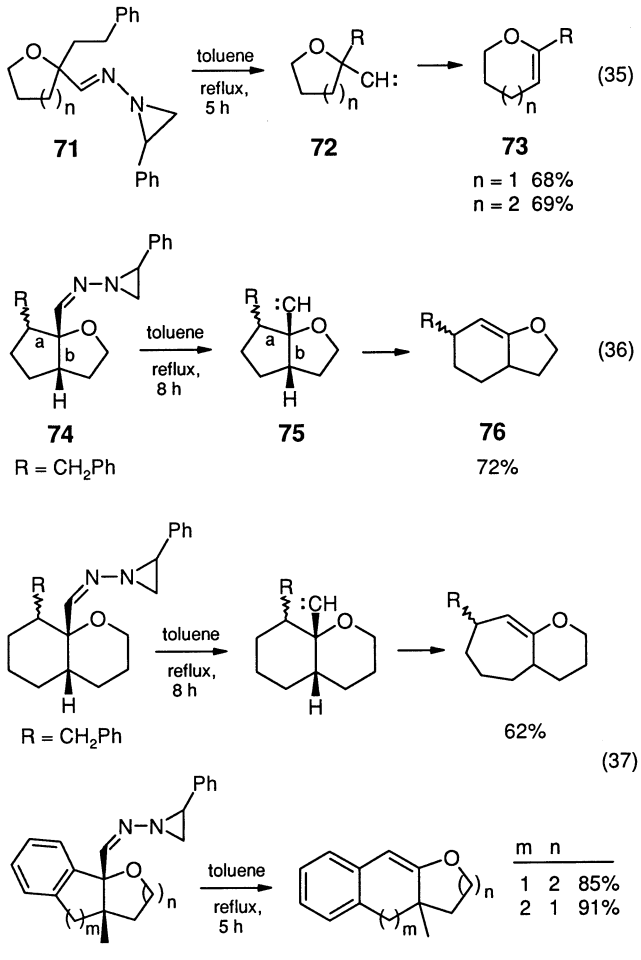

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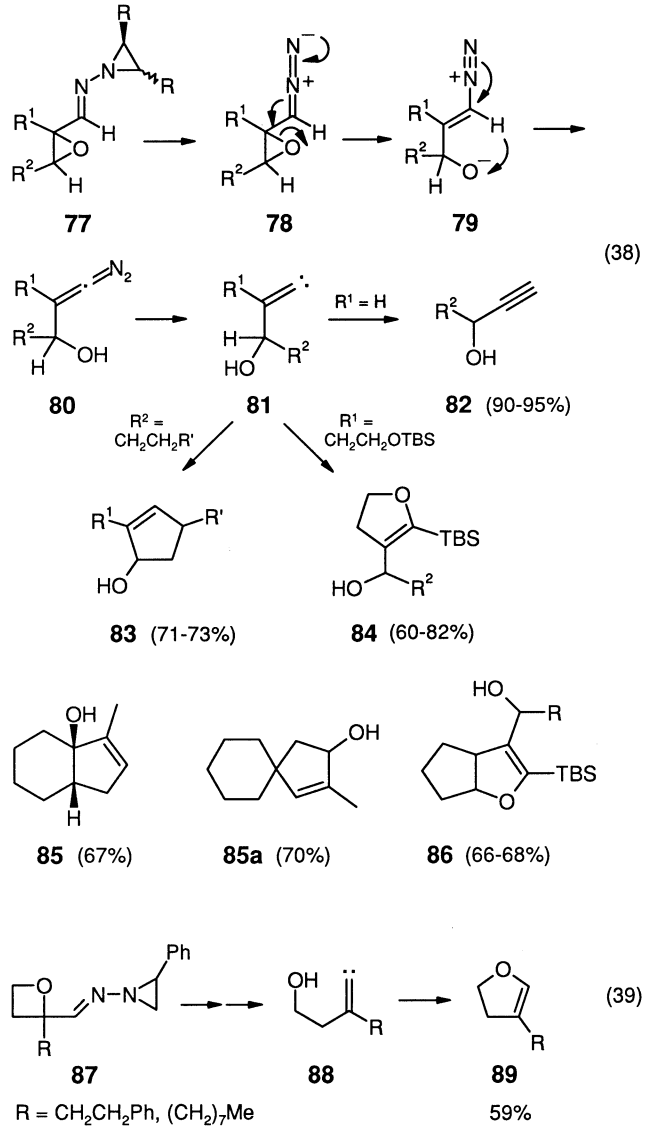
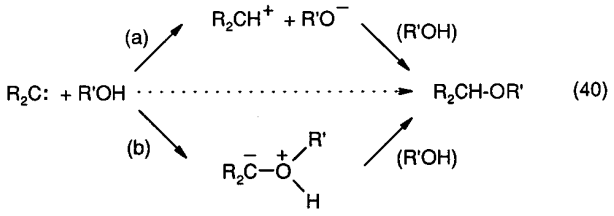


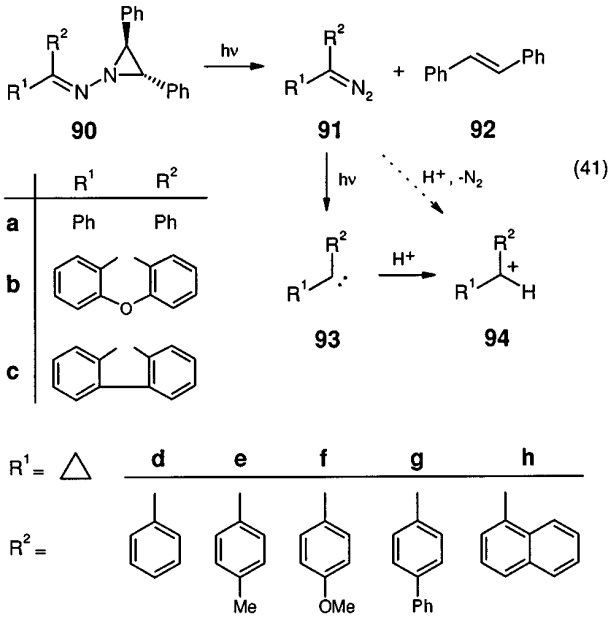
75 → **76**[37]. Further applications of this principle are shown in eq. 37.

The aziridinylimines of α,β-epoxyaldehydes (**77**) do not conform to the reaction patterns of eqs. 34−37. The first steps, extrusion of the alkene (**77** → **78**) and opening of the epoxide (**78** → **79**), are analogous to those of α,β-epoxyketone-derived aziridinylimines (eq. 8). The diazonium betaines **79**, however, undergo proton transfer (rather than fragmentation) to give the elusive 1-diazo-3-hydroxyalkenes **80** and the alkylidenecarbenes **82** (eq. 38). The reactivity of **82** depends on the nature of the substituents R^1 and R^2. With R^1 = H, 2-alkynols **82** are formed by a 1,2-H shift[38]. If R^1 and R^2 are alkyl groups, 1,5-C−H insertion of the carbene leads to the cyclopentenols **83**[38]. With R^1 = $CH_2CH_2OSi(Me_2)CMe_3$, the carbene inserts into the O−Si bond to give the dihydrofurans **84**[39]. Formulae **84**−**86** exemplify bicyclic compounds that were obtained by these methods. Aziridinylimines of 2-R-oxetane-2-carboxaldehydes (**87**) follow an analogous route to the alkenylidene **88** (eq. 39). In contrast to **81**, the hydroxyl group of **88** is in the correct position for O−H insertion to give the dihydrofurans **89**[37].

5. Generation of Carbocations

A variety of carbenes react with alcohols by way of proton transfer, generating carbocations that are eventually captured by nucleophiles (eq. 40a). Product and/or isotope distributions served to distinguish the carbocation route from the alternative ylide mechanism (eq. 40b)[40]. The protonation of diarylcarbenes has been demonstrated by time-resolved spectroscopy of the resulting diarylmethyl cations[41]. The application of laser flash photolysis (LFP) to O−H insertion reactions of carbenes is often hampered by the instability of diazo compounds in protic media[1]. For example, the lifetime of diphenylcarbenium ions (**94a**) in trifluoroethanol (TFE)[41a][42] is appropriate for nanosecond LFP experiments, but rapid decomposition of diphenyldiazomethane (**91a**) ($\tau \approx 10^2$ s) precluded the generation of diphenylcarbene (**93a**) from **91a** in neat TFE. In contrast to **91a**, the aziridinylimine **90a** persists in TFE for hours. LFP of **90a** in TFE (Figure 1) gave rise to a transient whose absorption (λ_{max} = 440 nm) and kinetics were in agreement with previous data for **94a**[43]. The long-lived absorption band at ca. 300 nm is due to *E*-stilbene (**92**). The optical density (OD) at 300 nm was found to increase linearly with the laser dose up to ca. 30 mJ and then





levels off, owing to depletion of **90a** (Figure 2a). An analogous plot of the OD at 440 nm is strongly curved-up at low laser doses (Figure 2b). These findings indicate that **94a** arises from a photoproduct of **90a** in a second light-induced step, thus confirming the reaction sequence **90a** → **91a** → **93a** → **94a**.

Figure 1. Time-dependent absorption spectra obtained after laser excitation (248 nm, 20 ns, 130 mJ/pulse) of **90a** (0.066 mM) in oxygen-saturated TFE; inset: decay of **94a**, recorded at 440 nm

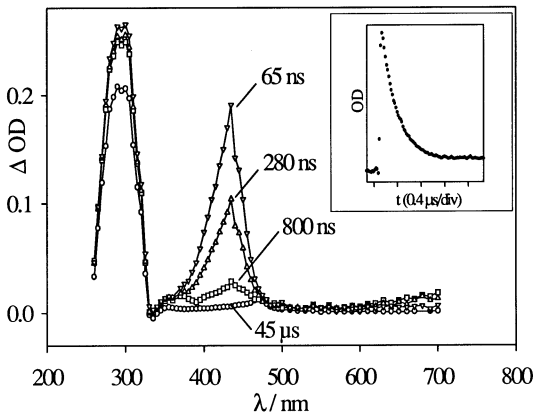
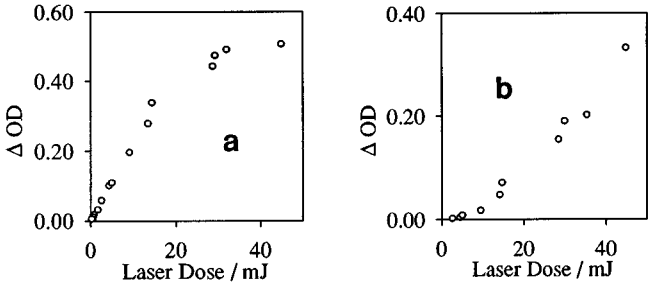


Figure 2. Yields of **92** (a) and **94a** (b) as a function of the laser dose (mJ/pulse), recorded 70 ns after LFP of **90a** (0.085 mM) as in Figure 1

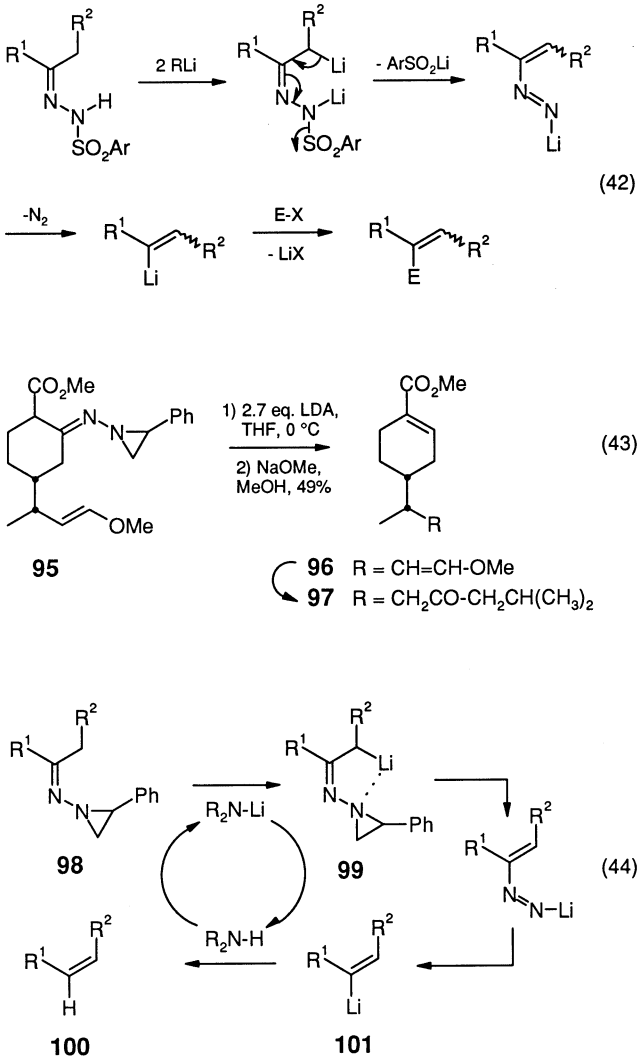


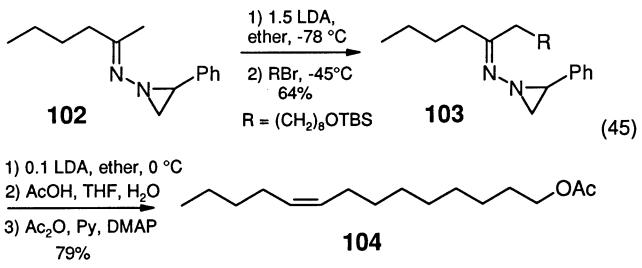
Similarly, LFP of **90b** in water/acetonitrile (4:1) gave rise to the xanthylium ion (**94b**), and LFP of **90c** in 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) generated the 9-fluorenyl cation (**94c**)[43]. Previous efforts with the analogous diazo compounds had failed; the lifetime of 9-diazofluorene (**91c**) in HFIP being only 0.5 s. Aziridinylimines served to explore the full range of diarylcarbene protonation (the hydride affinities of the cations **94b** and **94c** differ by 19 kcal/mol![44]).

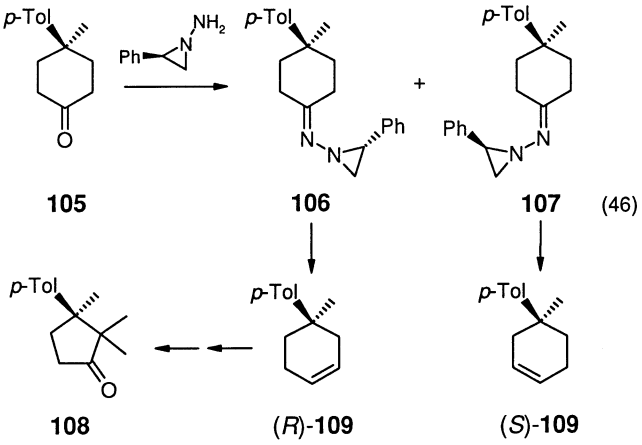
In contrast to diarylcarbenium ions, Ar_2CH^+, cyclopropylarylcarbenium ions, Ar(*c*-Pr)CH^+, are not accessible by LFP (photoheterolysis) of R^1R^2CH-X. Carbene protonation is the only approach so far to time-resolved spectroscopy of these species[9]. The cations **94d**−**h** were generated by LFP of the aziridinylimines **90d**−**h** in TFE and in TFE/MeOH. The rate constants obtained for **94d**−**h** and for analogous arylphenylcarbenium ions, $ArPhCH^+$, were found to be similar in magnitude, although cyclopropyl responds more strongly than phenyl to increasing electron demand by Ar. The cation stabilizing abilities of cyclopropyl and phenyl groups have been a matter of dispute[45] which is, hopefully, resolved by the new data for *nucleophilic capture* of Ar(*c*-Pr)CH^+ and $ArPhCH^+$. It appears that the faster *solvolysis* of Ar(*c*-Pr)CH−X, compared to that of ArPhCH−X, is influenced by conformational effects[9].

6. Reactions Involving Carbanions

Ketone arenesulfonylhydrazones afford alkenyllithiums on treatment with two or more equivalents of RLi (eq. 42). The Shapiro reaction[46] has found many applications in organic synthesis as the alkenyllithiums accept a variety of electrophiles (protons, carbonyl compounds, alkyl and silyl halides) to give useful products. An analogous elimination was performed with the aziridinylimine **95** in a synthesis of (±)-juvabione (**97**) (eq. 43)[47]. The use of **95** was prompted by the presence of the ester group; sodium methoxide served to equilibrate the alkene(s) formed from **95**. Recently, a catalytic procedure has been developed (eq. 44)[48], which appears to be superior, in some ways, to the Shapiro reaction: (a) The conversion of aziridinylimines **98** into alkenes **100** can be achieved with sub-stoichiometric amounts of lithium dialkylamides. The amine produced in the lithiation step, **98** → **99**, protonates the alkenyllithium, **101** → **100**, with regeneration of R_2NLi. Under standard con-



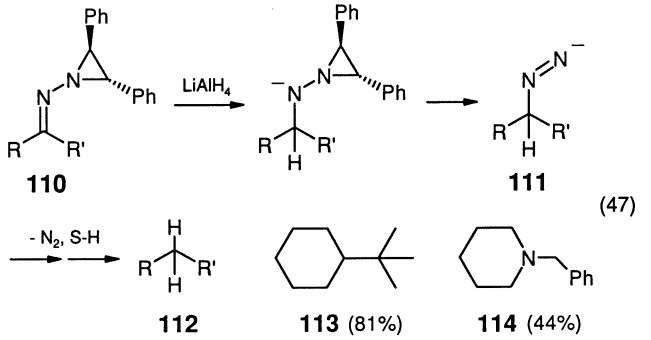


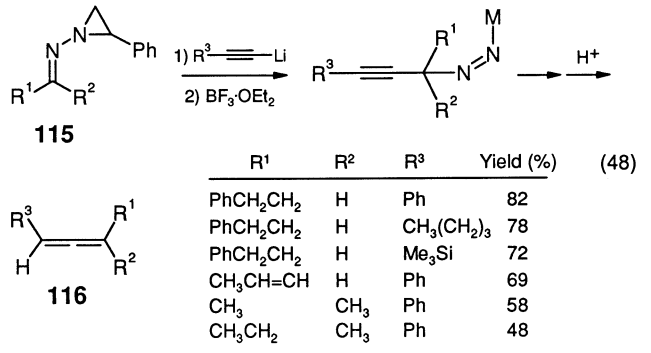


ditions (0.1 equiv. of LDA, 0°C, 1 h), the yields of **100** (R^1, R^2 = alkyl) range from 84 to 98%. (b) The chemoselectivity is excellent, secondary C−H bonds (RCH_2-) react to the virtual exclusion of tertiary C−H bonds (R_2CH-). The regioselectivity (ca. 98:2) is controlled by the configuration of **98**, probably due to internal complexation of Li in **99**. (c) The stereoselectivity, in favor of *Z*-**100**, is greatly enhanced over that of the Shapiro reaction. *E*:*Z* ratios ranging from 4:96 to 0.1:99.9 were observed (R^1, R^2 = alkyl)[48].

Moreover, the stability of **99** at low temperatures is sufficient for the construction of new C−C bonds, before the remaining steps of reaction (44) are performed. This strategy is illustrated by a synthesis of the insect pheromone (*Z*)-9-tetradecenyl acetate (**104**) (eq. 45)[48]. Note that **102**, obtained as the more stable *E* isomer, is alkylated to give (*Z*)-**103** whose configuration serves to place the double bond in the proper position of **104** (99.6% *Z*). The present methodology also opens a convenient route to optically active alkenes. The achiral ketone **105** reacted with (*R*)-1-amino-2-phenylaziridine to give diastereomeric aziridinylimines which were separated by chromatography. Individual treatment of **106** and **107** with 0.1 equiv. of LDA provided (*R*)-**109** (94% *ee*) and (*S*)-**109** (92% *ee*), respectively. The *R* enantiomer was converted into (+)-α-cuparenone (**108**) (eq. 46)[48].

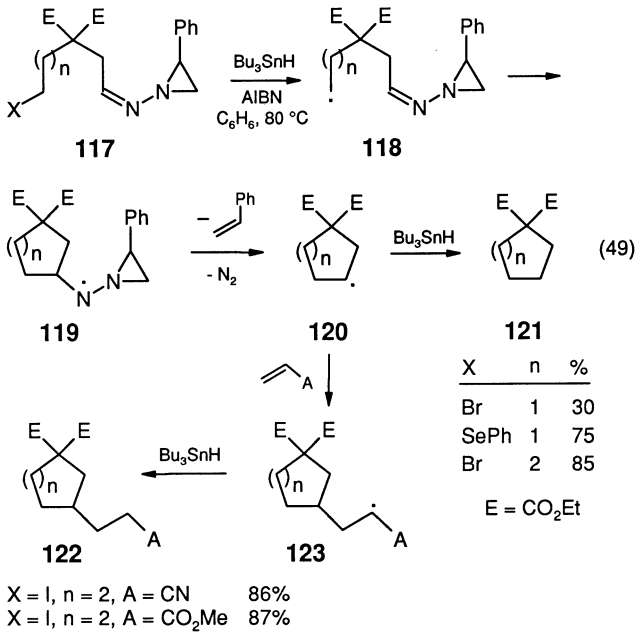
Carbanions are probably involved in the reduction of aziridinylimines with $LiAlH_4$, **110** → **112** (eq. 47)[49]. For example, **113** was obtained from 4-*tert*-butylcyclohexanone and **114** from *N*-benzyl-piperidin-4-one. In some cases, elimination according to eq. 44 was competitive or pre-

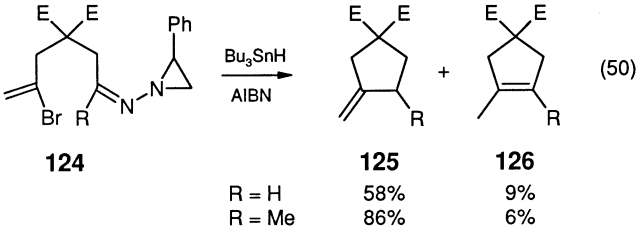




R^1	R^2	R^3	Yield (%)
$PhCH_2CH_2$	H	Ph	82
$PhCH_2CH_2$	H	$CH_3(CH_2)_3$	78
$PhCH_2CH_2$	H	Me_3Si	72
$CH_3CH{=}CH$	H	Ph	69
CH_3	CH_3	Ph	58
CH_3CH_2	CH_3	Ph	48

(48)

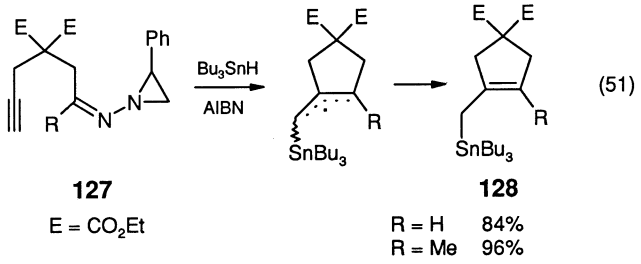




dominant (R = R′ = benzyl). The aziridinylimines **115** were found to add alkynylboranes (M = BF_2 or BF_3^- Li^+) with eventual formation of the allenes **116**[50]. A selection of products, and their yields, are shown in eq. 48. Alkynyllithiums, alkynyl Grignard reagents, and alkynyl cuprates failed to undergo this reaction. It appears that complexation of the aziridinylimines **115** with boranes promotes addition to the C=N bond.

7. Reactions Involving Free Radicals

N-Aziridinylimines can be utilized as radical acceptors as well as radical precursors. The former reactivity was demonstrated by cyclization of the radicals **118** which were generated from **117** by abstraction of X (Br, I, SePh) with $Bu_3Sn^{\cdot}$[51]. Intramolecular addition of **118** to the C=N bond (→ **119**) is followed by elimination of styrene and N_2 (→ **120**). The cycloalkyl radicals **120** abstract hydrogen from Bu_3SnH to give **121** or add to acceptor-substituted alkenes (→ **123**) with eventual formation of **122** (eq. 49). The low yield of **121** from **117**-Br (*n* = 1) and Bu_3SnH/AIBN at 80°C is due to competing intramolecular *N*-alkylation. This problem is obviated by the use of **117**-SePh[51] or by generating $Bu_3Sn^{\cdot}$ photochemically at 20°C[52]. Analogous cyclization of the vinyl bromides **124** leads to allylic radicals whose reaction with Bu_3SnH gives mixtures of isomeric alkenes, **125** > **126** (eq. 50)[51].



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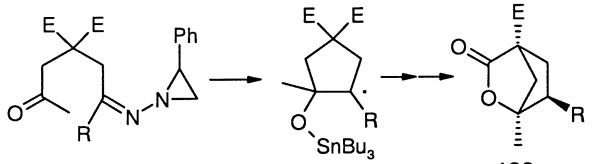

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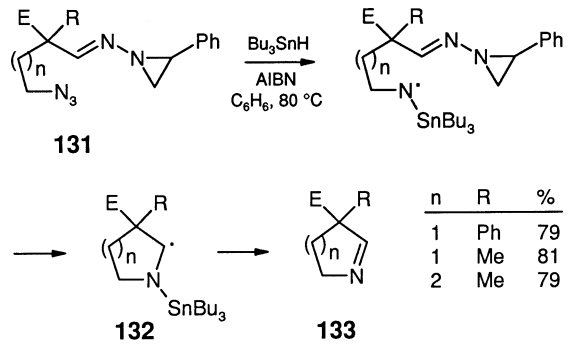
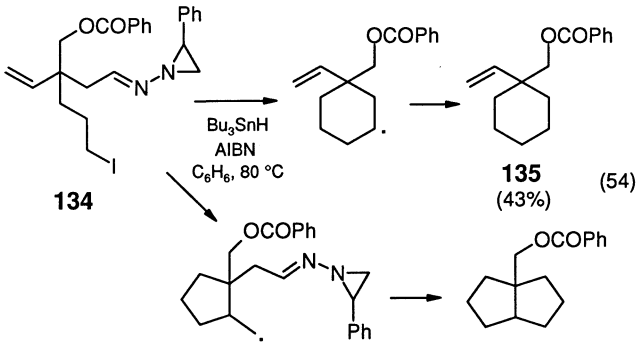


(53)

Radicals suitable for interaction with the C=N bond of aziridinylimines were also generated by addition of $Bu_3Sn^{\cdot}$ to triple bonds (eq. 51)[51], carbonyl groups (eq. 52)[53], and azides (eq. 53)[54]. While all cyclization steps are similar, the reaction sequences are terminated differently. Bu_3Sn is recovered in the products **128** obtained from **127** whereas the Bu_3SnO group produced from **129** undergoes transesterification with CO_2Et to give the cyclic lactones **130**. The cyclic radical **132** arising from **131** eliminates $Bu_3Sn^{\cdot}$ with formation of the cyclic imines **133**.

Competition studies were performed to compare the intramolecular addition rates of radicals to aziridinylimines with those of alkenes. In the case of *exo*-6 cyclization to aziridinylimine versus *exo*-5 cyclization to alkene, both reaction paths were observed. A mixture of the products **135** and **136** (1:1) was obtained from **134** (eq. 54)[52]. However, in cyclizations leading to the same ring size (*exo*-6 or *exo*-5), aziridinylimines are superior to alkenes (≥100:1). Thus, the photochemical reaction of **137** with Bu_3SnH afforded only **139**. Selective addition of the primary radical gener-



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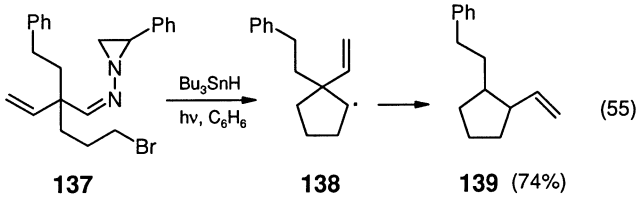

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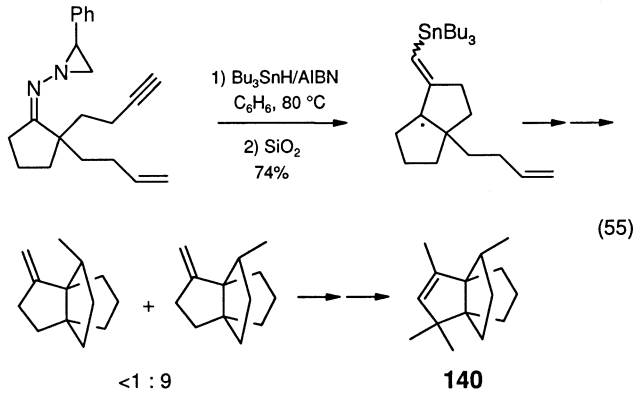
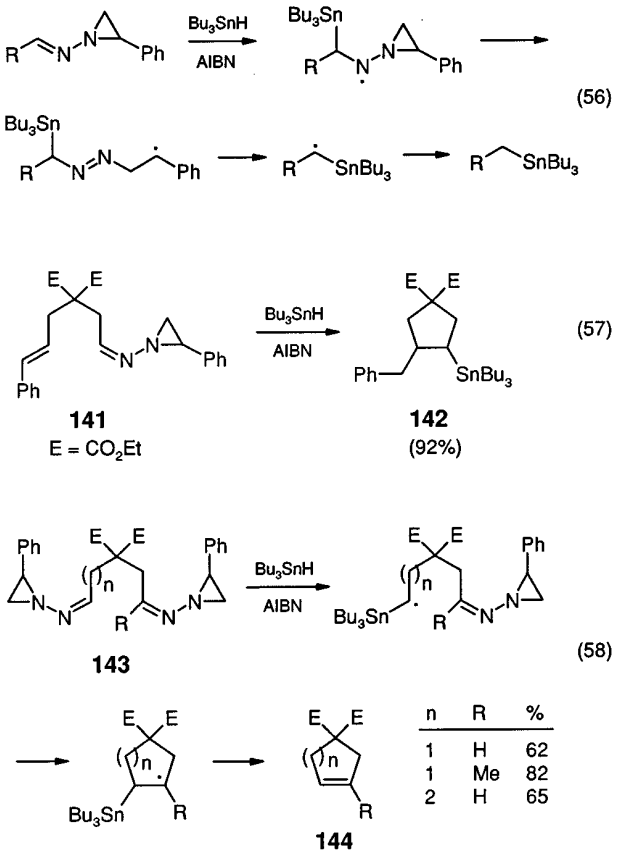


(55)

ated from **137** to the C=N bond is followed by a 1,2-vinyl shift of **138** (eq. 55)[52]. The discrimination in favor of C=N was utilized in tandem cyclization reactions leading to [3.3.3]propellanes, as illustrated by a synthesis of (±)-modhephene (**140**) (eq. 55)[55].

The role of aziridinylimines as radical precursors has been documented less extensively. In the absence of intramolecular radical traps, the treatment of aziridinylimines with Bu_3SnH/AIBN leads to alkyltributylstannanes (eq. 56)[52]. In the presence of alkenes, the intervening α-stannyl radicals undergo addition to the C=C bond, as shown by the nearly quantitative formation of **142** from **141** (eq. 57)[51]. The efficacy of aziridinylimines as both radical precursors and radical acceptors was demonstrated with **143** (eq. 58)[51]. The conversion of **143** into **144** is equivalent to the reductive coupling of 1,*n*-dicarbonyl compounds, which could be effected more directly (McMurry reaction). However, the aziridinylimine methodology is compatible with a wide range of substituents, such as the ester groups in **143** and **144**.



8. Conclusion

After a slow start some thirty years ago, the chemistry of aziridinylimines has gained momentum during the past decade. The utility of aziridinylimines as non-ionic diazo precursors is becoming more and more appreciated. Previously inaccessible carbenes have been generated and employed in synthesis, with the conversion of α,β-epoxyaldehydes into β-hydroxyvinylidenes as an outstanding example. LFP techniques, applied to persistent solutions of aziridinylimines in fluorinated alcohols, were used to demonstrate the protonation of carbenes and to measure absolute reaction rates of carbocations. The catalytic Shapiro reaction provides a powerful tool for the regio- and stereoselective synthesis of alkenes, including nonracemic compounds. The ability of aziridinylimines to behave as both radical acceptors and radical precursors offers unique opportunities, such as tandem cyclizations leading to tricyclic products. Various reactions of aziridinylimines have been utilized for the synthesis of natural products, and such applications are likely to increase in number and sophistication.

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