Table I. ^{13}C NMR Chemical Shift in D_2O^a

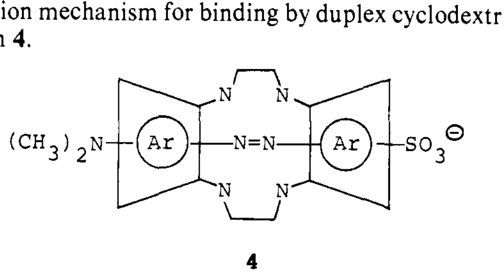
compd	^{13}C chemical shift, ppm
2	100.06 (C_1), 79.35 (C_4), 71.23 (C_3), 70.19 (C_2, C_5), 58.70 (C_6), 45.45 (C -NHR), 37.08 (C-NH_2)
3	100.45 (C_1), 79.66 (C_4), 71.75 (C_3), 70.39 (C_2, C_5), 58.77 (C_6), 47.66 (C-NHR)
$(CH_3CH_2)_2NH^b$	44.1 (C-NH-C)
$CH_3CH_2NH_2{}^c$	35.9 (C-NH_2)

[a] Acetone was used as an internal standard. [b] L. F. Johnson and W. C. Hankowski, "Carbon-13 Spectra", Wiley-Interscience, New York, 1972. [c] E. Breitmaier, G. Haas, and W. Voclter, "Atlas of Carbon-13 NMR Data", Plenum Press, New York, 1976.

solvent molecule(s) was usually bound much tighter than by parent cyclodextrin, Found: C, 45.21; H, 6,53; N, 3.02. Calcd for $C_{88}H_{148}N_4O_{66}\cdot(CH_3)_2NCHO$: C, 45.69; H, 6.54; N, 2.93. Calcd for $C_{88}H_{148}N_4O_{66}$; C, 45.58; H, 6.44; N, 2,42.

The NMR spectra of both **2** and **3** show the characteristic absorptions of the protons α to amino nitrogen at δ 3.4 in D_2O: **2**, δ 3.4 (12 H, N-CH_2), 3.7-4.9 (38 H), 5.4 (7 H, C_1 H); **3**, δ 3.4 (16 H, N-CH_2), 3.6-4.8 (76 H), 5.4 (14 H, C_1 H). More characteristic are the ^{13}C NMR spectra of **2** and **3**; the former, as listed in Table I, shows two types of methylene absorption adjacent to the primary and secondary amino groups while no methylene absorption adjacent to the primary amino group is observed in duplex cyclodextrin (**3**).

The present host duplex cyclodextrin shows unique and interesting binding characteristics toward guest molecules having two hydrophobic recognition sites. One typical example of this multiple recognition is the binding of 6-*p*-toluidinylnaphthalene-2-sulfonate (TNS) where its fluorescence maximum at 480 nm in aqueous solution[8] shifted to 444 nm in the presence of duplex cyclodextrin. This large shift due to the hydrophobic environment of the host-guest inclusion complex is approximately equal to that of 2:1 β-cyclodextrin-TNS complex but much larger than that of the corresponding 1:1 complex as the following data suggest: aqueous, 480; β-duplex 1:1 complex, 444; β-CD 1:1 complex, 457; β-CD 2:1 complex, 444; β-CD$(N_2C_2H_6)_2$ (**2**) 1:1 complex, 452 nm. This suggests that the binding of TNS by duplex cyclodextrin is very similar to that involved in 2:1 β-CD inclusion. Another example is binding of methyl orange where the association constant with duplex cyclodextrin was 3160 M^{-1}, much higher than that with the corresponding β-CD tetramine **2** (520 M^{-1}), demonstrating the additive contribution of the second hydrophobic binding site.[9] These examples strongly support the multiple recognition mechanism for binding by duplex cyclodextrin as shown in **4**.



4

References and Notes

(1) (a) F. Cramer and W. Kampe, *J. Am. Chem. Soc.*, **87**, 1115 (1965); (b) R. L. van Etten, J. F. Sebastian, G. A. Clowes, and M. L. Bender, *ibid.*, **89**, 3242 (1967); (c) D. L. Vander Jagt, F. L. Killian, and M. L. Bender, *ibid.*, **92**, 1016 (1970); (d) T. S. Straub and M. L. Bender, *ibid.*, **94**, 8875, 8881 (1972); (e) R. Breslow and P. Cambell, *Bioorg. Chem.*, 1, 140, (1971); (f) I. Tabushi, K. Fujita, and H. Kawakubo, *J. Am. Chem. Soc.*, **99**, 6456 (1977).

(2) (a) F. Cramer and G. Mackenson, *Angew. Chem.*, **78**, 641 (1966); (b) F. Cramer and G. Mackenson, *Chem. Ber.*, **103**, 2138 (1970); (c) R. Breslow and L. E. Overmann, *J. Am. Chem. Soc.*, **92**, 1075 (1970); (d) W. B. Gruhn and M. L. Bender, *Bioorg. Chem.*, **4**, 219, 237 (1975); (e) R. Breslow, J. B. Doherty, G. Guillot, and C. Lipsey, *J. Am. Chem. Soc.*, **100**, 3227 (1978).

(3) (a) I. Tabushi, Y. Kuroda, and Y. Kimura, *Tetrahedron Lett.*, 3327 (1976); (b) I. Tabushi, H. Sasaki, and Y. Kuroda, *J. Am. Chem. Soc.*, **98**, 5727 (1976); (c) I. Tabushi, Y. Kimura, and K. Yamamura, *ibid.*, **100**, 1304 (1978).

(4) J. Emert and R. Breslow, *J. Am. Chem. Soc.*, **67**, 670 (1975).

(5) (a) I. Tabushi, K. Shimokawa, N. Shimizu, H. Shirakata, and K. Fujita, *J. Am. Chem. Soc.*, **98**, 7855 (1976); (b) I. Tabushi, K. Shimokawa, and K. Fujita, *Tetrahedron Lett.*, 1527 (1977); (c) I. Tabushi, L. C. Yuan, and K. Fujita, *ibid.*, 2503 (1977).

(6) I, Tabushi, N. Shimizu, T. Sugimoto, M, Shiozuka, and K. Yamamura, *J. Am. Chem. Soc.*, **99**, 7100 (1977).

(7) The ^{13}C NMR spectrum of 1 supports the assignment of the disulfonyl group capping positions as the remote transannular ones (6A,6C and/or 6A,6D). See ref 2e. We have also observed the same ^{13}C NMR for 1. Therefore, if 1 is the mixture of 6A,6C and 6A,6D, six possible isomers of present duplex cyclodextrin should exist:

$$\binom{\text{6A,6C}}{\text{6A,6C}},\ \binom{\text{6A,6C}}{\text{6C,6A}},\ \binom{\text{6A,6C}}{\text{6A,6D}},\ \binom{\text{6A,6C}}{\text{6D,6A}},\ \binom{\text{6A,6D}}{\text{6A,6D}},\ \binom{\text{6A,6D}}{\text{6D,6A}}$$

(8) Since no fluorescence of TNS could be observed in pure water, the fluorescence maximum of free TNS employed here was measured in 10% ethanol solution.

(9) Most probably a part of the favorable interaction (such as the van der Waals interaction or the loss of water structure) is partially offset by a considerable loss of freedom of motion of the guest molecule in the duplex inclusion complex. Cf. I. Tabushi, Y. Kiyosuke, T. Sugimoto, and K. Yamamura, *J. Am. Chem. Soc.*, **100**, 916 (1978).

Iwao Tabushi,* Yasuhisa Kuroda, Kazuhiro Shimokawa
Department of Synthetic Chemistry, Kyoto University
Yoshida, Kyoto 606, Japan

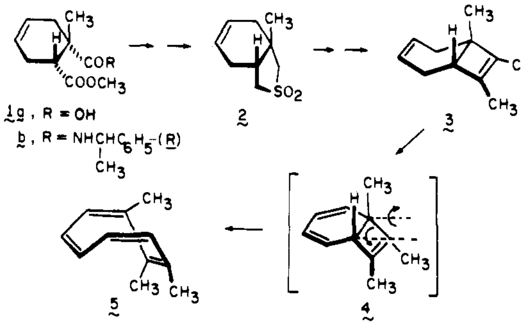
Received July 11, 1978

Bond Fixation in Annulenes. 5. Absolute Configuration and Chiroptical Properties of Optically Active 1,2,3-Trimethyl- and 1,2,3,4-Tetramethylcyclooctatetraenes[1]

Sir:

Whereas the smaller annulene ring systems (cyclobutadiene and benzene) are too planar to support optical activity[2] and the larger annulenes are too flexible to maintain chirality,[3] the medium-sized cyclooctatetraene nucleus is ideally suited for probing the interaction of light with a cyclic conjugated polyolefin network. The successful realization of this objective is dependent upon adequate inhibition of the high susceptibility of these tub-shaped molecules toward ring inversion and π-bond alternation,[4] processes which normally result in facile racemization. The control of these dynamic phenomena having been mastered,[1,5-7] we can now report the first absolute configurational assignments to two chiral [8]annulene hydrocarbons and the elucidation of their chiroptical properties.

The assignment of absolute stereochemistry to (−)-**5** began by sequential reaction of fully resolved acid ester **1a,** $[\alpha]^{25}{}_D$ −13.8° (*c* 10.8, C_2H_5OH),[1] with oxalyl chloride and excess (*R*)-(+)-α-methylbenzylamine to give **1b,** mp 95-97 °C, $[\alpha]^{25}{}_D$ + 66.5° (*c* 18.8, C_2H_5OH).[8] This compound was isolated as monoclinic crystals of space group $P2_1$ with lattice constants a = 10.084 (3), b = 9.429 (3), c = 18.234 (4) Å; β = 96.36 (2)°. An observed and calculated density of ~1.16 g/cm^3 indicated four molecules in the unit cell or two molecules of composition $C_{18}H_{23}NO_3$ in the asymmetric unit. All unique diffraction maxima with $\theta \leq 57°$ were collected (Cu



0002-7863/79/1501-1615$01.00/0

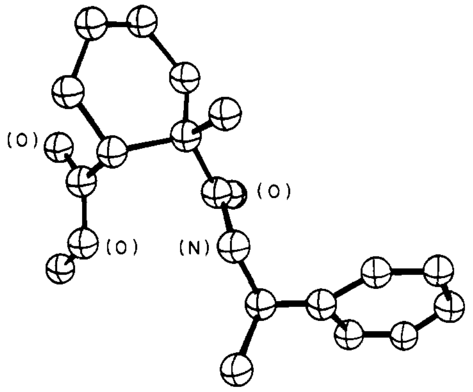


Figure 1. A structural view of (+)-**1b** as seen by X-ray analysis.

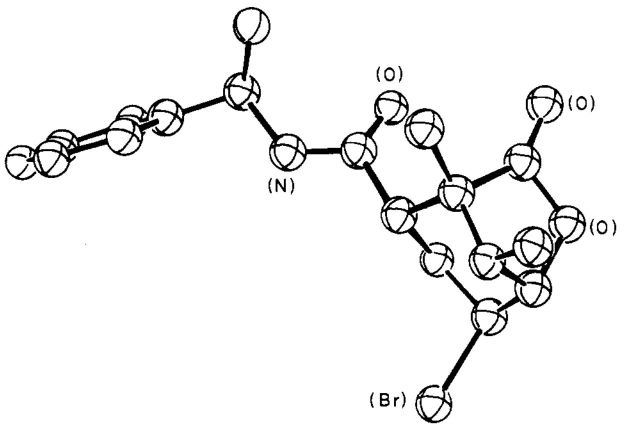


Figure 2. A structural view of (+)-**7b** as seen by X-ray analysis.

Kα radiation) and a total of 1663 (67%) reflections were considered observed after correction for Lorentz, polarization, and background effects ($F_o^2 \geq 3\sigma(F_o^2)$).

In spite of the size of the asymmetric unit and the paucity of high angle scattering data, the structure emerged uneventfully from standard direct methods.[9] Tables describing fractional coordinates and temperature factors, bond distances and angles, as well as observed and calculated structure factors have been placed in the microfilm version of the journal. As the computer generated perspective drawing (Figure 1) indicates, our prior knowledge of the absolute configuration of the α-methylbenzylamine moiety permits depiction of the correct absolute stereochemistry for the remainder of structure **1b**.

It then follows that the precedented[10] sequence of steps employed to transform (−)-**1a** to (+)-**2** and subsequently **3**, $[\alpha]^{25}{}_D$ +141° (*c* 12.7, hexane), must deliver a product having the 1*S*,6*R* configuration. Furthermore, since the disrotatory opening of **4**, prepared by regiospecific bromination-dehydrobromination of (+)-**3**, likely proceeds with full orbital symmetry control,[5] this optically active cyclooctatetraene, $[\alpha]^{25}{}_D$ −148° (*c* 21.1, diglyme), must have the absolute stereochemistry indicated.[11]

To gain access to (+)-**9**, diacid **6a**, obtained by hydrolysis of the citraconic anhydride-1,3-pentadiene adduct,[12] was resolved with (*R*)-(+)-α-methylbenzylamine. The enantiomeric purity of this material, $[\alpha]^{25}{}_D$ −110.1° (*c* 98.2, C_2H_5OH), was established by conversion via **6b*** (Ac_2O, then CH_3OH, reflux) to **6c*** whose ^1H NMR spectrum showed a single methyl ester absorption at δ 3.62. For comparison, amide prepared from racemic **6b** displayed a pair of equally intense signals at δ 3.62 and 3.56. Bromolactonization of optically pure **6a** proceeded with full stereochemical control[13] to give bromolactone **7a**, $[\alpha]^{25}{}_D$ −25.68° (*c* 25.9, CH_2Cl_2). The derived amide **7b**, $[\alpha]^{25}{}_D$ + 10.75° (*c* 14.6, CH_2Cl_2), formed stout acicular crystals which proved to be nicely suited to X-ray analysis by heavy-atom techniques: *a* = 10.675 (7), *b* 18.047 (8), *c* = 19.533 (11) Å; density, 1.34 g/cm^3 with two molecules of composition $C_{18}H_{22}BrNO_3$ per asymmetric unit. A total of 1505 (52%) reflections were judged observed (see supplemental material). Figure 2 shows the final X-ray model with absolute stereochemistry.

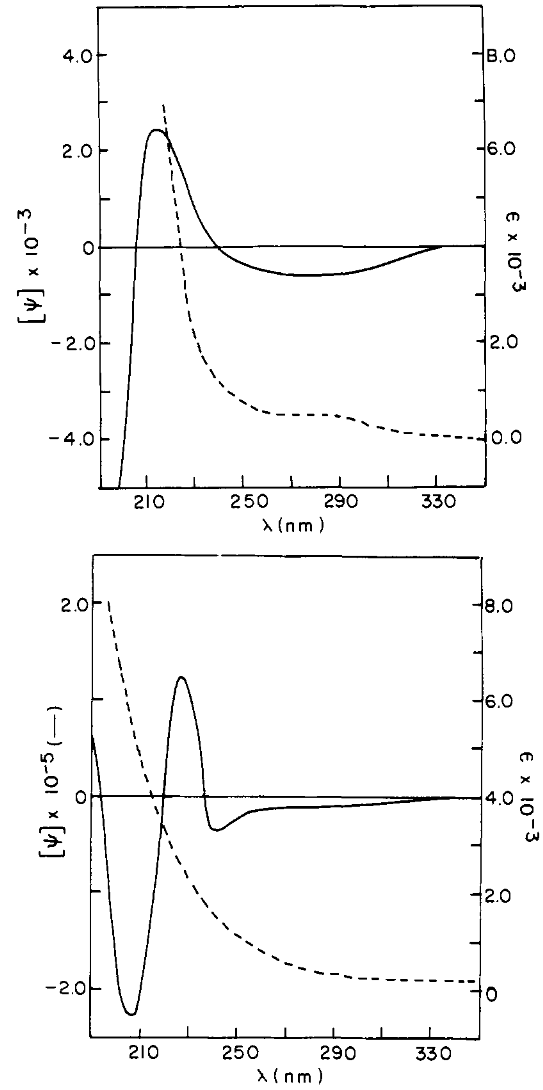
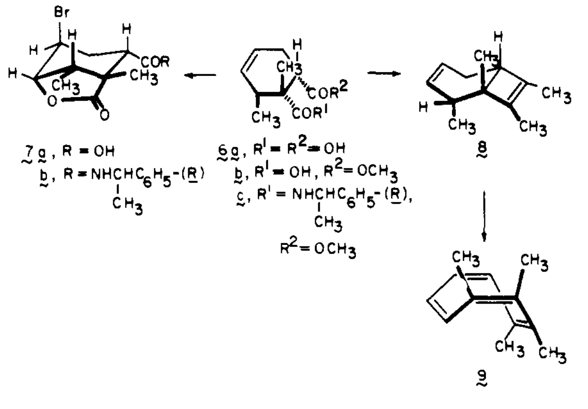


Figure 3. UV (---) and CD (—) spectra of (−)-**5** (top) and of (−)-**9** (bottom). *n*-Hexane was used as solvent.



Starting with optically pure (−)-**6a**, cyclobutene **8** was obtained as a colorless liquid, $[\alpha]^{25}{}_D$ −109.3° (*c* 38.2, pentane). Bromination-dehydrobromination of material of this quality led to **9**, $[\alpha]^{25}{}_D$ + 87.8° (*c* 7.8, pentane), whose absolute stereochemistry must be as indicated. This substance was not optically pure, however, as revealed through application of an alternative method of resolution[14] which afforded the levorotatory enantiomer of **9** having substantively higher rotatory power, $[\alpha]^{25}{}_{\mathrm{D}}$ −310° (*c* 0.15, hexane).

Whereas **5** belongs to the C_1 point group, **9** has C_2 symmetry; both molecules are therefore dissymmetric although **5** is also asymmetric.[15] Because the parent cyclooctatetraene ring system is achiral (D_{2d} symmetry), any chiral moiety contained therein must be balanced by an enantiomeric moiety, a common occurrence. Thus, if C_1–C_2–C_3–C_4–C_5 has left-handed helicity, the segment C_1–C_8–C_7–C_6–C_5 has the enantiomeric right-handed helicity. For this reason, the substituted derivatives **5** and **9** cannot be referred to as "inherently dissymmetric" hydrocarbons, a designation which would be appropriate only if the substituents caused the [8]annulene framework to distort significantly to a chiral geometry or if the methyl groups participated so significantly in the electronic transitions under consideration that they would have to be considered an integral part of the chromophore.

In the present circumstances, therefore, neither the homoannular diene helicity rule[16] nor the allylic chirality rule[17] apply. Twisting about individual double bonds[18] similarly cannot be playing a significant role. In actual fact, the two CD curves taken in conjunction with the UV spectra (which show minimal π–π interaction, Figure 3) clearly reveal that "conjugated" polyene systems with distinct near-UV absorptions are *not* being dealt with. Rather, these systems consist essentially of four virtually unconjugated ethylene chromophores coupled principally by the electrostatic potential between the $\pi \rightarrow \pi^*$ transition dipoles.

The CD spectra of the pair of optically active cyclooctatetraenes unmistakably reveal that antipodes of like sign belong to the same enantiomeric series. The curve due to **9** is more complex, however, perhaps because of a higher concentration of the bicyclo[4.2.0]octatriene valence tautomer.[5] Notwithstanding, it remains difficult to know at this time which CD band is pertinent for any given analysis. Obviously, further study of the matter is required, a goal currently being pursued in these laboratories.

Acknowledgment. This investigation was supported in part by the National Cancer Institute, DHEW (Grant No. CA-12115), and the National Science Foundation (Grant No. CHE7608764). The authors are indebted to Professors A. W. Burgstahler, S. Mason, K. Mislow, A. Moscowitz, and A. I. Scott for their helpful comments.

Supplementary Material Available: Fractional coordinates and temperature factors, bond distances, bond angles, and observed and calculated structure factors for **1b** (Tables 1–4, respectively) and **7b** (Tables 5–8, respectively) (24 pages). Ordering information is given on any current masthead page.

References and Notes

(1) For part 4, see Paquette, L. A.; Gardlik, J. M.; Photis, J. M. *J. Am. Chem. Soc.* **1976,** *98*, 7096.
(2) Multilayered paracyclophanes having two para bridges spanning the benzene rings can be constructed with C_2 or D_2 symmetry. Such helical structures have recently been prepared in optically active form: Nakazaki, M.; Yamamoto, K.; Tanaka, S.; Kametani, H. *J. Org. Chem.* **1977,** *42*, 287.
(3) Oth, J. F. M. *Pure Appl. Chem.* **1971,** *25*, 573 and the many references cited therein.
(4) (a) Paquette, L. A. *Tetrahedron* **1975,** *31*, 2855. (b) Fray, G. I.; Saxton, R. G. "The Chemistry of Cyclo-octatetraene and its Derivatives", Cambridge University Press: New York, 1978. (c) Schröder, G. "Cyclooctatetraen", Verlag Chemie: Weinheim/Bergstr., Germany, 1965.
(5) Paquette, L. A.; Photis, J. M.; Ewing, D. G. *J. Am. Chem. Soc.* **1975,** *97*, 3538. Paquette, L. A.; Photis, J. M. *ibid.* **1976,** *98*, 4936.
(6) Gardlik, J. M.; Johnson, L. K.; Paquette, L. A. *J. Am. Chem. Soc.*, following paper in this issue.
(7) π bond alternation may be arrested by benzo fusion; the problem then reduces to one of sterically inhibiting ring inversion. Recent attention has been directed to inversion barriers in aryl fused cyclooctatetraenes. See the following. Mislow, K.; Perlmutter, H. D. *J. Am. Chem. Soc.* **1962,** *84*, 3591. Figeys, H. P.; Dralants, A. *Tetrahedron Lett.* **1971,** 3901. Buchanan, G. W. *ibid.*, **1972,** 665. Gust, D.; Senkler, G. H., Jr.; Mislow, K. *J. Chem. Soc., Chem. Commun.* **1972,** 1345. Senkler, G. H., Jr.; Gust, D.; Riccobono, P. X.; Mislow, K. *J. Am. Chem. Soc.* **1972,** *94*, 8626. Rosdahl, A.; Sandström, J. *Tetrahedron Lett.* **1972,** 4187. FINDER= C. J.; Chung, D.; Allinger, N. L. *ibid.* **1972,** 4677. Allinger, N. L.; Sprague, J. T.; Finder, C. J. *Tetrahedron* **1973,** *29*, 2519.
(8) ^{1}H NMR ($CDCl_3$, δ): 7.28 (s, 5 H), 5.66 (m, 2 H), 5.4–5.0 (m, 1 H), 3.59 (s, 3 H), 3.20–1.65 (series of m, 6 H), 1.47 (d, J = 6.0 Hz, 3 H), 1.22 (s, 3 H). Amide prepared from racemic 1a showed *two* methyl ester absorptions, each of relative area 1.5 H at δ 3.66 and 3.59.
(9) The following library of crystallographic programs was used. Hubbard, C. R.; Quicksall, C. O.; Jacobson, R. A. "The Fast Fourier Algorithm and the Programs ALFF, ALFFDP, ALFFT and FRIEDEL", USAEC Report IS-2625, Iowa State University–Institute for Atomic Research, Ames, Iowa, 1971. Busing, W. R.; Martin, K. O.; Levy, H. A. "A Fortran Crystallographic Least Squares Program", USAEC Report ORNL-TM-305, Oak Ridge National Laboratory, Oak Ridge, Tenn., 1965. Johnson, C. "ORTEP, A Fortran Thermal-Ellipsoid Plot Program", U.S. Atomic Energy Commission Report ORNL-3794, Oak Ridge National Laboratory, Oak Ridge, Tenn., 1965. MULTAN: Germain, G.; Main, P.; Woolfson, M. M. *Acta Crystallogr., Sect. B*, **1970,** *26*, 274.
(10) Photis, J. M.; Paquette, L. A. *J. Am. Chem. Soc.* **1974,** *96*, 4715.
(11) The efficient separation of (−)-**5** from impurities without incurring racemization is a difficult laboratory manipulation. In our earlier report,[1] a dextrorotatory rotation was erroneously given for **5.** We have since come to recognize that those early samples had been unwittingly enriched with the optically active precursor (+)-**3** (owing to incomplete bromination). Consult ref 6.
(12) Huang, W.-Y.; Holmes, H. L.; Fieser, L. F. *J. Am. Chem. Soc.* **1952,** *74*, 5920.
(13) Corey, E. J.; Sachdev, H. S. *J. Org. Chem.* **1975,** *40*, 579.
(14) The procedure involved Diels–Alder addition of a chiral triazolinedione to racemic **9,** separation of the resulting diastereomers, and liberation of the cyclooctatetraene through hydrolysis–oxidation of a urazole of high diastereomeric purity. Details of this method will be reported separately.
(15) Mislow, K. "Introduction to Stereochemistry", W. A. Benjamin: New York, 1965; p 25.
(16) Moscowitz, A.; Charney, E.; Weiss, U.; Ziffer, H. *J. Am. Chem. Soc.* **1961,** *83*, 4661. Jacobs, H. J. C.; Havinga, E. *Recl. Trav. Chim. Pays-Bas* **1965,** *84*, 932. Weiss, U.; Ziffer, H.; Charney, E. *Tetrahedron* **1965,** *21*, 3105. Charney, E. *ibid.*, **1965,** *21*, 3126. Maestro, M.; Moccia, R.; Taddei, G. *Theoret. Chim. Acta* **1967,** *8*, 80. Gould, R. R.; Hoffmann, R. *J. Am. Chem. Soc.* **1970,** *92*, 1813. Hug, W.; Wagnière, G. *Helv. Chim. Acta* **1971,** *54*, 633. Caldwell, D. J.; Eyring, H. "The Theory of Optical Activity", Wiley-Interscience: New York, 1971, pp 223–232. Charney, E.: Edwards, J. M.; Weiss, U.; Ziffer, H. *Tetrahedron* **1972,** *28*, 973. Hug, W.; Wagnière, H. *ibid.* **1972,** *28*, 1241. Nolte, H. J.; Buss, V. *ibid.* **1975,** *31*, 719. Rosenfield, J. S.; Charney, E. *J. Am. Chem. Soc.* **1977,** *99*, 3209.
(17) Burgstahler, A. W.; Barkhurst, R. C. *J. Am. Chem. Soc.* **1970,** *92*, 7601. Beecham, A. F.; Mathieson, A. M.; Johns, S. R.; Lamberton, J. A.; Sioumis, A. A.; Batterham, T. J.; Young, I. G. *Tetrahedron* **1971,** *27*, 3725. Beecham, A. F. *ibid.* **1971,** *27*, 5207. Gawronski, J. K.; Kielczewski, M. A. *Tetrahedron Lett.* **1971,** 2493. Scott, A. I.; Wrixon, A. D. *Tetrahedron* **1971,** *27*, 4787. Andersen, N. H.; Costin, C. R.; Syrdal, D. D.; Svedberg, D. P. *J. Am. Chem. Soc.* **1973,** *95*, 2049. Burgstahler, A. W.; Weigel, L. O.; Gawronski, J. K. *ibid.* **1976,** *98*, 3015. Burgstahler, A. W. Boger, D. L.; Naik, R. C. *Tetrahedron* **1976,** *32*, 309.
(18) Robin, M. B.; Basch, H.; Kuebler, N. A.; Kaplan, B. E.; Meinwald, J. *J. Chem. Phys.* **1968,** *48*, 5037. Yaris, M.; Moscowitz, A.; Berry, R. S. *ibid.*, **1968,** *49*, 3150. Scott, A. I.; Wrixon, A. D. *Tetrahedron* **1970,** *26*, 3695, 3706. Levin, C. C.; Hoffmann, R. *J. Am. Chem. Soc.* **1972,** *94*, 3446. Andersen, N. H.; Costin, C. R.; Shaw, J. R. *ibid.* **1974,** *96*, 3692.
(19) The Ohio State University Dissertation Fellow, 1977–1978.

John M. Gardlik,[19] Larry K. Johnson, Leo A. Paquette*
Evans Chemical Laboratories, The Ohio State University
Columbus, Ohio 43210

Barbara A. Solheim, James P. Springer, Jon Clardy*
Department of Chemistry, Cornell University
Ithaca, New York 14853

Received December 14, 1978

Bond Fixation in Annulenes. 6. Equalization of Ring Inversion and Bond Shifting Energetics in Methyl-Substituted Cyclooctatetraenes. Use of Buttressing Effects for Comparing Transition-State Geometries[1]

Sir:

Cyclooctatetraenes are recognized to be capable of conformational ring inversion (RI) and bond shifting (BS).[2] While it is generally accepted that RI occurs through the D_{4h} planar alternate transition state **1** ($\Delta G^{\ddagger}$ = 12–15 kcal/mol for monosubstituted derivatives[3]), the mechanism for BS has remained controversial. The planar symmetric D_{8h} species **2** has been advanced to explain the permutation of ring carbon

0002-7863/79/1501-1617$01.00/0