

**Synthesis of Dihydroactiniolide [5,6,7,7a-Tetrahydro-4,4,7a-trimethylbenzofuran-2(4*H*)-one] and 6,7,8,8a-Tetrahydro-5,5,8a-trimethylnaphthalene-1,3(5*H*)-dione from 6,7,8,8a-Tetrahydro-2,5,5,8a-tetramethyl-5*H*-chromen**

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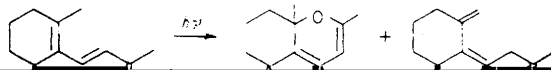
Autoxidation of 6,7,8,8a-tetrahydro-2,5,5,8a-tetramethyl-5*H*-chromen (2), obtained by photolysis of  $\beta$ -ionone, afforded a mixture of dihydroactiniolide (4), a cyclohexylideneacetaldehyde (5), and 3,5,6,7,8,8a-hexahydro-2,5,5,8a-tetramethyl-2*H*-chromen-2,3-diol (6). By refluxing in benzene, compound (6) was converted into a hexahydroindenone (15), which, in several steps, afforded 6,7,8,8a-tetrahydro-5,5,8a-trimethylnaphthalene-1,3(5*H*)-dione (20).

THE photoreactions of  $\beta$ -ionone and  $\beta$ -ionol have been studied extensively and some have been used in the syntheses of natural products such as grasshopper ketone<sup>1</sup> and sesquiterpenes.<sup>2</sup> The 2*H*-pyran derivative (2),<sup>3</sup> a photoproduct from  $\beta$ -ionone, was of interest to us as a potential synthetic precursor of more complex terpenes.

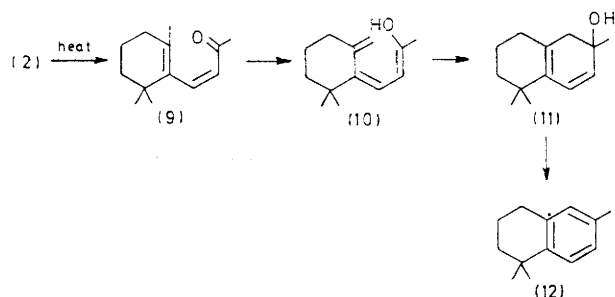
The present paper describes the synthesis of dihydro-

The product (5) was identified on the basis of its i.r. ( $\alpha\beta$ -unsaturated aldehyde and acetoxy-bands) and n.m.r. spectra (see Experimental section).

Compound (6), the major product, contained two hydrogen and two oxygen atoms more than the pyran



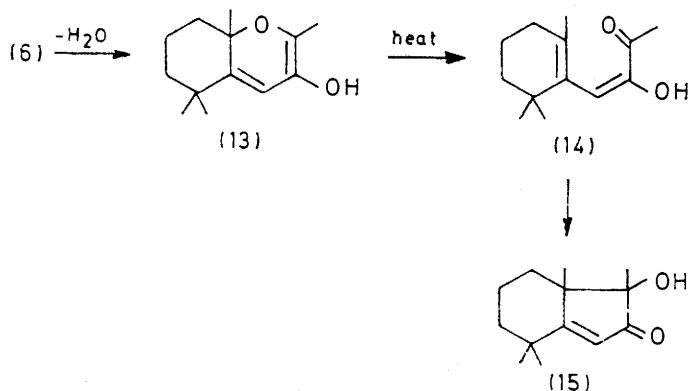
The foregoing reaction suggests that the 2,3-double bond of the pyran (2) is more reactive than the 4,4a-bond, which may suffer steric hindrance. This coincides with observation that the pyran reacted with tetracyanoethylene to afford the [2 + 2] addition product (8). Diels-Alder reactions of the pyran (2) with various dienophiles including maleic anhydride did not proceed, but afforded an aromatic compound, in low yield, identified as ionene (12) from its spectral properties. A possible mechanism for its formation is shown in Scheme 1.



SCHEME 1

Dihydroactiniolide (4) was synthesized from the hemiacetal (6) as follows. Oxidation with periodate afforded the acetoxy-aldehyde (5), base-catalysed hydrolysis of which afforded the unstable hemiacetal (7); this was oxidised with chromic acid to dihydroactiniolide (4) in a good yield.

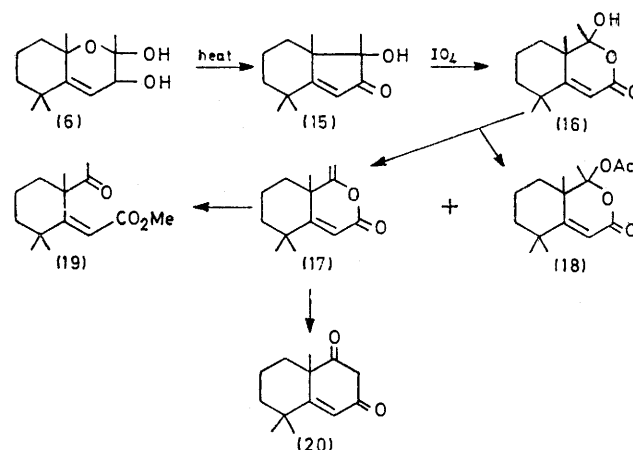
The hemiacetal (6) was also converted into the trimethyloctalindione (20), which was expected to be a useful intermediate for the synthesis of various terpenoids. Refluxing a solution of the hemiacetal (6) in benzene afforded a dehydration product (15) in quantitative yield. The u.v. and i.r. spectra indicated the presence of a  $\beta\beta$ -disubstituted cyclopentenone group bearing a hydroxy-substituent, and n.m.r. signals were observed for four methyl groups, an olefinic proton, and a hydroxy-proton. A possible mechanism for the formation of the hexahydroindenone (15) is shown in Scheme 2.



SCHEME 2

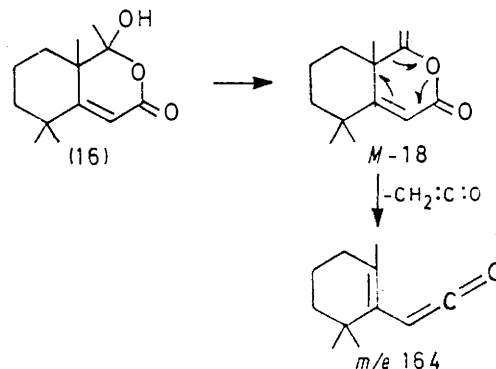
Support for structure (15) was obtained by its oxidation with periodic acid to the lactol (16). The presence

of a hydroxy-function and an  $\alpha\beta$ -unsaturated  $\delta$ -lactone group was deduced from the u.v. and i.r. spectra, and



the mass spectrum showed the molecular ion, an  $M - 18$  fragment, and the base peak at  $m/e$  164, generated through loss of keten from the  $M - 18$  fragment.

Refluxing the lactol (16) in acetic anhydride afforded an enol lactone (17) in 80% yield and a lactol acetate (18) in 13% yield. Treatment of the enol lactone (17) with sodium methoxide gave an oxo-ester (19) in



SCHEME 3

quantitative yield. In contrast, the enol lactone (17) was converted into the  $\beta$ -diketone (20)<sup>8</sup> on treatment with methanolic potassium hydroxide, in high yield.

#### EXPERIMENTAL

I.r. spectra were recorded with a Hitachi 215 grating spectrophotometer. U.v. spectra were measured with a Hitachi EPS-3T spectrophotometer. N.m.r. spectra were obtained with a Hitachi H 60 instrument.

6,7,8,8a-Tetrahydro-2,5,5,8a-tetramethyl-5H-chromen (2).—A solution of  $\beta$ -ionone (40 g) in ethanol (500 ml) was irradiated with a high-pressure mercury lamp (450 W) through a Pyrex filter for 15 h at room temperature. The ethanol was removed under reduced pressure; distillation of the residue gave the pyran (2) (28 g), b.p. 42–45° at 0.1 mmHg;  $\nu_{\max}$  1 650 and 1 598  $\text{cm}^{-1}$ ;  $\delta(\text{CCl}_4)$  1.08, 1.14,

<sup>8</sup> P. Beak and B. M. Monroe, *J. Org. Chem.*, 1967, **32**, 2778.

1.33, and 1.73 (each 3 H, s), 4.86 (1 H, d,  $J$  6 Hz), and 5.6 (1 H, d,  $J$  6 Hz).

4-(2,2-Dimethyl-6-methylenecyclohexylidene)butan-2-one (3).—A solution of  $\beta$ -ionone (5 g) in ethanol (400 ml) was irradiated without filter for 4 h at room temperature. Evaporation of the solvent afforded the diene (3) (4.8 g), b.p. 57–60° at 0.2 mmHg;  $\nu_{\max}$  1 710, 1 625, and 890  $\text{cm}^{-1}$ ;  $\delta(\text{CCl}_4)$  1.07 (6 H, s), 2.05 (3 H, s), 3.16 (2 H, d,  $J$  7.1 Hz), 4.51 and 4.96 (2 H, m), and 5.33 (1 H, t,  $J$  7.1 Hz).

Autoxidation of the Pyran (2).—The pyran (2) (28 g) was exposed to the atmosphere for 2 weeks at room temperature. White crystals were filtered off and washed with a small amount of hexane. Recrystallization from benzene-hexane afforded the hemiacetal (6) (8 g, 28%), m.p. 141–146°;  $\nu_{\max}$  3 460, 3 330, 1 650, and 1 220  $\text{cm}^{-1}$ ;  $\delta(\text{CCl}_4)$  1.14 (6 H, s), 1.47 (3 H, s), 1.60 (3 H, s), 2.0–2.3 and 2.5–2.8 (2 H, br, disappeared on treatment with  $\text{D}_2\text{O}$ ), 4.0 (1 H, m), and 5.47 (1 H, d,  $J$  4 Hz) (Found: C, 69.0; H, 9.55.  $\text{C}_{13}\text{H}_{22}\text{O}_3$  requires C, 69.0; H, 9.8%). The filtrate was fractionated by column chromatography on silicic acid. Elution with hexane gave the starting material and  $\beta$ -ionone. Elution with 1 : 1 hexane-benzene afforded dihydroactinoliide (4) (see later). The acetoxy-aldehyde (5) was obtained by elution with benzene; its properties were identical with those of the product from the following experiment.

(2-Acetoxy-2,6,6-trimethylcyclohexylidene)acetaldehyde (5) and 2,4,5,6,7,7a-Tetrahydro-4,4,7a-trimethylbenzofuran-2-ol (7).—A solution of the hemiacetal (6) (452 mg) and periodic acid (768 mg) in ethanol (30 ml) was stirred at 0 °C for 16 h, then extracted with ether to give the acetoxy-aldehyde (5) (428 mg) as an oil;  $\nu_{\max}$  1 740, 1 660, and 1 597  $\text{cm}^{-1}$ ;  $\delta(\text{CCl}_4)$  1.18, 1.29, and 1.75 (each 3 H, s, Me), 1.92 (3 H, s, Ac), 5.77 (1 H, d,  $J$  8 Hz, :CH), and 10.21 (1 H, d,  $J$  8 Hz, CHO) (Found: C, 69.45; H, 9.05.  $\text{C}_{13}\text{H}_{20}\text{O}_3$  requires C, 69.6; H, 9.0%).

The acetoxy-aldehyde (5) (310 mg) was hydrolysed with methanolic sodium hydroxide to afford the unstable hemiacetal (7) (213 mg),  $\nu_{\max}$  3 430  $\text{cm}^{-1}$  (OH),  $\delta$  3.22 (CH·OH), which was used directly for the next reaction.

Dihydroactinoliide [5,6,7,7a-Tetrahydro-4,4,7a-trimethylbenzofuran-2(4H)-one] (4).—A solution of chromic oxide (531 mg) and pyridine (861 mg) in methylene chloride (10 ml) was stirred for 15 min at room temperature. The acetal (7) (165 mg) dissolved in a small amount of methylene chloride was then added and the mixture was stirred for an additional 15 min at room temperature, and extracted with ether. The extract was successively washed with aqueous 5% sodium hydroxide, aqueous 5% hydrochloric acid, saturated sodium hydrogen carbonate solution, and brine. Evaporation afforded an oil (129 mg), which was distilled under reduced pressure; b.p. 85–90° at 0.2 mmHg. The distillate crystallized on cooling; m.p. 39°;  $\lambda_{\max}$  (EtOH) 212 nm ( $\epsilon$  13 800);  $\nu_{\max}$  1 750 and 1 621  $\text{cm}^{-1}$ ;  $\delta(\text{CCl}_4)$  1.22, 1.28 and 1.51 (each 3 H, s), and 5.50 (1 H, s);  $m/e$  180 ( $M^+$ ), 165 ( $M^+ - \text{CH}_3$ ), 152 ( $M^+ - \text{CO}$ ), and 137 (165 - CO).

Ionene (12).—To a solution of the 2H-pyran (2) (1.0 g) in dry benzene (2 ml) was added maleic anhydride (0.5 g). The mixture was sealed in a glass tube under nitrogen and heated at 100 °C for 20 h, then poured into ice-water and extracted with ether. After drying ( $\text{Na}_2\text{SO}_4$ ) the extract was evaporated to yield a tar, which was chromatographed on silicic acid. Ionene (12) (220 mg) was eluted by hexane;  $\lambda_{\max}$  265, 270, 272, and 278 nm;  $\nu_{\max}$  1 610 and 810  $\text{cm}^{-1}$ ;

$\delta(\text{CCl}_4)$  1.25 (6 H, s), 1.62 (4 H, m), 2.20 (3 H, s), 2.66br (2 H, t,  $J$  6 Hz), 6.69br (1 H, s), 6.77br (1 H, d,  $J$  8 Hz), and 7.06 (1 H, d,  $J$  8 Hz).

Addition of Tetracyanoethylene to the 2H-Pyran (2).—A solution of the 2H-pyran (2) (582 mg) and tetracyanoethylene (388 mg) in dry tetrahydrofuran (20 ml) was kept at room temperature for 19 h. The solvent was evaporated off under reduced pressure to leave 2,2a,3a,4,5,6,7,8a-octa-hydro-2a,3a,7,7-tetramethyl-1H-cyclobuta[b]chromen-1,1,2,2-tetracarbonitrile (850 mg);  $\nu_{\max}$  2 250 and 1 645  $\text{cm}^{-1}$ ;  $\delta(\text{CCl}_4)$  1.14, 1.26, 1.51, and 1.89 (each 3 H, s), 3.51 (1 H, d,  $J$  4 Hz), and 5.75 (1 H, d,  $J$  4 Hz) (Found: C, 71.35; H, 6.45; N, 17.35.  $\text{C}_{19}\text{H}_{20}\text{N}_4\text{O}$  requires C, 71.2; H, 6.3; N, 17.5%).

Thermal Reaction of the Hemiacetal (6).—A solution of the hemiacetal (6) (7.0 g) in benzene was refluxed for 3 h. The benzene was removed under reduced pressure, and the residue was recrystallized from benzene-hexane to afford 1,4,5,6,7,7a-hexahydro-1-hydroxy-1,4,4,7a-tetramethylinden-2-one (15) (4.2 g), m.p. 104–110°;  $\lambda_{\max}$  237 nm ( $\epsilon$  12 400);  $\nu_{\max}$  3 450, 1 700, and 1 590  $\text{cm}^{-1}$ ;  $\delta(\text{CCl}_4)$  1.21 and 1.25 (each 3 H, s), 1.30 (6 H, s), 2.7–3.1br (1 H, disappeared with  $\text{D}_2\text{O}$ ), and 5.90 (1 H, s);  $m/e$  208 ( $M^+$ ), 193 ( $M^+ - \text{CH}_3$ ), 175 (193 -  $\text{H}_2\text{O}$ ), and 165 (193 - CO) (Found: C, 74.75; H, 9.75.  $\text{C}_{13}\text{H}_{20}\text{O}_2$  requires C, 74.95; H, 9.7%).

1,5,6,7,8,8a-Hexahydro-1-hydroxy-1,5,5,8a-tetramethyl-2-benzopyran-3-one (16).—A mixture of compound (15) (3 g) and periodic acid (5.3 g) in ethanol (30 ml) was stirred at 0 °C for 18 h, then treated with ether, and the ethereal mixture was washed with water, dried, and evaporated. Recrystallization from benzene-hexane gave the lactol (16) (2.66 g);  $\lambda_{\max}$  227 nm ( $\epsilon$  11 600);  $\nu_{\max}$  3 310, 1 680, and 1 595  $\text{cm}^{-1}$ ;  $\delta(\text{CDCl}_3)$  1.23 (6 H, s), 1.30 (3 H, s), 1.55 (3 H, s), and 5.92 (1 H, s);  $m/e$  224 ( $M^+$ ), 206 ( $M^+ - \text{H}_2\text{O}$ ), 209 ( $M^+ - \text{CH}_3$ ), 164 ( $M^+ - \text{C}_2\text{H}_4\text{O}_2$ ), 149 (164 -  $\text{CH}_3$ ), and 121 (149 - CO) (Found: C, 69.5; H, 8.8%;  $M^+$ , 224.1426.  $\text{C}_{13}\text{H}_{20}\text{O}_3$  requires C, 69.6; H, 9.0%;  $M$ , 224.1410).

Dehydration of the Lactol (16).—A solution of the lactol (16) (2.24 g) in acetic anhydride (50 ml) was refluxed for 3 h. Fused sodium acetate (500 mg) was then added and the mixture was refluxed for a further 4 h. The acetic anhydride was removed under reduced pressure and the residue was dissolved in ether; the solution was washed with saturated sodium hydrogen carbonate solution and water, dried, and evaporated. The resulting oil was chromatographed on silicic acid to give 1,5,6,7,8,8a-hexahydro-5,5,8a-trimethyl-1-methylene-2-benzopyran-3-one (17) and the lactol acetate (18) (0.31 g). The enol lactone (17) had m.p. 50–51°;  $\lambda_{\max}$  224 nm ( $\epsilon$  11 200);  $\nu_{\max}$  1 725, 1 645, 1 610, and 890  $\text{cm}^{-1}$ ;  $\delta(\text{CCl}_4)$  1.12, 1.28, and 1.49 (each 3 H, s), 4.31 (1 H, d,  $J$  2 Hz), 4.61 (1 H, d,  $J$  2 Hz), and 5.71 (1 H, s) (Found: C, 75.55; H, 8.9.  $\text{C}_{12}\text{H}_{18}\text{O}_2$  requires C, 75.7; H, 8.8%). The lactol acetate (18) had m.p. 104–107°;  $\lambda_{\max}$  230 nm;  $\nu_{\max}$  1 760, 1 715, and 1 610  $\text{cm}^{-1}$ ;  $\delta(\text{CCl}_4)$  1.22, 1.28, and 1.30 each (3 H, s), 1.81 (3 H, s), 1.91 (3 H, s), and 5.80 (1 H, s).

Methyl 2-Acetyl-2,6,6-trimethylcyclohexylideneacetate (19).—To a solution prepared from sodium (15 mg) and dry methanol (5 ml) was added the enol lactone (17) (41 mg). The solution was stirred for 3 h at room temperature, then acidified with hydrochloric acid and extracted with ether to afford the oily oxo-ester (19) in quantitative yield;  $\lambda_{\max}$  228 nm;  $\nu_{\max}$  1 710, 1 700, and 1 610  $\text{cm}^{-1}$ ;  $\delta(\text{CCl}_4)$

1.24, 1.29, 1.54, 2.18, and 3.64 (each 3 H, s) and 6.01 (1 H, s) (Found: C, 70.7; H, 9.25.  $C_{14}H_{22}O_3$  requires C, 70.55; H, 9.3%).

6,7,8,8a-Tetrahydro-5,5,8a-trimethylnaphthalene-1,3(5H)-dione (20).—A solution of the enol lactone (19) (1.6 g) in methanolic potassium hydroxide was set aside for 3 h at room temperature, then acidified with hydrochloric acid

and extracted with ether to afford the diketone (20) (1.4 g), m.p. 156–160° (from benzene);  $\lambda_{max}$  243 ( $\epsilon$  10 000) and 291 nm (5 100);  $\lambda_{max}$ (KOH) 329 nm;  $\nu_{max}$  2 520, 1 640, 1 620, and 1 560  $cm^{-1}$ ;  $\delta(CCl_4)$  1.22, 1.32, and 1.57 (each 3 H, s), 3.5 (2 H, q,  $J$  18 Hz), and 6.25 (1 H, s) (Found: C, 75.75; H, 8.65.  $C_{13}H_{18}O_2$  requires C, 75.7; H, 8.8%).

[5/1721 Received, 8th September, 1975]