Synthesis and Acidolysis of 3-*endo*-Azidomethyl- and 3-*endo*-Azidobicyclo[3.3.1]non-6-enes. A Novel Synthesis of 4-Azahomoadamant-4-enes [1]

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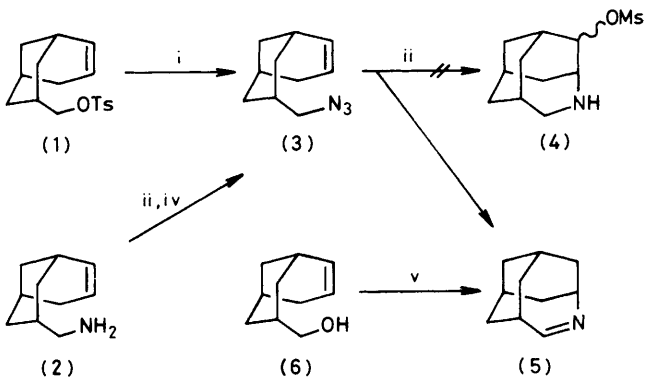
The acidolysis of 3-*endo*-azidomethylbicyclo[3.3.1]non-6-ene (3) with methanesulphonic acid gave 4-azahomoadamant-4-ene (5) which was also produced from 3-*endo*-hydroxymethylbicyclo[3.3.1]non-6-ene (6) on treatment with NaN_3–$MeSO_3H$. The formation of (5) was rationalized by a π route cyclization followed by acidolytic ring expansion of intermediate azides on the basis of acidolysis of dideuterio-derivatives. The above route was extended to synthesis of 2,2- (16) and 7,7-dimethyl-4-azahomoadamant-4-enes (17). The acidolysis of 3-*endo*-azidobicyclo[3.3.1]non-6-ene (23) gave 2-aza-adamantan-*anti*-4-ol (26) *via* a π-N^+ type cyclization.

Organic azides are well-known as excellent synthetic starting materials for various nitrogen-containing organic molecules, although, studies utilizing azide functionalization of carbocycles, particularly, bi- and tri-cycles seem, as yet, to be underdeveloped.[2] We have therefore been pursuing attractive synthetic routes to aza-adamantane and related derivatives by utilizing azide functionalization of bi- and tri-carbocycles in order to study their biological properties.[3] Previously, we reported convenient and efficient synthesis of 4-azahomoadamant-4-ene and its 5-substituted derivatives by acidolysis and/or photolysis of 2-azidoadamantanes.[4] Here, we report the synthesis of 3-*endo*-azidomethyl- and -azidobicyclo[3.3.1]non-6-enes and their acidolysis behaviour, the latter providing novel routes to 4-azahomoadamant-4-enes and 4-hydroxy-2-aza-adamantane, respectively.



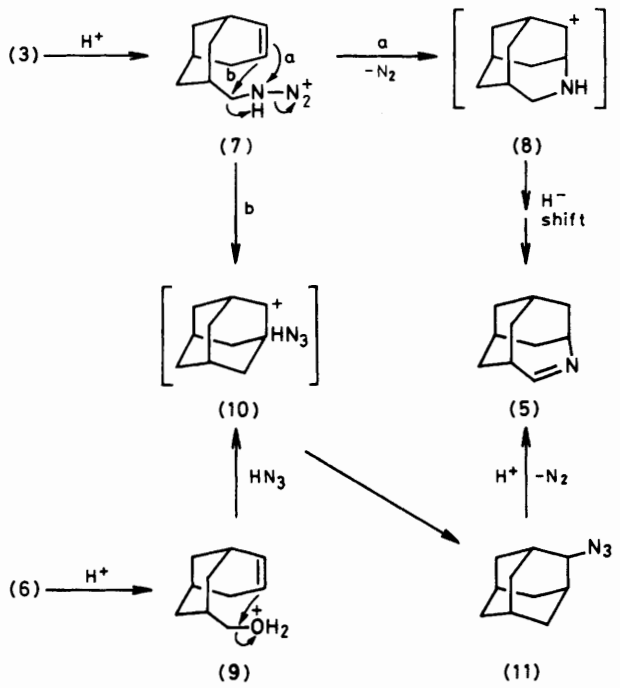
Scheme 1. *Reagents:* i, NaN_3; ii, $MeSO_3H$; iii, NaH; iv, TsN_3; v, NaN_3–$MeSO_3H$

Results and Discussion

Direct introduction of an azido group by nucleophilic substitution [5] on the tosylate (1) in dipolar aprotic solvents afforded the *endo*-azide (3) in only low yields; this was because of adamantan-2-ol formation *via* the so-called π route cyclization.[6,†] Thus, treatment of (1) with sodium azide (9-fold excess) in dimethyl sulphoxide (DMSO) at 90 °C for 5 days gave (3) and adamantan-2-ol in 34 and 65% yields respectively. Similar treatment of (1) with sodium azide (15-fold excess) in the presence of 15-crown-5 ether [7] in dimethylformamide (DMF) at room temperature (*ca.* 25 °C) for 4.5 days afforded (3) (21%) and adamantan-2-ol (12%), accompanied by unidentified side-products. Reactions under a variety of other conditions failed to give better yields of (3), and hence, the diazo transfer method [8] was examined. Treatment of the known amine (2) [9] with n-butyl-lithium (1.6 fold excess) and toluene-*p*-sulphonyl azide (tosyl azide) (1.3 fold excess) in THF at room temperature for 21 h afforded the azide (3) in 28% yield after work-up. The use of a large excess of sodium hydride as the base according to Quast and Eckert procedure [10] improved the yield of (3) up to 87%. The azide (3) was obtained as a volatile colourless oil ($\nu_{max.}$ 2 100 cm^{-1}) and was thermally stable (no change after 20 days at 110 °C in toluene).

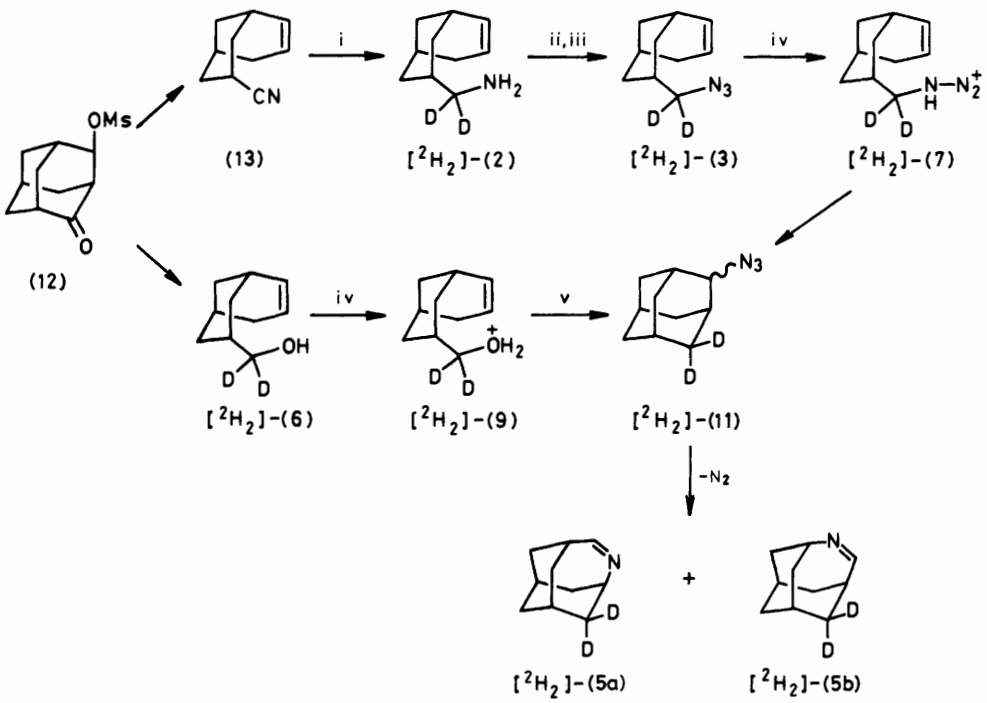
Treatment of (3) with methanesulphonic acid–dichloromethane (3 : 1, v/v) at room temperature for 0.5 h gave a sublimable solid (67%) which was characterized as 4-azahomoadamant-4-ene (5) by comparison with an authentic sample.[4a] No other cyclization products, such as 2-methylsulphonoxy-4-azahomoadamantane (4) were obtained (Scheme 1). Interestingly treatment of the *endo*-alcohol (6) with sodium azide in methanesulphonic acid–dichloromethane also afforded the imine (5) in 66% yield. The formation of (5) from (6) can most reasonably be explained by a π route cyclization to give 2-azidoadamantane (11) *via* (10), followed by its acidolysis to (5) (Scheme 2). The trapping of a π-route cyclization intermediate by acetonitrile (the Ritter reaction) has been reported recently,† and also the formation of (5) from adamantan-2-ol under similar conditions is known.[4a] The formation of (5) from the azide (3) could also be explained in terms of the π route cyclization (π-C^+ route: b in Scheme 2), although, another route involving a π-N^+ type cyclization to (8) followed by intra- or inter-molecular hydride shifts could also be operative, bearing in mind the facile transannular cyclization of appropriate derivatives of bicyclo[3.3.1]nonane-3-*endo*-carbonitrile [9] and the hydride transfers of adamantyl systems in strong acids.[11] In order to clarify the reaction pathway, dideuteriated azidomethyl [$^2H_2$]-(3) and carbinol derivatives [$^2H_2$]-(6) were prepared and treated by methanesulphonic acid as above (Scheme 3). An authentic sample of the dideuterio-imine as a 1 : 1 mixture (^{13}C n.m.r.) of [$^2H_2$]-(5a) and [$^2H_2$]-(5b) ($^2H_2$ content: 90% of theory by mass and ^1H n.m.r. spectra) was obtained by treatment of 3-(hydroxy[$^2H_2$]methyl)-

† For an elegant synthetic extension of the π route cyclization to 2,4-disubstituted adamantanes see R. M. Black, *J. Chem. Soc., Perkin Trans. 1*, 1982, 73.



Scheme 2.

It was of interest to apply the above route to the synthesis of 2,2- and/or 7,7-disubstituted 4-azahomoadamant-4-enes which might require a multistep preparation by other routes. The readily accessible 2-(bicyclo[3.3.1]non-6-en-3-yl)-*endo*-propan-2-ol alcohol (14) from (12) [13] was treated with sodium azide in methanesulphonic acid. Work-up and sublimation afforded a 35 : 65 mixture of 2,2-dimethyl- (16) and 7,7-dimethyl-4-azahomoadamant-4-enes (17) (n.m.r. and h.p.l.c. analyses) as a colourless solid in 90% yield. In their ^{1}H n.m.r. spectra, (16) and (17) revealed characteristic signals at δ 8.11 (1 H, d, *J* 6.0 Hz, 5-H), 3.72br (1 H, d, *J* ca. 4.5 Hz, 3-H), 2.58br (1 H, s, 6-H), 1.11 and 0.99 (each 3 H, s, 2,2-Me_2), and 7.98 (1 H, d, *J* 6.0 Hz, 5-H), 4.10br (1 H, s, 3-H), and 1.09 and 1.05 (each 3 H, s, 7,7-Me_2), respectively. The assignment was also supported by the use of the downfield shift reagent, $Eu(fod)_3$.* The 3-H signal at δ 4.10 for compound (17) showed a larger downfield shift than the 3-H signal at δ 3.72 for compound (16) on addition of $Eu(fod)_3$ (see Experimental section); this supported the presence of a bulky substituent (2,2-dimethyl) near to the N in (16) (results in steric hindrance to complex formation with the shift reagent.) [14] In their ^{13}C n.m.r. spectra, (16) and (17) had characteristically shifted carbon signals at δ 65.3 (C-3) for (16) and 49.0 (C-6) for (17) respectively compared with those (55.8 for C-3 and 37.6 for C-6) [4c] of unsubstituted (5); these were compatible with the presence of 2,2-dimethyl and 7,7-dimethyl substituents, respectively (β effect of the dimethyl group).[15] The observed preferential

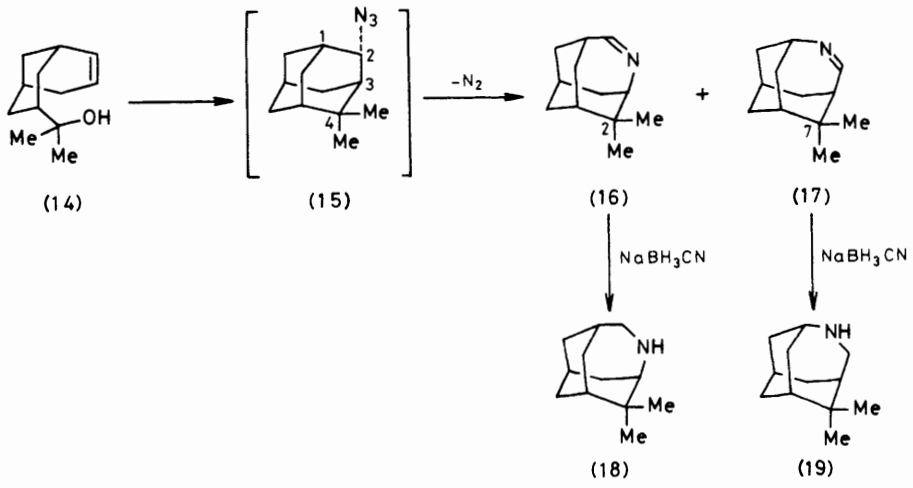


Scheme 3. *Reagents:* i, $LiAl^2H_4$; ii, NaH; iii, TsN_3; iv, H^+; v, HN_3

bicyclo[3.3.1]non-6-ene [$^2H_2$]-(6) [12] ($^2H_2$ content: 91%) with methanesulphonic acid–sodium azide in chloroform. The acidolysis of the azido[$^2H_2$]methyl derivative [$^2H_2$]-(3) ($^2H_2$ content: 92%) prepared by the route shown in Scheme 3 afforded also the dideuterioimine ($^2H_2$ content: *ca.* 81%), although the yield was low (15%). These results confirmed clearly the operation of path b: namely, the π route cyclization of (3) and (6) to give 2-azidoadamantane followed by its acidolytic ring expansion to form 4-azahomoadamant-4-ene (5).

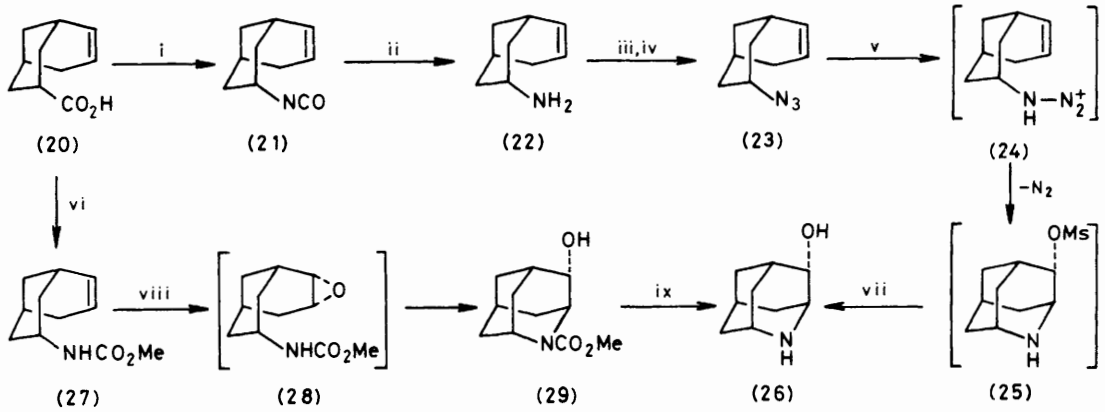
formation of (17) rather than (16) was unexpected since from the known alkyl migration tendency in the Schmidt reaction of tertiary alcohols [16] (Pr^i ≈ cyclohexyl ≫ Et ≈ Me), C-2,C-3 bond migration on the protonated azide nitrogen of (15) to afford (16) should be electronically favoured over C-1, C-2 bond migration to give (17). The preference for C-1, C-2, bond

* $Eu(fod)_3$ = tris-(6,6,7,7,8,8,8-heptafluoro-2,2-dimethyloctane-3,5-dionato)europium.



(14) (15) (16) (17) (18) (19)

Scheme 4.



(20) (21) (22) (23) (24) (27) (28) (29) (26) (25)

Scheme 5. *Reagents:* i, DPPA–Et_3N; ii, H_3O^+; iii, Bu^nLi; iv, TsN_3; v, $MeSO_3H$; vi, DPPA–Et_3N–MeOH; vii, aq. NaOH; viii, *m*-CPBA; ix, KOH–EtOH

migration over C-2,3 can tentatively be explained in terms of the difference of steric crowding at the corresponding transition states due to the $2_{ax.}$-Me group.

Reduction of the imines (16) and (17) with sodium cyanoborohydride gave the 2,2-dimethyl- (18) and 7,7-dimethyl-4-azahomoadamantane (19), respectively (Scheme 4).

Finally, 3-*endo*-azidobicyclo[3.3.1]non-6-ene (23) was prepared by the route shown in Scheme 5 [51.4% yield from (20)], and treated with methanesulphonic acid. Work-up gave the known 2-aza-adamantan-*anti*-4-ol (26) * (70%) which was identical with the sample prepared from (21) *via* (27), (28), and (29) by a modified procedure of that previously reported.[17]

As described above, the expansion of the π route cyclization to 2,4-disubstituted adamantanes using azide functionalization provides novel routes to 4-azahomoadamant-4-enes and 4-substituted 2-aza-adamantane.

Experimental

M.p.s were taken in a sealed tube on a Yanagimoto micro-melting point apparatus. I.r. spectra were obtained on a Jasco A-100 spectrometer. ^1H N.m.r. and ^{13}C n.m.r. were recorded on a JEOL JMN-C-60HL instrument at 60 MHz and a JEOL-FX-60 FT spectrometer at 15.04 MHz, respectively. Chemical shifts are reported in p.p.m. (δ) relative to Me_4Si as an internal standard in $CDCl_3$. Mass spectra were obtained with a JEOL JMS-D10 mass spectrometer at 75 eV. Microanalyses were performed with a Perkin-Elmer 240B elemental analyser. High performance liquid chromatography (h.p.l.c.) analyses were carried out on a Jasco Tri Rotar-II instrument fitted with a UVIDEC-100-III spectrophotometer operating at 210 nm.

3-endo-*Tosyloxymethylbicyclo*[3.3.1]*non-6-ene* (1).—Although this compound was reported in a preliminary communication,[6a] no physical data for it except for a m.p. were given. To an ice-cooled and stirred mixture of tosyl chloride (1.14 g, 6.00 mmol) in dry pyridine (4.5 ml) was added 3-*endo*-hydroxymethylbicyclo[3.3.1]non-6-ene [13] (0.85 g, 5.58 mmol). After being stirred for 12 h with ice-cooling, the mixture was diluted with cold water (30 ml) and extracted with n-hexane (5 × 7 ml). The combined extracts were washed with water, dried (Na_2SO_4), and concentrated to yield the tosylate (1) as colourless crystals (0.97 g, 57%), m.p. 45—48 °C (lit.,[6a] m.p. 52.2—53.8 °C) (Found: C, 66.75; H, 7.15. $C_{17}H_{22}O_3S$ requires C, 66.65; H, 7.24%); $\nu_{max.}$ (KBr) 2 930, 1 640, 1 600, 1 360, 1 180, 955, and 845 cm^{-1}; $\delta_H(CCl_4)$ 7.8—7.1 (AB type m, 4 H), 5.9—5.2 (m, 2 H), 4.2—3.6 (m, 2 H), 2.43 (s, 3 H), and 2.5—1.2 (m, 11 H).

3-endo-*Azidomethylbicyclo*[3.3.1]*non-6-ene* (3).—(*a*) *From*

* The terms *syn* and *anti* are used with reference to the aza function.

the tosylate (1). A mixture of the tosylate (1) (306 mg, 1.00 mmol) and sodium azide (585 mg, 9.00 mmol) in DMSO (dried on molecular sieves, 4A, 5 ml) was heated under argon at 90 °C for 5 days. The cooled mixture was diluted with water (20 ml) and extracted with dichloromethane (3 × 10 ml). The combined extracts were washed with water, dried (Na_2SO_4), and evaporated under reduced pressure to give an oily residue which was purified on a silica-gel column (Merck Kieselgel 60, 70—230 mesh, n-hexane–CH_2Cl_2–MeOH system) to afford the azide (3) as a colourless oil in the first fractions (61 mg, 34%), $n_D^{18.5}$ 1.5197 (Found: C, 68.05; H, 8.2; N, 23.75. $C_{10}H_{15}N_3$ requires C, 67.76; H, 8.53; N, 23.71%); $\nu_{max.}$ (film) 3 030, 2 920, 2 860, 2 100, 1 450, and 1 260 cm^{-1}; δ_H ($CDCl_3$) 6.10—5.34 (m, 2 H), 3.40—3.22 (m, 2 H), and 2.8—0.7 (m, 11 H). The second fractions afforded adamantan-2-ol (99 mg, 65.0%) which was identified by comparison with an authentic sample [18] (t.l.c., i.r. and ^1H n.m.r. spectra). The reaction of (1) (306 mg, 1.00 mmol) and sodium azide (975 mg, 15.0 mmol) in DMF (5 ml) containing 15-crown-5 ether (203 mg, 0.920 mmol) at room temperature (*ca.* 25 °C) for 4.5 days afforded the azide (3) (37 mg, 21%) and adamantan-2-ol (18 mg, 12%) accompanied with uncharacterized side-products after work-up and chromatography as above.

(B) *From* 3-endo-*aminomethylbicyclo*[3.3.1]*non*-6-*ene* (2). A mixture of the amine (2) [9] (151 mg, 1.00 mmol), sodium hydride (400 mg of 60% dispersion in mineral oil, 10.0 mmol), and *p*-tosyl azide (395 mg, 2.00 mmol) in anhydrous THF (5 ml) was stirred under nitrogen for 3 days at room temperature. The mixture was treated with methanol (2 ml) under ice-cooling, and poured onto ice–water, and extracted with ether (4 × 10 ml). The combined extracts were washed with water, dried (Na_2SO_4), and evaporated under reduced pressure to yield an oily residue which was chromatographed on a silica gel column with n-pentane as eluant to afford the azide (3) as a colourless oil (155 mg, 87.5%).

Acidolysis of (3): 4-*Azahomoadamant*-4-*ene* (5).—To a stirred ice-cooled mixture of methane sulphonic acid (3 ml) and dichloromethane (0.5 ml) was added the azide (3) (60 mg, 0.34 mmol) in dichloromethane (0.5 ml). After 0.5 h, the mixture was poured onto ice–water (10 ml) and the layers separated. The aqueous layer was basified with 50% aqueous potassium hydroxide under ice-cooling and then extracted with dichloromethane (5 × 6 ml). The combined extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give a solid residue which was sublimed (90 °C at 20 mmHg) to afford the imine (5) as a colourless solid (35 mg, 67%), m.p. 292—294 °C (lit.,[4a] 215—218 °C).* The hydrochloride had m.p. 276—279 °C [lit.,[4a] 276—279 °C (decomp.)]. I.r. and ^1H n.m.r. spectra were identical with those of an authentic sample.

Compound (5) *from* (6).—To a stirred ice-cooled mixture of (6) (110 mg, 0.723 mmol) in methanesulphonic acid (3 ml) and dichloromethane (2 ml) was added by portions sodium azide (120 mg, 1.85 mmol). After being stirred for 12 h at room temperature, the mixture was poured onto ice–water (10 ml) and the chloroform layer separated and washed with 10% hydrochloric acid (2× 5 ml). The washings and aqueous layer were combined and basified with 50% aqueous potassium hydroxide and then extracted with dichloromethane (5 × 6 ml). The combined extracts were dried (Na_2SO_4) and evaporated to give a solid residue which was sublimed (90 °C, 20 mmHg) to afford the imine (5) as a colourless solid (71 mg, 66%).

3-endo-*Hydroxy*[$^2H_2$]*methylbicyclo*[3.3.1]*non*-6-*ene* [$^2H_2$]-(6).—This compound was prepared by $LiAlD_4$ reduction of 4_{eq}-methylsulphonyloxyadamantan-2-one (12) [6e] in 84% yield according to the procedure of Numan and Wynberg,[12] and had $n_D^{27.0}$ 1.5161; δ_H($CDCl_3$) 6.05—5.22 (m, 2 H), 3.8—3.3 (m, 0.37 H), 1.93 (s, 1 H, D_2O exchangeable), and 2.7—0.8 (m, 11 H) {this corresponded to 98.1% of [$^2H_2$]-(6)}; *m*/*z* 156 (M^+ + 2, 2%), 155 (M^+ + 1, 9), 154 (M^+, 100), 153 (M^+ − 1, 9), and 152 (M^+ − 2, 8) (this corresponded to 83.9% of [$^2H_2$]-(6) {the average value of [$^2H_2$]-(6): 91.0%}.

[$^2H_2$]-*Imines* [$^2H_2$]-(5a) *and* [$^2H_2$]-(5) *from* [^2H]-(6).—To a stirred ice-cooled mixture of [$^2H_2$]-(6) (115 mg, 0.746 mmol) in methanesulphonic acid (3 ml) and chloroform (2 ml) was added sodium azide (150 mg, 2.31 mmol) and the stirring was continued for 12 h at room temperature. The mixture was poured onto ice–water and work-up as above gave the [$^2H_2$]-imines [$^2H_2$]-(5a) and [$^2H_2$]-(5b) in 1 : 1 ratio (^{13}C n.m.r.) as a colourless solid after three sublimations (90 °C, 20 mmHg) (55 mg, 49%), m.p. 279—281 °C (Found: C, 80.55; H, 10.1; N, 9.35. $C_{10}H_{13}D_2N$ as $C_{10}H_{15}N$ requires C, 80.48; H, 10.13; N, 9.39%), $\nu_{max.}$ 2 920, 1 650, and 1 640 cm^{-1}; δ_H ($CDCl_3$) 8.08 (d, *J* 6.0 Hz, 1 H), 4.12 (unsymmetrical t, *J* ca. 4 Hz, 1 H), 2.9—2.4 (m, 1 H), and 2.3—1.5 (m, 10.15 H) {this corresponded to 92.5% of [$^2H_2$]-(5)}; δ_C ($CDCl_3$) 171.66 and 171.59 (each d, *ca.* 1 : 1 ratio), 37.62 and 37.49 (each d, *ca.* 1 : 1 ratio), and other signals similar to (5); [4c] *m*/*z* 153 (M^+ + 2, 1%), 152 (M^+ + 1, 14), 151 (M^+, 100), 150 (M^+ − 1, 7), and 149 (M^+ − 2,6) (this corresponded to 86.8% of [$^2H_2$]-(6) {the average 89.7% of [$^2H_2$]-(5)}. The hydrochloride of [$^2H_2$]-(5) had m.p. 226—228 °C; $\nu_{max.}$ (KBr) 3 400—2 400, 2 930, 1 680, and 1 440 cm^{-1}; δ_H ($CDCl_3$) 9.12br (s, 1 H), 4.33br (s, 1 H), 3.6—2.5 (m, *ca.* 2 H, *ca.* 1 H on shaking with D_2O), and 2.5—1.5 (m, *ca.* 10 H).

3-endo-[$^2H_2$]*Aminomethylbicyclo*[3.3.1]*non*-6-*ene* [$^2H_2$]-(2).—3-*endo*-Cyanobicyclo[3.3.1]non-6-ene [6e] (13) (300 mg, 2.04 mmol) was reduced with $LiAlD_4$ (200 mg, 5.27 mmol) according to the procedure of Hassner *et al.* [Method (a)] [9] to yield the dideuterioamine [$^2H_2$]-(2) isolated as its hydrochloride (252 mg, 65%), m.p. 230—233 °C (Found: C, 64.15; H, 9.6; N, 7.35. $C_{10}H_{16}D_2ClN$ as $C_{10}H_{18}ClN$ requires C, 63.98; H, 9.67; N, 7.37%); $\nu_{max.}$ (KBr) 3 400—2 500, 2 940, 1 600, 1 510, 1 445, 905, and 720 cm^{-1}; δ_H ($CDCl_3$) 8.23br (s, 3 H, D_2O exchangeable), 6.2—5.4 (m, 2 H), 3.5—2.8 (m, 0.11 H), and 2.7—1.2 (m, 11 H) {this corresponded to 94.5% of [$^2H_2$]-(2)}.

3-endo-*Dideuterioazidomethylbicyclo*[3.3.1]*non*-6-*ene* [$^2H_2$]-(3).—To a stirred ice-cooled mixture of [$^2H_2$]-(2) hydrochloride (190 mg, 1.00 mmol) was added Bu^nLi (0.62 ml of 1.62 M hexane solution, 1.00 mmol) under nitrogen. Stirring was continued for 1 h, after which the mixture was treated with sodium hydride (400 mg of 60% dispersion in mineral oil, 10.0 mmol), and *p*-tosyl azide (395 mg, 2.00 mmol) as for (3) and stirred for 3 days at room temperature. The work-up as above and chromatography gave the dideuterioazide [$^2H_2$]-(3) as a colourless oil (145 mg, 81%), n_D^{17} 1.5155 (Found: C, 67.6; H, 8.5; N, 23.95. $C_{10}H_{13}D_2N_3$ as $C_{10}H_{15}N_3$ requires C, 67.76; H, 8.53; N, 23.71%), $\nu_{max.}$ (film) 3 020, 2 920, 2 080, 1 630, 1 440, 1 270, 1 040, and 720 cm^{-1}; δ_H ($CDCl_3$) 6.1—5.3 (m, 2 H), 3.4—3.2 (m, 0.16 H), and 1.5—1.1 (m, 11 H) {this corresponded to 92.0% of [$^2H_2$]-(3)}.†

Acidolysis of [$^2H_2$]-(3).—The dideuterioazide [$^2H_2$]-(3) (40 mg, 0.22 mmol) was decomposed in methanesulphonic acid (3 ml) and chloroform (2 ml) for 20 h at room temperature and then worked up as above for (3) to give the dideuterioimines (5 mg, 15%) after p.t.l.c. (Merck, aluminium oxide $60F_{254}$,

* Previously reported m.p. for (5) should be corrected as given.

† Mass spectral determination of D content was not successful since the M^+ ion was not observed.

type E, $CHCl_3$). The i.r. and ^1H n.m.r. spectra were identical with those of a sample of [$^2H_2$]-(5a) and [$^2H_2$]-(5b) prepared from [$^2H_2$]-(6); *m/z* 153 ($M^+ + 2$, 1%), 152 ($M^+ + 1$, 6), 151 (M^+, 100), 150 ($M^+ - 1$, 12), and 149 ($M^+ - 2$, 6) {this corresponded to *ca.* 81.0% of [$^2H_2$]-(5).* The acidolysis under a variety of other conditions failed to improve the yield of imine accompanied as it was by many side-products.

2,2-*Dimethyl-* (16) *and* 7,7-*Dimethyl*-4-*azahomoadamant*-4-*enes* (17).—To a stirred ice-cooled solution of bicyclo[3.3.1]-non-6-en-3-yl-*endo*-propan-2-ol [13] (14) (192 mg, 1.00 mmol) in methanesulphonic acid (3.5 ml) and chloroform (3 ml) was added in portions solid sodium azide (260 mg, 4.00 mmol). Stirring was continued for 12 h at room temperature after which the mixture was poured onto ice–water (20 ml). The aqueous layer was basified with 50% potassium hydroxide and extracted with chloroform (6 × 5 ml). The combined extracts were dried (Na_2SO_4) and evaporated to give a solid residue which was sublimed (90 °C at 0.5 mmHg) to afford the mixture of imines (16) and (17) as a colourless solid having the characteristic odour of imines (160 mg, 90%), m.p. 163—167 °C (Found: C, 81.6; H, 10.55; N, 7.85. $C_{12}H_{19}N$ requires C, 81.30; H, 10.80; N, 7.90%), $\nu_{max.}$ (KBr) 2 920, 1 665, 1 450, 1 365, 1 070, and 1 015 cm^{-1}. The ratio of (16) and (17) was 35 : 65 by h.p.l.c. [on a Jasco Finepak SIL-C_{18}-5 column (MeOH–H_2O containing 0.1% ammonium carbonate, 80 : 20 v/v)] and ^1H n.m.r. analyses. The imines were separable on a p.t.l.c. (Merck, aluminium oxide 60F_{254}, type E) after repeated development using a n-hexane–chloroform (3 : 2, v/v) system. The major imine (17) was obtained in the first fraction as a colourless solid after sublimation, m.p. 170—172 °C (Found: C, 81.15; H, 11.05; N, 7.8. $C_{12}H_{19}N$ requires C, 81.30; H, 10.80; N, 7.90%), $\nu_{max.}$ (KBr) 2 920, 1 655, 1 450, 1 370, 1 070, and 900 cm^{-1}; δ_H ($CDCl_3$) 7.98 (d, *J* 6.0 Hz, 1 H), 4.10br (s, 1 H), 2.4—1.2 (m, 10 H), and 1.09 and 1.05 (each s, each 3 H); δ_H [$CDCl_3$–Eu(fod)$_3$, mol. ratio to 17 = 0.0948] 9.27 (d, *J* 6.0 Hz, 1 H), 6.82br (s, 1 H), 3.7—1.7 (m, 10 H), and 1.60 and 1.40 (each s and 3 H); δ_C ($CDCl_3$) 171.0 (d, 1 C), 55.5 (d, 1 C), 49.0 (d, 1 C), 38.8 (d, 1 C), 33.7 (t, 1 C), 32.9 (s, 1 C), 31.8 (t, 1 C), 28.4 (t, 1 C), 28.2 (q overlapped d, 3 C), and 27.1 (t, 1 C); *m/z* 177 (M^+, 100%), 162 (54), 135 (13), 108 (22), 107 (32), 94 (21), 93 (39), 81 (11), 80 (19), 79 (32), 67 (14), and 41 (25). The minor imine (16) was obtained in the second fractions as a colourless solid after sublimation, m.p. 169—172 °C (Found: C, 81.35; H, 10.8; N, 7.85. $C_{12}H_{19}N$ requires C, 81.30; H, 10.80; N, 7.90%, $\nu_{max.}$ (KBr) 2 920, 1 665, 1 470, 1 450, 1 390, 1 365, 1 015, and 865 cm^{-1}; δ_H ($CDCl_3$) 8.11 (d, *J* 6.0 Hz, 1 H), 3.72br (d, *J ca.* 4.5 Hz, 1 H), 2.4—1.2 (m, 10 H), 1.11 and 0.99 (each s, each 3 H); δ_H [$CDCl_3$–Eu(fod)$_3$, mol. ratio 16 : 0.0948] 8.72 (d, *J* 6.0 Hz, 1 H), 4.50br (unsymmetrical d, *J ca.* 5 Hz, 1 H), 3.7—1.7 (m, 11 H), and 1.46 and 1.40 (each s and 3 H); δ_C ($CDCl_3$)† 170.4 (d, 1 C), 65.3 (d, 1 C), 38.8 (d, 1 C), 37.3 (d, 1 C), 33.8 (s, 1 C), 32.0 (t, 1 C), 31.6 (t, 1 C), 29.1 (t, 1 C), 28.7 (q, 1 C), 28.4 (d, 1 C), 27.1 (t, 1 C), and 26.6 (q, 1 C); *m/z* 177 (M^+, 100%), 162 (43), 108 (22), 107 (33), 94 (36), 93 (29), 91 (10), 81 (16), 80 (18), 79 (34), 77 (11), 67 (18), 57 (12), 56 (13), 55 (11), 53 (10), 43 (12), and 41 (34).

2,2-*Dimethyl*-4-*azahomoadamantane* (18).—To a stirred mixture of the 2,2-dimethylimine (16) (15 mg, 0.085 mmol), sodium cyanoborohydride (100 mg, 1.59 mmol), and Bromocresol Green (trace) in methanol (5 ml) was added a 2M HCl–MeOH solution until the blue colour turned yellow at room temperature; the stirring was continued whilst the yellow colour was maintained by occasional and dropwise addition of the HCl–MeOH solution for 8 h.[19] The mixture was poured into 20% aqueous NaOH and extracted with dichloromethane (7 × 5 ml). The combined extracts were dried (K_2CO_3) and evaporated to give a solid residue which was sublimed (80 °C, 0.5 mmHg). The sublimed material was treated with picric acid in ethanol to afford the picrate of (18) as yellow needles (14 mg, 40%), m.p. 265—268 °C (decomp.) (Found: C, 53.05; H, 5.7; N, 13.55. $C_{18}H_{24}N_4O_7$ requires C, 52.93; H, 5.92; N, 13.72%), $\nu_{max.}$ (KBr) 3 300—2 300, 3 220, 2 920, 1 640, 1 605, 1 560, 1 485, 1 430, 1 365, 1 335, 1 315, 1 275, 1 260, 1 160, 1 075, 1 045, 915, 790, 750, and 715 cm^{-1}; δ_H [$CDCl_3$–$(CD_3)_2$-SO] 8.89 (s, 2 H), 3.8—3.3 (m, 3 H), 2.6—1.2 (m, *ca.* 11 H), 1.76 (s, *ca.* 2 H, disappeared on shaking with D_2O), and 1.17 and 1.13 (each s, each 3 H).

7,7-*Dimethyl*-4-*azahomoadamantane* (19).—The imine (17) (25 mg, 0.14 mmol) was reduced in a similar way to that described above with sodium cyanoborohydride (100 mg, 1.59 mmol). Work-up and treatment with picric acid in ethanol afforded the picrate of (19) as yellow cubic crystals from ethanol–ether (25 mg, 44%), m.p. 250—252 °C (decomp.) (Found: C, 53.15; H, 6.0; N, 13.45. $C_{18}H_{24}N_4O_7$ requires C, 52.93; H, 5.92; N, 13.72%), $\nu_{max.}$ (KBr) 3 400, 3 080, 3 040, 2 930, 2 890, 2 850, 1 605, 1 565, 1 520, 1 320, 1 165, 1 075, 920, 800, 715, and 700 cm^{-1}; δ_H [$CDCl_3$–$(CD_3)_2SO$] 8.86 (s, 2 H), 4.27br (s, *ca.* 2 H, disappeared on shaking with D_2O), 4.0—3.0 (m, 3 H), 2.6—1.3 (m, 11 H), and 1.16 and 1.08 (each s, each 3 H).

3-endo-*Aminobicyclo*[3.3.1]*non*-6-*ene* (22).—Although this amine is reported by Staas and Spurlock,[17b] we prepared it by a modified procedure as follows. To a refluxing mixture of bicyclo[3.3.1]non-6-ene-3-*endo*-carboxylic acid [6e] (20) (1.66 g, 10.0 mmol) and triethylamine (1.05 g, 10.4 mmol) in dry xylene (mixed, b.p. 137—140 °C, 40 ml) was added dropwise DPPA (diphenylphosphoryl azide) [20] (2.82 g, 10.3 mmol) in xylene (5 ml) during 1 h under nitrogen, and the refluxing was continued for further 9 h. After removal of the solvent under reduced pressure, an oily residue was purified by Kugelrohr distillation (80—110 °C, 0.15 mmHg) to afford the isocyanate (21) as a colourless oil (1.43 g, 87.6%), $\nu_{max.}$ (film) 3 030, 2 930, 2 265, 1 640, 1 430, 1 102, and 1 000 cm^{-1}. The isocyanate (1.32 g, 8.09 mmol) was heated to reflux in a mixture of carbon tetrachloride (40 ml) and 8% hydrochloric acid (40 ml) for 3 days. The aqueous layer was separated, basified with 50% aqueous potassium hydroxide, and extracted with dichloromethane (7 × 5 ml). The combined extracts were dried (Na_2SO_4) and evaporated to afford the crude amine (22) as a solid which was dissolved in ether and treated with dry hydrogen chloride gas to afford hydrochloride of (22) as a colourless solid (0.97 g, 69%), m.p. >300 °C (lit.,[17b] >300 °C).

3-endo-*Azidobicyclo*[3.3.1]*non*-6-*ene* (23).—To a stirred and ice-cooled mixture of (22) hydrochloride (174 mg, 1.00 mmol) in dry THF (4 ml) was added Bu^nLi (1.6 ml of 1.62M hexane solution, 2.59 mmol) under argon. After 1 h, *p*-tosyl azide (395 mg, 2.00 mmol) in THF (2 ml) was added to the mixture, and stirring was continued for 1 day at room temperature. Work-up as above and chromatography (silica gel, n-pentane) afforded the azide (23) as a colourless oil (139 mg, 85%), n_D^{18} 1.5315 (Found: C, 66.45; H, 7.8; N, 25.85. $C_9H_{13}N_3$ requires C, 66.22; H, 8.03; N, 25.75%); $\nu_{max.}$ (film) 3 040, 2 920, 2 105, 1 460, 1 275, and 1 000 cm^{-1}; δ_H ($CDCl_3$) 6.1—5.5 (m, 2 H), 4.1—3.7 (m, 1 H), and 2.75—1.45 (m, 10 H).

* This should be considered approximate value because of background peak at 149.

† Obtained by substraction of the signals of (17) from the spectrum of the mixture, and hence, the overlapped signals should be considered as tentative.

3-endo-*Methoxycarbonylaminobicyclo*[3.3.1]*non*-6-*ene* (27).—The crude isocyanate (21) was prepared from (20) (0.83 g, 5.0 mmol), triethylamine (0.51 g, 5.1 mmol), and DPPA (1.41 g, 5.1 mmol) in xylene (30 ml) as above, and to the mixture was added methanol (3 ml); the mixture was heated to reflux for 3 days. After removal of the solvent under reduced pressure, the oily residue was chromatographed (silica gel, n-hexane–CH_2Cl_2) and then distilled (Kugelrohr, 90—100 °C at 0.5 mmHg) to afford the urethane (27) as a colourless oil (0.61 g, 62%), n_D^{15} 1.5421 (Found: C, 67.9; H, 8.5; N, 7.05. $C_{11}H_{17}NO_2$ requires C, 67.66; H, 8.78; N, 7.17%), $\nu_{max.}$ (film) 3 440, 3 350, 2 940, 1 720, 1 510, 1 455, 1 230, 1 100, and 955 cm^{-1}; δ_H (CCl_4) 6.3—5.3 (m, 3 H, *ca.* 2 H after shaking with D_2O), 4.2—3.7 (m, 1 H), 3.50 (s, 3 H), and 2.8—1.3 (m, 10 H).

2-*Methoxycarbonyl*-2-*aza-adamantan*-anti-4-*ol* (29).—A mixture of (27) (195 mg, 1.00 mmol) and *m*-CPBA (224 mg of 85% purity reagent, 1.10 mmol) in dichloromethane (10 ml) was stirred for 2 days at room temperature. The mixture was washed with 10% aqueous sodium hydrogen sulphite until a starch–iodine paper test became negative, and then, successively, with 5% aqueous sodium hydrogen carbonate and water; the solution was then dried (Na_2SO_4). Removal of the solvent gave an oil which was chromatographed (silica gel, $CHCl_3$–MeOH) to afford (29) as a crystalline solid (120 mg, 57%), m.p. 70—73 °C (Found: C, 62.45; H, 7.9; N, 6.4. $C_{11}H_{17}NO_4$ requires C, 62.54; H, 8.11; N, 6.63%); $\nu_{max.}$ (KBr) 3 440, 2 930, 1 680, 1 455, 1 360, 1 305, 1 120, 1 075, 1 050, and 1 025 cm^{-1}; δ_H ($CDCl_3$) 4.19br (s, 2 H), 3.95—3.55 (m, 1 H), 3.66 (s, 3 H), 3.55—3.05 (m, 1 H, D_2O exchangeable), and 2.5—1.3 (m, 10 H).

2-*Aza-adamantan*-anti-4-*ol* (26) *from* (29).—A mixture of (29) (50 mg, 0.24 mmol) 50% aqueous potassium hydroxide (1 ml) in ethyl cellosolve (1 ml) and ethanol (1 ml) was heated to reflux under nitrogen for 10 h. The cooled mixture was diluted with 20% aqueous sodium hydroxide and extracted with dichloromethane (6 × 5 ml). The combined extracts were dried (K_2CO_3) and evaporated to give a solid residue which was dissolved in ether and treated with dry hydrogen chloride gas to afford the hydrochloride of the amine (26). The hydrochloride was further purified on an alumina column (Wako, basic, activity grade I—II) with CH_2Cl_2–MeOH as eluant to give the analytically pure amine (26) as a colourless solid (33 mg, 90%), m.p. 302—305 °C (decomp.) (Found: C, 70.7; H, 10.0; N, 8.85. $C_9H_{15}NO$ requires C, 70.55; H, 9.87; N, 8.14%), $\nu_{max.}$ (KBr) 3 400, 3 260, 2 930, 1 450, 1 105, and 1 035 cm^{-1}; δ_H [$CDCl_3$–$(CD_3)_2SO$] 4.61 (s, 2 H, D_2O exchangeable), 4.08br (s, 1 H), 3.25br (s, 2 H), and 2.7—1.2 (m, 10 H). The hydrogen oxalate salt of (26) had m.p. 179—182 °C [301—304 °C (decomp.)] (lit.,[17b] 172—175 °C (decomp.), the i.r. spectrum of which was similar to that previously reported.[17b]

Acidolysis of (23).—The azide (23) (88 mg, 0.54 mmol) in dichloromethane (2 ml) was added to methanesulphonic acid (3 ml) with stirring at room temperature. The stirring was continued for 1 day after which the mixture was diluted with ice–water (10 ml). The aqueous layer was basified (40% aqueous sodium hydroxide) and extracted with dichloromethane (6 × 5 ml). The combined extracts were dried (K_2CO_3) and evaporated to afford (26) as a colourless solid (58 mg, 70%) identified by comparison of its i.r. and ^1H n.m.r. spectra with the sample obtained from (29).

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