

literature (Table I). The optical yields determined in this manner were verified by a series of 90-MHz ^1H NMR spectra (CDCl_3) at increasing concentration of the chiral shift reagent tris[3-((heptafluoropropyl)hydroxymethylene)-*d*-camphorato]europium(III) derivative $\text{Eu}(\text{hfc})_3$ or tris[3-((heptafluoropropyl)hydroxymethylene)-*d*-camphorato]praseodymium(III) derivative $\text{Pr}(\text{hfc})_3$. When the shift difference of the appropriate absorption was 6–9 Hz, the peak areas were determined by integration. Agreement between the two methods was approximately $\pm 1.0\%$ enantiomeric excess.

All asymmetric oxidations were carried out at least twice and the results averaged (Table I).

Acknowledgment. We gratefully acknowledge Professor Robert D. Bach, Wayne State University, for valuable discussions and for providing a sample of **3d**. We thank the National Science Foundation and Merck, Sharp and Dohme for generous support of this research.

Long-Range Control by Norbornane Frameworks of Cyclopentadienide Reactivity. Stereoselective Capture of Electrophiles by Tricyclo[5.2.1.0^{2,6}]deca-3,8-dienyl Anions¹

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Abstract: The π -facial stereoselectivities exhibited by cyclopentadienide anions **3** and **4** in their reactions with methyl iodide, three geminally deuterated 1,2-disubstituted ethanes, epichlorohydrin, $\text{Cl}(\text{CH}_2)_3\text{CD}_2\text{I}$, 1,4-dibromo-2-isopropylidenebutane, and deuterium oxide were determined. Analysis was achieved by a combination of ^1H and ^2H NMR spectroscopy, Diels–Alder chemistry, and $\text{Eu}(\text{fod})_3$ shift studies. Three sets of quantum mechanical calculations were applied to these anions, only the newly developed INDO procedure proving itself uniformly consistent in predicting the observed endo stereoselectivity of **3**. Loss of stereocontrol is experienced by **3** during spirocyclopropanation, a phenomenon attributed to the probable product-like nature of such transition states and the rather unusual ground-state electronic properties of the products. A model for the influence of the added norbornene double bond in **4** is proposed which calls attention to its substantial rate-retarding effect and consequently the late timing of its transition states. Because bond energies are substantially altered at this stage, the electronic features inherent to **4** are not made apparent. Allowance is also made for ion-pairing effects that may be influential in controlling the course of deuteration at -70°C .

Isodicyclopentadiene (**1**) and its dehydro derivative **2** have been



the focus of considerable attention as a consequence of the π -facial stereoselectivity which they exhibit in Diels–Alder cycloadditions.^{3–5} The intricate electronic interrelationship which exists between the framework σ electrons and the 1,3-diene π network in these hydrocarbons has generated high theoretical interest in their ground-state structures,^{4,5,7,8} particularly their π -bond nonequivalence. Our studies to date in this area have been focused not only on the behavior of the parent systems,⁵ but also on a detailed analysis of the consequences of cyclopentadiene ring

substitution.^{1,9} These more recent developments have removed from serious consideration the proposal^{7,10} that stereoselectivity might be governed by the stability of the isomeric adducts, as a consequence of adherence by these systems to the Bell–Evans–Polanyi principle.¹¹

The complications introduced by adduct formation are seen not to be present during the capture by anions **3** and **4** of suitable



electrophilic reagents. For steric reasons, bonding was expected to be directed to the cyclopentadienide center most remote from the bicyclic units to deliver C_s -symmetric products. In these examples, the causative factors which underlie the extent of endo/exo stereoselection must clearly be electronic in nature, since the reaction site is quite distant from the methano and ethano (or etheno) bridges which distinguish the π faces. Consequently, **3**, **4**, and related carbanions offer the potential for providing

(1) Electronic Control of Stereoselectivity. 14. For part 13, see: Paquette, L. A.; Kravetz, T. M.; Böhm, M. C.; Gleiter, R. *J. Org. Chem.*, in press.

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(8) Rondan, N. G.; Paddon-Row, M. N.; Caramella, P.; Houk, K. N. *J. Am. Chem. Soc.* 1981, 103, 2436.

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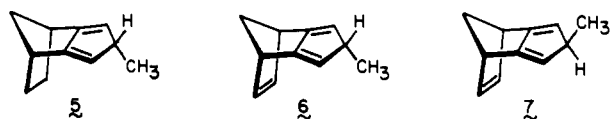
(11) Dewar, M. J. S.; Dougherty, R. C. "The PMO Theory of Organic Chemistry"; Plenum Press: New York, 1975; p 212.

additional independent *experimental* evidence for the fact that norbornyl, and to a lesser degree norbornenyl, ring systems can indeed exert long-range electronic perturbational effects.

Results

Reaction with Methyl Iodide. The first experiments to be conducted involved simple alkylation. Sequential treatment of **1** with *n*-butyllithium and methyl iodide in tetrahydrofuran solution cleanly afforded a single monomethylated product in 57% yield after distillation. ¹H and ¹³C NMR analysis before and after rectification told us that selective destruction of one or more additional isomers had not occurred during the requisite heating to approximately 75 °C. Given the existing detectability limits, **5** must therefore be formed with ≥97% selectivity. The methyl doublet appeared to be somewhat shielded (δ 1.06 in CDCl₃); the seven-line carbon spectrum confirmed the earlier assumption that a planar-symmetric product might result. Proof that endo alkylation had occurred as in **5** was derived from an X-ray crystal structure analysis of its *N*-methyltriazolinedione adduct.^{9a} This subject is considered in detail in the ensuing paper.

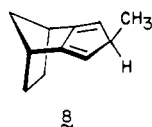
Comparable handling of **2** afforded a mixture of **6** and **7** in



approximately equivalent amounts. The 1:1 product distribution was ascertained by integration of the methyl doublets centered at δ 1.05 and 1.15. Attempts to separate these isomers by gas chromatography were not successful due to the incursion of 1,5-hydrogen shifts at the elevated temperatures needed.

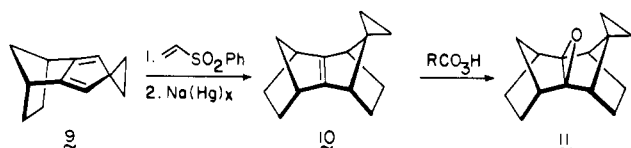
It is clear from these findings that the presence of a norbornene double bond reduces the ability of the bicyclo[2.2.1]heptane ring system to perturb the flanking cyclopentadienide anion. In our attempts to deprotonate **5–7** for the purpose of introducing a geminal CD₃ group (with CD₃I), the electrophile was seen to enter at one of the immediately adjacent sites, presumably to avoid steric congestion. The phenomenon of stereoelectronic control during geminal alkylation was therefore pursued only by means of spirocyclic ring formation.

Controlled catalytic hydrogenation of the **6/7** mixture provided a sample of **8** admixed with **5**. Since the ¹H NMR spectrum of



this sample was characterized by doublets at δ 1.06 and 1.10 and the first of these signals could be unequivocally assigned to **5** (see above), it becomes clear that the methyl group in **8** appears downfield of that in **5**.

Spirocyclopropanation Studies. The addition of sodium amide (2 equiv) and 1,2-dibromoethane (1 equiv) to **1** resulted in formation of the spirocyclopropane **9**. The ¹³C NMR spectrum of **9** revealed that the chemical shifts of the methylene groups on the three-membered ring are distinctively different (11.26 and 10.29 ppm), indicating that they are experiencing unequal perturbation by the distant norbornane framework. This distinction is not apparent in ¹H NMR spectroscopy where the four protons involved appear as a sharp singlet at δ 1.36. Consequently, some structural modification of **9** was necessary if its cyclopropyl CH₂ groups were to be spectroscopically distinguished.



To this end, conversion to the *syn*-sesquinorbornene **10** was achieved as described elsewhere^{9a} by Diels–Alder addition to

Scheme I

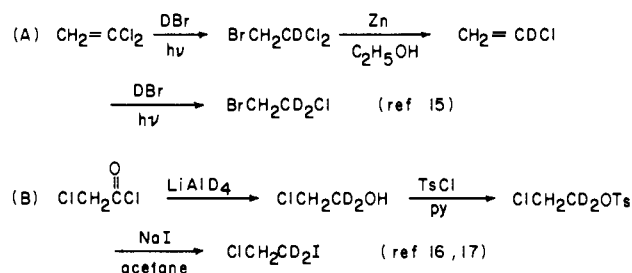


Table I. Deuterium-Labeled Spirocyclopropanation Product Ratios

electrophile	12a, %	12b, %
BrCH ₂ CD ₂ Cl	40	60
ClCH ₂ CD ₂ I	66	34
ClCH ₂ CD ₂ OTs	62	38

phenyl vinyl sulfone and reductive desulfonation. Subsequent epoxidation proceeded exclusively via *exo* delivery of oxygen¹² to produce **11**. The spectral changes which occur during this transformation are illustrated in Figure 1. In line with established precedent concerning oxirane ring anisotropy,¹³ H10'_{anti} should be shielded and H10'_{syn} deshielded in the epoxide relative to **10**. Additional factors need to be considered for the somewhat more distant cyclopropane methylene hydrogens. As seen in Figure 1, the relocation of the original A₂B₂ pattern due to H₂ (δ 0.42 → 0.07) and H₃ (δ 0.52 → 0.69) can be suitably interpreted in these terms. Whereas convincing support for the hydrocarbon assignments was gained from the deuterium labeling experiments which follow, confirmation for the epoxide was derived from standard Eu(fod)₃ shift studies. As anticipated a priori, the relative shift positions for H₂ and H₃ invert when approximately 0.25 mol % of the europium reagent is present (Figure 2). Additionally, the extrapolated ΔEu values¹⁴ for H₂ (4.07) and H₃ (1.75) necessitate that H₂ reside closer to the oxygen atom.

With the preceding observations as our basis for stereochemical assignment within the cyclopropane ring, alkylation studies involving **3** were carried out with three different isotopically labeled 1,2-disubstituted ethanes. The preparation of these materials (Scheme I) followed established procedures.^{15,17} For the present purposes, lithium aluminum deuteride reduction of chloroacetyl chloride is vastly preferred to ethyl chloroacetate^{18,19} because ethanol is not produced concomitantly as a troublesome byproduct. Note that while initial nucleophilic attack on BrCH₂CD₂Cl should occur at the nondeuterated carbon (Br/Cl ≈ 50),²⁰ the response of ClCH₂CD₂I (I/Cl ≈ 100)^{20,21} and ClCH₂CD₂OTs should be reversed. With sodium amide as base, the condensation reactions involving **1** were conducted as before to give mixtures of **12a** and **12b** (Table I). The first indication that a single isomer had not been produced was provided by ¹³C NMR spectroscopy. Although integration analysis was not performed by this technique, it was already apparent that the product distribution from the bromo chloride was the inverse of those obtained with the chloro tosylate.

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(20) This is an average value for intermolecular S_N2 displacement reactions: Streitwieser, A., Jr. "Solvolytic Displacement Reactions"; McGraw Hill: New York, 1962; p 30 (*Chem. Rev.* **1956**, *56*, 571).

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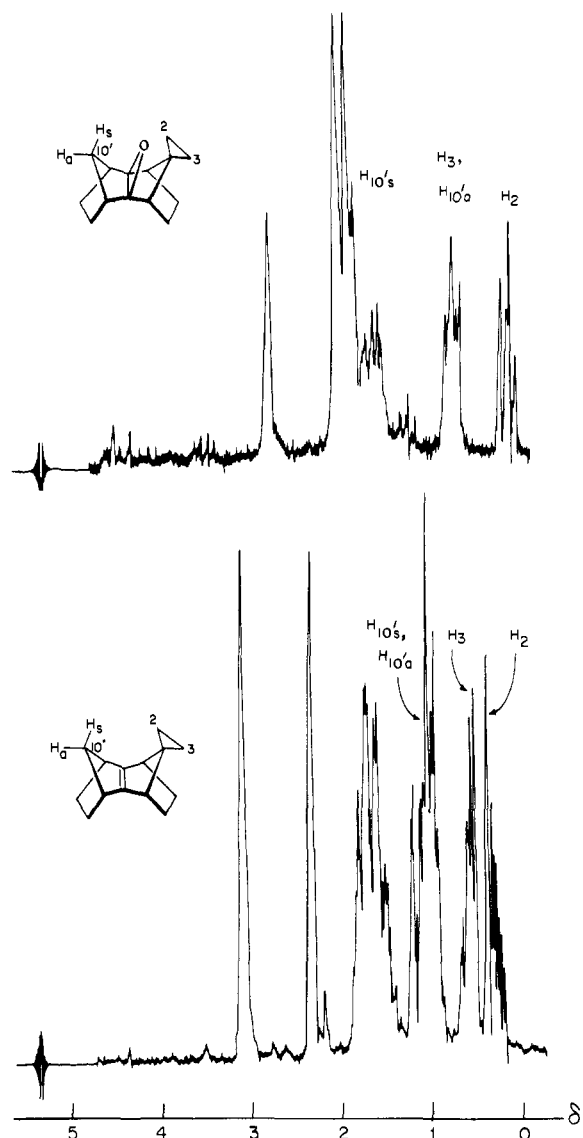
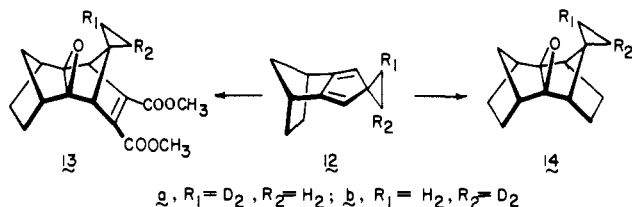


Figure 1. ^1H NMR spectra (90 MHz) of **10** and **11** (CDCl_3 solution).

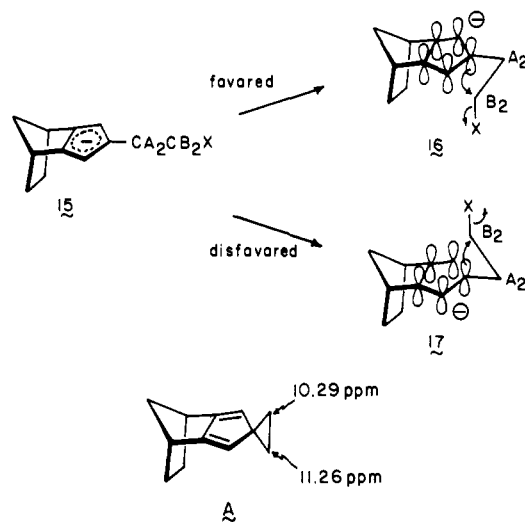
The precise location of the isotopic label in hydrocarbons **12a** and **12b** was ascertained by conversion to **13a** and **13b** as before,



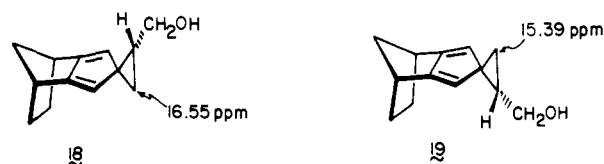
followed by careful integration of the ^1H NMR spectra. Independent assessment of the product distributions was realized by analogous conversion to **14a** and **14b** where the cyclopropane hydrogen pairs are comparably well separated.

The predominance of **12b** in the reaction mixture from $\text{BrC-H}_2\text{CD}_2\text{Cl}$ and of **12a** from $\text{ClCH}_2\text{CD}_2\text{X}$ show that carbanion **15** favors C-C bond formation from the endo surface as in **16** relative to exo capture of the electrophile as in **17**. The partitioning ratio in these cases is not large, and a major question remains about the drop-off in stereoselectivity during cyclopropane ring formation. This point will be addressed in the Discussion.

The ^{13}C NMR spectra of compounds **12a** and **12b** show that the above-plane cyclopropyl methylene carbon (C_2) appears at higher field than its below-plane counterpart (C_3). Consequently, the electronic effects prevailing within **9** are such that C_2 experiences the greater level of shielding (see A).²²



The stereoselection which occurs upon reaction of the same cyclopentadienide species with epichlorohydrin²³ is of comparable magnitude. With this reagent, there is produced a mixture of **18** (28%) and **19** (72%) as determined by quantitative ^{13}C NMR



analysis.²⁴ This technique was employed because of technical difficulties experienced during attempted separation of these isomers and because Diels-Alder addition with such dienophiles as dimethyl acetylenedicarboxylate proved unsatisfactory as a diagnostic tool. The individual structural assignments were made on the basis that the cyclopropyl CH_2 in **18** should exhibit a ^{13}C chemical shift at lower field than that in **19** (see A).

Five-Ring Spiroalkylation. Under kinetically controlled conditions as before, spiroalkylation of **1** with 1,4-dibromobutane provided **20**. Each of the four methylene carbons within the newly formed five-membered ring emerged at distinctively different chemical shifts (33.60, 33.06, 25.93, and 25.73 ppm). While individual assignments had to await completion of the isotopic studies which immediately follow, it was already quite apparent that the electronic influences within the norbornane moiety extend to remarkably long distances. A pivotal question was whether the shielding effects observed in **20** paralleled those in **9** or were reversed relative to those in the cyclopropyl analogue.



Condensation of **1** with $\text{Cl}(\text{CH}_2)_3\text{CD}_2\text{I}$ ^{17a} led cleanly to a single deuterium labeled hydrocarbon as seen from the appearance of only three intense ^{13}C signals at 33.06, 25.93, and 25.53 ppm.²² Identification of the product as **21** could not be achieved by conversion to its maleic anhydride, *N*-phenyl maleimide, benzoquinone, or *N*-methyltriazolinedione adduct. Because of stereospecific above-plane dienophile approach in each instance, *anti*-

(22) With the introduction of two deuterium atoms on C_2 or C_3 , the signals for these carbon atoms are not visible and the observed absorptions are those of the residual protio-substituted centers. Vicinal deuterium isotope effects induce only insignificant chemical shift changes as expected (Inamoto, Y.; Aigami, K.; Fujikura, Y.; Ohsugi, M.; Takaishi, N.; Tsuchihashi, K.; Ikeda, H. *Chem. Lett.* **1978**, 25 and pertinent references cited therein). For **12a**, δ_{C_3} 11.06. For **12b**, δ_{C_2} 10.04.

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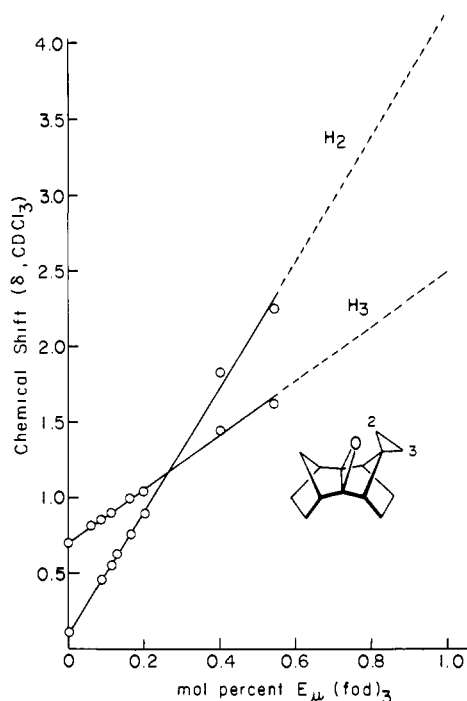
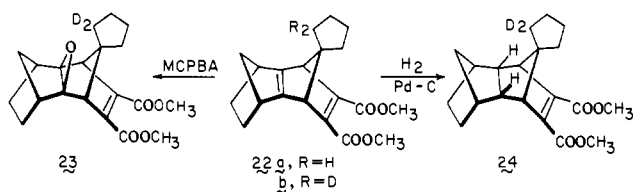


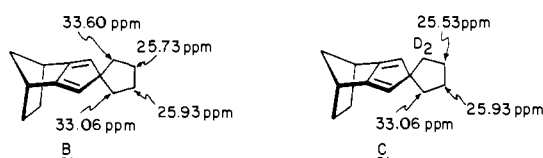
Figure 2. Field positions of the cyclopropyl protons of **11** plotted as a function of $\text{Eu}(\text{fod})_3$ concentration in ppm downfield from Me_4Si (CDCl_3 solution).

sesquinoxinorbornenes were produced^{9b} and the newly generated structural perturbations were inadequate for distinguishing between C_2 and C_5 . In addition, epoxidation of the central double bond did not proceed cleanly. Consequently, recourse was made to dimethyl acetylenedicarboxylate which adds to **20** with 70% below-plane stereoselectivity to give **22a** as the major product.^{9b}

The locus of isotopic substitution in **21** was established by comparable preparation of **22b** for which a ^2H chemical shift of



1.75 ppm was noted. Since deuterium substituents are subject to chemical shift alterations entirely comparable to those experienced by hydrogen atoms, epoxidation to give **23** and selective catalytic hydrogenation to give **24** were expected to be accompanied by enhanced shielding of the D_2 pair, if the labeling pattern is indeed as shown. Should the deuteriums be attached to the other surface of the spirocyclopentane ring, much less change in chemical shift would be expected. The ^2H signal in **23** (1.62 ppm) is clearly upfield of that in **22b**. In addition, saturation of the internal double bond as in **24** causes the ^2H signal to appear at 1.42 ppm, an observation anticipated only if the deuterium atoms in **22b** were originally subject to $\text{C}=\text{C}$ bond anisotropy. Consequently, the carbon shielding effects present in **20** (see **B** and **C**) are seen to be reversed relative to those in **9!**

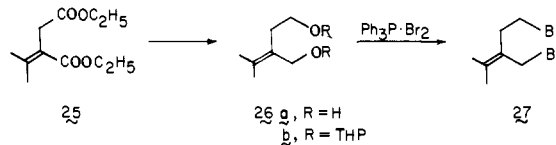


In view of the exceptionally high stereoselectivity exhibited by $\text{Cl}(\text{CH}_2)_3\text{CD}_2\text{I}$ toward **3**, the decision was made to investigate the outcome of five-ring spiroalkylation with at least one other reagent. For this purpose, we were attracted to the report by Stork and

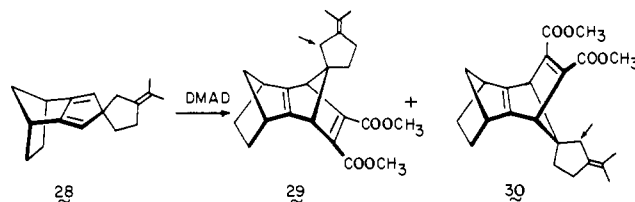
Table II. Chemical Shifts of the "Isolated" Allylic Methylene Group in Several Adducts (CDCl_3 solution, 90 MHz)

compd	chemical shift, δ
29	2.35
30	2.38
32	1.98
34	2.08

co-workers which described the use of 1,4-dichloro-2-isopropylidenebutane in order to gain rapid synthetic access to (\pm)-vetivone.²⁵ However, we, like the original investigators, experienced annoying irreproducibility problems in the preparation of this dihalide. To bypass these complications, we developed an alternative route to the related dibromide **27** which proceeds smoothly and is readily amenable to scale-up if desired. Following reduction of diester **25**²⁶ with lithium aluminum triethoxyhydride and quantitative conversion of resulting diol **26a** to its bis(tetrahydropyranyl) ether (**26b**),²⁷ reaction with triphenylphosphine dibromide²⁸ gave **27** in 66% yield.

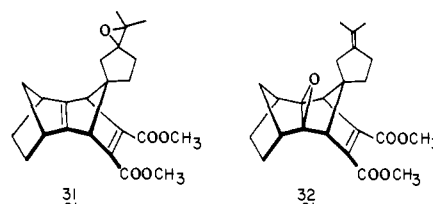


Condensation of **27** with the anion of **1** produced the spirocyclopentane derivative **28** as the only identifiable product (^{13}C NMR analysis; 28% isolated). To ascertain the stereoselectivity of this process, **28** was condensed with dimethyl acetylenedi-



carboxylate to provide a separable mixture of adducts **29** and **30** in a 2:1 ratio. The ^1H and ^{13}C NMR data for **29** and **30** agree very well with those of the parent systems and serve as the basis of the structural assignments. Especially noteworthy in these examples is the downfield nature of the "isolated" allylic CH_2 group in these adducts (see arrows) which removes it from the area of large upfield absorption and allows it to be readily identified (Table II).

Although attempts to oxidize **29** at its central double bond with molecular oxygen¹² were without success, probably due to excessive steric hindrance on its exo surface, this substance did undergo reaction with *m*-chloroperbenzoic acid at 0°C . The monoepoxides **31** and **32** which were formed could be chromatographically



separated without difficulty. Significantly, **32** shows a 0.37-ppm shielding for its "isolated" allylic methylene group relative to that of **29** (Table II). The indication of kinetically favored endo face stereoselectivity which was provided by this observation was

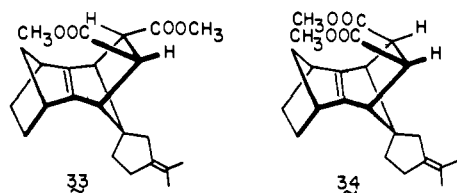
(25) Stork, G.; Danheiser, R. L.; Ganem, B. *J. Am. Chem. Soc.* **1973**, *95*, 3414. We thank Professor Stork for making available to us the details of his original experimental procedure.

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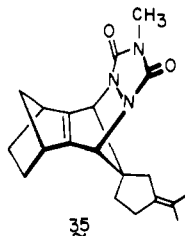
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(28) Schwarz, M.; Oliver, J. E.; Sonnet, P. E. *J. Org. Chem.* **1975**, *40*, 2410. Sonnet, P. E. *Synth. Commun.* **1976**, *6*, 21.

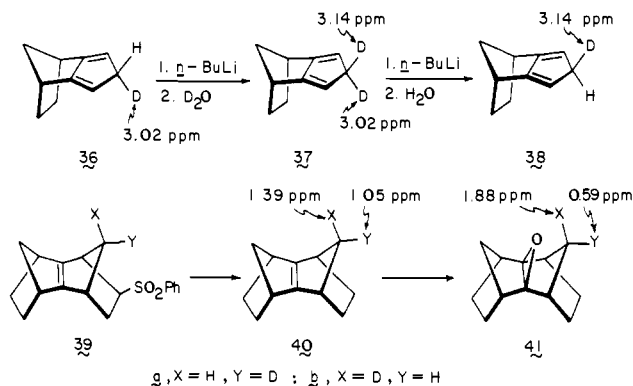
substantiated by chromous sulfate reduction²⁹ of **30**. The pair of diesters **33** and **34** was isolated from the reaction mixture in



a 5:1 ratio. Although the ¹H NMR spectrum of unsymmetrical trans isomer **33** proved too complex for analysis, that of the more symmetrical cis isomer (**34**) permitted ready assignment of the broadened singlet appearing at δ 2.08 to its "isolated" allylic methylene group. This represents an upfield shift at 0.30 ppm relative to **30** (Table II) and corresponds to the anticipated onset of shielding resulting from saturation of that double bond which carries the carbomethoxy groups. The spectral properties of **35** obtained from **28** and *N*-methyltriazolinedione were likewise in full agreement with precedent.⁹



Deuteration Studies. When solutions of cyclopentadienide anion **3** were quenched by addition to D₂O–THF mixtures at -70 °C, regioselective and π -facial stereoselective capture of deuterium resulted. The ²H NMR spectrum of the product (in CCl₄) was characterized by a pair of singlets at 3.02 and 3.14 ppm, with the upfield peak dominating (75–85%). Its ¹H NMR spectrum established that an isomeric product had not formed. Repetition of this procedure gave **37** having two signals of equal intensity



at the same chemical shift positions. When a third exchange was performed on **37** and the resulting *d*₁ anion was protonated at low temperature, the isolated hydrocarbon exhibited a deuterium singlet at 3.14 ppm. In order to confirm that the first isotopic label had entered from the below-plane direction, **36** and **38** were independently subjected to reaction with phenyl vinyl sulfone.³⁰ Following reductive desulfonylation of adducts **39a** and **39b**, the pair of *d*₁ *syn*-sesquinorbornenes (**40**) were epoxidized. In **41a** and **41b**, the anisotropy contributions of the oxirane oxygen^{13,31} induce deshielding of the inner D atom of **41b** by 0.49 ppm and shielding of the outer D atom of **41a** to the extent of 0.46 ppm (see formulas).

(29) Castro, C. E. *J. Am. Chem. Soc.* **1961**, *83*, 3262. Castro, C. E.; Stephens, R. D.; Mojè, S. *Ibid.* **1966**, *88*, 4964.

(30) The below-plane stereoselectivity of this Diels–Alder reaction has been established elsewhere.¹²

(31) (a) Tori, K.; Kitahonoki, K.; Takano, Y.; Tanida, H.; Tsuji, T. *Tetrahedron Lett.* **1964**, 559. (b) Tori, K.; Aono, K.; Kitahonoki, K.; Muneyuki, R.; Takano, Y.; Tanida, H.; Tsuji, T. *Ibid.* **1966**, 2921.

Accordingly, under the conditions employed herein, **3** is deuterated predominantly (75–85%), though not exclusively, from the below-plane direction.

Theoretical Considerations. The stereochemical preferences observed in the alkylation reactions of cyclopentadienyl anions **3** and **4** are reminiscent of the cycloaddition behavior of various diene systems containing a π fragment adjacent to a bicyclic system which provides σ/π nonorthogonality.^{1,4-7,9} In recent publications, we have demonstrated that unsymmetrical bicyclic frameworks such as norbornyl allow coupling between orbitals of pure π character and high-lying σ orbitals. As a result of this interaction, those canonical molecular orbitals endowed predominantly with π character are predicted to be rotated and/or tilted. In most of the examples, the destabilizing four-electron interaction between the highest occupied molecular orbital of the dienophile and a symmetrical π orbital of the diene was determined to be the factor principally responsible for the associated stereoselectivity. More specifically, a symmetrical diene π orbital under the influence of relatively strong σ/π mixing can be seen to experience a twisting of its 2p _{π} lobes with the ultimate consequence that dienophile approach from one face of the diene is rendered more facile than the other. As noted previously,^{1,5,9} the magnitude of such σ/π interactions is dependent upon the coupling element $H_{\pi\sigma}$, as well as the energy difference ($\epsilon_{\pi} - \epsilon_{\sigma}$) of the one-electron energies of the fragments. Quantum chemical procedures for the determination of $H_{\pi\sigma}$, ϵ_{π} , and ϵ_{σ} starting with canonical orbitals from an ordinary SCF calculation have been published some time ago.³² Due to the different semiempirical procedures available, one is very often confronted with divergent results regarding the energy differences between σ and π orbitals. Through suitable comparison of one-electron energies compiled by semiempirical LCAO procedures (e.g., EHT,³³ CNDO/2,³⁴ MINDO/3,³⁵ SPINDO,³⁶ and a recently developed INDO method³⁷) with He I photoelectron (PE) spectroscopic results, it proved possible to select that procedure which most consistently predicted the π/σ orderings given by the PE experiments. Usually, our recently developed INDO model turned out to be most satisfactory.

As the combined application of PE spectroscopy and quantum mechanical calculation is not possible in the case of **3** and **4**, we have compared the experimental stereochemical evidence with expectations derived from three different LCAO procedures (EHT, MINDO/3, and INDO). In our detailed analyses, the assumption has been made that the interaction which is dominant arises between a donor MO of the cyclopentadienyl anion and an acceptor orbital of the electrophilic agent, irrespective of the transition state involved in the particular alkylation reaction. That is to say that the acceptor orbital might be an empty 2p orbital if an S_N1 reaction is involved or a low-lying σ^* orbital if alkylation occurs via an S_N2 mechanism.

The three sets of calculations relating to **3** and **4** lead to the common result that the two highest occupied π MO's of these anionic systems (derived from e_1'' of the unsubstituted cyclopentadienyl anion) show negligible contributions from the σ frame. In contrast, the lowest occupied π combination (a_2'' of cyclopentadienide) contains significant contributions from the molecular σ frame. The LCAO coefficients of the lowest occupied π orbital of both **3** and **4** as obtained by all three computational procedures are compiled in Table III. A schematic representation of the corresponding wave functions is presented in Figure 3.

The strongest deformation along the *x*-axis direction is found at C₁. For both carbanions, INDO predicts a rotation toward the methylene bridge. However, the outcomes of the MINDO/3 and EHT calculations parallel those of the INDO method only

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(33) Hoffmann, R. *J. Chem. Phys.*, **1963**, *39*, 1397. Hoffmann, R.; Lipscomb, W. N. *Ibid.* **1962**, *36*, 2179; **1962**, *37*, 2872.

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(35) Bingham, R. C.; Dewar, M. J. S.; Lo, D. H. *J. Am. Chem. Soc.* **1975**, *97*, 1285. Bischof, P. *Ibid.* **1976**, *98*, 6844.

(36) Fridh, C.; Åsbrink, L.; Lindholm, E. *Chem. Phys. Lett.* **1972**, *15*, 282. Åsbrink, L.; Fridh, C.; Lindholm, E. *J. Am. Chem. Soc.* **1972**, *94*, 5501.

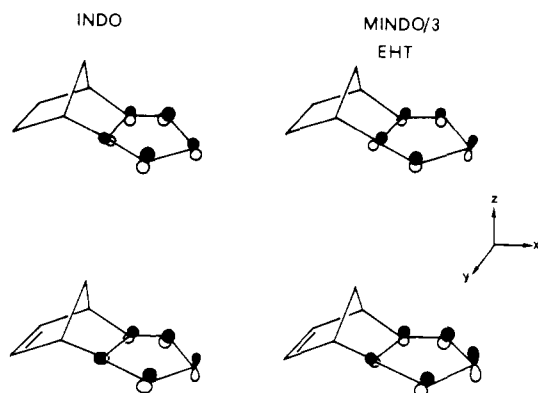
(37) Böhm, M. C.; Gleiter, R. *Theor. Chim. Acta*, in press.

Table III. LCAO Coefficients of the Lowest π Orbital within 3 and 4 as Calculated by INDO, MINDO/3, and EHT Procedures

anion	AO	INDO			MINDO/3			EHT		
		C ₁	C ₃ , C ₄	C ₂ , C ₅	C ₁	C ₃ , C ₄	C ₂ , C ₅	C ₁	C ₃ , C ₄	C ₂ , C ₅
3	2s	0.0276	-0.0090	0.0108	-0.0154	0.0202	-0.0085	-0.0092	0.0130	-0.0039
	2p _x	-0.2539	0.1970	-0.2386	-0.0713	-0.0353	0.0361	-0.0414	-0.0142	0.0267
	2p _y		-0.0760	-0.0335		-0.0125	0.0215		-0.0092	0.0157
	2p _z	0.3697	0.1892	0.3266	0.3786	0.1890	0.3254	0.2999	0.2844	0.2956
4	2s	0.0190	-0.0106	0.0087	0.0146	-0.0256	0.0105	0.0337	-0.0164	0.0032
	2p _x	0.1297	0.1290	-0.1644	0.0799	0.0345	-0.0413	0.1320	0.1061	-0.1189
	2p _y		-0.0470	-0.0200		0.0117	-0.0226		-0.0032	-0.0323
	2p _z	0.4600	0.2504	0.4100	0.4421	0.2520	0.3893	0.3563	0.0997	0.2912

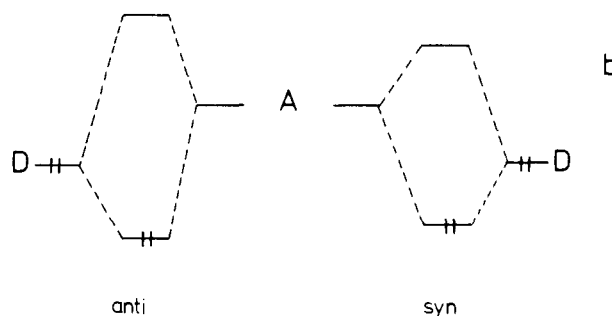
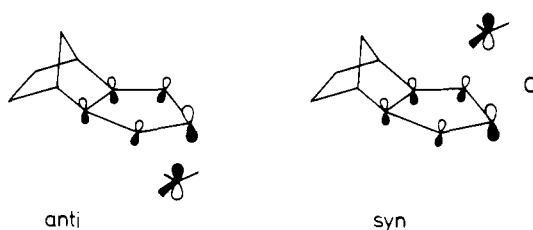
Table IV. Predicted Orbital Sequences for 3 According to INDO and MINDO/3

INDO		MINDO/3	
energy	orbital	energy	orbital
-2.74	16a'(π)	-2.24	16a'(π)
-3.29	10a''(π)	-2.68	10a''(ρ)
-5.71	15a'(σ)	-4.82	15a'(σ)
-6.77	9a''(σ)	-4.49	9a''(σ)
-7.13	14a'(ρ)	-5.63	14a'(σ)
-7.13	8a''(σ)	-6.37	8a''(σ)
-7.50	7a''(σ)	-6.46	13a'(π)
-7.75	13a'(σ)		

Figure 3. Schematic representation of the lowest occupied π orbital in 3 (top) and 4 (bottom) as determined by INDO, MINDO/3, and EHT procedures.

in the case of 4. Where 3 is concerned, the INDO protocol differs from those produced by MINDO/3 and EHT in its deduction of the manner in which the lowest occupied π orbital is deformed. The different rotations predicted for 3 can be traced back to different orbital sequences as summarized in Table IV, where the relevant INDO and MINDO/3 results are compared. While MINDO/3 (and EHT as well) places two σ MO's belonging to the irreducible representations A' above the lowest π MO, INDO predicts only one (15a') above the lowest π orbital. Since 15a' shows negligible coefficients in the cyclopentadienide moiety and large coefficients in the norbornane fragment (Figure 4), its interaction with the lowest occupied π orbital is predicted to be small. However, the other σ orbital (13a' in the INDO and 14a' in the MINDO/3 and EHT calculations) interacts appreciably with the lowest occupied π orbital because of existing large amplitudes in the cyclopentadiene ring. Both σ orbitals are shown in Figure 4. As a consequence of our own experiences^{1,5,9} and those of others,³⁸⁻⁴⁰ we believe the INDO model²⁸ to be a more reliable tool for the prediction of canonical MO sequences in π/σ non-orthogonal compounds than either MINDO/3 or EHT.

The observed preference for alkylation anti to the methano bridge in 3 and the loss of stereoselectivity experienced by 4 can

Figure 4. Schematic drawings of the highest occupied π orbitals belonging to the irreducible representation A' of 3 and 4.Figure 5. (a) Schematic representation of a transition state for S_N1 reaction between an electrophile and anion 3; (b) MO interaction diagram between the π orbital of a donor system and the empty orbital of a carbenium ion.

be explained in part by the predicted tilting of the lowest occupied π orbital. Inspection of the LCAO coefficients in Table III clearly shows that the π lobe of C₁ is tilted toward the CH₂ bridge. As a result of this tilting deformation, different group overlap integrals between the π donor (D) and the acceptor (A) are calculated for an attack from the endo (anti) and exo (syn) face (Figure 5). The simplified interaction diagram in Figure 5 shows that the bonding interaction of the attacking electrophile is more efficient if alkylation occurs from the endo side. Although lesser σ/π interaction is predicted for the lowest π MO in 4, a pronounced deformation at C₁ is still encountered. Therefore, the observed decrease in stereoselectivity experienced by 4 must arise from other factors not accounted for by the preceding analysis (see Discussion).

Discussion

The results compiled for the capture of anions 3 and 4 by electrophilic reagents reveal several interesting facets of π -facial stereoselectivity in these systems. As concerns 3, an overwhelming kinetic preference for endo attack occurs in the course of monomethylation and five-ring spiroannulation. This remarkable

(38) Nicholson, B. J. *Adv. Chem. Phys.* 1970, 18, 249.(39) Clardy, D. C.; Lewis, A. A.; Morland, D.; Murrell, J. N.; Heilbronner, E. *J. Chem. Soc., Faraday Trans. 2* 1974, 70, 1889.(40) Cook, D. B. *Theor. Chim. Acta* 1977, 46, 291.

stereochemical behavior is significantly attenuated when a spirocyclic three-membered ring is being formed or when a norbornene double bond is present as in **4**. The deuteration of **3** is also less than totally stereoselective. Given these facts, it first becomes important to recognize that steric influences are unlikely to be the source of the differing exo/endo rate ratios when they materialize, because the steric perturbation can only come from the differing size of the methano and ethano (or etheno) bridges and these are too remote from the nucleophilic reaction center. Furthermore, very low level isotope effect differences can be expected to make product stability an obviously irrelevant consideration in those studies which involve **12** and **21**. Since the stereoselections observed with epichlorohydrin and 1,4-dibromo-2-isopropylidenebutane parallel closely those observed with the isotopically substituted systems, it would appear that product stability plays an inconsequential role throughout the present investigation.

Consequently, the observed phenomena are presumed to have an electronic origin. The INDO calculations previously described correctly predict higher levels of nucleophilicity on the endo face of **3**. The principal contributory factor is σ/π interaction involving the norbornyl framework bonds and a subjacent π orbital of the cyclopentadienide moiety. The net consequence of this mixing is π orbital tilting in that direction which favors electrophilic attack from the endo surface (Figure 5). This analysis, which suggests the outcome of the methylation and five-ring spiroalkylation reactions to be normally responsible in direction and magnitude to this electronic perturbation, has close parallels in the ground-state nature of **1** and **2**^{5,9} and or norbornene, for which recent calculations show that σ/π interaction induces significant endo tilting of the π bond to favor exo stereoselection.^{8,41,42}

We may now inquire why stereoselectivity drops off during the cyclopropanation process. It has long been recognized that the relative rates of closure associated with three-membered rings do not parallel product stability and are much faster than those for five-membered rings.^{43,44} The activation energies for cyclization do not reflect entirely the thermodynamic stability of the cycle being formed because other factors intervene as well. The most important of these is activation entropy which in the case of cyclopropanation is particularly favorable due to the close proximity of the chain ends across which the bond is to be formed. For five-membered rings, the considerable reduction in strain is offset by a plethora of additional conformational possibilities available to the longer chain.

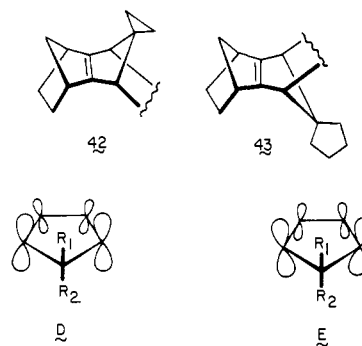
Although rate studies relating to the formation of **8** and **20** have not been carried out, the plausible assumption is made by analogy that **8** is formed more rapidly under the reaction conditions employed. If this is so, then the transition state leading to **8** might initially be misconstrued to resemble the cyclopentadienide more closely than that associated with the formation of **20**.⁴⁵ Were this so, higher π -facial stereoselectivity should be observed during spirocyclopropanation, in contradiction to the experimental results. Importantly, however, frequency factors associated with cyclopropane ring formation are usually very high. As a direct consequence, the trend normally observed is a *decrease* in activation enthalpy while progressing from three- to five-ring cyclizations.⁴³ In view of the higher ΔH^\ddagger for spirocyclopropanation, a later transition state develops and decreased stereoselectivity results because the effects of orbital tilting are made less evident.

We now return to the stereochemical response of **4**. Our previous experience with Diels–Alder additions to **2** and several structural congeners of this triene has shown the added site of

unsaturation to cause a sizeable drop-off in rate (relative to **1**, etc.)^{9b} and on several occasions a loss of stereoselectivity.^{1,5,9} We believe these effects to be intricately related. Thus, perturbation theory clearly denotes that the earlier the transition state, the more successful will be the application of molecular orbital analysis.⁴⁶ Accordingly, as transition states surface progressively later down the reaction profile, the activated complex is less and less likely to reflect the true electronic nature of the cyclopentadienide anion because bond energies have already become substantially altered at this stage.^{45,47} As a consequence, there remains very little, if any, of those electronic features which are characteristic of **4** as it enters into alkylation chemistry. Alternatively, the reduced π -facial stereoselectivity of **4** relative to its norbornyl analogues may arise from reduced levels of tilting in its ψ_1 .

The foregoing discussion has not given explicit consideration to ion-pairing effects involving the lithium counterion. In part, this is due to the fact that the alkylation reactions, which were conducted at relatively elevated temperatures (–30 to +25 °C), have enthalpy demands which almost certainly exceed those required for the Li⁺ to migrate below plane to above plane in **3** and vice versa.⁴⁸ However, the same conditions do not apply to the low-temperature deuteration and protonation experiments. Under the conditions employed (–70 °C), the D⁺ and H⁺ transfers were very probably diffusion controlled. Accordingly, the latter reactions can be expected to be more responsive in their stereoselectivity to the intimate structure of the ion pair. While rapid endo capture of these simple electrophiles is unquestionably preferred, it is not known whether D⁺ or H⁺ enters from the same or opposite side as the Li⁺. This esoteric question may prove resolvable by lithium NMR experiments which we hope to undertake shortly.

We close by calling specific attention to the NMR characteristics of isodicyclopentadiene derivatives prepared in this study. In particular, the differences which emerge between the cyclopropyl carbons in **9** (see A) and the spirocyclopentane carbons in **20** (see B) are especially striking. The ordering of their chemical shifts parallels exactly the differing stereoselectivities of dienophile capture.^{1,9} Thus, the more highly deshielded cyclopropyl methylene carbon in **9** is found below plane, and it is this surface of its cyclopentadiene ring which preferably becomes bonded to electron-deficient olefins with the formation of adducts of general formula **42**.^{1,9,49} Conversely, **20** generally engages in Diels–Alder



chemistry from the above-plane direction to give adducts of type **43**; interestingly, the more shielded of the two α -cyclopentyl carbon atoms resides on the endo surface.

As noted in accompanying papers,^{1,9} the conversion of **1** to **20** by replacement of the hydrogens at R₁ and R₂ by a tetramethylene

(41) Wipff, G.; Morokuma, K. *Tetrahedron Lett.* **1980**, 4445.

(42) Burkert, U., private communication.

(43) (a) House, H. O. "Modern Synthetic Reactions", 2nd ed; W. A. Benjamin: Menlo Park, CA, 1972; pp 541–544. (b) Eliel, E. L. "Steric Effects in Organic Chemistry"; Newman, M. S., Ed.; Wiley: New York, 1956; pp 114–120. (c) Eliel, E. L. "Stereochemistry of Carbon Compounds"; McGraw-Hill: New York, 1962; pp 198–202.

(44) (a) Knipe, A. C.; Stirling, C. J. M. *J. Chem. Soc. B* **1968**, 67; **1967**, 808. (b) Bird, R.; Stirling, C. J. M. *Ibid.* **1968**, 111.

(45) For another example of the use of this argument in another context, see: Huisgen, R.; Schug, R. *J. Am. Chem. Soc.* **1976**, 98, 7819.

(46) Sustmann, R.; Trill, H. *Angew. Chem., Int. Ed. Engl.* **1972**, 11, 838. Sustmann, R.; Schubert, R. *Ibid.* **1972**, 11, 840. Sustmann, R. *Pure Appl. Chem.* **1974**, 40, 569.

(47) Consult, for example: Kiselev, V. D.; Miller, J. G. *J. Am. Chem. Soc.* **1975**, 97, 4036.

(48) We make no distinction between intra- and intermolecular exchange in these systems.

(49) Exceptions to this behavior are sometimes encountered with those dienophiles, e.g., dimethyl acetylenedicarboxylate and *N*-methyltriazolinedione, which possess a second π bond or nonbonded electron pairs orthogonal to that π bond which constitutes the seat of reaction. The consequences of these secondary electronic perturbations are discussed elsewhere.⁹

chain is to cause the π_s diene orbital to be disrotatorily tilted as in **E**. This is the reverse of the state of affairs in **1** (viz., **D**). However, the high levels of spiroconjugation⁵⁰ which is believed to be operative within **9** as the result of strong π interaction with the symmetric Walsh orbitals of the three-membered ring⁵¹ induce its π_s orbital to become tilted as in the parent hydrocarbon (**D**). It would appear, therefore, that [4 + 2] cycloaddition occurs preferentially from the *less shielded* face of these dienes in order to profit from lower secondary antibonding influences along this pathway.^{1,5,9,12}

No technique has yet been uncovered to distinguish unequivocally the methyl carbons in the gem-dimethyl derivative (¹³C shifts: 23.55 and 22.92 ppm). We have established that the methyl signal in **5** (14.76 ppm) appears upfield of that in **8** (15.54 ppm). Additionally, **5** exhibits above-plane stereoselectivity in Diels-Alder reactions and appears on the basis of calculations to experience π_s disrotation as in **E**.⁹ Although good adherence to the general trend is seen, we caution that the absence of a symmetrical substitution pattern in these monomethyl derivatives may well lead to conformational distortions to which ¹³C shifts are very responsive.⁵² Accordingly, **5** and **8** are not regarded as necessarily suitable model substrates, although they well may be. Ultimately required is proof that the ¹³C shift of the exo methyl carbon in the gem-dimethyl compound does indeed appear at 23.55 ppm.

While ¹³C shieldings are dominated predominantly by local paramagnetic electron currents,⁵³ local diamagnetic effects are known to make the more important contribution to ²H chemical shifts.⁵⁴ These differences may account for the fact that the ²H spectral parameters of **36-38** do not conform in direction to those of the carbon shifts discussed above.

Experimental Section

Melting points were determined with a Thomas-Hoover apparatus and are uncorrected. The ¹H NMR spectra were determined with Varian EM-390, Bruker HX-90, Bruker WP-200 and Bruker WM-300 instruments, and apparent splittings are given in all cases. The ¹³C spectra were obtained with a Bruker WP-80 spectrometer and the ²H spectra on the WM-300 instrument. Mass spectra were measured on an AEI-MS9 spectrometer at an ionizing energy of 70 eV. Microanalytical determinations were performed at the Scandinavian Microanalytical Laboratory, Herlev, Denmark.

4,5,6,7-Tetrahydro-endo-2-methyl-4,7-methano-2H-indene (5). A cold (-78 °C), magnetically stirred solution of **1** (8.7 g, 0.066 mol) in anhydrous tetrahydrofuran was treated slowly under a nitrogen atmosphere with *n*-butyllithium in hexane (60.8 mL of 1.3 M, 0.079 mol). After 30 min, methyl iodide (37.4 g, 0.26 mol) was added to the pale yellow solution. After passage of an additional hour, ether (100 mL) was added and the organic phase was washed with water (3 × 100 mL), dried, and evaporated. The residue was distilled to give 5.5 g (57%) of **5** as a colorless liquid: bp 52–55 °C (4 torr); ¹H NMR (CDCl₃) δ 5.53 (s, 2 H), 3.56–3.16 (m, 1 H), 2.96 (s, 2 H), 2.0–1.16 (m, 6 H), 1.06 (d, *J* = 7.5 Hz, 3 H); ¹³C NMR (ppm, CDCl₃) 153.75, 121.62, 52.48, 45.98, 38.31, 28.89, 14.71; mass spectrum, *m/e* (*M*⁺) calcd, 146.1095; obsd, 146.1099.

4,7-Dihydro-exo and endo-2-methyl-4,7-methano-2H-indene (6 and 7). A 1.7 g (13.1 mmol) sample of **2** in dry tetrahydrofuran (100 mL) was treated sequentially with *n*-butyllithium in hexane (15 mL of 1.3 M, 19.6 mmol) and methyl iodide (2.8 g, 20.0 mmol) in the prescribed manner. The reaction mixture was stirred at room temperature for 1 h and worked up as before. Distillation of the residue furnished 1.1 g (58%) of a 50:50 mixture of **6** and **7** (bp 52–58 °C (5 torr)). Product analysis was achieved through integration of the ¹H NMR spectrum, especially the high-field methyl doublets centered at δ 1.15 and 1.05 (*J* = 8 Hz); ¹³C NMR (ppm, CDCl₃) 151.96, 137.98, 137.88, 122.29, 121.81, 58.79,

58.21, 54.42, 54.28, 43.35, 15.83, 14.61.

4',5',6',7'-Tetrahydrospiro[cyclopropene-1,2'-[4,7]methano[2H]indene (9). Into a solution of sodium amide in liquid ammonia [prepared from 0.70 g (30.4 mg-atom) of sodium and 30 mg of ferric nitrate in 100 mL of solution] was slowly syringed 2.0 g (15.1 mmol) of isodicyclopentadiene (**1**). After the reaction mixture had been stirred for 1 h, 1,2-dibromoethane (2.84 g, 15.1 mmol) was slowly introduced during 10 min. After 30 additional minutes, anhydrous ether (50 mL) was added and the ammonia was allowed to evaporate. The ether solution was washed with water (50 mL) and the aqueous phase was back-extracted with ether (2 × 50 mL). The combined organic layers were washed several times with water to neutrality, dried, and evaporated. Approximately 50% of starting diene can be recovered by fractional distillation. The fraction having bp 51–52 °C (1 torr) proved to be **9** (635 mg, 27%). The analytical sample was obtained by preparative VPC on a 5% SE-30 column at 110 °C; ¹H NMR (CDCl₃) δ 5.30 (s, 2 H), 3.10–2.96 (m, 2 H), 1.90–1.39 (series of m, 6 H), and 1.36 (s, 4 H); ¹³C NMR (ppm, CDCl₃) 152.88 (q), 121.13 (d), 46.51 (t), 40.04 (q), 38.94 (d), 28.84, 11.26, 10.29; mass spectrum, *m/e* (*M*⁺) calcd, 158.1095; obsd, 158.1100.

Epoxidation of 10. Spirodiene **9** was reacted with phenyl vinyl sulfone and the adducts were reductively desulfonated as described elsewhere.^{9b} To an ice-cold solution of **10** (30 mg, 0.16 mmol) in dichloromethane (10 mL) was slowly added a solution of *m*-chloroperbenzoic acid (33 mg, 0.19 mmol) in the same solvent (10 mL). After 30 min, the clear solution was washed with 5% sodium sulfite and saturated sodium bicarbonate solutions and with water prior to drying. Following the evaporation of solvent, the residue was purified by MPLC on silica gel (elution with 5% ethyl acetate in hexanes) and epoxide **11** was obtained as a colorless oil (26 mg, 82%); ¹H NMR (CDCl₃) δ 2.80 (br s, 2 H), 2.06–1.47 (series of m, 11 H), 0.90–0.63 (m, 3 H), and 0.27–0.03 (m, 2 H); ¹³C NMR (ppm, CDCl₃) 59.70, 47.70, 41.40, 38.35, 37.00, 27.25, 26.87, 11.96, 2.91; mass spectrum, *m/e* (*M*⁺) calcd, 202.1358; obsd, 202.1363.

Spirocyclopropanation with Deuterium-Labeled 1,2-Disubstituted Ethanes. General Procedure. Diene **1** (5.0 g, 37.8 mmol) was slowly syringed into a rapidly stirred mixture of sodium amide (106 mmol) in liquid ammonia (150 mL). After 30 min, BrCH₂CD₂Cl (5.5 g, 37.8 mmol) was added via syringe. The previous directives were followed and 2.0 g (33%) of a mixture of **12a** and **12b** was obtained, bp 42–43 °C (0.2 torr); ¹H NMR (CDCl₃) δ 5.30 (s, 2 H), 2.97 (br s, 2 H), 1.9–1.2 (series of m, 8 H); ¹³C NMR (ppm, CDCl₃) 152.83, 121.08, 46.51, 39.86, 38.89, 28.84, 11.07, 10.05.

A 300-mg sample of this mixture (1.9 mmol) was added to a solution of dimethyl acetylenedicarboxylate (400 mg, 2.8 mmol) in chloroform (25 mL) and stirred at room temperature for 3 h. The solvent was evaporated and the residue was purified by preparative TLC on silica gel (elution with 10% ethyl acetate in hexanes). There was isolated 360 mg (63%) of a mixture of adducts; ¹³C NMR (ppm, CDCl₃) 165.99, 158.03, 150.06, 66.08, 57.48, 51.95, 47.97, 43.01, 22.58, 9.86, 7.72.

To an ice-cold solution of the adducts (310 mg, 1.03 mmol) in dichloromethane (40 mL) was added *m*-chloroperbenzoic acid (243 mg, 1.13 mmol of 80% purity) dissolved in the same solvent (15 mL). After 30 min, the reaction mixture was washed with 5% sodium thiosulfate and saturated sodium bicarbonate solutions and with water prior to drying and solvent evaporation. The epoxides were purified by preparative TLC on silica gel (elution with 20% ethyl acetate in hexanes) to give 312 mg (95%) of **13a** and **13b**: ¹H NMR (CDCl₃) δ 3.85 (s), 2.96 (s), 2.70 (br s), 2.06–1.80 (m), 1.60–1.16 (m), 0.96–0.80 (m), 0.73 (s), and 0.33 (s); ¹³C NMR (ppm, CDCl₃) 165.07, 149.14, 66.22, 54.96, 54.13, 52.24, 39.81, 38.89, 24.95, 14.03, 2.18.

Condensation with Epichlorohydrin. Diene **1** (5.0 g, 0.038 mol) was added dropwise to a stirred solution of freshly prepared sodium amide [from 2.2 g (0.095 g-atom) of sodium metal and a few crystals of ferric nitrate in 125 mL of liquid ammonia]. After 0.5 h at the reflux temperature, epichlorohydrin (3.5 g, 0.038 mol) was added dropwise to the green solution which was maintained at reflux for an additional 3 h. Tetrahydrofuran (100 mL) was added and the ammonia was allowed to evaporate. The reaction mixture was stirred overnight at 20 °C, cautiously diluted with ice water, and extracted with ether (3 × 50 mL). The combined ether extracts were washed with water (3 × 25 mL), saturated ammonium chloride solution (2 × 25 mL), and water (25 mL) prior to drying and solvent evaporation. Bulb-to-bulb distillation afforded 1.7 g of recovered starting material (bp <50 °C (0.05 torr)) and 1.9 g (40% based upon recovered **1**) of a mixture of **18** and **19** as a light yellow oil (bp <150 °C (0.05 torr)); ¹H NMR (CDCl₃) δ 5.48 (m, 2 H), 5.31 (m, 2 H), 3.92 (d, *J* = 11.6 Hz, 1 H), 3.88 (d, *J* = 11.6 Hz, 1 H), 3.55 (d, *J* = 11.6 Hz, 1 H), 3.50 (d, *J* = 11.6 Hz, 1 H), 2.20–2.09 (m, 2 H), 1.87–1.34 (m, 18 H); ¹³C NMR (ppm, CDCl₃) 155.70, 155.45, 152.20, 152.01, 121.52, 121.37, 115.64, 115.45, 65.30, 65.15, 46.36, 44.28, 39.08, 38.79, 28.84, 28.69, 28.01, 27.28, 16.55, 15.29; mass spectrum *m/e* (*M*⁺) calcd, 188.1201; obsd, 188.1206.

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4',5',6',7'-Tetrahydrospiro[cyclopentane-1,2'-[4,7]methano[2H]indene] (20). Following the addition of **1** (2.0 g, 15.1 mmol) to sodium amide (37.8 mmol) in liquid ammonia (100 mL), 1,4-dibromobutane (3.27 g, 15.1 mmol) was introduced by syringe. After the usual workup, the residue was distilled and the fraction boiling at 61–62 °C (1 torr) was collected to give 703 mg (25%) of **20**: ¹H NMR (CDCl₃) δ 5.53 (s, 2 H), 3.00–2.83 (m, 2 H), 1.93–1.17 (series of m, 14 H); ¹³C NMR (ppm, CDCl₃) 151.23, 124.58, 69.33, 45.25, 38.35, 33.60, 33.06, 28.84, 25.93, 25.73; mass spectrum, *m/e* (M⁺) calcd, 186.1408; obsd, 186.1412.

Anal. Calcd for C₁₄H₁₈: C, 90.26; H, 9.74. Found: C, 90.02; H, 9.72.

Spiroalkylation of 1 with Cl(CH₂)₃CD₂I. Following the addition of **1** (1.87 g, 14.1 mmol) to sodium amide (39.6 mmol) in liquid ammonia (120 mL), 4-chloro-1-iodobutane-1,1-*d*₂ (3.12 g, 14.15 mmol) was introduced by syringe. After the customary workup, there was obtained 510 mg (19%) of **21**, bp 67–68 °C (0.05 torr); ¹H NMR (CDCl₃) δ 5.47 (s, 2 H), 3.10–2.80 (m, 2 H), and 1.90–1.17 (m, 12 H); ¹³C NMR (ppm, CDCl₃) 151.18, 124.53, 69.14, 45.25, 38.31, 33.06, 28.84, 25.93, 25.54.

The adducts of **21** with maleic anhydride, *N*-phenylmaleimide, benzoquinone, and *N*-methyltriazaolinedione were prepared and the ¹³C NMR spectrum of each product confirmed that a single isotopically labeled isomer had been formed.

Spiroalkylation of 2 with Cl(CH₂)₃CD₂I. Reaction of **2** (2.35 g, 18.1 mmol) with the labeled dihalide in the prescribed manner and fractional distillation furnished 1.64 g (29%) of spiroalkylated product, bp 52–53 °C (0.05 torr). The ¹H and ¹³C NMR spectra of this material indicated that a pair of isomers had been produced in a ratio approximately 1:1: ¹H (CDCl₃) δ 6.27 (t, *J* = 3 Hz, 2 H), 5.57 (s, 2 H), 3.37 (t, *J* = 3 Hz, 2 H), 2.07 (A₂B₂, *J*_{AB} = 9 Hz, 2 H), 1.83–1.50 (m, 6 H); ¹³C NMR (ppm, CDCl₃) 149.29, 137.64, 124.92, 71.22, 57.92, 43.35, 34.28, 32.87, 25.63, 25.39.

Dimethyl Acetylenedicarboxylate Cycloaddition to 21. A solution of **21** (700 mg, 3.72 mmol) and dimethyl acetylenedicarboxylate (582 mg, 4.10 mmol) in chloroform (50 mL) was stirred at room temperature overnight. The yellow solution was evaporated to dryness and the residue was purified by medium-pressure liquid chromatography (MPLC) on silica gel. Elution with 10% ethyl acetate in hexanes gave first the endo adduct **22b** (780 mg, 64%) as a colorless crystalline solid, mp 75–76 °C (from hexanes). Later fractions contained the exo isomer (300 mg, 24%), a pale yellow mobile oil.

For **22b**: ²H NMR (ppm, CCl₄) 1.75; ¹H NMR (δ, CDCl₃) 3.76 (s, 6 H), 3.46 (s, 2 H), 3.10–2.90 (m, 2 H), 1.8–1.0 (m, 10 H), 0.70–0.36 (m, 2 H); ¹³C NMR (ppm, CDCl₃) 166.52, 158.12, 149.92, 93.80, 61.12, 51.90, 48.06, 42.92, 34.37, 25.49, 24.91, 22.62.

Epoxidation of 22b. *m*-Chloroperbenzoic acid (107 mg, 0.62 mmol) dissolved in dichloromethane (10 mL) was added to an ice-cooled solution of **22b** (170 mg, 0.52 mmol) in the same solvent (20 mL). The solution was heated to reflux for 15 h, washed with 10% sodium sulfite and saturated sodium bicarbonate solutions and water, dried, and evaporated. There was isolated 150 mg (83%) of **23**, mp 132–133 °C (from hexanes); ²H NMR (ppm, CCl₄) 1.62; ¹H NMR (δ, CDCl₃) 3.73 (s, 6 H), 3.10 (s, 2 H), 2.53 (m, 2 H), 1.96–1.13 (m, 10 H), 0.83–0.63 (m, 2 H); ¹³C NMR (ppm, CDCl₃) 165.50, 149.48, 81.66, 65.93, 57.68, 52.29, 40.20, 38.60, 37.58, 27.92, 25.20, 24.66.

Hydrogenation of 22b. A solution of **22b** (1.80 g, 5.49 mmol) in ethyl acetate (150 mL) containing 100 mg of 10% palladium on carbon was hydrogenated at 53 psi in a Parr apparatus for 28 h. The mixture was filtered through Celite and the filtrate was evaporated to dryness. The oily residue was purified by HPLC on silica gel (elution with 7% ethyl acetate in petroleum ether) to give 1.5 g (83%) of **24**: mp 65–67 °C (from hexanes); ¹H NMR (CDCl₃) δ 3.77 (s, 6 H), 2.63 (s, 4 H), 2.20 (br, 2 H), 1.80–1.15 (series of m, 14 H); ¹³C NMR (ppm, CDCl₃) 165.79, 144.34, 83.84, 54.62, 51.95, 48.69, 46.90, 39.76, 32.67 (2C), 25.68, 25.40, 24.47; mass spectrum, *m/e* (M⁺) calcd, 330.1831; obsd, 330.1840.

1,4-Bis(tetrahydropyranyloxy)-2-isopropylidenebutane (26b). A solution of **26a** (2.0 g, 17 mmol) and dihydropyran (4.21 g, 50 mmol) in dichloromethane (50 mL) containing 10 mol % pyridinium *p*-toluenesulfonate was stirred at room temperature for 4 h. The reaction mixture was diluted with ether (25 mL), washed with brine (2 × 25 mL), dried, and evaporated to furnish 4.7 g (98%) of **26b** as a light yellow oil: ¹H NMR (CDCl₃) δ 4.5 (m, 2 H), 4.20–3.15 (m, 8 H), 2.42 (t, *J* = 7 Hz, 2 H), 1.72 (s, 6 H), 2.0–1.25 (m, 12 H).

1,4-Dibromo-2-isopropylidenebutane (27). A solution of triphenylphosphine dibromide was prepared by adding bromine (2.7 mL, 7.92 g, 0.049 mol) to a stirred, cooled (0 °C) solution of triphenylphosphine (12.97 g, 0.049 mol) in dichloromethane (120 mL). A solution of unpurified **26b** (3.24 g, 0.0112 mol) in dichloromethane (20 mL) was added and the reaction mixture was stirred overnight at room temperature. The dark solution was washed with water (2 × 100 mL), dried, and adsorbed

onto 45 g of neutral alumina. This solid was placed atop a column of silica gel (120 g) and the product was isolated as a colorless oil by petroleum ether elution: 3.3 g (66%); IR (cm⁻¹, neat) 2970, 2900, 1645, 1430, 1365, 1255, 1190; ¹H NMR (CDCl₃) δ 4.02 (s, 2 H), 3.40 (t, *J* = 8.5 Hz, 2 H), 2.72 (t, *J* = 8.5 Hz, 2 H), 1.78 (3 H), 1.75 (s, 3 H); ¹³C NMR (ppm, CDCl₃) 137.78, 127.00, 35.30, 34.03, 30.63, 21.31, 20.63; mass spectrum, *m/e* (M⁺ - HBr) calcd, 174.0045; obsd, 174.0049.

Spiroalkylation with 27. Diene **1** (5.0 g, 0.038 mol) was added dropwise to a stirred solution of freshly prepared sodium amide [from 2.2 g (0.095 g-atom) of sodium metal—see above] in 125 mL of liquid ammonia. After 0.5 h at the reflux temperature, **27** (10.33 g, 0.0403 mol) was added dropwise to the green anion solution and the reaction mixture was stirred for 2 h. Tetrahydrofuran (100 mL) was added and the ammonia was allowed to evaporate. Water was cautiously added and the product was extracted into ether (4 × 50 mL). The combined organic layers were washed with water (5 × 50 mL) and saturated ammonium chloride solution (2 × 50 mL), dried, and evaporated to afford 2.4 g (28%) of **28** as a colorless oil: IR (cm⁻¹, neat) 3045, 2950, 2910, 2860, 1440, 1365, 1100, 820, 810; ¹H NMR (CDCl₃) δ 5.56 (s, 2 H), 3.03–2.90 (m, 2 H), 2.58–2.33 (m, 4 H), 1.95–1.28 (m, 14 H); ¹³C NMR (ppm, CDCl₃) 151.67, 135.65, 124.19, 121.71, 68.79, 45.20, 38.30, 37.82, 33.55, 31.22, 28.79, 21.07, 20.92; mass spectrum, *m/e* (M⁺) calcd, 226.1721; obsd, 226.1727.

Anal. Calcd for C₁₇H₂₂: C, 90.20; H, 9.80. Found: C, 90.15; H, 9.82.

Reaction of 28 with Dimethyl Acetylenedicarboxylate. A solution of DMAD (250 mg, 1.77 mmol) in chloroform (5 mL) was added to a stirred solution of **28** (200 mg, 0.885 mmol) in chloroform (5 mL). After 24 h, the solvent was evaporated and the residue was separated into its components by MPLC on silica gel (elution with 10% ethyl acetate in petroleum ether).

For **29**: 173 mg (53%); IR (cm⁻¹, neat) 3080, 2950, 2860, 1710, 1620, 1430, 1300, 1260, 1200, 1160, 1085, 1056; ¹H NMR (CDCl₃) δ 3.68 (s, 6 H), 3.40 (s, 2 H), 2.94 (m, 2 H), 2.35 (br s, 2 H), 2.17 (br t, *J* = 6 Hz, 2 H), 1.82 (t, *J* = 6 Hz, 2 H), 1.55–1.25 (m, 10 H), 0.50–0.45 (m, 2 H); ¹³C NMR (ppm, CDCl₃) 166.47, 157.78, 149.58, 133.51, 121.81, 93.75, 59.81, 52.00, 48.16, 42.97, 38.79, 32.04, 28.79, 22.67, 20.78, 20.54; mass spectrum, *m/e* (M⁺) calcd, 368.1987; obsd, 368.1997.

For **30**: 88 mg (27%); IR (cm⁻¹, neat) 2950, 2850, 1710, 1620, 1430, 1305, 1270, 1255, 1190, 1155, 1090, 1050, 727; ¹H NMR (CDCl₃) δ 3.79 (s, 6 H), 3.52 (s, 2 H), 3.12–3.00 (m, 2 H), 2.38 (br s, 2 H), 2.12 (br t, *J* = 6 Hz, 2 H), 1.97–1.71 (m, 2 H), 1.60–0.79 (m, 12 H); ¹³C NMR (ppm, CDCl₃) 166.13, 160.16, 153.66, 133.07, 122.34, 99.48, 60.01, 55.10, 51.90, 42.92, 38.64, 32.28, 29.71, 28.79, 25.39, 20.78, 20.49; mass spectrum, *m/e* (M⁺) calcd, 368.1987; obsd, 368.1997.

Epoxidation of 29. A solution of **29** (200 mg, 0.54 mmol) in dichloromethane (10 mL) was treated at 0 °C with a solution of *m*-chloroperbenzoic acid (93 mg, 0.54 mmol) in the same solvent (10 mL). After 4 h at 0 °C, the reaction mixture was washed with 5% sodium thiosulfate (4 × 25 mL) and saturated sodium bicarbonate solutions (2 × 25 mL) prior to drying and evaporation. Separation of the epoxide mixture by mp on silica gel (elution with 20% ethyl acetate in petroleum ether) afforded:

For **31**: 110 mg (54%) as a pale yellow oil; IR (cm⁻¹, neat) 2970, 2870, 1715, 1433, 1375, 1305, 1255, 1100; ¹H NMR (CDCl₃) δ 3.80 (s, 6 H), 3.68 (m, 1 H), 3.48 (m, 1 H), 3.03 (m, 2 H), 2.28–1.74 (m, 6 H), 1.66–1.08 (m, 10 H), and 0.70–0.42 (m, 2 H); ¹³C NMR (ppm, CDCl₃) 166.28, 158.37, 157.35, 149.77, 148.71, 92.05, 72.14, 60.49, 60.15, 60.01, 52.04, 48.11, 43.01, 42.92, 39.28, 30.83, 29.37, 22.62, 21.51; mass spectrum, *m/e* (M⁺) calcd, 384.1937; obsd, 384.1944.

For **32**: 70 mg (34%) as a light tan oil; IR (cm⁻¹, neat) 2970, 2930, 2870, 1715, 1625, 1435, 1375, 1250, 1095, 1050; ¹H NMR (CDCl₃) δ 3.80 (s, 6 H), 3.67 (m, 1 H), 3.55 (m, 1 H), 3.08 (m, 2 H), 2.22–1.11 (series of m, 10 H), 1.98 (s, 3 H), 1.31 (s, 3 H), 0.71–0.48 (m, 2 H); ¹³C NMR (ppm, CDCl₃) 165.89, 157.69, 149.87, 91.95, 71.80, 60.01, 52.04, 48.21, 42.92, 37.53, 32.38, 29.91, 22.72, 21.65, 21.41; mass spectrum, *m/e* (M⁺) calcd, 384.1937; obsd, 384.1944.

Chromous Sulfate Reduction of 30. A solution of **30** (190 mg, 0.52 mmol) in dimethylformamide (8 mL) was added dropwise to a stirred aqueous solution of chromous sulfate (5 mL, 2.5 mequiv). After being stirred at room temperature for 30 min, the reaction mixture was diluted with water (20 mL) and extracted with ether (4 × 20 mL). The combined extracts were washed with water (4 × 20 mL) and brine (20 mL) prior to drying and evaporation. The products were separated by mp on silica gel (elution with 10% ethyl acetate in petroleum ether):

For **33**: 100 mg (52%) of colorless platelets, mp 93–94 °C (from methanol); IR (cm⁻¹, neat) 2950, 2910, 2850, 1735, 1435, 1270, 1200, 1015; ¹H NMR (CDCl₃) δ 3.72–3.52 (m, 1 H), 3.68 (s, 3 H), 3.63 (s, 3 H), 3.65–3.00 (m, 5 H), 2.20–1.04 (series of m, 18 H); ¹³C NMR (ppm, CDCl₃) 174.48, 174.19, 155.16, 151.33, 133.90, 121.81, 74.96,

54.57, 52.77, 52.58, 51.90, 51.70, 50.44, 48.65, 41.80, 41.56, 36.61, 31.95, 28.55, 25.29, 20.78, 20.54; mass spectrum, m/e (M^+) calcd, 370.2144; obsd, 360.2152.

Anal. Calcd for $C_{23}H_{30}O_4$: C, 74.56; H, 8.16. Found: C, 74.40; H, 8.17.

For **34**: 20 mg (10%) as a colorless oil; IR (cm^{-1} , neat) 2950, 2910, 2860, 1745, 1430, 1270, 1190, 1160, 1050; 1H NMR ($CDCl_3$) δ 3.64 (s, 6 H), 3.48 (m, 2 H), 2.90 (m, 2 H), 2.75 (m, 2 H), 2.08 (m, 4 H), 1.92–0.73 (series of m, 14 H); ^{13}C NMR (ppm, $CDCl_3$) 173.11, 151.64, 133.79, 122.01, 73.71, 53.48, 52.60, 51.41, 49.07, 42.48, 37.56, 31.17, 28.97, 25.62, 20.80, 20.59; mass spectrum, m/e (M^+) calcd, 370.2144; obsd, 370.2152.

Reaction of 28 with *N*-Methyltriazolinedione. A solution of *N*-methyltriazolinedione (100 mg, 0.885 mmol) in dichloromethane (5 mL) was added to a stirred, cold (-78 °C) solution of **28** (200 mg, 0.885 mmol) in the same solvent (5 mL). After being stirred at -78 °C for 30 min, the reaction mixture was warmed to room temperature and solvent was removed in vacuo. Purification by MPLC on silica gel (elution with 30% ethyl acetate in petroleum ether) afforded 100 mg (33%) of **35** as colorless needles: mp 161–162 °C (from hexanes); IR (cm^{-1} , KBr) 2990, 2940, 2850, 1773, 1710, 1440, 1387, 1260, 1190, 1165, 1007, 853, 780, 770; 1H NMR ($CDCl_3$) δ 4.51 (s, 2 H), 3.01 (m, 2 H), 2.95 (s, 3 H), 2.47 (br s, 2 H), 2.18 (br t, $J = 6$ Hz, 2 H), 2.00–1.75 (m, 2 H), 1.57 (br s, 6 H), 1.49–0.99 (m, 6 H); ^{13}C NMR (ppm, $CDCl_3$) 161.33, 150.06, 132.20, 123.17, 75.74, 70.44, 55.25, 41.36, 36.99, 30.00, 28.64, 25.39, 24.91, 20.88, 20.58; mass spectrum, m/e (M^+) calcd, 339.1947; obsd, 339.1939.

Anal. Calcd for $C_{20}H_{25}N_3O_2$: C, 70.77; H, 7.42. Found: C, 70.69; H, 7.44.

Deuterium Oxide Quench of 3. *n*-Butyllithium in hexane (26.3 mL of 0.95 M, 25.0 mmol) was added slowly via syringe to a cold (-70 °C) solution of **1** (3.0 g, 22.73 mmol) in 100 mL of freshly distilled anhydrous tetrahydrofuran. The pale yellow solution was stirred at this temperature for 1 h prior to being slowly transferred to a cold (-70 °C) solution of 100% deuterium oxide (0.5 mL, 25.0 mmol) in the same solvent (10 mL). The resulting mixture was allowed to warm to room temperature, stirred for 1 h, and treated with ether (100 mL). The organic phase was washed with water (3×100 mL), dried, and evaporated. The residue was distilled to give 1.8 g (60%) of a mixture of **36** and **38** as a colorless liquid, bp 64–67 °C (22 torr). The product ratio of 77:23 with **36** dominating was established by 2H NMR spectroscopy in CCl_4 : for **36** (major), 3.02 ppm; for **38**, 3.14 ppm.

4,5,6,7-Tetrahydro-4,7-methano-2*H*-indene-2,2- d_2 (37). Treatment of the preceding mixture (3.96 g, 29.77 mmol) with *n*-butyllithium (31.1 mL of 0.95 M, 32.75 mmol) in the predescribed manner, followed by a D_2O quench, afforded 1.56 g (39%) of **37**: bp 64–67 °C (22 torr); 2H NMR (ppm, CCl_4) 3.14 and 3.02 (equal intensity).

Water Quench of the Anion of 37. From 1.56 g (11.64 mmol) of **37** and *n*-butyllithium (13.5 mL of 0.95 M, 12.28 mL), there was produced the monodeuterated anion which was quenched in water to give 680 mg (44%) of **38**: bp 65–67 °C (22 torr); 2H NMR (ppm, CCl_4) 3.14 with a small shoulder at 3.02 due to the presence of residual d_2 -labeled diene.

Cycloaddition of Phenyl Vinyl Sulfone to 38. A solution of **38** (680 mg, 5.11 mmol) and phenyl vinyl sulfone (860 mg, 5.11 mmol) in di-

chloromethane (10 mL) was heated at the reflux temperature for 2.5 days. The solvent was evaporated and the residue was purified by MPLC on silica gel (elution with 10% ethyl acetate in petroleum ether). There was obtained 540 mg of exo sulfone **39b** which was contaminated with a small amount of the endo-phenylsulfonyl isomer (^{13}C NMR analysis). Recrystallization from hexanes gave **39b** as colorless needles (400 mg, 26%): mp 132.5–133.5 °C; 2H NMR (ppm, CCl_4) 1.45; 1H NMR ($CDCl_3$) δ 8.00–7.73 (m, 2 H), 7.70–7.40 (m, 3H), 3.37 (s, 1 H), 3.05 (br m, 1 H), 2.66 (s, 2 H), 2.77–2.51 (m, 1 H), 2.25–1.85 (m, 2 H), 1.70–0.90 (m, 5 H), 0.80–0.55 (m, 2 H); ^{13}C NMR (ppm, $CDCl_3$) 157.40, 150.55, 140.21, 133.36, 129.29, 128.12, 64.33, 50.35, 45.44, 42.82, 42.53, 42.19, 29.37, 25.88, 24.91.

Reductive Desulfonylation of 39b. To a stirred mixture of disodium hydrogen phosphate (1.70 g, 11.97 mmol) and 6% sodium amalgam (3.73 g, 6.65 mmol) in distilled methanol (20 mL) was added a solution of **39b** (400 mg, 1.33 mmol) in distilled tetrahydrofuran (10 mL). The reaction mixture was stirred overnight at room temperature, treated with hexane (50 mL), and washed with water (2×100 mL). Following drying and solvent evaporation, the residue was purified by filtration through basic alumina: 160 mg (75%) of **40b**, mp 32–34 °C; 2H NMR (ppm, $CDCl_3$) 1.39 with a weak signal at 1.05 due to the dideuterio compound; 1H NMR ($CDCl_3$) δ 3.00 (br s, 4 H), 1.7–0.7 (series of m, 11 H).

Epoxidation of 40b. An ice-cold (0 °C) solution of **40b** (160 mg, 0.99 mmol) in dichloromethane (10 mL) was slowly treated with a solution of *m*-chloroperbenzoic acid (206 mg, 1.2 mmol) in the same solvent (20 mL). After 10 min at room temperature, the reaction mixture was processed in the manner described above to give a residue which was purified by sublimation at 70 °C and 0.1 torr. Epoxide **41b** (130 mg, 73%) was obtained as a white powder: mp 88–89 °C; 2H NMR (ppm, CCl_4) 1.88 with a weak band at 0.59 for the d_2 impurity; 1H NMR ($CDCl_3$) δ 2.70 (br s, 4 H), 2.06–1.36 (series of m, 9 H), 0.76–0.50 (m, 2 H).

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Registry No. 1, 6675-72-5; 2, 6675-71-4; 3, 83877-21-8; 4, 85221-92-7; 5, 83134-57-0; 6, 85221-93-8; 7, 85234-90-8; 9, 81897-89-4; 10, 85221-94-9; 11, 81897-90-7; 12a, 81897-92-9; 12b, 81967-95-5; 13a, 85221-95-0; 13b, 85280-02-0; 18, 85221-96-1; 19, 85280-03-1; 20, 81897-93-0; 21, 81897-94-1; 21 8,9-dehydro (isomer 1), 85221-97-2; 21 8,9-dehydro (isomer 2), 85280-04-2; endo-22b, 81897-95-2; exo-22b, 85280-86-0; 23, 81897-96-3; 24, 81897-97-4; 26a, 42091-47-4; 26b, 85221-98-3; 27, 85221-99-4; 28, 85222-00-0; 29, 85222-01-1; 30, 85280-05-3; 31, 85222-02-2; 32, 85222-03-3; 33, 85222-04-4; 34, 85230-06-4; 35, 85222-05-5; 36, 81897-83-8; 37, 81897-84-9; 38, 81897-85-0; 39b, 81897-86-1; 40b, 81897-92-2; 41b, 81967-93-3; $BrCH_2CD_2Cl$, 61853-37-0; $Cl(CH_2)_3CD_2I$, 66502-81-6; methyl iodide, 74-88-4; 1,2-dibromoethane, 106-93-4; phenyl vinyl sulfone, 5535-48-8; epichlorohydrin, 106-89-8; 1,4-dibromobutane, 110-52-1; dimethyl acetylenedicarboxylate, 762-42-5; dihydrogen, 110-87-2; *N*-methyltriazolinedione, 13274-43-6.