319. *Studies in the Polyene Series. Part XLVII.* The Synthesis of Two Pentaene Esters related to Vitamin A.*

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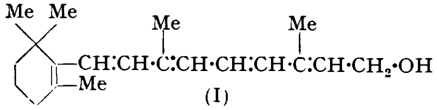
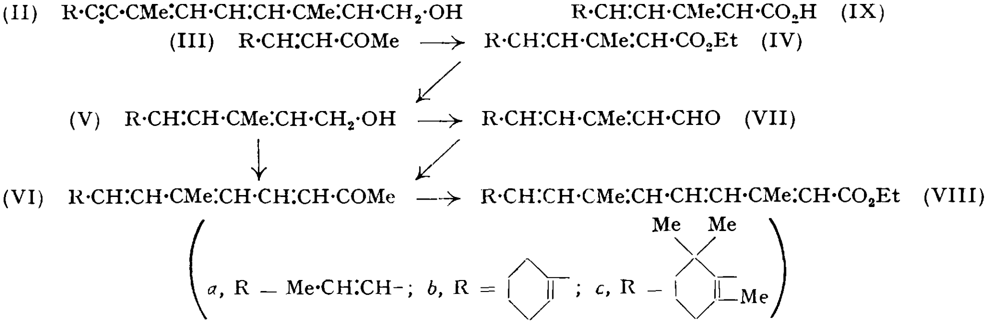
Syntheses of the pentaene esters (VIII*a* and *b*) are described, and the light-absorption properties of some polyenes derived from β-ionone are discussed.

Much information has now accumulated concerning the influence on biological activity of varying the functional group and of modifying the side chain of vitamin A (I) (cf. Isler, *Chimia*, 1950, **4**, 103). Scant information is however available concerning the specificity of the ring-methyl groups (cf. Weedon and Woods, *J.*, 1951, 2687). The crystalline alcohol (II*b*) (Cheeseman, Heilbron, Jones, and Weedon, *J.*, 1949, 3120) exhibited slight growth-promoting properties, but the presence of the acetylenic linkage in the side chain prevented an evaluation of the effect on activity of the ring modification. The investigations now reported were directed to the preparation of a polyene related to vitamin A, or the corresponding acid, but possessing an unmethylated ring system. Since β-ionone (III*c*) had been used in a number of syntheses of the natural vitamin, its lower homologue, 4-*cyclo*hexenylbut-3-en-2-one (III*b*) (Heilbron, Jones, Richardson, and Sondheimer, *J.*, 1949, 737), was selected as a suitable starting material. Model experiments were also carried out with the more readily available crotonylideneacetone (III*a*) and (see Experimental section) 5-ethylnona-3 : 5-dien-2-one.


(I)

Conversion of crotonylideneacetone (hepta-3 : 5-dien-2-one) into 3-methylocta-2 : 4 : 6-trien-1-ol (V*a*) was effected as described in Part XXXVIII (*J.*, 1951, 2687). Oxidation of the alcohol with acetone and aluminium *tert.*-butoxide gave the crystalline ketone (VI*a*) directly in 22% yield. Preliminary oxidation of the alcohol to the corresponding aldehyde (VII*a*) (Part XXXVIII), and condensation of the latter with acetone, gave an inferior overall yield of the tetraene ketone. The structure of (VI*a*) was confirmed by catalytic hydrogenation to 6-methylundecan-2-one, which was identical with a specimen prepared by treating 5-methyldecanoic acid with methyl-lithium. A Reformatsky reaction of (VI*a*) with ethyl bromoacetate, and dehydration of the resulting hydroxy-ester, furnished the pentaene ester (VIII*a*), an acyclic analogue of the ester (VIII*c*) of vitamin A acid.


(II) R·C⋮C·CMe:CH·CH:CH·CMe:CH·CH$_2$·OH   R·CH:CH·CMe:CH·CO$_2$H (IX)
(III) R·CH:CH·COMe ⟶ R·CH:CH·CMe:CH·CO$_2$Et (IV)
(V) R·CH:CH·CMe:CH·CH$_2$·OH ⟶ R·CH:CH·CMe:CH·CHO (VII)
(VI) R·CH:CH·CMe:CH·CH:CH·COMe ⟶ R·CH:CH·CMe:CH·CH:CH·CMe:CH·CO$_2$Et (VIII)
(*a*, R = Me·CH:CH–; *b*, R = ; *c*, R =)

Condensation of the *cyclo*hexenylbutenone (III*b*) with ethyl bromoacetate and zinc gave, in 66% yield a mixture of triene esters, one of which (IV*b*) was obtained crystalline. Reduction of the ester with lithium aluminium hydride afforded (83%) the alcohol (V*b*)

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* Part XLVI, preceding paper.

(3 : 5-dinitrobenzoate), which with acetone and aluminium *tert.*-butoxide gave the crystalline ketone (VI*b*) in 14% yield. The structure of (VI*b*) was confirmed by catalytic reduction to the known 8-*cyclo*hexyl-6-methyloctan-2-one (Heilbron, Jones, and Richardson, *J.*, 1949, 287). Oxidation of the alcohol (V*b*) with manganese dioxide gave (43%) the corresponding aldehyde (VII*b*) as a mixture of isomers, one of which was isolated by regeneration from its semicarbazone. Condensation of (VII*b*) with acetone furnished the crystalline ketone (VI*b*) in only 5% yield. A Reformatsky reaction of (VI*b*) with ethyl bromoacetate led to the pentaene ester (VIII*b*).

Unfortunately both the pentaene esters polymerised rapidly even at 0° in an inert atmosphere, and hence no significant biological assays were possible. Similar instability was also encountered in many of the intermediate compounds which, even after isolation as pure crystalline solids, decomposed rapidly. The ring-methyl groups in compounds of the vitamin A type clearly play an important rôle in stabilising the molecule.

Since the work described in this paper was completed, the preparation of dehydrovitamin A (II*c*), and the corresponding carboxylic acid, has been reported (Attenburrow, Cameron, Chapman, Evans, Hems, Jansen, and Walker, *J.*, 1952, 1094). A comparison of their biological potencies with those of related acetylenic compounds possessing modified cyclic systems (see Table 1) strongly suggests that the three ring-methyl groups of vitamin A are also necessary for high growth-promoting activity.

TABLE 1.

Substance	Method of administration *	Activity (as % of that of vitamin A)
$\mathrm{A{\cdot}C{\vdots}C{\cdot}CMe{:}CH{\cdot}CH{:}CH{\cdot}CMe{:}CH{\cdot}CO_2H}$ [1]	1	0·1
$\mathrm{A{\cdot}C{\vdots}C{\cdot}CMe{:}CH{\cdot}CH{:}CH{\cdot}CMe{:}CH{\cdot}CH_2{\cdot}OH}$ [2]	2	0·1
$\mathrm{B{\cdot}C{\vdots}C{\cdot}CMe{:}CH{\cdot}CH{:}CH{\cdot}CMe{:}CH{\cdot}CO_2H}$ [3]	1	<0·1
$\mathrm{D{\cdot}C{\vdots}C{\cdot}CMe{:}CH{\cdot}CH{:}CH{\cdot}CMe{:}CH{\cdot}CO_2H}$ [4]	1	<0·1
$\mathrm{E{\cdot}C{\vdots}C{\cdot}CMe{:}CH{\cdot}CH{:}CH{\cdot}CMe{:}CH{\cdot}CO_2H}$ [4]	1	0·1
$\mathrm{G{\cdot}C{\vdots}C{\cdot}CMe{:}CH{\cdot}CH{:}CH{\cdot}CMe{:}CH{\cdot}CO_2H}$ [5]	2	0·5—1
$\mathrm{G{\cdot}C{\vdots}C{\cdot}CMe{:}CH{\cdot}CH{:}CH{\cdot}CMe{:}CH{\cdot}CH_2{\cdot}OH}$ [5]	2	10 †
$\mathrm{G{\cdot}CH{:}CH{\cdot}CMe{:}CH{\cdot}CH{:}CH{\cdot}CMe{:}CH{\cdot}CO_2H}$ [6]	2	10
,, ,, ,,	1	100

A = *cyclo*hex-1-enyl; B = 4-methyl*cyclo*hex-1-enyl; D = 2-methyl*cyclo*hex-1-enyl; E = 6 : 6-dimethyl*cyclo*hex-1-enyl; G = 2 : 6 : 6-trimethyl*cyclo*hex-1-enyl.

* Fed orally to rats : (1) as an aqueous solution of sodium salt; (2) in arachis oil.

† 40% when fed as the anthraquinone-2-carboxylate.

[1] Heilbron, Jones, and Richardson, *J.*, 1949, 287. [2] Cheeseman, Heilbron, Jones, and Weedon, *J.*, 1949, 3120. [3] Toogood and Weedon, *J.*, 1949, 3123. [3] Heilbron, Jones, Lewis, and Weedon, *J.*, 1949, 2023. [5] Attenburrow, Cameron, Chapman, Evans, Hems, Jansen, and Walker, *J.*, 1952, 1094. [6] Arens and van Dorp, *Nature*, 1946, **158**, 60.

TABLE 2.

	Acyclic series (*a*)		*cyclo*Hexene series (*b*)		Trimethyl*cyclo*hexene series (*c*)	
	$\lambda_{\text{max.}}$ (mμ)	$\varepsilon_{\text{max.}}$	$\lambda_{\text{max.}}$ (mμ)	$\varepsilon_{\text{max.}}$	$\lambda_{\text{max.}}$ (mμ)	$\varepsilon_{\text{max.}}$
Diene ketones (III)	—	—	—	—	223 [3]	6,500
	270 [1]	28,500	281 [2]	20,800	296	10,700
Triene acids (IX)	—	—	—	—	255 [5]	13,500
	296 [4]	42,000	305 †	37,500	300	15,500
	302 *	38,000	—	—	—	—
Triene aldehydes (VII)	—	—	3140 ‡	22,000	265 [5] §	12,500
	322 [4]	30,500	323	22,000	315	16,500
Tetraene ketones (VI)	360	46,500	360	40,000	345 [6]	25,500
Pentaene esters (VIII)	352	49,000	347	>34,500	—	—
	364	49,000	364	>34,500	347 [7]	44,500

* Inflexion † Crystalline ethyl ester. ‡ Regenerated from semicarbazone; *n*-hexane solution. § *iso*Octane solution.

[1] Heilbron, Jones, and Richardson, *J.*, 1949, 287. [2] Heilbron, Jones, Richardson, and Sondheimer, *J.*, 1949, 737. [3] Young, Cristol, Andrews, and Lindenbaum, *J. Amer. Chem. Soc.*, 1944, **66**, 855; Braude, Jones, Koch, Richardson, Sondheimer, and Toogood, *J.*, 1949, 1890. [4] Weedon and Woods, *J.*, 1951, 2687. [5] Wendler, Slates, Trenner, and Tishler, *J. Amer. Chem. Soc.*, 1951, **73**, 719. [6] Attenburrow, Cameron, Chapman, Evans, Hems, Jansen, and Walker, *J.*, 1952, 1094. [7] Schwarzkopf, Cahnmann, Lewis, Swidinsky, and Wüest, *Helv. Chim. Acta*, 1949, **32**, 443.

The ultra-violet light absorptions of some of the compounds described above, and of their 2 : 6 : 6-trimethyl*cyclo*hexenyl analogues, derived from β-ionone, are collected in Table 2. The data for compounds of the acyclic and *cyclo*hexene series are in good agreement; it is however noteworthy that while the increased substitution of the chromophores results in a slight bathochromic shift of $\lambda_{\text{max.}}$ in the *cyclo*hexene derivatives (III*b*) and (IV*b*), this is not observed in the tetraene ketone (VI*b*) or the pentaene ester (VIII*b*).

Of considerable interest are the differences in the spectra of analogous compounds of the *cyclo*hexene and trimethyl*cyclo*hexene series. The light absorption properties of β-ionone (III*c*) (Braude *et al.*, *loc. cit.*), and of vitamin A (Oroshnik, Karmas, and Mebane, *J. Amer. Chem. Soc.*, 1952, **74**, 295), have been discussed previously, and shown to be consistent with the view that these two compounds possess an *s-trans*-configuration and that steric inhibition of resonance occurs, the unsaturated side chain being displaced out of the plane of the *cyclo*hexene ring by the neighbouring ring-methyl groups. This accounts in the case of β-ionone for the observed reduction in intensity of the long-wave-length band, and for the appearance of a partial chromophore band characteristic of the side chain. With vitamin A it was suggested that the observed spectrum, in which both $\lambda_{\text{max.}}$ and $\varepsilon_{\text{max.}}$ are lower than in spectra of analogous unhindered compounds, is due to a summation of the full and partial chromophore bands which lie sufficiently close to overlap.

The results now presented show that the spectra of the trimethy*cyclo*hexene derivatives (VI*c*—IX*c*) are also capable of adequate explanation on the basis of the principles summarised above. Both the tetraene ketone (VI*c*) and the pentaene ester (VIII*c*) are clearly of the vitamin A type; they exhibit single maxima which are both hypsochromically and hypochromically shifted with respect to their unhindered acyclic and *cyclo*hexene analogues. The triene acid (IX*c*) and the corresponding aldehyde (VII*c*) may be regarded as intermediate between the two extreme types represented in the above account by vitamin A and β-ionone; not only are the positions of maximal absorption slightly displaced to shorter wave-lengths, but partial chromophore bands are also apparent.

In conclusion it must be mentioned that the preparation of the triene alcohol (V*b*) and of the tetraene ketone (VI*b*), by two routes based on ethynyl*cyclo*hexene, has been claimed previously in a preliminary publication by Milas, Grossi, Penner, and Kahn (*J. Amer. Chem. Soc.*, 1948, **70**, 1292). Condensation of ethynyl*cyclo*hexene with methyl vinyl ketone gave the alcohol (X) which on partial catalytic hydrogenation to (XI) followed by allylic rearrangement, or, alternatively, by isomerisation to (XII) and subsequent catalytic reduction, was stated to yield (XIII = V*b*). However, by analogy with the isomerisation of 3-methylocta-1 : 4 : 6-trien-3-ol (Cheeseman, Heilbron, Jones, Sondheimer, and Weedon, *J.*, 1949; 2031), an acyclic analogue of (XI), rearrangement of the latter would not be expected to give the primary alcohol (XIII) initially. Furthermore no evidence was given by the American authors in support of the selectivity claimed for the partial reduction of (X) and (XII). In this connection it may be observed that the liquid C_{15} ketone obtained in 90% yield on Oppenauer oxidation of the product which they believed to be (XIII) exhibited light absorption properties ($\lambda_{\text{max.}}$ 333 mμ; $\varepsilon = 19{,}000$) more in agreement with those of the acetylenic ketone (XIV) ($\lambda_{\text{max.}}$ 335 mμ; $\varepsilon = 23{,}000$) (Heilbron, Jones, and Richardson, *loc. cit.*) than with those of the authentic tetraene ketone reported above. This disparity between the spectral properties cannot be attributed to a difference in configuration about the double bond adjacent to the ring system. This bond is of the "hindered" type and a tetraene ketone possessing a *cis*-configuration at this position, which the American authors might conceivably have obtained by their route involving the catalytic reduction of an acetylene, would be expected to exhibit a low-intensity broad absorption band (cf. Oroshnik, Karmas, and Mebane, *J. Amer. Chem. Soc.*, 1952, **74**, 299; Garbers, Eugster, and Karrer, *Helv. Chim. Acta*, 1952, **35**, 1850).

$$\begin{tikzcd}
\text{(X)} & \mathrm{R{\cdot}C{\vdots}C{\cdot}CMe(OH){\cdot}CH{:}CH_2} \arrow[r] \arrow[d] & \mathrm{R{\cdot}CH{:}CH{\cdot}CMe(OH){\cdot}CH{:}CH_2} \arrow[d] & \text{(XI)} \\
\text{(XII)} & \mathrm{R{\cdot}C{\vdots}C{\cdot}CMe{:}CH{\cdot}CH_2{\cdot}OH} \arrow[r] & \mathrm{R{\cdot}CH{:}CH{\cdot}CMe{:}CH{\cdot}CH_2{\cdot}OH} & \text{(XIII)} \\
 & (\mathrm{R} = \textit{cyclo}\text{hex-1-enyl.}) & \mathrm{R{\cdot}C{\vdots}C{\cdot}CMe{:}CH{\cdot}CH{:}CH{\cdot}COMe} & \text{(XIV)}
\end{tikzcd}$$

EXPERIMENTAL

(See notes preceding the Experimental in Part XLV.)

6-*Methylundeca*-3 : 5 : 7 : 9-*tetraen*-2-*one* (VI*a*).—(*a*) A solution of 3-methylocta-2 : 4 : 6-trien-1-ol (14·0 g.) (Weedon and Woods, *J.*, 1951, 2687) and aluminium *tert.*-butoxide (40 g.) in acetone (300 c.c.) and benzene (500 c.c.) was heated under reflux for 45 hours and then cooled. The mixture was shaken with 2N-sulphuric acid, and the benzene layer was separated, washed with aqueous sodium hydrogen crabonate, dried (Na_2SO_4), and evaporated under reduced pressure. Mesityl oxide was removed by warming the crude product to 70° (bath-temp.)/1 mm. for 1 hour. A solution of the residue (18·5 g.), n_D^{20} 1·61—1·62, in *n*-hexane (*ca.* 40 c.c.) at 0° deposited a solid, m. p. 81—83°. Recrystallisation from the same solvent gave the *ketone* (4·0 g.) as yellow prisms, m. p. 85—87°, which decomposed slowly even at 0° in an inert atmosphere (Found : C, 81·8; H, 9·45. $C_{12}H_{16}O$ requires C, 81·75; H, 9·15%). Light absorption : see table. The 2 : 4-*dinitrophenylhydrazone*, crystallised from ethyl acetate, had m. p. 194° (Found : N, 15·55. $C_{18}H_{20}O_4N_4$ requires N, 15·7%). Light absorption in chloroform (main band only) : max., 424 mμ; ε = 50,000.

Evaporation of the hexane mother-liquors gave a red oil (13 g.). Light absorption : max., 264, 278, 318, and 354 mμ; $E^{1\%}_{1\,\mathrm{cm.}}$ = 750, 740, 750, and 1280 respectively, indicating an appreciable content of the tetraene ketone, probably as a mixture of geometrical isomers. All attempts to isolate more crystalline ketone proved abortive.

(*b*) 3-Methylocta-2 : 4 : 6-trienal (6·3 g.) (*idem, loc. cit.*) and aluminium *tert.*-butoxide (28·8 g.) in acetone (150 c.c.) and benzene (170 c.c.) were heated under reflux for 34 hours. Decomposition of the complex and isolation of the product as in (*a*) gave an oil (9·8 g.), n_D^{26} 1·635. Distillation from a short-path still gave a yellow oil (4·62 g.), b. p. 110—120° (bath-temp.)/10^{-4} mm., n_D^{23} 1·65 (Light absorption: max., 268, 279, and 353 mμ; $E^{1\%}_{1\,\mathrm{cm.}}$ = 530, 530, and 1480 respectively) which deposited a yellow solid when kept at 0°. Crystallisation from *n*-hexane yielded the ketone (0·45 g.), m. p. 86—87°. The 2 : 4-dinitrophenylhydrazone had m. p. 194°, undepressed on admixture with a specimen from (*a*).

6-*Methylundecan*-2-*one*.—(*a*) A solution of the preceding crystalline ketone (0·1 g.) in methanol (10 c.c.) was shaken under hydrogen in the presence of 10% palladium–charcoal (50 mg.) until absorption was complete (hydrogen absorbed, 53 c.c. at 17°/755 mm., equiv. to 3·9 double bonds). After removal of catalyst and solvent, the crude ketone was converted into the 2 : 4-dinitrophenylsemicarbazone (65 mg.), m. p. 185°, undepressed on admixture with a specimen from (*b*).

(*b*) A solution of methyl-lithium in ether (42·5 c.c.; 0·582N) was added to one of 5-methyldecanoic acid (2·2 g.) (for which the authors are indebted to Drs. R. A. Raphael and C. L. Leese) in ether (40 c.c.). The solution was shaken with 2N-sulphuric acid, dried, and evaporated, giving the ketone (1·5 g.), b. p. 130—135°/18 mm. The 2 : 4-*dinitrophenylsemicarbazone* crystallised from ethanol and had m. p. 185° (Found : C, 56·3; H, 7·1; N, 17·15. $C_{19}H_{29}O_5N_5$ requires C, 56·0; H, 7·2; N, 17·2%).

Ethyl 2 : 6-*Dimethylundeca*-1 : 3 : 5 : 7 : 9-*pentaene*-1-*carboxylate* (VIII*a*).—A mixture of the crystalline methylundecatetraenone (2·6 g.), ethyl bromoacetate (2·6 g.; freshly distilled), zinc wool (1·0 g.), and benzene (50 c.c.), containing traces of mercuric chloride and iodine, was heated under reflux. The reaction commenced immediately and after ½ hour the mixture was cooled. The solution was decanted from a small amount of zinc, shaken with 5% (v/v) acetic acid (60 c.c.), washed with sodium carbonate solution, and dried (Na_2SO_4). A small portion of the benzene solution (*ca.* 2—3 c.c.) was evaporated under reduced pressure and gave the hydroxy-ester as a gum. Light absorption : max., 302 and 315 mμ; $E^{1\%}_{1\,\mathrm{cm.}}$ = 1450 and 1450.

The remainder of the benzene solution (50 c.c.) was heated under reflux for 3 hours in the presence of toluene-*p*-sulphonic acid (40 mg.) and then cooled, washed with aqueous sodium hydrogen carbonate, dried, and evaporated. The residue (3·1 g.) in benzene was poured on to a column of alumina (250 g.) and the chromatogram was developed with light petroleum (b. p. 40—60°). Elution of the least strongly adsorbed orange band yielded a viscous oil (0·5 g.). Distillation yielded the *ester* (0·2 g.), b. p. 130—140° (bath-temp.)/10^{-4} mm. (Found : C, 78·8; H, 9·3. $C_{16}H_{22}O_2$ requires C, 78·0; H, 9·0%). Light absorption : see table. It decomposed rapidly even at 0° in an inert atmosphere.

5-*Ethylnona*-3 : 5-*dien*-2-*one*.—A mixture of 2-ethylhex-2-enal (210 g.), acetone (375 c.c.; dried over K_2CO_3) and powdered potassium hydroxide (6·0 g.) was stirred at 20° for 12 hours, then neutralised by excess of solid carbon dioxide, and filtered. The filtrate was evaporated and the product was extracted with ether. Distillation gave (i) recovered aldehyde (70 g.), b. p. 73—76°/20 mm., n_D^{18} 1·4556, and (ii) 5-ethylnona-3 : 5-dien-2-one (88 g.), b. p. 43—44°/10^{-2} mm., n_D^{25} 1·5073. Light absorption : max., 282 mμ; ε = 21,000. The *semicarbazone* crystallised from alcohol in needles, m. p. 157° (Found : N, 19·1. $C_{12}H_{21}ON_3$ requires N, 18·85%). Light absorption : max., 290 mμ; ε = 47,000. Inflexions, 281 and 298 mμ; ε = 37,500 and 38,000 respectively. The 2 : 4-*dinitrophenylhydrazone*, crystallised from alcohol, had m. p. 156° (Found : N, 16·15. $C_{17}H_{22}O_4N_4$ requires N, 16·15%). Light absorption in chloroform (main band only) : max., 396 mμ; ε = 36,500.

5-*Ethylnonan*-2-*one*.—A solution of the preceding ketone (5·0 g.) in methanol (30 c.c.) was shaken in the presence of palladium–calcium carbonate (0·55 g.; from 10% of $PdCl_2$) in hydrogen until absorption was complete (1240 c.c. of hydrogen absorbed at 20°/774 mm., equiv. to 1·8 double bonds). Removal of catalyst and solvent and distillation of the residue gave 5-*ethylnonan*-2-*one* (2·0 g.), b. p. 36°/5 × 10^{-3} mm., n_D^{21} 1·4340 (Found : C, 77·45; H, 12·65. $C_{11}H_{22}O$ requires C, 77·6; H, 13·0%). The *semicarbazone* crystallised from aqueous alcohol in needles, m. p. 97° (Found : N, 19·15. $C_{12}H_{25}ON_3$ requires N, 18·5%).

Ethyl 5-*Ethyl*-2-*methylnona*-1 : 3 : 5-*triene*-1-*carboxylate*.—A Reformatsky reaction of 5-ethylnona-3 : 5-dien-2-one (90 g.) with ethyl bromoacetate (125 g.) and zinc (42 g.) gave the hydroxy-ester (43 g.), b. p. 80—100° (bath-temp.)/6 × 10^{-4} mm., n_D^{20} 1·5107. Dehydration with toluene-*p*-sulphonic acid in the usual way yielded the *ester* (20 g.) as a mixture of isomers, b. p. 88—91°/5 × 10^{-4} mm., n_D^{21} 1·5276 (Found : C, 75·6; H, 10·25. $C_{15}H_{24}O_2$ requires C, 76·2; H, 10·25%). Light absorption : max., 280 mμ; ε = 28,500. Inflexion, 288 mμ; ε = 26,500.

Hydrolysis of the ester (0·75 g.) under reflux with methanolic potassium hydroxide (20 c.c.; 10% w/v) overnight furnished an acidic product (0·45 g.) which partly solidified. Crystallisation from pentane gave 5-*ethyl*-2-*methylnona*-1 : 3 : 5-*triene*-1-*carboxylic acid* (7 mg.) as needles, m. p. 103—105° (Found : C, 75·1; H, 9·5. $C_{13}H_{20}O_2$ requires C, 74·95; H, 9·7%). Light absorption : max., 300 mμ; ε = 34,500.

6-*Ethyl*-3-*methyldeca*-2 : 4 : 6-*trien*-1-*ol*.—Reduction of the preceding ester (20 g.) at −60° with lithium aluminium hydride (4·95 g.) gave the *alcohol* (7·6 g.), b. p. 84—85°/5 × 10^{-5} mm., n_D^{19} 1·5368 (Found : C, 79·75; H, 11·3. $C_{13}H_{22}O$ requires C, 80·35; H, 11·4%). Light absorption : maxima, 271 and 280 mμ; ε = 29,000 and 31,000 respectively.

Oxidation of the alcohol with aluminium *tert.*-butoxide and acetone gave 9-ethyl-6-methyltrideca-3 : 5 : 7 : 9-tetraen-2-one which was isolated as its *semicarbazone* which crystallised from methanol and had m. p. 177° (Found : N, 14·35. $C_{17}H_{27}ON_3$ requires N, 14·5%). Light absorption : max., 352, and 368 mμ; ε = 63,500 and 58,000 respectively. Inflexion, 333 mμ; ε = 48,500.

4-*cyclo*Hex-1′-enylbut-3-en-2-one (III*b*) was prepared by the method of Heilbron, Jones, Richardson, and Sondheimer (*J.*, 1949, 737). The 2 : 4-*dinitrophenylsemicarbazone* crystallised from pyridine in prisms, m. p. 232° (decomp.) (Found : N, 18·4. $C_{17}H_{19}O_5N_5$ requires N, 18·75%). Light absorption : max., 298 mμ; ε = 35,500. Inflexion, 320 mμ; ε = 25,000.

Ethyl 4-cyclo*Hex*-1′-*enyl*-2-*methylbuta*-1 : 3-*diene*-1-*carboxylate* (IV*b*).—About one-quarter of a mixture of 4-*cyclo*hex-1′-enylbut-3-en-2-one (60 g.) and ethyl bromoacetate (84 g.) freshly distilled) was added to zinc wool (32 g.), benzene (500 c.c.), and a trace of iodine. The mixture was heated under reflux until reaction commenced and the remainder of the ketone–bromoacetate solution was added at such a rate that gentle refluxing was maintained (½ hour). After being heated for a further 15 minutes, the solution was cooled, decanted from unchanged zinc (4 g.), shaken with N-acetic acid, and sodium hydrogen carbonate solution, and dried. Evaporation of a small portion and distillation of the residue (2·8 g.) gave 4-cyclo*hex*-1′-*enyl*-2-*hydroxy*-2-*methylbut*-3-*ene*-1-*carboxylate* (1·83 g.), b. p. 105°/2 × 10^{-3} mm., n_D^{24} 1·5070 (Found : C, 71·25; H, 9·4. $C_{14}H_{22}O_3$ requires C, 70·6; H, 9·25%). Light absorption : max., 234 mμ; ε = 22,500. 4-*cyclo*Hex-1′-enylbut-3-en-2-ol, which possesses the same chromophore, has max., 235 mμ; ε = 23,000 (Braude and Coles, *J.*, 1950, 2014).

The remainder of the benzene solution was diluted (to 1 l.) and heated under reflux in the presence of toluene-*p*-sulphonic acid (0·7 g.) for 5 hours; the water which separated was removed by azeotropic distillation. Isolation of the product in the usual way yielded *ethyl* 4-cyclo*hex*-1′-*enyl*-2-*methylbuta*-1 : 3-*diene*-1-*carboxylate* (58 g.) as a mixture of isomers, b. p. 104—110°/1·4 × 10^{-3} mm., n_D^{24} 1·5630—1·5738 (Found : C, 76·4; H, 9·15. $C_{14}H_{20}O_2$ requires C, 76·35; H, 9·15%). Light absorption : max., 281 and 296 mμ; ε = 22,000 and 24,000 respectively. When the fractions having $n_D^{24} > 1·5700$ were kept at 0°, a small amount of one isomer, m. p. 44°, was obtained (Found: C, 76·35; H, 9·1%). Light absorption: see table. During 12 hours at 0° in an inert atmosphere, the crystals liquefied.

Attempts to hydrolyse the ester gave irreproducible results. In one experiment the liquid ester (0·1 g.) and methanolic potassium hydroxide (10 c.c.; 10% w/v) were heated under reflux for 3 hours and gave 4-cyclo*hex-1'-enyl-2-methylbuta-1 : 3-diene-1-carboxylic acid,* yellow needles (20 mg.) (from methanol), m. p. 126° (Found: C, 75·1; H, 8·8. $C_{12}H_{16}O_2$ requires C, 74·95; H, 8·4%). Light absorption: max., 304 mμ; ε = 29,500.

5-cyclo*Hex-1'-enyl-3-methylpenta-2 : 4-dien-1-ol* (V*b*).—The preceding triene ester (50 g.; liquid) in ether (200 c.c.) was added during ½ hour to a stirred solution of lithium aluminium hydride (10·0 g.; *ca.* 80% pure) in ether (400 c.c.) at −60°. The temperature of the mixture was kept at −30° for 1½ hours and then allowed to rise to 20° during 1 hour. Ethyl acetate (8 g.) was added, to decompose the excess of hydride, followed by saturated ammonium chloride solution (75 c.c.). Isolation of the product with ether and distillation gave the *alcohol* (32 g.), b. p. 115—117°/10⁻³ mm., n_D^{24} 1·5720—1·5828 (Found: C, 80·65; H, 10·3. $C_{12}H_{18}O$ requires C, 80·85; H, 10·2%. Unsaturation, equiv. to 3 double bonds). Light absorption: max., 270 and 280 mμ; ε = 35,500 and 35,500. Inflexion, 261 mμ; ε = 29,500. The 3 : 5-*dinitrobenzoate* crystallised from acetone in orange prisms, m. p. 128° (Found: C, 61·05; H, 5·55. $C_{19}H_{20}O_6N_2$ requires C, 61·25; H, 5·4%). Light absorption: max., 237, 270, and 280 mμ; ε = 27,000, 40,000 and 40,000 respectively.

5-cyclo*Hex-1'-enyl-3-methylpenta-2 : 4-dienal* (VII*b*).—The preceding alcohol (3·0 g.) in light petroleum (b. p. 40—60°) (200 c.c.) was shaken with manganese dioxide (30 g.; dried over P_2O_5) at 20° for 4 hours. Removal of oxide and solvent gave an oil (2·7 g.), n_D^{26} 1·6135. Chromatography on alumina (200 g.) from benzene yielded the *aldehyde* (1·3 g.), b. p. 80—90° (bath-temp.)/10⁻⁴ mm., n_D^{23} 1·6250 (Found: C, 81·6; H, 8·95. $C_{12}H_{16}O$ requires C, 81·8; H, 9·15%). Light absorption in *n*-hexane: max., 294, 308, and 324 mμ; ε = 19,000, 29,000, and 24,000 respectively. Inflexion, 314 mμ; ε = 23,500. The 2 : 4-*dinitrophenylhydrazone,* crystallised from ethyl acetate, had m. p. 211° (Kofler block) (Found: N, 15·45. $C_{18}H_{20}O_4N_4$ requires N, 15·75%). Light absorption in $CHCl_3$ (main band only): max., 415 mμ; ε = 41,500. The *semicarbazone,* crystallised from methanol, had m. p. 201° (decomp.) (Found: N, 18·05. $C_{13}H_{19}ON_3$ requires N, 18·0%). Light absorption: max., 328 and 340 mμ; ε = 42,000 and 38,000 respectively.

The yield was not improved by increasing the time of oxidation to 7 days (cf. Wendler, Slates, Trenner, and Tishler, *J. Amer. Chem. Soc.*, 1951, **73**, 719).

8-cyclo*Hex-1'-enyl-6-methylocta-3 : 5 : 7-trien-2-one* (VI*b*).—(*a*) 5-*cyclo*Hex-1'-enyl-3-methylpenta-2 : 4-dien-1-ol (20 g.) and aluminium *tert.*-butoxide (55 g.) in acetone (500 c.c.) and benzene (800 c.c.) were heated under reflux for 45 hours. Decomposition of the complex and isolation of the product in the usual way gave an oil (24 g.), n_D^{21} 1·628—1·630. Light absorption: max. 271, 281, 292, 352, and 362 mμ; $E^{1\%}_{1\,\text{cm.}}$ = 720, 780, 700, 680, and 680 respectively. A portion (11 g.) in light petroleum (b. p. 40—60°) was poured on alumina (300 g.) and the chromatogram was developed with benzene. The main yellow band gave the crude ketone (5·7 g.), n_D^{22} 1·650. Light absorption (main band only): max., 354 mμ; $E^{1\%}_{1\,\text{cm.}}$ = 900. The *semicarbazone* crystallised from alcohol in yellow prisms, m. p. 206° (decomp.) (Found: N, 14·85. $C_{16}H_{23}ON_3$ requires N, 15·35%). Light absorption: max. 367 mμ; ε = 71,000. The *phenylsemicarbazone,* crystallised from aqueous pyridine, had m. p. 210° (decomp.) (Found: N, 11·85. $C_{22}H_{27}ON_3$ requires N, 12·0%). Light absorption in $CHCl_3$: max., 355 mμ; ε = 59,500. The 2 : 4-*dinitrophenylsemicarbazone,* crystallised from aqueous pyridine, had m. p. 217° (decomp.) (Found: N, 15·7. $C_{22}H_{25}O_5N_5$ requires N, 15·95%). Light absorption in $CHCl_3$: max., 350 mμ; ε = 48,500. Inflexion, 360 mμ; ε = 44,000. The first two of these derivatives decomposed rapidly even at 0° in an inert atmosphere.

A portion (0·5 g.) of the crude ketone was distilled and the distillate (0·34 g.), b. p. 80° (bath-temp.)/10⁻⁵ mm., collected in three equal fractions. The last of these solidified partly. Subsequently the crude product, without chromatography, was distilled in small batches (1 g.). The distillates (620 mg.), on being seeded with the solid described above partly solidified. Crystallisation from aqueous methanol gave the *ketone* (140 mg. from each batch) as yellow needles, m. p. 74—75·5° (Kofler block) (Found: C, 83·0; H, 9·3. $C_{15}H_{20}O$ requires C, 83·3; H, 9·3%). Light absorption in EtOH: see table. In *n*-hexane: max., 347 mμ; ε = 47,500. Inflexion, 353 mμ; ε = 44,500.

(*b*) 5-*cyclo*Hex-1'-enyl-3-methylpenta-2 : 4-dienal (5·8 g.) and aluminium *tert.*-butoxide (20 g.) in acetone (150 c.c.) and benzene (175 c.c.) were heated under reflux for 32 hours. Decomposition of the complex and isolation of the product as in (*a*) gave an oil (6·0 g.), n_D^{24} 1·64—1·65. Distillation gave the crude ketone (3·7 g.), b. p. 90—100° (bath-temp.)/10⁻⁴ mm., n_D^{21} 1·655—1·665. Light absorption: max., 280, 305, 345, and 363 mμ; $E^{1\%}_{1\,\text{cm.}}$ = 600, 740, 1160, and 1040 respectively. Inflexion: 333 mμ; $E^{1\%}_{1\,\text{cm.}} = 100$. On seeding with a sample from (*a*), the crystalline ketone (0·4 g.), m. p. 74—76° (Kofler block), was obtained.

8-cyclo*Hexyl-6-methyloctan-2-one*.—The preceding crystalline ketone (170 mg.) was shaken in methanol (25 c.c.) in hydrogen in the presence of Adams's platinum catalyst (17 mg.) until absorption was complete (hydrogen absorbed, 69 c.c. at 22°/760 mm., equiv. to 3·6 double bonds). After removal of catalyst and solvent, the saturated ketone was converted into the semicarbazone which crystallised from aqueous methanol in plates (45 mg.), m. p. 98°, undepressed on admixture with an authentic specimen (Heilbron, Jones, and Richardson, *loc. cit.*, give m. p. 98°).

Ethyl 8-cyclo*Hex-1'-enyl-2* : *6-dimethylocta-1* : *3* : *5* : *7-tetraene-1-carboxylate* (VIII*b*).—The Reformatsky reaction between 8-*cyclo*hex-1'-enyl-6-methylocta-3 : 5 : 7-trien-2-one [2·9 g.; from route *b* above; partly crystalline; $E^{1\%}_{1\,\text{cm.}}$ (360 mμ) = *ca.* 1100, indicating a purity of *ca.* 60%], ethyl bromoacetate (2·9 g.) and zinc wool (1·1 g.) in benzene (30 c.c.), and the isolation of the product, were carried out in the usual way. Evaporation of a portion of the resulting benzene solution gave a gum which absorbed at 280—320 mμ., $E^{1\%}_{1\,\text{cm.}}$ = *ca.* 300, indicating complete reaction of the ketone.

The remainder of the benzene solution was diluted to 100 c.c. and heated under reflux for 5 hours with toluene-*p*-sulphonic acid (50 mg.). Isolation of the product gave an oil (3·2 g.), n_D^{23} 1·625. Light absorption : max., 330, 347, and 362 mμ; $E^{1\%}_{1\,\text{cm.}}$ = 560, 740, and 680 respectively. Chromatography on alumina (125 g.) from a mixture (2 : 1) of light petroleum (b. p. 40—60°) and benzene, and elution of the least strongly adsorbed, orange band yielded a viscous gum (1·6 g.), n_D^{23} 1·645—1·650. Light absorption : max., 328, 347, and 363 mμ; $E^{1\%}_{1\,\text{cm.}}$ = 820, 1070, and 780 respectively. Distillation of a portion (0·5 g.) from a short-path still gave the ester (0·22 g.) as a highly unstable viscous oil, b. p. 130—140° (bath-temp.)/10^{-4} mm. Light absorption : see table.

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