On the use of removable steric buttresses in cycloaddition reactions

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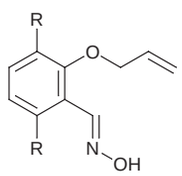
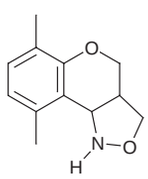
Use of bulky protecting groups, such as the trityl group, can be utilised to encourage cycloaddition reactions that otherwise do not proceed. Thus *N*-allylfurfurylamines, bearing the appropriate *N*-protecting group, can thermally cyclise; subsequent removal of the protecting group produces the thermodynamically unstable, free amine.

We have recently described the use of steric buttresses to accelerate intramolecular cycloaddition reactions.[1] These include examples of certain cycloadditions that otherwise do not proceed; thus, heating the oxime **1** at temperatures up to



1 R = H
2 R = Me



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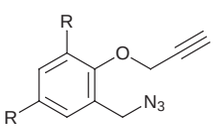
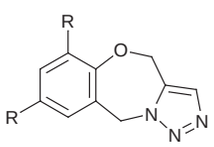


4 R = H
5 R = Br



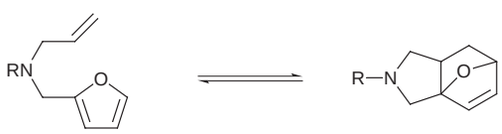
6 R = Br
7 R = H

110 °C for extensive periods does not result in cycloadduct formation, whilst heating at higher temperatures leads to other reactions setting in, such as dehydration and Claisen rearrangement.[2] The introduction of two methyl groups, as in the derivative **2**, is sufficient to restrict the available conformational space for the oxime and allyl groups, allowing the cyclisation path to be followed and leading to the cycloadduct **3**.

A limitation of these previous studies is that the steric buttresses are incorporated as constituent parts of the reacting components, *i.e.* they are not readily removed after performing their task.

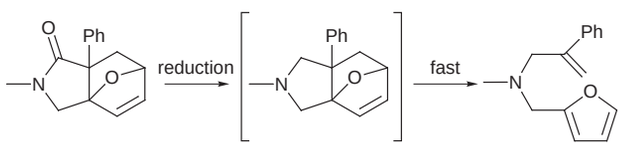
An initial attempt at introducing removable buttresses has been made, using bromine atoms as the bulky groups; thus, the dibromo derivative, **5**, can be thermally cyclised at 80 °C within 2 h to produce the cycloadduct **6**, followed by reductive removal of the bromine atoms, to form the product **7**; the unsubstituted starting material **4** only cycloadds slowly (2–3 days at 80 °C) to give **7**.[3] However, the introduction and removal of bromine atoms as steric buttresses is rather cumbersome and not generally applicable. We have therefore sought to explore systems in which a suitable steric buttress can be more readily introduced *and* removed.

This paper describes work on cyclisation of simple *N*-substituted derivatives of the parent amine **8**, to produce the corresponding *N*-substituted cycloadducts of the type **16**.[4] The system **8**, involving an unactivated double bond adding across the aromatic furan ring, was selected since it is known to be sensitive to structural changes about the nitrogen atom. Thus,



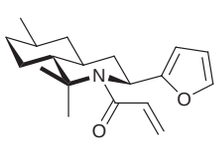
8 R = H
9 R = Ph
10 R = Ph_3C
11 R = Ph_2CH
12 R = $PhCH_2$
13 R = 2,4,6-$Me_3C_6H_2$
14 R = tosyl
15 R = benzoyl

16 R = H
17 R = Ph
18 R = Ph_3C
19 R = Ph_2CH
20 R = $PhCH_2$
21 R = 2,4,6-$Me_3C_6H_2$
22 R = tosyl
23 R = benzoyl



24 **25** **26**

we have shown that the unsubstituted amine **8** does *not* undergo cycloaddition to form compound **16**, whereas at room temperature the *N*-phenyl substituted amine **9** does, forming **17**, although ring opening occurs on heating, in an attempted distillation, to give back the starting olefin.[5] Similarly, the *N*-methyl cycloadduct **25**, prepared by reduction of the corresponding cyclic amide **24**, spontaneously ring opens to form the furan **26**.[6] Use of *N*-acrylamide groups (an 'activated' alkene), rather than the allyl group promotes cyclisation.[7] Thus Pedrosa and co-workers made the chiral acrylamide derivative **27** and



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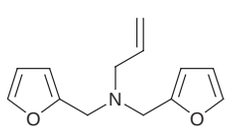

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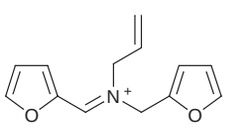

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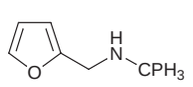

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showed that the cycloadduct, after a three-step oxidation, reduction and elimination process, could be used in a route to the (chiral) amine **16**,[8] although the thermal stability of this amine was not reported.

We have prepared the amine derivatives **10**–**15** and examined their tendency to cyclise to the corresponding cycloadducts, **18**–**23**, on heating.

Table 1 Thermal equilibration of the amine derivatives, **8**, **10**–**15**

Starting amine	Product[a]	Yield of isolated product (%)	Cyclisation conditions	Open : cyclic[b]
8	**16**	0	110 °C, toluene, several days	100 : 0
10	**18**	85	110 °C, toluene, 40 h	2.5 : 97.5
11	**19**	35	135 °C, xylene, 34 h	50 : 50
12	**20**	—[c]	135 °C, xylene, 60 h	98 : 2
13	**21**	—[c]	135 °C, xylene, 60 h	90 : 10
14	**22**	60	110 °C, toluene, 21 h	20 : 80[d]
15	**23**	60	110 °C, toluene, 21 h	20 : 80[d]

[a] Isolated by column chromatography. [b] Estimated by 360 MHz ^{1}H NMR spectroscopy after thermal equilibration. [c] Isolation not attempted. [d] Thermal equilibrium point not reached.

The parent amine **8** was prepared by direct allylation of furfurylamine, albeit in low yield (~30%), with over-alkylation also being observed. An alternative method tried was the reductive amination of allylamine with furfuraldehyde, using sodium cyanoborohydride at pH 6.[9] However, the yields from this latter reaction were also modest, some di(furfuryl)allylamine **28** forming, as a side product, by over-reaction of the required amine **8** with more furfuraldehyde (or displacement of the initially formed iminium species) to give the intermediate **29**, followed by further reduction.

The amine **8** was converted into the series of protected derivatives, **10**–**15** using standard protection methods.[10] Because of the modest yields observed in formation of the starting secondary amine **8**, an alternative route to the trityl-protected derivative **10** was investigated. This involves use of the tritylated furfurylamine **30**, which was formed selectively and in high yield by tritylation of furfurylamine. As expected, because of the steric bulk of the protecting group in the amine **30**, further alkylation, with allyl bromide, did not proceed, only minute amounts of the required amine **10** forming even after extensive reaction periods. In contrast, prior formation of the lithium salt of the secondary amine **30**, using butyllithium, proceeded smoothly and this reacted with allyl bromide, to produce the required product **10**, in reasonable yields. This has proven to be a convenient method for the preparation of tritylated secondary amines when the parent amine is difficult to obtain.

Cyclisation studies

The *N*-alkylated derivatives **10**–**13** were heated as solutions in either toluene or xylene, at temperatures between 110–135 °C, reactions being monitored by ^{1}H NMR spectroscopy for the appearance of cycloadduct and the attainment of thermodynamic equilibria.

Of these derivatives the tritylated amine, **10**, showed the greatest degree of intramolecular cycloaddition (Table 1). At equilibrium, at 110 °C, 97.5% of the cycloadduct **18** formed, the remainder being uncyclised starting material. Evidence for the formation of the cycloadduct at room temperature was also obtained but the reaction was exceedingly slow and no evidence for cyclisation of the amine **10** was observed when the starting amine was stored at −10 °C over several months.

The structure of the pure, isolated cycloadduct resulting from the intramolecular, regiospecific *exo*-cycloaddition process was as indicated in Fig. 1(b). The preference for *exo*-cycloaddition is caused by the constraints imposed by the connecting bridge of the reacting functions; *endo*-cycloaddition would lead to a highly strained tricyclic system. The observation of the *exo*-addition product is consistent with previous findings reported by Brieger and Bennett[11] on related processes. Molecular models of the starting amine **10** [Fig. 1(a)] illustrate the limited space available to the reacting arms in the presence of the bulky triphenylmethyl (trityl) substituent, a constraint which is relieved in the cycloadduct **18** [Fig. 1(b)].

A kinetic study was carried out on the cycloaddition reaction, following the progress of the reaction by ^{1}H NMR spectroscopy. This study showed that a smooth unimolecular process occurred over the range 50 to 80 °C. The activation energy was found to be 76.9 ± 10 kJ mol^{-1}, typical for Diels–Alder cycloaddition processes,[12] and equates to an enthalpy of activation of 74 ± 10 kJ mol^{-1} at 338 K. However, one would expect a slightly higher enthalpy of activation for cycloaddition reactions involving both an unactivated dienophile and an aromatic diene. The negative entropy of activation, −110 ± 15 J K^{-1} mol^{-1}, reflects the fact that, as expected (and despite the presence of the steric buttress), a considerable amount of organisation, involving loss of degrees of freedom, is required in the transition state.

These kinetic results confirm earlier studies,[2,3] that both an enthalpic as well as an entropic effect is operating. The enthalpic effect is most likely caused by a raising of the ground state energy of the tritylated amine **10**, as compared to the starting amine **8**, as a result of the steric interference between the steric buttress and the reacting arms. These are relieved in the transition state. Entropically there are fewer degrees of freedom (smaller available conformational space) in the trityl-

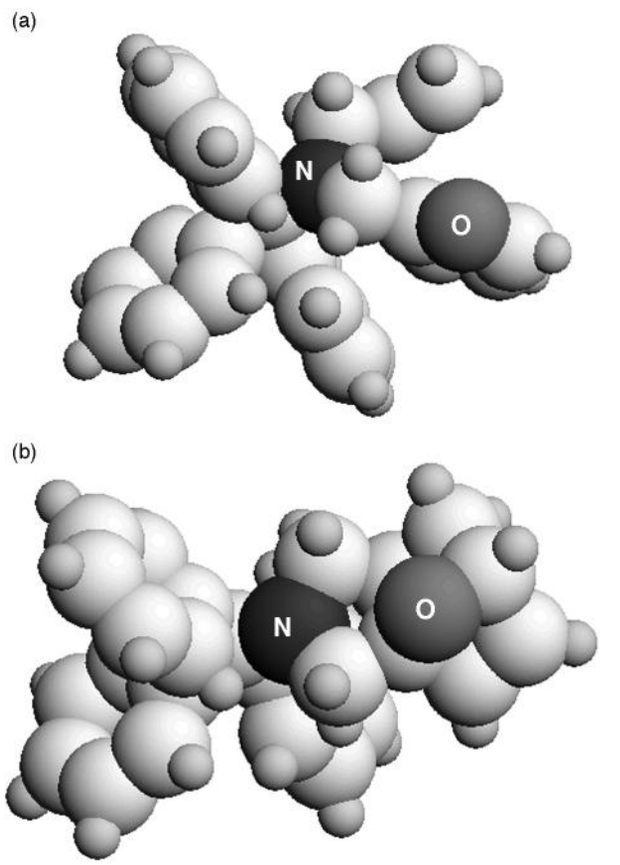

Fig. 1 (a) Energy minimised representation of the uncyclised tritylated amine **10** (b) cyclised derivative **18** (from the Alchemy 2000 molecular modelling program Alchemy 32, version 2.0, Tripos Inc., St. Louis, USA)

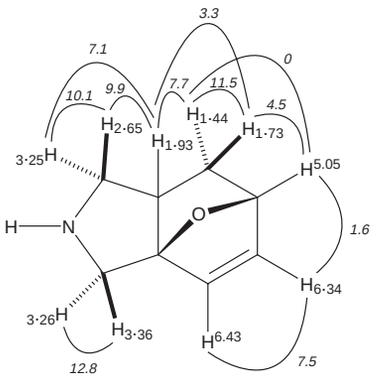

Fig. 2 ^{1}H Chemical shifts and coupling constants recorded for the cycloadduct **16** (360 MHz, $CDCl_3$)

ated amine compared to that in the unprotected amine **8**. The combination of these two effects serves to reverse the thermodynamic equilibrium, cyclisation being preferred in the presence of the buttress and the open form in its absence.

To explore the requirements of the steric buttress in this system, the cyclisation of the other protected analogues **11**–**13** was examined. The results are tabulated. As expected, as the steric bulk of the protecting group is decreased so is the observed degree of cyclisation. The benzhydryl derivative **11** formes an approximately 50 : 50 equilibrium between the closed and open forms, whereas the benzyl protected system **12**, with its much smaller size, results in only a few percent of the cyclic isomer being formed. Thus, in order to be effective in this reaction, the steric buttress has to occupy a considerable amount of the available conformational space that the two reacting arms would otherwise be expected to occupy.

Of interest was the observed result with the amine bearing the 2,4,6-trimethylbenzyl protecting group, **13**, which, despite having the benzylic position very shielded, only has a small effect on the cycloaddition reaction, producing approximately 10% of the cycloadduct. In this case the steric shielding is too distant from the reacting arms, and the total conformational space occupied, compared to the space covered by the reactant furyl and allyl groups, is only marginally larger than that occupied by the simpler benzyl group.

Having obtained the trityl-protected cycloadduct **18** in good yield, deprotection was effected. Although several deprotection methods were attempted, the simplest method was to warm a solution of the adduct in ethanol containing dilute hydrochloric acid for a few minutes.[13] The product amine **16** was isolated by acid/base extraction. The ^{1}H NMR spectrum was consistent with the assigned structure (Fig. 2) resulting from *exo*-cycloaddition. The latter amine was stable for considerable periods (days) at room temperature but, on heating at 110 °C, rapidly reverted to the open allyl-furfurylamine isomer **8**.

In order to confirm the behaviour of the other protected derivatives, the amine **16** was also re-protected with the benzhydryl and benzyl groups. The isolated cyclic products, **19** and **20** respectively, re-established the same equilibrium mixtures, when heated to 135 °C for several days, as were observed with the open isomers, compounds **11** and **12** respectively (see Table 1).

Besides the use of *N*-alkylated buttresses, the use of amide-type protecting groups has also been explored, namely use of the *N*-tosyl derivative **14** and the benzamide **15**. In earlier work Babayan *et al*.[14] briefly reported that aliphatic amides of *N*-allylfurfurylamine do undergo cyclisation. From X-ray crystallographic studies,[15] the sulfonamide group is known to freeze the inversion about the nitrogen atom and to occupy a large part of the (local) available conformational space, *viz*. it should behave as a bulky buttress. In both cases, heating the derivatives at 110 °C (refluxing toluene) gave the corresponding cycloadducts, **22** and **23**, although in neither case was the conversion quantitative. Of note, therefore, is that of all the buttresses explored, the trityl group was the most effective.

The ^{1}H NMR spectrum of the benzamide derivative **15** indicated the presence of two rotamers. At room temperature several of the peaks appeared as broadened signals, in particular the methylene groups attached to the nitrogen atom. The broadening disappeared at −20 °C, two distinct sets of signals, ratio *ca*. 1 : 1, appearing. Heating to 50 °C produced a coalescence of these signals into a single set. After heating for 40 h at 110 °C, cycloaddition occurred, to give the product **23**, together with the starting benzamide. The cycloadduct could be separated by column chromatography. At room temperature the ^{1}H NMR spectrum of the adduct showed two distinct sets of signals for the two rotamers present; on heating to 50 °C these only just started to broaden, indicating, rather unexpectedly, that rotation of the benzoyl group about the carbonyl–nitrogen bond is more difficult (higher activation energy) for the cycloadduct **23** than for the open system **15**. Presumably, intramolecular collisions between the groups in the more flexible open form result in a more frequent rotation about the amide bond than in the more ordered cycloadduct.

Experimental

Mps were determined on a Kofler hot-stage apparatus and are uncorrected. Mass spectra were obtained on an AEI MS902 spectrometer and infrared spectra on a PE1420 spectrophotometer, using either thin films or KBr discs. ^{1}H NMR Spectra were obtained on either a JEOL FX 200 or a Bruker AM360 spectrometer, using $CDCl_3$ solutions with tetramethylsilane as internal reference unless otherwise indicated. Coupling constants, *J*, are given in Hz. Accurate mass and FAB measurements were conducted by the EPSRC Mass Spectrometry Service, University of Wales, Swansea. Microanalytical determinations were carried out by MEDAC Ltd., Egham. Solvents were distilled before use, using literature procedures.[16] Thin layer chromatography was carried out on 0.25 mm GF60A silica plates and column chromatography utilised Sorbsil silica. Generally, solvents were removed, after drying over anhydrous sodium sulfate, under reduced pressure using a rotary evaporator. Ether refers to diethyl ether and light petroleum refers to the fraction of boiling range 40–60 °C. Xylene was redistilled, commercial, mixed isomers boiling range 137–142 °C.

N-Allylfurfurylamine 8[14]

Freshly distilled furfurylamine (7.52 g, 0.077 mol) was dissolved in dry tetrahydrofuran (25 cm^3) containing diisopropyl(ethyl)-amine (10.44 g, 0.08 mol). Allyl bromide (9.33 g, 0.077 mol) was then slowly added over 1 h, with stirring. The solution was stirred for a further 2 h, 3 M sodium hydroxide added (25 cm^3) and the organic layer collected, washed with brine (25 cm^3), dried, filtered and the solvent removed. The residue was fractionally distilled to give the title compound (3.23 g, 30%), bp 130–132 °C; δ_H 7.35 (1 H, br s), 6.30 (1 H, d, *J* 3.0), 6.16 (1 H, d, *J* 3), 5.86 (1 H, m), 5.17 (2 H, m), 3.77 (2 H, s), 3.09 (2 H, d, *J* 6), 1.52 (1 H, br s, exch. D_2O).

N-Triphenylmethyl-*N*-allylfurfurylamine 10

The amine **8** (0.95 g, 7 mmol) was added dropwise to solution of trityl chloride (2.23 g, 8 mmol) and diisopropyl(ethyl)amine (1.05 g, 8 mmol) in dichloromethane (7.5 cm^3). After 24 h the solution was washed with 3 M aqueous sodium hydroxide (10 cm^3) and brine (10 cm^3) before drying, filtering and evaporating off the solvent. The resulting gum was purified by column chromatography, using a 1 : 1 light petroleum–dichloromethane mixture as eluent, to produce the *title compound* (1.0 g, 53%) as a pale yellow, viscous gum; δ_H 7.68–7.20 (16 H, m, aromatic H), 6.31 (1 H, t, *J* 3), 6.14 (1 H, d, *J* 3), 5.47–5.34 (1 H, m), 4.74–4.66 (2 H, m), 3.47 (2 H, s), 3.04 (2 H, d, *J* 5.6); characterised as its cycloadduct **18**.

N-Benzhydryl-N-allylfurfurylamine 11
This was prepared in a similar manner to the trityl compound, using allyl bromide (0.74 g, 6 mmol) and *N*-benzhydrylfurfurylamine (1.32 g, 5 mmol), to give the *benzhydryl derivative* (0.9 g, 60%) as a colourless oil (Found: C, 83.1; H, 7.0; N, 4.4. $C_{21}H_{21}NO$ requires C, 83.1; H, 7.0; N, 4.6%); *m*/*z* 303; δ_H 7.45–7.16 (11 H, aromatic H), 6.30 (1 H, t, *J* 3.1), 6.11 (1 H, d, *J* 3.1), 5.94–5.83 (1 H, m), 5.21–5.11 (2 H, m), 4.81 (1 H, s), 3.67 (2 H, s), 3.08 (2 H, d, *J* 6.2).

N-Benzyl-N-allylfurfurylamine 12
This was prepared in a similar manner to the trityl compound, from allyl bromide (3.03 g, 25 mmol) and *N*-benzylfurfurylamine (4.68 g, 25 mmol) to give the *benzyl derivative* (3.4 g, 60%) as a colourless oil (Found: C, 79.5; H, 7.2; N, 6.3. $C_{15}H_{17}NO$ requires C, 79.3; H, 7.5; N, 6.2%); *m*/*z* 227; δ_H 7.42–7.21 (6 H, m, aromatic H), 6.32 (1 H, t, *J* 3.1), 6.18 (1 H, d, *J* 3), 5.95–5.84 (1 H, m), 5.25–5.15 (2 H, m), 3.63–3.59 (4 H, m), 3.11 (2 H, d, *J* 6.4).

N-2,4,6-Trimethylbenzyl-N-allylfurfurylamine 13
This was prepared in a similar manner to the trityl compound, to give the *title compound* as a colourless oil (41%) (Found: MH^+, 270.1858. $C_{18}H_{23}NO{\cdot}H^+$ requires 270.1858); δ_H 7.30 (1 H, br s), 6.73 (2 H, s, aromatic H), 6.25 (1 H, br d, *J* 3), 6.12 (1 H, d, *J* 3), 5.79 (1 H, m), 5.12 (2 H, m), 3.97 (2 H, s), 3.55 (2 H, s), 2.99 (2 H, d, *J* 6.4), 2.3–2.0 (9 H, 3 × CH_3).

N-4-Methylphenylsulfonyl-N-allylfurfurylamine 14
The amine **9** (1.03 g, 7 mmol) was dissolved in pyridine (5 cm^3) and cooled in a water bath at room temperature before adding toluene-*p*-sulfonyl (tosyl) chloride (1.54 g, 8 mmol) with stirring. After 3 h the solution was poured into ice–water (20 cm^3) and extracted with dichloromethane (20 cm^3). The organic extract was washed with 3 M HCl (3 × 10 cm^3) and water, before drying, filtering and removing the solvent *in vacuo* to give the crude product (*ca*. 100%) as a viscous oil. A sample of the crude product was purified by dissolving it in a little dichloromethane, filtering through silica gel, washing the solid with more dichloromethane, and removing the solvent under reduced pressure to yield the *title sulfonamide* as a pale yellow viscous oil (Found: C, 61.5; H, 5.8; N, 4.7. $C_{15}H_{17}NO_2S$ requires C, 61.8; H, 5.9; N, 4.8%); δ_H 7.65 (2 H, d, *J* 8.1), 7.25 (1 H, br s), 7.25 (2 H, d, *J* 8.1), 6.24 (1 H, br d, *J* 3.2), 6.14 (1 H, d, *J* 3.2), 5.61 (1 H, m), 5.15 (2 H, m), 4.39 (2 H, s), 3.77 (2 H, d, *J* 6.3), 2.40 (3 H, s).

N-Allyl-N-furfurylbenzamide 15
The amide was prepared in a similar manner to the sulfonamide. A sample was purified by filtration through silica gel, using dichloromethane as solvent, to give the *title benzamide* as a viscous oil (Found: C, 74.6; H, 6.4; N, 5.7. $C_{15}H_{15}NO_2$ requires C, 74.7; H, 6.3; N, 5.8%); ν_{max}/cm^{-1} 1641; δ_H(25 °C; broad signals) 7.39 (6 H, aromatic H), 6.28 (2 H), 5.83 and 5.73 (1 H, two broad signals), 5.23 (2 H, m), 4.7–4.4 (2 H), 4.1–3.8 (2 H). At −20 °C, the spectrum resolved into two overlapping sets of signals, corresponding to the two rotamers, in a *ca*. 1 : 1 ratio.

Cycloaddition reactions
Solutions of the uncyclised amine (5–10 mmol) in either toluene or xylene were heated under a nitrogen atmosphere at reflux. Aliquots of the solutions were taken for monitoring the progress of the reaction by ^1H NMR spectroscopy. Equilibria were established separately by following the progress of reactions heated in a sealed NMR tube suspended in the solvent of choice. After heating, the solvent was removed *in vacuo* and the residue isolated either by preparative TLC or by column chromatography, using basic alumina as support and dichloromethane–light petroleum as eluent.

Kinetic studies were carried out using solutions of the tritylated amine **10** in deuterated benzene in a sealed NMR tube. The tube was fully immersed in the solvent (xylene–toluene–benzene mixtures) and heated at reflux, using a calibrated thermometer to measure the temperature. At intervals the NMR tube was retrieved, rapidly cooled to room temperature and the ^1H NMR spectrum immediately recorded before continuing the heating.

8-Triphenylmethyl-8-aza-1,4-epoxybicyclo[4.3.0]non-2-ene 18†
Obtained in 85% yield as a viscous gum that slowly crystallised, mp 141–143 °C (Found: C, 85.2; H, 6.9; N, 3.4. $C_{27}H_{25}NO$ requires C, 85.4; H, 6.6; N, 3.7%); δ_H 7.54–7.13 (15 H, m, aromatic H), 6.36 (1 H, d, *J* 5.9), 6.18 (1 H, dd, *J* 1.5, 5.8), 4.83 (1 H, dd, *J* 1.5, 4.6), 3.55 (1 H, d, *J* 11.9), 3.25 (1 H, dd, *J* 6.85, 9.9), 2.73 (1 H, d, *J* 11.9), 1.95 (1 H, dd, *J* 9.6, 9.9), 1.71 (1 H, dddd, *J* 4.1, 6.9, 7.8, 9.6), 1.47 (1 H, ddd, *J* 4.1, 4.6, 11.6), 1.18 (1 H, dd, *J* 7.7, 11.6).

8-Diphenylmethyl-8-aza-1,4-epoxybicyclo[4.3.0]non-2-ene 19
Obtained in 40% yield as a viscous gum (Found: C, 83.0; H, 7.0; N, 4.4. $C_{21}H_{21}NO$ requires C, 83.1; H, 7.0; N, 4.6%); δ_H 7.51–7.15 (10 H, m, aromatic H), 6.38 (1 H, d, *J* 5.8), 6.24 (1 H, dd, *J* 1.3, 7.1), 4.97 (1 H, dd, *J* 1.3, 5.5), 4.49 (1 H, s), 3.48 (1 H, d, *J* 12.2), 3.08 (1 H, dd, *J* 5.5, 7.5), 2.62 (1 H, d, *J* 12.2), 2.05 (1 H, dd, *J* 5.7, 7.5), 1.66 (1 H, dddd, *J* 3.1, 5.5, 5.7, 7.3), 1.61 (1 H, ddd, *J* 3.1, 4.8, 11.5), 1.30 (1 H, dd, *J* 7.3, 11.5).

8-Benzyl-8-aza-1,4-epoxybicyclo[4.3.0]non-2-ene 20
Compound **20** could not be readily isolated from the equilibrium mixture produced from the cyclisation of the starting amine **12**. An authentic sample was prepared by benzylation of the free cyclic amine **16**, using benzyl chloride in dichloromethane as alkylating agent and diisopropyl(ethyl)amine as the base. The *amine* (94%), isolated as a viscous oil, showed δ_H 7.39–7.24 (5 H, m), 6.40 (1 H, d, *J* 6.0), 6.25 (1 H, dd, *J* 1.3, 6.0), 4.99 (1 H, dd, *J* 1.3, 4.3), 4.58 (2 H, s), 3.54 (1 H, d, *J* 11.9), 3.17 (1 H, dd, *J* 7.0, 10.4), 2.68 (1 H, d, *J* 11.9), 2.19 (1 H, dd, *J* 10.0, 10.4), 2.03 (1 H, dddd, *J* 3.5, 7.0, 7.7, 10.0), 1.7 (1 H, ddd, *J* 3.5, 4.3, 11.5), 1.31 (1 H, dd, *J* 7.7, 11.5). The cycloadduct was characterised by heating to give, mainly, the uncyclised amine **12**.

8-4-Methylphenylsulfonyl-8-aza-1,4-epoxybicyclo[4.3.0]non-2-ene 22
Compound **22** was isolated, after heating the material in toluene under the standard conditions for 21 h. After this time, TLC indicated some of the uncyclised tosylamide was still present in solution. The pure cycloadduct was isolated in 60% yield by column chromatography through silica gel (light petroleum–dichloromethane) as a viscous gum, which eventually crystallised, mp 88–90 °C (Found: C, 61.7; H, 5.8; N, 4.7. $C_{15}H_{17}NO_3S$ requires C, 61.8; H, 5.9; N, 4.8%); δ_H 7.75 (2 H, m), 7.35 (2 H, m), 6.32 (2 H, m), 4.93 (1 H, d, *J* 4.5), 3.90 (1 H, d, *J* 12.3), 3.89 (1 H, m), 3.51 (1 H, d, *J* 12.3), 2.68 (1 H, t, *J* 9.6), 2.44 (3 H, s), 2.05 (1 H, m), 1.63 (1 H, m), 1.32 (1 H, dd, *J* 7.8, 11.7).

8-Benzoyl-8-aza-1,4-epoxybicyclo[4.3.0]non-2-ene 23
Compound **23** was obtained as a mixture of cyclic rotamers after heating the material in toluene under the standard conditions for 24 h. The rotamers were separated from remaining starting material by column chromatography through silica gel (light petroleum–dichloromethane) and showed the following spectroscopic data (Found: MH^+, 242.1181. $C_{15}H_{15}NO_2{\cdot}H^+$ requires 242.1811); δ_H 7.39 (5 H, m), 6.43 (1 H, m), 6.30 (1 H,

† The correct IUPAC name for this compound is 3-triphenylmethyl-10-oxa-3-azatricyclo[5.2.1.$0^{1,5}$]dec-8-ene.

m), 5.09 (1 H, m), 4.27 (1 H, m), 3.95 (1 H, m), 3.85 (1 H, m), 3.28 (1 H, m), 2.10 (1 H, m), 1.8 (1 H, m), 1.45 (1 H, m).

Deprotection of tritylated amine 18

The tritylated cycloadduct **18** (0.50 g, 1.32 mmol) was added to ethanol (10 cm^3) containing 4 M HCl (3 cm^3) and the mixture warmed on a steam bath until the solid dissolved, keeping the temperature <60 °C. The solution was warmed for a further 10 min before removing most of the ethanol under reduced pressure, whereby a solid formed. Water (10 cm^3) was added and the solid removed by extraction into ether (2 × 10 cm^3). The aqueous layer was basified with 4 M aqueous NaOH and the solution extracted with dichloromethane (2 × 15 cm^3). The organic extract was dried, filtered and the solvent evaporated off at room temperature, under reduced pressure, to afford 8-*aza*-1,4-*epoxybicyclo*[4.3.0]*non*-2-*ene* **16** (0.15 g, 83%) as a pale yellow oil, which readily oxidised in air to give a brown material. The product showed the chemical shifts and coupling constants shown in Fig. 2 (Found: M^+, 137.0841. $C_8H_{11}NO$ requires 137.084 06).

Samples were alkylated with either benzhydryl chloride or benzyl chloride, under the conditions used to alkylate the uncyclised amine **8**, to give pure samples of the cyclic derivatives **19** and **20**, respectively, identical in their TLC behaviour to those formed thermally from the uncyclised isomers.

Heating the cyclic amine **16** under nitrogen at 140 °C for several hours resulted in retro-addition and complete formation of the starting amine **8**.

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