

TERPENES—IV¹

THE STEREOCHEMISTRY AND OPTICAL ROTATORY DISPERSION CURVES OF SOME CYCLIC KETONES RELATED TO (-)-UMBELLULONE

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Abstract—A number of optically active cyclic ketones derived from (-)-umbellulone were prepared, and their UV absorption and NMR spectra and ORD curves measured. The sign of the Cotton effect associated with the $n - \pi^*$ transition of the CO group for each ketone is related to its configuration and preferred conformation.

RECENTLY there have been a number of reports concerning the ORD of cyclic ketones. The Octant Rule³ has been extended to cyclopropyl and epoxy ketones, and a "reverse" Octant Rule⁴ has been introduced for these chromophoric systems. Snatzke⁵ has discussed the relationship between the chirality of nonplanar, cyclic α,β -unsaturated ketones and the sign of the CD maximum associated with the CO $n - \pi^*$ transition. This discussion included both transoid^{5b} and cisoid^{5c} enones and was extended to cyclic α,β -unsaturated cyclopropyl ketones.⁶

Of the cyclic α,β -unsaturated and cyclopropyl ketones studied, the ring incorporating the carbonyl group generally has been part of a more extensive ring system,⁴⁻⁸ and only a limited number of studies have been made with bicyclo[3.1.0]-hex-3-en-2-ones, bicyclo[3.1.0]hexan-2-ones and monocyclic cyclopent-2-en-1-ones.^{4,6,7} We now wish to present the results of a stereochemical and ORD study on a number of such compounds. Included in this series is (-)-umbellulone (I),⁹ a thujane terpene of known absolute configuration,¹⁰ and a number of optically active ketones (II-VIII) derived from I (Chart 1).

¹ Paper III: H. E. Smith, J. C. D. Brand, E. H. Massey and L. J. Durham, *J. Org. Chem.* **31**, 690 (1966).

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³ W. Moffitt, R. B. Woodward, A. Moscowitz, W. Klyne and C. Djerassi, *J. Am. Chem. Soc.* **83**, 4013 (1961).

⁴ C. Djerassi, W. Klyne, I. Norin, G. Ohloff and E. Klein, *Tetrahedron* **21**, 163 (1965).

⁵ ^a G. Snatzke, *Tetrahedron* **21**, 413 (1965); ^b *ibid.* **21**, 421 (1965); ^c *ibid.* **21**, 439 (1965).

⁶ K. Schaffner and G. Snatzke, *Helv. Chim. Acta* **48**, 347 (1965).

⁷ C. Djerassi, R. Riniker and B. Riniker, *J. Am. Chem. Soc.* **78**, 6377 (1956).

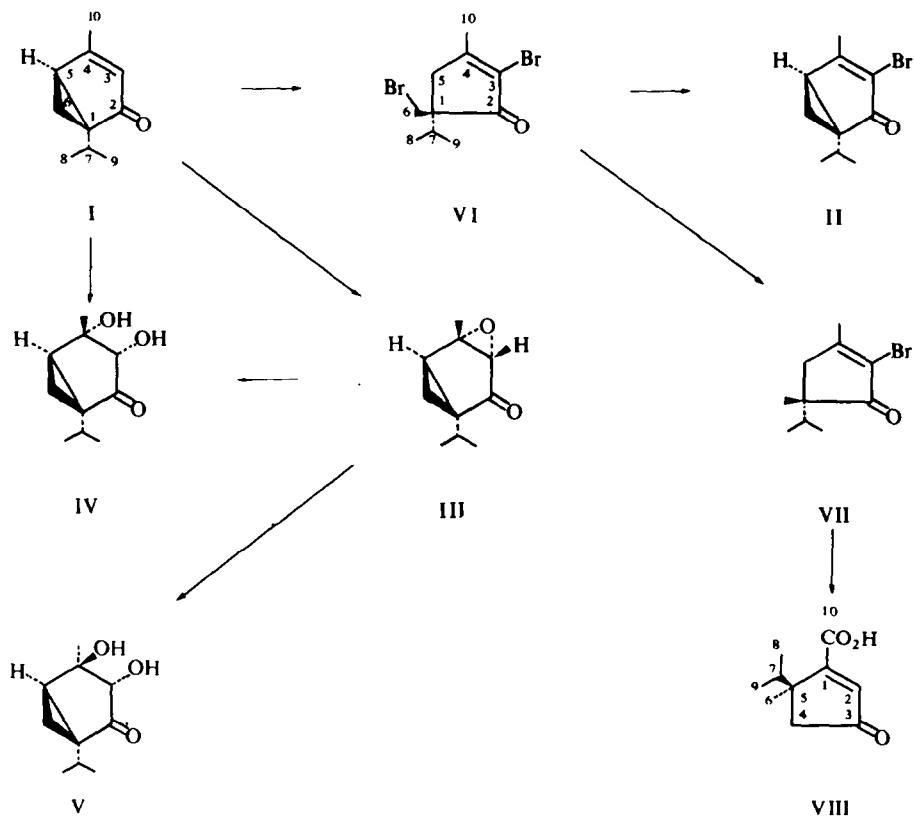
⁸ ^a C. Djerassi, *Optical Rotatory Dispersion* pp. 60, 83 and 101, McGraw-Hill, New York, N.Y. (1960);

^b L. Velluz, M. Legrand and M. Grosjean, *Optical Circular Dichroism* p. 126 Academic Press, New York, N.Y. (1965); ^c P. Crabbé, *Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry* pp. 166 and 191, Holden-Day, San Francisco, Calif. (1965).

⁹ F. B. Power and F. H. Lees, *J. Chem. Soc.* **85**, 629 (1904).

¹⁰ E. H. Massey, H. E. Smith and A. W. Gordon, *J. Org. Chem.* **31**, 684 (1966)

Chart I



RESULTS AND DISCUSSION

Bicyclo[3.1.0]hex-3-en-2-ones. The ORD curve of (–)-umbellulone (I)¹¹ in dioxan has been measured previously,⁷ and only one extremum, a peak at 367 m μ , reported. The curve has now been measured¹⁴ to shorter wavelengths (Fig. 1). A peak at 350 m μ ($[\phi] + 7300^\circ$) was observed, below 334 m μ the curve going strongly negative with a trough at 290 m μ ($[\phi] - 43,800^\circ$). As evidenced by CD measurements with I in dioxan,⁶ this intense trough is the result of two overlapping optically active absorption bands, a positive Cotton effect associated with the carbonyl $n - \pi^*$

¹¹ Signs in parenthesis for compounds I through VIII refer to rotatory powers observed with sodium D-light with methanol as the solvent. It is to be noted that (–)-umbellulone dibromide (VI) is dextrorotatory in chloroform.^{10 12 13}

¹² F. H. Lees, *J. Chem. Soc.* **85**, 639 (1904).

¹³ R. H. Eastman and A. Oken, *J. Am. Chem. Soc.* **75**, 1029 (1953).

¹⁴ The ORD curves reported here were obtained at room temperature with methanol as the solvent. It has been reported,⁷ however, that a solvent change from methanol to dioxan increases the observed fine structure of the Cotton effect associated with the carbonyl $n - \pi^*$ transition of an α,β -unsaturated ketone. With the one compound (VI) for which both solvents were used, a slight alteration in the fine structure was observed, but as in previous measurements,⁷ there was no change in over-all shape.

transition seen in the UV spectrum (Fig. 1) as a shoulder centered at 327 $m\mu$, and a negative Cotton effect associated with the absorption band at 263 $m\mu$.

The ORD of $(-)\alpha$ -bromoumbellulone (II) has now also been measured (Fig. 1).

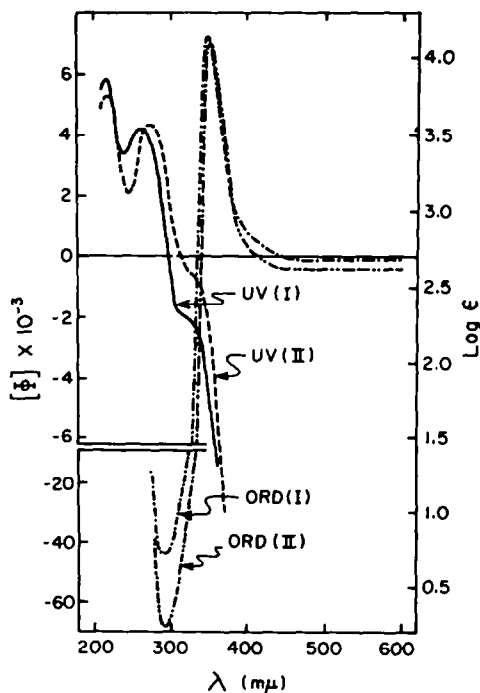


FIG. 1. The UV spectra and ORD curves of $(-)$ -umbellulone (I) and $(-)\alpha$ -bromoumbellulone (II) in methanol

This compound was prepared by dehydrobromination of $(-)$ -umbellulone dibromide (VI) with potassium acetate in boiling ethanol, VI being one of the bromination products of umbellulone.^{12,13} The structure of II was assigned^{13,15} on the basis of its preparation from VI by this dehydrobromination reaction.¹³ The assigned structure of II is compatible with its chemical properties and its IR and UV spectra,^{13,15} the latter (Fig. 1) being very similar to that of I. The NMR spectrum of II, compared to that of I (Table 1), now confirms the structural assignment for the former. The configuration of II follows from the known configuration of VI (see below).¹⁰

$(-)\alpha$ -Bromoumbellulone (II) was also formed by the reaction of I at 0° with bromine in carbon tetrachloride followed by treatment of the reaction product with piperidine at room temperature for 1 hr.¹⁵ It is to be noted, however, that this latter sequence of reactions does not give information concerning the absolute configuration of II, since this dehydrobromination proceeds much more readily than the dehydrobromination of VI with potassium acetate. In fact, after we had treated VI with

¹⁵ R. H. Eastman and J. C. Selover, *J. Am. Chem. Soc.* **76**, 4118 (1954).

piperidine in boiling carbon tetrachloride for 4 hr, VI was returned unchanged with almost no loss, indicating that II arises by dehydrobromination with piperidine, as outlined above, from an intermediate or intermediates other than VI.

The ORD curve of II is essentially the same as that of I (Fig. 1). This extends the earlier findings that a bromine or chlorine atom at C-2 in a cyclohex-2-en-1-one¹⁶ or Me group at C-3 in bicyclo[3.1.0]hex-3-en-2-one,⁶ the halogen atoms and the Me group lying in or near the plane of the CO group, in the absence of other more remote conformational changes, has no gross effect on the Cotton effect associated with the $n - \pi^*$ transition of the CO group.*

Bicyclo[3.1.0]hexan-2-ones. Of the three compounds studied (III-V), (-)-(3*S*)-epoxyumbellulone (III) and (-)-(3*S*,4*R*)-3,4-dihydroxydihydroumbellulone (V) have been prepared and characterized previously.¹⁵ Their configurations, however, were not specified.

The epoxide III was prepared by oxidation of I with hydrogen peroxide in methanolic sodium hydroxide.¹⁵ The NMR spectrum of III (Table 1) is compatible

TABLE 1. SUMMARY OF NMR DATA^a

Protons ^b	I	II	III	IV	V	VI	VII	VIII
Chemical shifts assigned, ^c ppm from TMS = 0								
2								6.75(s)
3	5.14(q)	<i>d</i>	2.93(d)	3.72(d) ^e	4.12(d) ^e			
4 α , 4 β ^f								2.10(d) ^g 2.61(d) ^g
5 α , 5 β ^f						2.56(q)	2.20(d) ^g 2.60(d) ^g	
6						3.53(s)	1.11(s)	1.45(s)
8, 9 ^f	0.95(d) 1.02(d)	0.99(d) 1.07(d)	0.88(d) 0.99(d)	0.88(d) 0.95(d)	0.93(d)	0.83(d) 0.90(d)	0.70(d) 0.90(d)	0.77(d) 0.99(d)
10	2.07(d)	2.18(s)	1.41(s)	1.41(s)	1.25(s)	2.19(t)	2.16(s)	
3-OH, 4-OH 10-OH				3.42(s) ^h	3.87(s) ^h			10.33(s)
Coupling constants assigned, ± 0.5 c/s								
3-10	1.5							
3-5			1.5	1.5	1.5			
4 α -4 β								19.0
5 α -5 β							18.5	
5-10						1.0		
7-8	7.0	7.0	7.0	7.0	7.0	7.0	6.5	7.0
7-9								

^a Measured at 60 Mc/s in CDCl₃. Abbreviations used: s, singlet; d, doublet; t, triplet; q, quartet.

^b See Chart 1 for numbering sequence.

^c Signal integrations were in agreement with all proton assignments.

^d No signal 2.50-8.30 ppm.

^e No change in multiplicity on exchange with D₂O.

^f No differentiation between these protons is made or implied.

^g AB type doublet of doublets; calculated chemical shift¹⁸

^h Vanished on exchange with D₂O.

* Added in proof. For a recent report in this connection see J.-C. Bloch and S. R. Wallis, *J. Chem. Soc. B, Phys. Org.* 1177 (1966).

¹⁶ Ref. 8a, p. 129.

with its assigned structure. Since this epoxide is essentially the only product formed in the oxidation reaction,¹⁵ the reported¹⁷ stereoselectivity of this reaction with structurally similar α,β -unsaturated ketones such as (-)-verbenone (IX) yielding the epoxide X¹⁷ implies the (3*S*) configuration for (-)-epoxyumbellulone. More recently it has been shown with (\pm)-piperitone that of the two stereoisomeric epoxides



which could be formed by a similar oxidation, it is the more thermodynamically stable isomer which is formed in the greater amount.¹⁹ A critical inspection of Dreiding molecular models²⁰ of the two epoxides of I and of IX, suggests that III and X are, respectively, the more thermodynamically stable.

The ORD curve of III (Fig. 2), reported earlier⁷ and now remeasured, may be compared with that reported^{4,7} for (-)-(1*S*,2*S*)-1-methyl-4-isopropyltricyclo[4.1.0]¹⁻⁶

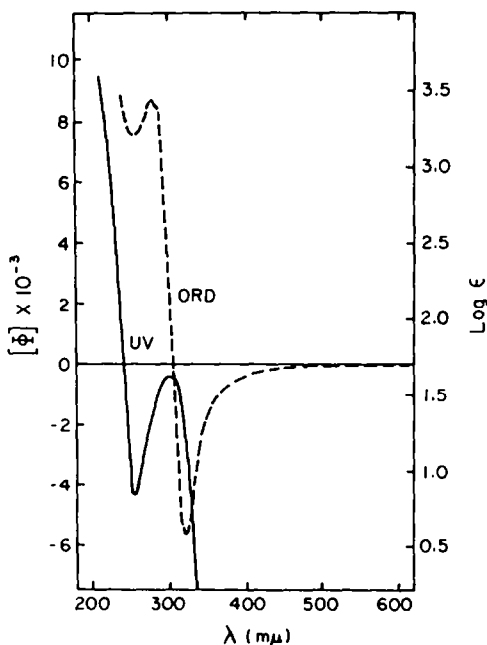


FIG. 2. The UV spectrum and ORD curve of (-)-(3*S*)-epoxyumbellulone (III) in methanol

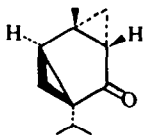
¹⁷ E. Klein and G. Ohloff, *Tetrahedron* **19**, 1091 (1963).

¹⁸ N. S. Bhacca and D. H. Williams, *Applications of NMR Spectroscopy in Organic Chemistry*, p. 42, Holden-Day, San Francisco, Calif. (1964).

¹⁹ W. R. Jackson and A. Zurqiyah, *J. Chem. Soc., B, Phys. Org.* **49** (1966).

²⁰ A. S. Dreiding, *Helv. Chim. Acta* **42**, 1339 (1959).

.0²,⁴]heptan-5-one (XI).²¹ Both ketones show a negative Cotton effect for the carbonyl $n - \pi^*$ transition, with a somewhat larger negative apparent amplitude for XI. The two cyclopropyl rings in XI and the oxirane and cyclopropyl rings in III both occupy,



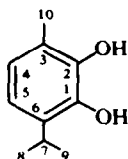
XI

according to the "reverse" Octant Rule,⁴ negative octants with each tricyclic system having a chair-like conformation with a planar cyclopentanone ring.

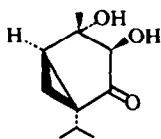
For XI, also prepared from I,²¹ the total configuration has been inferred²² from its mode of preparation,²¹ the configuration of the additional cyclopropane ring being assigned on the basis that the Michael addition of diethyl malonate to I, producing the key intermediate in the synthesis of XI, occurs from the less hindered side, remote from the cyclopropyl ring in I.

The two keto diols IV and V were formed by the acid catalyzed hydrolysis of the oxirane ring in III, and were isolated in about a 1:4 ratio, respectively. The ketone IV, (-)-(3*S*,4*S*)-3,4-hydroxydihydroumbellulone, was also formed by potassium permanganate and osmium tetroxide oxidations of I, and is assigned the (3*S*,4*S*) configuration on the basis of the latter two oxidations, the oxidizing agents attacking I from its less hindered side.²³ The structure of IV is confirmed by its UV (Fig. 3) and NMR (Table 1) spectra, the former being similar to those of other conjugated cyclopropyl ketones,^{21, 24} and by its conversion on treatment with hot, aqueous sodium hydroxide and then acidification to 2-hydroxythymol (XII).

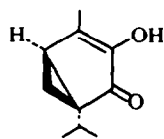
Since IV is certainly a *cis*-glycol, the keto diol V is assigned a *trans*-glycol configuration. This assignment is in agreement with the expectation that the predominant



XII



XIII



XIV

product from the acid catalyzed hydrolysis of an oxirane ring would lead to a *trans*-glycol.²⁵ Of the two possible *trans*-glycols V and XIII, it is concluded that it

²¹ R. H. Eastman, *J. Am. Chem. Soc.* **76**, 4115 (1954).

²² T. Norin, *Acta Chem. Scand.* **17**, 738 (1963).

²³ E. L. Eliel, N. L. Allinger, S. J. Angyal and G. A. Morrison, *Conformational Analysis* p. 284. Interscience, New York, N.Y. (1965).

²⁴ H. E. Smith and R. H. Eastman, *J. Am. Chem. Soc.* **79**, 5500 (1957).

²⁵ R. E. Parker and N. S. Isaacs, *Chem. Revs.* **59**, 737 (1959).

is the former which results from acid hydrolysis since the electron-withdrawing effect of the carbonyl group would be expected to favour the back-side attack of the entering nucleophile on the oxirane ring at C-4.²⁵ The structure of V is confirmed by its UV (Fig. 3) and NMR (Table 1) spectra and its reported¹⁵ conversion on treatment with hot, aqueous sodium hydroxide and then acidification to α -hydroxyumbellulone (XIV).

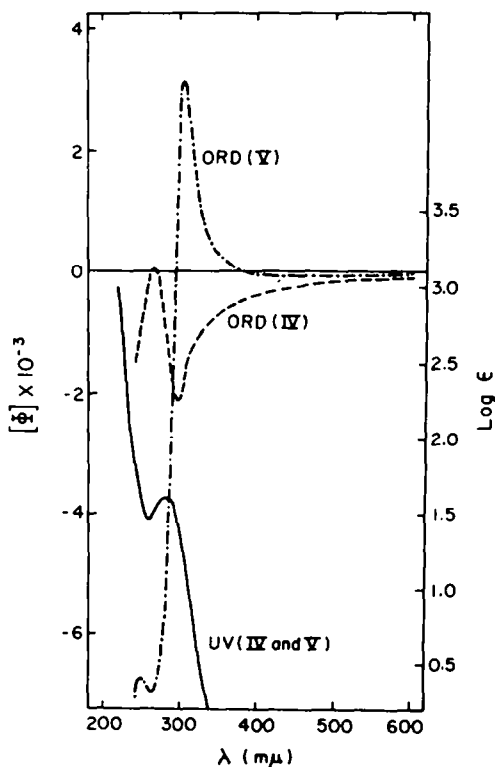
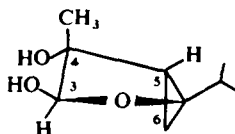


FIG. 3. The UV spectra and ORD curves of (-)-(3*S*,4*S*)-3,4-dihydroxydihydroumbellulone (IV) and (-)-(3*S*,4*R*)-3,4-dihydroxydihydroumbellulone (V) in methanol.

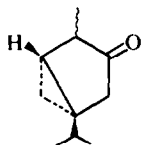
The ORD curves of IV and V (Fig. 3) are of considerable interest and confirm their respective assignments of configuration, the change in configuration of C-4 resulting in a change in the sign of the Cotton effect associated with the carbonyl $n - \pi^*$ transition near 284 $m\mu$. For V, an inspection of Dreiding models²⁰ and the positive Cotton effect suggest that the bicyclic system, in order to relieve the torsional strain



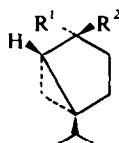
XV

between substituents at C-3, C-4 and C-5, has a boat-like conformation, the extreme form of which is shown as XV. In the preferred conformation the cyclopropane ring is somewhat symmetrically orientated with regard to the plane of the carbonyl group, and the positive Cotton effect results from both the ring carbon C-4 and the methyl group at C-4 occupying the far, upper left octant. It is assumed that, as with the α -hydroxycyclohexanones,²⁶ the influence on the ORD curve of the hydroxyl groups at C-3 and C-4 is insignificant. A chair-like conformation, although relieving the torsional strain between the groups at C-3 and C-4, would result in the C-4 methyl group eclipsing the hydrogen atom at C-5 and the hydroxyl group at C-4 being close to one of the methylene hydrogens at C-6.

It is to be noted that a similar boat-like conformation has been deduced for the two isomeric thujones (XVI),²⁷ for the thujyl alcohols^{27a} and amides¹ derived from these ketones and for (+)-isothujane (XVIIa).²⁸ In comparison, (-)-thujane (XVIIb) has a half-chair conformation.²⁸



XVI

XVIIa: R¹ = CH₃; R² = HXVIIb: R¹ = H; R² = CH₃

A comparison of a Dreiding model²⁰ of the *cis*-glycol IV with those of the thujane derivatives mentioned above suggests that the former has preferentially a flattened boat-like conformation similar to that of V, the OH groups still being close enough for effective intramolecular hydrogen bonding.

It is to be noted that in the NMR spectra of the epoxy ketone III and the two glycol ketones IV and V, the hydrogen atom at C-3 is coupled to the hydrogen atom at C-5²⁹ with an equal coupling constant (Table 1). Since the cyclopentanone ring in III is essentially flat, the similarity of these coupling constants indicates that the cyclopentanone ring in both IV and V is distorted from planarity only to a small degree,²⁹ and that the difference in the sign of the Cotton effect in the ORD curves of IV and V is due to the Me group in its preferred conformation in the former occupying a positive (far, upper left) octant and in the latter being in a negative (far, lower left) octant or close to the plane of the CO group.

It is also likely that (-)- β -dihydrourbellulone (XVIII)¹⁵ which in methanol and in dioxan shows a negative Cotton effect near 290 m μ ,^{4,7} has a similar boat-like conformation. This ketone, prepared in almost quantitative yield by the Raney nickel catalyzed reduction of I,¹⁵ can be assigned the (4*S*) configuration on the basis of this reduction, the *cis* addition of hydrogen to the double bond in I occurring from the

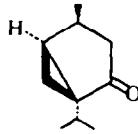
²⁶ Ref. 8a, p. 111.

²⁷ " M. S. Bergqvist and T. Norin, *Arkiv. Kem* **22**, 137 (1964); " K. Tori, *Chem. Pharm. Bull. Tokyo* **12**, 1439 (1964)

²⁸ A. Dieffenbacher and W. von Philipsborn, *Helv. Chim. Acta* **49**, 897 (1966).

²⁹ Ref. 18, p. 115

side remote from the cyclopropane ring. This configurational assignment for (-)- β -dihydroumbellulone is confirmed by the similarity of its ORD curve to that of IV.



XVIII

Cyclopent-2-en-1-ones. The three compounds with the monocyclic cyclopent-2-en-1-one system (VI-VIII) were obtained through the bromination of I.^{12,13} When the crude product from this reaction is distilled, hydrogen bromide is evolved and one product is (-)-umbellulone dibromide (VI)^{12,13} which on reduction with zinc in acetic acid gives (-)-bromodihydroumbellulone (VII).^{12,13} The configuration of each of these two ketones was deduced by the conversion of the latter to (-)-*S*-5-isopropyl-5-methyl-3-oxo-1-cyclopentene-1-carboxylic acid (VIII), which was finally oxidized to (+)-*S*- α -methyl- α -isopropylsuccinic acid.^{10,13} NMR measurements (Table I) are in agreement with these structural assignments for VI, VII and VIII.

The ORD curves for VI and VII (Fig. 4) both display a positive Cotton effect

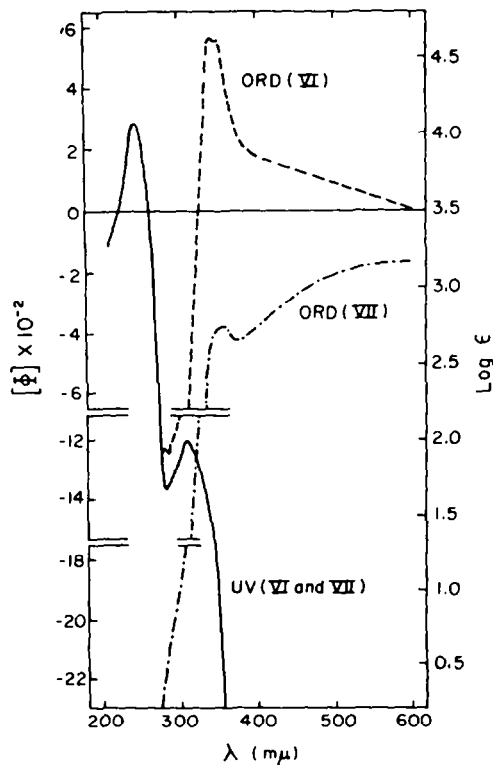


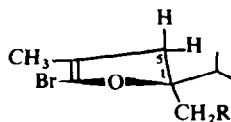
FIG. 4 The UV spectra and ORD curves of (-)-umbellulone dibromide (VI) and (-)-bromodihydroumbellulone (VII) in methanol

associated with the CO $n - \pi^*$ transition at about 308 m μ although for VII this Cotton effect is superimposed on a much stronger negative background curve, presumably associated with the transition at 244 m μ .

An inspection of Dreiding models²⁰ suggests that both VI and VII have, for relief of the torsional strain between the groups at C-1 and the hydrogen atoms at C-5,



XIX

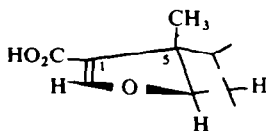


XXa: R = Br

XXb: R = H

a nonplanar conformation. On the basis of the preferred conformation of (-)- α -phellandrene (XIX),³⁰ for which it has been recently verified that the isopropyl group is quasi-equatorial,^{30b} it is concluded that the preferred conformation of both VI and VII is such that in each the isopropyl group is also quasi-equatorial (XX).³¹ Comparison of the Cotton effect displayed by bi- and tetracyclic cyclopent-2-en-1-ones^{5b, 32} with those shown by VI and VII supports the assignment of the preferred conformation for each of these ketones. In each the bromine atom at C-3 lies almost in the plane of the CO group and has, as in II when compared with I, only a small effect on the shape of the ORD curve.

For VIII, relief of torsional strain probably also causes a distortion of the ring to a nonplanar conformation with the isopropyl group quasi-equatorial (XXI). Assuming



XXI

that a carboxyl group at C-1 has an insignificant influence on the Cotton effect associated with the $n - \pi^*$ transition of a C-5 substituted cyclopent-1-en-3-one, the positive Cotton effect near 338 m μ shown by VIII (Fig. 5) also indicates a nonplanar conformation, such as XXI, for this ketone.^{5b}

³⁰ ^a H. Ziffer, E. Charney and U. Weiss, *J. Am. Chem. Soc.* **84**, 2961 (1962); ^b G. Snatzke, E. sz. Kovats and G. Ohloff, *Tetrahedron Letters* 4551 (1966).

³¹ In this latter connection and below, the term quasi-equatorial is used to mean that, due to the puckering of the cyclopentenone ring but without any specification as to the degree, the attachment bond of the group in question lies more in the best plane defined by the ring atoms that would be the case for a completely planar ring. In fact, a three-dimensional X-ray analysis (P. G. Lenhart, R. T. Gray, T. J. Shaffner and H. E. Smith, unpublished results) shows that VII in the crystalline state is nearly planar with C-5 not more than 0.1 Å out of the best plane defined by C-1, C-2, C-3 and oxygen. The deviation of C-5 from this plane, however, is in the direction which causes the isopropyl group to be quasi-equatorial, a crude representation of which is shown as XXb.

³² See especially XCI and XCIII in ref. 5b; F. Sondheimer, S. Burstein and R. Mechoulam, *J. Am. Chem. Soc.* **82**, 3209 (1960).

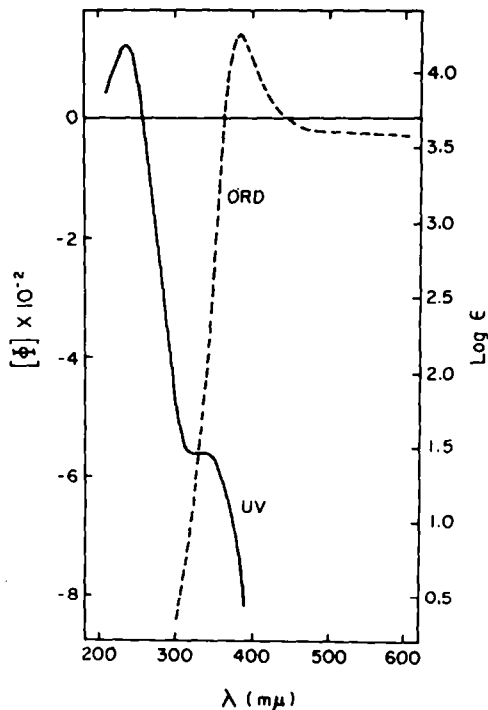


FIG 5. The UV spectrum and ORD curve of (—)(*S*)-5-isopropyl-5-methyl-3-oxo-1-cyclopentene-1-carboxylic acid (VIII) in methanol.

EXPERIMENTAL

M.ps were taken in capillary tubes and are corrected. B.ps are not corrected. Optical rotations at the sodium D-line were measured using 1-dm tubes and unless otherwise noted MeOH was the solvent. Microanalyses were done by Galbraith Laboratories Inc., Knoxville, Tenn. IR spectra were obtained using a Beckman Model IR-10 spectrophotometer and were measured as KBr pellets. UV spectra were measured with Cary Model 14 spectrophotometer using 10-mm cells and MeOH as solvent. ORD curves were obtained at 25° using a Rudolph automatic recording spectropolarimeter, Model 260/658/850/-810-614. The slit width was 0.4 mm with a scan speed of 7–28 mμ/min, a symmetrical angle of 4°, and a sample tube length of 100 mm. Unless otherwise noted the solvent was MeOH, and the curves are reported by indicating the molecular rotation, $[\phi]$, at 600 mμ or at the wavelength at which cut off occurred at the next higher concentration, at 589 mμ if included and at the wavelength of each extremum and inflection, at which the rotation changed sign, and at cut-off. The following abbreviations are used: pk = peak, tr = trough, i = inflection. Cut-off was indicated when the voltage on the photomultiplier tube reached 600 V. NMR spectra were measured with a Varian Model A-60 spectrometer³³ operating at 60 Mc/s on CDCl₃ solns with TMS as the internal standard. All chemical shifts are reported in ppm downfield from the standard. Coupling constants, *J*, are reported in c/s.

(—)-*Umbellulone*³⁴ (I), b.p. 52° (0.9 mm), n_D^{24} 1.4825, $[\alpha]_D^{26}$ –36.7° (neat, 1 dm), $[\alpha]_D^{25}$ –32° (c 1.14) [lit.¹³ $[\alpha]_D^{25}$ –39.4 (neat)]; UV: $\epsilon_{327\text{m}\mu}^{25}$ 190, $\epsilon_{263\text{m}\mu}^{25}$ 3700, $\epsilon_{217\text{m}\mu}^{25}$ 7400; ORD: (c 0.114) $[\phi]_{600}$ –110°, $[\phi]_{589}$

³³ We acknowledge the generosity of the National Science Foundation for a grant (GP-1683) to the Department of Chemistry, Vanderbilt University for the purchase of this instrument.

³⁴ We are grateful to Professor Richard H. Eastman, Stanford University for a generous gift of this compound

-110 . $[\phi]_{455} \pm 0$. $[\phi]_{350} + 7300$ (pk). $[\phi]_{334} \pm 0$; (c 0.0114) $[\phi]_{334} \pm 0$. $[\phi]_{290} - 43.800$ (tr). $[\phi]_{275} - 15.800$.

(-)- α -Bromoumbellulone (II) from (-)-umbellulone (I). As described previously.¹⁵ II was prepared by reaction of 7.5 g (0.050 mole) of I in 100 ml of CCl_4 at 0° with 8.0 g (0.050 mole) of Br_2 and the subsequent treatment of the reaction product with 20 ml of piperidine. The crude dehydrobromination product was distilled yielding a colourless oil, b.p. 120–125 (12 mm) which crystallized on standing. Two recrystallizations of this material from pet. ether (b.p. 40–60) gave 2.43 g of II (21%) as prisms, m.p. 33–34. $[\alpha]_D^{25} - 137$ (c 1.55) (lit.¹⁵ m.p. 31–32, no rotational data reported); UV: $\epsilon_{330}^{\text{max}}$ 380. $\epsilon_{276}^{\text{max}}$ 3800. $\epsilon_{220}^{\text{max}}$ 5800; ORD: (c 0.155) $[\phi]_{600} - 410$. $[\phi]_{589} - 410$. $[\phi]_{410} \pm 0$. $[\phi]_{355} + 7030$ (pk). $[\phi]_{338} \pm 0$; (c 0.031) $[\phi]_{338} \pm 0$. $[\phi]_{293} - 68.300$ (tr). $[\phi]_{279} - 39.100$.

(-)- α -Bromoumbellulone (II) from (-)-umbellulone dibromide (VI). A soln of 0.204 g (0.66 mmole) of VI and 0.401 g (4.1 mmoles) of AcOK in 10 ml abs EtOH was boiled for 118 hr. After having been cooled, the soln was diluted with ether and washed with water and then Na_2CO_3 aq. The aqueous washings were extracted with ether, the combined ether solns were dried over Na_2SO_4 and then the ether evaporated yielding a pale yellow oil. Molecular distillation of this oil at 90 (3 mm) gave 0.122 g of II (81%) as colourless needles, m.p. 31–32. $[\alpha]_D^{25} - 134$ (c 2.80). The IR spectrum was identical to that of II prepared directly from I as outlined above.

(-)-3(S)-Epoxyumbellulone (III), m.p. 27–28. $[\alpha]_D^{25} - 19$ (c 1.01) [lit.¹⁵ m.p. 25–26; $\alpha_D^{25} - 20.4$ (neat, 1 dm)]; UV: $\epsilon_{301}^{\text{max}}$ 44; ORD: (c 1.01) $[\phi]_{600} - 23$. $[\phi]_{589} - 23$. $[\phi]_{400} - 370$; (c 0.201) $[\phi]_{400} - 340^\circ$. $[\phi]_{324} - 5660^\circ$ (tr). $[\phi]_{307} \pm 0$. $[\phi]_{286} + 8570^\circ$ (i). $[\phi]_{278} + 8730^\circ$ (pk). $[\phi]_{256} + 7540^\circ$ (tr). $[\phi]_{240} + 8950^\circ$.

(-)-3(S,4S)-3,4-Dihydroxydihydrourbellulone (IV) and (-)-3(S,4R)-dihydroxydihydrourbellulone (V) from (-)-3(S)-epoxyumbellulone (III). A stirred mixture of 2.3 g (0.014 mole) of III, 10 ml of H_2O , and 5 drops of 20% H_2SO_4 was heated on a steam plate for 5 min, during which the mixture became homogeneous. The cooled soln was then thoroughly extracted of the ether and the ethereal soln dried over Na_2SO_4 . Evaporation of the ether left a pale yellow, viscous oil. Distillation of this oil yielded a colourless oil, b.p. 123–125 (1 mm), which solidified on cooling. Recrystallization of this solid from pet. ether (b.p. 40–60) gave 0.96 g of V (38%) as white needles, m.p. 67–68. $[\alpha]_D^{25} - 28$ (c 1.03) (lit.¹⁵ m.p. 65.9–66.7, no rotational data reported); IR: ν^{max} 1730 cm^{-1} (C=O); UV: $\epsilon_{285}^{\text{max}}$ 42; ORD: (c 0.206) $[\phi]_{600} - 60$. $[\phi]_{589} - 70^\circ$. $[\phi]_{390} \pm 0$. $[\phi]_{307} + 3120^\circ$ (pk). $[\phi]_{294} \pm 0$. $[\phi]_{262} - 6960^\circ$ (tr). $[\phi]_{250} - 6700^\circ$ (pk). $[\phi]_{240} - 7070$.

Evaporation of the pet. ether from the mother liquors yielded a solid which on sublimation at 50° (0.1 mm) yielded 0.22 g of IV (9%), m.p. 90–91 (sealed tube). The IR spectrum of this material was distinctly different from that of V but was identical with that of IV obtained as outlined below by the KMnO_4 oxidation of I.

(-)-3(S,4S)-3,4-Dihydroxydihydrourbellulone (IV) by oxidation of (-)-umbellulone (I) with potassium permanganate. An ice-cold mixture of 3.4 g (0.023 mole) of I and 40 ml of H_2O was shaken into an emulsion, and 3.5 g (0.022 mole) of KMnO_4 in 75 ml of H_2O was added with continuous agitation. The MnO_2 ppt was removed by filtration and washed thoroughly with water. The aqueous filtrate and washings were combined and thoroughly extracted with ether. The ethereal soln was dried over Na_2SO_4 and evaporation of the ether yielded a white solid which on sublimation at 50° (0.1 mm) gave 1.4 g of IV (33%) as long, white needles, m.p. 93–95 (sealed tube). $[\alpha]_D^{25} - 70$ (c 0.67); IR: ν^{max} 1740 cm^{-1} (C=O); UV: $\epsilon_{283}^{\text{max}}$ 41; ORD: (c 0.67) $[\phi]_{600} - 98$. $[\phi]_{589} - 100^\circ$. $[\phi]_{298} - 2100$ (tr). $[\phi]_{273} \pm 0$. $[\phi]_{267} + 79^\circ$ (pk). $[\phi]_{264} \pm 0$. $[\phi]_{240} - 1800$. (Found: C, 64.73; H, 8.79; mol. wt. 180, osmometric in CHCl_3 , $\text{C}_{10}\text{H}_{16}\text{O}_3$ requires: C, 65.19; H, 8.75%; mol. wt. 184.)

(-)-3(S,4S)-3,4-Dihydroxydihydrourbellulone (IV) by oxidation of (-)-umbellulone (I) with osmium tetroxide. To 0.66 g (0.26 mmole) of OsO_4 in 25 ml of ice-cold, Na-dried ether was added 0.59 g (0.39 mmole) of I in 15 ml of cold, dry ether. The mixture was allowed to stand at room temp for 3 weeks, after which the black osmate complex was collected and dissolved in dioxan and this soln saturated with H_2S . After removal of the black ppt by filtration, evaporation of the dioxan from the clear, colourless filtrate yielded 0.50 g of white solid which on sublimation at 50° (0.1 mm) gave 0.27 g of IV (56%) as long, white needles, m.p. 92–93 (sealed tube). The IR spectrum of this material was identical to that of IV obtained by the KMnO_4 oxidation of I.

(-)-Umbellulone dibromide (VI), m.p. 120–121. $[\alpha]_D^{26} - 6^\circ$ (c 1.02). $[\alpha]_D^{22} + 6.0^\circ$ (c 3.0, CHCl_3) [lit.¹² m.p. 119–119.5, $[\alpha]_D + 6.4^\circ$ (c 2.1, CHCl_3)]; UV: $\epsilon_{309}^{\text{max}}$ 100; $\epsilon_{247}^{\text{max}}$ 11,000; ORD: (c 1.02) $[\phi]_{600} + 9^\circ$. $[\phi]_{589} + 20$. $[\phi]_{350} + 560$ (pk). $[\phi]_{347} + 554$ (tr). $[\phi]_{340} + 575$ (pk). $[\phi]_{325} \pm 0$. $[\phi]_{285} - 1250$ (tr).

$[\phi]_{280} - 1230$ (pk), $[\phi]_{275} - 1250$; ORD in dioxan: (c 1.55) $[\phi]_{600} + 32$, $[\phi]_{589} + 32$, $[\phi]_{553} + 662$ (pk), $[\phi]_{340} + 467$ (i), $[\phi]_{328} \pm 0$, $[\phi]_{300} - 1010$ (tr), $[\phi]_{298} - 994$ (pk), $[\phi]_{295} - 1000$ (tr), $[\phi]_{270} - 976$.

(-)-*Bromodihydroumbellulone* (VII), m.p. 58-60, $[\alpha]_D^{25} - 60$ (c 1.03), $[\alpha]_D^{25} - 60$ (c 1.5, abs EtOH) [lit.¹² m.p. 58-59, $[\alpha]_D - 70.1$ (c 1.7, CHCl₃)]; UV: $\epsilon_{307\text{ m}\mu}^{\text{max}}$ 100, $\epsilon_{244\text{ m}\mu}^{\text{max}}$ 12,000; ORD: (c 1.03) $[\phi]_{600} - 160$, $[\phi]_{589} - 160$, $[\phi]_{375} - 423$ (tr), $[\phi]_{355} - 371$ (pk), $[\phi]_{270} - 2420$.

(-)-*(S)-5-Isopropyl-5-methyl-3-oxo-1-cyclopentene-1-carboxylic acid* (VIII), m.p. 194-195, $[\alpha]_D^{25} - 15$ (c 1.11) [lit.¹⁰ m.p. 194-196, $[\alpha]_D^{22-25} - 11$ (c 3.2, 95% EtOH)]; UV: $\epsilon_{338\text{ m}\mu}^{\text{max}}$ 29, $\epsilon_{236\text{ m}\mu}^{\text{max}}$ 15,000; ORD: (c 1.11) $[\phi]_{600} - 31$, $[\phi]_{589} - 29$, $[\phi]_{443} \pm 0$, $[\phi]_{387} + 140$ (pk), $[\phi]_{364} \pm 0$, $[\phi]_{300} - 840$.

2-Hydroxythymol (XII) from (-)-(3S,4S)-*dihydroxydihydroumbellulone* (IV) To a solution of 0.42 g (2.5 mmoles) of IV in 10 ml of water was added 1 ml of 10% sodium hydroxide solution. The mixture was refluxed for five minutes, and after it had cooled to room temperature, it was acidified with 10% hydrochloric acid. The brown solid which separated was collected by filtration, and recrystallization of this solid from *n*-hexane yielded 0.10 g of XII (24%) as small, white needles, m.p. 91-92° (lit.¹⁵ m.p. 90-1-90.8°).

The NMR spectrum is consistent with structure XII: 1.20 ppm (doublet, 6H, $J_{7-8/9} 7.0 \pm 0.5$ cps, assigned to C-8 and C-9 protons), 2.25 ppm (singlet, 3H, assigned to C-10 protons), ca. 2.6 ppm (multiplet, 1H, $J 7.0 \pm 0.5$ c/s, assigned to C-7 proton), 5.28 ppm (broad singlet, 2H, assigned to C-1 and C-2 hydroxyl protons), 6.60 ppm (singlet, 2H, assigned to C-4 and C-5 protons).

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