Tetrahedron Vol. 49, No. 20, pp. 4383-4408, 1993
Printed in Great Britain

0040-4020/93 $6.00+.00

1,3-Dipolar Cycloadditions of 2-Ethoxy- and 2-(Ethylthio)-1-azetines with Nitrile Oxides, Nitrile Ylides and Nitrilimines: An Unexpected 1,2,4-Triazole Formation.[1,2]

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(*Received in UK* 12 *March* 1993)

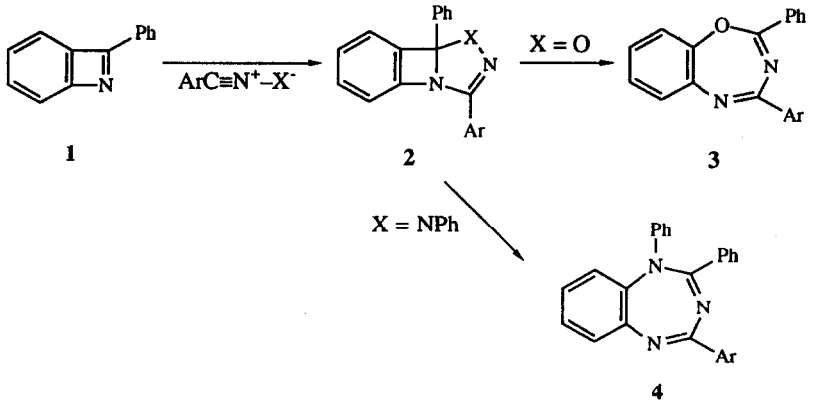
Abstract. 2-Ethoxy- and 2-(ethylthio)-1-azetines readily undergo 1,3-dipolar cycloadditions with nitrile oxides and nitrile ylides to give stable 4,5-bicyclic cycloadducts. With nitrilimines, however, the expected 1,3-dipolar cycloadducts and/or unexpected ring-opened products, namely 1,2,4-triazoles, are formed depending on the nature of the nitrilimine *N*-substituent. In contrast, the azetines fail to react with nitrile sulphides, azomethine ylides, nitrones, aryl azides, and various dienes.

X-ray crystallographic data on the nitrile oxide, nitrile ylide, and nitrilimine cycloadducts, and on the 1,2,4-triazoles, are presented. Also a mechanistic rationale for triazole formation is offered.

1,3-Dipolar cycloadditions of nitrile oxides to acyclic and alicyclic imines to form 1,2,4-oxadiazolines are well-documented.[3] Analogous cycloadditions are known with nitrilimines,[3d,4] which also enter into cycloadditions with the imine bond present in oximes, amidines and imidates.[5] In all instances, 1,2,4-triazolines are produced which, in the case of the imidates, aromatise spontaneously to the 1,2,4-triazoles. Likewise, the cycloadducts from nitrile oxides and imino-ethers,[6a,b] amidines[6b] and S-methylthioureas[6b] undergo heteroaromatisation to 1,2,4-oxadiazoles.

The cycloaddition of nitrile ylides to the strained imine bond of 2H-azirines has been rigorously investigated.[7] However, nitrile ylide additions to other imine-bonds are rare, and we are not aware of any examples involving imino-ethers.

The 1,3-dipolar cycloadducts **2** of benzazete **1** with nitrile oxides[10] and with nitrilimines[11] are known, and undergo ring-expansion and rearrangement to the benzoxadiazepines **3** and benzotriazepines, **4** respectively (Scheme 1).

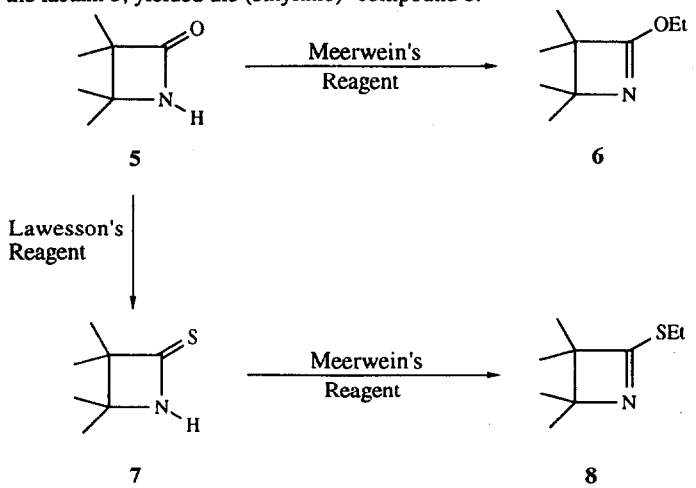


Scheme 1

However, apart from a recent report[8] on the trapping of transient azetinone species by Lewis-acid catalysed Diels-Alder cycloadditions with silyloxydienes, there appear to be no examples of cycloaddition to the imine-bond of a 1-azetine.[9] We were, interested, therefore, in the action of 1,3-dipoles on 2-alkoxy- and 2-(ethylthio)-1-azetines, as these heterocycles represent examples of a strained imino-ether.

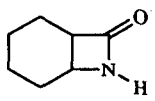
In this paper we describe our work on the 1,3-dipolar cycloadditions of several 2-ethoxy- and 2-(ethylthio)-1-azetines with nitrilimines, nitrile oxides and nitrile ylides, and the ring-opening of some of the nitrilimine cycloadducts to 1,2,4-triazoles.

The tetramethylazetine[12] **6** was obtained readily by ethylation of the azetidinone **5**[13] with Meerwein's reagent. Treatment of the azetidinone with Lawesson's reagent afforded the thiolactam **7**, which on ethylation in a like manner to the lactam **5**, yielded the (ethylthio)- compound **8**.



Scheme 2

The bicyclic 2-(ethylthio)-1-azetine **11** was prepared in a similar manner from the bicyclic 1-azetidinone **9**,[14] as were the methyl- and dimethyl-substituted bicyclic azetines **15a**, and **14a** and **14b**, from azetidinone **12a**[15] and thioazetidinones **13a** and **13b**, respectively.



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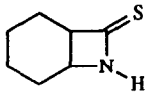

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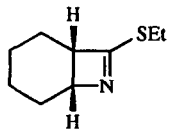

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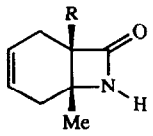
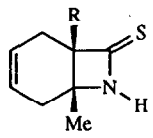
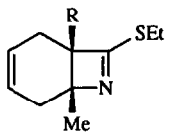


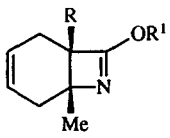
12 a, R = H; **b**, R = Me



13 a, R = H; **b**, R = Me



14 a, R = H; **b**, R = Me



15 a, R = H; R^1 = Me; **b**, R = R^1 = Me; **c**, R = H, R^1 = Et

Nitrilimine cycloadditions

The nitrilimines, in the initial studies, were generated by dehydrohalogenation of the appropriate hydrazonyl halides [ArC(X)=NNHPh; X = Cl or Br].[16] Latterley, however, an alternative procedure[17] which involved heating a benzaldehyde hydrazone (ArNHN=CHPh) with chloramine-T in boiling ethanol, was adopted. This method was particularly useful as it avoided the isolation and subsequent handling of the hydrazonyl halides, which are extremely vigorous skin-irritants.

The cycloaddition of C,N-diphenyl nitrilimine ($PhC\equiv\overset{+}{N}\text{-}\overset{-}{N}\text{-}Ph$), generated *in situ* by dehydrohalogenation (method A) of the hydrazonyl halide with triethylamine in boiling benzene, and 2-ethoxy-1-azetine **6** was complete (as shown by t.l.c.) in two hours. Removal of the solvent and triethylamine hydrochloride, followed by purification of the residue by flash chromatography, furnished a single product (57% yield). However, it was apparent immediately from the ^{1}H n.m.r. spectrum that this was not the expected 1:1 cycloadduct (**16**; X = O) since the ethoxy-hydrogen resonances were absent and only three, rather than four, methyl group signals were present. In addition, two one-proton signals at 4.5 and 4.6 δ were suggestive of a methylene unit; a feature which was confirmed by the ^{13}C n.m.r. spectrum. Interestingly, addition of the diphenylnitrilimine to the (ethylthio) azetine **8** furnished the same product in 60% yield. A single crystal X-ray crystallographic study (Figure 1) revealed that this unexpected product was in fact the 5-(butenyl)-1,2,4-triazole **19**.

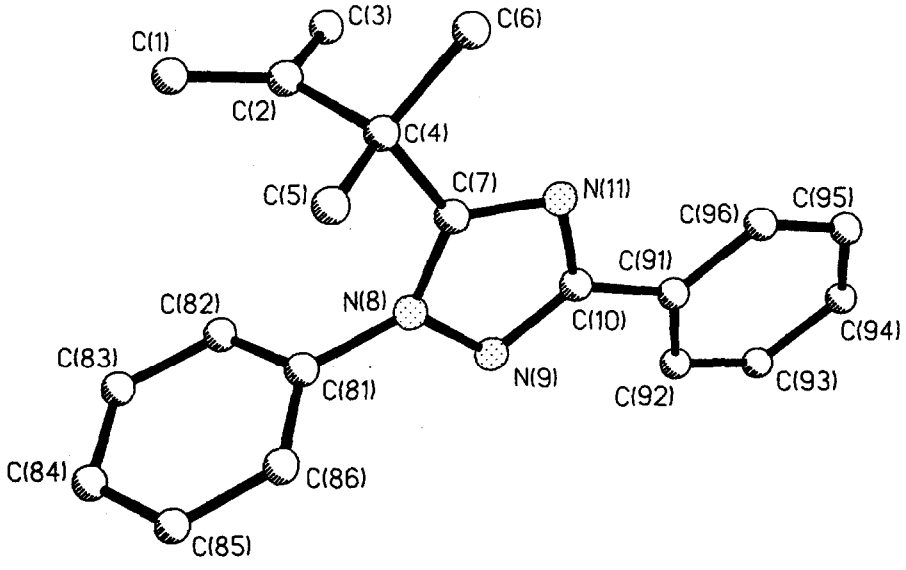
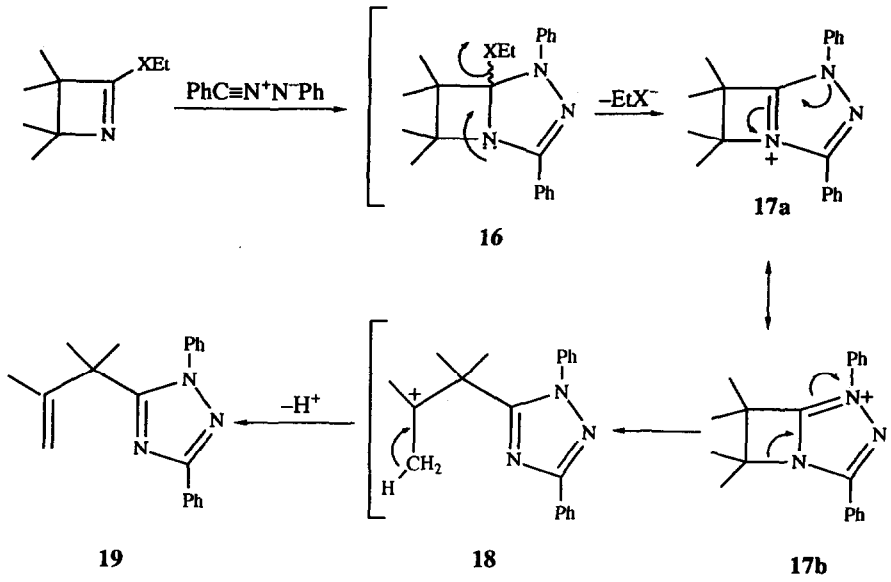
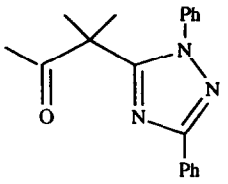


Figure 1. Molecular structure of 5-(2,3-dimethylbut-1-ene-3-yl)-1,3-diphenyl-1,2,4-triazole **19**

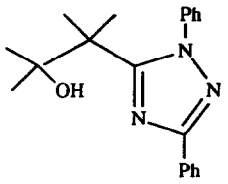


Scheme 3

Ozonolysis of alkene **19** yielded the expected methyl ketone **20** which with methyl lithium at -78° in dry ether produced the tertiary alcohol **21**.



20



21

A mechanistic rationale for this unexpected ring-opening is outlined in Scheme 3. Loss of EtX^- from the initially formed 1,3-dipolar cycloadduct **16** yields the resonance stabilised triazolium species **17a** <----> **17b** which, by scission of the strained 4-membered ring and loss of a proton from the resulting tertiary carbocation **18**, affords the aromatic 1,2,4-triazole system **19**.

It was argued that stabilisation of the triazolium species **17** should be dependent on the availability of the lone pair on N-1 for mesomeric interaction with the positively charged bridgehead nitrogen. Any factor that decreases this electron availability should increase the stability of cycloadduct **16** at the expense of the triazolium species **17**.

With this in mind, the *N*-(*p*-nitrophenyl)-C-phenylnitrilimine (p-$NO_2C_6H_4\bar{N}$-$\overset{+}{N}$≡C-Ph) was prepared and allowed to react with the 2-ethoxy- and 2-(ethylthio)-1-azetines **6** and **8** respectively, whereupon the bicyclic adducts **22a** and **22e** were obtained in high yields. The X-ray crystal structure for the ethoxy-derivative **22a** is shown in Figure 2.

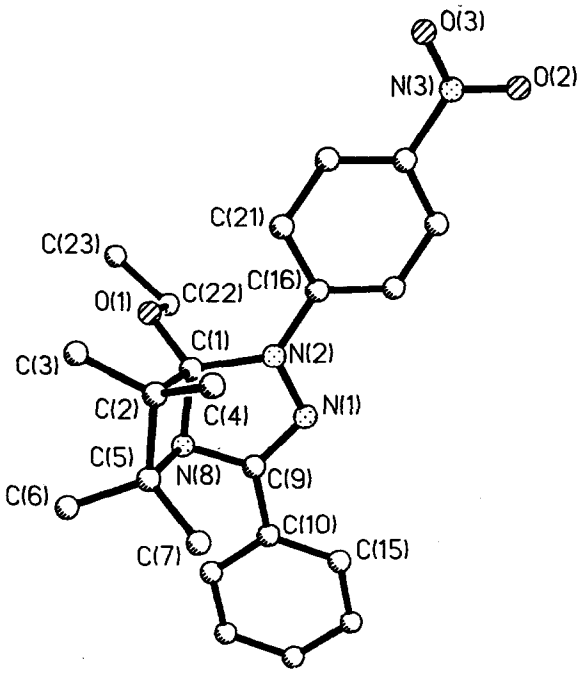


Figure 2. Molecular structure of 5-ethoxy-4-(*p*-nitrophenyl)-2-phenyl-6,6,7,7-tetramethyl-1,3,4-triaza-bicyclo[3.2.0]hept-2-ene **22a**

Furthermore, and in accord with the mechanism outlined in Scheme 3, these cycloadducts on heating in boiling dichlorobenzene, suffered loss of EtXH, and formation in each case, of the 1,2,4-triazole **23a** (Figure 3) in quantitative yield.

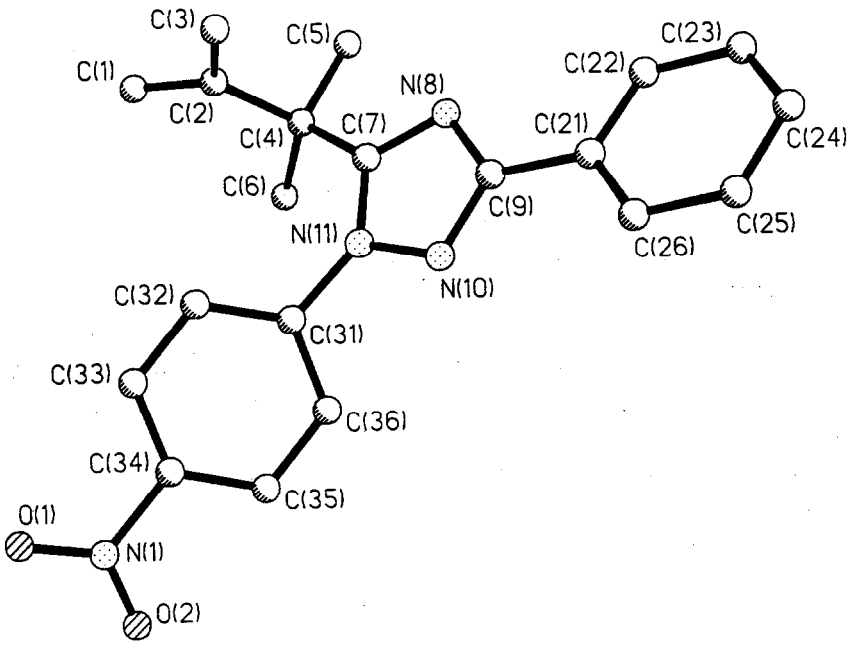
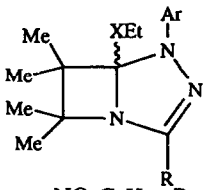


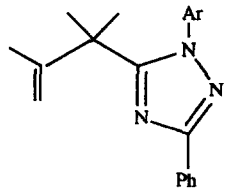
Figure 3. Molecular structure of 5-(2,3-dimethylbut-1-ene-3-yl)-1-(*p*-nitrophenyl)-3-phenyl-1,2,4-triazole **23a**

Further cycloadditions of 2-ethoxy- and 2-(ethylthio)-1-azetines **6** and **8** with other N-(*p*-nitrophenyl)-nitrilimines revealed that whereas the 4-ethoxy-azetine yielded only bicyclic cycloadducts **22b-d**, the (ethylthio)azetine afforded mixtures of 1,3-dipolar cycloadducts **22f-h** and butenyl-1,2,4-triazoles **23b-d**.

These mixtures proved to be difficult to separate, and on standing, slowly lost ethanethiol. As a consequence, the products were not isolated and the % yields cited in Table 2 are those estimated from the high-field ^{1}H n.m.r. spectra of the mixtures measured as soon as possible after purification of the mixture of products by flash chromatography. The difference in behaviour of the ethoxy- and (ethylthio)-azetines cycloadducts may be a reflection of the greater nucleofugacity of the ethylthio- group over that of the ethoxy-group.



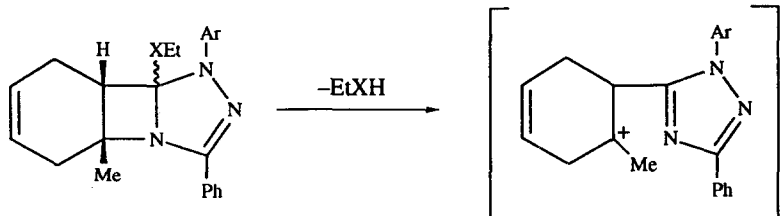
22 **a** X = O, Ar = p-$NO_2C_6H_4$, R = Ph
b X = O, Ar = p-$NO_2C_6H_4$, R = p-ClC_6H_4
c X = O, Ar = R = p-$NO_2C_6H_4$
d X = O, Ar = p-$NO_2C_6H_4$, R = CO_2Me
e X = S, Ar = p-$NO_2C_6H_4$, R = Ph
f X = S, Ar = p-$NO_2C_6H_4$, R = p-ClC_6H_4
g X = S, Ar = R = p-$NO_2C_6H_4$
h X = S, Ar = p-$NO_2C_6H_4$, R = CO_2Me



23 **a** Ar = p-$NO_2C_6H_4$, R = Ph
b Ar = p-$NO_2C_6H_4$, R = p-ClC_6H_4
c Ar = R = p-$NO_2C_6H_4$
d Ar = p-$NO_2C_6H_4$, R = CO_2Me

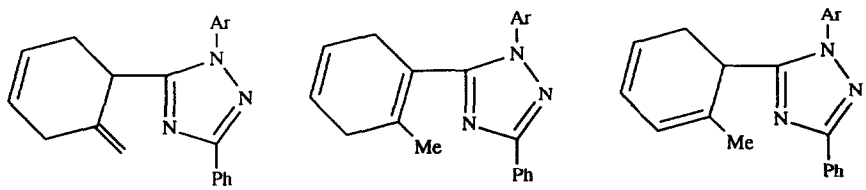
Interestingly, cycloaddition of the *N*-(*p*-nitrophenyl)-C-phenyl nitrilimine (*p*-$NO_2C_6H_4\bar{N}\text{-}\overset{+}{N}\equiv CPh$), generated by the action of chloramine-T in hot ethanol on benzaldehyde-*p*-nitrophenylhydrazone (*p*$NO_2C_6H_4NHN{=}CHPh$), with the (ethylthio) azetine **8**, yielded the cycloadduct **22e** contaminated by a small amount (5%) of the triazole **23a**. In view of the previous results, the appearance of the ring-opened product at this lower temperature (boiling ethanol) was surprising. In fact, we have now found that the rearrangement of cycloadduct **22e** to triazole **23a** can be accomplished in quantitative yield, in boiling ethanol (3 h.), or in boiling benzene (5 h.).

As a further probe into the mechanism of triazole formation, the methyl- and dimethyl-substituted bicyclic azetines **14a,b** and **15a** were prepared and their 1,3-dipolar cycloadditions with nitrilimines studied. The monomethyl substituted cycloadducts **24a,b** were of interest in that the carbocation intermediate **25**, formed by ring-opening of the 4-membered ring, offered the choice of 3-possible primary reaction products, namely the *exo*-methylene structure **26**, the non-conjugated diene **27**, and the conjugated diene **28** (Scheme 4).



24 **a** X = O, Ar = p-$NO_2C_6H_4$
b X = S, Ar = p-$NO_2C_6H_4$

25



26 **27** **28**

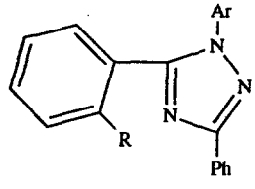
Scheme 4

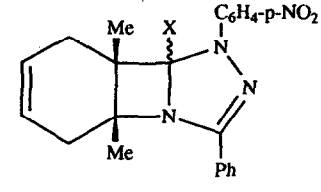
Surprisingly, with *N*-(*p*-nitrophenyl)-C-phenylnitrilimine, generated from the hydrazonyl chloride, a cycloadduct **24a** (40%) was obtained only from the ethoxy-azetine **15**. No reactions were observed with the (ethylthio)-azetines **14a,b**.

However, on generation of the (nitrophenyl)nitrilimine, with chloramine-T in ethanol, cycloadduct **24b** was obtained from (ethylthio)azetine **14a**, along with a trace amount (by ^{1}H n.m.r.) of a ring-opened product (no SEt group), which exhibited terminal methylene proton resonances at 4.5 and 5.05 δ in its proton magnetic resonance spectrum [*exo*-methylene structure **26**?]. Unfortunately, all attempts to reproduce this result have failed. For example, on scaling up the experiment cycloadduct (**24b**; 53%) was obtained, which was stable in boiling benzene, toluene, and mixed xylenes, but which on heating in boiling *o*-dichlorobenzene suffered ring-scission and dehydrogenation to the fully unsaturated 5-(*o*-tolyl)-1,2,4-triazole **29a** (62%). In addition to adduct **24b**, trace amounts of by-products were detected, which, from the complex alkene resonances in the ^{1}H n.m.r. spectrum of the mixture, could have been the cyclohexadiene derivatives **27** and **28**. In an attempt to produce these cyclohexadienes in greater yields, the cycloaddition, using chloramine-T as the nitrilimine generator, was repeated under prolonged (8h) reflux in ethanol solution. In this instance, a mixture of products was obtained, which from the complex vinyl resonances, and the two distinct methyl singlets at 1.61 and 1.87 δ, were assigned tentatively as the sought-after conjugated and non-conjugated dienes **27** and **28**. So far, however, we have been unable to separate and characterise any of these partially unsaturated products.

In accord with the result obtained with the tetramethyl-azetine, the bicyclic (ethylthio) azetine **14a** and diphenylnitrilimine, afforded no primary cycloadduct, but only fully aromatised 1,3,5-triaryl-1,2,4-triazole **29b**.

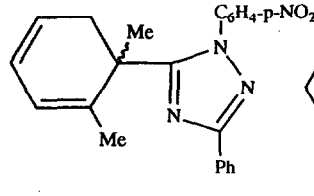
The cycloadduct **30a**, formed from the dimethylcyclohexyl-azetine **14b** and *N*-(*p*-nitrophenyl)-C-phenylnitrilimine, on heating in *o*-dichlorobenzene gave, as anticipated, the ring-opened conjugated diene **31** along with traces (by ^{1}H n.m.r.) of what could be an *exo*-methylene compound analogous to product **26**.

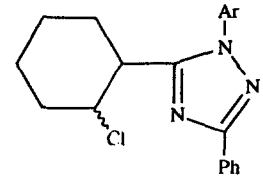


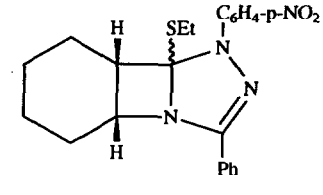


29 a Ar = p-$NO_2C_6H_4$, R = Me
b Ar = C_6H_5, R = Me
c Ar = C_6H_5, R = H

30 a X = SEt
b X = OMe







31 **32 a** Ar = Ph **33**
b Ar = p-$NO_2C_6H_4$

In our preliminary report it was noted that the bicyclic azetine **11** with diphenylnitrilimine, generated from the hydrazonyl chloride, yielded a major product (73%) which clearly had lost ethanethiol, and which, from the mass spectrum (M^+, 337, 339; 3:1) contained chlorine. On the basis of its ^1H n.m.r. spectrum, which showed no alkene protons, but rather a significant downfield proton shift (4.48) for one of the 1H complex multiplets of the cyclohexyl-ring, the product was assigned tentatively as a diastereoisomeric mixture of the 5-(chlorocyclohexyl)-1,2,4-tetrazoles **32a**.

Surprisingly, repetition of this reaction using diphenylnitrilimine generated by Hassner's chloramine-T method, produced only the 1,3,5- triphenyl-1,2,4-triazole **29c** in 69% yield. We are not aware of other examples of aromatisation of cyclohexanes or cyclohexenes with chloramine-T,[18] although *N,N*-dichlorobenzenesulphonamide is known to effect dehydrogenation of cyclohexene to cyclohexa-1,3-diene in 47% yield.[19]

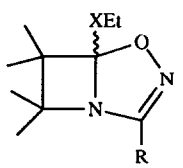
With *N*-(*p*-nitrophenyl)-C-phenylnitrilimine generated from the hydrazonyl chloride, the bicyclic azetine **11** gave a separable mixture of the tricyclic adduct **33** and what are thought to be the diastereoisomeric chloro-compounds **32b**.

Nitrile oxide cycloadditions

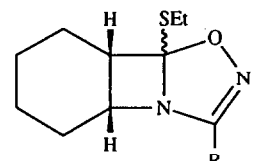
The nitrile oxides were generated mainly by the standard method[16] i.e. by dehydrodehalogenation of α-chloroaldoximes (benzhydroximoyl chlorides) with triethylamine, and by a more recent method,[20] involving the action of chloramine-T on the arylaldoxime in boiling ethanol.

Addition of α-chloro-*p*-methoxybenzaldoxime to a mixture of triethylamine and 2-ethoxy-1-azetine **6** in dry benzene resulted in an almost instantaneous precipitation of triethylamine hydrochloride. Reaction was complete (as shown by t.l.c.) in about 2 hours and removal of the amine salt and solvent, followed by purification by flash chromatography gave the 1:1 cycloadduct **34a**.

The ^1H n.m.r. spectrum displayed four non-equivalent methyl groups and, as a consequence of the adjacent chiral bridgehead carbon, two distinct 1 proton signals for the diastereotopic geminal protons of the methylene unit of the ethoxy-group.



34 **a** X = O, R = p-$MeOC_6H_4$
b X = O, R = Ph
c X = O, R = o-$NO_2C_6H_4$
d X = S, R = p-$MeOC_6H_4$
e X = S, R = Ph
f X = S, R = o-$NO_2C_6H_4$
g X = S, R = CO_2Et



35 **a** R = p-$MeOC_6H_4$
b R = Ph
c R = o-$NO_2C_6H_4$

Analogous cycloadducts **34b,c** and **34e,f** respectively, were obtained from benzonitrile oxide and *o*-nitrobenzonitrile oxide, and azetine **6** and the corresponding 2-(ethylthio) azetine **8**.

An X-ray crystal structure (Figure 4) for the cycloadduct **34d** has been determined, and confirms the regiochemistry expected for the nitrile oxide cycloaddition.

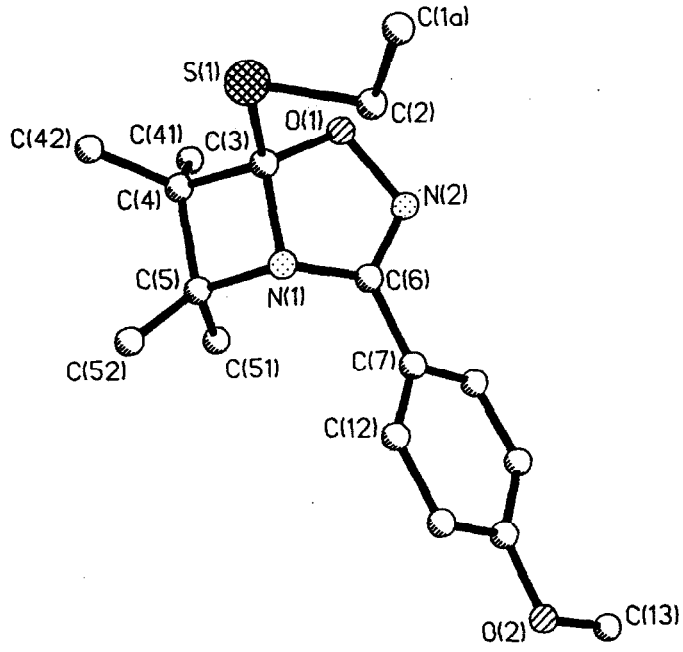
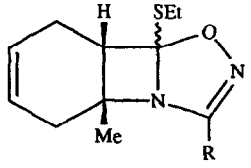


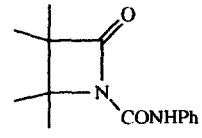
Figure 4. Molecular structure of 5-(ethylthio)-2-(*p*-methoxyphenyl)-6,6,7,7-tetramethyl-4-oxa-1,3-diaza-bicyclo[3.2.0]hept-2-ene **34d**

Nitrile oxide cycloadditions to the bicyclic azetine **11** under similar conditions gave the 9-oxa-1,10-diazatricyclo[6.3.0.$0^{2,7}$]undec-10-enes **35a-c** as mixtures of diastereoisomers, which were distinguishable by ^{1}H n.m.r. and t.l.c., but which on attempted separation by h.p.l.c. decomposed to unknown products.

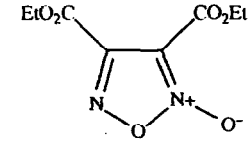
Adducts **34e** and **36a** respectively, have been obtained from the tetramethylazetine **8** and the bicyclic azetine **14a** and benzonitrile oxide generated by Hassner's method[20] i.e. benzaldoxime and chloramine-T in hot ethanol.



36 a R = Ph
b R = CO_2Et



37



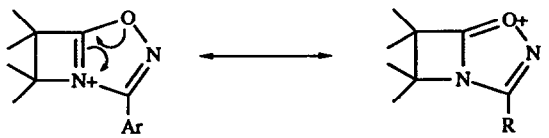
38

Attempts to add ethoxycarbonylnitrile oxide, generated by treatment of ethyl nitroacetate with triphenylphosphine and phenylisocyanate,[21] to azetine **8** failed. Only urea **37**, along with the nitrile oxide dimer, 3,4-(diethoxycarbonyl)-1,2,5-oxadiazole 2-oxide **38**, were isolated.

However, generation of nitrile oxide by base-catalysed elimination from the chlorooxime [Cl(EtO$_2$C)C=NOH] in the presence of the azetines **8** or **14a** furnished the adducts **34g** and **36b** in high yields.

The thermal rearrangement of azetine-diarylnitrilimine cycloadducts **22** to 1,2,4-triazoles has been referred to earlier (Scheme 3). An analogous reaction of the nitrile oxide-azetine cycloadducts should yield the corresponding oxadiazoles. However, the nitrile oxide adducts **34a** and **36a** proved to be remarkably stable, and were recovered unchanged even after prolonged boiling in 1-methylnaphthalene (b.p. 240°C).

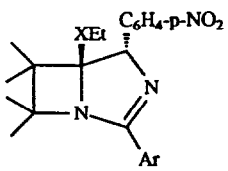
Possibly, the enhanced stability of these adducts, compared to those from the nitrilimines, is due to the reluctance of the lone-pair electrons on the more electronegative oxygen to enter into mesomeric stabilisation of the corresponding intermediate oxadiazolium ion **39**, a feature which appears to be of paramount importance in determining the stability of the corresponding triazolium ions **17**.



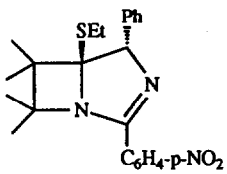
39

Nitrile ylide cycloadditions

Additions of nitrile ylides (*p*-NO$_2$C$_6$H$_4$$\bar{C}$H-$\overset{+}{N}$≡CAr; Ar = Ph, *p*-NO$_2C_6H_4$, or *p*-MeC$_6H_4$), generated by dehydrohalogenation of the corresponding imidoyl chlorides with triethylamine in benzene,[7] with azetines **6**and **8** were slow (12 hours), but gave the 1,3-diaza-bicyclo[3.2.0]hept-2-enes **40a-f** in practicable yields (Table 5).



40
a X = O, Ar = Ph
b X = O, Ar = p-NO$_2$C$_6$H$_4$
c X = O, Ar = p-MeC$_6$H$_4$
d X = S, Ar = Ph
e X = S, Ar = p-NO$_2$ C$_6$H$_4$
f X = S, Ar = p-MeC$_6$H$_4$



41

The 300 MHz spectra of the products were consistant with the assigned structures, and again, revealed clearly the diastereotopic character of the methylene protons of the ethoxy and (ethylthio) groups. However, despite the presence in the cycloadduct of two chiral centres, only one set of diastereoisomers could be detected in the high field n.m.r. spectrum of adduct **40a**. Furthermore, an X-ray crystal structure of **40b** (Figure 5) revealed, that the ethoxy- and *p*-nitrophenyl- groups located at the two chiral carbon centres, adopt a

trans-configuration. It is likely, although not confirmed, that the other cycloadducts are also formed as the single '*trans*-' diastereoisomeric pairs.

An attempt to prepare the regio-isomer **41** of nitrile ylide cycloadduct **40d** from the isomeric nitrile ylide **43** and azetine **8** failed.

Generation of the nitrile ylide **43** from chloro-compound **42**, derived from N-(*p*-nitrobenzoyl)benzylamine,[22] with triethylamine in the presence of azetine **8** gave only cycloadduct **40d**. This result is in accord with the work of Huisgen and his co-workers[23] who demonstrated clearly that nitrile ylide **43** readily transforms into the isomeric ylide **44**. A base-catalysed tautomerism of the chloro-compound is suggested to account for this isomerism.

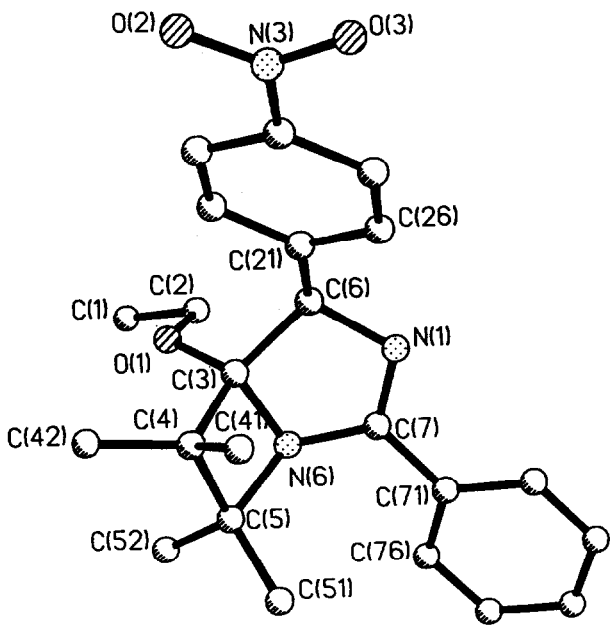
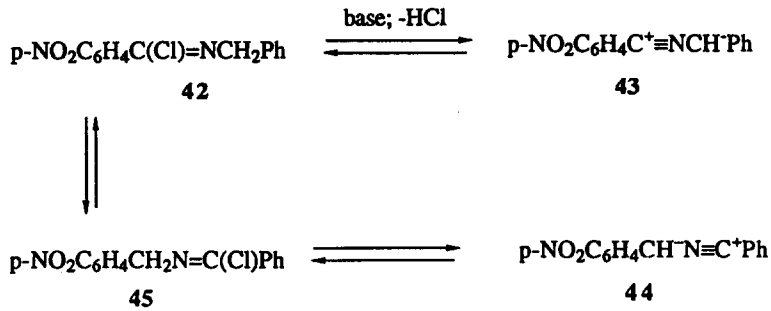


Figure 5. Molecular structure of 5-ethoxy-4-(*p*-nitrophenyl)-2-phenyl-6,6,7,7-tetramethyl-1,3-diazabicyclo-[3.2.0]hept-2-ene

It is most likely, therefore, that the slow rate of nitrile ylide-azetine addition allows isomerisation of the nitrile ylide precursor **42** to the more stable form **45** prior to cycloaddition.



Other Cycloadditions

Curiously, we have been unable to effect cycloaddition of the azetines with nitrile sulphides,[24] non-stabilised nitrile ylides (e.g. $CH_3C{\equiv}\overset{+}{N}\text{-}\bar{C}H_2$),[25] azomethine ylides (generated by thermal ring-opening of aziridines,[26] or by prototropic shifts in anils[27]) nitrones,[28] and surprisingly, in view of their known[29] propensity to add to strained double bonds, aryl azides.

In addition, all attempts so far to coax the azetines into Diels-Alder [4 + 2] cycloadditions with electron-rich or electron-deficient dienes, have failed.

EXPERIMENTAL

I.r., mass, and ^{1}H n.m.r. spectra were measured on a Perkin-Elmer 1710 Fourier Transform Infrared spectrometer, a Finnegan 4000 mass spectrometer, and a Bruker AC 300 MHz n.m.r. spectrometer, respectively. I.r. spectra were recorded as nujol mulls, and ^{1}H n.m.r. spectra in $CDCl_3$ solution, unless stated otherwise. X-Ray crystallographic data were obtained on a NICOLET R3 mV/V diffractometer. T.l.c. was conducted on Camlab. Polygram silica G/UV_{254} and flash chromatography was carried out on silica gel 60 (Merck 9385). Unless stated otherwise light petrol refers to the fraction of b.p. 60-80°C.

All m.p.'s are uncorrected.

2-Ethoxy-3,3,4,4-tetramethyl-1-azetine **6**,[12] obtained by ethylation of 3,3,4,4-tetra-methylazetidin-2-one **5**[13] with Meerwein's reagent, was purified by flash chromatography on silica [light petrol-ethyl acetate (4:1) as eluant]. Colourless liquid (54%); b.p. 78-80°/50 mm. Prepared similarly were 8-methoxy-6-methyl- **15a**, 8-methoxy-1,6-dimethyl- **15b** and 7-azabicyclo[4.2.0]oct-3,7-diene pale yellow oils (^{1}H n.m.r. data in agreement with lit.[15] values) and 8-ethoxy-6-methyl-7-azabicyclo[4.2.0]oct-3,7-diene **15c** as an unstable oil which was used directly without further investigation: δ_H ($CDCl_3$: 300 MHz) 1.35 (3H, t, OCH_2CH_3), 1.36 (3H, s, Me), 2.0-2.4 (4H, m, 2 x CH_2CH=CH), 2.94 (1H, dd, CH), 4.16 (2H, q, OCH_2CH_3), 5.75 (2H, m, CH=CH).

3,3,4,4-Tetramethylazetidin-2-thione **7**

To a stirred solution of 3,3,4,4-tetramethylazetidin-2-one (1 g; 7.9 mmol) in dry THF was added Lawesson's reagent (1.59 g; 3.9 mmol), and the mixture stirred under nitrogen at room temperature for 20 min. The mixture was heated at 60° for a further 20 min. then cooled, the solvent removed under reduced pressure, and the residue purified by flash chromatography on silica [light petrol - ethyl acetate (7:3)] as eluant. 3,3,4,4-

Tetramethylazetidin-2-thione was obtained as a white solid (1 g; 89%) which was crystallised from light petrol as white needles, m.p. 123-4°; (Found C, 58.7; H, 9.0; N, 9.8; S, 22.7 $C_7H_{13}NS$ requires C, 58.7; H, 9.15; N, 9.8; S, 22.4%). ν_{max} (nujol) 1240 cm^{-1} (C=S); δ_H (90 MHz, $CDCl_3$) 1.25 (6H, s, 2 x CH_3), 1.4 (6H, s, 2 x CH_3), 8.4 (1H, bs, NH).

Prepared similarly were 7-azabicyclo[4.2.0]octan-8-thione **10**, white needles from light petrol, m.p. 85-7° (62%), from 7-azabicyclo[4.2.0]octan-8-one **9**.[14] (Found: C, 59.6; H, 7.8; N, 10.0; S, 22.75 $C_7H_{11}NS$ requires C, 59.5; H, 7.85; N, 9.9; S, 22.7%); ν_{max} (Nujol) 1240 cm^{-1} (C=S); δ_H (90 MHz; $CDCl_3$) 1.35-1.95 (8H, m, 4 x CH_2), 3.15 (1H, bm, bridgehead CH), 4.32 (1H, m, bridgehead CH), 8.15 (1H, bs, NH):

6-methyl-7-azabicyclo[4.2.0]oct-3-ene-8-thione **13a**, from 6-methyl-7-azabicyclo-[4.2.0]oct-3-ene-8-one **12a**,[15] as a white crystalline solid, m.p. 124-6° (93%) after flash chromatography on silica [light petrol (b.p. 40-60°C) - ethyl acetate 7:3 as eluant] ν_{max} (nujol) 1503 cm^{-1} (C=S): δ_H (300 MHz, $CDCl_3$) 1.52 (3H, s, Me), 2.06-2.28 (2H, m, CH_2C=C), 2.29-2.61 (2H, m, CH_2-C=C), 2.92 (1H, d, CH), 5.72-5.89 (2H, m, CH=CH), 7.8 (1H, bs, NH): HRMS (NH_3: CI) Found 154.0684 (M + 1). $C_8H_{11}NS$ (M + 1) requires 154.0690; and 1,6-dimethyl-7-azabicyclo[4.2.0]oct-3-ene-8-thione **13b**, from 1,6-methyl-7-azabicyclo-[4.2.0]oct-3-ene-8-one **12b**,[15] as a white crystalline solid, m.p. 146-7° (91%) after flash chromatography on silica [light petrol-ethyl acetate (5:3) as eluant], and crystallisation from light petrol-ethyl acetate (7:2) ν_{max} 3122 (NH); 1504 cm^{-1} (C=S); δ_H (300 MHz, $CDCl_3$) 1.21 (3H, s, Me), 1.4 (3H, s, Me), 1.89 (1H, ddd, CH_2C=C), 2.07 (1H, ddd, CH_2C=C), 2.29 (1H, dd, C*H*-C=C), 2.38 (1H, dd, C*H*-C=C), 5.69-5.86 (2H, m, C*H*=CH), 8.27 (1H, bs, NH). HRMS (NH_3:CI) Found 168.0841 (M + 1): $C_9H_{13}NS$ (M + 1) requires 168.0847.

2-(Ethylthio)-3,3,4,4-tetramethyl-1-azetine **8**, prepared in a similar manner to the 2-ethoxy-derivative **6**, was obtained as a colourless oil by flash chromatography on silica [light petrol - ethyl acetate (4:1)] as eluant. Yield 89%: (Found: C, 63.1; H, 9.9; N, 8.2 $C_9H_{17}NS$ requires C, 63.1; H, 10.0; N, 8.2%); ν_{max} (liquid film) 1640 cm^{-1} (C=N); δ_H ($CDCl_3$: 90 MHz) 1.12 (6H, s, 2 x CH_3), 1.22 (6H, s, 2 x CH_3), 1.28 (3H, t, CH_2CH_3), 2.99 (2H, q, CH_2CH_3).

Also prepared were a) 8-(ethylthio)-7-azabicyclo[4.2.0]oct-7-ene **11**, colourless oil from flash chromatography on silica (eluant as in previous example). Yield 77%; (Found: C, 63.9; H, 8.9; N, 8.2 $C_9H_{15}NS$ requires C, 63.9; H, 8.9; N, 8.3%). ν_{max} (liquid film) 1635 cm^{-1} (C-N): δ_H ($CDCl_3$, 90 MHz) 1.3 (3H, t, CH_2CH_3), 1.2-1.8 (8H, m, cyclohexyl), 2.95 (2H, dq, SCH_2CH_3), 3.25 (1H, m, 1-CH), 4.05 (1H, m, 1-CH);

b) 8-(Ethylthio)-6-methyl-7-azabicyclo[4.2.0]oct-3,7-diene **14a**: Pale yellow oil from flash chromatography on silica [eluant light petrol - ethyl acetate 3:1]. Yield 60%: δ_H ($CDCl_3$: 300 MHz), 1.29 (3H, t, CH_2CH_3), 1.37 (3H, s, CH_3), 1.96-2.38 (4H, m, 2 x CH_2-C=C), 2.38-2.7 (3H, m, CH_3CH_2S and CH), 5.72-5.78 (2H, m, CH=CH); HRMS $(M + 1)^+$ Found 182.0998: $C_{10}H_{15}NS$ $(M + 1)^+$ requires 182.1003;

c) 1,6-Dimethyl-8-(ethylthio)-7-azabicyclo[4.2.0]oct-3,7-diene **14b**: Pale yellow oil from flash chromatography on silica [light petrol-ethyl acetate (6:5) as eluant]: Yield 54%: δ_H ($CDCl_3$: 300 MHz) 1.11 (3H, s, Me), 1.25 (3H, s, Me), 1.25 (3H, t, SCH_2CH_3), 1.8-2.4 (4H, m, 2 x CH_2-CH=CH), 2.8-3.0 (2H, m, SCH_2CH_3), 5.69 (2H, m, C*H*=C*H*-) HRMS Found: 196.1168 $(M + 1)^+$, $C_{11}H_{17}NS$ (M + 1) requires 196.1160.

Preparation of Hydrazonyl Halides - The hydrazonyl chlorides [ArNH-N=C(Cl)Ph] were obtained by a) chlorination of the corresponding *N*-acylarylhydrazines (ArNHNHCOPh) with phosphorus pentachloride[4d,30] [CAUTION: the hydrazonyl halides are vigorous skin irritants and great care needs to be exercised in their handling. All operations with these products were carried out in an efficient fume-hood, and all skin-contact avoided:]. α-Chloro-benzaldehyde phenyl hydrazone [PhNHN=C(Cl)Ph], m.p. 129-31°; (lit.,[30] m.p. 130°); yield 59%: α-chlorobenzaldehyde *p*-nitrophenylhydrazone [*p*-$NO_2C_6H_5NHN$=C(Cl)Ph] m.p. 188-90° (lit.,[4d] m.p. 189-91°); yield 79%.

The hydrazonyl bromides [ArNHN=C(Br)Ar[1]] were obtained by bromination of the corresponding *N*-acylphenylhydrazines with bromine in acetic acid[31]: α-Bromo-(*p*-chloro-benzaldehyde) *p*-nitrophenyl-hydrazone [*p*-$NO_2C_6H_4NHN$=C(Br)C_6H_4-*p*-Cl], m.p. 222-4° (lit.,[31] m.p. 222-4°) Yield 55%: α-Bromo-(*p*-nitrobenzaldehyde)-*p*-nitrophenylhydrazone [*p*-$NO_2C_6H_4NHN$=C(Br)C_6H_4-*p*-NO_2]; m.p. 280-2° (lit.,[31] m.p. 280°) Yield 49%.

Addition of nitrilimines to 2-ethoxy- and 2-(ethylthio)-1-azetines: General method A - To a stirred solution of the 1-azetine (1.46 mmol) and the hydrazonyl halide (1.75 mmol) in dry benzene (20 ml) was added dropwise, triethylamine (4 mol. equivalents). The mixture was heated under reflux, and the reaction followed by t.l.c. When the reaction was complete (2-4 h), the mixture was filtered to remove triethylamine hydrochloride, and the filtrate evaporated to give the crude solid product, which was purified by flash chromatography.

5-(2,3-Dimethylbut-1-ene-3-yl)-1,3-diphenyl-1,2,4-triazole **19** was obtained from diphenylnitrilimine [$PhN^{-}\text{-}N^{+}\equiv$C-Ph] and a) 2-ethoxy-1-azetine **6** and b) 2-(ethylthio)-1-azetine **8**: [light petrol - ethyl acetate 19:1 as eluant] m.p. 94-5°. Yield a) 57%; b) 60%: [Found C, 78.9; H, 6.9; N, 13.65: $C_{20}H_{21}N_3$ requires C, 79.2; H, 7.0; N, 13.9%); δ_H ($CDCl_3$; 250 MHz) 1.4 (6H, s, Me_2C), 1.63 (3H, s, CH_3), 4.54 (1H, s, =CH), 4.68 (1H, s, =CH), 7.38 (8H, m, Ar), 8.15 (2H, dd, Ar); δ_C ($CDCl_3$; 75.5 MHz) 19.9 (q, *Me* C=C), 27.2 (q, Me_2C), 41.6 (s, CMe_2), 111.1 (t, $=CH_2$), 126.3, 127.5, 128.4, 128.6, 129.2, 129.5 (d, 6 x aromatic, CH), 131.1 (s, $C(Me)=CH_2$), 139.2 (s, Ar*C*), 148.9 (s, Ar*C*-N), 160.05 (s, C=N), 161.7 (s, C=N); m/z (EI) 303 (M^+).

Ozonolysis of the butenyl-triazole was carried out in dichloromethane solution at 0° over 40 mins. An excess of dimethyl sulphide was added and the mixture stirred at room temperature. Removal of the solvent under vacuum and purification of the residue by flash chromatography (SiO_2; light petrol-ethyl acetate 9:1) as eluant gave 3-(1,3-diphenyl-1,2,4-triazol-5-yl)-3-methyl-2-butanone **20** as a white solid (60%) which recrystallised from light petrol, m.p. 91-3°C; (Found C, 74.5; H, 6.25; N, 13.7. $C_{19}H_{19}N_3O$ requires C, 74.7; H, 6.3; N, 13.8%). ν_{max} (nujol) 1720 cm^{-1} (CO); δ_H ($CDCl_3$; 90 MHz) 1.46 (6H, s, 2 CH_3), 2.09 (3H, s, CH_3), 7.45 (8H, m, ArH), 8.13 (2H, dd, ArH).

To a stirred solution of the ketone **20** (0.2 g; 0.66 mmol) in dry diethyl ether (10 ml) maintained at -78°C and under a dry nitrogen atmosphere, was added 0.5 ml of a 1.55 M solution of methyl lithium in diethyl ether. The mixture was stirred and allowed to reach room temperature. After 3 hours at room temperature the mixture was quenched by addition of ammonium chloride solution (10 ml) and the organic layer separated. The aqueous layer was extracted with diethyl ether (2 x 10 ml) and the combined ether extracts dried over anhydrous magnesium sulphate. Removal of the solvent yielded an oily product which was purified by flash chromatography on silica (light petrol-ethyl acetate 9:1) as eluant. 2,3-Dimethyl-3-(1,3-diphenyl-1,2,4-triazol-5-yl)-2-butanol was obtained as an oil (0.11 g; 52%): (Found: C, 74.7; H, 7.3; N,

13.15. $C_{20}H_{23}N_3O$ requires C, 74.7; H, 7.2; N, 13.1%): ν_{max} (liquid film) 3400 cm^{-1} (OH); δ_H ($CDCl_3$; 90 MHz) 1.16 (12H, s, 4 x CH_3), 6.3 (1H, bs, OH), 7.4 (5H, m, ArH), 7.51 (3H, m, ArH), 8.06 (2H, dd, ArH).

Under the conditions of method (A) the addition of *N*-(*p*-nitrophenyl)-C-phenyl-nitrilimine to 2-(ethylthio)-1-azetine **8** gave 5-(ethylthio)-4-(*p*-nitrophenyl)-2-phenyl-6,6,7,7-tetramethyl-1,3,4-triaza-bicyclo[3.2.0]hept-2-ene **22e** (88%) which was crystallised from light petrol - ethyl acetate, m.p. 153-4°C, (Found: C, 64.6; H, 6.3; N, 14.0; S, 7.1. $C_{22}H_{26}N_4O_2S$ requires C, 64.4; H, 6.4; N, 13.7; S, 7.8%); δ_H (250 MHz, $CDCl_3$) 0.98 (3H, s, CH_3), 1.05 (3H, t, CH_3CH_2), 1.13 (3H, s, CH_3), 1.4 (3H, s, CH_3), 1.69 (3H, s, CH_3), 2.15 (1H, dq, s-CH_2CH_3), 2.45 (1H, dq, SCH_2CH_3), 7.3 (2H, dd, *p*-$NO_2C_6H_4$), 7.42 (3H, m, Ph), 7.75 (2H, dd, *p*-$NO_2C_6H_4$), 8.12 (2H, d, Ph).

Similarly, the addition of other N-(*p*-nitrophenyl)nitrilimines (*p*-$NO_2C_6H_4\bar{N}\overset{+}{N}\equiv CR$) to ethoxy-azetine **6** yielded the 5-ethoxy-6,6,7,7-tetramethyl-1,3,4-triazabicyclo[3.2.0]hept-2-enes **22a-d** (Table 1).

Table 1 5-Ethoxy-6,6,7,7-tetramethyl-1,3,4-triazabicyclo[3.2.0]hept-2-enes (22)

Compound No.	Yield (%)	m.p. °C	Found (%)	Molecular Formula	Required (%)	δ_H ($CDCl_3$: 250 MHz) CH_3 (3H, s)	OC_2H_5	ArH [Others]
(22a)	89	143[a]	C, 67.1		C, 67.0	0.94	1.22[c]	7.2[e]
			H, 6.7	$C_{22}H_{26}N_4O_3$	H, 6.6	1.05	3.0[d]	7.4[e]
			N, 14.3		N, 14.2	1.34	3.5[d]	7.75[f]
						1.53		
(22b)	55	189-91[b]	C, 61.6		C, 61.7	0.93	1.11[c]	7.18[f]
			H, 5.8	$C_{22}H_{25}ClN_4O_3$	H, 5.9	1.02	3.0[d]	7.35[f]
			N, 13.2		N, 13.1	1.32	3.98[d]	7.67[f]
						1.51		8.11[f]
(22c)	57	211-3[b]	C, 60.3		C, 60.1	0.95	1.15[c]	7.22[f]
			H, 5.7	$C_{22}H_{25}N_5O_5$	H, 5.7	1.05	3.0[d]	7.88[f]
			N, 16.2		N, 15.9	1.36	3.49[d]	8.13[f]
						1.58		8.25[f]
(22d)	43	124-6[b]	C, 57.2		C, 57.4	1.0	1.1[c]	7.22[f]
			H, 6.4	$C_{18}H_{24}N_4O_5$	H, 6.4	1.18	2.96[d]	8.12[f]
			N, 15.6		N, 14.9	1.3	3.5[d]	[3.89][g]
						1.5		

Crystallised from [a] light petrol (b.p. 40-60°); [b] from hexane-ethyl acetate; [c] (3H, t, CH_3CH_2); [d] (1H, dq; OCH_2CH_3; diastereotopic geminal protons adjacent to the chiral bridge-head carbon; [e] (2H, dd); [f] (3H, m); [g] (3H, s, OCH_3).

In all other cases, mixtures of bicyclic cycloadducts **22f, g, h** and butenyl-1,2,4-triazoles **23b, c, d** (Table 2) were formed. % Yields were estimated from the 250 MHz ^1H n.m.r. spectra of the purified, (flash chromatography) but unseparated mixtures.

Table 2 5-(Ethylthio)-6,6,7,7-tetramethyl-1,3,4-triazabicyclo[3.2.0]hept-2-enes (22) and 1,3-Diaryl-5-(2,3-dimethylbut-1-ene-3-yl)-1,2,4-triazoles (23)

Compound No.	Yield (%)	δ_H (250 MHz:$CDCl_3$) Me (3H)	SEt [other]	Compound No.	Yield (%)	δ_H (250 MHz:$CDCl_3$) Me_2C (6H, s)	Me-C=C (3H, s)	$=CH_2$ 2 x (1H, s)	Ar (2H, dd)
(22f)	18	0.98 1.05 1.14 1.4	1.05[a] 2.15[b] 2.43[b]	(23b)	37	1.45	1.67	4.61 4.79	7.38 7.61 7.68 7.9 8.05 8.11 8.29 8.33
(22g)	21	0.99 1.05 1.16 1.56	1.05[a] 2.14[b] 2.41[b]	(23c)	39	1.45	1.67	4.61 4.8	7.22 7.25 7.88 7.91 8.12 8.13 8.23 8.25
(22h)	34	1.05 1.18 1.37 1.62	1.65[a] [3.88][c]	(23d)	15	1.43	2.0	4.55 4.74	7.3 7.54 8.1 8.26

[a] (3H, t, CH_3CH_2-S); [b] (1H, dq, SCH_2CH_3) diastereotopic geminal protons adjacent to the chiral bridge-head carbon; [c] (3H, s, OCH_3).

Method B

To the 2-(ethylthio)-1-azetine **8** (0.3 g; 1.8 mmol) in ethanol (20 ml) was added benzaldehyde-*p*-nitrophenylhydrazone (m.p. 192-3°: lit.[32] 192°) (0.41 g; 1.7 mmol) and chloramine-T (Aldrich) (0.46 g; 2.0 mmol) and the mixture heated under reflux for 2.5 h. The mixture was cooled to room temperature, filtered to remove solids and the filtrate evaporated *in vacuo* to give the crude product. Purification by flash chromatography [light petrol (b.p. 40-60°) - ethyl acetate as eluant)] gave 5-(ethylthio)-4-(*p*-nitrophenyl)-2-phenyl-6,6,7,7-tetramethyl-1,3,4-triazabicyclo[3.2.0]hept-2-ene **22e** (57%), m.p. 153-4°, and a small amount (5%) of the 1-(*p*-nitrophenyl)-1,2,4-triazole **23a**.

5-(2,3-Dimethylbut-1-ene-3-yl)-1-(4-nitrophenyl)-3-phenyl-1,2,4-triazole **23a**. A solution of cycloadduct **22e** (0.2 g; 0.5 mmol) in *o*-dichlorobenzene (5 ml) was heated under reflux for 30 min. The solvent was removed under reduced pressure to leave a dark oily residue which was purified by flash chromatography on silica [light petrol - ethyl acetate - 9:1] as eluant. 5-(2,3-Dimethylbut-1-ene-3-yl)-1-(4-nitrophenyl)-3-phenyl-1,2,4-triazole **23a** (0.17 g; 98%) was obtained as a solid, which was crystallised from light petrol, m.p. 131-3°C (Found C, 68.95; H, 5.8; N, 16.1 $C_{20}H_{20}N_4O_2$ requires C, 68.85; H, 5.9; N,

15.9%); δ_H ($CDCl_3$; 250 MHz) 1.46 (6H, s, 2 x CH_3), 1.68 (3H, s, CH_3), 4.62 (1H, s, =CH), 4.78 (1H, s, $=CH_2$), 7.40 (3H, m, ArH), 7.62 (2H, dd, ArH), 8.11 (2H, d, *p*-NO_2ArH), 8.28 (2H, d, *p*-NO_2ArH).

Addition of diphenylnitrilimine to the bicyclic azetine **11** was carried out as in Method A to give, after flash chromatography on silica [light petrol - ethyl acetate 6:1 as eluant], a semi-solid unstable mixture (73%) of diastereoisomers tentatively assigned as 5-(2-chlorocyclohexyl)-1,3-diphenyl-1,2,4-triazoles: **32a**; δ_H ($CDCl_3$; 250 MHz) 1.2-2.0 (7H, bm, cyclohexyl), 2.3-2.4 (1H, m), 3.0 (1H, m, CH), 4.43 (1H, m, CHCl), 7.37 (3H, m, Ar), 7.52 (5H, m, Ar), 8.14 (2H, dd, Ar). EIMS m/e 339 $(M + 2)^+$, 337 $(M)^+$:

Similarly cycloaddition of *N*-(*p*-nitrophenyl)-C-phenylnitrilimine (0.55 g, 2 mmol) to bicyclic azetine (**15c**; 0.25 g, 1.5 mmol) gave 8-ethoxy-2-methyl-9-(*p*-nitrophenyl)-11-phenyl-1,9,10-triazatricyclo-[6.3.0.$0^{2,7}$]undeca-4,10-diene **24a** as an orange oil (0.24 g; 40%) from flash chromatography [light petrol - ethyl acetate (8:1) as eluant]. HRMS (CI; NH_3) Found (M + 1) 405.1947. $C_{23}H_{24}N_4O_3$ (M + 1) requires 405.1927; δ_H (300 MHz: $CDCl_3$) 1.0 and 1.1 (3H, t, CH_3CH_2O), 1.55 (3H, s, Me), 1.9-2.8 (4H, m, allylic), 2.95 and 3.3 (2H, dq, CH_3CH_2O), (diastereotopic protons), 3.6 (1H, dd, CH), 6.05 (2H, m, CH=CH), 7.3-8.2 (9H, m, Ar).

Addition of *N*-(*p*-nitrophenyl)-C-phenylnitrilimine (prepared by Method B), to bicyclic azetine (14a) furnished 8-(ethylthio)-2-methyl-9-(*p*-nitrophenyl)-11-phenyl-1,9,10-triaza-tricyclo[6.3.0.$0^{2,7}$]undeca-4,10-diene **24b**. Orange oil: (53% yield) from flash chromatography, [light petrol-ethyl acetate (6:1) as eluant]. HRMS (CI-NH_3) $(M + 1)^+$ 421.1690. $C_{23}H_{24}N_4O_2S$ $(M + 1)^+$ requires 421.1698; δ_H ($CDCl_3$; 300 MHz) 0.97 (3H, t, CH_3CH_2), 1.43 (3H, s, Me), 2.15-3.0 (4H, m, 2 x allylic CH_2), 3.25-3.45 (3H, m, CH_3 CH_2-S and CH), 5.6-5.8 (2H, m, CH=CH), 7.4-8.4 (9H, m, ArH).

Likewise addition of N-(*p*-nitrophenyl)-C-phenylnitrilimine (Method B) to the dimethyl(ethylthio)-azetine **14b** (0.2 g; 1 mmol) yielded after flash chromatography on silica [light petrol-ethyl acetate (8:1) as eluant] 2,7-dimethyl-8-(ethylthio)-9-(*p*-nitrophenyl)-11-phenyl-1,9,10-triazatricyclo[6.3.0.$0^{2,7}$]undeca-4,10-diene **30a** (0.21 g; 47%) as an orange oil.

HRMS Found 435.1838 (M + 1) $C_{24}H_{26}N_4O_2S$ $(M + 1)^+$ requires 435.1855. δ ($CDCl_3$; 300 MHz) 1.23 (3H, s, Me), 1.42 (3H, dt, CH_3CH_2S), 1.54 (3H, s, Me), 2.05 (1H, m, CH_2CH=CH), 2.15 (1H, m, CHCH=CH), 2.52 (1H, dd, CHCH=CH), 2.65 (1H, dd, CHCH=CH), 2.95 (1H, dq, CH_3CH_2S), 3.35 (1H, dq, CH_3CH_2S), 5.9-6.1 (2H, m, CH=CH), 7.3-7.8 (5H, m, ArH), 8.1-8.3 (4H, m, ArH). Azetine **14b** was also recovered (20%).

Addition of the nitrilimine, under the same conditions, to the dimethylmethoxy-azetine **15b** (0.04 g; 0.26 mmol) gave, after flash chromatography on silica [light petrol-ethyl acetate (3:1) as eluant] 2,7-dimethyl-8-methoxy-9-(*p*-nitrophenyl)-11-phenyl-1,9,10-triazatricyclo-[6.4.0.$0^{2,7}$]undeca-4,10-diene **30b** (0.059 g; 56%) as an oil. HRMS Found $(M + 1)^+$ 405.1900. $C_{23}H_{24}N_4O_3$ requires $(M + 1)^+$ 405.1927. δ ($CDCl_3$: 300 MHz), 0.97 (3H, s, Me), 1.16 (3H, s, Me), 1.85-2.0 (2H, m, CH_2CH=CH), 2.45 (1H, dd, CH-CH=CH), 2.66 (1H, dd, CHCH=CH), 2.86 (3H, s, OMe), 5.95-6.14 (2H, m CH=CH), 7.4 (3H, m, ArH), 7.8 (2H, m, ArH), 8.1 (2H, m, ArH).

1-(*p*-Nitrophenyl)-3-phenyl-5-(*o*-tolyl)-1,2,4-triazole **29a**: A solution of the cycloadduct **24b** (0.2 g, 0.47 mmol) in *o*-dichlorobenzene (10 ml) was heated under reflux for 8 h. The dichlorobenzene was removed under reduced pressure and the residue purified by flash chromatography on silica [light petrol - ethyl acetate (4:1) as eluant] to give unchanged cycloadduct **24b** and 1-(*p*-nitrophenyl)-3-phenyl-5-(*o*-tolyl)-1,2,4-triazole as an orange oil (0.11 g; 62%) which on trituration with light petrol (b.p. 40-60°) and crystallisation from light

petrol-ethyl acetate had m.p. 184-6° [lit.[33] m.p. 178°]. HRMS (CI: NH_3), Found $(M + H)^+$ 357.1361. $C_{21}H_{16}N_4O_2$ $(M + H)^+$ requires 357.1351; δ_H ($CDCl_3$, 300 MHz) 2.13 (3H, s, Me), 7.2-7.7 (9H, m, Ar), 8.1-8.3 (4H, m, Ar).

1,3-Diphenyl-5-(*o*-tolyl)-1,2,4-triazole (29b): To a solution of bicyclic azetine (14a) (0.1 g; 0.6 mmol) in ethanol (10 ml) was added benzaldehyde phenylhydrazone (0.12 g; 0.6 mmol) and chloramine-T (0.16 g; 0.7 mmol) and the mixture heated under reflux for 4 h. The solution was cooled, filtered, and evaporated to dryness to yield the crude product, which was purified by flash chromatography on silica [light petrol - ethyl acetate (6:1) as eluant] to give 1,3-diphenyl-5-(*o*-tolyl)-1,2,4-triazole (0.06 g; 37%), oil (lit.[4b] m.p. 75-7°); δ_H ($CDCl_3$; 300 MHz) 2.17 (3H, s, Me), 7.3-8.2 (14H, m, Ar). Found 312.1513 (M + 1) $C_{21}H_{17}N_3$ (M + 1) requires 312.1501.

1,3,5-Triphenyl-1,2,4-triazole **29c**: (69%) m.p. 103-4°C (lit.,[4b] 103-4°C) was obtained in a similar manner from bicyclic azetine **11** and benzaldehyde-phenylhydrazone.

5-(1,2-Dimethylcyclohexa-2,4-diene-1-yl)-1-(*p*-nitrophenyl)-3-phenyl-1,2,4-triazole **31**. A solution of the cycloadduct **30a** (0.15 g; 0.35 mmol) in freshly distilled *o*-dichloro-benzene was heated under reflux for 1 h., after which time no starting material remained (t.l.c.). Removal of the solvent under reduced pressure yielded a dark-oily residue which was purified by flash chromatography on silica light petrol-ethyl acetate (8:1) as eluant to give 5-(1,2-dimethylcyclohexa-2,4-diene-1-yl)-1-(*p*-nitrophenyl)-3-phenyl-1,2,4-triazole as an orange oil (0.11 g; 85%).δ_H ($CDCl_3$; 300 MHz); 1.6 (3H, s, Me), 1.69 (3H, s, Me), 2.2 (1H, dd, C*H*CH=CH), 2.64 (1H, d, *C*HCH=CH), 5.53 (1H, m, CH=CH), 5.68 (1H, m, CH=CH), 5.82 (1H, m, CH=CH), 7.42 (3H, m, ArH), 7.8 (2H, m, ArH), 8.15 (2H, m, ArH), 8.31 (2H, m, ArH). HRMS Found 373.1657 (M + 1) $C_{22}H_{20}N_4O_2$ $(M + 1)^+$ requires 373.1664.

Cycloaddition of diphenylnitrilimine to bicyclic azetine **14a**. To a solution of azetine **14a** (0.285 g; 1.6 mmol) and chloramine-T (0.5 g; 2.2 mmol) in ethanol (10 ml) was added benzaldehyde phenylhydrazone (0.392 g; 2 mmol) in ethanol (10 ml). The mixture was heated under reflux (nitrogen atmosphere) for 1.5 h, then cooled to room temperature and filtered. Concentration of the filtrate under reduced pressure and flash chromatography on silica [light petrol-ethyl acetate (8:1) as eluant] gave a mixture of products [cyclohexadienes **27** and **28**] (0.23 g; 45%) which were not separated further. HRMS $(M + H)^+$ 314.1667 $C_{21}H_{19}N_3$ requires $(M + H)^+$ 314.1657; δ_H ($CDCl_3$, 300 MHz) 1.63 (3H, s, Me), 1.9 (3H, s, Me), 1.92-3.00 (m, CH_2-C=C), 5.6-6.0 (m, CH=CH), 7.5 (m, Ar*H*), 8.2 (m, ArH). Also present were proton resonances at 4.51-5.05 (possibly compound **26**).

The benzohydroximoyl chlorides (α-chloroaryldoximes) were prepared from the corresponding oximes using N-chlorosuccinimide in dimethylformamide. Benzohydroximoyl chloride yield 55%; m.p. 43-5° (lit.[34] 45°C); 4-methoxybenzohydroximoyl chloride yield 95%: m.p. 88-90°C (lit.,[35] 88-9°); 2-nitrobenzohydroximoyl chloride: yield 77%: m.p. 92-4°C (lit.,[34] 90-3°C).

Cycloaddition of nitrile oxides to 1-azetines **6** and **8** -

General Method A - To a stirred solution of the 1-azetine (1.17 mmol) and the benzohydroximoyl chloride (1.17 mmol) in dry benzene (20 ml), under nitrogen, was added dropwise triethylamine (1.3 mmol). The mixture was stirred at room temperature for 2 hours, and then the precipitated triethylamine hydrochloride removed by filtration and the residue washed with dichloromethane. Evaporation of the combined filtrate and

dichloromethane washings under vacuum, gave the crude product, which was purified by flash column chromatography on silica. For details see Table 3.

Table 3 5-Ethoxy- (34a-c) and 5-(ethylthio)- (34d-f) 4-oxa-1,3-diazabicyclo[3.2.0]hept-2-enes

Compound No.	Yield (%)	m.p. °C	Found (%)	Molecular Formula	Required (%)	δ_H (CDCl3: 250 MHz) CH_3	X CH_2CH_3(3H, s)	ArH [Others]
(34a)	72[a,b]	107-9	C, 66.8 H, 7.9 N, 9.1	$C_{17}H_{24}N_2O_3$	C, 67.1 H, 7.95 N, 9.2	0.95 1.2 1.25 1.43	1.22[h] 3.55[i]	6.9[l] 7.68[l] [3.83][m]
(34b)	60[c,d]	106-8	C, 70.2 H, 7.95 N, 10.3	$C_{16}H_{22}N_2O_2$	C, 70.0 H, 8.1 N, 10.2	0.9 1.18 1.22 1.41	1.20[h] 3.49[i]	7.35-7.58[n] 7.67-7.7[l]
(34c)	34[a,b]	103-4	C, 60.0 H, 6.55 N, 12.9	$C_{16}H_{21}N_3O_4$	C, 60.2 H, 6.6 N, 13.2	0.88 1.11 1.16 1.25	1.23[h] 3.55[j] 3.65[j]	7.5-7.63[n] 7.73[o]
(34d)	80[a,b]	106-8	C, 63.6 H, 7.5 N, 8.7 S, 9.9	$C_{17}H_{24}N_2O_2S$	C, 63.7 H, 7.6 N, 8.75 S, 10.0	1.0 1.27[g] 1.55	1.27[k] 2.68[i]	6.93[l] 7.65[l] [3.85][m]
(34e)	62[b,e]	132-4	C, 66.3 H, 7.4 N, 9.4	$C_{16}H_{22}N_2OS$	C, 66.2 H, 7.6 N, 9.65	0.95 1.2-1.25[g] 1.52	1.2-1.25[k] 2.64[i]	7.38[n] 7.69[l]
(34f)	42[b,f]	90-1	C, 57.3 H, 6.3 N, 12.5	$C_{16}H_{21}N_3O_3S$	C, 57.3 H, 6.3 N, 12.5	0.96 1.15 1.27 1.42	1.27[h] 2.7[i]	7.5-7.65[n] 7.73[o]

[a] light petrol-EtOAc (4:1) as eluant; [b] crystallised from hexane; [c] light petrol-dichloromethane (4:1) as eluant; [d] crystallised from light petrol; [e] light petrol-EtOAc (8.5:1.5) as eluant; [f] light petrol-dichloromethane (3:1) as eluant; [g] (6H, m, 2 x CH_3); [h] (3H, t, $\underline{CH_3}CH_2S$); [i] (2H, dq, or m, $S\underline{CH_2}CH_3$) and [j] (1H, m), diastereotopic geminal hydrogens adjacent to chiral bridgehead carbon; [k] (3H, m, $\underline{CH_3}CH_2S$); [l] (2H, dd); [m] (3H, s, OMe); [n] (3H, m); [o] (1H, dd).

Table 4 8-(Ethylthio)-9-oxa-1,10-diazatricyclo[6.3.0.0^{2,7}]undec-10-enes (35)

Compound No.	Yield (%)	m.p. °C	Found (%)	Molecular Formula	Required (%)	δ_H (CDCl3: 300 MHz) cyclohexyl	SCH_2CH_3 [Others]	Ar [Others]
(35a)	95[a,b]	69-71	C, 63.6 H, 6.9 N, 8.8 S, 10.1	$C_{17}H_{22}N_2O_2S$	C, 64.1 H, 7.0 N, 8.8 S, 10.1	1.1-2.1[e] 3.45[f] 3.85[f]	1.28[g] 2.69[h] [3.8][i]	6.98[j] 7.62[j]
(35b)	54[c,d]	-	C, 66.4 H, 7.1 N, 9.7	$C_{16}H_{20}N_2OS$	C, 66.6 H, 7.0 N, 9.7	1.1-2.1[e] 3.5[f] 3.9[f]	1.25[g] 2.68[h]	7.4[k] 7.69[j]
(35c)	43[c,d]	-	C, 57.6 H, 5.7 N, 12.5	$C_{16}H_{19}N_3O_3S$	C, 57.6 H, 5.7 N, 12.6	1.1-2.0[e] 3.56[f] 3.90[f]	1.32[g] 2.75[h]	7.3-7.55[k] 7.69[l]

[a] light petrol-EtOAc (4:1) as eluant; [b] crystallised from light petrol; [c] light petrol-EtOAc (9.5:0.5) as eluant; [d] semi-solid; [e] (8H, m); [f] (1H, m); [g] (3H, t, CH_3CH_2S); [h] (2H, m, SCH_2CH_3), diastereotopic geminal protons adjacent to the chiral bridgehead carbon; [i] (3H, s, OCH_3); [j] (2H, dd); [k] (3H, m); [l] (1H, m).

Method B - 8-(Ethylthio)-2-methyl-11-phenyl-9-oxa-1,10-diazatricyclo[6.3.0.0^{2,7}]undeca-4,10-diene **36a**. To a solution of 2-(ethylthio)-1-azetine **14a** (0.9 g; 4.2 mmol) and chloramine-T (0.64 g; 2.8 mmol) in boiling ethanol (25 ml) was added dropwise over 4 h a solution of benzaldehyde oxime (0.17 g; 1.4 mmol) in ethanol (15 ml). The solution was cooled, filtered, and the solvent, removed *in vacuo* to give a yellow residue, which was purified by flash chromatography, on silica [light petrol-EtOAc (7:2) as eluant]. 8-(Ethylthio-2-methyl-11-phenyl-9-oxa-1,10-diazatricyclo[6.3.0.0^{2,7}]undeca-4,10-diene was obtained as a colourless oil (0.26 g; 61%); HRMS Found $(M + 1)^+$ 301.1363, $C_{17}H_{20}N_2OS$ requires $(M + 1)^+$ 301.1374. δ_H ($CDCl_3$: 300 MHz) 1.1 (3H, t, CH_3CH_2S), 1.31 (3H, s, CH_3-C); 2.1-3.1 (5H, m, CH_2-C=C and bridgehead CH), 3.3-3.6 (2H, m, -CH_2S), 5.6-5.8 (2H, m, CH=CH), 7.45 and 8.05 (5H, m, Ph).

2-Ethoxycarbonyl-5-(ethylthio)-6,6,7,7-tetramethyl-4-oxa-1,3-diazabicyclo[3.2.0]-hept-2-ene **34g**: To a vigorously stirred solution of ethyl chloroximidoacetate[36] [**CAUTION** - an extremely vigorous skin irritant] - (1 g; 6.6 mmol) and 2-(ethylthio)-3,3,4,4-tetramethyl-1-azetine (1.69 g; 10 mmol) in diethyl ether (20 ml) at room temperature was added dropwise over 5 hours, a solution of triethylamine (0.71 g; 7 mmol) in diethyl ether (15 ml). The solution was then filtered and the solvent removed to give the crude product, which was purified by flash chromatography using light petrol-ethyl acetate (7:2) as eluant.
2-Ethoxycarbonyl-5-(ethylthio)-6,6,7,7-tetramethyl-4-oxa-1,3-diazabicyclo[3.2.0]-hept-2-ene was obtained as a pale yellow oil (1.77 g; 94%). HRMS $(M + 1)^+$ 287.1427 Calc. for $C_{13}H_{22}N_2O_3S$ $(M + 1)^+$ 287.1429. δ_H ($CDCl_3$: 300 MHz) 1.15 (3H, s, Me), 1.16 (3H, s, Me), 1.18 (3H, s, Me), 1.2 (3H, t, CH_3CH_2S), 1.3 (3H, t, CH_3CH_2O), 2.55 (2H, m, CH_3CH_2S), 4.3 (2H, m, CH_3CH_2O), FT i.r. 1735 (C=O), 1547 cm^{-1} (C=N).

11-(Ethoxycarbonyl)-8-(ethylthio)-2-methyl-9-oxa-1,10-diazatricyclo[6.3.0.0^{2,7}]-undeca-4,10-diene **36b**, obtained as a pale yellow oil (0.4 g, 81%) after flash chromatography on silica [light petrol-ethyl acetate

(7:2) as eluant], was prepared similarly from bicyclic azetine (14a) (0.3 g; 1.6 mmol) and ethyl chloroximidoacetate[36] (0.27 g; 1.7 mmol) in the presence of triethylamine (0.28 ml; 2 mmol). HRMS Found $(M + 1)^+$ 297.1276, $C_{14}H_{20}N_2O_3S$ $(M + 1)^+$ requires 297.1273. FT i.r. 1737 cm^{-1} (C=O), 1547 cm^{-1} (C=N) δ_H ($CDCl_3$; 300 MHz) 1.19-1.44 [9H, 2 x over-lapping triplets (-OCH_2CH_3, SCH_2CH_3), and (s, Me)], 1.84-2.16 (2H, m, CH_2CH=CH), 2.3-3.10 (5H, m, CH_2CH=CH, CH, and -SCH_2CH_3), 4.3 (2H, q, OCH_2CH_3), 5.7-6.0 (2H, bm, CH=CH).

Cycloaddition of nitrile ylides to azetines 6 and 8

The imidoyl chlorides were prepared from the corresponding N-acyl-*p*-nitrobenzyl-amines in boiling thionyl chloride. N-(*p*-Nitrobenzyl)benzimidoyl chloride. Yield 85%: m.p. 71-3°C (lit.[22] m.p. 73-4°C): N-(*p*-nitrobenzyl)-*p*-toluimidoyl chloride. Yield 64%. M.p. 86-7°C (lit.[37] 89°C); N-(*p*-nitrobenzyl)-*p*-nitrobenzimidoyl chloride: Yield 59% m.p. 93-5°C; General Method. To a solution of the 1-azetine and the imidoyl chloride (2.18 mmol) in dry benzene (20 ml), under nitrogen, was added trimethylamine (1.5 equiv.). The mixture was stirred for 12-15 h at room temperature after which time the mixture was filtered and the solvent removed under reduced pressure. The oily residue was purified by flash chromatography on silica to give the 1,3-diazabicyclo[3.2.0]hept-2-ene as a crystalline solid. See Table 5 for analytical and spectroscopic details.

Acknowledgements

We thank Roussel Scientific Institute, U.K. Ltd. for a generous studentship (to A-B.N.L.) and Roussel Scientific Institute and SERC for a CASE award to (K.H.).

Table 5 5-Ethoxy- (40a-c) and 5-(Ethylthio)- (40d-f) 2-aryl-4-(*p*-nitrophenyl)-6,6,7,7-tetramethyl-1,3-diazabicyclo[3.2.0]hept-2-enes

Compound No.	Yield (%)	m.p. (°C)	Found (%)	Molecular formula	Required (%)	Me (3H, s)	δ_H ($CDCl_3$: 300 MHz XCH_2CH_3 [Others]	Ar (1H, s)	CHAr
(40a)	46[a,b]	165-7	C, 70.2		C, 70.2	0.38	1.38[e]	7.40[h]	5.48
			H, 7.0	$C_{23}H_{27}N_3O_3$	H, 6.9	0.70	3.59[f]	7.76[i]	
			N, 10.7		N, 10.7	0.95	3.84[f]	7.83[j]	
						1.49		8.19[j]	
(40b)	42[b,c]	173-5	C, 62.8		C, 63.0	0.43	1.31[e]	7.85[j]	5.52
			H, 6.3	$C_{23}H_{26}N_4O_5$	H, 6.0	0.62	3.58[f]	8.11[j]	
			N, 13.3		N, 12.8	0.97	3.84[f]	8.19[j]	
						1.49		8.27[j]	
(40c)	53[b,d]	166-8	C, 70.1		C, 70.7	0.43	1.36[e]	6.98[i]	5.41
			H, 7.5	$C_{24}H_{29}N_3O_3$	H, 7.2	0.76	3.54[f]	7.14[i]	
			N, 10.7		N, 10.3	0.94	3.79[f]	7.82[j]	
						1.51	[2.26][g]	8.18[j]	
(40d)	68[a,b]	148-9	C, 67.5		C, 67.45	0.46	1.36[e]	7.41[h]	5.71
			H, 6.7	$C_{23}H_{27}N_3O_2S$	H, 6.65	0.72	2.6[f]	7.85[i]	
			N, 10.3		N, 10.3	1.08	2.74[f]	8.0[j]	
			S, 7.9		S, 7.8	1.74		8.19[j]	
(40e)	45[b,d]	164-6	C, 62.1		C, 60.8	0.45	1.21[e]	7.9[j]	5.78
			H, 6.0	$C_{23}H_{26}N_4O_4S$	H, 5.8	0.73	2.61[f]	8.0[j]	
			N, 12.2		N, 12.3	1.65	2.73[f]	8.18[j]	
							1.77	8.29[j]	
(40f)	61[b,c]	182-4	C, 67.3		C, 68.0	0.44	1.34[e]	7.03[i]	5.6
			H, 7.0	$C_{24}H_{29}N_3O_2S$	H, 6.9	0.69	2.59[f]	7.18[i]	
			N, 10.3		N, 9.9	1.14	2.73[f]	8.12[j]	
						1.76	[2.25][g]	8.26[j]	

[a] light petrol-EtOAc (8.5:1.5) as eluant; [b] crystallised from light petrol; [c] light petrol-EtOAc (4:1) as eluant; [d] (light petrol-EtOAc (9:1) as eluant; [e] (3H, t, $\underline{CH_3}CH_2X$); [f] (1H, dq, XCH_2CH_2) diastereotopic geminal protons adjacent to the chiral 4-carbon centre; [g] (3H, s, $Ar\underline{CH_3}$); [h] (3H, m, Ar); [i] (2H, Ar); [j] (2H, d, $ArNO_2$)

Summary of X-Ray Crystallographic Data

Compound	19	22a	23a	34d	40b
Formula	$C_{20}H_{21}N_3$	$C_{32}H_{26}N_4O_2$	$C_{20}H_{20}N_4O_2$	$C_{17}H_{24}N_2O_2S$	$C_{23}H_{27}N_3O_3$
Formula Weight	303.4	394.5	348.4	320.4	393.5
Crystal system	Monoclinic	Monoclinic	Monoclinic	Monoclinic	Monoclinic
Space group	$P2_1/c$	$P2_1/n$	$P2_1/n$	$P2_1/n$	$P2_1/c$
a(A)	10.056(2)	7.520(3)	17.990(6)	8.035(3)	7.402(1)
b(A)	13.418(4)	16.409(7)	10.257(3)	23.163(12)	11.090(3)
c(A)	13.014(3)	17.240(6)	21.613(6)	9.514(4)	25.503(6)
β°	101.01(2)	102.44(3)	112.34(2)	97.89(3)	92.51(2)
Volume(A^3)	1723.6(7)	2077(1)	3689(2)	1753(1)	2091.5(8)
Z	4	4	8	4	4
μ(MoKα) mm^{-1}	0.065	0.080	0.078	0.184	0.078
D_c(Mg m^{-3})	1.169	1.261	1.255	1.214	1.250
F(000)	648	840	1472	688	840
Temperature (K)	293	293	293	293	293
Index ranges h	0 → 11	-8→0	0 → 21	0→9	0→8
k	-15 → 15	0→19	0 → 12	0→27	0→13
l	-15 → 15	-19→20	-25 → 23	-11→11	-30→30
Total no. of reflections	6489	4083	7188	3443	4240
Independent reflections	3057	3632	6553	3109	3701
R_{int}	0.03	0.02	0.04	0.03	0.01
F> nσ(F)	4	4	6	4	4
Observed reflections	1943	1601	2179	1010	2207
$w^{-1}= \sigma^2(F)+gF^2$, g	0.001	0.0003	0.001	0.003	0.0007
No. of parameters	208	263	469	133	262
R(observed data, all data)	0.044, 0.083	0.059,0.141	0.051, 0.162	0.12, 0.24	0.048, 0.090
wR(observed data, all data)	0.057, 0.070	0.052, 0.076	0.059, 0.094	0.14, 0.19	0.055, 0.096
Goodness of Fit	1.18	1.45	1.27	1.74	1.34
Largest shift:esd	0.001	0.001	0.001	0.117	0.001
Data:parameter ratio	9.3:1	6.1:1	4.6:1	7.6:1	8.4:1
Δρ max(eA^{-3})	+0.13	+0.22	+0.18	+0.52	+0.22
Δρ min(A^{-3})	-0.23	-0.22	-0.19	-0.37	-0.22

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