Terpenes. V. The Preferred Conformation and Spectral Properties of Some Optically Active 2-Cyclopenten-1-ones[1]

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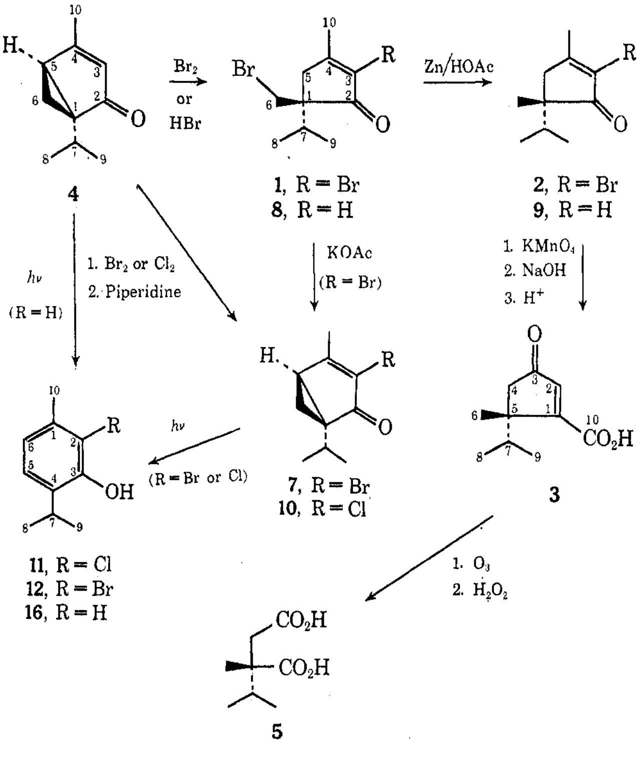
Received May 27, 1968

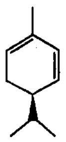
A single crystal X-ray diffraction study reveals that for (−)-bromodihydroumbellulone (**2**) [(−)-(S)-3-bromo-1,4-dimethyl-1-isopropyl-3-cyclopenten-2-one], the attachment bond of the isopropyl group is oriented closer to the ring plane than is that of the methyl group at C-1. In addition, a comparison of the uv absorption spectra of two 3-methyl-2-cyclopenten-1-ones (**8** and **9**) and two 2-bromo-3-methyl-2-cyclopenten-1-ones (**1** and **2**) shows that the more intense π–π^* absorption band, centered at about 229 mμ in the former two ketones, has been bathochromically shifted by 16–17 mμ in the latter. In the ORD curves of these ketones, the Cotton effect associated with the n–π^* transition centered at about 309 mμ is affected hardly at all by the presence of a bromine atom at C-2. In attempts to prepare chloro analogs of **1** and **2**, only (−)-α-chloroumbellulone (**10**) was formed by chlorination of (−)-umbellulone (**4**). Both **10** and (−)-α-bromoumbellulone (**7**) were isomerized to the respective 2-halothymols (**11** and **12**) by a photochemical reaction.

Recently we have reported[1] the ORD curves of three 2-cyclopenten-1-ones, (−)-umbellulone dibromide (**1**),[3–6] (−)-bromodihydroumbellulone (**2**),[4,5] and (−)-(*S*)-5-isopropyl-5-methyl-3-oxo-1-cyclopentene-1-carboxylic acid (**3**).[5] These three compounds were obtained through the bromination of (−)-umbellulone (**4**)[4–6] and subsequent transformations of **1**, one of the products of this bromination reaction (see Scheme I).[4–6] The configuration of each of these ketones had been deduced by the oxidation of **3** to (*S*)-α-methyl-α-isopropylsuccinic acid (**5**),[5,6] a compound of known absolute configuration.[7–9]

The ORD curves of these ketones were of special interest in that only a limited number of ORD and CD studies have been made with 2-cyclopenten-1-ones,[10–15] and in most of the cases studied the ring incorporating the carbonyl group generally has been part of a more extensive ring system[10–15] which constrains the 2-cyclopenten-1-one ring to a particular nonplanar conformation. For the 2-cyclopenten-1-ones **1**, **2**, and **3** a constraint of this type is not present. However, an inspection of Dreiding models[16] suggests that these three ketones have, for relief of the torsional strain between the groups at C-1 and the hydrogens at C-5 in **1** and **2** and the groups at C-5 and the hydrogens at C-4 in **3**, a nonplanar conformation. In addition, on the basis of the preferred conformation of (*R*)-α-phellandrene (**6**)[17,18] for which it has been recently verified by ORD measurements that the isopropyl group is quasi-

Scheme I





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equatorial,[19] it was concluded that the preferred conformation of **1**, **2**, and **3** is such that in each the isopropyl group is quasiequatorial. Comparison of the Cotton effect displayed by each ketone at about 320 mμ with those shown by bi- and tetracyclic 2-cyclo-

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(1) Paper IV: R. T. Gray and H. E. Smith, *Tetrahedron*, **23**, 4229 (1967).

(2) Monsanto Fund Fellow, 1966–1968.

(3) Signs in parentheses refer to rotatory powers observed with sodium D light using methanol as the solvent. It is to be noted that **1** is dextrorotatory in chloroform.[1,4–6] For clarity the carbon atom numbering in **1**, **2**, **8**, and **9** is the same as in **4**.

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

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

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

(7) J. Porath, *Arkiv Kemi*, **1**, 385 (1949).

(8) K. Freudenberg and W. Lwowski, *Ann. Chem.*, **587**, 213 (1954).

(9) M. R. Cox, H. P. Koch, W. B. Whalley, M. B. Hursthouse, and D. Rogers, *Chem. Commun.*, 212 (1967).

(10) C. Djerassi, "Optical Rotatory Dispersion," McGraw-Hill Book Co., Inc., New York, N. Y., 1960, pp 60, 83.

(11) C. Djerassi, *Proc. Chem. Soc.*, 314 (1964).

(12) C. Djerassi and J. E. Gurst, *J. Amer. Chem. Soc.*, **86**, 1755 (1964).

(13) P. Crabbé, "Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry," Holden-Day, Inc., San Francisco, Calif., 1965, p 191.

(14) G. Snatzke, *Tetrahedron*, **21**, 413 (1965).

(15) G. Snatzke, *ibid.*, **21**, 421 (1965).

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

(17) H. Ziffer, E. Charney, and U. Weiss, *J. Amer. Chem. Soc.*, **84**, 2961 (1962).

(18) U. Weiss, H. Ziffer, and E. Charney, *Tetrahedron*, **21**, 3105 (1965).

(19) G. Snatzke, E. sz. Kováts, and G. Ohloff, *Tetrahedron Lett.*, 4551 (1966).

penten-1-ones[15] supports the assignments of this preferred conformation to **1**, **2**, and **3**. It was also concluded, on the basis of a comparison of the ORD curves of (−)-umbellulone (**4**) and (−)-α-bromoumbellulone (**7**),[20] which are very similar,[1] that the bromine at C-3 in **1** and **2**, lying in or near the plane of the carbonyl group, and the carboxyl group at C-1 in **3** have only a small or an insignificant influence on the Cotton effect associated with the carbonyl n–π* transition at about 320 mμ, much the same as is observed with 2-halo-2-cyclohexen-1-ones.[21,22]

We now wish to report measurements which give direct, experimental confirmation concerning the preferred conformation of 5-substituted 2-cyclopenten-1-ones and in these same compounds the effect of bromine at C-2 on the Cotton effect associated with the n–π* transition. First, we have done a single crystal X-ray diffraction[23] study of (−)-bromodihydroumbellulone (**2**) which reveals its preferred conformation in the crystalline state. Second, we have prepared and measured the ORD curves of (−)-(*R*)-1-(bromomethyl)-1-isopropyl-4-methyl-3-cyclopenten-2-one (**8**) and (−)-(*S*)-1,4-dimethyl-1-isopropyl-3-cyclopenten-2-one (**9**), both ketones being derived from (−)-umbellulone (**4**) (Scheme I). We also report the preparation and ORD curve of (−)-α-chloroumbellulone (**10**). In connection with the assignment of structure to **10**, both this ketone and (−)-α-bromoumbellulone (**7**) were converted into the respective 2-halothymols (**11** and **12**) by a photochemical reaction.[24]

Results and Discussion

Crystallographic Measurements.—The structure of (−)-bromodihydroumbellulone (**2**) was determined by single crystal X-ray diffraction.[23] Details of the structure analysis, final atomic coordinates (Table IV), and thermal parameters (Table IV) are given in the Experimental Section.

In the crystal there are two crystallographically independent molecules, denoted A and B. Their conformations are nearly identical. Figure 1 is an arbitrary projection of A showing the numbering of the atoms.

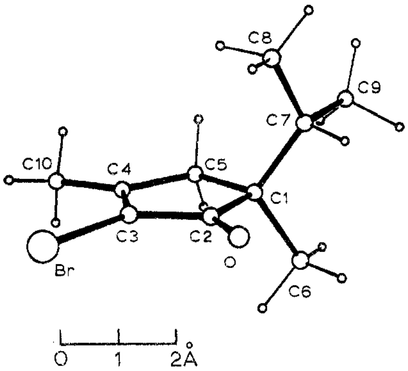

Figure 1.—An arbitrary projection of molecule A in crystalline (−)-bromodihydroumbellulone (2).

One can see in Figures 2a and 2b, referring to A and B, respectively, that in each molecule, four ring atoms, C-2, C-3, C-4, and C-5, the oxygen and bromine atoms and C-10 of the methyl group are all coplanar to within about one standard deviation. The remaining ring atom, C-1, lies below the least-squares plane determined by these atoms. The methyl and isopropyl substituents are displaced downward by a corresponding amount. Figures 2c and 2d, referring to A and B, respectively, show projections down the carbonyl bond, from oxygen to C-2. In Table I are listed the observed bond lengths and angles with standard deviations for each molecule, and for an average of the two. Most values differ by less than one standard deviation.

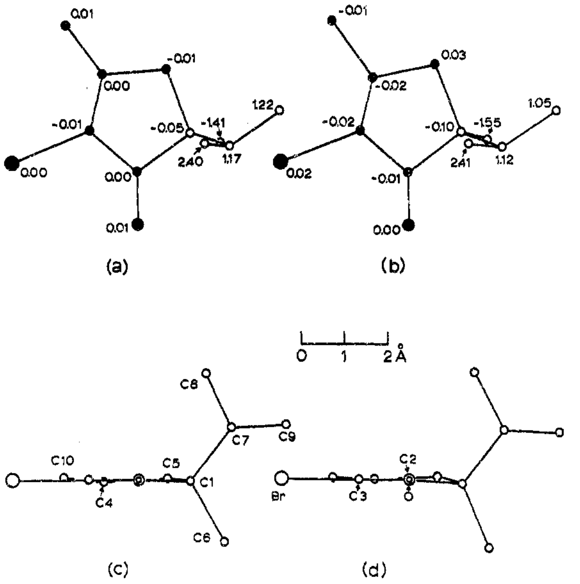

Figure 2.—(−)-Bromodihydroumbellulone (2) molecules A and B are shown in a and b, respectively, as projected normal to the best least-squares plane defined by the atoms represented by filled circles (C-2, C-3, C-4, C-5, C-10, oxygen, and Br). The distance of all atoms from this plane are given in angstroms. Molecules A and B are shown in c and d, respectively, as projected down the carbonyl bond, from oxygen to C-2. The atoms in c and d are directly below the corresponding atoms in a and b.

The only significant conformational difference between A and B involves the substituents at C-1. This difference is described in Figures 2a and 2b where the distances from the ring planes are given. The isopropyl group in A is rotated about the C-7 to C-1 bond in a counterclockwise direction, as viewed from C-7 toward C-1. This rotation decreases the dihedral angle between the planes defined by C-1, C-7, and C-8 and by C-2, C-1, and C-7 from 53.5° in B to 50.6° in A. A 3.8-Å contact between C-9 of A and C-10 of B, translated by $-a$ and $+c$ with respect to the coordinates in Table IV, may be responsible for the rotation. All other intermolecular contacts correspond to normal van der Waals distances.

In the absence of contrary steric factors, one would expect a 2-cyclopenten-1-one to be planar or to be only slightly puckered for relief of torsional strain between the substituents at C-4 and C-5. For (−)-bromodihydroumbellulone (**2**) any puckering of the ring, causing either the methyl or isopropyl group at C-1 to be quasiequatorial, would relieve torsional strain between the substituents at C-1 and the hydrogen

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[20] R. H. Eastman and J. C. Selover, *J. Amer. Chem. Soc.*, **76**, 4118 (1954).

[21] Reference 10, p 129.

[22] J.-C. Bloch and S. R. Wallis, *J. Chem. Soc., B*, 1177 (1966).

[23] M. J. Buerger, "Crystal-Structure Analysis," John Wiley & Sons, Inc., New York, N. Y., 1960.

[24] J. W. Wheeler, Jr., and R. H. Eastman, *J. Amer. Chem. Soc.*, **81**, 236 (1959).

Table I

Bond Lengths and Angles in Crystalline (−)-Bromodihydroumbellulone (**2**)[a]

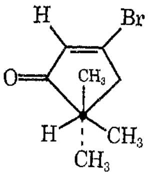
Bond		Molecule A[a]		Molecule B[a]		Average	
		Length, Å	σ^b	Length, Å	σ^b	Length, Å	σ^b
Br	C-3	1.90	0.02	1.90	0.02	1.90	0.01
O	C-2	1.20	0.03	1.20	0.03	1.20	0.02
C-1	C-2	1.49	0.03	1.49	0.03	1.49	0.02
C-1	C-5	1.58	0.03	1.56	0.04	1.57	0.03
C-2	C-3	1.46	0.03	1.43	0.03	1.44	0.02
C-3	C-4	1.34*	0.04	1.28*	0.04	1.31	0.03
C-4	C-5	1.50	0.03	1.47	0.02	1.48	0.02
C-6	C-1	1.57	0.04	1.59	0.04	1.58	0.03
C-7	C-8	1.36*	0.04	1.46*	0.04	1.41	0.03
C-7	C-9	1.50	0.03	1.52	0.03	1.51	0.02
C-7	C-1	1.55	0.04	1.59	0.03	1.57	0.03
C-4	C-10	1.47*	0.03	1.56*	0.04	1.51	0.02

Angle			Molecule A		Molecule B		Average	
Apex	End	End	Deg	σ^b	Deg	σ^b	Deg	σ^b
C-1	C-2	C-5	104	3	103	3	104	2
C-1	C-6	C-2	109	3	107	2	108	2
C-1	C-6	C-5	110	1	111	2	110	1
C-1	C-6	C-7	112*	2	116*	2	114	2
C-1	C-7	C-2	111	2	109	2	110	1
C-1	C-7	C-5	111	2	111	2	111	1
C-2	O	C-1	125	2	125	2	125	2
C-2	C-1	C-3	107	2	108	2	107	1
C-3	Br	C-2	120	2	122	2	121	1
C-3	Br	C-4	127	2	126	2	126	1
C-3	C-2	C-4	113	2	112	2	113	1
C-4	C-3	C-5	110	2	112	2	111	1
C-4	C-10	C-3	128	2	128	2	128	1
C-4	C-10	C-5	123*	2	119*	2	121	2
C-5	C-1	C-4	105	3	104	3	105	2
C-7	C-8	C-1	117*	2	113*	2	115	2
C-7	C-8	C-9	108*	3	113*	3	111	2
C-7	C-9	C-1	115*	2	111*	2	113	2

[a] An asterisk indicates values that differ by more than one standard deviation between molecules A and B. [b] Estimated standard deviation.

atoms at C-5. Puckering in a particular direction must be the summation of the nonbonded interactions, attractive or repulsive, of the methyl and isopropyl groups with the adjacent ring moieties. In both A and B the intramolecular distance between C-8 and C-2 and between C-8 and C-5 is increased by puckering the ring in the direction observed.[25] The ring pucker is 2.8° for A and 6.7° for B,[26] each with the isopropyl group quasiequatorial. Hence an unfavorable repulsive interaction between the C-8 methyl group and the adjacent ring moieties has been relieved by the observed direction of ring pucker.

Since a steric relief between the C-8 methyl group and the adjacent ring moieties appears to be crucial in determining the direction and, for the most part, the degree of ring pucker in A and B in the crystalline state, one should ask whether the isopropyl group assumes the same position in solution. Three staggered orientations, **13**, **14**, and **15**,[27] for this group seem possible. Two of these orientations, **13** and **14**, would give similar interactions between adjacent ring moieties and a methyl group of the isopropyl group. A similar ring pucker is to be expected in both cases. The other



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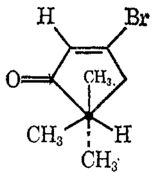

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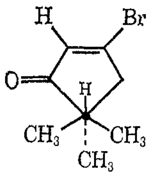

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orientation, **15**, would have some crowding between the isopropyl group and the methyl group at C-1. This position for the isopropyl group might be less likely, but, if present, would not be expected to cause the same degree of ring pucker as is observed for A and B in the crystalline state.

Chemical Conversions and ORD Measurements.—As has been reported earlier,[4,5] on addition of bromine to (−)-umbellulone (**4**) in carbon tetrachloride or chloroform and subsequent distillation of the reaction mixture, one of the products is (−)-umbellulone dibromide (**1**), the other products being hydrogen bromide and an unsaturated bromo ketone, $C_{10}H_{13}BrO$.[4] There has been some speculation concerning the mechanism of the reaction[28-31] and the nature of the unsaturated bromo ketone.[28,29] Our observations[32] indicate that the reaction proceeds by way of an electrophilic addition of bromine to the double bond of **4** followed by rearrangement of the adduct or adducts. Hydrogen bromide should also add electrophilically to the double bond of **4**. The stereochemical course of the reaction is expected to be similar to that in the addition of bromine. Indeed, this is the course of the hydrobromination reaction, and as outlined in the Experimental Section a modest yield of (−)-(*R*)-1-(bromomethyl)-1-isopropyl-4-methyl-3-cyclopenten-2-one (**8**) was obtained by the hydrobromination of **4** in carbon tetrachloride (Scheme I).

The nmr spectrum of **8** (Experimental Section) is compatible with its assigned structure. In addition, as with the conversion of **1** into **2**,[4,5] **8** was smoothly reduced with zinc in acetic acid to (−)-(*S*)-1,4-dimethyl-1-isopropyl-3-cyclopenten-2-one (**9**), the nmr spectrum of the latter also being compatible with its assigned structure. The configuration of **8** and **9** were both confirmed when **9** was oxidized to (−)-(*S*)-5-isopropyl-5-methyl-3-oxo-1-cyclopentene-1-carboxylic acid (**3**), the configurational assignment of which has been discussed above.

The uv absorption spectra of the 2-cyclopenten-1-ones **1**, **2**, **8**, and **9** also confirm their structures. As shown in Table II for the two ketones, **8** and **9**, with hydrogen at C-3, the more intense π–π^* band at 230 and 228 mμ, respectively, has been bathochromically shifted by about 15 mμ from the base value of 214 mμ for 2-cyclopenten-1-one[33,34] to just within the predicted

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(25) In A the distances are 2.92 and 3.11 Å and in B, 2.91 and 3.06 Å, respectively.

(26) The pucker angle is defined as the acute dihedral angle formed by the least-squares plane of Figure 2 and the C-2, C-5, and C-1 plane.

(27) **13**, **14**, and **15** are Newman projections down the bond C-7 to C-1.

(28) A. Oken, Ph.D. Dissertation, Stanford University, Stanford, Calif., 1952.

(29) J. C. Selover, Ph.D. Dissertation, Stanford University, Stanford, Calif., 1953.

(30) P. de Mayo in "The Chemistry of Natural Products," Vol. II, K. W. Bentley, Ed., Interscience Publishers, New York, N. Y., 1959, p 110.

(31) J. F. King and P. de Mayo in "Molecular Rearrangements," part II, P. de Mayo, Ed., Interscience Publishers, New York, N. Y., 1964, p 807.

(32) R. T. Gray and H. E. Smith, unpublished data.

(33) R. L. Frank, R. Armstrong, J. Kwiatek, and H. A. Price, *J. Amer. Chem. Soc.*, **70**, 1379 (1948).

(34) J. C. D. Brand and A. I. Scott in "Elucidation of Structures by Physical and Chemical Methods," part I, K. W. Bentley, Ed., Interscience Publishers, New York, N. Y., 1963, p 61.

value of 224–226 ± 5 mμ for 3-alkyl-2-cyclopenten-1-ones.[33–35] The presence of a bromine atom at C-3 in **1** and **2** also produces a bathochromic shift, the increment being 17 and 16 mμ, respectively. This shift is somewhat smaller than the 25-mμ increment assigned for a bromine atom at this position,[34,35] and it may be that, for 2-bromo-2-cyclopenten-1-ones, 16–17 mμ is a more correct value.

TABLE II
SUMMARY OF ULTRAVIOLET ABSORPTION DATA FOR 2-CYCLOPENTEN-1-ONES IN METHANOL

Compd	$\lambda^{\max}$, mμ	ϵ
1	309	100
	247	11,000
2	307	100
	244	12,000
8	310	80
	230	13,000
9	310	84
	228	14,000

The ORD curves of the ketones **8** and **9** are compared with those of **1** and **2** in Figure 3. As predicted,[1] and in agreement with 2-halo-2-cyclohexen-1-ones,[21,22] the bromine atom at C-2 in these optically active 2-cyclopenten-1-ones (**1** and **2**), lying almost in the plane of the carbonyl group, has only a small effect on the ORD curve. For the change **1** to **8**, removal of the bromine atom at C-3 in **1** causes the Cotton effect associated with the n–π* transition of **8** at 310 mμ to be superimposed on a stronger background curve, presumably associated with the transition at 230 mμ. As with the change **1** to **2**, removal of the bromine atom at C-6 in **8** causes the negative background curve of **9** to be even stronger, the result being that **2** and **9** have almost identical ORD curves.

In experiments to prepare chloro-substituted 2-cyclopenten-1-ones analogous to **1**, **2**, and **8**, both chlorine and hydrogen chloride were added to (−)-umbellulone (**4**) in carbon tetrachloride.[32] In the case of chlorine, addition to the double bond occurs but the adduct or adducts did not rearrange to a monocyclic dichlorocyclopentenone. Rather, on heating hydrogen chloride is evolved and the sole product is (−)-α-chloroumbellulone (**10**). As outlined in the Experimental Section, this compound was also prepared, similar to a preparation of (−)-α-bromoumbellulone (**7**),[20] by treatment of the chlorination product of **4** in cold carbon tetrachloride with piperidine. The structure of **10** is confirmed by its nmr spectrum (Experimental Section) and may be compared with those of **4** and **7**, published earlier.[1] The uv spectra and ORD curves of these three ketones are very similar,[1] the ORD curve of **10** being in accord with its assigned configuration.

In the case of the addition of hydrogen chloride to (−)-umbellulone (**4**) in carbon tetrachloride, reaction occurred but again the adduct or adducts did not rearrange to a chlorocyclopentenone.[32] Heating of the reaction mixture or treatment of the product in cold carbon tetrachloride with piperidine returned only **4**.[32]

Earlier it had been reported that on uv irradiation (−)-umbellulone (**4**) is isomerized to thymol (**16**).[24] This general reaction of bicyclo[3.1.0]hex-3-en-2-ones[24,36] should yield the corresponding 2-halothymols, **11** and **12**, on irradiation of (−)-α-chloroumbellulone (**10**) and (−)-α-bromoumbellulone (**7**). Indeed, irradiation of **7** and **10** afforded the corresponding thymols **12** and **11**, respectively (Scheme I), thus confirming the assignments of the structures of **7** and **10**. The nmr spectra of **11** and **12** are compatible with their assigned structures. The physical properties of **12** were identical with those of an authentic sample but different from those of 6-bromothymol, the two latter compounds being prepared by the direct bromination of thymol.

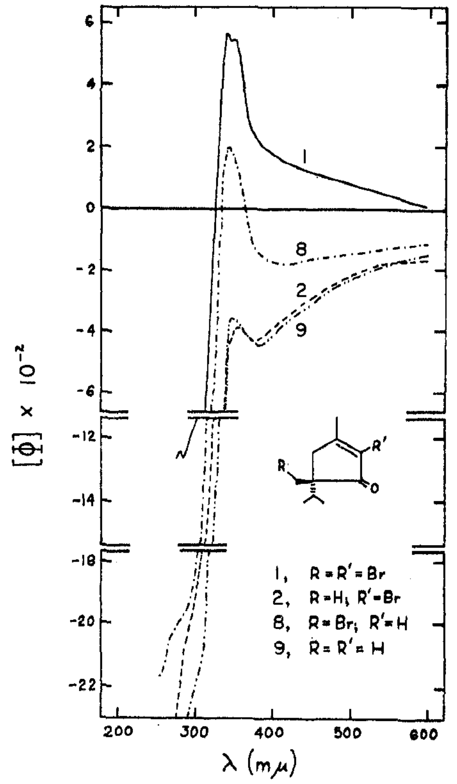

Figure 3.—The ORD curves of (−)-umbellulone dibromide (**1**), (−)-bromodihydroumbellulone (**2**), (−)-(*R*)-1-(bromomethyl)-1-isopropyl-4-methyl-3-cyclopenten-2-one (**8**), and (−)-(*S*)-1,4-dimethyl-1-isopropyl-3-cyclopenten-2-one (**9**) in methanol.

Experimental Section

Crystallographic Measurements.—(−)-Bromodihydroumbellulone (**2**) crystallizes in the monoclinic space group $P2_1$ with four molecules in the unit cell (two in each asymmetric unit). The cell constants are a = 10.19, b = 11.13, and c = 10.11 Å and β = 103.4°. Crystals grown by sublimation were found to be suitable for X-ray diffraction. The experimental density, determined by flotation in a CsCl solution, is 1.39 g/cm³ and the calculated density is 1.38 g/cm³. The linear absorption coefficient is 38.56 cm⁻¹ for molybdenum Kα radiation.

Intensity measurements were made using a crystal approximately 0.5 mm square coated with a thin layer of silicone stopcock grease and mounted in a thin-walled glass capillary. This prevented sublimation which takes place in a few hours under X-radiation at room temperature. Intensities of the Bragg reflections were measured with a Picker full circle diffractometer using the 2θ scan technique.[23] All measurements were made with molybdenum Kα radiation at a scan rate of 2°/min in 2θ. Of

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[35] J. C. D. Brand and G. Eglinton, "Applications of Spectroscopy to Organic Chemistry," Oldbourne Press, London, 1965, p 171.

[36] R. Fraisse-Jullien, C. Frejaville, V. Toure, and M. Derieux, *Bull. Soc. Chim. Fr.*, 3725 (1966).

the 1884 reflections with $2\theta \leq 50°$, 1442 were observed.[37] Table III summarizes data taking procedures.

TABLE III

DATA TAKING PROCEDURES

2θ, deg	Resolution, Å	Technique
0–10	4.08	Ross balanced filters (Zr and Y) in the diffracted beam
10–42	1.00	No filters
42–50	0.85	0.015-mm Zr filter in the incident beam

Coordinates of the two bromine atoms were found with little difficulty from a three-dimensional Patterson synthesis, and the coordinates of the remaining atoms were determined by minimum function techniques. The first difference synthesis, phased on the complete trial structure, gave an initial residual $R = \Sigma \,||F_o| - |F_c|| / \Sigma |F_o|$ of 27.7%. Three rounds of differential synthesis[38] refined the bromine coordinates and anisotropic thermal parameters to a residual of 16.0%. A second difference synthesis followed by three rounds of differential synthesis with all atoms refined anisotropically brought the residual to 9.5%. Hydrogen coordinates uniquely determined by the positions of their bonding carbon atoms were calculated; hydrogen coordinates for the methyl groups were estimated from a third difference synthesis.

Six cycles of full-matrix least squares[39,40] were calculated with all hydrogen parameters fixed. The five ring carbon atoms were refined isotropically and all other atoms anisotropically. All observed and unobserved reflections were included; the final residual was 9.3%. Since the ring atoms showed nearly isotropic thermal motion following differential synthesis, they were refined isotropically in order to allow all variables to be included in the normal equations simultaneously. Full-matrix refinement was desirable because of a pseudo-*n*-glide symmetry which gave correlation matrix elements as large as 0.4 between some parameters of atoms related by the pseudosymmetry. Generally, thermal motion was large, as expected for soft crystals with a low melting point. Final coordinates and thermal parameters are given in Table IV.

General Procedures.—Melting points were taken in capillary tubes and are corrected. Boiling points are not corrected. Optical rotations at the sodium D line were measured using 1-dm tubes and, unless otherwise noted, methanol 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 potassium bromide pellets (ν_{KBr}) or as capillary films (ν_{cap}) between potassium bromide plates. Uv spectra were measured with a Cary Model 14 spectrophotometer using 10-mm cells. ORD curves were obtained at 25° using a Rudolph automatic recording spectropolarimeter, Model 260/658/850/810-614.[41] The slit width was variable (0.4–1.0 mm) with a scan speed of 7–28 mμ/min, a symmetrical angle of 4°, and a sample tube length of 10 mm,[42] cutoff being indicated when the voltage on the photomultiplier tube reached 600 V. The solvent was methanol, and the curves are reported as outlined previously.[1] Nmr spectra were measured with a Varian Model A-60 spectrometer[43] operating at 60 MHz on deuteriochloroform solutions. Chemical shifts are reported in parts per million from TMS = 0. Coupling constants were estimated to ±0.5 Hz.

The photochemical reactions were done by irradiation with a Sylvania 400-W medium pressure mercury lamp (H33-1CD/RS) immersed in an American Instrument Co. constant-temperature laboratory bath at 25°. The Pyrex tubes containing the samples during irradiation did not transmit light below 300 mμ.

The oxyacetic acid derivatives of phenols **11** and **12** and of 6-bromothymol were prepared according to a previously described procedure.[44] Owing to the cryptophenolic nature of these compounds, only low yields of the derivatives were obtained.

(−)-**Bromodihydroumbellulone** (**2**) had mp 58–60° and $[\alpha]^{25}_{\text{D}}$ −60° (*c* 1.03) [lit.[4] mp 58–59°, $[\alpha]_{\text{D}}$ −70.1° (*c* 1.7, $CHCl_3$)].

(−)-(*R*)-**1-(Bromomethyl)-1-isopropyl-4-methyl-3-cyclopenten-2-one** (**8**).—Hydrogen bromide gas was passed for 5 min through a stirred, ice-cold solution of 14.1 g (0.0939 mol) of (−)-umbellulone (**4**),[45] α^{26}_{D} −36.7° (neat, 1 dm),[46] $[\alpha]^{25}_{\text{D}}$ −32° (*c* 1.14) [lit.[5] $[\alpha]^{25}_{\text{D}}$ −39.4° (neat)], in 100 ml of carbon tetrachloride. The pale brown solution was washed with 50 ml of water and then dried ($MgSO_4$). Evaporation of the solvent left a fuming, brown oil. On fractional distillation of this oil, first there was evolved a substantial amount of hydrogen bromide, and then 10.0 g of a colorless oil was distilled, bp 74–75° (1.7 mm), which did not contain bromine[47] and 3.92 g of a pale yellow oil, bp 85–91° (1.7 mm), which partially crystallized on cooling. Recrystallization of this latter material from petroleum ether (bp 40–60°) gave 1.51 g of **8** (7.0%) as long white needles, mp 83–84°. Elemental analyses of this material indicated solvation by petroleum ether.

Anal. Calcd for $C_{10}H_{15}BrO$: C, 51.96; H, 6.54; Br, 34.57. Found: C, 56.01; H, 7.36; Br, 32.46.

Sublimation then at 60° (0.3 mm) gave an analytically pure sample of **8** as white needles: mp 85–86°; $[\alpha]^{25}_{\text{D}}$ −40° (*c* 1.40); ir, $\nu^{\text{max}}_{\text{KBr}}$ 1610, 1690 cm^{-1}; ORD (*c* 1.03), $[\phi]_{600}$ −107°, $[\phi]_{589}$ −109°, $[\phi]_{410}$ −172° (tr), $[\phi]_{365}$ ±0°, $[\phi]_{343}$ +205° (pk), $[\phi]_{334}$ ±0°, $[\phi]_{275}$ −2000° (i), $[\phi]_{255}$ −2160°; nmr, 5.90 (q, 1, $J = 1.5$ Hz, C-3 H), 3.51 (s, 2, C-6 H), 2.47 (q, 2, $J = 1.0$ Hz, C-5 H), 2.13 (m, 3, $J = 1.0$ and 1.5 Hz, C-10 H), 0.90 (d, 3, $J = 7.0$ Hz, C-8 or C-9 H), and 0.84 ppm (d, 3, $J = 7.0$ Hz, C-8 or C-9 H).

Anal. Calcd for $C_{10}H_{15}BrO$: C, 51.96; H, 6.54; Br, 34.57. Found: C, 52.05; H, 6.38; Br, 34.51.

(−)-(*S*)-**1,4-Dimethyl-1-isopropyl-3-cyclopenten-2-one** (**9**).—A mixture of 1.18 g (5.10 mmol) of (−)-(*R*)-1-(bromomethyl)-1-isopropyl-4-methyl-3-cyclopenten-2-one (**8**) and 5 g (0.08 g-atom) of zinc dust in 35 ml of glacial acetic acid was heated on a steam plate for 12 hr. The hot solution was filtered and diluted with 30 ml of water. This mixture was neutralized with solid sodium bicarbonate and then thoroughly extracted with ether. The combined ether extracts were washed with saturated, aqueous sodium bicarbonate, water, and saturated, aqueous sodium chloride and dried ($MgSO_4$). Evaporation of the ether left 0.594 g of a pale brown oil. Molecular distillation of this oil at 55° (0.5 mm) gave 0.413 g of **9** (53%) as a colorless oil: $[\alpha]^{26}_{\text{D}}$ −95.5° (*c* 1.21); n^{25}_{D} 1.4706; ir, $\nu^{\text{max}}_{\text{cap}}$ 1630, 1705 cm^{-1}; ORD (*c* 1.21), $[\phi]_{600}$ −144°, $[\phi]_{589}$ −150°, $[\phi]_{380}$ −436° (tr), $[\phi]_{347}$ −346° (pk), $[\phi]_{340}$ −385°; (*c* 0.121) $[\phi]_{340}$ −500°, $[\phi]_{300}$ −2180° (i), $[\phi]_{270}$ −3320°; nmr, 5.85 (q, 1, $J = 1.5$ Hz, C-3 H), 2.54[48] and 2.11[48] (AB d of d,[49,50] 2, $J = 18.5$ Hz, C-5 H), 2.13 (m, 3, $J = 1.5$ and <1.0 Hz, C-10 H), 1.08 (s, 3, C-6 H), 0.90 (d, 3, $J = 6.5$ Hz, C-8 or C-9 H), and 0.70 ppm (d, 3, $J = 6.5$ Hz, C-8 or C-9 H).

Anal. Calcd for $C_{10}H_{16}O$: C, 78.89; H, 10.59. Found: 78.84; H, 10.73.

Oxidation of (−)-(*S*)-**1,4-Dimethyl-1-isopropyl-3-cyclopenten-2-one** (**9**) **to** (−)-(*S*)-**5-Isopropyl-5-methyl-3-oxo-1-cyclopentene-1-carboxylic Acid** (**3**).—To a stirred mixture of 0.102 g (0.67 mmol)

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(37) A measurement was said to be observed if the value of the measured intensity was greater than or equal to three times its standard deviation.

(38) R. Shiono, "IBM 7070 Programs for Crystallographic Computing," Technical Reports No. 29, 42, and 44, Crystallography Laboratory, University of Pittsburgh, Pittsburgh, Pa., 1962.

(39) J. M. Stewart, "Crystal Structure Calculation System for the IBM 709, 7090, 7094," Technical Report TR-64-6, Computer Science Center, University of Maryland, College Park, Md., and Research Computer Laboratory, University of Washington, Seattle, Wash., 1964.

(40) These calculations were performed on the IBM 7094 computer at the U. S. Army Missile Support Command, Redstone Arsenal, Ala.

(41) We wish to thank the Department of Microbiology, Vanderbilt University, for the use of its spectropolarimeter, purchased with a grant (AI-06191) from the U. S. Public Health Service.

(42) In ref 1, the sample tube length should also read 10 mm. This was inadvertently changed by the printer to 100 mm.

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

(44) S. M. McElvain, "The Characterization of Organic Compounds," Revised Edition, The MacMillan Co., New York, N. Y., 1953, p 264.

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

(46) In ref 1, the rotation of (−)-umbellulone (**4**) should also read α^{26}_{D} −36.7° (neat 1 dm). This was inadvertently changed by the printer to specific rotation.

(47) The composition, $C_{10}H_{14}O$, and structure[32] of this substance are analogous to those of the compound, $C_{10}H_{13}BrO$, reported[4] to be formed in the bromination of **4**. See Results and Discussion above.

(48) Broad owing to coupling between C-5 and C-10 protons, $J < 1.0$ Hz.

(49) Calculated chemical shifts.[50]

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

TABLE IV

CRYSTALLINE (−)-BROMODIHYDROUMBELLULONE (**2**), ATOMIC COORDINATES AND THERMAL PARAMETERS[a]

Atom	X/a	Y/b	Z/c	B or B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
				Molecule A					
Br	0.0474	0.2500	0.2368	7.130	8.865	3.524	0.687	2.660	0.991
O	−0.1450	0.3151	0.4383	4.643	8.047	3.679	2.473	0.819	0.397
C-1	−0.0191	0.2033	0.6272	4.612					
C-2	−0.0495	0.2526	0.4869	4.020					
C-3	0.0547	0.2084	0.4209	3.726					
C-4	0.1497	0.1432	0.5036	3.607					
C-5	0.1173	0.1322	0.6399	5.036					
C-6	−0.1339	0.1138	0.6413	7.653	8.075	9.718	0.216	5.991	1.085
C-7	−0.0029	0.3064	0.7331	8.193	6.909	3.021	5.448	2.412	1.340
C-8	0.0822	0.3978	0.7202	18.520	5.384	5.795	4.520	−1.935	−0.591
C-9	0.0290	0.2668	0.8785	11.128	12.541	3.741	6.156	0.426	−0.426
C-10	0.2682	0.0864	0.4716	6.076	6.630	6.235	0.584	2.541	−0.355
				Molecule B					
Br	0.5443	0.3332	−0.2912	8.269	9.303	3.881	−1.211	2.885	−1.243
O	0.3942	0.2027	−0.0828	5.036	5.508	5.301	−2.128	0.741	−1.070
C-1	0.5374	0.2866	0.1177	4.585					
C-2	0.4860	0.2674	−0.0314	3.883					
C-3	0.5703	0.3349	−0.0994	3.853					
C-4	0.6589	0.3973	−0.0166	3.518					
C-5	0.6472	0.3851	0.1251	4.418					
C-6	0.6038	0.1628	0.1784	6.524	6.507	6.256	−1.179	−1.943	0.927
C-7	0.4168	0.3333	0.1793	4.677	6.988	4.007	−2.041	2.369	−1.014
C-8	0.3496	0.4391	0.1084	7.213	8.080	8.754	1.545	4.649	−1.207
C-9	0.4625	0.3501	0.3324	8.699	15.159	4.035	−6.876	2.527	−2.676
C-10	0.7675	0.4835	−0.0497	5.138	5.282	8.217	−1.714	4.303	−0.593

[a] The temperature factor expression is $\exp[-{}^1/_4(B_{11}h^2a^{*2} + B_{22}k^2b^{*2} + B_{33}l^2c^{*2} + B_{12}2hka^*b^* + B_{13}2hla^*c^* + B_{23}2klb^*c^*)]$.

of **9** and 1.0 g of sodium bicarbonate in 5 ml of water was added 0.20 g (1.3 mmol) of potassium permanganate over a period of 30 min. The mixture was stirred for an additional 90 min, and then the excess potassium permanganate was destroyed by the addition of aqueous sodium bisulfite. The solution was filtered, and the precipitate of manganese dioxide washed with 5 ml of hot water. To the combined filtrate and washing was added 2.0 g of solid sodium hydroxide; the solution was heated at 70° for 30 min. The solution was then made acidic with concentrated hydrochloric acid and cooled. The brown solid which formed was collected and recrystallized twice from aqueous acetic acid. Thus was obtained 8 mg of **3** (7%) as fine needles: mp 190–191°; $[\alpha]^{25}\text{D}$ −19° (*c* 0.40) [lit.[1] mp 194–195°; $[\alpha]^{25}\text{D}$ −15° (*c* 1.11, MeOH)]. The ir spectrum was identical in all respects with that of an authentic sample of **3**: mp 194–195°; $[\alpha]^{25}\text{D}$ −15° (*c* 1.11).

(−)-α-Chloroumbellulone (10).—Chlorine gas was passed for 5 min through a stirred, ice-cold solution of 3.41 g (0.0227 mol) of (−)-umbellulone (**4**) in 40 ml of carbon tetrachloride. To this mixture was slowly added 15 ml of piperidine, and the subsequent mixture stirred overnight at room temperature. Dilute hydrochloric acid was then added until the aqueous layer was acidic to litmus. The organic layer was separated, washed with aqueous sodium bicarbonate and water, and dried ($MgSO_4$). Evaporation of the solvent left 3.80 g of crude **10** (91%). Nmr analysis of this material showed that it was greater than 95% **10**. Fractional distillation of the crude product gave 1.73 g of **10** (41%)[51] as a pale yellow oil: bp 68–70° (1.5 mm); $[\alpha]^{25}\text{D}$ −115° (*c* 2.49); $n^{25}\text{D}$ 1.5002; ir, $\nu_{\text{cap}}^{\text{max}}$ 1625, 1720 cm^{-1}; uv, $\epsilon_{327\ m\mu}^{\text{sh}}$ 320, $\epsilon_{273\ m\mu}^{\text{max}}$ 3120, $\epsilon_{219\ m\mu}^{\text{max}}$ 5420; ORD (*c* 0.0103), $[\phi]_{600}$ −200°, $[\phi]_{589}$ −200°, $[\phi]_{425}$ ±0°, $[\phi]_{353}$ +7140° (pk), $[\phi]_{339}$ ±0°, $[\phi]_{298}$ −51,900° (tr), $[\phi]_{280}$ −12,500°; nmr, 2.15 (s, 3, C-10 H), 1.07 (d, 3, J = 7.0 Hz, C-8 or C-9 H), and 0.99 ppm (d, 3, J = 7.0 Hz, C-8 or C-9 H).

Anal. Calcd for $C_{10}H_{13}ClO$: C, 65.04; H, 7.10; Cl, 19.20. Found: C, 64.94; H, 7.01; Cl, 18.96.

2-Chlorothymol (11) by Irradiation of (−)-α-Chloroumbellulone (10).—A solution of 2.08 g (0.0113 mol) of **10** in 10 ml of purified dioxane was irradiated for 168 hr. Evaporation of the solvent yielded a brown, viscous oil. This oil was chromatographed on silica gel, using hexane, chloroform, and benzene as eluting solvents. The main fraction of oil was eluted with benzene. Molecular distillation of this oil at 70° (1 mm) gave 1.27 g of **11** (61%) as a colorless oil: $n^{25}\text{D}$ 1.5254; ir, $\nu_{\text{cap}}^{\text{max}}$ 625, 800, 1610, 3530 cm^{-1}; nmr, 6.99 and 6.75 (AB type d of d,[49,50] 2, J = 8.0 Hz, C-5 and C-6 H), 5.68 (s, 1, C-3 OH), 3.29 (septet, 1, J = 7.0 Hz, C-7 H), 2.32 (s, 3, C-10 H), and 1.22 ppm (d, 6, J = 7.0 Hz, C-8 and C-9 H).

Anal. Calcd for $C_{10}H_{13}ClO$: C, 65.04; H, 7.10; Cl, 19.20. Found: C, 65.01; H, 6.96; Cl, 19.37.

The oxyacetic acid derivative was recrystallized from water: white needles; mp 76–77°.

2-Bromothymol (12) by Irradiation of (−)-α-Bromoumbellulone (7).—A solution of 0.660 g (2.88 mmol) of **7**, mp 33–34°, $[\alpha]^{25}\text{D}$ −137° (*c* 1.55) (lit.[20] mp 31–32°, no rotational data reported) in 5 ml of purified dioxane was irradiated for 70 hr. Evaporation of the solvent gave, on the basis of its ir and nmr spectra, a quantitative yield of **12** as a pale yellow oil: ir, $\nu_{\text{cap}}^{\text{max}}$ 615, 805, 1610, 3520 cm^{-1}; nmr, 6.84 and 6.57 (AB type d of d,[49,50] 2, J = 8.0 Hz, C-5 and C-6 H), 5.41 (s, 1, C-3 OH), 3.21 (septet, 1, J = 7.0 Hz, C-7 H), 2.28 (s, 3, C-10 H), and 1.18 ppm (d, 6, J = 7.0 Hz, C-8 and C-9 H).

The oxyacetic acid derivative of this material was recrystallized from water: mp 90–91°; mmp 91–92° with the authentic sample described below.

2-Bromothymol (12) by Bromination of Thymol (16).—A solution of 3.80 g (0.0253 mol) of **16** in 100 ml of dry toluene was cooled to −65°. Approximately 0.025 mol of N-bromo-*t*-butylamine[52,53] in 50 ml of dry toluene was added rapidly, and the resulting light yellow solution allowed to warm slowly to room temperature over a period of 16 hr. Evaporation of the solvent left 5.52 g of a colorless oil. Distillation of this oil gave 4.63 g of a pale yellow oil (80%): bp 83–84° (0.5 mm) (lit.[54] bp 240° for 2-bromothymol). The ir and nmr spectra of this material were essentially the same as those for **12** characterized above.

A sample of this oil was treated with dimethyl sulfate and the product subjected to glpc using a 6-ft silicone rubber column. This analysis showed methyl ethers as follows: 5% thymol (**16**), 95% 2-bromothymol (**12**), and a trace of 6-bromothymol, eluted in the order given.

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(51) A heavy, black residue was also obtained in this fractional distillation.

(52) C. E. Boozer and J. W. Moncrief, *J. Org. Chem.*, **27**, 623 (1962).

(53) D. E. Pearson, R. D. Wysong, and C. V. Breder, *ibid.*, **32**, 2358 (1967).

(54) Ad. Claus and E. Krause, *J. Prakt. Chem.*, **43**, 344 (1891).

From another sample of oil, the oxyacetic acid derivative was prepared and was recrystallized from water: white needles; mp 91–92° (lit.[53] mp 90.5–91.5°).

6-Bromothymol from Thymol (16).—As described previously,[55] **16** in dioxane was brominated with dioxane dibromide.[55] The product (46%) distilled as a colorless oil, bp 103–105° (0.5 mm), which crystallized on cooling: mp 54–55° (lit.[55] mp 55–56°); ir, $\nu_{\text{cap}}^{\text{max}}$ 610, 810, 870, 1620, 3400–3600 cm^{-1}; nmr, 7.14 (s, 1, C-5 H), 6.41 (s, 1, C-2 H), 4.83 (s, 1, C-3 OH), 3.05 (septet, 1, J = 7.0 Hz, C-7 H), 2.20 (s, 3, C-10 H), and 1.18 ppm (d, 6, J = 7.0 Hz, C-8 and C-9 H).

The oxyacetic acid derivative was recrystallized from water: white needles; mp 133–134°.

Anal. Calcd for $C_{12}H_{15}BrO_3$: C, 50.19; H, 5.27; Br, 27.83. Found: C, 49.99; H, 5.27; Br, 27.73.

Registry No.—**1**, 16934-58-0; **2**, 17693-33-3; **8**, 17693-34-4; **9**, 17693-35-5; **10**, 17693-36-6; **11**, 1408-66-4; **12**, 13019-31-3; oxyacetic acid derivative of 6-bromothymol, 17693-39-9.

Acknowledgment.—We wish to thank the National Science Foundation for a grant (GP-5772) supporting part of this work. X-ray diffraction measurements were made using equipment purchased with the support of a U. S. Public Health Service grant (AM-09085) for which we are very grateful.

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(55) L. A. Yanovskaya, A. P. Terent'ev, and L. I. Belen'kii, *Zh. Obshch. Khim.*, **22**, 1594 (1952); *Chem. Abstr.*, **47**, 8032 (1953).

Experiments Directed toward the Total Synthesis of Terpenes. XIII. The Construction of the Lactone Ring of Rosenonolactone[1]

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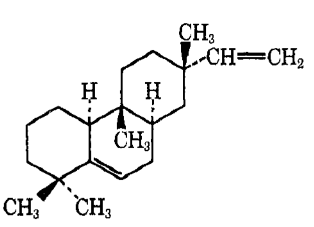
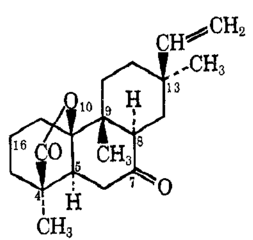
Received June 4, 1968

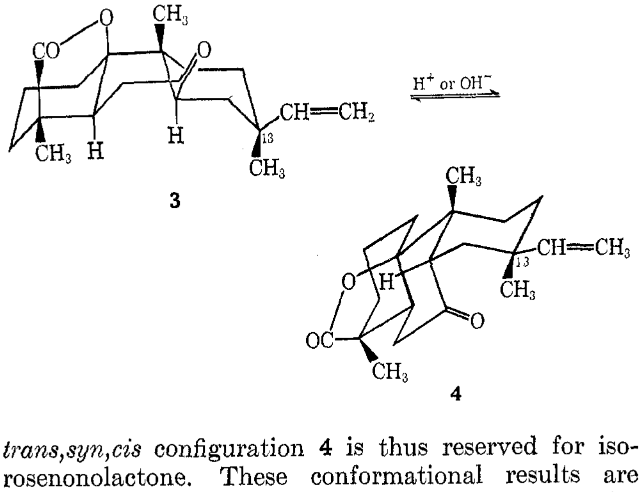
The use of the lead tetraacetate–iodine transannular oxidation has been explored as a method forthe construction of the lactone bridge of rosenonolactone (**2**). Attempts were made to isomerize the 9β→12 lactone **20**, formed on *oxidation of the 9β alcohol* **16**, *to the requisite 4bβ→12 lactone* **6** *under acid conditions with no success.* The 9β→12 ether **18**, also available from the same precursor on oxidation with lead tetraacetate alone, could only be cleaved so as to generate the chlorodiacetate **27**. Oxidation of the 12-hydroxyacetate **30**, obtained in 20% yield by an alternate synthetic scheme from the aromatic enone **33**, with lead tetraacetate iodine established the desired oxygen bridge in 28% yield. The acetoxylactone **6** could then be obtained in 50% yield by further chromic acid oxidation of the ether.



1



2



Our earlier work that led to the total synthesis[2] of (±)-rimuene (**1**) and (±)-13-epirimuene aroused our interest in the closely related, but considerably more complex mold metabolite, rosenonolactone (**2**), and its congeners.[3] While the structural as well as possibly biosynthetic[4] relationship between these substances is clear, rosenonolactone (**2**) poses a much more difficult synthetic problem in view of the higher degree of oxygenation present. Not only are the methyl and vinyl substituents at C-13 in the less readily synthesized[2] configuration and a ketone function present in the relatively inaccessible C-7 position, but also there is present a lactone bridge that terminates at the C-10β position and thereby forces the B ring to adopt the boat conformation. In spite of the potential lability conferred on the C-8 hydrogen by the adjacent C-7 ketone the *trans,syn,trans* configuration **3** is not irreversibly convertible into the all-chair *trans,syn,cis* configuration **4**. The strain of the *trans,syn,trans* configuration **3** with the attendant boat conformation of ring B is approximately the same as that of the all-chair *trans,syn,cis* configuration **4** owing to the severe steric congestion of the C-13 methyl group in the latter arrangement. The two configurations have been found[3a] to be present in nearly equal proportions in both mild acidic and basic media, and rosenonolactone (**2**) has conclusively been shown[3b] by X-ray crystal structure analysis of a derivative to be represented by the *trans,syn,trans* configuration **3**. The epimeric *trans,syn,cis* configuration **4** is thus reserved for isorosenonolactone. These conformational results are particularly important to a synthetic program, for the establishment of a lactone bridge across a *trans*-fused B/C structure would probably not result in the rosenonolactone structure **2**. In fact, such a transformation has been investigated[3a] with acid **5**, a degradation product of rosenonolactone (**2**), and found

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[1] Acknowledgment is made to the Alfred P. Sloan Foundation and the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

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[3] (a) G. A. Ellestad, B. Green, A. Harris, W. B. Whalley, and H. Smith, *J. Chem. Soc.*, 7246 (1965); (b) A. I. Scott, S. A. Sutherland, D. W. Young, I. Guglielmetti, D. Arigoni, and G. A. Sim, *Proc. Chem. Soc.*, 19 (1964).

[4] A. J. Birch, R. W. Richards, H. Smith, A. Harris, and W. B. Whalley, *Tetrahedron*, **7**, 241 (1959).