

anchimeric assistance by a neighboring carboxyl group resulting in a ratio in the rate of reduction of isomeric *cis*-3-benzylsulfanylbicyclo[2.2.1]-heptane-2-carboxylic acids of syn/anti = 3×10^3 in methanol. Comparison of the third-order rate constant for **1** in water with the second-order rate constant for the syn isomer gives a factor of 7.11.

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Neutral Products from Deprotonation of Tertiary Cations in the Gas Phase

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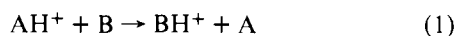
Abstract: The products of gas-phase proton transfer from cations with chemically nonequivalent acidic protons have been examined experimentally. The neutral products of deprotonation of 1-methylcyclopentyl cation (**1**) and of *tert*-amyl cation (**2**) have been collected using an electron bombardment flow (EBFlow) reactor. The cations were generated by 70-eV electron impact on bromocyclohexane and isoamyl bromide, respectively, at pressures of 4×10^{-4} Torr in the presence of 2×10^{-4} Torr triethylamine. The products from **1**, 1-methylcyclopentene and methylenecyclopentane, are recovered in a ratio of 1.2:1, which is closer to the statistical value of 4/3 than it is to the equilibrium value $\sim 10^3$. Analysis of the products from **2** requires the use of deuterium-labeled isoamyl bromides to exclude the products of dehydrohalogenation of the molecular ions. When the products of EBFlow radiolysis of $(\text{CH}_3)_2\text{CDCH}_2\text{CH}_2\text{Br}$ and of $(\text{CH}_3)_2\text{CHCH}_2\text{CH}_2\text{DBr}$ are compared, the ratio of 2-methyl-1-butene to 2-methyl-2-butene from **2** is estimated to be 2.5:1. Both results support the notion that statistical effects predominate in deprotonations of *tert*-alkyl cations by triethylamine. Generation of **2** by addition of isopropyl cation to ethylene in the presence of di-*n*-propyl ether affords 2-methyl-1-butene and 2-methyl-2-butene in a ratio of 1.2:1, which implies that thermodynamic effects play more important roles in deprotonations by weaker bases.

Proton transfer in the gas phase, reaction 1, represents a prototype for Brønsted acid-base chemistry. Despite widespread interest in this reaction, only a few investigations have probed the identities of the neutral products (A) produced by gas-phase proton transfer.¹ One question, in particular, has received scant attention: what is the distribution of isomers of A when proton transfer may yield more than one neutral product? There are at least three different surmises which predict different outcomes when two acidic sites in the same ion compete for reaction with a gaseous base:

(1) Proton transfer is dominated by statistical effects. The product distribution reflects the number of protons which can be removed to give each product.

(2) Ion and molecule form a long-lived complex in which the proton is exchanged between A and B many times before the products separate from one another. Under such conditions thermodynamic control is expected, and an equilibrium distribution of products should be formed.

(3) The more weakly bound protons are preferentially transferred, by analogy to hydrogen abstractions by recoil tritium atoms.² This surmise predicts that even under kinetic control reaction 1 may yield the thermodynamically more stable product.



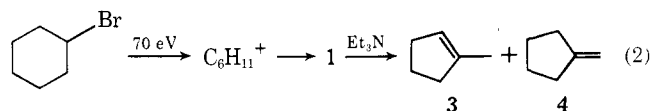
The tertiary cations **1** and **2** represent two of the simplest examples of ions with nonequivalent acidic protons. Analysis of the neutral products from their deprotonations can distinguish among the surmises regarding reaction 1. Two considerations dominate the contemplation of such a neutral product study: ion currents on the order of microamperes are required for adequate yields of neutrals to be recovered within a rea-

sonable time, and the products of reaction 1 must be distinguishable from other reaction products. Electron impact at 70 eV is well known as an efficient method of generating cations from neutral substrates in the gas phase.³ The construction of an electron bombardment flow (EBFlow) reactor for collection of neutral products from reactions of ions in the gas phase



provides the capability to realize the yields necessary for such an experiment.⁴

Electron bombardment can efficiently generate excited neutrals as well as cations. Therefore, it is necessary to choose neutral substrates from which the products of nonionic pathways are distinct from the products of cationic pathways. For this reason, electron bombardment of *tert*-methylcyclopentyl compounds ought not to be used to generate ion **1**, since 1-methylcyclopentyl radicals could give the same products, **3** and **4**, as deprotonation of **1**. Bromocyclohexane was chosen instead as a source of **1**, since the stable $\text{C}_6\text{H}_{11}^+$ cation generated from



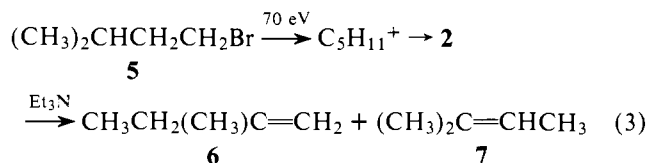
this compound in solution has been reported to be **1**.⁵ The $\text{C}_6\text{H}_{11}^+$ cation is the base peak in the mass spectrum of bromocyclohexane, composing at least one-third of the total ionization at 70 eV. Other conceivable ionic sources of **3** and **4** are produced in negligible quantities.⁶

Irradiation of a mixture of bromocyclohexane and triethylamine with nominal 70-eV electrons yields the rearranged hydrocarbons **3** and **4** among the reaction products. As there is no precedent for forming either of these products from bromocyclohexane via nonionic pathways, the observed 3:4 ratio is taken as the product distribution from reaction 2. Cyclohexane is recovered in approximately the same yield as **3**. The recovered 3:4 ratio is 1.22, with a standard deviation of 0.02.

Two types of control experiment are required to validate this result. The EBFlow reactor consists of three main sections, an electron source, a reaction vessel, and a collector. The first type of control shows that the recovered **3** and **4** do not result from pyrolysis on the hot filament in the electron source. The reaction is run under ordinary conditions, except that the electric fields are adjusted so that electrons do not enter the reaction vessel. In this control, products **3** and **4** are recovered in less than 0.05 of the yield which is recovered under electron impact.

The second type of control attests that **1** produces **3** and **4** via reaction 2. The reaction vessel of the EBFlow reactor is enclosed in a solenoid electromagnet. The flux lines inside the solenoid run axially from the electron source to the collector. Ions and electrons travel helical paths within the reaction vessel, and the solenoid is adjusted so that the radii of these helical paths (the cyclotron radii) are less than the diameter of the reaction vessel. If the solenoid is not turned on, or if the pressure of base is very low, unreacted **1** may collide with the wall of the reaction vessel, which is lined with stainless steel cage set at a constant potential. Neutralization of **1** could produce radicals which might also yield **3** and **4**. Radiolysis of bromocyclohexane with insufficient base or in the absence of a magnetic field produces a diminished yield of **3** and **4** with a ratio 3:4 = 1.35. When the solenoid field is increased and the base pressure elevated, this ratio reaches a limiting value of 1.22 which is unaffected by further increases in base pressure or magnetic field strength.

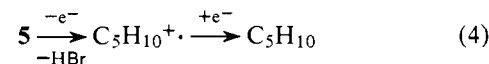
The observed ratio from reaction 2 is sufficiently close to the statistical value of 4/3 and is so far from the equilibrium constant ($\sim 10^3$ at 300 K)⁷ as to suggest that statistical effects predominate. This interpretation probably cannot be generalized for reaction 1, since the ions AH⁺ formed by 70-eV electron impact are likely to have a broad distribution of internal energies and since the proton transfer in reaction 2 is at least 1 eV exothermic (based on gas-phase basicities of 9.9⁸ and 8.9 eV⁹ for triethylamine and **4**, respectively). Nevertheless, if statistical effects do predominate under these reaction conditions, then deprotonation of *tert*-amyl cation by triethylamine, reaction 3, ought to yield a contrathermodynamic distribution of products **6** and **7**. The equilibrium constant $K_{eq} = 6:7$ is 0.09 at 298 K and approaches unity in the high-temperature limit.¹⁰ The statistical product ratio from reaction 3 ought to be 3:1.



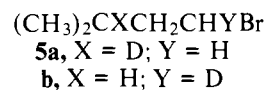
The *tert*-amyl cation, **2**, is generated by 70-eV electron impact on isoamyl bromide (**5**). Electron impact on *tert*-amyl compounds would be unsatisfactory because products **6** and **7** could be produced via nonionic pathways. Since **2** is the most stable isomer,¹¹ formation of other branched cations should lead to **2**. If a primary cation is initially formed from **5**, we estimate the value of ΔH for its isomerization to **2** to be the same as ΔH for isomerization of isobutyl cation to *tert*-butyl cation, -1.4 eV.¹¹ Previous studies have shown that primary

cations in the gas phase rearrange rapidly on the microsecond time scale to more stable structures,^{12,13} and we further note that **2** thus formed has an internal energy which is greater than the 0.8-eV barrier reported for complete intramolecular hydrogen randomization.¹⁴ Since the bimolecular rate constant for reaction 3 may be estimated to be on the order of 1×10^{-9} cm³ molecule⁻¹ s⁻¹,¹⁵ the mean lifetime of AH⁺ cations in the EBFlow reactor is on the order of 10^{-4} s before deprotonation occurs. We assume that in this time span other branched structures, such as *sec*-isoamyl cation or protonated cyclopropanes, have isomerized to **2** and contribute negligibly to production of **6** and **7**.

The C₅H₁₁ cation composes about one-sixth of the total ionization from **5** in the 70-eV mass spectrum,⁶ and 70-eV EBFlow radiolysis of **5** with triethylamine produces **6** and **7** as 70% of the C₅H₁₀ yield. We cannot separate 3-methyl-1-butene from 1,1-dimethylcyclopropane on the GLC columns used for analyses; together these two isomers constitute approximately 15% of the C₅H₁₀ yield. Other C₅H₁₀ olefins detected (each on the order of 3–4% of the C₅H₁₀ yield) are 1-pentene, *trans*-2-pentene, and *cis*-2-pentene. The GLC analysis shows smaller peaks (1–2% of the C₅H₁₀ yield) whose retention times correspond to ethylcyclopropane and *cis*-dimethylcyclopropane (*trans*-dimethylcyclopropane is not seen, but may be obscured by a large 1,3-butadiene peak).



The production of 3-methyl-1-butene via electronic or vibrational excitation of **5** is plausible, but there is no precedent for production of any of the other isomers by any pathway not involving ionic intermediates. However, the possibility of an alternative ionic pathway to **6** and **7**, reaction 4, complicates the analysis of reaction 3. An [M – HBr] fragment ion is nearly as abundant as the C₅H₁₁ cation in the 70-eV mass spectrum of **5**, and neutralization of this fragment could produce the same products as reaction 2. No other conceivable ionic sources of **6** and **7** are produced in significant quantities.⁶ A deuterium-labeling experiment which distinguishes the products of reaction 3 from those of reaction 4 should therefore suffice to characterize the product distribution from deprotonation of **2**.



Comparison of the EBFlow radiolysis products of **5a** and **5b** permits the dissection of reaction products. The 70-eV mass spectrum of **5a** shows a prominent [M – DBr] ion and virtually no [M – HBr] when corrections are made for insufficient deuteration and ¹³C natural abundance. In other words, the odd-electron species in reaction 4 is produced by a nominal 1,3-elimination of HBr from the molecular ion. The product of **5a** from reaction 4 will thus be C₅H₁₀. We assume that complete hydrogen randomization occurs in **2** when it is generated by 70-eV electron impact on **5**. If this assumption is correct, then deprotonation of the *tert*-amyl cation from **5a** should yield mostly C₅H₉D. Therefore the 6-*d*₁:7-*d*₁ ratio from **5a** ought to give the product distribution from reaction 3. This ratio has been determined from molecular ion intensities in the mass spectra of the products from **5a**.

Mass spectrometric determination of isotropic abundances in **6** and **7** are complicated by the presence of [M – 1] peaks approximately one-tenth the intensity of the parent peaks in the mass spectra of C₅H₁₀ isomers. Consequently, the mass spectra of **6** and **7** from EBFlow radiolysis of **5b** have been used to calibrate the analysis. Because some isotopic fractionation occurs on the GLC column, a direct GLC–mass spectrometer interface cannot be used. Instead, it is necessary to collect each

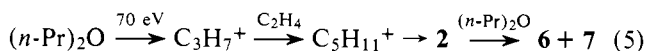
GLC peak in its entirety for subsequent mass spectrometric analysis. The peaks of interest are m/e 71 (C_5H_9D) and 70 (C_5H_{10} and C_5H_8D), and correction for ionization potential, cross section, and fragmentation rate differences between C_5H_{10} and C_5H_9D have been ignored.

The m/e 70:71 ratios from **6** and **7** collected from **5b** are within experimental error of one another, having a mean value of 0.28 (standard deviation 0.04). The m/e 70:71 ratios from the products of EBFlow radiolysis of **5a** are 0.30 for **6** and 1.17 for **7**, implying that **7** is the major product from reaction 4. This result is consistent with photochemical studies of $C_5H_{10}^{+16}$ and with the suggestion that molecular ions of unsaturated hydrocarbons rearrange to the most stable isomers.¹⁷ Since the product ratio **6:7** from **5a** is 1.36, the ratio **6-d₁:7-d₁** is calculated to equal 2.6. If we are correct in assuming hydrogen randomization in **2**, then the **6-d₁:7-d₁** ratio is the product distribution from reaction 3.

An independently determined value of **6-d₁:7-d₁** from **5a** can be calculated from product ratios alone. One effect of γ -substitution of deuterium in **5** is partial suppression of dehydrohalogenation of the molecular ion. The ratio $[M - Br]/[M - DBr]$ in the 70-eV mass spectrum of **5a** is 1.98 ± 0.05 , while the $[M - Br]/[M - HBr]$ ratio in the 70-eV mass spectra of **5** and **5b** is 1.14 ± 0.02 . Correspondingly, the **6:7** ratio from GLC analyses of the EBFlow reaction products decreases from 1.36 (standard deviation 0.05) for **5a** to 1.09 (standard deviation 0.04) for **5** and **5b**. If the **6:7** ratio from reaction 4 is taken to be <0.1 and if the change in the overall **6:7** ratio is going from **5a** to **5b** is entirely due to suppression of $C_5H_{10}^{+}$ ion formation, then the **6:7** ratio from reaction 3 is computed to equal 2.1 ± 0.4 .

These results support the notion that statistical effects predominate in reaction 1 when it is very exothermic. The control experiments lend further credence to this surmise. When **5** and **5a** are radiolyzed without an axial magnetic field or in the absence of sufficient base, the observed **6:7** ratios are 0.7 and 1.0, respectively. It is noteworthy that, when conditions for reaction 1 are optimized, the **3:4** ratio from bromocyclohexane and the **6:7** ratios from **5** and **5a** are shifted in the direction away from equilibrium.

Cation **2** can also be generated by addition of isopropyl cation to ethylene. Bombardment of di-*n*-propyl ether with 70-eV electrons yields $C_3H_7^+$ cation as more than half of the total ionization,¹⁸ and $C_3H_7^+$ cations in the gas phase have been shown to rearrange to the most stable structure, isopropyl cation.¹³ Mass spectrometric studies have shown that silyl cations add to ethylene at pressures above 10^{-4} Torr to form long-lived intermediates,¹⁹ and the analogous reaction of isopropyl cation ought to generate $C_5H_{11}^+$ cations, as shown in reaction 5. If these cations rearrange to **2**, then the **6:7** ratio from 70-eV electron bombardment of a mixture of di-*n*-propyl ether with ethylene should reflect the product distribution from reaction 1 where the base is di-*n*-propyl ether. The *tert*-amyl cations formed under these conditions are still likely to be excited, since the addition step of reaction 5 is at least 1 eV exothermic,¹¹ but the proton transfer step will be less exothermic for **B** = di-*n*-propyl ether (whose proton affinity is 9.0 eV)²⁰ than for **B** = triethylamine.



Radiolysis of di-*n*-propyl ether in the presence of ethylene produces **6** and **7** as 40% of the C_5H_{10} yield. These products are not observed when di-*n*-propyl ether or ethylene are radiolyzed neat. If reaction 5 is properly assumed to be the sole source of **6** and **7**, then deprotonation of **2** by di-*n*-propyl ether affords a **6:7** ratio of 1.2, which is closer to equilibrium than the ratio of products from deprotonation by triethylamine. The

implications of this trend are the subject of a continuing investigation.

Experimental Section

EBFlow radiolyses were performed as described in ref 4 with the following modifications of operating voltages: the repeller was removed and the anode set at 150 V. A separate inlet was used for each reactant. Unless otherwise specified, alkyl bromide radiolyses were all performed under the same conditions and pressures (2×10^{-4} Torr triethylamine, 4×10^{-4} Torr bromide, reaction vessel solenoid current at 4 A) for periods varying from 0.5 to 5 h. Lowering the bromide pressure to 1×10^{-4} Torr and raising the triethylamine pressure to 6×10^{-4} Torr did not change the reported product ratios within experimental error. For control experiments in the bromide radiolyses, current in the reaction vessel solenoid was varied from 0 to 5 A. The axial method magnetic field in the reaction vessel is linear with solenoid current and equals $32 \pm 2 \text{ G A}^{-1}$. Variation in the ratios of collected products was noted up to a solenoid current of 4 A, but no further variation was observed upon raising the solenoid current to 5 A. At these solenoid settings irradiating electron currents were measured to be 10–25 μA on the reaction vessel cage and $<1 \mu\text{A}$ at the collector.

Product analyses were performed on a Perkin-Elmer 881 gas chromatograph equipped with a flame ionization detector. Large yields of C_2 – C_4 hydrocarbons were recovered from all radiolyses. Products from bromocyclohexane radiolyses were analyzed on a 20 ft \times 1/8 in. 20% β,β -oxydipropionitrile on 100/110 Chromosorb P (acid-washed DMCS) column at room temperature. Products from isoamyl bromide radiolyses were analyzed on a 37 ft \times 1/8 in. 20% dimethylsulfolane on 100/120 Chromosorb P (acid-washed DMCS) column at room temperature. Products were identified by comparison of retention times with those of authentic samples. Relative GLC detector responses were calibrated for **3–4** and **6–7** and found to be the same (within 5%) for pairs of isomers. Reported **3:4** and **6:7** ratios are the averages of at least three independent radiolyses and have estimated uncertainties of ± 0.02 . For mass spectrometric analyses, small quantities of the C_5 olefin products (on the order of 50 nmol) were purified by preparative GLC on a 30 ft \times 1/8 in. *n*-octane on Porasil column at 80 °C mounted in an Aerograph 900. Mass spectra were recorded on a Hitachi Perkin-Elmer RMU 6-D with chamber set at 70 V and target set at 110 V. No significant changes in ion distributions were noted in varying the inlet and chamber temperatures from room temperature to 200 °C.

Commercial 3-methyl-1-bromobutane (MCB), bromocyclohexane (Fluka), and di-*n*-propyl ether (Aldrich) were purified by preparative GLC on an 8 ft \times 14 in. 10% TCEPE on 60/80 Chromosorb P (acid-washed DMCS) column at 80 °C prior to EBFlow radiolysis. Triethylamine was distilled from calcium hydride and purified by preparative GLC on the TCEPE column prior to EBFlow radiolysis.

1-Deuterio-3-methyl-1-bromobutane (5b) was prepared by reduction of isovaleraldehyde (Fluka, purum) with lithium aluminum deuteride (Merck) and treatment of the recovered alcohol with phosphorus tribromide. This bromide was purified by preparative GLC on the TCEPE column prior to EBFlow radiolysis, and the mass spectrum of the purified material showed it to be 98% d_1 : IR (thin film) ν_{C-D} 2230 cm^{-1} ; mass spectrum (70 eV) m/e (rel intensity) 153 (9), 151 (9), 73 (5), 72 (57), 71 (49), 70 (4), 56 (43), 55 (8), 44 (26), 43 (100). The mass spectra of **5–5b** are sensitive to changes in the nominal voltages and inlet temperature and were all recorded under the same conditions.

3-Deuterio-3-methyl-1-bromobutane (5a) was prepared by partial reduction of 3-methyl-1,3-dibromobutane with tri-*n*-butyltin deuteride. A mixture of 1.15 g (5 μmol) of 3-methyl-1,3-dibromobutane (prepared by reaction of 2-methyl-3-buten-2-ol with hydrobromic acid) and 1.45 g (5 μmol) of tri-*n*-butyltin deuteride (prepared by the method of Menapace and Kuivila²¹) was sealed in a Pyrex tube under vacuum and set in a steam bath for 4 weeks. Distillation (90–110 °C) of the contents afforded 0.46 g (3 μmol) of crude **5a**, which GLC and NMR analyses showed to be approximately 90% pure: IR (thin film) ν_{C-D} 2160 cm^{-1} ; ^1H NMR (CHCl_3) δ 0.91 (t, $J_{\text{HD}} = 1.0 \text{ Hz}$, $(\text{CH}_3)_2\text{CD}$), 1.76 (t, $J = 7 \text{ Hz}$, CDCH_2), 3.41 (t, $J = 7 \text{ Hz}$, CH_2Br). A mass spectrum of GLC-purified material showed it to be 88% d_1 . Repetition of this reduction using a 50% excess of 3-methyl-1,3-dibromobutane afforded **5a** that was 96% d_1 , which was purified by

preparative GLC prior to EBFlow radiolysis: mass spectrum (70 eV) m/e (rel intensity) 153 (6), 151 (6), 73 (3), 72 (58), 71 (4), 70 (30), 56 (27), 55 (16), 44 (100), 43 (22).

Radiolysis of 3-Methyl-1-bromobutane (5). The GLC retention times of all C_5H_{10} isomers were determined using authentic samples, and C_5H_{10} neutral products not reported were not observed. Absolute yields were measured by dissolving all of the product from one radiolysis in 10 mm³ of dichloromethane which was 25 mM in *cis*-4-methyl-2-pentene and comparing GLC peak areas. The yields of **6** and **7** determined in this fashion were 2.3 and 2.0 $\mu\text{mol A}^{-1} \text{s}^{-1}$, respectively.

Radiolysis of Di-*n*-propyl Ether with Ethylene. Absolute yields of C_5H_{10} isomers were determined for a 5-h radiolysis of a mixture of 3×10^{-4} Torr di-*n*-propyl ether and 1×10^{-3} Torr ethylene with an average cage current of 35 μA . The C_5H_{10} yields were (units of $\mu\text{mol A}^{-1} \text{s}^{-1}$), in order of GLC retention time, 3-methyl-1-butene plus 1,1-dimethylcyclopropane (0.12), 1-pentene (0.11), 2-methyl-1-butene (**6**, 0.09), *trans*-2-pentene (0.03), *cis*-2-pentene (0.02), and 2-methyl-2-butene (**7**, 0.08). GLC peaks corresponding to traces of ethylcyclopropane and *cis*- and *trans*-1,2-dimethylcyclopropane were also seen.

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High-Yield Synthesis and Crystal Structure of 1,5,9,13-Tetraazacyclohexadecane ([16]aneN₄)

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Abstract: The title compound, 1,5,9,13-tetraazacyclohexadecane (**I**), has been prepared in 60% yield on both a 0.01- and a 0.2-mol scale by the condensation of the ditosylate of 1,3-propanediol with the disodium salt of *N,N',N'',N'''*-tetra-*p*-toluenesulfonyl-*N,N'*-bis(3-aminopropyl)-1,3-propanediamine, followed by the removal of the tosylate groups in 98% sulfuric acid. The crystal structure of **I** was determined from x-ray diffraction data collected by counter methods. The overall symmetry of the molecule, excluding the nitrogen hydrogen atoms is D_{2d} . That the amine hydrogens on adjacent nitrogens are *trans* lowers the molecular symmetry to S_4 , which is obeyed within experimental error. The four nitrogens form a square with an average edge length of 2.925 (4) Å. The trimethylene groups are in chair configurations with adjacent groups folding toward opposite sides of the nitrogen plane. Refinement on F^2 using all 1866 measured independent reflections by full-matrix least-squares led to an R factor of 6.6%. Unit cell dimensions in the space group $P2_1/n$ are $a = 12.764$ (6), $b = 12.201$ (6), $c = 9.579$ (4) Å; $\beta = 108.13$ (3)°; and the calculated density is 1.07 g cm⁻³ for $z = 4$.

Introduction

In the course of the design and synthesis of sequestering agents selective for the actinides, the tetraazacycloalkanes have been selected as "backbones" for the proposed ligands. The four nitrogens of these macrocyclic rings provide convenient sites for the attachment of bidentate groups which bind strongly to actinides. The size of the cavity thus formed is predicted to be the optimum size and geometry for the selective encapsulation of Pu(IV) and other tetravalent actinide ions.¹ To gain insight into the conformation and geometry of the proposed sequestering agents the structure of 1,5,9,13-tetraazacyclohexadecane (designated as **I** or by [16]aneN₄) has been determined, and a convenient high yield synthesis has been developed. The structure of **I** is also of interest in that it

may be considered as a prototype for porphyrin, and other tetraazamacrocycles, about which there is much current interest and activity.²⁻⁴

Although [16]aneN₄ is the first tetraazacycloalkane to have its structure determined as the free amine, some related nitrogen macrocycles have been studied. The structure of the dihydroperchlorate salt of 1,4,7,11-tetraazacyclotetradecane ([14]aneN₄)⁵ and a completely unsaturated analogue⁶ as well as neutral prophine,⁷ are known. Many structures of metal complexes of tetraazacycloalkanes,⁸⁻¹⁷ tetraazacycloalkenes,^{12,18-31} related macrocycles,^{6,32-40} and metalloporphyrins⁴¹ have been reported. A few of these structures contained a 16-membered tetraaza ring,^{7,31,36,37,41} all of which were at least partially unsaturated.