Transannular Orbital Interaction between Ketone and Olefin Chromophores Detected by Circular Dichroism and ^{13}C-NMR Spectroscopy. Dimethanonaphthalenones and Trimethanoanthracenones

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Abstract: A series of δ,ε-unsaturated ketones and their saturated ketone analogs were synthesized on the dimethanonaphthalene skeleton with endo-endo (**1**), endo-exo (**2**), and exo-exo (**3**) configurations. The corresponding norbornylogs (trimethanoanthracenes) with ζ,η-unsaturated ketones (**4**, **5**, and **6**) and their saturated analogs were also synthesized. Their ^{13}C-NMR and circular dichroism (CD) spectra were measured in order to examine transannular orbital interactions. Transannular orbital interaction was detected by a relatively more shielded ^{13}C=O resonance in the unsaturated ketones. The shielding was largest when the C=O and C=C chromophores could interact through σ–pp orbital overlap, as in **1**. That is, orbital interaction through space is an important component of the ground state of **1**. In the CD spectra, the ketone n–π* $\Delta\epsilon_{max}$ values were typically larger for the unsaturated ketones, as compared with their saturated ketone analogs. The n–π* $\Delta\epsilon_{max}$ enhancements fall off with increasing interchromophoric distance, as seen in the trimethanoanthracenes. The presence of "charge-transfer" CD bands near 230 nm in the unsaturated ketones suggests a component of "through-space" orbital interaction. The intensity of the CD charge-transfer bands is greatest when the chromophores are oriented for σ–pp orbital interaction. Orbital interaction through space appears to be an important component of the excited state of **1** and **2**, and even **4**, but it appears to play a less important role in **3**, **5**, and **6**.

Introduction

Some twenty years ago, using the language of perturbation theory, Hoffmann[1] described how localized sets of orbitals or chromophores may interact with each other directly, through space, or indirectly, through bonds, as in homoconjunction and transannular orbital interactions. This division, seen possibly as an arbitrary distinction between normal bonding and nonbonding interactions, has proved, nonetheless, to be a very useful way to picture electronic interactions in terms of molecular structure. Orbital interactions through space (OITS), which involve direct spatial overlap, have long fascinated organic chemists. They have been detected in diverse circumstances, e.g., anchimeric assistance in solvolysis[2] and in spectral shifts,[3] and they have been explored in σ-aromaticity.[4] Orbital interactions through bonds (OITB) may operate over long distances, typically through the σ-bond molecular electronic framework, as has been demonstrated in kinetic[2,5] and spectroscopic studies.[3] In recent years, ground-state OITS and OITB in organic molecules have been detected and studied by photoelectron spectroscopy.[6,7] For example, the 0.86-eV splitting of the π orbitals of norbornadiene has been attributed predominantly to OITS;[6] the large splitting (~1 eV) of the $\pi(b_{3u})$ from the $\pi(b_{2u})$ orbital of [2.2]paracyclophane is thought to be due largely to orbital interaction through the σ-bond framework[6] (three σ bonds); the even larger (1.55 eV) splitting of the two linear combinations from the in-plane MOs of cyclodeca-1,6-diyne has been attributed to both OITS and OITB.[8] In select examples, OITB can be seen to operate over surprisingly large distances, as in a trimethanoanthracene, where an 0.32-eV π-orbital splitting is due to coupling through six σ bonds (7.5 Å).[9] At the even greater distances (eight σ bonds) of tetramethanotetracenes, π-orbital splittings as large as 0.29 eV have been explained as a combination of OITB and laticyclic hyperconjugation.[10,11]

Most of the observations of homoconjugation and transannular orbital interaction have been studied for ground-state orbitals, especially by photoelectron spectroscopy (PES)[3,6-11] and electron transmission spectroscopy (ETS).[12] However, orbital interactions can also lead to interesting and unusual excitation bands in the electronic spectrum, often seen with difficulty in the UV[13] but with greater clarity in the UV–circular dichroism (CD) spectra, e.g., in the "mystery" bands of norbornadiene,[14a] 7-norbornenone,[14b] and barrelene.[14c] Except for such small systems[14] and for dissymmetric β,γ-unsaturated ketones,[15,16] β,γ-cyclopropyl

(1) Hoffmann, R. *Acc. Chem. Res.* **1971**, *4*, 1–9.
(2) There are many examples. See: (a) Bruck, P.; Thompson, D.; Winstein, S. *Chem. Ind.* **1960**, 590–591. (b) Winstein, S.; Hansen, R. L. *Tetrahedron Lett.* **1960**, *25*, 1–8, and references therein. (c) See also, *Carbonium Ions*; Olah, G., Schleyer, P. v. R., Eds.; Wiley: New York, 1972; Vol. III.
(3) A representative collection may be found in Martin, H.-D.; Mayer, B. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 283–314.
(4) McEwen, A. B.; Schleyer, P. v. R. *J. Org. Chem.* **1986**, *51*, 4357–4368.
(5) See, for example: Sargent, G. D. The 2-Norbornyl Carbon. In *Carbonium Ions*; Olah, G., Schleyer, P. v. R., Eds.; Wiley: New York, 1972; Vol. III and references therein.
(6) For leading references, see: (a) Heilbronner, E.; Maier, J. P. Some Aspects of Organic Photoelectron Spectroscopy. In *Electron Spectroscopy: Theory, Techniques and Applications*; Brindle, C. R., Baker, A. D., Eds.; Academic Press: New York, 1977; Vol. 1, Chapter 5. (b) Paddon-Row, M. N. *Acc. Chem. Res.* **1982**, *15*, 245–251.
(7) The theoretical explanations typically involve a delocalized orbital description; however, whether a delocalized or a localized picture should be involved depends on the intramolecular relaxation time. Consequently, the OITS and OITB situations seen by PES might just as well be described with a localized orbital picture. Sawatzky, G. A.; Lenseline, A. *J. Chem. Phys.* **1980**, *72*, 3748–3753.
(8) Gleiter, R.; Karcher, M.; Schäfer, W. *Tetrahedron Lett.* **1985**, *26*, 1635–1638.
(9) Paddon-Row, M. N.; Patney, H. K.; Brown, R. S.; Houk, K. N. *J. Am. Chem. Soc.* **1981**, *103*, 5575–5577.
(10) For leading references, see: Paddon-Row, M. N.; Cotsaris, E.; Patney, H. K. *Tetrahedron* **1986**, *42*, 1779–1788.
(11) Paddon-Row, M. H. *J. Chem. Soc., Perkin Trans. II* **1985**, 257–263.
(12) (a) Balaji, V.; Ng, L.; Jordan, K. D.; Paddon-Row, M. N.; Patney, H. K. *J. Am. Chem. Soc.* **1987**, *109*, 6957–6969. (b) Balaji, V.; Jordan, K. D.; Burrow, P. D.; Paddon-Row, M. N.; Patney, H. K. *J. Am. Chem. Soc.* **1982**, *104*, 6849–6851. (c) Dürr, H.; Albert, K.-H.; Kausch, M. *Tetrahedron* **1979**, *35*, 1285–1295.
(13) For examples of long-range interaction between ketone and olefin chromophores seen by UV, see: (a) Winstein, S.; DeVries, L.; Orloski, R. *J. Am. Chem. Soc.* **1961**, *83*, 2020–2021. (b) Wijekoon, W. M. D.; Lightner, D. A. *J. Org. Chem.* **1987**, *52*, 4171–4175. (c) Toan, V. V.; Lightner, D. A. *Tetrahedron* **1987**, *43*, 5769–5774. (d) Orloski, R. Ph.D. Dissertation, UCLA, 1964.
(14) (a) Lightner, D. A.; Gawroński, J. K.; Bouman, T. D. *J. Am. Chem. Soc.* **1980**, *102*, 5749–5754, and references therein. (b) Lightner, D. A.; Gawroński, J. K.; Hansen, Aa. E.; Bouman, T. D. *J. Am. Chem. Soc.* **1981**, *103*, 4291–4296, and references therein. (c) Lightner, D. A.; Paquette, L. A.; Chayangkoon, P.; Lin, H.-S.; Peterson, J. R. *J. Org. Chem.* **1988**, *53*, 1969–1973.

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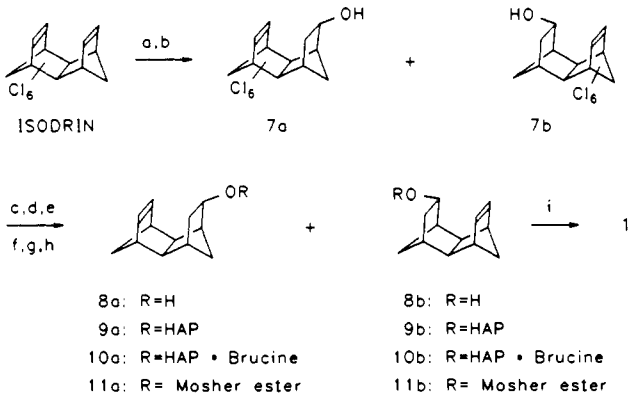
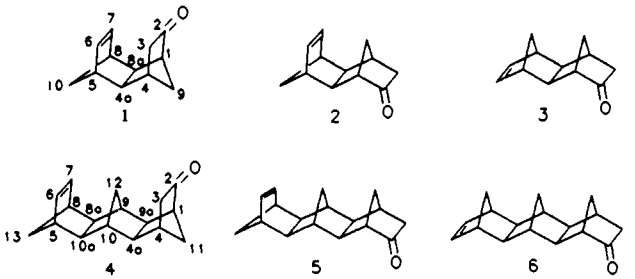
Scheme I[a]



[a] (a) B_2H_6. (b) $H_2O_2/NaOH$. (c) Na/C_2H_5OH on **7** to give **8**. (d) Phthalic anhydride/pyr on **8** to give **9**. (e) Brucine, fractional crystallization of **9**. (f) HCl, H_2O. (g) $NaOH/CH_3OH$. (h) (*R*)-MTPA chloride on **8** or **8a**. (i) Jones oxidation of **8** or **8a**.

ketones,[17] and 1,3-diones,[18] long-range OITS and OITB have been largely unexplored by the combination of UV and CD spectroscopy, techniques which have been shown previously[14] to offer a powerful way of extracting a detailed understanding of electronic structure and excited-state properties. Our target compounds were the isomeric δ,ϵ-unsaturated ketones possessing the endo-endo (**1**), endo-exo (**2**), and exo-exo (**3**) dimethanonaphthalene skeletons and their corresponding ζ,η-unsaturated ketone norbornylogs (**4–6**) possessing trimethanoanthracene skeletons. In these systems,

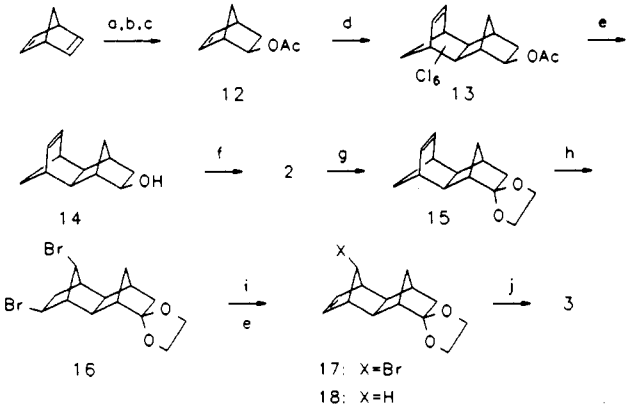


orbital interaction through space may be governed by nonbonded interatomic distances as short as 2.9 Å (**1**) and orbital interaction through bonds over as many as six σ bonds (**4–6**). Their CD spectra were run and compared with the CD spectra of the corresponding saturated ketone analogs in order to detect $\Delta\epsilon$ exaltations and the presence of "charge-transfer" bands. Since shielding of carbonyl carbon ^{13}C-NMR chemical shifts has been shown recently[19] to be useful in detecting transannular (ground-state) orbital interaction, $^{13}C{=}O$ chemical shifts of the unsaturated ketones were measured and compared to those of the saturated analogs.

Results and Discussion

Syntheses and Absolute Configuration. Ketone **1** could be prepared in racemic form from the chlorinated endo-endo dimethanonaphthalene isodrin in a relatively straightforward way

Scheme II[a]



[a] (a) $(IPC)_2BH$. (b) $H_2O_2/NaOH$. (c) Ac_2O/pyr. (d) Hexachlorocyclopentadiene. (e) Na/C_2H_5OH. (f) Jones oxidation. (g) $HOCH_2CH_2OH$, pTSA. (h) Br_2/CH_2Cl_2. (i) KOtBu/THF. (j) H_3O^+.

(Scheme I) by a modification of Howe's procedures.[20] Its successful synthesis in its optically active form followed from resolution of the intermediate racemic alcohol **8a + 8b** as its half-acid phthalate derivative. Although isodrin easily hydroborates with diborane, an attempted asymmetric hydroboration with diisopinocampheylborane was unsuccessful, as there was no reaction. Although asymmetric hydroboration of the sensitive dechlorinated diene[20] analog of isodrin succeeded, the yields were too low to be useful. Consequently, isodrin was converted to the dechlorinated racemic alcohol **8a + 8b** first by hydroboration with diborane in tetrahydrofuran (to give **7a + 7b**), followed by dechlorination. Sodium in liquid ammonia gave the highest yields of the dechlorinated alcohol. Reaction of the alcohol with phthalic anhydride gave half-acid phthalates **9a + 9b**, which were resolved by fractional crystallization of the brucine salt **10a + 10b**. The less soluble salt **10a** was converted to the alcohol **8a**, and its enantiomeric excess was determined by ^{19}F-NMR spectroscopy on its Mosher ester (**11a**)[21] with (*R*)-α-methoxy-α-(trifluoromethyl)phenylacetic acid and comparison with the Mosher ester **11a + 11b** of the racemic alcohol **8a + 8b**. The latter showed a 1.0:1.0 integrated ratio (instrument or cut-and-weigh) of ^{19}F resonances at −72.18 and −72.26 ppm upfield from the ^{19}F resonance of $CFCl_3$. Mosher ester **11a** from the most highly resolved alcohol **8a** showed the same two ^{19}F resonances, but with a 2.44:1 ratio of peaks at −76.26 and −72.18 ppm, corresponding to a 41.9% enantiomeric excess of **8a**.

The absolute configuration of **8a** was determined by LIS NMR of the Mosher ester.[21] Addition of aliquots of a 0.04 M EuFOD solution in $CDCl_3$ to a $CDCl_3$ solution of **8a** caused differential rates of downfield shifts of the two ^{19}F-NMR signals at −72.18 and −72.26 ppm. The initial $\Delta\delta$ was 0.078 ppm, which decreased successively to 0.0703, 0.0677, 0.0599, 0.0442, and finally 0.000 (broad) ppm upon addition of the EuFOD solution. This indicates that the more intense −72.26 ppm resonance moved downfield at a faster rate than the −72.18 ppm resonance because it was complexed more effectively to the shift reagent. Consistent with previous applications of the LIS NMR method,[21b] we would assign the *S* configuration to the major enantiomer **8a**. The saturated ketone dihydro-**1** was obtained following catalytic hydrogenation of **1**.

Ketones **2** and **3** were prepared from an optically active precursor (2-norbornenyl acetate) of known absolute configuration and enantiomeric excess[22] (**12**, Scheme II) following the Diels–

(15) For a summary, see: (a) Paquette, L. A.; Farnham, W. B.; Ley, S. V. *J. Am. Chem. Soc.* **1975**, *97*, 7273–7279. (b) Schippers, P. H.; Dekkers, H. P. J. M. *J. Am. Chem. Soc.* **1983**, *105*, 79–84. (c) Lightner, D. A.; Jackman, D. E.; Christiansen, G. D. *Tetrahedron Lett.* **1978**, 4467–4470.

(16) (a) Hansen, Aa. E.; Lic. Thesis. Copenhagen; HC. Ørsted Inst., 1964. (b) Bouman, T. D.; Hansen, Aa. E. *Croat. Chem. Acta* **1989**, *62*, 227–243.

(17) Lightner, D. A.; Beavers, W. A. *J. Am. Chem. Soc.* **1970**, *92*, 2677–2684.

(18) (a) Lightner, D. A.; Christiansen, G. D.; Melquist, J. L. *Tetrahedron Lett.* **1972**, 2045–2048. (b) Hill, R. K.; Morton, G. H.; Peterson, J. R.; Walsh, J. A.; Paquette, L. A. *J. Org. Chem.* **1985**, *50*, 5528–5533.

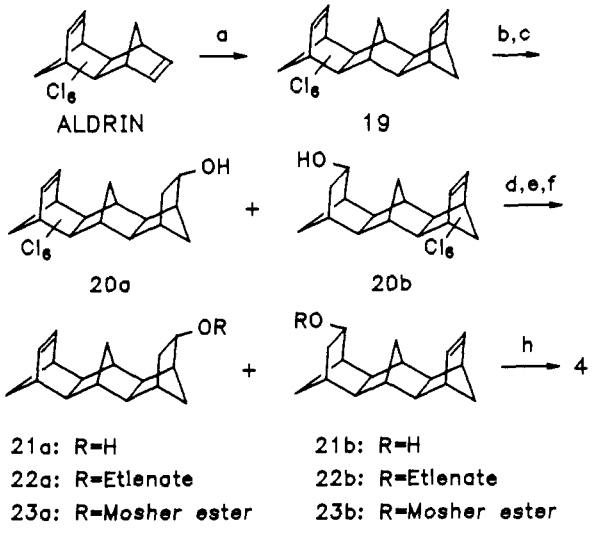
(19) (a) Bishop, R.; Lee, G. H. *Aust. J. Chem.* **1987**, *40*, 249–255. (b) Bishop, R. *Aust. J. Chem.* **1984**, *37*, 319–325. (c) Bicker, R.; Kessler, H.; Steigel, A.; Zimmermann, G. *Chem. Ber.* **1978**, *111*, 3215–3221.

(20) Howe, R. Ph.D. Dissertation, UCLA, 1965.

(21) (a) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543–2549. (b) Kalyanam, N.; Lightner, D. A. *Tetrahedron Lett.* **1979**, 415–418.

(22) (a) Lightner, D. A.; Bouman, T. D.; Crist, B. V.; Rodgers, S. L.; Knobeloch, M. A.; Jones, A. M. *J. Am. Chem. Soc.* **1987**, *109*, 6248–6259. (b) Mislow, K.; Berger, J. G. *J. Am. Chem. Soc.* **1962**, *84*, 1956–1961.

Scheme III[a]



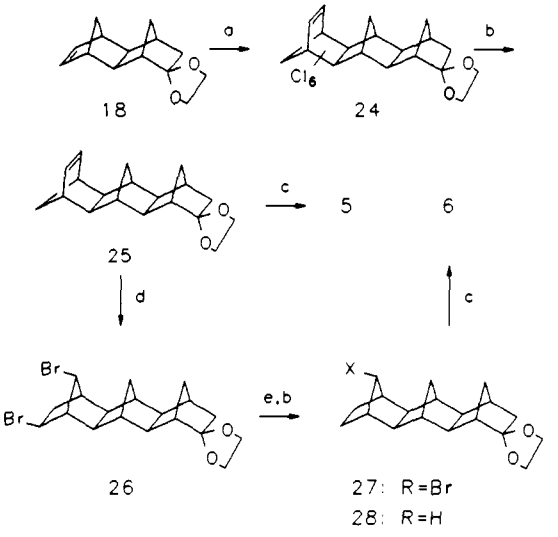
[a](a) Cyclopentadiene. (b) B_2H_6. (c) $H_2O_2/NaOH$. (d) Na/C_2H_5OH. (e) 3-β-Acetoxyetienic acid chloride on **21**, then fractional crystallization. (f) $LiAlH_4$. (g) (*R*)-MTPA chloride on **21** or **21a**. (h) $(CH_3)_2SO$/oxalyl chloride/Et_3N on **21** or **21a**.

Alder addition of hexachlorocyclopentadiene (to give the endo-exo adduct **13**). Dechlorination using sodium in ethanol smoothly gave **14**, which could be converted to **2** by oxidation with Jones reagent. Rearrangement of the endo-exo skeleton to exo-exo was achieved following the method of Paddon-Row.[10,23] Thus, ketalization of **2** (to give **15**) followed by bromination gave entry to the exo-exo dimethanonaphthalene system in dibromo ketal **16**—a suspected toxic material.[24] Base-catalyzed elimination of HBr followed by reductive debromination afforded the unsaturated exo-exo ketal **18**, from which **3** could be generated by acid catalysis. Catalytic hydrogenation of **2** and **3** gave the corresponding saturated ketones dihydro-**2** and dihydro-**3**.

Trimethanoanthracene ketone **4** was readily prepared in racemic form following hydroboration of diene **19**, the Diels–Alder adduct of aldrin with cyclopentadiene, to give **20** (Scheme III). Dechlorination of **20** using sodium in ethanol afforded **21**, and Swern oxidation[25] of **21** smoothly gave racemic **4**; the use of chromium-based oxidizing agents caused skeletal rearrangements. Attempts at asymmetric hydroboration of **19** with diisopinocampheylborane led to no reaction, and attempted resolution of racemic **21** through its half-acid phthalate produced no diastereomeric separation on crystallization with brucine or cinchonidine. However, the diastereomeric esters with the steroid etienic acid[26] separated easily and completely by fractional crystallization from hot hexane or by column chromatography on silica gel. The enantiomeric excess of the more hexane-soluble diastereomer **22a** was determined to be >99%, as shown by comparison of the ^{19}F-NMR spectrum of the Mosher ester **23a** of the derived alcohol **21a** to that of the Mosher ester of racemic alcohol **21**. The latter showed a 1.0:1.0 integrated ratio of the ^{19}F resonances at −72.055 and −72.148 ppm upfield from that of $CFCl_3$. The former showed only one signal at −72.030 ppm, indicating complete resolution.

The absolute configuration of the resolved alcohol **21a** was determined by LIS NMR[21] of the Mosher ester with (*R*)-α-methoxy-α-(trifluoromethyl)phenylacetic acid. By adding approximately 0.04 M equivalent aliquots of a EuFOD/$CDCl_3$ solution and noting the differential shifts to lower field of the ^{19}F resonances of racemic **23** at −72.055 and −72.148 ppm, the absolute configuration of the (−)-alcohol was determined to be that of **21a**. The initial chemical shift difference ($\Delta\delta$) was 0.093 ppm. This value changed but at different increments, as the concentration of EuFOD increased and both peaks shifted to lower field until one signal was observed. Since both peaks moved to lower field with added shift reagent, the peak initially at highest field "caught up" with the lower field peak as they shifted, indicating that the stereoisomer exhibiting the peak at −72.148 ppm complexed more efficiently to the EuFOD than did the lower field signal. According to earlier applications of this method in the determination of absolute configuration of secondary alcohols, the *S* configuration may be assigned to the (−)-alcohol,[21b] e.g., **21a**. Swern oxidation[25] of **21a** gave **4**, and catalytic hydrogenation of **4** gave dihydro-**4**.

Scheme IV[a]



[a](a) Hexachlorocyclopentadiene. (b) Na/C_2H_5OH. (c) H_3O^+. (d) Br_2/CH_2Cl_2. (e) KOtBu/THF.

Ketones **5** and **6** were both prepared (Scheme IV) from the optically active ketal **18** (derived from **12** of known absolute configuration and enantiomeric excess[22] (Scheme II)). Diels–Alder reaction of **18** with hexachlorocyclopentadiene afforded the trimethanoanthracene ketal **24**, from which **5** was obtained in two steps following reductive dechlorination by sodium in alcohol then deketalization. Ketal **25** was rearranged to the exo-exo-exo system by addition of bromine in methylene chloride to give **26**, which, as before (Scheme II), was dehydrobrominated (to give **27**) and then reductively debrominated (to give **28**). Deketalization afforded **6**. Dihydro-**5** and dihydro-**6** were obtained from **5** and **6**, respectively, by catalytic hydrogenation.

Carbon-13 NMR Assignments. The carbon-13 resonances are particularly difficult to assign by inspection of the trimethanoanthracene NMR spectra: **4**, **5**, and **6** each have ten methine and four methylene carbons; their dihydro analogs have eight methine and six methylene carbons. With the assistance of the 2D-INADEQUATE technique, most of the carbon resonances could be assigned unambiguously (Figure 1) with the connectivity starting from the unambiguously assignable $^{13}C{=}O$ resonances. It is interesting to note that (1) the $^{13}C{=}O$ resonances are generally deshielded in **1** and **4** (and their dihydro derivatives) relative to the isomeric ketones, (2) the C=C resonances are deshielded in **3** and **6** relative to **1**, **2**, **4**, and **5**, and (3) the CH_2–CH_2 bridge carbon resonances in dihydro-**3** and -**6** are deshielded relative to the corresponding bridge carbon resonances in dihydro-**1**, -**2**, -**4**, and -**5**. These are all useful diagnostics which would readily allow one to distinguish all of the isomeric ketones under investigation. The shielding (δ 29.3) of the central CH_2 bridge at C-12 of **4** relative to those of **5** and **6** is not attributable to the opposing C=C because it remains essentially unchanged in dihydro-**4**. But the deshielding of the C-12 resonance in **5** (δ 34.7) is apparently due

(23) Paddon-Row, M. N.; Patney, H. K.; Warrener, R. N. *J. Org. Chem.* **1979**, *44*, 3908–3917.
(24) Winstein, S. *J. Am. Chem. Soc.* **1961**, *83*, 1516–1517.
(25) Omura, K.; Swern, D. *Tetrahedron* **1978**, *34*, 1651–1660.
(26) (a) Djerassi, C.; Staunton, J. *J. Am. Chem. Soc.* **1961**, *83*, 736–743. (b) Woodward, R.; Katz, T. *Tetrahedron* **1959**, 70–89. (c) Djerassi, C.; Burakevich, J.; Chamberlin, J.; Elad, D.; Toda, T.; Stork, G. *J. Am. Chem. Soc.* **1964**, *86*, 465–471. (d) Staunton, J.; Eisenbraun, E. *Org. Synth.* **1973**, *5*, 8–11.

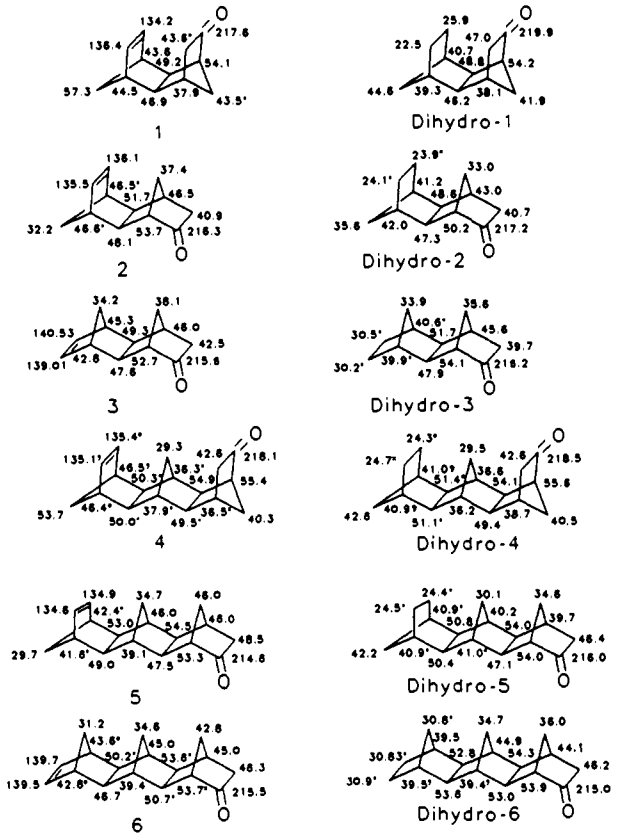
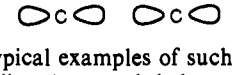


Figure 1. Assignments of carbon resonances in the ^{13}C-NMR spectra of unsaturated ketones **1**–**6** and their saturated ketone analogs in $CDCl_3$ solvent at 21 °C.

to the C=C, as it moves strongly upfield (to δ 30.1) in dihydro-**5**. Other interesting shifts may be found by inspecting Figure 1.

Orbital Interaction through Space. In the laticyclic topology,[27] p(π) orbitals of, e.g., carbon–carbon and/or carbon–oxygen double bonds, overlap in the unusual σ–pp



alignment. Archetypical examples of such alignments may be found in endo-endo dimethanonaphthalenes **1** and **29**, and in **30**, in which the C=C and C=O interchromophoric distance is very short, i.e., 2.8–2.9 Å in **29**,[28] thus providing for substantial σ–pp orbital overlap. The importance of this type of orbital interaction

29 30 31 32

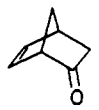
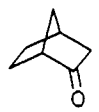
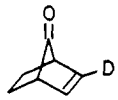
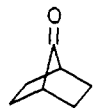
through space[1] was discovered many years ago in these skeletal systems by Winstein and co-workers[2] in solvolytic studies and can be seen clearly in the very large splittings of the π (1.26 eV) and π* (1.45 eV) orbitals of dimethanonaphthalene revealed by photoelectron spectroscopy and electron transmission spectroscopy, respectively.[29] The dominant mechanism leading to the large orbital splittings of **29** is thought to come largely (~70%) from through-space interactions, with the remainder coming from orbital interaction through bonds,[1] in this case four σ bonds.[12,29] In marked contrast, the dimethanonaphthalene **31** with the all-exo-exo arrangement of the C=Cs shows significant but smaller π (0.87 eV) and π* (0.80 eV) orbital splittings, as does the

(27) Goldstein, M.; Hoffmann, R. *J. Am. Chem. Soc.* **1971**, *93*, 6193–6204.

(28) Ermer, O.; Bodecker, C.-D.; Preut, H. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 55–56.

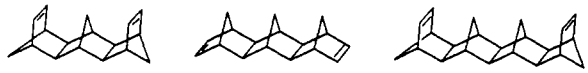
(29) Prinzbach, H.; Sedelmeier, G.; Martin, H.-D. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 103–104, and references therein.

Table I. Influence of Homoconjugation on (A) ^{13}C-NMR,[a] (B) Ultraviolet,[b] and (C) Circular Dichroism[b] Spectra of β,γ-Unsaturated Bicyclo[2.2.1]heptenones and Saturated Bicyclo[2.2.1]heptanones

	A		B	C
structures	$\delta_{C=O}$	$\Delta\delta^c$	ϵ_{max} (λ)	$\Delta\epsilon_{max}$ (λ)
	212.9		300 (294)[d]	−19 (294)[d]
			2000 (214)[sh]	+4.4 (224)[d]
				−5.4 (205)[d]
		−2.1		
	215.0		23 (293)	+0.76 (304)
	205.1		35 (272)	−0.033 (273)
			450 (220)[sh]	−0.028 (224)
				+0.029 (219)
		−11.1		
	216.2		18 (293)	0

[a] From ref 19c. [b] In *n*-heptane, 2 × 10^{-3} M, at 21 °C. [c] $\delta_{enone} - \delta_{ketone}$. [d] In CF_3CH_2OH, 1 × 10^{-3} M, at 21 °C. In *n*-heptane the values are −19 (307), −5.1 (219). CD values are corrected to 100% ee.

endo-exo isomer **32**, with the principal splitting mechanism being due, in both cases, to OITB.[12,29] The magnitude of the orbital splitting is attenuated with increasing distance between the chromophores, with OITS falling off rapidly (predicted to become negligible for interorbital separations greater than 4 Å) and optimal OITB falling off much less rapidly (predicted to show π-orbital splittings of 0.2 eV at 10-Å interorbital separation).[10] As expected, PES of the norbornylogs **33** and **34**, of **29** and **31**, respectively, show much reduced, yet significant, π-orbital splittings. The surprisingly large splitting for the bisnorbornylog



33 34 35

35 has been attributed to orbital interaction through the methano-bridge orbitals.[10,30] The PES splitting data summarized in Figure 2 clearly indicate orbital interactions over very large distances that might be probed by CD, UV, and ^{13}C-NMR studies of suitable derivatives.

NMR Evidence for Orbital Interaction. Electronic interaction in 1,3-homoconjugated unsaturated ketones has been detected previously by ^{13}C-NMR chemical shifts of the unsaturated ketone C=O, compared with that of the saturated ketone analog.[19] For example, as shown in Table I, $\delta_{C=O}$ for the homoconjugated ketone 2-norbornenone is more shielded than that of 2-norbornanone. Even more impressive is the very large relative shielding of 7-norbornenone compared with 7-norbornanone. Similar transannular interaction has been reported[19a,b] for 1,5-homoconjugated cyclic ketones where the carbocyclic framework brings the C=O and (exocyclic) C=C chromophores into a close nonbonded alignment, as in 7-methylenebicyclo[3.3.1]nonan-3-one and in the dimethanonaphthalenone **30** (Table II). These systems exhibit a larger Δδ than does the 1,5-homoconjugated adamantanone, where the C=O and C=C groups are held farther apart. The nature of the interaction has been attributed to through-space π interaction or a cross-ring field effect.

Our $\delta_{C=O}$ data for the dimethanonaphthalene system **30** of Table II are particularly instructive, because the enone possesses

(30) Jørgensen, F. S.; Paddon-Row, M. N. *Tetrahedron Lett.* **1983**, *24*, 5415–5418.

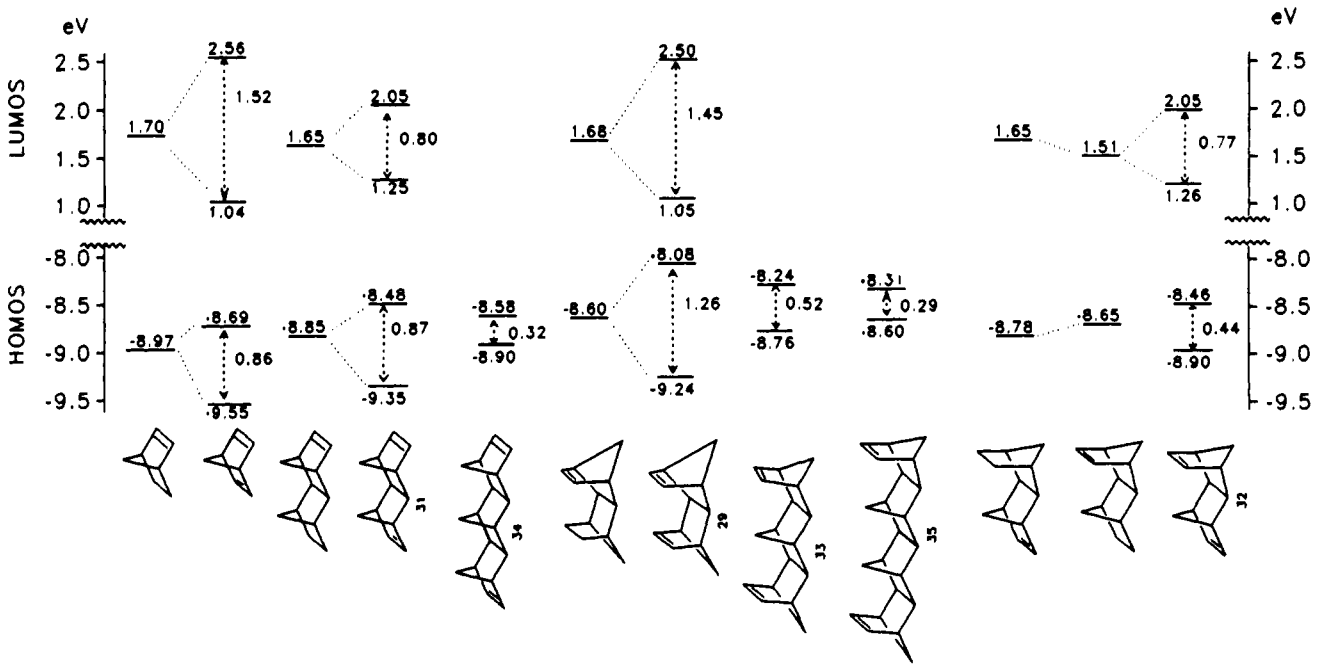


Figure 2. (Lower, HOMOS) π-Orbital vertical ionization potentials from photoionization spectroscopy (PES). (Upper, LUMOS) π^*-Orbital electron affinities from electron transmission spectroscopy (ETS). Data are from refs 10 and 12.

the unusual σ–pp alignment of the C=C and C=O π systems and also shows a large deshielding relative to the saturated ketone ($\Delta\delta$ −2.9). As in 2-norbornenone ($\Delta\delta$ −2.1, Table I), the strong deshielding would appear to indicate a strong electronic interaction between the C=C and C=O chromophores. And as in the PES (Figure 2) of the endo-endo dimethanonaphthalene **29** (in which π systems are oriented for σ–pp orbital overlap), the electronic interaction is thought to come mainly from orbital interaction through space rather than orbital interaction through the four σ bonds connecting the two chromophores.

It is not surprising, therefore, that enone **1** shows a large $\delta_{C=O}$ deshielding ($\Delta\delta$ −2.5) relative to dihydro-**1** (Table III) because σ–pp orbital overlap operates over essentially the same distance in **1** as in **30**. When the C=C and C=O chromophores are not oriented for favorable σ–pp orbital overlap, as in **2** and **3**, the $\Delta\delta$ values drop (to −0.8 and −0.6, respectively). However, since the enone C=O resonance is deshielded (relative to the saturated ketone analog) in **2** and **3**, some sort of orbital interaction through four σ bonds would appear to be operating in these enones, as well as in **1**. At present, it is difficult to assign the relative importance of OITS and OITB, but the latter would appear to be the major source of interaction between the C=C and C=O chromophores of **2** and **3**, and in **1** the former would appear to predominate.

When the C=C and C=O chromophores are held in the same relative positions as in **1–3** but are pushed farther apart by an intervening norbornane unit, the trimethanoanthracene norbornylogs (**4–6**) show much reduced $\Delta\delta$ values, as might be expected for decreased orbital interaction between the chromophores (Table III).

Circular Dichroism Evidence for Orbital Interaction. Through-space π interaction was the subject of studies by Winstein and co-workers, principally from reaction kinetics and product analyses.[2,5] However, the Winstein group also examined UV spectral shifts of ketone carbonyl chromophores and the emergence of new UV bands (near 230 nm), which were thought originally to come from an intramolecular $\pi \rightarrow \pi^*$ charge-transfer excitation.[13] In the case of 7-norbornenone, the presence of a 230 nm band was disputed and then later confirmed and has been detected clearly by circular dichroism spectroscopy (of 2-deuterio-7-norbornenone, Table I).[31] It has been assigned to a mixed transition[31] with roughly 15% $\pi_{C=C} \rightarrow \pi^*_{C=O}$ (π–π^* charge transfer), ~15% $\sigma_{C=C\alpha} \rightarrow \pi^*_{C=O}$ (σ–π^* charge transfer), ~30% $n(\sigma)_{C=O} \rightarrow \pi^*_{C=O}$, and ~30% $\sigma_{C=O} \rightarrow \pi^*_{C=O}$. Although the transition is composed mainly of localized σ–π^* excitations, it does have a significant (~15%) intramolecular $\pi \rightarrow \pi^*$ charge-transfer component, which is consistent with the model for orbital interaction through space.

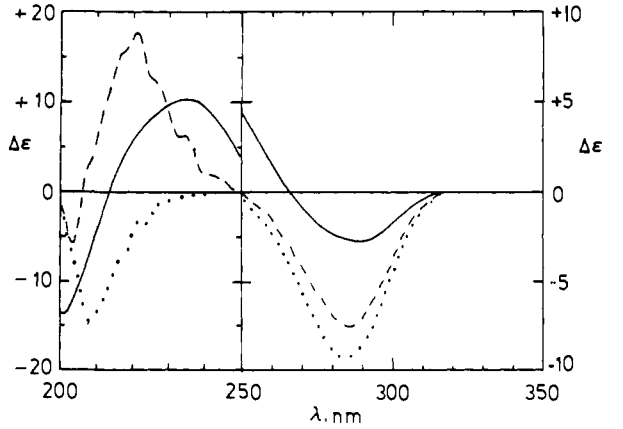


Figure 3. Circular dichroism spectra of δ,ϵ-unsaturated dimethanonaphthalenones **1** (—), **2** (– –), and **3** (···) in 2,2,2-trifluoroethanol solvent at 2×10^{-3} to 2×10^{-4} M concentration at 22 °C.

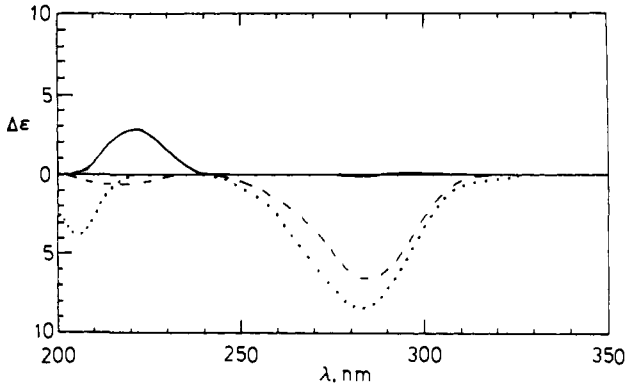
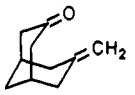
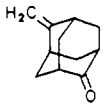
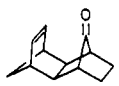
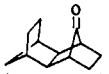


Figure 4. Circular dichroism spectra of ζ,η-unsaturated trimethanoanthracenones **4** (—), **5** (– –), and **6** (···) in 2,2,2-trifluoroethanol solvent at 2×10^{-3} to 2×10^{-4} M concentration at 22 °C.

(31) Lightner, D. A.; Gawroński, J. K.; Hansen, Aa. E.; Bouman, T. D. *J. Am. Chem. Soc.* **1981**, *103*, 4291–4296.

Table II. Influence of 1,5-Homoconjugation and Orientation on the $^{13}C{=}O$ NMR Chemical Shifts[a] of Polycyclic Enones in $CDCl_3$

structure	$\delta_{C=O}$	$\Delta\delta^c$
	209.3[b]	
		−3.2
	212.5[b]	
	216.9[b]	
		−1.4
	218.3[b]	
 (30)	215.9	
		−2.9
 (Dihydro-30)	218.8	

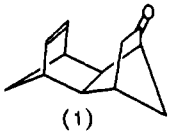
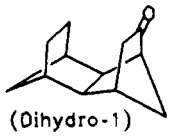
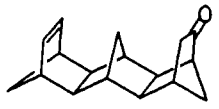
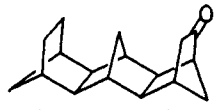
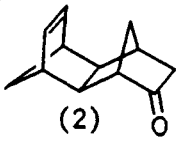
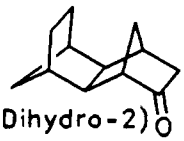
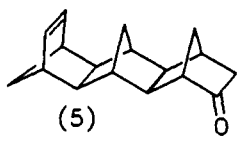
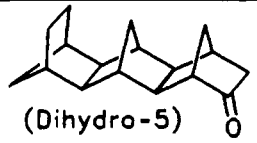
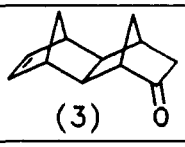
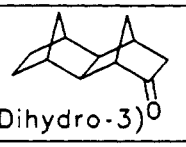
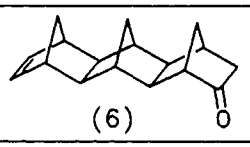
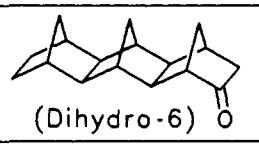
[a] Chemical shifts in ppm downfield from $(CH_3)_4Si$. [b] Data from refs 19a and b. [c] $\delta_{enone} - \delta_{ketone}$.

A moderately strong UV absorption near 230 nm can be seen more clearly (Table III, Figure 3) in the CD spectrum of **1**, whose C=O and C=C chromophores are oriented for σ–pp orbital overlap over a short (2.9 Å) nonbonded interatomic distance. No corresponding band could be detected in dihydro-**1**. Even in its norbornylog (**4**), a moderately intense band near 220 nm can be seen but is absent in dihydro-**4** (Table III, Figure 4). This new band, appearing in an unusual spectral region (220–230 nm), bears a strong similarity to that seen in a chiral 7-norbornenone[31] and likewise probably contains a $\pi_{C=O} \rightarrow \pi^*_{C=O}$ charge-transfer component. Keeping the same orbital alignment but increasing the distance between the C=C and C=O chromophores (as in **4**) decreases the intensity of the band. However, when the relative orientation is altered to disfavor σ–pp overlap (as in **3**), the ~230 nm charge-transfer band is absent and apparently is replaced by a band near 206 nm.

The interchromophoric geometry of **2** lies somewhere between that of **1** and **3**, and although **2** does not share the same favorable orientation for σ–pp overlap found in **1**, it exhibits a very intense band near 218 nm, again probably due to a charge-transfer component. As with **1** and **4**, increasing the distance between the chromophores of **2** (as in **5**) drastically weakens the 218 nm band and even changes its sign. The intense band near 206 nm in **3** finds a counterpart in its norbornylog (**6**) and also in the 205 nm band of 2-norbornenone of the same absolute configuration (Table I). These observations, related to excited states, are consistent with the conclusions drawn from an analysis of $^{13}C{=}O$ chemical shifts for the ground state, viz., that orbital interaction through space is an important component of transannular orbital interaction in **1** and probably **2** but is less important in **3**, where OITB may dominate. On the basis of CD charge-transfer bands, one might also conclude that OITS is more important in **4** than in **5** or **6**.

In addition to the 220–230 nm charge-transfer bands, further evidence for excited-state interaction may be found in the ketone n–π^* transitions, where the $\Delta\epsilon_{max}$ values are substantially larger for the unsaturated ketones **1**, **2**, and **3** than for their saturated analogs (Table III). Not surprisingly, the largest increase (factor of 4) in $\Delta\epsilon_{max}$ is found in **1** (vs dihydro-**1**), and smaller increases (factors of 1.5–1.6) are found for **2** and **3**. This exaltation presumably comes from coupling of locally excited states, as in 2-norbornenone.[16] And when the chromophores are separated more widely, as in **4**, **5**, and **6**, the difference between $\Delta\epsilon_{max}$ of the unsaturated ketone and $\Delta\epsilon_{max}$ of the saturated analog becomes

Table III. Influence of Homoconjugation on the (A) ^{13}C-NMR,[a] (B) Circular Dichroism,[b] and (C) Ultraviolet[b] Spectra for Dimethanonaphthalene and Trimethanoanthracene Ketones

	 (1)	 (Dihydro-1)	 (4)	 (Dihydro-4)
A ($\delta_{C=O}$)	217.1	219.6	217.6	217.8
B ($\Delta\epsilon_{max}$ (λ))	−3.3 (288) +10 (233)	−0.83 (280)	<−0.01 (284) +2.8 (221)	<−0.01 (284)
C (ϵ_{max} (λ))	30 (277) 321 (227)[sh]	11 (280)	40 (281) 840 (217)[sh]	41 (279)
	 (2)	 (Dihydro-2)	 (5)	 (Dihydro-5)
A ($\delta_{C=O}$)	216.4	217.2	214.8	216.0
B ($\Delta\epsilon_{max}$ (λ))	−7.5 (284) +21 (218)	−4.7 (281)	−6.7 (285) −0.68 (215)	−6.8 (284)
C (ϵ_{max} (λ))	118 (283)	71 (281)	296 (284) 1265 (219)[sh]	119 (285)
	 (3)	 (Dihydro-3)	 (6)	 (Dihydro-6)
A ($\delta_{C=O}$)	215.6	216.2	215.5	216.0
B ($\Delta\epsilon_{max}$ (λ))	−8.9 (283) −16 (206)	−5.8 (282)	−8.5 (284) −4.0 (206)	−8.0 (284)
C (ϵ_{max} (λ))	150 (283)	85 (282)	154 (279)	165 (279)

[a] In $CDCl_3$, 2×10^{-2} M, at 22 °C. [b] In CF_3CH_2OH, 2×10^{-3} M, at 22 °C for the C=O n–π^* transition. CD values corrected to 100% ee.

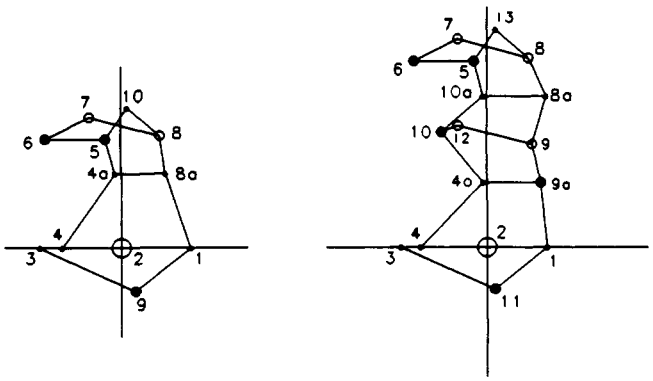


Figure 5. Octant projection diagrams for ketones dihydro-**1** (left) and dihydro-4 (right). The carbonyl carbon (C-2) is at the intersection of the horizontal and vertical coordinates. Small dots lie either on or very close to a symmetry plane. Large filled circles lie in back octants, and large open circles lie in front octants.

trivial (Table III, Figure 4). Whatever the origin of the enhanced $\Delta\epsilon_{max}$ found in **1**, **2**, and **3** (vs their dihydro analogs), it falls off very rapidly with distance.

The extremely weak n–π^* $\Delta\epsilon_{max}$ values of **4** and dihydro-4 are interesting. They are far weaker than those of either dihydro-**1** or 2-norbornanone (Table I), which, curiously, have the same $\Delta\epsilon$ magnitude but opposite signs. The (1*S*)-2-norbornanone moiety is found in both dihydro-**1** and dihydro-**4**, but its octant contributions[17] (which give (1*S*)-2-norbornanone its $\Delta\epsilon_{304}^{max}$ +0.76 value) are largely overcome by the added octant contributions of the expanded skeleton of the higher homologs. Thus, although the major octant perturbers at C-6 and C-7 of norbornanone are still present in dihydro-**1** (as C-8a and C-9) and dihydro-**4** (as C-9a and C-11), these perturbers are, surprisingly, dominated by contributions from more remote perturbers, which are normally considered to make weaker contributions (Figure 5).[32] In dihydro-**1**, remote perturbers at C-6 and C-8 are probably the major contributors, for C-5, C-7, and C-10 are near an octant symmetry. A positive back contribution is made by C-6, but its contribution should be weaker than that of C-8a, which dominates the CD Cotton effect of (1*S*)-2-norbornanone. C-8 lies in a positive *front* octant[32] and apparently makes an unanticipated dominant positive octant contribution. In dihydro-**4**, the expected negative back octant contributions of C-8a and C-9a appear to be offset by positive *front* octant contributions of C-8 and C-9, leading to a net, near zero $\Delta\epsilon$ value for the n–π^* CD. There are few, if any, front octant perturbers in **2**, **3**, **5**, and **6** and their dihydro analogs, and their n–π^* CD Cotton effects show major, dominating contributions from a large number of back octant perturbers.

Concluding Comments

Evidence for transannular molecular orbital interaction in the ground states of structurally rigid δ,ϵ- and ζ,η-unsaturated ketones **1–6** may be found in the relatively more shielded $^{13}C{=}O$ resonances compared with their saturated ketone analogs. The largest effect was found with **1**, where the endo-endo geometry of the dimethanonaphthalene orients the C=C and C=O π systems toward σ–pp orbital overlap. The effect falls off rapidly with distance (**4**) and in the endo-exo and exo-exo systems where σ–pp overlap is less favored. Ketones **1–3** exhibit strongly enhanced n–π^* CD Cotton effects relative to their saturated ketone analogs and may also exhibit shorter wavelength transitions (220–235 nm) of mixed origin but probably containing $\pi_{C=C} \rightarrow \pi^*_{C=O}$ components. The n–π^* CD exhaltation disappears in trimethanoanthracene analogs **4–6**, but much weaker, shorter wavelength bands near 220 nm can be found. The CD data provide evidence for excited-state transannular interchromophoric interaction.

(32) (a) Bouman, T. D.; Lightner, D. A. *J. Am. Chem. Soc.* **1976**, *98*, 3145–3154. (b) Lightner, D. A.; Bouman, T. D.; Wijekoon, W. M. D.; Hansen, Aa. E. *J. Am. Chem. Soc.* **1986**, *108*, 4484–4497. (c) Lightner, D. A.; Toan, V. V. *Tetrahedron* **1987**, *43*, 4905–4916.

Experimental Section

General Procedures. Circular dichroism spectra were obtained on a JASCO J-600 circular dichroism spectrophotometer. Solutions were run in cylindrical 1-cm or 0.05-cm path length cuvettes at 20 °C. Ultraviolet–visible (UV–vis) spectra were recorded on a Perkin-Elmer 3840 diode array detector spectrophotometer using 1-cm rectangular cuvettes at room temperature. Optical rotations were recorded at the indicated wavelengths in a 10-cm path length cell on a Perkin-Elmer 141 automatic polarimeter at 20 °C or the cited temperature. High resolution mass spectra were determined either at the University of California, Riverside on a Nicolet FTMS-1000 Fourier transform mass spectrometer (upgraded to accommodate a dual differentially pumped cell with a super conducting magnet of 3.0 T, with either a batch inlet or a heated inlet probe for sample introduction), or at the Midwest Center for Mass Spectrometry, University of Nebraska, Lincoln. Routine mass spectra (MS or GC-MS) were recorded on a Hewlett-Packard 5970 mass selective detector/8890 capillary gas chromatograph (70 eV) using a 30-m HP-1 column. Infrared (IR) spectra were recorded in CCl_4, unless otherwise noted, on a Perkin-Elmer 1610 Fourier transform spectrophotometer. ^{1}H-NMR spectra were recorded in $CDCl_3$, unless otherwise noted, on either a General Electric QE-300 or GN-300 (300 MHz) spectrometer, all with TMS as reference set to 0.0 parts per million (ppm). ^{13}C-NMR spectra were recorded in $CDCl_3$, unless otherwise noted, on either a General Electric QE-300 or GN-300 (75 MHz) spectrometer, all in $CDCl_3$ set to 77.00 ppm reference. ^{19}F-NMR measurements were determined on a JEOL FX-100 or GE GN-300 instrument, with $C^{19}FCl_3$ (Freon-11) reference set to $\delta = 0.00$. All NMR work was recorded at room temperature. All melting points were recorded on either a Thomas-Hoover Uni-Melt capillary or a Laboratory Devices Mel-Temp apparatus and are reported uncorrected. Spectrograde solvents for UV and CD were purchased from Aldrich, MCB, Eastman, or Fischer. All solvents used in synthesis were distilled and/or dried before use. Diglyme was distilled from CaH_2 or sodium metal. Boron trifluoride etherate was distilled from CaH_2. Acetone was distilled from $KMnO_4$. Benzene was azeotropically dried using a Dean–Stark trap. Pyridine was distilled from KOH. Dichloromethane was distilled from CaH_2. Tetrahydrofuran (THF) was predried with $LiAlH_4$ under N_2 and then distilled from sodium metal and benzophenone under N_2. Dimethyl sulfoxide (DMSO) was distilled from CaH_2. (*R*)-(+)-α-methoxy-α-(trifluoromethyl)phenylacetic acid, $[\alpha]^{20}_D$ +72° (*c* 1.6, CH_3OH), and EuFOD were from Aldrich.

Conversion of Isodrin to Dimethanonaphthalenone 1. This conversion was achieved by modification of a procedure described by Howe[20] involving hydroboration and dechlorination to afford (±)-(1β,4β,4aα,5β,8β,8aα)-5,6,7,8,9,9-hexachloro-1,2,3,4,4a,5,8,8a-octahydro-1,4:5,8-dimethanonaphthalen-2-*exo*-ol (**7a + 7b**). Technical-grade isodrin starting material was recrystallized three times. In the first recrystallization, the isodrin was dissolved in hot acetone containing a little methanol, treated with decolorizing charcoal, filtered hot, and concentrated to half its original volume. Twice that volume of hot methanol was added to the boiling solution, and, upon cooling, crystals formed. After two additional recrystallizations, the crystals appeared as white plates, mp 240–242 °C: IR (KBr) ν 3070, 2965, 1605, 880, 675; ^{1}H NMR δ 1.6 (1 H, m) and 1.8 (1 H, m) geminal Hs, 2.9 (2 H, m), 3.3 (2 H, m) HCC=C allylic Hs, 6.0 (2 H, m) C=CH.

Into a 1-L flask equipped with a mechanical stirrer, nitrogen inlet, and pressure equalizing addition funnel were placed recrystallized isodrin (45 g, 0.123 mol, 1 equiv), powdered sodium borohydride (4.3 g, 0.112 mol, 0.91 equiv), and 200 mL of dry tetrahydrofuran. At 25 °C, boron trifluoride etherate (18.2 mL, 0.148 mol, 1.2 equiv) in 75 mL of dry THF was added dropwise over a period of 130 min with stirring. The solution became milky white. When the addition was complete, the stirring rate was increased and the reaction continued for 105 min. Water (100 mL) was *slowly* added to the solution to quench the reaction (much frothing occurs). A solution of 23.6 g of sodium hydroxide (0.59 mol, 4.8 equiv) in 75 mL of water was then added. The solution was then brought to 0 °C with an ice bath, and 33.6 mL of 30% hydrogen peroxide (1.427 mol) was added dropwise over 25 min. Following complete addition, the ice bath was removed, and the reaction mixture was stirred for 15 h. Two hundred and fifty milliliters of ether and 100 g of sodium chloride were then added, and the solution was stirred for 15 min before extraction. The aqueous layer was reextracted with 2 × 250 mL of ether, and the combined ethereal extracts were filtered to remove a small amount of gray, viscous material. The organic layer was concentrated (Rotovap) to leave a thick, pale yellow material. Boiling hexane was added in many small portions (totaling 300 mL) and decanted from the undissolved gummy material. The hexane extracts were concentrated to about half the original volume and allowed to cool. Pure hexachloro alcohol **7a + 7b** was obtained as white crystals (34.01 g, 72% yield), mp 222–223 °C [lit.[33] mp 222 °C dec]: IR (KBr) ν 3330, 2975, 1600, 885, 675; ^{1}H NMR

δ 1.3 (1 H, m), 1.7 (1 H, m), 1.8 (2 H, m), 2.1 (1 H, s), 2.5 (2 H, m), 3.2 (2 H, m), 3.95 (1 H, m, HCR_2OH).

(±)-(1β,4β,4aα,5β,8β,8aα)-1,2,3,4,4a,5,8,8a-Octahydro-1,4:5,8-dimethanonaphthalen-2-ol (8a + 8b). Dechlorination of hexachloro alcohol **7a + 7b** to **8a + 8b** was accomplished by any of three methods, as described below.

Method 1. In a 1-L flask, a solution of 18.5 g (0.05 mol, 1 equiv) of **7a + 7b** was dissolved in 300 mL of hot absolute ethanol. To the refluxing solution were added small pieces of sodium metal (43.5 g, 1.9 g-atoms, 37 equiv) over a period of 2 h. The reaction mixture was heated at reflux for two more hours following addition of the sodium before being allowed to cool. Five hundred grams of crushed ice was added, and the solution was transferred to a large separatory funnel. After addition of 400 mL each of pentane and water, the phases were separated, and the aqueous layer was extracted with 2 × 200 mL of fresh pentane. The combined pentane extracts were washed with 6 × 110 mL of water and 100 mL of saturated sodium chloride and then dried over sodium sulfate before being filtered and distilled through an 18-in. fractionating column to remove the pentane. (The fractionating column was packed with 0.5-× 0.2-in. hollow glass cylinders.) The remaining material was recrystallized from hexane to yield 3.1 g of **8a + 8b** as white crystals in 36% yield.

Method 2. Utilizing a 3-L flask with dual reflux condensers, nitrogen inlet, and a magnetic stirrer, 12 g of the hexachloro alcohol **7a + 7b** was dissolved in 250 mL of dry tetrahydrofuran and 80 g of *tert*-butyl alcohol, and this solution was then treated with 30 g of lithium wire. Within 5 min, an exothermic reaction began which required cooling by an ice bath to remain under control. However, after several trial runs of this dechlorination procedure, it was obvious that the reaction worked best if allowed to run as hot as possible. When the spontaneous reflux subsided, heat was applied to maintain boiling for a total reaction time of 1.5 h. The hot mixture was poured through a wire screen (to remove the excess lithium pieces) and cooled with the addition of crushed ice before being transferred to the separatory funnel. Four hundred milliliters each of pentane and water were added, and the solution was extracted with 3 × 100 mL of pentane. The pentane extracts were washed with 5 × 100 mL of water and once with saturated sodium chloride and then dried over sodium sulfate, filtered, and concentrated. Reduced pressure and 100 °C temperature were used to remove the last traces of solvent, and the residual material was crystallized from hexane to yield 3.1 g of **8a + 8b** as a white solid in 56% yield.

Method 3. In a flame-dried 1-L flask fitted with a cold finger style dry ice/acetone condenser and a mechanical stirrer with a glass paddle was distilled 300 mL of ammonia. The apparatus was then immersed into a −78 °C bath, 17.7 g (0.77 g-atom, 24 equiv) of sodium metal was added, and then the mixture was stirred. The characteristic deep blue color of solvated electrons was immediately visible. A pressure equalizing addition funnel containing 12.25 g (0.03 mol, 1 equiv) of compound **7a + 7b** dissolved in a mixture of 115 mL of dry ether and 20 mL of absolute ethanol was fitted to the neck of the reaction flask, and the dropwise addition of starting material was initiated. The reaction was stirred for an additional hour following total addition and then quenched with the careful introduction of solid ammonium chloride until no blue color remained. The cooling bath and condenser were removed, and the liquid ammonia was allowed to evaporate. The remaining white slurry was dissolved in 200 mL of water, extracted with 3 × 150 mL of pentane, and then dried with anhydrous magnesium sulfate and filtered. The pentane was removed by rotary evaporation. The resulting semisolid material was flash chromatographed on silica gel using first 5:1 hexane/ethyl acetate and then dichloromethane. The desired product (4.1 g) was obtained in 71% yield and had mp 103–104 °C [lit.[34] mp 102.5–103.5 °C]. There was no evidence in any of the methods of partially dechlorinated material. Unsaturated alcohol **8a + 8b**: IR (KBr) ν 3300, 3050, 2940, 2895, 1050, 965, 740; ^{13}C NMR δ 132.58, 131.93, 70.80, 58.75, 48.22, 46.48, 45.88, 44.41, 44.18, 43.54, 38.97, 37.63; ^1H NMR δ 1.3 (2 H, m), 1.5 (2 H, m), 1.6 (2 H, m), 1.7 (2 H, m), 1.9 (1 H, s), 2.1 (2 H, m), 2.5 (1 H, m), 2.7 (1 H, m), 3.75 (1 H, m, HCR_2OH), 6.05 (2 H, s, C=CH).

(±)-(1β,4β,4aα,5β,8β,8aα)-1,2,3,4,4a,5,8,8a-Octahydro-1,4:5,8-dimethanonaphthalen-2-*exo*-ol Half-Acid Phthalate (9a + 9b). This reaction was found to work best with freshly sublimed (50 °C/2 mmHg) phthalic anhydride. (Alternatively, phthalic anhydride can be purified by dissolving the mixture in chloroform and removing any solid phthalic acid by filtration. Evaporation of the chloroform leaves the anhydride.) In a 250-mL flask, a solution of 18.8 g of alcohol **8a + 8b** (107 mmol, 1 equiv), 15.8 g of phthalic anhydride (107 mmol, 1 equiv), 90 mL of pyridine, and a catalytic amount of 4-(*N*,*N*-dimethylamino)pyridine were stirred together for 16 h at 40 °C and then for 1 h at 110 °C. The solution was allowed to cool to 20 °C before being poured into 1500 mL of cold water and extracted with 4 × 200 mL of benzene. The combined organic extracts were washed with 2 × 600 mL of 2% aqueous HCl followed by saturated sodium chloride. The original aqueous phase was treated with 100 mL of cold 12 N HCl, extracted with 2 × 200 mL of dichloromethane, and washed once with 100 mL of saturated sodium chloride. The combined organic extracts were then dried over anhydrous sodium sulfate and filtered, and the solvents were evaporated. The yield was 27.4 g (79%) of product: IR ($CHCl_3$) ν 3420, 2975, 1719, 1697, 1286; ^1H NMR (d_6-DMSO) δ 1.6 (6 H, m), 2.0 (2 H, m), 2.2 (2 H, m), 2.5 (2 H, m), 4.79 (1 H, d, J = 3.5 Hz, $HCR_2OC(=O)$), 6.11 (2 H, m, C=C*H*), 7.62 (4 H, m, Ar-*H*); ^{13}C NMR (d_6-DMSO) δ 33.60, 43.47, 43.82, 44.31, 45.53, 45.72, 50.30, 58.26, 75.21, 128.09, 128.33, 130.53, 130.62, 131.46, 132.25, 132.40, 132.87, 166.72, 168.09. Anal. Calcd for $C_{20}H_{20}O_4$ (324.4): C, 74.06; H, 6.21. Found: C, 73.97; H, 6.25.

Resolution of 9a + 9b. Ethanol (120 mL) and **9a + 9b** were placed in a flask. At this point, the solid did not dissolve, but after addition of brucine dihydrate (10.6 g, 1 equiv), the solids dissolved. The solution was concentrated to 50 mL and, after the addition of a few drops of water, allowed to crystallize. The crystals so obtained were recrystallized six times, with the optical rotations of the crystalline salt dropping as shown in Table IS (supplementary material). Decomposition of the brucine salt to regenerate half-acid phthalate was accomplished with aqueous HCl and acetone; thus, 7.05 g of salt was combined with 30 mL of acetone and 11 mL of 1 N aqueous HCl and stirred. A white precipitate formed and was collected by centrifugation and washed twice with 35 mL of water. Samples of the half-acid phthalate so obtained from each crystallization step (above) of the salt had the rotations noted in Table IIS (supplementary material). Saponification of the half-acid phthalate regenerated the optically active alcohol, which had the optical rotations noted in Table IIIS (supplementary material).

The enantiomeric excess and absolute configuration of the alcohol with $[\alpha]_D$ +8.59° was determined from ^{19}F-NMR measurements on its Mosher ester[21] (**11a**), as described in the section Syntheses and Absolute Configuration. The standard reference substance was the Mosher ester **11a + 11b** of racemic alcohol **8a + 8b**.

Mosher Ester 11 and 11a. To a dry, argon-flushed vial containing 100 μL of dichloromethane, 200 μL of pyridine, a few crystals of 4-(*N*,*N*-dimethylamino)pyridine and 17.6 mg of alcohol was added 55 μL of the acid chloride of (*R*)-(+)-α-methoxy-α-(trifluoromethyl)phenylacetic acid.[21] This mixture was then stoppered and placed in a 0 °C refrigerator. Precipitation of pyridine hydrochloride (a white solid) was evident. To work up the reaction, 30 μL of 3-(diethylamino)propylamine was added, followed by dilution with 15 mL of diethyl ether, and the reaction mixture was transferred to a separatory funnel. The ethereal solution was washed with 5 mL of 0.5 N aqueous HCl, 2 × 10 mL of saturated sodium bicarbonate, and finally 10 mL of saturated brine. The organic layer was then dried over magnesium sulfate and filtered, and the solvent was removed (Rotovap) to afford the desired alcohol product.

(±)-(1β,4β,4aα,5β,8β,8aα)-1,2,3,4,4a,5,8,8a-Octahydro-1,4:5,8-dimethanonaphthalen-2-one (Racemic 1). Method 1. A solution of alcohol **8a + 8b** (4.0 g) in 30 mL of acetone was prepared in a 100-mL flask and brought to 0 °C using an ice bath. Eight milliliters of 2 N Jones reagent was added in 0.5-mL portions over a period of 30 min to the stirred reaction mixture and was noted to decolorize between additions. The stirring was continued for another 30 min at room temperature before isopropyl alcohol was added in order to consume any excess oxidant. The solution was then made neutral with solid sodium bicarbonate and then filtered. The green residue was washed twice with additional acetone before the extracts were combined and the solvent was removed. The oil was then diluted with 40 mL of ether and washed twice with dilute sodium bicarbonate and then once with brine before being dried over magnesium sulfate and filtered. The ether was then removed. Flash chromatography on silica gel of the semisolid was achieved with 225 mL of 10:1 hexane/ethyl acetate to yield 2.49 g of white solid. The yield of purified product was 63%.

Method 2. The unsaturated alcohol (0.15 g, 0.85 mmol, 1 equiv) was dissolved in 10 mL of dichloromethane, and, with magnetic stirring, solid pyridinium chlorochromate was added in small portions totaling 0.28 g (1.28 mmol, 1.5 equiv). This suspension was stirred at room temperature for 30 min before isopropyl alcohol was added to decompose any excess oxidant. The reaction was then worked up and purified as in method 1. The yield of product was 69%.

Method 3. Pyridinium chlorochromate was generated as a complex with alumina. In order to do this, 6.0 g of chromium trioxide and 11 mL of 6 N aqueous hydrochloric acid were placed in a 250-mL round-bottom flask and brought up to 40 °C before the dropwise addition of 4.85 mL

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of pyridine. After this was swirled for 5 min, the reaction was cooled to 0 °C with an ice bath and noted to solidify. Upon being reheated to 40 °C, the mixture again became a solution. At this time, 50.0 g of neutral aluminum oxide (Woelm, activity grade I) was slowly streamed in with swirling, and an even coating of oxidant was achieved on the alumina. The 250-mL flask was then placed on a rotary evaporator and slowly turned for 30 min under aspirator vacuum. This orange sandy material was then pumped dry at 1 mmHg on a vacuum line for 2 h. This procedure generates 1 mmol of oxidant per gram of reagent. The pyridinium chlorochromate–alumina was then used to oxidize the alcohol by combining 5.7 g (5.7 mmol, 2 equiv) of reagent, 0.5 g of alcohol (2.85 mmol, 1 equiv), and 10 mL of benzene in a 50-mL round-bottom flask and then rotating it (using no vacuum) on the rotary evaporator in order to thoroughly combine the reagents. Within 5 min, the orange color became dark. This heterogeneous mixture was rotated as such for 2 h before the benzene solution was filtered through Celite. The inorganic residue was washed once with 50 mL of ether, and the organic phases were combined and evaporated to yield 81% of the crude product. After purification by flash column chromatography (method 1), the purified enone had mp 128–130 °C [lit.[32] mp 128–130 °C]: IR ($CHCl_3$) ν 3030, 2960, 1728, 850, 800, 750; ^1H NMR δ 1.6 (2 H, m), 1.8 (2 H, m), 2.3 (3 H, m), 2.5 (2 H, m), 2.8 (3 H, m), 5.60 (1 H, dd, J = 6.5, 8.0, C=CH), 5.97 (1 H, dd, J = 6.5, 7.5, HC=C); ^{13}C NMR δ 37.95 (d), 43.57 (d), 43.76 (t), 43.86 (t), 44.59 (d), 46.98 (d), 49.24 (d), 54.08 (d), 57.28 (d), 134.28 (d), 136.24 (d), 217.08 (s); UV (*n*-heptane) ϵ_{285}^{max} 13, ϵ_{215}^{sh} 548.

(1*S*)-(1β,4β,4aα,5β,8β,8aα)-1,2,3,4,4a,5,8,8a-Octahydro-1,4:5,8-dimethanonaphthalen-2-one (1). Unsaturated alcohol **8a** ($[\alpha]_D$ +8.59 (*c* 0.41, C_2H_5OH) was oxidized according to method 2 or 3 (above) to give ketone **1**, mp 127–129 °C and the same spectroscopic properties as reported above.

(1β,4β,4aα,5β,8β,8aα)-1,2,3,4,4a,5,6,7,8,8a-Decahydro-1,4:5,8-dimethanonaphthalen-2-*exo*-ol (Dihydro-8). Catalytic hydrogenation of unsaturated alcohol **8** was achieved on a 2.0-g scale using 75 mg of catalyst (10% palladium on powdered charcoal, Matheson, Coleman & Bell) in 65 mL of argon-flushed ethyl acetate. The stirred hydrogenation mixture was exposed to 1 atm of hydrogen gas for 1 h to take up 1 equiv of H_2. Vacuum filtration of the catalyst through a pad of Celite/magnesium sulfate and rotary evaporation of the solvent afforded 1.9 (94% yield) of a white solid, mp 101–102 °C [lit.[35] mp 102 °C]: IR ($CHCl_3$) ν 3300, 3000, 2945, 2880, 1060, 1115; ^1H NMR δ 1.4 (2 H, m), 1.5 (4 H, m), 1.7 (4 H, m), 1.9 (1 H, s, RO–*H*), 2.2 (6 H, m), 4.55 (1 H, m, *H*–CR_2–OH).

(1*S*)-(1β,4β,4aα,5β,8β,8aα)-1,2,3,4,4a,5,6,7,8,8a-Decahydro-1,4:5,8-dimethanonaphthalen-2-one (Dihydro-1). Catalytic hydrogenation of ketone **1** was achieved on a 100-mg scale using 75 mg of palladium/carbon catalyst and 50 mL of argon-flushed methanol solvent. The stirred hydrogenation mixture was exposed to 1 atm of hydrogen gas for 5 h before vacuum filtration of the catalyst through a pad of Celite/magnesium sulfate and rotary evaporation of the solvent. The product obtained from this procedure consisted of an 80:20 ratio of saturated dimethoxy ketal and saturated ketone. The mixture was suspended in 20 mL of water, and 20 mg of *p*-toluenesulfonic acid was added. The mixture was heated to 50 °C for 1 h and then allowed to cool. The solution was diluted with 50 mL each of water and ether, extracted twice with 25 mL of additional ether, dried over magnesium sulfate, and evaporated to yield 89 mg (88% yield) of the saturated ketone, mp 90–91 °C [lit.[36] 91.5–92 °C]: IR (KBr) ν 2880, 1734, 1080; ^1H NMR δ 1.3 (2 H, m), 1.5 (2 H, m), 1.6 (3 H, m), 1.8 (2 H, m), 2.1 (2 H, m), 2.5 (2 H, m), 2.6 (1 H, m), 2.9 (2 H, m); ^{13}C NMR δ 22.53 (t), 25.89 (t), 38.09 (d), 39.32 (d), 40.72 (d), 41.89 (t), 44.59 (t), 46.17 (d), 47.05 (t), 48.80 (d), 54.24 (d), 219.57 (s); UV (*n*-heptane) ϵ_{296}^{max} 12.

(1*S*)-(1α,4α,4aα,5β,8β,8aα)-1,2,3,4,4a,5,8,8a-Octahydro-1,4:5,8-dimethanonaphthalen-2-one (2). This ketone, of known absolute configuration and ee, was prepared in three steps from the known (−)-norbornenyl acetate as follows.

(1*S*)-*exo*-Bicyclo[2.2.1]hept-5-en-2-yl Acetate (12).[22] Into a 3-L flask equipped with a magnetic stirrer and blanketed with N_2 was placed $NaBH_4$ (28.66 g, 758.2 mmol) suspended in 900 mL of diglyme (distilled from CaH_2). The α-pinene (Aldrich, $[\alpha]^{20}_D$ = −136.8°, neat) (240 g, 1.76 mol) was added at room temperature to the suspension. After the addition of α-pinene, the mixture was cooled to 0 °C with an ice bath. To this slurry was added $BF_3{\cdot}Et_2O$ (144 g, 1.01 mol) over 2 h with stirring. After the addition of $BF_3{\cdot}Et_2O$, the mixture was allowed to stir an additional 2 h. During this time, the mixture turned opaque and a white precipitate slowly formed. The white suspension was transferred to a separatory funnel and then added to bicyclo[2.2.1]hepta-2,5-diene (190 g, 2.06 mol) at 0 °C with stirring. The temperature should not be allowed to rise above 20 °C during the addition of the white suspension. After the addition of the white suspension, the mixture was allowed to stir at room temperature for 15–20 h. After stirring, the excess bicyclo[2.2.1]hepta-2,5-diene was removed at 30 °C with a Rotovap. To the residue was added 50 mL of 3 M NaOH, and the solution was cooled to 0 °C with an ice bath. To this was added 350 mL of 30% H_2O_2, while not allowing the temperature to rise over 30 °C. After the addition of H_2O_2, the ice bath was removed, and the solution was stirred at room temperature for 2 h. The white precipitate was gravity filtered, and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 and washed with brine. After the solution was dried over $MgSO_4$, the solvent was removed by rotary evaporation. To this residue was added 240 mL of pyridine, followed by 300 mL of acetic anhydride; each was added dropwise with stirring at room temperature. After the addition of acetic anhydride, the solution was allowed to stir at room temperature for 40 h. This solution was then diluted with 4 L of water. The organic layer was separated, and the aqueous layer was extracted with diethyl ether. The combined organic layers were washed with water (12 × 1 L), 6 M HCl (1 × 200 mL), water (2 × 200 mL), 5% aqueous $NaHCO_3$ (2 × 200 mL), and water (2 × 200 mL). After the solution was dried over $MgSO_4$, the solvent was removed on a Rotovap. The residue was fractionally distilled through a 3-ft vacuum-jacketed column filled with glass beads to give 51.81 g (34% yield) of **12**: bp 64–66 °C (5 mmHg); $[\alpha]^{20}_D$ −20.5° (neat), corresponding to 43% ee[22]: IR (neat) ν 3062, 2936, 1740, 1244, 1034 cm^{-1}; ^1H NMR δ 1.2–1.6 (4 H, m), 1.86 (3 H, s), 2.68 (2 H, d, J = 8.4 Hz), 4.47 (1 H, d, J = 6.3 Hz), 5.80 (1 H, m), 6.06 (1 H, m); ^{13}C NMR δ 21.1, 34.5, 40.5, 46.0, 47.1, 75.0, 132.5, 140.9, 170.7.

(1*S*)-(1α,4α,4aα,5β,8β,8aα)-5,6,7,8,9,9-Hexachloro-2α-acetoxy-1,2,3,4,4a,5,8,8a-octahydro-1,4:5,8-dimethanonaphthalene (13). Into a thick-walled glass tube with a Teflon-brand screw cap were placed **12** ($[\alpha]^{20}_D$ = −20.5°, 43% ee) (8 g, 52.6 mmol), hexachlorocyclopentadiene (20 g, 73.3 mmol), and 1 mL of propylene oxide. This mixture was heated at 160 °C for 40 h. The excess hexachlorocyclopentadiene was removed by Kugelrohr distillation at 170 °C (0.5 mmHg), and the solid product was collected at 200–240 °C (0.5 mmHg). The yellow crystals were chromatographed on a column of silica gel (predried at 175 °C). Elution with 5% ethyl acetate in hexane gave white crystals; mp 144–145 °C [lit.[37] mp 144–145 °C]: $[\alpha]^{25}_D$ +9.44° (*c* 0.146, C_2H_5OH), 43% ee; IR ν 3038, 3014, 2978, 1736, 1598; ^1H NMR δ 1.36 (1 H, q, J = 12.3 Hz), 1.48 (1 H, dt, J = 4.0, 13.7 Hz), 1.72 (1 H, ddd, J = 2.1, 6.7, 13.9 Hz), 1.95 (3 H, s), 2.39 (1 H, d, J = 4.2 Hz), 2.43 (2 H, s), 2.55 (2 H, s), 4.51 (1 H, d, J = 6.6 Hz); ^{13}C NMR δ 21.14, 31.18, 34.94, 40.99 (double intensity), 51.56, 55.40, 76.08, 80.19, 80.54, 104.29, 130.42, 130.46, 170.23.

(1*S*,2*R*)-(1α,4α,4aα,5β,8β,8aα)-1,2,3,4,4a,5,8,8a-Octahydro-1,4:5,8-dimethanonaphthalen-2-ol (14). Into a 2-L flask equipped with a water condenser and magnetic stirrer was placed acetate **13** ($[\alpha]^{25}_D$ = +9.44°, 43% ee) (7.59 g, 17.8 mmol) dissolved in 1200 mL of absolute ethanol. This was brought to reflux with stirring. Sodium (120 g, 5.2 mol) was then added in small pieces over a 3-h period. After the addition of sodium, refluxing was continued for 12 h. The hot solution was poured into ice water and extracted with diethyl ether (2 × 200 mL). The combined organic layers were washed with water (2 × 100 mL) and 100 mL of brine. After the solution was dried over $MgSO_4$, the solvent was removed with a Rotovap. A small quantity of the sample was Kugelrohr distilled at 100 °C (0.5 mmHg) [racemic **14**[2a,10,28]], while the remainder of the product was used without further purification. **14**: $[\alpha]^{25}_D$ +10.36° (*c* 0.145, C_2H_5OH), 43% ee; IR ν 3319, 3051, 2957, 1056; ^1H NMR δ 0.95 (1 H, d, J = 10.5 Hz), 1.15 (1 H, m), 1.32 (1 H, dt, J = 2.4, 9.0 Hz), 1.4–1.6 (2 H, m), 1.72 (1 H, dd, J = 4.2, 8.1 Hz), 1.81 (1 H, dd, J = 4.2, 8.4 Hz), 1.91 (1 H, s), 1.99 (1 H, m), 2.04 (1 H, m), 2.80 (2 H, m), 3.08 (1 H, s), 3.55 (1 H, d, J = 6 Hz), 5.93 (2 H, m); ^{13}C NMR δ 29.94 (t), 36.93 (t), 43.59 (t), 44.88 (d), 46.04 (d), 46.21 (d), 47.91 (2 × d), 53.13 (d), 76.11 (d), 135.25 (d), 135.30 (d).

(1*S*)-(1α,4α,4aα,5β,8β,8aα)-1,2,3,4,4a,5,8,8a-Octahydro-1,4:5,8-dimethanonaphthalen-2-one (2). Into a 250-mL Erlenmeyer flask equipped with a magnetic stirrer was placed alcohol **14** ($[\alpha]^{25}_D$ +10.36°, 43% ee) dissolved in 150 mL of acetone (distilled from $KMnO_4$). The solution was cooled to 0 °C with an ice bath while stirring. Jones reagent (18 mL) was added slowly until an orange-brown color persisted for 30 min. Isopropyl alcohol was added to reduce any excess Jones reagent. The solution was decanted to remove the chromium slats, and 5% aqueous $NaHCO_3$ was added to neutralize the solution. This decanted solution was extracted with diethyl ether (2 × 200 mL). The combined organic layers were washed with 100 mL of brine. After the solution was dried

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(36) Rothberg, I. *J. Am. Chem. Soc.* **1968**, 268–269.
(37) Bird, C. W.; Cookson, R. C.; Crundwell, E. *J. Chem. Soc.* **1961**, 4809–4816.

over $MgSO_4$, the solvent was removed with a Rotovap. The crude product was Kugelrohr distilled at 115 °C (2 mmHg) [racemic **2**[10,23]] to give 2.89 g (69% yield) of product: $[\alpha]^{20}_D$ −61° (*c* 2.07, C_2H_5OH, 43% ee); IR ν 3049, 2962, 1747, 1153; ^1H NMR δ 0.99 (1 H, d, J = 11 Hz), 1.25 (1 H, dm, J = 7.8 Hz), 1.40 (1 H, dt, J = 7.8, 1.6 Hz), 1.68 (1 H, dd, J = 17.0, 5.0 Hz), 1.92 (1 H, ddm, J = 17.0, 4.6 Hz), 2.14 (1 H, dd, J = 8.1, 4.1 Hz), 2.23 (1 H, dd, J = 8.1, 3.8 Hz), 2.42 (2 H, m), 2.52 (1 H, m, J = 11 Hz), 2.91 (2 H, m), 5.97 (1 H, ddm, J = 8.2, 3.1 Hz), 6.01 (1 H, ddm, J = 8.2, 2.9 Hz); ^{13}C NMR δ 32.24 (t), 37.41 (t), 40.93 (t), 46.46 (d), 46.58 (d), 48.09 (2 × d), 51.69 (d), 53.67 (d), 135.48 (d), 136.12 (d), 216.33 (s) ppm; UV (heptane) ϵ^{sh}_{315} 25.4, ϵ^{max}_{303} 46.5, ϵ^{max}_{294} 51.5, ϵ^{sh}_{241} 74.5; HRMS calcd for $C_{12}H_{16}O$ 174.103 916, found 174.1038.

(1*S*)-(1α,4α,4aα,5β,8β,8aα)-1,2,3,4,4a,5,6,7,8,8a-Decahydro-1,4:5,8-dimethanonaphthalen-2-one (Dihydro-2). Unsaturated ketone **2** (270 mg, 1.55 mmol) in 40 mL of THF was hydrogenated at atmospheric pressure in the presence of 90 mg of 10% Pd–C during 20 h at room temperature. After the catalyst was removed by filtration through Celite, the solvent was evaporated (Rotovap), and the residue was distilled (Kugelrohr) to give 190 mg (70%) of pure dihydro-**2** as a colorless oil, bp 150 °C (1.0 mmHg) [racemic dihydro-**2**[23]]: $[\alpha]^{20}_D$ −55° (*c* 1.18, C_2H_5OH, 43% ee); IR (film) ν 2950, 2890, 1745; ^1H NMR δ 1.03–1.83 (8 H, m), 1.80–2.03 (4 H, m), 2.33 (2 H, br s), 2.50 (2 H, br s); ^{13}C NMR δ 23.88 (t), 24.11 (t), 32.95 (t), 35.76 (t), 40.67 (t), 41.20 (d), 41.96 (d), 43.01 (d), 47.34 (d), 48.57 (d), 50.20 (d), 217.17 (s); UV (*n*-heptane) ϵ^{sh}_{314} 20.5, ϵ^{max}_{303} 33.2, ϵ^{max}_{293} 36.6.

(1*S*)-(1α,4α,4aα,5α,8α,8aα)-1,2,3,4,4a,5,8,8a-Octahydro-1,4:5,8-dimethanonaphthalen-2-one (3). This ketone, of known absolute configuration and ee, was prepared from the isomeric ketone **2** as follows.

(1*S*)-(1α,4α,4aα,5β,8β,8aα)-1,2,3,4,4a,5,8,8a-Octahydro-1,4:5,8-dimethanonaphthalen-2-one Ethylene Ketal (15).[10] Into a 500-mL flask equipped with a water condenser and a Dean–Stark trap were placed 20 mL of ethylene glycol and 200 mL of benzene. This mixture was refluxed with stirring overnight to azeotropically remove water. To the dried benzene were added ketone **2** (43% ee) (5.73 g, 32.9 mmol) and a catalytic amount of *p*-toluenesulfonic acid. This mixture was refluxed with stirring, and water was again removed azeotropically. After 0.6 mL of water had been collected, the reaction was cooled to room temperature. The solution was washed with 150 mL of 5% aqueous $NaHCO_3$, and the two layers were separated. The aqueous layer was extracted with diethyl ether (2 × 150 mL). The combined organic layers were washed with cold water (2 × 200 mL) and 100 mL of brine. After the solution was dried over $MgSO_4$, the solvent was removed on a Rotovap. This gave 6.82 g (95% yield) of ketal **15**, which was >95% pure by GC-MS. The product was used without further purification: ^1H NMR δ 1.05 (d, J = 10.8 Hz), 1.22–1.38 (m), 1.76 (dd, J = 4.8, 12.9 Hz), 2.0 (s), 2.05–2.38 (m), 2.53 (dd, J = 4.2, 8.1 Hz), 2.9 (s), 3.9 (4 H, m), 5.96 (2 H, m); ^{13}C NMR δ 33.92, 37.79, 40.10, 45.71, 46.03, 46.57, 46.82, 48.21, 53.42, 63.52, 64.32, 116.88, 135.56, 135.92.

(1*S*)-(1α,4α,4aβ,5α,8α,8aβ)-1,2,3,4,4a,5,6,7,8,8a-Decahydro-7,9-dibromo-1,4:5,8-dimethanonaphthalen-2-one Ethylene Ketal (16).[10] Into a 100-mL flask equipped with a Claisen connecting tube, an addition funnel, a water condenser, and a magnetic stirrer was placed ketal **15** (11.88 g, 54.5 mmol) dissolved in 30 mL of CH_2Cl_2. This solution was cooled to 0 °C with an ice bath. Bromine (8.7 g, 5.5 mL, 57.5 mmol) dissolved in 20 mL of CH_2Cl_2 was added slowly with stirring. After complete addition of Br_2, the solution was stirred at room temperature for 30 min. The solution was then washed with 3 M NaOH and brine. After the solution was dried over $MgSO_4$, the solvent was removed with a Rotovap. GC-MS showed no starting material present and a major peak for product. The product **16** was not further characterized or purified due to its suspected high toxicity.[24] It was assumed to have a 43% ee.

(1*S*)-(1α,4α,4aβ,5α,8α,8aβ)-1,2,3,4,4a,5,8,8a-Octahydro-9-bromo-1,4:5,8-dimethanonaphthalen-2-one Ethylene Ketal (17).[23] Into a 200-mL flask equipped with a Claisen connecting tube, an addition funnel, a water condenser, and a magnetic stirrer, blanketed with N_2, was placed potassium *tert*-butoxide (12.0 g, 107.1 mmol, 2 equiv) dissolved in 100 mL of THF (distilled from $LiAlH_4$). This mixture was stirred at room temperature, and dibromo-**16** dissolved in 50 mL of dry THF was added dropwise. After complete addition of **16**, the dark solution was brought to reflux for 12 h. After being cooled to room temperature, the solution was poured into 200 mL of water and extracted with diethyl ether (2 × 200 mL). The combined organic layers were washed with 100 mL of water and 100 mL of brine. After the solution was dried over $MgSO_4$, the solvent was removed with a Rotovap. GC-MS showed no starting material present and a major peak for product. The product **17** was not further characterized or purified due to its suspected high toxicity.[24] It was assumed to have a 43% ee.

(1*S*)-(1α,4α,4aβ,5α,8α,8aβ)-1,2,3,4,4a,5,8,8a-Octahydro-1,4:5,8-dimethanonaphthalen-2-one Ethylene Ketal (18),[10] Into a 1-L flask equipped with a water condenser and a magnetic stirrer was placed bromo ketal **17** (12.4 g, 41.8 mmol, 43% ee) dissolved in 250 mL of absolute ethanol. This solution was brought to reflux, and sodium (24.5 g, 1.06 mol) was added in small pieces over 3 h. After the addition of sodium, the mixture was allowed to reflux overnight. The hot solution was then poured into 600 mL of water and extracted with CH_2Cl_2 (2 × 200 mL). The combined organic layers were washed with water (2 × 200 mL) and 100 mL of brine. After the solution was dried over $MgSO_4$, the solvent was removed by rotary evaporation. Ketal **18** was purified by Kugelrohr distillation at 120 °C (0.5 mmHg) and assumed to have a 43% ee.

(1*S*)-(1α,4α,4aβ,5α,8α,8aβ)-1,2,3,4,4a,5,8,8a-Octahydro-1,4:5,8-dimethanonaphthalen-2-one (3). Ketal **18** (0.90 g, 4.1 mmol) was dissolved in 20 mL of THF and stirred with 18 mL of 1 M aqueous H_2SO_4 at room temperature for 24 h. The solution was then poured into water (100 mL) and extracted with ether (50 mL). After the solution was dried over anhydrous $MgSO_4$, the ether was removed (Rotovap), and the residue was chromatographed on a 1-cm (diameter) × 30-cm (length) column of silica gel (60–200 mesh). The main fraction eluted with ether. Kugelrohr distillation of the product (following evaporation of the ether) gave 0.55 g (77%) of ketone **3** as a colorless oil, bp 140–143 °C (0.5 mmHg): $[\alpha]^{20}_D$ −125° (*c* 1.5, C_2H_5OH, 43% ee); IR (film) ν 3050, 2960, 1750, 1560; ^1H NMR δ 1.00–2.45 (8 H, m), 2.56 (2 H, br s), 2.88 (2 H, br s), 6.22 (2 H, br s); ^{13}C NMR δ 34.18 (t), 38.10 (t), 42.25 (t), 42.78 (d), 45.29 (d), 45.99 (d), 47.63 (d), 49.27 (d), 52.66 (d), 139.01 (d), 140.53 (d), 215.59 (s); UV (heptane) ϵ^{sh}_{313} 34.8, ϵ^{max}_{303} 60.5, ϵ^{max}_{293} 64.5, ϵ^{sh}_{240} 156.5. HRMS calcd for $C_{12}H_{16}O$ 174.103 916, found 174.1041.

(1*S*)-(1α,4α,4aβ,5α,8α,8aβ)-1,2,3,4,4a,5,6,7,8,8a-Decahydro-1,4:5,8-dimethanonaphthalen-2-one (Dihydro-3). Unsaturated ketone **3** from above (230 mg, 1.3 mmol) in 20 mL of THF was hydrogenated at atmospheric pressure in the presence of 80 mg of 10% Pd–C during 20 h at room temperature. After removal of the catalyst by filtration through Celite, evaporation of the THF (Rotovap) and Kugelrohr distillation afforded 190 mg (81%) of dihydro-**3** as a colorless oil, bp 140 °C (0.5 mmHg): $[\alpha]^{20}_D$ −79° (*c* 1.1, C_2H_5OH); IR (film) ν 2960, 2880, 1750, 1500; ^1H NMR δ 0.60–2.70 (16 H, m); ^{13}C NMR δ 30.19 (t), 30.49 (t), 33.94 (t), 35.76 (t), 39.73 (t), 39.91 (d), 40.61 (d), 45.64 (d), 47.86 (d), 51.73 (d), 54.07 (d), 216.24. HRMS calcd for $C_{12}H_{18}O$ 176.118 84, found 176.1189.

(1*S*)-(1α,4α,4aα,5α,8α,8aα,9β,9aβ,10β,10aα)-1,2,3,4,4a,5,8,8a,9,9a,10,10a-Dodecahydro-1,4:5,8:9,10-trimethanoanthracen-2-one (4). This ketone was synthesized from aldrin in six steps, including the optical resolution, as follows.

(1α,4α,4aα,5β,8β,8aα)-5,6,7,8,9,9-Hexachloro-1,4,4a,5,8,8a-hexahydro-1,4:5,8-dimethanonaphthalene (Aldrin).[38] Into a 500-mL flask equipped with a water condenser and a magnetic stirrer were placed norbornadiene (75 g, 815 mmol) and hexachlorocyclopentadiene (75 g, 275 mmol). This was heated at reflux with stirring overnight. After refluxing, the excess norbornadiene was removed by distillation at 20 mmHg. The product was distilled at 180 °C (2 mmHg) to give a colorless solid. Recrystallization of the solid in 600 mL of acetone–methanol (5:2) gave, after drying, 375 g (65% yield) of product: mp 103–104 °C [lit.[38] mp 104–105 °C]: ^1H NMR δ 1.57 (1 H, d, J = 10.8 Hz), 2.72 (2 H, s), 2.89 (2 H, t, J = 1.5 Hz), 3.33 (1 H, d, J = 10.8 Hz); ^{13}C NMR δ 40.72, 40.85, 54.53, 79.95, 105.12, 130.54, 141.02.

(1α,4α,4aα,5α,8α,8aα,9β,9aβ,10β,10aα)-5,6,7,8,13,13-Hexachloro-1,4,4a,5,8,8a,9,9a,10,10a-decahydro-1,4:5,8:9,10-trimethanoanthracene (19). Into a thick-walled glass tube with a Teflon-brand screw cap were placed aldrin (20 g, 54.8 mmol) and cyclopentadiene (4.8 g, 6 mL, 72.9 mmol). This mixture was heated at 170 °C for 3 days. After being cooled to room temperature, the viscous oil was checked by ^1H NMR, which showed 20% of the aldrin had not reacted. Next, 0.2 equiv of cyclopentadiene was added, and the mixture was heated at 170 °C for 24 h. After being cooled to room temperature, the oil was again checked by ^1H NMR, which showed that 12% of the aldrin had not reacted. The viscous oil was used in the next step without further purification. Purified **19**: ^1H NMR δ 0.74 (1 H, d, J = 13.3 Hz), 1.17 (1 H, d, J = 7.9 Hz), 1.30 (1 H, d, J = 7.9 Hz), 1.92 (2 H, s), 2.11 (1 H, d, J = 13.3 Hz), 2.30 (2 H, s), 2.52 (2 H, s), 2.89 (2 H, m), 5.96 (2 H, s); ^{13}C NMR δ 135.84, 130.35, 104.75, 80.42, 58.68, 53.76, 49.83, 46.59, 37.73, 28.31.

(1α,4α,4aα,5α,8α,8aα,9β,9aβ,10β,10aα)-5,6,7,8,13,13-Hexachloro-1,2,3,4,4a,5,8,8a,9,9a,10,10a-dodecahydro-1,4:5,8:9,10-trimethanoanthracene-2-ol (20). Into a 500-mL flask equipped with a mechanical stirrer with a glass paddle and blanketed with N_2 were placed diene **19** (22.9 g, 53.1 mmol) and $NaBH_4$ (3 g, 79.3 mmol) suspended in dry diglyme. While stirring, this mixture was cooled with an ice bath, and $BF_3{\cdot}Et_2O$ (15 g, 13 mL, 105.7 mmol) was added slowly without allowing

(38) Lidov, R. E.; U.S. Patent 2635977, 1953. *Chem. Abstr.* **1954**, *48*, 2769–2770.

the temperature to rise above 10 °C. After the addition of BF_3·Et_2O, the ice bath was removed, and the mixture was left stirring for 12 h. After stirring, 10 mL of water was added slowly to decompose the excess borane. Next, 30 mL of 3 M NaOH and 30 mL of 30% H_2O_2 were added successively. After the addition of H_2O_2, the solution was heated at 50 °C for 1 h. The solution was poured into 500 mL of ice water and extracted with diethyl ether (3 × 200 mL). The organic layers were combined and washed with water (4 × 1 L) and 200 mL of brine. After the solution was dried over $MgSO_4$, the solvent was removed with a Rotovap. The oily residue was used without further purification: IR ν 3406.

(1α,4α,4aα,5α,8α,8aα,9β,9aβ,10β,10aα)-1,2,3,4,4a,5,8,8a,9,9a,10,10a-Dodecahydro-1,4:5,8:9,10-trimethanoanthracen-2-ol (21). Into a 2-L flask equipped with a water condenser and a magnetic stirrer was placed alcohol **20** (23.5 g, 53.2 mmol) in 500 mL of absolute EtOH. This solution was brought to reflux, and sodium (56 g, 2.4 mol) was added in small pieces over 2 h. After the addition of sodium, the solution was refluxed for an additional 8 h. The hot solution was poured into 500 mL of ice water, and the aqueous layer was extracted with diethyl ether (2 × 300 mL). The organic layers were combined and washed with 300 mL of brine. After the solution was dried over $MgSO_4$, the solvent was removed under reduced pressure (Rotovap). The gummy residue was boiled in hexanes, and the hexanes were decanted off. This procedure was repeated several times. All of the hexanes were combined, and the volume was reduced by half. This solution was put aside for crystallization. Alcohol **21**: mp 130 °C dec: HRMS calcd for $C_{17}H_{22}O$ 242.166 516, found 242.166 99.

Preparation and Resolution of Etienate Ester 22. 3β-Acetoxy-Δ⁵-etiocholenyl chloride was freshly prepared by allowing 3β-acetoxyetienic acid[26] (6.5 g, 18.9 mmol) and 50 mL of thionyl chloride to react at room temperature for 4 h. Removal of the excess thionyl chloride by rotary evaporation yielded the crystalline acid chloride. The acid chloride was dissolved in 40 mL of dry pyridine and cooled with an ice bath. Alcohol **22** (4.5 g, 18.6 mmol) was dissolved in 40 mL of dry pyridine and added dropwise to the acid chloride. After the addition of the alcohol, the solution was allowed to stir overnight at room temperature. The solution was then poured into 190 mL of 10% aqueous HCl in 1 L of water. The precipitate that formed was filtered and washed with 10% HCl and water and then was air dried.

Resolution was achieved by fractional crystallization as follows. *n*-Hexane was added to the solid, and the mixture was heated to boiling. The hot hexane was decanted from undissolved solid, and the process was repeated twice more. The combined hot hexane washings were concentrated then cooled to 0 °C to afford 1.5 g of crystals, which are shown below to consist of only one diastereomer (**22a**). (Alternatively, the diastereomeric esters could be separated on a column of silica gel eluting with methylene chloride.)

Regeneration of Resolved Alcohol 21a. The etienate ester **22a** obtained from hexane crystallization above was dissolved in 40 mL of dry THF and was added to a cooled suspension of $LiAlH_4$ (1.0 g) in 60 mL of dry THF. After the addition of the ester, the mixture was stirred for 1 h. Next, 10 mL of water was cautiously added, after which 50 mL of 2 M H_2SO_4 was added. The aqueous solution was extracted with 100 mL of diethyl ether. The organic layer was washed with 5% aqueous $NaHCO_3$ and then water. After the solution was dried over $MgSO_4$, the solvent was removed with a Rotovap. The residue was chromatographed on a column of silica gel. Elution with methylene chloride gave alcohol **21a** with $[\alpha]^{25}_D$ −49° (*c* 0.115, C_2H_5OH, ≥95% ee).

Mosher Ester of Alcohol 21 or 21a with (*R*)-(+)-MTPA (23 and 23a). Into a vial purged with N_2 were added alcohol **21a** or racemic **21** (16.5 mg), 100 μL of methylene chloride, and 200 μL of pyridine. Next, 60 μL of the acid chloride of (*R*)-(+)-α-methoxy-α-(trifluoromethyl)-phenylacetic acid and a few crystals of 4-(dimethylamino)pyridine were added. The vial was capped and placed into a freezer (−30 °C) overnight. A precipitate of pyridine hydrochloride (a white solid) became evident. To the mixture were added 30 μL of 3-(diethylamino)propylamine and 15 mL of diethyl ether. The ethereal solution was washed with 10% aqueous HCl, 5% aqueous $NaHCO_3$, and water. After the solution was dried over $MgSO_4$, the solvent was removed by rotary evaporation. The crude product was filtered through a column of silica gel, and the solution was eluted with methylene chloride to give the MTPA ester (**23a** or **23**).

(1*S*)-(1α,4α,4aα,5α,8α,8aα,9β,9aβ,10β,10aα)-1,2,3,4,4a,5,8,8a,9,-9a,10,10a-Dodecahydro-1,4:5,8:9,10-trimethanoanthracen-2-one (4). Into a 100-mL flask equipped with an addition funnel and a magnetic stirrer, blanketed with N_2, was placed oxalyl chloride (0.1 mL, 1.1 mmol) in 10 mL of CH_2Cl_2. This was cooled to −78 °C with an acetone/dry ice bath. Next, Me_2SO (0.1 mL, 1.1 mmol) in 5 mL of CH_2Cl_2 was added dropwise while the solution was stirred. The Swern oxidation[34] mixture was stirred for 2 min, and then alcohol **21a** (1.0 g, 0.41 mmol), dissolved in 5 mL of CH_2Cl_2, was added dropwise within 5 min. After the addition of **21a**, stirring was continued for 15 min. Next, 1 mL of triethylamine was added, and the reaction mixture was stirred for 5 min and allowed to warm to room temperature, after which 50 mL of water was added. The aqueous layer was extracted with 50 mL of CH_2Cl_2, and the organic layers were combined. After the solution was dried over $MgSO_4$, the solvent was removed with a Rotovap. The crude residue was purified on a column of silica gel. Elution with 10% EtOAc in hexanes gave 0.8 g (80% yield) of ketone **4**, mp 131–132 °C: $[\alpha]^{25}_D$ −23° (*c* 0.65 C_2H_5OH, 8.3% ee); IR ν 1735; ^{1}H NMR δ 0.58 (1 H, d, *J* = 12.9 Hz), 1.23 (2 H, m), 1.54 (2 H, m), 1.78–2.20 (9 H, m), 2.53 (1 H, d, *J* = 4.5 Hz), 2.63 (1 H, br s), 2.81 (2 H, s), 5.95 (2 H, m); ^{13}C NMR δ 29.31 (CH_2), 37.91 (CH), 38.32 (CH), 38.48 (CH), 40.34 (CH_2), 42.62 (CH_2), 46.39 (CH), 46.47 (CH), 49.99 (CH), 50.28 (CH), 53.73 (CH_2), 54.85 (CH), 55.35 (CH), 135.13 (CH), 135.37 (CH), 218.07 (C=O); UV (ethanol) ϵ^{max}_{287} 51, ϵ^{sh}_{216} 812; UV (trifluoroethanol) ϵ^{max}_{281} 40, ϵ^{sh}_{217} 840; HRMS calcd for $C_{17}H_{20}O$ 240.150 866, found 240.151 07.

(1*S*)-(1α,4α,4aα,5α,8α,8aα,9β,9aβ,10β,10aα)-1,2,3,4,4a,5,6,7,8,8a,9,9a,10,10a-Tetradecahydro-1,4:5,8:9,10-trimethanoanthracen-2-one (Dihydro-4). Into a 250-mL flask equipped with a magnetic stirrer were placed ketone 4, 50 mg of Pd–C, and 100 mL of EtOAc. This mixture was purged for 3 min with N_2 which was catalytically hydrogenated at atmospheric pressure. After the uptake of hydrogen had stopped, the mixture was filtered through a 1-cm pad of Celite. The solvent was removed by rotary evaporation, and the remaining solid was chromatographed on a column of silica gel. Elution with 10% EtOAc in hexanes gave pure product. Dihydro-**4**: mp 144–145 °C; $[\alpha]^{25}_D$ −19° (*c* 0.60, C_2H_5OH, 8.3% ee); IR ν 1740; ^{1}H NMR δ 0.70–2.5 (22 H, m); ^{13}C NMR δ 24.29 (CH_2), 24.68 (CH_2), 29.47 (CH_2), 36.23 (CH_2), 36.60 (CH_2), 38.65 (CH), 40.45 (CH), 40.89 (CH), 40.99 (CH), 42.60 (CH double density), 49.38 (CH_2), 51.07 (CH), 51.40 (CH), 54.07 (CH), 55.62 (CH), 218.52; UV (ethanol) ϵ^{max}_{286} 35; UV (trifluoroethanol) ϵ^{max}_{279} 165; HRMS calcd for $C_{17}H_{22}O$ 242.166 516, found 242.167 52.

(1*S*)-(1α,4α,4aβ,5α,8α,8aα,9α,9aβ,10β,10aα)-1,2,3,4,4a,5,8,8a,9,-9a,10,10a-Dodecahydro-1,4:5,8:9,10-trimethanoanthracen-2-one (5). This ketone was prepared in three steps from optically active ketal **18** as follows.

(1*S*)-(1α,4α,4aβ,5α,8α,8aα,9α,9aβ,10β,10aα)-5,6,7,8,9,9-Hexachloro-1,2,3,4,4a,5,8,8a,9,9a,10,10a-dodecahydro-1,4:5,8:9,10-trimethanoanthracen-2-one Ethylene Ketal (24). Into a thick-walled glass tube with a Teflon-brand screw cap were placed ketal **18** (3.68 g, 16.9 mmol), hexachlorocyclopentadiene (6.00 g, 21.9 mmol), and 1 mL of propylene oxide. The tube was sealed and heated at 140 °C for 24 h. The solution was cooled to room temperature and chromatographed on a column of silica (dried at 175 °C). Elution with hexanes removed the excess hexachlorocyclopentadiene, followed by elution with 10% EtOAc in hexanes to give 5.07 g (61% yield) of product **24** [racemic **24**[10]]. GC-MS showed only one major peak, and **24** was used directly in the next step. It was assumed that **24** had the same ee as its precursor **18** (43% ee).

(1*S*)-(1α,4α,4aβ,5α,8α,8aα,9α,9aβ,10β,10aα)-1,2,3,4,4a,5,8,8a,9,-9a,10,10a-Dodecahydro-1,4:5,8:9,10-trimethanoanthracen-2-one Ethylene Ketal (25). Into a 500-mL flask equipped with a water condenser and a magnetic stirrer was placed hexachloro ketal **24** (43% ee, 5.07 g, 10.3 mmol) dissolved in 200 mL of absolute ethanol. This solution was brought to reflux with stirring, and sodium (20 g, 0.87 mol) was added in small pieces over 2 h. After the addition of sodium, refluxing was continued overnight. The hot solution was poured into ice water and extracted with diethyl ether. The combined organic layers were washed with 200 mL of water and 100 mL of brine. After the solution was dried over $MgSO_4$, the solvent was removed by rotary evaporation. GC-MS showed only one major peak for **25** [racemic **25**[10]], which was used directly in the next step.

(1*S*)-(1α,4α,4aβ,5α,8α,8aα,9α,9aβ,10β,10aα)-1,2,3,4,4a,5,8,8a,9,-9a,10,10a-Dodecahydro-1,4:5,8:9,10-trimethanoanthracen-2-one (5). Into a 250-mL flask equipped with a magnetic stirrer were placed ketal **25**, *p*-toluenesulfonic acid (50 mg), 100 mL of acetone (distilled from $KMnO_4$), and 10 mL of water. This solution was stirred at room temperature for 12 h. One hundred milliliters of water was added, and the aqueous solution was extracted with diethyl ether (2 × 100 mL). The combined organic layers were washed with 5% aqueous $NaHCO_3$ (2 × 100 mL) and 50 mL of brine. After the solution was dried over $MgSO_4$, the solvent was removed with a Rotovap. The crude product was chromatographed on a column of silica gel (dried at 175 °C), and elution with 10% ethyl acetate in hexane gave a solid, which was distilled (Kugelrohr) at 130 °C (0.5 mmHg) to give a white solid, mp 95–97 °C: $[\alpha]^{25}_D$ −69° (*c* 0.37, C_2H_5OH, 43% ee); IR ν 1747; ^{1}H NMR δ 1.1–1.3 (m), 1.4–1.5 (m), 1.7–2.0 (m), 2.1 (s), 2.15–2.30 (m), 2.8 (m), 5.9 (2 H, s); ^{13}C NMR δ 29.65 (CH_2), 34.73 (CH_2), 39.08 (CH), 41.56 (CH), 42.42 (CH), 46.01 (CH, double intensity), 47.51 (CH), 47.99 (CH_2), 48.48 (CH), 48.97 (CH), 52.98 (CH_2), 53.31 (CH), 54.49 (CH), 134.83 (CH),

134.92 (CH), 214.73; UV (ethanol) ϵ_{293}^{max} 64, ϵ_{209} 1062; UV (trifluoroethanol) ϵ_{284}^{max} 296, ϵ_{219} 1265; HRMS calcd for $C_{17}H_{20}O$ 240.150866, found 240.151 36.

(1*S*)-(1α,4α,4aβ,5α,8α,8aα,9α,9aβ,10β,10aα)-1,2,3,4,4a,5,6,7,8,8a,9,9a,10,10a-Tetradecahydro-1,4:5,8:9,10-trimethanoanthracen-2-one (Dihydro-5). Into a 250-mL 1-necked round-bottom flask equipped with a magnetic stirrer were placed unsaturated ketone **5**, 50 mg of Pd–C, and 100 mL of ethyl acetate. This mixture was purged for 30 min with N_2 which was catalytically hydrogenated at atmospheric pressure. After the uptake of hydrogen had stopped, the mixture was filtered through a 1-cm pad of Celite. The solvent was removed by rotary evaporation, and the remaining solid was Kugelrohr distilled at 130 °C (0.5 mmHg) to give a white solid. Dihydro-**5**: mp 127–129 °C; $[\alpha]^{25}_D$ −64° (*c* 0.34, C_2H_5OH, 43% ee); IR *ν* 3056, 1742; ^{1}H NMR δ 1.1–2.6 (22 H, m); ^{13}C NMR δ 24.43 (CH), 24.49 (CH_2), 30.10 (CH_2), 34.75 (CH_2), 39.65 (CH), 40.15 (CH), 40.89 (CH, double intensity), 41.03 (CH), 42.14 (CH_2), 47.09 (CH), 48.44 (CH), 50.36 (CH), 50.78 (CH), 53.95 (CH, double intensity), 216.04; UV (ethanol) ϵ_{293}^{max} 65; UV (trifluoroethanol) ϵ_{285}^{max} 119; HRMS calcd for $C_{17}H_{22}O$ 242.166516, found 242.166 81.

(1*S*)-(1α,4α,4aβ,5α,8α,8aβ,9α,9aβ,10α,10aβ)-1,2,3,4,4a,5,8,8a,9,-9a,10,10a-Dodecahydro-1,4:5,8:9,10-trimethanoanthracen-2-one (6). This ketone was prepared from optically active ketal **25** in three steps, as shown below.

(1*S*)-(1α,4α,4aβ,5α,8α,8aα,9α,9aβ,10β,10aα)-6,13-Dibromo-1,2,3,4,4a,5,6,7,8,8a,9,9a,10,10a-tetradecahydro-1,4:5,8:9,10-trimethanoanthracen-2-one Ethylene Ketal (26). Into a 250-mL flask equipped with a Claisen connecting tube, an addition funnel, a water condenser, and a magnetic stirrer were placed ketal **25** (11% ee) (4.7 g, 16.5 mmol) and 50 mL of CH_2Cl_2. This solution was cooled to 0 °C with an ice bath. Bromine (2.6 g, 1.6 mL, 16.5 mmol) dissolved in 20 mL of CH_2Cl_2 was added slowly with stirring. After addition of Br_2, the solution was stirred at room temperature for 30 min. The solution was then washed with 50 mL of 3 M NaOH and 100 mL of brine. After the solution was dried over $MgSO_4$, the solvent was removed by rotary evaporation. GC-MS showed no starting material present and a major peak for product. Dibromo ketal **26** was not further characterized or purified due to its suspected high toxicity.[24] It was assumed to have an 11% ee and was used directly in the next step.

(1*S*)-(1α,4α,4aβ,5α,8α,8aβ,9α,9aβ,10α,10aβ)-6-Bromo-1,2,3,4,4a,5,6,7,8,8a,9,9a,10,10a-tetradecahydro-1,4:5,8:9,10-trimethanoanthracen-2-one Ethylene Ketal (27). Into a 100-mL flask equipped with a Claisen connecting tube, an addition funnel, a water condenser, and a magnetic stirrer, blanketed with N_2, was placed potassium *tert*-butoxide (4.0 g, 35.7 mmol, 2 equiv), which was dissolved in 15 mL of THF (distilled from $LiAlH_4$). This mixture was stirred at room temperature, and dibromo ketal **26** dissolved in 25 mL of dry THF was added dropwise. After complete addition of **26**, the dark solution was brought to reflux for 12 h. After being cooled to room temperature, the solution was poured into 200 mL of water and extracted with diethyl ether (2 × 100 mL). The combined organic layers were washed with 100 mL of water and 50 mL of brine. After the solution was dried over $MgSO_4$, the solvent was removed by rotary evaporation. GC-MS showed no starting material present and a major peak for product. Monobromo ketal **27** was not further characterized or purified due to its suspected high toxicity.[24] It was assumed to have an 11% ee and was used directly in the next step.

(1*S*)-(1α,4α,4aβ,5α,8α,8aβ,9α,9aβ,10α,10aβ)-1,2,3,4,4a,5,6,7,8,8a,9,9a,10,10a-Tetradecahydro-1,4:5,8:9,10-trimethanoanthracen-2-one Ethylene Ketal (28). Into a 500-mL flask equipped with a water condenser and a magnetic stirrer was placed monobromo ketal **27** dissolved in 200 mL of absolute ethanol. This solution was brought to reflux with stirring, and sodium (10 g, 0.43 mol) was added in small pieces over 2 h. After the addition of sodium, refluxing was continued overnight. The hot solution was poured into 1 L of ice water and extracted with CH_2Cl_2. The combined organic layers were washed with 200 mL of water and 100 mL of brine. After the solution was dried over $MgSO_4$, the solvent was removed by rotary evaporation. GC-MS showed only one major peak for **28**, which was used directly in the next step.

(1*S*)-(1α,4α,4aβ,5α,8α,8aβ,9α,9aβ,10α,10aβ)-1,2,3,4,4a,5,8,8a,9,-9a,10,10a-Dodecahydro-1,4:5,8:9,10-trimethanoanthracen-2-one (6). Into a 250-mL flask equipped with a magnetic stirrer were placed ketal **28**, 50 mL of THF, 20 mL of water, and 20 mL of 2 M H_2SO_4. This solution was stirred at room temperature for 12 h. One hundred milliliters of water was added, and the aqueous solution was extracted with diethyl ether (2 × 100 mL). The combined organic layers were washed with 5% aqueous $NaHCO_3$ (2 × 100 mL) and 50 mL of brine. After the solution was dried over $MgSO_4$, the solvent was removed with a Rotovap. The crude product was chromatographed on a column of silica gel (dried at 175 °C), and elution with 10% ethyl acetate in hexane gave a solid. Unsaturated ketone **6** had mp 84–85 °C: $[\alpha]^{25}_D$ −33° (*c* 0.58, C_2H_5OH, 11% ee); IR *ν* 1747; ^{1}H NMR δ 0.70–2.8 (m), 6.06 (2 H, s); ^{13}C NMR δ 31.24 (CH_2), 34.77 (CH_2), 39.40 (CH), 42.78 (CH, CH_2, double intensity), 43.60 (CH), 44.98 (CH, double intensity), 46.73 (CH), 48.34 (CH_2), 50.24 (CH), 50.74 (CH), 53.57 (CH), 53.65 (CH), 139.54 (CH), 139.65 (CH), 215.49; UV (ethanol) ϵ_{293}^{max} 113, ϵ_{240}^{sh} 336, ϵ_{216} 639; UV (trifluoroethanol) ϵ_{279}^{max} 154, ϵ_{203} 1543; HRMS calcd for $C_{17}H_{20}O$ 240.150866, found 240.150 86.

(1*S*)-(1α,4α,4aβ,5α,8α,8aβ,9α,9aβ,10α,10aβ)-1,2,3,4,4a,5,6,7,8,8a,9,9a,10,10a-Tetradecahydro-1,4:5,8:9,10-trimethanoanthracen-2-one (Dihydro-6). Into a 250-mL flask equipped with a magnetic stirrer were placed unsaturated ketone **6**, 50 mg of Pd–C, and 100 mL of EtOAc. This mixture was purged for 30 min with N_2 which was catalytically hydrogenated at atmospheric pressure. After the uptake of hydrogen had stopped, the mixture was filtered through a 1-cm pad of Celite. The solvent was removed by rotary evaporation, and the remaining solid was chromatographed on a column of silica gel. Elution with 10% ethyl acetate in hexane gave pure dihydro-**6**, mp 73–74 °C: $[\alpha]^{25}_D$ −28° (*c* 0.088, C_2H_5OH, 11% ee); IR *ν* 1747; ^{1}H NMR δ 0.70–2.5 (22 H, m); ^{13}C NMR δ 30.79 (CH_2), 30.83 (CH_2), 30.86 (CH_2), 34.53 (CH_2), 35.86 (CH_2), 39.24 (CH), 39.37 (CH, double intensity), 43.92 (CH), 44.74 (CH), 46.12 (CH), 48.21 (CH_2), 52.81 (CH), 53.43 (CH), 53.94 (CH), 54.31 (CH), 214.97; UV (ethanol) ϵ_{284}^{max} 126, ϵ_{218} 355; UV (trifluoroethanol) ϵ_{279}^{max} 165; ϵ_{215} 375; HRMS calcd for $C_{17}H_{22}O$ 242.166 516, found 242.167 86.

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Supplementary Material Available: Tables IS–IIIS of observed optical rotations of recrystallized products (2 pages). Ordering information is given on any current masthead page.