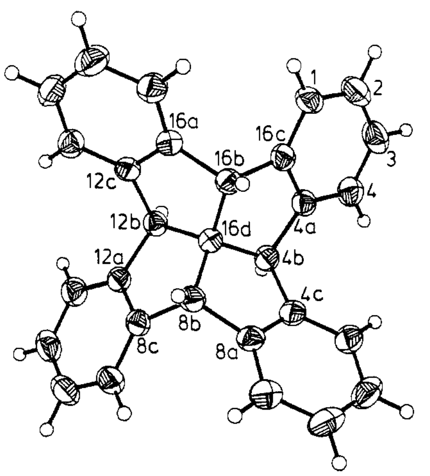

Figure 1. Perspective drawing of the solid-state structure of **4**, viewed along the S_4 axis. Selected bond lengths (pm) and angles (deg): C(4a)–C(4b), 150.6; C(4b)–C(16d), 155.1; C(4a)–C(4b)–C(4c), 117.4; C(4a)–C(4b)–C(16d), 104.2; C(4b)–C(16d)–C(8b), 106.0; C(4b)–C(16d)–C(12b), 116.5.

However, it is interesting to note that the molecular symmetry of **4** is S_4 rather than D_{2d}. An X-ray crystal structure analysis[20] reveals (Figure 1) that the mutual fusion of the two 2,2′-spirobiindan moieties of **4** still allows for the envelope-like bending of each of the four cyclopentene rings. In this way, the central neopentane unit avoids the all-eclipsed conformation which should represent the D_{2d} transition state for interconversion of the two equivalent S_4 conformers. Thus a torsional angle of 20.6° is found for the central C–C bonds (e.g. ∠ H(8b)–C(8b)–C(16d)–C(16b)), and the slightly concave (convex) *o*-xylylene moieties are situated 38 (±1) pm above (below) the central carbon atom. Nevertheless, the dihedral angles between two opposite and respectively two adjacent xylylene moieties are found to remain 90 (±1)° and 120 (±1)°, as anticipated for the D_{2d} conformation. A similar situation should apply to the related tetraene **2**.[3,21]

The UV absorption spectrum of fenestrindan[19] gives no evidence for electronic interactions between the benzo nuclei, the α band closely resembling those of indan and the tribenzocentrotriquinanes.[1] Efforts are under way in this laboratory to investigate the chemistry of fenestrindan and the synthetic potential for bridging the remaining two edges of the central tetrahedron of **4**, producing benzoannelated centropolyquinanes with topologically nonplanar structures.[22]

Acknowledgment. We thank Prof. Dr. A. Müller and Prof. Dr. H.-F. Grützmacher, University of Bielefeld, for their kind support of this work. Thanks are due also to Dr. W.-D. Fessner, University of Freiburg, West Germany, for a helpful discussion.

Supplementary Material Available: ^{1}H NMR (300 MHz) data of compounds **7–13** and positional parameters, bond lengths and angles, anisotropic thermal parameters, and hydrogen positions of **4** (6 pages). Ordering information is given on any current masthead page.

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(19) Fenestrindan (**4**): ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.89 (s, 4 H), 7.27 and 7.53 (AA′BB′, 16 H); ^{13}C NMR (75 MHz, $CDCl_3$) (ppm) 62.17 (d), 71.93 (s), 124.57 (d), 127.63 (d), 144.11 (s); IR (KBr) (cm^{-1}) 3065, 3035, 3018, 2925, 2895 (w), 1478, 1475, 1463, 1454 (s), 763, 760, 754, 730 (s); MS (EI, 70 eV), *m/z* 368 ($M^{\bullet+}$, 100%), 367 (46), 291 (33), 290 (25), 289 (36), 145 ($[M - C_6H_6]^{2+}$, 31); UV (*n*-heptane, $c = 2.5 \cdot 10^{-5}$ mol L^{-1}) λ_{max} (nm) 273.5 (ε 5000), 267.0 (4130), 261.5 (2380).

(20) Crystals of **4** are triclinic, space group $P\bar{1}$, $a = 1041.4$ (2) pm, $b = 1077.7$ (2) pm, $c = 1099.0$ (2) pm, $\alpha = 115.20$ (2)°, $\beta = 105.67$ (2)°, $\gamma = 104.73$ (2)°, $Z = 2$, $\rho_c = 1.257$ g cm^{-3}. The structure was refined (with hydrogen atoms in calculated positions) to $R = 0.053$ and $R_w = 0.050$ for 2681 independent reflections ($F_o > 3.92\sigma(F_o)$).

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Torands: Rigid Toroidal Macrocycles. Calcium Sequestration by a Member of This New Ligand Class

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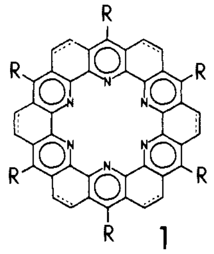
Discovery of new host families is crucial to the development of tailored molecules capable of molecular recognition and selective catalysis.[1] Heretofore, effective neutral hosts for alkali-metal and alkaline-earth ions have been largely restricted to three main classes: crown ethers,[2] cryptands,[3] and spherands.[4] Model studies of a fully unsaturated nitrogen analogue of 18-crown-6 suggested that fusion of six-membered rings to every position on the periphery of 1,4,7,10,13,16-hexaaza[18]annulene would afford a planar toroidal macrocycle, **1**, having potentially useful metal binding properties.[5] We have now synthesized the first substituent-solubilized ligand of this type, **2**, and we find that this new "torand" complexes calcium.



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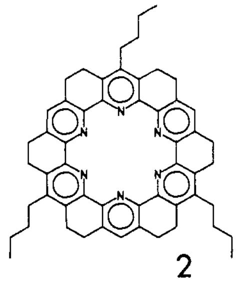

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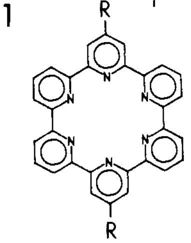
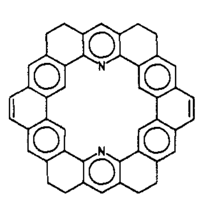


3a R=H
3b R=C_6H_5 or $C_6H_4CH_3$



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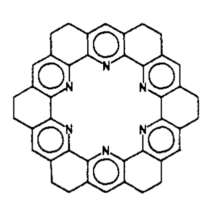

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Formula **1** represents a general ligand structure in which the outer two-carbon bridges may be saturated or unsaturated and the pyridine 4-positions bear up to six substituents (R). Our choice of target system **2** was determined by balancing considerations of solubility and spectroscopic simplicity. In particular, low solubility has hindered studies of "sexipyridines" **3a**[6] and **3b**,[7]

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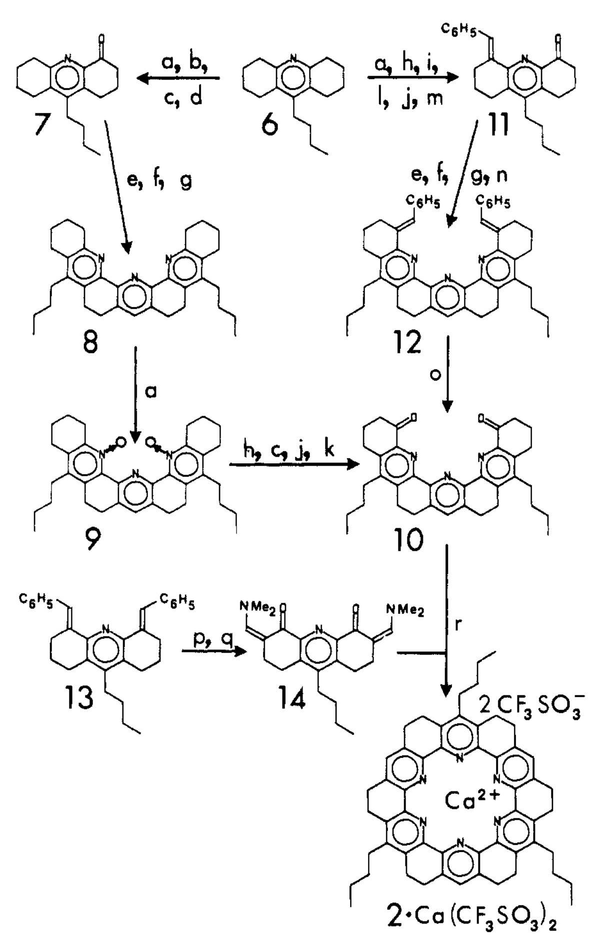

Figure 1. Synthesis of torand **2** as its calcium triflate complex: (a) MCPBA, CH_2Cl_2; (b) Ac_2O, 110 °C; (c) 3 M HCl, 100 °C; (d) CrO_3, HOAc, H_2O, H_2SO_4; (e) Me_2NNH_2, cyclohexane, EtOH–H_2O; (f) Me_3OBF_4, CH_2Cl_2; (g) 210–230 °C, N_2 flow; (h) Ac_2O, AcCl, NaOAc, 100 °C; (i) Ac_2O, C_6H_5CHO, reflux; (j) Dess–Martin periodinane, CH_3CN (oxidation of H_2SO_4 salts); (k) 35% from **8**; (l) 0.5 M H_2SO_4, distillation of excess C_6H_5CHO; (m) 46% from **6**; (n) 31% from **11**; (o) O_3, CH_2Cl_2, CH_3OH, −78 °C/Me_2S, 15 h (60%); (p) O_3, CH_2Cl_2, CH_3OH, −42 °C/Me_2S, 15 h; (q) *t*-BuOCH$(NMe_2)_2$, 70 °C, 2 h (35% from **13**); (r) CF_3SO_3H, HOAc, 100 °C, 1 h/NH_4OAc, 160–165 °C, 4 h/$CHCl_3$, 2 M LiOH (12%).

"diazakekulene" **4**,[8] and "dodecahydrohexaazakekulene" **5**.[9] Moreover, the parent benzenoid hydrocarbon, kekulene, is notoriously insoluble.[10] The three *n*-butyl groups of **2** were expected to enhance its solubility, relative to **5** or to the unknown, fully unsaturated parent system, hexaazakekulene.

We have reported the preparation of 9-*n*-butyl-1,2,3,4,5,6,7,8-octahydroacridine (**6**) and its conversion to heptacyclic terpyridine **8** via pyrolysis of a trimethylhydrazonium salt of ketone **7** (Figure 1).[11] We have now found that di-*N*-oxide **9** also undergoes rearrangement in acetic anhydride.[12] The resulting stereoisomeric diacetates are hydrolized to a mixture of diols, which are oxidized by using Dess–Martin periodinane[13] to afford key diketone intermediate **10**[14] (35% overall from **8**). An alternative approach to **10** combines the rearrangement of **6** *N*-oxide in acetic anhydride with benzaldehyde condensation in the same solvent.[15] The resulting benzylidene acetate is hydrolized to the alcohol, which, as the H_2SO_4 salt, is oxidized to benzylidene ketone **11**.[16] Compound **11** undergoes conversion to dibenzylideneheptacycle **12**[16] in somewhat higher yield than observed for the transformation of **7** to **8**.[11] Ozonolysis of **12** then provides key intermediate **10**[14] more expeditiously and in higher overall yield than by the former route.

The choice of reaction partners is often crucial to the success of macrocyclization reactions. Since conversion of **10** to **2** by trimethylhydrazonium salt pyrolysis would require unselective cross-coupling of two different diketones, an alternative, directed approach was sought. We have found that the condensation of β-dimethylamino enones with ketones can be used to form pyridines, such as **8**, in comparable yields.[17] Therefore, **6** was converted to dibenzylidene derivative **13**,[18] which was ozonolyzed. The resulting diketone was treated with Brederick's reagent[19] to afford the bis(β-dimethylamino enone) **14**.[14] Macrocycle **2** may be prepared in low yield by heating a 1:1 solution of **10** and **14** in *N*,*N*-dimethylformamide with an ammonium salt at 150 °C. An alternative procedure was modeled after the known synthesis of pyrylium salts by reaction of ketones with β-chlorovinyl aldehydes in the presence of trifluoromethanesulfonic acid (triflic acid)[8]. Thus, **10** and **14** were heated with triflic acid in acetic acid; then excess ammonium acetate was added and the resulting mixture was heated at 165 °C. Neutralization of the acidic reaction mixture with 2 N lithium hydroxide was followed by chloroform extraction of the crude product. Chromatography (silica gel/CH_2Cl_2, isopropyl alcohol, triethylamine (44:5:1)) gave a high R_f fraction which was triturated with ethyl acetate–acetonitrile to afford a yellow solid.

Proton NMR[20] and ^{13}C NMR[21] spectra of the macrocyclization product are consistent with ligand structure **2**; however, the IR spectrum revealed the presence of triflate. Recrystallization by evaporation of a 1:1 methylene chloride/ethyl acetate solution afforded fine yellow needles (mp > 400 °C), which gave correct microanalytical data for the composition $\mathbf{2}\cdot Ca(CF_3SO_3)_2$.[22] Mass spectrometry (FAB) corroborated this result, since the two most intense ions observed above 400 amu were *m/z* 975 ($\mathbf{2}\cdot CaCF_3SO_3^+$) and *m/z* 826 ($\mathbf{2}\cdot Ca^+$). The presence of calcium in the product is accounted for by a 0.3% Ca impurity in the triflic acid used in these experiments.

This synthesis of the first substituent-solubilized rigidly toroidal macrocyclic ligand paves the way for development of a new family of metal ion receptors related to the nascent cycloarene hydrocarbons.[10,23] The ready access of solvent to rigid cavities in toroidal ligands suggests that metal ion complexes of these hosts may exhibit useful kinetic and thermodynamic properties. Indeed, we have observed sequestration of calcium from a low-concentration source. The torus shape of planar macrocyclic ligands that consist of multiply fused rings suggests the same "torand" for these unique molecules.

Acknowledgment. This research was supported by the National Institutes of Health (PHS Grant GM 32937), and the National

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(17) Reaction of **7** with Brederick's reagent[19] gave the β-dimethylamino enone, which was treated with **7** and NH_4BF_4 in DMF at 150 °C, yielding **8** (30%).

(18) Benzaldehyde, acetic anhydride, reflux, 11 h (76%).[16]

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(20) δ ($CDCl_3$, 300 MHz) 7.54 (s, 3 H), 3.05 (s, 24 H), 2.78 (m, 6 H), 1.53 (m, 12 H), 1.01 (t, J = 7 Hz).

(21) δ ($CDCl_3$) 150.6, 149.5, 148.3, 136.4, 133.7, 132.5, 31.3, 28.5, 27.0, 23.6, 23.0, 13.8 (^{19}F-coupled triflate resonance expected to escape detection at sample concentration employed).

(22) Calcd for $C_{56}H_{54}N_6F_6O_6S_2Ca$: C, 59.78; H, 4.80; N, 7.47; F, 10.14; S, 5.69; Ca, 3.56. Found: C, 59.56; H, 4.72; N, 7.26; F, 9.84; S, 5.55; Ca, 3.27%.

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Electrophilic Capture by "Conjugated" Bis(bicyclo[1.1.0]butanes). Site Specificity of the Initiation Step and Thermodynamic Control of the Ensuing Electronic Reorganization

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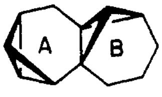
The intramolecular capture of cyclopropylcarbenes (or carbenoids) has emerged as one of the more important bicyclo[1.1.0]butane-forming reactions by virtue of its simplicity and selectivity.[2] Several years ago, we observed that twofold cyclopropylidene C–H insertion is an equally powerful synthetic technique that provides ready access to bis(bicyclo[1.1.0]butanes).[3] The elaboration of **1** and **2** in three convenient steps (Na, NH_3; KO-*t*-Bu, $CHBr_3$; CH_3Li, C_6H_6[4]) from tetralin and indan, respectively, is illustrative. We have been intrigued by the multiple sites offered by **1** and **2** to electrophilic reagents and now present



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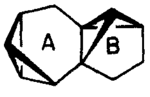

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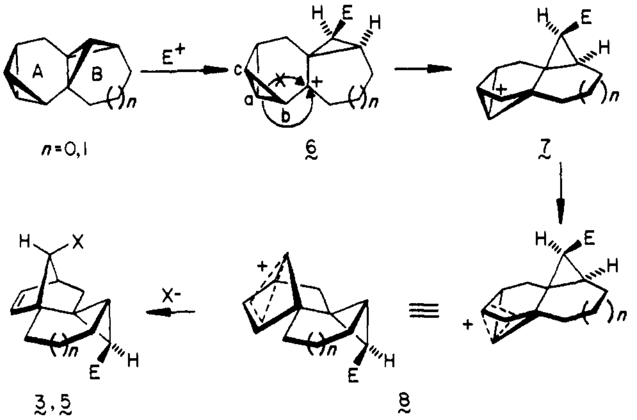
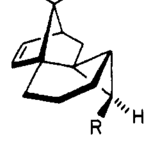
experimental evidence indicating that (a) only *one* of the *ten* available strained C–C σ bonds is cleaved by the attacking E^+ in remarkably regiospecific fashion; (b) this initiation step proceeds with retention of configuration at the reaction center; (c) the ensuing cascade of electronic rearrangements proceeds unidirectionally irrespective of the length of the polymethylene tether in ring B, presumably as a direct consequence of product stabilities; and (d) gradation in the nucleophilicity of the counter anion does in no case result in interception of the rearrangement prior to arrival at the 7-norbornenyl cation stage.

Addition of trifluoroacetic acid (8.2 equiv) to a chloroform solution of **1** at 20 °C resulted in rapid conversion to a single trifluoroacetate (86% isolated). Although the presence in this product of a trisubstituted cyclopropane ring, a pair of olefinic hydrogens, and a proton of the H–C–O type could be clearly inferred from the 300-MHz ^1H NMR spectrum, the remaining multiplets proved uninformative. Product identification as **3a** was achieved, however, by saponification (K_2CO_3, CH_3OH) to alcohol **3b** (mp 71–72 °C) whose three-dimensional structure was established by X-ray crystallographic analysis.[5]

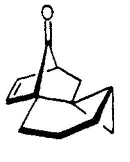
Scheme I



The extendability of this unusual addition–rearrangement was investigated by next reacting **1** with acetic acid (8.2 equiv, $CHCl_3$, 20 °C) and with 70% perchloric acid (0.22 equiv, aqueous THF, 20 °C) to give **3c** (70%) and **3b** (77%), respectively. The corresponding conversion to **3d** (31%) was realized through the agency of anhydrous $AlCl_3$ (0.20 equiv) in ether under otherwise identical conditions. Improved access to chloride **3d** was achieved by displacement with retention of the hydroxyl group in **3b** using thionyl chloride in refluxing anhydrous ether.[6]



3a, X=$OCOCF_3$, R=H
b, X=OH, R=H
c, X=$OCOCH_3$, R=H
d, X=Cl, R=H
e, X=$OCOCF_3$, R=D
f, X=OH, R=D



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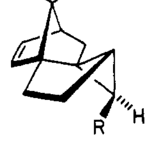

5a, X=$OCOCF_3$, R=H
b, X=OH, R=H
c, X=ODNB, R=H
d, X=Cl, R=H
e, X=$OCOCF_3$, R=D

From a reactivity standpoint, treatment with silver ion[7] was also of interest. In actuality, when **1** was exposed to silver nitrate in aqueous THF, qualitatively comparable conversion to **3b** was seen.[8] Swern oxidation of **3b** furnished **4** in 32% yield.

Usefully, the 300-MHz ^1H NMR spectra of **3a** and **3b** (in $CDCl_3$) cleanly distinguish the pair of cyclopropyl methylene hydrogens. For example, the endo proton in **3b** (δ 0.40) appears downfield of its exo counterpart (δ 0.27) and is seen to be equivalently coupled (J = 4.7 Hz) to its geminal and vicinal neighbors. In contrast, the dd pattern for H_{exo} (J = 4.7, 8.5 Hz) features a large spin interaction that is compatible with its cis relationship to the methine proton.

The stage was therefore set for the critical deuterium labeling experiments. Since treatment of **1** with CF_3COOD as before gave trifluoroacetate lacking the 0.40 signal, conversion to **3e** had obviously materialized. Isomerically pure **3f** was similarly obtained upon mixing **1** with $AgNO_3$ in a D_2O–THF solvent system.

Transformations involving **2** were conducted analogously and provided **5a** (58%) and **5d** (63%). As in the higher homologous series, trifluoroacetate **5a** exhibits well separated cyclopropyl methylene protons [δ 0.45 (dd, J = 4.9, 7.8 Hz) and 0.36 (dd, J = 4.9, 4.9 Hz)].[9] Following confirmation of the endo con-

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[1] Undergraduate research scholar, 1984–1986.

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[4] Benzene has supplanted ether as the solvent originally employed for this step because it precludes formation of carbene insertion products into the reaction medium.

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[8] Two isomeric polyolefinic hydrocarbons are produced concurrently (ca. 25% combined yield). For details of their structure, see ref 3b.

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