

After acidolysis⁹ of the Boc group, mixed anhydride coupling⁷ of Ac-Gly and the resulting pentapeptide dimer (2:1 molar ratio, THF/DMF) gave the acetylated hexapeptide **6a**, Ac replacing Z, in 76% yield. The latter was reduced, activated, and cyclized to thiolactone **1e** in 55–60% yield as described^{11,18} for the conversion of **6a** into **1c**.

The protected thiolactones **1a**, **1c**, and **1e** were deprotected (9:1 (v/v) HF/anisole, 0 °C, 15 min) and purified by reverse-phase liquid chromatography to furnish 10-mg quantities of the desired¹⁹ macrocyclic thiolactones **1b**, **1d**, and **1f**. The yields over four steps were 16% from thiolester **4a** to **1b** by the first strategy and both 24% from dimeric hexapeptide **6a** to **1d** and 22% from **6a**, Ac replacing Z, to **1f** by the second strategy. In order to study the binding of thiolactone **1f** to biological particles,²¹ tritiated **1f**, R = [³H]Ac-Gly (2960 cpm/nmol), was prepared from [³H]Ac-Gly and the pentapeptide dimer as described above.

These results (1) constitute the first chemical synthesis of the 1-thia-5,8,11-triazacyclopentadecane ring system, (2) present the first examples of reduction of a peptide disulfide with a trialkylphosphine,¹¹ and (3) introduce the formation of peptide thiolesters¹⁵ and thiolactones¹⁸ by coupling of cysteine thiol groups with 1-benzotriazolone esters.

The 300-MHz NMR spectrum^{22,23} of macrocyclic thiolactone **1f** revealed that the chemical shifts of the β -methylene protons of Cys differ by 0.58 ppm and those of the γ -methylene protons of the second Glu differ by 0.20 ppm. In addition, the coupling constant between one of the Cys β -methylene protons and the α proton is only 2 Hz. A plausible explanation for these large chemical shift differences and the small coupling constant is that the 15-membered thiolactone ring exists in a single, relatively rigid conformation.

Thiolactones **1d** and **1f** undergo hydrolytic ring opening about 2000 times faster than the acyclic model thiolester *N,S*-diacetylcysteine methylamide.²⁴ Macrocyclic thiolactone **1f** (half-life²⁴ 0.20 h) hydrolyzes about 10³ times faster than the latent binding site of C3 (half-life²⁴ 186 h) but about 10⁷ times slower than the metastable binding site of nascent C3b (estimated half-life⁵ 30 μ s). The 15-membered thiolactone ring **1** is evidently necessary but not sufficient to explain the pronounced biological reactivity of the metastable binding site of human C3b.

Acknowledgment. We thank Professors Brian T. Chait and Frank H. Field for the mass spectra, Professor David Cowburn

(19) The following thiolactones were homogeneous by thin-layer chromatography and reverse-phase liquid chromatography and gave acceptable mass spectral molecular weights, amino acid molar ratios, and elemental analyses. Thin-layer systems: A, 4:1:1 (v/v/v) 1-butanol/acetic acid/water; B, 23:10:3 (v/v/v) ethanol/acetic acid/water; C, 3:1:1:1 (v/v/v/v) 1-butanol/ethyl acetate/acetic acid/water. Reverse-phase conditions: 30-cm μ Bondapak C₁₈ column was eluted isocratically with 2% CH₃CN in water; $k' = (t_{\text{comp}}/t_{\text{solvent}}) - 1$, where t = retention time. Molecular ions were observed as ($M + \text{Na}$)⁺ in the positive-ion portion of the ²⁵²Cf fission fragment-induced mass spectrum.²⁰ Molar ratios for Cys are uncorrected for losses due to oxidation during acid hydrolysis (6 N HCl, 110 °C, 24 h). The counterion for the protonated amines **1b** and **1d** is assumed to be fluoride because the only acid present during purification was HF. (a) Pentapeptide **1b**: R_f (A) 0.73, (B) 0.17, (C) 0.21; $k' = 2.27$; m/e (C₁₉H₂₉N₇O₉SNa) calcd 554.16, found 554.22; Asp_{1.07}Glu_{1.97}Gly_{1.00}Cys_{0.27}. Anal. (C₁₉H₂₉N₇O₉S·HF·0.5 H₂O) C, H, N. (b) Hexapeptide **1d**: R_f (A) 0.69, (B) 0.13, (C) 0.14; $k' = 2.10$; m/e (C₂₁H₃₂N₈O₁₀SNa) calcd 611.19, found 611.23; Asp_{1.05}Glu_{2.10}Gly_{2.00}Cys_{0.74}. Anal. (C₂₁H₃₂N₈O₁₀S·HF) C, H, N. (c) Acetylated hexapeptide **1f**: R_f (A) 0.85, (B) 0.42, (C) 0.24; $k' = 3.64$; m/e (C₂₃H₃₄H₈O₁₁SNa) calcd 653.20, found 653.27; Asp_{1.07}Glu_{2.05}Gly_{2.00}Cys_{0.47}. Anal. (C₂₃H₃₄N₈O₁₁S·1.5H₂O) C, H, N; calcd 17.04, found 16.58. Thiolactones **1d** and **1f** contained <2% free thiol as measured with 5,5'-dithiobis(2-nitrobenzoic acid) (Ellman's reagent).

(20) Chait, B. T.; Agosta, W. C.; Field, F. H. *Int. J. Mass Spectrom. Ion Phys.*, in press.

(21) Khan, S. A.; Pangburn, M. K.; Müller-Eberhard, H. J.; Erickson, B. W., unpublished results.

(22) ¹H NMR (CF₃CO₂D) 2.2–2.6 (4 H, m, Glu β), 2.40 (3 H, s, Ac), 2.78 (2 H, t, Glu γ), 2.93 (1 H, m, Glu γ 1), 3.13 (1 H, m, Glu γ 2), 3.23 (2 H, d, Asn β), 3.38 (1 H, d15 d6, Cys β 1), 3.96 (1 H, d15 d2, Cys β 2), 4.24 and 4.31 (2 H, ABq17.5, Gly α), 4.38 and 4.42 (2 H, ABq17.5, Gly α), 4.98 (1 H, d9 d5, Glu α), 5.03 (1 H, d9 d3, Glu α), and 5.17–5.28 ppm (2 H, m, Cys α and Asn α).

(23) Khan, S. A.; Cowburn, D.; Erickson, B. W., unpublished results.

(24) Khan, S. A.; Erickson, B. W.; Müller-Eberhard, H. J.; Pangburn, M. K. In "Peptides: Synthesis, Structure, Function"; Rich, D. H.; Gross, E., Eds.; Pierce Chemical Co.: Rockford, IL, in press.

for the NMR spectra, and Patricia M. Bihn for valuable editorial assistance. The National Institutes of Health (AI 15301 and CA 24435) provided financial support, the National Science Foundation (PCM 79-12083) and the Dreyfus Foundation supported the 7 T Nicolet NMR spectrometer, and the NIH (RR 00862) supported the Mass Spectrometric Biotechnology Research Resource.

Encircling of Water by Crown Compounds

George R. Newkome,* Hellen C. R. Taylor,
Frank R. Fronczek, Terry J. Delord, and Dalip K. Kohli

Department of Chemistry, Louisiana State University
Baton Rouge, Louisiana 70803

Fritz Vögtle

Institut für Organische Chemie und Biochemie
Universität Bonn, D-5300 Bonn 1, West Germany

Received May 22, 1981

Despite the fact that various authors have stressed the importance of water complexation by crown ethers¹ and although several stoichiometric water complexes of crown-type ligands have been reported,² in no previous case has water been found to be encircled by an uncharged³ host molecule. We report here on the first proven "neutral-component complexes" of crown hosts⁴ (**1** and **2**) which contain water bound exclusively in the center of the cavity by hydrogen bonding with several crown ether oxygen atoms.

Polar guest compounds have recently been found to be bound by crowns.^{11,12} Water has been proven to interact strongly with

(1) de Jong, F.; Reinhoudt, D. N.; Smit, C. J. *Tetrahedron Lett.* **1976**, 1371–1374, 1375–1378.

(2) Vögtle, F.; Sieger, H.; Müller, W. M. *Top. Curr. Chem.* **1981**, *98*, 107.

(3) The definitions for complex, adduct, addition compound, molecular compound, molecular complex associates, inclusion compound, clathrate, host-guest complex, key-lock complex, etc. seem not to be used consistently in the literature.² We propose that the above overall "neutral complexes" can be further subdivided into two classes: (a) those which are composed of two or more neutral (or uncharged) components, to be considered "neutral-component complexes"; and (b) those which are formed from one or more charged components, resulting in the formation of "charged-component complexes".

(4) Previously described water complexes of uncharged crown ethers possess either phenolic (acidic) OH² or pyridine *N*-oxide⁶ groups to which the hydrogen bond(s) form; the remainder of the reports are actually of aza crown cations as hosts⁷ or hydronium ion complexes. Older claims of water-containing macrocyclic polyamines⁸ or diketones,⁹ based mainly on IR data, have never been proven by X-ray analysis to bind the water molecules inside the cavity. A triple crown ether has been analyzed as a dihydrate, but X-ray analysis has not been conducted.¹⁰

(5) (a) Goldberg, I. *Acta Crystallogr., Sect. B* **1978**, *B34*, 3387–3390. (b) Koenig, K. E.; Helgeson, R. C.; Cram, D. J. *J. Am. Chem. Soc.* **1976**, *98*, 4018–4020.

(6) (a) Vögtle, F.; Müller, W. M.; Weber, E. *Chem. Ber.* **1980**, *113*, 1130–1137. (b) Vögtle, F.; Oepen, G.; Raschhofer, W. *Liebigs Ann. Chem.* **1979**, 1577–1584.

(7) (a) Gokel, G. W.; Garcia, B. J. *Tetrahedron Lett.* **1977**, 317–320. (b) Khanna, R. K.; Gokel, G. W., unpublished results, 1980. (c) Similarly, the hydronium ion complex of the dicyclohexane derivative of 18-crown-6 has been discussed: Haymore, B. L.; Huffman, J. C. Fourth Symposium on Macrocyclic Compounds, Provo, Utah, Aug 1980.

(8) Zahn, H.; Spoor, H. *Chem. Ber.* **1956**, *92*, 1375–1380.

(9) Borgen, G.; Dale, J. *Chem. Commun.* **1970**, 1342–1343.

(10) Frensch, K.; Vögtle, F. *Liebigs Ann. Chem.* **1979**, 2121–2123.

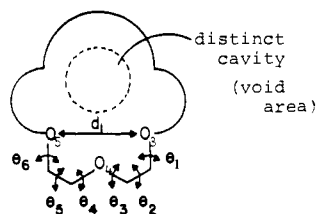
(11) (a) El Basyony, A.; Klimes, J.; Knöchel, A.; Oehler, J.; Rudolph, G. *Z. Naturforsch. b* **1976**, *31*, 1192–1200. (b) Kaufmann, R.; Knöchel, A.; Kopf, J.; Oehler, J.; Rudolph, G. *Chem. Ber.* **1977**, *110*, 2249–2253. (c) von Deuten, K.; Knöchel, A.; Kopf, J.; Oehler, J.; Rudolph, G. *J. Chem. Res. (S)* **1979**, 358. *J. Chem. Res. (M)* **1979**, 4035–4037. (d) Chang, C. K. *J. Am. Chem. Soc.* **1977**, *99*, 2819–2822. (e) Vögtle, F.; Müller, W. M. *Naturwissenschaften* **1980**, *67*, 255–256. (f) Vögtle, F.; Müller, W. M. *Chem. Ber.* **1980**, *113*, 2081–2085. (g) Vögtle, F.; Müller, W. M. *Ibid.* **1981**, *114*, 3179–3183.

(12) (a) Goldberg, I. *Acta Crystallogr., Sect. B* **1975**, *B31*, 754–762. (b) Bandy, J. A.; Truter, M. R.; Vögtle, F. *Ibid.* **1981**, *B37*, 1568–1571. (c) Saenger, W.; Hilgenfeld, R. *Z. Naturforsch.*, in press.

Table I. Critical Torsion Angles (Deg) and Distances (Å)^a

	1	2	NH ₄ SCN complex	free ligand	3
O3-O5	5.010	5.022	4.84	4.534	4.258
O3-O4	2.886	2.881	2.83	3.047	2.840
O4-O5	2.849	2.889	2.82	2.830	2.835
θ_1	155.5	-166.6	-175.7	175.5	172.7
θ_2	-68.9	-62.6	-66.2	-67.6	-69.7
θ_3	-169.4	-179.9	-173.9	165.8	151.5
θ_4	-174.5	177.3	-177.3	-155.2	-168.8
θ_5	73.9	65.9	68.1	75.4	63.7
θ_6	-174.1	174.0	-176.9	79.7	87.8

a



crowns in solution¹ but to date has not been observed to form a crystalline complex with 18-crown-6 or related uncharged crown compounds.¹³ A question arises as to what prerequisites must be fulfilled to allow the encircling of water by **1** and **2**, but not by **3** and **4** (Table I), as we have observed.

Complex **1**·2H₂O (lit.¹⁴ mp 65–66 °C) exists in an approximately planar conformation with six potential donor atoms lying in a plane to within 0.26 Å. The ether-coordinated water molecule lies below this plane, 1.49 Å from its center, to optimize the hydrogen bond with O4 (O–O = 2.92 Å) and to minimize heteroatom repulsion. The second water molecule is hydrogen bonded to the first (3.01 Å); both water oxygen atoms are located in well-defined positions and the hydrogen atoms appear as peaks of electron density 0.26–0.51 e Å⁻³.

Ketone macrocycle **2**, an oil prepared by standard methods,¹⁵ was shown to be anhydrous,¹⁶ but upon treatment with isopropyl alcohol–water was transformed to the crystalline monohydrate.^{16,17} Complex **2**·H₂O exists in the crystal in a conformation which approximates C₂ symmetry (Figure 1). The pyridine rings are twisted out of the carbonyl plane by an average of 34.6°, and the five oxygen atoms O2–O6 lie in a plane to within 0.6 Å. The water O9 lies 1.34 Å out of this plane, making its closest contact with the central bridge oxygen atom O4 (O4...O9 = 3.00 Å). Contacts with O5, O6, O7, and O8 range from 3.19 to 3.61 Å, generally too long for strong hydrogen bonding. This water molecule is also located in a well-defined position with reasonable thermal parameters, and the residual electron density (0.12–0.20 e Å⁻³) around O9 is indicative of disorder of the hydrogen atoms.

(13) von Deuten, K.; Dickel, M.; Knöchel, A.; Kopf, J.; Rudolph, G. "Abstracts of Papers", Symposium on Macrocyclic Ligands, Basel, Switzerland, 2–4 July 1980; Lecture 37.

(14) Newkome, G. R.; Fronczek, F. R.; Kohli, D. K. *Acta Crystallogr.*, in press.

(15) Newkome, G. R.; Taylor, H. C. R. *J. Org. Chem.* **1979**, *44*, 1362–1363.

(16) Acceptable analytical and spectral data were obtained for all new compounds.

(17) Crystal data: C₂₃H₃₀N₂O₈·H₂O, triclinic space group P $\bar{1}$, *a* = 10.265 (1) Å, *b* = 10.925 (1) Å, *c* = 11.633 (2) Å, α = 106.41 (1)°, β = 96.02 (1)°, γ = 97.14 (1)°, *Z* = 2, *d*_{calcd} = 1.299 g cm⁻³, *R* = 0.060 for 2330 observed data.

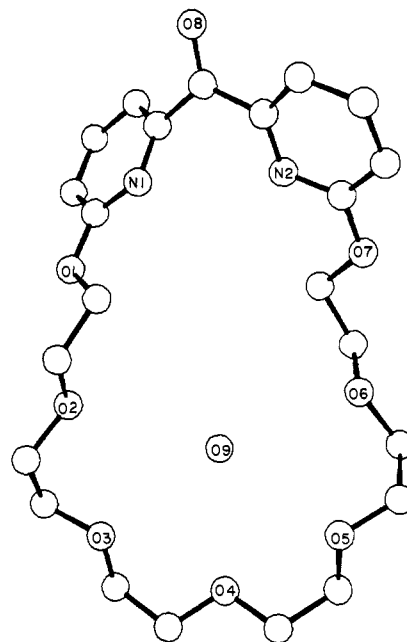


Figure 1. Crystal structure of the water complex of the hexaethylene glycol bis(2-pyridyl) ketone macrocycle.

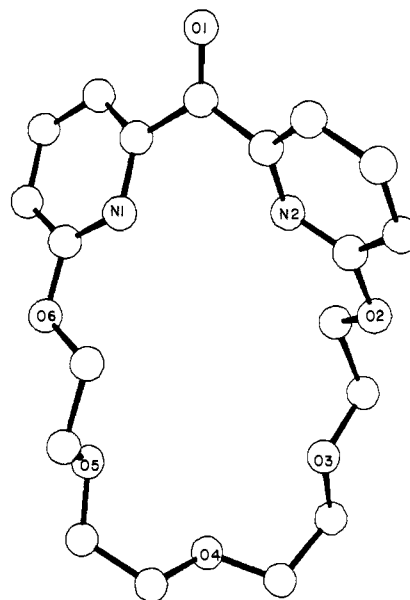


Figure 2. Crystal structure of the tetraethylene glycol bis(2-pyridyl) ketone macrocycle.

Ketone **3**¹⁸ crystallized easily from a mixture of chloroform and aqueous ethanol to afford large, colorless crystals that display no evidence¹⁶ of complexed water. Macrocycle **3** exists in the crystal in a conformation of ca. C₂ symmetry (Figure 2). The pyridine rings twist out of the carbonyl plane by an average of 30.1°, and the linkage of polyether to pyridine is *cis* to N (average N–C–O–C torsion angle = 5.0°) in both cases. The nitrogen and five oxygen atoms are within 0.23 Å of the defined plane.

Comparison of the X-ray crystal structures of the water complexes **1** and **2** with those of similar macrocycles which do not possess water (**3** and **4b**) and with that of a benzylammonium cation complex of 18-crown-6 (**4a**)¹⁹ suggests a structural parameter that enables these ethereal compounds to encircle a water

(18) Crystal Data: C₁₉H₂₂N₂O₆, monoclinic space group P2₁/c, *a* = 10.238 (2) Å, *b* = 13.140 (2) Å, *c* = 14.540 (3) Å, β = 109.35 (2)°, *Z* = 4, *d*_{calcd} = 1.347 g cm⁻³, *R* = 0.044 for 1775 observed data.

(19) Bovill, M. J.; Chadwick, D. J.; Sutherland, I. O. *J. Chem. Soc., Perkin Trans. 2* **1980**, 1529–1543.

molecule. Compounds **4a** and **4b** illustrate the differences in conformation of the complexed and free forms of a single ligand.

With respect to the section of polyether from O3 to O5, the conformation of **3** corresponds to that of **4b**, as would be expected for optimum electrostatic interactions. Alleviation of disadvantageous electrostatic interactions by the presence of a hydrogen bond allows the polyether chains of **1** and **2** to assume the conformation found in **4a**. In each example, the distance from O4 to the adjacent oxygen atoms (O3 and O5) is quite similar, on the order of 2.8 Å. The O3 to O5 separations, however, vary significantly (**1**, 5.010 Å; **2**, 5.022 Å; **4a**, 4.84 Å vs. **3**, 4.258 Å; **4b**, 4.534 Å), as do the torsion angles θ_4 and especially θ_6 (vide Table I).

The ability of these ethereal compounds to encircle a water molecule depends on both the conformation of the polyether chain and on the inherent structural spacing produced by the heteroaromatic moiety in the macrocycle. This combination of conformation and spacing in **1** and **2** creates a distinct cavity in the central portion of the host and apparently provides sufficient space in the extreme ether portion so that the water molecule can hydrogen bond well.

Monte Carlo calculations²⁰ based on the available structural parameters are in progress to determine an energy profile for the complexation of water by these crown compounds.

na

Acknowledgment is made to the National Institutes of Health and the National Science Foundation for partial support of this work.

(20) See: Mattice, W. L.; Newkome, G. R. *J. Am. Chem. Soc.* **1979**, *101*, 4477-4480 and references cited therein.

Experimental Evidence for the Absence of Bonding Electron Density between Inverted Carbon Atoms

Pinakpani Chakrabarti, Paul Seiler, and Jack D. Dunitz*

*Organic Chemistry Laboratory
of the Swiss Federal Institute of Technology
CH-8092 Zürich, Switzerland*

Arnulf-Dieter Schlüter and Günter Szeimies*

*Institute of Organic Chemistry of the University of Munich
D-8000 Munich, Germany
Received July 17, 1981*

The nature of the bonding at inverted^{1,2} carbon atoms is problematical.³ Reported distances between such atoms lie in the range 1.55–1.64 Å,⁴⁻⁹ most are only slightly (0.01–0.03 Å) longer than the normal C–C single-bond distance of about 1.541 Å and are thus similar to bond distances between quaternary carbon

(1) The bridgehead atoms of small-ring propellanes have been dubbed "inverted"² because the interatomic vectors emanating from each of them to its four nearest neighbors are directed to one side of a plane.

(2) Wiberg, K. B.; Burgmaier, G. J.; Shen, K.; La Placa, S. J.; Hamilton, W. C.; Newton, M. D. *J. Am. Chem. Soc.* **1972**, *94*, 7402-7406.

(3) For general discussions of the problems involved, see: Ginsburg, D. "Propellanes"; Verlag Chemie: Weinheim, 1975; Chapter 4. Greenberg, A.; Liebman, J. F. "Strained Organic Molecules"; Academic Press: New York, 1978; Chapter 6B.

(4) For example, 1.64 Å in a [3.3.1]propellane (1,3-dehydroadamantane derivative);⁵ 1.57 Å in a [3.2.1]propellane;² 1.55 Å in [4.2.1]-⁶; [4.1.1]-⁷ and [3.1.1]propellanes;⁸ 1.54 Å in another [4.1.1]propellane.⁹

(5) Gibbons, C. S.; Trotter, J. *Can. J. Chem.* **1973**, *51*, 87-91.

(6) Harnisch, J.; Baumgärtel, O.; Szeimies, G.; van Meersche, M.; Germain, G.; Declercq, J.-P. *J. Am. Chem. Soc.* **1979**, *101*, 3370-3371.

(7) Declercq, J.-P.; Germain, G.; van Meersche, M. *Acta Crystallogr., Sect. B* **1978**, *34*, 3472-3474.

(8) Szeimies-Seebach, U.; Szeimies, G.; van Meersche, M.; Germain, G.; Declercq, J.-P. *Nouv. J. Chim.* **1979**, *3*, 357-358.

(9) Szeimies-Seebach, U.; Harnisch, J.; Szeimies, G.; van Meersche, M.; Germain, G.; Declercq, J.-P. *Angew. Chem.* **1978**, *90*, 904-905. *Angew. Chem. Int. Ed. Engl.* **1978**, *17*, 848-849.

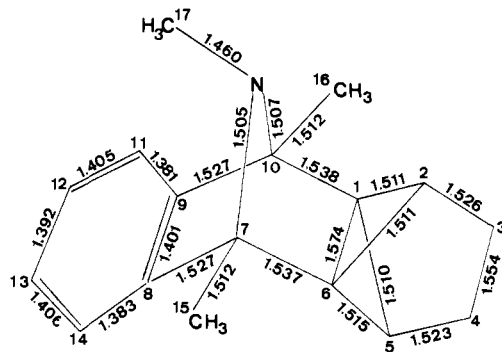
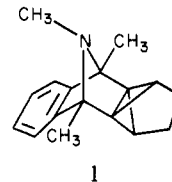


Figure 1. Atom numbering and bond distances. Standard deviations estimated by inversion of the least-squares normal equation matrix are in the range 0.001–0.002 Å.

atoms in less highly strained systems. On the other hand, it is obviously difficult to describe the bond between a pair of inverted carbon atoms in traditional terms. This is a problem where experimental information on the electron-density distribution¹⁰ in the crystalline compound would be helpful. Here we provide such evidence from electron-density difference maps obtained by a low-temperature (95 K) X-ray analysis¹¹⁻¹⁴ of a crystalline [3.1.1]propellane derivative, 11-aza-9,10-benzo-1,8,11-trimethylpentacyclo[6.2.1.0^{2,6}.0^{2,7}.0^{3,7}]undec-9-ene (**1**).¹⁵



Bond distances (Figure 1) from our analysis are quite normal for this type of molecule; in particular, the distance of 1.574 Å between the inverted carbon atoms C(1) and C(6) corresponds to a slightly stretched single bond and is by no means extraor-

(10) Dunitz, J. D. "X-ray Analysis and the Structure of Organic Molecules"; Cornell University Press: Ithaca, NY, 1979; Chapter 8 and references therein.

(11) Colorless crystals of C₁₇H₁₉N are triclinic space group P $\bar{1}$, cell dimensions $a = 8.405$ Å, $b = 8.550$, $c = 10.332$ Å, $\alpha = 80.19^\circ$, $\beta = 84.67^\circ$, and $\gamma = 62.87^\circ$ at 95 K, $Z = 2$. Intensity measurements were made with an Enraf-Nonius CAD-4 diffractometer equipped with graphite monochromator (Mo K α radiation) and cooling device for 8474 reflections [6394 with $F > 10\sigma(F)$ out to $(\sin \theta)/\lambda = 0.994$ Å⁻¹]. Structure determined by direct methods (MULTAN¹²) and refined by full-matrix least-squares analysis using XRAY system.¹³ Final $R = 0.032$ with exponentially modified weighting system ($r = 1.5$ Å²)¹⁴ and including extinction correction. The difference maps shown in Figure 2 are based on 4875 ($F_o - F_c$) coefficients with $(\sin \theta)/\lambda < 0.857$ Å⁻¹ and $F_o \geq 10\sigma(F_c)$. A table of atomic coordinates and vibrational parameters is provided as supplementary material. Full details will be reported later.

(12) Main, P. "MULTAN 80; a System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data"; Department of Physics, University of York: York, England, 1980.

(13) Stewart, J. M.; Kruger, G. J.; Ammon, H. L.; Dickenson, C.; Hall, S. R. "The XRAY system: Version of June 1972"; Technical Report TR 192; Computer Science Center, University of Maryland: College Park, MD.

(14) Dunitz, J. D.; Seiler, P. *Acta Crystallogr., Sect. B* **1973**, *29*, 589-595.

(15) To a stirred solution of 52.4 mmol of lithium 2,2,6,6-tetramethylpiperidide and 10.0 g (62.8 mmol) of 1,2,3-trimethylisindole¹⁶ in 30 mL of THF at -30 °C a solution of 4.00 g (34.9 mmol) of 1-chlorotricyclo[3.1.0.0^{2,6}]hexane⁹ in 20 mL of THF was added dropwise. After stirring the mixture for 1 h at -30 °C and after workup with ether and water, the oily residue of the organic layer was purified by a short-path distillation affording 4.30 g (52%) of **1**, bp 100–120 °C (bath) (0.001 torr), mp 89 °C, after recrystallization from CH₃CN and ether. ¹H NMR (CDCl₃) δ 1.00–1.60 (m, 4 H, 3-H₂, 4-H₂), 1.55 (s, 6 H, CH₃-C), 1.58 (s, 3 H, CH₃-N), 1.72 (dt, $J = 5$ Hz and $J = 1$ Hz, 1 H, 5-H), 3.99 (dt, $J = 5$ Hz and $J = 1$ Hz, 1 H, 2-H), and 7.10 (s, 4 H, aromatic H); ¹³C NMR (C₆D₆) δ 16.5 (q, CH₃-C), 2.6 (t, C-4), 26.9 (t, C-3), 30.7 (q, CH₃-N), 34.7 (s, C-1, C-6), 58.2 (d, C-5), 64.1 (d, C-2), 71.6 (s, C-7, C-10), 121.4 (d), 126.3 (d), and 147.2 (s); MS (70 eV), m/e (relative intensity) 237 (M⁺, 36%), 222 (40%), 56 (100%).

(16) Anderson, P. S.; Christy, M. E.; Dylion, C.; Halczenko, W.; Ponticello, G. S.; Shepard, K. L. *J. Org. Chem.* **1979**, *44*, 1519-1533 and references therein.