Dissymmetric Non-conjugated Chromophores. Optical Rotatory Dispersion of Bicyclo[2.2.1]hept-5-en-2-one and Bicyclo[2.2.2]oct-5-en-2-one[1]

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Optically active β,γ-unsaturated ketones I and II of known absolute configuration have been prepared and the optical rotatory dispersion characteristics corresponding to the long wave length n → π*-transition have been determined. These compounds represent the simplest examples known of ketones containing dissymmetric non-conjugated chromophores. The sign and shape of the respective O.R.D. curves are in excellent agreement with those theoretically calculated on the basis of the generalized octant rule.[2]

In the preceding paper[2] diverse instances were cited of optically active β,γ-unsaturated ketones whose long wave length Cotton effects were most usefully discussed in terms of the relevant dissymmetric non-conjugated chromophore. The present work is concerned with the study of optically active bicyclo[2.2.1]hept-5-en-2-one (dehydronorcamphor, I) and bicyclo[2.2.2]oct-5-en-2-one (II). These molecules contain the twisted chromophore rigidly fixed and embedded in a structural skeleton of minimum complexity: they may be regarded as archetypes of previously discussed dissymmetric β,γ-unsaturated carbonyl chromophores. The shape of the O,R.D, curves of I and II had been predicted[2] from the respective ultraviolet spectra and the sign from the chirality of the twisted chromophores. An experimental verification of these predictions would serve to support the theoretical framework of the previously enunciated[2] generalized octant rule.

Syntheses.—The essential transformations described in the present work are collected in Chart 1.

CHART 1[a]
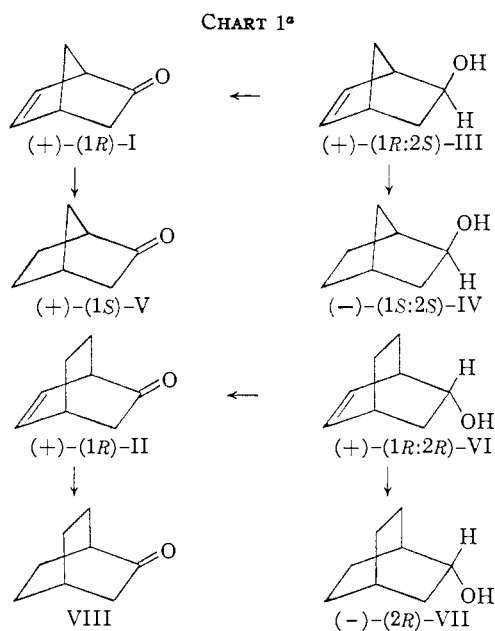
a Signs of rotation refer to the D-line, solvent chloroform.

(2) A. Moscowitz, K. Mislow, M. A. W. Glass and C. Djerassi, J. Am. Chem. Soc., 84, 1945 (1962); cf. also K. Mislow, M. A. W. Glass, A. Moscowitz and C. Djerassi, ibid., 83, 2771 (1961).

Direct entry into the optically active bicyclo[2.2.1]hept-5-en-2-yl series was achieved by subjecting bicyclo[2.2.1]hepta-2,5-diene (norbornadiene) to Brown's elegant asymmetric hydroboration,[3] using diisopinocampheylborane. The resulting dehydronorborneol (III) was epimerically homogeneous (exo)[4] and optically active ([α]^{25}D +5.8° (chf.)). Hydrogenation of III gave exo-norborneol (IV), [α]^{26}D −1.36° (chf.); hydrogenation of the corresponding III-acetate (α^{25}D +22.9° (neat, l 1)) afforded IV-acetate, α^{25}D +6.31° (neat, l 1). Based on the maximum values for IV and IV-acetate reported by Berson and Suzuki,[5] the optical purity of IV is 45–48% and that of IV-acetate 48–51%; we have therefore taken 48% as the optical purity of III and IV.[6] Derivatives I and V (norcamphor) were obtained, respectively, by Oppenauer oxidation[7] of III and by catalytic hydrogenation of I. Since they were isolated by methods (distillation, sublimation) not conducive to optical fractionation, I and V are considered 48% optically pure. Further, the configurations of I, III, IV and V have been unequivocally interrelated by the reaction sequences just described.

Optical activation of the bicyclo[2.2.2]oct-5-en-2-yl series was conveniently initiated by partial optical resolution of endo-bicyclo[2.2.2]oct-5-en-2-yl hydrogen phthalate. The hydrogen phthalate, obtained by conventional transformations from the Diels–Alder product[8] of 1,3-cyclohexadiene and vinyl acetate (endo:exo = 87:13), formed a salt with ephedrine[9] which on recrystallization from ethanol concentrated both enantiomers of the exo

(3) H. C. Brown and G. Zweifel, ibid., 83, 486 (1961).

(4) Hydroboration of the diene with diborane yields a mixture (88% exo, 12% endo) of epimers, m.p. 92–93° (H. C. Brown and G. Zweifel, ibid., 81, 5832 (1959)).

(5) J. A. Berson and S. Suzuki, ibid., 81, 4088 (1959), report [α]D 2.85–3.02° (chf.) and αD 12.3–13.0° (neat, l 1) for enantiomerically pure IV and IV-acetate, respectively. These values were established by the isotope dilution method and may be accepted as completely reliable.

(6) Asymmetric hydroboration of norbornene[3] gives IV and IV-acetate of ca. 65% optical purity (based on the maximum values[5]). Since the optical purity of our α-pinene ([α]$^{22.5}$D +43°) was only 90% of that employed by Brown and Zweifel,[3] the asymmetric hydroborations of norbornadiene and of norbornene appear in fact to yield products of comparable optical purity, as well as of the same configuration.

(7) N. J. Toivonen and J. Kaila, Suomen Kemi., 28B, 91 (1955), modified according to P. D. Bartlett and W. P. Giddings, J. Am. Chem. Soc., 82, 1240 (1960); cf. S. J. Cristol and P. K. Freeman, ibid., 83, 4427 (1961).

(8) J. Hine, J. A. Brown, L. H. Zalkow, W. E. Gardner and M. Hine, ibid., 77, 594 (1955).

(9) Several other optically active bases (brucine, strychnine, cinchonidine, quinine, quinidine, morphine, amphetamine) gave unsatisfactory results.

epimer as well as the (−)-*endo* isomer in the mother liquors: the seventh head fraction was 99⁺% diastereomerically pure and enriched in the (+)-*endo* epimer. Further recrystallizations effected a gradual increase in optical purity; lack of material precluded achievement of constant optical rotation.

We note that epimerically pure *rac-endo*-bicyclo-[2.2.2]oct-5-en-2-ol may thus be conveniently prepared on a massive scale by recrystallization of the hydrogen phthalate (±)ephedrine salt. The alternative procedure of purification *via* the *p*-nitrobenzoate was not successful in our hands (Experimental Part).

The VI-hydrogen phthalate of highest optical purity obtained in the present work had $[\alpha]^{25}$D +50.5°(chf.). Saponification of this sample yielded VI, $[\alpha]^{23}$D +68.2° (chf.), which in turn afforded VII, $[\alpha]^{21}$D −28.0° (chf.), on catalytic hydrogenation. Based on the maximum value for VII reported by Berson and Willner,[10] these materials are all *ca.* 70% optically pure.

Since hydrogenation of VI-hydrogen phthalate, $[\alpha]^{25}$D +38.4° (chf.), yielded VII-hydrogen phthalate, $[\alpha]^{22}$D −18.0° (chf.), the value $[\alpha]$D −34° may be calculated for optically pure VII-hydrogen phthalate, in agreement with the findings of Berson and Willner.[10]

Oxidation of *ca.* 40% optically pure VI, $[\alpha]^{26}$D +39.6°, gave II, $[\alpha]^{28}$D +267° (chf.). The oxidation was carried out conveniently using "active" manganese dioxide[11]–methylene chloride; the product was identical in every respect with that obtained by the Oppenauer procedure. Further investigation revealed that even saturated alcohols are readily oxidized by this reagent (Experimental Part) in shorter periods than heretofore realized.[12]

Hydrogenation of (+)-II gave optically inactive VIII. This experiment adds weight to the structural assignments in this series.

As seen from the flowsheet below, oxidation of the epimers of VI having the *same* absolute configuration at C-1 gives the *same* isomer of II, whereas hydrogenation gives *enantiomeric* forms of VII. From the point of view of correlating configurations *and* optical purities of II, VI and VII, identity and homogeneity, respectively, of VI are thus of crucial import. Assignment of the *endo* configuration to VI rests primarily on the infrared spectral characteristics in the hydroxyl region[13]; gas chromatographic analysis proves epimeric homogeneity. The desired correlations have therefore been achieved.

In connection with the gas chromatographic analyses of *endo-exo* mixtures, we have noted that the relative *order* of retention times may be a func-

(10) J. A. Berson and D. Willner, *J. Am. Chem. Soc.*, **84**, 675 (1962), report [α]D 40.0 ± 4.8° (chf.) and [α]D 30.5 ± 3.7 (chf.) for enantiomerically pure VII and VII-hydrogen phthalate, respectively. These values were established by the isotope dilution method.

(11) J. Attenburrow, A. F. B. Cameron, J. H. Chapman, R. M. Evans, B. A. Hems, A. B. A. Jansen and T. Walker, *J. Chem. Soc.*, 1094 (1952); *cf.* also J. C. Bloch, J. Boissier and G. Ourisson, *Bull. soc. chim. France*, 540 (1961).

(12) R. J. Gritter and T. J. Wallace, *J. Org. Chem.*, **24**, 1051 (1959). E. F. Pratt and J. F. Van de Castle, *ibid.*, **26**, 2973 (1961), have recently come to similar conclusions.

(13) H. L. Goering, R. W. Greiner and M. F. Sloan, *J. Am. Chem. Soc.*, **83**, 1391 (1961).
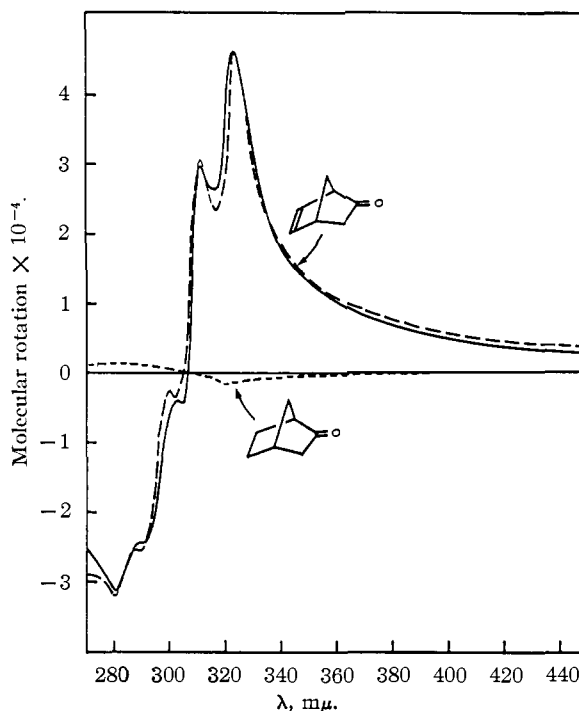

Fig. 1.—Rotatory dispersion curves (isoöctane) of dehydronorcamphor (solid line) and norcamphor (short dashes), both corrected to optical purity. Calculated curve for dehydronorcamphor (long dashes) with scale factor adjusted to experimental.

tion of the column substrate, as summarized in Table I. In view of the important use to which such information has been put in the elucidation of epimeric identity of unsaturated bicyclic alcohols,[13,14] it might be pointed out that some reservation should be attached to the unqualified generalization that internal hydrogen bonding is accompanied by shorter g.c. retention times.

TABLE I

GC RETENTION TIMES (MIN.)ᵃ

Compound	20% Carbowax 1500-on-Chromosorb	30% glycerol-on-Chromosorb
Dehydronorborneol		
exo-	19.8	7.0
endo-	15.9	7.0
Bicyclo[2.2.2]oct-5-en-2-ol		
exo-	34.2	10.0
endo-	27.6	11.7

ᵃ 6′ × 0.25″ column, helium carrier, 15 p.s.i., 120–130 cc./min., 120–130°.

Optical Rotatory Dispersions.—Three features of the O.R.D. curves of I (Fig. 1) and II (Fig. 2) are of paramount concern: *sign, shape* and *amplitude*.

According to the preceding analysis,[2] the sign of the Cotton effects is determined solely by the handedness of the dissymmetric chromophore (*i.e.*, by the absolute disposition of the double bond relative to the carbonyl group): for the isomers of I and II which have the (1*R*)-configuration,

(14) C. H. DePuy and P. R. Story, *Tetrahedron Letters*, No. **6**, 20 (1959).
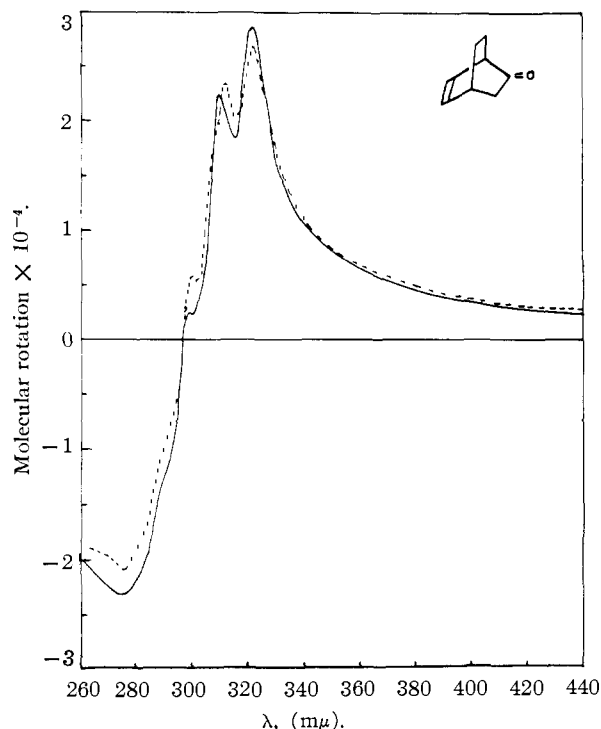
Fig. 2.—Rotatory dispersion curves (isoöctane) of bicyclo-[2.2.2]oct-5-en-2-one: experimental (solid line); calculated (dashed line) with scale factor adjusted to experimental. Curves are corrected to optical purity.

positive Cotton curves were predicted. This prediction has now been verified (Figs. 1 and 2) for (1R)-I and (1R)-II, whose absolute configurations are established by direct correlations (previous section) with unequivocal standards (1S:2S)-IV (or (1S)-V)[15] and (2R)-VII,[10,16] respectively.
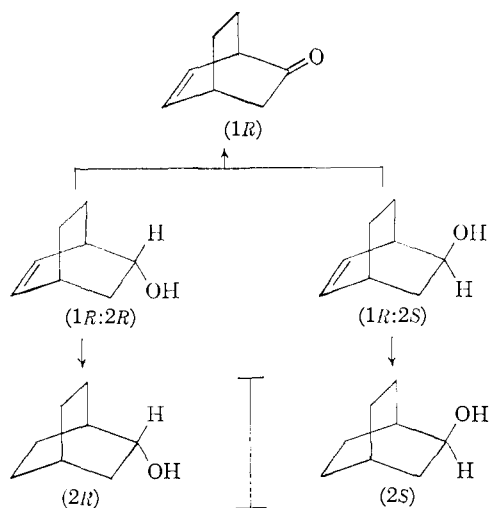

When the dissymmetric chromophore makes the dominant contribution to the optical activity, the shape of the absorption and of the dichroism curve is the same.[17] In consequence[2] the shape

(15) J. A. Berson, J. S. Walia, A. Remanick, S. Suzuki, P. Reynolds-Warnhoff and S. Willner, J. Am. Chem. Soc., **83**, 3986 (1961).

(16) H. M. Walborsky, M. E. Baum and A. A. Youssef, ibid., **83**, 988 (1961).

of the partial O.R.D. curve is uniquely determined by that of the corresponding partial absorption curve in β,γ-unsaturated ketones such as I and II. As seen in Figs. 1 and 2, the experimental curves, *exclusive of scale factor*, have precisely the shapes predicted[2] for I and II on the basis of absorption spectra *alone*, including every detail of the vibrational contour. In Figs. 1 and 2 the calculated curves have been fitted to those experimentally obtained.

Dissymmetric chromophores are associated with greatly enhanced rotational strengths,[17] as generally reflected in Cotton effects of high amplitude: it was thus predictable[2] that I and II would exhibit anomalously high optical rotations. However, owing to the asymmetry of I and II, the projection of $\bar{\mu}_e$ on $\bar{\mu}_m$ is unknown and the rotational strength (and hence the scale factor for the molecular rotation [ϕ]) can therefore not be calculated with confidence. This is in contrast to IX in which $\bar{\mu}_e$ and $\bar{\mu}_m$ are collinear with the twofold symmetry axis and the O.R.D. curve *including* scale factor
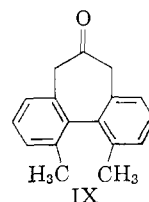
is *a priori* calculable.[2] Fortunately, the present experimental work supplies the scale factor for both I and II, since the optical purities of both compounds are known (ca. 48% resp. 40%).

In the case of I, the molecular amplitude, corrected to optical purity, is 78 ± 4 × 10³. In striking contrast, the O.R.D. curve of V (Figs. 3 and 1) is not only of a different shape and sign,[18] but the corresponding molecular amplitude of 2.8 × 10³ (after correction to optical purity) is smaller by a factor of 28, as also reflected in the lower ϵ-values of the absorption spectrum.

The molecular amplitude of II, corrected to optical purity, is 52 ± 5 × 10³. Calculations carried out by Moscowitz[19] on the assumption that the mixing coefficients[2] λ of I and II are the same have led to the prediction that the amplitude of I is roughly twice that of II. This prediction is in reasonable agreement with the present experimental findings.

The molecular amplitudes of I and II are smaller than those found[2,20] for IX and parasantonide (ca.140 × 10³) in the same solvent (isoöctane), though all are of the same order of magnitude (10⁵). Following completion of the work described in this and the preceding papers,[2,20] a further example of the type of compound under discussion was

(17) A. Moscowitz, Ph.D. Dissertation, Harvard University, 1957; W. Moffitt and A. Moscowitz, J. Chem. Phys., **30**, 648 (1959).

(18) Sign and shape are solvent dependent, as already noted for the trimethyl derivatives isofenchone and epiisofenchone by H. P. Gervais and A. Rassat, Bull. soc. chim. France, 743 (1961).

(19) A. Moscowitz, private communication. We thank Professor Moscowitz for the many illuminating discussions in this connection.

(20) K. Mislow, M. A. W. Glass, R. E. O'Brien, P. Rutkin, D. H. Steinberg and C. Djerassi, J. Am. Chem. Soc., **82**, 4740 (1960); K. Mislow and C. Djerassi, ibid., **82**, 5247 (1960).

provided by Cookson and MacKenzie,[21] who reported that 5-phenylborn-5-en-2-one has a long-wave length extremum with $[\phi]_{345}$ 108 × 10³ (ethanol). Unfortunately the complete Cotton curve was not obtained and the corresponding amplitude therefore remains unknown. Until the possibility has been eliminated that background rotations from Cotton effects centered at shorter wave lengths contribute significantly to the rotations above 300 mμ, a comparison with our results is clearly unprofitable.

Experimental Part[22]

(±)-"*endo*"-Bicyclo[2.2.2]oct-5-en-2-ol was prepared by the procedure of Hine, *et al.*[8] Condensation of cyclohexadiene[23] and vinyl acetate at 180° (5 days) in sealed glass Carius tubes gave a fraction, b.p. 90–91° (9 mm.), $n^{25}D$ 1.4971 (lit.[8] b.p. 125–130° (44 mm.), $n^{27}D$ 1.5020), which g.c.-analysis revealed to be a mixture of cyclohexadiene dimer (37%, retention time 14.4 min.), *exo*-bicyclo[2.2.2]oct-5-en-2-yl acetate (7.7%, 19.2 min.), the *endo* isomer (53%, 22.4 min.) and a small shoulder (*ca.* 2.3%) on the last peak of undetermined identity. Saponification of this fraction with aqueous methanolic sodium hydroxide gave the desired alcohol, m.p. 167.5–169° after three recrystallizations from petroleum ether followed by sublimation (lit.[13] m.p. 167.5–169°; lit.[24] m.p. 166–167°), which g.c.-analysis on two columns (Table I) revealed to be a mixture of *endo* (81%) and *exo* (19%) isomers. This analysis was confirmed by acetylation (acetic anhydride–pyridine) and g.c.-analysis of the esters (b.p. 89–90°(9 mm.), $n^{25}D$ 1.4791): the mixture was found to consist of *exo*-acetate (18%), *endo*-acetate (79%) and an unidentified material (as a shoulder after *endo*-acetate, *ca.* 3%).

Preparation of the *p*-nitrobenzoate, m.p. 107–109° after five recrystallizations from aqueous ethanol (lit. m.p. 109.8–110.8°,[13] m.p. 108.5–109.5°,[24] m.p. 108–110°[25]), followed by saponification with aqueous methanolic sodium hydroxide, gave alcohol, m.p. 167.5–168.5° after sublimation. Gas chromatographic analysis showed this material to be essentially unchanged in composition (87% *endo* isomer, 12% *exo* isomer, 1.7% of unidentified component having a shorter retention time).

(±)-"*endo*"-Bicyclo[2.2.2]oct-5-en-2-yl hydrogen phthalate was prepared by heating a mixture of the "*endo*"-alcohol (20 g.), phthalic anhydride (24 g.) and anhydrous pyridine (35 ml.) for 3.5 hr. at 95–105°. The reaction mixture was poured into dilute hydrochloric acid and the mixture was extracted with chloroform. The chloroform layer was washed with dilute acid, filtered to clarity, and extracted with 10% sodium bicarbonate. Acidification of the basic solution and extraction with chloroform afforded the desired hydrogen phthalate (35.4 g., 81%), m.p. 168–168.5°.

Anal. Calcd. for $C_{16}H_{16}O_4$: C, 70.57; H, 5.92. Found: C, 71.11; H, 5.95.

(+)-*endo*-Bicyclo[2.2.2]oct-5-en-2-yl Hydrogen Phthalate. —A mixture of the (±)-"*endo*"-hydrogen phthalate (pre-

(21) R. C. Cookson and S. MacKenzie, *Proc. Chem. Soc.*, 423 (1961).

(22) Melting points are corrected and boiling points are uncorrected. Microanalyses by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y. Rotatory dispersions were obtained by use of an automatic recording Rudolph spectropolarimeter. Gas chromatographies were run using a 6' × 0.25" column packed with 20% Carbowax 1500-on-Chromosorb at 120–130°, helium carrier at 15 p.s.i., 120–130 cc./min., unless otherwise specified.

(23) Prepared according to Hine, *et al.*[8] The material had b.p. 79–82°, $n^{25}D$ 1.4690 (lit.[8] b.p. 79–82°, $n^{24}D$ 1.4689); g.c.-analysis using 20% Carbowax 1500-on-Chromosorb (6' × 0.25", helium carrier, 15 p.s.i., 76 cc./min., 85°) revealed this to be a mixture of: cyclohexene (16%, retention time 9.1 min.), 1,3-cyclohexadiene (72%, 12.7 min.), 1,4-cyclohexadiene (8.5%, 17.2 min.), benzene (3.5%, 20.4 min.), and an unknown component (*ca.* 0.5%, 23.5 min.). Components were identified by comparison of retention times with authentic materials; lit.[8] product composition: 81% 1,3-cyclohexadiene, 15% cyclohexene, 4% benzene.

(24) W. C. Wildman and D. R. Saunders, *J. Org. Chem.*, 19, 381 (1954).

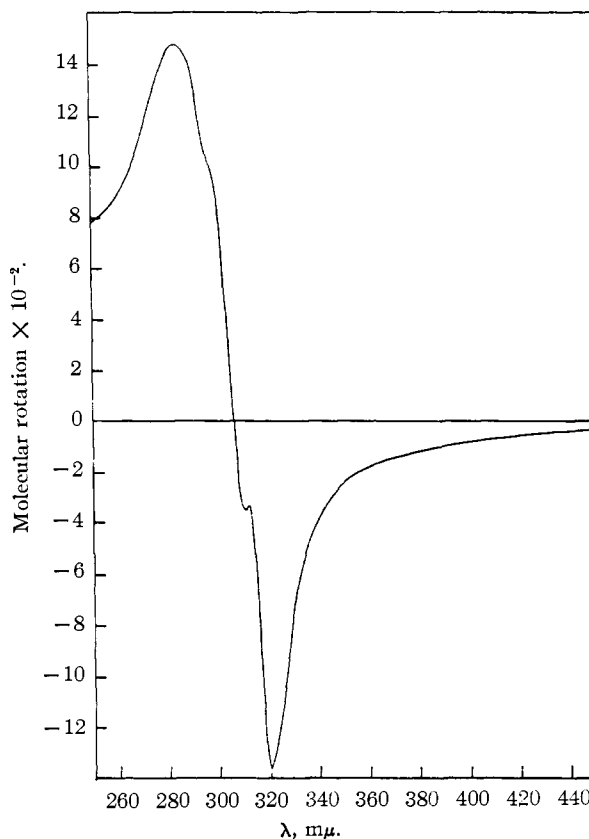(25) A. Gagneux and C. A. Grob, *Helv. Chim. Acta*, 42, 2006 (1959).

Fig. 3.—Rotatory dispersion curve (isoöctane) of norcamphor, corrected to optical purity.

ceding section) (35.3 g., 0.130 mole), (−)-ephedrine (24.5 g., 0.148 mole) and 320 ml. of abs. ethanol was heated briefly on the steam-bath. The clear solution was allowed to cool to room temperature and the precipitated crop of crystals was collected. Successive recrystallizations of the head fractions from ethanol were monitored by examining the rotation of hydrogen phthalate of VI liberated from aliquots of each salt fraction. The results are collected in Table II.

TABLE II

Ephedrine salt head fraction[a]	Hydrogen phthalate[b,d] Wt., g.	[α]D	Alcohol VI[c,d] [α]D	*endo*, %
1	39.5	+ 8.8°		
2	32.5	+13.9		
3	27.3	+18.6		
4	22.0	+21.0		
5	18.4	+26.0		
6	15.6	+29.9	+ 5.8°	98.7
7	12.8	+35.4	+20.5	99.4
8	10.5	+37.5	+19.9	99.7
9	9.30	+39.5		
10	7.95			
11	6.74	+42.8	+39.6	99.9
12	5.61			
13	4.50	+46.8		
14	3.60	+43.2		
15	2.85	+50.5	+68.2	100

[a] Fract. 1 = original crop; fract. 2–5 by crystallization from 175 ml. of ethanol, fract. 6–8 from 100 ml., fract. 9–15 from 75 ml. [b] Recovered from aliquots of salt. [c] Liberated from mother liquors of corresponding fractions; g.c.-analysis revealed only *endo* and *exo* components. [d] Rotation in chloroform.

Evaporation of the mother liquors from fraction 15 gave the white, powdery ephedrine salt, m.p. 173–173.5° after one recrystallization from ethanol, $[\alpha]^{23}$D + 16.7° (c 1.2, methanol).

Anal. Calcd. for $C_{26}H_{31}NO_5$: C, 71.37; H, 7.14; N, 3.20. Found: C, 71.53; H, 7.31; N, 3.84.

Decomposition of this salt with dilute hydrochloric acid–methanol yielded hydrogen phthalate, $[\alpha]^{23}$D + 43.1° (c 1.4, chf.). Similarly, decomposition of head fraction 15 gave hydrogen phthalate of VI, m.p. 158.5–159.5°, $[\alpha]^{25}$D + 50.5° (c 1.1, chf.).

Anal. Calcd. for $C_{16}H_{16}O_4$: C, 70.57; H, 5.92. Found: C, 70.76; H, 6.03.

Changes in epimeric composition were determined as follows. Hydrogen phthalate liberated from aliquots of the mother liquors of corresponding fractions was dissolved in concd. aqueous sodium hydroxide and the mixture was steam distilled. The alcohol thus obtained was analyzed by g.c. The results are listed in Table II.

(−)-Bicyclo[2.2.2]octan-2-yl Hydrogen Phthalate.—A solution of (+)-*endo*-bicyclo[2.2.2]oct-5-en-2-yl hydrogen phthalate (0.239 g., $[\alpha]^{25}$D + 38.4° (chf.)) in 15 ml. of abs. ethanol was hydrogenated over 10% Pd–C (81 mg.). In 10 minutes at 20° and 1 atm., 101% of the theoretical hydrogen was taken up. Filtration of the catalyst and evaporation of the filtrate gave 195 mg. (81%) of large white crystals, m.p. 157–158.5°, $[\alpha]^{22}$D − 18.0° (c 1.0, chf.) (lit.[16] m.p. 157–158°, $[\alpha]$D − 7.03° (c 0.521, chf.)).

(+)-*endo*-Bicyclo[2.2.2]oct-5-en-2-ol (VI).—A solution of (+)-*endo*-bicyclo[2.2.2]oct-5-en-2-yl hydrogen phthalate (1.40 g., $[\alpha]^{25}$D + 50.5° (chf.)) and 5.2 g. of sodium hydroxide in 20 ml. of water was steam distilled until 50 ml. of distillate had been collected. The clear distillate was saturated with sodium chloride and the precipitated material was filtered, dried and sublimed to give 282 mg. of alcohol VI. The filtrate was extracted with methylene chloride and the solvent was removed by distillation through a short column. Sublimation of the residue gave an additional amount (176 mg.) of material. The combined product (458 mg., 72%) had m.p. 167.5–168°, $[\alpha]^{23}$D +68.2° (c 1.1, chf.). Analysis by g.c. showed only a single peak, corresponding to the *endo* epimer.

Anal. Calcd. for $C_8H_{12}O$: C, 77.37; H, 9.74. Found: C, 76.82; H, 9.81.

(±) and (−) Bicyclo[2.2.2]octan-2-ol (VII).—A solution of (±)-bicyclo[2.2.2]oct-5-en-2-ol (81% *endo* + 19% *exo* epimer by g.c.-analysis) in ethanol was hydrogenated (10% Pd–C) at room temperature and 1 atm. pressure (110% theoretical uptake of hydrogen). The product was worked up as usual to give a 72% yield of bicyclo[2.2.2]octan-2-ol, m.p. 216–217°, unchanged by sublimation (lit. m.p. 216–217°,[24,26] m.p. 210–212°[27]). Analysis by g.c. showed only a single peak.

A solution of (+)-*endo*-bicyclo[2.2.2]oct-5-en-2-ol (VI, 240 mg., $[\alpha]^{23}$D + 68.2°) in 2.5 ml. of abs. ethanol similarly hydrogenated (96% theoretical uptake of hydrogen) afforded 147 mg. (61%) of (−)-bicyclo[2.2.2]octan-2-ol (VII), m.p. 221–222°, $[\alpha]^{21}$D − 28.0° (c 1.2, chf.) (lit.[16] $[\alpha]^{25}$D −7.45° (c 0.75, chf.)). Analysis by g.c. showed a minimum purity of 99.5%, the remainder being starting alcohol. The infrared spectrum of this material was superimposable on that of authentic (±)-alcohol (above) and also on that of a sample of (−)-*endo*-alcohol, $[\alpha]$D − 7° (c 1.0, chf.), which was very kindly furnished to us by Prof. Walborsky.

Anal. Calcd. for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 76.60; H, 11.18.

(±) Bicyclo[2.2.2]oct-5-en-2-one. A. Openauer Oxidation.—A mixture of 3.1 g. of bicyclo[2.2.2]oct-5-en-2-ol (85% *endo* + 15% *exo* epimer by g.c.) and freshly distilled aluminum isopropoxide (1.7 g.) was slowly heated to 180° in a flask equipped with a heat-jacketed Vigreux column and a cold-finger total-reflux head vented to the atmosphere through a calcium chloride drying tube. At that temperature 1.1 g. of isopropyl alcohol (b.p. 82°) was collected. Benzophenone (4.5 g.) was then added to the pot residue, and the contents of the flask were evacuated (9 mm.) and slowly heated to 180°. The glassy, translucent solid (2.1 g.)

which gradually accumulated on the cold-finger was sublimed three times to give a material, m.p. 88–94°, 96% of which, according to g.c.-analysis, consisted of the desired ketone, while 4% consisted of a mixture of the epimeric starting alcohols in a ratio of *endo*:*exo* = 75:25. A small quantity of this ketone was purified by g.c. using Carbowax 1500. The material so obtained readily sublimed to give soft, well-defined crystals, m.p. 90–91.5° (lit. m.p. 79°,[28] m.p. 75.0–83.5°[29]) whose infrared spectrum was identical in every respect with material prepared by the alternate procedure (below).

B. Manganese Dioxide Oxidation.—A mixture of 1.01 g. of bicyclo[2.2.2]oct-5-en-2-ol (88% *endo* + 12% *exo* epimer by g.c.), 15 g. of "active" manganese dioxide[11] and 30 ml. of methylene chloride was continuously stirred for 17 hr. at room temperature. The reaction mixture was then rapidly steam distilled. The organic layer was separated and the aqueous layer was saturated with sodium chloride and extracted with methylene chloride. The combined organic layers were dried and the solvent was removed by distillation through a short column. Sublimation of the residue gave 0.64 g. (64%) of bicyclo[2.2.2]-oct-5-en-2-one, m.p. 91.5–93°. Analysis by g.c. showed a purity of 99.5+%.

Anal. Calcd. for $C_8H_{10}O_2$: C, 78.65; H, 8.25. Found: C, 78.62; H, 8.33.

Reduction with lithium aluminum hydride[25] (0.205 g.) of the above ketone (0.329 g.) in 40 ml. of ether, followed by destruction of the complex with concd. aq. sodium hydroxide, extraction with ether, distillation of the ether and sublimation of the residue, gave 0.226 g. (68%) of product, m.p. 168.5–169.5° (lit.[25] m.p. 165–167°), which g.c.-analysis revealed to be a mixture of epimeric bicyclo[2.2.2]-oct-5-en-2-ols containing 70% of the *endo* and 30% of the *exo* isomer.

Oxidation of Alcohols by Manganese Dioxide.—The oxidation procedure B described in the preceding section was employed on a variety of alcohols and the products were analyzed by gas chromatography. A typical procedure follows.

Cyclohexanol (0.60 g.) in 10 ml. of methylene chloride was added to a slurry of "active" manganese dioxide[11] (10 g.) in 5–8 ml. of methylene chloride. The mixture was stirred for 1 hour at room temperature, a small aliquot was removed, the oxide was removed by centrifugation, and the supernatant clear liquid was analyzed gas chromatographically.[22] The composition was estimated at 59% cyclohexanone and 41% cyclohexanol.

The data obtained are collected in Table III.

TABLE III

OXIDATION OF VARIOUS ALCOHOLS BY ACTIVE MANGANESE DIOXIDE[a]

Alcohol[b]	Contact time, hr.	Conversion,[c] %
Bicyclo[2.2.1]heptan-2-ol [23% *exo* + 77% *endo*]	1	96
Bicyclo[2.2.2]octan-2-ol	1	100
Cyclohexanol	1	59
Cyclohexanol	3	66
4-Methyl-2-pentanol	1	85[d]
Bicyclo[2.2.1]hept-5-en-2-ol [21% *exo* + 79% *endo*]	1	57
	19	76
Bicyclo[2.2.2]oct-5-en-2-ol [12% *exo* + 88% *endo*]	19	100

[a] Alcohol:MnO_2[11] ≃ 1:20 by wt., CH_2Cl_2 solvent, room temp. [b] Preparation of the bicyclic alcohols described in Experimental Part. [c] As estimated by g.c.-analysis on 6' × 0.25" Carbowax-1500 at 130°, 15 p.s.i. and 100–105 cc./min., unless otherwise indicated. [d] G.c.-analysis at 100° and 140 cc./min.

Preparation and Hydrogenation of (+)-Bicyclo[2.2.2]-oct-5-en-2-one (II).—A mixture of (+)-*endo*-bicyclo[2.2.2]-oct-5-en-2-ol (0.81 g., $[\alpha]^{26}$D + 39.6° (chf)), "active"

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(27) H. M. Walborsky and D. F. Loncrini, *J. Am. Chem. Soc.*, **76**, 5396 (1954).

(28) C. A. Grob, H. Kny and A. Gagneux, *Helv. Chim. Acta*, **40**, 130 (1957).

(29) H. L. Goering and M. F. Sloan, *J. Am. Chem. Soc.*, **83**, 1397 (1961).

manganese dioxide[11] (12 g.) and 20 ml. of methylene chloride was stirred for 23 hours at room temperature. The product was worked up as described for the racemic modification. There was thus obtained 0.50 g. of material, m.p. 92–94°, which was shown by g.c.-analysis to contain 2.5% of unoxidized alcohol. Reoxidation of this material (10 g. of MnO$_2$, 14 hr.) gave 0.21 g. of product, m.p. 90.5–92°, 100% pure by g.c.-analysis, $[\alpha]^{28}$D + 267° (c 1.2, chf.); O.R.D. in isoöctane (c 0.208, 28°): $[\alpha]_{589}$ +265°, $[\alpha]_{321}$ + 9420°, $[\alpha]_{315}$ + 6050°, $[\alpha]_{309.5}$ +7400°, $[\alpha]_{300}$ +770°, $[\alpha]_{299}$ +816°, $[\alpha]_{290}$ −4515°, $[\alpha]_{275}$ −7600°, $[\alpha]_{260}$ −6450°; cf. also Fig. 2.

Anal. Calcd. for C$_8$H$_{10}$O: C, 78.65; H, 8.25. Found: C, 78.63; H, 8.30.

Hydrogenation of (+)-ketone II (in ethanol over 10% Pd–C at room temperature and atmospheric pressure) resulted in 102% of the theoretical uptake of hydrogen. The produced bicyclo[2.2.2]octan-2-one (VIII), worked up as usual, had m.p. 175.5–177.5° after three sublimations (lit. m.p. 176°,[26] m.p. 178–179°[30]) and was ca. 99.5% homogeneous by g.c.-analysis. It was optically inactive at all accessible wave lengths.

Anal. Calcd. for C$_8$H$_{12}$O: C, 77.37; H, 9.74. Found: C, 76.72; H, 9.65.

Preparation and Hydrogenation of (+)-exo-Bicyclo[2.2.1]-hept-5-en-2-yl Acetate.—α-Pinene[31] (distilled from calcium hydride, b.p. 155–157°, $[\alpha]^{22.5}$D +43° (c 2.0, ethanol), 272 g.) was added to a solution of sodium borohydride (28.6 g.) in 900 ml. of diglyme (distilled from calcium hydride, b.p. 162–165°). Boron trifluoride etherate (b.p. 125–126°, 142 g.) was added dropwise over a period of 1 hour to the stirred, chilled (0°) solution which was blanketed with nitrogen throughout. The solution was stirred for an additional hour at 0° and the resulting suspension was slowly added to norbornadiene (b.p. 89–90°, 190 g.) with stirring and sufficient cooling to maintain the temperature near 20°. The mixture was allowed to stand overnight at room temperature, volatile components (excess norbornadiene and ether) were removed at reduced pressure and 50 ml. of 3 N sodium hydroxide was added to the residue, followed by the dropwise addition of 400 ml. of 30% hydrogen peroxide. The reaction temperature was maintained at 30–50° throughout the addition by external cooling. Stirring was continued for another 2 hours and the reaction mixture was poured into a large volume of cold water and extracted with ether. The ether extracts were washed with water, dried and the ether was removed by careful distillation through a packed column. The residue was treated with 400 ml. of dry pyridine and 540 g. of acetic anhydride. After standing overnight, the reaction mixture was concentrated by distillation, poured into water and extracted with ether. The ether extracts were washed with 10% sodium bicarbonate, dried and distilled to give a 15% yield of crude ester. Repeated fractionation through a heated column packed with glass helices afforded product, b.p. 77.0–77.5° (14 mm.), n^{25}D 1.4645, α^{25}D +22.9° (neat, l 1), which contained 97% of the desired exo-dehydronorbornyl acetate according to g.c.-analysis.

Anal. Calcd. for C$_9$H$_{12}$O$_2$: C, 71.02; H, 7.95. Found: C, 71.17; H, 8.20.

Hydrogenation of this material in ethanol over 10% Pd–C at room temperature and atmospheric pressure resulted in 102% of the theoretical uptake of hydrogen. The

produced exo-norbornyl acetate, worked up as usual, after distillation (b.p. 84.0° (14 mm.)) had n^{25}D 1.4560 (lit.[32] n^{25}D 1.4565, α^{25}D +10.39° (neat, l 1)), α^{25}D +6.31° (neat, l 1), 99% homogeneous by g.c.-analysis, infrared spectrum identical with published spectrum.[32]

Preparation and Hydrogenation of (+)-exo-Bicyclo[2.2.1]hept-5-en-2-ol, exo-Dehydronorborneol (III).—The alcohol was prepared by lithium aluminum hydride (2.93 g.) reduction of the acetate (α^{25}D +22.9° (neat, l 1), 12.35 g.) in ether. After 30 min. of refluxing following addition, the complex was destroyed with concd. sodium hydroxide. The product, worked up as usual, was sublimed, and the sublimate was pressed on filter paper to remove traces of oily contaminant. Recrystallization (pentane) of this material, followed by sublimation, gave 5.50 g. of the desired product, m.p. 86–92° (lit.[3] m.p. 92–93°), $[\alpha]^{52}$D +5.8° (c 8.7, chf.), 99$^+$% homogeneous by g.c.-analysis.

Anal. Calcd. for C$_7$H$_{10}$O: C, 76.32; H, 9.15. Found: C, 76.04; H, 9.06.

Hydrogenation of this material in ethanol over 10% Pd–C at room temperature and atmospheric pressure resulted in 99.5% of the theoretical uptake of hydrogen. The produced exo-norborneol (IV), worked up as usual, had m.p. 125.5–127°, $[\alpha]^{16}$D − 1.36° (c 10.65, chf.) (lit.[32] m.p. 126–126.5°, $[\alpha]^{24}$D −2.41 (c 10.0, chf.)); g.c.-analysis showed only one peak.

Anal. Calcd. for C$_7$H$_{12}$O: C, 74.95; H, 10.78. Found: C, 75.05; H, 10.58.

Preparation and Hydrogenation of (+)-Bicyclo[2.2.1]-hept-5-en-2-one, Dehydronorcamphor (I).—A mixture of (+)-exo-bicyclo[2.2.1]hept-5-en-2-ol (III, 4.82 g., $[\alpha]^{25}$D +5.8° (chf.)), aluminum t-butoxide (21.6 g.), resublimed quinone (5.61 g.) and 250 ml. of benzene was refluxed for 49 hr. under exclusion of moisture. The reaction mixture was then shaken with 2 × 250 ml. of 5% sulfuric acid, followed by several washings with 5% sodium hydroxide until the extracts were colorless. Fractionation of the organic layer afforded 0.79 g. of product, b.p. 65.5–66.5° (19 mm.), n^{25}D 1.4834, m.p. 17–21°, 98% homogeneous by g.c. (repd. for racemic modification: (a)[7] b.p. 64° (19 mm.), n^{25}D 1.4857, m.p. 22–23°; (b)[33] b.p. 59–59.3° (18 mm.), n^{25}D 1.4839, m.p. 22–23°). The infrared spectrum was superimposable on that of racemic dehydronorcamphor prepared according to Toivonen and Kaila,[7] $[\alpha]^{28}$D + 592° (c 1.7, chf.); O.R.D. in isoöctane (c 0.107 − 0.0097, 28°): $[\alpha]_{589}$ +548°, $[\alpha]_{322}$ + 20,600°, $[\alpha]_{316}$ +11,800°, $[\alpha]_{311}$ +13,700°, $[\alpha]_{305}$ − 1,970°, $[\alpha]_{303}$ − 1,630°, $[\alpha]_{292}$ − 10,800°, $[\alpha]_{289}$ − 10,800°, $[\alpha]_{281}$ −13,900°, $[\alpha]_{270}$ −11,100°; cf. also Fig. 1.

Anal. Calcd. for C$_7$H$_8$O: C, 77.75; H, 7.46. Found: C, 77.68; H, 7.57.

Hydrogenation of this material in ethanol over 10% Pd–C at room temperature and atmospheric pressure resulted in 101% of the theoretical uptake of hydrogen. The product, worked up as usual, was sublimed to give the desired norcamphor (V), m.p. 93.5–96°, $[\alpha]^{22}$D +15.0° (c 2.8, chf.) (lit.[15] m.p. 90–91°, $[\alpha]^{30}$D +17.0 (chf.)), 98% pure by g.c.-analysis (2% norborneols), infrared spectrum superimposable on that of authentic racemic norcamphor; O.R.D. in isoöctane (c 1.44 −0.204, 26°): $[\alpha]_{450}$ −14°, $[\alpha]_{325}$ −592°, $[\alpha]_{312}$ −141°, $[\alpha]_{311}$ −148°, $[\alpha]_{296}$ +450°, $[\alpha]_{283}$ +646°, $[\alpha]_{250}$ +343°; cf. also Fig. 3; ultraviolet spectrum: $\lambda\lambda_{\text{inf}}^{\text{isoöct}}$ 272.5 mμ (ϵ 16.8), 282 mμ (ϵ 24.2), 295 mμ (ϵ 29.0, max), 305 mμ (ϵ 25.4), 317 mμ (ϵ 12.7).

Anal. Calcd. for C$_7$H$_{10}$O: C, 76.32; H, 9.15. Found: C, 76.74; H, 9.28.

(30) O. Diels and K. Alder, Ann., 478, 137 (1930).

(31) As térébenthine de Pin d'Alep, a sample of which was generously provided for us by courtesy of Marius Brémond et Fils, Septèmes-les-Vallons, Bouches-du-Rhône, France.

(32) S. Winstein and D. Trifan, J. Am. Chem. Soc., 74, 1154 (1952).

(33) P. D. Bartlett and B. E. Tate, ibid., 78, 2473 (1956).