194. *A Synthesis of Vitamin A from* cyclo*Hexanone.*

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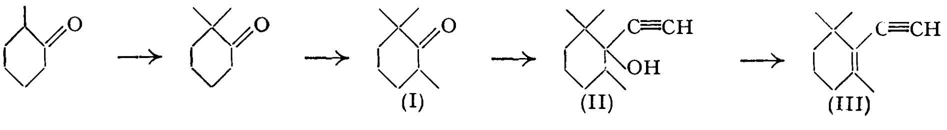
8 : 9-Dehydrovitamin A has been prepared by two routes (cf. Heilbron, *J.*, 1948, 386; 1949, 2031), and by a modification of the scheme vitamin A itself was also synthesised by two routes.

2-Ethynyl-1 : 3 : 3-trimethyl*cyclo*hex-1-ene (III) and 6-methylocta-3 : 5 : 7-trien-2-one are coupled together by Grignard reaction and the tertiary alcohol (XI) so obtained rearranges to give 8 : 9-dehydrovitamin A (IX). Condensation of ethynyl-2 : 6 : 6-trimethyl*cyclo*hex-1-ene (III) with crotonylideneacetone, rearrangement, and oxidation give the 7 : 8-dehydro-C_{18} ketone (VI), which is converted into the same dehydrovitamin A by condensation with ethyl bromoacetate, followed by dehydration and reduction of the ethyl ester of 8 : 9-dehydrovitamin A acid (VIII; R = Et) with lithium aluminium hydride.

1-Ethynyl-2 : 2 : 6-trimethyl*cyclo*hexanol (II) condenses with crotonylideneacetone and with 6-methylocta-3 : 5 : 7-trien-2-one to give C_{18} and C_{20} glycols, (XII) and (XVIII), respectively, in which compounds, after rearrangement, the triple bond is selectively semi-reduced with lithium aluminium hydride. Dehydration of the reduced C_{20} glycol monoacetate (XXII; R = Ac) gives vitamin A acetate, and oxidation of the reduced C_{18} glycol (XX) with subsequent dehydration gives the known C_{18} ketone, which is converted into vitamin A by one of the published methods. The C_{18} acetylenic glycol (XIV) is alternatively obtained by condensation of 2 : 2 : 6-trimethyl*cyclo*hexanone with a C_9 acetylenic alcohol (XIII).

Several syntheses of vitamin A have now been described and excellent reviews of previous work are available (Milas, *Recent Advances in Vitamins and Hormones*, 1947, **5**, 1; Heilbron, *J.*, 1948, 386; Isler, *Chimia*, 1950, **4**, 103; Johnson, *Ann. Reports*, 1949, **46**, 168). It will be noted that all the syntheses described are from β-ionone, which has 13 of the 20 carbon atoms of vitamin A already correctly disposed. It has, however, certain obvious disadvantages as a starting material for the preparation of vitamin A, and Heilbron (*loc. cit.*) has suggested several possible routes for the synthesis of vitamin A and its lower homologues from *cyclo*hexanone, and has prepared several analogues by this method (Heilbron *et al.*, *J.*, 1949, 287, 742, 2023, 3120, 3123; 1950, 633). It was the object of our work to effect a synthesis of vitamin A itself from *cyclo*hexanone by one such route.

The key condensation of the routes outlined by Heilbron is of an ethynyl*cyclo*hexene with a C_7 or C_9 ketone, leading (with a trimethyl-substituted ring) to a C_{18} or C_{20} skeleton; several routes from the C_{18} to the C_{20} skeleton are now well substantiated (Arens and van Dorp, *Rec. Trav. chim.*, 1946, **65**, 338; 1949, **68**, 604; Schwarzkopf, Cahnmann, Lewis, Swidinsky, and Wuest, *Helv. Chim. Acta*, 1949, **32**, 443). 2-Methyl*cyclo*hexanone is available commercially and was selected as starting material. From this point the route envisaged to the ethynyltrimethyl*cyclo*hexene (III) was as follows:



The methylation of *cyclo*hexanone had been examined previously (Cornubert and Haller, *Bull. Soc. chim.*, 1927, **41**, 367, 894; Colonge and Duroux, *ibid.*, 1940, **7**, 459; Adamson, Marlow, and Simonsen, *J.*, 1938, 774; Fischer and Wunderlich, *Ber.*, 1941, **74**, 1544), and the published method of methylation with methyl iodide and sodamide in a non-polar solvent was found suitable. The methylation was carried out in two stages, the separation of homologues at each stage being effected by fractionation through an 80-plate column with a gauze packing (Dixon, *J. Soc. Chem. Ind.*, 1949, **68**, 88). The earlier method of separation by fractional crystallisation of the semicarbazones was rejected as practicable only for small samples of the pure ketones.

It may be noted that the m. p. of 2 : 2 : 6-trimethyl*cyclo*hexanone semicarbazone, 209—211°, was found to be lower than those previously recorded, 220—221° (Masson, *Compt. rend.*, 1912, **154**, 517) and 214—216° (Cornubert and Haller, *loc. cit.*). However, repeated recrystallisation did not raise the m. p. and solubility analysis did not indicate the presence of any substantial amount of impurity.

The physical constants of the homologous ketones are shown in Table 1, the m. p.s having been newly determined. It will be seen that methods for analysing mixtures of the ketones based on the measurement of physical constants are largely precluded by the small range of these constants. However, a method of limited applicability was developed, based on the measurement of setting-points. By this means it was possible to determine the composition of mixtures of 2 : 2-dimethyl-, 2 : 2 : 6-trimethyl-, and 2 : 2 : 6 : 6-tetramethyl-*cyclo*hexanones with an accuracy of ± *ca.* 0·5%, provided that the trimethyl compound accounted for more than 85% of the mixture. Preliminary experiments have indicated that a more complete solution of the problem is to be found in the determination of infra-red absorption spectra.

TABLE 1. *Physical properties of methylated* cyclo*hexanones.*

Substituent	B. p.	M. p.	n_D^{20}	d_4^{20}
None	155°	−40·5°	1·4507	0·9478
2-Methyl	166	−14·4	1·4456	0·9250
2 : 2-Dimethyl	173	−20·5	1·4486	0·9145
2 : 6-Dimethyl	170—173	—	1·4508 *	0·9146 *
2 : 2 : 6-Trimethyl	178	−31·8	1·4493 *	0·9043 *
2 : 2 : 6 : 6-Tetramethyl	185	+11·2	1·4470	0·8923

* Both physical properties relate to 18°, not 20°.

By adding the trimethyl ketone (I) to a solution of sodium acetylide in liquid ammonia, 1-ethynyl-2 : 2 : 6-trimethyl*cyclo*hexanol (II) was readily obtained in high yield. This condensation has now been carried out with both *cyclo*hexanone (Heilbron, Jones, and Richardson, *J.*, 1949, 287) and its 2 : 2 : 6-trimethyl homologue (Milas, MacDonald, and Black, *J. Amer. Chem. Soc.*, 1948, **70**, 1829).

Dehydration of the alcohol (II) to 2-ethynyl-1 : 3 : 3-trimethyl*cyclo*hex-1-ene (III) proved to be difficult. After many attempts to effect it directly had given small or erratic yields of the required hydrocarbon, this was obtained in moderate yield by pyrolysis of its acetate. The acetate and other esters were prepared by treating (II) with one equivalent of ethylmagnesium bromide and reaction of the product with the appropriate acid anhydride (Houben, *Ber.*, 1906, **39**, 1736). The acetate was subsequently prepared by other acetylation procedures, of which the one preferred is given on p. 1102 : methods involving the use of pyridine were not satisfactory. The acetate was best pyrolysed in silicone oil in the presence of zinc oxide, whereupon it gave a 36% yield of hydrocarbon (III). Inferior yields were obtained in the absence of a solvent and substitution of the propionate, *n*-hexanoate, or benzoate for the acetate gave rather smaller yields. The use of zinc, iron, lead monoxide, lead dioxide, ferric oxide, sodium acetate, or lead acetate as catalyst gave a smaller yield of hydrocarbon (III) (10—25%). Silver, copper, magnesium, aluminium, tin, nickel, cobalt, manganese, molybdenum, or tungsten, the oxides of copper, magnesium, calcium, barium, mercuric, aluminium, or bismuth, and manganese dioxide or calcium hydroxide gave very small yields (0—10%).

The resulting product gave the correct analysis and had the ultra-violet absorption to be expected for such a compound. On ozonolysis it gave a 25% yield of geronic acid. Its physical constants agreed with those given by Sobotka and Chanley (*J. Amer. Chem. Soc.*, 1949, **71**, 4136) but not with those by Milas, MacDonald, and Black (*loc. cit.*). Moreover, we had earlier (B.P. 627 453/47) obtained the same compound by direct pyrolysis of the alcohol (II) over aluminium phosphate, as described by Milas (*loc. cit.*) and Heilbron, Jones, and Richardson (*loc. cit.*). This method gave very variable yields, as has also been noted by Sobotka and Chanley (*loc. cit.*). We were also able to repeat the method used by these authors and obtained identical material.

The acetylenic compound (III) was converted into its Grignard derivative and condensed with crotonylideneacetone (of which an improved preparation is described, p. 1103) to give the tertiary alcohol (IV).

The data for the light absorption of this and the other C_{18} and C_{20} compounds described are collected in Table 2.

TABLE 2.

	$\lambda_{\text{max.}}$, Å	$\epsilon_{\text{max.}}$		$\lambda_{\text{max.}}$, Å	$\epsilon_{\text{max.}}$
IV	2300	30 000	XVI	3160	4 300
V	3010	21 000		2660	24 200
	2260	12 600		Infl. 2930—3045	4 400
	Infl. 3110—3120	16 400	XVII	3385	15 000
VI	3400	23 300		2630	9 850
	2440	11 200	XVIII	2810	31 600
VII	3000	25 600		2700	40 600
	2250	17 000	XIX	3170 *	39 400
VIII	3510	33 600		3020 *	47 600
	2650	12 200		2260 *	8 350
IX	3280	35 000		Infl. 2870—2960 *	35 650
	2520	19 400	XX	2850	22 400
XI	2810	36 000		2740	28 200
	2710	34 600		2650	23 400
	Infl. 2350—2450	17 800	XXI	3110	29 400
XII	2290	25 000		2280	8 000
XIV	2800	23 600	XXII	3230 *	46 600
	2690	32 300		3070 *	58 000
XV	3050	25 000		2960 *	43 500
	2400	3 400		2300 *	5 700
	3130 *	25 400			
	2510 *	3 500			

	$\lambda_{\text{max.}}$, Å	$\epsilon_{\text{max.}}$
† R·CH:CH·CMe:CH·CH:CH·COMe	3310	30 000
	3450 *	25 500
† R·CH:CH·CMe:CH·CH:CH·CMe:CH·CH_2·OH	3250	50 000

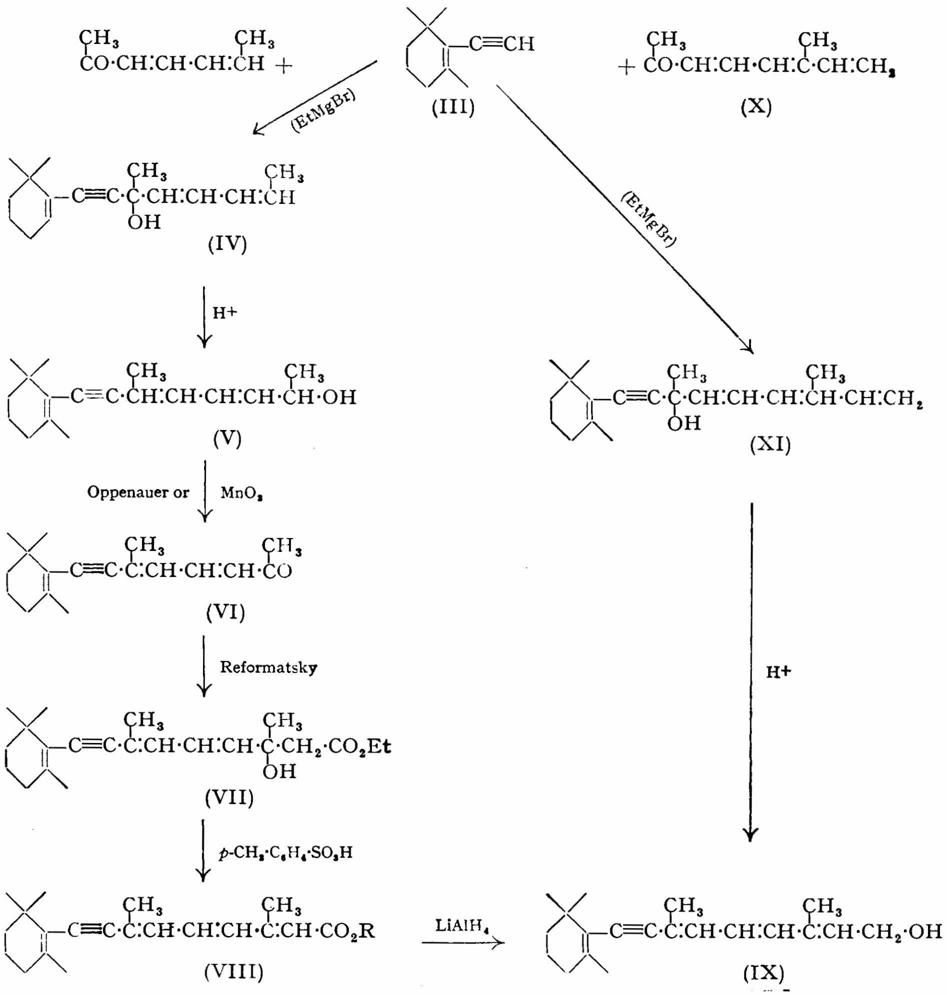
* Determination carried out in ethanol. The remaining determinations were made in *n*-hexane.
† R as in Table 3.

When shaken in ethereal solution with 0·5% sulphuric acid, (IV) underwent rearrangement to give the secondary alcohol (V) in 60% yield. Total hydrogenation of this compound gave the saturated 6-methyl-8-(2 : 2 : 6-trimethyl*cyclo*hexyl)octan-2-ol which was oxidised to the corresponding known ketone (semicarbazone) (Karrer and Morf, *Helv. Chim. Acta*, 1933, **16**, 625).

For the Reformatsky reaction required to complete the C_{20} skeleton it was necessary to oxidise the alcohol (V) to the corresponding ketone (VI); this was effected by Oppenauer oxidation, followed by isolation as the semicarbazone and regeneration, or directly in 80% yield by oxidation with manganese dioxide in light petroleum. The ketone (VI) gave the above saturated ketone (semicarbazone) on total hydrogenation.

Manganese dioxide had previously been used by Ball, Goodwin, and Morton (*Biochem. J.*, 1948, 42, 516) for the oxidation of vitamin A to retinene; 2-β-ionylidene-ethanol (Wendler, Slates, and Tishler, *J. Amer. Chem. Soc.*, 1949, **71**, 3267) and vitamin A_2 (Henbest and Jones, *Chem. and Ind.*, 1951, 49) have recently been oxidised to the corresponding aldehydes in the same way. In this work five successful oxidations with manganese dioxide are described, and we have also tested the method, with positive results, on simpler alcohols, *i.e.*, allyl alcohol, cinnamyl alcohol, oct-3-yn-2-ol, and 3-dehydro-β-ionol. It therefore appears that the method may be general for alcohols of the allylic type, whether they are primary or secondary and possibly when the unsaturation is acetylenic. Of acetylenic alcohols three were successfully oxidised in this way; a fourth, hex-1-yn-3-ol, was recovered unchanged after treatment with manganese dioxide: it may be significant that this was the only one of the four having acetylenic hydrogen.

The reaction conditions have been examined in some detail and it has been found possible to prepare precipitated manganese dioxide by means of which a substantially complete oxidation can be effected in ½—1 hour at room temperature, in contrast with the 6—10 days used by Morton and his colleagues. Normal commercial samples of precipitated manganese dioxide commonly have a much lower activity and are often inactive. In the preparation of active material (see p. 1104), it has been found essential to precipitate it in the presence of alkali, or to treat it with alkali after precipitation and before drying. The latter process is also critical and both under- and over-drying can profoundly reduce the activity of the oxide. The active material is a hydrated oxide and of a chocolate-brown colour.

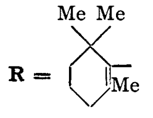


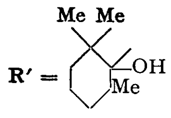
The ketone (VI) obtained by this method was subjected to a Reformatsky reaction to give an ester (VII). On dehydration this gave the oily ester (VIII; R = Et), which on hydrolysis gave the corresponding acid (VIII; R = H) as a crystalline solid, m. p. 161°. The acid showed only slight vitamin A activity; the results of animal-growth tests on this and other compounds described in this paper are collected in Table 3.

The ester (VIII; R = Et) was reduced to 8 : 9-dehydrovitamin A (IX) with lithium aluminium hydride, as described by Schwarzkopf *et al.* (*loc. cit.*) for vitamin A itself.

The crude (70%) dehydrovitamin thus obtained was, after chromatography, converted into the anthraquinone-2-carboxylate, which, like that of vitamin A, crystallised in two modifications, yellow needles, m. p. 113°, and red needles, m. p. 137°. However, in this instance the red form was the stable one; the yellow form was stable when dry but changed to the red on contact with acetone. On hydrolysis, 8 : 9-dehydrovitamin A was obtained as a crystalline solid, m. p. 47—50° (*p*-phenylazobenzoate).

TABLE 3.



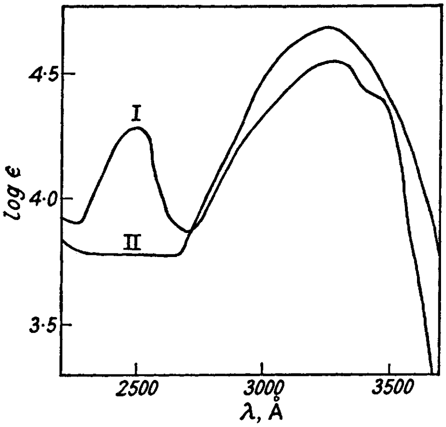


Compound	Activity, as a percentage of that of vitamin A
$\mathrm{R{\cdot}C{\vdots}C{\cdot}CMe{:}CH{\cdot}CH{:}CH{\cdot}CMe{:}CH{\cdot}CO_2Et}$	5
$\mathrm{R{\cdot}C{\vdots}C{\cdot}CMe{:}CH{\cdot}CH{:}CH{\cdot}CMe{:}CH{\cdot}CO_2H}$	0·5—1
$\mathrm{R{\cdot}C{\vdots}C{\cdot}CMe(OH){\cdot}CH{:}CH{\cdot}CH{:}CMe{\cdot}CH{:}CH_2}$	4
$\mathrm{R{\cdot}C{\vdots}C{\cdot}CMe{:}CH{\cdot}CH{:}CH{\cdot}CMe{:}CH{\cdot}CH_2{\cdot}OH}$	40 *
$\mathrm{R'{\cdot}C{\vdots}C{\cdot}CMe{:}CH{\cdot}CH{:}CH{\cdot}CMe{:}CH{\cdot}CH_2{\cdot}OH}$	1
$\mathrm{R'C{\vdots}C{\cdot}CMe{:}CH{\cdot}CH{:}CH{\cdot}CMe{:}CH{\cdot}CH_2{\cdot}OAc}$	1

* This figure has been calculated from the results of tests carried out with the anthraquinone-2-carboxylate (yellow form).

On a column of alumina the dehydrovitamin A showed a blue fluorescence under ultra-violet radiation, similar to that shown by the vitamin. It differed from the vitamin in giving, with the Carr–Price reagent, a blue colour that rapidly faded to a stable purple.

A second route to the dehydrovitamin employed ketone (X), which gave the C_{20} tertiary alcohol (XI) on condensation with the same acetylenic hydrocarbon (III).



I, 8 : 9-*Dehydrovitamin A*. II, *Vitamin A*.

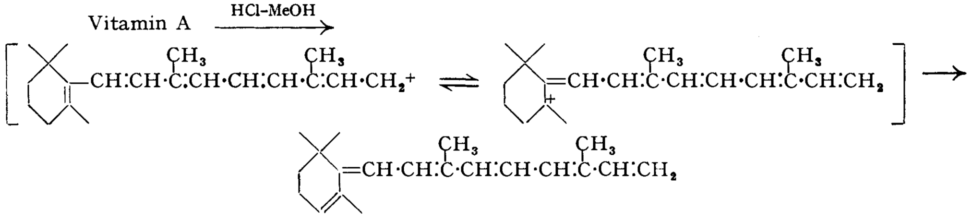
The ketone (X) was prepared by the route of Cheeseman, Heilbron, Jones, Sondheimer, and Weedon (*J.*, 1949, 2031), but it was found possible to substitute calcium for lithium in the ethynylation of crotonylideneacetone, and the rearranged condensation product was oxidised by manganese dioxide in light petroleum, instead of by the Oppenauer method, giving a better conversion and a purer product. The use of the less pure ketone obtained by the Oppenauer oxidation led to complex mixtures, which it was found impossible to purify sufficiently to yield a crystalline anthraquinone-2-carboxylate after rearrangement.

The crude condensation product (XI) was, after purification by chromatography and distillation, rearranged in a homogeneous acidic medium to give a mixture containing dehydrovitamin A (60% of IX). Chromatography of the mixture gave a product (75% of IX) that yielded a crystalline anthraquinone-2-carboxylate, identical in all respects with that previously obtained.

The ultra-violet absorption curves for vitamin A and 8 : 9-dehydrovitamin A are shown for comparison in the figure.

8 : 9-Dehydrovitamin A differs markedly from vitamin A in its ease of dehydration. Whereas vitamin A is well known to be readily dehydrated by, *e.g.*, methanolic hydrogen chloride, yet the dehydrovitamin when treated with this reagent retained its ultra-violet absorption maximum at 325 mμ and no absorption at longer wave-lengths appeared. The triple bond clearly exerts a stabilising effect, and this fact strengthens the case for a formulation of anhydrovitamin A involving a shift of the whole conjugated system during the dehydration, as opposed to formulations involving changes in only the first four carbon atoms of the side chain (Meunier, Dulou, and Vinet, *Bull. Soc. Chim. biol.*, 1942, **25**, 371; *Compt. rend.*, 1943, **216**, 907; Shantz, Cawley, and Embree, *J. Amer. Chem. Soc.*, 1943, **65**, 901). The presence of the triple bond in the conjugated system would be expected to make

the contribution of the " rearranged " form of the carbonium ion very small and thus for 8 : 9-dehydrovitamin A to render largely inoperative the mechanism suggested by Meunier *et al.*



Anhydrovitamin A

Animal tests on the anthraquinone 2-carboxylate of 8 : 9-dehydrovitamin A showed the activity of the free alcohol to be 40% of that of vitamin A. Tests on the free 8 : 9-dehydrovitamin showed its activity to be only 10% of that of vitamin A, but under the conditions of the tests this is likely to have been due to decomposition of the samples. It can, therefore, only be asserted that its activity lies between 10 and 40% of that of vitamin A, but it is thus considerably more active than any other analogue yet prepared.

The considerable difficulties encountered in the dehydration of the alcohol (II) to the hydrocarbon (III) had prompted the suggestion that this might more readily be accomplished if the unsaturated side-chain was first built up by condensation with the carbinol (II) : in fact it was found that the desired effect was produced even by a saturated side-chain, and 1-hex-1′-yn-1′-yl-2 : 2 : 6-trimethyl*cyclo*hexanol, prepared by condensing hex-1-yne and 2 : 2 : 6-trimethyl*cyclo*hexanone (I), was dehydrated to 2-hex-1′-yn-1′-yl-1 : 3 : 3-trimethyl*cyclo*hex-1-ene by aqueous sulphuric acid, acetic anhydride containing a trace of. sulphuric acid, boiling acetic anhydride, or several other reagents, of which none had effected the dehydration of (II) to (III).

Accordingly, a Grignard compound was prepared by the addition of the alcohol (II) to two mols. of ethylmagnesium bromide in ether and was treated with crotonylideneacetone to give the glycol (XII), which was rearranged under the usual homogeneous conditions to give a second C_{18} glycol (XIV). This compound was also obtained by condensation of the Grignard derivative of 6-methylocta-3 : 5-dien-7-yn-2-ol (XIII) (Cheeseman *et al.*, *loc. cit.*) with 2 : 2 : 6-trimethyl*cyclo*hexanone (I).

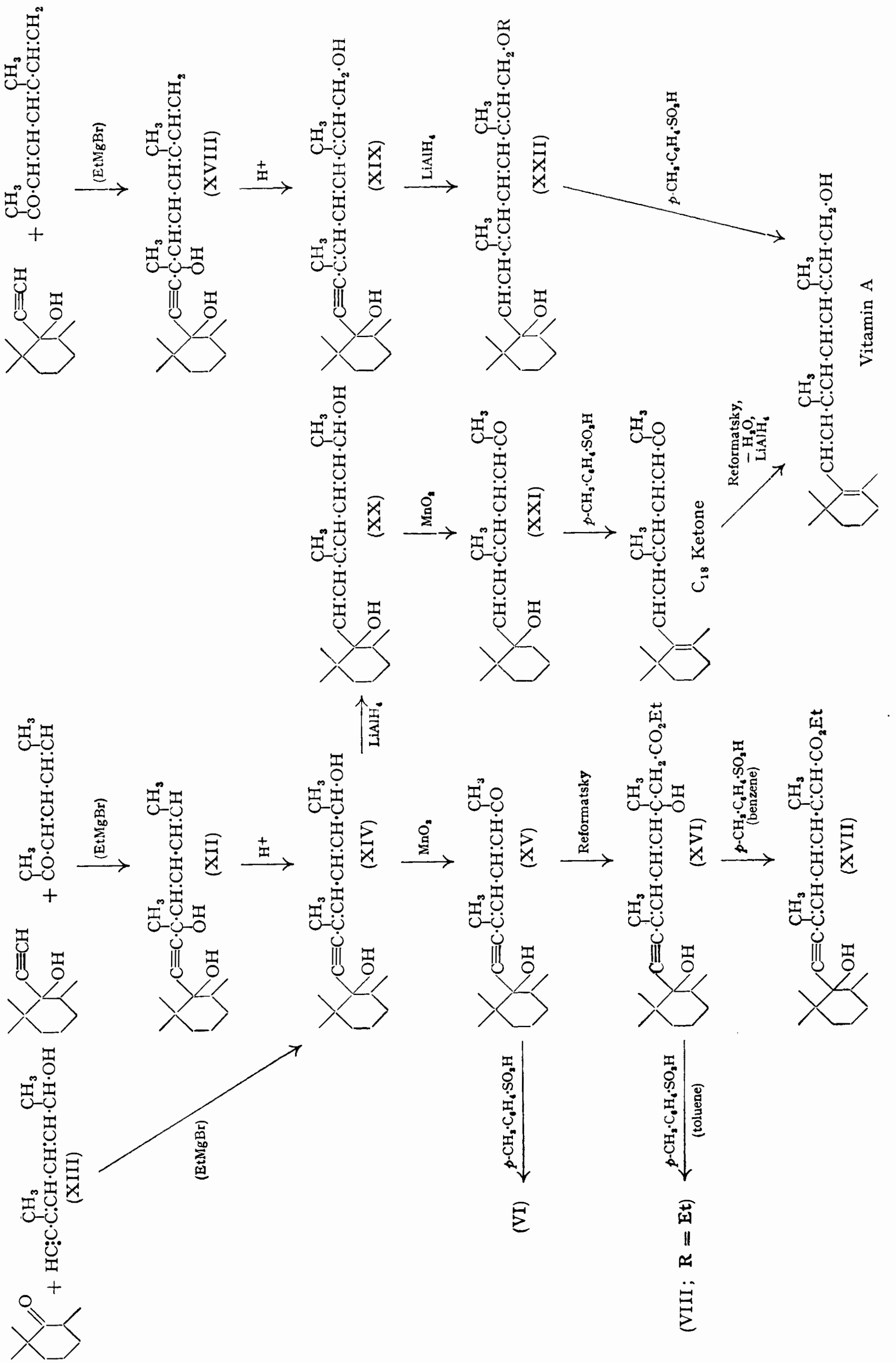
The acetylenic alcohol (XIII) has also been oxidised with manganese dioxide to the corresponding ketone (semicarbazone). Both the alcohol and the ketone show considerable instability : the former has been distilled on many occasions, but occasionally polymerised explosively during the process; the latter cannot be heated above room temperature without vigorous decomposition occurring and has not been distilled.

Glycol (XIV) was oxidised to the corresponding ketone (XV) (semicarbazone; 2 : 4-dinitrophenylhydrazone) with manganese dioxide, and (XV) was readily dehydrated, preferably by toluene-*p*-sulphonic acid in boiling toluene, to the 7 : 8-dehydro-C_{18} ketone (VI).

The hydroxy-ketone (XV) was subjected to a Reformatsky reaction and gave with two molecular proportions of ethyl bromoacetate the glycol-ester (XVI). Dehydration of this substance with toluene-*p*-sulphonic acid in boiling benzene gave a hydroxy-ester, which, on the basis of its light absorption, had formula (XVII), whereas the same reagent in boiling toluene gave the 8 : 9-dehydrovitamin A ester (VIII; R = Et) previously obtained.

Similarly, the di-Grignard complex from 1-ethynyl-2 : 2 : 6-trimethyl*cyclo*hexanol (II), in this instance in benzene, was condensed with 6-methylocta-3 : 5 : 7-trien-2-one (X) to give the ditertiary glycol (XVIII); this, under homogeneous acidic conditions, rearranged to give a crystalline glycol (XIX). The crystalline material was first obtained by regeneration from its anthraquinone-2-carboxylate, but later directly from the reaction product. It gave a green colour with the Carr–Price reagent and had only slight vitamin A activity. Neither it nor its anthraquinone-2-carboxylate has been dehydrated to 8 : 9-dehydrovitamin A.

The acetylenic alcohol (II) has also been condensed, by the same procedure, with


HC:C·C:CH·CH:CH·CH·OH (XIII)
(EtMgBr)
CO·CH:CH·CH:CH
(XII)
(XIV)
(XV)
(XVI)
(XVII)
(VI)
(VIII; R = Et)
H+
MnO2
LiAlH4
Reformatsky
p-CH3·C6H4·SO3H
p-CH3·C6H4·SO3H (benzene)
p-CH3·C6H4·SO3H (toluene)
CO·CH:CH·CH:C·CH:CH2
(XVIII)
(XIX)
(XX)
(XXI)
(XXII)
C18 Ketone
Reformatsky, − H2O, LiAlH4
CH:CH·C:CH·CH:CH·C:CH·CH2·OR
Vitamin A
CH:CH·C:CH·CH:CH·C:CH·CH2·OH

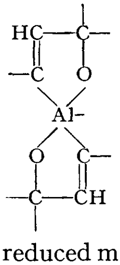
acetaldehyde, and with acetic anhydride at −70° to give 4-(1-hydroxy-2 : 2 : 6-trimethyl*cyclo*hexyl)but-3-yn-2-ol (3 : 5-dinitrobenzoate) and 4-(1-hydroxy-2 : 2 : 6-trimethyl*cyclo*hexyl)but-3-yn-2-one, respectively, compounds analogous to the 3-dehydro-β-ionol and -ionone recently described by Sobotka and Chanley (*J. Amer. Chem. Soc.*, 1949, **71**, 4136). The hydroxy-ketone was also prepared from the glycol in good yield by oxidation with manganese dioxide.

The outstanding problem remaining in the synthesis of vitamin A itself was the semi-reduction of the triple bond. Many attempts had been made in the *cyclo*hexene serias and more were made in the *cyclo*hexanol series: a considerable hindrance was the difficulty of determining whether any reduction occurring was selective. Attempts to analyse reduction products by the preparation and separation of derivatives were unsuccessful, and vitamin A activity tests were precluded by the comparatively high activity of the 8 : 9-dehydrovitamin. Certain colour reactions were also examined, but the acetylenic compounds and the corresponding ethylenic compounds gave very similar colours. In fact, in the early part of this work the only useful criteria available were measurements of unsaturation by total hydrogenation and of ultra-violet absorption spectra.

Triple carbon–carbon linkages in otherwise saturated systems have been shown to exhibit an absorption band in the infra-red between 2100 and 2240 cm.$^{-1}$ (Wotiz and Miller, *J. Amer. Chem. Soc.*, 1949, **71**, 3441); the band showed greatest intensity when the triple bond was near the end of the chain and weakened rapidly as it moved towards the centre of the molecule. No previous examination of a polyenyne system has been reported. However, an examination of the infra-red absorption of a series of pairs consisting of an acetylenic compound and the corresponding ethylenic compound [3-methylocta-4 : 6-dien-1-yn-3-ol and 3-methylocta-1 : 4 : 6-trien-3-ol; 6-methylocta-3 : 5-dien-7-yn-2-ol (XIII) and 6-methylocta-3 : 5 : 7-trien-2-ol; acetylenic ketone (VI) and C_{18} ketone semicarbazones; 3-dehydro-β-ionone and β-ionone semicarbazones] showed the acetylenic compounds all to have at 2100—2240 cm.$^{-1}$ a well-defined band which was entirely absent from the ethylenic compounds. Thus a comparison of the intensity of this band before and after an attempted semi-reduction, taken in conjunction with the ultra-violet absorption (and total hydrogenation figures, when necessary) gave a satisfactory measure of the extent of selective semi-reduction achieved.

Sobotka and Chanley (*J. Amer. Chem. Soc.*, 1949, **71**, 4140) had recently announced the selective semi-reduction of the triple bond in *cyclo*hex-1-en-1-ylethynylmethylcarbinol with lithium aluminium hydride, but when applied to our compounds this reagent did not reduce the triple bond selectively in either the analogous alcohol (IV) or the alcohol (V). It did so, however, when applied in the *cyclo*hexanol series to the glycols (XIV and XIX).

Thus a hydroxyl group in the allyl position with respect to the acetylenic linkage appears to be necessary for its reduction, and the mechanism may well be that suggested by Hochstein and Brown (*J. Amer. Chem. Soc.*, 1948, **70**, 3484) in the reduction of cinnamyl alcohol to dihydrocinnamyl alcohol, involving a cyclic intermediate, in our examples of the type inset. The unsaturated linkage in the groups $>\mathrm{C(OH)\cdot C{\vdots}C\cdot}$ appears to be reduced preferentially to that in the groupings $-\mathrm{CH{:}CH\cdot CH(OH)\cdot CH_3}$ and $>\mathrm{C{:}CH\cdot CH_2\cdot OH}$, *e.g.*, in glycols (XIV) and (XIX), respectively, but total hydrogenation and ultra-violet spectroscopy indicated that in the alcohol (IV), containing the grouping $-\mathrm{C{\vdots}C\cdot C(CH_3)(OH)\cdot CH{:}CH\cdot}$, the double bond was preferentially reduced.



In the reduction of the C_{18} acetylenic glycol (XIV) it was found that over-reduced material could be separated chromatographically, and the mixture containing the triene glycol (XX), thus purified, was oxidised with manganese dioxide to give a hydroxy-ketone (XXI), which was dehydrated with toluene-*p*-sulphonic acid in boiling toluene. From the mixture obtained after chromatography the known C_{18} ketone was isolated as its semicarbazone. Its identity was confirmed by m. p., mixed m. p., ultra-violet absorption spectrum, and finally, by conversion into vitamin A by the method of Schwarzkopf *et al.* (*loc. cit.*).

The C_{20} glycol (XIX) on reduction with lithium aluminium hydride gave a crystalline polyene glycol (XXII; R = H). This glycol was found to occur in two forms, m. p. 79° and 120°, the former being considerably less stable. It was isolated from the reaction mixture only occasionally and was readily converted into the high-melting form on attempted recrystallisation; it also absorbed atmospheric oxygen more rapidly. Acetylation of either form under very mild conditions gave one monoacetate only (XXII; R = Ac), and this on mild hydrolysis gave the higher-melting isomer. It seems probable that the two forms are related as *cis-trans*-isomers about the newly formed double bond.

Dehydration of the monoacetate (XXII; R = Ac) with toluene-*p*-sulphonic acid in toluene at 80°, boiling benzene, or chloroform gave a mixture of vitamin A acetate (50%), unchanged starting material, and anhydrovitamin A. Chromatography readily separated unchanged starting material from the other components, giving a mixture containing about 80% of vitamin A acetate from which crystalline vitamin A anthraquinone-2-carboxylate was readily obtained. Its identity was confirmed by m. p., mixed m. p., ultra-violet absorption, and animal-growth tests.

EXPERIMENTAL

All experiments were carried out in a nitrogen atmosphere and products were generally stabilised by the addition of small quantities of quinol or α-tocopherol. Active hydrogen was determined by Zerewitinoff's method, and unsaturation by use of platinum oxide in acetic acid, unless otherwise specified.

*2-Ethynyl-*1 : 3 : 3-*trimethyl*cyclo*hex*-1-*ene* (III).—(A) 1-Ethynyl-2 : 2 : 6-trimethyl*cyclo*hexanol (150 g.) was distilled slowly (*ca.* 25 g./hour) at 130—140° (bath-temp.)/30 mm. through a glass tube (70 cm. × 2 cm.) containing a supported aluminium phosphate catalyst (Heilbron, Jones, and Richardson, *J.*, 1949, 287) kept at 300—310°. The emergent gases were condensed by a water-condenser and collected in a flask equipped with a solid carbon dioxide–acetone trap. Ether (100 ml.) was added to the pyrolysis product, and the ethereal extract separated, dried ($CaCl_2$), and evaporated. Fractional distillation gave the crude dehydration product (34 g.), b. p. 66—70°/18 mm., n_D^{15} 1·491. This was added to an ethanolic solution of silver nitrate (10%; 75 ml.) and kept overnight. The precipitated silver salt was filtered off, washed with alcohol and water, and refluxed with a solution of potassium cyanide (70 g.) in water (200 ml.), and the mixture steam-distilled. The distillate was extracted with ether, and the ethereal extract dried ($CaCl_2$) and evaporated. Distillation of the residue gave 2-ethynyl-1 : 3 : 3-trimethyl*cyclo*hex-1-ene as a colourless liquid (20 g.), b. p. 68—69°/18 mm., n_D^{14} 1·4925 (Milas, MacDonald, and Black, *J. Amer. Chem. Soc.*, 1948, **70**, 1829, give b. p. 56—57°/18 mm., n_D^{25} 1·4745; Sobotka and Chanley, *ibid.*, 1949, **71**, 4136, give b. p. 69—70°/13 mm., n_D^{20} 1·4915) (Found: C, 88·9; H, 10·8. Calc. for $C_{11}H_{16}$: C, 89·2; H, 10·8%). Active H: 1·0. Unsaturation: 2·9, 3·2$|^{=}$. Light absorption (in *n*-hexane): Maximum at 2270 Å, ε 13 000 (Sobotka and Chanley, *loc. cit.*, give $\lambda_{max.}$ 2270 Å, ε 13 000).

1-*Ethynyl*-2 : 2 : 6-*trimethyl*cyclo*hexyl acetate*. (i) 1-Ethynyl-2 : 2 : 6-trimethyl*cyclo*hexanol (73 g.) was added to a stirred solution of ethylmagnesium bromide (1 mol.; determined by titration of an aliquot with standard acid) in ether (*ca.* 400 ml.) which was kept at −5°. The stirring was continued for a further 30 minutes at 0°, and the mixture refluxed for 1 hour. It was cooled to −5°, and acetic anhydride (90 g., 2 mols.) in ether (150 ml.) added. Stirring was continued at −5° for 2 hours and at room temperature overnight. The mixture was poured into 2N-sulphuric acid, and the product isolated with ether. Removal of the solvent gave a solid which was recrystallised from ethanol, giving 1-*ethynyl*-2 : 2 : 6-*trimethyl*cyclo*hexyl acetate* (64 g., 70%), m. p. 57·5—58·5° (Found: C, 74·95; H, 9·65; OAc, 27·9. $C_{11}H_{17}$·OAc requires C, 74·95; H, 9·7; OAc, 28·35%). Active H: 1·09.

(ii) The alcohol (II) (50 g.), acetic anhydride (68 g., 2 mols.), and acetyl bromide (1 ml.) were heated together on a steam-bath for 16 hours. The mixture was poured into water, and the product isolated with light petroleum (b. p. 40—60°). After the removal of solvent the residue crystallised; recrystallisation from ethanol gave the acetate (29·1 g., 46%). From the mother-liquors a liquid (22 g.) was obtained by evaporation, and by adding this to the next preparation the overall yield was raised, after a few cycles, to 60%.

By method (i) the following 1-*ethynyl*-2 : 2 : 6-*trimethyl*cyclo*hexyl* esters were obtained by means of the appropriate acid anhydrides: *propionate*, platelets from ethanol, m. p. 43—44°, b. p. 118—128°/12 mm. (Found: C, 75·1; H, 9·7. $C_{14}H_{22}O_2$ requires C, 75·65; H, 9·95%); n-*butyrate*, b. p. 139—141°/12 mm., $n_D^{13·5}$ 1·4802 (Found: C, 76·5; H, 10·55. $C_{15}H_{24}O_2$ requires C, 76·25; H, 10·25%); n-*valerate*, b. p. 78—80°/1 mm., n_D^{14} 1·4730 (Found: C, 77·15; H, 10·25. $C_{16}H_{26}O_2$ requires C, 76·75; H, 10·5%); n-*hexanoate*, b. p. 93—94°/0·03 mm., $n_{\rm D}^{14}$ 1·4750 (Found: C, 77·4; H, 10·45. $C_{17}H_{28}O_2$ requires C, 77·2; H, 10·7%); *crotonate*, m. p. 40—41°, b. p. 76°/0·04 mm. (Found: C, 76·7; H, 9·25. $C_{15}H_{22}O_2$ requires C, 76·9; H, 9·45%); *benzoate*, m. p. 97—98°, b. p. 164°/13 mm. (Found: C, 79·8; H, 8·0. $C_{18}H_{22}O_2$ requires C, 79·95; H, 8·2%).

(B) 1-Ethynyl-2 : 2 : 6-trimethyl*cyclo*hexyl acetate (25 g.), zinc oxide (5 g., 1 equiv.), and silicone oil (20 ml.; Dow Corning 550) were stirred together vigorously at 160 mm. and heated in an oil-bath to 160—180°, whereupon a liquid began to distil. As the rate of distillation became slower, the bath temperature was gradually raised to 200° and the pressure lowered, finally to 14 mm. The distillate (17 g.) was taken up in light petroleum (b. p. 40—60°), and the solution washed with saturated sodium hydrogen carbonate solution and dried. The product was distilled at 12 mm , and the fraction boiling up to 90° (7·5 g.) collected [light absorption (in *n*-hexane): maximum at 2280 Å; $E^{1\%}_{1\,\text{cm.}}$ 815]. Purification through the silver salt gave 2-ethynyl-1 : 3 : 3-trimethyl*cyclo*hex-1-ene (6·5 g., 36%), identical in all respects with that described under (A) above.

Crotonylideneacetone. Crotonaldehyde (2800 ml.) was added during 2 hours to a refluxing suspension of barium hydroxide (octahydrate; 195 g.) in " AnalaR " acetone (7500 ml.), and the mixture stirred for a further 1½ hours without further heating. A solution of 2N-hydrochloric acid (700 ml.) was then added to the cooled mixture, the precipitated barium chloride filtered off, and excess of acetone removed from the filtrate on a steam-bath. The residue was steam-distilled, and the product isolated with ether. After removal of the solvent the residue was fractionated through a 24″ Fenske column. A fraction having b. p. 84—86°/22 mm. and $n_{\rm D}^{15}$ 1·5210—1·5250 was collected (1520 g., 41%).

3-*Methyl*-1-(2 : 6 : 6-*trimethyl*cyclo*hex*-1-*en*-1-*yl*)*octa*-4 : 6-*dien*-1-*yn*-3-*ol* (IV).—2-Ethynyl-1 : 3 : 3-trimethyl*cyclo*hex-1-ene (14·8 g.) in ether (50 ml.) was added during 30 minutes to a solution of ethylmagnesium bromide (from magnesium, 2·92 g., and ethyl bromide, 16·4 g.) in ether (100 ml.), the temperature being kept between −30° and −40°. After being stirred overnight at room temperature, the solution was cooled to −40° and crotonylideneacetone (13·2 g.) in ether (50 ml.) was added during 30 minutes. The mixture was allowed to warm to room temperature and stirred for a further 90 minutes. A saturated solution of ammonium chloride (50 ml.) diluted with water (50 ml.) was added slowly to the ice-cold mixture, and the ethereal layer separated. After drying ($MgSO_4$), the solvent and unchanged starting material were removed, finally at 1 mm. Distillation of the residue gave 3-*methyl*-1-(2 : 6 : 6-*trimethyl*-cyclo*hex*-1-*en*-1-*yl*)*octa*-4 : 6-*dien*-1-*yn*-3-*ol* (18·8 g., 73%), b. p. 110°/10^{-5} mm., $n_{\rm D}^{15}$ 1·5345 (Found: C, 83·6; H, 10·6. $C_{18}H_{26}O$ requires C, 83·7; H, 10·1%). Active H: 1·1. Unsaturation: 4·5╒. Light absorption: see Table 2.

6-*Methyl*-8-(2 : 6 : 6-*trimethyl*cyclo*hex*-1-*en*-1-*yl*)*octa*-3 : 5-*dien*-7-*yn*-2-*ol* (V).—The acetylenic alcohol (IV) (19 g.) was dissolved in acetone (500 ml.), and sulphuric acid (3·5 g.) in water (200 ml.) was added. The clear solution was kept at room temperature for 24 hours. Saturated sodium hydrogen carbonate solution (250 ml.) was added, and the product isolated with light petroleum (b. p. 40—60°). After removal of the solvent *in vacuo* the residue was distilled to give the *alcohol* (V) (15·5 g., 60%), as a pale yellow viscous oil, b. p. 100—120°/10^{-5} mm., $n_{\rm D}^{14}$ 1·5650 (Found: C, 84·1; H, 10·2. $C_{18}H_{26}O$ requires C, 83·7; H, 10·1%). Active H: 1·05. Unsaturation: 4·9╒. Light absorption: see Table 2.

6-*Methyl*-8-(2 : 6 : 6-*trimethyl*cyclo*hexyl*)*octan*-2-*one*.—A solution of the secondary alcohol (V) (1 g.) in glacial acetic acid (15 ml.) was shaken with hydrogen in the presence of Adams's catalyst until absorption ceased. After removal of the catalyst by filtration, the product was oxidised by dropwise addition of a solution of chromic acid (0·5 g.) in acetic acid (5 ml.), and the solution kept overnight at room temperature and then poured into a mixture of ice and sodium hydroxide solution (6·5 g.; in 500 ml.), and the product isolated with ether. Removal of the solvent and distillation gave 6-methyl-8-(2 : 6 : 6-trimethyl*cyclo*hexyl)octan-2-one (0·72 g.) as a colourless liquid, b. p. 110°/0·1 mm., $n_{\rm D}^{15}$ 1·4696 (Found: C, 81·0; H, 13·0. Calc. for $C_{18}H_{34}O$: C, 81·2; H, 12·9%). The semicarbazone, prepared in the usual manner, crystallised from methanol in colourless cubes, m. p. 119—120° (Found: N, 12·6. Calc. for $C_{19}H_{37}ON_3$: N, 12·9%) (Karrer and Morf, *Helv. Chim. Acta*, 1933, **16**, 625, give m. p. 114°).

6-*Methyl*-8-(2 : 6 : 6-*trimethyl*cyclo*hex*-1-*en*-1-*yl*)*octa*-3 : 5-*dien*-7-*yn*-2-*one* (VI).—(i) A solution of the secondary alcohol (V) (10 g.) and aluminium *tert.*-butoxide (30 g.) in dry acetone (400 ml.) and dry benzene (600 ml.) was refluxed for 48 hours. The cold solution was poured into 2N-sulphuric acid (1 l.), the mixture shaken, and the organic layer separated, washed with sodium hydrogen carbonate solution and water, and dried. Removal of the solvent and distillation of the residue gave a viscous yellow liquid (7 g.), b. p. 90—100°/10^{-5} mm., $n_{\rm D}^{15}$ 1·5728.

The crude material was treated with semicarbazide acetate in aqueous methanol and gave a product (4·7 g.), m. p. 192—198°. Further recrystallisation from methanol gave the pure *semicarbazone*, m. p. 204—205° as very fine colourless needles (Found : N, 13·3. $C_{19}H_{27}ON_3$ requires N, 13·4%). Light absorption (in ethanol) : maxima at 3420 and 2640 Å, ε 43 500 and 14 200, respectively. Inflection at 3060—3110 Å, ε 21 600.

The semicarbazone (4 g.), 3N-sulphuric acid (150 ml.), and light petroleum (300 ml. ; b. p. 80—100°) were refluxed with vigorous stirring for 16 hours. The cooled mixture was filtered from unchanged semicarbazone, and the petroleum layer washed with saturated sodium hydrogen carbonate solution and dried (Na_2SO_4). Removal of the solvent and distillation of the product gave the *ketone* (VI) (1 g.), b. p. 100°/10^{-5} mm., n_D^{14} 1·6022 (Found : C, 84·5; H, 9·7. $C_{18}H_{24}O$ requires C, 84·3; H, 9·4%). Light absorption : see Table 2.

Hydrogenation. The ketone (340 mg.) on hydrogenation in ethyl acetate with platinic oxide catalyst absorbed 170 ml. of hydrogen at 20°/764 mm., equivalent to 5·2$|^{=}$ per molecule. Isolation of the product and treatment with semicarbazide acetate gave the semicarbazone of 6-methyl-8-(2 : 6 : 6-trimethyl*cyclo*hexyl)octan-2-one m. p. 118—120° undepressed when the sample was mixed with the specimen described previously.

(ii) A solution of the secondary alcohol (V) (1 g.) in light petroleum (b. p. 40—60°; 50 ml.) was shaken with manganese dioxide (10 g.) for 1 hour. Isolation and distillation gave the ketone (VI) (0·8 g.), n_D^{15} 1·5975. Light absorption (in *n*-hexane) : maxima at 3360 and 2430 Å, $E^{1\%}_{1\,\text{cm.}}$ 842 and 440, respectively.

Active Manganese Dioxide.—A solution of manganese sulphate (tetrahydrate; 1110 g.) in water (1500 ml.) and a solution of sodium hydroxide (40% ; 1170 ml.) were added simultaneously during 1 hour to a hot stirred solution of potassium permanganate (960 g.) in water (6 l.). Manganese dioxide was precipitated soon after the start as a fine brown solid. Stirring was continued for a further hour and the solid was then collected with a centrifuge and washed with water until the washings were colourless. The solid was dried in an oven at 100—120° and ground to a fine powder (920 g.) before use.

Oxidations with Manganese Dioxide.—*Cinnamaldehyde.* Cinnamyl alcohol (5 g.) was stirred for 30 minutes with a suspension of manganese dioxide (commercial sample; 50 g.) in carbon tetrachloride (250 ml.). The mixture was filtered and the filtrate evaporated. The residue was dissolved in an aqueous-alcoholic solution of semicarbazide hydrochloride (7·5 g.) and sodium acetate (9 g.), heated to 60°, and then kept at room temperature for 2 hours. The cinnamaldehyde semicarbazone (5 g.), m. p. 212—215° (lit., m. p. 215°), was collected.

Acraldehyde. Allyl alcohol (2 g.) was stirred for 30 minutes with a suspension of manganese dioxide (commercial sample; 20 g.) in light petroleum (b. p. 40—60°; 100 ml.) and the mixture was quickly filtered without suction. The precipitate was washed with solvent and the combined filtrates were added to a solution of Brady's reagent (8 g. of 2 : 4-dinitrophenylhydrazine, 16 ml. of concentrated sulphuric acid, and methanol to a total volume of 200 ml.). Water was added, and red crystalline acraldehyde 2 : 4-dinitrophenylhydrazone (4·7 g.), m. p. 165° (lit., m. p. 165°), separated.

*Oct-*3*-yn-*2*-one.* Oct-3-yn-2-ol (1 g.) (Bowden, Heilbron, Jones, and Weedon, *J.*, 1946, 43) was stirred for 30 minutes with a suspension of manganese dioxide (commercial sample; 10 g.) in light petroleum (b. p. 40—60°; 50 ml.). The mixture was filtered and evaporated, and the residue was treated with semicarbazide hydrochloride in the usual fashion to give the desired semicarbazone (1·45 g.), m. p. 109° (lit., m. p. 109°).

3-*Dehydro*-β-*ionone.* 3-Dehydro-β-ionol (0·5 g.) (Sobotka and Chanley, *J. Amer. Chem. Soc.*, 1949, **71**, 4136) in light petroleum (b. p. 40—60°; 25 ml.) was shaken with active manganese dioxide (5 g.) for 1 hour. After removal of the solvent the residue was treated with a 1% solution of 2 : 4-dinitrophenylhydrazine in ethanol containing 1% of hydrochloric acid (50 ml.). The orange crystals deposited (0·36 g.) had m. p. 140—141° undepressed when the sample was mixed with a specimen prepared from 3-dehydro-β-ionone synthesised by another route (Sobotka and Chanley, *loc. cit.*).

Ethyl 3-*Hydroxy*-3 : 7-*dimethyl*-9-(2 : 6 : 6-*trimethyl*cyclo*hex*-1-*en*-1-*yl*)*nona*-4 : 6-*dien*-8-*yne*-1-*carboxylate* (VII). The ketone (VI) (6 g.) in benzene (150 ml.) reacted with ethyl bromoacetate (4·1 g.) and activated zinc (1·18 g.) to give a red viscous liquid (7·0 g.), n_D^{15} 1·550. Light absorption (in *n*-hexane) : maxima at 3000 and 2250 Å; $E^{1\%}_{1\,\text{cm.}}$ 710 and 448, respectively. Distillation gave the pure *hydroxy-ester*, b. p. 140°/10^{-5} mm., n_D^{14} 1·5490 (Found : C, 76·8; H, 9·3; OEt, 12·2. $C_{20}H_{27}O_2{\cdot}OEt$ requires C, 76·7; H, 9·4; OEt, 13·1%). Unsaturation : 4·5$|^{=}$. Active H : 1·0. Light absorption : see Table 2.

Ethyl 3 : 7-*Dimethyl*-9-(2 : 6 : 6-*trimethyl*cyclo*hex*-1-*en*-1-*yl*)*nona*-2 : 4 : 6-*trien*-8-*yne*-1-*carb*-

oxylate (VIII; R = Et).—The hydroxy-ester (VII) (5·7 g.) was refluxed with toluene-*p*-sulphonic (0·05 g.) in benzene (90 ml.) for 4 hours. The solution was washed with saturated sodium hydrogen carbonate solution, dried (Na_2SO_4), and evaporated, to give the crude ester as a dark red liquid (5·0 g.), n_D^{14} 1·610. It was chromatographed on deactivated alumina (Grade III Brockmann) with *n*-hexane as solvent and developer, and gave the *ethyl* ester (VIII; R = Et) as a dark yellow oil (2·8 g.), n_D^{14} 1·622 (Found: C, 81·1; H, 9·4; OEt, 14·2. $C_{29}H_{25}O\cdot OEt$ requires C, 80·9; H, 9·3; OEt, 13·8%). Unsaturation: 6·3$|^{=}$. Light absorption: see Table 2.

3 : 7-*Dimethyl*-9-(2 : 6 : 6-*trimethyl*cyclo*hex*-1-*en*-1-*yl*)*nona*-2 : 4 : 6-*trien*-8-*yne*-1-*carboxylic Acid* (VIII; R = H).—The ester (VIII; R = Et) (3·0 g.) in alcoholic potassium hydroxide (10%; 100 ml.) was shaken for several hours until solution was complete, and set aside for 5 days. Water (300 ml.) was added, the solution extracted with ether, and the pH of the aqueous portion lowered to 3·0 by addition of phosphoric acid. The emulsion was extracted with ether, and the ethereal extract dried ($MgSO_4$) and evaporated, giving a yellow crystalline solid. Recrystallisation from ether gave the *acid* as fine yellow needles, m. p. 161° (Found: C, 80·6; H, 8·9. $C_{20}H_{26}O_2$ requires C, 80·4; H, 8·8%). Light absorption: see Table 2.

3 : 7-*Dimethyl*-9-(2 : 6 : 6-*trimethyl*cyclo*hex*-1-*en*-1-*yl*)*nona*-2 : 4 : 6-*trien*-8-*yn*-1-*ol* (8 : 9-*Dehydrovitamin A*) (IX).—The above ester (VIII; R = Et) (5·7 g.) in ether (40 ml.) was added dropwise to a stirred and cooled solution of lithium aluminium hydride (10 g.) in ether (36 ml.) at such a rate that the temperature did not exceed −65°. The temperature was then allowed to rise to and was kept at −30° for 1 hour. Ethyl acetate (0·8 g.) was added, the complex decomposed by addition of a saturated ammonium chloride solution (20 ml.), and the ethereal extract washed with water, dried (Na_2SO_4), and evaporated to give the crude alcohol (IX) (4·8 g.), n_D^{14} 1·6032. Light absorption (in *n*-hexane): maxima at 3280 and 2520 Å, $E_{1\,\text{cm.}}^{1\%}$ 890 and 493, respectively. This was purified either by distillation at 140°/10^{-5} mm. or by chromatography on a column of deactivated alumina (Brockmann Grade III) shielded from the light, light petroleum (b. p. 40—60°) being used as solvent, and, with the addition of 5% ether, as developer. The dehydrovitamin separated as a colourless band at the top of the column, its presence being indicated by a pale blue fluorescence in ultra-violet light. The column was cut and extracted with ether. Evaporation gave a pale yellow oil (1·2 g.), n_D^{14} 1·610. Light absorption (in *n*-hexane): maxima at 3280 and 2520 Å, $E_{1\,\text{cm.}}^{1\%}$ 1080 and 557, respectively. This oil (1·5 g.) in benzene (15 ml.) containing pyridine (5 ml.) was added to anthraquinone-2-carboxyl chloride (2·0 g.) in benzene (10 ml.), and the mixture heated on a steam-bath for 30 minutes. The material was worked up in the usual manner and the ester purified by chromatography on activated alumina, benzene–light petroleum (b. p. 40—60°) (1 : 1) being used as solvent and developer. Isolation of the chromatographed product yielded a red oil which on cooling in acetone solution gave the *anthraquinone*-2-*carboxylate* as fine red needles (1·1 g.), m. p. 137° (Found: C, 81·3; H, 6·8. $C_{35}H_{34}O_4$ requires C, 81·1; H, 6·5%). Light absorption (in ethanol): maxima at 3280 and 2550 Å, ε 39 400 and 66 300, respectively. If the acetone solution of the ester was subjected to rapid cooling the product was obtained in the form of small yellow needles, m. p. 113° (Found: C, 80·9; H, 6·7%). Light absorption (in ethanol): maxima at 3280 and 2550 Å, ε 39 800 and 60 600, respectively.

The above ester (0·4 g.) in 2N-alcoholic potassium hydroxide (10 ml.) was heated at 50° for 10 minutes. The product was isolated with light petroleum (b. p. 40—60°), and the crystalline residue recrystallised from *n*-pentane at −50°, to give 8 : 9-*dehydrovitamin A* as colourless needles, m. p. 47—50° (Found: C, 84·2; H, 9·8. $C_{20}H_{28}O$ requires C, 84·5; H, 9·9%). Light absorption: see Table 2.

p-*Phenylazobenzoate.* 8 : 9-Dehydrovitamin A (0·8 g.) was converted into its *p*-phenylazobenzoate by the method of Isler *et al.* (*Helv. Chim. Acta*, 1947, **30**, 1911). The crude ester was chromatographed on a column of alumina (Brockmann Grade III) in light petroleum (b. p. 40—60°)–ether (9 : 1) and crystallised from light petroleum (b. p. 40—60°) at −70°, to give the p-*phenylazobenzoate* as orange needles, m. p. 93° (Found: N, 5·7. $C_{33}H_{36}O_2N_2$ requires N, 5·7%). Light absorption (in ethanol): maxima at 3310 and 2520 Å, ε 60 800 and 24 700, respectively.

3-*Methylocta*-4 : 6-*dien*-1-*yn*-3-*ol*.—A rapid stream of acetylene was passed for 1¾ hours into liquid ammonia (6 l.), stirred and cooled in a solid carbon dioxide–alcohol bath. Calcium turnings (90 g.) were added during 1 hour, and after a further hour the acetylene flow was reduced, and crotonylideneacetone (300 g.) in dry ether (300 ml.) run in during 1 hour. The cooled mixture was stirred for another 4 hours, then ammonium chloride (470 g.) was added gradually and the ammonia evaporated on a steam-bath. Water was added to the residue and the product was collected in ether, washed, dried, and distilled, giving a colourless oil (280 g.), b. p. 52—54°/0·8 mm., n_{D}^{15} 1·5075.

The oil was freed from unchanged crotonylideneacetone as described by Cheeseman, Heilbron, Jones, Sondheimer, and Weedon (*J.*, 1949, 2032), giving the desired product (200 g.), b. p. 58°/1 mm., n_{D}^{14} 1·5050. Light absorption (in ethanol) : maximum at 2270 Å, ε 26 500.

6-*Methylocta*-3 : 5 : 7-*trien*-2-*one* (X).—A solution of 6-methylocta-3 : 5 : 7-trien-2-ol (20 g.) in light petroleum (b. p. 40—60°; 1 l.) was stirred with manganese dioxide (200 g.) for 30 minutes. The mixture was filtered and the precipitate was washed well with fresh solvent. Evaporation of the combined filtrate and washings gave a crude product (16·7 g.), n_{D}^{14} 1·5965. On distillation this gave a yellow oil (11·4 g.), b. p. 65°/0·4 mm., n_{D}^{14} 1·6025. Light absorption (in *n*-hexane) : maximum at 3030 Å, ε 32 600; (in ethanol) : maximum at 3110 Å, ε 31 000.

A portion of the ketone was converted into its semicarbazone and then regenerated as follows. The semicarbazone (4·5 g.) was dissolved in a mixture of glacial acetic acid (5 ml.) and pyruvic acid (50%; 5 ml.), and water was added until cloudiness appeared. The mixture was heated on a steam-bath for 15 minutes, then cooled,. and treated with light petroleum (b. p. 40—60°) and much water. The light petroleum layer was dried and evaporated and the residue (2·4 g.) was distilled, giving a product (1·5 g.), b. p. 65°/0·4 mm., n_{D}^{16} 1·6035. Light absorption (in *n*-hexane) : maximum at 3050 Å, ε 32 200.

3 : 7-*Dimethyl*-1-(2 : 6 : 6-*trimethyl*cyclo*hex*-1-*en*-1-*yl*)*nona*-4 : 6 : 8-*trien*-1-*yn*-3-*ol* (XI).—2-Ethynyl-1 : 3 : 3-trimethyl*cyclo*hex-1-ene (III) (12 g.) in ether (20 ml.) was added during 1 hour to a solution of ethylmagnesium bromide (from ethyl bromide, 13·4 g.; magnesium, 2·37 g., and ether, 30 ml.), the temperature being kept at −20°. After being stirred overnight at room temperature, the solution was cooled to −40°, and 6-methylocta-3 : 5 : 7-trien-2-one (10·4 g.) in ether (20 ml.) added during 1 hour. After a further 2 hours' stirring at −40° the complex was decomposed with ammonium chloride (30 g.) in water (120 ml.). The ethereal layer was separated, washed with water, and dried ($MgSO_4$). The solvent was evaporated *in vacuo*, finally at 10^{-5} mm. for several hours. The product (20 g., 95%) was a clear red viscous oil, n_{D}^{15} 1·5600. Light absorption (in *n*-hexane) : maxima at 2810, 2710, and 2350 Å, $E_{1\,\text{cm.}}^{1\%}$ 950, 1100, and 625, respectively. The crude alcohol (5 g.) in light petroleum (b. p. 40—60°; 50 ml.) was chromatographed on a column of Brockmann Grade III alumina. When development with light petroleum was complete the top colourless band was cut out and eluted with ether. Distillation gave 3 : 7-*dimethyl*-1-(2 : 6 : 6-*trimethyl*cyclo*hex*-1-*en*-1-*yl*)*nona*-4 : 6 : 8-*trien*-1-*yn*-3-*ol* as a colourless viscous oil, b.p. 80—90°/10^{-5} mm., n_{D}^{15} 1·5630 (Found : C, 84·3; H, 9·8. $C_{20}H_{28}O$ requires C, 84·5; H, 9·85%). Active H : 1·1. Unsaturation : 5·92|=. Light absorption : see Table 2.

3 : 7-*Dimethyl*-9-(2 : 6 : 6-*trimethyl*cyclo*hex*-1-*en*-1-*yl*)*nona*-2 : 4 : 6-*trien*-8-*yn*-1-*ol* (IX).—A cold solution of concentrated sulphuric acid (0·4 g.) in water (80 ml.) was added to a solution of the tertiary alcohol (XI) (4 g.) in acetone (320 ml.), and the whole kept for 2 hours at room temperature in the dark; saturated sodium hydrogen carbonate solution (600 ml.) was then added, and the mixture extracted with light petroleum (b. p. 40—60°). The extracts were washed with water and dried ($MgSO_4$) and the solvent was removed *in vacuo*, to give a yellow viscous oil (4·0 g.), n_{D}^{15} 1·5910. Light absorption (in *n*-hexane) : maxima at 3260, 2810, 2690, and 2520 Å, $E_{1\,\text{cm.}}^{1\%}$ 727, 581, 557, and 543, respectively. The crude alcohol was chromatographed on Brockmann Grade III alumina in ether–light petroleum (b. p. 40—60°) (1 : 9), the dark blue fluorescence of the purified material in ultra-violet light being used to locate it on the column. Elution with ether and evaporation of the solvent gave the alcohol (IX) (2·4 g.) as a golden-yellow viscous oil, n_{D}^{14} 1·6010. Light absorption (in *n*-hexane) : maxima at 3280 and 2520 Å, ε 27 000 and 14 200, respectively. The identity of this material was proved by the preparation in good yield of the crystalline anthraquinone-2-carboxylate and *p*-phenylazobenzoate, whose m. p.s. were undepressed when the samples were mixed with authentic specimens (above).

Action of anhydrous methanolic hydrogen chloride on 8 : 9-*dehydrovitamin A*. (i) The alcohol (IX) (0·55 g.) was dissolved in methanolic hydrogen chloride (N/30; 50 ml.) and kept for 15 minutes. The solution was then diluted with iced water (50 ml.), neutralised with sodium hydroxide solution, and extracted with light petroleum (b. p. 40—60°), the extract dried ($MgSO_4$), and the solvent removed under reduced pressure. The residue was a pale yellow viscous liquid (0·25 g.), n_{D}^{14} 1·6005. Active H : 0·6. Light absorption (in *n*-hexane) : maxima at 2520 and 3280 Å, $E_{1\,\text{cm.}}^{1\%}$ 508 and 1148, respectively: inflexions at 3130—3210 and 3390—3460 Å, $E_{1\,\text{cm.}}^{1\%}$ 1041 and 867, respectively.

(ii) The quantities of materials were the same as in the preceding experiment but the solution was kept for 16 hours before being worked up. The product was a pale yellow viscous oil

(0·15 g.), n_D^{16} 1·5840 (Found: C, 82·9; H, 10·2. Calc. for $C_{20}H_{28}O$: C, 84·5; H, 9·8%). Light absorption (in *n*-hexane): maxima at 2510 and 3260 Å, $E_{1\,cm.}^{1\%}$ 436 and 828, respectively: inflexion at 3360—3450 Å, $E_{1\,cm.}^{1\%}$ 649.

1-*Hex*-1′-*yn*-1′-*yl*-2 : 2 : 6-*trimethyl*cyclo*hexanol*.—Hex-1-yne (50 g.) in ether (100 ml.) was added dropwise to a stirred solution of ethylmagnesium bromide (from magnesium, 16 g.) in ether (250 ml.), and the solution heated under reflux for 2 hours. 2 : 2 : 6-Trimethyl*cyclo*hexanone (77 g.) in ether (150 ml.) was added during 30 minutes to the cooled solution (0°), which was then stirred overnight; cold saturated ammonium chloride solution (500 ml.) was added, the product extracted with ether, and the ethereal extract washed with sodium hydrogen carbonate, dried (Na_2SO_4), and evaporated. Distillation of the product through a 12″ Fenske column gave 1-*hex*-1′-*yn*-1′-*yl*-2 : 2 : 6-*trimethyl*cyclo*hexanol* as a colourless liquid (62 g.), b. p. 133—140°/12 mm., n_D^{15} 1·4800 (Found: C, 81·0; H, 11·6. $C_{15}H_{26}O$ requires C, 81·0; H, 11·8%). Active H: 1·15. Unsaturation: 2·0|=.

Dehydration of 1-*hex*-1′-*yn*-1′-*yl*-2 : 2 : 6-*trimethyl*cyclo*hexanol*.

(2 G. of alcohol were used in all these experiments.)

		Product			
Dehydrating agent	Conditions of reaction	Wt., g.	n_D^{14}	$\lambda_{max.}$, Å	$E_{1\,cm.}^{1\%}$
Ac_2O containing 1% H_2SO_4 (7 ml.)	0°, 20 min.	0·6	1·4927 *	2320	607
H_2SO_4 (50%; 10 ml.)	50°, 4 hours	1·3	1·4860 *	2330	288
Toluene-*p*-sulphonic acid (1·0 g.)	Refluxed in PhMe (300 ml.) until no further water evolved	1·0	1·4940	2410	180
Iodine (0·1 g.)	As above	1·0	1·4900	2330	181
$H\cdot CO_2H$ (98%; 10 ml.)	Reflux for 10 min.	1·1	1·4798	2270	121
$POCl_3$ (1·0 g.)	Heated in pyridine (8·0 ml.) at 50° for 2 hours	1·1	1·4799	2280	38
Ac_2O (10 ml.)	Reflux for 2 hours	1·2	1·4947	2320	512

* n_D^{15}.

Prepared by the first method and isolated in the usual way, 1-*hex*-1′-*yn*-1′-*yl*-2 : 6 : 6-*trimethyl*cyclo*hex*-1-*ene* was obtained after fractionation twice through a short column; b.p. 130°/13 mm., n_D^{14} 1·4940 (Found: C, 88·3; H, 12·1. $C_{15}H_{24}$ requires C, 88·2; H, 11·8%). Unsaturation: 2·95 |=. Light absorption (in ethanol): maximum at 2300 Å, ε 12 540.

1-(1-*Hydroxy*-2 : 2 : 6-*trimethyl*cyclo*hexyl*)-3-*methylocta*-4 : 6-*dien*-1-*yn*-3-*ol* (XII).—1-Ethynyl-2 : 2 : 6-trimethyl*cyclo*hexanol (20 g.) in ether (50 ml.) was added dropwise to a refluxing solution of ethylmagnesium bromide (from magnesium, 7·2 g.) in ether (400 ml.), and the mixture stirred for a total of 2 hours. It was cooled to 20° and freshly distilled crotonylideneacetone (19·8 g.) in ether (50 ml.) was added. After being stirred for a further 2 hours, it was cooled to 0°, and aqueous ammonium chloride (20% solution; 500 ml.) added at such a rate that the temperature did not exceed 20°. The product was extracted with ether, the ethereal extract evaporated under reduced pressure, and the residue distilled, giving the *diol* (XII) as a pale yellow viscous oil (20·3 g.), b. p. 120°/10^{-5} mm.; n_D^{15} 1·5240 (Found: C, 78·3; H, 10·5. $C_{18}H_{28}O_2$ requires C, 78·2; H, 10·2%). Active H: 2·1. Unsaturation 3·8|=. Light absorption: see Table 2.

8-(1-*Hydroxy*-2 : 2 : 6-*trimethyl*cyclo*hexyl*)-6-*methylocta*-3 : 5-*dien*-7-*yn*-2-*ol* (XIV).—(i) The foregoing glycol (XII) (5·25 g.) in ether (20 ml.) was shaken for 16 hours with dilute hydrochloric acid (0·5%; 20 ml.). The aqueous layer was re-extracted with ether, and the combined ethereal solutions washed with saturated sodium hydrogen carbonate solution, dried (Na_2SO_4), and evaporated. Distillation gave the *glycol* (XIV) as a very viscous yellow gum (3·3 g.), b. p. 120°/10^{-4} mm., n_D^{14} 1·5445 (Found: C, 78·0; H, 10·2. $C_{18}H_{28}O_2$ requires C, 78·2; H, 10·2%). Active H: 2·0. Unsaturation: 3·8|=. Light absorption: see Table 2.

(ii) The glycol (XII) (8·9 g.) in acetone (250 ml.) was added to an aqueous solution of hydrochloric acid (1%; 100 ml.) and kept for 4 hours. The solution was neutralised by addition of saturated sodium hydrogen carbonate solution (350 ml.), and the product isolated with light petroleum (b. p. 40—60°). Distillation gave the rearranged glycol (XIV) (7·2 g.), b. p. 130°/10^{-5} mm., n_D^{15} 1·5431.

(iii) 6-Methylocta-3 : 5-dien-7-yn-2-ol (XIII) (13·6 g.) in ether (50 ml.) was added dropwise to a stirred solution of ethylmagnesium bromide (from magnesium, 5·34 g.) in ether (200 ml.). The mixture was heated under reflux for 30 minutes, cooled to room temperature, and 2 : 2 : 6-trimethyl*cyclo*hexanone (14 g.) in ether (50 ml.) added during 2 hours. The mixture was again heated under reflux for 30 minutes and cooled to 20°. Saturated ammonium chloride solution (100 ml.) was added, and the product isolated with ether. Distillation gave the glycol (XIV)

(12·6 g.) as a viscous yellow gum, b. p. 120°/10^{-5} mm., n_D^{14} 1·5447. Light absorption (in *n*-hexane) : maxima at 2690 and 2810 Å, ε 30 400 and 23 000, respectively.

6-*Methylocta*-3 : 5-*dien*-7-*yn*-2-*one*.—6-Methylocta-3 : 5-dien-7-yn-2-ol (4·0 g.), dissolved in light petroleum (b. p. 40—60°; 200 ml.), was shaken with manganese dioxide (40 g.) for 45 minutes. The dioxide was removed by filtration, and the filtrate split into two equal portions which were treated as follows : (*a*) The solvent was removed under reduced pressure, the temperature of the solution being kept below 5°, leaving 6-*methylocta*-3 : 5-*dien*-7-*yn*-2-*one* (1·3 g.) as a pale red liquid, n_D^{14} 1·5665 (Found : C, 80·4; H, 7·5. $C_9H_{10}O$ requires C, 80·3; H, 7·5%). Light absorption (in *n*-hexane) : maximum at 3030 Å, ε 18 300; inflection at 2630—2710 Å, ε 12 000. (*b*) After removal of the solvent the residue (1·5 g.) was converted in the usual manner into the *semicarbazone*, pale yellow plates (from ethanol), m. p. 120° (decomp.) (Found : C, 62·7; H, 6·8; N, 20·4. $C_{10}H_{13}ON_3$ requires C, 62·8; H, 6·9; N, 22·0%). Light absorption (in ethanol) : maxima at 3270 and 3130 Å, ε 47 700 and 50 000, respectively.

8-(1-*Hydroxy*-2 : 2 : 6-*trimethyl*cyclo*hexyl*)-6-*methylocta*-3 : 5-*dien*-7-*yn*-2-*one* (XV).—(i) The C_{18} glycol (XIV) (20 g.), aluminium *tert.*-butoxide (45 g.) in dry acetone (1 l.), and dry benzene (750 ml.) were heated under reflux for 40 hours. The cooled mixture was decomposed with 2N-sulphuric acid (2 l.), and the benzene layer washed with sodium hydrogen carbonate solution, dried ($MgSO_4$), and evaporated. Distillation gave a viscous yellow liquid (15 g.), b. p. 135°/10^{-5} mm., n_D^{14} 1·5595. Light absorption (in *n*-hexane) : maxima at 3020 and 2240 Å, $E_{1\,cm.}^{1\%}$ 742 and 450, respectively.

(ii) The glycol (XIV) (30 g.) in carbon tetrachloride (900 ml.) was stirred with manganese dioxide (300 g.) for 1 hour. After filtration, the filtrate was evaporated and the residue distilled to give a viscous oil (20 g.), n_D^{14} 1·5678. Light absorption (in *n*-hexane) : maximum at 3000 Å, $E_{1\,cm.}^{1\%}$ 946. Inflection at 3030—3130 Å, $E_{1\,cm.}^{1\%}$ 831.

The *semicarbazone*, prepared in the usual manner, formed fine needles (from aqueous methanol), m. p. 194° (sintered, 140—145°) (Found : N, 12·6. $C_{19}H_{29}O_2N_3$ requires N, 12·7%). Light absorption (in ethanol) : maxima at 3330, 3160, and 2320 Å, ε 43 500, 49 800, and 4300, respectively.

The semicarbazone (8·5 g.), 2N-sulphuric acid (100 ml.), and light petroleum (b. p. 80—100°; 200 ml.) were heated under reflux with rapid stirring for 6 hours. The organic layer was separated, washed with sodium hydrogen carbonate solution, dried (Na_2SO_4), and evaporated. Distillation gave 8-(1-*hydroxy*-2 : 2 : 6-*trimethyl*cyclo*hexyl*)-6-*methylocta*-3 : 5-*dien*-7-*yn*-2-*one* as a viscous yellow liquid (4·2 g.), b. p. 140°/10^{-4} mm., n_D^{15} 1·5708 (Found : C, 78·8; H, 9·6. $C_{18}H_{26}O_2$ requires C, 78·6; H, 9·6%). Active H : 1·05. Unsaturation : 3·9|=. Light absorption : see Table 2.

6-*Methyl*-8-(2 : 6 : 6-*trimethyl*cyclo*hex*-1-*en*-1-*yl*)*octa*-3 : 5-*dien*-7-*yn*-2-*one* (VI).—A mixture of the hydroxy-ketone (XV) (50 g.) and toluene-*p*-sulphonic acid (2 g.) in toluene (2 l.) was distilled slowly until the distillate was free from traces of water (2½ hours). The residue was washed with saturated sodium hydrogen carbonate solution, dried (Na_2SO_4), and evaporated. Distillation gave the dehydro-C_{18} ketone (VI) (34 g.) as a pale yellow liquid, b. p. 140°/10^{-5} mm., n_D^{15} 1·5960. Light absorption (in *n*-hexane) : maxima at 3380 and 2440 Å, $E_{1\,cm.}^{1\%}$ 741 and 447, respectively. The semicarbazone was prepared and had m. p. 204—205° undepressed when the sample was mixed with an authentic specimen (above).

Ethyl 3-*Hydroxy*-9-(1-*hydroxy*-2 : 2 : 6-*trimethyl*cyclo*hexyl*)-3 : 7-*dimethylnona*-4 : 6-*dien*-8-*yne*-1-*carboxylate* (XVI).—The hydroxy-ketone (XV) (5·5 g.), ethyl bromoacetate (8·0 g.), activated zinc (3·0 g.), and a crystal of iodine in benzene (50 ml.) were heated under reflux for 2 hours. The product gave the *ethyl* ester (XVI) as a viscous red liquid (5·7 g.), n_D^{14} 1·5318 (Found : C, 72·8; H, 9·1; OEt, 11·1. $C_{20}H_{29}O_3{\cdot}OEt$ requires C, 72·9; H, 9·5; OEt, 12·4%). Active H : 2·2. Light absorption : see Table 2.

Ethyl 9-(1-*Hydroxy*-2 : 2 : 6-*trimethyl*cyclo*hexyl*)-3 : 7-*dimethylnona*-2 : 4 : 6-*trien*-8-*yne*-1 *carboxylate* (XVII).—The foregoing ester (XVI) (2·0 g.) and toluene-*p*-sulphonic acid (0·05 g.) in benzene (150 ml.) were heated under reflux for 5 hours. Isolation of the product in the usual manner gave a dark viscous oil (0·9 g.), n_D^{14} 1·6000, which was chromatographed on a column of deactivated alumina with light petroleum (b. p. 40—60°) as solvent and developer, and gave the *ethyl* ester (XVII) as a pale yellow viscous liquid, n_D^{14} 1·605—1·610 (Found : C, 77·0; H, 8·8; OEt, 11·4. $C_{20}H_{27}O_2{\cdot}OEt$ requires C, 76·7; H, 9·4; OEt, 13·1%). Active H : 0·85. Light absorption : see Table 2.

Ethyl 3 : 7-*Dimethyl*-9-(2 : 6 : 6-*trimethyl*cyclo*hex*-1-*en*-1-*yl*)*nona*-2 : 4 : 6-*trien*-8-*yne*-1-*carboxylate* (VIII; R = Et).—The glycol ester (XVI) (2·9 g.), toluene-*p*-sulphonic acid (0·85 g.), and toluene (150 ml.) were heated under reflux for 5 hours. Isolation of the crude product and purification by chromatography on a column of deactivated alumina by use of light petroleum (b. p. 40—60°) as solvent and developer gave 8 : 9-dehydrovitamin A acid ethyl ester (VIII; R = Et) (0·7 g.), n_D^{14} 1·620—1·623 (Found : C, 80·9 ; H, 9·2; OEt, 13·6. Calc. for $C_{20}H_{25}O_2{\cdot}OEt$: C, 80·9; H, 9·3; OEt, 13·8%).

1-(1-*Hydroxy*-2 : 2 : 6-*trimethyl*cyclo*hexyl*)-3 : 7-*dimethylnona*-4 : 6 : 8-*trien*-1-*yn*-3-*ol* (XVIII).—A solution of 1-ethynyl-2 : 2 : 6-trimethyl*cyclo*hexanol (16·6 g.) in benzene (150 ml.) was added to a solution of ethylmagnesium bromide (from magnesium, 5·84 g.) in ether (50 ml.), the mixture stirred under reflux for 30 minutes and then cooled to room temperature, and 6-methylocta-3 : 5 : 7-trien-2-one (13·6 g.) in benzene (150 ml.) was added in about 30 minutes. The solution was refluxed for 15 minutes, cooled, and poured on ice and ammonium chloride solution. The benzene layer was washed, dried, and evaporated *in vacuo,* leaving an oil (31·1 g.). Light absorption (in ethanol) : maximum at 2690 Å, $E^{1\%}_{1\,\text{cm.}}$ 1180. A sample of this material was purified for analysis by chromatography on alumina (Brockmann Grade I), followed by distillation, giving the *diol* (XVIII) as a yellow oil, b. p. 160—180°/10^{-5} mm., n_D^{15} 1·5493 (Found : C, 79·4; H, 10·2. $C_{20}H_{30}O_2$ requires C, 79·4; H, 10·0%). Light absorption : see Table 2.

9-(1-*Hydroxy*-2 : 2 : 6-*trimethyl*cyclo*hexyl*)-3 : 7-*dimethylnona*-2 : 4 : 6-*trien*-8-*yn*-1-*ol* (XIX).—The preceding product (XVIII) (16·5 g.) was dissolved in aqueous acetone (90%; 330 ml.) containing sulphuric acid (0·1% w/v), and the solution, after 3 hours at room temperature, was poured into a large volume of water. The product was collected in ether (sodium sulphate being used to break emulsions), the solution washed with alkali and water, and the solvent evaporated. The residual viscous oil (15·9 g.) was taken up in *cyclo*hexane (50 ml.), and, on cooling and seeding, the solution deposited the *diol* (XIX) as colourless hexagonal plates (4·3 g.), m. p. 76—80°, raised by recrystallisation from the same solvent to 78—80° (Found : C, 79·3; H, 10·1. $C_{20}H_{30}O_2,\frac{1}{4}C_6H_{12}$ requires C, 79·8; H, 10·3%). Active H : 2·05. Light absorption (in ethanol) : maxima at 3170, 3020, and 2260 Å, ε 36 500, 45 300, and 7730, respectively; inflection at 2870—2960 Å, ε 34 400. The compound gave a green colour with the Carr–Price reagent.

When the crystals were heated at 56°/0·1 mm. they lost 6·5% of their weight (corresponding to $\frac{1}{4}$ mol. of *cyclo*hexane of crystallisation) and then had m. p. 93—95° (Found : C, 79·2; H, 10·1. $C_{20}H_{30}O_2$ requires C, 79·4; H, 10·0%). Light absorption : see Table 2. The same unsolvated *compound* was also obtained by recrystallisation of the *cyclo*hexane-containing crystals from ether. The higher-melting solid reverted to the original solvated modification on recrystallisation from *cyclo*hexane.

The necessary seed crystals were obtained *via* the *anthraquinone*-2-*carboxylate* as follows. Dry pyridine (6 ml.) was added to a solution of the crude glycol (6 g.) and anthraquinone-2-carboxyl chloride (3·2 g.) in dry benzene (50 ml.) and the mixture was refluxed for 45 minutes. Water (6 ml.) was added to the mixture which was then shaken for a few minutes and filtered. The filtrate was washed successively with dilute hydrochloric acid, sodium hydroxide solution and water, dried, and evaporated. The residue, after trituration with ether, afforded a solid product (1·3 g.), m. p. 180—182°, which separated from benzene in pale yellow prisms, m. p. 181—182°, resolidifying sharply at 183°, and again melting gradually with decomposition up to about 220° (Found : C, 78·3; H, 6·7. $C_{35}H_{36}O_5$ requires C, 78·3; H, 6·7%). Light absorption (in chloroform) : maxima at 2580, 2800, 3060, and 3200 Å, ε 62 500, 31 400, 41 600, and 38 000, respectively.

The anthraquinone-2-carboxylate (0·2 g.) was hydrolysed by heating it with 2N-alcoholic potassium hydroxide (5 ml.) at 50° for 10 minutes. The mixture was then filtered, and the filtrate poured into water. The product was collected by means of ether and recrystallised twice from *cyclo*hexane, to give material, m. p. 78—80°, identical with that described above.

4-(1-*Hydroxy*-2 : 6 : 6-*trimethyl*cyclo*hexyl*)*but*-3-*yn*-2-*ol*.—1-Ethynyl-2 : 2 : 6-trimethyl*cyclo*hexanol (14·3 g.) in ether (50 ml.) was added to a stirred refluxing solution of ethylmagnesium bromide (magnesium, 5 g.; ethyl bromide, 28 g.; ether, 70 ml.), and the product refluxed for 2 hours. It was cooled to −10°, and freshly distilled acetaldehyde (3·8 g.) in ether (25 ml.) added with stirring. Stirring was continued for 2 hours while the mixture warmed to 5°. On isolation of the product in the usual way, followed by distillation at 0·15 mm. through a short column, the *diol* (13·1 g., 72·5%) was obtained, b. p. 107—108°/0·15 mm. It solidified and gave prisms, m. p. 112—113°, from light petroleum (b. p. 100—120°) (Found : C, 74·1; H, 10·35. $C_{13}H_{22}O_2$ requires C, 74·25; H, 10·55%). Active H : 2·1.

The standard procedure gave the 3 : 5-*dinitrobenzoate* as pale yellow needles, m. p. 132·5—133·5°, from ethanol (Found : C, 59·2; H, 6·0; N, 7·15. $C_{20}H_{24}O_7N_2$ requires C, 59·4; H, 6·0; N, 6·95%).

4-(1-*Hydroxy*-2 : 2 : 6-*trimethyl*cyclo*hexyl*)*but*-3-*yn*-2-*one*.—(i) The foregoing diol (1 g.) in light petroleum (b. p. 40—60°; 50 ml.) was stirred with active manganese dioxide (10 g.) for 1 hour. The product was distilled and gave the *hydroxy-ketone* (0·65 g.), b. p. 100°/0·1 mm., n_{D}^{14} 1·4994 (Found: C, 74·7; H, 9·5. $C_{13}H_{20}O_2$ requires C, 74·95; H, 9·7%). Active H: 0·8. Light absorption (in *n*-hexane): maxima at 2190 and 2980 Å, ε 7500 and 97, respectively. (ii) 1-Ethynyl-2 : 2 : 6-trimethyl*cyclo*hexanol (10·6 g.) in ether (30 ml.) was treated with a solution of ethylmagnesium bromide (magnesium, 3·7 g.; ethyl bromide, 20 g.; ether, 50 ml.) as above, and after 2 hours' refluxing the solution was cooled to room temperature. It was added to a stirred solution of acetic anhydride (6·6 g.) in ether (50 ml.) at −65°, and the product stirred for 2 hours while it warmed to 10°. On isolation in the normal way and distillation at 0·1 mm., a fraction, b. p. 100—105° (6·06 g.; 45%), was collected and redistilled. It had b. p. 90°/0·05 mm., n_{D}^{14} 1·4957. Light absorption (in *n*-hexane): maxima at 2200 and 2950 Å, $E_{1\,\mathrm{cm.}}^{1\%}$ 340 and 4·35, respectively.

8-(1-*Hydroxy*-2 : 2 : 6-*trimethyl*cyclo*hexyl*)-6-*methylocta*-3 : 5 : 7-*trien*-2-*ol* (XX).—A solution of the C_{18} acetylenic glycol (XIV) (20·2 g.) in ether (500 ml.) was added to a stirred solution of lithium aluminium hydride (3·5 g.) in ether (167 ml.) during 20 minutes. The mixture was stirred under reflux for 3 hours, then cooled at 0° and treated cautiously with ice, followed by a solution of tartaric acid (10 g.) in water (500 ml.). The ethereal layer was washed, dried, and evaporated *in vacuo*, leaving an oil (19 g.). Light absorption (in *n*-hexane): maxima at 2410, 2750, and 3130 Å, $E_{1\,\mathrm{cm.}}^{1\%}$ 550, 615, and 295, respectively. This oil was dissolved in light petroleum (b. p. 40—60°; 50 ml.) and chromatographed on Brockmann Grade III alumina (400 g.). The chromatogram was developed with light petroleum until the two yellow bands which fluoresced in ultra-violet light had reached the middle of the column. The portion of the column above these bands was eluted with ether and gave, on evaporation, a yellow oil (10·5 g.), which was used for the next stage. Light absorption (in *n*-hexane): maxima at 2740 and 3130 Å, $E_{1\,\mathrm{cm.}}^{1\%}$ 911 and 235, respectively. Infra-red absorption analysis showed 91% reduction of the triple bond. Further purification of this material by chromatography gave 8-(1-*hydroxy*-2 : 2 : 6-*trimethyl*cyclo*hexyl*)-6-*methylocta*-3 : 5 : 7-*trien*-2-*ol* as a colourless viscous oil, n_{D}^{15} 1·5530 (Found: C, 77·9; H, 10·8. $C_{18}H_{30}O_2$ requires C, 77·7; H, 10·8%). Active H: 2·0. Unsaturation: 3·15|=. Light absorption: see Table 2.

8-(1-*Hydroxy*-2 : 2 : 6-*trimethyl*cyclo*hexyl*)-6-*methylocta*-3 : 5 : 7-*trien*-2-*one* (XXI).—A solution of the triene glycol (XX) (7 g.) in light petroleum (b. p. 40—60°; 350 ml.) was stirred with manganese dioxide (70 g.) for 30 minutes. The mixture was filtered, and the solid washed with light petroleum (350 ml.) The filtrate was evaporated *in vacuo*, leaving a yellow oil (6·1 g.), n_{D}^{17} 1·5720, which was used for the next stage. Light absorption (in *n*-hexane): maxima at 2250 and 3130 Å, $E_{1\,\mathrm{cm.}}^{1\%}$ 340 and 925, respectively. A sample of this *hydroxy-ketone* was purified by chromatography in light petroleum (b. p. 40—60°) on Brockmann Grade II alumina, followed by distillation, and was obtained as a viscous yellow oil, b. p. 130°/10^{-4} mm., n_{D}^{15} 1·5773 (Found: C, 78·2; H, 10·4. $C_{18}H_{28}O_2$ requires C, 78·2; H, 10·2%). Active H: 1·15. Unsaturation: 2·9|=. Light absorption: see Table 2. The *semicarbazone* separated from methanol as yellow microcrystalline powder, m. p. 213—215° (Found: C, 68·5; H, 9·4; N, 12·6. $C_{19}H_{31}O_2N_3$ requires C, 68·5; H, 9·3; N, 12·6%). Light absorption (in ethanol): maxima at 2350, 3250, and 3400 Å, ε 4900, 57 500, and 48 600, respectively.

The semicarbazone (1·0 g.) was refluxed with light petroleum (b. p. 100—120°; 10 ml.) and 2N-hydrochloric acid (20 ml.) for 2 hours. A yellow oil (0·4 g.), n_{D}^{15} 1·6024, was isolated from the petroleum layer. Light absorption (in *n*-hexane): maxima at 2250 and 3240 Å, $E_{1\,\mathrm{cm.}}^{1\%}$ 253 and 1088, respectively.

6-*Methyl*-8-(2 : 6 : 6-*trimethyl*cyclo*hex*-1-*en*-1-*yl*)*octa*-3 : 5 : 7-*trien*-2-*one*.—A solution of the hydroxy-ketone (XXI) (9·2 g.) and toluene-*p*-sulphonic acid (0·18 g.) in dry toluene (230 ml.) was refluxed for 30 minutes. The solution was washed with aqueous sodium hydrogen carbonate and water, and the solvent removed *in vacuo*. The residue was partly purified by chromatography on Brockmann Grade II alumina in light petroleum (b. p. 40—60°). The chromatogram was developed until the area which appeared brown in ultra-violet light had reached the bottom of the column. Extraction of the column with ether, evaporation of the solvent, and distillation of the residue gave a pale yellow viscous oil (1·9 g.), b.p. 120°/10^{-4} mm., n_{D}^{16} 1·5900. Light absorption (in *n*-hexane): maximum at 3280 Å, $E_{1\,\mathrm{cm.}}^{1\%}$ 755. The semicarbazone separated from methanol as yellow plates, m. p. 190—192° (decomp.) undepressed when the sample was mixed with an authentic specimen prepared from β-ionone by the method of van Dorp and Arens (*Rev. Trav. chim.*, 1946, **65**, 338) (Found: C, 72·3; H, 9·4; N, 13·2. Calc. for $C_{19}H_{29}ON_3$: C, 72·4; H, 9·2; N, 13·3%). Light absorption (in ethanol): maximum at 3450 Å, ε 53 900.

The semicarbazone (0·54 g.) was refluxed with light petroleum (b. p. 100—120°; 15 ml.)

and 2N-hydrochloric acid (15 ml.) for 2 hours. A viscous yellow oil, b. p. 120°/10^{-4} mm, n_D^{17} 1·6230, was isolated from the petroleum layer (Found : C, 83·7; H, 10·2. Calc. for $C_{18}H_{26}O$: C, 83·9; H, 10·1%). Unsaturation : 3·8|=. Light absorption : see Table 2.

9-(1-*Hydroxy*-2 : 2 : 6-*trimethyl*cyclo*hexyl*)-3 : 7-*dimethylnona*-2 : 4 : 6 : 8-*tetraen*-1-*ol* (XXII ; R = H).—A solution of 9-(1-hydroxy-2 : 2 : 6-trimethyl*cyclo*hexyl)-3 : 7-dimethylnona-2 : 4 : 6-trien-8-yn-1-ol (XIX) (3 g.) in ether (150 ml.) was added to a stirred solution of lithium aluminium hydride (0·75 g.) in dry ether (190 ml.) during 1 hour. The mixture was stirred under reflux for 3 hours, then cooled to 0° and treated cautiously with ice and a saturated solution of tartaric acid. The ethereal layer was washed with saturated tartaric acid solution and water, dried, and evaporated *in vacuo*, leaving a pale yellow oil (2·8 g.). Crystallisation from *cyclo*hexane gave the *diol* (XXII ; R = H) as needles, m. p. 122—127° (Found : C, 78·7; H, 10·6. $C_{20}H_{32}O_2$ requires C, 78·95; H, 10·5%). Active H : 1·8. Unsaturation : 3·6|=. Light absorption : see Table 2.

9-(1-*Hydroxy*-2 : 2 : 6-*trimethyl*cyclo*hexyl*)-3 : 7-*dimethylnona*-2 : 4 : 6 : 8-*tetraen*-1-*yl Acetate* (XXII; R = Ac).—A solution of acetyl chloride (1·75 g.) in dry ether (70 ml.) was added during 30 minutes to a solution of the above glycol (XXII; R = H) (3·4 g.) and dry pyridine (5·4 ml.) in dry ether (70 ml.) cooled to 0°, so that the temperature did not exceed 10°. The mixture was kept at room temperature for 40 minutes, and decomposed with N-sulphuric acid with cooling, so that the temperature did not exceed 10°. The ethereal layer was washed with N-sulphuric acid and saturated sodium hydrogen carbonate solution, dried, and evaporated *in vacuo*, leaving a crystalline residue (3·6 g.; m. p. 96—104°). Recrystallisation from *cyclo*hexane gave the *acetate* (XXII; R = Ac), m. p. 110—111° (Found : C, 75·9; H, 9·75. $C_{22}H_{34}O_3$ requires C, 76·3; H, 9·8%). Active H : 1·15. Unsaturation: 3·95|=.

Vitamin A Acetate.—A solution of the hydroxy-acetate (XII; R = Ac) (3 g.) and toluene-*p*-sulphonic acid (18 mg.) in toluene (450 ml.) was heated at 80° for 30 minutes. The cooled solution was washed with saturated sodium hydrogen carbonate solution and water, dried, and evaporated *in vacuo*. The residue [light absorption (in ethanol) : maxima at 3270, 3680, and 3900 Å, $E^{1\%}_{1\,\text{cm.}}$ 741, 514, and 321, respectively. Inflexion at 3390—3490 Å, $E^{1\%}_{1\,\text{cm.}}$ 641] was chromatographed on Brockmann Grade III alumina in a 1 : 1 mixture of light petroleum (b. p. 40—60°) and benzene. Development was continued until the required fraction, which had a bright blue fluorescence in ultra-violet light, had been washed through. Evaporation *in vacuo* gave impure vitamin A acetate (1·66 g.). Light absorption (in ethanol) : maxima at 3300, 3680, and 3910 Å, $E^{1\%}_{1\,\text{cm.}}$ 892, 767, and 503, respectively.

Vitamin A Anthraquinone-2-*carboxylate.*—The above impure vitamin A acetate (1·66 g.) was warmed with methanol (5 ml.) and N-methanolic potassium hydroxide (14 ml.) to 50° for 10 minutes. The product was poured into iced water, extracted with light petroleum (b. p. 40—60°), and washed with water until neutral. The dried solution was evaporated *in vacuo*, leaving a residue (1·5 g.) which was dissolved in benzene (15 ml.) and dry pyridine (5 ml.). This solution was treated with anthraquinone-2-carboxyl chloride (1·95 g.) in benzene (15 ml.) and heated on a steam-bath for 35 minutes. A dark red oil (1·55 g.) was isolated in the usual way. This was chromatographed on Brockmann Grade III alumina in a 1 : 1 mixture of light petroleum (b. p. 40—60°) and benzene. A chocolate-brown band, which moved slowly down the column, was extracted with ether to yield a fraction (0·6 g.). Light absorption (in alcohol) : maxima at 2560 and 3280 Å, $E^{1\%}_{1\,\text{cm.}}$ 858 and 737, respectively. This fraction crystallised from acetone and gave vitamin A anthraquinone-2-carboxylate as pale yellow prisms, m. p. 124°, undepressed when the sample was mixed with a specimen prepared from natural vitamin A. Light absorption in (ethanol) : maxima at 2550 and 3290 Å, $E^{1\%}_{1\,\text{cm.}}$ 983 and 1010, respectively. The red modification, m. p. 117—119°, was also obtained.

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