by National Science Foundation Undergraduate Research Participation Grants SPI-7826903 and SPI-7926823. Gratitude is expressed to Mrs. Joan S. Murphy, Merck Sharp & Dohme Research Laboratories, for the ^{13}C NMR spectra and to Dr. Bryon H. Arison, Merck Institute for Therapeutic Research, for the 300-MHz ^{1}H NMR spectra. Appreciation is extended to Mr. Henry J. Albert, Jr., for aid in the initial phases of this study.

Registry No. *meso*-**1a**, 54105-33-8; (±)-**1c**, 79803-35-3; (±)-**1d**, 79815-46-6; (±)-**2a**, 79803-36-4; (±)-**2b**, 79803-37-5; (±)-**2c**, 79803-38-6; (±)-**2d**, 79803-39-7; *meso*-**3a**, 79803-40-0; (±)-**3b**, 79803-41-1; (±)-**3c**, 79803-42-2; (±)-**4a**, 79803-43-3.

Octant Rule. 9.[1] Circular Dichroism of Axial and Equatorial 4-(Trideuteriomethyl)adamantan-2-ones and a Comparison with 4-Methyladamantan-2-ones

David A. Lightner* and W. M. Donald Wijekoon

Department of Chemistry, University of Nevada, Reno, Nevada 89557

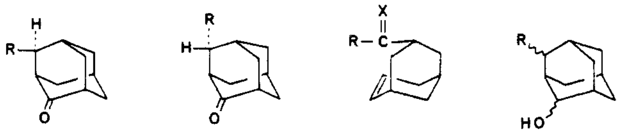
Received August 18, 1981

The title compounds were prepared optically active, and their variable-temperature circular dichroism (CD) spectra were measured. The β-axial ketones (1*S*,3*R*,4*S*)-4(a)-(trideuteriomethyl)adamantan-2-one (1) and (1*S*,3*R*,4*S*)-4(a)-methyladamantan-2-one (2) underwent considerable changes in their CD spectra: at −175 °C moderately intense ($\Delta\epsilon \sim 0.5$) negative n → π* Cotton effects (CEs) were observed in both polar (EPA) and nonpolar (methylcyclohexane–isopentane) solvents. Those findings contrast with the room temperature n → π* CE signs and magnitudes of 1 and 2: $\Delta\epsilon \sim -0.04$ in ethyl ether–isopentane–ethanol and $\Delta\epsilon \sim +0.02$ in methylcyclohexane–isopentane. The β-equatorial ketones (1*S*,3*R*,4*R*)-4(e)-(trideuteriomethyl)adamantan-2-one (3) and (1*S*,3*R*,4*R*)-4(e)-methyladmantan-2-one (4) gave the expected (+) CEs ($\Delta\epsilon \sim 1$) which are relatively insensitive to temperature and solvent. Comparison of CD_3 and CH_3 rotatory strengths indicates that the heavier isotope makes the inherently more dissignate octant contribution.

Introduction

During recent years there has been an increasing interest in understanding how deuterium influences the conformational[2-4] and chiroptical[4-7] properties of ketones with special reference to the octant rule.[8,9] Most of this work has focused on cyclic compounds in which optical activity was due to substitution of a ring hydrogen by deuterium. There are, however, relatively few examples which contrast the behavior of the rotatory contributions of CD_3 and CH_3 to the carbonyl n → π* Cotton effect (CE). In the first of those examples, Meyer and Lobo[10] found that (+)-camphor-*9,9,9-d*$_3$ had an ORD molecualr amplitude (+60.92°) 3% smaller than that of the protio analogue.[7] Subsequently, Pak and Djerassi[11] found that 3(*S*)-methyl-5(*R*)-(trideuteriomethyl)cyclohexanone exhibited a negative CE, $[R]^{20} = -0.082$, and concluded that *the heavier isotope is the weaker* perturber—as has proved true in other examples involving deuterium[2-13] and even carbon-13.[11,12,14] That conclusion was supported by more recent work with α-(trideuteriomethyl)-4-*tert*-butylcyclohexanones and other α-(trideuteriomethyl)-4-alkylcyclohexanones and prompted Djerassi et al.[12] to suggest that the emerging generalization, if upheld, could "lead to a useful application for obtaining estimates of methyl octant contributions in more complicated situations where the observed Cotton effect amplitude results from a larger

Chart I



1: R = CD_3
2: R = CH_3

3: R = CD_3
4: R = CH_3

5: R = OH, X = O
6: R = CD_3, X = O
7: R = CD_3, X = $<^{OH}_{H}$
8: R = CH_3, X = O
9: R = CH_3, X = $<^{OH}_{H}$

10: R = CD_3
11: R = CH_3

---

[1] For preceding paper, see: Lightner, D. A.; Eng. F. P. C. *Steroids* **1980**, *35*, 189–207.

[2] Lee, S-F.; Barth, G.; Djerassi, C. *J. Am. Chem. Soc.* **1981**, *103*, 295–301.

[3] Dauphin, G.; Gramain, J. C.; Kergomard, A.; Renard, M. F.; Veschambre, H. *Tetrahedron Lett.* **1980**, *21*, 4275–4278.

[4] (a) Sundararaman, P.; Barth, G.; Djerassi, C. *J. Org. Chem.* **1980**, *45*, 5231–5236. (b) Sing, L. Y.; Lindley, M.; Sundararaman, P.; Barth, G.; Djerassi, C. *Tetrahedron, Suppl.* **1981**, *37*, 181–189.

[5] Lightner, D. A.; Gawroński, J. K., Bouman, T. D. *J. Am. Chem. Soc.* **1980**, *102*, 1983–1990.

[6] Edgar, M. T.; Barth, G.; Djerassi, C. *J. Org. Chem.* **1980**, *45*, 2680–2684.

[7] Meyer, W. L.; Lobo, A. P.; Ernstbrunner, E. E.; Giddings, M. R.; Hudec, J. *Tetrahedron Lett.* **1978**, 1771–1774. These authors report: (+)-camphor, $\Delta\epsilon = +1.50$; camphor-*9,9,9-d*$_3$, $\Delta\epsilon = +1.36$, yielding a 9% reduction in intensity for CD_3 substitution.

[8] Moffitt, W.; Woodward, R. B.; Moscowitz, A.; Klyne, W.; Djerassi, C. *J. Am. Chem. Soc.* **1961**, *83*, 4013–4018.

[9] Bouman, T. D.; Lightner, D. A. *J. Am. Chem. Soc.* **1976**, *98*, 3145–3154.

[10] Meyer, W. L.; Lobo, A. P.; *J. Am. Chem. Soc.* **1966**, *88*, 3181–3182.

[11] Pak, C. S.; Djerassi, C. *Tetrahedron Lett.* **1978**, 4377–4378.

[12] Lee, S-F.; Edgar, M.; Pak, C. S.; Barth, G.; Djerassi, C. *J. Am. Chem. Soc.* **1980**, *102*, 4784–4790.

[13] Ringdahl, B.; Craig, J. C.; Keck, R.; Retey, J. *Tetrahedron Lett.* **1980**, *21*, 3965–3968.

[14] Sing. Y. L.; Numan, H.; Wynberg, H.; Djerassi, C. *J. Am. Chem. Soc.* **1979**, *101*, 5155–5158.

0022-3263/82/1947-0306$01.25/0

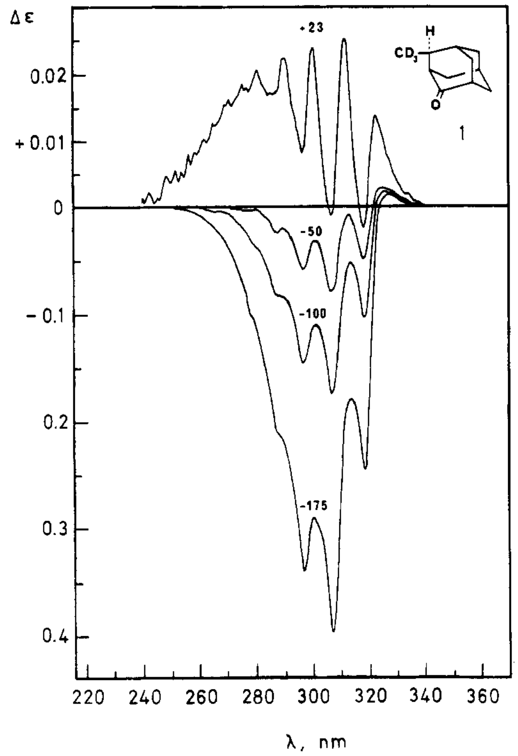


Figure 1. Variable-temperature circular dichroism spectra of 4.33 mM 1 in MI4:1. Temperatures (°C) are indicated above the curves, which are to be read as all being on the same scale as the majority of the curve. Corrections are made to 100% ee.

number of other group contributions..." In this paper we address the question of whether the heavier isotope is the weaker octant perturber for the n → π* CEs of β-axial and β-equatorial adamantanones, polycyclic systems where the rings are conformationally immobile.

Synthesis and Stereochemistry

Optically active methyl- and (trideuteriomethyl)-adamantanones (1–4) were prepared from the same known (+)-*endo*-bicyclo[3.3.1]non-6-ene (3*R*)-carboxylic acid (5)[15] whose absolute configuration had been established previously.[16] Treatment of the lithium salt of 5 with either CD_3Li or CH_3Li gave the corresponding trideuteriomethyl or methyl ketones (6 and 8, respectively), which were reduced smoothly and in high yields by $LiAlH_4$ to the corresponding secondary alcohols (7 and 9, respectively). Cyclization[15-17] of the secondary alcohols in hot formic acid followed by $LiAlH_4$ treatment gave mixtures of epimeric adamantanols (four isomers, **10** and **11**). The mixtures of epimeric admantanols were simplified by Jones oxidation, which led to mixtures of the epimeric β-(trideuteriomethyl)- or β-methyladamantanones (**1** and **3**, or **2** and **4**, respectively; Chart I). The epimers could be separated by preparative gas chromatography. The axial epimers had shorter retention times than the equatorial epimers, as expected, and axial 4-methyladmantanone (**2**) exhibited the expected higher field doublet in the ^1H NMR (δ 0.95) than the equatorial epimer (**4**) (δ 1.07). Both **2** and **4** were identical with Snatzke et al.'s reported β-methyladamantanones[18-20] and identical with β-methyladamantanones that we had prepared previously[21] by Snatzke et al.'s method.[18-20] The β-(trideuteriomethyl)adamantanones were essentially identical with their protio analogues in GC retention times and melting points.

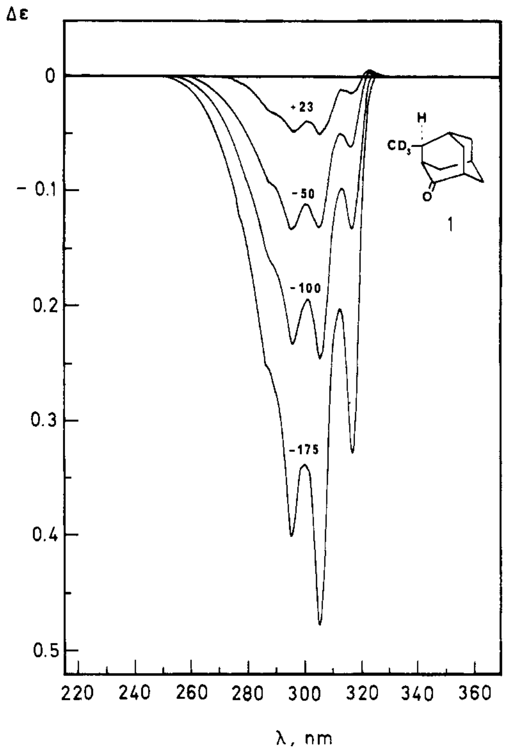


Figure 2. Variable-temperature circular dichroism spectra of 3.98 mM 1 in EPA. Temperatures (°C) are indicated above the curves. Corrections are made to 100% ee.

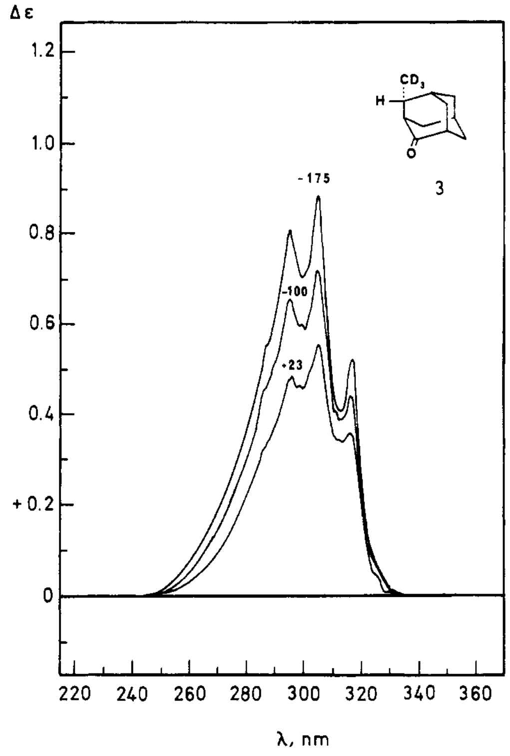


Figure 3. Variable-temperature circular dichroism spectra of 2.90 mM 3 in MI4:1. Temperatures (°C) are indicated above the curves. Corrections are made to 100% ee.

---

(15) Numan, H.; Wynberg, H. *J. Org. Chem.* **1978**, *43*, 2232–2236.

(16) Numan, H.; Troostwijk, C. B.; Wieringa, J. H.; Wynberg, H. *Tetrahedron Lett.* **1977**, 1761–1764.

(17) McKervey, M. A.; Faulkner, D.; Hamill, H. *Tetrahedron Lett.* **1970**, 1971–1974.

(18) Snatzke, G.; Ehrig, B.; Klein, H. *Tetrahedron* **1969**, *25*, 5601–5609.

(19) Snatzke, G.; Eckhardt, G. *Tetrahedron* **1968**, *24*, 4543–4558.

(20) Snatzke, G.; Eckhardt, G. *Chem. Ber.* **1968**, *101*, 2010–2027.

(21) Lightner, D. A.; Chang, T. C. *J. Am. Chem. Soc.* **1974**, *96*, 3015–3016. Chang, T. C., unpublished synthesis.

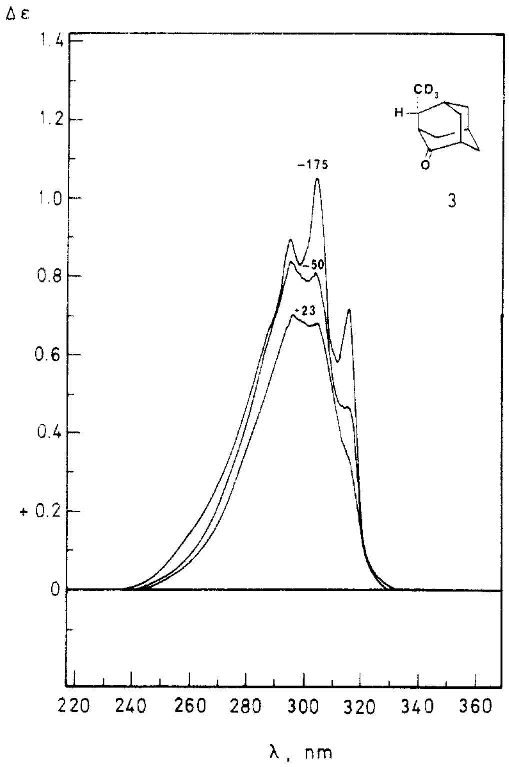


Figure 4. Variable-temperature circular dichroism spectra of 2.61 mM **3** in EPA. Temperatures (°C) are indicated above the curves. Corrections are made to 100% ee.

Results and Discussion

The room temperature CD curves for the n–π^* CEs of **1** and **3** (Figures 1–4) are nearly identical with those of their protio analogues (**2** and **4**). They are also qualitatively similar to the CD curves of Snatzke and co-workers, who showed nearly 15 years ago[22] that whereas β-equatorial substituted adamantanones obey the octant rule, β-axial may not. They determined that (1*S*,3*R*)-4(e)-methyladamantan-2-one (**4**) obeyed the octant rule[8] (consignate[23] methyl contribution)[19,20] but that (1*R*,3*S*)-4(a)-methyladamantan-2-one (enantiomer of **2**) did not obey the octant rule in polar solvents.[18] In dioxane and ethanol the β-axial methyl group exhibited a weak ($\Delta\epsilon \sim -0.1$), dissignate[23] contribution to the circular dichroism (CD) CE, but in isooctane it exhibited a weak ($\Delta\epsilon \sim +0.05$) consignate contribution.[18] The apparent dissignate ("anti-octant")[18,24] behavior was subsequently explained by locating the β-axial methyl group in a front octant by studies which investigated the third nodal surface of the octant rule.[9] However, the solvent-dependent CE sign change remained puzzling, especially in light of the unvaryingly positive CE of (1*S*,4*R*)-*exo*-2-methylbicyclo[2.2.1]heptan-7-one, whose dissignate methyl perturber is located in a position nearly identical with that of the CH_3 group of **3**, both relative to the C=O group.[24]

Interestingly, although the room temperature CD CE signs of **1** (Figures 1 and 2) correspond to those reported for the enantiomer of **2**,[18] in hydrocarbon solvent at low temperatures the situation changes considerably (Figure 1). From our point of view, the inherent, moderately intense dissignate contributions found at −175 °C for the β-axial CD_3 and CH_3 groups became an order of magnitude weaker at room temperature, or even weakly consignate. On the basis of CNDO/S calculations[25] we could not find a strong rotamer effect for the CH_3 group. Consequently, we do not attribute the considerable reduction in CE intensity in going from low temperature to room temperature to a redistribution of the CH_3 or CD_3 rotamer populations, with a concomitant differing mix of CH_3 C–H contributions and CD_3 C–D contributions. (The importance of C–H octant contributions in ketones has been stressed previously.[9,26]) Vibronic effects,[27] aggregation, and/or solvation effects[4b,12,28,29] presumably play an important role in determining whether the CE sign is weakly positive or weakly negative at room temperature. At this time, however, we cannot offer a more complete explanation.

Our conclusion in favor of an inherent dissignate contribution for the β-axial CH_3 (or CD_3) group in adamantanone is contrary to the view of Djerassi et al.,[28] who favor an inherent consignate contribution based on CD studies with 3-methyl-4-*tert*-butycyclohexanones and other 4-substituted-3-methylcyclohexanones. We have no explanation for our dissonant results, which may reflect differences in ring conformations and preferences for rotational isomers at C-4 in the cyclohexanones. The adamantanones of our work are assumed to have a fairly rigid ring skeleton with all ring substituents symmetrically disposed, except a β-CH_3 or CD_3 and β'-H.

The CD curves of the corresponding β-equatorial-CD_3 adamantanone (**3**) are presented in Figures 3 and 4. Both CH_3 and CD_3 groups exhibit the expected and previously observed (in the case of CH_3)[19,20] consignate octant contributions, the magnitudes of which are in good agreement with the assigned β-equatorial CH_3 values.[12,30] The CE magnitudes do not vary greatly with changes in temperature and solvent[31]—observations which suggest that solvent–aggregation effects play only a minor role.[4b,12] We also point out that the observed −175 °C CE signs and ~1:2 ratio of rotatory strengths for fully staggered β-axial and β-equatorial methyladamantanones are predicted by theory.[9]

As revealed in Table I, deuterium in β-equatorial CD_3 (of **3**) makes a *more consignate* contribution to the octant rule than hydrogen in β-equatorial CH_3 (of **4**) at 25 °C. Our calculated $\Delta[R]$ values at room temperature differ in sign from that determined by Pak and Djerassi,[11] using (3*S*,5*R*)-3-methyl-5-(trideuteriomethyl)cyclohexanone, $\Delta[R]^{20} = -0.082$ in 4:1 isopentane–methylcyclohexane. However, at −175 °C the situation with **3** and **4** reverses such that, as we see it, deuterium in β-equatorial CD_3 makes an *inherently more dissignate* contribution to the octant rule than hydrogen in β-equatorial CH_3, as expected[5]—and in qualitative agreement with Djerassi et al.[11,12] The reasons for the reversal at room temperature are not clear but may be attributed to a combination vibronic[27] and/or aggregation–solvation[4b,12,28,29] effects. What is clear is that caution must be exercised in assuming that deuterium will always *exhibit* a more dissignate contribution than hydrogen (or that the heavier isotope is the weaker perturber). Deuterium in β-axial CD_3, on the other

---

[22] Snatzke, G.; Eckhardt, G.; Ehrig, B. *Agnew. Chem., Int. Ed. Engl.* **1967**, *6*, 998–999. Paper given at the September 1967 Centennial Meeting of the Gesellschaft Deutscher Chemiker.

[23] Klyne, W.; Kirk, D. N. *Tetrahedron Lett.* **1973**, 1483–1486.

[24] Lightner, D. A.; Jackman, D. E. *J. Am. Chem. Soc.* **1974**, *96*, 1938–1939. Bouman, T. D.; Lightner, D. A.; Kalyanam, N., unpublished work.

[25] Bouman, T. D., Southern Illinois University, Edwardsville, IL. See ref 9.

[26] Kirk, D. N. *J. Chem. Soc., Perkin Trans. 1*, **1976**, 2171–2177.

[27] Weigang, O. E., Jr.; Ong, E. C. *Tetrahedron* **1974**, *30*, 1783–1793.

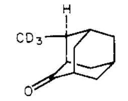
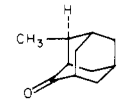
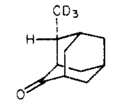
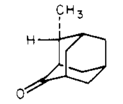
[28] Konopelski, J. P.; Sundararaman, P.; Barth, G.; Djerassi, C. *J. Am. Chem. Soc.* **1980**, *102*, 2737–2745.

[29] Allinger, J.; Allinger, N. L. *Tetrahedron* **1958**, *2*, 64–74.

[30] Kirk, D. N.; Klyne, W. *J. Chem. Soc., Perkin Trans. 1* **1974**, 1076–1103.

[31] Solvent-induced changes in the CEs have been explained in terms of differing refractive indices of the solvents, see ref 22.

Table I. Reduced Rotatory Strengths for the n → π* Transitions of β-(Trideuteriomethyl)- and β-Methyladamantanones

compd	EPA[a]		MI[b]		$[R]_{EPA}$ - $[R]_{MI}$[c]	
	$[R]^{25±2}$	$[R]^{-175±5}$	$[R]^{25±2}$	$[R]^{-175±5}$	25 ± 2 °C	-175 ± 5 °C
 1	-0.0860	-0.8214	+0.09137	-0.6681	-0.177	-0.153
 2	-0.1004	-0.9157	+0.07840	-0.7582	-0.179	-0.158
$[R]_1$ - $[R]_2$	+0.0144	+0.0943	+0.01297	+0.0901		
 3	+2.157	+1.849	+1.561	+1.621	+0.596	+0.228
 4	+2.097	+2.077	+1.537	+1.847	+0.560	+0.230
$[R]_3$ - $[R]_4$	+0.060	-0.228	+0.024	-0.226		

[a] Ethanol-isopentane-ether (2:5:5, v/v/v). [b] Methylcyclohexane-isopentane (4:1, v/v). [c] Reduced rotatory strength, $[R]$ (= rotatory strength (cgs) × 1.08 × 10^{40}); superscript temperatures are in °C.

hand, exhibits a solvent and temperature-independent, *inherently more dissignate* contribution to the octant rule than hydrogen in β-axial CH_3 (Table I)—relative to both CD_3 and CH_3 in a front octant.

In summary, one can conclude, as has been suggested,[12] that the heavier isotope is the *inherently* weaker octant perturber for CD_3 vs. CH_3 in both 3-equatorial and 3-axial substituted cyclohexanone systems.

Experimental Section

General Procedures. Circular dichroism (CD) spectra were recorded on a JASCO J-40 instrument equipped with a photoelastic modulator and a J-DPY data processor. Variable-temperature CD measurements were performed with a cryoscopic Dewar. Ultraviolet spectra were recorded on a Cary 219 spectrophotometer, and rotations were determined in 96% ethanol unless otherwise indicated on a Perkin-Elmer 141 polarimeter. All nuclear magnetic resonance (NMR) spectra were determined in $CDCl_3$ and reported in parts per million downfield from tetramethylsilane unless otherwise indicated on a Perkin-Elmer R-24B or JEOL FX-100 instrument. Mass spectra (MS) were recorded at 70-, 20-, or 14-eV ionizing voltage on a JEOL JMS-07 or AEI MS-9 spectrometer. Infrared (IR) spectra were measured on a Perkin-Elmer Model 599 instrument. All melting points are uncorrected and were determined on a Thomas-Hoover or Mel-Temp capillary apparatus. Analytical gas chromatography (GC) was performed on a Varian-Aerograph Model 2400 F/I instrument, using a 6 ft × $^1/_8$ in. diameter column A with 5% FFAP stationary phase adsorbed on 80/100 Chromosorb W AW-DMCS. Preparative gas chromatography (GC) was performed on 5 ft × $^3/_8$ in. diameter column B (15% QF-1 on 80/100 Chromosorb W), using a Varian-Aerograph Model 1720 T/C instrument.

Spectral data were obtained with spectra grade solvents (MCB): MI4:1 (methylcyclohexane–isopentane, 4:1, v/v) and EPA (ethyl ether–isopentane–ethanol, 5:5:2, v/v/v). Diethyl ether was first distilled from CaH_2 and then from $LiAlH_4$ all under N_2. Other solvents used were freshly distilled or stored over 4A molecular sieves (Linde). Trideuteriomethyl iodide (CD_3I) used in this work was >99 atom % D from Aldrich. LiH and $LiAlH_4$ were from Alfa/Ventron.

(+)-(1*S*,5*R*,3*R*)-*endo*-3-Bicyclo[3.3.1]non-6-enyl Trideuteriomethyl Ketone (6). Sixteen hundred milligrams (9.64 mmol) of (+)-*endo*-bicyclo[3.3.1]non-6-ene (3*R*)-carboxylic acid [**5**, $[\alpha]^{25}_{578}$ +79.6° (*c* 1.0), 52.97% ee[15,16]] was dissolved in dry ethyl ether and converted to its lithium salt by the addition of 60 mg of finely powdered LiH. The mixture was stirred at room temperature for 1 h, and then the solvent was removed by rotary evaporation. The resulting lithium salt was dried under vacuum at 80 °C. The dried salt (1.65 g) in 25 mL of dry ether was stirred vigorously while an ethereal solution of (trideuteriomethyl)lithium[32] (0.99 M, 12.0 mL, 11.88 mmol) was added to it at 0 °C. The mixture was stirred for 0.5 h at 0 °C after final addition and then 3 h at room temperature, after which it was quenched by the addition of saturated aqueous NH_4Cl. The aqueous layer was separated and extracted with (3 × 25 mL) ether. The combined ether layers were washed with water (25 mL) and then with 5% aqueous $NaHCO_3$ and dried ($MgSO_4$). Evaporation of the ether gave a pale yellow oil which was distilled [Kugelrohr, 78 °C (2 mm)] to give 1.38 g (87%) of the colorless, semisolid ketone **6**. It was >99% pure by GC on column A and had $[\alpha]^{25}_{589}$ +55.73°, $[\alpha]^{25}_{578}$ +58.69° (*c* 3.5); IR (neat) ν 3010, 2900, 2250 (C–D), 1700, 1450, 1170 cm^{-1}; ^1H NMR δ 1.2–2.5 (br m, 11 H), 5.4 (m, 2 H, =CH).

(+)-(1*S*,5*R*)-*endo*-3-(1-Hydroxy-2,2,2-trideuterioethyl)-bicyclo[3.3.1]non-6-ene (7). Ketone **6** from above (1.23 g, 7.37 mmol) in 20 mL of dry ether was added dropwise to stirred slurry of $LiAlH_4$ (0.4 g) in ether (20 mL). The mixutre was heated to reflux following complete addition. After 4 h at reflux, the mixture was cooled and added to 50 mL of a 1:1 mixture of water–10% aqueous H_2SO_4. The aqueous layer was separated and extracted with ether (3 × 25 mL). The combined ether layers were washed with water (25 mL) and then 5% aqueous $NaHCO_3$ and dried ($MgSO_4$). After removal of the solvent by rotary evaporation and Kugelrohr [94 °C (2.5 mm)] distillation, 1.12 g (90%) of alcohol **7** was obtained. It was >99% pure by GC on column A and had the following: $[\alpha]^{25}_{589}$ +107.97°, $[\alpha]^{25}_{578}$ +112.87° (*c* 1.7); IR (neat) ν 3680–3080, 3030, 2920, 2220 (C–D), 1460, 1040 cm^{-1}; ^1H NMR δ 1.0–2.5 (br m, 12 H), 3.3–3.7 (br m, 1 H, OH), 5.2–5.9 (br m, 2 H, =CH).

(+)-(1*S*,3*R*,4*S*)-4(a)-(Trideuteriomethyl)adamantan-2-one (1). Alcohol **7** (1.0 g, 5.9 mmol) from above was heated in formic

---

[32] (a) Prepared according to the method described for 1-propenyllithium; Linstrumelle, G. M. *Org. Synth.* **1976**, *55*, 103–113. (b) The concentration was estimated using the standard method; Whitesides, G. M.; Casey, C. P.; Krieger, J. K. *J. Am. Chem. Soc.* **1971**, *93*, 1379–1389.

acid (88%, 18 mL) at 100 °C. After heating 4 h, the solution was cooled, poured into water (25 mL), and basified with 50% aqueous NaOH. The products were extracted with ether (3 × 25 mL), and the combined ether extracts were washed with water (2 × 25 mL) and dried ($MgSO_4$). Evaporation of the ether gave a mixture of pale yellow liquid formate esters. Hydrolysis was achieved by dissolving the esters in ether (20 mL) and adding the ether solution dropwise to a stirred slurry of $LiAlH_4$ in ether (20 mL). The mixture was heated at reflux for 1 h after complete addition, cooled, and quenched by adding to 50 mL of a 1:1 mixture of water 10% aqueous H_2SO_4. The desired alcohol mixture was obtained by ether extraction, and the alcohol mixture in acetone was oxidized to the corresponding ketones (**1** and **3**) by Jones reagent.[33] Excess oxidant was decomposed by adding 2-propanol. The solution was diluted with ether (25 mL) and neutralized with 5% aqueous $NaHCO_3$. Solids were removed by filtration, and the filtrate was extracted with ether and the ether layer dried ($MgSO_4$) and evaporated to give a pale yellow solid. The solid was sublimed [110 °C (1 atm)] to yield white crystals (820 mg, 83%) of a 1:1 mixture of **1** and **3** (GC, column A). The mixture was separated by preparative GC on column B to give a 41% yield of >99% pure **1**: mp 187–188 °C (sealed capillary); $[\alpha]^{25}_{589}$ +8.53°, $[\alpha]^{25}_{578}$ +9.47°, $[\alpha]^{25}_{436}$ +18.44°, $[\alpha]^{25}_{365}$ +26.13° (*c* 0.75); UV (MI4:1) ϵ_{290} 17, UV (EPA) ϵ_{287} 21; CD (MI4:1) $\Delta\epsilon_{247} = 0$, $\Delta\epsilon_{281} = +0.020$, $\Delta\epsilon_{291} = +0.022$, $\Delta\epsilon_{301} = +0.024$, $\Delta\epsilon_{312.5} = +0.025$, $\Delta\epsilon_{323.5} = +0.014$, $\Delta\epsilon_{339} = 0$; CD (EPA) $\Delta\epsilon_{273} = 0$, $\Delta\epsilon_{288} = -0.023$, $\Delta\epsilon_{296} = -0.039$, $\Delta\epsilon_{305.5} = -0.040$, $\Delta\epsilon_{316} = -0.017$, $\Delta\epsilon_{320} = 0$ (CD run at room temperature and data corrected to 100% ee); IR (CH_2Cl_2) ν 2920, 2860, 2205 (C–D), 1710, 1445, 1055 cm^{-1}; ^1H NMR δ 1.82 (s, 2 H), 2.02 (br m, 8 H), 2.28 (m, 2 H), 2.44 (br m, 1 H); mass spectrum, *m/z* (relative intensity) 167.1391 [$M^{+\cdot}$, calcd for $C_{11}H_{13}D_3O$ 167.1389] (100), 166.1326 (1.5), 121.1004 (11), 97.0969 (37), 79.0551 (26).

(+)-(1*S*,3*R*,4*R*)-4(e)-(Trideuteriomethyl)adamantan-2-one (3). The equatorial CD_3 epimer (**3**) formed above and separated by preparative GC (column B) had the following: mp 163–165 °C (sealed capillary); $[\alpha]^{25}_{589} \simeq 0$, $[\alpha]^{25}_{578} \simeq 0$, $[\alpha]^{25}_{436}$ +9.62°, $[\alpha]^{25}_{365}$ +49.59° (*c* 0.75); UV (MI4:1) ϵ_{293} 19; UV (EPA) ϵ_{290} 22; CD (MI4:1) $\Delta\epsilon_{250} = 0$, $\Delta\epsilon_{287} = +0.344$, $\Delta\epsilon_{296} = +0.484$, $\Delta\epsilon_{305} = +0.554$, $\Delta\epsilon_{316.5} = +0.363$, $\Delta\epsilon_{333} = 0$; CD (EPA) $\Delta\epsilon_{252} = 0$, $\Delta\epsilon_{294.5} = +0.651$, $\Delta\epsilon_{304} = +0.636$, $\Delta\epsilon_{316} = +0.296$, $\Delta\epsilon_{330} = 0$ (CD run at room temperature and data corrected to 100% ee); IR (CH_2Cl_2) ν 2930, 2870, 2220 (C–D), 1710, 1450, 1040, cm^{-1}; ^1H NMR δ 1.72 (s, 3 H), 1.98 (m, 7 H), 2.24 (d, 2 H), 2.52 (s, 1 H); mass spectrum, *m/z* (relative intensity) 167.1391 ($M^{+\cdot}$, calcd for $C_{11}H_{13}D_3O$ 167.1389,100), 121.1010 (22), 97.0969 (70), 96.0894 (69), 79.0546 (49), 71.0817 (11) 67.0557 (12).

(+)-(1*S*,5*R*,3*R*)-*endo*-3-Bicyclo[3.3.1]non-6-enyl Methyl Ketone (8).[34] This ketone was prepared exactly as in the preparation of **6**, using a sample of the same acid (**5**; 1.0 g, 6.02 mmol), with precisely the same rotation values but with the ethereal CH_3Li (1.52 M, 5 mL, 7.6 mmol) in place of CD_3Li. The final product **8** [bp 78 °C (2 mm)] [lit.[34] bp 70–73 °C [0.5 mm)] was >99% pure by GC on column A and had the following: $[\alpha]^{25}_{589}$ +63.01°, $[\alpha]^{25}_{578}$ +64.97 (*c* 1.1); IR (neat) ν 3040, 1710, 1350 cm^{-1}; ^1H NMR δ 1.2–2.7 (br m, 11 H), 2.0 (s, 3 H, CH_3), 5.2–5.7 (m, 2 H, =CH).

(+)-(1*S*,5*R*,3*R*)-*endo*-3-(1-Hydroxyethyl)bicyclo[3.3.1]non-6-ene (9). This alcohol was prepared from **8** (above) exactly as in the preparation of **7**. It was >99% pure by GC on column A and had the following: $[\alpha]^{25}_{589}$ +115.7°, $[\alpha]^{25}_{578}$ +121.8° (*c* 0.99); IR (neat) ν 3600–3200, 3025 cm^{-1}; ^1H NMR δ 0.9–2.5 (br m, 11 H), 1.0 (d, 3 H, *J* = 6 Hz, CH_3), 3.4 (br, 1 H, OH), 5.51–5.9 (br t, 2 H, =CH).

Anal. Calcd for $C_{11}H_{18}O$ (166): C, 79.46; H, 10.91. Found: C, 79.20; H, 10.77.

(+)-(1*S*,3*R*,4*S*)-4(a)-Methyladamantan-2-one (2).[18,21] The axial CH_3 ketone (**2**) was prepared from **9** (above) as a mixture with the equatorial CH_3 epimer (**4**) exactly as in the synthesis of **1** and **3**. It was separated by preparative GC on column B to give a 41% yield of **2** and a 41% yield of **4**. The axial methyl epimer (**2**) had the following: mp 187–189 °C (sealed capillary) (lit.[21] mp 185–187 °C); $[\alpha]^{25}_{589}$ +10.11°, $[\alpha]^{25}_{578}$ +10.62°, $[\alpha]^{25}_{436}$ +20.29, $[\alpha]^{25}_{365}$ +30.15 (*c* 0.68); UV (MI4:1) ϵ_{290} 17; UV (EPA) ϵ_{287} 21; CD (MI4:1) $\Delta\epsilon_{250} = 0$, $\Delta\epsilon_{281.5} = +0.020$, $\Delta\epsilon_{291} = +0.022$, $\Delta\epsilon_{301} = +0.023$, $\Delta\epsilon_{312.5} = +0.025$, $\Delta\epsilon_{323.5} = +0.013$, $\Delta\epsilon_{339} = 0$; CD (EPA) $\Delta\epsilon_{272} = 0$, $\Delta\epsilon_{288} = -0.026$, $\Delta\epsilon_{296.5} = -0.045$, $\Delta\epsilon_{305.5} = -0.046$, $\Delta\epsilon_{316} = -0.019$, $\Delta\epsilon_{321} = 0$ (CD run at room temperature and data corrected to 100% ee); IR (CCl_4) ν 2920, 2860, 1715, 1065 cm^{-1}; ^1H NMR δ 0.95 (d, 3 H, *J* = 7 Hz, CH_3), 1.6–2.55 (br m, 13 H).

(+)-(1*S*,3*R*,4*R*)-4(e)-Methyladamantan-2-one (4).[19-21] The equatorial methyl epimer (**4**) formed and separated above by preparative GC had the following: mp 165–167 °C (sealed capillary); $[a]^{25}_{589} \simeq 0°$, $[\alpha]^{25}_{578} \simeq 0°$, $[\alpha]^{25}_{436}$ +11.19°, $[\alpha]^{25}_{365}$ +54.29° (*c* 0.97); UV (MI4:1) ϵ_{293} 19; UV (EPA) ϵ_{290} 22; CD (MI4:1) $\Delta\epsilon_{252} = 0$, $\Delta\epsilon_{287} = +0.393$, $\Delta\epsilon_{295.5} = +0.479$, $\Delta\epsilon_{305} = +0.544$, $\Delta\epsilon_{316.5} = +0.362$, $\Delta\epsilon_{332} = 0$; CD (EPA) $\Delta\epsilon_{242} = 0$, $\Delta\epsilon_{294.5} = +0.671$, $\Delta\epsilon_{303} = +0.643$, $\Delta\epsilon_{310} = +0.306$, $\Delta\epsilon_{332} = 0$ (CD data run at room temperature and data corrected to 100% ee); IR ($CHCl_3$) ν 2920, 2860, 1710, 1055 cm^{-1}; ^1H NMR δ 1.07 (d, 3 H, *J* = 7 Hz, CH_3), 1.4–2.47 (br m, 13 H).

Acknowledgment. We thank the National Science Foundation for support of this work. We also thank Professor T. D. Bouman, Southern Illinois University, Edwardsville, for stimulating discussions on this work and for carrying out the CNDO/S calculation on the various methyl rotamers of **2**.

Registry No. **1**, 79815-97-7; **2**, 19301-60-1; **3**, 79854-62-9; **4**, 79854-63-0; **5**, 64937-51-5; **6**, 79815-98-8; **7**, 79815-99-9; **8**, 79854-64-1; **9**, 79816-00-5.

---

[33] Eisenbraun, E. J. "Organic Syntheses", Collect. Vol. 5; Wiley: New York, 1973; pp 310–314.

[34] Murray, R. K., Jr.; Goff, D. L. *J. Org. Chem.* **1978**, *43*, 3844–3848.