131. *The Synthesis of Some Thiophens Related to Vitamin A.*

By R. M. Acheson, J. A. Barltrop, M. Hichens, and R. E. Hichens.

Perhydro-2,2- and -4,4-dimethyl- and -2,4,4-trimethyl-3-oxothiophen have been synthesised by cyclisation of the corresponding dicarboxylic acids in the presence of barium hydroxide. The ethynylcarbinols, obtained from the last two ketones, gave with crotonylideneacetone or 6-methylocta-3,5,7-trien-2-one the expected ditertiary alcohols which rearranged with acid to the more conjugated tertiary-secondary and tertiary-primary alcohols respectively. Reduction of the products from 6-methylocta-3,5,7-trien-2-one with lithium aluminium hydride gave perhydro-3-hydroxy-3-(9-hydroxy-3,7-dimethylnona-1,3,5,7-tetraenyl)-4,4-dimethyl- and -2,4,4-trimethyl-thiophen which soon polymerised.

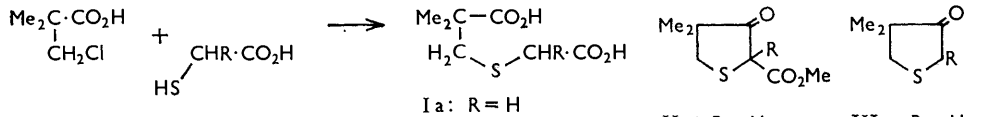
Many analogues of vitamin A have been synthesised and the growth-promoting properties in rats of a proportion of these compounds have been measured relative to that of vitamin A itself.[1] It is unfortunate that biological data are not available for all the analogues prepared, and it is particularly regrettable that, with one exception, no tests of possible anti-vitamin A activity have been reported. The one exception is a mixture of two compounds which is claimed [2] to possess anti-vitamin A activity and was prepared [2] from vitamin A by oxidation with vanadium tetroxide; the structures of the constituents have not been convincingly demonstrated. The ingestion of certain chlorinated naphthalenes

[1] Milas, in "The Vitamins," Vol. I, ed. Sebrell and Harris, Academic Press, New York, 1954; Bharucha and Weedon, *J.*, 1953, 1571.

[2] Meunier, Jouanneteau, and Ferrando, *Compt. rend.*, 1950, **230**, 140; Meunier, *Fortschr. Chem. org. Naturstoffe*, 1952, **9**, 102; Meunier, Zwingelstein, Jouanneteau, and Mallein, *Compt. rend.*, 1950, **230**, 1323.

can cause a condition that resembles the symptons of vitamin A deficiency,[3,4] but the functions of vitamin A *in vivo*, with the exception [5] of the cycle involving the retinenes in the eye, are not understood [6] and experiments [7] involving ^{14}C-labelled vitamin A have so far thrown little light on the problem. As structural analogues have proved useful in other instances in investigating the function of compounds essential to animal life the synthesis of some potential anti-vitamin A compounds was undertaken.

Although the cyclohexene ring can be modified in vitamin A analogues without total loss of growth-promoting activity, alteration in the side chain usually leads to activity only when conversion into the vitamin *in vivo* is possible. This, coupled with the fact that the replacement of two carbon atoms by sulphur, and *vice versa*, has led to anti-metabolite activity in the cases of nicotinamide and thiazole-5-carboxyamide,[8] phenylalanine and thienylalanine,[9] biotin and ureidocyclohexylvaleric acid,[10] and thiamine and pyrithiamine,[11] suggested the synthesis of the dihydrothiophen analogues of vitamin A. Comparatively little is known about dihydrothiophens; the 2,3-isomer polymerises slowly at room temperature or on prolonged heating,[12] but the 2,5-isomer is reported to be stable.[12] It was therefore considered worth while to try to synthesise both the 2,3- and the 2,5-dihydrothiophen analogues of vitamin A, and most of the experiments described here are in connexion with the former compound (XIV).



Ia: R = H
Ib: R = Me

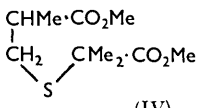
IIa: R = H
IIb: R = Me

IIIa: R = H
IIIb: R = Me

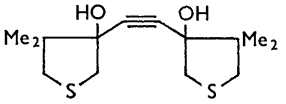
The route chosen was based on the synthesis of vitamin A carried out by Attenburrow *et al.*,[13] and the preparation of the requisite ketones was undertaken. Perhydro-4,4-dimethyl-3-oxothiophen (IIIa) was prepared by cyclisation of dimethyl ester of the acid (Ia); the corresponding sequence involving the diethyl ester had been described previously.[14] A number of attempts to methylate the intermediate keto-ester (IIa) at position 2, with a view to obtaining the trimethylthiophen derivatives (IIb) and (IIIb), were unsuccessful as ionic products were invariably formed. 3-Chloropivalic acid was then condensed with α-mercaptopropionic acid, and a number of attempts were made to cyclise the methyl ester of the product (Ib). As only one α-hydrogen atom is present triphenylmethylsodium was used as the condensing agent, and in most experiments perhydro-2,4,4-trimethyl-3-oxothiophen (IIIb) was obtained in poor yield. On one occasion, unaccountably, a liquid with a higher boiling point than the oxothiophen (IIIb) was obtained. Its composition was that required of the keto-ester (IIb), but hydrolysis under conditions successful for the corresponding dimethyl compound (IIa) gave none of the desired ketone (IIIb). Attempts to cyclise the isomeric ester (IV) [which had been

[3] Engel and Bell, *Nutrit. Abs. Rev.*, 1953, **11**, 97.
[4] Editorial, *Nutrit. Abs. Rev.*, 1954, **12**, 180; Ferrando, *ibid.*, 1957, **15**, 319; Hove, *J. Nutrit.*, 1953, **51**, 609.
[5] Morton and Pitt, *Fortschr. Chem. org. Naturstoffe*, 1957, **14**, 244; Dartnell, " The Visual Pigments," Methuen, London, 1957.
[6] Lowe and Morton, *Vitamins and Hormones*, 1956, **14**, 97.
[7] Wolf, Lane, and Johnson, *J. Biol. Chem.*, 1957, **225**, 995; Wolf, Kahn, and Johnson, *J. Amer. Chem. Soc.*, 1957, **79**, 1208.
[8] Erlenmeyer and Wurgler, *Helv. Chim. Acta*, 1942, **25**, 249; Erlenmeyer, Bloch, and Kiefer, *ibid.*, 1942, **25**, 1066.
[9] Garst, Campaigne, and Day, *J. Biol. Chem.*, 1949, **180**, 1013.
[10] English, Clapp, Cole, Halverstadt, Lampen, and Roblin, *J. Amer. Chem. Soc.*, 1945, **67**, 295.
[11] Woolley and White, *J. Biol. Chem.*, 1943, **149**, 285.
[12] Birch and McAllan, *J.*, 1951, 2556.
[13] Attenburrow, Cameron, Chapman, Evans, Hems, Jansen, and Walker, *J.*, 1952, 1094.
[14] Truce and Knospe, *J. Amer. Chem. Soc.*, 1955, **77**, 5063.

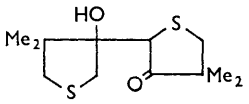
prepared by base-catalysed (Michael) addition of methyl α-mercapto-α-methylpropionate to methyl methacrylate] with triphenylmethylsodium were less successful. No cyclisation could be detected and a reverse Michael reaction, as sometimes occurs in the presence of molar quantities of strong bases, took place. At this stage it was found that the pyrolysis of the acid (Ia) over barium hydroxide gave the ketone (IIIa) in excellent yield, and the reaction has been applied with success to the synthesis of the trimethyl analogue (IIIb) and of perhydro-2,2-dimethyl-3-oxothiophen.



(IV)



(V)

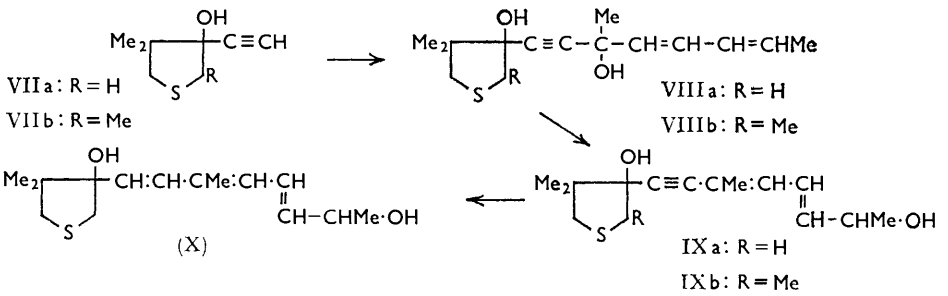


(VI)

In contrast to 2,2,6-trimethylcyclohexanone, perhydro-2,4,4-trimethyl-3-oxothiophen does not react with 2,4-dinitrophenylhydrazine, although it yields a semicarbazone. The failure may be due to steric hindrance as the corresponding dimethyl compound (IIIa) yields a 2,4-dinitrophenylhydrazone without difficulty. Oxidation of the trimethyl-ketone (IIIb) with hydrogen peroxide did not give the expected sulphone: the ring was opened giving di-(2-carboxy-2-methylpropyl) disulphide, which had been obtained earlier by a similar oxidation of perhydro-4,4-dimethyl-3-oxothiophen.[14]

Ethynylation of the ketones (IIIa, b) has been tried under a variety of conditions with only moderate success. 3-Ethynylperhydro-3-hydroxy-4,4-dimethylthiophen (VIIa) was obtained with least difficulty from the ketone (IIIa), acetylene, and calcium acetylide in liquid ammonia; a small amount of the glycol (V) was also isolated. When the ethynylation was effected with ethynylmagnesium bromide in tetrahydrofuran [15] it proved much more difficult to isolate the desired product and a small amount of the aldol (VI) was formed. In the case of the trimethyl-ketone (IIIb), however, the corresponding ethynyl-carbinol (VIIb) was best prepared by the ethynylmagnesium bromide method.

Both ethynylcarbinols (VII) gave bismagnesium derivatives with ethylmagnesium bromide, and these combined with hepta-3,5-dien-2-one which had been prepared and



purified by the method of Attenburrow *et al.*[13] The products were the ditertiary alcohols (VIII) which isomerised in the presence of acid to the more highly conjugated secondary-tertiary alcohols (IX). The ditertiary alcohols (VIII) showed infrared absorption at 1709 cm.$^{-1}$, and their isomers (IX) at 1710 cm.$^{-1}$. Such absorption in the carbonyl region has been observed previously [16] for acetylenic compounds carrying functional groups on a carbon atom directly attached to the acetylene group although the origin of the absorption is not clear.

Reduction of the acetylenic bond in (IXa) was achieved with lithium aluminium

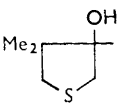
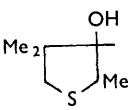
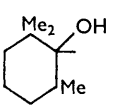
[15] Jones, Skattebol, and Whiting, 1956, 4765.

[16] Wotiz, Miller, and Palchak, *J. Amer. Chem. Soc.*, 1950, **72**, 5055; Wotiz and Miller, *ibid.*, 1949, **71**, 3441.

hydride, and oxidation of the product (X) with manganese dioxide gave a poor yield of perhydro-3-hydroxy-4,4-dimethyl-3-(6-methyl-2-oxo-octa-3,5,7-trienyl)thiophen. Much material remained adsorbed on the manganese dioxide, as was the case in the similar oxidation of the secondary alcohol (IXb) to the corresponding ketone. The ultraviolet absorption spectra of all these products based on the heptadienone are very similar to those of the corresponding derivatives in the 2,2,6-trimethylcyclohexanol series (Table) and thus confirm their structures.

As the experiments with hepta-3,5-dien-2-one were successful, 6-methylocta-3,5,7-trien-2-one was prepared by the modifications introduced by Attenburrow *et al.*[13] into the five-stage synthesis used by Cheeseman *et al.*[17] This ketone condensed with the bismagnesium

Ultraviolet absorption data [$\lambda_{max.}$ (Å); $10^{-4}\varepsilon$ *in parentheses*] *for the perhydrothiophens and their cyclohexane analogues.*

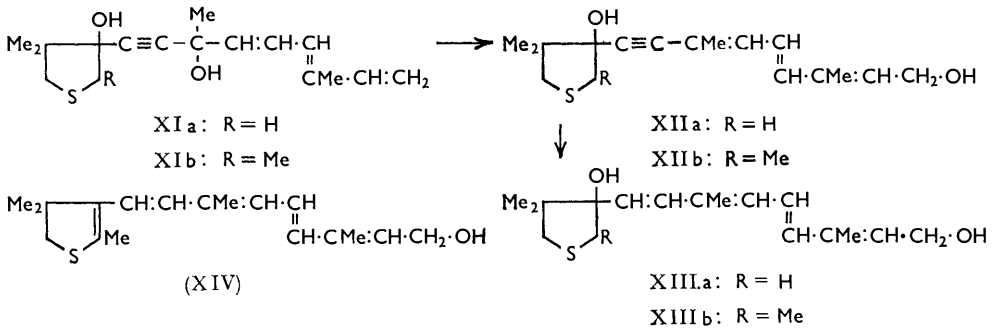
Compound	Formula	Cyclic substituent R					
							
R·C≡C·CMe(OH)·CH=CH·CH=CHMe	(VIII)	2290	(2·86)	2285	(2·80)	2290	(2·50)
R·C≡C·CMe=CH·CH=CH·CHMe·OH	(IX)	2685	(2·98)	2680	(3·25)	2690	(3·23)
		2795	(2·31)	2790	(2·30)	8200	(2·36)
R·C≡C·CMe=CH·CH=CH·COMe semicarbazone	—	—	—	2290*	(0·54)	2320*	(0·43)
		—	—	3180	(3·60)	3160	(4·98)
		—	—	3325	(3·17)	3330	(4·35)
R·CH=CH·CMe=CH·CH=CH·CHMe·OH	(X)	2655	(3·00)	—	—	2650	(2·34)
		2755	(3·58)	—	—	2740	(2·82)
		2850	(2·66)	—	—	2850	(2·24)
R·CH=CH·CMe=CH·CH=CH·COMe semicarbazone	—	2340	(0·25)	—	—	2350	(0·49)
		3100	(4·23)	—	—	—	—
		3220	(5·60)	—	—	3250	(5·75)
		3370	(4·68)	—	—	3400	(4·86)
R·C≡C·CMe(OH)·CH=CH·CH=CMe·CH=CH_2	(XI)	2590–2630*	(3·25)	2590–2630*	(3·14)	—	—
		2690	(4·10)	2690	(3·98)	2700	(4·06)
		2800	(3·25)	2800	(3·14)	2810	(3·16)
R·C≡C·CMe=CH·CH=CH·CMe=CH·CH_2·OH	(XII)	2250	(1·04)	2260	(0·92)	2260	(0·84)
		2880–2935*	(4·70)	2880–2935*	(3·57)	2870–2960*	(3·57)
		3010	(6·39)	3010	(4·95)	3020	(4·76)
		3150	(5·29)	3150	(4·08)	3170	(3·94)
Anthraquinone-2-carboxylate of (XII)		2590	(6·19)	2580	(5·15)	2580	(6·25)
		2780	(4·07)	2760	(3·30)	2800	(3·14)
		2940–2965*	(4·55)	2930–2960*	(3·82)	—	—
		3060	(5·81)	3050	(4·80)	3060	(4·16)
		3210	(4·94)	3190	(4·14)	3200	(3·80)
R·CH=CH·CMe=CH·CH=CH·CMe=CH·CH_2·OH	(XIII)	2290	(0·68)	2260	(0·74)	2300	(0·57)
		2835–2860*	(2·44)	2835–2855*	(2 86)	—	—
		2950	(4·04)	2950	(4·40)	2960	(4·35)
		3075	(5·29)	3070	(5·93)	3070	(5·80)
		3220	(4·18)	3225	(4·65)	3230	(4·66)

* Inflexion.

derivatives of the ethynylcarbinols (VII), and the products (XI) rearranged with acid to the more highly conjugated primary alcohols (XII). Three crystalline modifications of one of these (XIIb) were obtained and, although all had identical ultraviolet absorption spectra, the identical infrared absorption spectra (determined in paraffin paste) of the two lower-melting modifications differed in small ways from that of the highest-melting

[17] Cheesman, Heilbron, Jones, Sondheimer, and Weedon, *J.*, 1949, 2031.

modification. Reduction of the diols (XII) by lithium aluminium hydride gave only a 5% yield of the alcohol (XIIIa) and 20% of the analogue (XIIIb) in contrast to the good yields obtained in the corresponding stage of the vitamin A synthesis; and the ether-soluble material left after the reduction was only about half the weight of the starting material. There is little in the literature to suggest that the hydride would cause sulphur–carbon scission, and it is likely that polymerisation of the reduced diols took place. Both



diols were unstable and in the case of (XIIIa) the best crystalline sample obtained deteriorated rapidly at 0° under nitrogen. No satisfactory analysis was obtained for this compound although the light absorption indicates that the material was substantially pure when these measurements were made. The trimethylthiophen derivative (XIIIb) was obtained analytically pure and was characterised as the acetate, but sufficient material was not obtained to attempt dehydration to the vitamin A analogue (XIV). The ultraviolet absorption spectra of the perhydrothiophens (Table) were very similar to those of the corresponding cyclohexanes.[13]

Experimental

The alumina used for chromatography was Spence type H, 100—200 mesh, which had been deactivated by shaking it with 5% of its weight of 10% aqueous acetic acid. The light petroleum used had b. p. 40—60°. Magnesium sulphate was used as the drying agent, unless otherwise specified. The solvent ratios in mixed solvents are all v/v. Polyenes were distilled under nitrogen, and fractionations were through a 24″ vacuum-jacketed, heated column filled with Dixon rings or glass helices. The ultraviolet absorption spectra were measured for EtOH solutions. Alkali-washings of ether extracts were with sodium hydrogen carbonate solution.

(Carboxymethylthio)pivalic acid.—Mercaptoacetic acid (200 g.) in aqueous potassium hydroxide (286 g. in 500 ml.) was added to chloropivalic acid [18] (324 g.) in aqueous sodium carbonate (130 g. in 1 l.), and after 6 hours' refluxing the mixture was acidified and extracted with ether. Distillation of the dried extract gave *(carboxymethylthio)pivalic acid* (280 g.) as a yellow viscous oil, b. p. 154°/0·02 mm. (Found: C, 43·7; H, 6·7; S, 16·6. $C_7H_{12}O_4S$ requires C, 43·7; H, 6·3; S, 16·2%). This solidified to a glass which resisted all attempts at crystallisation.

This acid (25 g.) was heated under reflux with methanol (120 ml.) containing hydrogen chloride (6 g.) for 5 hr. and then the excess of methanol was removed *in vacuo*. The residue, in ether, was washed with aqueous sodium hydrogen carbonate, dried, and distilled, and gave the *ester* (18 g.), b. p. 104—106°/0·05 mm., n_D^{10} 1·4734 (Found: C, 49·3; H, 7·3; S, 14·5. $C_9H_{16}O_4S$ requires C, 49·1; H, 7·3; S, 14·5%).

Methyl Perhydro-4.4-dimethyl-3-oxothiophen-2-carboxylate (IIa).—The preceding ester (9·0 g.) in dry toluene (75 ml.) was stirred at 50° for 5 hr. with sodium methoxide (1·4 g.), and the mixture left at room temperature for 2 days. Acetic acid (10 ml.), ice, and ether were added. An ether extract was made and washed with aqueous sodium hydrogen carbonate, dried, and distilled, giving the *keto-ester* (5·0 g.), b. p. 78—79°/1 mm., n_D^{10} 1·4950 (Found: C, 50·6; H, 6·4; S, 16·9. $C_8H_{12}O_3S$ requires C, 51·0; H, 6·4; S, 17·0%). The *2,4-dinitrophenylhydrazone*

[18] Kharasch and Brown, *J. Amer. Chem. Soc.*, 1940, **62**, 925.

separated from methanol in orange needles, m. p. 122° (Found: C, 45·5; H, 4·3. $C_{14}H_{16}N_4O_6S$ requires C, 45·6; H, 4·5%).

Perhydro-4,4-dimethyl-3-oxothiophen (IIIa).—(i) The preceding ester (5·0 g.) was heated under reflux with 2N-sulphuric acid (40 ml.) for 4 hr. and extracted with ether. Distillation of the extract (washed with sodium hydrogen carbonate solution and dried) gave perhydro-4,4-dimethyl-3-oxothiophen (2·0 g.), b. p. 62—63°/10 mm., n_D^{10} 1·4970 (Found: C, 55·0; H, 7·7; S, 24·8. Calc. for $C_6H_{10}OS$: C, 55·3; H, 7·7; S, 24·6%). Truce and Knospe [14] give b. p. 78—78·5°/20 mm. and n_D^{25} 1·4948 but do not describe derivatives. The *2,4-dinitrophenylhydrazone*, orange needles from methanol, had m. p. 125° (Found: C, 45·9; H, 4·7. $C_{12}H_{14}N_4O_4S$ requires C, 46·3; H, 4·5%), and the *semicarbazone*, colourless needles from water, had m. p. 205° (Found: C, 44·9; H, 7·0; N, 22·1. $C_7H_{13}N_3OS$ requires C, 44·9; H, 7·0; N, 22·4%).

(ii) (Carboxymethylthio)pivalic acid (270 g.) was heated to 200° with finely powdered barium hydroxide (10 g.). The non-aqueous layer of the distillate was dried ($CaCl_2$), and distillation gave perhydro-4,4-dimethyl-3-oxothiophen (140 g.), b. p. 60—62°/6 mm., with refractive index, infrared absorption spectrum, and semicarbazone identical with those of the compound prepared as under (i).

α-Mercaptopropionic Acid.—α-Chloropropionic acid (21 g.) and thiourea (15 g.) were refluxed in ethanol (50 ml.) for 1 hr. *2-Amino-4-hydroxy-5-methylthiazole hydrochloride* separated on cooling, and after crystallisation from ethanol had m. p. 200° (26 g.) (Found: C, 28·8; H, 4·3; N, 16·6; S, 18·9. $C_4H_6N_2OS$,HCl requires C, 28·8; H, 4·2; N, 16·8; S, 19·2%). This hydrochloride was heated under reflux with 10% aqueous sodium hydroxide (250 ml.) for 3 hr., acidified, and extracted with ether. Distillation of the dried extract gave α-mercaptopropionic (thiolactic) acid, b. p. 97—98°/8 mm., n_D^{13} 1·4827, as a foul-smelling colourless liquid (7 g.). Dixon [19] has described the preparation of the thiazole hydrochloride in outline, but gave no analysis, and he mentioned its decomposition with barium hydroxide to thiolactic acid.

(1-Carboxyethylthio)pivalic Acid.—α-Mercaptopropionic acid (240 g.) and potassium hydroxide (350 g.) in water (1 l.) were added to chloropivalic acid (300 g.) and sodium hydrogen carbonate (200 g.) in water (800 ml.), and the mixture was refluxed for 18 hr. After acidification, with ice-cooling, the mixture was extracted with ether, and the extract washed with water and dried. Distillation gave a viscous oil, b. p. 172°/0·03 mm. (324 g.), which solidified. Recrystallisation from light petroleum gave the *acid* as colourless rhombs, m. p. 83° (Found: C, 46·9; H, 6·8; S, 15·7. $C_8H_{14}O_4S$ requires C, 46·6; H, 6·8; S, 15·6%).

This acid (2·3 g.) and 30% hydrogen peroxide (4 ml.) were mixed in glacial acetic acid, heat being evolved. After being kept overnight the mixture was heated under reflux for 3 hr. and evaporated to dryness *in vacuo*. The residue on crystallisation from ethyl acetate–light petroleum gave the *sulphone* (1·5 g.) as colourless needles, m. p. 149·5—150·5° (Found: C, 40·5; H, 6·1; S, 12·9. $C_8H_{14}O_6S$ requires C, 40·3; H, 5·9; S, 13·4%).

Methyl (1-methoxycarbonylethylthio)pivalate, obtained from the crude acid and hydrogen chloride in methanol in the usual way, in 73% yield, had b. p. 86—88°/0·06 mm., n_D^{12} 1·4699 (Found: C, 51·5; H, 7·9; S, 13·4. $C_{10}H_{18}O_4S$ requires C, 51·3; H, 7·7; S, 13·7%).

Perhydro-2,4,4-trimethyl-3-oxothiophen (IIIb).—(i) The preceding ester (7·4 g.) was added under nitrogen to triphenylmethylsodium, prepared from triphenylmethyl chloride (11 g.) and 1% sodium amalgam (200 g.), in ether (270 ml.). The intense red colour was discharged immediately and, after 24 hr., acetic acid (2 g.) was added. The mixture was washed with aqueous sodium hydrogen carbonate, dried, and evaporated and ethanol containing 5% of water was added. Triphenylmethane was precipitated and was collected, and distillation of the filtrate gave first ethanol, which smelled strongly of mercaptan and gave a red colour with sodium nitroprusside (it was not investigated further), and then *perhydro-2,4,4-trimethyl-3-oxothiophen* (1·0 g.), b. p. 78°/16 mm., n_D^{19} 1·4963 (Found: C, 58·0; H, 8·0; S, 22·7. $C_7H_{12}OS$ requires C, 58·4; H, 8·3; S, 22·2%). The *semicarbazone* separated from aqueous ethanol in needles, m. p. 188° (Found: C, 48·0; H, 7·5; S, 15·8. $C_8H_{15}N_3OS$ requires C, 47·8; H, 7·5; S, 15·9%). Higher-boiling fractions were the initial diester, b. p. 82°/0·2 mm. (2·5 g.), and triphenylmethane, b. p. 134°/0·2 mm.

On one occasion, instead of the expected product, the above experiment yielded a pale yellow oil, b. p. 85—90°/0·5 mm., n_D^{16} 1·4780, which appeared to be *methyl perhydro-2,4,4-trimethyl-3-oxothiophen-2-carboxylate* (IIb) (15% yield) (Found: C, 53·0; H, 6·7; S, 16·0. $C_9H_{14}O_3S$ requires C, 53·4; H, 6·9; S, 15·8%). Attempted hydrolysis of this oil (1·9 g.) by

[19] Dixon, *J.*, 1893, 819.

heating it under reflux for 5 hr. with 2N-sulphuric acid (20 ml.) followed by ether-extraction and distillation of the alkali-washed and dried extract gave an oily *substance* (1·5 g.), b. p. 150°/0·5 mm., that was not identified (Found: C, 58·8; H, 7·5; S, 11·5. $C_{14}H_{22}O_4S$ requires C, 58·9; H, 7·6; S, 11·3%).

(ii) (1-Carboxyethylthio)pivalic acid (270 g.) was heated to 220° with finely powdered barium hydroxide (10 g.), and the distillate (208 g.) collected. The non-aqueous layer was separated and on distillation gave perhydro-2,4,4-trimethyl-3-oxothiophen (140 g.), b. p. 60—62°/6 mm., n_D^{19} 1·4963. The semicarbazone had m. p. and mixed m. p. 188°.

Perhydro-2,4,4-trimethyl-3-oxothiophen (3·0 g.) in acetic acid (20 ml.) was mixed with 30% hydrogen peroxide (7 ml.) and after 24 hr. the solvent was removed *in vacuo*. The residual red oil partially crystallised, and recrystallisation from aqueous ethanol gave di-(2-carboxy-2-methylpropyl) disulphide as colourless plates, m. p. 145—146° (Found: C, 44·6; H, 6·6; S, 24·1. Calc. for $C_{10}H_{18}O_4S_2$: C, 45·1; H, 6·8; S, 24·0%) (lit.,[14] m. p. 147·5—148·5°).

α-(2-*Carboxyethylthio*)-α-*methylpropionic Acid*.—α-Bromo-α-methylpropionic acid (13 g.) from bromine, isobutyric acid, and its anhydride in the presence of pyridine, was neutralised with sodium hydroxide and added to β-mercaptopropionic acid (8·5 g.) in 5% aqueous sodium hydroxide (120 ml.). After 12 hr. the mixture was heated under reflux for 5 hr., cooled, acidified with hydrochloric acid, and extracted with ether. Distillation of the dried extract gave the substituted *propionic acid* (3·2 g.), b. p. 170—180°/0·03 mm., which solidified. It separated from light petroleum as colourless crystals, m. p. 53° (Found: C, 43·5; H, 6·3; S, 16·4. $C_7H_{12}O_4S$ requires C, 43·7; H, 6·2; S, 16·7%).

Perhydro-2,2-dimethyl-3-oxothiophen.—The preceding acid (2·5 g.) was heated at 200—220° with finely powdered barium hydroxide (0·1 g.), and the distillate collected with ether and dried ($MgSO_4$). Distillation gave the *ketone* (1·0 g.), b. p. 115—120°/18 mm., n_D^{17} 1·4532 (Found: C, 55·5; H, 7·8; S, 24·3. $C_6H_{10}OS$ requires C, 55·3; H, 7·7; S, 24·6%).

Methyl α-Mercapto-α-methylpropionate.—Sodium hydrogen sulphide in methanol, prepared by passing hydrogen sulphide into a solution of sodium (9·2 g.) in dry methanol (80 g.) until the required increase in weight (13 g.) had taken place, was added to methyl α-bromo-α-methylpropionate (30 g.), and the mixture refluxed for 40 min. Precipitated sodium bromide was removed and the filtrate was acidified with acetic acid, diluted to 500 ml. with water, and extracted with benzene. The extract was alkali-washed, dried, and distilled, giving the ester (8 g.) as an evil-smelling liquid, b. p. 86°/100 mm.

Methyl α-(2-*Methoxycarbonylpropylthio*)-α-*methylpropionate* (IV).—Freshly redistilled methyl methacrylate (11 g.) was added dropwise to methyl α-mercapto-α-methylpropionate (8 g.) containing sodium methoxide (0·1 g.) with stirring during 30 min., and stirring continued for a further 90 min. After filtration the mixture was distilled and gave the *diester* (10 g.), b. p. 64—66°/0·02 mm., n_D^{17} 1·4683 (Found: C, 51·5; H, 7·8; S, 13·4. $C_{10}H_{18}O_4S$ requires C, 51·3; H, 7·7; S, 13·7%).

In an attempt at cyclisation this ester (8·0 g.) was added under nitrogen to triphenylmethylsodium [from triphenylmethyl chloride (14 g.) and 1% sodium amalgam (300 g.)] in ether (300 ml.), and the mixture shaken for 6 hr. The precipitate was collected, suspended in ether, and acidified with acetic acid (2 ml.). Evaporation and distillation yielded only methyl α-mercapto-α-methylpropionate (2·0 g.), b. p. 87°/100 mm., which was characterised as its *S*-triphenylmethyl derivative, m. p. 148—150° (Found: C, 75·9; H, 6·1. Calc. for $C_{23}H_{22}O_2S$: C, 76·2; H, 6·1%) (lit.,[20] gives m. p. 155—156°).

3-*Ethynylperhydro-4,4-dimethylthiophen-3-ol* (VIIa).—(i) Liquid ammonia (3 l.) was saturated with dry, acetone-free acetylene, and calcium turnings (30 g.) were added during 2 hr. with stirring. The stream of acetylene was continued while perhydro-4,4-dimethyl-3-oxothiophen (70 g.) in ether (70 ml.) was added dropwise, and after overnight stirring ammonium chloride (100 g.) was added cautiously. The ammonia was allowed to evaporate, the residue was extracted with ether, and the extracts were washed with water and dried. Distillation gave first pure perhydro-4,4-dimethyl-3-oxothiophen (20 g.), and then a mixture of this and the desired product which had b. p. 92—108°/17 mm., n_D^{23} 1·5030, and could not be resolved by further fractionation. The next fraction was a colourless oil (18 g.), b. p. 117—124°/17 mm., n_D^{23} 1·5160—1·5250, that solidified slowly and crystallised from light petroleum giving the *ethynylcarbinol*, m. p. 38° (Found: C, 61·3; H, 7·9; S, 20·6. $C_8H_{12}OS$ requires C, 61·5; H, 7·8; S, 20·5%). The presence of the ethynyl group was shown by absorption at 2210 $cm.^{-1}$.

[20] Iskander and Tewkif, *J.*, 1951, 2050.

The residue from the distillation solidified overnight, and crystallisation from benzene gave a colourless solid, m. p. 132°, which showed absorption in the hydroxyl region (3400 cm.$^{-1}$) and may be *bis(perhydro-3-hydroxy-4,4-dimethyl-3-thienyl)acetylene* (V) (Found: C, 58·9; H, 7·5; S, 22·6. $C_{14}H_{22}O_2S_2$ requires C, 58·7; H, 7·7; S, 22·4%).

Poorer results were obtained when the initial reaction mixture was allowed to remain at room temperature in a steel bomb for 2 days before being worked up.

(ii) Perhydro-4,4-dimethyl-3-oxothiophen (18·2 g.) in an equal volume of dry tetrahydrofuran was added to ethynylmagnesium bromide (from 4·8 g. of magnesium) in tetrahydrofuran (220 ml.), prepared according to Jones *et al.*,[15] with ice-cooling. After overnight stirring saturated aqueous ammonium chloride was added. The organic layer, combined with ether extracts of the aqueous layer, was washed with water, dried, and evaporated, and the residual oil (20 g.) treated with a small quantity of light petroleum. A colourless solid (1·7 g.) separated at 0°, and after crystallisation from benzene had m. p. 79°. Absorption at 3510 and 1735 cm.$^{-1}$ indicated the presence of hydroxyl and carbonyl groups respectively, and the compound is tentatively formulated as *perhydro-4,4-dimethyl-3-oxo-2-(perhydro-3-hydroxy-4,4-dimethyl-3-thienyl)thiophen* (VI) (Found: C, 55·2; H, 7·9; S, 24·3. $C_{12}H_{20}O_2S_2$ requires C, 55·4; H, 7·7; S, 24·6%).

The remainder of the product (18·3 g.) was chromatographed on alumina. Elution with light petroleum and with benzene gave oils, which were combined, and subsequent elution with ether gave some of the bisthienylacetylene described under (i), as shown by m. p. and infrared absorption spectrum comparisons. The oils (9·7 g.) were dissolved in ethanol (100 ml.) and added dropwise to silver nitrate (48 g.) in 95% ethanol (1 l.). The colourless precipitate was collected, washed with ethanol, added to ammonium thiocyanate (30 g.) in water (108 ml.), and extracted successively with light petroleum, benzene, and ether. Evaporation of the petroleum gave a colourless oil (3·5 g.) which was not examined as the benzene fraction gave the desired ethynylcarbinol (1·3 g.); the ether extract gave a colourless solid, m. p. 140°, which was not identified. Trial experiments with the pure ethynylcarbinol showed that an 80% recovery was obtainable through the thiocyanate procedure after conversion into the silver salt.

Distillation of the crude product of an identical experiment gave an oil, b. p. 102—110°/15 mm., n_D^{12} 1·5055, which showed maxima at both 1725 and 2210 cm.$^{-1}$ and could not be resolved by further fractionation. It was treated with semicarbazide hydrochloride (6 g.) and potassium acetate (7 g.) in aqueous methanol; after warming to 60° and cooling, perhydro-4,4-dimethyl-3-oxothiophen semicarbazone was collected. The filtrate was poured into water (250 ml.) and extraction with light petroleum gave some of the ethynylcarbinol (3·7 g.), m. p. 38°.

3-Ethynylperhydro-2,4,4-trimethylthiophen-3-ol (VIIIb).—(i) Lithium (21 g.) was added in portions with stirring to liquid ammonia (4 l.) previously saturated with acetylene, while the acetylene stream was continued. Perhydro-2,4,4-trimethyl-3-oxothiophen (180 g.) in ether (500 ml.) was added in 1 hr. and stirring continued for 2 hr. After evaporation of the ammonia, ammonium chloride and ice were added, and the mixture was extracted with ether. Distillation of the washed, dried extracts gave the original ketone (89 g.) and a brown oil, b. p. 98—102°/6 mm., n_D^{21} 1·5101. Fractionation of this gave a brown liquid, b. p. 100—102°/6 mm., n_D^{19} 1·5129, containing the desired acetylene and original ketone, as shown by absorption at 2210 and 1730 cm.$^{-1}$; this mixture could not be resolved by fractionation. The liquid, in light petroleum, was chromatographed on deactivated alumina. Elution with benzene–light petroleum (1 : 1) gave *3-ethynylperhydro-2,4,4-trimethylthiophen-3-ol* (8·0 g.), m. p. 78° (from light petroleum) (Found: C, 64·0; H, 8·2. $C_9H_{14}OS$ requires C, 63·6; H, 8·2).

(ii) Perhydro-2,4,4-trimethyl-3-oxothiophen (130 g.) was added to ethynylmagnesium bromide under the same conditions as in the reaction with perhydro-4,4-dimethyl-3-oxothiophen; distillation of the crude product gave the original ketone (40 g.) and the desired ethynylcarbinol (49 g.), b. p. 108—110°/14 mm., n_D^{20} 1·5221, m. p. and mixed m. p. 78°.

The crude product from a similar reaction involving 10 g. of the perhydro-3-oxothiophen was chromatographed as above and yielded unchanged ketone (2 g.), and the ethynylcarbinol (3 g.). Final elution of the alumina with methanol gave an unidentified *substance* which separated from benzene as rhombs, m. p. 134° (Found: C, 58·6; H, 7·9; S, 19·3. $C_{16}H_{26}O_3S_2$ requires C, 58·1; H, 7·9; S, 19·4%).

Perhydro-3-hydroxy-3-(3-hydroxy-3-methylocta-4,6-dien-1-ynyl)-4,4-dimethylthiophen (VIIIa).—3-Ethynylperhydro-4,4-dimethylthiophen-3-ol (5·5 g.) in ether (10 ml.) was added dropwise to a stirred refluxing solution of ethylmagnesium bromide (from 2·1 g. of magnesium)

in ether (200 ml.), and the mixture stirred for 2 hr. Dry tetrahydrofuran was added to dissolve the precipitated complex and thus facilitate stirring. Hepta-3,5-dien-2-one [16] (5·8 g.) in tetrahydrofuran (10 ml.) was added to the mixture at 20° and the whole was stirred overnight. 20% Aqueous ammonium chloride (140 ml.) and ice were added and the product was collected with ether. The ether solution was then washed, dried, and evaporated. The residual oil, in light petroleum, was chromatographed on alumina, and elution with the same solvent, followed by benzene, gave starting materials. Elution with benzene–ether (1 : 1) gave the desired *diol* (5·36 g.) as a viscous yellow-green oil, b. p. 50°/10^{-6} mm., n_D^{13} 1·5410 (Found: C, 67·2; H, 8·1; S, 12·2. $C_{15}H_{22}O_2S$ requires C, 67·6; H, 8·3; S, 12·0%).

Perhydro-3-hydroxy-3-(7-hydroxy-3-methylocta-3,5-dien-1-ynyl)-4,4-dimethylthiophen (IXa).—The previous diol (4·0 g.) was dissolved in acetone (100 ml.), and 1% aqueous hydrochloric acid (40 ml.) was added. After 4 hr. the mixture was neutralised with saturated aqueous sodium hydrogen carbonate (150 ml.), and the product extracted with light petroleum. After drying, the extract was chromatographed on alumina. Elution with benzene–ether (1 : 1) gave the substituted *octa-3,5-dien-1-yn-7-ol* (2·8 g.) as a green-yellow viscous oil, b. p. 60°/10^{-5} mm., n_D^{12} 1·5798 (Found: C, 67·2; H, 8·1; S, 12·5. $C_{15}H_{22}O_2S$ requires C, 67·6; H, 8·3; S, 12·0%).

Perhydro-3-hydroxy-3-(7-hydroxy-3-methylocta-1,3,5-trienyl)-4,4-dimethylthiophen (X).—The octa-3,5-dien-1-yn-7-ol (IXa) (2·4 g.) in ether (50 ml.) was added dropwise to a stirred solution of lithium aluminium hydride (0·45 g.) in ether (20 ml.), and the mixture was refluxed for 3 hr. After cooling to 0°, ice and saturated aqueous tartaric acid were added, and the ether layer was washed, dried, and evaporated; a pale yellow oil (2·1 g.), n_D^{20} 1·5650, was obtained. It was chromatographed on alumina from benzene–light petroleum (1 : 1), and elution with benzene–ether (1 : 1) gave the *octa-1,3,5-trien-7-ol derivative* (1·6 g.) as a viscous yellow oil, b. p. 60°/10^{-5} mm., n_D^{12} 1·5860 (Found: C, 66·8; H, 8·6; S, 11·5. $C_{15}H_{24}O_2S$ requires C, 67·1; H, 8·9; S, 11·9%).

Perhydro-3-hydroxy-3-(3-methylocta-1,3,5-trien-7-onyl)-4,4-dimethylthiophen.—The preceding alcohol (X) (1·4 g.) in ether (40 ml.) was shaken for 4 hr. with active manganese dioxide (15 g.), and the mixture centrifuged. Evaporation of the supernatant liquid gave a green viscous oil (0·5 g.) which was chromatographed, in benzene–light petroleum (1 : 1), on alumina. Elution with benzene–ether (1 : 1) gave the ketone as a viscous yellow oil (0·45 g.), n_D^{12} 1·6032. The *semicarbazone* crystallised from ethanol in yellow needles, m. p. 167—169° (Found: C, 59·5; H, 7·6; N, 12·7; S, 10·0. $C_{16}H_{25}N_3O_2S$ requires C, 59·5; H, 7·7; N, 13·0; S, 9·9%).

Perhydro-3-hydroxy-3-(3-hydroxy-3,7-dimethylnona-4,6,8-trien-1-ynyl)-4,4-dimethylthiophen (XIa) —3-Ethynylperhydro-4,4-dimethylthiophen-3-ol (35 g.) in benzene (300 ml.) was added slowly to ethylmagnesium bromide (from 13·2 g. of magnesium) in ether (200 ml.) and stirred under reflux for 30 min. After cooling to room temperature, 6-methylocta-3,5,7-trien-2-one [16] (31 g.) in benzene (300 ml.) was added slowly, with stirring. After refluxing for 30 min. the mixture was cooled and poured on to aqueous ammonium chloride and ice, and the organic layer was collected, washed, and dried. Evaporation gave the crude 4,6,8-trien-1-yn-3-ol derivative as a viscous brown oil (65 g.). A portion was purified by chromatography on alumina, and gave the *diol* as a viscous yellow oil, b. p. 70°/10^{-5} mm., n_D^{12} 1·5560 (Found: C, 69·7; H, 8·0; S, 11·1. $C_{17}H_{24}O_2S$ requires C, 69·9; H, 8·2; S, 10·9%).

Perhydro-3-hydroxy-3-(9-hydroxy-3,7-dimethylnona-3,5,7-trien-1-ynyl)-4,4-dimethylthiophen (XIIa).—The above crude diol (60 g.) was dissolved in 1 : 9 aqueous acetone (1 l.) containing 0·1% of sulphuric acid and left for 3 hr. at 20°, then poured into water (1·5 l.). The product was isolated with ether, and the alkali-washed extracts were dried and evaporated. The residual brown oil (59 g.; n_D^{18} 1·5550) in benzene was chromatographed on alumina. Elution with benzene–ether (1 : 1) gave a dark red oil (12 g.), n_D^{18} 1·5830, which solidified, and crystallisation from benzene gave the *3,5,7-trien-1-yn-9-ol* as yellow needles, m. p. 138—139° (Found: C, 69·6; H, 8·1; S, 11·2. $C_{17}H_{24}O_2S$ requires C, 69·9; H, 8·2; S, 10·9%).

This diol (0·2 g.) was converted into the *anthraquinone-2-carboxylate* by refluxing it with the appropriate acid chloride (0·5 g.) and pyridine (1 ml.) in dry benzene (25 ml.) for 45 min. After addition of a little water the mixture was filtered, and the benzene layer washed with dilute acid and then alkali, and water, and dried. Trituration, with ether, of the residue obtained on evaporation gave the orange ester which crystallised from benzene. It had m. p. 172°; it resolidified sharply at 178°, and decomposed on further heating without melting (Found: C, 73·1; H, 6·0; S, 6·0. $C_{32}H_{30}O_5S$ requires C, 73·0; H, 5·7; S, 6·1%).

Perhydro-3-hydroxy-3-(9-hydroxy-3,7-dimethylnona-1,3,5,7-tetraenyl)-4,4-dimethylthiophen (XIIIa).—The above diol (6·0 g.) in ether (300 ml.) was added dropwise with stirring to lithium aluminium hydride (3 g.) in ether (400 ml.), and the mixture was heated under reflux for 3 hr. The product was isolated in the usual way and was a yellow viscous oil (3·5 g.) which resisted all attempts at crystallisation. The oil, in benzene, was chromatographed on alumina and elution with benzene–ether (1 : 1) gave the tetraenol (0·3 g.) which separated from benzene in yellow needles, m. p. 142°. The compound rapidly became oily at 0° under nitrogen, and neither satisfactory analytical data nor crystalline derivatives could be obtained.

Perhydro-3-hydroxy-3-(3-hydroxy-3-methylocta-4,6-dien-1-ynyl)-2,4,4-trimethylthiophen (VIIIb).—3-Ethynylperhydro-2,4,4-trimethylthiophen-3-ol (3·0 g.) in ether (10 ml.) was added dropwise to ethylmagnesium bromide (from 1·1 g. of magnesium) in ether (100 ml.), and the mixture stirred for 3 hr.; some tetrahydrofuran was added to facilitate stirring. Hepta-3,5-dien-2-one (2·9 g.) in tetrahydrofuran (10 ml.) was added at 0° and stirring continued for 3 hr. at 19°. 20% Aqueous ammonium chloride was then added at 0°, and the product isolated in the usual way with ether. It was a yellow-green oil (5·7 g.) which was chromatographed on alumina from light petroleum. Elution with benzene–light petroleum (1 : 1) gave the original acetylene (1 g.), and benzene–ether (1 : 1) then gave the *methylocta-4,6-dien-1-yn-3-ol derivative* (1·94 g.), n_D^{20} 1·5355, which distilled at 60°/10^{-5} mm. as a yellow-green viscous oil, n_D^{13} 1·5388 (Found: C, 68·2; H, 8·7; S, 10·9. $C_{16}H_{24}O_2S$ requires C, 68·6; H, 8·6; S, 11·4%).

Perhydro-3-hydroxy-3-(7-hydroxy-3-methylocta-3,5-dien-1-ynyl)-2,4,4-trimethylthiophen (IXb).—The above methylocta-4,6-dien-1-yn-3-ol derivative (0·69 g.) in acetone (20 ml.) was added to 1% aqueous hydrochloric acid (10 ml.) under nitrogen and set aside at 19° for 3 hr. After neutralisation with saturated aqueous sodium hydrogen carbonate, the product was isolated with ether and obtained as a pale yellow oil (0·62 g.), n_D^{19} 1·5598. It was chromatographed on alumina, and elution with benzene–light petroleum (1 : 1) gave the substituted *methylocta-3,5-dien-1-yn-7-ol* (0·5 g.) as a pale yellow oil, b. p. 70°/10^{-5} mm., n_D^{11} 1·5560 (Found: C, 68·6; H, 8·6; S, 11·4. $C_{16}H_{24}O_2S$ requires C, 68·6; H, 8·6; S, 11·4%).

Perhydro-3-hydroxy-2,4,4-trimethyl-3-(3-methylocta-3,5-dien-1-yn-7-onyl)thiophen.—The 3,5-dien-1-yn-7-ol (IXb) (0·32 g.) in carbon tetrachloride (10 ml.) was shaken for 1 hr. with activated manganese dioxide (3 g.). The mixture was centrifuged and evaporation of the supernatant liquid gave the desired ketone as a viscous green oil (0·20 g.). The *semicarbazone* separated from aqueous methanol in colourless needles, m. p. 178—179° (Found: C, 61·2; H, 7·4; S, 12·7. $C_{17}H_{25}N_3O_2S$ requires C, 60·9; H, 7·5; S, 12·5%).

Perhydro-3-hydroxy-3-(3-hydroxy-3,7-dimethylnona-4,6,8-trien-1-ynyl)-2,4,4-trimethylthiophen (XIb).—3-Ethynylperhydro-2,4,4-trimethylthiophen-3-ol (17 g.) was treated with ethylmagnesium bromide (from 6·0 g. of magnesium), followed by 6-methylocta-3,5,7-trien-2-one (13·6 g.), the solvents and conditions being as described for the similar reaction with 3-ethynylperhydro-4,4-dimethylthiophen-3-ol. The crude *4,6,8-trien-1-yn-3-ol* (31 g.) was a red viscous oil, and a portion (8 g.) in benzene–light petroleum (1 : 1) was chromatographed on alumina. Elution with the same solvent gave the original acetylenic alcohol (1·0 g.), and benzene–ether (1 : 1) subsequently eluted the required trienyn-ol (3·8 g.), n_D^{25} 1·5599. This distilled at 70°/10^{-5} mm. giving a viscous yellow oil, n_D^{12} 1·5550 (Found: C, 70·1; H, 8·6; S, 10·4 $C_{18}H_{26}O_2S$ requires C, 70·5; H, 8·5; S, 10·5%).

Perhydro-3-hydroxy-3-(9-hydroxy-3,7-dimethylnona-3,5,7-trien-1-ynyl)-2,4,4-trimethylthiophen (XIIb).—The crude 4,6,8-trien-1-yn-3-ol (22 g.) from the previous reaction was dissolved in 90% aqueous acetone (600 ml.) containing 0·1% of sulphuric acid, and after 3 hr. at 18° was poured into water (1 l.) and extracted with ether. The alkali-washed ether extract was dried and then evaporated *in vacuo* to an orange viscous oil (21 g.). This crude diol (15 g.) was seeded in cyclohexane solution with a crystal of the pure 3,5,7-trien-1-yn-9-ol of m. p. 128—129°, obtained from the hydrolysis of the anthraquinone-2-carboxylate described below. Some of the desired diol (2·5 g.) was precipitated, and the filtrate was chromatographed in benzene on alumina. Elution with benzene–ether (1 : 1) gave a further quantity (2·6 g.).

Recrystallisation of the material, obtained by chromatography, from aqueous ethanol gave yellow needles, m. p. 141—142°, while that obtained by seeding had m. p. 128—129° and separated from benzene as a microcrystalline powder without change in m. p. Recrystallisation from aqueous ethanol, however, gave yellow needles, m. p. 141—142°. When kept at room temperature a benzene solution of the seeded material gave large yellow rhombs of the *diol*, m. p. 120°, which recrystallised under similar conditions without change in m. p. (Found:

C, 70·4; H, 8·1; S, 10·9. $C_{18}H_{26}O_2S$ requires C, 70·5; H, 8·5; S, 10·5%). Recrystallisation of this material from aqueous ethanol also gave yellow needles, m. p. 141—142°. The three forms had almost identical ultraviolet and infrared (paraffin paste) absorption characteristics, and mixtures melted between the values given for the constituents. This diol slowly gave a feeble green colour with antimony trichloride in chloroform.

The *anthraquinone-2-carboxylate* was prepared by refluxing the crude diol (6 g.) with anthraquinone-2-carbonyl chloride (3·2 g.) and pyridine (6 ml.) in benzene (50 ml.) for 45 min. Water (6 ml.) was then added, and the benzene solution was filtered, washed, dried, and evaporated. Trituration of the residue with ether gave the orange ester (1·3 g.), which crystallised from benzene. It had m. p. 172—173°, resolidified sharply at 177°, and decomposed without melting at 225° (Found: C, 73·3; H, 5·9; S, 5·8. $C_{33}H_{32}O_5S$ requires C, 73·3; H, 5·9; S, 5·9%).

The pure 3,5,7-trien-1-yn-9-ol was initially obtained by hydrolysing this ester with 2N-alcoholic potassium hydroxide at 50° for 10 min. After the solution had been filtered and poured into water the trienynol was extracted with ether; crystallisation from benzene gave very small crystals, m. p. 128—129°.

Perhydro-3-hydroxy-3-(9-hydroxy-3,7-dimethylnona-1,3,5,7-tetraenyl)-2,4,4-trimethylthiophen (XIIIb).—The previous 3,5,7-trien-1-yn-9-ol (2·1 g.) in ether was added dropwise to a stirred solution of lithium aluminium hydride (1·0 g.) in ether (150 ml.). The mixture was heated under reflux for 3 hr., cooled to 0°, and treated cautiously with ice and saturated aqueous tartaric acid. The aqueous layer was extracted with ether, and the combined ether solutions were washed with saturated aqueous tartaric acid and then water, dried, and evaporated. The residual yellow oil (1·1 g.), dissolved in benzene, was chromatographed on alumina. Elution with benzene–ether (1 : 1) gave unreduced trienynol (0·18 g.), followed by the *tetraen-9-ol* (0·43 g.), which separated from benzene in pale yellow needles, m. p. 143—144° (Found: C, 69·6; H, 8·8; S, 10·1. $C_{18}H_{28}O_2S$ requires C, 70·0; H, 9·1; S, 10·4%). The m. p. was depressed on mixture with the initial trienynol, and the compound gave a green colour with antimony trichloride in chloroform.

Acetyl chloride (0·13 g.) in ether (5 ml.) was added to the tetraen-9-ol (0·25 g.) in ether (5 ml.) and pyridine (0·04 ml.) at 0°. After 40 min. at room temperature the mixture was shaken successively with cooled N-sulphuric acid and aqueous sodium hydrogen carbonate, and then the ethereal layer was dried and evaporated. The residual *acetate* (0·06 g.) separated from benzene as colourless needles, m. p. 107—108° (Found: C, 68·3; H, 8·4; S, 9·4. $C_{20}H_{30}O_3S$ requires C, 68·6; H, 8·6; S, 9·1%).

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