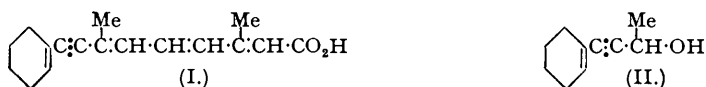


158. Studies in the Polyene Series. Part XXVII. The Synthesis of a Biologically Active C₁₆ Acid.

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Developing the scheme previously outlined for the synthesis of simplified analogues of vitamin A, ethynylcyclohexene (III) has been condensed with various aldehydes. The polyene aldehydes crotonaldehyde, sorbaldehyde, and octatrienal give the carbinols (IV; $n = 1, 2,$ and 3) which on treatment with acids undergo anionotropic rearrangement to the fully-conjugated carbinols (V), which are converted into the corresponding ketones (VI) by Oppenauer oxidation. Reaction of the ketone (VI; $n = 1$) with methyl bromoacetate gives the C₁₄ acid (VIII). Condensation of the ketone (VI; $n = 2$) with methyl bromoacetate leads to the isolation of a crystalline C₁₆ acid (IX) which, when administered orally to young rats as the sodium salt, shows small but definite growth-promoting properties.

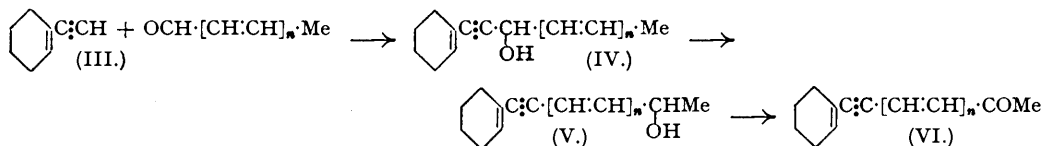
In Part XXV of this series (this vol., p. 287) schemes were outlined for the synthesis of a variety of analogues of vitamin A with simplified structures, and the preparation of a biologically active C₁₇ acid (I) was described. This paper records some further progress made.



The condensations of the Grignard reagent from the now readily-available ethynylcyclohexene (III; cf. Part XXV) with acetaldehyde gave the *carbinol* (II) in 55% yield. Hydrogenation of the latter yielded 4-cyclohexylbutan-2-ol which was oxidised to the known ketone.

Similar condensations of cyclohexenylethynylmagnesium bromide with the $\alpha\beta$ -unsaturated aldehydes, crotonaldehyde, sorbaldehyde, and octatrienal, yielded the *carbinols* (IV; $n = 1, 2,$ and 3) in yields of 42, 45, and 28%, respectively. Hydrogenation of (IV; $n = 1$) gave 1-cyclohexylhexan-3-ol which was oxidised by chromic acid to the corresponding *ketone*.

The carbinols (IV) underwent anionotropic rearrangement on shaking with dilute sulphuric acid (cf. Heilbron, Jones, *et al.*, *J.*, 1943—1946) to give the fully conjugated *carbinols* (V).



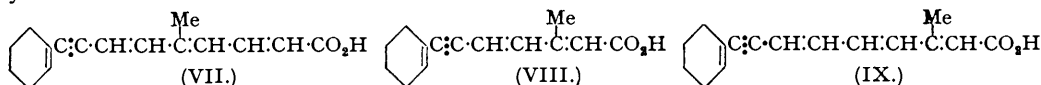
Confirmation of the structure of (V; $n = 1$) was obtained by reduction to the corresponding saturated *carbinol* which on treatment with chromic acid gave 6-cyclohexylhexan-2-one. The latter on oxidation with alkaline hypobromite yielded ω -cyclohexylvaleric acid which was identified by preparation of the crystalline amide.

To enable further extensions of the side chains to be attempted, the secondary carbinols (V) were converted into the corresponding ketones (VI) by oxidation with aluminium *tert.*-butoxide and acetone. It was observed that the yields increased with increasing values of n ; apparently the Oppenauer oxidation of the carbinols is hindered by the presence in the molecule of an acetylenic linkage, but as the number of double bonds between the latter and the hydroxyl group is increased, the effect diminishes. The $\alpha\beta$ -acetylenylcarbinol (II) could not be oxidised under the conditions used successfully with the carbinols (V).

The pure ketones (VI; $n = 1$ and 2) were obtained by regeneration from the *semicarbazones* using Heilbron, Jones, and O'Sullivan's procedure (*J.*, 1946, 866).

An analogue of (I) was prepared by means of a Reformatsky condensation of the ketone (VI; $n = 1$) with methyl ω -bromocrotonate. Extensive decomposition occurred under the conditions previously employed in similar reactions with β -ionone (Heilbron, Jones, and O'Sullivan, *loc. cit.*) and 4-cyclohex-1'-enylbut-3-yn-2-one (Heilbron, Jones, and Richardson, this vol., p. 287). However, by dehydration and hydrolysis of the crude condensation product, an acidic fraction was obtained which was estimated to contain 25—30% of the acid (VII) on the basis of light-absorption measurements. Unfortunately the crude acid could not be induced to crystallise. The decomposition during the Reformatsky reaction may be attributed mainly to the comparatively low reactivity of the bromocrotonate since with the more reactive methyl bromoacetate condensation occurred readily with the ketone (VI; $n = 1$) to give,

after dehydration of the hydroxy-ester and hydrolysis, the crystalline C_{14} acid (VIII) in 45% yield.




The ketone (VI; $n = 2$) also underwent normal condensation with methyl bromoacetate yielding the crystalline C_{16} acid (IX), m. p. 168°, in 12% yield.

When the sodium salt of this C_{16} acid, in aqueous solution buffered at pH 10, was administered orally in daily doses of one milligram to young rats on a vitamin-A deficient diet definite growth responses were produced which indicated that the acid exhibited activity of the same order as that of (I) (*i.e.*, one-thousandth of that of vitamin A itself).

The secondary carbinol (V; $n = 3$) possesses a conjugated system differing from that of vitamin A in the replacement of an ethylenic by an acetylenic linkage. However, when administered orally in arachis oil to vitamin-A deficient rats, in doses of 0.5 mg. daily, it exhibited no growth-promoting properties, *i.e.*, no activity approaching the order of one-thousandth of that of vitamin A itself.

The various compounds described in this paper all exhibited the expected light-absorption properties (see table).

	$\lambda_{\text{max.}}$ A.	$\epsilon_{\text{max.}}$		$\lambda_{\text{max.}}$ A.	$\epsilon_{\text{max.}}$
Carbinol (II)	2270	14,500	Ketone (VI; $n = 1$)	3120	20,000
	2340 *	12,500		2220	7,500
Carbinol (IV; $n = 1$).....	2300	15,500	(VI; $n = 2$)	3300	24,000
	2350 *	15,000		3460 *	22,500
(IV; $n = 2$) ...	2290	24,000	C_{14} acid (VIII)	3130	22,000
	2380	22,500		2370	16,500
(IV; $n = 3$) ...	2690	60,000		2420 *	14,500
	2780 *	52,000		3250	32,500
Carbinol (V; $n = 1$)	2640	19,500	C_{16} acid (IX)	3380	45,000
	2780	13,500	C_{17} acid A (I) ²	3390	27,500
(V; $n = 2$)	2950	21,000		2600	12,900
	3060	18,500		2570	11,000
(V; $n = 3$)	3210	36,000	Vitamin-A acid ³	3400	37,500
	3350	29,500			
	2390	12,500			

* Inflection.

¹ Heilbron, Jones, and O'Sullivan, *loc. cit.*

² Heilbron, Jones, and Richardson, *loc. cit.*

³ Arens and van Dorp, *Rec. Trav. chim.*, 1946, **65**, 338.

EXPERIMENTAL.

Light-absorption measurements were carried out in ethanol except where stated otherwise. All the operations were carried out in an atmosphere of nitrogen.

4-cycloHex-1'-enylbut-3-yn-2-ol (II).—Ethylnylcyclohexene (60 g.) in ether (50 c.c.) was added dropwise to a solution of ethylmagnesium bromide (prepared from 12.5 g. of magnesium) in ether (500 c.c.), the solution heated under reflux for 3 hours, and then cooled to 10°. Acetaldehyde (28 g.) in ether (30 c.c.) was added dropwise, and the mixture left at room temperature overnight. The complex was decomposed by the addition of ice and ammonium chloride (200 g.), and the product isolated by means of ether. After the solution had been washed with water until it was neutral, and dried, distillation gave 4-cyclohex-1'-enylbut-3-yn-2-ol (43 g.) as a pale yellow, viscous oil with a characteristic odour, b. p. 82°/0.2 mm., n_D^{20} 1.5218 (Found: C, 79.65; H, 9.5. $C_{10}H_{14}O$ requires C, 79.95; H, 9.4%). Light absorption: see Table. Active hydrogen (Zerewitinoff): The carbinol (163 mg.) evolved 27.1 c.c. of methane at 16°/767 mm., equivalent to 1.05 atoms of active hydrogen per mol.

4-cycloHexylbutan-2-ol.—The carbinol (II; 3.0 g.) in ethyl acetate (25 c.c.) was shaken with hydrogen and platinum oxide catalyst until absorption was complete (1310 c.c. at 20°/762 mm., equivalent to 2.75 \bar{H}). After separation of the catalyst by filtration and removal of solvent, distillation gave 4-cyclohexylbutan-2-ol (1.6 g.) as a pleasant-smelling mobile liquid, b. p. 118°/15 mm., n_D^{20} 1.4671 (Vavon, *Compt. rend.*, 1912, **154**, 359, gives b. p. 112°/14 mm., n_D^{20} 1.467) (Found: C, 77.1; H, 12.45. Calc. for $C_{10}H_{20}O$: C, 76.85; H, 12.9%). The *a*-naphthylurethane crystallised from light petroleum (b. p. 60—80°) as small prismatic needles, m. p. 99° (Found: C, 78.45; H, 8.75. $C_{21}H_{27}O_2N$ requires C, 78.15; H, 8.8%).

4-cycloHexylbutan-2-one.—The saturated carbinol was oxidised with chromium trioxide in glacial acetic acid, and the crude ketone isolated. The 2:4-dinitrophenylhydrazone, crystallised from methanol, had m. p. 106°, undepressed on admixture with the derivative previously described (Heilbron, Jones, and Richardson, *loc. cit.*).

1-cycloHex-1'-enylhex-4-en-1-yn-3-ol (IV; $n = 1$).—Ethylnylcyclohexene (31 g.) in ether (50 c.c.) was

added dropwise to a solution of ethylmagnesium bromide (prepared from 6.1 g. of magnesium) in ether (100 c.c.), and the solution was then heated under reflux for 3 hours. Crotonaldehyde (17.5 g., freshly distilled) in ether (50 c.c.) was added dropwise to the solution (or in some cases fine suspension) of Grignard complex cooled to 0°, and the mixture left overnight at room temperature. The complex was decomposed by pouring on ice and ammonium chloride (100 g.); isolation of the product with ether and distillation gave 1-cyclohex-1'-enylhex-4-en-1-yn-3-ol (22 g.) as a very pale yellow, viscous liquid, b. p. 115°/0.1 mm., n_D^{20} 1.5381 (Found: C, 81.55; H, 9.05. $C_{12}H_{18}O$ requires C, 81.8; H, 9.1%). Light absorption: see Table. Active hydrogen (Zerewitinoff): The carbinol (95.5 mg.) evolved 12.3 c.c. of methane at 18°/765 mm., equivalent to 0.96 active hydrogen atom per mol. The 3:5-dinitrobenzoate crystallised from light petroleum (b. p. 40—60°) in small rosettes of needles, m. p. 107° (Found: C, 61.65; H, 5.0. $C_{18}H_{18}O_6N_2$ requires C, 61.45; H, 4.9%). Light absorption: Maxima, 2500, 2400, and 2270 Å.; $\epsilon = 28,000, 35,000$, and $37,000$ respectively.

1-cycloHexylhexan-3-ol and cycloHexylhexane.—1-cycloHex-1'-enylhex-4-en-1-yn-3-ol (7.5 g.) in ethyl acetate (75 c.c.) was shaken with hydrogen and platinum oxide catalyst (25 mg.) until absorption was complete (3850 c.c. at 15°/770 mm., equivalent to 3.9 [F]). After separation of the catalyst by filtration through alumina, and removal of the solvent, distillation gave 1-cyclohexylhexan-3-ol (3.9 g.) as a pleasant-smelling, viscous liquid, b. p. 93°/0.5 mm., n_D^{20} 1.4668 (Found: C, 78.6; H, 13.0. $C_{12}H_{22}O$ requires C, 78.2; H, 13.1%). The *a*-naphthylurethane crystallised in rosettes or clusters of small needles from light petroleum (b. p. 40—60°) after long standing at 0°, m. p. 74—75° (Found: C, 73.45; H, 8.75. $C_{23}H_{31}O_2N$ requires C, 78.15; H, 8.8%). From the hydrogenation experiment was also obtained a mobile liquid (1.9 g.), b. p. 102°/16 mm., n_D^{20} 1.4492 (Found: C, 84.65; H, 13.9. Calc. for $C_{12}H_{24}$: C, 85.6; H, 14.4%). (Bourguel, *Bull. Soc. chim.*, 1927, **41**, 1476, gives b. p. 102°/16 mm., n_D^{20} 1.446, for cyclohexylhexane.)

1-cycloHexylhexan-3-one.—1-cycloHexylhexan-3-ol (3.1 g.) in glacial acetic acid (15 c.c.) was oxidised by the dropwise addition of a solution of chromium trioxide (1.2 g.) in water (2 c.c.) and acetic acid (5 c.c.). After being kept overnight at room temperature the mixture was partially neutralised by pouring on ice and aqueous sodium hydroxide (6.5 g. in 50 c.c. of water), and extracted with ether. After the extract had been washed with sodium hydrogen carbonate solution and water and dried, distillation gave 1-cyclohexylhexan-3-one (2.4 g.), b. p. 130°/15 mm., n_D^{20} 1.4583 (Found: C, 79.5; H, 12.3. $C_{12}H_{22}O$ requires C, 79.0; H, 12.2%). The semicarbazone crystallised from aqueous methanol in glistening needles, m. p. 127.5° (Found: C, 65.5; H, 10.3. $C_{12}H_{23}ON_3$ requires C, 65.2; H, 10.5%).

6-cycloHex-1'-enylhex-3-en-5-yn-2-ol (V; $n = 1$).—1-cycloHex-1'-enylhex-4-en-1-yn-3-ol (25 g.), 5% (w/v) aqueous sulphuric acid (250 c.c.), and a trace of quinol were shaken for 36 hours. The product was isolated by means of ether giving 6-cyclohex-1'-enylhex-3-en-5-yn-2-ol (20.7 g.) as a pale yellow viscous liquid, b. p. 70—80° (bath temp.)/10⁻⁵ mm., n_D^{21} 1.5550 (Found: C, 81.0; H, 9.0. $C_{12}H_{18}O$ requires C, 81.8; H, 9.1%). Light absorption: see Table. Active hydrogen (Zerewitinoff): The carbinol (148 mg.) evolved 20.3 c.c. of methane at 16°/767 mm., equivalent to 1.03 atoms of active hydrogen per mol. The 3:5-dinitrobenzoate crystallised from light petroleum (b. p. 60—80°) in feathery crystals, m. p. 104—105° (Found: C, 61.1; H, 4.9. $C_{18}H_{18}O_6N_2$ requires C, 61.45; H, 4.9%). Light absorption: Maxima, 2820, 2650, 2500, and 2280 Å.; $\epsilon = 17,500, 25,000, 28,500$, and $32,500$ respectively.

6-cycloHexylhexan-2-ol.—The carbinol (V; $n = 1$) (5.55 g.) in ethyl acetate (25 c.c.) was shaken with hydrogen and platinum oxide catalyst (25 mg.) until absorption was complete (2938 c.c. at 16°/773 mm.; equivalent to 4.0 [F]). After separation of the catalyst, distillation gave 6-cyclohexylhexan-2-ol (4.2 g.) as a pleasant-smelling, viscous liquid, b. p. 137°/15 mm., n_D^{17} 1.4659 (Found: C, 78.35; H, 12.8. $C_{12}H_{22}O$ requires C, 78.2; H, 13.1%). The *a*-naphthylurethane crystallised from light petroleum (b. p. 60—80°) as feathery crystals, m. p. 93° (Found: C, 78.7; H, 8.65. $C_{23}H_{31}O_2N$ requires C, 78.15; H, 8.85%).

6-cycloHexylhexan-2-one.—6-cycloHexylhexan-2-ol (3.35 g.) in glacial acetic acid (15 c.c.) was oxidised with chromium trioxide (1.25 g.) in acetic acid (5 c.c.) as previously described. Isolation as before gave 6-cyclohexylhexan-2-one (2.85 g.) as a pleasant-smelling liquid, b. p. 130°/14 mm., n_D^{15} 1.4594 (Found: C, 78.75; H, 11.8. $C_{12}H_{22}O$ requires C, 79.05; H, 12.2%). The semicarbazone crystallised from aqueous methanol in plates or prisms, m. p. 154° (Found: C, 65.85; H, 10.1. $C_{13}H_{25}ON_3$ requires C, 65.2; H, 10.55%).

ω -cycloHexylvaleramide.—6-cycloHexylhexan-2-one (0.6 g.) was shaken for 15 hours with excess of alkaline sodium hypobromite (prepared from bromine, 7 g., and sodium hydroxide, 5 g., in water 50 c.c.). The solution was diluted to 100 c.c. with water, cooled, and decolourised by the careful addition of a solution of sodium metabisulphite. After a single extraction with ether, the aqueous phase was acidified with 2N-sulphuric acid, and the liberated acid isolated by means of ether, giving crude ω -cyclohexylvaleric acid (0.7 g.). This acid and thionyl chloride (5 c.c.) were heated under reflux for 3 hours, the excess of reagent removed under reduced pressure, and the crude acid chloride dropped into concentrated ammonium hydroxide solution (5 c.c.; d 0.88). Crystallisation of the separated amide from aqueous methanol gave ω -cyclohexylvaleramide (0.25 g.), m. p. 121° (Katznelson and Bubinin, *Compt. rend. Acad. Sci. U.R.S.S.*, 1936, **4**, 405, give m. p. 122—123°).

6-cycloHex-1'-enylhex-3-en-5-yn-2-one (VI; $n = 1$).—6-cycloHex-1'-enylhex-3-en-5-yn-2-ol (30 g.) and aluminium *tert.*-butoxide (75 g.) in dry acetone (750 c.c.) and dry benzene (1500 c.c.) were heated under reflux for 60 hours. The product was then poured on 2N-sulphuric acid (500 c.c.) and ice, and the organic layer removed. After being washed with sodium hydrogen carbonate solution and water, and dried, the benzene was removed at 40°/250 mm. Distillation of the residue gave a mixture (24.1 g.) of ketone and unchanged carbinol, b. p. 85° (bath temp.)/10⁻⁵ mm., n_D^{20} 1.572. Light absorption: Maxima, 3100, 2650, and 2230 Å.; $E_{1\text{cm}}^{1\%} = 430, 900$, and 490 . Inflection, 2780 Å.; $E_{1\text{cm}}^{1\%} = 820$. The crude ketone (24 g.) was left with a solution of semicarbazide acetate (from 11 g. of semicarbazide hydrochloride) in methanol (250 c.c.) for 24 hours at room temperature and then for a further 24 hours at 0° to -5°. The solid was filtered off and recrystallised from methanol giving the semicarbazone (9.85 g.), m. p. 185° (Found: N, 18.65. $C_{13}H_{17}ON_3$ requires N, 18.15%). The semicarbazone (9.8 g.) was heated under reflux with stirring with 2N-sulphuric acid (100 c.c.) and light petroleum (200 c.c., b. p. 80—100°) until

all solid material had dissolved. After being heated for a further 0.5 hour, the mixture was cooled, and the petroleum layer removed. After being washed free from acid with sodium hydrogen carbonate solution and dried, the solution was evaporated, and the residue distilled giving 6-cyclohex-1'-enylhex-3-en-5-yn-2-one (6.25 g.) as a pale yellow, viscous liquid, b. p. 80° (bath temp.)/10⁻⁶ mm., n_D^{25} 1.5906 (Found: C, 82.65; H, 8.1. C₁₂H₁₄O requires C, 82.75; H, 8.1%). Light absorption: see Table. From the mother liquors obtained in the preparation of the semicarbazone the carbinol (V, $n = 1$; 5.5 g.) was recovered.

6-cycloHexylhexan-2-one Semicarbazone.—A solution of this ketone (508 mg.) in ethyl acetate (25 c.c.) was shaken with hydrogen and platinum oxide catalyst until absorption was complete (272 c.c. at 13°/778 mm.; equivalent to 4.05 F). The semicarbazone of the saturated ketone crystallised from aqueous methanol, m. p. (and mixed m. p. with specimen described above) 154°.

6-cycloHex-1'-enyl-2-methylhexa-1 : 3-dien-5-yne-1-carboxylic Acid (VIII).—6-cycloHex-1'-enylhex-3-en-5-yn-2-one (2.75 g.), methyl bromoacetate (2.5 g.), zinc turnings (1.1 g.), and benzene (35 c.c.) were heated under reflux with stirring for 1 hour with the addition of a small crystal of iodine. The mixture was then cooled and poured into *n*-acetic acid (100 c.c.). The crude hydroxy-ester (4.05 g.), n_D^{18} 1.554, was isolated in the usual manner. Light absorption: Maxima, 2790 and 2640 Å.; $E_{1\text{cm}}^{1\%} = 450$ and 600 respectively.

The ester was heated with anhydrous oxalic acid (10 g.) for 3 hours at 95–100°. Isolation with light petroleum (b. p. 40–60°) gave the crude unsaturated ester (3.3 g.), n_D^{19} 1.598. Light absorption: Maxima, 3250 and 3090 Å.; $E_{1\text{cm}}^{1\%} = 680$ and 740 respectively.

The ester was dissolved in a solution of potassium hydroxide in methanol (100 c.c.; 10% w/v), and the mixture was kept at 20° for 60 hours. After the addition of water (250 c.c.) to the solution, and extraction of the non-saponifiable portion with ether, the acid was liberated from the aqueous phase by acidifying to pH 3 with phosphoric acid (50% w/v), and was isolated by means of ether. The crude acid (2.4 g.) was triturated with aqueous methanol (5 c.c., 70% w/v) at 0°, and was filtered off. Crystallisation of the solid from light petroleum (b. p. 80–100°) gave 6-cyclohex-1'-enyl-2-methylhexa-1 : 3-dien-5-yne-1-carboxylic acid (1.55 g.) as pale yellow needles, m. p. 115–116° (Found: C, 77.35; H, 7.55. C₁₄H₁₆O₂ requires C, 77.7; H, 7.45%). Light absorption: see Table.

Condensation of the Ketone (VI; $n = 1$) with Methyl ω -Bromocrotonate.—The ketone (1.0 g.), methyl ω -bromocrotonate (1.0 g.), and zinc turnings (0.37 g.) were allowed to react in sulphur-free benzene (20 c.c.), and the product was isolated, as described in the previous experiment. After the final hydrolysis with potassium hydroxide in methanol (15 c.c.; 10% w/v) for 48 hours, an acidic fraction was obtained (0.3 g.) as a light brown, viscous oil. Light absorption: Maximum, 3370 Å.; $E_{1\text{cm}}^{1\%} = 330$, indicating an appreciable content of an acid of structure (VII). On long keeping at –5° with a few drops of acetone the oil partially solidified, but no crystalline material could be isolated.

1-cycloHex-1'-enyl-4 : 6-dien-1-yn-3-ol (IV; $n = 2$).—Ethynylcyclohexene (42 g.) was added slowly to a well-stirred solution of ethylmagnesium bromide, from magnesium (9.5 g.), in ether (250 c.c.). After addition was complete, the liquid was heated under reflux for 1½ hours, then cooled, and diluted with dry ether to 1500 c.c. To the cooled suspension, sorbaldehyde (38 g., n_D^{23} 1.5320) in ether (50 c.c.) was added dropwise. After a further 2 hours at 20°, the mixture was added to a solution of ammonium chloride (50 g.) in water (2 l.) at 0°. The ethereal layer was separated, washed free from acid, dried, and evaporated. Distillation yielded 1-cyclohex-1'-enyl-4 : 6-dien-1-yn-3-ol as a viscous, yellow oil (36 g.), b. p. 90–95° (bath temp.)/10⁻⁶ mm., n_D^{23} 1.5612 (Found: C, 82.9; H, 9.15. C₁₄H₁₈O requires C, 83.2; H, 9.0%). Light absorption: see Table.

8-cycloHex-1'-enyl-3 : 5-dien-7-yn-2-ol (V; $n = 2$).—The carbinol (IV; $n = 2$) (22 g.) was shaken for 14 hours with acetone (400 c.c.) and 2*N*-sulphuric acid (500 c.c.). The mixture was added to water (2 l.), and the product was isolated with ether. Distillation gave 8-cyclohex-1'-enyl-3 : 5-dien-7-yn-2-ol (16.5 g.) as a very viscous, yellow oil, b. p. 80–90° (bath temp.)/10⁻⁶ mm., n_D^{23} 1.5955 (Found: C, 83.1; H, 8.95. C₁₄H₁₈O requires C, 83.2; H, 9.0%). Light adsorption: see Table.

8-cycloHex-1'-enyl-3 : 5-dien-7-yn-2-one (VI; $n = 2$).—A mixture of the re-arranged carbinol (15 g.), aluminium *tert.*-butoxide (45 g.), acetone (500 c.c.), and benzene (1000 c.c.) was heated under reflux for 48 hours. After cooling, the liquid was poured into excess of 0.5*N*-sulphuric acid (2 l.) at 0°. The aqueous layer was extracted with ether. The ethereal extract, together with the benzene layer, was washed with sodium hydrogen carbonate solution and water, dried, and evaporated. Distillation of the residue gave the crude ketone (11.6 g.), b. p. 110–130° (bath temp.)/10⁻⁴ mm., n_D^{21} 1.6088. This crude material was treated with an excess of semicarbazide acetate in 90% aqueous methanol; the mixture was warmed to 60°, then left for 24 hours at 20° and for a further 24 hours at 0°. The precipitate was crystallised from methanol giving the *semicarbazone* (9.1 g.) as pale yellow needles, m. p. 186° (Found: N, 16.0. C₁₅H₁₉ON₃ requires N, 16.3%). Light absorption: Maximum, 3380 Å.; $\epsilon = 41,000$. Inflexion, 3550 Å.; $\epsilon = 36,000$.

A suspension of the semicarbazone (5 g.; m. p. 185°) in light petroleum (250 c.c.; b. p. 80–100°) and 2*N*-sulphuric acid (250 c.c.) was heated under reflux with vigorous stirring until all the solid had disappeared (3 hours). Isolation gave the *ketone* as a light yellow oil (3.2 g.), b. p. 90–95° (bath temp.)/10⁻⁶ mm., n_D^{21} 1.6094 (Found: C, 83.8; H, 8.2. C₁₄H₁₆O requires C, 84.0; H, 8.1%). Light absorption: see Table.

8-cycloHex-1'-enyl-2-methyl-3 : 5-trien-7-yn-1-carboxylic Acid (IX).—A mixture of the regenerated ketone (VI; $n = 2$) (3.2 g.), methyl bromoacetate (2.5 g.), activated zinc turnings (1.1 g.), mercuric chloride (0.1 g.), and thiophen-free benzene (100 c.c.) was heated under reflux for 2 hours, during which time most of the zinc dissolved. The liquid was then cooled, and was shaken with 5% acetic acid (200 c.c.). The benzene layer was separated, washed free from acid, dried, and evaporated. Anhydrous oxalic acid (3 g.) was added to the residual orange-red oil, and the mixture was heated to 100°/0.1 mm. for 2 hours. After cooling, the dark red product was extracted with light petroleum (b. p. 40–60°). The extract was washed with sodium hydrogen carbonate solution and water, dried, and evaporated. The residual crude ester was dissolved in a solution of potassium hydroxide in

methanol (500 c.c., 10%), and was kept at 20° for 48 hours. Water (2 l.) was then added, the non-saponifiable material was extracted with ether, and the aqueous portion acidified with phosphoric acid (50% w/v). The liberated acid was isolated with ether. Trituration of the resulting viscous, orange oil with benzene gave a yellow solid which was recrystallised from methanol yielding the *acid* (0.45 g.) in rhombic needles, m. p. 168° (Found : C, 79.6; H, 7.6. $C_{16}H_{18}O$ requires C, 79.3; H, 7.5%). Light absorption : see Table.

1-cycloHex-1'-enyldeca-4 : 6 : 8-trien-1-yn-3-ol (IV; $n = 3$).—Ethynylcyclohexene (10 g.) was added slowly to a well-stirred solution of ethylmagnesium bromide (prepared from magnesium, 2.5 g.) in ether (100 c.c.). After addition was complete, the solution was heated under reflux for 1½ hours, cooled, and diluted with ether (400 c.c.). Octatrienal (12 g., m. p. 51°) in ether (100 c.c.) was then added dropwise at 0°. After being stirred at 20° for 2 hours, the mixture was poured into a solution of ammonium chloride (20 g.) in water (1000 c.c.). The ethereal layer was washed with sodium hydrogen carbonate solution and water, dried, and evaporated. On adding light petroleum (b. p. 40–60°) the residue partially solidified. The solid was filtered off, and was recrystallised from aqueous methanol, yielding 1-cyclohex-1'-enyldeca-4 : 6 : 8-trien-1-yn-3-ol (6.1 g.) in clusters of colourless needles, m. p. 108° (Found : C, 83.9; H, 9.0. $C_{16}H_{20}O$ requires C, 84.2; H, 8.85%). Light absorption : see Table.

10-cycloHex-1'-enyldeca-3 : 5 : 7-trien-9-yn-2-ol (V; $n = 3$).—The carbinol (IV; $n = 3$) (4.2 g.) was shaken for 14 hours with acetone (100 c.c.) and 2N-sulphuric acid (200 c.c.). The mixture was poured into water, and extracted with ether. The ethereal extracts were washed with sodium hydrogen carbonate solution and water, dried, and evaporated. The residue was distilled, giving the rearranged *carbinol* as a viscous yellow oil (2.7 g.), b. p. 115–120° (bath temp.)/10⁻⁵ mm., n_D^{25} 1.6254 (Found : C, 84.0; H, 9.2. $C_{16}H_{20}O$ requires C, 84.2; H, 8.85%). Light absorption : see Table.

10-cycloHex-1'-enyldeca-3 : 5 : 7-trien-9-yn-2-one *Semicarbazone*.—A solution of the rearranged carbinol (V; $n = 3$) (1.5 g.) and aluminium *tert.*-butoxide (5 g.) in acetone (50 c.c.) and benzene (120 c.c.) was heated under reflux for 48 hours. After cooling, the mixture was poured into 0.5N-sulphuric acid (500 c.c.) at 0°, and the crude product was isolated as an orange-red oil. The latter was treated with excess of semicarbazide acetate in 90% aqueous methanol, warmed to 60°, and left for 24 hours at 20° and finally for 24 hours at 0°. The resulting precipitate (1.3 g.) was recrystallised from ethyl acetate, yielding the *semicarbazone* as light yellow plates, m. p. 203° (decomp.) (Found : N, 14.7. $C_{17}H_{21}ON_3$ requires N, 14.8%). Light absorption : Maxima, 2650, 3640, and 3780 Å.; $\epsilon = 8,500, 59,500, \text{ and } 46,500$ respectively.

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