Rotatory Dispersion of Some Brominated α-Tetralones[1]

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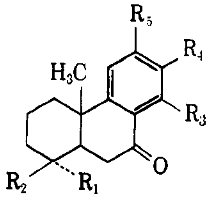
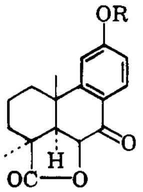
The rotatory dispersion and circular dichroism spectra of several brominated α-tetralones have been studied. The configuration of the bromine atom was determined from n.m.r. data. For a ketone chromophore the wave length at which the Cotton-effect curve crosses the zero-degree axis should coincide with the extremum in the circular dichroism spectrum and also with the n → π* transition maximum of the >C═O group in the ultraviolet spectrum. Our observations show that this relationship holds only very approximately in the case of the brominated α-tetralones described here.

Rotatory dispersion (R.D.) of α-halo ketones has attracted considerable attention particularly in connection with the axial halo ketone rule.[2] Only very limited data on halogen-substituted conjugated ketones have, however, appeared in the literature. We wish to report here on the rotatory dispersion of α-bromo derivatives of cyclohexanone in which the keto group is conjugated with an aromatic ring.

The parent ketones for our studies were derivatives of totarol, sugiol, podocarpic acid, and dehydroabietic acid, represented by the general formulas I–IV. In each case, only one isomer was obtained when the bromination of the ketones was carried out in glacial acetic acid solution containing a small amount of hydrobromic acid. During the bromination of methyl 7-oxomethylpodocarpic acid (IIIb) by this method the lactone Va was isolated. This lactone had previously been prepared by Bible[3] by the reaction of N-bromosuccinimide with IIIb. An analogous lactone Vb was obtained during the bromination of 7-oxo-O-acetylpodocarpic acid (IIIc). Such lactones had been obtained earlier *via* dehydrobromination of 6-bromo-7-oxo esters with collidine.



I (sugiol), R_1, R_2 = Me; R_3 = H; R_4 = *i*-Pr; R_5 = OH
II (7-oxototarol), R_1, R_2 = Me; R_3 = *i*-Pr; R_4 = OH; R_5 = H
III (7-oxopodocarpic acid), R_1 = Me; R_2 = COOH; R_3, R_4 = H, R_5 = OH
IV (7-oxodehydroabietic acid), R_1 = COOH; R_2 = Me; R_3 = *i*-Pr; R_4, R_5 = H



Va, R = CH_3
b, R = $COCH_3$

All the bromo ketones described here showed a positive Cotton effect with the peak at 360–370 mμ. The rotatory dispersion curve crossed the zero-degree axis in the 335–355-mμ region (see Table I).

It has been shown that the n → π* transition of the carbonyl of α-bromo ketones is responsible for the abnormal rotatory dispersion of these compounds. The introduction of an equatorial bromine in the α-position in cyclohexanone leads to a hypsochromic shift of 5 mμ, whereas the corresponding axial bromine atom causes a bathochromic shift of about 28 mμ.[4] Such a shift in the ultraviolet spectrum can be expected to be reflected in the rotatory dispersion curves.[5]

An inspection of Table I shows that, of all the ketones studied, sugiol methyl ether alone shows on bromination a hypsochromic shift of 5 mμ in the position of the extremum in the R.D. spectrum in isooctane. The wave length at which the R.D. curve crosses the zero-degree axis also undergoes a hypsochromic shift of 5 mμ. The ultraviolet spectrum of sugiol methyl ether in methanol did not show any measurable maxima in the neighborhood of 335–345 mμ. In isooctane solution, however, a very weak maximum at 345 mμ was noted for sugiol methyl ether. This maximum was shifted to a lower wave length by 4 mμ on bromination to the corresponding 6-bromo ether. In the case of all other compounds listed in Table I, bathochromic shifts ranging from 1 to 30 mμ were observed for the R.D. extremum on bromination of the ketones. Bathochromic shifts of approximately the same order were noticed in the ultraviolet spectra of these bromo ketones.

Proton n.m.r. spectroscopy has been used recently for determining the stereochemistry of α-halo ketones. Thus Bible[6] has observed that the proton at C-5 and C-6 in methyl 6-bromo-7-oxo-O-methylpodocarpate shows a coupling of 7 c.p.s. He has assigned the 6α-configuration to the bromine in this ketone. We have studied the proton n.m.r. spectra of several of the bromo ketones discussed here. With one exception, all of them show a coupling constant of 6–7 c.p.s. which is indicative of the 6α-configuration of the bromine atom. In the case of bromosugiol methyl ether the coupling constant is only 3 c.p.s. It is, therefore, necessary to assign the 6β-configuration to the halogen

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[1] Molecular Rotation and Absolute Configuration, part VI. For part V, see R. C. Cambie, L. N. Mander, A. K. Bose, and M. S. Manhas, *Tetrahedron*, **20**, 409 (1964).

[2] C. Djerassi, "Optical Rotatory Dispersion: Applications to Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1960, Chapter 9.

[3] R. H. Bible, U. S. Patent 2,753,357 (1956); *Chem. Abstr.*, **51**, 2869 (1957).

[4] R. C. Cookson, *J. Chem. Soc.*, 282 (1954); R. C. Cookson and S. H. Dandegaonker, *ibid.*, 352 (1955).

[5] C. Djerassi, J. Osiecki, R. Riniker, and B. Riniker, *J. Am. Chem. Soc.*, **80**, 1216 (1958), and subsequent papers.

[6] R. H. Bible, private communication.

TABLE I

Compd.	Solvent	$\lambda_{\max}$, mμ (ε)	R.D. peak, mμ	$[\phi]_{\max}$, mμ	Zero-degree crossing, mμ
Sugiol benzoate	Methanol	Sh 300 (2190) 256 (13,450)	355	+3610	331
6α-Bromosugiol benzoate	Methanol	Sh 302 (4120) 264 (12,000) 227 (21,700)	365	+5520	345
	Isooctane	Sh 299 (2210) 261 (12,300) 224 (24,200)	370	+5000	350
Sugiol methyl ether	Methanol	281 (19,500) 232 (15,500)	Plain	. . .	. . .
	Isooctane	345 (82.5)	365	+1130	340
6β-Bromosugiol methyl ether	Methanol	304 (4060) 242 (949)	Plain	. . .	. . .
	Isooctane	341 (206)	360	+2315	335
7-Oxototaryl acetate	Ethanol	297 (2820) 248 (10,260)	355	+2603	342
6α-Bromo-7-oxototaryl acetate	Methanol	Sh 292 (2270)	361	+3675	345
7-Oxototaryl methyl ether	Methanol	320 (2912) 257 (8181)	367	+2190	350
6α-Bromo-7-oxototaryl methyl ether	Methanol	321 (2470) 263 (5240)	367	+3902	355[a]
7-Oxototaryl benzoate	Methanol	296 (2300) 283 (2662) 233 (23,340)	353	+4437	331
6α-Bromo-7-oxotataryl benzoate	Methanol	340 (12,740)	365	3640	351
Methyl 7-oxo-O-methylpodocarpate	Methanol	276 (15,870) 227 (12,870)	346	+4646	317[a]
	Isooctane	320 (686)	351	+2764	332
Methyl 6α-bromo-7-oxo-O-methylpodocarpate	Methanol	295 (11,750)	360	+12,500	344[a]
	Isooctane	336 (603)	. . .	. . .	. . .
Methyl 7-oxo-13-isopropyl-O-methylpodocarpate	Methanol	279 (13,350) 230 (13,500)	342	+4830	315[a]
Methyl 6α-bromo-7-oxo-13-isopropyl-O-methylpodocarpate	Ethanol	306 (7300) 242 (2481)	364	+15,420	347[a]
Methyl 7-oxopodocarpate	Methanol	277 (15,700) 225 (12,200)	338	+3989	316[a]
Methyl 6α-bromo-7-oxopodocarpate	Methanol	297 (18,200) 232 (15,000)	360	+14,500	345
Methyl 7-oxo-O-acetylpodocarpate	Methanol	. . .	362	+1500	. . .
Methyl 6α-bromo-7-oxo-O-acetylpodocarpate	Methanol	Sh 337 (1058) Sh 294 (4130) 263 (8650)	365	+8700	347
Methyl 7-oxo-O-methyl-13-isopropylpodocarpate	Methanol	279 (13,350) 230 (14,300)	342	+4184	313[a]
Methyl 6α-bromo-7-oxo-O-methyl-13-isopropylpodocarpate	Methanol	305 (8700) 257 (3100) 235 (12,400)	364	+15,420	347[a]
	Ethanol	306 (7300) 242 (2481)	. . .	. . .	. . .
Methyl 7-oxodehydroabietate	Methanol	. . .	350	+3144	325
Methyl 6α-bromo-7-dehydroabietate	Methanol	310 (891) 262 (5250)	364	+3607	338

[a] By extrapolation.

atom in this bromo ketone. Such an assignment is in conformity with the small hypsochromic shift in the ultraviolet spectrum observed on the bromination of sugiol methyl ether. A fused aromatic ring causes considerable departure from the chair form of a cyclohexane ring: the 6α- and 6β-positions in I–IV correspond only approximately to the equatorial and axial conformation, respectively. If the axial halo ketone rule be valid for such compounds, one can predict that 6β-bromosugiol methyl ether should show a positive Cotton effect. The R.D. data of bromosugiol methyl ether is in agreement with the conformational assignment (6β, pseudo-axial) made here.

Some other features of Table I are worth notice. For the bromo compound from 7-oxototaryl methyl ether the bathochromic shift is negligible both in the ultraviolet and rotatory dispersion spectra. The n.m.r. data, however, clearly indicates the 6α-configuration (pseudo-equatorial) for the bromine atom.

Bromination of a ketone increases the molecular rotation. This increase, however, was much higher for the podocarpic acid derivatives than for the other compounds in Table I. The presence of a hydroxyl group (or its ester) at C-12 could lead to resonance with the carbonyl group at C-7 and thereby influence the rotational strength of the carbonyl chromophore. Sugiol

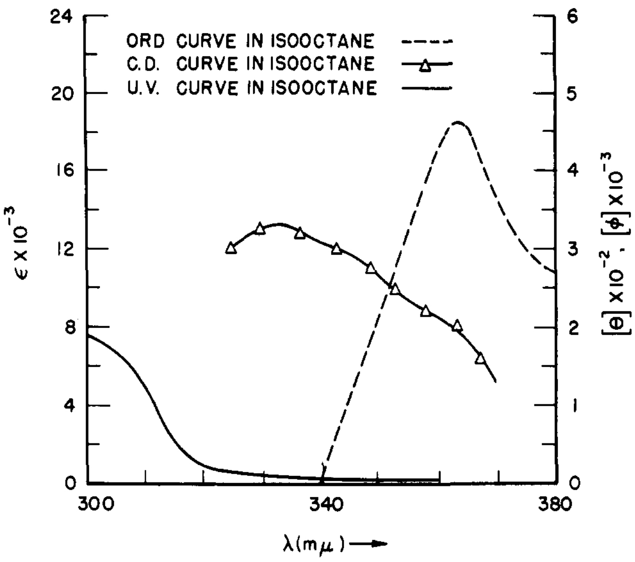

Figure 1.—Sugiol methyl ether.

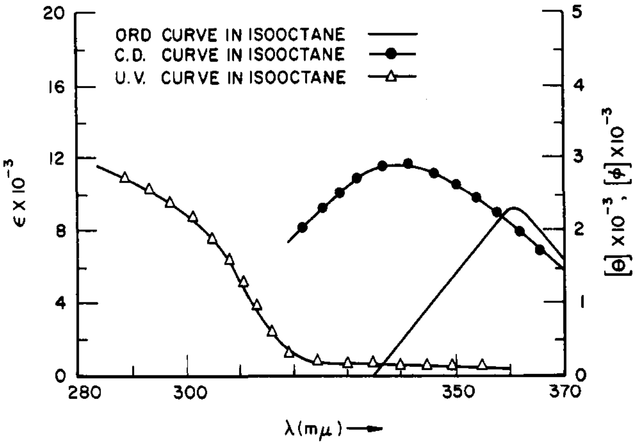

Figure 2.—6β-Bromosugiol methyl ether.

benzoate which also has a hydroxy group at C-12 shows a large bathochromic shift on bromination at C-6. However, bromination does not increase the rotation as much as in podocarpic acid derivatives.

The ultraviolet spectrum in methanol solution of the bromo ketones did not show any noticeable maxima in the neighborhood of 350 mμ—the region in which the rotatory dispersion curves cross the zero-degree axis. When isooctane rather than methanol was used as the solvent, small maxima were revealed in the 340–360-mμ region.

R.D., circular dichroism (C.D.), and ultraviolet spectra for a carbonyl chromophore are intimately related to the n → π* transition. In general the wave length at which the Cotton-effect curve of a ketone crosses the zero-degree axis should approximately coincide with the extremum in the corresponding C.D. spectrum as well as the n → π* transition maximum of the carbonyl in the ultraviolet spectrum.[7] An examination of Table I and Figures 1–5 reveals that this relationship is only very approximate in the case of brominated α-tetralones.

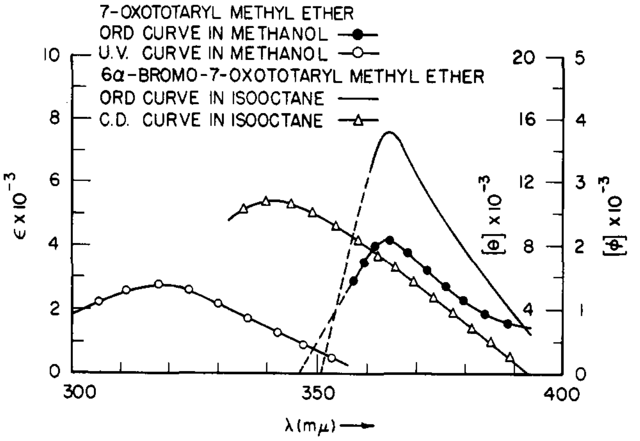

Figure 3.—7-Oxototaryl methyl ether and 6α-bromo-7-oxototaryl methyl ether.

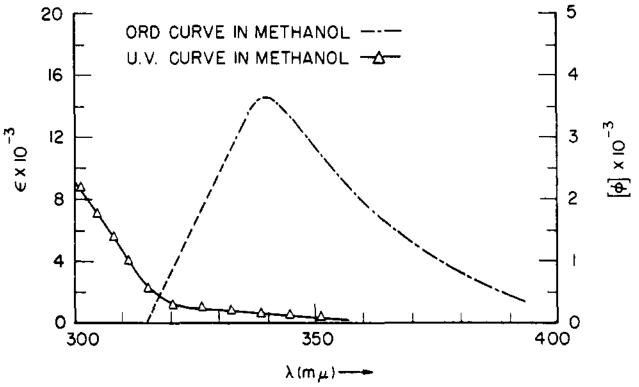

Figure 4.—Methyl 7-oxo-13-isopropyl-O-methyl podocarpate.

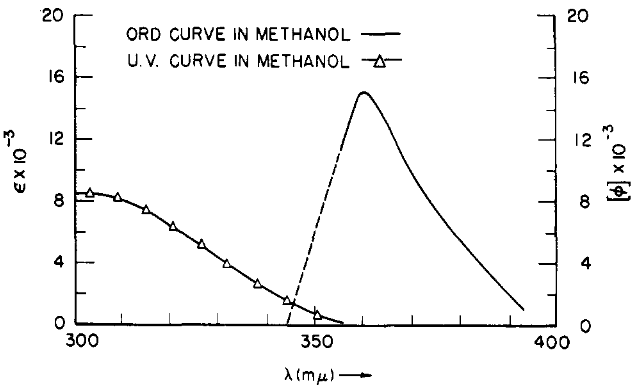

Figure 5.—Methyl 7α-bromo-7-oxo-13-isopropyl-O-methyl podocarpate.

Experimental[8]

6β-Bromosugiol Methyl Ether.—A solution of bromine (0.5 ml.) in glacial acetic acid (1 ml.) was added dropwise with stirring to a solution of sugiol methyl ether (50 mg.) in glacial acetic acid (1 ml.) containing 1 drop of 48% hydrobromic acid while the temperature was maintained at 40–45°. Heating was continued for a further period of 45 min. The solvent was then removed under reduced pressure. The residue was crystallized several

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[7] C. Djerassi, H. Wolf, and E. Bunnenberg, *J. Am. Chem. Soc.*, **85**, 324 (1963).

[8] The O.R.D. measurements were made on a Rudolph self-recording spectropolarimeter (*c* being defined in g./100 ml.). Circular dichroism measurements were performed with a Baird-Atomic/Jouan Dichrograph. Molecular ellipticities [θ] were calculated according to E. Bunnenberg, C. Djerassi, K. Mislow, and A. Moscowitz [*ibid.*, **84**, 2833 (1962)]. In these calculations *c* is defined in g./l. All melting points are uncorrected. The compounds were analyzed by Dr. A. D. Campbell and his associates, University of Otago, New Zealand, and by Drs. Weiler and Strauss, University of Oxford, England.

times from methanol to yield irregular crystals of 6α-bromosugiol methyl ether (43 mg.): m.p. 185–187°; $\lambda_{\max}^{\text{Nujol}}$ 1684 cm.$^{-1}$ (-CHBrCOC=C-); C.D. (c 0.2634, isooctane, 400–320 mμ) $[\Theta]_{335}$ +2953; R.D. (methanol) plain positive curve, R.D. (c 0.01104, isooctane) $[\phi]_{360}$ +2315° and $[\phi]_{335}$ 0°; ultraviolet spectrum (methanol) ϵ_{304} 4060 and ϵ_{242} 949, (isooctane) ϵ_{341} 206, $\epsilon_{307}^{\text{sh}}$ 6590, ϵ_{282} 11,860, $\epsilon_{238}^{\text{sh}}$ 10,150, and ϵ_{232} 11,750; n.m.r. peak, doublet centered at τ 5.09 (C-6 H), J_{HH} = 3 c.p.s.

Anal. Calcd. for $C_{21}H_{29}BrO_2$: C, 64.1; H, 7.4; Br, 20.3. Found: C, 63.65; H, 7.4; Br, 20.1.

6α-Bromosugiol Benzoate.—Bromination of sugiol benzoate (40 mg.) under the above conditions gave the 6α-bromo derivative (46 mg.) which crystallized from aqueous methanol as small needles: m.p. 127–128°, with shrinking at 76°; $\lambda_{\max}^{CS_2}$ 1730 (benzoate) and 1678 cm.$^{-1}$ (-CHBrCOC=C-); R.D. (c 0.05268, methanol) $[\phi]_{450}$ +177°, $[\phi]_{400}$ +1600°, $[\phi]_{365}$ +5520°, $[\phi]_{345}$ 0°; ultraviolet spectrum (methanol) $\epsilon_{302}^{\text{sh}}$ 4120, ϵ_{264} 12,000, and ϵ_{227} 21,700, (isooctane) $\epsilon_{299}^{\text{sh}}$ 2210, ϵ_{261} 12,300, and ϵ_{224} 24,200.

Anal. Calcd. for $C_{27}H_{31}BrO_3$: C, 67.1; H, 6.5. Found: C, 67.1; H, 6.6.

6α-Bromo-7-oxototaryl Methyl Ether.—A solution of bromine (50 mg.) in glacial acetic acid (0.5 ml.) was added dropwise over a period of 10 min. to a stirred solution of 7-oxototaryl methyl ether (100 mg.) in glacial acetic acid (5 ml.) containing 1 drop of 48% hydrobromic acid. The product was isolated by precipitation with water. Three crystallizations from methanol gave 6α-bromo-7-oxototaryl methyl ether as long needles (65 mg.): m.p. 168–170°; $\lambda_{\max}^{\text{Nujol}}$ 1692 (conjugated CO), 1040 (—OCH_3), and 818 cm.$^{-1}$ (two adjacent aromatic hydrogens); C.D. (c 0.277, isooctane, 400–335 mμ) $[\Theta]_{340}$ +10,881; R.D. (c 0.0866, methanol) $[\phi]_{367}$ +3902° and $[\phi]_{355}$ 0° (by extrapolation); ultraviolet spectrum (methanol) ϵ_{321} 2470 and ϵ_{263} 5240; n.m.r. peak, doublet centered at τ 5.45 (C-6 H), J_{HH} = 6.6 c.p.s.

Anal. Calcd. for $C_{21}H_{29}BrO_2$: C, 64.1; H, 7.45; Br, 20.3. Found: C, 63.9; H, 7.5; Br, 20.2.

6α-Bromo-7-oxototaryl Acetate.—Bromination of 7-oxototaryl acetate (50 mg.) under the above-mentioned conditions gave the 6α-bromo derivative which formed needles (45 mg.), m.p. 176–177° (lit.[9] m.p. 176–178°), from aqueous methanol: $\lambda_{\max}^{\text{Nujol}}$ 1761 (ester CO), 1686 (-CHBrCOC=C-), and 811 cm.$^{-1}$ (two adjacent aromatic hydrogens); R.D. (c 0.0788, methanol) $[\phi]_{361}$ +3675° and $[\phi]_{345}$ 0°; ultraviolet spectrum (methanol) ϵ_{290} 2270 and ϵ_{258} 6385; n.m.r. peak, doublet centered at τ 5.46 (C-6 H), J_{HH} = 7.2 c.p.s.

Anal. Calcd. for $C_{22}H_{29}BrO_3$: C, 62.65; H, 6.95; Br, 19.0. Found: C, 62.4; H, 7.05; Br, 19.1.

6α-Bromo-7-oxototaryl Benzoate.—7-Oxototaryl benzoate (50 mg.) in glacial acetic acid (2 ml.) containing 1 drop of 48% hydrobromic acid was treated with bromine (0.1 ml.) in acetic acid (1 ml.) for 10 min. at room temperature. The product, isolated by pouring into water, crystallized from aqueous acetic acid as needles (33 mg.): m.p. 202–203°; $\lambda_{\max}^{\text{Nujol}}$ 1739 (benzoate), 1689 (-CHBrCOC=C-), and 819 cm.$^{-1}$ (two adjacent aromatic hydrogens); R.D. (c 0.0962, methanol) $[\phi]_{366}$ +3640° and $[\phi]_{351}$ 0°; ultraviolet spectrum (95% ethanol) ϵ_{340} 12740; n.m.r. peak, doublet centered at τ 5.40 (C-6 H), J_{HH} = 7.2 c.p.s.

Anal. Calcd. for $C_{27}H_{31}BrO_3$: C, 67.1; H, 6.5; Br, 16.5. Found: C, 67.1; H, 6.5; Br, 16.5.

Methyl 6α-Bromo-7-oxo-O-methylpodocarpate.—Methyl 7-oxo-O-methylpodocarpate (40 mg.) in Analar carbon tetrachloride (20 ml.) was treated with N-bromosuccinimide (200 mg.) and the mixture was exposed to sunlight for 36 hr. Succinimide was removed and the residue, after removal of solvent, was chromatographed on silica gel. Fractions eluted with benzene gave an oil which yielded methyl 6α-bromo-7-oxo-O-methylpodocarpate (25 mg.) on seeding with an authentic material. Recrystallization from aqueous methanol gave irregular crystals: m.p. 141–142° (lit.[8] m.p. 142–144.5°); R.D. (c 0.0495, methanol) $[\phi]_{360}$ +12,500° and $[\theta]_{344}$ 0° (by extrapolation); ultraviolet spectrum (methanol) ϵ_{295} 11,750 and ϵ_{235} 8511; n.m.r. peak, doublet centered at τ 4.25 (C-6 H), J_{HH} = 7.8 c.p.s.

Anal. Calcd. for $C_{19}H_{23}BrO_4$: C, 57.7; H, 5.9; Br, 20.2. Found: C, 57.7; H, 6.0; Br, 20.3.

Methyl 6α-Bromo-7-oxo-13-isopropyl-O-methylpodocarpate.—Bromination of methyl 7-oxo-13-isopropyl-O-methylpodocarpate (40 ml.) was carried out at 40–45° in acetic acid solution containing 1 drop of 48% hydrobromic acid, giving methyl 6α-bromo-7-oxo-13-isopropyl-O-methylpodocarpate which, when recry tallized from 90% aqueous methanol, afforded 38 mg. of the product: m.p. 165–166°; $\lambda_{\max}^{\text{Nujol}}$ 1723 (ester CO) and 1684 cm.$^{-1}$ (-CHBrCOC=C-); R.D. (c 0.0189, methanol) $[\phi]_{364}$ +15,420 and $[\phi]_{347}$ 0° (by extrapolation); ultraviolet spectrum (95% ethanol) ϵ_{306} 7300 and ϵ_{242} 2481, (methanol) ϵ_{305} 8700, ϵ_{257} 3100, and ϵ_{235} 12,400; n.m.r. peak, doublet centered at τ 4.21 (C-6 H), J_{HH} = 6.6 c.p.s.

Anal. Calcd. for $C_{22}H_{29}BrO_4$: C, 60.4; H, 6.7; Br, 18.3. Found: C, 60.0; H, 6.5; Br, 18.2.

Methyl 6α-Bromo-O-acetyl-7-oxopodocarpate.—Bromination of methyl O-acetyl-7-oxopodocarpate under the above conditions gave the 6α-bromo derivative (85% yield) which formed rods, m.p. 125–126°, from aqueous methanol (lit.[10] m.p. 130–132°): $\lambda_{\max}^{CS_2}$ 1760 (acetate), 1720 (ester CO), and 1687 cm.$^{-1}$ (-CHBrCOC=C-); R.D. (c 0.055, methanol) $[\phi]_{550}$ +153°, $[\phi]_{365}$ +8700°, and $[\phi]_{347}$ 0°; ultraviolet spectrum (methanol) $\epsilon_{337}^{\text{sh}}$ 1058, $\epsilon_{294}^{\text{sh}}$ 4130, and ϵ_{263} 8650; n.m.r. peak, doublet centered at τ 4.15 (C-6 H), J_{HH} = 7.2 c.p.s.

Anal. Calcd. for $C_{20}H_{23}BrO_5$: C, 56.7; H, 5.5; Br, 18.9. Found: C, 56.8; H, 5.4; Br, 19.0.

Methyl 6α-Bromo-7-oxopodocarpate.—Methyl 6α-bromo-O-acetyl-7-oxopodocarpate (150 mg.) was warmed on the water bath with concentrated sulfuric acid (5 ml.) for 2 min. and the mixture was kept at room temperature for 30 min. Isolation of the product by pouring the mixture onto crushed ice and crystallization from methanol gave methyl 6α-bromo-7-oxopodocarpate (130 mg.) as shining plates: m.p. 196–198° dec. (lit.[10] m.p. 200–204°); $\lambda_{\max}^{\text{Nujol}}$ 3356 (OH), 1730 (ester CO), and 1672 cm.$^{-1}$ (-CHBrCOC=C-); R.D. (c 0.07954, methanol) $[\phi]_{600}$ +237°, $[\phi]_{360}$ +14,500, and $[\phi]_{345}$ 0°; ultraviolet spectrum (methanol) ϵ_{297} 18,200 and ϵ_{232} 15,000.

Anal. Calcd. for $C_{18}H_{21}BrO_4$: C, 56.7; H, 5.5; Br, 21.0. Found: C, 56.6; H, 5.5; Br, 20.9.

Methyl 6α-Bromo-7-oxodehydroabietate.—Methyl 7-oxodehydroabietate (30 mg.) in glacial acetic acid (2 ml.) containing a drop of 48% hydrobromic acid was treated with bromine (0.1 ml.) in glacial acetic acid (1 ml.) at room temperature. After 30 min. the product was isolated by pouring into water and crystallized from aqueous methanol to yield needles (29 mg.) of methyl 6α-bromo-7-oxodehydroabietate: m.p. 159–160° (lit.[11] m.p. 153–155°); $\lambda_{\max}^{\text{Nujol}}$ 1719 (ester CO) and 1686 cm.$^{-1}$ (-CHBr-COC=C-); R.D. (c 0.0817, methanol) $[\phi]_{364}$ +3607° and $[\phi]_{338}$ 0°; ultraviolet spectrum (methanol) ϵ_{310} 891 and ϵ_{262} 5250.

Anal. Calcd. for $C_{21}H_{27}BrO_3$: C, 61.8; H, 6.8; Br, 19.6. Found: C, 61.9; H, 6.7; Br, 19.2.

Acknowledgment.—We wish to thank Dr. E. M. Kosower for the use of the dichrograph in his laboratory and Dr. U. Weiss for valuable discussions.

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(9) Y. L. Chou and H. Erdtman, *Acta Chem. Scand.*, **13**, 1305 (1962).

(10) E. Wenkert, P. Beak, R. W. J. Carney, J. W. Chamerlin, D. B. R Johnston, C. D. Roth, and A. Tahara, *Can. J. Chem.*, **41**, 1924 (1963).

(11) E. Wenkert, R. W. J. Carney, and C. Kaneko, *J. Am. Chem. Soc.* **83**, 4440 (1961).