Hückel line is common to the neutral and charged species (eq 8), it is close to the PPP results for the latter but too high for the former. Hückel theory has long been known to overestimate the ring current in [18]annulene. The assumption of bond alternation[12] to explain the reduced ^{1}H NMR shifts is not supported by X-ray structural data.[13] Vogler[14] obtained much improved, but still too high, ^{1}H shifts for the observed geometry by an elaborate SCF-MO-PPP method that includes local anisotropic contributions. We emphasize here the role of electron correlation in selectively depressing the ring current of neutral species. The enhanced ring current of charged vs. neutral annulenes requires going beyond MO theory.

Acknowledgment. We gratefully acknowledge NSF support for this work under DMR-8403819.

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Stereochemical Control of Transannular Radical Cyclizations. A New Approach to the Synthesis of Linearly Fused Cyclopentanoids[1]

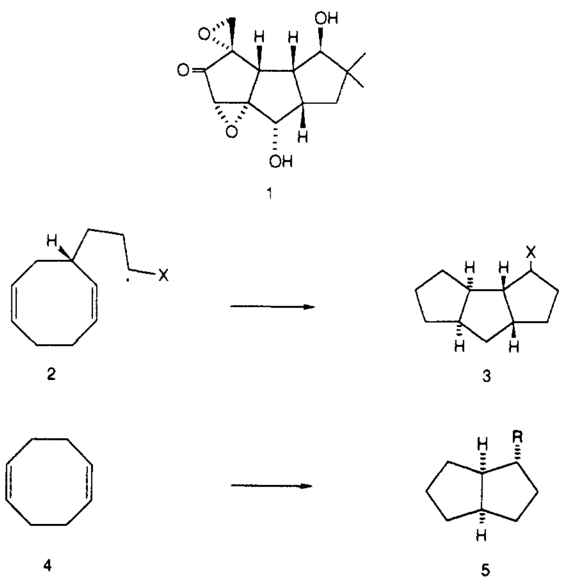
Jeffrey D. Winkler* and V. Sridar

Searle Chemical Laboratories, Department of Chemistry
University of Chicago, Chicago, Illinois 60637

Received November 19, 1985

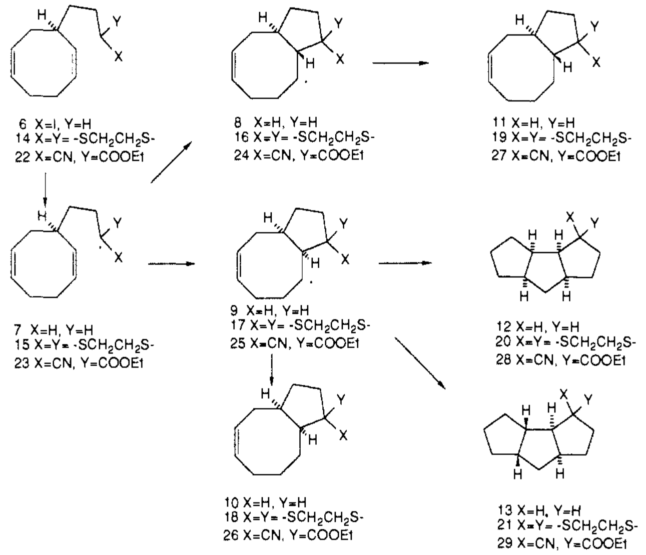
Most of the existing strategies for the synthesis of linearly condensed cyclopentanoids, such as the hirsutane sesquiterpenes, i.e., coriolin (**1**), sequentially construct each ring in the tricyclic system, with some notable exceptions.[2] We report herein our preliminary results with a conceptually novel approach to this problem—the application of transannular radical cyclizations to the control of stereochemistry in the formation of carbocyclic ring systems.[3] By judicious choice of X (Scheme I) the cyclization of **2** leads to the formation of **3**, in which three five-membered rings and four contiguous centers of asymmetry are produced in a single chemical step.

Scheme I

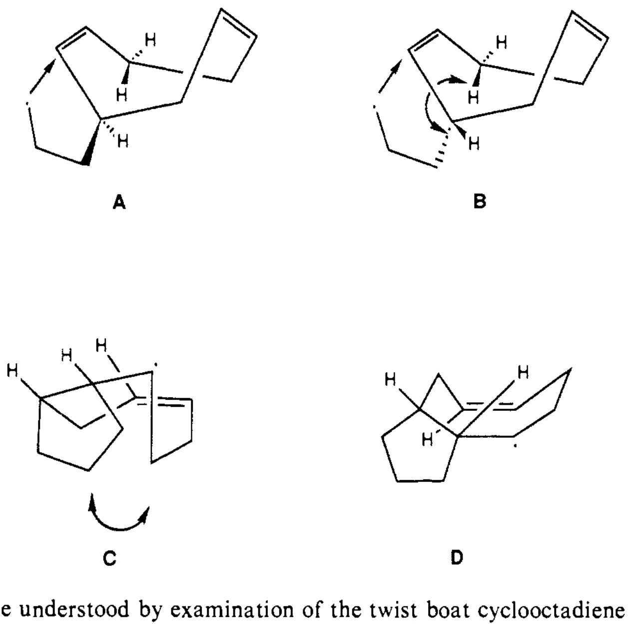


Several years ago, Dowbenko[4] and Friedman[5] independently reported that the addition of exogenous radicals to 1,5-cyclooctadiene (**4**) produces exo-substituted bicyclo[3.3.0]octanes, i.e., **5**, in which three contiguous stereocenters are produced in a single synthetic operation from achiral precursors. To examine the intramolecular version of this reaction, we prepared **6** (Scheme II) and submitted it to the usual radical cyclization conditions. Irradiation (150-W lamp) of **6** in the presence of 1.1 equiv of tri-*n*-butyltin hydride in benzene (0.02 M) containing a catalytic amount of azoisobutyronitrile (AIBN) for 4 h led to the formation of four new products, **10–13**, in a ratio of 11:73:5:11, respectively (61% yield).[6]

Scheme II



Scheme III



The kinetic preference for trans-fused products (73:27 ratio of trans-/cis-fused products) in the intial cyclization reaction can be understood by examination of the twist boat cyclooctadiene conformations shown below (Scheme III).[7] The preferred con-

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[1] Presented at the 190th National Meeting of the American Chemical Society, Chicago, IL, Sept 8–13, 1985; paper ORGN 142.

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[3] (a) Sutherland, J.; Sam, T. *J. Chem. Soc., Chem. Commun.* **1971**, 970. (b) van der Line, L.; van der Weerdt, A. *Tetrahedron Lett.* **1984**, 1201. (c) Paquette, L.; Colapret, J.; Andres, D. *J. Org. Chem.* **1985**, *50*, 201.

[4] Dowbenko, R. *Tetrahedron* **1964**, *20*, 1843.

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[6] The identities of **10–13** were unambiguously established by correlation with independently prepared authentic samples (see supplementary materials for experimental details).

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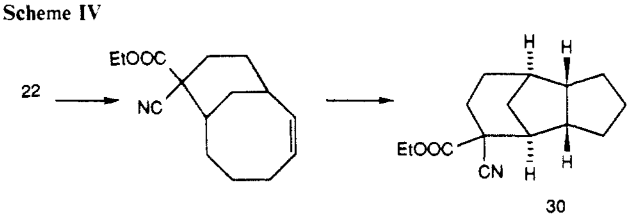
Scheme IV



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 reversible[9] 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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(10) Desulfurization of **19** and **21** with tri-*n*-butyltin hydride (Gutierrez, C.; Srringham, R.; Nitasaka, T.; Gilasscock, 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**.

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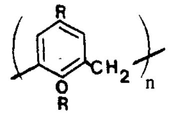
Inclusion of Both Cation and Neutral Molecule by a Calixarene. Structure of the [*p*-*tert*-Butylmethoxycalix[4]arene–sodium–toluene]$^+$ Cation

Simon G. Bott, Anthony W. Coleman, and Jerry L. Atwood*

Department of Chemistry, University of Alabama
University, Alabama 35486

Received November 14, 1985

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 Pedersen[2] 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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