Dissymmetric Chromophores. 7.[1] On the Optical Activity of Conjugated Cisoid Dienes: An Experimental-Theoretical Study of 5-Alkyl-1,3-cyclohexadienes

David A. Lightner,*[2a] Thomas D. Bouman,*[2b] Jacek K. Gawroński,[2c] Krystyna Gawrońska,[2c] Jacques L. Chappuis,[2a] B. Vincent Crist,[2a] and Aage E. Hansen[2d]

Contribution from the Departments of Chemistry, University of Nevada, Reno, Nevada 89557, and Southern Illinois University, Edwardsville, Illinois 62026, the Institute of Chemistry, Natural Products Laboratory, Adam Mickiewicz University, Poznan, Poland, and the Department of Physical Chemistry, H. C. Ørsted Institute, DK-2100 Copenhagen, Denmark.
Received January 12, 1981

Abstract: (+)-(5*R*)-Methyl-1,3-cyclohexadiene (**1**) was synthesized stereoselectively from (+)-pulegone via (-)-(5*R*)-methylcyclohex-2-enone tosylhydrazone (**15**), which was shown to undergo highly regioselective elimination with alkyllithiums. Similarly, (+)-(5*R*)-*tert*-butyl-1,3-cyclohexadiene (**3**) was prepared stereoselectively from (+)-(5*R*)-*tert*-butylcyclohex-2-enone tosylhydrazone (**16**). Variable-temperature circular dichroism (CD) measurements of **1** indicate only small changes in the rotatory strength (*R*) associated with the long-wavelength transition, $\Delta\epsilon_{256} = +5.56$ (25 °C) and $\Delta\epsilon_{258} = +4.10$ (-153 °C); substantial changes but no sign reversal were found in the CD spectra of (-)-(*R*)-α-phellandrene (**2**), $\Delta\epsilon_{265} = -3.88$ (23 °C) and $\Delta\epsilon_{270} = -0.50$ (-179 °C); and a sign reversal was found for **3**, $\Delta\epsilon_{265} = +2.78$ (30 °C) and $\Delta\epsilon_{259} = -3.04$ (-180 °C). The data suggest that **1** exists as a 1:1 mixture of conformers with axial and equatorial methyl groups, whereas the equatorial isopropyl group (of **2**) and *tert*-butyl group (of **3**) are only slightly ($\Delta G^\circ \approx 250$ and 400 cal/mol, respectively) more favored than the corresponding axial group. Ab initio calculations in the localized orbital random phase approximation (LORPA) for **1** and other methyl-1,3-cyclohexadienes show that: (1) the *net* Cotton effect (CE) for the 260-nm transition in these molecules follows the diene helicity rule, (2) the sign and magnitude of the CE of this transition are dominated by the axial allylic bonds (groups), and (3) the sign of the contribution to the CE due to the cisoid diene moiety *alone* is opposite to that predicted by the helicity rule, as is also the sign of the contributions due to the equatorial allylic bonds (groups) and the C_5-C_6 bond in the cyclohexadiene rings.

Introduction

The relationship between the molecular structure of chiral cisoid 1,3-dienes and their optical rotatory dispersion (ORD) or circular dichroism (CD) spectra has been a subject of long-standing interest.[3] The earliest proposed relationship focused on the relative orientation of the carbon-carbon bonds of an inherently dissymmetric diene chromophore and assumed that the skewness or helicity of the diene controlled the Cotton effect (CE) sign associated with the long-wavelength electronic transition.[4-6] Thus, with the support of Hückel π-electron calculations and ORD curves for about a dozen compounds, the diene helicity rule[6] emerged: a strong (+) CE means a cisoid diene with right-handed (**P**) helicity; a strong (-) CE means a cisoid diene with left-handed (**M**) helicity (Figure 1). At that time, only one diene (-)-(*R*)-α-phellandrene, seemed not to fit the rule,[5] which required a predominantly axial isopropyl conformer.

The diene helicity rule was subsequently extended to transoid dienes[7] and even conjugated ketones.[3c] Despite the early ambiguities with α-phellandrene, however, it remained a widely accepted guide for cisoid diene stereochemistry until it was challenged[8] by one of its original authors,[5] who convincingly showed that some steroid cisoid dienes and enones do not obey the rule.[8] In the expanded view, allylic axial bonds are throught to contribute in a significant, often sign-determining way to the CE[3b,8,9] as shown in Figure 2.

Subsequently, the concept of allylic axial bond contributions was extended to transoid dienes and other conjugated systems.[3b] It was also supported by CNDO/S SCF molecular orbital calculations on 1,3-cyclohexadiene (assumed skew angle = 14°) substituted with one or more methyl groups at C_5 and C_6.[10a] Those calculations and more recent ab initio SCF-CI calculations on 1,3-butadiene and 1-butene[10b] confirmed that CE contributions from allylic substituents can outweigh those from the skewed diene chromophore. They also indicated that contributions from allylic axial groups are especially large. Calculations on 1,3-butadiene[10,11] also indicated that **P** helicity gives rise to a (+) CE. However, as has been pointed out,[11] the angle between the computed induced electric and magnetic moments associated with the long-wavelength diene transition is very close to 90° in a molecular coordinate system centered on the C_2-C_3 bond; consequently, the magnitude of the rotatory strength and perhaps even the sign are sensitive to details of the computational method. Recently, the diene helicity and allylic chirality rules have been blended into sector rules for cisoid dienes.[12]

In this work we present a reexamination of cisoid diene chirality in the form of a detailed experimental and theoretical analysis

(1) Presented in part at the Second Chemical Congress of the North American Continent, Las Vegas, NV, Aug. 24-29, 1980. For part VI, see: Lightner, D. A.; Crist, B. V. *Tetrahedron* **1981**, *37*, 685-688.

(2) (a) University of Nevada. (b) Southern Illinois University at Edwardsville. (c) Adam Mickiewicz University. (d) H. C. Ørsted Institute.

(3) For reviews of this field, see: (a) Charney, E. "The Molecular Basis of Optical Activity"; Wiley: New York, 1979; pp 217-226. (b) Burgstahler, A. W.; Barkhurst, R. C.; Gawronski, J. K. In "Modern Methods of Steroid Analysis"; E. Heftmann, Ed.; Academic Press: New York, 1973; Chapter 16. (c) Snatzke, G.; Snatzke, F. In "Fundamental Aspects and Recent Developments in Optical Rotatory Dispersion and Circular Dichroism"; F. Ciardelli and P. Salvadori, Eds.; Heyden & Son: New York, 1973; Chapter 3.5. (d) Snatzke, G. In "Optical Activity and Chiral Discrimination"; S. F. Mason, Ed.; D. Reidel: Dordrecht, 1979; pp 48-55. (e) Weiss, H.; Ziffer, H.; Charney, E. *Tetrahedron* **1965**, *21*, 3105-3120.

(4) Deen, R.; Jacobs, H. J. C. *Proc. K. Ned. Akad. Wet.* **1961**, *64*, 313-315.

(5) Burgstahler, A. W.; Ziffer, H.; Weiss, U. *J. Am. Chem. Soc.* **1961**, *83*, 4660-4661.

(6) (a) Moscowitz; A.; Charney, E.; Weiss, U.; Ziffer, H. *J. Am. Chem. Soc.* **1961**, *83*, 4661-4663. (b) Charney, E. *Tetrahedron*, **1965**, *21*, 3127-3139. Diene **25** was recently prepared by Professor J. E. Gurst (University of West Florida); it has $R = +24.2 \times 10^{-40}$, $\Delta\epsilon_{259} = +7.55$, and $\epsilon_{261} = 3731$ (*n*-heptane).

(7) Charney, E.; Ziffer, H.; Weiss, U. *Tetrahedron* **1965**, *21*, 3121-3126.

(8) Burgstahler, A. W.; Barkhurst, R. C. *J. Am. Chem. Soc.* **1970**, *92*, 7601-7603.

(9) Burgstahler, A. W.; Weigel, L. O.; Gawroński, J. K. *J. Am. Chem. Soc.* **1976**, *98*, 3015-3016.

(10) (a) Rosenfield, J. S.; Charney, E. *J. Am. Chem. Soc.* **1977**, *99*, 3209-3214. (b) Rauk, A.; Peoples, H. A. *J. Comput. Chem.* **1980**, *1*, 240-256.

(11) Bouman, T. D.; Hansen, Aa. E. *Chem. Phys. Lett.* **1977**, *45*, 326-329.

(12) (a) Weigang, O. E. *J. Am. Chem. Soc.* **1979**, *101*, 1965-1975. (b) Moriarty, R. M.; Paaren, H. E.; Weiss, U.; Whalley, W. B. *Ibid.* **1979**, *101*, 6804-6810.

0002-7863/81/1503-5314$01.25/0

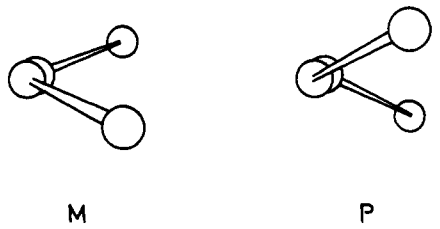


Figure 1. Models showing the helicity of cisoid 1,3-dienes. **M** (minus) corresponds to left-handed helicity and a negative Cotton effect in the diene helicity rule; **P** (plus) corresponds to right-handed helicity and a positive Cotton effect.

Figure 2. Signs of allylic axial chirality contributions for cisoid 1,3-dienes. The **M** and **P** helicities of the dienes correspond to a left- and a right-handed helicity, respectively.

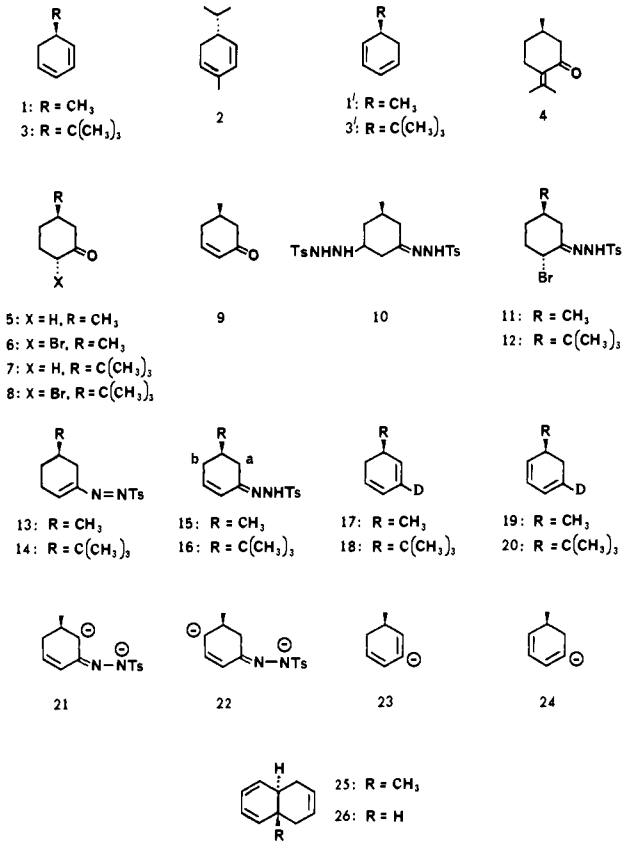
of the chiroptical properties of (+)-(5*R*)-methyl-1,3-cyclohexadiene (**1**), (-)-(*R*)-α-phellandrene (**2**) [(-)-(5*R*)-isopropyl-2-methyl-1,3-cyclohexadiene],[13] and (+)-(5*R*)-*tert*-butyl-1,3-cyclohexadiene (**3**). The theoretical analysis is based on ab initio calculations of the chiroptical properties for the lower energy electronic transitions in a number of isomers and conformers of methyl-1,3-cyclohexadienes, using a localized molecular orbital framework, followed by the full random-phase approximation (RPA) for the excitation properties (for leading references see ref 14a,c,d). In general, the use of a localized molecular orbital basis allows a more direct analysis of the contributions to the total chiroptical properties due to individual fragments and/or bonds in the molecules. In this paper it allows us to discuss more quantitatively the respective contributions from the twisted diene chromophore and from the allylic bonds and/or substituents. We find, in fact, that we can extract approximately additive bond and group contributions to the rotatory strength of the lowest transition in these molecules, and that these bond and group contributions can be employed to yield qualitatively satisfactory chiroptical properties for the equatorial and axial conformers of **2** and **3**.

In what follows we shall first describe the synthesis and determination of absolute stereochemistry of **1** and **3**. Then we present the experimental temperature-dependent CD and NMR spectra of **1**, **2**, and **3**, from which we extract conformer properties. Following an outline of the computational method, the calculations and the theoretical analysis of **1** and other methyl-substituted and unsubstituted 1,3-cyclohexadienes are presented next in the localized orbital RPA (LORPA). The theoretical results are compared with the experimental CD curves for **1**, **2**, and **3** and discussed in relation to other work, followed finally by a section containing concluding remarks.

Synthesis and Stereochemistry

It was essential to this work that the absolute configuration and enantiomeric excess (ee) of **1**, **2**, and **3** be known with certainty. Preferably, the dienes would be optically pure. The natural product, (-)-(*R*)-α-phellandrene (**2**), used herein has the highest reported rotation $[\alpha]_D$ -229° (*c* 1.0, *n*-hexane); we assume it to be optically pure. Its absolute configuration has been determined

Chart I



by classical degradation methods.[15] Optically active 5-methyl-1,3-cyclohexadiene, apparently mainly **1**, has been prepared[16] by bis-dehydrobromination of (+)-3,4-dibromo-1-methylcyclohexane obtained from bromine addition to (+)-3-methylcyclohexene. Because we were not entirely certain that we could know the ee of the diene prepared in this way, we conceived of a potentially more stereoselective route involving *n*-butyllithium reaction[17] with the tosylhydrazone of α,β-unsaturated ketone **9**. Conveniently, the natural product (+)-pulegone (**4**) of known,[18] classically determined absolute configuration[19] could serve as the starting material. Optically pure **4** was converted to (+)-(3*R*)-methylcyclohexanone (**5**) to retroaldolization[20] and brominated to give the previously described,[21] crystalline bromo ketone **6**. Dehydrobromination of **6** using $CaCO_3$ in dimethylacetamide[22] led to an improved yield of previously reported **9**.[21] Unfortunately, **9** reacts with *p*-toluenesulfonylhydrazine, as does 2-cyclohexenone,[23a] to give the bis-adduct (**9** → **10**)—even under carefully controlled conditions with 1 equiv of tosylhydrazine. The desired derivative **15** could be prepared, however, via **11**, the tosylhydrazone of **6**.[23b] Thus, **11** was dehydrobrominated under mild conditions using $NaHCO_3$ to give the unstable, crystalline tosylazine **13**, treatment of which with excess triethylamine led to the desired hydrazone **15** (presumably a mixture of syn and anti isomers). Tosylhydrazone **15** could be prepared more conveniently directly from

(13) (a) Snatzke, G.; Kovats, E. Sz.; Ohloff, G. *Tetrahedron Lett.* **1968**, 4551–4553. (b) Snatzke, G. *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 14–25. (c) The differing CD data might be due to difficulties associated with obtaining CD spectra of strongly allowed electronic transitions and attributable to high sample concentrations (>10^{-4} M) and instrumental factors.

(14) (a) Bouman, T. D.; Hansen, Aa. E. *J. Chem. Phys.* **1977**, *66*, 3460–3467. (b) Hansen, Aa. E.; Bouman, T. D. *Mol. Phys.* **1979**, *37*, 1713–1724. (c) *Adv. Chem. Phys.* **1980**, *44*, 545–644. (d) Bouman, T. D.; Voigt, B.; Hansen, Aa. E. *J. Am. Chem. Soc.* **1979**, *101*, 550–558.

(15) Freudenberg, K.; Lwowski, W. *Justus Liebigs Ann. Chem.* **1954**, *587*, 213–225, and references therein.

(16) Mousseron, M.; Winternitz, F. *Bull. Soc. Chim. Fr.* **1946**, 232–239.

(17) Shapiro, R. H. *Org. React.* **1976**, *23*, 405–507. Stemke, J. E.; Chamberlin, R. A.; Bond, F. T. *Tetrahedron Lett.* **1976**, 2947–2950.

(18) Djerassi, C.; Krakower, G. W. *J. Am. Chem. Soc.* **1959**, *81*, 237–242.

(19) Eisenbraun, E. J.; McElvain, S. M. *J. Am. Chem. Soc.* **1955**, *77*, 3383–3384.

(20) Lightner, D. A.; Docks, E. L. *Tetrahedron* **1979**, *35*, 713–720.

(21) Allinger, N. L.; Riew, C. K. *J. Org. Chem.* **1975**, *40*, 1316–1321.

(22) See, for example, Green, G. F.; Long, A. G. *J. Chem. Soc.* **1961**, 2532–2543. Zurflüh, R.; Tamm, Ch. *Helv. Chim. Acta* **1972**, *55*, 2495–2517.

(23) (a) Kirmse, W.; Ruetz, L. *Justus Liebigs Ann. Chem.* **1969**, *726*, 30–35. (b) Dondini, A.; Rossini, G.; Caglioti, L. *J. Chem. Soc. B* **1968**, 1404–1407.

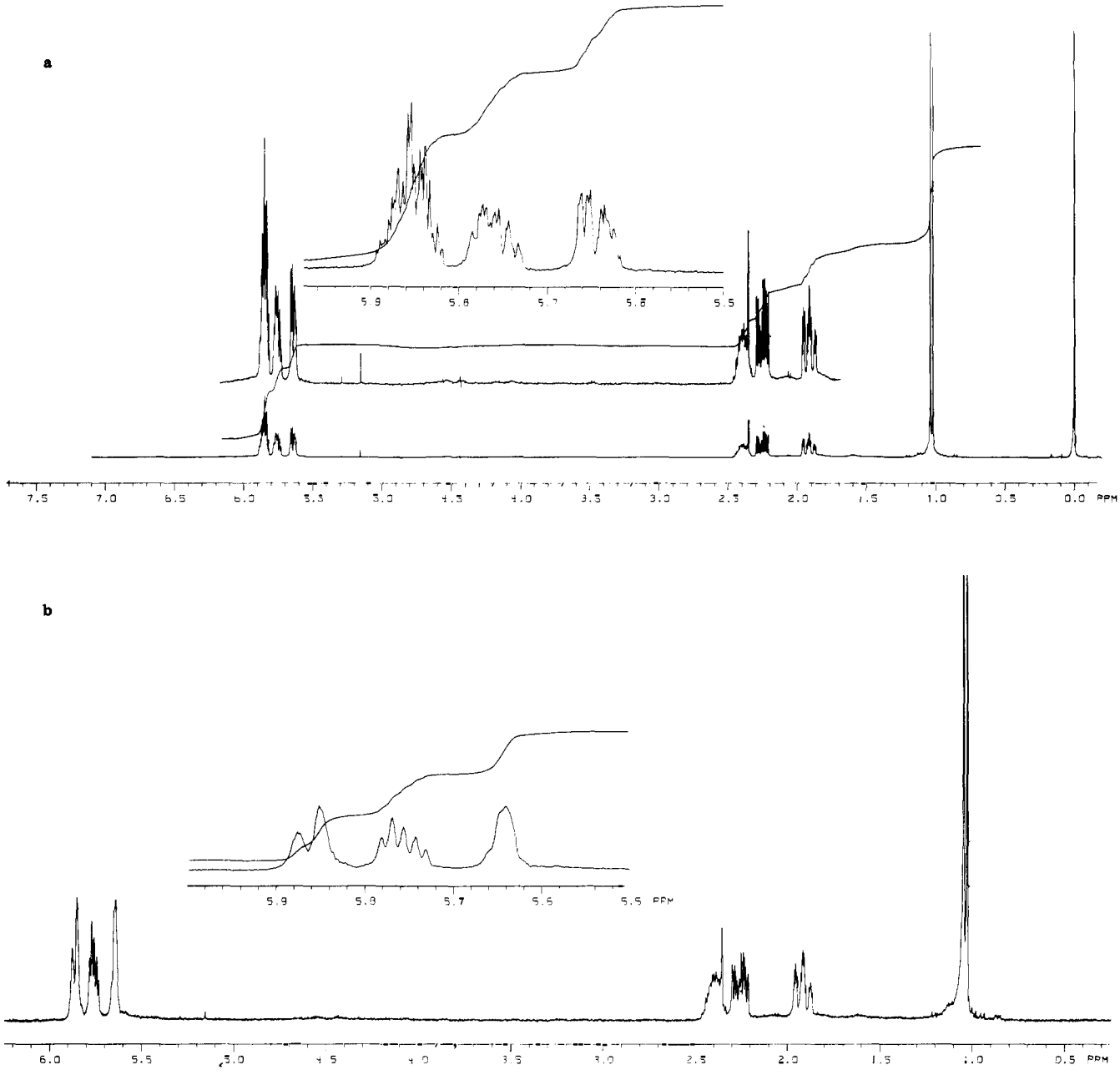


Figure 3. 360-MHz ^{1}H NMR spectra of: (a) (+)-(5*R*)-methyl-1,3-cyclohexadiene (**1**) and (b) (+)-(5*R*)-methyl-3-deuterio-1,3-cyclohexadiene (**17**) run in $CDCl_3$ at 25 °C and reported in δ (ppm) downfield from tetramethylsilane. The vinyl proton region of each spectrum is offset and scale expanded for clarity of integration. In (a) integration gives: 474.93 from δ 5.92 to 5.80, 246.42 from δ 5.80 to 5.69, and 245.30 from δ 5.69 to 5.59, yielding ratios 1.936:1.005:1.000, respectively. In (b) integration gives 357.15 from δ 5.90 to 5.81, 337.88 from δ 5.81 to 5.69, and 336.92 from δ 5.69 to 5.59, yielding ratios 1.060:1.003:1.000, respectively.

11 by careful reaction with triethylamine. Treatment of **15** with *n*-BuLi at −60 °C led to **1**.

In each step leading from **4** to **15** it seems clear that the reactions proceed with unchanging absolute stereochemistry at the single asymmetric center. The final step, **15** → **1**, is, however, less clear. The absolute stereochemistry of the diene product depends on the reaction mechanism, and if two mechanisms compete, the relative rates will determine the ee. If the *n*-BuLi base removes a proton from the α position *a* of **15**, intermediate **21** should lead to diene product **1**, but if the allylic proton at *b* is removed to give **22**, the enantiomeric diene **1′** would be the expected product—or possibly a mixture of **1** and **1′** would obtain leading to (partially) racemized diene. In order to clarify the situation, if D_2O is used in the quenching step (in place of H_2O), the product from intermediate **21** would proceed via **23** to give **17**, whereas that from **22** would proceed via **24** to give **19**. Dienes **17** and **19** are equivalent to the protio enantiomers **1** and **1′**, respectively, but they are, in principle, distinguishable by NMR.

In practice we found that the 360-MHz ^{1}H NMR (Figure 3) of 5-methyl-1,3-cyclohexadiene cleanly separated the four olefinic protons signals into three groups of relative intensities 2:1:1 at δ 5.86, 5.76, and 5.64, respectively. We assign the latter two signals to the outer protons of the diene system, and the lowest field signal we assign to the inner two protons. These assignments are consistent with those for 1,3-cyclohexadiene.[24] Therefore, if product **17** is formed exclusively, the lowest field signal should decrease in intensity, and the relative integration of the three sets of signals should become 1:1:1. If **19** is formed exclusively, the signal at δ 5.76 should vanish, leaving a 2:1 relative intensity of signals at δ 5.86 and 5.64. Furthermore, if both elimination mechanisms operate, the ^{1}H NMR should show decreases in both the δ 5.86 and 5.76 signals relative to the δ 5.64 signal. In fact, when the tosylhydrazone elimination reaction is quenched with

(24) A. d. Heyde, W.; Lüttke, W. *Chem. Ber.* **1978**, *111*, 2384–2395. Crews, P. *J. Am. Chem. Soc.* **1973**, *95*, 636–638.

D_2O, the resultant monodeuterio 5-methyl-1,3-cyclohexadiene ^1H NMR spectrum shows a 1:1:1 ratio of peaks, and very careful integration of the δ 5.64 and 5.76 signals reveals an intensity ratio of 1.003 (consistent with **17**) for the deuterio analog and 1.005 for the protio analog (**1**). These findings are supported qualitatively by the ^{13}C NMR spectra: the ^{13}C-3 signal of the deuterated diene is no longer an OFR doublet and is considerably reduced in intensity. Therefore, we conclude that the *n*-BuLi induced tosylhydrazone elimination of **15** at −60 °C proceeds by one mechanism only (**15** → **21** → **23** → **1**) with complete retention of configuration. At 0 °C the reaction is less selective but proceeds with at least 96% retention of configuration (see Experimental Section). Consequently, we believe that **1** has the same *R* absolute configuration and ee (100%) as the starting (+)-pulegone (**4**). And, on the basis of comparative specific rotations, we can further conclude that the sample of optically active 5-methyl-1,3-cyclohexadiene prepared by Mousseron and Winternitz[16] also has the 5*R* absolute configuration but only a 44% ee.

Similar stereochemical arguments obtain in the synthesis of **3**. Optically pure **7** of known absolute configuration[25] was obtained as described[25,26] following reduction of 3-*tert*-butylphenol to *cis*-3-*tert*-butylcyclohexanol and resolution of its half-acid phthalate ester with brucine.[26] Optical rotations of the cis alcohol agree with the highest reported rotations.[26] Futhermore, both the ee and absolute configuration were confirmed by LIS NMR measurements[27] on the Mosher ester of *trans*-3-*tert*-butylcyclohexanol obtained by catalytic hydrogenation of **7**.[25] Bromo ketone **8** was converted smoothly to tosylhydrazone **16** either via the tosylazine (**14**) or directly (vide supra). Stereospecific reaction of *n*-butyllithium with **16** gave the desired (5*R*)-*tert*-butyl-1,3-cyclohexadiene (**3**). In this reaction, as with that involving the methyl isomer (**15**), D_2O quenching revealed that only the α proton (*a*) had been abstracted. Product analysis by ^1H and ^{13}C NMR, as before, showed that >99.5% of **18** (relative to **20**) is formed at −60 °C.

Experimental Results and Discussion

Molecular Geometries, NMR and CD Spectra, and Rotatory Strengths. If the cyclohexadiene rings of **1**, **2**, and **3** assume the same 1,-diplanar conformation as that of 1,3-cyclohexadiene,[28] two classically different conformational isomers obtain: one with a pseudo (ψ)-axial 5-alkyl group, the other with a ψ-equatorial 5-alkyl group. As shown in Figure 4, the conformer with a ψ-axial methyl or *tert*-butyl group (**a**) has a right-handed (**P**) diene helicity, whereas that with a ψ-equatorial group (**e**) has a left-handed (**M**) diene helicity. Because **2** belongs to the mirror-image series, its conformer with a ψ-axial isopropyl group has **M** diene helicity, and that with a ψ-equatorial isopropyl group has **P** diene helicity. Since the conformational inversion barrier (**P** ⇄ **M**) for 1,3-cyclohexadiene is small (~3 kcal/mol),[29] we expect a similarly small barrier for the interconversion of the **P** and **M** conformers of **1**, **2**, and **3**. Indeed, consistent with this expectation we have not been able to detect any additional splitting of the ^{13}C or ^1H NMR signals of **1**, **2**, or **3** in going from 25 to −100 °C. It therefore appears that the **1a** ⇄ **1e**, **2a** ⇄ **2e**, and **3a** ⇄ **3e** equilibria are facile.

An understanding of factors influencing the relative stabilities of axially and equatorially substituted cyclohexanes has long been a goal of conformational analysis.[30-34] Conformational free-energy

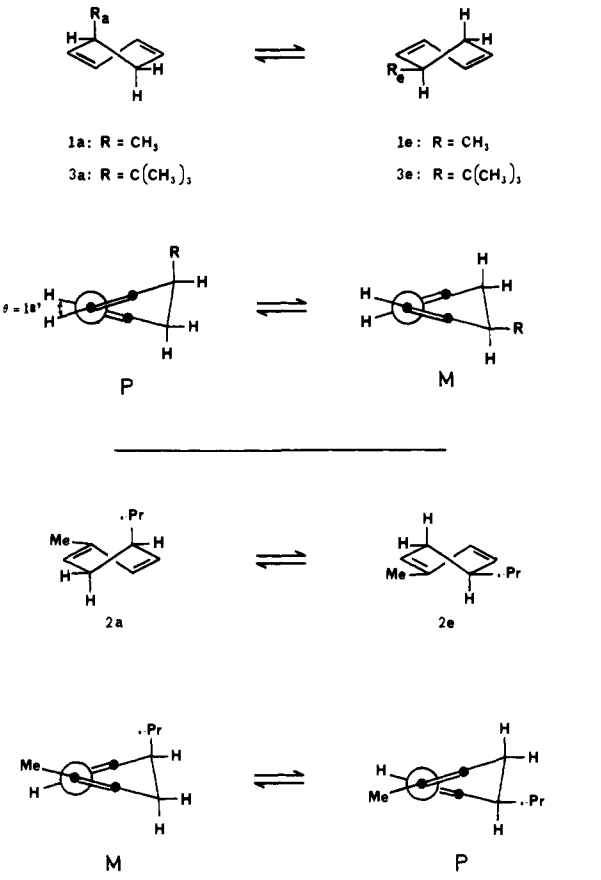


Figure 4. Upper half: Conformational drawings of (+)-(5*R*)-methyl-1,3-cyclohexadiene (**1**) and (+)-(5*R*)-*tert*-butyl-1,3-cyclohexadiene (**3**) showing the ψ-axial CH_3 or $C(CH_3)_3$ group associated with **P** diene chirality, and the ψ-equatorial group with **M** diene chirality. The skew angle (θ) indicated at 18° comes from ref 28. Lower half: conformational drawings of (−)-(*R*)-α-phellandrene (**2**) showing the ψ-axial isopropyl group associated with **M** diene helicity, and the ψ-equatorial isopropyl group associated with P diene helicity.

differences ($\Delta G°_{ax\text{-}eq}$) have been determined for methyl- (1.7 kcal/mol[35]), isopropyl- (2.15 kcal/mol[35]), and *tert*-butyl- (>4.4,[35] 5.4[34] kcal/mol) substituted cyclohexanes, which are interconverted by a chair ⇄ chair ring conformational isomerism. The principal destabilizing influence on the axial alkyl configuration is seen commonly as a combination of gauche interactions and across the ring 1,3-diaxial interactions,[30,31,33,36] although gauche H|H interactions may explain the observations just as well.[34] When 1,3-diaxial interactions are reduced, the axial conformer becomes more populated. For example, $\Delta H°_{ax\text{-}eq}$ = 585 ± 27 and 972 ± 83 cal/mol for 3-methyl- and 4-methylcyclohexene, respectively;[36] $\Delta G°_{ax\text{-}eq}$ = 0.80–0.97, 0.98, and 1.36≃1.46 kcal/mol for 5-methyl-, 5-isopropyl-, and 5-*tert*-butyl-1,3-dioxane, respectively.[31] Similar trends might reasonably be expected for 5-alkyl-1,3-cyclohexadienes.

The question of the relative stabilities of conformers **2a** and **2e** has been associated with diene chirality rules from the beginning.[3,5,10,12b,37-39] At first it appeared that the diene helicity

(25) Djerassi, C.; Warawa, E. J.; Wolff, R. E.; Eisenbraun, E. J. *J. Org. Chem.* **1960**, *25*, 917–921.
(26) Belluci, G.; Ingrosso, G.; Marsili, A.; Mastrorilli, E.; Morelli, I. *J. Org. Chem.* **1977**, *42*, 1079–1081.
(27) Kalyanam, N.; Lightner, D. A. *Tetrahedron Lett.* **1979**, *20*, 415–418.
(28) The diene C=C to C=C torsion angle has been reported as 18.3°: Oberhammer, H.; Bauer, S. H. *J. Am. Chem. Soc.* **1969**, *91*, 10–16.
(29) Carreiera, L. A.; Carter, R. O.; Durig, S. R. *J. Chem. Phys.* **1973**, *59*, 812–816.
(30) (a) Eliel, E. L.; Allinger, N. L.; Angyal, S. J.; Morrison, G. A. "Conformational Analysis"; Wiley-Interscience: New York, 1965; Chapter 2. (b) Testa, B. "Principles of Organic Stereochemistry"; Marcel Dekker: New York, 1979; pp 116–119. (c) Dale, J. "Stereochemistry and Conformational Analysis"; Verlag Chemie: Weinheim, 1978; pp 153–156.
(31) Eliel, E. L.; Knoeber, M. C. *J. Am. Chem. Soc.* **1968**, *90*, 3444–3458.
(32) Allinger, N. L.; Hirsch, J. A.; Miller, M. A.; Tyminski, I. J.; VanCatledge, F. A. *J. Am. Chem. Soc.* **1968**, *90*, 1199–1210.
(33) Garbisch, E. W.; Hawkins, B. L., Jr.; MacKay, K. D. In "Conformational Analysis"; Chiurdoglu, G., Ed.; Academic Press: New York, 1971; pp 93–109.
(34) Wertz, D. H.; Allinger, N. L. *Tetrahedron* **1974**, *30*, 1579–1586.
(35) Hirsch, J. A. *Top. Stereochem.* **1967**, *1*, 199–227.
(36) (a) Tan, H.-W., Ph.D. Dissertation, University of Minnesota, 1971; *Chem. Abstr.* **1972**, *76*, 139772r. (b) MacKay, K. D., Ph.D. Dissertation, University of Minnesota, 1969; *Chem. Abstr.* **1970**, *73*, 14006a. Hawkins, B. L. Ph.D. Dissertation, University of Minnesota, 1969; *Chem. Abstr.* **1971**, *75*, 151256n.
(37) Ziffer, H.; Charney, E.; Weiss, U. *J. Am. Chem. Soc.* **1962**, *84*, 2961–2963.

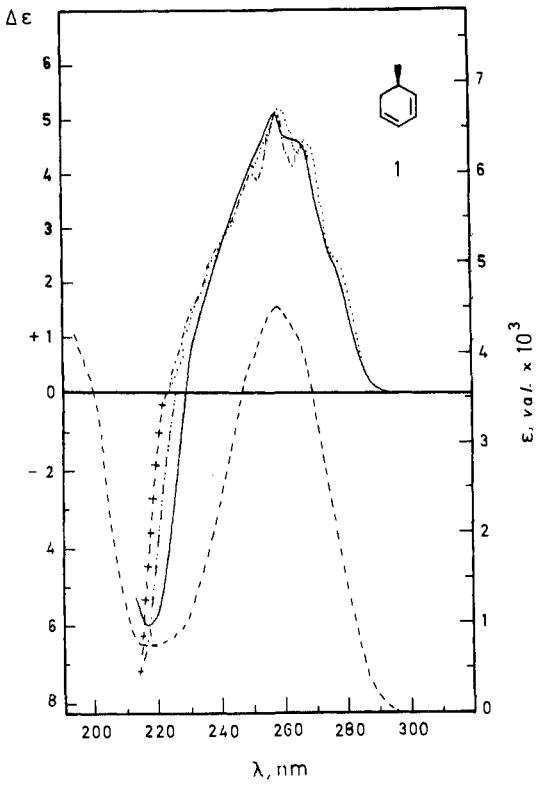


Figure 5. Ultraviolet (---) spectrum of (+)-(5*R*)-methyl-1,3-cyclohexadiene (**1**) at 25 °C in methylcyclohexane. Circular dichroism spectra of **1** were measured in 4:1 methylcyclohexane–isopentane at 25.5 °C (—), −44 °C (-··-··-), −70 °C (···), 100 °C (-+-+-), and −152 °C (-·-·-) and are uncorrected for solvent contraction.

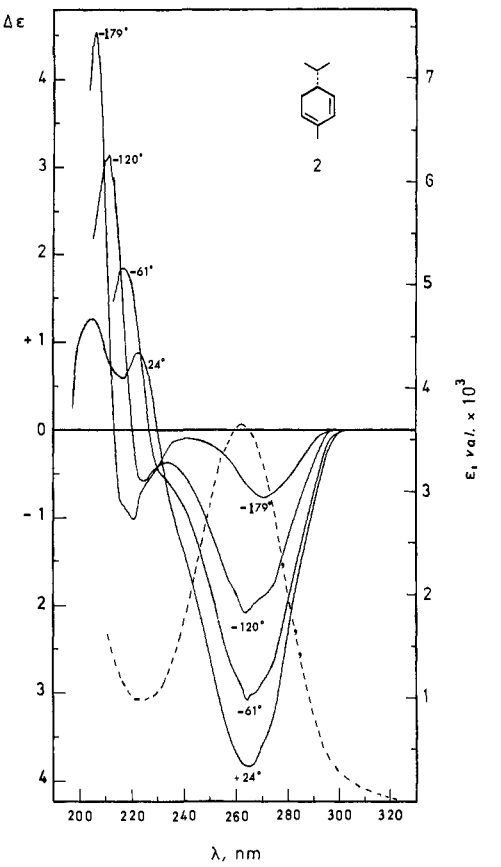


Figure 6. Ultraviolet (---) spectrum of (−)-(*R*)-α-phellandrene (**2**) at 25 °C in methylcyclohexane. Circular dichroism (—) spectra of **2** were measured in 4:1 methylcyclohexane–isopentane with the temperatures (°C) indicated on the curves and are uncorrected for solvent contraction.

rule predicted the wrong CE sign for **2**.[5] The observed room-temperature (−)-CE required a predominate left-handed helical diene isomer with an associated ψ-axial isopropyl group; i.e., the diene helicity rule seemed to say that an axial isopropyl group was favored over equatorial.[3b,5] This surprising conclusion was readdressed subsequently by measuring an increasing negative molecular rotation of **2** at 302 nm over the temperature range +11 to +82 °C—an observation which showed that the less stable conformer has a more negative CE and also suggested, on the basis of helicity, that **2a** is less stable than **2e** but has an inherently larger magnitude (−)-CE.[37] Shortly thereafter, ORD measurements supported these contentions by showing that the CE of **2** decreased in amplitude in going from +20 to −150 °C.[39]

The actual values of the conformational energies for **2a** ⇄ **2e**, **1a** ⇄ **1e**, and **3a** ⇄ **3e** were determined by several methods. Conformer **2e** has been estimated to be more stable than **2a** by ΔH° = 460 cal/mol (with ΔS° = 0) by a study of the temperature dependence of the product ratios for photochemical electrocyclic ring opening of **2**.[40] A similar study on a series of 5-alkyl-1,3-cyclohexadienes obtained ΔG°_{300} = 240, 950, and 2980 cal/mol for methyl, isopropyl, and *tert*-butyl substituents, respectively.[41] Curiously, the same method gives two different conformational energies for isopropyl (460 and 950 cal/mol). However, neither of these studies[40,41] assumed any dynamic effects on the product ratios. The results are based on the assumption that there are no differences in rates of ring opening for each reacting conformer, and also that the conformations of the excited states leading to products are identified with (only two) ground-state conformations. An even different value (ΔH° = 280 cal/mol, ΔS° = 2.2 eu)

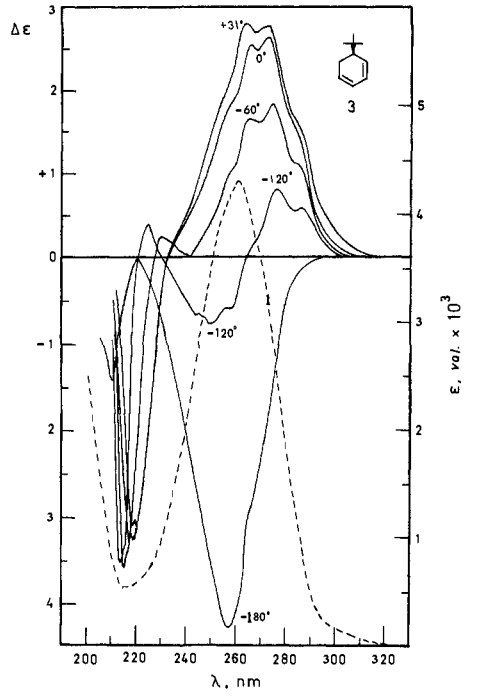
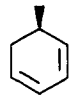


Figure 7. Ultraviolet (---) spectrum of (+)-(5*R*)-*tert*-butyl-1,3-cyclohexadiene (**3**) at 28 °C in methylcyclohexane–isopentane (4:1). Circular dichroism (—) spectra of **3** were measured in the same solvent mixture, and temperatures (°C) are indicated on the curves and are uncorrected for solvent contraction.

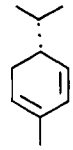
finding **2e** more stable than **2a**[3c] was determined from low-temperature CD measurements in which the room-temperature (−)-CE ($\Delta\epsilon \sim -10$) became (+) ($\Delta\epsilon \sim +6$) at −177 °C.[13] In unpublished

(38) Charney, E.; Lee, C.-H.; Rosenfield, J. S. *J. Am. Chem. Soc.* **1979**, *101*, 6802–6804.
(39) Horsman, G.; Emeis, C. A. *Tetrahedron* **1966**, *22*, 167–173.
(40) Baldwin, J. E.; Kruger, S. M. *J. Am. Chem. Soc.* **1969**, *91*, 6444–6447.
(41) (a) Spangler, C. W.; Hennis, R. P. *J. Chem. Soc., Chem. Commun.* **1972**, 24–25. (b) Hennis, R. P. Ph.D. Dissertation, Northern Illinois University, 1972.

Table I. Circular Dichroism Data for (+)-(5*R*)-Methyl-1,3-cyclohexadiene (**1**), (−)-(*R*)-α-Phellandrene (**2**), and (+)-(5*R*)-*tert*-Butyl-1,3-cyclohexadiene (**3**)[a]



1



2

3

T, °C	λmax	Δε	R[b]	T, °C	λmax	Δε	R[b]	T, °C	λmax	Δε	R[b]
+25.2	256	+5.56	+17.0	+23	265	−3.88	−12.4	+30.5	265	+2.78	+8.98
−29.5	257.5	+5.25	+16.6	−30	265	−3.45	−11.3	+0.3	274	+2.51	+7.32
−60.0	256.5	+5.18	+16.2	−70	265	−3.07	−9.96	−60.4	275	+1.61	+3.97
−99.7	258	+4.59	+14.8								
−128.7	258	+4.28	+14.4	−110	265	−2.43	−7.76	−120.2	277 250	+0.638 −0.638	−0.0966
−152.8	258	+4.10	+12.4	−150	268	−1.45	−4.73				
−174.8[c]	258	+3.36	+9.35	−179	270	−0.505	−1.49	−180	259	−3.04	−8.16

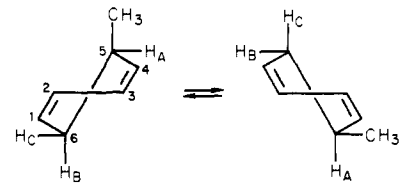
[a] Determined in methylcyclohexane-isopentane (4:1 v/v) and corrected for solvent contraction as per Korver, O.; Bosma, J. *Anal. Chem.* 1971, *43*, 1119. [b] Rotatory strength, value × 10^{-40}. [c] At this temperature, some crystallization occurred.

work involving a study of the temperature dependence of the vicinal coupling constants in the ^{1}H NMR of 5-trideuteriomethyl-1,2,3,4-tetradeuterio-1,3-cyclohexadiene, conformer **1e** has been estimated to be more stable than **1a** ($\Delta H°$ = 538 ± 23 cal/mol with $\Delta S° \sim 0$).[36a] The numbers give cause for concern because they suggest that a ψ-axial isopropyl group may be more stable than a ψ-axial methyl group, each relative to its ψ-equatorial isomer.

Analyses of the variable-temperature CD data (Figures 5, 6, and 7, and Table I) clarify the situation. Strikingly, the rotatory strength (*R*) values for the long-wavelength transition of **1** are essentially invariant, whereas those for **2** show substantial changes, and those for **3** show a CE sign inversion. Moreover, in contrast to the data reported by Snatzke[3c,13] and by Rauk,[10b] the long-wavelength CE of **2** does not reverse sign upon temperature lowering to −179 °C,[42] and the room-temperature Δε value (−3.88) is considerably smaller than Snatzke's (Δε ∼ −10) on the one hand, but greater than Rauk's (Δε ∼ −2.8) on the other.[13c] Assuming only a **2a** ⇄ **2e** conformational equilibrium, and applying the free-energy extrapolation method of Moscowitz, Wellman, and Djerassi,[43] we estimate that the **2e** conformer is more stable than **2a** by $\Delta G°_{ax\text{-}eq} \approx 250$ cal/mol with corresponding rotatory strength values, $R_{2a} = -48.2 \times 10^{-40}$ cgs and $R_{2e} = +10.9 \times 10^{-40}$ cgs. The data for **1** do not lend themselves as easily to a similar treatment; we estimate that **1e** is only slightly more stable than **1a** (with $\Delta G°_{ax\text{-}eq}$ less than 50 cal/mol). The data for **3** lead to a conformational free-energy value, $\Delta G°_{ax\text{-}eq} \approx 400$ cal/mol, for *tert*-butyl, with $R_{3a} = +55.6 \times 10^{-40}$ cgs and $R_{3e} = -15.0 \times 10^{-40}$ cgs. We believe that these data, although different from earlier estimates,[3b,13,36a,40,41] are more nearly correct [$\Delta G°_{ax\text{-}eq} <$ 50 cal/mol for methyl (**1**), ≈250 cal/mol for isopropyl (**2**), and ≈400 cal/mol for *tert*-butyl (**3**)] because they are derived by a thermodynamic method that is sufficiently sensitive to use in the determination of conformational energies of deuterium (vs. hydrogen).[44]

We note that Rauk and Peoples,[10b] in their minimal basis set SCF calculations of molecular mechanics optimized conformers of α-phellandrene, find that the energy difference between the lowest energy equatorial and the lowest energy axial forms is 170 cal/mol, and that all other conformers have significantly higher energies, consistent with our assumption of an effective two-state

Table II, ^{1}H Coupling Constants (*J*, Hz) for (+)-(5*R*)-Methyl-1,3-cyclohexadiene (**1**) (Upper Half) and 1,2,3,4-Tetradeuterio-5-trideuteriomethyl-1,3-cyclohexadiene (Lower Half) at 25 °C.



location of H atom

	1	2	3	4	H_A	H_B	H_C	CH_3
1		9.3	1	1		3.6	1	
2			5	1		1.9	1	
3				9.3	1.9			
4					3.6	4.8		
H_A				(10.52)[a]	(7.73)[b]	8.4	12.9	6.7
H_B					8.5		17.1	
					(3.31)[a]	(16.33)[b]		
H_C					12.6	17.0		
CH_3								

[a] CONAL 2 calculated "best" value for conformer with ψ(a)-CH_3 group (corresponding to 1a). [b] CONAL 2 calculated "best" value for conformer with ψ(e)-CH_3 group (corresponding to 1e).

equilibrium and with our estimates of $\Delta G°_{ax\text{-}eq}$ from our CD data. It may also be noted that, as predicted, the conformational free energies of 5-alkyl-1,3-cyclohexadienes are considerably reduced over the corresponding alkylcyclohexanes, and they follow the same order with increasing group size.

It was of interest to determine whether deuterium (D) at C-3 has an influence on the CE of **1**. In principle, D serves as a steric probe on the diene torsion angle; i.e., the torsion angle of the C=C groups of the diene might be expected to be slightly different in **1** and **17** because of the smaller steric requirement of D vs. H.[44] On the other hand, the angle would be expected to be different in both isomers equivalent to **1a** and **1e**, and might, of course, lead to cancelling effects. We observed no real difference in the CE's of **1** and **17** prepared under identical conditions: $\Delta\epsilon_{256}(\mathbf{1}) = +5.56$, $\Delta\epsilon_{256}(\mathbf{17}) = +5.56$; $\Delta\epsilon_{216.5}(\mathbf{1}) = -6.53$, $\Delta\epsilon_{216.5}(\mathbf{17}) = -6.50$. This system is apparently insensitive to D substitution at C-3, as we have also found in the **3** and **18** pair. Whether D substitution at C-1 or C-4 also leads to the same conclusion has not been tested, nor has the conformational equilibrium been determined for 5-deuterio-1,3-cyclohexadiene.

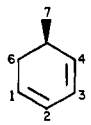
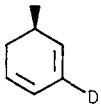
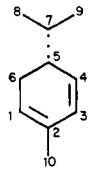
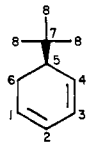
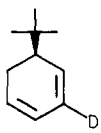
Conformational analysis of **1**, **2**, and **3**, based on variable-temperature CD measurements should be consistent with NMR measurements. Tan[36a] analyzed the dependence of the allylic

(42) The CE sign inversion with temperature lowering has been questioned (ref 38) on the basis of data in ref 37 and 39. In another study, involving gas-phase CD of α- and β-phellandrene, the question of conformational mobility was not addressed: Gross, K. P.; Schnepp, O. *J. Chem. Phys.* **1978**, *68*, 2647–2657.

(43) Moscowitz, A.; Wellman, K.; Djerassi, C. *J. Am. Chem. Soc.* **1963**, *85*, 3515–3516.

(44) Configurational preferences for D vs. H have been determined in conformationally mobile cyclohexanones; see: Lee, S.-F.; Barth, G.; Djerassi, C. *J. Am. Chem. Soc.* **1978**, *100*, 8010–8012.

Table III. Natural Isotopic Abundance ^{13}C NMR and ^{1}H NMR Chemical Shifts[a] for (+)-(5*R*)-Methyl-1,3-cyclohexadiene (1), (+)-(5*R*)-Methyl-1,3-cyclohexadiene-3*d*, (17), (−)-(*R*)-α-Phellandrene (2), (+)-(5*R*)-*tert*-Butyl-1,3-cyclohexadiene (**3**), and (+)-(5*R*)-*tert*-Butyl-**1**,3-cyclohexadiene-3*d* (**18**)

position	1		17		2		3		18	
	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C[b]	^{1}H	^{13}C	^{1}H	^{13}C	^{1}H
1	125.78 (d)	5.76	125.72 (d)	5.76	120.46 (d)	5.65	126.89[d] (d)	5.81	126.78[d] (d)	5.81
2	123.79 (d)	5.86	123.67 (d)	5.86	131.10 (s)		123.97[d] (d)	5.86	123.91[d] (d)	5.86
3	123.32 (d)	5.86	123.26 (s)		129.99[c] (d)	5.42	124.79 (d)	5.91		
4	133.09 (d)	5.64	132.91 (d)	5.64	128.06[c] (d)	5.65	128.71 (d)	5.77	128.47 (d)	5.77
5	27.96 (d)	2.40	27.91 (d)	2.40	39.78 (d)		43.88 (d)	2.11	43.82 (d)	2.11
6	30.83 (t)	2.25 (eq) 1.92 (ax)	30.76 (t)	2.25 (eq) 1.92 (ax)	25.98 (t)	1.99	24.28 (t)	2.19 (eq) 2.06 (ax)	24.28 (t)	2.19 (eq) 2.06 (ax)
7	20.01 (q)	1.03 (d, J = 6.7 Hz)	20.01 (q)	1.03 (d, J = 6.7 Hz)	31.36 (d)		33.00 (s)		33.00 (s)	
8					19.89 (q)	0.873/0.939 (d, J = 6.6 Hz)	27.50 (q)	0.91 (s)	27.44 (q)	0.91 (s)
9					19.89 (q)	0.858/0.924 (d, J = 6.6 Hz)				
10					21.06 (q)	1.71 (s)				

[a] Expressed in δ (ppm) downfield from tetramethylsilane. ^{1}H spectra were run in $CDCl_3$; ^{13}C spectra were run in CD_2Cl_2. [b] Run in $CDCl_3$ solvent. [c] These assignments may be interchanged. [d] Assignments would be interchanged if Δδ values between corresponding carbon signals in 3 and **18** are to parallel those Δδ values found for 1 and 17. The assignments for **1** and 17 follow the relationship that the larger Δδ value (associated with C-1 and C-2) belongs to the carbon closer to the point (C-3) of isotopic substitution: see Wehrli, F. W.; Wirthlin, T. "Interpretation of Carbon-13 NMR Spectra"; Heyden: Philadelphia, 1978; p 108.

vicinal ^{1}H–^{1}H coupling constants and chemical shifts over the range 173 to 373 K using the Garbisch CONAL 2 method[33] to "best fit" a conformational ΔH° = 538 ± 22 cal/mol (ΔS° = 0.0 eu) for 1,2,3,4-tetradeuterio-5-trideuteriomethyl-1,3-cyclohexadiene. The allylic coupling constants observed at 298 K are quite similar to ours for **1** (Table II), which show large vicinal couplings (J_{AB} = 8.4 Hz and J_{AC} = 12.9 Hz) and a very large geminal coupling, J_{BC} = 17.1 Hz (see also Figure 3). Unfortunately, it cannot be easily shown that those values are indeed the averaged coupling constants, e.g., J_{AB}(obsd) = [J_{AB}(**1e**) + J_{AB}(**1a**)]/2, for a dynamic **1a** ⇄ **1e** equilibrium with a 1:1 conformer population, because the "expected" static coupling constants for each conformer are strongly perturbed by the π system. The strong perturbation is exemplified in the large geminal (J_{BC}) coupling. According to the Barfield–Grant analysis for the dependence of the magnitude of the geminal coupling constant on dihedral angle between the methylene group and the adjacent π bond,[45] the π contribution to J_{BC} of **1** should be ~|3|Hz (for an angle of ~8°, as determined from Dreiding models). We therefore feel that the conformational energies (ΔH° = 538 ± 22 cal/mol with ΔS° = 0.0 eu) derived from NMR analyses of vicinal coupling constants[36a] represent upper limits. We believe that the CD value of $\Delta G^\circ_{a\text{-}e}$ < 50 cal/mol is a better one.

Chemical shift values at 25 °C for the ^{1}H and ^{13}C NMR spectra of **1** and **2** are summarized in Table III. Upon lowering the temperature to −100 °C, we can observe no significant signal broadening (or splitting) for **1** in Freon-11 ($CFCl_3$). In **2**, the diastereotopic hydrogens of the *gem*-dimethyl group show clearly as two doublets (25 °C). Slight broadening (but no further splitting) of the ^{1}H signals, including the CH_3 doublets, and their corresponding ^{13}C signals is observed upon cooling to −100 °C in Freon-11. It is unclear why broadening occurs here; it may be due simply to solvational changes rather than changes in the rates of conformational isomerization.

Computational Method

Among the essential ingredients for reliable calculations of electronic intensities are inclusion of all valence electrons and estimates of electron correlation.[14] In this study, we generate SCF molecular orbitals using the ab initio GAUSSIAN 70 program system,[46] in a minimal (STO-4G) atomic orbital basis set, and electron correlation is treated properly through first-order by calculating the excitation properties in the random-phase approximation (RPA).[14b] Previous studies using this scheme[11,14,47] have yielded acceptably accurate intensities for valence-shell transitions, even with small basis sets. To facilitate analysis of the results in terms of structural features of the molecules, we transform the SCF molecular orbitals into localized orbitals (LO's); occupied and virtual MO sets are localized separately, and virtual LO's are spatially paired with their occupied counterparts.[14d] For the double bonds our localization procedure retains local σ and π character for the LO's in these regions.

The electric dipole transition moment for an electronic excitation from the ground state $|0\rangle$ into an excited state $|n\rangle$ can be expressed in a number of equivalent forms,[14c] of which we shall consider only the length form $\langle 0|\mathbf{r}|n\rangle$ and the velocity form $\langle 0|\hat{\nabla}|n\rangle$. In the RPA method these two transition moments are calculated from the following expressions[14]

$$\langle 0|\mathbf{r}|n\rangle = \sqrt{2}\sum_{lm} (X^n_{lm} + Y^n_{lm})\langle l|\mathbf{r}|m\rangle \quad (1)$$

$$\langle 0|\hat{\nabla}|n\rangle = \sqrt{2}\sum_{lm} (X^n_{lm} - Y^n_{lm})\langle l|\hat{\nabla}|m\rangle \quad (2)$$

and the magnetic dipole transition moment is calculated from

$$\langle 0|\mathbf{r} \times \hat{\nabla}|n\rangle = \sqrt{2}\sum_{lm} (X^n_{lm} - Y^n_{lm})\langle l|\mathbf{r} \times \hat{\nabla}|m\rangle \quad (3)$$

Here $\langle l|\mathbf{r}|m\rangle$ is the electric dipole length transition moment for the primitive one-electron excitation from the occupied orbital l into the unoccupied orbital m; $\langle l|\hat{\nabla}|m\rangle$ and $\langle l|\mathbf{r} \times \hat{\nabla}|m\rangle$ are the corresponding electric dipole velocity and magnetic dipole transition moments. The coefficients $X^{(n)}_{lm}$ and $Y^{(n)}_{lm}$, which determine

(45) Barfield, M.; Grant, D. M. *J. Am. Chem. Soc.* **1963**, *85*, 1899–1904.

(46) Hehre, W. J.; Lathan, W. A.; Ditchfield, R.; Newton, M. D.; Pople, J. A. Program QCPE 236, Quantum Chemistry Program Exchange, Indiana University, Bloomington, Ind.

(47) Lightner, D. A.; Gawroński, J. K.; Bouman, T. D. *J. Am. Chem. Soc.* **1980**, *102*, 5749–5754.

the contributions from the individual primitive excitations to the total transition moments, are determined together with the transition energies ΔE_{0n} by solving the following set of coupled equations

$$\boldsymbol{A}\mathbf{X}^{(n)} + \boldsymbol{B}\mathbf{Y}^{(n)} = \Delta E_{0n}\mathbf{X}^{(n)} \quad (4)$$

$$\boldsymbol{B}\mathbf{X}^{(n)} + \boldsymbol{A}\mathbf{Y}^{(n)} = -\Delta E_{0n}\mathbf{Y}^{(n)} \quad (5)$$

Here $\mathbf{X}^{(n)}$ and $\mathbf{Y}^{(n)}$ are column vectors containing the coefficients $X_{lm}^{(n)}$ and $Y_{lm}^{(n)}$, respectively, for the primitive excitations. The $\boldsymbol{A}$ matrix contains the matrix elements of the Hamiltonian between the singly excited configurations, i.e., all $\langle l \rightarrow m|\hat{H}|l' \rightarrow m'\rangle$ elements, whereas the $\boldsymbol{B}$ matrix contains the matrix elements between the Hartree–Fock ground state Δ_0 and the doubly excited configurations, i.e., all $\langle \Delta_0|\hat{H}|_{l'\rightarrow m'}^{l\rightarrow m}\rangle$ elements. In a localized orbital picture the matrices $\boldsymbol{A}$ and $\boldsymbol{B}$ contain the elements[14c]

$$A_{lm,l'm'} = F_{mm'}\delta_{ll'} - F_{ll'}\delta_{mm'} + 2(ml|l'm') - (ll'|mm') \quad (6)$$

$$B_{lm,l'm'} = 2(ml|m'l') - (m'l|l'm) \quad (7)$$

where F_{ij} is the Fock matrix element between LO's i and j and $(ij|kl)$ are electron repulsion integrals in Mulliken's notation; the indexes l,l' refer to LO's occupied in the ground state, and m,m' refer to virtual LO's. The contribution of each primitive excitation $l \rightarrow m$ to the normalization is given by $(X_{lm}^{(n)})^2 - (Y_{lm}^{(n)})^2$. We refer to this method as localized orbital RPA, or LORPA.[14c] Of the various equivalent intensity expressions,[14] the mixed oscillator strength

$$f_{0n}^{\nabla} = \tfrac{2}{3}\langle 0|\mathbf{r}|n\rangle \cdot \langle 0|\hat{\nabla}|n\rangle \quad (8)$$

and the electric dipole length expression for the rotatory strength

$$R_{0n}^{r} = \frac{e^2\hbar}{2mc}\langle 0|\mathbf{r}|n\rangle \cdot \langle 0|\mathbf{r} \times \hat{\nabla}|n\rangle \quad (9)$$

do not contain the transition energy. In an exact calculation the electric dipole transition moments $\langle 0|\mathbf{r}|n\rangle$ and $\langle 0|\hat{\nabla}|n\rangle$ are parallel, and the various equivalent expressions[14] for respectively the oscillator strength and the rotatory strength provide identical results. It is an important feature of the RPA method that in a calculation including all the primitive excitations that can be constructed from the chosen orbital basis, any discrepancy between computed values from the various equivalent intensities or any deviation from colinearity of the two electric dipole transition moments is due solely to incompleteness of the atomic orbital basis. One consequence of obtaining nonparallel $\langle 0|\mathbf{r}|n\rangle$ and $\langle 0|\hat{\nabla}|n\rangle$ transition moments is that the expression for R_{0n}^{r} given above yields results that depend upon the choice of origin for the molecular coordinate system. As advocated elsewhere,[14c,d] we shall therefore use the modified length expression

$$R_{0n}^{[r]} = \frac{\langle 0|\mathbf{r} \times \hat{\nabla}|n\rangle \cdot \langle 0|\hat{\nabla}|n\rangle}{|\langle 0|\hat{\nabla}|n\rangle|^2} f_{0n}^{r\nabla} \quad (10)$$

which provides the origin-invariant part of R_{0n}^{r}. In the tables of results given below, the angles between the computed $\langle 0|\mathbf{r}|n\rangle$ and $\langle 0|\hat{\nabla}|n\rangle$ moments are included as an indication of the accuracy of the calculations. The reason for our choice of the energy-independent intensity expressions is that we have found, in general, that for molecules of the sort considered here, the effects of truncating the atomic orbital basis in an RPA calculation are more severe for the transition energies than for the transition moments.

Computational Results

In this study we calculated the chiroptical properties of the low-lying transitions in seven molecules or conformers: 1,3-cyclohexadiene ("CHD"), (5*R*)-*axial*-methyl-1,3-cyclohexadiene (**1a**, "MCA"), the same with methyl group rotated 60° ("MCAR"), the enantiomer of **1e** ("MCE"), 1-methyl-1,3-cyclohexadiene ("MC1"), 2-methyl-1,3-cyclohexadiene ("MC2"), and *cis*-1,3-butadiene twisted out of plane ("B17"). All compounds were taken to have **P** diene helicity, and a standard geometry, obtained from Dreiding models with a 17° diene twist angle, was used for all molecules studied to facilitate comparisons (see Figure 8). In addition, all methyl groups were staggered relative to the ring bonds, except in MCAR where the methyl group is in an eclipsed position. The results shown for MCA and MCAR in Table IV show that rotation of the methyl group has little consequence for the chiroptical properties; hence, no rotamer optimizations were attempted. The actual calculations employed a minimal atomic orbital set; further details concerning the SCF calculations and the localization of the molecular orbitals are given in the Experimental Section. We chose not to include diffuse functions or other extensions of the minimal basis set in our calculations. The lowest transition in conjugated dienes is considered to be essentially a valence shell excitation; moreover, our comparisons are made to spectra obtained in solution, where diffuse, Rydberg-type excitations are quenched or shifted to higher energy. Whether or not diffuse *configurations* would contribute strongly to the overall chiroptical properties of course cannot be determined from our calculations. Excitations into s-type Rydberg orbitals, at any rate, would be expected to have very small magnetic moment contributions.

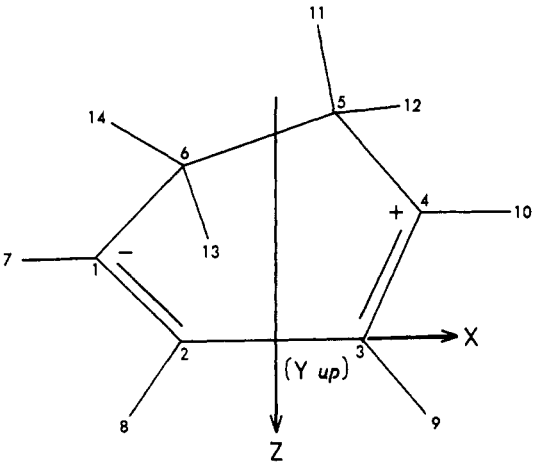


Figure 8. Coordinate system, numbering system, and geometry used in calculations. The unsubstituted ring system has C_2 symmetry. Atoms 11 and 13 are ψ-axial. Bond lengths (in Å): $C_1C_2 = 1.392$, $C_2C_3 = 1.464$, $C_4C_5 = 1.500$, $C_5C_6 = 1.536$, $C_1C_7 = C_2C_8 = 1.052$, $C_5C_{11} = C_5C_{12} = 1.088$, $C_1C_7 = C_2C_8 = 1.500$, $C_5C_{11} = 1.536$ (methyl CH = 1.088). Bond angles: $sp^2 = 120°$, $sp^3 = 109.5°$. $\angle C_1C_2C_3C_4 = 17°$.

Table IV, Calculated Chiroptical Properties for the Two Lowest Excitations in the Molecule Studied[b]

molecule	excitation	ΔE	$f^{r\Delta}$	$R^{[r]}$	$\angle_{r}^{\nabla}$ [a]	$\angle_{\nabla}^{r\times\nabla}$ [a]
B17	1	6.79	0.23	+20	0.62	83.2
	2	9.27	0.03	−69	0.00	180.0
CHD	1	6.05	0.11	+48	0.14	79.0
	2	8.96	0.01	−29	0.00	180.0
MC1	1	5.96	0.14	+34	0.55	82.6
	2	8.92	0.01	−30	1.23	156.7
MC2	1	5.96	0.10	+51	2.02	77.3
	2	8.88	0.02	−42	1.66	177.7
MCA	1	6.02	0.10	+83	2.00	76.1
	2	8.90	0.01	−37	2.31	150.8
MCAR	1	6.00	0.10	+88	2.59	75.2
	2	8.87	0.01	−37	3.00	152.6
MCE	1	6.03	0.11	+38	0.58	83.6
	2	8.90	0.00	−21	4.21	161.9

[a] Angle (deg) between indicated transition moments. [b] See text for notation. Units of ΔE are eV, and of R, 10^{-40} cgs. All singly excited configurations are included.

Our calculations indicate that the lowest four transitions in the molecules considered here can be characterized as predominantly $\pi \rightarrow \pi^*$, $\sigma \rightarrow \pi^*$, $\sigma \rightarrow \pi^*$, and $\pi \rightarrow \pi^*$, respectively, and in Table IV we present the optical properties of the lowest two transitions for the seven systems studied, calculated in the full LORPA, i.e., including all possible single excitations among the valence-shell LO's. In CHD there are 256 such excitations, while in each of the methyl derivatives there are 361. Besides these excitations,

Table V, Components of the Two Lowest Transitions in B17 and CHD in Terms of Localized Orbital Excitations[a]

excitation (symmetry)	component	CHD X	CHD Y	CHD N	B17 X	B17 Y	B17 N
1(B)	$\pi_{1,2} \rightarrow \pi^*_{1,2}$	−0.5253	0.0411	0.548	−0.5587	0.0565	0.617
	$\pi_{1,2} \rightarrow \pi^*_{3,4}$	0.4018	−0.0338	0.320	0.4248	−0.0413	0.355
	$\sigma_{5,6} \rightarrow \pi^*_{1,2}$	0.1145	−0.0034	0.026	0	0	0
	$\sigma_{6,13} \rightarrow \pi^*_{1,2}$	−0.1040	0.0011	0.022	0	0	0
	$\sigma_{5,6} \rightarrow \sigma^*_{5,6}$	0.0845	−0.0307	0.006	0	0	0
	$\sigma_{6,13} \rightarrow \sigma^*_{6,13}$	0.0189	0.0027	0.000	0	0	0
				0.922			0.972
2(A)	$\sigma_{1,2} \rightarrow \pi^*_{1,2}$	0.4148	−0.0086	0.344	0.4377	−0.0096	0.383
	$\sigma_{1,6} \rightarrow \pi^*_{1,2}$	−0.3171	0.0056	0.202	0.2316	−0.0040	0.107
	$\sigma_{2,8} \rightarrow \pi^*_{1,2}$	0.2614	−0.0034	0.136	−0.2740	0.0040	0.150
	$\sigma_{1,6} \rightarrow \pi^*_{3,4}$	0.1681	0.0022	0.056	−0.1091	0.0013	0.024
	$\sigma_{1,2} \rightarrow \pi^*_{3,4}$	−0.1617	0.0011	0.052	−0.1695	0.0011	0.057
	$\sigma_{2,8} \rightarrow \pi^*_{3,4}$	−0.1562	0.0004	0.048	0.1655	−0.0008	0.055
	$\pi_{1,2} \rightarrow \pi^*_{1,2}$	−0.1044	0.0129	0.021	0.2036	−0.0266	0.081
	$\pi_{1,2} \rightarrow \pi^*_{3,4}$	0.1337	0.0038	0.036	−0.2185	−0.0050	0.095
				0.895			0.952

[a] N is the normalized fraction of the total excitation contributed by a given pair of local excitations, related by the C_2 axis. X and Y are defined in the text. Related components implied by symmetry.

Table VI, Partial LORPA Results on the Chiroptical Properties of the Lowest Excitation of Each of the Molecules Studied[a]

molecule	bond set	no. of configurations	ΔE, eV	$f^{r\nabla}$	$R^{[r]} \times 10^{-40}$, cgs	$\angle \overset{r}{\nabla}{}^{\times\nabla}$, deg
B17	LE = full	121	6.79	0.23	+20	83.2
CHD	LE	121	7.20	0.24	−13	95.7
MC1	LE	121	7.35	0.23	−7	93.0
MC2	LE	121	7.33	0.25	−13	96.0
MCA	LE	121	7.26	0.24	−16	93.0
MCE	LE	121	7.26	0.24	−13	92.4
CHD	LE + AX	169	6.82	0.22	+107	56.0
MCA	LE + AX	169	6.86	0.22	+104	73.0
MCE	LE + AX	169	6.87	0.22	+105	72.4
CHD	LE + AX + $\sigma_{5,6}$	196	6.20	0.12	+55	77.0
CHD	LE + $\sigma_{5,6}$	144	6.75	0.15	−68	109.7
MCE	LE + EQ	169	6.98	0.23	+28	85.5
MCA	LE + AX + ME	256	6.77	0.21	+142	67.0
MC1	LE + ME	196	7.07	0.30	−22	101.0
MC1	LE + $\sigma_{5,6}$ + ME	225	6.63	0.20	−77	112.0
MC1	LE + AX + $\sigma_{5,6}$ + ME	289	6.10	0.15	+41	80
MC2	LE + ME	192	7.18	0.21	−10	96
MC2	LE + $\sigma_{5,6}$ + ME	225	6.67	0.13	−63	110
MC2	LE + AX + $\sigma_{5,6}$ + ME	289	6.10	0.10	+56	75

[a] LE means the set of σ and π bonds corresponding to *cis*-1,3-butadiene, AX refers to $\sigma_{5,11}$ and $\sigma_{6,13}$, EQ refers to $\sigma_{5,12}$ and $\sigma_{6,14}$, ME refers to the set of methyl CH bonds. MCA results are averages of MCA and MCAR.

the effects on the transition energies and moments of, respectively, some 16 300 and 32 500 doubly excited configurations are included implicitly in the RPA method.[14b] In addition to the two intensities f^{∇}_{0n} and $R^{[r]}_{0n}$ and the angle between $\langle 0|\mathbf{r}|n\rangle$ and $\langle 0|\hat{\nabla}|n\rangle$, as discussed in the preceding section, we include also the angle between the computed electric dipole transition moment, in the form $\langle 0|\hat{\nabla}|n\rangle$, and the computed magnetic dipole transition moment. However, it is important to stress that the latter angle depends upon the choice of molecular coordinate system.[14] For B17 and CHD we display in Table V the major components of the excitation eigenvectors for the lowest two transitions, as obtained from the full LORPA calculations.

The use of localized molecular orbitals allows us to examine the diene helicity and allylic axial chirality rules further through a series of partial LORPA calculations, in which only the singly excited configurations involving orbitals localized in specific bonds are included in the RPA procedure. In this way, the "chromophore" may be built up bond-by-bond, as it were, until the optical properties show no further significant change. The results for the lowest excitation in the molecules studied are tabulated in Table VI and form the basis for the (approximately) additive bond contributions shown in Figure 9 (see following section).

Discussion

Inspection of the full LORPA results displayed in Table IV shows that the chiroptical properties of the two lowest transitions are qualitatively the same for all these molecules, and that the lowest transition indeed does follow the helicity rule. For the second transition, which is essentially a $\sigma \rightarrow \pi^*$ excitation within the diene chromophore (see Table V), Table IV shows that the ordinary and rotatory intensities are very nearly the same for all the ring systems. The drop in absolute magnitude of the rotatory strength for this transition going from twisted butadiene (B17) to the ring system is largely associated with the corresponding decrease in the $\pi \rightarrow \pi^*$ contributions (see Table V).

Turning now to the lowest transition, Table IV shows immediately the strongly enhanced rotatory strength of the ψ-axial conformer of **1** (MCA), relative to the unsubstituted CHD. We see also that a ψ-equatorial methyl group (MCE) makes a weakly dissignate[48] contribution to R. A 1-methyl group (MC1) makes a similarly dissignate contribution, as well as leading to a small bathochromic shift, in accord with Woodward's rules.[49] A 2-

(48) We use the terms consignate and dissignate to describe rotatory strength contributions of sign respectively equal to or opposite to the sign predicted for the molecule by the diene helicity rule.

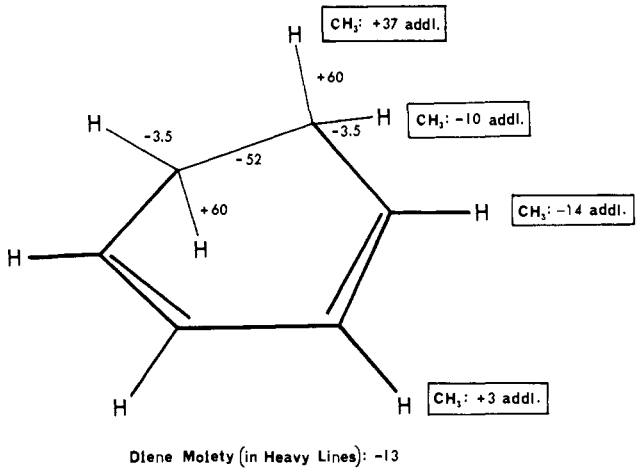


Figure 9. Estimated bond contributions to $R^{[r]}$ ($\times 10^{40}$ cgs) for the lowest transition of **P**-helicity 1,3-cyclohexadiene. The total value, R_{CHD}, for 1,3-cyclohexadiene is +48 (**P** helicity), obtained by summing the appropriate contributions shown.

methyl group (MC2) causes a similar bathochromic shift but has little effect on R.

The most striking effect, from the standpoint of the diene helicity rule, is seen by examining the LE–LORPA calculations for the ring systems (Table VI). The results show that the diene part of the ring system, including the σ bonds, consistently makes a contribution to R *of sign opposite to that implied by its* **P** *helicity, and therefore in violation of the diene helicity rule*, whereas, *cis*-1,3-butadiene itself (B17), held in a twisted conformation, is seen to obey the helicity rule (cf. also ref 10b). Inspection of the localized molecular orbitals in B17 and CHD (say) shows that the orbitals in the diene part of CHD are very similar to those of B17; in fact, the centroids of corresponding orbitals are the same to within 0.02 Å, even for the σ_{1-6} bond which is a C–C bond in one case and a C–H bond in the other. Also, the LORPA coefficients for the leading local excitations are very nearly the same. These similarities are reflected in the fact that the electric dipole transition moment is essentially identical for the LE–LORPA of CHD and the LORPA of B17, and the sign change in the rotatory strengths therefore arises from a change in the magnetic moment. In the coordinate system chosen, the angle between the electric and magnetic dipole transition moments changes from 95.6° in CHD to 83.2° in B17, thereby effecting the sign change in R. This observation reemphasizes the instability of the computed rotatory strength of the lowest transition in an "isolated" diene system with respect to small changes in the wave functions and/or computational methods, as has been demonstrated in previous work.[10a,11]

The contributions to the chiroptical properties of the lowest transition from other bonds in the ring systems can be assessed from the results of the series of partial LORPA calculations in Table VI, noting that the contributions from the individual bonds and groups are additive to within 10% for these molecules. We believe that this extraction of approximate bond and group contributions is justified by the additivity found in the actual LORPA calculations and by the qualitatively satisfactory results reported below for compounds **2** and **3**. Assignments of the estimated bond contributions are given in Figure 9. Beginning with the basic twisted diene contribution to R of −13 (all values $\times 10^{-40}$ cgs), we see that the C_5–C_6 bond contributes a strongly dissignate −52, whereas each allylic equatorial C–H bond adds only −3.5. Only when the allylic axial C–H bonds are added, each contributing a strongly consignate[48] +60, does the overall molecule obey the "helicity rule". By comparing these results with those for the methyl derivatives, we arrive at the following approximate *relative* contributions for CH_3 vs. H: 5-axial, +37; 5-equatorial, −10; 1-subst, −14; 2-subst, +3. All numbers refer to **P** helicity for the diene and would change sign for **M** helicity. Finally, we note that not only do the allylic axial bonds give the largest consignate enhancement of R, but a methyl substitution in an allylic axial position also yields a numerically much larger contribution than do methyl substitutions on other ring positions. Closer analysis of the contributions due to the most important bonds, namely, the C_5–C_6 and the allylic bonds, shows that they affect both the electric and the magnetic transition moments mainly through a combination of contributions from local $\sigma \rightarrow \sigma^*$ excitations in these bonds and from charge-transfer excitations from the σ orbitals in these bonds into the π^* orbitals (see Table V). We notice again therefore that the essential chiroptical properties of an electronic transition can be dominated by excitations that contribute only about 5% to the total normalization. We shall comment further on these findings in the concluding section.

We can now compare our calculated results to the experimental CD spectra for **1**, **2**, and **3**. In the Experimental Results section above we showed that the experiments provide an estimate of $\Delta G^\circ_{ax\text{-}eq} < 50$ cal/mol for **1**. Assuming therefore that **1** is present as an essentially equimolar mixture of MCA and the enantiomer of MCE, the values in Table IV yield $R^{[r]} = +22$ for the lowest transition and −8.5 for the second band (obsd $R = +17, -9$, all $\times 10^{-40}$ cgs). The agreement is seen to be excellent, probably better than we have a right to expect. For **2** and **3** we can use the bond contributions in Figure 9 to estimate the essential features of the rotatory strength of the lowest transition, provided we assume that the isopropyl or *tert*-butyl group can be adequately represented by a methyl group and that the contributions are additive; the first of these assumptions is presumably the most severe. If our estimates of ring and vicinal bond contributions remain approximately valid for these systems, then the departure from the experimental results could be taken as a measure of the combined importance of longer-range terms and of rotamer contributions, particularly in **2**, where there is no (pseudo)symmetry about the allylic axial C–C bond. From these assumptions and using Figure 9, we estimate $R^{[r]}_{ax}$ for **2** and **3** to be −88 and +85, respectively,[50] whereas our experimental estimates (vide supra) are −48 and +56, all in 10^{-40} cgs units. For the equatorial forms we estimate $R^{[r]}_{eq}$ to be +41 and −38 for **2** and **3**, respectively,[50] whereas the experimental estimates are +11 and −15. The theoretical estimates are seen to be numerically too high, but qualitatively in fair agreement with the experimental estimates.

Comparisons with Previous Work

We are now in a position to comment on the results of previous work. The molecule on which the original diene rule was based, **25**, has a rotatory strength of about $+24 \times 10^{-40}$ cgs.[6] The presence of two allylic equatorial groups should tend to lower the R value somewhat from that expected for the allylic axial methyl alone (cf. **1a**, MCA). Our analysis of approximate relative contributions suggests that the corresponding 11-nor triene (**26**) would be expected to have the same long-wavelength CE sign but an R value approximately one-half that of **25**.[56] The allylic axial chirality rules of Burgstahler et al.[8,9] are amply confirmed by our calculations. The sign inversions noted in ref 9 upon progressive demethylation of the allylic axial positions in steroidal dienes are consistent with our computed estimates of axial CH_3 vs. H, provided that the remainder of the steroidal framework, attached at the allylic equatorial sites, exerts a sufficiently dissignate effect. The steroid, 3,3-dimethoxy-19-norandrosta-5(10),6-dien-17-one, cited as an exception to the diene helicity rule,[51] can be understood in terms of its lack of allylic axial substituents, and the combined dissignate effect of three equatorial and ring substituents.

(49) Woodward, R. B. *J. Am. Chem. Soc.* **1941**, *63*, 1123–1126; **1942**, *64*, 72–75, 76–80.

(50) Using the bond contributions of Figure 9, for **2a** (**M**-diene helicity) $R_{ax} \approx -(R_{CHD} + R_{ax(CH_3)} + R_{2\text{-}CH_3}) = -(48 + 37 + 3) = -88$. For **3a** (**P**-diene helicity), $R_{ax} \approx R_{CHD} + R_{ax(CH_3)} = (48 + 37) = +85$. For the ψ-equatorial isomers, **2e** (**P**-diene helicity) has $R_{eq} \approx R_{CHD} + R_{eq(CH_3)} + R_{2\text{-}CH_3} = (48 - 10 + 3) = +41$; **3e** (**M**-diene helicity) has $R_{eq} \approx -(R_{CHD} + R_{eq(CH_3)}) = -(48 - 10) = -38$.

(51) Ahmad, R.; Carrington, R.; Midgely, J. M.; Whalley, W. B.; Weiss, U.; Ferguson, G.; Roberts, P. J. *J. Chem. Soc., Perkin Trans. 2* **1978**, 263–267.

In terms of other theoretical studies, our calculations are closest in spirit to the CNDO/S calculations of Rosenfield and Charney,[10a,38] who studied CHD as well as several of its di-, tri-, and tetramethyl derivatives and α-phellandrene itself. Their assessment of the importance of allylic axial substitution and the dissignate character of allylic equatorial substitution is substantially the same as ours, and they also believe that the reported sign reversal of the long-wavelength CD band at low temperatures[13] is erroneous. Weigang[12a] has developed a sector rule for electric dipole-allowed transitions and has applied it to substituted CHD. His estimates, like ours, show the dissignate effect of the C_5–C_6 bond and allylic equatorial substituents, and the strongly consignate effect of allylic axial groups. Our calculations support his assumption that perturber contributions are additive, but not the neglect of contributions to R from C–H bonds. Moriarty et al.[12b] have proposed a quadrant rule for homoannular cisoid 1,3-dienes. In their formulation, allylic axial H is assumed to predominate over allylic axial CH_3, although they present little evidence for this. They point out that all exceptions to the diene helicity rule have two allylic axial H atoms. The equatorial substituents in the cases cited, however, are OH or OR; the electronic characteristics of such highly polar groups can be expected to differ markedly from those of an alkyl substituent. Both the present work and that of ref 10a assign a greater effect to axial CH_3 than to axial H. Rauk and Peoples[10b] have recently used an ab initio SCF-CI method to calculate the rotatory strength of 1,3-butadiene as a function of twist angle and find, as we do, that the diene helicity rule is obeyed. From calculations on 1-butene vs. angle of twist about C_2–C_5, they are able to support the large effect of allylic axial vs. equatorial substituents. For α-phellandrene they use a molecular exciton model to estimate the rotatory strength of the lowest transition in a number of different conformers. In analogy to our results for MCA and MCAR (Table IV), they find that the chiroptical properties of different rotamers of the isopropyl group are very nearly the same. (See, however, ref 38 for a much larger computed rotamer effect in **2**.) Their results are numerically about twice as large as our theoretical estimates, but agree both in sign and in the general magnitude of R_{eq}/R_{ax}.

Concluding Remarks

The results of the theoretical analysis presented here illustrate clearly the difficulties involved in defining a model system for the alleged chromophoric parts of a molecule. More specifically, twisted butadiene can definitely not be considered a reliable model system for the long-wavelength circular dichroism of molecules containing a homoannular, cisoid diene system. This is in part due to the observation that the computed rotatory strength associated with the diene group itself appears to be unstable with respect to small variations in structural parameters or computation scheme, and in part because some "nonchromophoric" parts of the molecules play a decisive role in the resulting chiroptical properties. We find that the use of a localized orbital basis provides a convenient and direct procedure for the definition of the proper chromophore, and for a semiquantitative representation of the various "helicity rule" and "antihelicity rule" contributions in the form displayed in Figure 9.

Experimental Section

General. Circular dichroism spectra were recorded on a JASCO J-40 instrument equipped with a photoelastic modulator and cryostat, and on a JOBIN-YVON dichrographe III equipped with a cryostat. The data were collected using dilute solutions (10^{-4} M) and 10-mm pathlength cuvettes with instrument sensitivity settings of 10^{-5} Δ(absorbance)/cm, slow scanning speeds, and long time constants. (Chromophores which absorb strongly in the UV and have small $\Delta\epsilon/\epsilon$ ratios, such as the dienes of this work, require very dilute solutions and a sensitive detector response in order to obtain accurate measurements of CD data.) Ultraviolet spectra were recorded on a Cary 219 spectrophotometer; all rotations, [α], were determined (in $CHCl_3$ unless otherwise noted) on a Perkin-Elmer 141 polarimeter. Nuclear magnetic resonance (NMR) spectra were determined on a JEOL FX-100 or Varian 360 MHz instrument; mass spectra were recorded at 70 eV on a JEOL JMS-07 spectrometer; and infrared spectra were recorded on a Perkin-Elmer 599 spectrophotometer. All melting points are uncorrected and were determined on a Thomas-Hoover capillary apparatus. Analytical gas chromatography (GC) was performed on column A (6 ft × $^1/_8$ in., 5% SE-30 on Chromosorb W AQ-DMCS), column B (6 ft × $^1/_8$ in., 5% FFAP on Chromosorb W AW-DMCS), or column C (6 ft × $^1/_8$ in., 3% QF-1 on Chromosorb W AW-DMCS) on a Varian-Aerograph Model 2400 instrument. Preparative gas chromatography (GC) was performed on a Varian-Aerograph 1700 instrument using column D (8 ft × $^3/_8$ in., 15% Carbowax 20M on Chromosorb-W AW-DMCS) or column E (6 ft × $^3/_8$ in., 12% QF-1 on Chromosorb W). Combustion analyses were performed by Chemalytics, Tempe, Ariz., or by Micro-analytical Laboratory, Mountain View, Calif. Spectral data were obtained using spectral grade solvents (MCB). Other solvents were distilled and dried before use: diethyl ether (from $LiAlH_4$ under N_2) and benzene (azeotropically dried) were used freshly distilled or stored over 4A molecular sieves (Linde). Tetramethylethylenediamine (TMEDA), Aldrich, was distilled twice from CaH_2 and stored over 5A molecular sieves. Dimethylacetamide was dried over CaH_2 and filtered through alumina (act. I). Triethylamine was distilled from CaH_2 and stored over 4A molecular sieves. Deuterium oxide (D_2O) used in this work was 99.8%, from Bio-Rad. Column chromatography was accomplished on Merck neutral or basic alumina.

(+)-(3*R*)-Methylcyclohexanone (5). This ketone was prepared from (+)-pulegone (**4**) [Aldrich, $[\alpha]^{20}_D$ +22° (neat)] by a retro-aldol reaction according to the published procedure.[18-20]

(−)-*trans*-(2*R*)-Bromo-(5*R*)-methylcyclohexanone (6). The *trans*-bromo ketone mp 83–4 °C, was obtained in 32% yield by direct bromination of **5** according to the published procedure.[21] It was >99% pure by GC on column B.

(+)-*trans*-(2*R*)-Bromo-(5*R*)-methylcyclohexanone *p*-Toluenesulfonylhydrazone (11). To an ice-cooled solution of 9.55 g (55 mmol) of the bromo ketone **6** in 120 mL of diethyl ether was added at once 9.3 g (50 mmol) of *p*-toluenesulfonylhydrazine (Aldrich); the mixture was stirred vigorously. After a few minutes, the *p*-toluenesulfonylhydrazine was dissolved and stirring interrupted. The bromotosylhydrazone crystallized readily as colorless plates which were separated below 0 °C. The yield (in two crops) was 16.2 g (90%) with mp 129–130 °C dec. It had $[\alpha]^{25}_D$ +148° (*c* 2.0, CH_2Cl_2): IR (Nujol) ν 3200, 1600, 1340, 1155 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.97 (br s, 3 H), 2.33 (s, 3 H), 4.74 (br s, 1 H), 7.10 (d, J = 8 Hz, 2 H), 7.64 (d, J = 8 Hz, 2 H) ppm; MS m/z (rel intensity) 278 [M − HBr], 95 (100%).

Anal. Calcd for $C_{14}H_{19}O_2N_2SBr$ (359.28): C, 46.80; H, 5.33; N, 7.80; Br, 22.24. Found: C, 46.50; H, 5.39; N, 8.04; Br, 22.65.

(5*R*)-Methylcyclohex-1-enyl *p*-Toluenesulfonylazine (13). Bromotosylhydrazone (**11**) (10.78 g, 30 mmol) in 300 mL of diethyl ether was cooled to 0 °C and was shaken vigorously with 200 mL of a saturated solution of $NaHCO_3$ for 3–5 min. The intense yellow solution was washed twice with a saturated solution of NaCl and dried with $MgSO_4$. After removal of the diethyl ether under reduced pressure, there was obtained 7.60 g (91%) of the yellow, crystalline tosylazo compound, mp 59–60 °C. It had UV ϵ_{418} 81 (methylcyclohexane); CD $\Delta\epsilon_{423.5}$ = −0.11, $\Delta\epsilon_{368}$ = +0.028, $\Delta\epsilon_{322}$ = −0.024 (methylcyclohexane); IR (Nujol) ν 1635, 1600, 1340, 1170, 680 cm^{-1}; ^1H NMR (CCl_4) δ 0.98 (d, J = 5.5 Hz, 3 H), 2.40 (s, 3 H), 6.83 (t, J = 4 Hz, 1 H), 7.17 (d, J = 8 Hz, 2 H), 7.53 (d, J = 8 Hz, 2 H) ppm. This compound is very unstable, particularly in solution, and was taken immediately to the next step.

(−)-(5*R*)-Methylcyclohex-2-enone *p*-Toluenesulfonylhydrazone (15), (A). The tosylazo compound **13** (6.96 g, 25 mmol) was dissolved in 500 mL of dry benzene and treated at once with 34 mL (10 equiv) of triethylamine. The characteristic absorption of the tosylazo compound ($\epsilon \approx 80$ at 420 nm) disappeared after 15 min. The solvents were evaporated under vacuum, and the solid residue was digested with hexane. Crystallization from methanol afforded, in several crops, a total amount of 5.5 g (79%) of the tosylhydrazone as needles.

(B). The bromotosylhydrazone (**11**) (188 mg, 0.52 mmol) in 5 mL of dry benzene was treated dropwise, while stirring and cooling in an ice bath, with 5 mL of 0.1 M NEt_3 in benzene. The mixture became yellow with a white deposit. The mixture was filtered to give 90 mg (95%) of NEt_3·HBr, mp 245–7 °C dec. The filtrate was treated with 10 equiv of NEt_3 as described above to give 73 mg (51%) of the tosylhydrazone in two crops, as needles, mp 145–6 °C. It had $[\alpha]^{25}_D$ −71.6° (*c* 2.0, CH_2Cl_2): UV λ_{max} 255, 224 nm (CH_3OH); IR (Nujol) ν 3240, 1625, 1600, 1495, 1330, 1170 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.96 (br s, 3 H), 2.36 (s, 3 H), 6.05 (br s, 2 H), 7.13 (d, J = 8 Hz, 2 H), 7.74 (d, J = 8 Hz, 2 H), 8.03 (br s, 1 H, NH) ppm; MS m/z (rel intensity): 278 [M^+], 79 (100%).

Anal. Calcd for $C_{14}H_{18}O_2N_2S$ (278.37): C, 60.40; H, 6.52; N, 10.06. Found: C, 60.33; H, 6.31; N, 9.83.

(+)-(5*R*)-Methyl-1,3-cyclohexadiene (1), (A). To a suspension of 1.73 g (6.2 mmol) of tosylhydrazone (**15**) in 5 mL of tetramethylethylenediamine (TMEDA) was added at 0 °C with stirring 9 mL (2.32 equiv) of 1.6 M MeLi in Et_2O (Alfa). The tosylhydrazone dissolved

Table VII. Variation of Yields and Spectroscopic Properties with Reaction Temperature[a]

temp of BuLi add., °C	% yield	$[\alpha]_D$ in hexane, deg before distill.	$[\alpha]_D$ in hexane, deg after distill.	$\Delta\epsilon$ at 256 nm	$\Delta\epsilon$ at 216.5 nm
−60	59	+230°	+233°	+5.56	−6.53
−30	50	+233°	+236°	+5.50	−6.50
0	47	+223°	+225°	+5.33	−6.25

[a] All concentrations are calculated using $\epsilon_{257} = 4510$.

completely during addition of the first 4 mL of MeLi solution (vigorous methane evolution). The addition of the next 4 mL of MeLi solution caused the solution to become dark brown with further gas (nitrogen) evolution. The solution was stirred for an additional 45 min, and subsequently water (5 mL) was slowly added. The almost colorless mixture was extracted with pentane; the extracts were washed with H_2O and dried over $MgSO_4$. The extracts (26 mL), after 1:100 dilution with hexane, had $A = 0.575$ at 257 nm (0.1 cm). That corresponds to a 54% yield of the diene. The extracts were concentrated to ca. 1 mL volume by careful column distillation (water bath temperature 40 °C). The UV of the distillate shows that it contains less than 1.5 mg of the diene. The diene was finally purified by preparative GC on column D. The isolated yield of 99.9% pure diene (GC on column A) was 58 mg (10%). It had $[\alpha]^{25}_D$ +250.0° (*c* 2.6): UV ϵ_{258} 4510 (methylcyclohexane–isopentane, 4:1 v/v); CD Table I; IR (neat) ν 3040, 1630, 680 cm^{-1}; ^1H NMR and ^{13}C NMR, Table III; MS *m/z* (rel intensity) 94 [M^+], 79 (100%).

(B), The tosylhydrazone **15** (1 mmol, 279 mg) was suspended in 1 mL of TMEDA, and the mixture was cooled to the temperature indicated in Table VII. At this step 2.5 mL of 1.6 M *n*-butyllithium in hexane was slowly added under nitrogen, and the mixture was allowed to warm up slowly to room temperature and stirred for additional 3 h (a deep-brown color begins to appear only at ca. 0 °C). The mixture was decomposed with water (1 mL) at 0 °C and the hexane layer was washed several times with water. The combined aqueous layers were extracted with 3 mL of hexane. The combined hexane extracts were dried ($MgSO_4$), filtered through activity II basic alumina, and combined. At this stage the yield of reaction was determined by means of UV absorption at 256–257 nm and the rotation was taken. The diene product was finally purified by codistillation with hexane and the distillate was checked by running rotations, UV, and CD spectra.

(+)-(5*R*)-Methyl-3-deuterio-1,3-cyclohexadiene (17), To a suspension of 1.67 g (6 mmol) of tosylhydrazone **15** in 5 mL of TMEDA was added at −62 °C with stirring 15 mL of 1.6 M MeLi in Et_2O (4 equiv). The mixture was allowed to warm up to room temperature. The solution became dark and homogeneous only after the temperature rose above 0 °C. The dark solution was stirred at room temperature for 2 h 45 min (slow nitrogen evolution) and then quenched with 1 mL of D_2O (the solution becomes almost colorless). Workup with pentane–H_2O gave 41 mL of the extracts, having $A = 0.567$ at 257 nm (0.1 cm), after dilution 1:100 with hexane. This corresponds to 5.15 mmol of the diene, i.e., 86% yield (longer reaction time!). Further concentration of the solution and purification by means of preparative GC on column D afforded 198 mg (35%) of the pure diene which was 94% d_1 as determined from 360-MHz NMR. Alternatively, the material could be prepared using *n*-butyllithium in hexane at −60 °C as per method B for the preparation of **1**. This sample was 80–85% d_1 as determined by mass spectrometry on a JEOL JMS D-100 instrument equipped for GC-MS with a 3% OV-17 on Chrom. Q column (40 °C) that allowed for clean separation of **2** from hexane solvent. Diene **17** had $[\alpha]^{25}_D$ +249.5° (*c* 4.7): UV ϵ_{258} 4510 (*n*-hexane); CD $\Delta\epsilon_{256} = +5.56$, $\Delta\epsilon_{216.5} = -6.50$ (methylcyclohexane–isopentane, 4:1, v/v); IR (neat) ν 3040, 2265 (C–D), 680, 620 cm^{-1}; ^1H NMR and ^{13}C NMR, Table III; MS *m/z* (rel intensity) 95 [M^+], 80 (100%).

(−)-(5*R*)-Methylcyclohex-2-enone (9), A mixture of 14.48 g (0.076 mol) of the *trans*-bromo ketone **6**, 15.2 g of powdered calcium carbonate, and 76 mL of dimethylacetamide (DMA) was stirred vigorously under argon at 130–140 °C for 1.5 h and at room temperature for 2 h. Water (100 mL) was added and the ketone distilled as an azeotropic mixture. The distillate was saturated with NaCl and extracted with diethyl ether–pentane (1:1 v/v). After drying with $MgSO_4$ and removal of the solvents there was obtained 7.6 g of the unsaturated ketone as an oil (yield 91%), purity (GC on column B) >90%.

A sample of the product was purified by preparative GC on column D and the side products separated and identified by NMR as 5-methyl-3-cyclohexenone, yield ~3%; 3-methyl-2-cyclohexenone, yield ~5%. The desired product (**9**) had $[\alpha]^{25}_D$ −94.6° (*c* 3.2, $CHCl_3$) [lit.[21] $[\alpha]_D$ −90.17° (*c* 0.77, $CHCl_3$)]; UV ϵ_{341} 26, ϵ_{330} 25, ϵ_{217} 12 860 (methylcyclohexane–isopentane, 4:1 v/v); CD $\Delta\epsilon_{341} = +0.223$, $\Delta\epsilon_{218} = -3.0$ (methylcyclohexane–isopentane, 4:1 v/v); IR (neat) ν 3040, 1685, 1620 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.07 (d, J = 4.6 Hz, 3 H), 1.8–2.7 (m, 5 H), 5.97 (d, J = 10 Hz, 1 H), 6.98 (dm, J = 10 Hz, 1 H) ppm.

(−)-(5*R*)-Methyl-3-*p*-toluenesulfonylhydrazinocyclohexanone *p*-Toluenesulfonylhydrazone (10), Enone **9** (318 mg, 2.89 mmol) and 539 mg (2.90 mmol) of *p*-toluenesulfonylhydrazine was dissolved at room temperature in 3.5 mL of methanol. The solution was left at room temperature overnight. The crystalline product was collected (after cooling to 5 °C) and washed with methanol to yield 300 mg, mp 182–3° dec. It could be recrystallized from dioxane–methanol, mp 185–7° dec. It had $[\alpha]^{25}_D$ −17° (*c* 2.0, dioxane): IR (Nujol) ν 3240, 1650, 1600, 1310, 1155, 815, 665 cm^{-1}; ^1H NMR (DMSO-d_6) δ 0.90 (br s, 3 H), 2.30 (s, 3 H), 2.35 (s, 3 H), 7.30 (d, J = 8 Hz, 4 H), 7.60 (d, J = 8 Hz, 4 H) ppm; MS *m/z* (rel intensity): 278 [M^+ − $TsNHNH_2$], 91 (100%), 79 (100%).

(−)-(*R*)-α-Phellandrene (2), This diene was obtained from Fluka A.-G. as >99% pure material by GC (rechecked before using), and had $[\alpha]^{22}_D$ −229° (*c* 1.0, *n*-hexane).

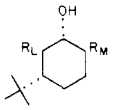
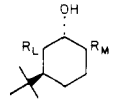
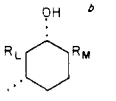
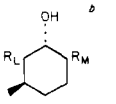
(+)-(3*R*)-*tert*-Butylcyclohexanone (7), Preparation of optically pure **7** involved the synthesis and resolution of *cis*-3-*tert*-butylcyclohexanol as the key step. The cis alcohol resolves more easily than the trans.[25,26] Several synthetic steps are required. (1) Catalytic hydrogenation of 3-*tert*-butylphenol (Aldrich) in methanol using 5% Rh(C) catalyst (Aldrich)[25] led to a 98% yield of a 1:1 mixture of *cis*- and *trans*-3-*tert*-butylcyclohexanols, as determined by GC on column C, bp 60–65 °C (2 mm). (2) Jones oxidation (CrO_3–H_2SO_4/acetone)[52] of the 1:1 mixture of cis and trans alcohols gave an 89% yield of 3-*tert*-butylcyclohexanone, bp 86–88 °C (6 mm). (3) Reduction of 3-*tert*-butylcyclohexanone with $LiAlH_4$ in ethyl ether[53] afforded a 90% yield of a 95:5 mixture (GC, column C) of cis and trans alcohols, bp 68–70 °C (2–3 mm). This mixture, predominantly the cis isomer, was converted in 94% yield to the half-acid phthalate (mp 133–134 °C) with phthalic anhydride in pyridine.[25,54] Saponification of the ester gave back 3-*tert*-butylcyclohexanol that was >99% pure cis isomer (GC, column C). (4) Resolution of the half-acid phthalate (above) with brucine[25,26] gave, in three crystallizations, a salt that yielded optically pure (100% ee) *cis*-(1*S*,3*R*)-*tert*-butylcyclohexanol, mp 41–42 °C, $[\alpha]^{25}_D$ +8.5°, $[\alpha]^{25}_{546}$ +10.2°, $[\alpha]^{25}_{436}$ +17.1°, $[\alpha]^{25}_{365}$ +26.3° (*c* 4.38). The absolute configuration and ee of the cis alcohol were determined by comparison with previous reported data: $[\alpha]_D$ +8.9°, $[\alpha]_{546}$ +10.1°, $[\alpha]_{436}$ +17.0°, $[\alpha]_{365}$ +26.0° (*c* 4.4);[26] $[\alpha]^{30}_D$ +7.9° (*c* 3.1).[25] They were confirmed by LIS-NMR studies (see Table VIII) of its Mosher ester[55] and the Mosher ester of the trans isomer. *trans*-(1*R*,3*S*)-*tert*-Butylcyclohexanol was obtained from partially resolved *cis*-(1*R*,3*S*)-*tert*-butylcyclohexanol, $[\alpha]^{25}_D$ −4.4° (*c* 2.83), following oxidation of the latter to (3*S*)-*tert*-butylcyclohexanone with Jones reagent,[52] then catalytic reduction with H_2/5% Rh(C). The resultant alcohol mixture (99% yield) contained a 6:4 ratio of cis:trans alcohols. The trans alcohol, $[\alpha]^{25}_D$ −9.7° (*c* 1.09), was isolated by preparative GC (column E) and >99% pure by analytical GC (column B). The Mosher esters of the cis and trans alcohols were prepared as before[27] using the acid chloride of (*R*)-(+)-α-methoxy-α-trifluoromethylphenylacetic acid [*R*-(+)-MTPA, Aldrich]. The ^{19}F NMR spectra of the Mosher esters of the partially resolved alcohols (above) indicated a 53 ± 3% ee, and the ^{19}F NMR spectrum of the Mosher ester of highly resolved *cis*-(1*S*,3*R*)-*tert*-butylcyclohexanol, $[\alpha]^{25}_D$ +8.5° (*c* 4.38), showed it to have >99% ee. The data are in close agreement and allow us to predict a value of $[\alpha]^{25}_D$ +18.3° ± 3% (*c* 1.1) for *trans*-(1*R*,3*R*)-*tert*-butylcyclohexanol of 100% ee; lit.[25] $[\alpha]^{28}_D$ +19.8° (*c* 0.85).

Lanthanide-induced shifts (LIS) of the methoxy and trifluoromethyl groups in the NMR spectra of the Mosher esters prepared from 53 ± 3% ee cis and trans alcohols are summarized in Table VIII.

The LIS of the *R*-(+)-MTPA esters of *cis*-3-*tert*-butylcyclohexanol have magnitudes opposite to those predicted using the empirical "bulkiness sequence subrule": the Mosher ester of the 1*R*,3*S* alcohol showed lower [LIS]-OCH_3 and [LIS]-CF_3 values than the Mosher ester of the 1*S*,3*R* enantiomer, leading to negative Δ[LIS] values. Other exceptions have been recognized (Yamaguchi et al., footnote *b*, Table

(52) Bowden, K.; Heilbron, I. M.; Jones, E. R. H.; Weedon, B. C. L. *J. Chem. Soc.* **1946**, 39–45.
(53) Winstein, S.; Holness, J. *J. Am. Chem. Soc.* **1955**, *77*, 5562–5578.
(54) Lightner, D. A.; Gawroński, J. K.; Bouman, T. D. *J. Am. Chem. Soc.* **1980**, *102*, 1983–1990.
(55) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543–2549.
(56) **Note Added in Proof**: Professor Burgstahler has just informed us of his synthesis of the parent diene analogue of **26** (*trans*-$\Delta^{1,3}$-hexalin). Its observed negative CE ($\Delta\epsilon = -2.35$) contrasts with our prediction based on the bond contributions (Figure 9), which suggests that longer range effects may also need to be considered. We are currently investigating this point.

Table VIII[a]

struct of the carbinyl moiety	[LIS]-OCH_3 *R*-(+)-B-*R* deriv	[LIS]-OCH_3 *R*-(+)-B-*S* deriv	Δ[LIS]-OCH_3	[LIS]-CF_3 *R*-(+)-B-*R* deriv	[LIS]-CF_3 *R*-(+)-B-*S* deriv	Δ[LIS]-CF_3
	9.4	10.4	−1.0	40.3	43.5	−3.2
	8.7	6.7	2.0	43.4	33.4	10.0
 [b]	8.4	8.5	−0.1			
 [b]	12.0	11.6	0.4			

[a] Values in ppm relative to tetramethylsilane (^{1}H NMR) or $CFCl_3$ (^{19}F NMR) as internal standards. [b] Values taken from Yamaguchi, S.; Yasuhara, F; Kubuto, K. *Tetrahedron* **1976**, *32*, 1363-1367.

VIII): *trans*-carveol, *cis*-3-methylcyclohexanol (shown in Table VIII), and α- and β-tetralol. The *R*-(+)-MTPA esters of *trans*-3-*tert*-butylcyclohexanol showed larger [LIS] values than the cis derivatives and positive Δ[LIS] values, as predicted.

The *tert*-butyl groups of the derivatives always appeared as separated singlets in the ^{1}H NMR. The *R*-(+)-MTPA esters of *trans*-3-*tert*-butylcyclohexanol showed small but reasonable [LIS]-*tert*-butyl values: [LIS]-*tert*-butyl (for *R*-(+)-B-*R*) ≃ 0.06; [LIS]-*tert*-butyl (for *R*-(+)-B-*S*) ≃ 0.39; Δ[LIS]-*tert*-butyl ≃ 0.3.

(5) Jones oxidation of optically pure *cis*-(1*S*,3*R*)-*tert*-butylcyclohexanol afforded optically pure (3*R*)-*tert*-butylcyclohexanone (**7**) in 94% yield, bp 60 °C (0.25 mm). It had $[\alpha]^{25}_{D}$ +24.1°, $[\alpha]^{25}_{578}$ +25.6°, $[\alpha]^{25}_{546}$ +32.1°, $[\alpha]^{25}_{436}$ +85.2°, $[\alpha]^{25}_{365}$ +252.7° (*c* 2.15); UV ϵ_{287} 18.7 (methylcyclohexane–isopentane, 4:1 v/v); CD $\Delta\epsilon_{297}$ 0.96 (methylcyclohexane–isopentane, 4:1 v/v); IR ($CHCl_3$) ν 2960, 2870, 1710, 1480, 1365, 1265, 1220 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.89 (s, 9 H), 1.2–2.4 (m, 9 H) ppm. This material was >99% pure by GC on column B.

(+)-*trans*-(2*R*)-Bromo-(5*R*)-*tert*-butylcyclohexanone (8),[25] The yield of this bromo ketone was improved by brominating its trimethylsilyl enol ether. (+)-(3*R*)-*tert*-butylcyclohexanone (**7**) (12.6 g, 82 mmol) in 40 mL of dry tetrahydrofuran was added to a stirred solution of lithium diisopropylamide [prepared in situ by addition of 14 mL (9.92 g, 98 mmol) of diisopropylamine to 38 mL (87 mmol) of 2.3 N *n*-butyllithium in 110 mL of dry tetrahydrofuran] over 20 min, all under N_2 and at −78 °C. The solution was stirred for an additional 5 min; then 18 mL (15.1 g, 139 mmol) of chlorotrimethylsilane was added over 10 min. The solution was allowed to warm to room temperature, and after stirring for 20 min the solvent was evaporated under vacuum. The concentrated reaction mixture was diluted with pentane and filtered, the pentane evaporated, and the residue distilled (85–90 °C (0.2 mm)) to yield 18.25 g (99% yield) of the silylenol ether. GC (column B) showed it to be a 9:1 mixture of the 5-*tert*-butyl and 3-*tert*-butyl isomers, respectively. Use of lithium dicyclohexylamide gave a 93% isolated yield of silylenol ether with no significant change of the 9:1 ratio of double bond isomers.

A solution of 12.9 g (80.6 mmol) of bromine in 30 mL of carbon tetrachloride was added over a period of 15 min to a stirred solution of 18.25 g (80.6 mmol) of the silylenol ether prepared above in 160 mL of carbon tetrachloride at −15 °C. The solution was allowed to warm to room temperature, and the solvent and bromotrimethylsilane were removed on a rotary evaporator. The residue was extracted with light petroleum ether, and the organic extracts were washed with cold aqueous $NaHCO_3$, then cold aqueous NaCl, and dried ($MgSO_4$). The petroleum ether was removed by rotary evaporation, and the residue was distilled (78–86 °C (0.1 mm)) to give 19.75 g of colorless oil. The oil was dissolved in ca. 50 mL of pentane and cooled to −78 °C to effect crystallization. Recrystallization from ether–pentane at −10 °C gave 5.03 g (27%) of white crystals, mp 96–97 °C (lit.[25] mp 82–83 °C), and 8.56 g (46%) of a yellow oil with the same spectroscopic properties as the crystalline material. The total yield was 73%. The bromo ketone had: $[\alpha]^{25}_{D}$ +25.4°, $[\alpha]^{25}_{578}$ +27.1°, $[\alpha]^{25}_{546}$ +33.7°, $[\alpha]^{25}_{436}$ +82.7°, $[\alpha]^{25}_{365}$ +226.8° (*c* 1.23); UV ϵ_{285} 24.2 (methylcyclohexane–isopentane, 4:1 v/v); CD $\Delta\epsilon_{296}$ +1.13 (methylcyclohexane–isopentane, 4:1 v/v); IR (CCl_4) ν 2940, 2845, 1725, 1355, 1135 cm^{-1}; ^{1}H NMR (C_6D_6) δ 0.62 (s, 9 H), 0.9–2.5 (m, 7 H), 4.09 (ddd, *J* = 12.8, 6.2, 0.98 Hz, 1 H) ppm.

(+)-*trans*-(2*R*)-Bromo-(5*R*)-*tert*-butylcyclohexanone *p*-Toluenesulfonylhydrazone (12). To an ice-cold solution of 1.40 g (6.0 mmol) of bromo ketone **8** (prepared above) in 20 mL of dry ether was added 1.02 g (5.5 mmol) of *p*-toluenesulfonylhydrazine. The vigorously stirred mixture was allowed to warm to room temperature. The bromotosylhydrazone (**12**) crystallized readily and was removed by filtration after cooling to −20 °C. The total yield was 1.74 g (79%) with mp 127–128 °C dec. It had: $[\alpha]^{25}_{D}$ +211.1° (*c* 0.47, CH_2Cl_2); IR (KBr) ν 3220, 2950, 2865, 1600, 1335, 1165, 1065, 665, 555 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.93 (s, 9 H), 1.0–2.3 (m, 7 H), 2.48 (s, 3 H), 4.87 (m, 1 H), 7.30 (d, *J* = 8 Hz, 2 H), 7.83 (d, *J* = 8 Hz, 2 H), 8.29 (m, 1 H) ppm.

Anal. Calcd for $C_{17}H_{25}O_2N_2SBr$ (401.36): C, 50.87; H, 6.28; N, 6.98; Br, 19.91. Found: C, 50.82; H, 6.30; N, 6.99; Br, 20.03.

(5*R*)-*tert*-Butylcyclohex-1-enyl *p*-Toluenesulfonylazine (14), Bromotosylhydrazone (**12**) from above, 1.25 g (3.1 mmol), was dissolved in 40 mL of ether and cooled to 0 °C. The solution was shaken vigorously with 25 mL of saturated aqueous $NaHCO_3$ for 3 min and treated as above in the preparation of **13** to afford 990 mg (99%) of the yellow, crystalline tosylazo compound, mp 88–90 °C. The compound was light-sensitive and decomposed rapidly in solution. It had: UV ϵ_{418} 25.2 (methylcyclohexane); CD $\Delta\epsilon_{495}$ = +0.014, $\Delta\epsilon_{421}$ = −0.061, $\Delta\epsilon_{322}$ = −0.18 (methylcyclohexane); IR (KBr) ν 2960, 2880, 1600, 1345, 1165, 1145, 1090, 815, 665, 590, 560 cm^{-1}; ^{1}H NMR (CCl_4) δ 0.89 (s, 9 H), 2.40 (s, 3 H), 1.0–2.1 (m, 7 H), 5.97 (m, 1 H), 7.13 (d, *J* = 7 Hz, 2 H), 7.57 (d, *J* = 7 Hz, 2 H) ppm.

(−)-(5*R*)-*tert*-Butylcyclohex-2-enone *p*-Toluenesulfonylhydrazone (16), Tosylhydrazone **16** was prepared by the two methods described for the methyl analog (**15**). Thus (method A), 882 mg (2.75 mmol) of tosylazine **14** as dissolved in 50 mL of dry benzene and treated at once with 3.8 mL (2.76 g, 27.3 mmol) of triethylamine. After 15 min the solvents were rotary evaporated to give a yellow-orange solid, which was crystallized from 95% ethanol to give 558 mg (64%) of desired tosylhydrazone, mp 148–150 °C.

Using method B, 9.48 g (23.6 mmol) of bromotosylhydrazone **12** in 400 mL of dry benzene as treated dropwise, with stirring and cooling in an ice bath, with 3.3 mL (2.4 g, 23.6 mmol) of triethylamine in 100 mL of dry benzene. The ice bath was removed and the deep yellow solution was treated with another 32.9 mL (23.9 g, 236 mmol) of triethylamine. After stirring for 30 min, the reaction mixture was filtered [to give 3.87 g (90%) of NEt_3·HBr, mp 247–249 °C dec.], and the filtrate was evaporated under reduced pressure. Recrystallization of the residue from ethanol afforded a total yield of 5.45 g (72%) of white crystals, mp 166–168 °C, as the desired tosylhydrazone **16**. The NMR spectrum (^{1}H and ^{13}C) showed it to be a 3:1 mixture of *E* and *Z* isomers. It had $[\alpha]^{25}_{D}$ −9.6° (*c* 1.17, CH_2Cl_2); UV ϵ_{256} 18 000, ϵ_{224} 19 600 (methanol); IR (KBr) ν 3440, 2970, 2880, 1635, 1600, 1400, 1355, 1165, 810, 660, 590, 553 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.83/0.94 (s/s, 9 H), 1.0–2.2 (m, 5 H), 2.35/2.39 (s/s, 3 H), 6.13 (m, 2 H), 7.29 (d, *J* = 8 Hz, 2 H), 7.89 (d, *J* = 8 Hz, 2 H), 8.46 (m, 1 H) ppm; ^{13}C NMR ($CDCl_3$) δ 155.9 (s, C-1), 143.7 (s, C-1′), 137.3 (d, C-3*), 135.6 (s, C-4′), 129.4 (d, 2 C, C-3′), 127.9 (d, 2 C, C-2′), 126.8 (d, C-2*), 43.1 (d, C-5), 32.2 (s, C-7), 27.0 (q, 3 C, C-8), 26.1 (t, C-6†), 25.6 (t, C-4†), 21.5 (q, C-5′), with lower intensity, 161.0 (s) and 27.3 (q) ppm. [Assignments * are interchangeable, as are those noted †.] A sample recrystallized from

CH_2Cl_2-light petroleum ether had mp 159-161 °C.

Anal. Calcd for $C_{17}H_{24}O_2N_2S$ (320.45): C, 63.72; H, 7.55; N, 8.74. Found: C, 63.89; H, 7.44; N, 8.80.

(+)-(5*R*)-*tert*-Butyl-1,3-cyclohexadiene (3). To a suspension of 421 mg (1.31 mmol) of tosylhydrazone **16** in 1.5 mL of TMEDA was added at -62 °C with stirring 2.3 mL (3.9 mmol) of 1.7 M *n*-BuLi in hexane. The tosylhydrazone dissolved completely, and the solution became orange-brown. The reaction mixture was allowed to warm up to room temperature, stirred for an additional 1.5 h under N_2, and treated dropwise with 2 mL of H_2O. The almost colorless mixture was extracted with pentane, and the organic extracts were washed with H_2O, dried ($MgSO_4$), and filtered through 30 g of activity II basic alumina. The filtrate (50 mL), after 1:100 dilution with hexane, had $A = 0.605$ at 260 nm (1 cm), corresponding to a 54% yield of diene (ϵ_{261} 4311). The filtrate was concentrated by distillation, and the residue was distilled (kugelrohr) at 74-76 °C (50 mm). The diene (70 mg, 39% yield) was obtained as a colorless oil, 96% pure by analytical GC (columns A and B). Samples for spectroscopy were further purified by preparative GC (column E) to yield 7% of diene **3** of >99.5% purity. [Racemic diene has been reported previously[41] and had bp 45-49 °C (10 mm); UV ϵ_{259} 4021 (isooctane)]. Diene **7** had $[\alpha]^{25}_D$ +187°, $[\alpha]^{25}_{578}$ +195°, $[\alpha]^{25}_{546}$ +228°, $[\alpha]^{25}_{436}$ +433°, $[\alpha]^{25}_{365}$ +815° (*c* 0.63); UV ϵ_{261} 4311 (methylcyclohexane-isopentane, 4:1 v/v); CD, Table I; IR (neat) ν 3050, 2970, 2920, 2880, 2835, 1480, 1470, 1395, 1370, 735, 720, 670, 650 cm^{-1}; ^1H NMR and ^{13}C NMR, Table III; MS *m/z* (rel intensity) 136 [M^+], 121 (20%), 79 (100%) amu.

(+)-(5*R*)-*tert*-Butyl-3-deuterio-1,3-cyclohexadiene (18). The deuterated diene was prepared exactly as for its protio analog (**3**) by quenching with D_2O instead of H_2O (see also preparation of **17**). The purified material (GC, column E) had $[\alpha]^{25}_D$ +186°, $[\alpha]^{25}_{436}$ +431° (*c* 0.79); UV ϵ_{261} 4308 (methylcyclohexane-isopentane, 4:1 v/v); CD $\Delta\epsilon_{303} = 0$, $\Delta\epsilon_{273} = +3.00$, $\Delta\epsilon_{265} = +3.19$, $\Delta\epsilon_{234} = 0$, $\Delta\epsilon_{219} = -3.64$, $\Delta\epsilon_{209} = 0$ (methylcyclohexane-isopentane, 4:1 v/v); IR (neat) ν 3050, 2970, 2920, 2880, 2835, 2260 (C-D), 1475, 1395, 1360, 745, 625 cm^{-1}; ^1H NMR and ^{13}NMR in Table III; MS *m/z* (rel intensity) 137 [M^+], 122 (18%), 80 (100%) amu.

Computational Details. Idealized geometries were used as in Figure 8. The STO-4G minimal basis set,[46] in conjunction with the unoptimized geometries used here, yielded the following SCF total energies in hartrees (1 hartree = 627.5 kcal/mol): B17, -154.0961; CHD, -230.6749; MCA, -269.5287; MCAR, -269.5211; MCE, -269.5303; MC1, -269.5000; MC2, -269.5340. Molecular orbitals were localized using the Foster-Boys-Coffey procedure.[14d] Computations were carried out in double precision on the IBM 3033 computer at the Northern Europe Computation Center at Lundtofte, Denmark, and on the IBM 370/145 system at Southern Illinois University at Edwardsville.

Acknowledgment. D.A.L., J.K.G., K.G., B.V.C., and J.L.C. thank the National Science Foundation for support of this work. T.D.B. and Aa.E.H. thank the Scientific Affairs Division of NATO for a grant in support of this work. Aa.E.H. thanks the Danish Natural Science Research Council for a travel grant. Additional support was provided to T.D.B. by the Office of Research and Projects of Southern Illinois University at Edwardsville. We wish to thank Drs. Lois Durham and C. S. Pak of Stanford University for their assistance in obtaining 360-MHz ^1H NMR spectra of dienes **1** and **17**, and Dr. Anthony Ribeiro for assistance with dienes **2** and **18**, all at the Stanford Magnetic Resonance Laboratory (NSF No. GP23633 and NIH No. RR00711). We also thank Dr. Jerome Gurst for a critical reading of the manuscript and for preparing a sample of diene **25** and providing us with its CD and UV spectra.

Carbon-13 Exchange Maps for the Elucidation of Chemical Exchange Networks

Y. Huang,[‡] S. Macura,[†] and R. R. Ernst*

Contribution from the Laboratorium für Physikalische Chemie, Eidgenössische Technische Hochschule, 8092 Zürich, Switzerland. *Received February 2, 1981*

Abstract: The application of two-dimensional carbon-13 NMR spectroscopy for the elucidation of chemical exchange networks is proposed. The utility of carbon-13 chemical exchange maps is demonstrated by application to systems involving conformational rearrangements, bond shifts, and solvation exchange processes.

I. Introduction

Recently, two-dimensional (2D) NMR exchange spectroscopy has been introduced for the elucidation of molecular exchange processes.[1] It has been found that 2D exchange spectroscopy is of significance for the investigation of cross-relaxation,[2-6] as well as for the study of chemical exchange networks.[1,7] The analysis of complex processes is greatly facilitated by the recording of informative 2D exchange maps.

So far, all 2D exchange studies have been based on proton resonance spectroscopy.[1-8] It has, however, been found that homonuclear spin-spin couplings in systems of abundant spins can lead to undesirable features in a 2D exchange map. Whenever two nuclei are connected by a network of spin-spin couplings, so-called *J* cross-peaks may appear in the 2D exchange spectrum.[8] These peaks are caused by a coherent magnetization transfer through the spin-spin coupling network. The resulting cross-peaks may be misinterpreted as cross-relaxation or chemical exchange cross-peaks.

We propose here to utilize carbon-13 resonance for the recording of 2D exchange maps. For low abundance nuclei, complicating effects like *J* cross-peaks are completely absent. Each spin represents an ideal tracer which allows one to trail the exchange pathways.

[‡]Physics Department, Huadong Normal University, Shanghai, P.R. China.
[†]Academic Guest 1979-1980 from the Institute of Physical Chemistry, Faculty of Sciences, 11000 Beograd, Yugoslavia.

(1) J. Jeener, B. H. Meier, P. Bachmann, and R. R. Ernst, *J. Chem. Phys.*, **71**, 4546 (1979).
(2) S. Macura and R. R. Ernst, *Mol. Phys.*, **41**, 95 (1980).
(3) Anil Kumar, R. R. Ernst, and K. Wüthrich, *Biochem. Biophys. Res. Commun.*, **95**, 1 (1980).
(4) Anil Kumar, G. Wagner, R. R. Ernst, and K. Wüthrich, *Biochem. Biophys. Res. Commun.*, **96**, 1156 (1980).
(5) R. Baumann, Anil Kumar, R. R. Ernst, and K. Wüthrich, *J. Magn. Reson.*, in press.
(6) Anil Kumar, G. Wagner, R. R. Ernst, and K. Wüthrich, submitted for publication.
(7) B. H. Meier and R. R. Ernst, *J. Am. Chem. Soc.*, **101**, 6441 (1979).
(8) S. Macura, Y. Huang, D. Suter, and R. R. Ernst, *J. Magn. Reson.*, **43**, 259 (1981).

0002-7863/81/1503-5327$01.25/0