(20) A. C. Larson, *Acta Crystallogr., Sect. A*, **23**, 664 (1967).
(21) D. T. Cromer and D. Liberman, *J. Chem. Phys.*, **53**, 1891 (1970).
(22) "International Tables for X-Ray Crystallography," Vol. III, Kynoch Press, Birmingham, England, p 202.
(23) R. F. Stewart, E. R. Davidson, and W. T. Simpson, *J. Chem. Phys.*, *42*, 3175 (1965).
(24) R. L. Shriner and R. C. Fuson, "The Systematic Identification of Organic Compounds", Wiley, New York, N.Y., 1935.

Syntheses and Chiroptical Properties of (+)-2-Brendanone and Its Analogues[1]

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Syntheses of (+)-2-brendanone (**12**), (+)-2-norbrendanone (**14**), and (−)-2-isobrendanone (**16**) from the respective optically active bicyclic intermediates (**38**, **37**, and **54**) with known absolute configurations establish their absolute configurations. As the lowest homologue of 2-brendanone, (+)-tricyclo[2.2.2.$0^{2,6}$]octan-3-one (**18**) was prepared by the oxidative decarboxylation of (−)-*endo*-5-bicyclo[2.2.2]octene-2-carboxylic acid (**43**). Absolute rotations and chiroptical properties of these 2-brendanone analogues are discussed.

Simultaneous bridging C-2 to C-5 and C-3 to C-6 positions of cyclohexane with short carbon chains ($m,n \leq 2$) freezes the cyclohexane moiety in a twist-boat conformation (Chart I) to yield the rigid tricyclic hydrocarbons (**1**) which have D_2 symmetry when $m = n = 2$, C_2 symmetry when $m \neq n$, and D_{2d} symmetry when $m = n = 1$. (−)-Twistane (**3**) (D_2 symmetry)[2] and (−)-*twist*-brendane (**5**) (C_2 symmetry)[3] can be cited as the typical representatives of these gyrochiral[4] cage-shaped hydrocarbons whose syntheses and absolute configurations have been reported from our laboratory. Starting from cyclohexanone, the same diagonal C-2 to C-5 and C-3 to C-6 bridgings afford tricyclic ketones with lower symmetries, among which (−)-2-twistanone (**4**) (C_2 symmetry),[2] (−)-2-*twist*-brendanone (**6**) (C_1 symmetry),[3] and (−)-2-bis(noradamantanone) (**8**) (C_2 symmetry)[5] have been synthesized with known absolute configurations. In contrast with these doubly diagonal bridging, simultaneous C-2 to C-4 and C-3 to C-6 bridgings (Chart II) fix the cyclohexane ring in a boat conformation giving achiral tricyclic hydrocarbons (**9**) all belonging to the C_s point group as can be seen in brendane (**11**),[6] norbrendane (**13**),[7] isobrendane (**15**),[7] and tricyclo[2.2.2.$0^{2,6}$]octane (**17**).[9] Introduction of carbonyl group breaks the bilateral symmetry inherent to these brendane analogue cage-shaped hydrocarbons to provide the tricyclic ketones **12**, **14**, **16**, and **18** with cyclohexanone moieties frozen in a boat conformation. Natural extention of our current interest in syntheses and chiroptical properties[10] as well as microbial stereodifferentiating reduction[11] of the cage-shaped tricyclic ketones led us to investigate the preparation of these types of tricyclic ketones in optically active modification from the intermediates with known absolute configurations.

Chart I

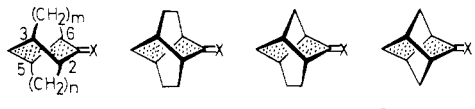
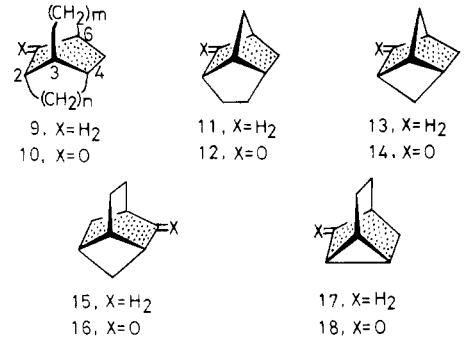


Chart II



Results and Discussion

Since previous synthetic routes for both 2-brendanone (**12**)[6] and 2-norbrendanone (**14**)[8] appeared inconvenient either for obtaining them in optically active modification or for correlating them with the intermediates with known absolute configurations, we designed the sequence of steps encompassed in Scheme I in which the bicyclic endo-keto ester (**27**) is a strategic intermediate which correlates (−)-(1*S*,2*S*,4*S*)-*endo*-5-bicyclo[2.2.1]heptene-2-carboxylic acid (**19**) with the bicyclic keto mesylates **37** and **38** whose intramolecular alkylation should lead to optically active 2-brendanone (**12**) and 2-norbrendanone (**14**), respectively.

Preparation of (−)-(1*S*,2*S*,4*S*)-*endo*-2-Carbomethoxybicyclo[2.2.1]heptan-5-one (27) (Scheme I). Spurlock's procedure[12] reported for the racemic compounds was applied with a slight modification to the conversion of the (−)-unsaturated carboxylic acid (**19**) into the optically active keto ester (**27**). A mixture of the hydroxy esters **21** obtained by hydroboration–oxidation of (−)-(1*S*,2*S*,4*S*)-*endo*-2-carbomethoxybicyclo[2.2.1]hept-5-ene (**20**), $[\alpha]^{16}_{D}$ −91.1° (optical purity 67%),[13] was treated with Jones' reagent to afford a 2:3 mixture of 5- and 6-keto esters **22** whose sodium borohydride reduction gave a mixture of 5- and 6-*endo*-hydroxy esters **23**. Separation of these regioisomers was carried out by saponification of the mixture of methyl esters followed by acidification which, while converting the 6-endo isomer into the (−)-lactone (**24**), mp 153.5–155 °C, $[\alpha]D^{15}_{D}$ −2.8° (EtOH), left the 5-endo isomer as the free 5-*endo*-hydroxycarboxylic acid (**25**). The separated hydroxy acid **25** was converted into methyl ester **26** whose Corey's oxidation yielded (−)-(1*S*,2*S*,4*S*)-keto ester **27**, $[\alpha]^{15}_{D}$ −21.3° (EtOH).

Synthesis of (+)-2-Norbrendanone (14) [(+)-Tricyclo[3.2.1.$0^{3,6}$]octan-2-one] (Scheme I). Continuation of the synthesis would involve (1) modification of the carboxyl group to give the keto mesylate (**37**) and (2) its intramolecular al-

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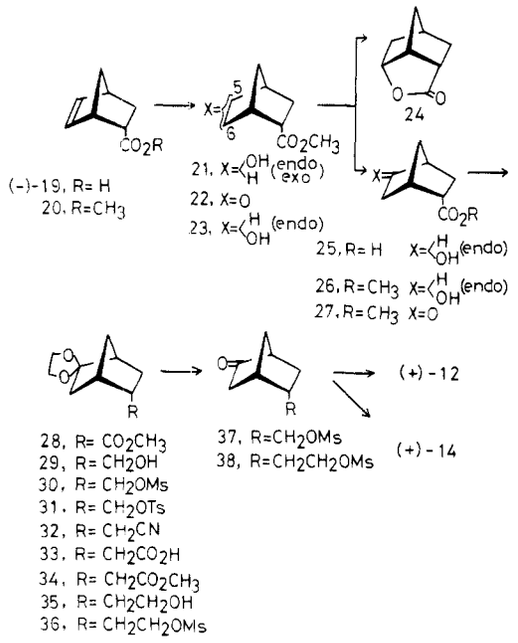
Scheme I



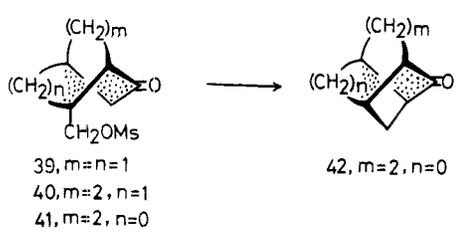
kylation. After protection of the ketone group by ketalization, the resulting ketal ester (**28**) was reduced with $LiAlH_4$ to give the alcohol (**29**) which was then treated with mesyl chloride with pyridine to give the mesylate (**30**). Acidic hydrolysis of **30** removed the protective group to yield the keto mesylate (**37**) which was cyclized by heating with sodium hydride in dimethylformamide. Chromatography followed by sublimation of the cyclization product gave a 40% yield of (+)-2-norbrendanone (**14**): mp 126.5–128 °C; $[\alpha]^{16}_D$ +82.6° (EtOH) (racemic modification, mp 126–127 °C).[8]

Synthesis of (+)-2-Brendanone (12) [(+)-Tricyclo[4.2.1.0^{3,7}]nonan-2-one] (Scheme I). Homologation of the alcohol (**29**) was carried out rather straightforwardly via the following sequence of intermediates: the tosylate (**31**), the cyanide (**32**), the carboxylic acid (**33**), and the methyl ester (**34**). Lithium aluminum hydride reduction of the methyl ester (**34**) provided the homologous alcohol (**35**) which was converted into the mesylate (**36**). After the protective group was removed by acidic hydrolysis, the resulting mesylate (**38**) was heated with sodium hydride in dimethylformamide to afford (+)-2-brendanone (**12**) (36% yield): mp 116.5–118 °C; $[\alpha]^{16}_D$ +31.3° (EtOH) (racemic modification, mp 118.5–119.5 °C).[6]

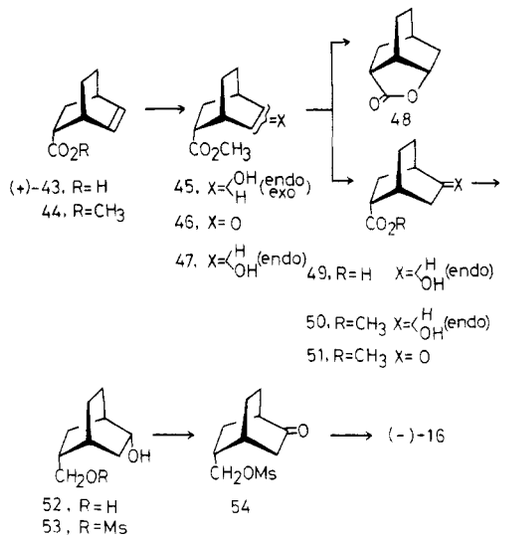
It may be relevant to note here that similar attempted intramolecular diagonal alkylations have failed with compounds **39** and **40**[14] (Chart III), and a single example so far successful for this kind of conversion can be found in the cyclization of **41** into **42** with a 3.5% yield.[4]

Synthesis of (−)-2-Isobrendanone (16) [(−)-Tricyclo[3.3.1.0^{3,6}]nonan-2-one] (Scheme II). As Scheme II illustrates, the sequence of steps from (+)-(1*R*,2*R*,4*R*)-*endo*-5-bicyclo[2.2.2]octene-2-[carboxylic acid (**43**), $[\alpha]^{19}_D$ +48.2° (optical purity 95%),[2b] to (−)-2-isobrendanone (**16**) involving intramolecular alkylation of the keto mesylate (**54**)

Chart III



Scheme II



was almost parallel to the one described for the synthesis of (+)-2-norbrendanone (**14**) (Scheme I). Hydroboration–oxidation converted the (+)-unsaturated ester (**44**), $[\alpha]^{14}_D$ +46.9° (EtOH), into a mixture of endo and exo alcohols (**45**) whose Jones' oxidation afforded a 1:1 mixture of 5- and 6-oxo carboxylates (**46**) which was reduced with sodium borohydride to yield a mixture of 5- and 6-endo alcohols (**47**). Alkaline hydrolysis of the mixture of the methyl esters (**47**) followed by acidification preferentially lactonized the resulting 6-endo alcohol to afford the lactone (**48**), mp 202–203.5 °C, $[\alpha]^{16}_D$ +8.4° (EtOH), while leaving the 5-endo alcohol as the free carboxylic acid (**49**), whose esterification followed by Jones' oxidation provided the (−)-keto ester (**51**). Lithium aluminum hydride reduction of **51** led to the formation of the diol (**52**) which was treated with 1 equiv of mesyl chloride in pyridine to afford the monomesylate (**53**). Chromic acid oxidation of **53** followed by intramolecular alkylation of the resulting keto mesylate (**54**) with sodium hydride in dimethylformamide gave a 39% yield of (−)-2-isobrendanone (**16**): mp 146–149 °C, $[\alpha]^{13}_D$ −199° (EtOH).

Synthesis of (+)-Tricyclo[2.2.2.0^{2,6}]octan-3-one (18) (Scheme III). Upon lead tetraacetate decarboxylation of racemic *exo*-5-bicyclo[2.2.2]octene-2-carboxylic acid (**55**), LeBel[9] observed the formation of a 20:53 mixture of racemic acetates **58** and **61** with a minor amount of racemic *axial*-

Scheme III

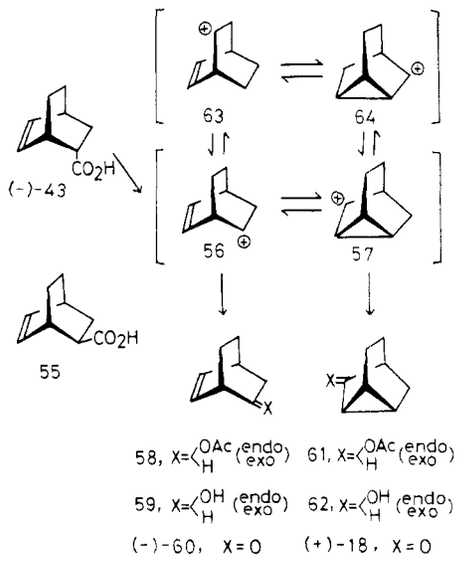


Table I. Absolute Configurations and Absolute Rotations of (+)-2-Brendanone (12), (+)-2-Norbrendanone (14), (−)-2-Isobrendanone (16), and (+)-Tricyclo[2.2.2.0^{3,6}]octan-3-one (18)

	registry no.	absolute configuration	absolute rotation
(+)-12	68069-46-5	(+)-(1*R*,3*S*,6*S*,7*R*)-tricyclo[4.2.1.0^{3,7}]nonan-2-one	$[\alpha]_D$ +46.7°[a]
(+)-14	68069-47-6	(+)-(1*R*,3*S*,5*S*,6*R*)-tricyclo[3.2.1.0^{3,6}]octan-2-one	$[\alpha]_D$ +123°[a]
(−)-16	68024-12-4	(−)-(1*R*,3*R*,5*S*,6*S*)-tricyclo[3.3.1.0^{3,6}]nonan-2-one	$[\alpha]_D$ −210°[a]
(+)-18	68069-48-7	(+)-(1*R*,2*R*,4*S*,6*S*)-tricyclo[2.2.2.0^{2,6}]octan-3-one	$[\alpha]_D$ +188°[b,c]

[a] In EtOH. [b] In $CHCl_3$. [c] Calculated on assuming the same degree of skeletal inversion from (−)-**43** to **58** and **61**.

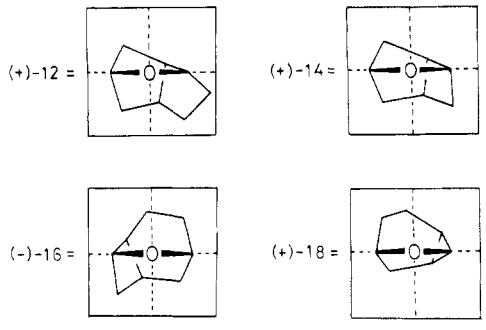
Table II. CD Spectra of (+)-2-Brendanone (12), (+)-2-Norbrendanone (14), (−)-2-Isobrendanone (16), and (+)-Tricyclo[2.2.2.0^{2,6}]octan-3-one (18) (in Isooctane)

(+)-12		(+)-14	
[θ]	nm	[θ]	nm
+4.13 × 10^3	296 (sh)	+3.90 × 10^3	284 (sh)
+5.25 × 10^3	306	+5.73 × 10^3	294
+4.00 × 10^3	316 (sh)	+6.19 × 10^3	303
		+3.90 × 10^3	315 (sh)
(−)-16		**(+)-18**	
[θ]	nm	[θ]	nm
−9.61 × 10^3	292	+2.41 × 10^4	287
−9.00 × 10^3	298.5 (sh)	+2.49 × 10^4	291.5
−4.43 × 10^3	312 (sh)	+2.55 × 10^4	296
		+1.36 × 10^4	306.5

bicyclo[3.2.1]oct-3-en-2-yl acetate. He also noted that the same oxidative decarboxylation of a mixture (82:18) of racemic endo-unsaturated carboxylic acid (**43**) and exo-unsaturated carboxylic acid (**55**) afforded a nearly identical mixture of products. Since this oxidative decarboxylation apparently involves cationic species **56** and **57** as intermediates, this process can correlate the absolute configurations of acetates **58** and **61** with that of the optically active endo-unsaturated carboxylic acid (**43**). Refluxing of a benzene solution of (−)-(1*S*,2*S*,4*S*)-*endo*-5-bicyclo[2.2.2]octene-2-carboxylic acid (**43**), $[\alpha]^{25}_D$ −14.5° (optical purity 29%), with lead tetraacetate and pyridine for 7 h gave a mixture of acetates **58** and **61** which was treated with $LiAlH_4$ to afford a mixture of alcohols **59** and **62**. Column chromatography of a mixture of ketones **60** and **18**, obtained by Collins' oxidation of the mixture of alcohols **59** and **62**, separated two ketones yielding (−)-bicyclo[2.2.2]-oct-5-en-2-one (**60**), mp 89–91 °C, $[\alpha]^{25}_D$ −70.1° ($CHCl_3$) (8.5% yield), and the tricyclic ketone (**18**),[15] bp 110–115 °C (35 mm), $[\alpha]^{27}_D$ +26.3° ($CHCl_3$) (23% yield). Although the levo-rotation of **60** and (+) Cotton effect (vide infra) exhibited by the tricyclic ketone (**18**) respectively support their absolute configurations, a rather low degree of configurational retention observed in the conversion of (−)-**43** into the acetates (**58**) will require a comment. Goering[16] gave $[\alpha]_D$ ±497° for the absolute rotation of the unsaturated bicyclic ketone (**60**) which indicates 14% optical purity for our ketone (**60**). Comparing this value with 29% optical purity of the starting (−)-unsaturated carboxylic acid (**43**), we can conclude that nearly 50% skeletal inversion had occurred during this oxidative decarboxylation. We are presently explaining this phenomena by assuming the intervention of enantiomeric cations (**63** and **64** presumably formed from their parent cations by 6,2-hydride shift.

Chiroptical Properties. Table I shows the IUPAC names together with the Cahn–Ingold–Prelog absolute configuration notations for the optically active 2-brendanone and its analogues whose preparations are reported in this paper. Purification of the final products as well as their intermediates was carried out only by distillation or sublimation. This with known optical purities of their starting materials permits us to calculate their absolute rotations listed in Table I. The value for (+)-**18**, $[\alpha]_D$ +188°, was obtained by assuming that the same degree of skeletal inversion would have occurred in the transformation of the (−)-*endo*-carboxylic acid (**43**) into acetates **58** and **61**. Analyses of the circular dichroism (CD) spectra exhibited by the various tricyclic ketones with known absolute configurations so far prepared in our laboratory indicated that the sign of the CD curve due to n–π* transition can be predicted by applying the octant rule to the "outer ring".[10,17] An inspection of the octant projections of (+)-2-brendanone (**12**), (+)-2-norbrendanone (**14**), (−)-2-isobrendanone (**16**), and (+)-**18** illustrated in Chart IV predicts the (+)-Cotton effects for (+)-**12**, (+)-**14**, and (+)-**18** whereas the (−)-Cotton effect for (−)-**16**. This conclusion is supported by their CD spectra tabulated in Table II in which their experimental [θ] values are corrected to 100% optical purity according to their known optical purities except for (+)-**18** whose optical purity was assumed on some analogy (vide supra). The above results emphasize that the octant rule holds also for the 2-brendanone analogues of compounds with tricyclic cage-shaped structure.

Chart IV



Experimental Section

Infrared spectral data were obtained from a Hitachi EPI-S2 spectrophotometer. Nuclear magnetic resonance spectra were obtained from a JNM-MH-100 spectrometer. Ultraviolet spectra were recorded on a Beckman DB spectrometer. Optical rotations were measured with a JASCO-DPI-SL automatic polarimeter. Circular dichroism data were measured on a JASCO-J-40 spectropolarimeter. Elemental analyses were performed on a Yanagimoto CHN-Corder type II. All melting points and boiling points are uncorrected.

(−)-*endo*-5-Bicyclo[2.2.1]heptene-2-carboxylic Acid (19). The carboxylic acid **19** was prepared by the same method previously reported:[3] bp 126–130 °C (8 mm); $[\alpha]^{16}_D$ −96.7° (*c* 0.608, EtOH) (67% optical purity).[13]

Anal. Calcd for $C_8H_{10}O_2$: C, 69.54; H, 7.30. Found: C, 69.44; H, 7.40.

(−)-Methyl *endo*-5-Bicyclo[2.2.1]heptene-2-carboxylate (20). (−)-Carboxylic acid to **19**, $[\alpha]^{16}_D$ −96.7° (16.5 g, 0.119 mol), was esterified with an ethereal solution of CH_2N_2 to afford 16.0 g of **20** (88% yield): bp 125–129 °C (96 mm); $[\alpha]^{16}_D$ −91.1° (*c* 0.530, EtOH).

Anal. Calcd for $C_9H_{12}O_2$: C, 71.02; H, 7.95. Found: C, 70.95; H, 7.99.

Methyl *exo*-5(6)-Hydroxy-*endo*-bicyclo[2.2.1]heptene-2-carboxylate (21).

A solution of (−)-**20**, $[\alpha]^{16}_D$ −91.1° (15.9 g, 0.105 mol), in 40 mL of THF was cooled to 0 °C. Diborane, generated by addition of a solution of sodium borohydride (4.0 g, 0.105 mol) in diglyme (100 mL) to a

solution of boron trifluoride etherate (26.4 mL, 0.209 mol) in diglyme (23 mL), was passed into the olefin–THF solution (maintained at 20 °C) by applying a slight flow of dry nitrogen through the generator. After generation of diborane ceased, the excess hydride in the reaction mixture was decomposed by an addition of water. To the mixture was added 3 N NaOH solution (12 mL) and then 30% hydrogen peroxide (14 mL). The reaction mixture was stirred for an additional 1 h at 30–50 °C and saturated NaCl solution was added to the mixture. The organic phase was separated and the aqueous phase was extracted with ether. The combined extracts were washed with water, dried ($MgSO_4$), and condensed. The residue was distilled to give 13.9 g of **21** (78% yield): bp 125–132 °C (8 mm); $[\alpha]^{13}_D$ +4.6° (*c* 0.724, EtOH); IR (neat film) 3400, 1307, 1200, 1080, 1036, 1000 cm^{-1}.

Methyl 5(6)-Oxo-*endo*-bicyclo[2.2.1]heptene-2-carboxylate (22). To a solution of **21**, $[\alpha]^{13}_D$ +4.6° (13.9 g, 0.0818 mol), in acetone (200 mL) was added an excess of Jones' reagent[18] with ice cooling and the mixture was stirred for 2 h at 0–5 °C. After addition of water, the mixture was extracted with ether. The extract was washed with saturated $NaHCO_3$ solution and water, dried ($MgSO_4$), and concentrated. Distillation of the residue gave 8.50 g of **22** (62% yield): bp 120–124 °C (8 mm); $[\alpha]^{15}_D$ −18.0° (*c* 0.524, EtOH); IR (neat film) 1735, 1270, 1200, 1150, 1076, 1028, 877 cm^{-1}; NMR (CCl_4) δ 3.59 and 3.64 (3:2 ratio; $-OCOCH_3$).

(−)-Methyl 5-Oxo-*endo*-bicyclo[2.2.1]heptane-2-carboxylate (27). To a solution of **22**, $[\alpha]^{15}_D$ −18.0° (8.42 g, 0.0501 mol), in methanol (160 mL) was added slowly sodium borohydride (1.90 g, 0.0500 mol) with ice cooling and the mixture was stirred for 4.5 h at room temperature. After most of the methanol was removed under reduced pressure, a solution of NaOH (4.0 g) in water (45 mL) was added to the residue. After being stirred for 2 h at room temperature, the alkaline solution was cooled in an ice-bath, acidified with 6 N HCl, and then kept for 2 days at room temperature. The acidic mixture was then made weakly basic with saturated $NaHCO_3$ solution. Continuous extraction of the solution with ether gave a white solid, which was sublimed at 100–110 °C (7 mm) to yield 1.93 g of (−)-**24**: mp 153.5–155 °C (racemic modification; mp 155–156 °C);[12] $[\alpha]^{15}_D$ −2.8° (*c* 0.613, EtOH); IR (KBr) 1765, 1188, 1167, 1091, 1043, 1000, 983 cm^{-1}.

Anal. Calcd for $C_8H_{10}O_2$: C, 69.54; H, 7.30. Found: C, 69.49; H, 7.21.

The alkaline solution which was acidified to pH 2 with HCl was continuously extracted with ether to give 3.20 g of **25**, which was esterified with CH_2N_2 to yield 3.11 g of **26**. A methylene chloride solution (10 mL) of **26** (3.11 g, 0.0183 mol) was added to a stirred suspension of pyridinium chlorochromate[19] (6.0 g, 0.0280 mol) in dry methylene chloride (40 mL), and the stirring was kept up for 2 h at room temperature. The organic phase was separated and the residue was rinsed with ether. The combined organic solutions were chromaographed on Florisil, and elution with ether gave 2.85 g of **27**, which was distilled to yield 2.71 g of **27**: bp 113–117 °C (7 mm); $[\alpha]^{15}_D$ −21.3° (*c* 0.514, EtOH); IR (neat film) 1735, 1270, 1200, 1028 cm^{-1}; NMR (CCl_4) δ 1.7–2.1 (m, 6 H), 2.4–2.6 (br s, 1 H), 2.8–3.0 (m, 2 H), 3.64 (s, 3 H).

Anal. Calcd for $C_9H_{12}O_3$: C, 64.27; H, 7.19. Found: C, 63.92; H, 7.26.

(−)-Methyl 5,5-Ethylenedioxy-*endo*-bicyclo[2.2.1]heptane-2-carboxylate (28). A mixture of (−)-**27**, $[\alpha]^{15}_D$ −21.3° (2.63 g, 0.0156 mol), ethylene glycol (2.0 mol), *p*-toluenesulfonic acid (20 mg), and benzene (80 mL) was heated until the benzene–water azeotrope ceased to distil. After cooling to room temperature, the reaction mixture was washed with saturated $NaHCO_3$ solution and water, dried ($MgSO_4$), and concentrated. Distillation of the residue gave 3.16 g of **28** (95% yield): bp 108–110 °C (6 mm); $[\alpha]^{16}_D$ −24.9° (*c* 0.566, EtOH); IR (neat film) 1730, 1200, 1175, 1100, 1030, 855 cm^{-1}.

Anal. Calcd for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60. Found: C, 61.90; H, 7.65.

(−)-5,5-Ethylenedioxy-*endo*-2-hydroxymethylbicyclo-[2.2.1]heptane (29). A solution of **28** $[\alpha]^{16}_D$ −24.9° (3.12 g, 0.0147 mol), in dry ether (15 mL) was added to a suspension of $LiAlH_4$ (0.62 g, 0.0155 mol) in dry ether (30 mL) and the mixture was refluxed for 3 h. After cooling with ice, saturated ammonium chloride solution was added to the chilled mixture. An inorganic solid was filtered off and rinsed with ether. Combined ether solutions were washed with water, dried ($MgSO_4$), and concentrated. Distillation gave 2.56 g of **29** (95% yield): bp 124–130 °C (6 mm); $[\alpha]^{15}_D$ −13.5° (*c* 0.462, EtOH); IR (neat film) 3400, 1180, 1100, 1060, 1020, 853 cm^{-1}.

Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 64.90; H, 8.69.

(5-Oxo-*endo*-2-bicyclo[2.2.1]heptyl)methyl Methanesulfonate (37). To a solution of **29**, $[\alpha]^{15}_D$ −13.5° (0.79 g, 4.29 mmol), in pyridine (3 mL) was added methanesulfonyl chloride (1.00 g, 8.77 mmol) at −5 to −10 °C and the mixture was stirred for 2.5 h at this temperature. After being stirred overnight at room temperature, the reaction mixture was poured onto ice and made acidic with HCl and was extracted with $CHCl_3$. The extract was washed with saturated $NaHCO_3$ solution and water and dried ($MgSO_4$). Evaporation of the solvent gave 1.16 g of **30**, to which was added 5% sulfuric acid (30 mL). After being stirred for 2 days at room temperature, the reaction mixture was extracted with $CHCl_3$. The extract was washed with saturated $NaHCO_3$ solution and water, dried ($MgSO_4$), and concentrated to give 0.85 g of **37** (91% yield) as a pale yellow oil: IR (neat film) 1738, 1350, 1175, 955 cm^{-1}.

(+)-2-Norbrendanone [(+)-Tricyclo[3.2.1.$0^{3,6}$]octan-2-one] (14). A solution of **37** (0.85 g, 3.90 mmol) in *N,N*-dimethylformamide (DMF) (10 mL) was added to a suspension of sodium hydride (0.40 g, 0.0167 mol) in DMF (10 mL) and the mixture was stirred for 11 h at 60 °C under a nitrogen atmosphere. After addition of a few drops of methanol, the reaction mixture was poured onto ice and extracted with ether. The extract was washed with diluted HCl, saturated $NaHCO_3$ solution, and water, dried ($MgSO_4$), and concentrated. The residue was chromatographed on neutral alumina (Woelm, activity II). Eluate with pentane–ether (9:1 v/v) was sublimed at 60–70 °C (30 mm) to give 196 mg of **14** (40% yield): mp 126.5–128 °C (in a sealed tube) (racemic modification, mp 126–127 °C);[8] $[\alpha]^{16}_D$ +82.6° (*c* 0.540, EtOH); IR (Nujol) 1750, 1159, 1049, 957 cm^{-1}; NMR ($CDCl_3$) δ 1.18–1.80 (m, 3 H), 1.8–2.1 (m, 2 H), 2.1–2.9 (m, 4 H), 3.1–3.4 (m, 1 H); UV $\lambda_{max}^{isooctane}$ 280 nm (sh) (ε 15), 294 (19), 304 (sh) (18), 316 (sh) (11); MS *m/e* 122 (M^+).

Anal. Calcd for $C_8H_{10}O$: C, 78.65; H, 8.25. Found: C, 78.18; H, 8.22.

(−)-5,5-Ethylenedioxy-*endo*-2-cyanomethylbicyclo[2.2.1]-heptane (32). To a solution of **29**, $[\alpha]^{15}_D$ −13.5° (1.77 g, 9.61 mmol), in pyridine (4 mL) was added *p*-toluenesulfonyl chloride (3.70 g, 19.5 mmol) and the mixture was stirred for 4 h at −5 to −10 °C. After standing overnight at room temperature, the reaction mixture was poured onto ice and made acidic with HCl. It was extracted with $CHCl_3$ and the extract was washed with saturated $NaHCO_3$ solution and water, dried ($MgSO_4$), and concentrated to give 3.24 g of the tosylate **31**, which was dissolved in DMF (2 mL). To the solution was added sodium cyanide (1.30 g, 26.5 mmol) and the mixture was stirred for 11 h at 120 °C. After an inorganic solid was filtered off, the filtrate was concentrated in vacuo. The residue was diluted with water and extracted with ether. The extract was washed with diluted HCl, saturated $NaHCO_3$ solution, and water, dried ($MgSO_4$), and concentrated. The residue was distilled to give 1.52 g of **32** (82% yield): bp 133–136 °C (6 mm); $[\alpha]^{15}_D$ −20.9° (*c* 0.510, EtOH); IR (neat film) 2300, 1180, 1100, 1050, 1016, 853 cm^{-1}.

Anal. Calcd for $C_{11}H_{15}O_2N$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.04; H, 7.82; N, 7.29.

(−)-Methyl (5,5-Ethylenedioxy-*endo*-2-bicyclo[2.2.1]-heptyl)acetate (34). A mixture of (−)-**32**, $[\alpha]^{15}_D$ −20.9° (1.48 g, 7.66 mmol), KOH (1.20 g, 21.4 mmol), and ethylene glycol (13 mL) was heated for 4.5 h at 150–160 °C. The reaction mixture was diluted with ice-water and washed with ether to remove neutral substances. After being made acidic with HCl, the mixture was extracted with ether. Washing with water and drying ($MgSO_4$) followed by condensation gave 1.39 g of **33**, which was esterified with CH_2N_2 without further purification. Distillation of the crude product gave 1.27 g of **34** (73% yield): bp 112–115 °C (6 mm); $[\alpha]^{15}_D$ −6.0° (*c* 0.493, EtOH); IR (neat film) 1733, 1172, 1100, 1018, 851 cm^{-1}.

Anal. Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found: C, 63.45; H, 8.22.

(+)-2-(5,5-Ethylenedioxy-*endo*-2-bicyclo[2.2.1]heptyl)ethanol (35). Reduction of **34**, $[\alpha]^{15}_D$ −6.0° (1.24 g, 5.48 mmol), with $LiAlH_4$ was carried out as described for the preparation of **29**. The crude product was distilled to give 1.06 g of **35** (97% yield): bp 136–140 °C (6 mm); $[\alpha]^{15}_D$ +3.5° (*c* 0.450, EtOH); IR (neat film) 3400, 1100, 1070, 1015, 852 cm^{-1}.

Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.25; H, 9.34.

2-(5-Oxo-*endo*-2-bicyclo[2.2.1]heptyl)ethyl Methanesulfonate (38). Treatment of **35**, $[\alpha]^{15}_D$ +3.5° (1.02 g, 5.14 mmol), with methanesulfonyl chloride (1.20 g, 10.5 mmol) followed by hydrolysis as described for the preparation of **37** gave 1.15 g of **38** (88% yield), which was converted into **12** without further purification (vide infra): IR (neat film) 1735, 1350, 1175, 975, 945 cm^{-1}.

(+)-2-Brendanone [(+)-Tricyclo[4.2.1.$0^{3,7}$]nonan-2-one] (12). Intramolecular alkylation of **38** (1.05 g, 4.53 mmol) was carried out by the same procedure described for the preparation of **14**. The crude product was chromatographed on neutral alumina (Woelm, activity II), and elution with pentane–ether (9:1 v/v) gave a white solid, which was sublimed at 60–70 °C (30 mm) to afford 224 mg of **12** (36% yield): mp 116.5–118 °C (in a sealed tube) (racemic modification, mp

118.5–119.5 °C);[6] $[\alpha]^{16}_D$ +31.3° (*c* 0.457, EtOH); IR (Nujol) 1745, 1168, 1022, 901 cm^{-1}; UV $\lambda_{max}^{isooctane}$ 282 nm (sh) (ϵ 16), 272 (22), 307 (sh) (21), 318 (sh), (13); MS *m/e* 136 (M^+).

Anal. Calcd for $C_9H_{12}O$: C, 79.37; H, 8.88. Found: C, 79.07; H, 8.81.

(+)-Methyl *endo*-5-Bicyclo[2.2.2]octene-2-carboxylate (44). Esterification of (+)-*endo*-5-bicyclo[2.2.2]octene-2-carboxylic acid (**43**),[20] $[\alpha]^{19}_D$ +48.2° (optical purity 95%)[2b] (8.80 g, 0.0578 mol), with CH_2N_2 afforded 9.25 g of **44** (96% yield): bp 112–114 °C (20 mm); $[\alpha]^{14}_D$ +46.9° (*c* 0.526, EtOH); IR (neat film) 1730, 1197, 1175, 1056, 889, 700 cm^{-1}.

Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 71.98; H, 8.52.

Methyl *exo*-5(6)-Hydroxy-*endo*-bicyclo[2.2.2]octane-2-carboxylate (45). Treatment of a THF solution of **44**, $[\alpha]^{14}_D$ +46.9° (9.12 g, 0.0549 mol), with diborane as described for the preparation of **21** gave 6.40 g of **45** (63% yield): bp 138–142 °C (8 mm); $[\alpha]^{16}_D$ −71.3° (*c* 0.666, EtOH); IR (neat film) 3400, 1725, 1198, 1175, 1078, 1029, 1011 cm^{-1}.

Methyl 5(6)-Oxo-*endo*-bicyclo[2.2.2]octane-2-carboxylate (46). A solution of **45**, $[\alpha]^{16}_D$ −71.3° (6.36 g, 0.0345 mol), in acetone was treated with Jones' reagent by the same method described for the preparation of **22**. Distillation of the product afforded 4.86 g of **46** (77% yield): bp 128–134 °C (8 mm); $[\alpha]^{14}_D$ −43.8° (*c* 0.512, EtOH); IR (neat film) 1725, 1196, 1172, 1101, 1072, 1020 cm^{-1}; NMR (CCl_4) δ 3.60 and 3.62 (ratio 1:1) ($OCOCH_3$).

Anal. Calcd for $C_{10}H_{14}O_3$: C, 65.91; H, 7.74. Found: C, 65.71; H, 7.70.

(−)-Methyl 5-Oxo-*endo*-bicyclo[2.2.2]octane-2-carboxylate (51). Reduction of **46**, $[\alpha]^{14}_D$ −43.8° (4.76 g, 0.0261 mol), with sodium borohydride followed by saponification as described for **27** afforded 1.02 g of **48** as a neutral fraction: mp 202.5–203.5 °C; $[\alpha]^{16}_D$ +8.4° (*c* 0.484, EtOH); IR (KBr) 1759, 1187, 1150, 1041, 970, 959 cm^{-1}.

Anal. Calcd for $C_9H_{12}O_2$: C, 71.02; H, 7.95. Found: C, 71.08; H, 7.87.

The hydroxy acid **49** (2.86 g) isolated as an acidic fraction was esterified with CH_2N_2 to provide the ester **50** which was treated with Jones' reagent to afford 2.30 g of **51**: bp 130–134 °C (7 mm); $[\alpha]^{12}_D$ −42.8° (*c* 0.522, EtOH); IR (neat film) 1725, 1196, 1172, 1101, 1075, 1022 cm^{-1}; NMR (CCl_4) δ 1.7–2.1 (m, 6 H), 2.10–2.31 (m, 3 H), 2.35–2.55 (m, 2 H), 3.62 (s, 3 H).

Anal. Calcd for $C_{10}H_{14}O_3$: C, 65.91; H, 7.74. Found: C, 65.61; H, 7.68.

(5-Oxo-*endo*-2-bicyclo[2.2.2]octyl)methyl Methanesulfonate (54). Reduction of **51**, $[\alpha]^{12}_D$ −42.8° (2.20 g, 0.0121 mol), with $LiAlH_4$ by the similar procedure described for the preparation of **29** gave 1.84 g of **52**. Treatment of **52** (1.84 g, 11.8 mmol) with methanesulfonyl chloride (1.53 g, 11.8 mmol) as described for the preparation of **30** afforded 1.77 g of **53**. The monomesylate **53** (1.77 g) was oxidized with Jones' reagent by the same method described for **22** to give 1.65 g of **54** as a pale yellow oil, which was converted into **16** without further purification (vide infra): IR (neat film) 1720, 1350, 1175, 955 cm^{-1}.

(−)-2-Isobrendanone [(−)-Tricyclo[3.3.1.$0^{3,6}$]nonan-2-one] (16). Compound **16** was prepared from **54** (1.65 g, 7.11 mmol) by the procedure described for the preparation of **14**. The product was chromatographed on neutral alumina (Woelm, activity II) and elution with pentane–ether (9:1 v/v) gave a white solid which was sublimed at 50–60 °C (30 mm) to give 379 mg of **16** (39% yield): mp 146–149 °C (in a sealed tube); $[\alpha]^{13}_D$ −199° (*c* 0.417, EtOH); IR (Nujol) 1722, 1216, 1125, 1062, 1007 cm^{-1}; UV $\lambda_{max}^{isooctane}$ 291 nm (ϵ 23), 301 (sh) (20), 312 (sh) (10); MS *m/e* 136 (M^+).

Anal. Calcd for $C_9H_{12}O$: C, 79.37; H, 8.88. Found: C, 79.06; H, 8.71.

(+)-Tricyclo[2.2.2.$0^{2,6}$]octan-3-one (18) and (−)-Bicyclo[2.2.2]oct-5-en-2-one (60). A mixture of partially resolved *endo*-5-bicyclo[2.2.2]octene-2-carboxylic acid (**43**), $[\alpha]^{25}_D$ −14.5° (optical purity 29%)[2b] (6.08 g, 40.0 mmol), lead tetraacetate (16.8 g, 90% pure, 80.0 mmol), dry pyridine (4.74 g, 60.0 mmol), and dry benzene (80 mL) was heated under reflux for 7 h under a nitrogen atmosphere. After cooling, the reaction mixture was filtered through a column of 100 g of neutral alumina (Woelm, activity II). Eluats with benzene and with ether were combined, washed with 1 N NaOH solution, diluted HCl, and water, dried ($MgSO_4$), and concentrated. Distillation gave 3.31 g of a mixture of **58** and **61**, bp 114–120 °C (50 mm). A solution of this mixture (3.11 g) in dry ether was added to a suspension of $LiAlH_4$ (0.80 g) in dry ether (50 mL) and the mixture was refluxed for 4 h. After cooling with ice, saturated ammonium chloride solution was added to the chilled reaction mixture and an inorganic solid was filtered off. The filtrate was dried ($MgSO_4$) and concentrated to afford 2.66 g of a mixture of **59** and **62**, which was dissolved in methylene chloride (10 mL). The solution was added to Collins' reagent[21] prepared from 12.8 g of chromium trioxide, 20.5 of dry pyridine, and methylene chloride (320 mL), and the mixture was stirred for 20 min at room temperature. The organic phase was separated and an inorganic residue was rinsed with methylene chloride. Combined organic solutions were washed with 5% NaOH solution, diluted HCl, and water, dried ($MgSO_4$), and concentrated. The residue was chromatographed on neutral alumina (Woelm, activity III). Elutions with pentane gave a solid, which was sublimed at 45–50 °C (5 mm) to give 410 mg of **60**: mp 89–91 °C (in a sealed tube); $[\alpha]^{25}_D$ −70.1° (*c* 0.473, $CHCl_3$); IR (KBr) 3020, 1725, 1090, 860 cm^{-1}; NMR ($CDCl_3$) δ 1.4–1.9 (m, 4 H), 2.0–2.1 (m, 2 H), 2.9–3.2 (m, 2 H), 3.1–3.3 (m, 1 H), 3.4–3.6 (m, 1 H); CD (*c* 1.71 × 10^{-2}, isooctane) [θ] (nm) +1.18 × 10^4 (196.5), −4.21 × 10^3 (217.5), −2.54 × 10^3 (sh) (278.5), −3.86 × 10^3 (286.5), −5.00 × 10^3 (295.5), −4.80 × 10^3 (306.0), −2.43 × 10^3 (317.5), +7.31 × 10^2 (324.0).

Anal. Calcd for $C_8H_{10}O$: C, 78.65; H, 8.25. Found: C, 78.35; H, 8.20.

Further elution with pentane–ether (1:1 v/v) gave an oily product which was purified by distillation to yield 1.10 g of **18**: bp 110–115 °C (35 mm); $[\alpha]^{27}_D$ +26.3° (*c* 0.638, $CHCl_3$); IR (neat film) 1724, 1320, 1300, 950, 920, 865, 820, 745 cm^{-1}; MS *m/e* 122 (M^+).

Anal. Calcd for $C_8H_{10}O$: C, 78.65; H, 8.25. Found: C, 78.30; H, 8.19.

Registry No.—**19,** 20507-53-3; **20,** 68069-49-8; **21** isomer 1, 68024-13-5; **21** isomer 2, 68024-14-6; **22,** 68069-50-1; **23,** 68069-51-2; **24,** 68035-53-0; **25,** 68069-52-3; **26,** 68069-53-4; **27,** 68069-54-5; **28,** 68024-15-7; **29,** 68024-16-8; **30,** 68024-17-9; **31,** 68024-18-0; **32,** 68024-19-1; **33,** 68024-20-4; **34,** 68024-21-5; **35,** 68024-22-6; **36,** 68024-23-7; **37,** 68024-24-8; **38,** 68024-25-9; (+)-**43,** 20507-56-6; (−)-**43,** 20507-57-7; **44,** 68069-55-6; **45** isomer 1, 68024-26-0; **45** isomer 2, 68069-56-7; **46,** 68069-57-8; **47,** 68069-58-9; **48,** 68069-59-0; **49,** 68069-60-3; **50,** 68069-61-4; **51,** 68069-62-5; **52,** 68024-27-1; **53,** 68024-28-2; **54,** 68024-29-3; *endo*-**58,** 68069-63-6; *exo*-**58,** 68069-64-7; *endo*-**59,** 68069-65-8; *exo*-**59,** 68069-66-9; **60,** 68069-67-0; *endo*-**61,** 68024-30-6; *exo*-**61,** 68069-68-1; *endo*-**62,** 68069-69-2; *exo*-**62,** 68069-70-5.

References and Notes

(1) Presented at the 36th Annual Meeting of the Chemical Society of Japan, Osaka, April 1977, Preprints, Vol. II, p 1097.
(2) (a) K. Adachi, K. Naemura, and M. Nakazaki, *Tetrahedron Lett.*, 5467 (1968); (b) M. Tichy and J. Sicher, *Collect. Czech. Chem. Commun.*, **37**, 3106 (1972); M. Tichy, *Tetrahedron Lett.*, 2001 (1972).
(3) K. Naemura and M. Nakazaki, *Bull. Chem. Soc. Jpn.*, **46**, 888 (1972).
(4) M. Nakazaki, K. Naemura, and H. Kadowaki, *J. Org. Chem.*, **41**, 3725 (1976).
(5) M. Nakazaki, K. Naemura, and N. Arashiba, *J. Chem. Soc., Chem. Commun.*, 678 (1976).
(6) A. Nickon, H. Kwasnik, T. Swartz, R. O. Williams, and J. B. DiGiorgio, *J. Am. Chem. Soc.*, **87**, 1615 (1965).
(7) We suggested the trivial name "norbrendane" for tricyclo[3.2.1.$0^{3,6}$]-octane[8] and "isobrendane" for tricyclo[3.3.1.$0^{3,6}$]octane.
(8) R. R. Sauers, R. A. Parent, and S. B. Damle, *J. Am. Chem. Soc.*, **88**, 2257 (1966), and references cited therein.
(9) N. A. LeBel and J. E. Huber, *J. Am. Chem. Soc.*, **85**, 3193 (1963).
(10) M. Nakazaki and K. Naemura, *J. Synth. Org. Chem., Jpn.*, **35**, 883 (1977).
(11) M. Nakazaki, H. Chikamatsu, K. Naemura, and Y. Hirose, presented at the 26th International Congress of Pure and Applied Chemistry, Sept. 8, 1977, Tokyo, Abstracts p 63.
(12) J. G. Henkel and L. A. Spurlock, *J. Am. Chem. Soc.*, **95**, 8339 (1973).
(13) J. A. Berson and D. A. Ben-Efraim, *J. Am. Chem. Soc.*, **81**, 4083 (1959); J. A. Berson, J. S. Walia, A. Remanick, S. Suzuki, P. Reynolds-Warnhoff, and D. Willner, *ibid.*, **83**, 3986 (1961).
(14) R. R. Sauers and J. C. Oppelt, *Tetrahedron*, **25**, 613 (1969).
(15) J. A. Berson, D. Wege, G. M. Clarke, and R. G. Bergman, *J. Am. Chem. Soc.*, **91**, 5594 (1969).
(16) H. L. Goering and D. L. Towns, *J. Am. Chem. Soc.*, **85**, 2295 (1963).
(17) G. Snatzke and F. W. Zamojska, *Tetrahedron Lett.*, 1665 (1971).
(18) J. Meinwald, J. Crandall, and W. E. Hymans, "Organic Syntheses", Collect. Vol. V, Wiley, New York, N.Y., 1973, p 866.
(19) E. J. Corey and J. W. Suggs, *Tetrahedron Lett.*, 2647 (1975).
(20) M. Nakazaki, K. Naemura, and S. Harita, *Bull. Chem. Soc. Jpn.*, **48**, 1907 (1975).
(21) J. C. Collins, W. W. Hess, and F. J. Frank, *Tetrahedron Lett.*, 3363 (1968).