Synthesis of Novel Carbo- and Hetero-polycycles. Part 7.[1] Synthesis of 6-Azatricyclo[6.3.1.0^{4,10}]dodecane and 5-Azatricyclo[5.3.1.1^{3,9}]dodecane Derivatives *via* Intramolecular Cycloaddition of *N*-{(*endo*-Bicyclo[3.3.1]non-6-en-3-yl)methyl}nitrones

Shoji Eguchi,* Yoshio Furukawa, Takanori Suzuki, and Tadashi Sasaki
Institute of Applied Organic Chemistry, Faculty of Engineering, Nagoya University, Furo-cho, Chikusa-ku, Nagoya 464, Japan

The intramolecular cycloaddition of *N*-{(*endo*-bicyclo[3.3.1]non-6-en-3-yl)methyl}nitrones (**4a—c**), generated *in situ* from the corresponding hydroxylamine with formaldehyde, benzaldehyde, and 2-furaldehyde, afforded both regioisomers (**5a—c**) and (**6a—c**). The regioisomeric ratios were dependent on the nitrone's α-substituent. Reductive cleavages of (**5**), (**6**), or their methiodides give the corresponding azatricyclododecane derivatives (**9a, b**) and (**10, b**).

Recently, we have reported a convenient synthesis of 2-amino-4-hydroxy derivatives and 2-hydroxy-5-aza analogues of tricyclononane, -decane, and -undecane derivatives *via* intramolecular 1,3-dipolar cycloaddition reactions of appropriate α-bicycloalkenylnitrones[2] and *N*-bicycloalkenylnitrones.[3] These are some examples of our efforts to pursue attractive synthetic routes for functionalized carbo- and hetero-polycyclic ring systems.[4] In this paper, we report on a convenient synthesis of 3-*endo*-hydroxy-6-azatricyclo[6.3.1.0^{4,10}]dodecane and 2-*endo*-hydroxy-5-azatricyclo[5.3.1.1^{3,9}]dodecane derivatives based on *N*-{(*endo*-bicyclo[3.3.1]non-6-en-3-yl)methyl}nitrones.[5–8]

Results and Discussion

N-{(*endo*-Bicyclo[3.3.1]non-6-en-3-yl)methyl}nitrone (**4a**) was generated *in situ* by heating paraformaldehyde and *N*-{(*endo*-bicyclo[3.3.1]non-6-en-3-yl)methyl}hydroxylamine (**3**) prepared from the corresponding aldehyde (**1**)[9] *via* oxime (**2**). The intramolecular cycloaddition of (**3**) occurred smoothly upon heating in xylene at 100 °C (135 h) to afford a 62:38 mixture of regioisomers (**5a**) and (**6a**) in 76% yield (Scheme). These regioisomers were isolated after chromatography on a silica gel column to give (**5a**) (46.8%) and (**6a**) (28.8%) both as crystals. The major product (**5a**) showed characteristic ^{1}H n.m.r. signals at δ 4.13 (dd, *J* 7.5 and 5.0 Hz, 1 H) due to 3-H. The coupling constants of this signal were compatible with structure (**5a**) but not with structure (**6a**).[10,†] The ^{13}C n.m.r. spectrum had 11 lines (5 doublets and 6 triplets)[11] and hence compound (**5a**) was confirmed as 13-oxa-6-azatetracyclo[6.3.1.1^{3,6}.0^{4,10}]tridecane. The minor product (**6a**) was assigned structure 5-oxa-6-azatetracyclo[6.3.1.1^{3,6}.0^{4,10}]tridecane on the basis of the characteristic ^{1}H n.m.r. signal at δ 4.60 (t, *J* 9.0 Hz, 1 H) due to 4-H ‡ and ^{13}C n.m.r. signals (5 d and 6 t signals). Reaction at 130 °C for 46 h gave a 56:44 mixture of compound (**5a**) and (**6a**) based on ^{13}C n.m.r. analysis, indicating scant regioselectivity of this intramolecular cycloaddition of the nitrone (**4a**). In order to examine the substituent effect on the regio- and stereo-selectivities, the intramolecular cycloaddition of α-phenyl- and α-2-furylnitrones (**4b**) and (**4c**) were studied. The results are summarized in the Table. It is of interest that the nitrones (**4b**) and (**4c**) led to more selective formation of isomers (**5**) than did the unsubstituted nitrone (**4a**), because the nitrone's α-substituent is generally considered to be less important in determining the regiochemistry of intramolecular cycloaddition of *N*-alkenylnitrones.[6c]

Table. Intramolecular cycloaddition products of nitrones (**4a—c**)

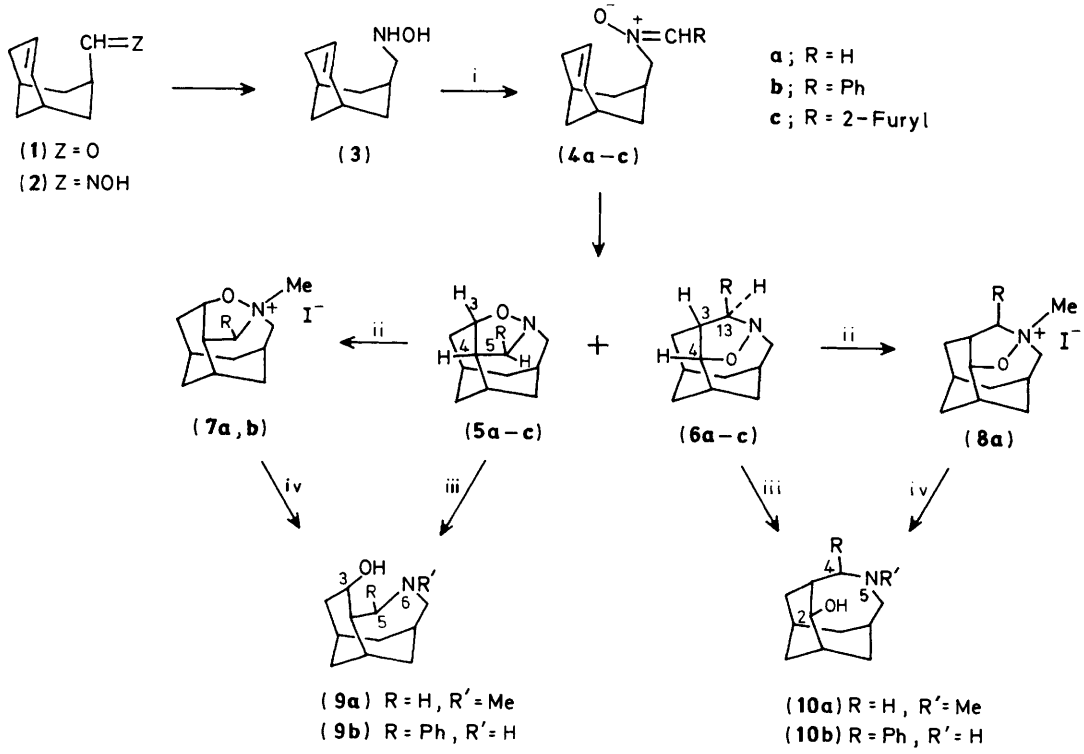
Nitrone	R	Reaction conditions[a] *T* (°C)	*t* (h)	Total yield[c] (%)	Product ratio (**5**):(**6**)
(**4a**)	H	100	135	75.6	62:38[c]
(**4a**)	H	130	46	27.3	56:44[d]
(**4b**)	Ph	140	30	66.0	74:26[d]
(**4b**)[b]	Ph	140	20	60.0	74:26[d]
(**4c**)	2-Furyl	140	30	44.5	95:5[d]

[a] All reactions were carried out in xylene (b.p. 138.5—141.5 °C) and unless otherwise stated the nitrones were generated *in situ* from (**3**) and the corresponding aldehyde. [b] The isolated nitrone was used. [c] Based on isolated amounts. [d] Based on ^{13}C n.m.r. analysis.

When a mixture of compound (**3**) (0.50 mmol) and benzaldehyde (0.75 mmol) in benzene was heated to reflux for 10 h, only nitrone (**4b**) was isolated (in 50% yield) after chromatography. But the same reaction at 140 °C for 30 h in xylene afforded a 74:26 mixture (based on ^{13}C n.m.r. analysis) of the cycloadducts (**5b**) and (**6c**) in 66% yield after chromatography. The nitrone (**4b**) on heating at 140 °C for 20 h in xylene also afforded a 74:26 mixture of (**5b**) and (**6b**), in 60% yield. The regioisomers could be separated on a Lobar LiChroprep Si 60 column ($CHCl_3$) to give (**6b**) (3.9% yield) from the first fractions and (**5b**) (39.5%) from the second fractions, both as crystals. The structures of these cycloadducts were determined by spectral data. The regio- and stereo-chemical assignments were based on characteristic ^{1}H n.m.r. signals at δ 4.06 (dd, *J* 7.1 and 4.6 Hz, 1 H, 3-H) and 4.77 (s, 1 H, 5-H) for (**5b**),† and at δ

† Examination of molecular models of (**5a**) indicates that the CH–CH dihedral angles for 3-H–4-H, 3-H–2-H$_{exo}$, and 3-H–2-H$_{endo}$ are 25, 35, and 90°, respectively; hence, the coupling constants calculated by the Karplus equation are 6.5, 5.4, and 0 Hz, respectively. These values are close to those observed. On the other hand, the dihedral angles for 4-H–3-H and 4-H–10-H of (**6a**) are both 15°, and hence a triplet pattern with the coupling constant 7.5 Hz is expected; the observed pattern is compatible with this calculation.

‡ Examination of molecular models indicates that the dihedral angles for 3-H–4-H, 3-H–2-H$_{exo}$, and 5-H–4-H of (**5b**) are 25, 35, and 90° respectively; these values correspond to coupling constants of 6.5, 5.4, and 0 Hz respectively, compatible with the observed values. Similarly, the dihedral angles 4-H–3-H, 4-H–10-H, and 13-H–3-H of (**6b**) are 15, 15, and 120°, respectively, corresponding to calculated coupling constants of 7.5, 7.5, and 2.2 Hz, respectively. These values are close to those observed.



Scheme. *Reagents:* i, RCHO; ii, MeI; iii, Zn/AcOH; iv, $LiAlH_4$

4.74 (t, *J* 10.0 Hz, 1 H, 4-H) and 4.06 (d, *J* 3.0 Hz, 1 H, 13-H) for (**6b**).† Other spectral and analytical data were compatible with the given structures. Thus, compounds (**5b**) and (**6b**) were characterized as 5-*exo*-phenyl-13-oxa-6-azatetracyclo-[6.3.1.$1^{3,6}$.$0^{4,10}$]tridecane and 13-*exo*-phenyl-5-oxa-6-aza-tetracyclo[6.3.1.$1^{3,6}$.$0^{4,10}$]tridecane, respectively.*

The reaction of a 1:1 mixture of (**3**) and 2-furaldehyde in xylene at 140 °C for 30 h afforded a 95:5 mixture of regio-isomers (**5c**) and (**6c**) (^{13}C n.m.r. analysis) in 44.5% yield after chromatography. The major isomer (**5c**) was isolated after pre-parative t.l.c. (p.l.c.) (Wakogel B-5F, CH_2Cl_2) as crystals (24.4%). The regio- and stereo-chemical assignments were aided by characteristic ^{1}H n.m.r. signals at δ 4.78 (s, 1 H, 5-H) and 4.25 (dd, *J* 7.5 and 4.5 Hz, 1 H, 3-H).

The observed regioselective and stereospecific formation of compound (**5c**) deserve some comments. In intramolecular cycloadditions of *N*-alk-5-enylnitrones, preferred cyclization of the C–C bond to a 7-membered ring, *i.e.* the ring system (**5**) for the present case, rather than to an 8-membered ring, *i.e.* the ring system (**6**), is entropically favoured as was discussed by Oppolzer *et al.* recently.[6c] But this factor cannot be the predominant one for the present relatively rigid *N*-alkenyl-nitrones compared with the acyclic examples.[6c] Inspection of stereomodels of *Z*-nitrones† clearly indicates that a cyclic transition state A leading to (**5**) suffers from less geometrical constraint for an ideal parallel and simultaneous overlap of the nitrone moiety compared with a transition state B leading to (**6**), which suffers from a considerable geometrical constraint (taking a nearly half-chair–half-boat conformation) and extra severe non-bonded interactions between 8-H_{endo} and the nitrone's CH and substituent (Figure). The α-substituent of the nitrone increases the non-bonded interactions, leading to more selective formation of isomer (**5**) as observed. Such regiochemical control by non-bonded interactions in an α-alkenylnitrone has been reported recently.[6d]

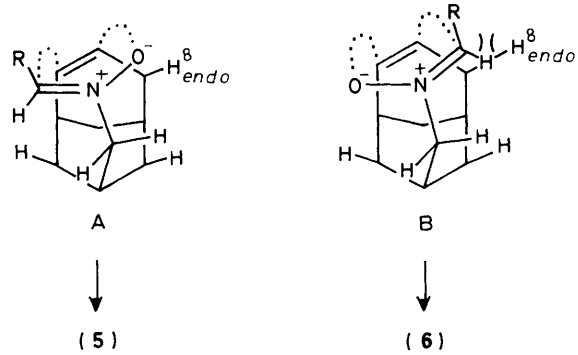


Figure.

Treatment of adducts (**5a**), (**5b**), and (**6a**) with a large excess of methyl iodide gave the corresponding methiodides (**7a**), (**7b**), and (**8a**) in goods yields, respectively (Scheme).

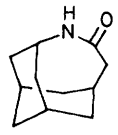
Usual reductive cleavage of (**5a**) with zinc in aq. AcOH gave only an intractable complex mixture, but $LiAlH_4$ reduction of the methiodide (**7a**) gave 6-methyl-6-azatricyclo[6.3.1.$0^{4,10}$]-dodecan-3-*endo*-ol (**9a**) as an oil (60.5%) which gave a crystal-line picrate. The phenyl derivative (**5b**) was cleanly cleaved by zinc in aq. AcOH to give 5-*endo*-phenyl-6-azatricyclo-[6.3.1.$0^{4,10}$]dodecan-3-*endo*-ol (**9b**) as crystals (57.9%). On the

* In this paper, a substituent is designated conventionally as *exo* if it is oriented toward the smaller ring of the polycyclic skeleton and *endo* if it faces the larger ring.

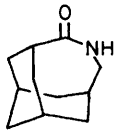
† Considerable steric repulsions between the substituent and 2-H_{endo} and/or 8-H_{endo} apparently disfavour the transition state for the *E*-nitrone. The observed stereochemistry is also in accord with the proposed transition states. See also refs. 6*c* and 6*d*.

other hand, zinc reduction of (**6a**) again gave complex products, but $LiAlH_4$ reduction of the methiodide (**8a**) afforded 5-methyl-5-azatricyclo[5.3.1.1^{3,9}]dodecane-2-*endo*-ol (2-*endo*-hydroxy-5-methyl-5-aza-1,1-bishomoadamantane)[12] (**10a**) as an oil which gave a crystalline picrate. The zinc reduction of (**6b**) afforded cleanly 2-*endo*-hydroxy-4-*syn*-phenyl-5-aza-1,1-bishomoadamantane* (**10b**) as crystals. The given structure of these novel monoazatricyclic derivatives were compatible with their spectral data (see Experimental section).

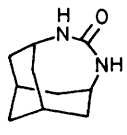
Although 4-azatricyclo[5.3.1.1^{3,9}]dodecan-5-one (**11**) is readily obtainable by the Beckmann rearrangement route, although 5-azatricyclo[5.3.1.1^{3,9}]dodecan-4-one (**12**) is difficult to obtain in pure form by the Beckmann or Schmidt reaction route[13] and 4,6-diazatricyclo[5.3.1.1^{3,9}]dodecan-5-one (**13**) is in fact prepared by the double Beckmann rearrangement route,[14] the 5-monoaza derivatives of this ring system seem not to have been recorded previously. In view of this, the intramolecular cycloaddition route of *N*-bicycloalkenylnitrones is very useful for synthesis of these functionalized monoazatricyclic ring systems.



(**11**)



(**12**)



(**13**)

Experimental

M.p.s were taken in a sealed tube on a Yanagimoto micro-melting point apparatus and are uncorrected. I.r. spectra were obtained on a JASCO IRA-100 spectrometer. ^1H and ^{13}C n.m.r. spectra were recorded on a JEOL JNM-60HL instrument at 60 MHz and a JEOL-60 FT n.m.r. spectrometer at 15.04 MHz, respectively. Chemical shifts are reported in parts per million (δ) relative to Me_4Si as internal standard. Unless otherwise stated, all n.m.r. spectra were run in $CDCl_3$. Mass spectra were obtained with a JEOL JMS-D10 mass spectrometer at 75 eV, and an ESCO EMD-05B mass spectrometer at 70 eV. Microanalyses were performed with a Perkin-Elmer 240B elemental analyzer.

Bicyclo[3.3.1]*non*-6-*ene*-3-endo-*carbaldehyde Oxime* (**2**).—To a cooled (−10 to −15 °C) and stirred solution of $NaBH_4$ (190 mg, 5.02 mmol) in methanol (25 ml) and water (5 ml) was added 4(eq)-(methylsulphonyloxy)adamantan-2-one[15] (2.20 g, 8.93 mmol). After the mixture had been stirred for 2 h (the reaction was monitored by t.l.c.; silica gel–$CHCl_3$), the remaining $NaBH_4$ was decomposed by addition of AcOH (0.5 ml). The reaction mixture was allowed to attain room temperature, and then stirred and treated with hydroxylamine hydrochloride (1.30 g, 18.7 mmol), followed by a solution of KOH (2.60 g) in water (10 ml). The mixture was stirred for 3 h, concentrated to *ca.* 20 ml under reduced pressure, and neutralized with 10% hydrochloric acid. The precipitated oxime was collected by filtration and washed with cold water to afford practically pure *oxime* (**2**) as crystals (1.08 g, 73.2%), m.p. 88.89 °C (Found: C, 72.8; H, 8.89; N, 8.18. $C_{10}H_{15}NO$ requires C, 72.69; H, 9.15; N, 8.48%); $\nu_{max.}$(KBr) 3 240, 3 020, 2 900, 1 640, 1 440, 1 300, 920, 720, and 680 cm^{-1}; δ_H 9.2—8.8 (m, 1 H, D_2O-exchangeable), 7.50 (d, *J* 5.5 Hz, 1 H), 6.1—5.3 (m, 2 H), and 2.9—1.5 (m, 11 H). On shaking with D_2O, new signals at δ 6.98 (d, *J* 6.0 Hz, 0.4 H) and 3.5—2.9 (m, 0.4 H) appeared, with concomitant decrease in the δ 7.50 and 2.9—1.5 signals. These new signals may be due to an *E*-oxime formed during the deuteriation.[16]

N-{(endo-*Bicyclo*[3.3.1]*non*-6-*en*-3-*yl*)*methyl*}*hydroxylamine* (**3**).—To a stirred mixture of the oxime (**2**) (496 mg, mmol) and a trace of Bromocresol Green in methanol (30 ml) was added $NaBH_3CN$ (380 mg, 6.00 mmol).[17] The resulting deep blue mixture was stirred and acidified by 2M-HCl–MeOH to produce the yellow mixture. After 1.5 h, the mixture was concentrated to *ca.* 10 ml, diluted with water (10 ml), basified strongly with 20% KOH, saturated with sodium chloride, and extracted with chloroform (20 ml × 4). The combined extracts were dried ($MgSO_4$), and evaporated under reduced pressure. The obtained residue was chromatographed on a silica gel column (CH_2Cl_2–AcOEt) to afford the hydroxylamine (**3**) as a solid (392 mg, 78.1%), m.p. 89—91 °C. The *hydrochloride*, m.p. 98—100 °C (Found: C, 58.7; H, 8.9; N, 7.15. $C_{10}H_{18}ClNO$ requires C, 58.96; H, 8.91; N, 6.88%); $\nu_{max.}$(KBr) 3 440, 2 940, 1 545, 1 455, 1 445, 1 395, 1 015, 935, and 720 cm^{-1}; δ_H 9.78 (br, s 3 H, D_2O-exchangeable), 6.10—5.35 (m, 2 H), 3.29 (d, *J* 6.0 Hz, 2-H), and 2.7—1.3 (m, 11 H).

13-*Oxa*-6-*azatetracyclo*[6.3.1.1^{3,6}.0^{4,10}]*tridecane* (**5a**) *and* 5-*Oxa*-6-*azatetracyclo*[6.3.1.1^{3,6}.0^{4,10}]*tridecane* (**6a**).—A mixture of the hydroxylamine (**3**) (390 mg, 2.33 mmol), paraformaldehyde (440 mg, 14.7 mmol of CH_2O), and 4A molecular sieves (1.0 g) in xylene (b.p. 138.5—141.5 °C; 10 ml) was heated under argon at 100 °C for 135 h in a sealed tube. After removal of the solvent under reduced pressure, the residue was purified on a silica gel column (Merck Kieselgel 60; $CHCl_3$) to afford the *cycloadduct* (**6a**) (first fractions) as crystals (from hexane–CH_2Cl_2) (120 mg, 28.8%), m.p. 212—214 °C (decomp.) (Found: C, 73.7; H, 9.6; N, 7.8. $C_{11}H_{17}NO$ requires C, 73.70; H, 9.56; N, 7.81%); $\nu_{max.}$(KBr) 2 930, 1 460, 1 045, 945, and 820 cm^{-1}; δ_H 4.60 (1 H, t, *J* 9.0 Hz, 4-H), 4.0—3.2 (m, 2 H), and 3.0—1.2 (m, 14 H); δ_C 80.0 (d),† 64.8 (t), 64.2 (t), 38.4 (t), 37.8 (d), 34.2 (t), 32.8 (t), 32.4 (d), 32.3 (t), 31.1 (d), and 26.0 (d); *m/z* (%) 180 (28), 179 (M^+, 52), 162 (27), 150 (34), 149 (68), 94 (57), 90 (69), 78 (100), and 76 (65).

The second fractions gave the cycloadduct (**5a**) as crystals (from hexane–CH_2Cl_2) (195 mg, 46.8%), m.p. 230—231 °C (Found: C, 73.6; H, 9.44; N, 7.9%); $\nu_{max.}$(KBr) 2 940, 1 460, 1 440, 1 035, 1 010, 825, 785, and 755 cm^{-1}; δ_H 4.13 (dd, *J* 7.5, 5.0 Hz, 1 H, 3-H), 3.51 (d, *J* 12.0 Hz, 1 H, 7-H_{endo}), 3.17 (d, *J* 12.0 Hz, 1 H, 7-H_{exo}), 3.55—2.55 (m, 3 H), and 2.35—1.40 (m, 11 H); δ_C 76.4 (d), 63.8 (t), 56.8 (t), 43.1 (d), 37.2 (t), 34.6 (t), 34.1 (t), 31.9 (t), 30.5 (d), 27.6 (d), and 25.3 (d); *m/z* (%) 179 (M^+, 22), 149 (100), 93 (25), 81 (21), 57 (23), and 55 (22)

The same reaction at 130 °C for 46 h gave a 56:44 mixture (based on ^{13}C n.m.r. analysis) of (**5a**) and (**6a**) in 27.3% yield after chromatography.

N-{(endo-Bicyclo[3.3.1]*non*-6-*en*-3-*yl*)*methyl*}-α-*phenylnitrone* (**4b**).—A mixture of (**3**) hydrochloride (103 mg, 0.50 mmol) and triethylamine (55 mg, 0.54 mmol) in benzene (4 ml) was stirred at room temperature for 1 h. The precipitate was filtered off and washed with benzene (1 ml). To the combined filtrate and washings were added benzaldehyde (80 mg, 0.75 mmol) and 4A molecular sieves (0.3 g), and the mixture was heated to reflux for 10 h under argon. Removal of the solvent and remaining benzaldehyde under reduced pressure, and chromatography of the residue on a silica gel column ($CHCl_3$) afforded the *nitrone* (**4b**) as crystals from CH_2Cl_2 (64 mg, 50.2%), m.p. 97—98 °C (Found: C, 80.0; H, 8.0; N, 5.3.

* In this paper, a substituent is designated as *syn* if it is oriented toward the hydroxy group.

† Unless otherwise noted, all ^{13}C peaks corresponded one carbon atom.

$C_{17}H_{21}NO$ requires C, 79.96; H, 8.29; N, 5.49%); $\nu_{max.}$(KBr) 3 040, 2 940, 1 590, 1 450, 1 430, 1 160, 760, and 690 cm^{-1}; δ_H 8.43—7.15 (m, 6 H), 6.20—5.45 (m, 2 H), 4.1—3.8 (m, 2 H), and 3.0—1.2 (m, 11 H); *m/z* (%) 255 (M^+, 34), 238 (57), 135 (30), 118 (100), and 91 (75).

5-exo-*Phenyl*-13-*oxa*-6-*azatetracyclo*[6.3.1.1^{3,6}.0^{4,10}]*tridecane* (**5b**) *and* 13-exo-*Phenyl*-5-*oxa*-6-*azatetracyclo*[6.3.1.1^{3,6}.0^{4,10}]*tridecane* (**6b**).—A mixture of compound (**3**) (350 mg, 2.09 mmol), benzaldehyde (400 mg, 3.67 mmol), and 4A molecular sieves (1.0 g) in xylene (5 ml) was heated under argon at 140 °C for 30 h in a sealed tube. After removal of the solvent under reduced pressure, the residue was chromatographed on a silica gel column (CH_2Cl_2) to afford a 74:26 mixture (^{13}C n.m.r. analysis) of title products (**5b**) and (**6b**) (352 mg, 60.0%). Further purification of this mixture on a Lobar LiChroprep Si 60 column (size B; $CHCl_3$) gave the *adduct* (**6b**) (the first fractions) as crystals from hexane–CH_2Cl_2 (21 mg, 3.9%), m.p. 103.0—103.5 °C (Found: C, 79.95; H, 8.2; N, 5.7. $C_{17}H_{21}NO$ requires C, 79.96; H, 8.29; N, 5.49%); $\nu_{max.}$(KBr) 2 930, 2 880, 1 600, 1 500, 1 455, 1 105, 1 000, 900, and 695 cm^{-1}; δ_H 7.5—7.0 (m, 5 H), 4.74 (t, *J* 10.0 Hz, 1 H, 4-H), 4.06 (d, *J* 3.0 Hz, 1 H, 13-H), 3.65 (d, *J* 15.0 Hz, 1 H, 7-H$_{endo}$), 2.95 (d, *J* 15.0 Hz, 1 H, 7-H$_{exo}$), and 2.8—1.2 (m, 12 H); δ_C 146.8 (s), 128.5 (d, 2 C), 126.3 (d), 125.4 (d, 2 C), 81.0 (d), 79.5 (d), 65.2 (t), 48.6 (d), 38.4 (d), 34.7 (t), 32.9 (t), 32.8 (t), 32.0 (t), 31.3 (d), and 26.4 (d); *m/z* (%) 255 (M^+, 67), 205 (20), 149 (49), 104 (49), 94 (33), 91 (100), 80 (29), 77 (20), and 67 (36).

The second fractions gave the *adduct* (**5b**) as crystals from hexane–CH_2Cl_2 (211 mg, 39.5%), m.p. 113—114 °C (Found: C, 80.0; H, 8.35; N, 5.4%); $\nu_{max.}$(KBr) 3 080, 3 040, 2 920, 1 600, 1 500, 1 450, 1 030, 720, and 690 cm^{-1}; δ_H 7.6—7.0 (m, 5 H), 4.77 (s, 1 H, 5-H), 4.06 (dd, *J* 7.1, 4.6 Hz, 1 H, 3-H), 3.59 (d, *J* 15.0 Hz, 1 H, 7-H$_{endo}$), 2.96 (d, *J* 15.0 Hz, 1 H, 7-H$_{exo}$), 2.83 (t, *J* 7.5 Hz, 1 H, 4-H), and 2.52—1.20 (m, 11 H); δ_C 143.3 (s), 128.2 (d, 2 C), 126.4 (d), 125.9 (2 C), 74.4 (d), 69.8 (d), 64.1 (t), 50.4 (d), 37.0 (t), 35.5 (t), 34.5 (t), 32.0 (t), 30.8 (d), 28.0 (d), and 25.3 (d); *m/z* (%) 255 (M^+, 50), 238 (55), 149 (60), 135 (36), 118 (93), 92 (100), 79 (49), 77 (30), and 57 (32).

Heating of the nitrone (**4b**) (50 mg, 0.20 mmol) in xylene (2 ml) at 140 °C for 20 h and purification on a silica gel column (CH_2Cl_2) gave a 74:26 mixture (^{13}C n.m.r. analysis) of compounds (**5b**) and (**6b**) (30 mg, 60.0%).

5-exo-(2-*Furyl*)-13-*oxa*-6-*azatetracyclo*[6.3.1.1^{3,6}.0^{4,10}]*tridecane* (**5c**).—A mixture of (**3**) hydrochloride (204 mg, 1.10 mmol) and triethylamine (120 mg, 1.19 mmol) in xylene (5 ml) was stirred for 1 h. The precipitate was filtered off and washed with xylene (1 ml). To the combined filtrate and washings were added 2-furaldehyde (106 mg, 1.10 mmol) and 4A molecular sieves (0.6 g). The mixture was heated under argon at 140 °C for 30 h. Removal of the solvent, and chromatography of the residue on a silica gel column ($CHCl_3$), gave a 95:5 mixture (^{13}C n.m.r. analysis) of compound (**5c**) and (**6c**) as a solid (110 mg, 44.5%), m.p. 82—84 °C. Further purification by p.l.c. (Wakogel B-5F; CH_2Cl_2) afforded the *adduct* (**5c**) as crystals from hexane–CH_2Cl_2 (60 mg, 24.4%), m.p. 89—90 °C (Found: C, 73.6; H, 7.9; N, 5.5. $C_{15}H_{19}NO_2$ requires C, 73.44; H, 7.81; N, 5.71%); $\nu_{max.}$(KBr) 3 120, 2 920, 1 600, 1 450, 1 340, 1 200, 1 020, 800, and 750 cm^{-1}; δ_H 7.4—7.2 (m, 1 H), 6.4—6.2 (m, 2 H), 4.78 (s, 1 H, 5-H), 4.25 (dd, *J* 7.5, 4.5 Hz, 1 H, 3-H), 3.24 (ABq, *J* 15.0 Hz, Δ/J 2.320, 2 H, 7-H$_2$), 3.08 (t, *J* 7.5 Hz, 1 H, 4-H), and 2.6—1.3 (m, 11 H); δ_C 155.6 (s), 141.2 (d), 110.3 (d), 105.5 (d), 75.4 (d), 65.1 (d), 64.0 (t), 46.5 (d), 37.1 (t), 35.1 (t), 34.4 (t), 32.0 (t), 30.7 (d), 27.3 (d), and 25.2 (d); *m/z* (%) 245 (M^+, 50), 228 (100), 216 (10), 108 (84), and 91 (25).

Attempts to isolate the minor regioisomer (**6c**) were unsuccessful.

6-*Methyl*-13-*oxa*-6-*azoniatetracyclo*[6.3.1.1^{3,6}.0^{4,10}]*tridecane Iodide* (**7a**).—A mixture of compound (**5a**) (100 mg, 0.56 mmol) and methyl iodide (2.30 g, 16.0 mmol) in methylene dichloride (5 ml) was kept at ambient temperature for 2 days. The resulting crystals were filtered off and washed with ether to afford the *methiodide* (**7a**) (180 mg, 100%), m.p. 184—185 °C (decomp.) (Found: C, 45.15; H, 6.4; N, 4.5. $C_{12}H_{20}INO$ requires C, 44.87; H, 6.28; N, 4.36%); $\nu_{max.}$(KBr) 3 000, 2 920, 2 860, 1 460, 1 065, 1 015, 950, 920, 830, and 790 cm^{-1}; δ_H 5.5—5.0 (m, 2 H), 4.75—4.20 (m, 2 H), 3.83 (s, 3 H), 3.95—3.20 (m, 2 H), and 2.8—1.5 (m, 11 H); δ_C 82.9 (d), 72.9 (t), 69.0 (t), 57.6 (q), 40.2 (d), 35.1 (t), 32.4 (t, 2 C), 30.4 (t), 28.7 (d), 26.5 (d), and 23.9 (d).

6-*Methyl*-5-*oxa*-6-*azoniatetracyclo*[6.3.1.1^{3,6}.0^{4,10}]*tridecane Iodide* (**8a**).—A solution of compound (**6a**) (30 mg, 0.17 mmol) and methyl iodide (0.50 g, 3.52 mmol) in methylene dichloride (0.5 ml) was kept at ambient temperature for 2 days to give a crystalline precipitate, which was filtered off and washed with ether to give the *methiodide* (**8a**) (40 mg, 73.3%), m.p. 225—227 °C (decomp.) (Found: C, 45.15; H, 6.4; N, 4.5%); $\nu_{max.}$(KBr) 3 000, 2 925, 1 460, 1 380, 960, and 775 cm^{-1}; δ_H 5.25 (t, *J* 9.0 Hz, 1 H 4-H), 5.05—3.50 (m, 4 H), 3.83 (s, 3 H), and 2.85—1.50 (m, 12 H); δ_C 83.9 (d), 74.1 (t), 72.6 (t), 58.8 (q), 36.2 (d), 36.0 (t), 32.8 (t), 31.5 (t), 30.3 (d), 30.1 (d), 29.3 (t), and 24.4 (d).

6-*Methyl*-5-exo-*phenyl*-13-*oxa*-6-*azoniatetracyclo*[6.3.1.1^{3,6}.0^{4,10}]*tridecane Iodide* (**7b**).—A solution of compound (**5b**) (60 mg, 0.23 mmol) and methyl iodide (1.0 g, 7.05 mmol) in methylene dichloride (0.5 ml) was kept at ambient temperature for 2 days, to afford a crystalline precipitate, which was filtered off and washed with ether to give the *methiodide* (**7b**) (90 mg, 100%), m.p. 212—213 °C (decomp.) (Found C, 54.4; H, 6.1; N, 3.6. $C_{18}H_{24}INO$ requires C, 54.42; H, 6.09; N, 3.53%); $\nu_{max.}$(KBr) 2 930, 1 500, 1 460, 950, 725, and 695 cm^{-1}; δ_H 7.60—7.35 (m, 5 H), 6.24 (s, 1 H, 5-H), 5.90—5.05 (m, 3 H), 3.88—1.60 (m, 12 H), and 3.15 (s, 3 H).

6-*Methyl*-6-*azatricyclo*[6.3.1.0^{4,10}]*dodecan*-3-endo-*ol* (**9a**).—The methiodide (**7a**) (120 mg, 0.43 mmol) was added into a suspension of $LiAlH_4$ (190 mg, 5.00 mmol) in anhydrous ether (10 ml) and the mixture was heated to reflux for 5 h under argon. The cooled mixture was carefully diluted with water (0.5 ml) followed by 10% NaOH (0.5 ml), and was then dried (Na_2SO_4). Removal of the solvent gave the practically pure alcohol (**9a**) as an oil (50 mg, 60.5%), *picrate* m.p. 234—237 °C (decomp.) (Found: C, 50.7; H, 6.0; N, 13.1. $C_{18}H_{24}N_4O_8$ requires C, 50.94; H, 5.70; N, 13.20%); $\nu_{max.}$ (**9a**) (neat film) 3 380, 2 900, 2 780, 2 730, 1 455, 1 440, 1 220, 1 050, 970, 940, and 790 cm^{-1}; δ_H (**9a**) 4.3—3.8 (m, 1 H), 3.8—3.4 (m, 1 H, D_2O-exchangeable), 2.26 (s, 3 H), and 3.1—0.9 (m, 16 H); δ_C 68.2 (d), 66.9 (t), 55.3 (t), 48.4 (q), 39.0 (d), 34.8 (t), 32.0 (t), 30.3 (d), 29.7 (t), 29.3 (t), 29.0 (d), and 25.2 (d); *m/z* (%) 195 (M^+, 43), 178 (26), 135 (22), 93 (21), 91 (21), 84 (21), 79 (22), 71 (37), 67 (21), and 58 (100).

5-endo-*Phenyl*-6-*azatricyclo*[6.3.1.0^{4,10}]*dodecan*-3-endo-*ol* (**9b**).—A stirred mixture of the adduct (**5b**) (60 mg, 0.23 mmol) and zinc dust (0.5 g) in a mixture of AcOH (1 ml) and water (0.5 ml) was heated to reflux for 6 h. The cooled mixture was basified with 20% aqueous KOH and extracted with chloroform (10 ml × 5). The combined extracts were dried ($MgSO_4$), and evaporated under reduced pressure. The residue was chromatographed (silica gel; $CHCl_3$) to give *compound* (**9b**) as crystals from hexane–CH_2Cl_2 (35 mg, 57.9%), m.p. 131—132 °C (Found: C, 79.4; H, 9.3; N, 5.4. $C_{17}H_{23}NO$ requires C, 79.33; H, 9.01; N, 5.44%); $\nu_{max.}$(KBr) 3 600—3 000, 2 950, 1 600, 1 455, 1 090, 1 070, and 890 cm^{-1}; δ_H 7.60—7.05 (m, 5 H), 4.35 (s, 1 H, 5-H), 4.15 (t, *J* 8.5 Hz, 1 H, 3-H), 1.70 (br s, 2 H, D_2O-exchangeable), 3.2—1.0 (m, 14 H); *m/z* (%) 257 (M^+, 54), 240

(40), 233 (23), 149 (28), 144 (21), 93 (34), 79 (34), 57 (57), and 41 (100).

5-*Methyl*-5-*azatricyclo*[5.3.1.1^{3,9}]*dodecan*-2-endo-*ol* (**10a**).—The methiodide (**8a**) (200 mg, 0.71 mmol) was added to a suspension of $LiAlH_4$ (380 mg, 10.0 mmol) in anhydrous ether (30 ml) and the mixture was heated to reflux for 5 h under argon. The cooled mixture was treated successively with water (0.5 ml) and 10% NaOH (1.0 ml) as above and was then dried (Na_2SO_4). Removal of the solvent under reduced pressure gave the practically pure alcohol (**10a**) as an oil (50 mg, 36.1%), which gave a crystalline *picrate*, m.p. 218—221 °C (decomp.) (Found: C, 50.7; H, 6.0; N, 13.15. $C_{18}H_{24}N_4O_8$ requires C, 50.94; H, 5.70; N, 13.20%); $\nu_{max.}$ (neat film of free base) 3 520, 2 920, 1 460, 1 290, 1 060, 1 005, and 800 cm^{-1}; δ_H 3.98 (dd, *J* 8.0, 5.5 Hz, 1 H, 2-H), 4.3—4.0 (br s, 1 H, D_2O-exchangeable), 2.25 (s, 3 H), and 3.4—1.2 (m, 16 H); δ_C 74.1 (d), 68.1 (t), 63.8 (t), 49.3 (q), 38.9 (t), 36.4 (t), 34.1 (t), 33.7 (d), 32.9 (d), 27.2 (d), 26.3 (t), and 25.3 (d); *m/z* (%) 195 (M^+, 43), 136 (33), 84 (34), 82 (23), 79 (21), 71 (31), 58 (100), and 57 (58).

4-syn-*Phenyl*-5-*azatricyclo*[5.3.1.1^{3,9}]*dodecan*-2-endo-*ol* (**10b**).—A stirred mixture of compound (**6b**) (12 mg, 0.05 mmol) and zinc dust (0.2 g) in a mixture of AcOH (1 ml) and water (0.5 ml) was heated to reflux for 5 h. The cooled mixture was basified with 20% aqueous KOH and extracted with chloroform (5 ml × 4). The combined extracts were dried ($MgSO_4$), and evaporated under reduced pressure. The residue was purified by p.l.c. (silica gel; $CHCl_2$) to give the *title compound* (**10b**) as crystals from hexane–CH_2Cl_2 (10 mg, 82.7%), m.p. 58—60 °C (Found: C, 79.5; H, 9.3; N, 5.6. $C_{17}H_{23}NO$ requires C, 79.33; H, 9.01; N, 5.44%); $\nu_{max.}$(KBr) 3 600—3 000, 2 920, 1 600, 1 450, 1 065, 795, 755, and 690 cm^{-1}; δ_H 7.7—7.1 (m, 5 H), 4.4—3.8 (br m, 2 H, D_2O-exchangeable), 4.02 (dd, *J* 7.5, 5.0 Hz, 1 H, 2-H), 3.62 (d, *J* 3.0 Hz, 1 H, 4-H), 3.2—2.5 (m, 3 H), and 2.5—1.2 (m, 11 H); δ_C 148.4 (s), 128.8 (d, 2 C), 127.1 (d, 2 C), 126.9 (d), 74.3 (d), 73.0 (d), 60.3 (t), 40.3 (d), 39.4 (t), 34.8 (t), 34.6 (t), 34.4 (d), 27.1 (d), 27.0 (t), and 26.2 (d); *m/z* (%) 257 (M^+, 21), 144 (10), 118 (16), 106 (19), 91 (19), and 86 (100).

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