318. *Studies in the Polyene Series. Part XLVI.* The Synthesis of* o-*Tolyl and Mesityl Analogues of Vitamin A Acid.*

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Syntheses of the *o*-tolyl and mesityl analogues of vitamin A acid have been achieved. When these analogues were fed as their crystalline methyl esters to rats, the *o*-tolyl compound showed no biological activity, whereas the mesityl compound exhibited slight but definite growth-promoting properties of the vitamin A type.

Some apparent anomalies in the spectra of the ester and its precursors of the mesityl series are discussed, and attributed to steric interference of resonance.

RECENTLY syntheses of the phenyl analogue (I*a*) of vitamin A acid, and the corresponding alcohol, were reported (Weedon and Woods, *J.*, 1951, 2687). As further examples of compounds of the vitamin A type possessing modified ring systems, the *o*-tolyl (I*b*) and the mesityl (I*c*) acid have now been prepared. The cyclic moiety of these acids approximates more closely to the ring system in vitamin A_1 and A_2, and, in the case of the mesityl compound, is isomeric with that found in metabolic products which are possibly of carotenoid origin (Prelog, Führer, Hagenbach, and Schneider, *Helv. Chim. Acta*, 1948, **31**, 1799).

(II) OCH·CH:CMe·CH:CH·CH:CHMe ⟶ R·CH(OH)·CH:CMe·CH:CH·CH:CHMe (III)

↙

(IV) R·CH:CH·CMe:CH·CH:CH·CHMe·OH ⟶ R·CH:OH·CMe:CH·CH:CH·COMe (V)

↙

(VI) R·CH:CH·CMe:CH·CH:CH·CMe:CH·CO_2Me ⟶ R·CH:CH·CMe:CH·CH:CH·CMe:CH·CO_2H (I)

(*a*, R = Ph; *b*, R = *o*-C_6H_4Me; *c*, R = 2 : 4 : 6-$C_6H_2Me_3$.)

Of the two routes developed for the synthesis of (I*a*), that based on 3-methylocta-2 : 4 : 6-trienal (II) seemed the more suitable for the introduction of substituted benzene rings.

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* Part XLV, *J.*, 1953, 658.

Reaction of *o*-tolylmagnesium bromide with this aldehyde, and anionotropic rearrangement of the product (III*b*), gave the alcohol (IV*b*), which on oxidation furnished the crystalline ketone (V*b*). This with methyl bromoacetate and zinc gave, after dehydration of the initial hydroxy-ester, the ester (VI*b*) as a mixture of stereoisomers, one of which was obtained crystalline. Hydrolysis of the solid and the liquid esters yielded different crystalline isomers of the *o*-tolyl analogue (I*b*) of vitamin A acid.

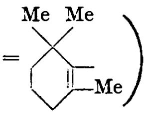
Analogous reactions were carried out with mesitylmagnesium bromide as far as the crystalline ketone (V*c*). The yields by this route of the *o*-tolyl and, especially, of the mesityl ketone were however much lower than in the phenyl series. Accordingly a new approach was examined, based on the *o*-tolyl (VII*b*) and the mesityl analogue (VII*c*) of β-ionone (VII*d*). The *o*-tolyl ketone (VII*b*) was prepared by oxidation of 4-*o*-tolylbut-3-en-2-ol (Braude, Jones, and Stern, *J.*, 1947, 1094). The mesityl ketone (VII*c*) was obtained both from the corresponding alcohol and, more conveniently, by condensation of mesitaldehyde with acetone (cf. Kohler and Blanchard, *J. Amer. Chem. Soc.*, 1935, **57**, 367). In the latter reaction 1 : 5-dimesitylpenta-1 : 4-dien-3-one was also formed.

Reformatsky reactions of 4-*o*-tolyl- (VII*b*) and 4-mesityl-but-3-en-2-one (VII*c*) with ethyl bromoacetate led to the esters (VIII*b* and *c*). Reduction of these with lithium aluminium hydride yielded the alcohols (IX*b* and *c*), which on oxidation with acetone and aluminium *tert.*-butoxide gave the ketones (V*b* and *c*) directly by condensation of the aldehydes formed initially with excess of acetone. After regeneration from the semicarbazones these ketones were obtained as crystalline solids, identical with those prepared by the alternative route described above.

Similar reactions have been used previously on a number of occasions for the extension of a polyene chain. Of particular interest is the conversion of β-ionone (VII*d*) into the C_{18} ketone (V*d*) (Milas and Harrington, *J. Amer. Chem. Soc.*, 1947, **69**, 2247), a key intermediate for the synthesis of vitamin A. Other workers (Wendler, Slates, Trenner, and Tishler, *ibid.*, 1951, **73**, 719), however, having experienced difficulty in repeating the final stage, recommended oxidation of β-ionylidene–ethanol (IX*d*) with manganese dioxide to the aldehyde (X*d*), and subsequent condensation of the latter with acetone. Similar modification of the synthesis of (V*c*) afforded no advantage.

$$\underset{\text{(VII)}}{\mathrm{R{\cdot}CH{:}CH{\cdot}COMe}} \longrightarrow \underset{\text{(VIII)}}{\mathrm{R{\cdot}CH{:}CH{\cdot}CMe{:}CH{\cdot}CO_2Et}} \longrightarrow \underset{\text{(XI)}}{\mathrm{R{\cdot}CH{:}CH{\cdot}CMe{:}CH{\cdot}CO_2H}}$$

$$\underset{\text{(IX)}}{\mathrm{R{\cdot}CH{:}CH{\cdot}CMe{:}CH{\cdot}CH_2{\cdot}OH}} \longrightarrow \underset{\text{(X)}}{\mathrm{R{\cdot}CH{:}CH{\cdot}CMe{:}CH{\cdot}CHO}} \longrightarrow \text{(V)} \longrightarrow \text{(VI)}$$

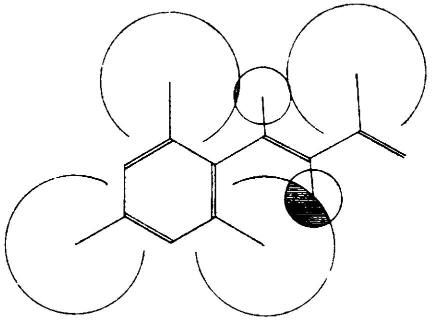
(*a*, $\mathrm{R = Ph}$; *b*, $\mathrm{R} = o\text{-}\mathrm{C_6H_4Me}$; *c*, $\mathrm{R = 2:4:6\text{-}C_6H_2Me_3}$; *d*, R = )

Reformatsky condensation of the ketone (V*c*) with methyl bromoacetate led to (VI*c*), one isomer of which was obtained crystalline. The solid and the liquid ester furnished two different modifications of the mesityl analogue (I*c*) of vitamin A acid.

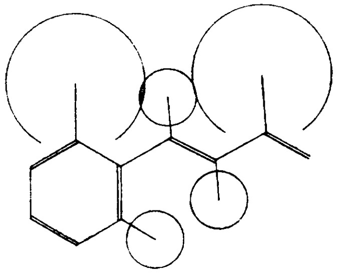
The crystalline esters (VI*b* and *c*) were fed in arachis oil to young rats reared on a vitamin-A-free diet. No growth responses were observed with the *o*-tolyl compound at doses which would have revealed activity of the order of one-thousandth of that of vitamin A. [The phenyl analogue of vitamin A acid, fed in aqueous solution as the potassium salt, was also inactive at this dose level (Weedon and Woods, *loc. cit.*).] The mesityl compound however had about one five-hundredth of the growth-promoting activity of vitamin A. Apart from esters and ethers of vitamin A itself, this is believed to be the first aromatic derivative to exhibit activity of the vitamin A type.

Spectral characteristics of a number of the new compounds, together with those for the corresponding phenyl compounds, are given in the Table ($\lambda_{\max.}$ in mμ). The *o*-tolyl and phenyl compounds exhibit very similar light-absorption properties, though the maxima are at slightly longer wave-lengths in the *o*-tolyl series, as would be expected owing to the increased methyl substitution of the chromophores. However, the additional substitution of the benzene ring in the mesityl compounds leads to marked reduction in the intensity of absorption, and either the appearance of partial chromophores or a hypsochromic shift of $\lambda_{max.}$. These effects are believed to be similar in origin to those observed with various *cyclo*hexene derivatives (Braude, Jones, Koch, Richardson, Sondheimer, and Toogood, *J.*, 1949, 1890; Oroshnik, Karmas, and Mebane, *J. Amer. Chem. Soc.*, 1952, **74**, 295; Braude, Bruun, Weedon, and Woods, *J.*, 1952, 1419; Bharucha and Weedon, following paper), and are attributed to steric inhibition of resonance in the mesitylene derivatives, the unsaturated side chain being displaced out of the plane of the benzene ring by an *o*-methyl group. The differences in steric interference are clearly illustrated in the Figures.* The *o*-tolyl compounds are only slightly hindered in the configuration shown, and therefore their spectral properties do not differ appreciably from those of their phenyl analogues.

o-*Mesityl Series.*



o-*Tolyl Series.*



Interference of the type envisaged for the mesityl compounds would be expected to give rise to partial chromophores characteristic of the aromatic ring and of the polyene side chain (cf. Braude, Jones, *et al.*, *loc. cit.*); these are clearly manifested in the spectra

Compound	Phenyl series		*o*-Tolyl series		Mesityl series	
	$\lambda_{max.}$	$\varepsilon_{max.}$	$\lambda_{max.}$	$\varepsilon_{max.}$	$\lambda_{max.}$	$\varepsilon_{max.}$
Ar·CH:CH·C(OH)·CH_3	—	—	—	—	227	9,000
	248 [1]	19,000	248 [1]	16,000	246	7,500
	251	19,500	255	16,000	251	7,500
	281	2,000	288	1,300	—	—
	291	1,550	297	700	—	—
(VII)	—	—	—	—	227	12,000
	—	—	—	—	280	11,500
	285 [2]	23,000	290	16,000	293	14,000
	—	—	—	—	301	14,000
Ar·CH:CH·CO·CH:CHAr	—	—	—	—	227	16,500
	—	—	—	—	242	13,500
	330 [3]	31,000	—	—	338	18,000
XI)	229 [4]	13,500	227 ‡	10,500	227	10,500
	—	—	—	—	290 *	14,000
	309	28,000	307	27,500	304	16,000
	—	—	312 *	24,000	312 *	14,000
V)	360 [5]	42,000	360	42,500	348	28,000
(VI)	354 *, [5]	44,500	—	—	—	—
	367	48,500	369	52,000	358	37,500
(I) †	364 [5]	56,000	367	56,000	—	—

* Inflexion. † High-melting isomer. ‡ Ethyl ester.

[1] Braude, Jones, and Stern, *J.*, 1947, 1087. [2] Lowry, Moureu, and MacConkey, *J.*, 1928, 3167. [3] Rădulescu, *Ber.*, 1931, **64**, 2243. [4] Heilbron, Jones, Julia, and Weedon, *J.*, 1949, 1823. [5] Weedon and Woods, *J.*, 1951, 2687.

of 4-mesitylbut-3-en-2-ol, the corresponding ketone (VII*c*), 1 : 5-dimesitylpenta-1 : 4-dien-3-one, and the acid (XI*c*). With 8-mesityl-6-methylocta-3 : 5 : 7-trien-2-one (V*c*) and the derived ester (VI*c*), however, the partial and full chromophore bands apparently lie sufficiently close to overlap. The observed maxima are therefore due to a summation of the

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* Drawn by using covalent radii, except for hydrogen. The radius of the latter has been taken as 0·75 Å (cf. Crombie, *Quart. Reviews*, 1952, **6**, 101).

two and are consequently displaced to shorter wave-lengths by comparison with the maxima of analogous unhindered compounds (cf. Braude, Jones, *et al.*; Oroshnik *et al.*, *locc. cit.*).

The present results indicate that the carbon–carbon double bond and the aromatic ring in 2 : 4 : 6-trimethylbenzylidene derivatives are not coplanar, as has been suggested by Fuson and Bannister (*J. Amer. Soc. Chem.*, 1952, **74**, 1631) in the case of 4-mesitylbut-3-en-2-one (VII*c*). It is however noteworthy that in the latter ketone the deformation, and consequently the shielding of the β-position by the *o*-methyl groups, is insufficient to preclude conjugate addition of hydrogen cyanide to the double bond (*idem, loc. cit.*).

EXPERIMENTAL

Light absorptions were determined in alcohol unless otherwise stated. Unsaturation was determined by hydrogenation in acetic acid with a platinum catalyst unless otherwise stated. All the operations were carried out in nitrogen. Chromatography was on partially deactivated alumina (Cheeseman, Heilbron, Jones, and Weedon, *J.*, 1949, 3120). Manganese dioxide was selected from commercial sources (cf. Weedon and Woods, *J.*, 1951, 2687). Zinc used in the Reformatsky reactions was activated, immediately before use, as described by Inhoffen, Bohlmann, and Bohlmann (*Annalen*, 1950, **568**, 47).

*3-Methyl-*1-*o-tolylocta-*2 : 4 : 6-*trien-*1-*ol* (III*b*) *and 6-Methyl-*8-*o-tolylocta-*3 : 5 : 7-*trien-*2-*ol* (IV*b*).—3-Methylocta-2 : 4 : 6-trienal (24·0 g.; freshly distilled) (Weedon and Woods, *loc. cit.*) in ether (50 c.c.) was added during 1 hr. to a stirred and cooled (ice-bath) solution of *o*-tolylmagnesium bromide (from 4·3 g. of magnesium) in ether (200 c.c.). Stirring was continued for 4 hr. at 20° and the complex was then decomposed by saturated ammonium chloride solution (200 c.c.). The ethereal layer was separated, washed with water, dried (Na_2SO_4 + trace of K_2CO_3) and evaporated, giving crude 3-methyl-1-*o*-tolylocta-2 : 4 : 6-trien-1-ol (36·5 g.) as an orange mobile oil, n_D^{18} 1·5908. Light absorption : max., 270, 280, and 328 mμ; $E^{1\%}_{1\,\text{cm.}}$ = 1100, 1100, and 250 respectively. Distillation of a portion (0·7 g.) gave the alcohol as a pale yellow oil (0·34 g.), b. p. 100—110°(bath-temp.)/10^{-4} mm., n_D^{17} 1·5939 (unsaturation, in EtOAc, equiv. to 3·1 double bonds). Light absorption : max., 270 and 279 mμ; $E^{1\%}_{1\,\text{cm.}}$ = 2100 in each case.

The crude alcohol (20·0 g.) was dissolved in a 0·01M-solution of hydrochloric acid in water (320 c.c.) and acetone (680 c.c.), and kept at 20° for 14 hr. A saturated solution of sodium hydrogen carbonate was added until the pH of the mixture rose to 7—8. The bulk of the acetone was removed under reduced pressure and the product isolated with ether in the usual way. This gave a red viscous oil (19·7 g.), n_D^{20} 1·6122, which was dissolved in light petroleum (20 c.c.). The solution was cooled at −80° for 48 hr. and then allowed to warm to 0°. The yellow solid (0·6 g.) which separated was removed and had m. p. 62—65°. Crystallisation of a portion (110 mg.) from light petroleum (b. p. 60—80°) gave *6-methyl-*8-*o-tolylocta-*3 : 5 : 7-*trien-*2-*ol* (52 mg.) as yellow plates, m. p. 67—68° (Found : C, 83·85; H, 8·9. $C_{16}H_{20}O$ requires C, 84·15; H, 8·8%). Light absorption : max., 317 mμ; ε = 42,000.

Evaporation of the mother-liquors gave a red oil (19 g.), n_D^{18} 1·605. Light absorption : max., 270, 280, and 317 mμ; $E^{1\%}_{1\,\text{cm.}}$ = 1000, 1000, and 900 respectively, indicating a ~50% content of the rearranged alcohol.

4-o-*Tolylbut-*3-*en-*2-*one* (VII*b*).—4-*o*-Tolylbut-3-en-2-ol (50 g.) (Braude, Jones, and Stern, *J.*, 1947, 1094) in light petroleum (b. p. 40—60°) (450 c.c.) was shaken with manganese dioxide (250 g.) at 20° for 7 days. Removal of oxide and solvent, and distillation, gave the ketone (43 g.), b. p. 72—73°/5 × 10^{-4} mm., n_D^{25} 1·5805. The semicarbazone (prepared in 85% yield) had m. p. 205° (decomp.) (Braude and Sondheimer, forthcoming publication, found m. p. 206°). The ketone after regeneration from this derivative and distillation had n_D^{26} 1·5858. Light absorption : see table.

*Ethyl 2-Methyl-*4-o-*tolylbuta-*1 : 3-*diene-*1-*carboxylate* (VIII*b*).—About half of a mixture of 4-*o*-tolylbut-3-en-2-one (44·0 g.) and ethyl bromoacetate (48 g.) was added to zinc wool (18 g.) and benzene (150 c.c.). The mixture was heated under reflux until reaction commenced, and then the remainder of the ketone–ester mixture was added at such a rate (15 min. required) that gentle refluxing was maintained. Heating was then recommenced and continued for ½ hr. The mixture was cooled and shaken with N-acetic acid (400 c.c.). The benzene layer was separated, washed with saturated sodium carbonate solution, and dried (Na_2SO_4). The solution was diluted (to 500 c.c.) with the same solvent and heated under reflux for 5 hr. with toluene-*p*-sulphonic acid (0·5 g.), water being removed by azeotropic distillation. The resulting benzene solution was washed with aqueous sodium hydrogen carbonate, dried and evaporated. Distillation gave the *ester* (33·0 g.), b. p. 112—114°/3 × 10^{-3} mm., n_D^{19} 1·5961 (Found: C, 78·5; H, 8·05. $C_{15}H_{18}O_2$ requires C, 78·2; H, 7·85%). Light absorption: see Table.

Hydrolysis of the ester for 2 hr. at 60—65° with methanolic potassium hydroxide (10% w/v) gave the corresponding acid as a mixture of stereoisomers which crystallised from aqueous methanol in prisms, m. p. 138—156°.

3-*Methyl*-5-o-*tolylpenta*-2 : 4-*dien*-1-*ol* (IX*b*).—The preceding ester (30·0 g.) in ether (125 c.c.) was added during ½ hr. to a cooled (−50°) solution of lithium aluminium hydride (7·0 g.) in ether (200 c.c.). The mixture was then stirred for 1½ hr. at −30°. Ethyl acetate (10 c.c.) was added, to decompose any excess of hydride, and then a saturated solution of ammonium chloride (50 c.c.). The mixture was filtered and the product isolated in the usual way, giving the *alcohol* (23 g.), b. p. 70—80° (bath-temp.)/10^{-5} mm., n_D^{24} 1·6059 (Found: C, 82·55; H, 8·65. $C_{13}H_{16}O$ requires C, 82·95; H, 8·5%). Light absorption: max., 280 mμ; ε = 20,500; inflexion, 289 mμ; ε = 18,500.

6-*Methyl*-8-o-*tolylocta*-3 : 5 : 7-*trien*-2-*one* (V*b*).—(*a*) 6-Methyl-8-*o*-tolylocta-3 : 5 : 7-trien-2-ol (400 mg.; m. p. 62—65°) in light petroleum (b. p. 40—60°) (50 c.c.) was shaken with manganese dioxide (10 g.), at 20° for 15 hr. The mixture was filtered and the filtrate evaporated, giving a solid (400 mg.) which on crystallisation from light petroleum (b. p. 60—80°) yielded the *ketone* (200 mg.) as yellow pyramids, m. p. 83° [Found: C, 84·8; H, 8·15. $C_{16}H_{18}O$ requires C, 84·9; H, 8·0%. Unsaturation (in EtOAc; Pd) equiv. to 2·7 double bonds)]. Light absorption: see Table. The *semicarbazone* (from 52 mg. of ketone) crystallised from alcohol in yellow needles (45 mg.), m. p. 198° (decomp.) (Found: C, 71·65; H, 7·45; N, 15·2. $C_{17}H_{21}ON_3$ requires C, 72·05; H, 7·45; N, 14·85%). Light absorption: max., 361 mμ; ε = 85,000.

(*b*) The crude triene alcohol (IV*b*) (17 g.; liquid) and aluminium *tert.*-butoxide (30 g.) in a mixture of acetone (400 c.c.) and benzene (600 c.c.) were heated under reflux for 15 hr. Isolation of the product in the usual way gave an oil (17 g.), n_D^{23} 1·637, which was converted into the semicarbazone (7·3 g.), m. p. 183—188°, raised by recrystallisation from methanol to 195° (decomp.), undepressed on admixture with a specimen from (*a*).

Attempts to oxidise the crude alcohol by the manganese dioxide method were unsuccessful.

(*c*) 3-Methyl-5-*o*-tolylpenta-2 : 4-dien-1-ol (20·0 g.) and aluminium *tert.*-butoxide (40 g.) in acetone (175 c.c.) and benzene (400 c.c.) were heated under reflux for 45 hr. The crude product (24 g.) was converted into the semicarbazone, needles (9·2 g.) (from methanol), m. p. and mixed m. p. 198° (decomp.).

A mixture of the finely powdered semicarbazone (9·0 g.), light petroleum (b. p. 100—120°) (75 c.c.) and 2N-sulphuric acid (75 c.c.) was heated under reflux with vigorous stirring for 1 hr., then cooled and filtered. Recovered semicarbazone was treated in the same way. The petroleum solutions were combined, washed with water, dried (Na_2SO_4), and evaporated. The residual oil (6·2 g.), n_D^{20} 1·69—1·70, solidified and had m. p. 46—71°. A small portion recrystallised from light petroleum (b. p. 60—80°) yielded the ketone as pyramids, m. p. 82°, undepressed on admixture with a specimen from (*a*).

Methyl 2 : 6-*Dimethyl*-8-o-*tolylocta*-1 : 3 : 5 : 7-*tetraene*-1-*carboxylate* (VI*b*).—A mixture of the preceding ketone (m. p. 46—71°) (6·0 g.), methyl bromoacetate (freshly prepared from crystalline bromoacetic acid and diazomethane) (4·8 g.), zinc (2·0 g.), and benzene (50 c.c.) was heated under reflux until all the zinc had reacted (½ hr.). The mixture was cooled, then shaken with dilute (5% w/v) acetic acid. The benzene layer was separated, washed with water, and dried (Na_2SO_4). The resulting solution was diluted with benzene (to 250 c.c.) and then heated under reflux for 5 hr. with toluene-*p*-sulphonic acid (200 mg.). The acid was extracted with aqueous sodium hydrogen carbonate, and the benzene solution was dried and evaporated. The residue (7 g.) was chromatographed on alumina (250 g.) from light petroleum (b. p. 40—60°). The chromatogram was developed with the same solvent. The least strongly absorbed band gave an oil (3·7 g.) which partly solidified. Crystallisation from light petroleum (b. p. 60—80°) gave the *ester* (425 mg.) as yellow needles, m. p. 94° (Found: C, 80·5; H, 7·6. $C_{19}H_{22}O_2$ requires C, 80·8; H, 7·85%). Light absorption: see table. Evaporation of the mother-liquors furnished a liquid ester.

2 : 6-*Dimethyl*-8-o-*tolylocta*-1 : 3 : 5 : 7-*tetraene*-1-*carboxylic acid* (I*b*).—A solution of the preceding crystalline ester (31 mg.) in methanolic potassium hydroxide (1·5 c.c.; 10% w/v) was warmed for 2 hr. at 60—65° and then cooled. Water (30 c.c.) was added and the resulting suspension was acidified with aqueous (1 : 1 v/v) phosphoric acid. Isolation of the product with ether and crystallisation from methanol gave the *acid* (20 mg.) as yellow plates, m. p. 189° (decomp.) (Found: C, 80·35; H, 7·95. $C_{18}H_{20}O_2$ requires C, 80·55; H, 7·5%). Light absorption: see Table.

Similar hydrolysis of the crude liquid ester (3·2 g.) furnished an *isomer* (900 mg.) of the acid which crystallised from methanol in yellow needles, m. p. 159° (decomp.) (Found: C, 80·7; H, 7·75. $C_{18}H_{20}O_2$ requires C, 80·55; H, 7·5%). Light absorption: max., 366 mμ; ε = 53,500.

4-*Mesitylbut*-3-*en*-2-*ol*.—A solution of crotonaldehyde (8·5 g.) in ether (30 c.c.) was added during 45 min. to a stirred and cooled (ice) solution in ether (100 c.c.) of mesitylmagnesium bromide, prepared from bromomesitylene (20 g.) and magnesium (2·4 g.) (Smith, *Org. Synth.*, Coll. Vol. II, p. 360). The mixture was stirred for a further 3 hr. at 20°, the complex was decomposed by the addition of saturated ammonium chloride, and the crude product (20 g.) isolated with ether. Distillation gave a fraction (5·0 g.), b. p. 90—100° (bath-temp.)/5 × 10^{-4} mm., n_D^{21} 1·5491. Of this a portion (4·0 g.) in acetone (100 c.c.) and 0·2N-sulphuric acid (100 c.c.) was kept at 20° for 13 hr. Isolation of the product with ether gave a liquid (2·4 g.), b. p. 50—60° (bath-temp.)/10^{-5} mm., n_D^{19} 1·5500, which at 0° deposited a solid (0·51 g.), m. p. 46—48°. Crystallisation from *n*-pentane gave 4-*mesitylbut*-3-*en*-2-*ol*, m. p. 49° (Found: C, 82·45; H, 9·55. $C_{13}H_{18}O$ requires C, 82·05; H, 9·55%). Light absorption: see Table.

4-*Mesitylbut*-3-*en*-2-*one* (VII*c*) *and* 1 : 5-*Dimesitylpenta*-1 : 4-*dien*-3-*one*.—(*a*) The method used is similar to that reported recently by Fuson and Bannister (*J. Amer. Chem. Soc.*, 1952, **74**, 1631), but gives much higher yields. Sodium hydroxide (3·5 g.) was added to a solution of mesitaldehyde (38 g.) in acetone (175 c.c.) and water (20 c.c.). The mixture was stirred at 20° for 17 hr. and then poured into 2N-sulphuric acid (400 c.c.). Isolation of the product with ether gave a crude solid (43·5 g.), m. p. 49—63°. Distillation gave a product (36 g.), b. p. 108—113°/0·4 mm., m. p. 59—64°. One recrystallisation from aqueous methanol gave 4-mesitylbut-3-en-2-one as colourless needles, m. p. 67° (Kohler and Blanchard, *J. Amer. Chem. Soc.*, 1935, **57**, 367, give m. p. 67°). The 2 : 4-*dinitrophenylhydrazone* crystallised from ethyl acetate in plates, m. p. 216° (Found: N, 15·4. $C_{19}H_{20}O_4N_4$ requires N, 15·25%). Light absorption in chloroform (main band only): max., 394 mμ; ε = 23,000. The residue from the distillation solidified on cooling. Crystallisation from ethyl acetate gave 1 : 5-*dimesitylpenta*-1 : 4-*dien*-3-*one* (2·4 g.) as pale yellow needles, m. p. 170° (Found: C, 86·75; H, 8·2. $C_{23}H_{26}O$ requires C, 86·75; H, 8·25%). Light absorption: see Table.

(*b*) A solution of crystalline 4-mesitylbut-3-en-2-ol (400 mg.) in light petroleum (b. p. 40—60°; 40 c.c.) was shaken with manganese dioxide (10 g.) at 20° for 60 hr. Removal of the oxide and solvent, and crystallisation of the residue from light petroleum (b. p. 40—60°), gave the ketone (203 mg.) as needles, m. p. 67°, undepressed on admixture with a specimen from (*a*).

Ethyl 4-*Mesityl*-2-*methylbuta*-1 : 3-*diene*-1-*carboxylate* (VIII*c*).—A Reformatsky reaction with 4-mesitylbut-3-en-2-one (35 g.), ethyl bromoacetate (35 g.), and zinc (14 g.) in benzene (125 c.c.), and dehydration of the hydroxy-ester with toluene-*p*-sulphonic acid (0·5 g.) in the usual way gave the *ester* (39 g.), b. p. 60—70° (bath-temp.)/10^{-5} mm., n_D^{20} 1·5791—1·5849 (Found: C, 78·6; H, 8·55. $C_{17}H_{22}O_2$ requires C, 79·0; H, 8·6%). Light absorption: max., 228, 237, 245, 251, and 307 mμ; ε = 14,000, 10,500, 10,500, 10,500, and 18,500 respectively. Inflexions, 292 and 316 mμ; ε = 17,500 and 17,500.

Evaporation of the benzene solution before dehydration, and distillation of the residue, yielded the *hydroxy*-ester, b. p. 75—85° (bath-temp.)/10^{-5} mm., n_D^{22} 1·5191 (Found: C, 74·05; H, 8·85. $C_{17}H_{24}O_3$ requires C, 73·8; H, 8·75%). Light absorption: max., 247 and 251 mμ; ε = 9,000 and 9,000.

4-*Mesityl*-2-*methylbuta*-1 : 3-*diene*-1-*carboxylic Acid* (XI*c*).—The preceding ester (0·5 g.) was heated in methanolic potassium hydroxide (10 c.c.; 10% w/v) at 60—65° for 2 hr. Isolation of the acidic product gave a solid (430 mg.), m. p. 167—191°. Fractional crystallisation from methanol yielded one stereoisomer of the *acid* as plates (75 mg.), m. p. 207° (decomp.) (Found: C, 78·0; H, 8·05. $C_{15}H_{18}O_2$ requires C, 78·2; H, 7·85%). Light absorption: see table.

5-*Mesityl*-3-*methylpenta*-2 : 4-*dien*-1-*ol* (IX*c*).—Reduction of ethyl 4-mesityl-2-methylbuta-1 : 3-diene-1-carboxylate (36 g.) in ether at −60° with lithium aluminium hydride (7 g.) gave the *alcohol* (27·9 g.), b. p. 75—85° (bath-temp.)/10^{-5} mm., n_D^{20} 1·5860 (Found: C, 83·05; H, 9·4. $C_{15}H_{20}O$ requires C, 83·3; H, 9·3%). Light absorption: max., 227, 268, and 280 mμ; ε = 19,000, 19,000, and 20,500 respectively.

5-*Mesityl*-3-*methylpenta*-2 : 4-*dienal* (X*c*).—The preceding alcohol (3·0 g.) was shaken in light petroleum (b. p. 40—60°) (125 c.c.) with manganese dioxide (15 g.) at 20° for 96 hr. Filtration, evaporation and distillation gave the *aldehyde* (2·4 g.) as a mixture of geometrical isomers, b. p. 70—80° (bath-temp.)/10^{-5} mm., m. p. 40—53°, n_D^{21} 1·6268 (Found: C, 84·0; H, 8·6. $C_{15}H_{18}O$ requires C, 84·05; H, 8·45%). Light absorption: max., 251, 256, and 323 mμ; ε = 9,500, 9,500, and 20,000 respectively. Attempts to separate the isomers by fractional crystallisation from *n*-pentane were unsuccessful. The *semicarbazone* crystallised from alcohol in needles, m. p. 220° (decomp.) (Found: C, 70·2; H, 7·85; N, 15·5. $C_{16}H_{21}ON_3$ requires C, 70·8; H, 7·8; N, 15·45%). Light absorption: max., 270, 280, and 325 mμ; ε = 18,000, 18,000 and 46,500 respectively.

8-*Mesityl*-6-*methylocta*-3 : 5 : 7-*trien*-2-*one* (V*c*).—(*a*) 5-Mesityl-3-methylpenta-2 : 4-dien-1-ol (12·0 g.) and aluminium *tert.*-butoxide (20 g.) in acetone (100 c.c.) and benzene (250 c.c.) were heated under reflux for 45 hr. The oily product (14·5 g.), n_D^{22} 1·635, was chromatographed on alumina (600 g.) from light petroleum (b. p. 40—60°). Elution of the least strongly adsorbed yellow band gave an oil (8·5 g.), n_D^{13} 1·652, which with excess of aqueous-methanolic semicarbazide acetate yielded a solid (7·2 g.), m. p. 211—216°. Crystallisation from alcohol gave the *semicarbazone* as yellow prisms, m. p. 217° (decomp.) (Found: N, 13·0. $C_{19}H_{25}ON_3$ requires N, 13·5%). Light absorption: max., 348 mμ; ε = 56,000.

The finely powdered semicarbazone (8·0 g.; m. p. 211—216°) was heated, with stirring, with 2N-sulphuric acid (160 c.c.) and light petroleum (b. p. 100—120°) (160 c.c.) under reflux for 45 min. The petroleum layer was separated, dried (Na_2SO_4), and evaporated to an oil (4·9 g.) which solidified. Crystallisation from light petroleum (b. p. 60—80°) gave the *ketone* as yellow plates, m. p. 89° (Found: C, 84·8; H, 8·95. $C_{18}H_{22}O$ requires C, 85·0; H, 8·7%). Light absorption: in alcohol, see Table; in *n*-hexane, max., 338 mμ; ε = 37,500.

(*b*) Sodium hydroxide (0·14 g.) in water (1 c.c.) was added to 5-mesityl-3-methylpenta-2 : 4-dienal (1·4 g.) in acetone (7 c.c.), and the mixture was kept at 20° for 21 hr. and then poured into 2N-sulphuric acid (30 c.c.). Isolation with ether yielded the crude ketone (1·25 g.), n_D^{22} 1·663. Light absorption: max., 280, 290, and 348 mμ; $E^{1\%}_{1\,\text{cm.}}$ = 430, 430, and 830 respectively. The semicarbazone, after chromatographic adsorption on alumina from chloroform, crystallised from alcohol in prisms, m. p. 217° (decomp.), undepressed on admixture with a specimen from (*a*).

(*c*) [With R. J. Woods.] Reaction of mesitylmagnesium bromide (from 8 g. of magnesium) with 3-methylocta-2 : 4 : 6-trienal (38 g.), rearrangement of the crude alcohol (68 g.) as described for the *o*-tolyl analogue, and chromatographic purification of the product on alumina from light petroleum (b. p. 40—60°), gave crude 8-mesityl-6-methylocta-2 : 4 : 6-trien-2-ol (*ca.* 19 g.). A portion (13 g.) in light petroleum (b. p. 40—60°) was oxidised with manganese dioxide, and the crude ketone converted into the semicarbazone (3·4 g.), m. p. 216°, undepressed on admixture with a specimen from (*a*). Regeneration from this derivative furnished the crystalline ketone, m. p. and mixed m. p. 89°.

Methyl 8-*Mesityl*-2 : 6-*dimethylocta*-1 : 3 : 5 : 7-*tetraene*-1-*carboxylate* (VI*c*).—A mixture of the preceding ketone (4·9 g.), zinc wool (2·0 g.), methyl bromoacetate (4·5 g.; freshly prepared), and benzene (75 c.c.) was heated under reflux until all the zinc had reacted (30 min.). Decomposition of the complex, and dehydration of the hydroxy-ester with toluene-*p*-sulphonic acid, gave an oil (6 g.) which was purified by chromatography on alumina (200 g.) from light petroleum (b. p. 40—60°). The least strongly adsorbed band yielded an oil (3·9 g.), a solution of which in light petroleum (b. p. 60—80°) (5 c.c.) deposited a solid at 0°. Crystallisation from methanol gave the *ester* as yellow plates (250 mg.), m. p. 90° (Found: C, 80·6; H, 8·5. $C_{21}H_{26}O_2$ requires C, 81·25; H, 8·45%). Light absorption: see Table. Evaporation of the mother-liquors gave a crude liquid ester (3·1 g.), n_D^{25} 1·64. Hydrolysis of the crystalline ester (30 mg.) with methanolic potassium hydroxide (10% w/v) for 2 hr. at 60° led to an acid (24 mg.), m. p. 185—195°. In another experiment the liquid ester (0·6 g.) was hydrolysed similarly and furnished another form of 8-*mesityl*-2 : 6-*dimethylocta*-1 : 3 : 5 : 7-*tetraene*-1-*carboxylic acid* (0·1 g.) which, crystallised from aqueous methanol, had m. p. 175° (decomp.) (Found: C, 81·1; H, 8·3. $C_{20}H_{24}O_2$ requires C, 81·05; H, 8·15%). Light absorption: maximum, 349 mμ; ε = 38,000.

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