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CHEMISTRY OF THE PODOCARPACEAE—XVI[1]

HETEROLYTIC FRAGMENTATION OF 6α-BROMO-7-OXOTOTAROL

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Abstract— Treatment of 6α-bromo-7-oxototaryl acetate (II, R = OAc) with $NaHCO_3$/DMSO gives 6α-bromo-7-oxototarol (II, R = OH, 5%), Δ^5-dehydro-7-oxototaryl acetate (III, R = OAc, 45%), Δ^5-dehydro-7-oxototarol (III, R = OH, 15%), and, by fission of the A/B ring junction, 7-oxo-5,10-secototara-5,8,10(20),11,13-pentaen-13-ol (IV, R = H, 5%). The yield of the secoditerpenoid is improved markedly (80%) when 6α-bromo-7-oxototarol rather than its acetate is the substrate.

The action of $NaHCO_3$/DMSO on other 6α-bromo-7-oxo-diterpenoids is examined and formation of the secoditerpenoid shown to be by a fragmentation reaction which is explicable in terms of the structure and stereochemistry of the parent and the nature of the dipolar aprotic medium.

FROM an examination of the action of $NaHCO_3$–DMSO on steroidal α-bromo-ketones Nace and Iacona[2] have shown that when the halogen atom and a vicinal hydrogen have a *trans* diaxial relationship elimination is normally the predominant reaction. When the vicinal halogen and H atoms possess a *trans* equatorial-axial relationship however, elimination to form the αβ-unsaturated ketone is relatively difficult and where it is possible oxidation becomes an important competing reaction yielding the α-diketone or its diosphenol.

During a search for a simple pathway to 6,7-dioxototarol (I),[3] the acetate (II, R = OAc)* of 6α-bromo-7-oxototarol[3,5] which possesses a *cis*-pseudoequatorial-axial relationship† between its 6α-Br and 5α-H atoms, was treated with $NaHCO_3$–DMSO in an attempt to effect oxidation rather than elimination. A product was obtained, TLC of which showed that it was composed of four compounds besides unreacted starting material (20%). These were separated by repeated column chromatography on alumina and three were identified as 6α-bromo-7-oxototarol (II, R = OH, 5%), Δ^5-dehydro-7-oxototaryl acetate (III, R = OAc, 45%), and Δ^5-dehydro-7-oxototarol (III, R = OH, 15%), respectively, by direct comparison with authentic samples prepared by established procedures. The remaining and most polar compound (5%) was identified from the following evidence as 7-oxo-5,10-secototara-5,8,10(20),-11,13,-pentaen-13-ol (IV, R = H) in which a 10-membered ring had been formed by fission of the A/B ring junction.

The crystalline solid, m.p. 195–196·5°, analysed for $C_{20}H_{26}O_2$ in agreement with a

* During the course of this work it was noted that Taylor *et al.*[4] had claimed to have prepared 12-bromo-7-oxototaryl acetate, m.p. 176–178°, by a similar method to that which in our hands[5] had led to 6α-bromo-7-oxototaryl acetate, m.p. 176–177°. Repetition of our experiment and of Taylor's led to an identical product whose NMR spectrum (2 aromatic protons) showed beyond doubt that the compound was the 6-bromo derivative.

† Wenkert *et al.*[7] distinguish a "half-boat" conformation for the B-ring of totarol as a result of the strong buttressing effect of the C_{13} and C_{14} substituents on the aromatic ring. In this conformation the C_6-α-bromine atom deviates considerably from a true equatorial conformation.[6]

mol wt of 298 from the mass spectrum while its UV spectrum showed strong absorption (ε 13,850) at 248 mμ characteristic of the electron transfer band of an aryl ketone intensified by an aryl substituent (OH) possessing non-bonded electrons.[9] Its IR spectrum which was devoid of acetyl absorption in the 1760 cm^{-1} region showed phenolic bands at 3950, 3400, and 1284 cm^{-1} and a strong CO peak at 1648 whose bathochromic shift from the normal range indicated the presence of a cross-conjugated CO group [cf. Δ^5-dehydro-7-oxototarol (III, R = OH), ν_{max} 1649 cm^{-1}]. In addition to a band at 819 cm^{-1} typical of that for the two adjacent protons of the totaryl aromatic substitution pattern[10] the IR spectrum also showed bands at 985 and 910 cm^{-1} which could be assigned to a *trans*-disubstituted double bond and an exocyclic methylene group, respectively.

In accord with the presence of the cross-conjugated CO group the compound formed a bright red 2,4-dinitrophenylhydrazone and it gave monoacetyl ($C_{22}H_{28}O_3$) and monomethyl ether ($C_{21}H_{28}O_2$) derivatives which rapidly decolourized bromine solution. The uptake of 2·18 moles of hydrogen/mole over Adams' catalyst confirmed the presence of two double bonds while the formation of formaldehyde, isolated as its dimedone derivative, from ozonolysis showed that one of them was terminal. The absence of optical activity at all wavelengths in the normal ORD range reflected the loss of the two asymmetric centres of the parent acetate (II, R = OAc) in opening of the A/B ring junction to form the secoditerpenoid.

The NMR spectrum of the compound showed features which were in agreement with its postulated structure (IV, R = H). A two-proton AB quartet centred at 6·87 δ (J = 8 c/s) corresponded to the adjacent C_{11} and C_{12} protons of the tetrasubstituted aromatic nucleus while a 2-proton AB quartet centred at 6·30 δ possessed a coupling constant (J = 16·5 c/s) which allowed assignment to a *trans*-disubstituted double bond (cf. *cis*-disubstituted double bonds, J = 6–14 c/s).[11] Two one-proton peaks at 4·96 and 4·78 δ showed a *geminal* coupling constant (J = 1·6 c/s) which was within the range (0–3 c/s)[11, 12] expected for non-equivalent protons of a terminal methylene group (cf. styrene, J = 1·3 c/s[12, 13]). The Me region of the spectrum was marked by the absence of a peak corresponding to that of the C_{10}-angular Me group (1·22 δ) of 6α-bromo-7-oxototaryl acetate. The presence of the aryl isopropyl group was clearly shown by a characteristic septet (J = 7 c/s) of the C_{15}-methine proton centred at 3·17 δ, by a doublet at 1·36 δ (J = 7 c/s) representing the isopropyl Me groups,[14, 15] and by their mutual coupling with spin decoupling experiments. A 6-proton singlet at 1·03 δ represented two magnetically equivalent Me groups. Examination of a Dreiding model of the secoditerpenoid showed that its 10-membered ring possessed considerable flexibility resulting in a vast array of possible conformers. From the lack of evidence for restricted rotation de la Mare and Klyne[16] have concluded that equilibrium is always established between the conformers of simple medium ring compounds even although they represent constrained systems.[17] Substitution of trigonal (sp^2) C atoms for tetrahedral (sp^3) C atoms in a cyclodecane relieves I-strain[18] by reducing non-bonded interaction and spreading the C—C—C bond angles.[16, 19] From this it follows that the secoditerpenoid will exist in a number of rapidly equilibrating conformations whose C_4-*gem* methyls would experience equivalent average magnetic environments accounting for the single peak in the NMR spectrum.

Reaction of the secoditerpenoid with $NaBH_4$ resulted in the unexpected formation of 7-oxo-5,10-secototara-8,10(20),11,13-tetraen-13-ol (V) from the reduction of the

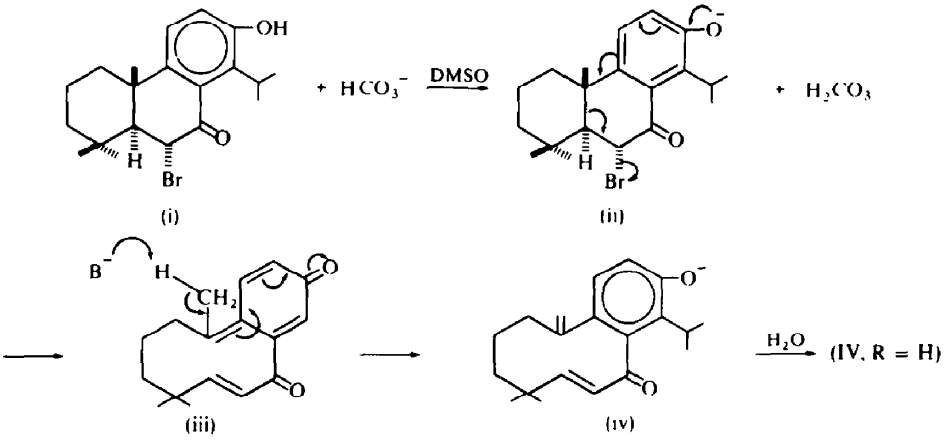
C_5-double bond of the αβ-unsaturated keto-group. While LAH or $NaBH_4$ reduction of C=C double bonds in conjugated systems has been observed previously[20] such reductions are normally accompanied by concomitant reduction of the CO group. However, a similar selective reduction of the double bond of an enone system in cedrelone has been reported by Hodges *et al.*[21] who suggest steric shielding and potential non-bonded interaction as the reasons for the resistance of the CO group to reduction. Presumably the buttressing effect of the C_{14}-arylisopropyl group results in steric shielding of the C_7-keto group in the present case. The structure of the reduction product followed from examination of its IR, UV and NMR spectra. The IR spectrum was similar to that of the parent but a shift of the carbonyl peak towards higher wavenumber (ν_{max} 1678 cm^{-1}) and the disappearance of the 985 cm^{-1} band indicated saturation of the *trans*-double bond as did also the sharp drop in intensity (ε, 7200) of the UV absorption at 246 mμ. The NMR spectrum also showed the loss of the *trans*-double bond and that the exocyclic double bond was still present. As was the case in the parent the C_4 *gem* methyls were again equivalent giving rise to a sharp 6-proton singlet which showed an upfield shift of ca. 0·3 ppm from that of the parent. A Dreiding model of the tetraene indicates that its 10-membered ring is even more flexible than that of the pentaene, the increased spatial freedom of the C_4 *gem*-methyls enabling them to reside in the cones of magnetic shielding of the C_7-CO group, the C_{20}-exocyclic methylene group, and the aromatic nucleus. That the increased shielding is not simply due to the removal of the adjacent magnetic environment of the *trans*-double bond can be seen by the upfield shift of only 0·12 ppm for the C_2-*gem* dimethyl singlet when *trans*-2-methylhex-3-ene is converted to the saturated alkane, 2-methylhexane.

With the constitution of the secoditerpenoid established its mode of formation and the structural features necessary for secoditerpenoid formation were investigated. The action of $NaHCO_3$–DMSO on some other 6α-bromo-7-oxoditerpenoids was therefore examined. With 6α-bromo-7-oxototaryl methyl ether (II, R = OMe)[4] a product was obtained from which starting material (20%), Δ^5-dehydro-7-oxototaryl methyl ether (III, R = OMe, 70%), and 7-oxototaryl methyl ether (VI, R = OMe, 10%) were isolated. Comparative TLC with the methyl ether (IV, R = Me) of the secoditerpenoid showed that there was no trace of this compound in the reaction product. In the case of methyl 6α-bromo-7-oxo-O-methylpodocarpate (VII, R = Br)[22,*] the compounds identified in the product were unchanged material (5%), the lactone (VIII, 85%) of 6β-hydroxy-7-oxo-O-methylpodocarpic acid,[22] and methyl-7-oxo-O-methylpodocarpate (VII, R = H, 5%). With 6α-bromo-7-oxototara-8,11,13-triene (II, R = H)[15] unreacted material accounted for 25% of the product, 7-oxo-5,8,11,13-tetraene (III, R = H) for 60% and 7-oxototara-8,11,13-triene (VI, R = H) for 5%. In neither of the latter cases was there any evidence for the formation of a seco-compound indicating that the presence of an aryl acetate group in the C_{13}-position was of some significance in the production of such a compound. Careful checking of the products from the original $NaHCO_3$–DMSO reaction with 6α-bromo-7-oxototaryl acetate and variation of the reaction conditions showed that no

* Contrary to previous evidence[5,23] Wheeler *et al.*[8] have suggested that this compound possesses a β-bromine atom. A recently completed three-dimensional X-ray structure determination on the compound by Professor T. N. M. Waters and Mr. G. R. Clark of this Department shows that the bromine atom is definitely α.

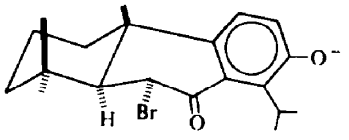
trace of the acetoxy-secoditerpenoid (IV, R = Ac) was present in the crude reaction mixture. From this and the fact that none of the other α-bromoketones (II, R = OMe; VI, R = Br, and II, R = H) were phenols or afforded phenols from their reaction with $NaHCO_3$–DMSO, it was inferred that the precursor of the secoditerpenoid (IV, R = H) was 6α-bromo-7-oxototarol (II, R = OH) and not its acetate, the low yield of secoditerpenoid from the acetate being a consequence of its partial deacetylation under the reaction conditions. This was confirmed when the phenol (II, R = OH) was treated with $NaHCO_3$–DMSO, the secoditerpenoid (IV, R = H) now being obtained in markedly increased yields of 70–80%. Similar yields were obtained when the dipolar aprotic solvent DMF was substituted for DMSO in the reactions but as expected, only deacetylation occurred when 6α-bromo-7-oxototaryl acetate was reacted with $NaHCO_3$ in the protic solvent methanol. No reaction occurred if 7-oxototarol which is devoid of halogen was treated with $NaHCO_3$–DMSO while in the absence of $NaHCO_3$, reaction of the acetate (II, R = OAc) with DMSO–acetonitrile[24,25] afforded the elimination products, Δ^5-dehydro-7-oxototarol, Δ^5-dehydro-7-oxototaryl acetate, and 6α-bromo-7-oxototarol over a long period of time but gave no secoditerpenoid.

With the structural requirements for high yields of secoditerpenoid more clearly defined a rational explanation for its mode of formation could now be advanced. The secoditerpenoid is undoubtedly formed via a heterolytic fragmentation[26] whose suggested pathway is shown in the following scheme.



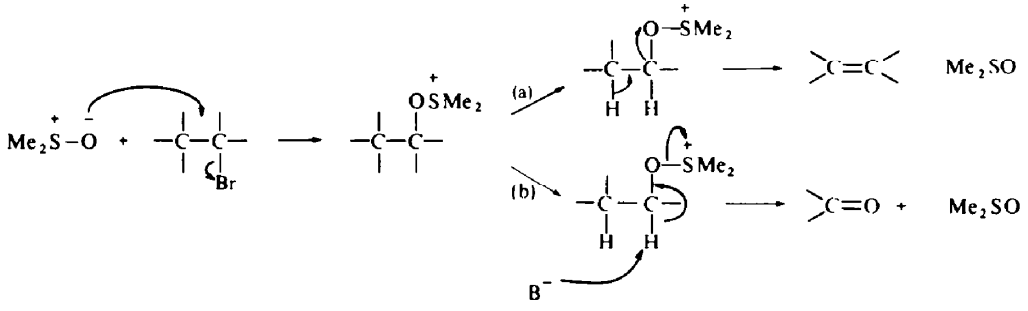
The success of this fragmentation is due to two factors *viz.* the nature of the reaction medium and the configuration of the reacting molecule. In the dipolar aprotic medium the anion HCO_3^- exists as a powerful base[27–29] promoting formation of the phenoxide ion (ii). Since stabilization of the negative charge by solvation or ion-pair formation will not occur to any significant extent[27,28] the charge on the phenoxide ion can be released via the *para* position of the aryl nucleus to the site of electron deficiency at C_6 caused by polarization of the C—Br bond.[31] Attack by base on the C_{20}—proton of the heterolytically fragmented product (iii) would then afford a new phenoxide ion (iv) which in turn would yield the secoditerpenoid (IV, R = H) on quenching the reaction with water. Fragmentation is favoured since the C_6—Br

bond, the C_5—C_{10} bond, and the C_9—C_{11} bond of the bromoderivative (ii) possess an antiperiplanar configuration (IX) necessary for a concerted one-step reaction.[32] The formation of a *trans* C_5 double bond in the product is in accord with the stereochemical implications of the fragmentation.[33]

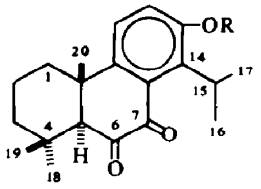


IX

Jarreau *et al.*[34] have suggested that the action of DMSO on a halogenated compound results in the formation of an intermediate salt[35] by nucleophilic displacement of the halogen, the salt then undergoing elimination (a) or oxidation (b) by two competitive reactions. The non-observance of 6,7-diketones in the present work is



explicable in terms of the conformation of the intermediate salt. With the exception of 6α-bromo-7-oxototarol where ionization of the C—Br bond leads to a more favorable concerted fragmentation, displacement of the pseudoequatorial bromine of all the other α-bromoketones by DMSO leads to inversion of configuration at C_6. The C_6-DMSO substituent and the C_5-proton then possess a *trans*-diaxial relationship favourable for 1,2-elimination. Examination of Dreiding models show that owing to the close proximity of the C_4-axial and C_{10}-Me groups the C_6-proton is more hindered from attack by a base from the β-face than is the axial C_5-proton by attack from the α-face. Elimination therefore occurs to give Δ^5-dehydro products rather than oxidation to form α-diketones. In the case of the action of DMSO–acetonitrile on methyl 6α-bromo-7-oxodehydroabietate (XI) where Wenkert *et al.*[24] postulated the intermediacy of a 6,7-diketo derivative during the formation of a ketolactone (X), the equatorial C_4-carboxymethyl could block the C_5-axial proton from attack by base (the effectiveness of this blocking would depend on the exact conformation of the carboxy Me group) such that C_5-proton elimination would become highly unfavourable in comparison with the removal of a proton from C_6 to give an α-diketone. Such an explanation is in accord with Wenkert's observation that the reaction was a slow one requiring ten days to give a high yield of the product.



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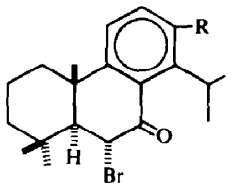

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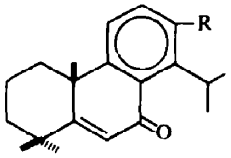

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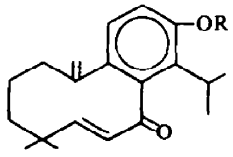

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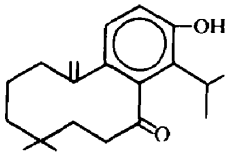

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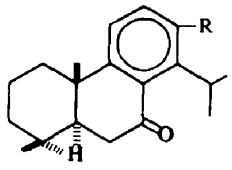
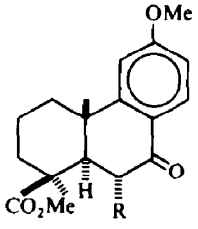
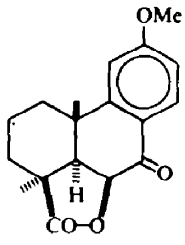


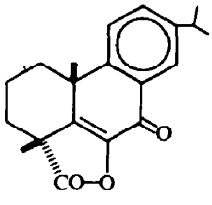
VI



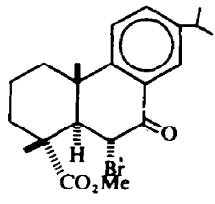
VII



VIII



X



XI

EXPERIMENTAL

Microanalyses were by Dr. A. D. Campbell and his associates, University of Otago, New Zealand. IR spectra were measured with a Perkin–Elmer 237 instrument and UV spectra were determined for EtOH solns with a Perkin–Elmer 137 UV spectrophotometer. ORD curves were determined with a Jasco ORD/UV-5 spectrophotometer at 25° and, unless otherwise stated, are for solns in MeOH. Unless otherwise stated NMR spectra were determined in $CDCl_3$ with a Varian A-60 spectrometer, using TMS as internal reference.

Light petroleum had b.p. 50–60°; alumina for column chromatography was P. Spence Type H material deactivated with 5% by vol of 10% HOAcaq. Silica gel G. was used for TLC and m.ps, determined on a Kofler block, were uncorrected.

6α-Bromo-7-oxototarol (II, R = OH)

Bromination of 7-oxototaryl acetate[36] as described[5] gave II (R = OAc, 82%) as needles, m.p. and mixed m.p. 176–177°, ν_{max} (CCl_4) 1767 (aryl acetate) and 1694 cm^{-1} (aryl COCHBr), RD (*c*, 0·096) $[\phi]_{589}$ +115°, $[\phi]_{400}$ +435°, $[\phi]_{361}$ +3,690°, $[\phi]_{346}$ 0°, $[\phi]_{320}$ −12,500. NMR (CCl_4) 1·09, 1·17 (C_4-*gem* diMe), 1·22 (C_{10}-angular Me), 1·37 (d, J = 7·0 c/s, $C_{16,17}$-isopropyl Me's), 2·29 (aryl acetate), 3·42 (5 members of septet, J = 7·0 c/s, C_{15}-methine proton), 4·47 (d, J = 7·2 c/s, C_6-proton), and 7·08 δ (2 proton s, $C_{11,12}$-aromatic protons).

Repetition of Taylor's experiment[4] gave an identical product (m.p., mixed m.p., TLC, IR, and NMR).

Hydrolysis of the bromo derivative (1·5 g) with KOH (0·5 g) and MeOHaq (90%, 50 ml) under reflux for 1 hr gave II (R = OH; 1·05 g, 76%) which formed needles, m.p. 218–220°, from MeOH (cf.[4] m.p. 225° for "12-bromo-7-oxototarol"). (Found: C, 63·8; H, 7·4; Br, 21·0. $C_{20}H_{27}O_2Br$ requires C, 63·3; H, 7·2; Br, 21·1%); ν_{max} ($CHCl_3$) 3583 sharp, 3310 broad (phenol), 1687 (aryl COCHBr), and 1280 cm^{-1} (phenol); RD (*c*, 0·115) $[\phi]_{450}$ +30°, $[\phi]_{400}$ +850°, $[\phi]_{365}$ +4,420°, $[\phi]_{350}$ +760°, $[\phi]_{344}$ 0° (by extrapolation); NMR 1·08, 1·15 (C_4-*gem* diMe), 1·23 (C_{10}-angular Me), 1·39 (d, J = 7·0 c/s, $C_{16,17}$-isopropyl Me's), 2·18 (d, J = 7·5 c/s, C_5-proton), 3·58 (5 members of septet, J = 7·0 c/s, C_{15}-methine proton), 4·64 (d, J = 7·5 c/s, C_6-proton), and 7·03 δ (quartet, $C_{11,12}$-aromatic protons).

Δ^5-Dehydro-7-oxototarol (III, R = OH)

III (R = OAc) was prepared in 46% yield from II (R = OAc) by Chow and Erdtman's method.[3] Recrystallization from light petroleum gave prisms, m.p. 164–165° (lit.[3] m.p. 163–165°). ν_{max} ($CHCl_3$) 1755 (aryl OAc), 1615 (conj. trisub. C=C), and 1188 cm^{-1} (OAc), RD (*c*, 0·163) $[\phi]_{589}$ −70°, $[\phi]_{450}$ −310°, $[\phi]_{383}$ −2,140°, $[\phi]_{360}$ 0°, $[\phi]_{320}$ +3,340°. NMR (CCl_4) 1·16 (C_4-axial Me), 1·28 (C_4-equatorial Me), 1·35 (C_{10}-angular Me), 1·35, 1·46 (2 doublets each with J = 7·0 c/s, isopropyl Me's), 2·28 (acetate), 4·34 (5 members of septet, J = 7·0 c/s, C_{15}-methine proton), 6·32 (C_6-proton), and 7·16 δ (quartet, $C_{11,12}$-aromatic protons).

Hydrolysis of the acetate by Chow and Erdtman's method[3] gave III (R = OH), needles, m.p. 243–244·5° (Lit.[3] m.p. 243–245°), from MeOH. ν_{max} ($CHCl_3$) 3588 sharp, 3305 broad (phenol), 1649 (aryl COC=C), 1619 (conj. trisub. C=C), 1580, 1290, 1286, and 1070 cm^{-1}. RD (*c*, 0·117) $[\phi]_{589}$ −120°, $[\phi]_{450}$ −715°, $[\phi]_{400}$ −2910°, $[\phi]_{380}$ −5210, $[\phi]_{355}$ 0° (by extrapolation).

Δ^5-Dehydro-7-oxototaryl methyl ether (III, R = OMe)

(a) III (R = OH; 48·5 mg), anhyd K_2CO_3 (50 mg), dry Me_2CO (10 ml), and MeI (5 ml) were heated under reflux for 84 hr and the mixture was poured into water (200 ml). Extraction with ether and crystallization of the product from EtOH gave *Δ^5-dehydro-7-oxototaryl methyl ether* (50 mg) as needles, further purified by vacuum sublimation, m.p. 152–154°. (Found: C, 81·0; H, 9·4. $C_{21}H_{28}O_2$ requires: C, 80·7; H, 9·0%); ν_{max} ($CHCl_3$) 1646 (aryl COC=C), 1612 (conj. trisub. C=C), and 817 cm^{-1} (2 adj. aromatic hydrogens). RD (*c*, 0·040) $[\phi]_{589}$ −85°, $[\phi]_{450}$ −426°, $[\phi]_{366}$ −3920, $[\phi]_{340}$ −1360°, $[\phi]_{330}$ 0°, $[\phi]_{306}$ +2470°, $[\phi]_{296}$ +1700°; NMR 1·21, 1·25 (C_4-*gem* diMe), 1·33 (C_{10}-angular Me), 1·42 (d, J = 7·0 c/s, $C_{16,17}$-isopropyl Me's), 3·85 (OMe), 4·38 (5 members of septet, J = 7·0 c/s, C_{15}-methine proton), 6·44 (C_6-proton), and 7·22 δ (quartet, $C_{11,12}$-aromatic protons).

(b) A mixture of II (R = OMe[5]; 540 mg), LiBr (1·24 g), dry $LiCO_3$ (280 mg) and DMF (22 ml) was heated at 120° for 46 hr. Isolation of the product followed by crystallization from EtOH gave fine needles (400 mg) of III (R = OMe), identical in all respects with that from (a).

7-Oxototara-5,8,11,13-tetraene (III, R = H)

A mixture of 6α-bromo-7-oxototara-8,11,13-triene (500 mg),[15] LiBr (1·18 g), dry $LiCO_3$ (246 mg), and DMF (20 ml) was heated with stirring at 120° for 23 hr. Isolation of the product from water and crystallization from MeOH gave *7-oxototara-5,8,11,13-tetraene* (180 mg, 47%) as short needles, m.p. 84–85°. (Found, for sample dried at 20°: C, 82·7, 82·6; H, 9·1, 9·0. $C_{20}H_{26}O \cdot \frac{1}{2}MeOH$ requires: C, 82·5; H, 9·5%); NMR 1·12, 1·25 (C_4-*gem* diMe), 1·32 (C_{10}-angular Me), 1·30, 1·42 (2 doublets each with J = 7·0 c/s, $C_{16,17}$-isopropyl Me's), 4·42 (5 members of a septet, J = 7·0 c/s, C_{15}-methine proton), 6·42 (C_6-proton), and 7·42 δ (m, $C_{11,12,13}$-aromatic protons).

Methyl 6α-bromo-7-oxo-O-methylpodocarpate (VII, R = Br)

Br_2 (1·9 g) in glacial HOAc (20 ml) was added over 10 min to a stirred soln of VII (R = H; 6·1 g)[37] in glacial HOAc (32·5 ml) containing 0·1 ml 48% HBr. Isolation of the product followed by two crystallizations from EtOH gave VII (R = Br; 1·2 g) as prisms, m.p. 142–144° (lit.[5] m.p. 142–144·5°); ν_{max} ($CHCl_3$) 1724 (CO_2Me), and 1678 cm^{-1} (aryl COCHBr); NMR 0·86 (C_4-equatorial Me), 1·56 (C_{10}-angular Me), 2·51 (d, J = 7·6 c/s, C_5-proton), 3·76 (CO_2Me), 3·90 (OMe), 5·88 (d, J = 7·6 c/s, C_6-proton), 6·93 (m, $C_{13,14}$-aromatic protons), and 7·85 δ (d, J = 9·0 c/s, C_{11}-aromatic proton).

A second crop of crystals from the first mother liquors gave the lactone VIII (3·2 g)[38] as needles, m.p. and mixed m.p. 198–201° (identical IR spectra).

Reactions of 6α-bromo-diterpenoids with $DMSO/NaHCO_3$

DMSO was added to a stirred mixture of equal weights of the 6α-bromo-diterpenoid and $NaHCO_3$ and the temp raised to 120–140° for 1–2 hr during which the mixture bubbled vigorously and continually darkened in colour. The cooled mixture was poured into sat. NaCl aq, extracted with ether, and the ether extract washed with water, dried, and evaporated under vacuum. The crude product was examined by TLC and then chromatographed on Al_2O_3 eluting with solvents of increasing polarity.

TABLE 1

Reactant	Quantities used: ketone (g)	$NaHCO_3$ (g)	DMSO (ml)	Temp (hr)	Time (hr)	Products	%	RR_f* (TLC)
II, R = OAc	0·5	0·5	12	135	1·0	IV, R = H	5	0·20
						III, R = OH	15	0·31
	5·0	5·0	115	130	1·5	III, R = OAc	45	0·55
	19·6	19·6	450	130	1·5	II, R = OH	5	0·73
						II, R = OAc	20	1·00
II, R = OH	0·1	0·1	4	100	1·5			
	0·3	0·3	12	120	1·5	IV, R = H	80	0·20
	7·0	7·0	160	120	1·6	III, R = OH	5	0·31
	0·1	0·1	8(DMF)	100	1·5	II, R = OH	2	0·73
II, R = OMe	1·0	1·0	25	140	1·5	VI, R = OMe	10	0·75
						III, R = OMe	70	0·61
						II, R = OMe	20	1·00
VI, R = Br	4·5	4·5	115	125	1·5	VII, R = H	5	0·44
						VIII	85	0·57
						VII, R = Br	5	1·00
II, R = H	1·0	1·0	25	130	2·0	III, R = H	60	0·63
						VI, R = H	5	0·77
						II, R = H	25	1·00
V, R = OH	0·5	0·5	12	130	1·0	VI, R = OH	95	

* RR_f = relative R_f.

7-Oxo-5,10-secotolara-5,8,10(20),11,13-pentaen-13-ol (IV, R = H)

Elution of the appropriate columns with benzene gave the *secoditerpenoid* IV (R = H) which crystallized from MeOH as plates, m.p. 195–196·5°. (Found: C, 80·6; H, 8·9; O, 10·7. $C_{20}H_{26}O_2$ requires: C, 80·5; H, 8·9; O, 10·7%); MW (mass-spectrum) 298; ν_{max} ($CHCl_3$) 3950, 3400 (phenol), 1648 (aryl COC=C), 1572 (aromatic C=C), 1367, 1357 (*gem*-diMe), 1284 (phenol), 985 (disub. *trans* C=C), 910 (C=CH_2), and

819 cm^{-1} (2 adj. aromatic hydrogens), λ_{max} 248 (ε, 13,850), 285 sh (ε, 2500), 318 nm (ε, 1330), $[\alpha]_{300-650}$ 0°, NMR 1·03 (6 protons, C_4-*gem* diMe), 1·36 (d, J = 7·0 c/s, $C_{16,17}$-isopropyl Me's), 3·17 (5 members of septet, J = 7·0 c/s, C_{15}-methine proton), 4·78, 4·96 (C_{20}-protons, J = 1·6 for 4·78 peak), 6·0–6·5 (s, variable with conc, phenolic proton), 6·30 (quartet, J = 16·5 c/s, $C_{5,6}$-*trans* protons), and 6·87 δ (quartet, $C_{11,12}$-aromatic protons).

IV (R = H, 13·7 mg) on hydrogenation in EtOAc (8 ml) over 5% palladium charcoal absorbed H_2 (2·25 ml) ≡ 2·18 double bonds. TLC (benzene) indicated the formation of one major product (RR_f 0·2).

Ozonolysis of the secoditerpenoid

The secoditerpenoid (IV, R = H; 80·0 mg, 0·268 mmol), dissolved in HOAc (20 ml), absorbed 2 mol/mol ozone. In a second run the secoditerpenoid (20·0 mg, 0·067 mmol), dissolved in ethyl acetate (20 ml) at −70°, absorbed 0·13 mmol of ozone (≡ 2 mol/mol).

The crude product from the first reaction was steam distilled from a Zn dust–H_2O–HOAc mixture and the clear distillate was neutralized to phenolphthalein. Subsequent treatment with a dimedone soln gave formaldehyde-dimedone (5 mg) which after sublimation had m.p. and mixed m.p. 190–192° (identical IR spectra and TLC behaviour).

No crystalline product was isolated from the distillation residue.

7-*Oxo*-5,10-*secotota*ra-5,8,10(20),11,13-*pentaene*-13-*yl acetate* (IV, R = Ac)

Compound IV (R = J, 83 mg) was acetylated with Ac_2O (5 ml) and pyridine (2 drops) for 3 hr under reflux Successive crystallization of the product from EtOH, EtOAc, and MeOH gave the *acetate*, IV (R = Ac) as fine needles (162 mg, 66%), m.p. 121–121·5°. (Found: C, 77·35; H, 8·4. $C_{22}H_{28}O_3$ requires: C, 77·6; H, 8·3%); ν_{max} (CCl_4) 1768 (aryl acetate) and 1658 cm^{-1} (aryl COC=C); NMR 1·04 (6 protons, C_4-*gem* diMe), 1·26 (d, J = 7·0 c/s, $C_{16,17}$-isopropyl Me's), 2·35 (OAc), 3·17 (5 members of septet, J = 7·0 c/s, C_{15}-methine proton), 4·90 (d, C_{20}-protons), 6·25 (d, $C_{5,6}$-*trans* protons), and 7·07 δ (quartet, $C_{11,12}$-aromatic protons).

7-*Oxo*-5,10-*secotota*ra-5,8,10(20),11,13-*pentaene*-13-*yl methyl ether* (IV, R = Me)

Compound IV (R = H, 200 mg), dissolved in benzene (10 ml) and dry xylene (5 ml), was added to K (50 mg) in dry xylene (5 ml) and the mixture was heated under reflux for 2 hr. MeI (5·15 ml) was added over 3 hr and the refluxing continued for a further 3 hr. The mixture was diluted with dry ether, excess K was destroyed with t-BuOH, and the product was isolated from water. Crystallization from MeOH gave the *methyl ether* IV (R = Me) as prisms (160 mg, 76%) further purified as needles, m.p. 105·5–108°, by vacuum sublimation. (Found: C, 80·75; H, 8·9. $C_{21}H_{28}O_2$ requires: C, 80·7; H, 9·0%); ν_{max} ($CHCl_3$) 1648 (aryl COC=C), 1567 (aromatic C=C), 986 (*trans* disub. C=C), 913 (C=CH_2), and 819 cm^{-1} (2 adj. aromatic hydrogens), λ_{max} 248 (ε, 12,700) and 310 nm (ε, 1000). NMR 1·03 (6 protons, C_4-*gem* diMe), 1·31 (d, $C_{16,17}$-isopropyl Me's), 3·18 (5 members of septet, C_{15}-methine proton), 3·91 (OMe), 4·82, 5·02 (d, C_{20}-protons), 6·29 (quartet, J = 16·5 c/s, $C_{5,6}$-*trans* protons, and 7·03 (quartet, $C_{11,12}$-aromatic protons).

7-*Oxo*-5,10-*secotota*ra-8,10(20),11,13-*tetraen*-13-*ol* (V)

To IV (R = H, 300 mg) in EtOH (25 ml) was added $NaBH_4$ (27 mg) in three portions over 24 hr and the mixture was left overnight. Isolation of the product followed by crystallization from EtOH gave the *tetraene* (V) as fine needles (240 mg, 80%), m.p. 169–172°. (Found: C, 80·0; H, 9·5; O, 10·9. $C_{20}H_{28}O_2$ requires: C, 80·0; H, 9·4; O, 10·65%); ν_{max} ($CHCl_3$) 3590, 3310 (phenol), 1678 (aryl CO), 1576 (aromatic C=C), 912 (C=CH_2), and 822 cm^{-1} (2 adj. aromatic hydrogens), λ_{max} 246 (ε, 7200) and 292 nm (ε, 2040); NMR 0·75 (6-protons, C_4-*gem* diMe), 1·35 (d, J = 7·0 c/s, $C_{16,17}$-isopropyl Me's), 2·71 (multiplet composed of a triplet, J = 7·0 c/s, due to C_6-protons superimposed on a septet, J = 7·0 c/s, due to C_{15}-methine proton), 4·99, 5·22 (d, C_{20}-protons, J = 1·8 c/s for 4·99 peak), 5·97 (OH), and 6·91 δ (quartet, $C_{11,12}$-aromatic protons).

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