

## Deprotonation of Hydrazinium Dications in the Diazoniapropellane Series to form Bridgehead Iminium Ions; External and Intramolecular Trapping

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The reactions of hexa-alkylhydrazinium dications with bases and nucleophiles are described. 1,5-Diazoniatriacyclo[3.3.2.0]decane (1) is hydrolysed rapidly by  $S_N2$  attack on the four-membered ring with ring opening (C–N<sup>+</sup> cleavage). In all other cases deprotonation at  $\alpha$ -C with concomitant N<sup>+</sup>–N<sup>+</sup> cleavage (*E2* reaction) is the only primary process. The *cis*-1,6-dimethyl-1,6-diazoniabicyclo[4.4.0]decane ion (6), is exclusively deprotonated at a methyl group (Hofmann orientation). 1,5-Diazoniatriacyclo[3.3.3.0]undecane (2), 1,6-diazoniatriacyclo[4.3.3.0]dodecane (3), 1,6-diazoniatriacyclo[4.4.3.0]tridecane (4), and 1,6-diazoniatriacyclo[4.4.4.0]tetradecane (5) ions generate bridgehead iminium ions, which may be trapped intramolecularly by the transannular amino group or externally by added nucleophiles. Reaction with cyanide ion gives detailed information on the regio- and stereo-chemistry of the trapping sequence. Although intramolecular/external trapping is truly competitive, the products of these reactions ( $\alpha$ -aminoammonium ions and  $\alpha$ -aminonitriles) may be interconverted under different reaction conditions. The solvolysis of 1-(3-phenoxypropyl)-1,5-diazabicyclo[3.3.0]octanium bromide in aqueous 48% HBr is  $10^3$  faster than that of 3-phenoxypropyltrimethylammonium bromide, and the products are consistent with the intermediacy of the dication (2). These observations provide an explanation for the formation of 1,5-diazacyclo-octane in the reaction of 1,3-dibromopropane with hydrazine.

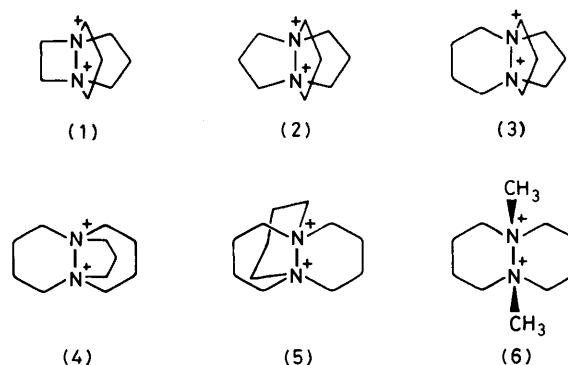
Dications with adjacent positively charged atoms are quite rare and their reactions are of considerable interest. Diprotonated hydrazines are commonly intermediates in benzidine rearrangements,<sup>1</sup> but apart from this their only known reaction is loss of a proton.<sup>2</sup> Stable salts of a series of hexa-alkylhydrazinium dications (1)–(6) have been prepared at Bristol recently;<sup>3–5</sup> these compounds provide an opportunity to examine reactions with nucleophiles and this is the subject of the present paper. At least five primary reaction steps are plausible for these dications (see Scheme 1). After preliminary publications had appeared,<sup>3,4</sup> the Bristol group became aware of much earlier unpublished work in Basel<sup>6</sup> which implicated the dication (2) as a (non-isolated) reaction intermediate. Since the Basel observations nicely complement the Bristol work, joint publication seemed appropriate.

### Experimental

The preparation of the bistetrafluoroborate salts of the dications (1)–(5) have been fully described.<sup>5</sup> The preparation of *cis*-1,6-dimethyl-1,6-diazoniabicyclo[4.4.0]decane bistetrafluoroborate (6)2BF<sub>4</sub><sup>-</sup> has been briefly described,<sup>7</sup> but is given here in full.

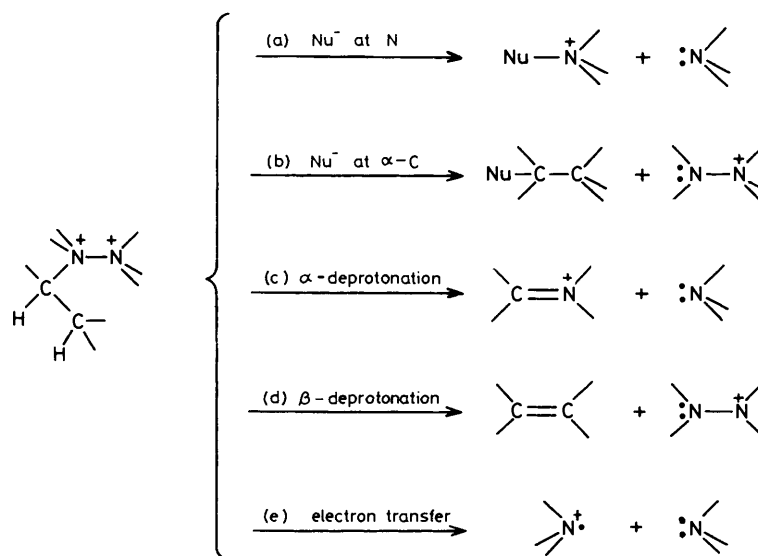
**1-(4-Bromobutyl)-1,2-dimethylpiperidazinium Bromide.**—*N,N'*-Dimethylpiperidazine<sup>8</sup> (0.29 g) and 1,4-dibromobutane (2 ml) were heated to 100 °C for 15 min. The resulting solid mass was broken up under ether and filtered to give 1-(4-bromobutyl)-1,2-dimethylpiperidazinium bromide (0.8 g, 96%) as a pale brown powder,  $\delta_H$  (D<sub>2</sub>O) 1.9 (8 H, m), 2.67 (3 H, s), 3.20 (3 H, s), and 2.8–3.9 (8 H, m). This material, which is hygroscopic, was used without further purification.

***cis*-1,6-Dimethyl-1,6-diazoniabicyclo[4.4.0]decane Bistetrafluoroborate (6)2BF<sub>4</sub><sup>-</sup>.**—The bromo-bromide salt just described (0.5 g) was stirred with a solution of silver oxide (0.33 g) in aqueous 40% tetrafluoroboric acid (5 ml). After 5 min, the silver bromide formed was filtered off and washed with aqueous 40% HBF<sub>4</sub> (2 ml). Ethanol (10 ml) was added to



the combined filtrates, causing (6)2BF<sub>4</sub><sup>-</sup> to precipitate (0.26 g, 50%). Recrystallisation from ethanol–aqueous 40% HBF<sub>4</sub> gave off-white crystals, m.p. 166–167 °C (Found: C, 33.8; H, 6.5; N, 8.1. C<sub>10</sub>H<sub>22</sub>B<sub>2</sub>F<sub>8</sub>N<sub>2</sub> requires C, 34.9; H, 6.4; N, 8.1%);  $\delta_H$  (D<sub>2</sub>O) 2.36 (8 H, m), 4.00 (6 H, s), and 3.8–5.2 (8 H, m);  $\delta_C$  (D<sub>2</sub>O), ambient temperature 16.4 (double intensity), 49.7, 61.6, and 65.6 (on warming to 60 °C the lines at 61.6 and 65.6 coalesced to a single line, and became resolved again on cooling; some decomposition was evident during this experiment as several new peaks appeared irreversibly). The temperature-variable <sup>13</sup>C n.m.r. is indicative of the *cis*-isomer and inconsistent with the *trans*, which would show only three <sup>13</sup>C peaks at all temperatures. The fact that one line at  $\delta$  16.4 is seen for the  $\beta$ -methylene carbon atoms at all temperatures must indicate a very small chemical shift difference between the pairs of  $\beta$ -methylene carbons in the frozen *cis*-decalin structure; this is not unexpected in view of the <sup>13</sup>C data for the methyldecalins,<sup>9</sup> as both types of  $\beta$ -methylene experience the same number of  $\gamma$ -*gauche* interactions.

**12,12-Dideuterio-1,6-diazoniatriacyclo[4.4.3.0]tridecane Bistetrafluoroborate.**—Diethyl malonate (5 g) was washed successively with three portions of NaOD–D<sub>2</sub>O [each Na (0.2 g) in D<sub>2</sub>O (2 ml)] and D<sub>2</sub>O (2 × 1 ml) and dried. The



Scheme 1.

resultant  $\text{CD}_2(\text{CO}_2\text{Et})_2$  (3.5 g) in ether (10 ml) was added dropwise to lithium aluminium hydride (2 g) in ether (50 ml), and the reaction mixture refluxed for 2 h after addition was complete. Water (5 ml) was added cautiously, followed by  $10\text{N-H}_2\text{SO}_4$  (40 ml). The aqueous solution was saturated with sodium chloride and continuously extracted with ether. Distillation of the residue from the ether extract gave 2,2-dideuteriopropene-1,3-diol (0.61 g), which showed only a singlet at  $\delta$  3.6 in its  $^1\text{H}$  n.m.r. spectrum ( $\text{D}_2\text{O}$  solution).

2,2-Dideuteriopropene-1,3-diol (1.0 g) was treated with triphenylphosphine and bromine in  $\text{CH}_2\text{Cl}_2$  solution to give 2,2-dideuterio-1,3-dibromopropane (0.75 g, 26% after distillation). This material was then heated for 4 h at  $70^\circ\text{C}$  with 1,6-diazabicyclo[4.4.0]decane as described for the per-protio material,<sup>3</sup> and subsequently converted into 12,12-dideuterio-1,6-diazoniatricyclo[4.4.3.0]tridecane bistetrafluoroborate, again by the published procedure.<sup>5</sup> This sequence was only performed once and the yield was very poor (63 mg, 7%); it is likely that the use of a 1 : 1 ratio of the dibromopropane and the 1,6-diazoniabicyclo[4.4.0]decane is responsible; in the per-protio series a large excess of dibromopropane was used.

**Standard Procedures for Reaction of Hydrizinium Dications with Potassium Cyanide.**—(a) *Preparative procedure.* A solution of KCN (1.5 g) in water (5 ml) was placed in a separating funnel together with dichloromethane (20 ml). The dication salt (0.5 g) was added as a solid and the mixture shaken thoroughly. The aqueous layer was extracted with more dichloromethane ( $4 \times 20$  ml), these extractions being spread out over 1 h in the case of the less reactive dications (4) and (5). The combined organic layers were dried and evaporated to yield the crude product.

(b) *N.m.r.-scale procedure.* The dication salt (0.1 g) was added to  $\text{CDCl}_3$  (1.0 ml) and potassium cyanide (0.3 g) in  $\text{D}_2\text{O}$  (1.0 ml). After thoroughly shaking, the layers were separated and each was analysed by  $^1\text{H}$  and  $^{13}\text{C}$  n.m.r. spectroscopy.

**Physical and Spectroscopic Data for  $\alpha$ -Amino Nitriles.**—2-Cyano-1,5-diazabicyclo[3.3.3]undecane (14). This was obtained from (2)  $2\text{BF}_4^-$  as an air-sensitive oil which slowly solidified. The  $^{13}\text{C}$  n.m.r. spectrum ( $\text{CDCl}_3$ ) showed lines at  $\delta$  23.5, 24.4, 28.2, 45.3, 46.7, 47.1, 47.3, 47.8, 50.4, and 120.9

(CN) assignable to (14), but indicated that the material was only ca. 80% pure. The  $^1\text{H}$  n.m.r. spectrum ( $\text{CDCl}_3$ ) showed  $\delta$  1.0–2.5 (complex multiplet, 6 H,  $\beta\text{-CH}_2$ ), 2.5–3.4 (complex multiplet, 10 H,  $\alpha\text{-CH}_2$ ), and 4.03 (dd, 1 H,  $\text{CHCN}$ ,  $J$  12 and 4 Hz). The high resolution mass spectrum showed a molecular ion at  $m/z$  179.142(4) [Calc. for  $\text{C}_{10}\text{H}_{17}\text{N}_3$ : 179.142(2)]. A trifluoroacetate salt was crystallized; m.p.  $160\text{--}165^\circ\text{C}$  (decomp.) (Found: C, 49.2; H, 6.3; N, 14.1.  $\text{C}_{12}\text{H}_{18}\text{F}_3\text{N}_3\text{O}_2$  requires C, 49.15; H, 6.2; N, 14.35%).

11-Cyano-1,6-diazabicyclo[4.4.3]tridecane (18). This was obtained by procedure (a) from (4)  $2\text{BF}_4^-$  in 43% yield as an air-sensitive liquid which slowly crystallized. The  $^{13}\text{C}$  n.m.r. spectrum ( $[\text{C}_6\text{H}_6]$ toluene) showed this material to be one of the three possible  $\alpha$ -amino nitriles, with lines at  $\delta$  28.9, 29.6, 30.3, 31.1, 33.2, 50.4, 52.0, 53.9, 55.7, 60.5, and 117.6 (CN) (one coincidence in the  $\alpha$ -carbon resonances). The  $^1\text{H}$  n.m.r. spectrum, besides complex multiplets for  $\alpha$ - and  $\beta\text{-CH}_2$ , showed the  $\text{CHCN}$  signal as a double doublet,  $J$  12 and 4 Hz at  $\delta$  4.02 in  $\text{CDCl}_3$  and  $\delta$  3.2 in  $[\text{C}_6\text{H}_6]$ toluene. In nitrile prepared from 12,12-dideuterio-(4)  $2\text{BF}_4^-$  (labelled at the middle methylene of the  $[\text{CH}_2]_3$  bridge), the  $\text{CHCN}$  signal appeared as a broad singlet, confirming that the compound was the 11-cyano isomer (18).

2-Cyano-1,6-diazabicyclo[4.4.4]tetradecane (19). Procedure (a), applied to the [4.4.4.0]dication (5)  $2\text{BF}_4^-$ , cleanly gave (19) as an air-sensitive white solid in 98% yield, pure according to  $^1\text{H}$  and  $^{13}\text{C}$  n.m.r.;  $M^+$  221.189(5) [Calc. for  $\text{C}_{13}\text{H}_{23}\text{N}_3$ : 221.189(2)];  $\delta_{\text{C}}$  ( $[\text{C}_6\text{H}_6]$ toluene) 29.9, 30.0, 30.4, 30.6, and 34.3 ( $\beta$ -carbons, only five of expected six lines resolved), 51.2, 52.5, 53.9, 54.4 (double intensity, coincidence), 55.3, and 119.7 (CN);  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ ) 3.33 ( $\text{CHCN}$ , dd,  $J$  10 and 4 Hz) and complex multiplets for  $\alpha$ - and  $\beta\text{-CH}_2$ .

1-Cyanomethyl-6-methyl-1,6-diazacyclodecane (20). When applied to (6)  $2\text{BF}_4^-$ , procedure (b) gave 20% 1-methyl-1-azonia-6-azabicyclo[4.4.1]undecane ion (12) and 80% of (20). No isomeric nitrile was detected. The  $^{13}\text{C}$  n.m.r. spectrum of (20) in  $\text{CDCl}_3$  showed  $\delta$  23.8, 24.1, 42.6, 43.1, 51.6, 55.0, and 115.4 (CN); the  $^1\text{H}$  n.m.r. spectrum ( $\text{CDCl}_3$ )  $\delta$  1.6 (8 H, m,  $\beta\text{-CH}_2$ ), 2.05 (3 H, s), 2.2–2.9 (8 H, m,  $\alpha\text{-CH}_2$ ), and 3.40 (2 H, s,  $\text{CH}_2\text{CN}$ ). The high resolution mass spectrum showed a molecular ion at  $m/z$  195.172(8) [Calc. for  $\text{C}_{11}\text{H}_{21}\text{N}_3$ : 195.173(5)].

1-(3-Phenoxypropyl)-1,5-diazabicyclo[3.3.0]octanium

**bromide** (21). 1,5-Diazabicyclo[3.3.0]octane<sup>10,11</sup> (10.68 g, 0.095 mol) and 3-phenoxypropyl bromide<sup>12</sup> (20.41 g, 0.095 mol) in acetone (500 ml) were refluxed for 4 h. After cooling overnight to  $-12^{\circ}\text{C}$  the acetone was decanted. The hygroscopic crystals were washed with acetone (20 ml) and then dried *in vacuo* at  $80^{\circ}\text{C}$  to constant weight; yield 26.5 g (85%); m.p.  $141\text{--}142^{\circ}\text{C}$  (Found: C, 55.1; H, 7.1; N, 8.5.  $\text{C}_{15}\text{H}_{23}\text{BrN}_2\text{O}$  requires C, 55.05; H, 7.1; N, 8.5%).

**1-(3-Phenoxypropyl)-1,5-diazacyclo-octane bishydrobromide** (22a). 1-(3-Phenoxypropyl)-1,5-diazabicyclo[3.3.0]octanium bromide (21) (22.0 g, 0.067 mol) and aluminium amalgam (12.5 g), prepared according to Vogel,<sup>13</sup> in ether (250 ml) were cooled with ice. Water (25 ml) was added in small portions with occasional shaking. After 14 h at  $0^{\circ}\text{C}$ , 50% potassium hydroxide (20 ml) was added to the mixture. Repeated extraction with ether yielded the crude base of (22a) (15.5 g) which was dissolved in ethanol (115 ml). After cooling to  $-30^{\circ}\text{C}$ , 48% hydrobromic acid (14.6 g) was added. Cooling, filtration, and drying *in vacuo* yielded (22a) (23.4 g, 85%) as platelets, which were recrystallized from ethanol (Found: C, 44.2; H, 6.5; Br, 39.1.  $\text{C}_{15}\text{H}_{26}\text{Br}_2\text{N}_2\text{O}$  requires C, 43.9; H, 6.4; Br, 38.95%).

**1-(3-Bromopropyl)-1,5-diazacyclo-octane bishydrobromide** (22b). 1-(3-Phenoxypropyl)-1,5-diazacyclo-octane bishydrobromide (22a) (2.22 g, 0.0054 mol) was heated with 66% hydrogen bromide (22 ml) to  $120^{\circ}\text{C}$  for 3.5 h in a sealed tube. After cooling, the solution was evaporated to dryness *in vacuo*. The crystals (2.2 g) were dissolved in hot 48% HBr (1.5 ml), and warm ethanol (20 ml) was added together with charcoal. After filtration through Celite and cooling the colourless salt (22b) crystallized (yield 2.03 g, 95%); m.p. (decomp.)  $218\text{--}220^{\circ}\text{C}$  (Found: C, 27.3; H, 5.4; Br, 60.2.  $\text{C}_9\text{H}_{21}\text{Br}_3\text{N}_2$  requires C, 27.25; H, 5.35; Br, 60.35%).

**1-(3-Phenoxypropyl)trimethylammonium bromide** (23a). 3-Phenoxypropyl bromide<sup>12</sup> (12.5 g) and trimethylamine (10 ml) were dissolved in dry acetone (200 ml), from which the quaternary salt (23a) began to crystallize within 30 min. After 40 h at  $0^{\circ}\text{C}$  the mixture was filtered to yield the salt (23a) (13.5 g, 85%), m.p.  $156\text{--}157.5^{\circ}\text{C}$  (from propan-2-ol) (Found: C, 52.8; H, 7.5; Br, 29.2; N, 5.3.  $\text{C}_{12}\text{H}_{26}\text{BrNO}$  requires C, 52.55; H, 7.35; Br, 29.15; N, 5.1%).

**1-(3-Bromopropyl)trimethylammonium bromide** (23b). 1-(3-Phenoxypropyl)trimethylammonium bromide (23a) (2.03 g) was heated with 66% hydrogen bromide (20 ml) to  $120^{\circ}\text{C}$  for 3.5 h. Evaporation to dryness *in vacuo* yielded a dark residue which was heated with charcoal in propan-2-ol. Ether was added to the filtered solution until white crystals of (23b) (1.9 g, 97%) appeared, m.p.  $225\text{--}226^{\circ}\text{C}$  (from propan-2-ol-acetone) (Found: C, 27.7; H, 5.6; Br, 60.6.  $\text{C}_6\text{H}_{15}\text{Br}_2\text{N}$  requires C, 27.6; H, 5.8; Br, 61.25%).

**Reaction of 1-(3-Phenoxypropyl)-1,5-diazabicyclo[3.3.0]octanium Bromide (21) with 48% Hydrobromic Acid.**—A solution of (21) (1.0 g) in 48% HBr (75 ml) was steam-distilled until the distillate no longer gave a precipitate with a solution of 2,4-dinitrophenylhydrazine (1.6 g) in conc. sulphuric acid (8 ml) and water (12 ml). The precipitate consisted of a mixture of the 2,4-dinitrophenylhydrazones of formaldehyde and acetaldehyde [yield 75% based on (21)] which was separated on silica gel using chloroform-pentane (80:20) as eluant. Mixed m.p. with the authentic derivatives showed no depression. The non-volatile contents of the distilling flask were treated with charcoal and filtered through Celite. Evaporation of the clear filtrate *in vacuo* gave a crystalline residue (770 mg) which was recrystallized from propan-2-ol containing 48% hydrobromic acid (1 ml). The resulting crystals of diazacyclo-octane dihydrobromide melted at  $248\text{--}250^{\circ}\text{C}$  (lit.,<sup>10</sup>  $240\text{--}250^{\circ}\text{C}$ ) and were identical with an

**Table.** Pseudo first-order rate constants for ether cleavage of (21), (22a), and (23a) in aqueous 8.74N-HBr

	$T/^{\circ}\text{C}$	$k/\text{s}^{-1}$	$k_{\text{rel}}$
(23a)	101.40	$1.97 \times 10^{-5}$	1
(22a)	101.40	$2.41 \times 10^{-5}$	1.2
(21)	27.82	$2.84 \times 10^{-5}$	
	37.87	$8.38 \times 10^{-5}$	
	47.70	$2.24 \times 10^{-4}$	
	101.40	$1.96 \times 10^{-2}$ <sup>a</sup>	$10^3$

<sup>a</sup> Extrapolated.

authentic sample (Found: C, 26.4; H, 6.0; Br, 57.9; N, 10.1. Calc. for  $\text{C}_6\text{H}_{16}\text{Br}_2\text{N}_2$ : C, 26.11; H, 5.84; Br, 57.95; N, 10.15%).

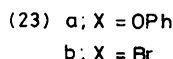
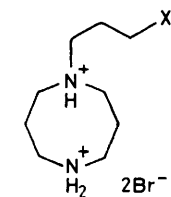
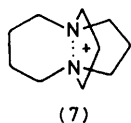
**Rate Measurements.**—Freshly distilled constant-boiling 8.74N-hydrobromic acid (b.p.  $125^{\circ}\text{C}$ ) was used throughout. Samples of the pure salts (21), (22a), and (23a) (150–200 mg) were dissolved in the acid (100 ml). Ten 12 ml samples of each solution were kept in sealed tubes at the temperatures listed in the Table. After a given time the samples were withdrawn, cooled, and extracted with pure ether to remove phenol. The reactions were followed by determining the decrease of the phenoxy u.v. absorption at 270 nm in the aqueous solution. The constants listed in the Table are the averages of three runs; mean deviation of 8–12 instantaneous constants from the average rate constant,  $\pm 2.14\%$ .

## Results

**Hydrolyses of Dications.**—1,5-Diazoniatriacyclo[3.3.2.0]-decane bistetrafluoroborate (1) was hydrolysed so rapidly, even at pH 2, that the reaction could not be followed by n.m.r., but the  $^1\text{H}$  n.m.r. spectrum of the resulting solution (in  $\text{D}_2\text{O}$ ) was identical with that of 1-(2-hydroxyethyl)-1,5-diazabicyclo[3.3.0]octanium bromide.<sup>5</sup>

The hydrolyses of the dications (2)–(6) were much slower. As reported earlier,<sup>5</sup> one can follow the disappearance of dication by  $^1\text{H}$  n.m.r. in  $\text{D}_2\text{O}$  solution. When this is done,  $t_{\frac{1}{2}}$  is about 1 day for (6) and 2 days for (2), and  $t_{\frac{1}{2}}$  increases in the order (2) < (3) < (4) < (5), (which appears almost indefinitely stable under these conditions). However the hydrolyses produce acid, and since it is likely that the observed rate is a composite of  $k_{\text{H}_2\text{O}}$  and  $k_{\text{OH}^-}$  terms (with the latter much greater than the former), the reactions slow down as the acid is formed. We shall not discuss the kinetics of these reactions any further at this time, but concentrate on the products. After 2 weeks in  $\text{D}_2\text{O}$ , the [3.3.3.0] dication (2) produced an  $^1\text{H}$  n.m.r. spectrum similar to that of 1,5-diazacyclo-octane in a solution of similar pH. When a  $\text{D}_2\text{O}$  solution of (2)  $2\text{BF}_4^-$  was treated with NaOH, a very complex  $^1\text{H}$  n.m.r. spectrum appeared. A sharp doublet at  $\delta$  1.50 could be due to some derivative of acetaldehyde [e.g.  $\text{HCMe}(\text{N}^<)_2$ ], and a singlet at  $\delta$  3.9 is consistent with the presence of 1,5-diazabicyclo[3.3.1]nonane.<sup>14</sup> When the [3.3.3.0] dication salt (2)  $2\text{BF}_4^-$  was heated in aqueous 40%  $\text{HBF}_4$  for 0.5 h, the product seemed to be a relatively clean mixture of (diprotonated) 1,5-diazacyclo-octane and 1,5-diazabicyclo[3.3.1]nonane.

When an equivalent of sodium carbonate was added to a solution of the [4.3.3.0] dication (3) in  $\text{D}_2\text{O}$ , the solution became a deep red colour, suggesting the presence of the radical cation (7).<sup>3</sup> After 0.5 h, the red colour had faded and the solution was dark brown. A  $^{13}\text{C}$  n.m.r. spectrum showed a major set of lines at  $\delta$  16.6, 19.6, 20.6, 21.6, 40.0, 51.6, 52.3, 62.5 (double intensity), and 85.8 corresponding exactly with



those of a solution of 1-azonia-6-azatricyclo[4.3.3.0<sup>1,5</sup>]dodecane chloride <sup>15</sup>(8)Cl<sup>-</sup> (see Scheme 6) in D<sub>2</sub>O, together with at least 15 other less intense lines between δ 17 and 75. When this solution was heated to 100 °C for 0.5 h, a new set of lines appeared in the <sup>13</sup>C n.m.r. spectrum. It was suspected that these were due to 1,5-diazacyclononane <sup>15</sup>[δ<sub>c</sub> (CDCl<sub>3</sub>) 28.7, 30.5, 50.3, and 50.8], and 1,5-diazabicyclo[4.3.1]decane <sup>16</sup>[δ<sub>c</sub> (CDCl<sub>3</sub>) 21.4, 30.6, 52.6, 54.7, and 66.1], although precise chemical shift correlations were affected by pH and solvent effects (in a separate experiment, this solution was extracted with CDCl<sub>3</sub> and the presence of the two amines conclusively verified by <sup>13</sup>C n.m.r. spectra). The solution was then acidified with trifluoroacetic acid, to pH < 1, and heated to 100 °C for 0.5 h. The <sup>13</sup>C n.m.r. spectrum now showed a clean mixture of (8) and (diprotonated) 1,5-diazacyclononane in roughly equal amounts (from <sup>13</sup>C peak intensities).

Treatment of the [4.4.3.0] dication salt (4) 2BF<sub>4</sub><sup>-</sup> in D<sub>2</sub>O with an excess of potassium carbonate gave a solution the <sup>13</sup>C n.m.r. spectrum of which indicated the major products to be the two stereoisomeric 1-azonia-6-azatricyclo[4.4.3.0<sup>1,5</sup>]tridecane ions (9) and (10) (see Scheme 7), also observed in the cyanide trapping reactions (see later), and in roughly the same ratio, 85:15. However other products are certainly formed and while these may belong to products arising from deprotonation in the [CH<sub>2</sub>]<sub>3</sub> bridge, the presence of a moderately intense line at δ 89.9 suggests the presence of another >N<sup>+</sup>-CH-N< salt.

The stereochemistry of (9) and (10) was assigned through <sup>1</sup>H decoupling and nuclear Overhauser effect (n.O.e.) experiments at 400 MHz on the resonances of the major isomer in the mixture. From the normal spectrum and by decoupling at δ 1.73 the protons within the [CH<sub>2</sub>]<sub>3</sub> bridge can be assigned as follows: H-11a δ 3.55, H-11e 3.28, H-12a 2.22, H-12e 1.73, H-13a 3.40, H-13e 2.80 [see (9), Scheme 7, for numbering]. Coupling constants are appropriate for a chair hexahydropyrimidinium ring; the high field shift for H-12e has precedents.<sup>17</sup> Assignments are further confirmed by the spectrum of the tricyclic product from 12,12-dideuteriated (4). Irradiation of the frequency of the methine signal at δ 5.12 for the major tricycle caused an n.O.e. at only one non-coupled proton, part of a close AB system at δ 3.0. By elimination this must be due to the protons on C-7 and hence the major isomer is (9) as shown in Scheme 7. An additional argument is that the methine proton signal at δ 5.12 shows small long-range couplings to H-11e and H-13e; this proton must therefore be equatorial in the hexahydropyrimidinium ring.

As reported already,<sup>5</sup> hydrolysis of the [4.4.4.0] dication salt (5)2BF<sub>4</sub><sup>-</sup> with potassium carbonate cleanly gives 1-azonia-6-azatricyclo[4.4.4.0<sup>1,5</sup>]tetradecane tetrafluoroborate (11)BF<sub>4</sub><sup>-</sup> (see Scheme 4) in 81% yield after recrystallisation.

*cis*-1,6-Dimethyl-1,6-diazoniabicyclo[4.4.0]decane bistetrafluoroborate (6)2BF<sub>4</sub><sup>-</sup>, on reaction with K<sub>2</sub>CO<sub>3</sub> in D<sub>2</sub>O, gave a solution whose <sup>13</sup>C n.m.r. spectrum indicated that the 1-methyl-1-azonia-6-azabicyclo[4.4.1]undecane ion (12)<sup>16</sup> (see Scheme 3) constituted >80% of the products (lines at δ 23.2, 26.5, 48.1, 51.9, 62.1, and 82.3) the remainder being 1-methyl-1,6-diazacyclodecane (13)<sup>16</sup> [lines at δ 26.3, 41.2, 44.8, and 54.6; the fifth line for this product at δ 26.5 being buried under a line for (12)]. The ratio (12):(13) did not change after 2 weeks and so (13) must arise not from (12) but from its precursor iminium ion. There is some evidence that the amount of (13) formed is pH-dependent, and it may be formed by attack of hydroxide ion, not water, on the iminium ion. The <sup>13</sup>C n.m.r. spectra of the hydrolysis products of (6)2BF<sub>4</sub><sup>-</sup> are very clean, with no sign of products derived from deprotonation at α-CH<sub>2</sub> groups.

*Reaction with Aqueous Potassium Cyanide.*—Procedure (a) (see Experimental section) when applied to (2)2BF<sub>4</sub><sup>-</sup> produced 2-cyano-1,5-diazabicyclo[3.3.3]undecane (14) (see Scheme 5) in ca. 80% yield, the remaining material being unidentified, but no tricyclic salt formation (internal trapping) occurred.

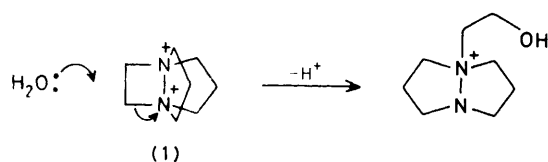
The [4.3.3.0] dication salt (3)2BF<sub>4</sub><sup>-</sup>, when treated under similar conditions, gave a colourless, air-sensitive oil in 68% yield (as a nitrile) which <sup>13</sup>C n.m.r. spectroscopy showed to be a mixture of the three nitriles 2-cyano-1,6-diazabicyclo[4.3.3]dodecane (15) (see Scheme 6), and the stereoisomeric 7-cyano-1,6-diazabicyclo[4.3.3]dodecane (16) and (17) in more or less equal amounts, based on the lines for the nitrile carbons at δ 119.4, 119.8, and 121.9 ([<sup>2</sup>H<sub>6</sub>]toluene solution). Seven major lines (out of twelve) were observed for carbons β to amino nitrogen between δ 28 and 36 and nine (out of eighteen) lines for α-carbons between δ 47 and 58. A high resolution mass measurement on the molecular ion gave *m/z* 193.159 (Calc. for C<sub>11</sub>H<sub>19</sub>N<sub>3</sub>: 193.158). When procedure (b) was applied to the [4.3.3.0] dication salt (3)2BF<sub>4</sub><sup>-</sup>, the D<sub>2</sub>O layer contained the 1-azonia-6-azatricyclo[4.3.3.0<sup>1,5</sup>]dodecane ion (8). Integration against an internal standard (CH<sub>3</sub>CN) indicated a yield of 33%, giving an excellent material balance with the nitriles formed.

The [4.4.3.0] dication salt (4)2BF<sub>4</sub><sup>-</sup> reacted with aqueous KCN [procedure (a)] to give a colourless, air-sensitive oil which slowly crystallized, in 43% yield (as a nitrile). As shown in the Experimental section, this material is 11-cyano-1,6-diazabicyclo[4.4.3]tridecane (18) (see Scheme 7), and it appears, from <sup>13</sup>C n.m.r. spectra, to be free of isomeric nitriles. A procedure (b) experiment on (4)2BF<sub>4</sub><sup>-</sup> produced roughly equal amounts of nitrile (18) and tricyclic ions (9) + (10) in the CDCl<sub>3</sub> and D<sub>2</sub>O layers, respectively. As discussed earlier, the major ionic product is (9).

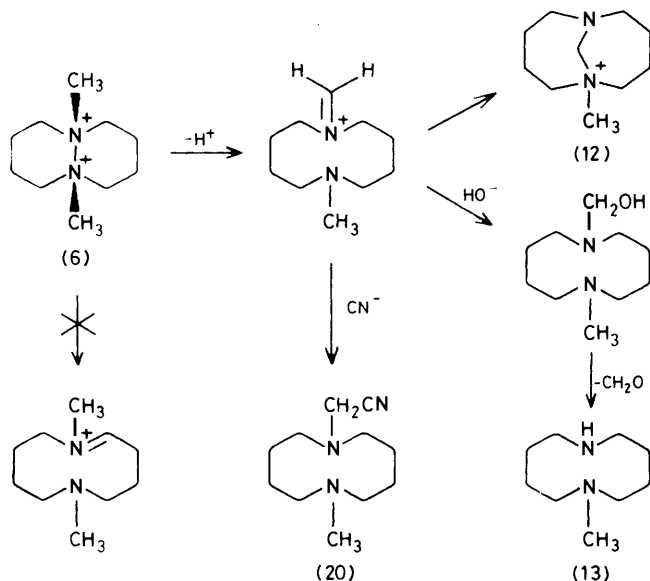
The [4.4.4.0] dication salt (5)2BF<sub>4</sub><sup>-</sup> gave an almost quantitative yield of 2-cyano-1,6-diazabicyclo[4.4.4]tetradecane (19) (see Scheme 4); there is no detectable internal trapping (tricyclic ion formation) in this case.

The bicyclic dication salt (6)2BF<sub>4</sub><sup>-</sup> gave only one nitrile product, (20) (see Scheme 3), in 80% yield, the remainder being internal trapping product (12).

*Interconversion of α-Amino Nitriles and α-Amino Ammonium Ions (Tricyclic).*—When 2-cyano-1,6-diazabicyclo[4.4.4]tetradecane (19) (145 mg) was heated at 100 °C for 5 min with iron(II) sulphate (60 mg; two-fold excess) and tetramethylammonium bromide (78 mg; internal integration standard) in D<sub>2</sub>O (1 ml) and the solution was cooled and filtered through



Scheme 2.



Scheme 3.

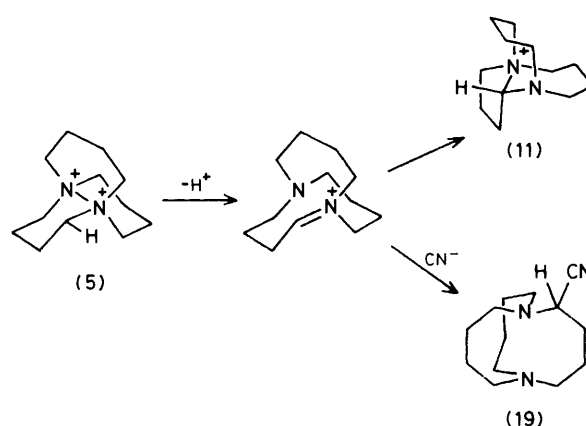
Celite,  $^1\text{H}$  n.m.r. spectroscopy indicated the formation of the 1-azonia-6-azatricyclo[4.4.4.0<sup>1,5</sup>]tetradecane ion (11) in 98% yield.

Conversely, when a solution of (11)BF<sub>4</sub><sup>-</sup> in CD<sub>3</sub>CN was heated to 80 °C for 1 h with an excess of KCN and 1 equiv. of 18-crown-6,  $^1\text{H}$  n.m.r. spectroscopy showed clean conversion into (19). However when this experiment was repeated with tricyclic salts (8)Cl<sup>-</sup> and [(9) + (10)]Cl<sup>-</sup> there was no detectable reaction even after 4 h heating.

**Reaction of 1-(3-Phenoxypropyl)-1-azonia-5-azabicyclo[3.3.0]octane bromide (21) (see Scheme 5) with 48% Hydrobromic Acid.**—As shown in the Table, this compound reacted *ca.* 10<sup>3</sup> times as fast with aqueous HBr as two model compounds (22a) and (23a).

## Discussion

With one exception, all the reactions of hydrazinium dications described in this paper can be interpreted in terms of  $\alpha$ -deprotonation to form an iminium ion [pathway (c), Scheme 1]. The exception is the rapid hydrolysis of the 1,5-diazoniatri-cyclo[3.3.2.0]decane dication (1), which proceeds by S<sub>N</sub>2 reaction at  $\alpha$ -carbon [pathway (b)], presumably owing to strain relief upon reaction, and unhindered access for the nucleophile (Scheme 2). Before proceeding to a detailed consideration of the reactions going *via* iminium ions, we draw the reader's attention to one other pathway, electron transfer (e) in Scheme 1, which is known<sup>3,4</sup> to be important in certain circumstances. The dications (2)—(5) react with the corresponding diamines (derived from them by two-electron reduction) to produce solutions of stable radical cations. The diamines are exceptionally easily oxidised and are therefore

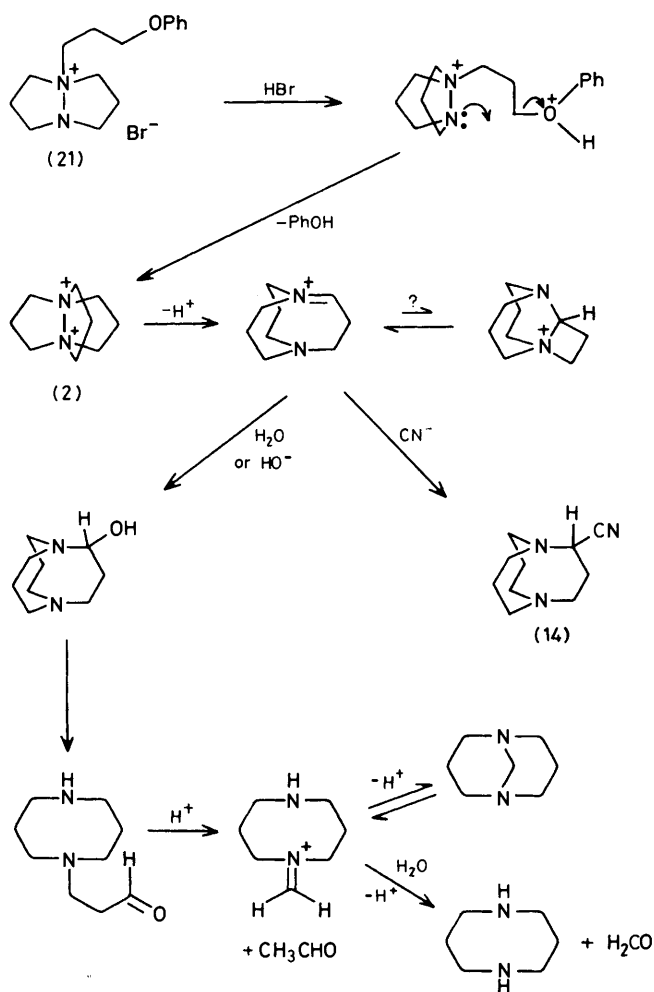


Scheme 4.

very 'soft' nucleophiles, and it is apparent that electron transfer will only be important in such circumstances. In fact, the electron transfer is only completely clean when the dication (5) reacts with its corresponding diamine, 1,6-diazabicyclo[4.4.4]tetradecane. With the dications (4), (3), and especially (2), radical cation generation is not quantitative and the major side reaction is undoubtedly  $\alpha$ -deprotonation, pathway (c). As described in the Results section, reaction of the dication (3) with aqueous sodium carbonate did produce a deep red colour, characteristic of the radical ion (7). It is unlikely however that (7) arose by electron transfer from OH<sup>-</sup> or HCO<sub>3</sub><sup>-</sup> to (3); the reducing agent was perhaps an  $\alpha$ -hydroxy diamine produced as an intermediate from the iminium ion.

Iminium ion formation from these hydrazinium dications is, in a sense, a rather unusual example of Hofmann elimination, and it is interesting that in the sole case which tests this point, the dication (6), Hofmann orientation is observed. All the observed products can be derived from the methylene-ammonium ion as shown in Scheme 3.

In the remaining examples, the iminium ions are at a bridgehead within a bicyclic ring system, and are presumably isostructural with the corresponding bridgehead alkenes. Bridgehead unsaturation within the medium-ring bicyclic ring systems discussed here can actually be favourable from the strain-energy point of view, as Maier and Schleyer<sup>18</sup> have pointed out with the aid of empirical force field calculations. We have recently reported<sup>19</sup> the preparation of 1-azabicyclo[4.4.4]tetradec-5-ene, the properties of which indicated a structure with an inside pyramidalised nitrogen. This monoamine reacts with acids by C-protonation to form a propellane, a process which is geometrically the precise reverse of the  $\alpha$ -deprotonation of (5). The reactions of (5) are particularly simple (Scheme 4). In the presence of CN<sup>-</sup>, external trapping of the iminium ion produces the  $\alpha$ -amino nitrile (19) in quantitative yield. In the absence of CN<sup>-</sup>, intramolecular trapping by the transannular nitrogen gives the  $\alpha$ -amino ammonium ion (11). External trapping by water or hydroxide is apparently uncompetitive, or, if it occurs, the  $\alpha$ -hydroxy amine does not undergo ring opening to an aldehyde (a reaction which would surely be irreversible); it simply reionises to the iminium ion. The intramolecular/external trapping of the iminium ion is truly competitive, because (11) does not form (19) with aqueous KCN, although when (11) is treated with KCN in CH<sub>3</sub>CN containing 18-crown-6, (19) is obtained in high yield. In these latter conditions the cyanide ion is presumably less solvated and more reactive. We also found it possible to convert (19) into (11), using Fe<sup>2+</sup> as a cyanide trap.

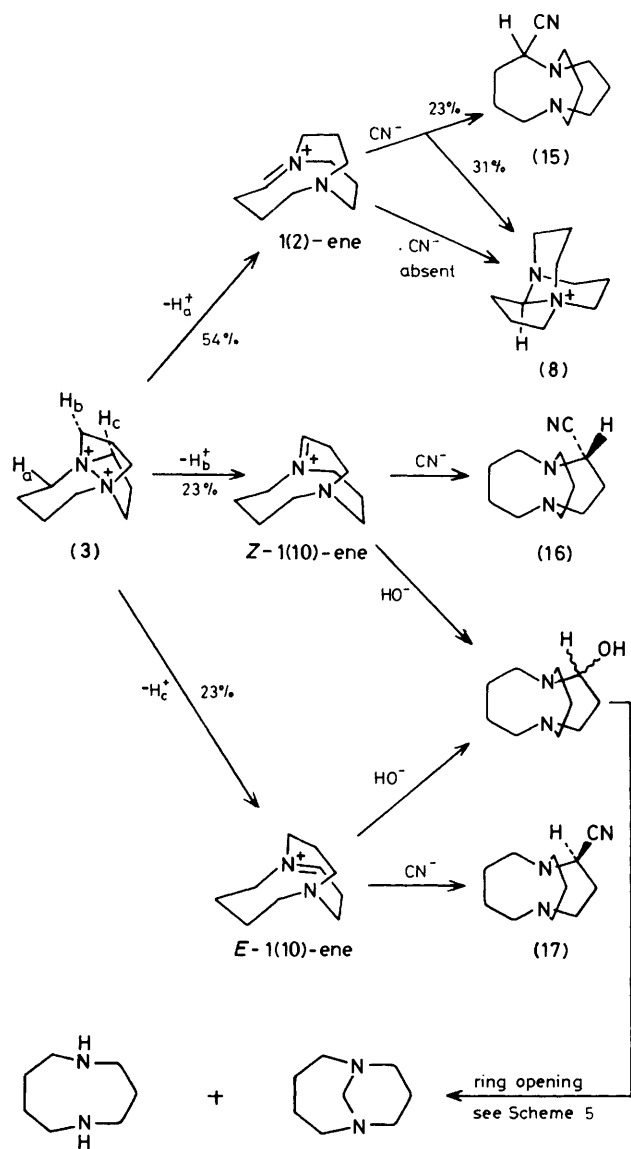


Scheme 5.

The reactions of the other three-fold symmetric dication (2) are rather different because no stable intramolecular trapping product is formed. If the tricyclic ion is formed, it must be in rapid equilibrium with the iminium ion (Scheme 5). Reaction of (2) with cyanide ion gives the nitrile in 80% yield but there are other products and these presumably arise from competitive trapping by water or hydroxide ion (see below). The iminium ion here is apparently less selective than that formed from (5), and this is not unexpected since it is a *trans*-cyclo-octene analogue and is presumably twisted. Maier and Schleyer<sup>18</sup> calculate that there is 16 kJ mol<sup>-1</sup> of olefinic strain in the corresponding alkene bicyclo[3.3.3]undec-1-ene.

Alkaline hydrolysis of (2)2BF<sub>4</sub><sup>-</sup> produced a complex mixture containing some 1,5-diazabicyclo[3.3.1]nonane, and this compound together with 1,5-diazacyclo-octane was obtained from hot acidic hydrolysis. Solvolysis of 1-(3-phenoxypropyl)-1,5-diazabicyclo[3.3.0]octanium bromide (21) (see Scheme 5) in constant-boiling HBr also gave 1,5-diazacyclo-octane. Formaldehyde and acetaldehyde were additionally detected as products of this solvolysis, which presumably involves (2) as an intermediate. These reactions are reasonably accounted for by the retro-Mannich sequence shown in Scheme 5.

The solvolysis of (21) is acid-catalysed, since the compound is unchanged after boiling for 8 h in H<sub>2</sub>O, but readily evolves phenol when heated with 2N-sulphuric acid. Acid-catalysed

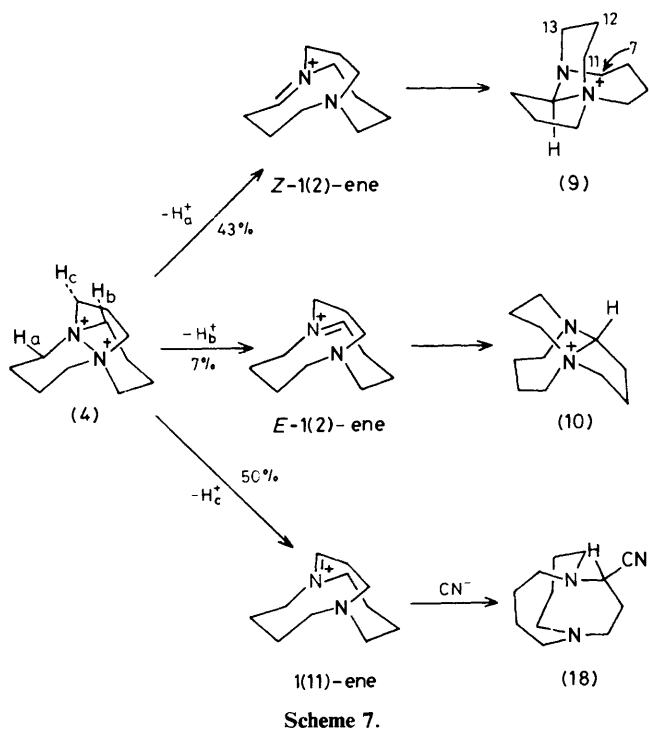


Scheme 6.

solvolysis of (21) is accelerated by a factor of 10<sup>3</sup> as compared with model substrates (22a) and (23a). Since (21), (22a), and (23a) should form very similar equilibrium concentrations of their *O*-protonated conjugated cations in 8.74N-HBr, the greater rate for (21) points to an anchimerically assisted solvolysis with N-5 participation as shown in Scheme 5. Actually (21) may be *N*-protonated to some extent,<sup>2</sup> so the observed acceleration is a minimum figure.

These results also permit a satisfactory interpretation of the observed formation of 1,5-diazacyclo-octane as a major product from the reaction of hydrazine with 1,3-dibromopropane in ethanol.<sup>10</sup> A sequence of alkylation reactions can lead to the analogue of (21) with Br in place of OPh. Cyclisation to (2) then occurs but this is unstable in the reaction conditions, breaking down as shown in Scheme 5.

The less symmetrical diazabicyclic dications, (3) and (4), can each give rise to three isomeric iminium ions, and in both cases it is possible to account for the products in the presence and in the absence of cyanide ion in terms of a partition between these isomeric ions which is independent of cyanide



ion, as shown in Schemes 6 and 7. As expected, intramolecular trapping by the transannular nitrogen occurs when a new five-membered ring can be formed. In fact this trapping occurs to some extent for the 1(2)-ene from (3) (Scheme 6) even in the presence of cyanide and with the *Z*- and *E*-1(2)-enes from (4) (Scheme 7) no cyanide trapping is observed at all. Thus the intramolecular trapping is more efficient here than in the case of (5) (Scheme 4). We suspect that formation of the bicyclic [3.3.1] unit in (8) and the [4.3.1] units in (9) and (10) is more favourable than that of the [4.4.1] unit in (11).

What controls the partition between the iminium ions from (3) and (4)? If the transition state for the *E2* elimination were very early, there might be a correlation with the dihedral angle H-C-N<sup>+</sup>-N<sup>+</sup> in the hydrazinium dication. MM2 calculation<sup>20</sup> on tricyclo[4.4.3.0]tridecane, the propellane parent for (4), gives a preferred structure with two chair-form six-membered rings and the appropriate dihedral angles are 171.3° for H<sub>a</sub>, 174.2° for H<sub>b</sub>, and 155.6° for H<sub>c</sub>. These numbers suggest no obvious correlation and we therefore presume that transition states may be later, so that the strain energies of the iminium ions become important. Force field calculations on the alkene analogues of these are possible,<sup>19</sup> but each may have several low energy conformations, and with the doubt concerning the iminium ion/alkene analogy, we have not felt it worthwhile to undertake calculations. Certainly, no simple explanations are forthcoming. The dication (3) produces as much *E*-1(10)-ene, a *trans*-cyclo-octene derivative, as *Z*-1(10)-ene, a *trans*-cyclononene, and while (4) gives more *Z*-1(2)-ene (*trans*-cyclodecene) than *E*-1(2)-ene (*trans*-cyclononene), the 1(11)-ene, another *trans*-cyclononene, is the major isomer formed.

Finally we note that these bridgehead iminium ions<sup>21,22</sup> may have synthetic potential and that under suitable conditions both the  $\alpha$ -amino nitriles and the  $\alpha$ -amino ammonium ions

may act as *in situ* sources of these ions. Thus the  $\alpha$ -amino ammonium ions are reduced by LiAlH<sub>4</sub> to bicyclic diamines. We have also observed that the nitrile (14) will react with Grignard reagents to form  $\alpha$ -alkyl-1,5-diazabicyclo[3.3.3]-undecanes.

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