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 mm^3 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 μmol A^{-1} 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 μmol A^{-1} 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]aneN_4)

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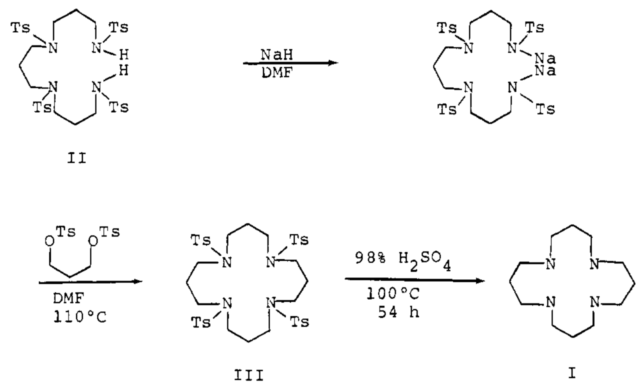
Abstract: The title compound, 1,5,9,13-tetraazacyclohexadecane (I), has been prepared in 60% yield on both a 0.01- and a 0.2-mol scale by the condensation of the ditosylate of 1,3-propanediol with the disodium salt of *N,N′,N″,N‴*-tetra-*p*-toluenesulfonyl-*N,N′*-bis(3-aminopropyl)-1,3-propanediamine, 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 countermethods. 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; β = 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]aneN_4) 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]aneN_4 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]aneN_4)[5] and a completely unsaturated analogue[6] 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 metalloporphyrins[41] 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.

Scheme I



Compound I was synthesized as shown in Scheme I. This method (which has been used for other macrocycles[42]) produced [16]aneN_4 in ~60% yield on both a 0.01- and a 0.2-mol scale. The same reaction using bromide as the leaving group, as reported previously,[43-46] gave much lower yields consistent with the results of Richman and Atkins.[47]

Excluding the amine hydrogens, the symmetry of the ring is D_{2d}, with the lower S_4 noncrystallographic molecular symmetry resulting from the alternation of the N-H bonds.

Experimental Section

Infrared spectra were obtained as KBr pellets on a Perkin-Elmer 283 spectrophotometer. ^{1}H NMR spectra were recorded on a Varian T-60 spectrophotometer. Melting points were taken in open capillaries on a Büchi apparatus and are uncorrected. Microanalyses were performed by Analytical Services, Chemistry Department, University of California, Berkeley.

The linear amine, *N,N'*-bis(3-aminopropyl)-1,3-propanediamine, was obtained from Eastman Kodak or prepared from 1,3-diaminopropane and 1,3-dibromopropane following the procedure for the preparation of *N,N'*-bis(3-aminoethyl)-1,3-propanediamine.[48]

The ditosylate of 1,3-propanediol was prepared as described in the literature.[49] Pyridine was distilled from barium oxide and *p*-toluenesulfonyl chloride was recrystallized from ether before use. The product was recrystallized from acetone-water: yield 65%, mp 91-92 °C (lit. 94 °C).

Compound II, *N,N',N'',N'''*-tetra-*p*-toluenesulfonyl-*N,N'*-bis(3-aminopropyl)-1,3-propanediamine, was prepared according to a published procedure.[45] The product was recrystallized twice from methanol and II was obtained in ~70% yield: mp 126-127 °: ^{1}H NMR ($CDCl_3$-Me_4Si) δ 1.81 (quintet, 6 H, β hydrogens), 1.86 (s, 2 H, NH), 3.0 (complex m, 12 H, α hydrogens), 2.40, 2.41 (two s, 12 H, $>NSO_2C_6H_4CH_3$), 7.75, 7.70, 7.31, and 7.27 (two sets of four lines), 7.65, 7.60, 7.30, 7.26 (8 H, aromatic); IR (KBr pellet) 3323 (sh), 3300 (s, NH), 3020 (w), 2945 (m), 2880 (m), 1600 (s, very sharp (sulfonamide)), 1495 (m), 1454 (s), 1435 (sh), 1420 (sh), 1404 (m), 1378 (m), 1325 (vs), 1305 (sh), 1292 (s), 1218 (m), 1188 (m), 1155 (vs), 1120 (m), 1090 (s), 1070 (sh), 1041 (m), 1019 (m), 968 (m), 948 (m), 933 (m), 895)w), 878 (w), 840 (m), 813 (s), 765 (m), 718 (s), 700 (m), 673 (m), 652 (s), 580 (s), 550 (s), 524 cm^{-1} (sh).

The disodium salt of II was prepared by the addition of sodium hydride (as a suspension in oil) in small portions to a solution of 0.1 mol (80.5 g) of II in 1 L of DMF. After the evolution of hydrogen ceased, the excess sodium hydride was removed by filtration. Before use, the DMF was distilled from calcium hydride under vacuum (bp ~29 °C at 1 × 10^{-2} Torr).

Compound III, 1,5,9,13-tetra-*p*-toluenesulfonyl-1,5,9,13-tetraazacyclohexadecane, was made by modification of published procedures.[43-45,47] The above filtrate was heated to 110 °C and a solution of 0.1 mol (39.4 g) of the ditosylate of 1,3-propanediol dissolved in 500 mL of DMF was added dropwise with stirring over a period of several hours, after which the stirring was continued for 2 h. The volume was reduced to 250 mL by vacuum distillation and 2 L of water were slowly added. The mixture was filtered and the product was washed with water. After drying at 60 °C under vacuum, III was obtained in >90% yield as a white powder. It was used in the next step without further purification although it may be recrystallized from $CHCl_3$-EtOH. Compound III decomposes at 252-255 °C: ^{1}H NMR ($CDCl_3$-Me_4Si) δ 2.00 (quintet, 8 H, β hydrogens), 3.22 (t, 16 H, α hydrogens), 2.47 (s, 12 H, $>NSO_2C_6H_4CH_3$), 7.21, 7.36, 7.58, and 7.68 (four lines, 16 H, aromatic hydrogens); IR (KBr pellet) 3095 (w), 3070 (w), 3040 (m), 2970 (sh), 2930 (s), 2880 (m), 1600 (m, sharp, sulfonamide), 1494 (m), 1482 (m), 1460 (s), 1400 (m), 1377 (m), 1340 (vs), 1310 (s), 1292 (m), 1256 (w), 1238 (w), 1218 (w), 1178 (sh), 1158 (vs), 1118 (m), 1090 (s), 1060 (w), 1040 (w), 1020 (m), 964 (s), 938 (s), 855 (m), 818 (s), 790 (sh), 780 (s), 759 (w), 685 (s), 655 (s), 580 (s), 565 (s), 549 (s), 464 ppm (w).

The title compound, 1,5,9,13-tetraazacyclohexadecane (I), was prepared by keeping a solution of 0.1 mol of III (80.5 g) in 200 mL of 98% H_2SO_4 at 100 °C for 56 h. The solution was cooled in an ice bath and 400 mL of ethanol was slowly added, followed by the addition of 1 L of ether. The precipitate was removed by filtration and dried. It was then dissolved in a minimum amount of water, and the pH adjusted to 10 with NaOH. This solution was extracted with equal volumes of chloroform four times. The chloroform extracts were dried with Na_2SO_4 and evaporated to dryness leaving a light yellow solid. The crude product was then sublimed (~60 °C at 1 × 10^{-3} Torr) to give white crystals of [16]aneN_4 in ~60% yield based on compound II, mp 84 °C (lit.[44] 82-83 °C). Anal. Calcd for $C_{12}H_{28}N_4$: C, 63.11; H, 12.36; N, 24.53. Found: C, 63.26; H, 12.13; N, 24.29. ^{1}H NMR ($CDCl_3$) agreed with that reported.[44] IR (KBr pellet) showed 3400 (s, br), 3285 (s, NH), 2925 (s), 2870 (s), 2805 (s), 2740 (m), 2665 (w), 1550 (m, broad), 1480 (s), 1468 (s), 1430 (m), 1413 (m), 1375 (w), 1338 (m), 1295 (m), 1257 (m), 1137 (s), 1070 (s), 1023 (w), 912 (w), 853 (m), 779 cm^{-1} (s).

Discussion

Crystallization and Diffraction Studies. Single crystals of [16]aneN_4 suitable for x-ray diffraction studies were grown by slow sublimation onto a cold finger cooled by air at ambient temperature. A colorless eight-sided parallelepiped of approximate dimensions of 0.55 × 0.34 × 0.38 mm was sealed in a thin-walled glass capillary. A series of precession photographs showed monoclinic symmetry with the following systematic absences: $h0l$, $h + l \neq 2n$; $0k0$, $k \neq 2n$. Space group $P2_1/n$ (an alternate setting of $P2_1/c$, $C_{2h}{}^5$) is the only choice consistent with these conditions. The general positions are $x, y, z; \bar{x}, \bar{y}, \bar{z}; \frac{1}{2} + x, \frac{1}{2} - y, \frac{1}{2} + z; \frac{1}{2} - x, \frac{1}{2} + y, \frac{1}{2} - z$. The crystal data follow: $C_{12}N_4H_{28}$; $M = 228.38$ g mol^{-1}; $a = 12.764$ (6), $b = 12.201$ (6), $c = 9.579$ (4) Å; $\beta = 108.13$ (3)°; $V = 1417.7$ Å^3; $z = 4$; $\rho_{calcd} = 1.07$, $\rho_{obsd} = 1.15$ g cm^{-3} (flotation in CCl_4/Et_2O); $F(0,0,0) = 512.0$ Å^{-3}.

Graphite-monochromatized Mo Kα radiation (λMo Kα = 0.70930 Å) was used for precise measurement of the cell constants and for data collection on a Picker FACS-1 four-circle diffractometer. The cell parameters were determined by a least-squares fit to the measured coordinates of 14 reflections ranging in 2θ from 19.3 to 25.4°. The intensities of all unique reflections with $2\theta \leq 45°$ were measured at least once at a constant scan rate of 1 deg min^{-1} with a base width of 1.25°. Background intensities were measured for 20 s at each extreme of the scan. Copper foil attenuators were inserted in the diffracted beam to prevent the rate from exceeding 10^3 Hz. Three standards measured every 100 reflections showed very little variation in intensity. The 2829 individual data (including monitors, systematic extinctions, and equivalent reflections) were reduced to F^2 and $\sigma(F^2)$ values with a parameter p equal to 0.04 introduced to avoid overweighting of the strong reflections as has been previously described.[50] Equivalent data were averaged and placed on an approximate absolute scale by the method of Wilson,[51] yielding a set of 1866 independent data, with 581 reflections having intensities $<2\sigma(F^2)$. No absorption correction was required ($\mu = 0.618$ cm^{-1}).

Structure Determination and Refinement. Phase determination was carried out with the program MULTAN[52] using 300 reflections having the highest E values. Four special reflections were permitted to generate 16 phase sets. The phase set found to contain the solution had the highest combined figure of merit

Table I. Positional and Anisotropic Thermal[a] Parameters ($\times 10^4$) for Nonhydrogen Atoms

Atom	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
N(1)	0.3623 (2)	0.3604 (2)	0.4450 (3)	75 (2)	72 (2)	83 (3)	3 (1)	21 (2)	4 (2)
C(2)	0.3413 (2)	0.4606 (2)	0.3573 (3)	77 (2)	98 (3)	108 (4)	7 (2)	34 (3)	36 (3)
C(3)	0.3305 (2)	0.5598 (2)	0.4447 (3)	88 (3)	72 (2)	159 (5)	0 (2)	27 (3)	42 (3)
C(4)	0.2346 (2)	0.5603 (2)	0.5065 (3)	88 (2)	65 (2)	161 (5)	19 (2)	29 (3)	22 (3)
N(5)	0.2469 (2)	0.4781 (2)	0.6200 (2)	77 (2)	62 (2)	122 (3)	17 (2)	39 (2)	12 (2)
C(6)	0.1622 (2)	0.4830 (3)	0.6931 (3)	67 (2)	93 (3)	135 (4)	16 (2)	34 (3)	−13 (3)
C(7)	0.1689 (2)	0.3891 (2)	0.7970 (3)	71 (2)	84 (2)	149 (4)	−5 (2)	53 (3)	−16 (3)
C(8)	0.2735 (2)	0.3824 (2)	0.9273 (3)	93 (2)	69 (2)	112 (4)	−3 (2)	52 (2)	−13 (3)
N(9)	0.3686 (2)	0.3546 (2)	0.8818 (2)	75 (2)	89 (2)	95 (3)	5 (2)	31 (2)	13 (2)
C(10)	0.4704 (2)	0.3368 (3)	1.0037 (3)	90 (2)	88 (3)	94 (4)	1 (2)	16 (2)	14 (3)
C(11)	0.5698 (2)	0.3269 (2)	0.9513 (3)	66 (2)	89 (3)	123 (4)	−8 (2)	−1 (2)	18 (3)
C(12)	0.5698 (2)	0.2304 (2)	0.8525 (3)	60 (2)	89 (3)	151 (4)	12 (2)	22 (2)	32 (3)
N(13)	0.4880 (2)	0.2415 (2)	0.7076 (2)	55 (2)	78 (2)	115 (3)	15 (1)	26 (2)	6 (2)
C(14)	0.4950 (2)	0.1581 (2)	0.6030 (3)	75 (2)	71 (2)	162 (5)	12 (2)	59 (3)	4 (3)
C(15)	0.3990 (2)	0.1615 (2)	0.4621 (3)	83 (2)	72 (2)	158 (5)	−6 (2)	55 (3)	−29 (3)
C(16)	0.3888 (2)	0.2652 (2)	0.3716 (3)	77 (2)	92 (3)	106 (4)	−7 (2)	37 (3)	−17 (3)

[a] The form of the anisotropic temperature factor is $\exp[-(\beta_{11}h^2 + \beta_{22}k^2 + \beta_{33}l^2 + 2\beta_{12}hk + 2\beta_{13}hl + 2\beta_{23}kl)]$.

Table II. Positional and Isotropic Thermal Parameters for Hydrogen Atoms

Atom	x	y	z	B
H(1)	0.401 (2)	0.368 (2)	0.505 (3)	4.8 (9)
H(2A)	0.272 (2)	0.446 (2)	0.274 (3)	5.4 (6)
H(2B)	0.400 (2)	0.467 (2)	0.314 (2)	4.7 (5)
H(3A)	0.325 (2)	0.622 (2)	0.385 (3)	5.9 (6)
H(3B)	0.393 (2)	0.569 (2)	0.522 (3)	4.9 (6)
H(4A)	0.164 (2)	0.547 (2)	0.425 (3)	6.2 (6)
H(4B)	0.229 (2)	0.630 (2)	0.550 (3)	6.9 (7)
H(5)	0.253 (2)	0.427 (2)	0.598 (3)	5.9 (9)
H(6A)	0.093 (2)	0.483 (2)	0.626 (3)	5.8 (6)
H(6B)	0.169 (2)	0.553 (2)	0.744 (3)	5.3 (6)
H(7A)	0.159 (2)	0.317 (2)	0.748 (2)	4.1 (5)
H(7B)	0.105 (2)	0.396 (2)	0.833 (2)	5.3 (6)
H(8A)	0.263 (2)	0.324 (2)	0.994 (2)	4.7 (5)
H(8B)	0.283 (2)	0.455 (2)	0.975 (2)	5.0 (6)
H(9)	0.379 (2)	0.396 (2)	0.843 (3)	4.5 (9)
H(10A)	0.482 (2)	0.399 (2)	1.077 (3)	6.3 (7)
H(10B)	0.461 (2)	0.269 (2)	1.060 (2)	4.8 (5)
H(11A)	0.633 (2)	0.321 (2)	1.034 (3)	5.5 (6)
H(11B)	0.578 (2)	0.398 (2)	0.901 (2)	5.1 (6)
H(12A)	0.557 (2)	0.158 (2)	0.896 (2)	5.0 (6)
H(12B)	0.641 (2)	0.225 (2)	0.834 (2)	5.9 (6)
H(13)	0.432 (2)	0.247 (2)	0.712 (3)	5.1 (8)
H(14A)	0.500 (2)	0.083 (2)	0.649 (3)	6.2 (6)
H(14B)	0.562 (2)	0.169 (2)	0.579 (2)	4.4 (5)
H(15A)	0.330 (2)	0.149 (2)	0.484 (2)	4.0 (5)
H(15B)	0.407 (2)	0.101 (2)	0.400 (3)	5.8 (6)
H(16A)	0.329 (2)	0.257 (2)	0.276 (3)	6.0 (6)
H(16B)	0.457 (2)	0.279 (2)	0.344 (2)	5.0 (5)

(3.0), the lowest residual (38.77), and the highest absolute figure of merit (0.9739). The coordinates of all 16 nonhydrogen atoms were generated by MULTAN and refined as carbon atoms. The four atoms that appeared with low temperature factors were then assigned as nitrogen atoms. The hydrogen positions were calculated from geometric considerations and confirmed in a difference Fourier.

Final refinement by full-matrix least-squares methods was performed using anisotropic temperature factors for carbon and nitrogen atoms (Table I) and isotropic temperature factors for hydrogen atoms (Table II), resulting in a total of 257 variables. Using 1285 data with $F_o^2 > 2\sigma(F_\sigma^2)$, refinement of the structure minimizing the function $\Sigma w_F(|F_o| - |F_c|)^2$, where $w_F = 1/\sigma^2(F_o)$, led to convergence with $R = 0.044$, $R_w = 0.045$, and the error in an observation of unit weight of 1.46.[53] To improve the parameter to data ratio, the structure was then refined using all 1866 unique data to minimize the function $\Sigma w_{F^2}(F_o^2 - F_c^2)^2$, where $w_{F^2} = 1/\sigma^2(F_o^2)$. Refinement led to convergence with $R = 0.066$, $R_w = 0.098$, and the error in an observation of unit weight of 1.26. The atom positions obtained in both refinements did not differ significantly. Since the refinement using all data results in better statistics[54] and lower esd's for atomic parameters all reported results use these parameters. Atomic scattering factors for neutral carbon and nitrogen are those tabulated by Cromer and Mann,[55] and those for hydrogen are from Stewart, Davidson, and Simpson.[56] Machine computations were performed on CDC 6400 and CDC 7600 computers.[57] A final difference Fourier showed maximum residual peaks of 0.17 e Å^{-3} and −0.15 e Å^{-3}. A list of observed and calculated structure factors is available.[58]

Discussion and Description of the Structure. The square-planar array of the nitrogen atoms is readily seen in Figure 1. The average edge length is 2.925 (4) Å, creating a cavity in 16-cyclam somewhat larger than that found in porphine[7] (2.901-Å edge). The nitrogens have an average deviation of 0.019 Å from their least-squares plane, which closely ap-

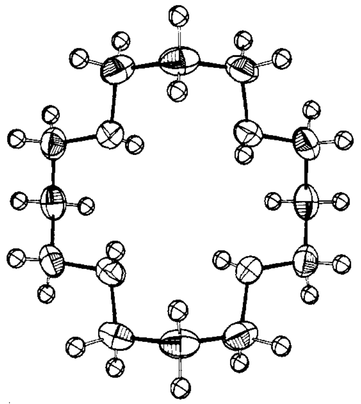


Figure 1. View of 16-cyclam down the S_4 axis showing thermal ellipsoids for nonhydrogen atoms at the 40% probability level. The shaded ellipsoids are carbon atoms.

proximates the least-squares plane calculated for all nonhydrogen atoms. The trimethylene chains connecting the nitrogen atoms assume chair configurations with adjacent chairs folding toward opposite sides of the nitrogen plane. The hydrogen atoms on adjacent nitrogen atoms are trans; there is no indication of partial occupancy at the lone-pair sites of the nitrogens as shown by the final difference Fourier and least-squares calculations. Further structural details may be ascertained from the stereopair in Figure 2.

Crystallographically, the molecule is not required to possess any symmetry since it occupies a general position in the unit cell. However, Figure 1 shows that the molecule has S_4 point group symmetry. Excluding the amine hydrogen atoms, the 16-cyclam molecule has nearly D_{2d} symmetry, with the nitrogen atoms lying on twofold axes and the trimethylene units bisected by dihedral mirror planes. The alternation of the N-H bonds lowers the symmetry of the ring to S_4.

The molecular symmetry of 16-cyclam was examined by applying the appropriate symmetry transformation to the atomic coordinates and comparing the transformed coordinates with the original ones. For simplicity, the fractional coordinates were first transformed to an orthonormal coordinate system by standard matrix methods, so that the origin corresponded to the center of mass of the nonhydrogen atoms. The molecule was then divided into four equal sections (asymmetric units). In each section, the atomic coordinates were added to give a vector representing that section. By taking the difference between the composite vectors in opposite sections, two vectors describing the best plane of the molecule were obtained. The cross product of these two vectors gives the best approximation to the S_4 axis of the molecule. The coordinates were then transformed so that this symmetry axis corresponded to the z axis of the orthogonal coordinate system. The symmetry axis thus obtained deviated slightly from the normal to the least-squares plane containing the four nitrogen atoms. The fractional coordinates in the unit cell for the center of the molecule are (0.3668, 0.3593, 0.6640) and the S_4 axis is defined by the vector (0.05795, 0.05830, 0.02375). Since the original fractional coordinates have similar esd's, unit weights were used.

The atomic coordinates in the orthogonal system were transformed by the matrices corresponding to possible symmetry elements. The distances between each transformed atom and the original position of its symmetry related atom was calculated. This gave an average deviation between original and transformed coordinates of 0.0305 Å with a standard deviation of the mean of 0.0088 Å for an S_4 rotation. The corresponding values for a C_2 (= $S_4{}^2$) rotation are 0.0155 and 0.0058 Å. From the esd's of the fractional coordinates, an average deviation, in terms of distance, of 0.0063 Å was calculated, which compares favorably to the standard deviation of the mean for both the S_4 and C_2 rotations. The average deviation for the C_2 rotation is 2.7 σ and that for the S_4 rotation is 3.5 σ. Therefore, this conformation of 16-cyclam displays S_4 symmetry within small error limits. Inclusion of the hydrogen atoms in this analysis does not cause any deviation from the S_4 symmetry.

As a consequence of the nearly D_{2d} symmetry, the carbon atoms C(2), C(4), C(10) and C(12) form a plane (least-squares average deviation 0.030 Å) as do the carbon atoms C(6), C(8), C(14), and C(16) (average deviation 0.025 Å). Both of these planes are parallel to the plane of the nitrogen atoms within experimental error. The carbon atom planes are separated from the nitrogen atom plane by 0.65 and 0.63 Å. The least-squares plane calculated for all nonhydrogen atoms approximates the least-squares plane of the nitrogen atoms. The angle between these planes is 1.2°, and the nitrogen atoms have an average deviation of 0.028 Å from the least-squares plane of the molecule.

Bond lengths and angles are shown in Figure 3 and their averages are tabulated in Table III. The average C-N bond length, 1.457 (2) Å, is shorter than the average C-N bond

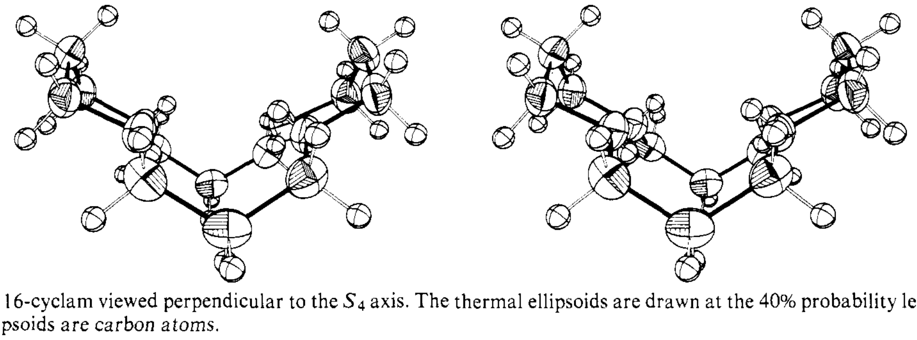


Figure 2. Stereopair of 16-cyclam viewed perpendicular to the S_4 axis. The thermal ellipsoids are drawn at the 40% probability level for the nonhydrogen atoms. The shaded ellipsoids are carbon atoms.

Table III. Average Bond Lengths and Angles[a] (Ångstroms and Degrees)

C-C	1.511 (1) Å	H_A-C-H_B	106.4 (6)°
C-N	1.457 (2) Å	N···N	2.925 (4) Å
C-C-C	116.0 (2)°	C-C-H	109.5 (4)°
C-N-C	114.4 (2)°	N-C-H	108.5 (5)°
N-C-C	112.4 (2)°	C-N-H	110.6 (9)°

[a] $\bar{x} = 1/n\Sigma x_i$; $\sigma(\bar{x}) = (\Sigma(x_i - \bar{x})^2/n(n-1))^{1/2}$. Owing to well-known polarization effects artifactually short N-H and C-H bond lengths of 0.68 (2) and 0.981 (6) Å were obtained (see ref 64).

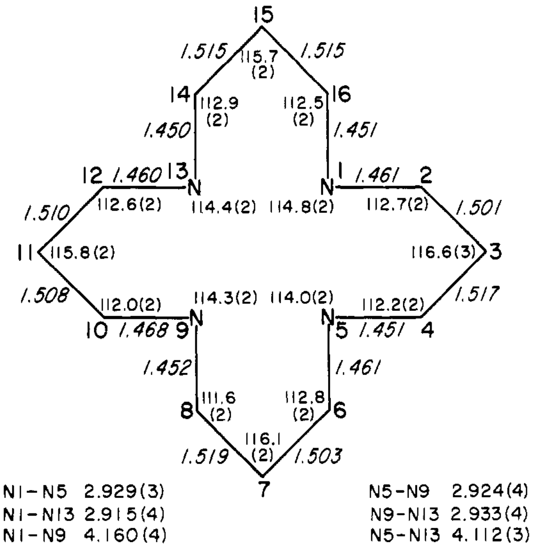


Figure 3. Bond lengths and angles in 16-cyclam (esd's for C-N bonds 0.003 Å, C-C bonds 0.004 Å).

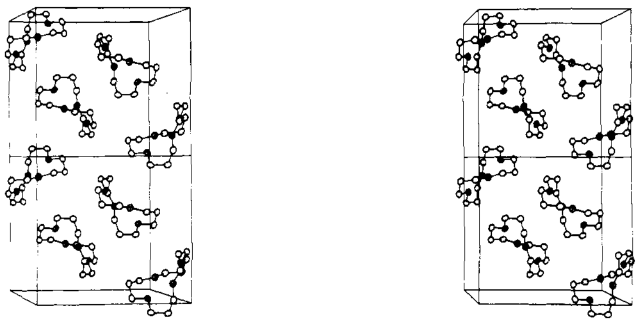


Figure 4. View of the contents of two units cells of 16-cyclam down the *c* axis; the *a* axis is horizontal. The size of the atom is arbitrary.

length reported for amines (1.472 (5) Å).[59] However, it is in good agreement with the C-N distance of 1.455 (2) Å found in gaseous dimethylamine by electron diffraction.[60] The average C-C bond length of 1.511 (2) Å is also shorter than the average reported value (1.537 (5) Å),[59] but is in good agreement with the C-C bond lengths of 1.51 (2) Å found in ethylenediamine,[61] 1.506 Å found in piperidine hydrochloride,[62] and 1.509 Å found in the dihydroperchlorate of 14-cyclam.[5]

As seen from Figure 4, the molecules of 16-cyclam are packed along the body diagonal of the unit cell. The closest intermolecular contact is 3.727 (4) Å between nonhydrogen atoms. The closest intermolecular distance between nitrogen atoms is >4.5 Å, which shows the absence of any intermolecular hydrogen bonding. The symmetry of the molecule divides the intramolecular nonbonded N-H interactions into two classes. The strongest interactions, with an average N···H-N distance of 2.26 (3) Å and an angle of 123.0 (2)°,[63] show the possibility of weak intramolecular hydrogen bonds. That the other class has an N···H-N distance of 2.86 (4) Å with an angle of 84.0 (2)° indicates that this class of interactions is unimportant. Thus, the hydrogen bonds occur in pairs such that the weak hydrogen bonds between N(1) and H(5) and N(9) and H(13) lie on one side of the nitrogen plane and those between N(5) and H(9) and N(13) and H(1) lie on the other side of the plane. These hydrogen bonds, in addition to the stability of the chair configuration of the trimethylene chain, hold the nitrogens in the square-planar arrangement.

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Supplementary Material Available: Listing of the structure factor amplitudes of tetraazacyclohexadecane (13 pages). Ordering information is given on any current masthead page.

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Antineoplastic Agents. 53. The Crystal Structure of Radiatin

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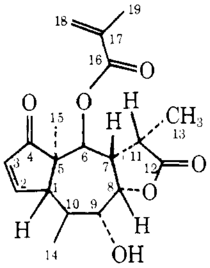
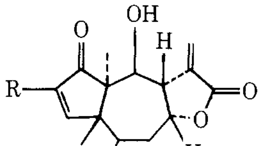
Abstract: Both *Baileya multiradiata* Harv. and Gray (Compositae) and *Baileya pleniradiata* Harv. and Gray have been shown to produce the cytotoxic and antineoplastic pseudoguaianolide radiatin (**1**). The crystal and molecular structure has been determined from single-crystal x-ray intensity data. The structure was solved by direct methods and refined by full-matrix least squares to a residual of 0.081 for 1589 independent observed reflections. The compound crystallizes in the monoclinic space group $P2_1$, $Z = 2$, with lattice parameters $a = 6.614$ (3), $b = 9.185$ (4), $c = 15.567$ (5) Å, and $\beta = 102.03$ (1)°. A most probable absolute stereochemical assignment was made by comparison with known and very similar natural products.

Introduction

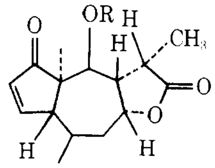
In 1969 Yoshitake and Geissman[2] reported isolation of a new pseudoguaianolide from *Baileya pleniradiata* Harv. and Gray collected in Cochise County, Arizona. The new terpene lactone was designated radiatin and on the basis of ^{1}H NMR and mass spectral data was assigned the ring system and relative positioning of substituents shown by structure **1.** Sufficient evidence for allowing stereochemical assignments was not available. While systematically investigating extracts of *Baileya multiradiata* Harv. and Gray for antineoplastic constituents we found one of the most promising (PS T/C 161 at 25 mg/kg, P388 ED_{50} 0.39) to be a substance resembling radiatin.[1] While our study formally began with a collection of *Baileya multiradiata* in 1966, radiatin was not isolated in sufficient quantity until large-scale processing of a 1973 collection (Mohave County, Arizona) was undertaken. ^{1}H NMR and mass spectral studies in our laboratory of the substance believed to be radiatin gave results consistent with assignment **1.** Because the substance assumed to be radiatin consistently inhibited progression of the National Cancer Institute's murine lymphocytic leukemia P388 (PS system) we undertook an investigation directed at defining the relationship of the two apparently identical pseudoguaianolides from *Baileya multiradiata* and *Baileya pleniradiata* and ascertaining the complete structure.



1, radiatin



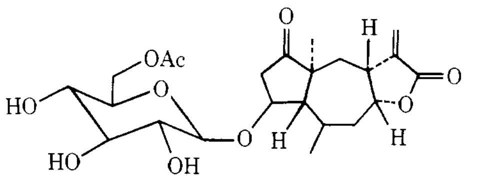
2a, R = H, helenalin
b, R = Br, bromohelenalin



3a, R = H, plenolin

b, R = $-\underset{\underset{\displaystyle O}{\|}}{C}-\mathrm{Ph}-\mathrm{I}$,

plenolinyl *p*-iodobenzoate



4, paucin

An authentic sample of radiatin was unavailable but Professor Geissman kindly provided fractions of *Baileya pleniradiata* containing this sesquiterpene. By utilizing the same chromatographic separation techniques developed for separating *Baileya multiradiata*[1] authentic radiatin was isolated and found by chromatographic and spectroscopic techniques to be identical with the substance from *Baileya m.* believed to be radiatin. The complete structure of radiatin obtained from *Baileya multiradiata* was then elucidated by x-ray crystallographic analysis.

Experimental Section

Introduction to the Experimental Section of part 52 provides a summary of experimental procedures and instrumental methods employed here. See ref 1.

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