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SYNTHESIS OF ADAMANTANE DERIVATIVES—XIII[1]

SYNTHESIS OF 9-METHYL-9-AZATRICYCLO[3.3.1.0^{3,7}]NONANE (9-METHYL-9-AZANORADAMANTANE) AND ITS DERIVATIVES[2]

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Abstract—Pyrolytic decomposition of the sodium salt of pseudopelletierine tosylhydrazone in diglyme gave 80% yield of 9-methyl-9-azatricyclo[3.3.1.0^{3,7}]nonane (IIIa), while the decomposition in ethylene glycol afforded IIIa (11%) and 9-methyl-9-azabicyclo-[3.3.1]nonene-2 (IV) (35%) and the pyrolysis without solvent gave IIIa (53%) and IV (19%). The photolytic decomposition in ether gave also IIIa (30·3%) and IV (33·3%), but in this case, together with 1-azatricyclo[4.3.0.1^{3,9}]nonane (V) (6·1%) and 9-methyl-9-azatricyclo[3.3.1.0^{1,3}]nonane (VI) (4·3%). The Hofmann degradation of the methiodide (VIIa) of IIIa afforded 7-dimethylaminobicyclo[3.3.0]octene-2 (VIII) which was further converted to bicyclo[3.3.0]octene-2 (XII) by repeated Hofmann degradation after the hydrogenation. IIIa was converted to 9-azatricyclo[3.3.1.0^{3,7}]nonane (IIIc) *via* an N-oxide (XIII), followed by an N-acetyl derivative (IIIb), and also by direct oxidation of IIIa with mercuric acetate. Bromination of IIIa and VIIa afforded the corresponding perbromides VIIb and VIIc respectively.

In carbenoid decomposition of diazocycloalkanes, the steric circumstances of the reacting molecules play a very important role in determining the reaction courses and the product distributions, as is demonstrated by several transannular insertion reactions including those involving 1,3-, 1,5- and 1,6-positions in seven ~ ten membered cycloalkyl carbenes.[3] Since no transannular reactions mediated by a carbene have been reported in the 3-carbenabicyclo[3.3.1]nonane ring system and since there is no information on the relation between the conformational effects and the intramolecular insertion reactions in contrast to acyclic,[4] monocyclic,[3] and more rigid bicyclo[2.2.1]heptyl,[5] and bicyclo[2.2.2]octyl systems,[6] we examined the possibility of transannular insertion reactions of the 3-carbenabicyclo[3.3.1]nonane ring system. This was linked with our deep interest in the synthesis of cage-compounds such as adamantane. In continuing our preliminary report,[2] this paper deals with the synthesis of 9-methyl-9-azatricyclo[3.3.1.0^{3,7}]nonane (9-methyl-9-azanoradamantane) (IIIa) by the 3,7-transannular C—H insertion reaction of 9-methyl-9-azabicyclo[3.3.1]nonanyl-3-carbene (I).

RESULTS AND DISCUSSION

The decomposition reactions of the sodium salt of pseudopelletierine tosylhydrazone

In the decomposition of 3-diazobicyclo[3.3.1]nonane, if the bicyclononane ring system is assumed to take up preferentially a chair-chair conformation,[7] a 3,7-transannular insertion would be expected rather than the 1,3-insertion from the proximity effects.[3b] From this point of view, 9-methyl-9-azabicyclo[3.3.1]nonanyl-3-carbene (I) seems to be a suitable intermediate for the synthesis of a novel norazaadamantane ring, because the corresponding ketone (IIa) is a readily available compound which has been known to take up preferentially a chair-chair conformation.[8] This expectation has been verified by the facile conversion of the sodium salt (IIc) of pseudopelletierine tosylhydrazone (IIb) to 9-methyl-9-azatricyclo[3.3.1.0^{3,7}]nonane (IIIa) in 80% yield on heating in dry diglyme at 165°, reported in our preliminary communication.[2] Inspection of the crude product by its NMR (100 MHz) spectrum and GLC analysis indicated the exclusive occurrence of the expected 3,7-transannular insertion reaction.[9] When ethylene glycol was used as a solvent at 195° instead of the aprotic diglyme, the decomposition yielded 46% of the basic products which were characterized as a mixture of IIIa (24%) and 9-methyl-9-azabicyclo [3.3.1]nonene-2 (IV) (76%) on the basis of NMR data following conversion to the picrates.[2] Dry pyrolysis of IIc gave a mixture of IIIa (74%) and IV (26%) in 72% yield on GLC. Considering that the relative extent of carbenic and cationic processes has been known to be much affected by the protonicity of the solvent,[10] the observed higher ratio of IIIa to IV even in ethylene glycol indicates a facile 3,7-transannular carbenic insertion in this ring system.[11]

For comparison, a photolytic decomposition of IIc was carried out. The crude product was found to be a mixture of IIIa (41%) and IV (45%) together with other products (14%) on GLC; these were isolated as a mixture of 1-azatricyclo[4.3.0.1^{3,9}] nonane (V) and 9-methyl-9-azatricyclo[3.3.1.0^{1,3}]nonane (VI) in the ratio of 6:4, tentatively assigned on the basis of the analytical and NMR data. In the NMR spectrum of the mixture (Fig 1), no signals due to olefinic protons at τ 3·92 and 4·40 for IV and N-methyl protons at τ 7·22 for IIIa were observed, but instead, characteristic signals were observed at τ 6·65, 7·05 and 8·92. A signal at τ 6·65 can be assigned to newly-formed pyrrolidine ring methylene protons of V, that at τ 8·92 to newly-formed cyclopropane ring methylene protons of VI, whilst that at τ 7·05 N-methyl is assigned to protons of VI, the latter being down-field shifted because of the presence of the cyclopropane ring. From the intensity ratio of the signals at τ 6·65 and 7·05, the ratio of the mixture of V and VI was estimated to be 6:4.

The product distribution under different conditions is summarized in Table 1.

TABLE 1. DECOMPOSITION PRODUCTS OF IIc UNDER VARIOUS CONDITIONS

Solvent	Temp	Total Yield (%)	Products (Relative Yield, %)
Diglyme	165°	80	IIIa (100)
Ethylene glycol	195°	46	IIIa (24) + IV (76)
None	160°	72	IIIa (74) + IV (26)
Ether	20° (hν)	74	IIIa (41) + IV (45) + [V + VI] (14)

The fact that somewhat different results were obtained from the photolysis and the pyrolysis of IIc seems to be of interest, assuming III and IV to be produced from a chair-chair conformation of I, and V and VI, from its chair-boat conformation. A study of the Dreiding stereomodel of I explains this situation as is depicted in Fig 2, showing various distances between C—H and C3 carbene.

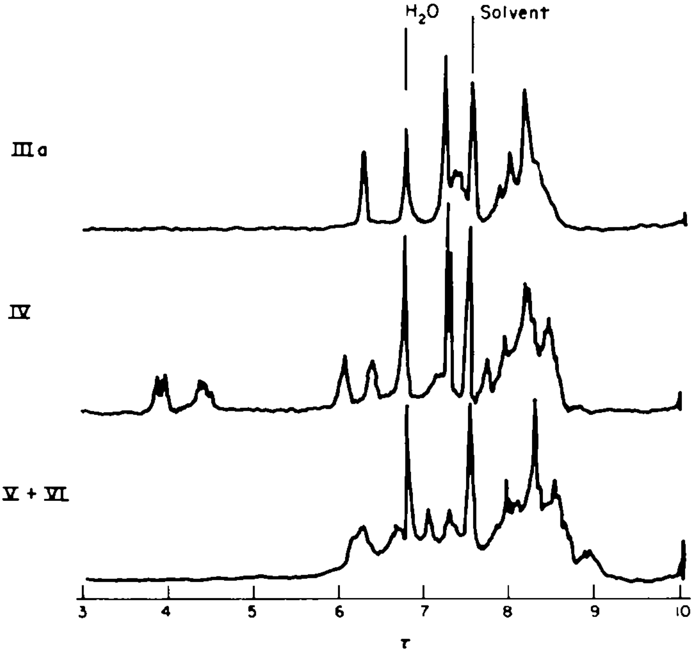


FIG 1. NMR Spectrum of a Mixture of V and VI (picrates) in Comparison with Those of IIIa and IV in $(CD_3)_2SO$ at 100 MHz.

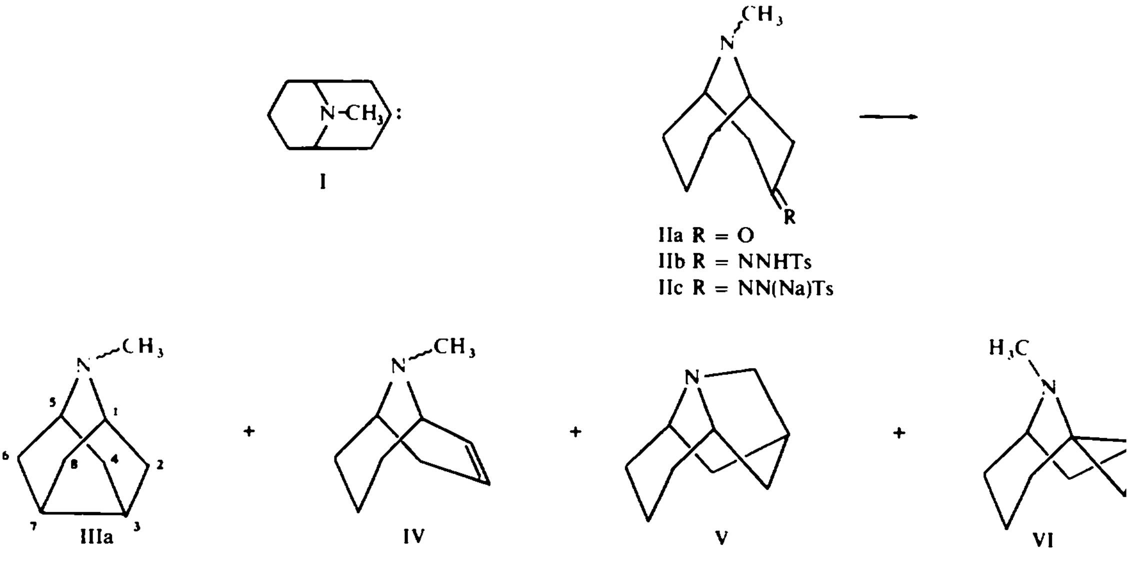
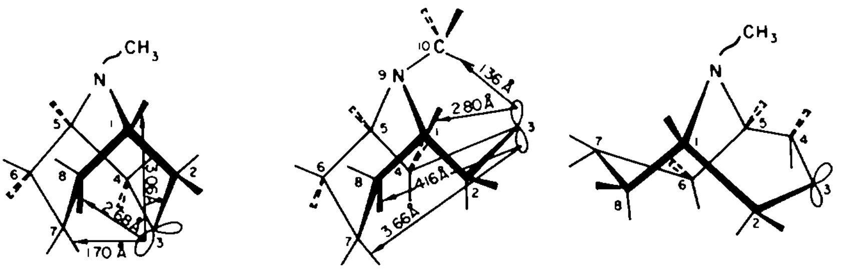


CHART 1



Chair-chair form Chair-boat form Boat-boat form

FIG 2. Various Interdistances between C- H Bonds and C-3 Carbene in I on The Dreiding Stereomodel: The Distances were measured between the centers of C- H bonds and the center of C-3- H bond.

Structural proofs of IIIa *by chemical properties*

The free base of IIIa was obtained as colorless prisms, m.p. 68–69°. It has an amine-like smell and sublimes easily. The NMR spectrum and the spin–spin decoupling results are shown in Figure 3a; the calculated coupling constants based on the

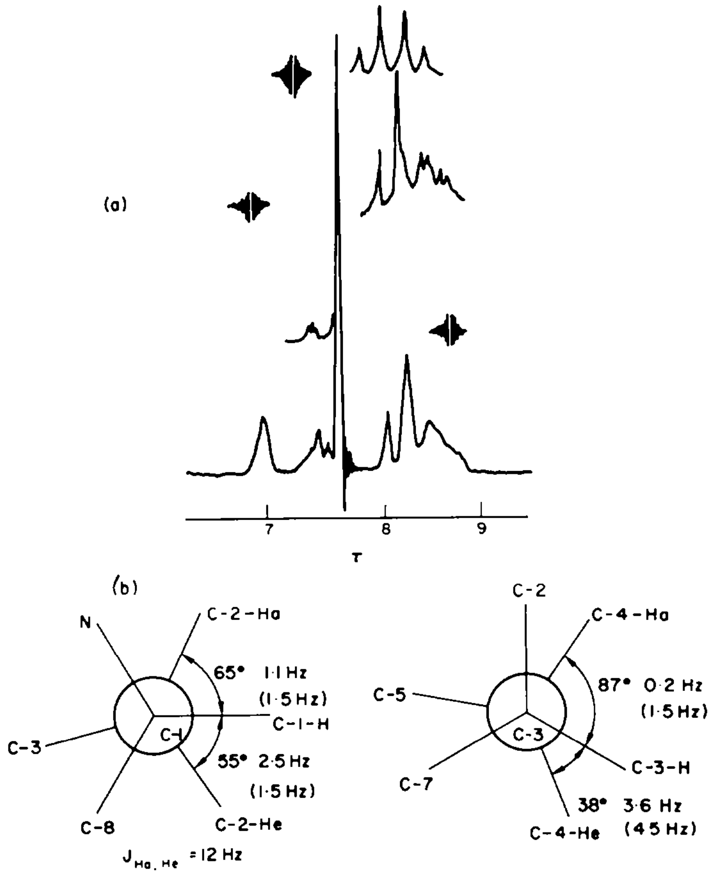
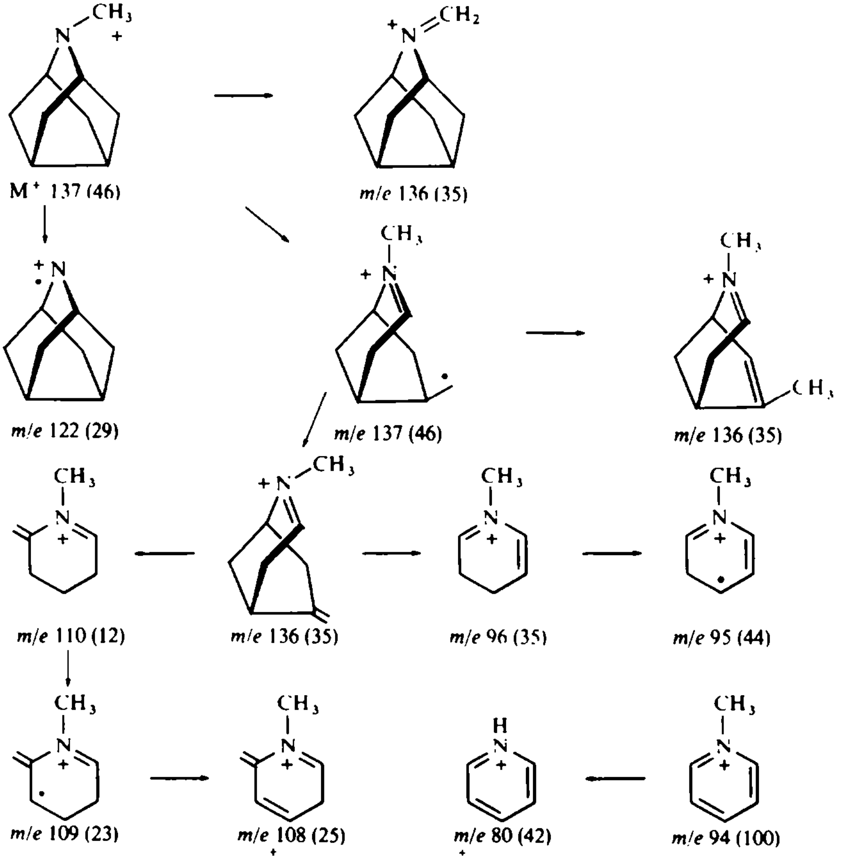


FIG 3. NMR Data of IIIa at 60 MHz in CDCl$_3$: (a) Normal and irradiated spectra; (b) Calculated coupling constants and observed ones in ( ).

dihedral angles obtained from the Dreiding stereomodel (Figure 3b) are in good agreement with the observed ones. The fragmentation pattern in the mass spectrum of IIIa (Chart 2) is very similar to that of the tropane alkaloids[13] supporting the assigned structure, but slightly different in the characteristic fragmentations at *m/e* 41 and 39. For further structural elucidation, successive Hofmann degradation reactions were carried out: VIIa was treated with silver oxide at 100° by the general procedure[14] to afford 7-dimethylaminobicyclo[3.3.0]octene-2 (VIII) which gave a methiodide (IX). The structures of VIII and IX were shown by the analytical and spectral (NMR and mass) data. IX afforded a tetrabromide (Xa) on treatment with bromine, which was characterized as 2,3-dibromobicyclo[3.3.0]octyl-7- trimethylammonium iodoperbromide. Catalytic hydrogenation of VIII afforded a dihydroderivative XI. The Hofmann degradation of the methiodide (Xb) of XI afforded a known bicyclo[3.3.0]octene-2 which was identified with an authentic sample[15] on GLC. Treatment of IIIa with bromine in refluxing carbon tetrachloride afforded a crystalline product (VIIb) in almost quantitative yield, which was assigned as above, a hydrobromide perbromide, on the basis of the analysis and of the fact that alkaline treatment yielded IIIa. Treatment of VIIa with bromine in carbon tetrachloride at 0°



$CH_3-\overset{+}{N}\equiv CH$ *m/e* 42 (22) $\overset{+}{\Delta}$ *m/e* 41 (27)

$H_2C=C=\overset{\oplus}{C}H$ *m/e* 39 (21)

CHART 2. Mass Spectral Fragmentations of IIIa

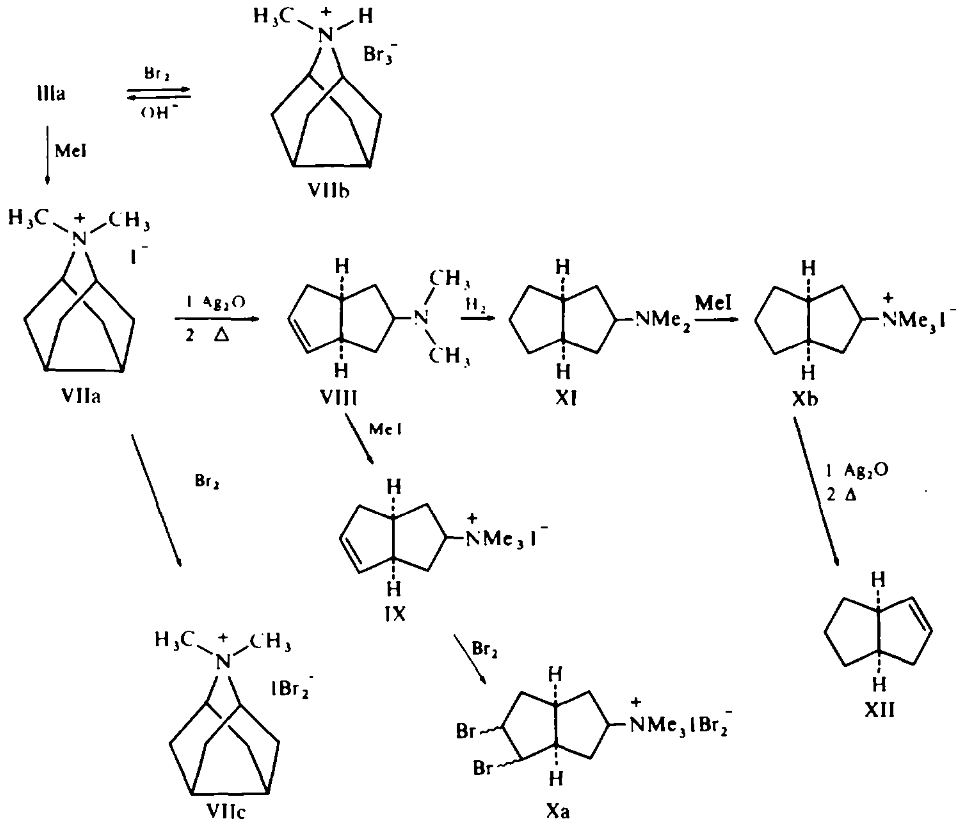


Chart 3

afforded a perbromide VIIc in 91% yield. Similar results were obtained in acetic acid at room temperature or when refluxed in carbon tetrachloride.

Oxidation of IIIa with hydrogen peroxide afforded an N-oxide (XIII), m.p. 72–74°, in 88% yield; XIII had an IR absorption band at 925 cm^{-1} due to the N—O bond and mass spectral peaks at *m/e* 153 (M$^+$), 137 (M$^+$-16) and 136 (M$^+$-17).[16] The NMR data were also compatible with the assigned structure.

The Polonovski reaction[17] of XIII afforded an oily amide (IIIb) in good yield, which exhibited a strong IR absorption band at 1630 cm^{-1} due to a tertiary amide, and mass spectral peaks at *m/e* 165 (M$^+$), 150 (M$^+$-15), 137 (M$^+$-28) and 122 (M$^+$-43).[18] The NMR spectrum in deuteriochloroform had signals at τ 4·90 (s, C-1), 5·54 (s, C-5), 7·25 (broad s, C-3 and C-7), 7·92 (s, $COCH_3$) and 8·35 (m, four methylene); the appearance of C-1 and C-5 proton signals separately at abnormally low fields compared with an α-carbon proton of a normal amide could be ascribed to the anisotropy of the N-acetyl group considering the reported $\Delta G^\ddagger_c$ values for hindered rotation in several amides.[19]

Acidic hydrolysis of IIIb afforded 9-azanoradamantane IIIc as sublimable crystals, m.p. 165–167°. The NMR spectrum in deuteriochloroform had signals at τ 6·54 (s, C-1 and C-5), 7·36 (broad s, C-3 and C-7), 7·53 (s, NH, exchangeable with deuterium) and 8·30 (m, four methylenes).[20] In the mass spectrum, the main frag-

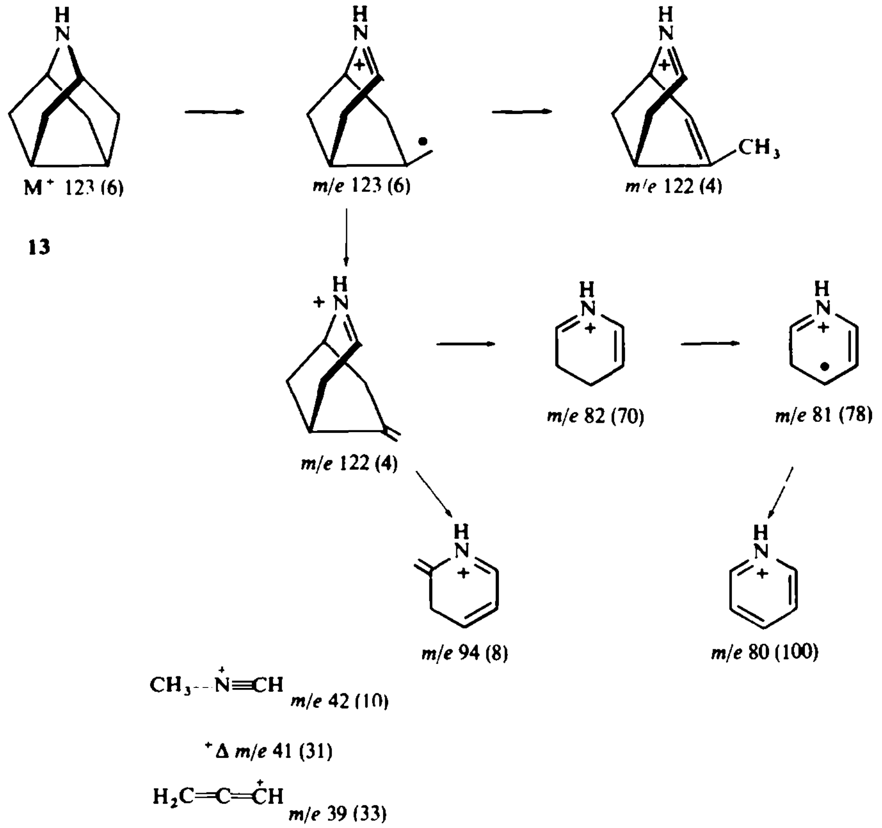


CHART 4. Mass Spectral Fragmentations of IIIc

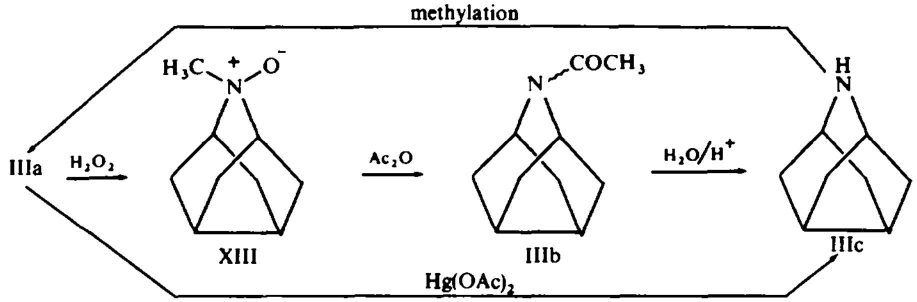


CHART 5

mentations could be explained similarly to those of IIIa as shown by the appearance of several common ions including those at *m/e* 41, 42 and 39 (Chart 4). IIIc was also obtained by oxidation of IIIa with mercuric acetate according to the method of Leonard and Morrow[21] but using a large excess of the oxidant. IIIc was readily methylated to IIIa. Thus, the integrity of the 9-azanoradamantane skeleton in IIIc was confirmed. In conclusion, it should be mentioned that the transannular carbene insertion reaction in a bicyclo[3.3.1]nonane ring is a useful method for the synthesis of tricyclic cage compounds.

EXPERIMENTAL

M.ps. were measured with a Yanagimoto micro-melting point apparatus (a hot-stage type) and are uncorrected. The NMR spectra were determined with a A-60 or HA-100 Varian spectrometer, using TMS as the internal standard and the chemical shifts are expressed as τ-values. Mass spectra were taken with a JEOL JMS-01SG spectrometer at 70 eV, and the IR with a JASCO IR/S spectromer. GLC analyses were performed on a Hitachi K-23 gas chromatograph, and microanalyses with a Perkin–Elmer 240 Elemental Analyzer.

Pseudopelletierine tosylhydrazone (IIb). To a stirred suspension of pseudopelletierine hydrochloride[22] (10·9 g, 0·057 mole) in EtOH (150 ml) tosylhydrazine (11·2 g, 0·06 mole) was added at 70°. At the end of the addition, the mixture became a clear soln which was refluxed for several hours to precipitate colourless crystals which were filtered to give the hydrochloride of IIb (15·3 g, 75%), m.p. 287–289°; IR ν_{max}^{KBr} 3015, 2930, 2800–2520, 1640, 1600, 1452, 1432, 1410, 1347, 1330, 1312, 1169, 1100, 1032, 1008, 928, 810, 771 and 668 cm^{-1}. (Found: C, 53·53; H, 7·16; N, 11·70. Calc for $C_{16}H_{24}N_3OSCl$: C, 53·41; H, 6·77; N, 11·74%).

Preparation of the sodium salt (IIc) *and the decomposition in diglyme*. A mixture of IIb hydrochloride (11 g, 0·03 mole) and NaOMe prepared from Na (2·1 g, 0·09 mole) and MeOH (100 ml) was stirred at room temp for 1 h under dry N_2. After removal of MeOH under reduced pressure (20 mm), the solid residue was dried at 70° for 2–3 h under high vacuum (0·1 mm), and dry diglyme (100 ml) was added. The resulting mixture was refluxed at 165° for 2 h under N_2 and distilled to afford a diglyme soln of crude products with b.p. 68°/24·5 mm. A portion of this soln was treated with MeI to give 9-methyl-9-azanoradamantane methiodide (VIIa) as colourless crystals; the total yield was 80% from IIb, m.p. > 320°; IR ν_{max}^{KBr} 3034, 2974, 2884, 1476, 1333, 1241, 1167, 1132, 1110, 1052, 1000, 980, 900 and 858 cm^{-1}. (Found: C, 42·96; H, 6·63; N, 5·17. Calc for $C_{10}H_{18}NI$: C, 43·02; H, 6·50; N, 5·02%).

Treatment of the soln with picric acid afforded the picrate of IIIa, m.p. 308–310°; IR ν_{max}^{KBr} 3005, 2880, 2710, 1632, 1614, 1565, 1518, 1498, 1440, 1369, 1333, 1332, 1320, 1278, 1164, 1080, 1051, 910, 789, 746 and 710 cm^{-1}. (Found: C, 49·57; H, 4·83; N, 15·31. Calc for $C_{15}H_{18}N_4O_7$: C, 49·18; H, 4·95; N, 15·30%).

A portion of the diglyme soln was diluted with an equal amount of dry Et_2O and saturated with dry HCl gas to give a hydrochloride as a colourless hygroscopic ppt (67% yield from IIb). NMR (D_2O) τ 6·18 (s, C-1 and C-5), 7·12 (s, NCH_3), 7·17 (broad t, J = 5·5 Hz, C-3 and C-7), 7·85 and 8·22 (partly overlapped d, J = 18 Hz, C-2, C-4, C-6 and C-8 methylene, the former in axial and the latter in equatorial position).

The hydrochloride was treated with 20% aq NaOH, followed by extraction with $CHCl_3$. The $CHCl_3$ extracts were dried (Na_2SO_4) and the solvent removed under reduced pressure to give a sticky residue which gave colourless crystals of IIIa on dry distillation at 58–60°/43 mm, m.p. 68·5–69°. IR ν_{max}^{KBr} 2930, 2915, 2830, 1450, 1370, 1322, 1250, 1100 and 1018 cm^{-1}. (Found: C, 78·51; H, 11·28; N, 10·45. Calc for $C_9H_{15}N$: C, 78·77; H, 11·02; N, 10·21%).

The decomposition in ethylene glycol. IIc was decomposed in ethylene glycol at 195° under dry N_2 for 2 h. The cooled mixture was acidified with HCl gas and most of ethylene glycol was removed. The concentrated mixture was made alkaline with KOH and distilled. A portion of this distillate was treated with MeI to give colourless crystals, m.p. 320° and with picric acid to give a yellow picrate, m.p. 302–307°. NMR inspection of the picrate disclosed it as a 24:76 mixture of IIIa and 9-methyl-9-azabicyclo[3.3.1] nonene-2 (IV).[2] An authentic sample of IV was prepared by the reported procedure[23] from 3-α-granatanol.

Dry pyrolysis of IIc. A mixture of IIc (0·14 g) and an equal amount of dry Celite was heated at 160–170° under reduced pressure (20 mm) and under N_2 in a flask connected with both an ice–MeOH trap and a dry ice–acetone trap. The decomposition products in the traps were collected by washing with $CHCl_3$ to give a semisolid (0·2 g, 72%) which was analyzed as a 74:26 mixture of IIIa and IV on GLC (Table 1).

Photolysis of IIc *in ether*. Dry powdered IIc prepared from IIb (0·01 mol) was suspended in dry Et_2O (100 ml) and the stirred mixture was irradiated with a 100 W high pressure mercury lamp through a quartz jacket under N_2 at 25° for 15 h. The end-point of the reaction was checked by measuring the amounts of N_2 evolved and the mixture was filtered to remove insoluble materials. The filtrate was condensed to give an oily residue (1·05 g, 73%) which was analyzed as given in Table 1 on GLC (Silicone SE-30). Chromatography on an alumina (Wako, grade 1) column using $CHCl_3$ as an eluent afforded pure IV (0·2 g, 5·8%) which was characterized as its picrate, m.p. 306–307° (lit[24], m.p. 299–302°) and a mixture of V and VI. Complete separation of this mixture was impossible at the present stage of the research and therefore, the picrate of this mixture, m.p. 297–302°, was analyzed. (Found: C, 49·57; H, 4·83; N, 15·31. Calc for $C_{15}H_{18}N_4O_7$: C, 49·18; H, 4·95; N, 15·30%).

Bromination of IIIa. To a stirred soln of IIIa (0·11 g, 0·8 mmole) in CCl_4 (5 ml) was added Br_2 (0·13 g, 0·8 mmole) under ice-cooling. After 10 min, the resulting ppts were filtered to give VIIb (0·17 g, 57%) as slightly brownish crystals, m.p. 47–55° ($CHCl_3$); IR ν_{max}^{KBr} 2940, 2750, 2660, 2560, 1457, 1417, 1263, 1327, 1305, 1222, 1134, 1130, 1108, 1043, 1013, 998, 972, 915, 860, 833, 813 and 783 cm^{-1}. (Found: C, 28·74; H, 3·99; N, 3·97. Calc for $C_9H_{16}NBr_3$: C, 28·75; H, 3·75; N, 3·73%).

Bromination of VIIa. To a stirred suspension of VIIa was added a small excess of Br_2 under ice-cooling. The resulting ppts were filtered and washed with CCl_4 to give VIIc in 91% yield, m.p. 255–258° (dec); IR ν_{max}^{KBr} 2965, 2880, 1470, 1450, 1330, 1228, 1166, 1133, 1106, 1050, 1002, 982, 967, 919, 900, 852 and 790 cm^{-1}. (Found: C, 27·26; H, 3·91; N, 3·49. Calc for $C_{10}H_{18}NIBr_2$: C, 27·36; H, 4·13; N, 3·19%).

Bromination in acetic acid at room temp and in refluxing CCl_4 using excess amounts of Br_2 afforded also VIIc.

The Hofmann degradation of VIIa *to* VIII. To a stirred suspension of VIIa (5·6 g, 0·02 mole) in water (50 ml) was added AgO freshly prepared from $AgNO_3$ (6·9 g, 0·04 mole). Stirring was continued at room temp for 1 h and then, at 60° for 1 h. The ppts were filtered and further refluxed in water (20 ml) for 1 h and again the mixture was filtered. The combined filtrate was distilled at the bath temp of 105–150°. The distillate was made alkaline with 20% NaOH and extracted several times with $CHCl_3$. The combined extracts were dried (Na_2SO_4) and the solvent removed under reduced pressure to give crude VIII (1·56 g, 52%) as an oil which was purified by dry distillation at 90–100°/0·25 mm. IR ν_{max}^{neat} 3060, 2960, 2880, 2840, 2790, 1619, 1462, 1355, 1299, 1214, 1154, 1105, 1060, 1047, 978, 940, 908 and 730 cm^{-1}; NMR ($CDCl_3$) τ 4·42 (m, 2H, vinyl protons), 7·77 (s, 6H, $N(CH_3)_2$) and 7·0–9·0 (broad m, 9H, methine and methylene protons); mass spectrum *m/e* (real intensity) 151 (100, M^+), 136 (81), 122 (99), 110 (74), 107 (18), 91 (38), 84 (54), 79 (51), 77 (35), 71 (98), 70 (50), 58 (25), 56 (39) and 44 (42). (Found: C, 78·99; H, 11·49; N, 9·53. Calc for $C_{10}H_{17}N$: C, 79·40; H, 11·34; N, 9·26%).

Treatment of VIII with MeI afforded the methiodide IX as colourless crystals, m.p. 215–217°. IR ν_{max}^{KBr} 3030, 2925, 2900, 1619, 942, 797, 753 and 725 cm^{-1}; NMR (D_2O) τ 4·26 (m, 2H, vinyl protons), 6·17 (p, 1H, J = 5·5 Hz, N^+—CH), 6·90 (s, 9H, $N^+(CH_3)_3$) and 6·60–8·90 (m, 8H, remaining protons). This was analyzed as the tetrabromide Xa.

IX gave a tetrabromide Xa in 90% yield on its bromination at 0° in CCl_4, m.p. > 320°. IR ν_{max}^{KBr} 3020, 2940, 1480, 1450, 1415, 1296, 1240, 1180, 957, 940, 883, 856, 784, 742 and 720 cm^{-1}. (Found: C, 21·47; H, 3·39; N, 2·50. Calc for $C_{11}H_{20}NIBr_4$: C, 21·56; H, 3·29; N, 2·29%).

Catalytic hydrogenation of VIII *to* XI. Catalytic hydrogenation of VIII (1·15 g, 7·6 mmole) in MeOH (50 ml) at room temp under H_2 at atm. pressure in the presence of 10% Pd/C (1 g) as a catalyst afforded the dihydro-derivative XI (0·96 g, 82·5%) as an oil which was converted to the methiodide (Xb) on treatment with MeI in MeOH in 52% yield, m.p. 264·5–266° (MeOH). IR ν_{max}^{KBr} 2926, 2820, 1470, 1440, 1410, 1388, 1239, 960, 940 and 850 cm^{-1}. (Found: C, 44·77; H, 7·40; N, 4·68. Calc for $C_{11}H_{22}NI$: C, 44·76; H, 7·51; N, 4·81%).

The Hofmann degradation of Xb. The decomposition was carried out similarly to that of VIIa using Xb (0·57 g, 1·9 mmole) and AgO. The product was trapped at dry ice–acetone temp and analyzed on GLC, which demonstrated the formation of bicyclo[3.3.0]octene-2 (XII) and Me_3N. An authentic sample of XII was prepared from cycloocta-1,5-diene by the method of Stapp and Kleinschmidt.[15]

Alkaline treatment of VIIb. VIIb (0·55 g, 1·5 mmole) was dissolved in a minimum amount of THF and to this soln was added 15% aq NaOH (20 ml). The mixture was stirred for 0·5 h and extracted several times with $CHCl_3$. The combined extracts were dried (Na_2SO_4) and concentrated to 1 ml and then treated with MeI to give VIIa (0·23 g, 56·5%), identified by an IR spectrum superimposable on that of VIIa.

9-*Methyl-9-azanoradamantane* N-*Oxide* (XIII). To a diglyme soln of IIIa (0·84 g, 6 mmole) was added 30% H_2O_2 (2·8 g, 24 mmole) with stirring under ice-cooling. Stirring was continued overnight at room temp. The excess H_2O_2 was decomposed by addition of Pt_2O (0·02 g). The mixture was filtered and the filtrate was dried under reduced pressure (0·2 mm) to leave the N-oxide (XIII) (0·8 g, 88%) as colourless crystals, m.p. 72–74° (CCl_4). IR ν_{max}^{KBr} 2980, 1460, 1335, 1310, 1157, 1130, 1100, 1010, 994 and 925 cm^{-1}; NMR (D_2O) τ 6·20 (s, C-1 and C-5), 6·65 (s, N—CH_3), 7·20 (broad s, C-3 and C-7) and 7·80 and 8·25 (partly overlapped d, J = 18 Hz, C-2, C-4, C-6 and C-8 methylenes, the former of axial and the latter of equatorial protons); mass spectrum *m/e* (rel intensity) 153 (58, M^+), 137 (7), 136 (13), 95 (9), 80 (20), 78 (11), 68 (47), 61 (36), 57 (98), 54 (100), 43 (18) and 42 (35). (Found: C, 70·27; H, 10·29; N, 8·90. Calc for $C_9H_{15}NO$: C, 70·55; H, 9·87; N, 9·14%).

9-*Acetyl-9-azanoradamantane* (IIIb) *by the Polonovski reaction of* XIII. A mixture of XIII (1 g, 6·5 mmole). Ac_2O (20 ml, 0·21 mole) and $CHCl_3$ (80 ml) was refluxed for 2 days. After removal of the solvent and excess Ac_2O under reduced pressure, the residue was chromatographed on a silica-gel column, eluting with $CHCl_3$–MeOH to give IIIb (0·75 g, 75%) as an oil. An analytical sample was obtained by dry distillation at 120°/0·25 mm. IR ν_{max}^{neat} 2960, 2880, 1635, 1426, 1367, 1348, 1222, 1112, 1045, 1002, 973, 900, 835 and 790 cm^{-1}. (Found: C, 72·74; H, 9·03; N, 8·45. Calc for $C_{10}H_{15}NO$: C, 72·69; H, 9·15; N, 8·48%).

Hydrolysis of IIIb *to 9-azanoradamantane* (IIIc). A mixture of IIIb (0·75 g, 4·5 mmole) in 10% HCl (30 ml) was refluxed for 2 days. After washing with $CHCl_3$, the mixture was made alkaline with 20% aq NaOH and extracted several times with Et_2O. The combined Et_2O-extracts were dried (Na_2SO_4) and evaporated to leave crude IIIc (0·37 g, 65%) as colourless crystals. An analytical sample was obtained by sublimation, m.p. 165–167°. IR ν_{max}^{KBr} 2950, 2860, 2750, 2630, 2480, 1450, 1426, 1335, 1320, 1310, 1228, 1157, 1110, 1080, 1010, 1040 and 830 cm^{-1}. (Found: C, 77·80; H, 10·42; N, 11·77. Calc for $C_8H_{13}N$: C, 77·99; H, 10·64; N, 11·37%).

Oxidation of IIIa *to* IIIc *with mercuric acetate*. A mixture of a diglyme soln (20 ml) containing IIIa (0·83 g, 6 mmole), water (50 ml), AcOH (2·5 g) and HgOAc (9·8 g, 38 mmole) was refluxed for 10 days. The ppts were filtered and the filtrate made alkaline to give further precipitation. The yellowish ppts were filtered and the filtrate extracted several times with $CHCl_3$. The combined extracts were dried (Na_2SO_4) and concentrated to 30 ml, into which dry HCl gas was introduced. The precipitated hydrochloride was dissolved in 20% aq NaOH and the soln was extracted with $CHCl_3$. The $CHCl_3$-extract afforded IIIc (0·52 g, 53%), which was identified by comparison of the IR spectrum with that of IIIc from IIIb.

Methylation of IIIc *to* IIIa. A suspension of NaH (50% dispersion in mineral oil, 0·05 g, 1 mmole) in dry benzene (5 ml) was washed with dry benzene several times under N_2 to remove mineral oil. To a benzene suspension (10 ml) of NaH, was added a benzene soln (20 ml) of IIIc (0·12 g, 1 mmole) with stirring at room temp. After stirring for 3 h, the mixture was mixed with a benzene soln (10 ml) of MeI (0·15 g, 1 mmole) at room temp. After stirring for 12 h, the mixture was filtered and the filtrate evaporated to give colourless solids (0·08 g, 58%), which were shown to be a 7:3 mixture of IIIa and IIIc from the NMR spectra.

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