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ROTATORY DISPERSION AND CIRCULAR DICHROISM STUDIES OF SOME α-TETRALONES[1]

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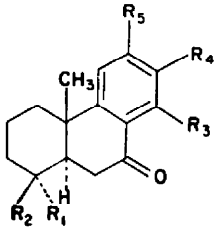
Abstract—The rotatory dispersion and circular dichroism spectra of several ketones conjugated with an aromatic ring (derived from diterpenoids and steroids) have been studied. These compounds show Cotton effect curves with peaks near 350 mμ. Extremely weak UV absorption maxima in the 320–350 mμ region can be detected for these ketones in iso-octane solution. This would indicate that the perturbing light wave induces in such conjugated ketones a very small electrical dipole moment but a large magnetic dipole moment.

IN THE course of our investigation of the family *Podocarpaceae* several diterpenoids of the general structure I became available to us.



I

Sugiol ($R_1 = R_2 = Me$, $R_3 = H$, $R_4 = i\text{-Pr}$, $R_5 = OH$)
7-Oxototarol ($R_1 = R_2 = Me$, $R_3 = i\text{-Pr}$, $R_4 = OH$, $R_5 = H$)
7-Oxopodocarpic acid ($R_1 = Me$, $R_2 = COOH$, $R_3 = R_4 = H$, $R_5 = OH$)
7-Oxodehydroabietic acid ($R_1 = COOH$, $R_2 = Me$, $R_4 = i\text{-Pr}$, $R_3 = R_5 = H$)

The carbonyl group conjugated with an aromatic ring which is present in these compounds constitutes a chromophoric system for optical rotatory dispersion that has received little attention. We have, therefore, studied the rotatory dispersion (R.D.) and circular dichroism (C.D.) spectra of several of these diterpenoid ketones.

Djerassi and his school have carried out extensive investigation of the R.D. of diverse types of ketones. The R.D. spectra of ketones are characterized by Cotton effect curves the sign of which can be predicted in cyclohexanone type compounds by

[1a] *Chemistry of the Podocarpaceae*—X. For Part IX, see L. H. Briggs and T. P. Cebalo, *Tetrahedron*, in press. For Part VIII, see S. M. Bocks, R. C. Cambie and T. Takahashi, *Tetrahedron* **19**, 1109 (1963).

[1b] *Molecular Rotation and Absolute Configuration*—V. For Part IV, see A. K. Bose, M. S. Manhas, R. C. Cambie and L. N. Mander, *J. Amer. Chem. Soc.* **84**, 3201 (1962).

using the Octant Rule.[2] For α, β-unsaturated ketones, e.g. testosterone, the R.D. spectrum consists of multiple peaks.

From theoretical considerations it has been shown that the phenomena of UV absorption, rotatory dispersion and circular dichroism are closely interrelated. The peak in the C.D. spectrum occurs at about the same wavelength at which the R.D. curve showing a Cotton effect crosses the zero degree axis; this wavelength coincides approximately with a weak absorption in the U.V. spectrum attributed to the $n \rightarrow \pi^*$ transition of the carbonyl group. Thus the R.D. spectra of steroid ketones cross the zero degree axis in the neighborhood of 300 mμ corresponding to the weak UV absorption band near 290 mμ of the carbonyl group. In the case of testosterone, for every peak in the R.D. curve a corresponding maximum at nearly the same wavelength in the UV curve has been found.[3]

A survey of the published literature before we started our investigation showed that the R.D. curves of two diterpenoid ketones, sugiol methyl ether and nimbiol methyl ether,[4] had been recorded and found to be plain curves at wavelengths higher than 350 mμ. We found that measurements at lower wavelengths were possible by using the acetates and benzoates in place of the methyl ethers of these two compounds. Both compounds revealed positive Cotton effect curves with peaks near 350 mμ. They crossed the zero degree axis at 330 to 335 mμ. The UV spectra of these compounds, however, showed no noticeable maxima between 300–350 mμ. This apparent lack of correspondence between the UV spectra and R.D. curves prompted us to examine a series of diterpenoid ketones.

Sugiol, nimbiol and 7-oxototarol did not show Cotton effect curves above 350 mμ. However, derivatives of these three diterpenoids and of 7-oxodehydroabietic acid exhibited positive Cotton effects. The peaks occurred between 340–367 mμ. These R.D. curves crossed the zero degree line at 312–335 mμ (see Table 1, ref. 1b). The UV spectra of several representative compounds of this series did not contain any noticeable maxima in the 300–350 mμ region in methanol solution.

The C.D spectrum of 7-oxototarol showed a peak at 340 mμ indicating that for some compounds C.D. measurement is more perceptive than R.D. measurement. In the C.D. spectrum of sugiol acetate a peak was found at 324 mμ; this coincides with the wavelength at which the R.D. spectrum of this compound crosses the zero degree axis. The C.D. spectra of sugiol benzoate, sugiol methyl ether and 7-oxo-O-acetylpodocarpic acid consisted of multiple peaks over the range 320–360 mμ.

One of these diterpenoid ketones, sugiol benzoate, has been studied in detail. On the basis of the multiple peaks in its C.D. spectrum, one can expect corresponding multiple maxima in its UV absorption spectrum. However, the UV spectrum in methanol failed to show any peaks at wavelengths higher than 300 mμ. Presumably the maxima at higher wavelengths are so weak that they are concealed under the tail end of the UV maxima at shorter wavelengths.

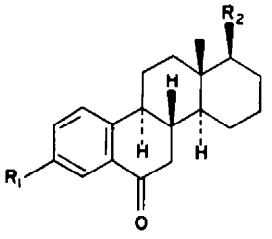
Methyl O-methyl-7-oxopodocarpate was found to be moderately soluble in iso-octane. Its R.D. and UV spectra were determined in this non-polar solvent.

[2] W. Moffitt, R. B. Woodward, A. Moscowitz, W. Klyne and C. Djerassi, *J. Amer. Chem. Soc.* **83**, 4013 (1961).
[3] C. Djerassi, *Optical Rotatory Dispersion* p. 40. McGraw-Hill, New York (1960).
[4] P. Sengupta, S. N. Chaudhuri and H. N. Khastgir, *Tetrahedron* **10**, 45 (1960).

The single Cotton effect peak as seen in methanol solution was now replaced by a set of multiple peaks. Increased resolution of R.D. spectra in non-polar media has been previously reported by Djerassi *et al.*[5] The UV spectrum, too, now showed a set of minor maxima in the longer wavelength region which corresponded closely with the C.D. and R.D. curves.[1b]

We have also examined the R.D spectra of some 6-oxoestrane derivatives of the general structure II where the keto group is again conjugated with an aromatic ring. An examination of the absolute configuration of I and II

6-Oxo-3,17β-estradiol ($R_1 = R_2 = OH$)
6-Oxo-3,17β-estradiol diacetate ($R_1 = R_2 = O{\cdot}CO{\cdot}CH_3$)
6-Oxo-17β-acetyl estradiol-3-methyl ether ($R_1 = OCH_3$, $R_2 = O{\cdot}CO{\cdot}CH_3$)

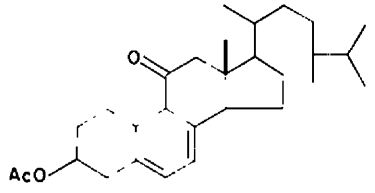


II

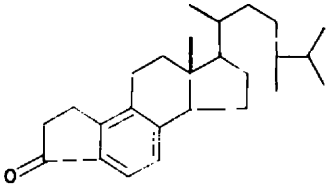
indicates that both families of ketones should show the same sign of Cotton effect. The data for these steroids was exactly analogous to those for the diterpenoids: the steroid ketones also showed positive Cotton effect curves, the R.D. peak appearing at 350–361 mμ. The R.D. curves of 6-oxo-3,17β-estradiol and its diacetate cross the zero degree axis at 335 mμ and 331 mμ, respectively.

The UV spectrum of 6-oxo-3,17β-estradiol diacetate in methanol solution showed no maxima at wavelengths higher than 300 mμ, but the UV spectrum in iso-octane revealed very weak maxima at 353 mμ (ε, 19) and 340 mμ (ε, 38).

We have studied the C.D. spectrum of 6-oxo-3,17β-estradiol in methanol solution. The R.D., C.D. and UV spectra of this compound are shown in Fig 1. It will be noticed that the R.D. curve crosses the zero degree line at 335 mμ which is near one of the peaks (345 mμ) in the C.D. spectrum. Again, we see an instance where the C.D. spectrum reveals more than the R.D. spectrum about a chromophore—thus the trough at 310 mμ indicates a second optically active UV absorption which could not be detected from the R.D. measurement.



III



IV

Through the courtesy of Dr. G. D. Meakins we have been able to study the spectra of 3β-acetoxy-19-norergosta-5,7,9-triene-11-one (III) and A-nor-19-norergosta-5,7,9-triene-3-one (IV). The former is antipodal to the diterpenoid ketones of type I and

[5] C. Djerassi, R. Riniker and B. Riniker, *J. Amer. Chem. Soc.* **78**, 6377 (1956).

the steroid ketones of type II, and shows a negative Cotton effect as would be expected. The C.D. spectrum of III shows inflections in the 338–365 mμ region (Fig. 2).

The steroid IV represents an interesting chromophoric system in view of the interposition of the aromatic B ring between the carbonyl group in ring A and the asymmetric centers (C_{13}, C_{14}, etc.). In iso-octane solution this compound showed a plain positive curve at wavelengths higher than 320 mμ. Its C.D. spectrum in iso-octane, however, consisted of three troughs at 325, 340 and 356 mμ.

According to present theory[6] the UV absorption, C.D. and R.D. of a chromophore are caused by charge displacements induced by the perturbing light wave. Induced electrical and magnetic dipoles result from these charge displacements. The intensity of the UV absorption has been shown to be directly dependent on the induced electrical dipole. The rotational strength (R_K) of a chromophore, however, is related to both the electrical dipole (μ_e^k) and magnetic dipole (μ_m^k) as shown in the following equation:

$$R_K = \mu_e^k \cdot \mu_m^k$$

The results presented here show that the R.D. and C.D. effects corresponding to a carbonyl conjugated to an aromatic ring are strong, but the n-π^* transition band in the carbonyl is exceedingly weak. One has to assume, therefore, that for this type of conjugated carbonyl group the induced electrical dipole moment is very small but the magnetic dipole moment is large.

EXPERIMENTAL[7]

Sugiol. It was isolated[8] from *Podocarpus dacrydioides* A. Rich, m.p. 292–293°. λ_{max}^{Etoh} 233 mμ (log ε 4·22) and 288 mμ (log ε 4·15). R.D. in methanol, plane positive curve above 350 mμ.

Sugiol benzoate. Ferruginyl benzoate (1·58 g) in glacial acetic acid (100 ml) was oxidized with chromic acid (1·106 g) in 80% aq. acetic acid (2·48 g) at room temp for 6 days. The product, sugiol benzoate, formed long needles, m.p. 183–184° (Lit.[9] m.p. 184°) when crystallized from ethanol (yield 94%). λ_{max} 230 mμ (log ε 4·35) and 300 mμ (log ε 3·37). C.D. dioxane: C, 0·092 (400 −270 mμ), $[\theta]_{364}$ +2046, $[\theta]_{361}$ +2013, $[\theta]_{349}$ +5412, $[\theta]_{343}$ +4818, $[\theta]_{335}$ +7029, $[\theta]_{332}$ +5313, $[\theta]_{310}$ +3300, $[\theta]_{307}$ 0, $[\theta]_{302}$ −6633. R.D. in methanol: C, 0·0793; $[\phi]_{600}$ +101·9°, $[\phi]_{500}$ +205·2°, $[\phi]_{450}$ +407·6°, $[\phi]_{355}$ +3617°, $[\phi]_{347}$ +3076°, $[\phi]_{331}$ 0°.

A similar oxidation of ferruginyl acetate[10] provided sugiol acetate,[8] m.p. 164–165°. $\lambda_{max}^{iso-octane}$ 209 mμ (log ε 4·46), 256 mμ (log ε 4·14), 292 mμ (log ε 3·43) and 297 mμ (log ε 3·47). C.D. in iso-octane: C 0·3594 (400–315 mμ), $[\theta]_{324}$ +10,594. R.D. in iso-octane: C 0·0556; $[\phi]_{600}$ +92·34° $[\phi]_{500}$ +123·1°, $[\phi]_{400}$ +684°, $[\phi]_{350}$ +3659°. $[\phi]_{345}$ +3837°, $[\phi]_{324}$ 0°.

Sugiol methyl ether. It was prepared by heating sugiol (100 mg) under reflux with anhydrous K_2CO_3 (2·0 g) and dimethylsulfate (2 ml) in dry acetone (100 ml) for 12 hr. The product (85 mg; 80%) was crystallized as plates, m.p. 145–146° from methanol (lit., m.p. 136–137°[10] and 137–138°[9]).

[6] E. V. Condon, W. Altar and H. Eyring, *J. Chem. Phys.* **5**, 753 (1937).

[7] All m.ps are uncorrected. The compounds were analysed by Dr. A. D. Campbell and his associates at the University of Otago, New Zealand and Drs. Weiler and Strauss, University of Oxford, England. Circular dichroism measurements were performed with a Baird-Atomic/Jouan Dichrograph. Molecular ellipticities [φ] were calculated according to E. Bunnenberg, C. Djerassi, K. Mislow and A. Moscowitz, *J. Amer. Chem. Soc.* **84**, 2833 (1962). In these calculations C is defined in g/l. For sugiol benzoate the molecular ellipticities were calculated by multiplying Δε with 3300. The optical rotatory dispersion measurements were made on a Rudolph Recording Spectropolarimeter using an Xenon lamp. In these calculations C is defined as g/100 cc.

[8] L. H. Briggs, R. C. Cambie, R. N. Seelye and A. D. Warth, *Tetrahedron* **7**, 270 (1959).

[9] P. Sengupta, S. N. Chaudhuri and H. N. Khastgir, *Tetrahedron* **10**, 45 (1960).

[10] C. W. Brandt and B. R. Thomas, *J. Chem. Soc.* 2442 (1952).

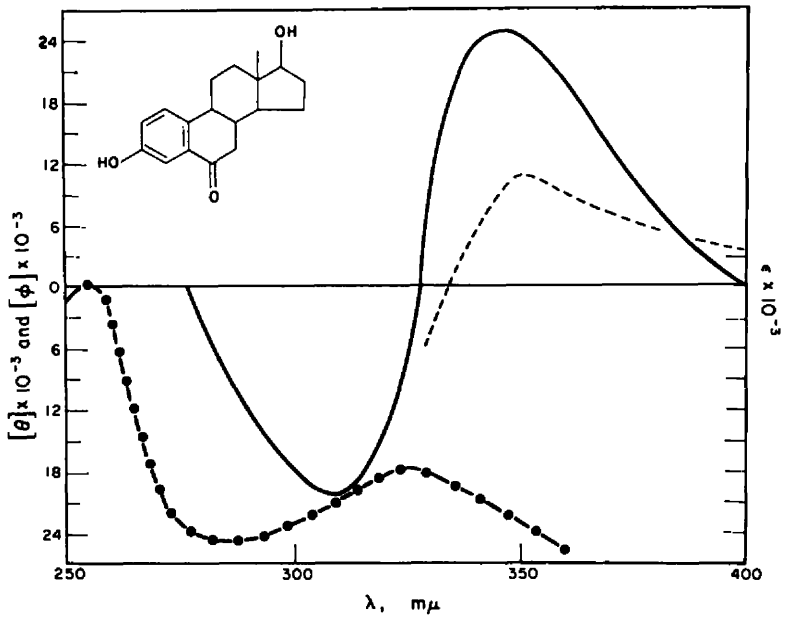


FIG. 1. Circular dichroism (——), optical rotatory dispersion (· · ·) and ultraviolet absorption (–·–·–) of 6-Oxo-3,17β-estradiol in methanol.

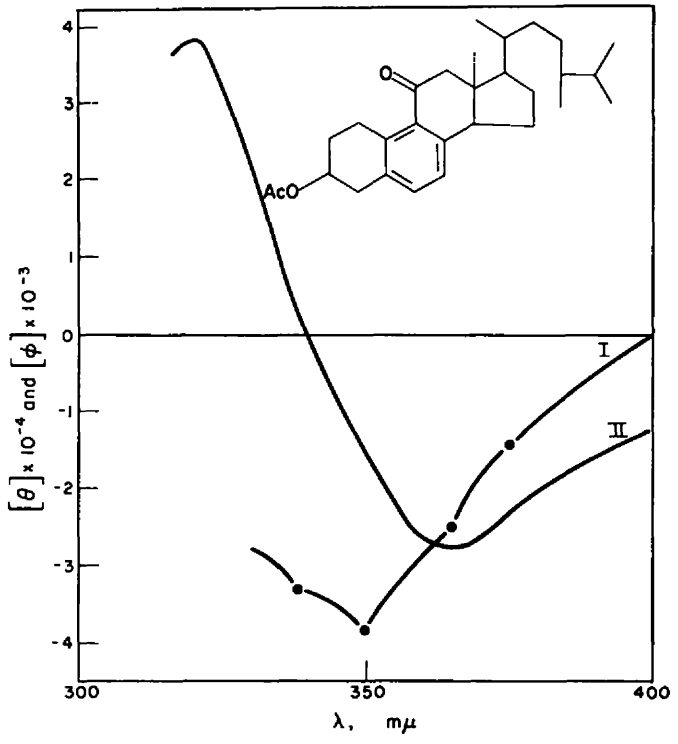


FIG. 2. Circular dichroism (I) and optical rotatory dispersion (II) curves of 3-acetoxy-19-norergosta-5,7,9-triene-11-one in iso-octane.

λ_{max} 232 mμ (log ε 4·29) and 281 mμ (log ε 4·19). $\lambda_{max}^{iso\text{-}octane}$ 345 mμ (log ε 1·92), Sh 306 mμ (log ε 3·81), 297 mμ (log ε 3·90), 274 mμ (log ε 3·96), 237 mμ (log ε 4·17), 231 mμ (log ε 4·25), 224 mμ (log ε 4·23). C.D. in iso-octane: C 0·02336 (400–320 mμ), $[\theta]_{363}$ +2000, $[\theta]_{346}$ +2993, $[\theta]_{333}$ +3326. R.D. in methanol: plain positive curve above 310 mμ.

7-Oxototarol.[11] m.p.240–241°, λ_{max}^{EtOH} 326 mμ (log ε 3·42), 258 mμ (log ε 3·74). C.D. in iso-octane: C 0·206 (400–335 mμ), $[\theta]_{340}$ +5765. R.D. in methanol: plain positive curve above 350 mμ.

7-Oxototaryl acetate.[11] m.p. 168–169° (lit.[12] m.p. 169–170°). λ_{max} 252 mμ (log ε 4·01) and 297 mμ (log ε 3·45). R.D. in methanol: C 0·0578; $[\phi]_{500}$ +59·2°, $[\phi]_{450}$ +177·5°, $[\phi]_{400}$ +591·7°, $[\phi]_{355}$ +2639°, $[\phi]_{332}$ 0°.

7-Oxototaryl benzoate.[11] m.p. 152–153°. R.D. in methanol: C 0·1275; $[\phi]_{500}$ +76·11°, $[\phi]_{450}$ +190·1°, $[\phi]_{400}$ +785·8°, $[\phi]_{355}$ −4437°, $[\phi]_{332}$ 0°.

7-Oxo-podocarpic acid. Methyl 7-oxo-0-methyl podocarpate (979 mg) was added to hot (90°) pyridine hydrochloride (7 g) and the mixture heated to 210° for 40 min. It was then cooled to 100° and poured into water (50 ml). The resultant precipitate was washed with water, 10% aq. HCl and finally with water. Crystallization of the washed precipitate from aq. methanol gave 7-oxo-podocarpic acid (476 mg, 53%) as needles, m.p. 304–305° (lit.[13] m.p. 296–298°). λ_{max} 228 mμ (log ε 4·10) and 293 mμ (log ε 4·19). R.D. in methanol: C 0·0672; $[\phi]_{550}$ +212°, $[\phi]_{450}$ +847°, $[\phi]_{400}$ +1949°, $[\phi]_{380}$ +11,647°, $[\phi]_{343}$ +13,680°, $[\phi]_{312}$ 0° (by extrapolation).

Methyl-7-oxopodocarpate. A solution of methyl-7-oxo-0-acetylpodocarpate (200 mg) in ethanol (2 ml) was warmed with 5% sodium hydroxide solution for 3 minutes and the mixture kept at room temperature for 5 hr. The solution was acidified, poured into water, and the crystalline precipitate recrystallised from methanol to yield *methyl-7-oxopodocarpate* (168 mg) as needles, m.p. 235–237° with softening at 205°. λ_{max}^{EtOH} 282 mμ (log ε 4·54) and 282 mμ (log ε 4·34) ν_{max}^{nujol} 3448 cm^{-1} (OH), 1706 cm^{-1} (ester CO), and 1667 cm^{-1} (CO), R.D. in methanol: C 0·065; $[\phi]_{550}$ + 492°, $[\phi]_{350}$ + 1860°, $[\phi]_{327}$ + 2070°, $[\phi]_{315}$ + 1925°, $[\phi]_{302}$ 0° (by extrapolation). (Found: C, 71·5; H, 7·3. $C_{18}H_{22}O_4$ requires C, 71·5; H, 7·3%).

Methyl 7-oxo-0-methylpodocarpate. A solution of chromic acid (2·45 g) in 80% acetic acid (5·7 g) was added dropwise to a stirred solution of methyl 0-methylpodocarpate (3·41 g) in glacial acetic acid (35·7 g). The mixture was stirred at room temp for 5 days and then poured into water (400 ml). The mixture was then extracted with ether (2 × 200 ml), the ether solution washed with water (3 × 100 ml) and dried. Evaporation of ether gave a yellow oil which afforded colourless needles (2·4 g, 70%) from aq. ethanol. Further crystallization from methanol gave pure product as long needles, m.p. 124–126° (lit.[13] m.p. 122–124°). λ_{max} 227 mμ (log ε 4·11) and 276 mμ (log ε 4·15). R.D. in methanol: C 0·0967; $[\phi]_{600}$ +196°, $[\phi]_{500}$ + 370°, $[\phi]_{400}$ + 979·6°, $[\phi]_{350}$ +4475°, $[\theta]_{347}$ +4640°, $[\theta]_{317}$ 0° (by extrapolation); in iso-octane: C 0·0423; $[\phi]_{600}$ +149·2°, $[\phi]_{400}$ +671·8°, $[\phi]_{367}$ +2615°, $[\phi]_{356}$ +1793°, $[\phi]_{351}$ +2764°, $[\phi]_{342}$ +37·4°, $[\phi]_{336}$ +1146°, $[\phi]_{332}$ 0°, $[\phi]_{327}$ −1711°, $[\phi]_{322}$ −747°, $[\phi]_{314}$ −2615°, $[\phi]_{308}$ −1942°.

Methyl 7-oxo-13-isopropyl-0-methyl podocarpate. A standard solution[14] of chromic acid (1·1 ml) was added dropwise to a solution of 13-isopropyl-0-methylpodocarpinol [1·13 g, m.p. 82–85° (lit.[15] m.p. 83–85°). From the collection of the late C. W. Brandt.] in acetone (15 ml) at 0°. The mixture was immediately poured into water and allowed to stand 30 min. The solid that separated was collected and crystallized from methanol to give needles (964 mg) of 13-isopropyl-0-methylpodocarpinal, m.p. 136–137° (lit.[16] m.p. 136–136·5°).

The above standard chromic acid solution (2 ml) was added to a solution of 13-isopropyl-0-methylpodocarpinal (225 mg) in acetone (10 ml). The mixture was allowed to stand at room temp 30 min and then poured into water. This aq. solution was extracted with ether (2 × 20 ml) and the ether solution washed and dried. Removal of ether gave a yellow gum which on recrystallization from methanol yielded needles (80 mg) of 13-isopropyl-0-methylpodocarpic acid, m.p. 182–184° (lit.[16] m.p. 183·5–184°).

[11] R. C. Cambie and L. N. Mander, *Tetrahedron* **18**, 465 (1962).
[12] Y. L. Chow and H. Erdtman, *Acta Chem. Scand.* **14**, 1852 (1960).
[13] R. H. Bible, U.S. Pat. 2,753,357 (1956); *Chem. Abstr.* **51**, 2869 (1957); U.S. Pat. 2,759,014 (1956); *Chem. Abstr.* **51**, 5838 (1957).
[14] See K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.* 39 (1946).
[15] M. M. Baizer, M. Karnowsky and W. G. Bywater, *J. Amer. Chem. Soc.* **72**, 3800 (1950).
[16] W. P. Campbell and D. Todd, *J. Amer. Chem. Soc.* **64**, 928 (1942).

Methylation of 13-isopropyl-0-methylpodocarpic acid was carried out by dissolving it in absolute methanol and treating this with an ethereal solution of diazomethane. Methyl 13-isopropyl-0-methylpodocarpate thus obtained was crystallized from aq. methanol as colourless needles, m.p. 109–110° (lit.[17] m.p. 109–109·5°).

A solution of chromic acid (432 mg) in 80% aq. acetic acid (1·2 g) was added dropwise to a solution of methyl 13-isopropyl-0-methylpodocarpate (402 mg) in glacial acetic acid. The mixture was allowed to stand 5 days at room temp and then poured into water. The resulting yellow oil which solidified at 0° was washed with water and repeatedly crystallized from methanol to give 356 mg of *methyl 7-oxo-13-isopropyl-0-methylpodocarpate* as colorless plates, m.p. 144–145·5°. λ_{max} 230 mμ (log ε 4·13), 280 mμ (log ε 4·10). R.D. in methanol: C 0·075; $[\phi]_{650}$ + 189·3°, $[\phi]_{500}$ − 225·1°, $[\phi]_{400}$ + 811·2°, $[\phi]_{342}$ + 4184°, $[\phi]_{313}$ 0° (by extrapolation). (Found: C, 73·97 and H, 8·25. $C_{22}H_{30}O_4$ requires: C, 73·71 and H, 8·44%.)

Methyl 7-oxo-13-acetyl-0-methylpodocarpate. Methyl 13-isopropenyl-0-methylpodocarpate (80 mg, m.p. 120·5–121·5°, from the collections of the late C. W. Brandt) was oxidized with 8N CrO_3–H_2SO_4 mixture in the normal manner and the solution allowed to stand overnight at room temp. Crystallization of the product from aq. methanol gave *methyl 7-oxo-13-acetyl-0-methylpodocarpate* (60 mg), m.p. 241–242°. C.D. in methanol: C 0·274 (400–320 mμ), $[\theta]_{326}$ + 4849. R.D. in methanol: C 0·0387; $[\phi]_{400}$ + 832·7°, $[\phi]_{343}$ + 2907°, $[\phi]_{315}$ 0° (by extrapolation). (Found: C, 70·60 and H, 7·00. $C_{21}H_{28}O_5$ requires: C, 70·37 and H, 7·31%.)

Methyl 7-oxodehydroabietate. Dehydroabietic acid in dry ether solution was methylated with an excess of ethereal diazomethane. Chromatography on alumina and crystallization of the product from aq. methanol gave methyl dehydroabietate, m.p. 61–63° (lit.[18] m.p. 62·5–63°).

A solution of chromic acid (340 mg) in 80% aq. acetic acid (1 g) was added dropwise to a solution of methyl dehydroabietate (459 mg) in glacial acetic acid. The mixture was allowed to stand 5 days and then poured into water. The product was extracted with ether. The ether solution was washed and dried. Removal of solvent gave a yellow oil which crystallized (with difficulty) from aq. methanol to yield methyl 7-oxo-dehydroabietate, m.p. 68–69°, undepressed by an authentic sample provided by Dr. T. F. Sanderson of Hercules Powder Company. $\lambda_{max}^{iso\text{-}octane}$ 248 mμ (log ε 4·06), Sh 255 mμ (log ε 3·97), 292 mμ (log ε 3·28), 303 mμ (log ε 3·23). R.D. in methanol: C 0·048; $[\phi]_{650}$ + 123°, $[\phi]_{400}$ − 410°, $[\phi]_{350}$ + 3144°, $[\phi]_{325}$ 0°.

9-Oxo-methoxy-trans-1,2,3,4,9,10,11,12-octahydro-1,1,12-trimethylphenanthrene. O-methyl-podocarpinal was converted to the semicarbazone, m.p. 203–205° in 91% yield by standard methods. The semicarbazone (600 mg), KOH (600 mg) and hydrazine (98%, 6 ml) were heated under reflux with trimethylene glycol (25 ml) for 1 hr. Excess hydrazine was removed by distillation and the mixture heated at 220° for 2 hr. The crude product, collected from the reaction mixture by extraction with light petroleum (b.p. 50–60°), was transferred to acetone (10 ml) and directly oxidized with 8N CrO_3–H_2SO_4 for 3 days at room temp. The resultant gum (450 mg) isolated on pouring into water was dissolved in ether, washed ($NaHCO_3$ aq.) and adsorbed on alumina (grade I). Elution with benzene gave a methoxy ketone as an oil (301 mg) which could not be induced to crystallize. IR spectra indicated the absence of an OH group.

A sample of this compound (200 mg) was demethylated by treatment with pyridine hydrochloride in the usual manner and the crude product reacted with 2,4-dinitrophenylhydrazine. The hydrazone after percolating through alumina in benzene solution was obtained as needles, m.p. 265–268° (lit.[18] m.p. 266–268°) from methanol. (Found: C, 62·96; H, 6·35 and N, 12·18. $C_{22}H_{26}N_4O_5$ requires: C, 63·00; H, 5·98 and N, 12·78%.)

7-Oxo-0-acetylpodocarpic acid. 7-Oxo-podocarpic acid (m.p. 304–305°, 60 mg) was heated under reflux with acetic anhydride (1 ml) and AnalaR pyridine (0·5 ml) for 3 hr. The product was isolated as a solid by pouring into ice water. Crystallization from aq. methanol gave *7-oxo-0-acetylpodocarpic acid* as needles (58 mg), m.p. 196–198°. ν_{max}^{nujol} 1742 cm^{-1} (ester CO), 1721 cm^{-1} (acid) and 1678 cm^{-1} (conjugated CO). R.D. in methanol: C 0·0783; $[\phi]_{600}$ + 462·3°, $[\phi]_{450}$ + 522·4°, $[\phi]_{400}$ + 994·6°, $[\phi]_{352}$ + 2290°, $[\phi]_{325}$ 0° (by extrapolation). (Found: C, 68·9 and H, 6·7. $C_{19}H_{22}O_5$ requires: C, 69·1 and H, 6·7%.)

17 *β-Acetyl estradiol-3-methyl ether.* Estradiol-3-methyl ether (1·06 g) was heated under reflux

[17] W. P. Campbell and D. Todd, *J. Amer. Chem. Soc.* **62**, 1287 (1940).

[18] P. F. Ritchie, T. F. Sanderson and L. F. McBurrey, *J. Amer. Chem. Soc.* **75**, 2610 (1953).

[19] R. Hodges and R. A. Raphael, *J. Chem. Soc.* 50 (1960)

with acetic anhydride (5 ml) and pyridine (1 ml) for 2 hr at 100°. Crystallisation of the product from methanol gave the 17 *β-acetate* (1·11 g, 90% yield) as shining plates. ν_{max}^{nujol} 1727 (Ac) and 1227 cm^{-1}. (OMe, broad). (Found: C, 76·8; H, 8·5. $C_{21}H_{28}O_3$ requires C, 76·8; H, 8·6%.)

17β-Acetyl-6-oxo-estradiol-3-methyl ether. 17β-Acetyl estradiol-3-methyl ether (900 mg) in dry acetone was treated dropwise with 8N CrO_3–H_2SO_4 reagent (20 ml) at room temp and allowed to stand 2 days. It was then poured into water and extracted with ether. The ethereal extract was freed from acids (by washing with sat. $NaHCO_3$ aq.). The neutral fraction so obtained was chromatographed on 5% deactivated alumina and the residues from initial fractions, eluted with benzene, rechomatographed to yield *17β-acetyl-6-oxo-estradiol-3-methyl ether* (400 mg, 43% yield) which formed long needles, m.p. 149–151°, from aq. methanol. λ_{max}^{nujol} 1724 cm^{-1} (ester CO), 1675 cm^{-1} (conjugated CO) and 1229 cm^{-1} (–OCH_3). R.D. in methanol: C 0·0986; $[\phi]_{400}$ +554°, $[\phi]_{361}$ +5421°. (Found: C, 73·5 and H, 8·0. $C_{21}H_{28}O_4$ requires: C, 73·7 and H, 7·9%.)

6-Oxo-3,17β-estradiol diacetate.[20] Estradiol diacetate (800 mg) in dry acetone (10 ml) was treated dropwise with 8N CrO_3–H_2SO_4 mixture (10 ml) at 0°. The mixture was kept at 20° for 12 hr, poured into water and extracted with ether. The ether extracts were separated into neutral and acidic fractions (with sat. $NaHCO_3$ aq.). The neutral portion was further separated into a ketonic fraction with Girard reagent T, following the method of Longwell and Wintersteiner,[20] and the fraction acetylated with acetic anhydride sodium acetate. Crystallization from absolute ethanol gave 6-oxo-estradiol diacetate (243 mg, 29% yield) as needles, m.p. 173–176°. λ_{max}^{EtOH} 250 mμ (log ε 3·94) and 300 mμ (log ε 3·23). $\lambda_{max}^{iso-octane}$ Sh 353 mμ (log ε 1·29), Sh 340 mμ (log ε 1·54), Sh 300 mμ (log ε 3·21), 292 mμ (log ε 3·24), Sh 251 mμ (log ε 3·86), 243 mμ (log ε 3·98). $\nu_{max}^{CS_2}$ 1764 cm^{-1} (aryl acetate), 1733 cm^{-1} (alkyl acetate) and 1686 cm^{-1} (conjugated CO). R.D. in methanol: C 0·0529; $[\phi]_{400}$ −416°, $[\phi]_{350}$ +2366°, $[\phi]_{331}$ 0°; in iso-octane: C 0·0281, $[\phi]_{362}$ +1177°, $[\phi]_{346}$ 0°.

6-Oxo-3,17β-estradiol[20]. 6-Oxo-estradiol diacetate (150 mg) was treated with 20% methanolic KOH (4 ml) in an atm of nitrogen. The mixture was kept at 20° for 24 hr and then poured into water, acidified and finally extracted with ether. After removing the ether, the residue was crystallized from abs. ethanol which gave 6-oxo-estradiol (70 mg) as plates, m.p. 279–281° (lit.[20] m.p. 281–283°). λ_{max}^{EtOH} 255 mμ (log ε 3·91) and 325 mμ (log ε 3·49). ν_{max}^{nujol} 3436 cm^{-1} (phenolic OH), 3125 (OH) and 1664 cm^{-1} (conjugated CO). C.D. in methanol: C 0·0596 (400–345 mμ), $[\theta]_{345}$ +24,982, $[\theta]_{310}$ −20,573. R.D. in methanol: C 0·01145; $[\phi]_{450}$ + 368°, $[\phi]_{400}$ −1724°, $[\phi]_{350}$ +9840°, $[\phi]_{336}$ 0°.

A-nor-19-norergosta-5,7,9-trien-3-one. C.D. in iso-octane: C 0·7612 (400–320 mμ), $[\theta]_{356}$ −238, $[\theta]_{340}$ −595, $[\theta]_{328}$ −595. R.D. in iso-octane: C 0·07612; $[\phi]_{600}$ +135°, $[\phi]_{500}$ +165°, $[\phi]_{400}$ +260°, $[\phi]_{350}$ −337°.

3-Acetoxy-19-norergosta-5,7,9-trien-11-one. C.D. in iso-octane: C 0·8796 (400–325 mμ), $[\theta]_{366}$ −25,466, $[\theta]_{350}$ −35,853, $[\theta]_{328}$ −33,615. R.D. in iso-octane: C 0·08796; $[\phi]_{600}$ −175°, $[\phi]_{500}$ −250°, $[\phi]_{400}$ −1256°, $[\phi]_{362}$ −2759°, $[\phi]_{330}$ 0°, $[\phi]_{320}$ +3833°.

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[20] B. B. Longwell and O. Wintersteiner, *J. Biol. Chem.* **133**, 219 (1940).