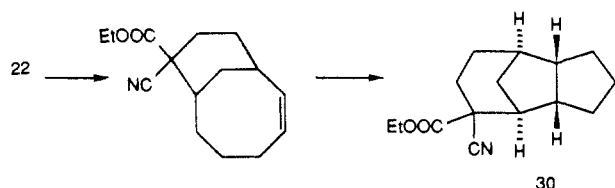


Scheme IV



formation, A, with the iodopropyl group disposed exo relative to the cyclooctadiene ring, leads to the trans-fused product. As expected on the basis of the relative strain energies of cis- and trans-fused bicyclo[3.3.0]octanes,⁸ the *trans*-[6.3.0]bicycloundecanyl radical **8** does not continue to react transannularly. The *cis*-fused bicycloundecanyl radical **9** partitions between reduction to **10** (40%) and formation of **13** (*cis-anti-cis*) and **12** (*cis-syn-cis*) in a ca. 2:1 ratio. The modest preference for the formation of the *cis-anti-cis* tricyclic product is analogous to that observed in the intermolecularly initiated reaction^{4,5} and can be rationalized by examination of conformations C and D of the intermediate product radical **9**.^{2b} The extended conformation, D, of the intermediate product radical which leads to **13**, does not suffer from the same eclipsing interaction which is present in C, the conformer leading to the formation of **12**.

Julia has demonstrated that substitution of radical-stabilizing groups on the 5-hexenyl radical makes the radical cyclization reaction reversible.⁹ In the present case (Scheme II), if X and Y are radical-stabilizing groups, the initial cyclization would be reversible, but the second, transannular cyclization would be irreversible, leading to the formation of exclusively *cis*-fused products. Treatment of **14** with di-*tert*-butyl peroxide (2 equiv, 150 °C, sealed tube) for 3 h provided a mixture of two products, **19** and **21**, in a 2.8:1 ratio in 90% yield (based on 40% recovered starting material).¹⁰ These results indicate that the addition of the dithiolanyl radical **15** is not reversible, since the *trans/cis* ratio (73:27) is the same as observed with **7**. However, unlike the previous case, the product which partitions through **17**, the *cis*-[6.3.0] system, leads to *cis-anti-cis* **21**, exclusively. The steric bulk of the dithiolane ring would appear to make the reduction of **17** slower relative to the transannular cyclization, so that none of **18**, the *cis*-[6.3.0] product, is observed. It also increases the energy difference between the transition states leading to the *syn* and *anti* transannular cyclization products, so that only **21** is formed.

Reaction of **22** with di-*tert*-butyl peroxide in cyclohexane at 150 °C for 40 h (sealed tube) led to a 45% yield of **29**,¹¹ with none of the *cis-syn-cis* tricyclic compound **28** or either the *trans*- or the *cis*-[6.3.0]bicycloundecanes **26** or **27**. The cyano ester makes the first cyclization reaction reversible⁹ and then serves as a control element for the transannular reaction of the *cis*-[6.3.0]bicycloundecanyl radical in the same manner as the dithiolane ring in the reaction of **14**. Also produced in this reaction is a 15% yield of *cis-anti-cis* **30**,¹² which results from attack of the cyano ester

stabilized radical on the distal olefin of the cyclooctadiene, followed by transannular closure (Scheme IV).

In conclusion, using **22**, we have been able to form the desired *cis-anti-cis*-triquinane as the major tricyclic reaction product. In this reaction, a single stereocenter in the starting material has been translated into four contiguous chiral centers. This transannular radical cyclization, in which four chiral centers and three five-membered rings are formed in a single chemical step, has counterparts in the Diels-Alder reaction, cationic polyene cyclization, and arene-olefin cycloaddition. More than one carbon-carbon bond and considerable stereochemical information are generated in a single synthetic operation. Further studies on the transannular reactions of radicals to control the stereochemistry of carbon-carbon bond formation are currently in progress in our laboratory.

Acknowledgment. We thank Professor Philip Eaton for a generous sample of the tricyclic enone **35** (see supplementary material). Acknowledgement is made to the donors of The Petroleum Research Fund, administered by the American Chemical Society, and the National Institutes of Health (CA-40250) for their support of this research. The NMR instruments used were funded in part by the NSF Chemical Instrumentation Program and by the NCI via the University of Chicago Cancer Research Center (CA 14599).

Supplementary Material Available: Experimental details for the preparation of cyclization substrates **6**, **14**, and **22** and the independent synthesis of authentic samples of **10-13** (4 pages). Ordering information is given on any current masthead page.

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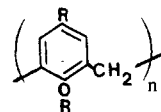
Inclusion of Both Cation and Neutral Molecule by a Calixarene. Structure of the [*p-tert*-Butylmethoxycalix[4]arene-sodium-toluene]⁺ Cation

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The liquid clathrate phenomenon has been investigated extensively by our group over recent years, starting with the reaction of simple salts with aluminum alkyls and proceeding to the recent enlargement of the area to include numerous ionic systems.¹ These newer results have hinged upon the use of crown ethers, either as catalysts or as integral parts of the final complex. The next step was to move up to the larger "three-dimensional" crown analogues. Of all the numerous cryptands and cavitands that have been synthesized since the pioneering work of Pedersen² and Lehn,³ calixarenes (**1**) were chosen for the initial investigations, primarily



due to their flexibility and the resultant potential for modification of the cavity size and shape.⁴

Unlike crown ethers, which were found to form adducts with aluminum alkyls that were easily dissociated upon addition of a

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(10) Desulfurization of **19** and **21** with tri-*n*-butyltin hydride (Gutierrez, C.; Srringham, R.; Nitasaka, T.; Gilascock, K. *J. Org. Chem.* 1980, 45, 3393) provided materials identical with **11** and **13**, respectively.

(11) The product was obtained as a mixture of epimers at the cyano ester carbon. Hydrolysis of **29** with potassium hydroxide in ethylene glycol, followed by decarboxylation of the resulting monoacid under Barton conditions (Barton, D.; Crich, D.; Motherwell, W. *J. Chem. Soc., Chem. Commun.* 1983, 939) furnished material which was identical with **13**.

(12) Hydrolysis and decarboxylation¹¹ furnished the known hydrocarbon (Golovkia, L.; Vorobeva, N.; Petrov, A. *Izv. Akad. Nauk SSR, Ser. Khim.* 1980, 591).

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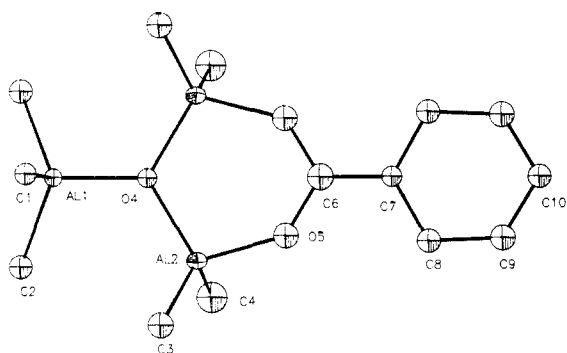
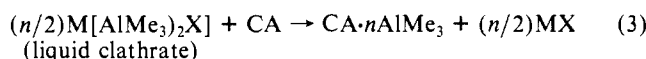
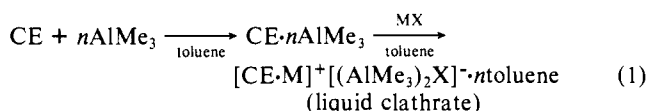


Figure 1. Structure of the $[\text{C}_6\text{H}_5\text{COO}(\text{AlMe}_2)_2\text{OAlMe}_3]^-$ anion which is bisected by a crystallographic mirror plane. Important distances: $\text{Al}(1)-\text{C}(1) = 2.04$ (2), $\text{Al}(1)-\text{C}(2) = 1.99$ (2), $\text{Al}(1)-\text{O}(4) = 1.81$ (1), $\text{Al}(2)-\text{O}(4) = 1.803$ (7), and $\text{Al}(2)-\text{O}(5) = 1.85$ (1) Å; angles, $\text{C}(1)-\text{Al}(1)-\text{C}(2) = 109.6$ (6)°, $\text{C}(1)-\text{Al}(1)-\text{O}(4) = 105.9$ (9)°, $\text{C}(2)-\text{Al}(1)-\text{O}(4) = 106.5$ (6)°, $\text{Al}(1)-\text{O}(4)-\text{Al}(2) = 119.5$ (4)°, $\text{O}(4)-\text{Al}(2)-\text{C}(3) = 113.1$ (7)°, $\text{O}(4)-\text{Al}(2)-\text{C}(4) = 111.0$ (8)°, and $\text{C}(3)-\text{Al}(2)-\text{C}(4) = 121.1$ (8)°.

salt,⁵ the methoxycalixarenes ($\text{R}' = t\text{-Bu}$; $\text{R} = \text{Me}$; $n = 4, 6$, or 8) form adducts that are generally difficult to dissociate. Indeed when the reaction is reversed and a methoxycalixarene is added to an existant liquid clathrate system (see Scheme I), adducts are often noted.⁶

Scheme I



CE = crown ether; CA = methoxycalix[4]arene;
M = alkali metal ion

A system that had been found to undergo reaction 2 is the adduct of methoxycalix[4]arene (1) ($\text{R}' = t\text{-Bu}$; $\text{R} = \text{Me}$; $n = 4$) and trimethylaluminum, together with hydrated sodium benzoate (of approximate composition one water to one sodium benzoate). From the liquid clathrate thus formed were isolated large, colorless, mildly air-sensitive crystals of the title complex.^{7a,b}

The anion, shown in Figure 1, is a new member of a growing series of aluminoxanes.⁸ However, it is the cation, Figure 2, that

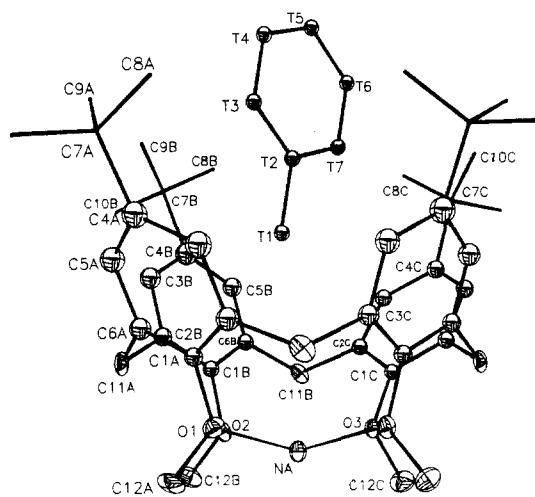


Figure 2. Structure of the $[p\text{-tert-butylmethoxycalix[4]arene-sodium-toluene}]^+$ cation. The crystallographic mirror plane contains the toluene molecule, bisects the A and C calixarene aromatic units, and reflects the B unit. Carbon atoms of the *tert*-butyl groups are shown as very small spheres for clarity.

exhibits the most interesting features. It has been shown that calixarenes will complex alkali metal ions, although generally not as strongly as do crown ethers or cryptands.^{9,10} We present here the first structure of such a complex. The sodium ion interacts with all four oxygen atoms of the methoxy groups in a strong fashion. The average $\text{Na} \cdots \text{O}$ separation of 2.30 Å may be compared with 2.38 Å in $\text{NaI}(\text{benzo-15-crown-5})\text{H}_2\text{O}$, in which the sodium is six-coordinate.¹¹ The sodium ion lies 0.44 Å out of the plane of the four oxygen atoms. The fifth coordination site is filled remotely by C(1) of the anion ($\text{Na} \cdots \text{C}(1) = 2.64$ Å), so that the geometry is virtually an ideal square pyramid. Note that the $\text{Na} \cdots \text{C}$ distance involving an ionic nearest neighbor interaction is 2.35 (2) Å in $\text{Na}[\text{CH}(\text{SiMe}_3)_2]$.¹²

The ability of the calixarene to include neutral molecules¹³ is not lost by this complexation. The main cavity of the calix contains a toluene molecule, which is oriented so that the methyl group is directly above the sodium at a separation of 4.35 Å (both lying on the crystallographic mirror plane that bisects the cation). There are two types of toluene-calix interactions: the methyl carbon is close to the aromatic rings of the calixarene at an average distance of 3.54 Å, and the toluene ring carbon atoms interact with the *tert*-butyl groups at an average $\text{C} \cdots \text{C}$ distance of 3.77 Å.

A liquid clathrate has now been prepared with a cation of preformed inclusion capability. In future contributions the use of this type of inclusion in separations problems will be discussed.

Acknowledgment. We are grateful to the National Science Foundation for support of this work.

Supplementary Material Available: Tables of bond distances and angles, final fractional coordinates, thermal parameters, and observed and calculated structure factors (17 pages). Ordering information is given on any current masthead page.

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(7) (a) Synthesis: The methoxycalix[4]arene was prepared by a modification of the literature procedure: Gutsche, C. D., personal communication. *p*-*tert*-Butylmethoxycalix[4]arene (7.05 g, 0.010 mol) was dissolved ca. 30 mL of toluene in a screw top tube. AlMe_3 (4 mL, 0.040 mol) was added via syringe (in a drybox!). Reaction was immediate as evidenced by a clearing of the solution and a warming of the tube. $\text{NaC}_6\text{H}_5\text{COO} \cdot \text{H}_2\text{O}$ (1.62 g, 0.010 mol) was added to the still-warm solution. A vigorous reaction ensued, presumably helped along by the water of hydration. The liquid layering, evidence of the liquid clathrate effect, was immediately noted. Colorless, mildly air-sensitive crystals of the title complex were obtained by allowing the mixture to cool to room temperature. The isolated yield was ca. 20%, but a substantial volume of liquid clathrate remained and further crops could have been obtained. (b) X-ray Structure Determination: The space group is the orthorhombic *Pnma* with cell constants, $a = 26.069$ (7) Å, $b = 15.269$ (6) Å, $c = 17.589$ (6) Å, and $D_c = 1.09$ g cm^{-3} for $Z = 4$. The cation and anion both lie on a crystallographic mirror plane. Least-squares refinement based on 4933 observed reflections led to a final $R = \sum(|F_o| - |F_c|) / \sum |F_o| = 0.090$. The rather high value is due to high thermal motion in the *t*-Bu groups and the included toluene molecule. Anisotropic thermal parameters were used for all non-hydrogen atoms except those of the toluene and the calixarene rings. Hydrogen atoms were not located. The details of data collection and refinement are given in Holton et al.: Holton, J.; Lappert, M. F.; Ballard, D. G. H.; Pearce, R.; Atwood, J. L.; Hunter, W. E. *J. Chem. Soc., Dalton Trans.* **1979**, 45.

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