1038. *Experiments Confirming the Structure of Shellolic Acid.*

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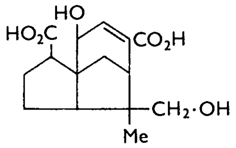
Experiments with shellolic acid support its formulation (I) proposed recently by Yates and Field.

In view of the report by Yates and Field [1] on the sesquiterpene shellolic acid, to which they assign the structure (I), we record some results of ours which confirm their findings.

For the isolation of the acid we employed Gidvani's method [2] but in our hands yields were variable and were considerably below those claimed.[2-4] The crude hydrolysis product of shellac contains a number of other acids closely related to shellolic acid,[4] and from mother liquors of dimethyl shellolate we obtained small amounts of an isomeric αβ-unsaturated ester.

(I)



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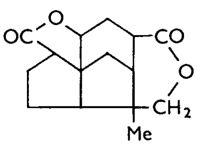

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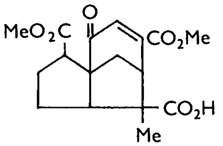

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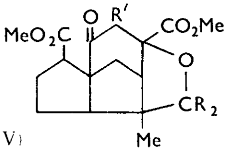

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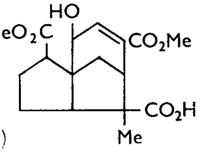
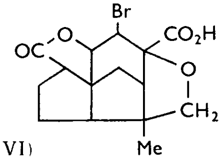


(VI)



In agreement with the proposed structure, dimethyl shellolate did not form an isopropylidene derivative, and Kuhn–Roth oxidation of the ester and of dihydroshellolic acid (below) showed the presence of one *C*-methyl group. With toluene-*p*-sulphonyl chloride in pyridine dimethyl shellolate gave only a monotoluene-*p*-sulphonate. The ultraviolet and infrared spectra of the acid and of dimethyl shellolate were consistent with the conjugated position of the double bond. In addition, three bands in the C–H deformation region ($\nu_{max.}$ in Nujol 772, 783, and 788 cm.$^{-1}$), absent in the spectrum of the dihydro-compound, strongly suggested the presence of a vinylic hydrogen atom for which the American workers obtained evidence by nuclear magnetic resonance. The double bond was rather unreactive and dimethyl shellolate did not react with perphthalic acid, but hydrogenation in presence of platinum oxide and treatment of the resulting oil with sodium hydrogen carbonate afforded the crystalline dilactone (II) obtained by Yates and Field [1]

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[1] Yates and Field, *J. Amer. Chem. Soc.*, 1960, **82**, 5764.

[2] Gidvani, *J.*, 1944, 306.

[3] Harries and Nagel, *Ber.*, 1922, **55**, 3833.

[4] Kirk, Spoerri, and Gardner, *J. Amer. Chem. Soc.*, 1941, **63**, 1243.

by a similar method. The same product was obtained directly by hydrogenation of shellolic acid. Oxidation of the dilactone with alkaline permanganate gave, in small yield, a crystalline dicarboxylic acid lactone, $C_{15}H_{18}O_6$, formed, presumably, by opening of the lactone ring and oxidation of the primary alcohol group.

By oxidation of dimethyl shellolate with six equivalents of chromic acid we obtained results essentially similar to those of Yates and Field.[1] The principal product was the oxo-acid formulated by them as (III); in some experiments the isomeric oxo-lactone (IV; $R_2 = O$, $R' = H$), which they describe, was also obtained. Both products were converted by methanol and sulphuric acid into the trimethyl ester, prepared also from the acid with methyl iodide and potassium carbonate. Reduction of the trimethyl ester with sodium borohydride led to a mixture from which the (oily) alcohol was isolated by chromatography. Catalytic reduction of the acid (III) with palladium in ethanol afforded an alcohol (V) by preferential reduction of the carbonyl group ($\lambda_{max.}$ 225 mμ, log ε 3·74; $\nu_{max.}$ in Nujol 3500, 1730, 1710, 1680sh cm.$^{-1}$).

With manganese dioxide,[5] dimethyl shellolate was converted in small yield into the dehydro-compound (IV; $R = R' = H$) obtained by Yates and Field.[1] In our hands, however, the main product was the acid (V) formed surprisingly by preferential oxidation of the non-conjugated, but more exposed, primary alcohol group. The product was identical with the acid obtained, as above, by catalytic reduction of the acid (III), and on oxidation with chromic acid afforded the oxo-lactone (IV; $R_2 = O$, $R' = H$) mentioned above.

Oxidation of dimethyl shellolate with hydrogen peroxide and osmium tetroxide afforded a crystalline lactone, $C_{16}H_{22}O_7$ ($\nu_{max.}$ in Nujol 1720 cm.$^{-1}$) by hydroxylation of the double bond and δ-lactonisation with loss of the elements of methanol. Again, treatment of the dihydroxy-dilactone, $C_{15}H_{18}O_6$, obtained by Nagel and Mertens [6] from shellolic acid and alkaline permanganate, with lead tetra-acetate gave an oily dicarbonyl compound, isolated as its bis-semicarbazone, $C_{17}H_{24}N_6O_7$. Both reactions proceeded in poor yield and were not pursued.

By bromination of shellolic acid Nagel and Mertens [6] obtained a crystalline bromo-lactonic acid, $C_{15}H_{17}BrO_5$, which was thought to contain an unreactive hydroxyl group. The infrared spectrum of the methyl ester of this substance has two carbonyl maxima, at 1770 (γ-lactone or α-bromo-ester) and 1720 cm.$^{-1}$ (δ-lactone or normal ester), and shows further that no hydroxyl group is present; in agreement, Zerewitinoff determination discloses only one reactive hydrogen atom, that in the carboxyl group. The methyl ester shows no ketonic properties, and the fifth oxygen atom must therefore be present in an ether group. From the bromo-lactonic acid and aqueous potassium carbonate Nagel and Mertens [6] obtained a dibasic acid, $C_{15}H_{18}O_6$, which has now been identified as (IV; CO_2H for CO_2Me; $R = R' = H$) by the fact that the dimethyl ester was identical with the neutral product (IV; $R = R' = H$) obtained by oxidation of dimethyl shellolate with manganese dioxide. On the basis of these facts the bromo-lactonic acid is represented by the structure (VI) with the bromine atom and the oxygen of the lactone ring in the *cis*-configuration, and its mode of formation recalls that of bromopicrotoxinin from picrotoxinin.[7] The ketone (IV; $R = R' = H$) is also produced by reaction of *N*-bromosuccinimide with dimethyl shellolate in presence of pyridine. A minor product of this reaction, $C_{17}H_{21}BrO_6$, was obtained also by Dr. R. A. W. Johnstone as the main product from reaction in absence of pyridine and is regarded as the α-bromo-ketone (IV; $R = H$, $R' = Br$) (cf. ref. 8). Its ultraviolet absorption ($\lambda_{max.}$ 278 mμ; log ε 1·93) indicates that the bromine is equatorial.[9] The infrared spectrum shows only one carbonyl maximum, at

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[5] Attenburrow *et al.*, *J.*, 1952, 1094; Evans, *Quart. Rev.*, 1959, **13**, 61.

[6] Nagel and Mertens, *Ber.*, 1939, **72**, 985.

[7] Conroy, *J. Amer. Chem. Soc.*, 1952, **74**, 491; 1957, **79**, 1726.

[8] Stuckwisch, Hammer, and Blau, *J. Org. Chem.*, 1957, **22**, 1678.

[9] Cookson, *J.*, 1954, 282.

1745 cm.$^{-1}$ (normal ester and α-bromo-ketone in a six-membered ring); there is no absorption indicating olefinic unsaturation and no hydroxyl band.

EXPERIMENTAL

Isolation of Shellolic Acid.—In the present work best results were obtained by using Super-Blonde Shellac. Shellolic acid was isolated as its zinc salt as described by Gidvani.[2] Yields from 500 g. of shellac varied from 37—78 g. depending on the shellac used.

For the isolation of dimethyl shellolate the dried and powdered zinc salts (70 g.) were esterified directly with methanol (1 l.) containing hydrogen chloride (3%) at room temperature for 4—5 days. The solution was partly neutralised with solid sodium hydrogen carbonate, and methanol removed under reduced pressure with slight warming. Water was added and the product was extracted with ether and washed with sodium hydrogen carbonate and with water. A reddish-brown viscous oil was obtained from which dimethyl shellolate was precipitated as an amorphous powder (11 g.), m. p. 142—150°, by trituration with ether. It crystallised from ethyl acetate as colourless prisms, m. p. 151—152·5° (Found: C, 63·1; H, 7·6. Calc. for $C_{17}H_{24}O_6$: C, 63·0; H, 7·5%), $[\alpha]_{5461}^{18\cdot1}$ +47·6°, +47·2°, $\lambda_{max.}$ (in EtOH) 229 mμ (log ε 3·77), $\nu_{max.}$ (in $CHCl_3$) 3350, 1720, 1705, 1658 cm.$^{-1}$.

The quantities of dimethyl shellolate isolated varied greatly in different experiments. The zinc salt should be esterified as soon as possible after isolation as changes occur on storage which lower the yield of ester.

In other experiments with different types of lac, very much smaller yields of dimethyl shellolate were obtained as shown in the Table. Usually about 25% of the oil resulting from esterification of the zinc salts was isolated as dimethyl shellolate. The remainder, consisting probably of a mixture of esters of several hydroxy-acids similar to shellolic acid (cf. Kirk, Spoerri, and Gardner[4]), remained for the most part uncrystallisable. On some occasions further crystalline material separated on prolonged storage. Fractional crystallisation of this afforded dimethyl shellolate and a small amount of another product, m. p. 152·5—153·5°, depressed to 126—131° when mixed with dimethyl shellolate (Found: C, 62·2, 62·8; H, 7·9, 6·9. Calc. for $C_{17}H_{24}O_6$: C, 63·0; H, 7·5%), $[\alpha]_{5461}^{20\cdot2}$ +58·6° (in EtOH), $\lambda_{max.}$ (in EtOH) 229 mμ (log ε 3·77). Hydrolysis of this ester afforded an acid, which softened at 208° and melted at 220° (decomp.).

Type of lac	Total quantity of lac (kg.)	Quantity of dimethyl shellolate obtained (g.)	(%)
Kusum (scraped)	18	20·1	0·112
Siam	2·5	1·4	0·056
Calcutta (dewaxed)	3·5	6·9	0·197
Ber	4·0	0·5	0·012
Palas	4·0	1·0	0·025
Kusmi	2·5	0·3	0·012
Angela deora shellac	23	182·6	0·794

Hydrolysis of the remaining syrupy material with sodium hydroxide afforded a gum.

Treatment of dimethyl shellolate (1 equiv.) with toluene-*p*-sulphonyl chloride (2 equiv.) in boiling pyridine for 2 hr. afforded, after chromatography, a *monotoluene*-p-*sulphonate*, m. p. 84—85° (from benzene–light petroleum), $[\alpha]_{5461}^{21}$ (*c* 2·351 in EtOH) +4·30° (Found: C, 59·8; H, 6·3; S, 6·85. $C_{24}H_{30}O_8S$ requires C, 60·2; H, 6·3; S, 6·7%).

Hydrolysis of dimethyl shellolate with sodium hydroxide as described by Kirk, Spoerri, and Gardner[4] afforded shellolic acid, m. p. 199—201° (decomp.) (from water), $\lambda_{max.}$ (in EtOH) 228 mμ (log ε 3·73), $[\alpha]_{5461}^{17\cdot6}$ +26·3°. Potentiometric titration of the acid with sodium hydroxide gave dissociation constants pK_1 4·00 and pK_2 5·08 (kindly determined for us by Dr. J. C. Speakman). The *di*-p-*bromophenacyl ester* (from methanol) had m. p. 141—142° (Found: C, 54·0; H, 4·45. $C_{31}H_{30}Br_2O_8$ requires C, 53·9; H, 4·35%).

Hydrogenation of Dimethyl Shellolate.—Microhydrogenation with platinum oxide in ethanol caused uptake of 0·88H_2. On a larger scale dimethyl shellolate (1 g.) in ethanol (10 c.c.) was hydrogenated with platinum oxide (50 mg.) (8 hr.); the viscous oil obtained was treated overnight at room temperature with potassium hydrogen carbonate (2·5 g.) in methanol (125 c.c.) and water (50 c.c.); methanol was removed under reduced pressure, the dihydro-dilactone being obtained on acidification. It crystallised from water or from aqueous ethanol as needles, m. p.

150—151° [Found: C, 68·4; H, 6·8%; equiv. (by titration), 119, 121. Calc. for $C_{15}H_{18}O_4$: C, 68·7; H, 6·9%; equiv., 131]. There was no high-intensity ultraviolet absorption above 215 mμ; $\nu_{max.}$ were at 1765 and 1740 cm.$^{-1}$ in $CHCl_3$.

The dihydro-dilactone was also obtained when shellolic acid (5 g.) was reduced with 2% palladised strontium carbonate (7 g.) in ethanol (300 c.c.) at 50°/120 atm.

The dihydro-dilactone (0·52 g.) was oxidised with potassium permanganate (0·42 g.) and potassium hydroxide (0·67 g.) in water (25 c.c.). Next morning manganese dioxide was filtered off and washed with boiling water, and the combined filtrates were evaporated to small volume and made acid to Congo Red. The precipitate was collected and crystallised from water, affording the *dicarboxylic acid lactone* as blades, m. p. 223—226° (Found: C, 61·4; H, 6·4. $C_{15}H_{18}O_6$ requires C, 61·2; H, 6·1%). Direct titration with barium hydroxide gave an equivalent weight of 157, but addition of an excess, warming, cooling, and back-titration gave a value of 92·7.

Oxidation of Dimethyl Shellolate with Chromic Acid.—Chromium trioxide in sulphuric acid [10] (2·45 c.c.) was added dropwise to a solution of the ester (1 g.) in acetone (100 c.c.) at 5°. When reaction was complete the solution was diluted with water and extracted with ether, and the extract was treated with aqueous sodium carbonate. The product (820 mg.) obtained from the alkaline solution crystallised from ether–methyl acetate and afforded the keto-acid (III) as prisms, m. p. 139—140° (Found: C, 60·8; H, 6·0. Calc. for $C_{17}H_{20}O_7$: C, 60·7; H, 6·0%), $\lambda_{max.}$ (in EtOH) 240, 343—353 mμ (log ε 3·97, 1·80). The *oxime* formed needles (from aqueous methanol), m. p. 161—162° (Found: N, 3·9. $C_{17}H_{21}NO_7$ requires N, 4·1%). Treatment of the keto-acid (100 mg.) with piperonaldehyde (50 mg.) in methanol (1 c.c.) containing 10N-sodium hydroxide (3 drops) afforded a *substance*, m. p. 233—236° (from ether), which appears to have resulted from hydrolysis of one of the ester groups (Found: C, 59·8; H, 5·75. $C_{16}H_{18}O_7$ requires C, 59·6; H, 5·6%). The trimethyl ester, prepared from the keto-acid with methyl iodide and potassium carbonate in acetone, formed needles, m. p. 94° (from ether) (Found: C, 61·6; H, 6·0. Calc. for $C_{18}H_{22}O_7$: C, 61·7; H, 6·3%), $\nu_{max.}$ (in CCl_4) 1740, 1696 cm.$^{-1}$, $\lambda_{max.}$ (in EtOH) 239, 345—355 mμ (log ε 3·97, 1·77).

In some experiments a mixture was obtained from which the keto-lactone (IV: R_2 = O, R′ = H) was isolated by crystallisation from ether as prisms, m. p. 144—146°, depressed when mixed with the keto-acid (Found: C, 60·5; H, 5·0. Calc. for $C_{17}H_{20}O_7$: C, 60·7; H, 6·0%), $\lambda_{max.}$ (in EtOH) 280 mμ (log ε 1·72), $\nu_{max.}$ (in Nujol) 1790, 1760, 1720 cm.$^{-1}$.

Esterification of either product (100 mg.) with methanol (10 c.c.) and sulphuric acid (1 c.c.) afforded an ester, m. p. 94—95°, not depressed when mixed with the trimethyl ester prepared from the acid as described above; the infrared spectra were identical.

Hydrogenation of the keto-acid with palladium–charcoal in ethanol afforded the *dihydro-compound* in quantitative yield as needles, m. p. 195—196° (from ether–methyl acetate) (Found: C, 60·4; H, 6·6. $C_{17}H_{22}O_7$ requires C, 60·3; H, 6·6%).

Reduction of the trimethyl ester (200 mg.) with sodium borohydride (250 mg.) in ethylene glycol dimethyl ether (10 c.c.) afforded a gum (120 mg.) which was chromatographed on silica gel. Benzene–ether (1 : 1) eluted fractions with only weak absorption at 3500 cm.$^{-1}$ and a pronounced band at 1780 cm.$^{-1}$ indicative of a γ-lactone. The *dihydro-compound* was eluted with ether and distilled at 180—190°/0·5 mm. (Found: C, 62·0; H, 7·4. $C_{18}H_{24}O_7$ requires C, 61·4; H, 6·9%), having $\lambda_{max.}$ (in EtOH) 225 mμ (log ε 3·58), $\nu_{max.}$ (in CCl_4) 3550, 1727 cm.$^{-1}$.

Oxidation of Dimethyl Shellolate with Manganese Dioxide.—The ester was recovered after treatment with manganese dioxide in chloroform solution at room temperature for 16 hr.

In another experiment a stirred solution of dimethyl shellolate (1 g.) in benzene (50 c.c.) was heated on the water bath with manganese dioxide [11] (8 g.) for 16 hr. Manganese dioxide was filtered off and washed with chloroform and with methanol. The recovered gum (900 mg.) partly crystallised when triturated with carbon tetrachloride. Crystallisation from benzene–methanol afforded needles, m. p. 197—199° alone or mixed with the reduction product prepared from the keto-acid as described above (Found: C, 61·0; H, 6·3. $C_{17}H_{22}O_7$ requires C, 60·3; H, 6·6%), $\lambda_{max.}$ (in EtOH) 225—226 mμ (log ε 3·71); the infrared spectra of the two products were identical. The *methyl ester*, prepared with methyl iodide and potassium carbonate, formed prisms, m. p. 109—111° (from ether) (Found: C, 61·0; H, 6·7. $C_{18}H_{24}O_7$ requires C, 61·35; H, 6·9%), $\lambda_{max.}$ (in EtOH) 226 mμ (log ε 3·76), $\nu_{max.}$ (in Nujol), 3550, 1724, 1708 cm.$^{-1}$. Oxidation

[10] Bowers, Halsall, Jones, and Lemin, *J.*, 1953, 2555.

[11] Mancera, Rosenkranz, and Sondheimer, *J.*, 1953, 2189.

of the acid with two equivalents of chromic acid as described above for dimethyl shellolate gave the keto-lactone, m. p. 142—146°, not depressed when mixed with a specimen obtained by oxidation of dimethyl shellolate. The infrared spectra were identical.

The remaining material from the manganese dioxide oxidation was extracted with sodium carbonate, yielding a further 85 mg. of acid. The neutral fraction was chromatographed on silica gel. Benzene–ether (4 : 1) eluted a gum (98 mg.) which partly crystallised when triturated with ether and therefrom afforded the oxo-ether (IV: R = R′ = H) as prisms, m. p. 120—122° (Found: C, 63·4; H, 6·7. Calc. for $C_{17}H_{22}O_6$: C, 63·3; H, 6·9%), $\nu_{max.}$ (in $CHCl_3$) 1725, 1741sh cm.$^{-1}$, no high-intensity absorption above 215 mμ. Elution with ether afforded dimethyl shellolate (145 mg.).

Oxidation of Dimethyl Shellolate with Osmium Tetroxide and Hydrogen Peroxide.—To a solution prepared from dimethyl shellolate (0·68 g.) and hydrogen peroxide (0·08 g.) in t-butyl alcohol (38 c.c.) was added at 0° a 0·5% solution of osmium tetroxide in t-butyl alcohol (5 drops). After 5 days at 25° the yellow solution was evaporated to dryness, benzene (75 c.c.) was added, and the mixture warmed and filtered. The residue (0·1 g.) crystallised from Cellosolve as prisms of the *product* which softened at 210° with evolution of gas and finally melted at 232—238° (Found: C, 58·9; H, 6·9; OMe, 10·3. $C_{16}H_{22}O_7$ requires C, 58·9; H, 6·75; OMe, 9·5%), $\nu_{max.}$ (KBr disc) 3300—3500, 1730 cm.$^{-1}$, no high-intensity absorption above 210 mμ.

Oxidation of Shellolic Acid with Potassium Permanganate.—The oxidation was carried out as described by Nagel and Mertens.[6] The product softened at 110° and melted at 123—124° (lit., swells at 124°, melts at 162°). This product (0·1 g.) was treated in water with lead tetra-acetate (0·14 g.) in acetic acid (7 c.c.). Next morning 0·1N-sulphuric acid (6·5 c.c.) was added, lead sulphate filtered off, and the solution evaporated to dryness. The sticky residue solidified when triturated with water, but the solid did not crystallise. It was converted into its *semicarbazone*, which prisms (from water), m. p. 270—272° (decomp.).

A slightly purer semicarbazone, m. p. 274—275° (decomp.), was obtained when the permanganate oxidation product (0·615 g.) was oxidised with sodium metaperiodate (0·528 g.) in water (16 c.c.) for 5 days (Found: C, 48·1; H, 5·6; N, 19·7. $C_{17}H_{24}N_6O_7$ requires C, 48·1; H, 5·7; N, 19·8%).

Bromination of Shellolic Acid.—The reaction was carried out as described by Nagel and Mertens.[6] The product formed colourless needles (from aqueous methanol), m. p. 235—237° (lit., 226°), after drying for 6 hr. at 110°/0·4 mm. (Found: C, 50·9; H, 4·7; active H, 0·28. Calc. for $C_{15}H_{17}BrO_5$: C, 50·4; H, 4·8; 1 active H, 0·25%), $[\alpha]_D^{18}$ $-103·5°$. The *methyl ester*, prepared with diazomethane, formed prisms m. p. 174—175° (from cyclohexane) (Found: C, 52·0; H, 5·1; OMe, 8·1. $C_{16}H_{19}BrO_5$ requires C, 51·8; H, 5·2; 1OMe, 8·4%).

Reduction of this product (150 mg.) with zinc (0·5 g.) and N-hydrochloric acid (6 c.c.) as described by Nagel and Mertens afforded deoxyshellolic acid as prisms, m. p. 181—184° (from water) (Found: C, 64·9; H, 6·4. Calc. for $C_{15}H_{18}O_5$: C, 64·7; H, 6·5%), log ε 600 at 220 mμ, 980 at 215 mμ. Treatment of the bromo-lactonic acid (215 mg.) with potassium carbonate (150 mg.) in water (0·6 c.c.) on the water bath for 1½ hr. and acidification to Congo Red afforded the dicarboxylic acid (described by Nagel and Mertens [6]) as prisms, m. p. 231—236° (from water) (Found: C, 61·4; H, 6·2. Calc. for $C_{15}H_{18}O_6$: C, 61·2; H, 6·2%), $\lambda_{max.}$ (in EtOH) 270—280 mμ (log ε 1·66), $\nu_{max.}$ (in Nujol) 1730, 1700sh cm.$^{-1}$.

The methyl ester, prepared with methyl iodide and potassium carbonate, formed colourless prisms (from ether), m. p. 119°, not depressed when mixed with the ketone produced by oxidation of dimethyl shellolate with manganese dioxide. The infrared spectra were identical.

Reaction of N-*Bromosuccinimide with Dimethyl Shellolate.*—A solution of dimethyl shellolate (970 mg.), *N*-bromosuccinimide (530 mg.), and pyridine (400 mg.) in carbon tetrachloride (20 c.c.) was heated at 60—70° for 4 hr. The recovered gum (890 mg.) partly crystallised in ether. The crystalline fraction (490 mg.) was chromatographed on alumina (Brockman grade II); elution with ether afforded the ketone (IV; R = R′ = H) (212 mg.), m. p. 119—120° alone or mixed with the neutral product from oxidation of dimethyl shellolate by manganese dioxide. The infrared spectra were identical. Further elution with chloroform gave dimethyl shellolate (150 mg.). The non-crystalline fraction was separately chromatographed on alumina (grade II). Elution with ether afforded first a fraction (200 mg.) from which the *bromo-ketone* (IV: R = H, R′ = Br) was obtained as plates (from methanol), m. p. 177—178° (Found: C, 50·7; H, 5·0. $C_{17}H_{21}BrO_6$ requires C, 50·9; H, 5·3%). Further elution with ether gave another fraction (30 mg.) from which the ketone (IV; R = R′ = H) was obtained by cystallisation from ether.

The bromo-ketone was also obtained, in high yield, when dimethyl shellolate (0·324 g.), *N*-bromosuccinimide (0·178 g.), and a few crystals of benzoyl peroxide in carbon tetrachloride (10 c.c.) were heated on the water bath. There was a vigorous reaction and hydrogen bromide was evolved. The bromo-ketone was isolated by chromatography on alumina. This substance did not react with silver nitrate and was recovered after being heated with silver acetate in acetic acid.

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