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Synthesis of Exo- and Endo-7,8-Epoxyhomotropanes

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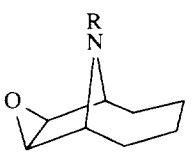
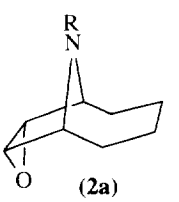
Abstract: Epoxidation of N-protected homotrop-7-ene (9-azabicyclo[4.2.1]non-7-ene) and 1-substituted derivatives occurs stereoselectively from the *exo*- (β-) face but a practical alternative approach to the *exo*- epoxides is based on a serendipitous hydride reduction of a 1-hydroxy-7β,8β-epoxyhomotropane derivative. The epoxidation of 4-aminocyclo-oct-2-enol derivatives occurs with total *anti*- stereoselectivity and opens the way to *endo*- (α-) 7,8-epoxyhomotropanes. Hydride reduction or hydrogenolysis provides a range of novel 7,8-epoxy- or 7-hydroxy- homotropanes and norhomo-tropanes, depending on conditions. Copyright © 1996 Elsevier Science Ltd

Introduction

We have described the synthesis of homotropane and norhomotropane together with 7,8-dehydro-, C_1-alkyl[1] and C_1-hydroxy derivatives.[2] Early work by Cope gave C_2-keto and hydroxy- derivatives by ring expansion of tropinone;[3] Hobson[4] approached the 2-hydroxy- compounds by solvolysis of 2-chloro-homotropanes. However, other oxygenated derivatives are rare and C_7,C_8 oxygenation is unknown. The scarcity of these compounds is surprising in view of the potent activity of anatoxin-a[5] (one of only two natural homotropanes) and the well established physiological properties of oxygenated tropanes.[6] We are also interested in higher homologues (based on the 1-hydroxyhomotropane skeleton) of the highly oxygenated 1-hydroxytropane derivatives known as the calystegins.[6b,7] We have therefore investigated the functionalisation of the 2-carbon bridge of homotropanes and now describe the stereoselective introduction of epoxy and hydroxy groups.[8]

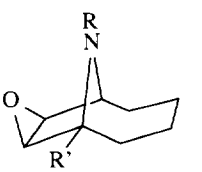


R = Me **(1a)**
R = H **(1b)**
R = CO_2CH_2Ph **(1c)**
R = CO_2CH_2Ph

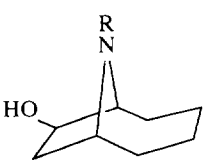


(2a)

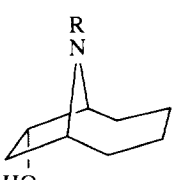
(2c)



(3a) [R' = OH]
(3b) [R' = OH]
(3c) [R' = OH]
(4) [R' = Me]



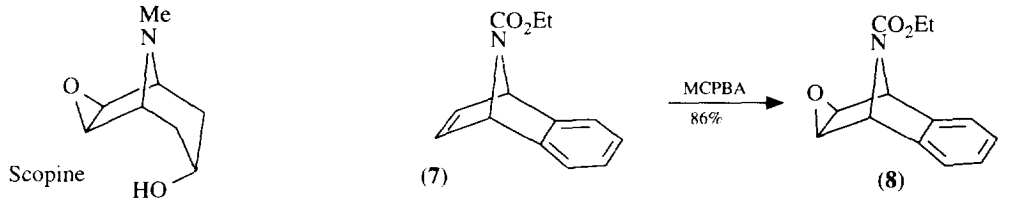
(5b) R = H
(5c) R = CO_2CH_2Ph



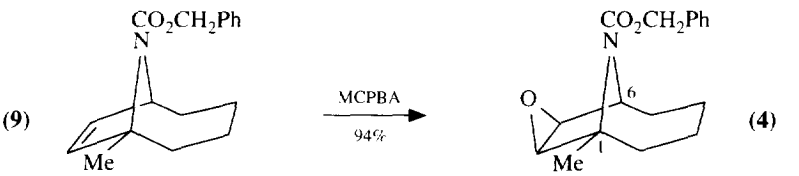
(6a) R = Me
(6b) R = H

Exo- (β-) epoxyhomotropanes

Our initial approach to *exo*-7,8-epoxyhomotropanes was based on epoxidation of N-protected 7,8-dehydro- derivatives; the presence of an amino- group had led to low yields and extended reaction times in the *exo*- epoxidation of 3α-acetoxytrop-6-ene (which formed the key step in the first partial synthesis of scopine).[9] *Exo*- epoxidation was observed in the epoxidation of norbornene with MCPBA[10a] and in our own model studies[10b] of N-protected 7-azabicyclo[2.2.1]heptene systems e.g. **(7)** → **(8)**.



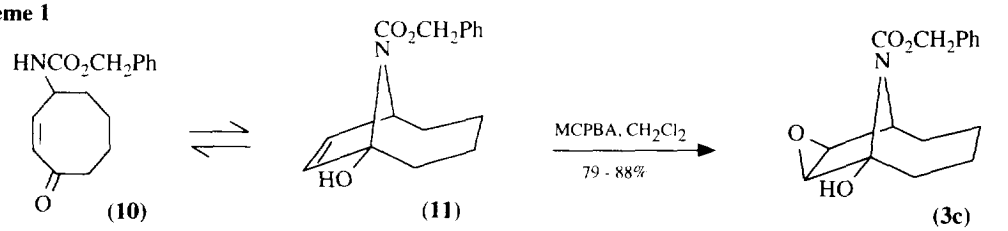
Initial studies of the epoxidation of homotrop-7-ene derivatives were carried out on simple N-alkoxycarbonyl-protected homotrop-7-ene derivatives. Treatment of **(9)**[1b] with 1.3 equivalents of MCPBA yielded **(4)** in excellent yield as the only stereoisomer.



The epoxide **(4)** existed as a pair of rotamers; the major rotamer displayed characteristic epoxide proton signals at δ 3.23 and δ 3.32 (J_{vic} = 3.1 Hz), with additional small coupling ($J_{6,7endo}$ = 0.4 Hz) indicative of the *exo*- stereoisomer. The assignment of *exo*-stereochemistry was also confirmed by detailed comparison of coupling constants and chemical shifts with those measured for *exo*- and *endo*-7,8-epoxy-homotropanes described below.

Epoxidation of **(10)** ⇌ **(11)**[2] occurred *via* the more reactive double bond of **(11)** (rather than with the α,β-unsaturated ketone) giving the *exo*-epoxide **(3c)** as the only product in good yield[10c] (scheme 1).

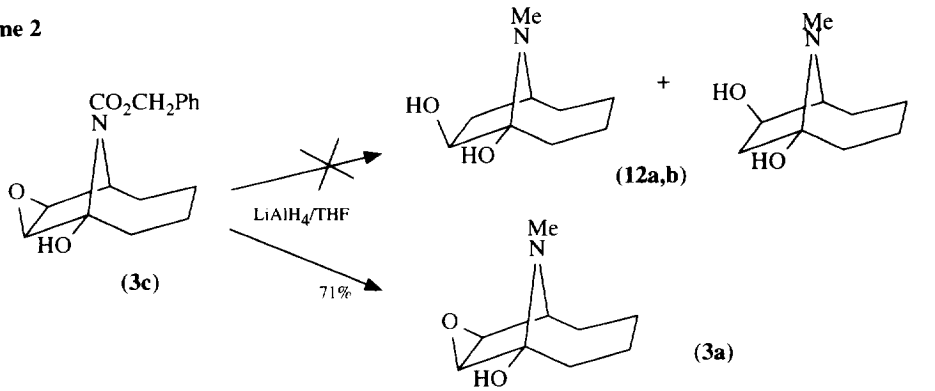
Scheme 1



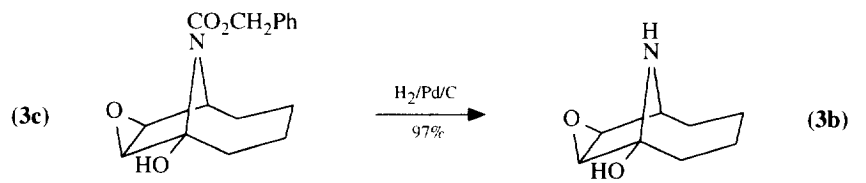
The ^{1}H NMR spectrum was consistent only with the bicyclic tautomer **(3c)** ($J_{6,7endo}$ ≈ 0 Hz) and two sets of well-resolved signals were again observed as a consequence of slow rotation about the N-CO bond. The ^{13}C NMR spectrum of **(3c)** included a quaternary (COH) signal at δ 91.4, characteristic of the bicyclic tautomer.

It was anticipated that reaction of **(3c)** with hydride would simultaneously reduce the carbamate to an N-methyl group and open the epoxide to yield a mixture of regioisomeric alcohols **(12a,b)**. However, the epoxide in **(3c)** survived treatment with lithium aluminium hydride in THF at reflux giving the novel epoxy-amine **(3a)** in good yield (scheme 2).

Scheme 2

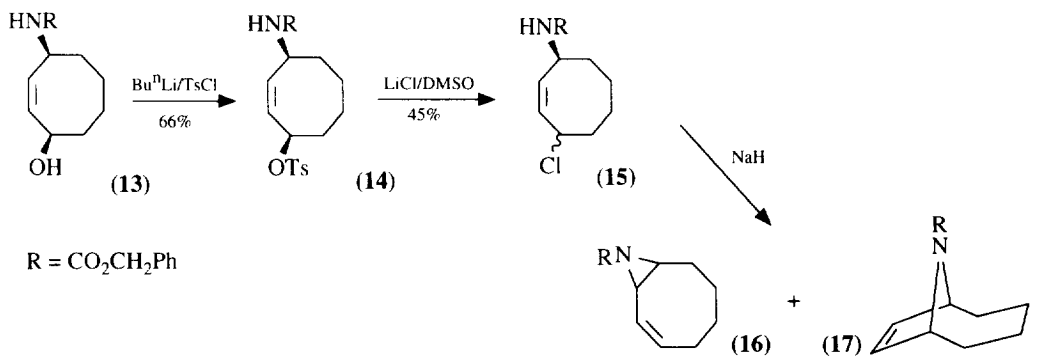


The ^{1}H NMR spectrum was very similar to that of (**3c**) and included an N-methyl singlet (δ 2.52). The ^{13}C NMR spectrum confirmed the bicyclic nature of (**3a**) (δ 89.6, s; C_1). Similar chemoselectivity was observed when (**3c**) was hydrogenolysed using a palladium on charcoal catalyst. The epoxide protons ($H_{7,8}$) of the product (**3b**) were magnetically equivalent in $CDCl_3$, but were resolved in D_6-acetone solution appearing as two doublets at δ 3.27 and 3.31 ($J_{7,8}$ = 2.7 Hz). The ^{13}C NMR spectrum showed a bridgehead (COH) signal at δ 91.2. Careful examination of the NMR spectra gave no evidence for tautomerism of (**3a**) or (**3b**) and spectra of crude samples of neither compound showed any indication of epoxide ring opening.



The exclusive formation of *exo*-7,8-epoxy derivatives in the two cases studied above led us to epoxidise the N-protected alkene (**17**) with the prospect of ultimate conversion into NH (**1b**) or NMe (**1a**) derivatives without reduction of the epoxide.

A modification of the previously described intramolecular displacement approach to homotropane[1] was employed to prepare the alkene (**17**) from the known intermediate (**13**)[1b] (scheme 3).



Scheme 3

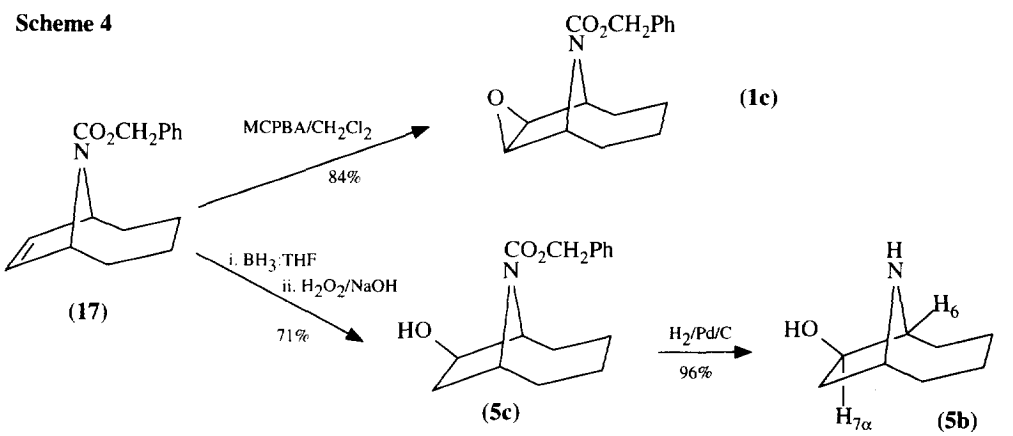
THF/Reflux :	10%	28%
THF/DME/60°C :	3%	40%

An alternative route involves the corresponding series of reactions where R is methyl (secondary amines have proved superior to carbamate groups in such cyclisations) but demethylation of the product, homotrop-7-ene, and reprotection with a benzyloxycarbonyl group is then necessary.[11] Difficulties were encountered with the production of **(15)** having the necessary *trans*-1,4- arrangement of nitrogen and leaving group. Firstly, the tosylate **(14)** was unstable and could only be prepared in modest yield; secondly, displacement of the tosylate using lithium chloride in DMSO solvent[12] resulted in epimerisation at the 4-position giving the chloride **(15)**, also in modest yield, as an inseparable mixture of stereoisomers in a 7:3 *trans*:*cis* ratio (calculated from ^{1}H NMR signal integrations). Attempts to produce the *trans*- chloride from **(13)** by other methods (such as thionyl chloride[1] or triphenylphosphine in carbon tetrachloride[13]) failed, giving complex mixtures. Nevertheless, base-induced cyclisation of **(15)** was achieved by refluxing with sodium hydride in THF solvent giving the homotrop-7-ene **(17)** in 28% yield together with a smaller quantity of aziridine by-product **(16)**, formed by a competitive 1,2-cyclisation. The formation of benzyl alcohol indicated some deprotection of the nitrogen. When the cyclisation of **(15)** was performed at a lower temperature (60°C) in THF/DME solvent, the yield of **(17)** increased to 40% and formation of aziridine was suppressed substantially. The NMR spectra of **(17)** were simplified somewhat as a result of the symmetry but displayed the typical signal duplication common in these bridged bicyclic carbamates. The ^{1}H and ^{13}C NMR spectra of **(16)** were predictably similar to those of related lower homologues (which were isolated as by-products from corresponding cyclisations in the tropane series[14]).

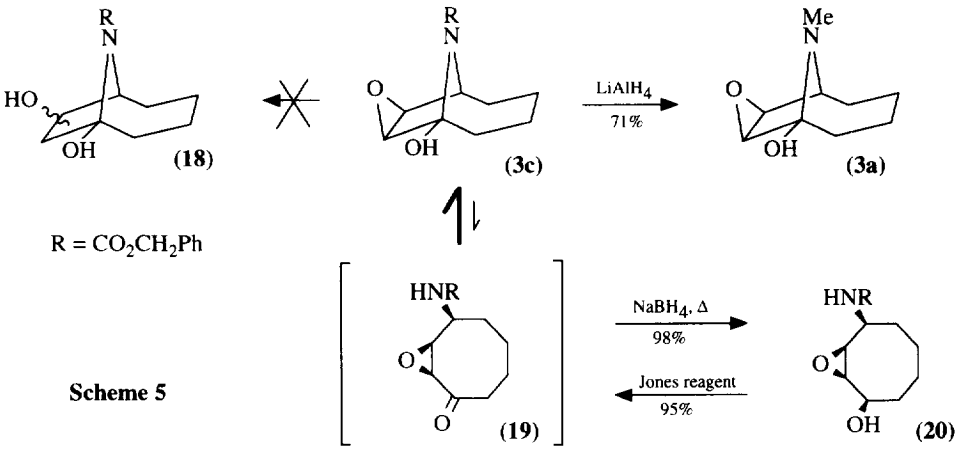
Epoxidation of **(17)** using MCPBA proceeded in high yield (scheme 4). The ^{1}H NMR spectrum of **(1c)** included two doublets at δ 3.36 (J = 3.0 Hz) and δ 3.37 (J = 3.0 Hz) for the epoxide protons in the two rotamers with no significant coupling to the bridgehead protons.

The investigation of facial selectivity using reagents other than MCPBA was of interest. Earlier studies have shown that hydroboration-oxidation of norbornene afforded the *exo*-alcohol as the sole product[15] and **(17)** was therefore treated with 0.6 equivalents of a borane:THF complex[16] giving the *exo*-alcohol **(5c)** as the only product in good yield. Hydrogenolysis with palladium on charcoal afforded norhomotropan- 7β-ol **(5b)** in near-quantitative yield (scheme 4). The duplication of signals in the ^{1}H NMR spectrum of **(5c)** was removed after hydrogenolysis; the ^{1}H NMR spectrum of **(5b)** now showed a doublet of doublets at δ 4.12 corresponding to the α-hydroxy proton H_7 ($J_{7endo,8endo}$ = 6.2, $J_{7endo,8exo}$ = 2.8 Hz) but no measurable coupling between H_7 and H_6.

Scheme 4



Despite the good yields in the later steps, the overall efficiency of production of **(1c)** and **(5b)** was low owing principally to the complications introduced by the presence of the double bond during the three steps involved in converting **(13)** into **(17)**. A more efficient approach would therefore involve introduction of the epoxide at an earlier stage in the synthesis and such a method was discovered fortuitously in an attempt to open the epoxide **(3c)** to the alcohol **(18)** (scheme 5).



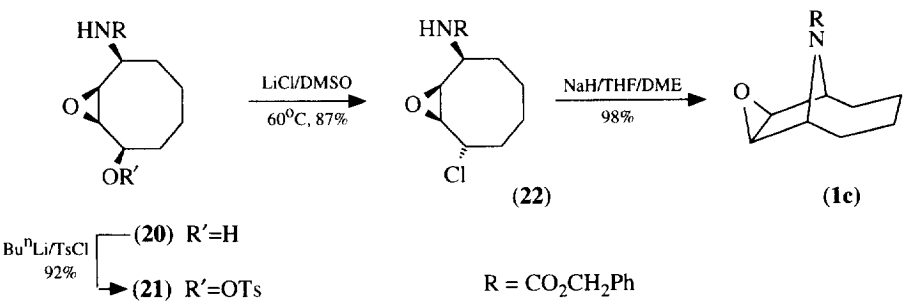
Scheme 5

Attempts to open the epoxide (**3c**) by acid or base hydrolysis gave only mixtures of starting materials and deprotected products. Many reductive ring opening methods have been reported in the literature.[17] Brown[18] used lithium metal in ethylenediamine to reduce norbornene oxide to norbornanols whilst Vankar[19] reduced epoxides with zinc and trimethlysilyl chloride, but the application of both of these methods to (**3c**) resulted in the isolation of starting material. Soai[20] used sodium borohydride in mixed alcohol solvents and this method was also applied to (**3c**); the product was not the expected alcohol (**18**) but, surprisingly, the epoxy-alcohol (**20**) isolated as a single stereoisomer.

Under these conditions, a very small stationary concentration of the monocyclic tautomer (**19**) must be present. Whilst this was not detectable spectroscopically, earlier studies of tautomerism of homotropan-1-ols have shown that the proportion of monocyclic tautomer in related systems increases with increase in temperature[2] and attack of hydride from the least hindered face of the ketone is reasonable. In contrast, the carbamate group in (**3c**) reacts rapidly with lithium aluminium hydride; the resulting amine (**3a**) presumably exists completely in the bicyclic form and is therefore resistant to further attack by hydride.

The conversion of (**3c**) into (**20**) could be reversed. Oxidation of the alcohol using Jones reagent gave (**3c**) in excellent yield, confirming the intermediacy of the epoxy-ketone structure (**19**). The all-*cis*-relationship of the substituents in (**20**) followed from the ^{1}H NMR spectrum which showed a doublet of doublets at δ 2.91 (J = 4.5, 3.6 Hz) and a pseudo- triplet at δ 3.11 (J ≈ 4.8 Hz) for the epoxide protons. The larger coupling of 4.5 Hz corresponds to a vicinal coupling between these protons, leaving two similar couplings of 3.6 Hz and *ca.* 4.8 Hz to the α-nitrogen and α-hydroxy protons. Had a *trans*-1,4 relationship of the 1- and 4- substituents existed, two significantly different values would have been observed (such an effect will be seen later for *trans*-1,4 systems). The successful conversion of (**20**) into the *exo*-epoxide (**1c**) is outlined in scheme 6.

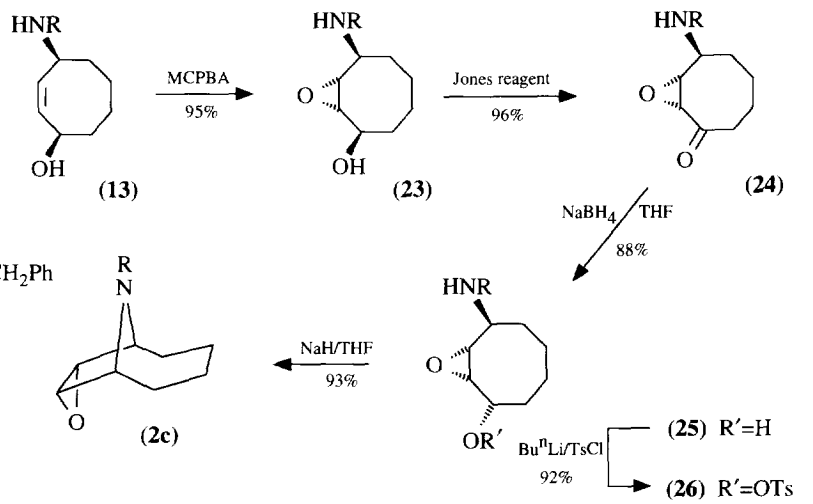
Scheme 6



The alcohol (**20**) was converted into the tosylate (**21**) in 92% yield and thence into the chloride (**22**), as a single stereoisomer as shown by NMR spectroscopy. The coupling between the α-epoxy- and the α-chloro- protons was much larger ($J_{3,4}$ = 8.9 Hz) than the corresponding *cis*-coupling ($J_{1,2}$ = 4.3 Hz) confirming the 1,4-*trans* stereochemistry. Cyclisation of (**22**) was achieved in near quantitative yield using sodium hydride and the product (**1c**) was identical to a sample prepared by epoxidation of the alkene (**17**).

Endo- (α-) 7,8-epoxyhomotropanes

The *exo-* selectivity illustrated above meant that the *endo*-7,8-epoxyhomotropanes were not available from 7,8-dehydrohomotropanes. It was necessary to introduce the epoxide prior to bicyclisation. Whilst syn-selectivity in the epoxidation of allylic alcohols has been widely studied,[21,22,23] earlier work with cyclooct-2-enol[24,25,26] showed that stereoselectivity was highly dependent on the oxidising agent chosen. Very high *anti*-selectivity (>99%) was observed in 8-ring allylic alcohols using monoperoxyphthalic acid whereas the use of $VO(acac)_2$/Bu^{t}OOH gave 97% *syn-* selection. Whilst allylic carbamate groups have also shown a pronounced *syn-* directing effect,[27] nevertheless reaction of (**13**) with 1.2 equivalents of MCPBA furnished the *trans*-epoxide (**23**) in 95% yield as a single stereoisomer (scheme 7).



Scheme 7
R = CO_2CH_2Ph

The *anti-* stereoselectivity shown in the epoxidation was unexpected, but welcome. Molecular modelling shows clearly that the *syn-* face of the π-bond in (**13**) is effectively shielded by the phenyl ring of the N-protecting group as a result of H-bonding interactions between the OH and NH groups in (**13**) (figure 1).

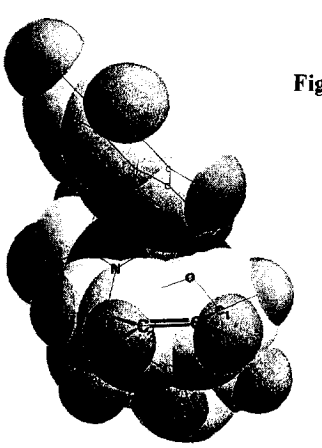


Figure 1

(**13**)

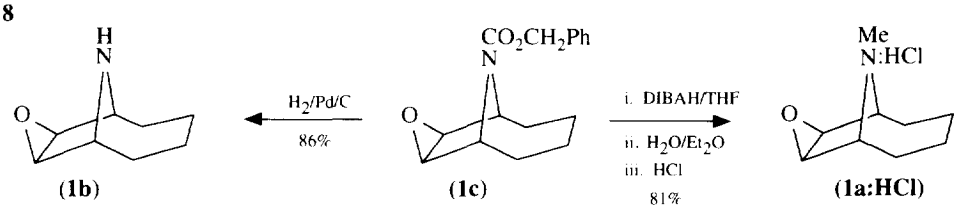
The ^{1}H NMR spectrum of (**23**) was generally similar to that of the *syn*-epoxide (**20**) including mutual vicinal coupling of 4.7 Hz between epoxide protons. However, two larger couplings of 8.2 Hz and 9.3 Hz to α-nitrogen and α-hydroxy protons were observed (contrast the respective values of 3.6 Hz and approximately 4.8 Hz for (**20**)), confirming the *anti-* relationship of the epoxide and α-substituents. There was no evidence in the ^{1}H NMR spectrum of the crude epoxide of any signals corresponding to the *syn*-epoxide.

Conversion of the epoxide (**23**) into the N-protected *endo*-epoxyhomotropane is shown in scheme 7. The configuration of the hydroxyl at C-1 was inverted by means of oxidation with Jones reagent [to (**24**)], followed by stereoselective reduction using sodium borohydride to yield (**25**) as a single stereoisomer. All spectroscopic data pointed to the epoxy-ketone (**24**) existing only as the monocyclic tautomer at room temperature with, for example, a characteristic carbonyl signal at δ 206.2 in the ^{13}C NMR spectrum. This is in sharp contrast to the epoxy-ketone (**3c**) with the opposite epoxide stereochemistry, which is completely bicyclic.[2b] The remaining two steps were straightforward; tosylation of (**25**) gave (**26**) which cyclised with base to give the *endo*-epoxyhomotropane (**2c**) in excellent yield. The ^1H NMR spectrum of (**2c**) differed from that of the *exo*-epoxide (**1c**) with the chemical shift of the epoxide protons appearing 0.53 ppm further downfield and a coupling of 3.6 Hz between epoxide and bridgehead protons.

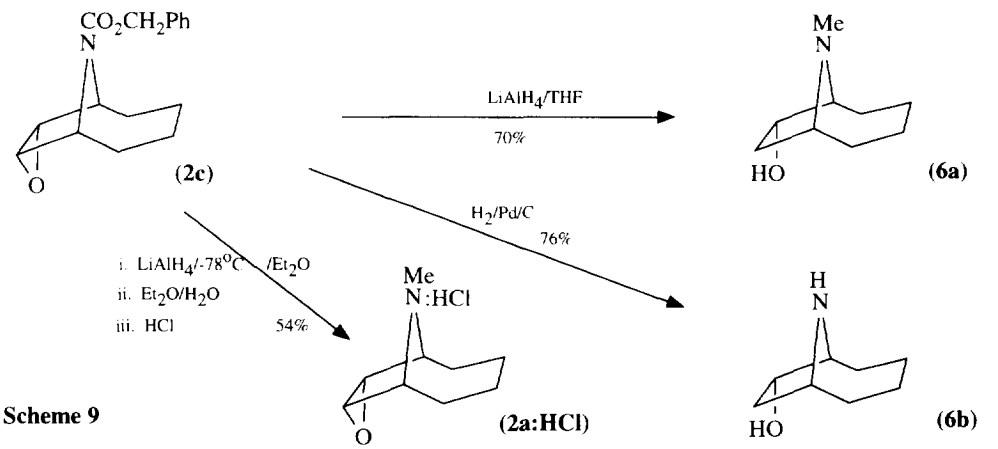
Reduction of N-protected epoxyhomotropanes

Reduction of (**1c**) with DIBAH in THF at ambient temperature afforded the N-methyl epoxide (**1a**) and hydrogenolysis using a palladium catalyst gave the corresponding nor derivative (**1b**) (scheme 8). The epoxide survived both reductions as anticipated from the earlier results with the 1-hydroxy derivative (**3c**). The N-methyl amine was stored as the hydrochloride salt.

Scheme 8



Reduction of the N-alkoxycarbonyl group restored the symmetry of the system in the NMR spectra of both amines. The ^1H spectrum of (**1a**) showed a singlet at δ 3.43 for the two equivalent epoxide protons. Five signals were observed in the ^{13}C spectrum; the spectra of (**1b**) were similar with only four signals in the ^{13}C spectrum.



Scheme 9

The *endo*-epoxide (**2c**) was considerably more reactive, being reduced to homotropan-7α-ol (**6a**) or norhomotropan-7α-ol (**6b**) under normal conditions (scheme 9). However, the N-methyl epoxide (**2a**) could be isolated [contaminated with 10% of the alcohol (**6a**)], if milder reducing conditions were employed.

The ^{1}H NMR spectrum of **(6a)** displayed a doublet of triplets at δ 4.55 for the α-hydroxy proton, due to vicinal coupling to both C_8 protons (J = 10.5, 6.4 Hz) and the C_6-bridgehead proton (J = 6.4 Hz). The observation of a doublet ($J_{6,7\text{-exo}}$ = 3.2 Hz) for the epoxide protons of **(2a)** confirmed the *endo*-stereochemistry.

The preferred conformation of the 7-membered ring in homotropane is known to be a boat[28] and this gives no reason to anticipate significant steric shielding of the *endo*- face. However, the established role of bridging nitrogen in the hydride reduction of an etheno- bridge in 7-azanorbornenes[29] suggests that the nitrogen is very likely to play a role in assisting the attack of hydride reducing agents from the *exo*- face, explaining the increased sensitivity of the *endo*- epoxide to hydride reducing agents. Adaptation of the overall strategy described here to the tropane series is reported in an accompanying paper.[30]

We are grateful to EPSRC for the award of a studentship to D.E.J.

Experimental

Routine ^{1}H NMR spectra were recorded on a Varian EM 390 (90MHz) spectrometer. Higher field ^{1}H NMR (300, 250 MHz) and ^{13}C NMR (75, 63 MHz) spectra were recorded on Bruker AM 300 or ARX 250 spectrometers. Spectra were measured in $CDCl_3$ with tetramethylsilane (TMS) as internal reference unless indicated otherwise. Signal characteristics are described using standard abbreviations: s (singlet), d (doublet), dd (doublet of doublets), t (triplet), q (quartet), quin (quintet), m (multiplet), br (broad) and v (very); protons identified as NH or OH were shown to be exchangeable with D_2O. In some circumstances, signals that appear in a more simplified form than the molecule allows are give the prefix ~. For example, a dddd which appears as a quintet is quoted as ~quin. Where data are quoted for two tautomers or rotamers, overlapping signals are shown in italics but may be quoted separately for reasons of clarity even though they are not fully resolved or assigned. In the ^{13}C spectra, C, CH, CH_2, CH_3 are used to indicate quaternary, methine, methylene and methyl carbons respectively, as shown by off-resonance decoupling or DEPT experiments.

IR spectra were recorded on PE 1604 FT or PE 298 IR spectrometers as solutions in CH_2Cl_2 unless indicated otherwise. Band intensities are described using standard abbreviations: s (strong), m (medium), w (weak), br (broad), v (very). Mass spectra were measured routinely on VG Micromass 14 or Kratos Concept spectrometers and were obtained using ionisation by electron impact except where chemical ionisation was used (shown CI) or fast atom bombardment (shown FAB); intensities are given as percentages of the base peak. Accurate mass measurements were obtained using the Kratos Concept mass spectrometer at Leicester University or through the SERC service at the University College of Swansea.

Melting point measurements were made using a Kofler hot stage apparatus and are uncorrected. Combustion Analyses were performed by Butterworth Laboratories Ltd., Teddington, Middlesex.

Reactions were performed under dry nitrogen using solvents dried by standard methods. Diethyl ether was dried over sodium wire and distilled from $LiAlH_4$. Dichloromethane, toluene and benzene were distilled from calcium hydride. Petroleum ether and ethyl acetate were distilled prior to use. Methanol and ethanol were purified with magnesium and iodine.[31] Tetrahydrofuran was distilled from sodium-benzophenone. Triethylamine and pyridine were distilled from potassium hydroxide. All other solvents were dried and purified as described by Perrin.[32] Flash chromatography was carried out according to the method of Still[33] using Merck Kieselgel 60 (230 - 400 mesh). Thin-layer chromatography was conducted on standard commercial aluminium sheets pre-coated with a 0.2 mm layer of silica gel (Merck 60 - 254).

Compounds **(9)**, **(10 ⇌ 11)**, and **(13)** were prepared as described in reference 1b.

N-Ethoxycarbonyl-exo-2,3-epoxy-1,2,3,4-tetrahydronaphthalene-1,4-imine (8)[10b]

MCPBA (80%; 1.10g, 6.36 mmol) was added portion-wise to a stirred solution of **(7)** (1.01g, 4.71 mmol) in dry dichloromethane (45 ml). Stirring was continued for 90h. The mixture was filtered, concentrated under vacuum, dissolved in diethyl ether, and washed with saturated sodium bicarbonate (10 x 15 ml). The organic layer was dried and the solvent removed under vacuum to leave the epoxide **(8)** as a pale yellow, waxy solid (0.94g; 86%). Slow rotation about the N-CO bond was observed and signals due to the two rotamers are quoted separately where these were resolved; overlapping signals are quoted in italics.

δ_H (300 MHz, $CDCl_3$): *1.28* (t, J = 7.2 Hz, 3H), 3.34 and 3.43 (d, J = 3.5 Hz, 1H), *3.46* (d, J = 3.5 Hz, 1H), *4.17* (q, J = 7.2 Hz, 1H), 5.11 and 5.19 (s, 2H), *7.12 - 7.33* (m, 4H). δ_C (75MHz, $CDCl_3$): 14.4 (CH_3), 54.6 (CH), 55.0 (CH), 61.5 (CH_2), 61.7 (CH), 62.0 (CH), 121.4 (CH), 121.6 (CH), 126.8 (CH), 126.9 (CH), 143.3 (C), 143.8 (C), 157.4 (C). m/z (%): 232 (MH^+, 3), 202 (21), 158 (36), 143 (33), 128 (99), 115 (11), 103 (17), 94 (41), 71 (41), 55 (21), 43 (37). $C_{13}H_{14}NO_3$ [MH^+] requires m/z 232.0974; observed 232.0974.

N-Benzyloxycarbonyl-7β,8β-epoxy-9-azabicyclo[4.2.1]nonan-1-ol (3c)

MCPBA (50-60% purity, 2.680g, 8.57 mmol) was added in portions to a stirred solution of (**10** ⇌ **11**)[1b] (1.942 g, 7.11 mmol) in dichloromethane (67 ml). After stirring for 24 hr a second portion of MCPBA (0.80 g, 2.54 mmol) was added and the mixture stirred for a further 48 hr. The solvent was concentrated under reduced pressure and the residual oil was dissolved in diethyl ether (65 ml) and washed repeatedly with saturated sodium bicarbonate (5 x 20 ml) and brine (20 ml). The ethereal layer was separated, dried over anhydrous magnesium sulphate, filtered and the solvent distilled under reduced pressure. After flash column chromatography using 3:2 diethyl ether:petroleum ether (b.p. 40 - 60°C) the epoxide (**3c**) was isolated as a white solid (1.626 g, 79%) which had m.p. 66 - 68°C after recrystallisation from toluene and petroleum ether (b.p. 40 - 60°C). δ_H (300 MHz, $CDCl_3$), Signals common to both rotamers are quoted in italics: *1.19 - 1.62* (series of m, 5H), *2.04* (m, 2H), *2.22* (m, 1H), 3.33 (d, J = 3.2 Hz, 1H, HCO, major rotamer), 3.37 (d, J = 3.2 Hz, 1H, HCO, minor rotamer), 3.46 (d, J = 3.2 Hz, 1H, HCO, minor rotamer), 3.48 (d, J = 3.2 Hz, 1H, HCO, major rotamer) 4.35 (d, J = 6.9 Hz, 1H, α-N major rotamer), 4.41 (d, J = 6.2 Hz, 1H, α-N minor rotamer), 5.05 & 5.18 (ABq, J = 12.3 Hz, 2H, CH_2Ph, major rotamer), 5.13 & 5.23 (ABq, J = 12.3 Hz, 2H, CH_2Ph, minor rotamer), *7.33* (m, 5H). δ_C (75MHz, $CDCl_3$), The heavy weighting towards the major rotamer resulted in the minor rotamer signals being too weak to be observed): 23.2 (2 x CH_2), 29.1 & 37.6 (2 x CH_2), 54.1 & 55.7 (2 x CHO), 58.0 (CHN), 66.8 (CH_2Ph), 91.4 (COH), 127.9, 128.1 & 128.5 (3 x aryl CH), 136.0 (aryl C), 155.9 (CO). ν_{max} (CH_2Cl_2): 3450brm, 3090w, 3050w, 3020w, 2920s, 2850m, 1670s, 1490w, 1420s, 1390s, 1345s, 1255w, 1235w, 1220w, 1190m, 1145m, 1110m, 1085m, 1050m, 1020m, 990m, 970m cm^{-1}. m/z (%): 289 (M^+, 27), 271 (19), 245 (17), 227 (27), 155 (25), 154 (76), 126 (49), 113 (19), 112 (59), 108 (61), 91 (100). $C_{16}H_{19}NO_4$ [M^+] requires m/z 289.1314; observed 289.131. Found: C, 66.46; H, 6.58; N, 4.66%. $C_{16}H_{19}NO_4$ requires: C, 66.42; H, 6.62; N, 4.84%.

N-Methyl-7β,8β-epoxy-9-azabicyclo[4.2.1]nonan-1-ol (3a)

A solution of (**3c**) (213 mg, 0.74 mmol) in dry THF (4 ml) was injected into a stirred slurry of lithium aluminium hydride in dry THF (2 ml). The solution was refluxed for 30 min under a nitrogen atmosphere and excess hydride was quenched by the addition of water-saturated diethyl ether and then dried with anhydrous sodium sulphate. The colourless solution was filtered through celite and the solvent was evaporated under reduced pressure to afford an oil. Repeated trituration with petroleum ether (b.p. 40 - 60°C) to remove benzyl alcohol left (**3a**) (89 mg, 71%) as a crystalline white solid having m.p. 119 - 120 °C (decomp.) after recrystallisation from ethanol. δ_H (300 MHz, $CDCl_3$): 1.55 (m, 5H), 1.97 (m, 3H), 2.52 (s, 3H), 2.99 (brs, exc, 1H), 3.34 (d, J = 3.3 Hz, 1H, HCO), 3.38 (d, J = 3.3 Hz, 1H, HCO), 3.41 (d, J = 4.9 Hz, 1H, α-N). δ_C (75MHz, $CDCl_3$): 22.7 & 24.0 (2 x CH_2), 28.9 (CH_3), 29.1 & 35.0 (2 x CH_2), 55.3 (CHN), 57.5 & 59.9 (2 x CHO), 89.6 (COH). ν_{max} (CH_2Cl_2): 3560w, 2930s, 2870m, 1465w, 1440w, 1370w, 1340w, 1240w, 1210w, 1190w, 1105w, 1080m, 1020m, 945w, 880m, 860w, 850w, 830w cm^{-1}. m/z (%): 169 (M^+, 72), 149 (17), 140 (46), 127 (26), 126 (78), 113 (36), 112 (100), 98 (21), 84 (42), 70 (40). Found: C, 63.82; H, 9.14; N, 8.31%. $C_9H_{15}NO_2$ requires: C, 63.88; H, 8.93; N, 8.23%.

7β,8β-Epoxy-azabicyclo[4.2.1]nonan-1-ol (3b)

A solution of (**3c**) (981 mg, 3.39 mmol) in absolute ethanol (54 ml) was hydrogenolysed at 1 atmosphere with a catalytic quantity of 5% palladium on charcoal. After 2.5 hr the solution was filtered through a Millipore 0.2μ Millex-FG disposable filter unit. Evaporation of ethanol under reduced pressure yielded (**3b**) (510 mg, 97%) as a gum. δ_H (300 MHz, $CDCl_3$): 1.35 (m, 1H), 1.47 - 1.73 (series of m, 4H), 1.82 (m, 2H), 2.00 (ddd, J = 13.9, 6.9, 4.4 Hz, 1H), 3.36 (m, 2H, HCO), 3.53 (d, J = 6.9 Hz, 1H, α-N). δ_H (300 MHz, CD_3COCD_3): 1.29 (m, 1H), 1.46 (m, 2H), 1.58 - 1.79 (series of m, 4H), 1.89 (m, 1H), 3.27 (d, J = 2.7 Hz, 1H, HCO), 3.31 (d, J = 2.7 Hz, 1H, HCO), 3.37 (d, J = 7.1 Hz, 1H, α-N), 3.72 (brs, 2H, exc, OH & NH). δ_C (75 MHz, $CDCl_3$): 23.2, 23.7, 30.7 & 38.9 (4 x CH_2), 54.6 (CHN), 58.4 & 59.4 (2 x CHO), 91.2 (COH). ν_{max} (CH_2Cl_2): 3560w, 3300brs, 2930s, 2860s, 1425brm, 1340m, 1300m, 1265m, 1185m, 1105s, 1025m, 990m, 980m, 945m, 930m cm^{-1}. m/z (%): 155 (M^+, 47), 126 (100), 112 (74), 98 (72), 85 (28), 72 (58). $C_8H_{13}NO_2$ [M^+] requires m/z 155.0946; observed 155.0946.

Cis-4-[(Benzyloxycarbonyl)amino]-1-[(_p_-toluenesulphonyl)oxycyclooct-2-ene (14)

A solution of _n_-butyllithium (2.5M in hexane, 2.69 ml, 6.72 mmol) was injected into a stirred solution of **(13)** (1.683 g, 6.23 mmol) in THF (28 ml) at -78°C under a nitrogen atmosphere. After 10 min a solution of _p_-toluenesulphonyl chloride (1.510 g, 7.91 mmol) in THF (8 ml) was added and warmed to room temperature. After stirring for 1 hr the reaction was quenched with water (1 ml) and the bulk of the solvent was distilled under reduced pressure. The residual oil was dissolved in diethyl ether (45 ml), dried over anhydrous magnesium sulphate, filtered and the solvent evaporated under reduced pressure. The crude oil was purified by flash chromatography using 1:1 diethyl ether:petroleum ether (b.p. 40 - 60°C) to yield **(14)** (1.740 g, 66%) as a yellow oil. Some decomposition occured during chromatography and also on standing. Full characterisation was not attempted and the tosylate was used immediately in the next reaction. δ_H (300 MHz, $CDCl_3$): 1.27 - 2.08 (series of m, 8H), 2.39 (s, 3H), 3.95 (m, 1H), 4.29 (m, 1H), 4.86 (brd, J = 5.4 Hz, NH), 5.11 (s, 2H, CH_2Ph), 5.28 (m, 1H), 5.40 (dd, J = 10.4, 6.9 Hz, 1H), 7.27 (part of AA'BB', 2H), 7.36 (m, 5H), 7.81 (part of AA'BB', 2H).

***Trans/cis*-4-[(Benzyloxycarbonyl)amino]-1-chlorocyclooct-2-ene (15)**

Lithium chloride (1.102 g, 26 mmol) was dissolved in DMSO (16 ml) and warmed with stirring to 60°C. A solution of **(14)** (1.610 g, 3.75 mmol) was added and stirred for 45 min. The solution was poured into water (15 ml) and extracted with diethyl ether (4 x 20 ml). The combined organic layers were washed with water (7 ml) and brine (5 ml). After drying with anhydrous magnesium sulphate and filtration, the solvent was distilled under reduced pressure. The crude oil was purified by flash chromatography eluting with 3:7 diethyl ether:petroleum ether (b.p. 40 - 60°C). The first fraction to be eluted (87 mg) was unidentifiable, but further elution afforded **(15)** (489 mg, 45%) as a white solid which had m.p. 87 - 88°C after recrystallisation from ethanol. The ^1H NMR indicated a 7:3 *trans*:*cis* mixture of isomers from signal integration; figures quoted in italics are common to both isomers. δ_H (300 MHz, $CDCl_3$): *1.34* (m, 1H), *1.45 - 1.74* (series of m, 3H), *1.86* (m, 2H), *2.13* (m, 2H), *4.44* (brm, 1H), *4.78* (brm, 1H), *4.91* (brm, 1H), *5.08* (s, 2H, CH_2Ph), 5.31 (ddd, J = 10.7, 8.1, 1.3 Hz, 1H, *trans*-isomer), 5.38 (dd, J = 12.4, 6.1, 1H, *cis*-isomer), 5.67 (ddd, J = 10.7, 8.0, 1.4 Hz, 1H, *trans*-isomer), 5.76 (dd, J = 12.1, 6.1 Hz, 1H, *cis*-isomer), *7.33* (m, 5H). δ_C (75 MHz, $CDCl_3$), *Trans*-isomer: 23.5, 24.9, 36.7 & 40.1 (4 x CH_2), 49.3 (CHN), 56.7 (CHCl), *66.6* (CH_2Ph), *128.0* (aryl CH), *128.4* (2 x CH), *130.9* (=CH_2), *132.1* (=CH_2), *136.2* (aryl C), *155.4* (C=O). *Cis*-isomer: 22.7, 23.9, 33.6 & 36.5 (4 x CH_2), 49.2 (CHN), 57.9 (CHCl), *66.6* (CH_2Ph), *128.0* (aryl CH), *128.4* (2 x CH), *130.9* (=CH_2), *132.1* (=CH_2), *136.2* (aryl C), *155.4* (C=O). υ_{max} (CH_2Cl_2): 3440m, 3340w, 3030w, 2940m, 2860w, 1715s, 1505s, 1465w, 1450m, 1395w, 1370w, 1325m, 1215s, 1130w, 1085w, 1025m, 980w, 910w, 800w, 790w cm^{-1}. $^m/z$ (%): 295 (M^+, 0.5), 293 (M^+, 2), 259 (18), 258 (100), 249 (8), 214 (37), 204 (4), 202 (11), 197 (9), 172 (41), 166 (9), 108 (10). Found: C, 65.12; H, 6.67; N, 4.76%. $C_{16}H_{20}NO_2Cl$ requires: C, 65.40; H, 6.86; N, 4.77%.

N-(Benzyloxycarbonyl)-9-azabicyclo[4.2.1]non-7-ene (17)

Sodium hydride (60% dispersion in mineral oil, 97 mg, 2.43 mmol) was slurried with THF (2 ml) under a nitrogen atmosphere. A solution of **(15)** (341 mg, 1.16 mmol) in THF (8 ml) was injected *via* syringe and stirred at ambient temperature for 1.5 hr and then refluxed for a further 2.5 hr. Excess hydride was destroyed by quenching with the minimum quantity of water at -78°C. The bulk of the solvent was distilled under reduced pressure and the oily residue was partitioned between diethyl ether (18 ml) and water (7 ml). After washing with further water (5 ml), the organic layer was separated, dried with anhydrous magnesium sulphate, filtered and the solvent distilled under vacuum. Purification by flash chromatography using 1:4 diethyl ether: petroleum ether (b.p. 40 - 60°C) afforded firstly the aziridine **(16)** (31 mg, 10%) as a pale yellow oil. δ_H (300 MHz, $CDCl_3$), Double irradiation of the two aziridine protons allowed for full measurement of the coupling constants: 1.22 - 1.44 (m, 2H), 1.51 - 1.84 (series of m, 3H), 1.99 (m, 1H), 2.15 (dddd, J = 13.8, 5.8, 3.4, J ≈ 3 Hz, 1H), 2.28 (m, 1H), 2.63 (ddd, J = 10.1, 6.3, 3.4 Hz, 1H, α-N), 3.07 (ddd, J = 6.3, 1.7, 1.1 Hz, 1H, α-N), 5.13 (s, 2H, CH_2Ph), 5.57 (dd, J = 11.1, 1.1 Hz, 1H, HC=), 5.75 (dddd, J = 11.1, 7.6, 5.8, 1.7 Hz, 1H, HC=), 7.35 (m, 5H). δ_C (75 MHz, $CDCl_3$): 25.7, 26.7, 27.1 & 28.8 (4 x CH_2), 40.0 & 44.4 (2 x CHN), 68.0 (CH_2Ph), 122.3 (=CH_2), 128.1, 128.2 & 128.5 (3 x aryl CH), 134.9 (=CH), 136.0 (aryl C), 163.8 (C=O). υ_{max} (CH_2Cl_2): 3030w, 2940m, 2860w, 1715s, 1495w, 1450w, 1425w, 1380w, 1270brs, 1215s, 1170w, 1110w, 1090w, 1045w, 1025w, 910w cm^{-1}. $^m/z$ (%): 257 (M^+, 1), 171 (10), 170 (16), 122 (14), 92 (9), 91 (100). $C_{16}H_{19}NO_2$ [M^+] requires $^m/z$ 257.1416; observed 257.1416.

Further elution with 3:7 diethyl ether:petroleum ether (b.p. 40 - 60°C) yielded **(17)** (86 mg, 28%) as a colourless oil; the signals quoted below in italics are common to both rotamers (in a 1:1 ratio). δ_H (300

MHz, $CDCl_3$): *1.27 - 1.66* (series of m, 6H), *1.94* (m, 1H), *2.07* (m, 1H), 4.72 (brd, J = 6.1 Hz, 1H, α-N), 4.78 (brd, J = 6.0 Hz, 1H, α-N), *5.13 & 5.18* (ABq, J = 12.5 Hz, 2H, CH_2Ph), 5.72 (dd, J = 6.8, 2.3 Hz, 1H), 5.75 (dd, J = 6.8, 2.3 Hz, 1H), *7.35* (m, 5H). δ_C (75 MHz, $CDCl_3$): 24.0 & 24.2 (2 x CH_2), 30.8 & 31.7 (2 x CH_2), 60.9 & 61.3 (2 x CHN), *127.7, 127.8 & 128.4* (3 x aryl CH), 130.9 & 131.0 (2 x =CH), *137.1* (aryl C), *153.2* (C=O). υ_{max} (CH_2Cl_2): 3030w, 2930s, 2860m, 1695s, 1615w, 1585w, 1495m, 1430s, 1365m, 1350m, 1315s, 1265brw, 1230w, 1210w, 1195w, 1180w, 1140m, 1115s, 1100s, 1095s, 1070s, 1025w, 975m, 960w cm^{-1}. $^m/z$ (%): 257 (M^+, 11), 171 (12), 170 (21), 92 (9), 91 (100). $C_{16}H_{19}NO_2$ [M^+] requires $^m/z$ 257.1416; observed 257.1418.

In a repeat experiment, the yield of **(17)** was increased to 40% by using a 6:1 mixture of THF:DME as solvent and stirring at 60°C for 2.5 hr, rather than refluxing. The yield of aziridine **(16)** was reduced to 3% using these conditions.

N-(Benzyloxycarbonyl)-7β,8β-epoxy-9-azabicyclo[4.2.1]nonane (1c)

A solution of **(17)** (39 mg, 0.15 mmol) in dichloromethane (4 ml) was epoxidised with MCPBA (50 - 60% purity, 57 mg, 0.18 mmol) using an identical procedure to that described for the conversion of **(10 ⇌ 11)** into **(3c)**. Purification of the crude product by flash chromatography using 1:1 diethyl ether:petroleum ether (b.p. 40 - 60°C) afforded the epoxide **(1c)** (34 mg, 84%) as a colourless oil. The chemical shifts quoted in italics refer to signals common to both rotamers (in a 1:1 ratio). δ_H (300 MHz, $CDCl_3$): *1.48* (m, 6H), *1.90* (m, 1H), *2.03* (m, 1H), 3.36 (d, J = 3.0 Hz, 1H, HCO), 3.37 (d, J = 3.0 Hz, 1H, HCO), 4.35 (d, J = 6.2 Hz, 1H, α-N), 4.41 (d, J = 6.2 Hz, 1H, α-N), *7.33* (m, 5H). δ_C (75 MHz, $CDCl_3$): *24.3* (2 x CH_2), 28.8 & 29.6 (2 x CH_2), 55.9 & 56.0 (2 x CHO), 56.8 & 57.3 (2 x CHN), *66.7* (CH_2Ph), *127.7, 127.9 & 128.4* (3 x aryl CH), *136.8* (aryl C), *155.1* (C=O). υ_{max} (CH_2Cl_2): 3040w, 2930m, 2860w, 1695s, 1495w, 1425s, 1350w, 1320m, 1295w, 1195w, 1155w, 1115m, 1095m, 1035w, 1025w, 980w, 900w, 850m cm^{-1}. $^m/z$ (%): 273 (M^+, 22), 166 (13), 138 (8), 110 (5), 92 (8), 91 (100). $C_{16}H_{19}NO_3$ [M^+] requires $^m/z$ 273.1365; observed 273.1363. An alternative route to **(1c)** from **(3c)** is described below.

N-(Benzyloxycarbonyl)-7β-hydroxy-9-azabicyclo[4.2.1]nonane (5c)

A solution of **(17)** (78 mg, 0.30 mmol) in THF (4 ml) was cooled with stirring to -78°C under a nitrogen atmosphere. Borane:THF complex (1M in THF, 0.18 ml, 0.18 mmol) was injected and the solution was slowly warmed to room temperature. After 2.5 hr the reaction was quenched by the sequential addition of water (200 µl), sodium hydroxide solution (6M, 200 µl) and hydrogen peroxide solution (30 weight %, 200 µl). The reaction mixture was stirred for a further 10 min, the bulk of the solvent distilled under reduced pressure and the residue partitioned between diethyl ether (20 ml) and water (5 ml) and then washed with further water (5 ml) and brine (5 ml). The diethyl ether layer was dried over anhydrous magnesium sulphate, filtered and the solvent distilled in vacuum. The resultant crude oil was purified by flash chromatography using 1:1 diethyl ether:petroleum ether (b.p. 40 - 60°C) to afford **(5c)** (59 mg, 71%) as a colourless oil. The chemical shifts quoted in italics refer to signals common to both rotamers. δ_H (300 MHz, $CDCl_3$): *1.24 - 1.64* (m, 4H), *1.81 - 2.16* (series of m, 6H), *2.89* (brs, 1H, exch), *4.17* (m, 1H), *4.49* (m, 1H), *5.05 & 5.18* (ABq, J = 12.4 Hz, 2H, CH_2Ph), *7.33* (s, 5H). δ_C (75 MHz, $CDCl_3$): 23.8, 23.9, 24.0 & 24.1 (4 x CH_2), 30.5, 31.5, 32.0 & 33.1 (4 x CH_2), 40.1 & 40.7 (2 x CH_2), 55.2 & 55.8 (2 x CHN), 65.2 & 65.4 (2 x CHN), 66.5 & 66.6 (2 x CH_2Ph), 77.4 & 78.4 (2 x CHOH), *127.4 & 127.5* (2 x aryl CH), 127.8 (aryl CH), 128.3 (aryl CH), 136.7 & 136.8 (2 x aryl C), 154.3 & 154.5 (2 x C=O). υ_{max} (CH_2Cl_2): 3600w, 3460brw, 3040w, 2940w, 2860w, 1690s, 1500w, 1445w, 1420m, 1360w, 1335m, 1215w, 1190w, 1115m, 1095m, 1020w, 1000w, 965w, 940w, 910 cm^{-1}. $^m/z$ (%): 275 (M^+, 17), 184 (11), 168 (5), 141 (4), 140 (40), 96 (20), 91 (100). $C_{16}H_{21}NO_3$ [M^+] requires $^m/z$ 275.1521; observed 275.1524.

Norhomotropan-7β-ol (5b)

The carbamate **(5c)** (49 mg, 0.18 mmol) was hydrogenolysed in absolute ethanol (5 ml) using the procedure described for the conversion of **(3c)** into **(3b)**. The amine **(5b)** (24 mg, 96%) was isolated as a thick oil after distillation of solvent under vacuum. δ_H (300 MHz, CD_3OD): 1.38 - 1.81 (series of m, 8H), 1.88 (ddd, J = 14.5, 8.7, 2.8 Hz), 1.97 (ddd, J = 14.5, 6.2, 3.3 Hz), 3.30 (brd overlapping with solvent signal, 1H, α-N), 3.77 (m, 1H, α-N), 4.12 (dd, J = 6.2, 2.8 Hz, 1H, α-OH). δ_C (75 MHz, $CDCl_3$): 24.3, 24.7, 33.4, 35.4 & 42.2 (5 x CH_2), 57.3 & 66.5 (2 x CHN), 79.8 (CHOH). υ_{max} (CH_2Cl_2): 3600w, 3300brw, 2930s, 2860w, 1460w, 1440w, 1255w, 1180w, 1120w, 1050w, 995w, 950w, 905m cm^{-1}. $^m/z$ (%): 141 (M^+, 31), 124 (31), 98 (33), 97 (100), 96 (17), 84 (17), 82 (51), 70 (11), 69 (30), 68 (36). $C_8H_{15}NO$ [M^+] requires $^m/z$ 141.1154; observed 141.1153.

1β-Hydroxy-2β,3β-epoxy-4β-[(benzyloxycarbonyl)amino]cyclooctane (20)

Using the procedure of Soai;[20] methanol (300 μl) was added over 45 min *via* a syringe pump to a refluxing solution of **(3c)** (126 mg, 0.44 mmol) and sodium borohydride (42 mg, 1.11 mmol) and the solution was then refluxed for 2 hr. After cooling to room temperature, saturated ammonium chloride solution (1 ml) was added to destroy excess hydride. Diethyl ether (20 ml) was added and washed with saturated ammonium chloride solution (12 ml). The ethereal layer was separated, dried with anhydrous magnesium sulphate, filtered and the solvent distilled under reduced pressure. The residual oil was purified by flash chromatography using 3:2 diethyl ether:petroleum ether (b.p. 40 - 60°C) to afford **(20)** (92 mg, 73%) as a colourless oil. In subsequent preparations the yield of **(20)** could be improved to 98% by refluxing in THF for 3 hr with 2 M equivalents of sodium borohydride (without the addition of methanol). The product isolated using this procedure was pure enough for further reactions without chromatography. δ_H (300 MHz, $CDCl_3$): 1.38 (m, 2H), 1.66 (m, 4H),1.86 (m, 2H), 2.91 (dd, J = 4.5, 3.6 Hz, 1H, HCO), 3.11 (t, J = 4.5, J ≈ 4.8 Hz, 1H, HCO), 3.62 (brs, 1H, exch), 4.42 (brd, J ≈ 3.4 Hz, 1H), 4.47 (m, 1H), 5.06 (s, 2H, CH_2Ph), 7.15 (d, J = 9.3 Hz, 1H, NH), 7.31 (m, 5H). δ_C (75 MHz, $CDCl_3$): 22.0, 22.9, 31.3 & 32.0 (4 x CH_2), 46.5 (CHN), 57.1 & 58.6 (2 x CHO), 65.5 (CHOH), 66.4 (CH_2Ph), 127.8, 127.9 & 128.3 (3 x aryl CH), 136.8 (aryl C), 156.2 (C=O). υ_{max} (CH_2Cl_2): 3570brw, 3330brw, 3030w, 2940m, 2870w, 1710s, 1525m, 1450w, 1380w, 1340w, 1305w, 1235m, 1165w, 1130w, 1085w, 1070w, 1040m, 1025w, 1005w, 925w, 905m cm^{-1}. $^m/z$ (%): 291 (M^+, 3), 156 (6), 146 (5), 108 (13), 91 (100). $C_{16}H_{21}NO_4$ [M^+] requires $^m/z$ 291.1471; observed 291.1474.

Oxidation of (20) to (3c)

Conversion of **(20)** back into **(3c)** was possible using the standard Jones procedure.[1b] Chromic acid, prepared from chromium trioxide (12.35 g), concentrated sulphuric acid (11.5 ml) and water (20 ml), was added dropwise to a solution of **(20)** (34 mg, 0.12 mmol) in dry acetone (6 ml). A persistent orange colouration indicated complete oxidation and excess oxidant was destroyed by dropwise addition of isopropanol. The mixture was filtered through celite and the bulk of the solvent was removed under vacuum. The residue was dissolved in dichloromethane and washed three times with brine. The organic layer was dried over magnesium sulphate, filtered, and the solvent removed under vacuum to yield **(3c)** (32 mg, 95%) which appeared pure from the 90 MHz ^1H NMR spectrum.

1β-[(*p*-Toluenesulphonyl)oxy]-2β,3β-epoxy-4β-[(benzyloxycarbonyl)amino]-cyclooctane (21)

A solution of **(20)** (520 mg, 1.78 mmol) in dry THF (11 ml) was stirred at 0°C under a nitrogen atmosphere. A solution of *n*-butyllithium (2.5M in hexane, 0.86 ml, 2.15 mmol) was injected and stirred for 5 min, before the addition of *p*-toluenesulphonyl chloride (443 mg, 2.32 mmol) in THF (4 ml). The solution was warmed to room temperature and stirred a further 1.5 hr and then quenched with water (0.5 ml). Diethyl ether (30 ml) was added, the solution transferred to a separating funnel, and washed with water (2 x 7 ml) and brine (7 ml). After separation the ethereal layer was dried over anhydrous magnesium sulphate, filtered, and the solvent distilled under reduced pressure. The tosylate **(21)** (728 mg, 92%) was isolated as a foam by purification of the crude oil using flash chromatography, eluting with 1:1 diethyl ether:petroleum ether (b.p. 40 - 60°C). δ_H (300 MHz, $CDCl_3$): 1.08 - 1.36 (brm, 2H), 1.44 - 1.73 (series of m, 5H), 2.02 (m, 1H), 2.42 (s, 3H, Me), 3.11 (m, 2H, CHO), 4.11 (m, 1H, α-N), 4.91 (brd, J = 9.1 Hz, 1H, α-OSO_2Ar), 5.09 (s, 2H, CH_2Ph), 5.41 (brd, J = 8.8 Hz, 1H, NH), 7.29 - 7.33 (s, 5H plus, part of AA'BB', 2H), 7.80 (part of AA'BB', 2H). δ_C (75 MHz, $CDCl_3$): 21.7 (CH_3), 22.3, 23.3, 27.3 & 27.4 (4 x CH_2), 49.3 (CHN), 59.1 & 59.5 (2 x CHO), 66.8 (CH_2Ph), 79.4 ($CHOSO_2$), 127.8, 128.0, 128.1, 128.5 & 130.0 (5 x aryl CH), 133.7 (aryl C), 136.4 (aryl CCH_2), 145.0 (aryl CSO_3), 155.6 (C=O). υ_{max} (CH_2Cl_2): 3440w, 3030w, 2940w, 2870w, 1720s, 1600w, 1505m, 1455w, 1365m, 1220w, 1190m, 1185s, 1095w, 1045w, 1025w, 900m, 855m, 810w cm^{-1}. $^m/z$ (%): 445 (M^+,9), 395 (23), 377 (21), 363 (74), 352 (21), 345 (58), 335 (61), 329 (59), 320 (100). $C_{23}H_{27}NO_6$ [M^+] requires $^m/z$ 445.1559; observed 445.1558.

1α-Chloro-2β,3β-epoxy-4β-[(benzyloxycarbonyl)amino]cyclooctane (22)

Lithium chloride (870 mg, 21 mmol) and **(21)** (1.538 g, 3.46 mmol) were added to DMSO (17 ml) and heated to 60°C with stirring for 1.5 hr. The solution was poured into an equal volume of water and extracted repeatedly with diethyl ether (3 x 25 ml). The organic layers were combined and washed with water (2 x 7 ml) and brine (5 ml), before drying over anhydrous magnesium sulphate. Filtration and distillation of solvent under reduced pressure gave a crude oil which was purified by flash chromatography using 3:7 diethyl ether:petroleum ether (b.p. 40 - 60°C) to afford **(22)** (928 mg, 87%) as a white solid. An analytical

sample was prepared by recrystallisation from ethanol (m.p. 94 - 95°C). δ_H (300 MHz, $CDCl_3$): 1.43 (m, 2H), 1.58 (m, 1H), 1.66 - 1.92 (series of m, 3H), 2.04 (m, 2H), 3.14 (dd, J = 8.9, 4.3 Hz, HCO, β-Cl), 3.37 (t, J ≈ 4.3 Hz, HCO, β-N), 4.24 (m, 2H, α-N & α-Cl), 5.08 & 5.12 (ABq, J = 12.2 Hz, 3H, CH_2Ph & NH), 7.35 (m, 5H). δ_C (75 MHz, $CDCl_3$): 22.6, 24.0, 29.8 & 36.2 (4 x CH_2), 49.3 (CHN), 58.6 & 59.1 (2 x CHO), 61.7 (CHCl), 66.9 (CH_2Ph), 128.1, 128.2 & 128.5 (3 x aryl CH), 136.2 (aryl C), 155.6 (C=O). υ_{max} (CH_2Cl_2): 3680w, 3430w, 2940w, 2860w, 1720s, 1605w, 1500m, 1450w, 1335w, 1310w, 1220m, 1165w, 1130w, 1105w, 1055w, 1035w, 895 cm^{-1}. $^m/_z$ (%): 311(M^+, 12), 309 (M^+, 32), 273 (18), 230 (11), 122(6), 108 (21), 107 (7), 92 (7), 91 (100). Found: C, 62.17; H, 6.41; N, 4.64%. $C_{16}H_{20}NO_3Cl$ requires: C, 62.02; H, 6.51; N, 4.52%.

N-(Benzyloxycarbonyl)-7β,8β-epoxy-9-azabicyclo[4.2.1]nonane (1c)

To a solution of **(22)** (414 mg, 1.34 mmol) in THF:DME (5:1, 8 ml) was added sodium hydride (60% dispersion in mineral oil, 107 mg, 2.68 mmol) and stirred for 2 hr. The solution was cooled to -78°C and excess hydride was destroyed by the addition of the minimum quantity of water. Diethyl ether (15 ml) was added and washed with water (2 x 5 ml) and brine (5 ml). The organic layer was dried with anhydrous magnesium sulphate, filtered, and the solvent distilled under reduced pressure. The crude oil was purified by flash chromatography, eluting with 2:3 diethyl ether:petroleum ether (b.p. 40 - 60°C), to afford **(1c)** (358 mg, 98%) as a colourless oil. The epoxide prepared using this method was identical to a sample prepared by epoxidation of the alkene **(17)**.

1β-Hydroxy-2α,3α-epoxy-4β-[(benzyloxycarbonyl)amino]cyclooctane (23)

MCPBA (50 - 60% purity, 4.21 g, 13.4 mmol) was added to stirred solution of **(13)** (3.07 g, 11.2 mmol) in dry dichloromethane and stirring was continued at room temperature for 3 hr. The solution was transferred to a separating funnel and washed with saturated sodium bicarbonate solution (2 x 20 ml), dried over anhydrous magnesium sulphate, filtered and the solvent distilled under vacuum. The residual oil was purified by flash chromatography, eluting with diethyl ether, to afford **(23)** (3.10 g, 95%) as a white solid which had m.p. 125 - 126°C after recrystallisation from ethanol. δ_H (300 MHz, $CDCl_3$): 1.39 - 1.70 (series of m, 6H), 1.86 (brm, 2H), 2.95 (dd, J = 4.7, 9.3 Hz, 1H, HCO), 3.03 (dd, J = 4.7, 8.2 Hz, HCO), 3.56 (m, 1H), 3.70 (m, 1H), 4.16 (brs, 1H, exch), 5.01 (m, 1H, NH), 5.29 (s, 2H, CH_2Ph), 7.34 (m, 5H). δ_C (75 MHz, $CDCl_3$): 23.2, 24.4, 33.6 & 34.8 (4 x CH_2), 51.3 (CHN), 57.9 & 60.3 (2 x CHO), 66.7 (CH_2Ph), 71.2 (CHOH), 128.0 (2 x aryl CH), 128.4 (aryl CH), 136.4 (aryl C), 155.7 (C=O). υ_{max} (CH_2Cl_2): 3600w, 3430w, 2930m, 2860w, 1720s, 1510m, 1450w, 1315brw, 1225m, 1145w, 1090w, 1045m, 1025w, 965w, 900w cm^{-1}. $^m/_z$ (%): 291 (M^+, 45), 256 (22), 237 (58), 213 (29), 200 (22), 184 (46), 167 (77), 108 (49), 91 (100). $C_{16}H_{21}NO_4$ [M^+] requires $^m/_z$ 291.1471; observed 291.1474. Found: C, 66.28; H, 7.46; N, 5.00%. $C_{16}H_{21}NO_4$ requires: C, 65.96; H, 7.27; N, 4.81%.

2α,3α-Epoxy-4β-[(benzyloxycarbonyl)amino]cyclooctanone (24)

A solution of **(23)** (551 mg, 1.90 mmol) in acetone (25 ml) was oxidised with Jones reagent using the procedure described previously for the conversion of **(20)** into **(3c)**. Recrystallisation of the crude product from ethanol afforded **(24)** (523 mg, 96%) as a crystalline white solid (m.p. 145 - 146°C). δ_H (300 MHz, $CDCl_3$): 1.48 (m, 1H), 1.62 - 1.94 (series of m, 5H), 2.35 (ddd, J = 13.4, 10.2, 3.7 Hz, 1H), 2.63 (m, 1H), 3.04 (m, 1H, α-N), 3.36 (m, 1H, HCO), 3.82 (d, J = 5.2 Hz, 1H, HCO), 5.03 (s, 2H, CH_2Ph), 5.61 (brd, J = 6.1 Hz, 1H, NH), 7.30 (s, 5H). δ_C (75 MHz, $CDCl_3$): 24.2, 24.7, 33.3 & 42.6 (4 x CH_2), 52.3 (CHN), 57.5 & 58.5 (2 x CHO), 66.6 (CH_2Ph), 128.0 (2 x aryl CH), 128.4 (aryl CH), 136.4 (aryl C), 155.5 (NC=O), 206.2 (C=O). υ_{max} (CH_2Cl_2): 3430w, 3030w, 2940w, 1725s, 1505m, 1450w, 1375w, 1315w, 1220m, 1185w, 1135w, 1100w, 1070w, 1020m, 950w, 915w, 845w cm^{-1}. $^m/_z$ (%): 289 (M^+,8), 183 (3), 112 (4), 108 (15), 107 (9), 92 (9), 91 (100). Found: C, 66.46; H, 6.46; N, 5.02%. $C_{16}H_{19}NO_4$ requires: C, 66.42; H, 6.62; N, 4.84%.

1α-Hydroxy-2α,3α-epoxy-4β-[(benzyloxycarbonyl)amino]cyclooctane (25)

A solution of **(24)** (1.105 g, 3.82 mmol) and sodium borohydride (350 mg, 9.46 mmol) in THF (45 ml) was refluxed for 1.5 hr. Saturated ammonium chloride solution (2 ml) was added to destroy excess hydride and the bulk of the solvent was distilled under reduced pressure. The residual oil was dissolved in diethyl ether (30 ml) and washed with saturated ammonium chloride solution (10 ml) and water (10 ml). The organic layer was dried over anhydrous magnesium sulphate, filtered and the solvent distilled under reduced pressure. The crude oil was purified by flash chromatography, eluting with 7:3 diethyl ether:petroleum

ether (b.p. 40 - 60°C), to afford **(25)** (982 mg, 88%) as a foam. The foam was triturated to a white solid with petroleum ether (b.p. 40 - 60°C) and an analytical sample was prepared by recrystallisation from ethanol (m.p. 103 - 104 °C). The ^{1}H NMR spectrum was broad when recorded in $CDCl_3$, but signals were better resolved in CD_3COCD_3. δ_H (300 MHz, $CDCl_3$): 1.20 (m, 1H), 1.39 - 1.66 (m, 4H), 1.82 (m, 2H), 2.09 (m, 1H), 2.75 (vbrs, 1H, exch), 3.04 (brm, 2H, HCO), 4.42 (brm, 2H, α-N & α-OH), 5.08 (m, 3H, CH_2Ph & NH), 7.33 (m, 5H). δ_H (300 MHz, CD_3COCD_3): 1.34 (m, 1H), 1.52 - 1.89 (series of m, 6H), 2.01 (m, 1H), 2.93 (dd, J = 9.4, 4.2 Hz, 1H, HCO, β-N), 3.06 (t, J = 4.2 Hz, 1H, HCO, β-OH), 3.41 (brs, 1H, exch), 4.39 (m, 1H), 4.52 (brm, 1H), 5.05 (s, 2H, CH_2Ph), 6.44 (brd, J = 6.8 Hz, NH, 1H), 7.35 (m, 5H). δ_C (75 MHz, $CDCl_3$): 19.3 & 25.0 (2 x CH_2), 32.6 (2 x CH_2), 48.8 (CHN), 57.2 & 59.3 (2 x CHO), 65.4 (CHOH), 66.7 (CH_2Ph), 128.1 (2 x aryl CH), 128.5 (aryl CH), 136.5 (aryl C), 156.0 (C=O). υ_{max} (CH_2Cl_2): 3560m, 3430m, 3350w, 3040w, 2940s, 2865m, 1720s, 1505s, 1455m, 1405w, 1305w, 1235s, 1220s, 1180w, 1165w, 1140w, 1095s, 1025s, 985w, 930w, 910w, 890m cm^{-1}. ^{m}/z (CI, %): 292 (MH^+, 100), 248 (9), 201 (10), 156 (27), 140 (16), 108 (26). $C_{16}H_{22}NO_4$ [MH^+] requires ^{m}/z 292.1549; observed 292.1549. Found: C, 65.95; H, 7.13; N, 4.72%. $C_{16}H_{19}NO_4$ requires: C, 65.96; H, 7.27; N, 4.81%.

1α-[(*p*-toluenesulphonyl)oxy]-2α,3α-epoxy-4β-[(benzyloxycarbonyl)amino]cyclooctane (26)

A solution of **(25)** (307 mg, 1.05 mmol) was tosylated using the procedure described previously for the tosylation of **(20)**. The residual oil was purified by flash chromatography, eluting with 4:1 diethyl ether:petroleum ether (b.p. 40 - 60°C), to afford **(26)** (451 mg, 96%) as a gum. The ^{1}H NMR spectrum was broad when recorded in $CDCl_3$, but signals were better resolved in CD_3COCD_3. δ_H (300 MHz, CD_3COCD_3): 1.38 - 1.59 (m, 2H), 1.61 - 1.83 (series of m, 5H), 1.98 (m, 1H), 2.43 (s, 3H), 2.90 (dd, J = 9.3, 4.2 Hz, 1H, HCO, β-N), 3.12 (t, J = 4.2 Hz, 1H, HCO, β-OSO_2Ar), 4.13 (m, 1H, α-N), 5.08 (s, 2H, CH_2Ph), 5.20 (ddd, J = 6.2, 3.7, 2.2 Hz, 1H, α-OSO_2Ar), 6.48 (m, 1H, NH), 7.38 (m, 5H, plus part of AA'BB', 2H), 7.89 (part of AA'BB', 2H). δ_C (75 MHz, $CDCl_3$): 20.7 (CH_2), 21.6 (CH_3), 23.8, 31.4 & 32.5 (3 x CH_2), 49.5 (CHN), 58.4 & 57.7 (2 x CHO), 66.5 (CH_2Ph), 75.7 ($CHOSO_2Ar$), 127.8 (2 x aryl CH), 128.1, 128.4 & 129.4 (3 x aryl CH), 133.7 (aryl CMe), 136.5 (aryl CCH_2), 144.5 (aryl CSO_2), 155.3 (C=O). υ_{max} (CH_2Cl_2): 3440m, 3040w, 2940m, 2865w, 1725s, 1600w, 1510s, 1455m, 1395w, 1360s, 1325w, 1305w, 1220s, 1190s, 1175s, 1140w, 1120w, 1095m, 1080m, 1040m, 1025m, 1015m, 930s, 880w, 825m, 815m cm^{-1}. ^{m}/z (%): 445 (M^+, 1), 273 (7), 187 (45), 186 (18), 170 (10), 169 (100), 155 (40), 149 (15), 138 (54), 123 (14), 109 (21), 95 (29), 91 (56). $C_{23}H_{27}NO_6S$ [M^+] requires ^{m}/z 445.1559; observed 445.1557.

N-(Benzyloxycarbonyl)-7α,8α-epoxy-9-azabicyclo[4.2.1]nonane (2c)

Sodium hydride (60% dispersion, 97 mg, 2.43 mmol) and THF (1 ml) were stirred in a 25ml two-necked flask under a nitrogen atmosphere at 0°C. A solution of **(26)** (451 mg, 1.01 mmol) in THF (4 ml) was injected, warmed to room temperature and stirred for 3 hr. The reaction was worked up using an identical procedure to that described for the *exo*-epoxide **(1c)**. Purification of the resultant crude oil by flash chromatography, eluting with 1:1 diethyl ether:petroleum ether (b.p. 40 - 60°C), afforded **(2c)** (258 mg, 93%) as an oil which solidified on standing. An analytical sample was prepared by recrystallisation from toluene and petroleum ether (b.p. 40 - 60°C) to give a white solid (m.p. 49 - 50°C). The NMR shifts given in italics refer to signals common to both rotamers (in a 1:1 ratio). δ_H (300 MHz, $CDCl_3$): *1.43* (m, 2H), *1.71 - 2.11* (series of m, 6H), 3.87 (dd, J = 7.4, 3.6 Hz, 1H, HCO), 3.89 (dd, J = 7.4, 3.6 Hz, 1H, HCO), *4.23* (m, 2H, α-N), *5.10* (s, 2H, CH_2Ph), *7.33* (m, 5H). δ_C (75 MHz, $CDCl_3$): 25.0 & 25.2 (2 x CH_2), 28.1 & 29.0 (2 x CH_2), 55.6 & 55.8 (2 x CHO), 62.6 & 62.7 (2 x CHN), *66.6* (CH_2Ph), *127.8, 127.9 & 128.4* (3 x aryl CH), *136.8* (aryl C), *152.7* (C=O). υ_{max} (CH_2Cl_2): 3040w, 2925m, 2860w, 1695s, 1440s, 1385w, 1370w, 1350w, 1325m, 1315m, 1300w, 1230w, 1200w, 1190w, 1155w, 1120m, 1095m, 1080w, 1030w, 1015w, 970w, 940w, 910m, 865w, 840w cm^{-1}. ^{m}/z (%): 273 (M^+, 28), 138 (12), 92 (8), 91 (100). $C_{16}H_{19}NO_3$ [M^+] requires ^{m}/z 273.1365; observed 273.1370. Found: C, 70.06; H, 7.02; N, 5.14%. $C_{16}H_{19}NO_3$ requires: C, 70.31; H, 7.02; N, 5.12%.

N-Methyl-7β,8β-epoxy-9-azabicyclo[4.2.1]nonane (1a)

A solution of **(1c)** (107 mg, 0.39 mmol) in dry THF (5 ml) was cooled with stirring to 0°C under a nitrogen atmosphere. A solution of DIBAH (1M in hexane, 2.16 ml, 2.16 mmol) was injected, warmed to room temperature and stirred for 3 hr. Excess hydride was destroyed by addition of the minimum quantity of water-saturated diethyl ether, the solution was dried over anhydrous sodium sulphate and then filtered through celite. The colourless solution was acidified with hydrogen chloride gas at 0°C and the solvent was distilled under reduced pressure. The residual white solid was repeatedly triturated with diethyl ether to remove benzyl alcohol yielding **(1a.HCl)** (60 mg, 81%) as a hygroscopic white solid. The amine was

volatile and NMR spectra of the free amine **(1a)** were recorded by dissolving the salt in the minimum quantity of $CDCl_3$, basifying with ammonia gas and filtering. The amine was stored as the hydrochloride salt. δ_H (300 MHz, $CDCl_3$): 1.33 - 1.52 (series of m, 4H), 1.58 (m, 2H), 1.74 (m, 2H), 2.55 (s, 3H, CH_3), 3.18 (dd, J = 7.0, 1.6 Hz, 2H, α-N), 3.43 (s, 2H, HCO). δ_C (75 MHz, $CDCl_3$): 24.7 (2 x CH_2), 30.8 (2 x CH_2), 46.5 (CH_3), 61.1 (2 x CHN), 63.6 (2 x CHO). υ_{max} ($CDCl_3$): 3030w, 2930m, 2850w, 1445w, 1340w, 1305w, 1220w, 1165w, 1125w, 1080w, 1035w, 950w, 845w cm^{-1}. m/z (%) [measured using **(1a.HCl)**]: 153 (M^+ - HCl, 41), 139 (23), 124 (22), 110 (100), 96 (85), 82 (48), 68 (36). $C_9H_{15}NO$ [M^+ - HCl] requires m/z 153.1154; observed 153.1154.

7β,8β-Epoxy-9-azabicyclo[4.2.1]nonane (1b)

A solution of **(1c)** (50 mg, 0.18 mmol) in dry methanol (4 ml) was hydrogenolysed using the procedure described for the conversion of **(3c)** into **(3b)**. Distillation of solvent under reduced pressure afforded **(1b)** (22 mg, 86%) as a waxy solid. δ_H (300 MHz, $CDCl_3$): 1.32 - 1.83 (series of m, 8H), 2.25 (s, 1H, NH), 3.34 (s, 2H, HCO), 3.42 (dd, J = 6.7, 1.7, 2H, α-N). δ_C (75 MHz, $CDCl_3$): 24.7 (2 x CH_2), 31.0 (2 x CH_2), 56.4 (2 x CHO), 58.9 (2 x CHN). υ_{max} (CH_2Cl_2): 3350w, 3030w, 2930s, 2860m, 1445w, 1425w, 1395w, 1340w, 1310w, 1265brw, 1215w, 1200w, 1160w, 1135w, 1110w, 1040w, 1010w, 950w, 930w, 860m, 840m, 825w, 815w, 795w cm^{-1}. m/z (%): 139 (M^+, 54), 110 (61), 97 (27), 96 (100), 83 (43), 82 (50), 80 (20), 68 (28), 55 (43). $C_8H_{13}NO$ [M^+] requires m/z 139.0997; observed 139.0998.

Homotropan-7α-ol (6a)

To a slurry of lithium aluminium hydride (21 mg, 0.55 mmol) in dry THF (1 ml) was injected a solution of **(2c)** (95 mg, 0.35 mmol) in THF (5 ml) which was then refluxed under nitrogen for 3 hr. Excess hydride was destroyed by the dropwise addition of the minimum quantity of water-saturated diethyl ether and the solution was then dried over anhydrous sodium sulphate. Filtration through celite and distillation of solvent under reduced pressure gave an oil which was purified by flash chromatography, eluting with 1:9 methanol:dichloromethane saturated with ammonia gas, to afford **(6a)** (38 mg, 70%) as a waxy solid. δ_H (300 MHz, $CDCl_3$): 1.40 (ddd, J = 13.7, 6.4, 3.1 Hz, 1H), 1.46 (m, 1H), 1.66 (m, 5H), 1.90 (m, 2H), 2.50 (s, 3H, CH_3), 2.63 (ddd, J = 13.7, 10.4, 9.5 Hz, 1H), 3.18 (m, 1H, α-N), 3.24 (m, 1H, α-N), 4.55 (dt, J = 10.4, 6.4, 6.4 Hz, 1H, α-OH). δ_C (75 MHz, $CDCl_3$): 24.8 (2 x CH_2), 26.7 & 33.6 (2 x CH_2), 39.2 (CH_3), 39.9 (CH_2), 61.1 & 65.3 (2 x CHN), 71.7 (CHOH). υ_{max} (CH_2Cl_2): 3620m, 3370brm, 3040w, 2920s, 1465w, 1375w, 1260brw, 1180w, 1125w, 1090w, 1050m, 1010w, 985w, 970w, 920w cm^{-1}. m/z (%): 155 (M^+, 50), 149 (17), 138 (80), 112 (68), 111 (90), 110 (26), 100 (12), 97 (24), 96 (60), 91 (25), 83 (63), 82 (100). $C_9H_{17}NO$ [M^+] requires m/z 155.1310; observed 155.1312.

Norhomotropan-7α-ol (6b)

A solution of the epoxide **(2c)** (38 mg, 0.14 mmol) in dry methanol (4 ml) was hydrogenolysed using the procedure described previously for the conversion of **(3c)** into **(3b)**. Reduction of both carbamate and epoxide occured to afford **(6b)** (15 mg, 76%) as a thick yellow oil. δ_H (300 MHz, $CDCl_3$): 1.37 (ddd, J = 13.4, 7.7, 4.2 Hz, 1H), 1.68 (m, 7H), 1.98 (m, 1H), 2.43 (dt, J = 13.4, 10.0, J ≈ 10.0 Hz, 1H), 3.46 (m, 1H, α-N), 3.57 (s, 1H, HN), 3.62 (m, 1H, α-N), 4.40 (dt, J = 10.0, 7.7, J ≈ 7.7 Hz, 1H, α-N). δ_C (75 MHz, $CDCl_3$): 24.4, 24.5, 27.5, 35.0 & 38.1 (5 x CH_2), 55.2 (CHN), 58.6 (CHN), 73.4 (CHOH). υ_{max} (CH_2Cl_2): 3610w, 3320brm, 3040w, 2920s, 2860m, 1445brw, 1335brw, 1255w, 1130w, 1070w cm^{-1}. m/z (%): 141 (M^+,32), 138 (17), 124 (39), 112 (18), 111 (20), 98 (37), 97 (100), 96 (34), 91 (33), 82 (55), 69 (43), 68 (47). $C_8H_{15}NO$ [M^+] requires m/z 141.1154; observed 141.1154.

N-Methyl-7α,8α-epoxy-9-azabicyclo[4.2.1]nonane (2a)

To a slurry of lithium aluminium hydride (65 mg, 1.71 mmol) was injected a solution of **(2c)** (140 mg, 0.51 mmol) in diethyl ether (7 ml) which was then stirred at -78°C for 3 hr. The reaction was then worked up as described previously for the *exo*-isomer **(1a)**: the amine was volatile and the solution was acidified with hydrogen chloride gas prior to distillation of solvent under reduced pressure. Trituration with diethyl ether afforded **(2a.HCl)** (52 mg, 54%) as a hygroscopic white solid. The free amine **(1a)** was used to record NMR spectra which displayed a 10% impurity of the ring opened product **(6a)**. δ_H (300 MHz, $CDCl_3$): 1.45 - 2.01 (brm, 8H), 2.41 (s, 3H, CH_3), 2.95 (brd, J = 4.1 Hz, 2H, α-N), 3.97 (d, J = 3.2 Hz, 2H, HCO). δ_C (75 MHz, $CDCl_3$): 25.7 (2 x CH_2), 29.8 (2 x CH_2), 46.7 (CH_3), 65.3 (2 x CHN), 65.8 (2 x HCO). υ_{max} ($CDCl_3$): 3600w, 3020w, 2920s, 2860w, 1440brw, 1380w, 1125w, 1110w, 1070w, 1000w, 905w cm^{-1}. m/z (%) [measured using **(6b.HCl)**]: 153 (M^+ - HCl, 45), 138 (16), 124 (31), 110 (100), 96 (69), 91 (55), 82 (42), 68 (29). $C_9H_{15}NO$ [M^+ - HCl] requires m/z 153.1154; observed 151.1154.

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