431. *Studies in the Polyene Series. Part XXXI. The Synthesis of C_{18} and C_{19} Acids related to Vitamin A.*

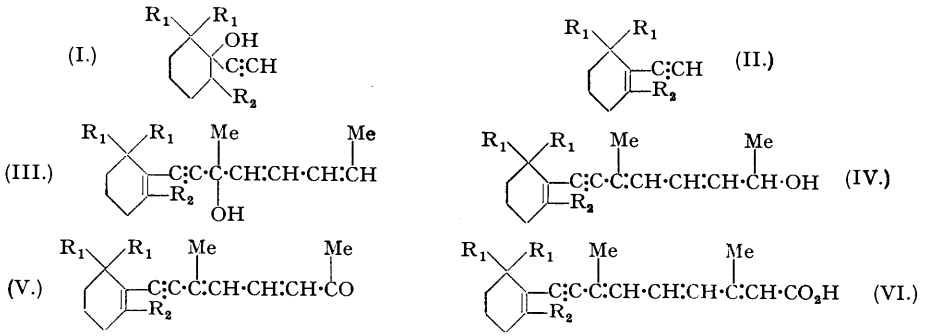
By Sir Ian Heilbron, E. R. H. Jones, D. G. Lewis, and B. C. L. Weedon.

The method previously developed for the preparation of the biologically active C_{17} acid (VI; $R_1 = R_2 = H$) has been applied to the synthesis of the C_{18} (VI; $R_1 = H$, $R_2 = Me$) and C_{19} (VI; $R_1 = Me$, $R_2 = H$) homologues.

Condensation of the ethynyl*cyclo*hexenes (II; $R_1 = H$, $R_2 = Me$) and (II; $R_1 = Me$, $R_2 = H$), obtained by dehydration of the corresponding ethynyl*cyclo*hexanols, with crotonylideneacetone gives the carbinols (III; $R_1 = H$, $R_2 = Me$) and (III; $R_1 = Me$, $R_2 = H$) which, on treatment with acids, undergo anionotropic rearrangement to the fully conjugated carbinols (IV; $R_1 = H$, $R_2 = Me$) and (IV; $R_1 = Me$, $R_2 = H$). The corresponding ketones, (V; $R_1 = H$, $R_2 = Me$) and (V; $R_1 = Me$, $R_2 = H$), prepared by Oppenauer oxidation of the carbinols, are condensed with methyl bromoacetate leading, after dehydration and hydrolysis, to the isolation of the crystalline acids (VI; $R_1 = H$, $R_2 = Me$) and (VI; $R_1 = Me$, $R_2 = H$). The latter acid, when administered orally as the sodium salt to young rats, shows small but definite growth-promoting properties.

A new synthetic approach to compounds related to vitamin A, and its application to the preparation of the biologically active C_{17} acid (VI; $R_1 = R_2 = H$), were described in Part XXV of this series (Heilbron, Jones, and Richardson, this vol., p. 287). As part of a comprehensive study of the relationship between molecular structure and growth-promoting activity of the vitamin-A type, the effect of introducing one and two methyl groups into the ring system, resulting in the formation of the C_{18} (VI; $R_1 = H$, $R_2 = Me$) and C_{19} (VI; $R_1 = Me$, $R_2 = H$) acids, has now been investigated.

Vapour-phase dehydration of both the solid and the liquid form of 2-methyl-1-ethynyl*cyclo*hexanol (I; $R_1 = H$, $R_2 = Me$) over a supported aluminium phosphate catalyst at 300—320° gave (*ca.* 40—55% yields) products consisting essentially of 2-methyl-1-ethynyl*cyclo*hex-1-ene (II; $R_1 = H$, $R_2 = Me$). The hydrocarbon obtained from the liquid carbinol was converted into 1-acetyl-2-methyl*cyclo*hexene (55% yield) by hydration, no other ketone being detected. On the other hand, hydration of the hydrocarbon from the solid carbinol, while giving 1-acetyl-2-methyl*cyclo*hexene as the major product (*ca.* 50%), yielded also an isomeric ketone (2 : 4-*dinitrophenylhydrazone*) (*ca.* 10%). Of the two dehydration products, both of which gave hexan-5-one-1-carboxylic acid (2 : 4-dinitrophenylhydrazone) on ozonolysis, that derived from the liquid carbinol appeared to be the more homogeneous and was therefore employed in the synthesis of the C_{18} acid (VI; $R_1 = H$, $R_2 = Me$) described below. Although the possibility that the starting material (II; $R_1 = H$, $R_2 = Me$) contained small amounts of other ethynyl*cyclo*hexenes cannot definitely be excluded, there can be no doubt as to the structure of the final C_{18} acid since the intermediate ketone (V; $R_1 = H$, $R_2 = Me$), which was purified by regeneration under mild conditions from a crystalline derivative, also gave hexan-5-one-1-carboxylic acid (2 : 4-dinitrophenylhydrazone) on ozonolysis.



While these investigations were in progress, Milas *et al.* (*J. Amer. Chem. Soc.*, 1948, **70**, 1829) published an account of the dehydration of 2-methyl-1-ethynyl*cyclo*hexanol under conditions very similar to those described above. From the solid and the liquid form of the carbinol, products were obtained both of which gave hexan-5-one-1-carboxylic acid (unstated yields) on ozonolysis. On this evidence alone, these authors concluded that the ethynyl*cyclo*hexenes produced in the two cases had essentially the same composition.

6 : 6-*Dimethyl*-1-*ethynyl*cyclo*hex*-1-*ene* (II; R_1 = Me, R_2 = H) was readily obtained (65% yield) by vapour-phase dehydration of 2 : 2-dimethyl-1-ethynyl*cyclo*hexanol (I; R_1 = Me, R_2 = H) and was converted into 1-acetyl-6 : 6-dimethyl*cyclo*hexene on hydration.

Condensation of the Grignard reagents from the ethynyl*cyclo*hexenes (II; R_1 = H, R_2 = Me) and (II; R_1 = Me, R_2 = H) with crotonylideneacetone gave the *carbinols* (III; R_1 = H, R_2 = Me) and (III; R_1 = Me, R_2 = H), in 45 and 70% yields respectively, which when shaken with dilute sulphuric acid yielded the isomeric fully conjugated *carbinols* (IV; R_1 = H, R_2 = Me) and (IV; R_1 = Me, R_2 = H). The *ketones* (V; R_1 = H, R_2 = Me) and (V; R_1 = Me, R_2 = H) were prepared by oxidation of (IV) with aluminium *tert.*-butoxide and acetone and were purified by regeneration from the *semicarbazones* by the procedure of Heilbron, Jones, and O'Sullivan (*J.*, 1946, 866). Condensation of the ketones with methyl bromoacetate and zinc gave, after dehydration of the crude hydroxy-esters and hydrolysis, the crystalline *acids* (VI; R_1 = H, R_2 = Me), m. p. 167°, and (VI; R_1 = Me, R_2 = H), m. p. 171°, in 8 and 20% yield respectively.

		$\lambda_{max.}$, A.	$\varepsilon_{max.}$
Ethynyl*cyclo*hexene	(II; $R_1 = R_2 =$ H)[1]	2230	12,500
		2280 *	9,500
	(II); R_1 = H, R_2 = Me)	2230	12,000
		2270	12,000
	(II; R_1 = Me, R_2 = H)	2230	9,000
		2280	9,000
Carbinol	(III; $R_1 = R_2 =$ H)[1]	2270	39,000
		2370	30,000
	(III; R_1 = H, R_2 = Me)	2270	29,000
		2350 *	24,000
	(III; R_1 = Me, R_2 = H)	2230	23,000
		2310 *	9,500
Carbinol	(IV; $R_1 = R_2 =$ H)[1]	2910	21,500
		3060	15,000
	(IV; R_1 = H, R_2 = Me)	2240	14,000
		2800	19,000
		2910	21,000
		3080	16,000
	(IV; R_1 = Me, R_2 = H)	2700	19,500
		2800	20,000
		2910	19,500
Ketone	(V; $R_1 = R_2 =$ H)[1]	2450	18,000
		3350	23,000
	(V; R_1 = H, R_2 = Me)	2440	11,500
		3350	18,000
	(V; R_1 = Me, R_2 = H)	2420	12,500
		3360	20,500
Acid	(VI; $R_1 = R_2 =$ H)[2]	2580	14,000
		3380	33,000
	(VI; R_1 = H, R_2 = Me)	3380	31,000
	(VI; R_1 = Me, R_2 = H)	2580	15,000
		3410	35,500

[1] Heilbron, Jones, and Richardson, this vol., p. 287.
[2] Heilbron, Jones, Julia, and Weedon, this vol., p. 1823.

* Inflexion.

When the C_{19} acid (VI; R_1 = Me, R_2 = H) was fed, as an aqueous solution of the sodium salt buffered at pH 10, in daily doses of 0·3 mg. to young rats on a vitamin-A-deficient diet, growth responses were produced which indicated that the acid possessed activity equivalent to about 5000 international units per gram, *i.e.*, of the same order as that of the C_{17} acid (VI; $R_1 = R_2$ = H) (*ca.* 1/1000th of that of vitamin A itself). Unexpectedly the C_{18} acid (VI; R_1 = H, R_2 = Me), when similarly tested in daily doses of 0·64 mg., exhibited no growth-promoting properties.

The various compounds described in this paper all showed the expected light absorption properties (see Table).

Experimental.

Light-absorption data were determined in ethanol except where stated otherwise. Data for most of the compounds described below are given in the Table. All the operations were carried out in an atmosphere of nitrogen.

2-*Methyl*-1-*ethynyl*cyclo*hexanol* (I; R_1 = H, R_2 = Me).—A solution of sodium acetylide in liquid ammonia (4 l.) was prepared from sodium (140 g.) and ferric nitrate (3 g.) by a method similar to that used by Heilbron, Jones, and Weedon (*J.*, 1945, 83). 2-Methyl*cyclo*hexanone (762 g.) in ether (500 c.c.) was added dropwise during 2 hours, and the mixture was stirred for a further 14 hours. The reaction

was terminated by the addition of ammonium chloride (400 g.), the ammonia was evaporated, and the crude product was isolated with ether in the usual way. Distillation gave 2-methyl-1-ethynyl*cyclo*hexanol (579 g.), b. p. 74—78°/14 mm., n_D^{20} 1·467—1·472. The carbinol was dissolved in pentane (600 c.c.), and the solution was set aside at −20° for 1 hour during which time a solid separated. Recrystallisation of the solid from pentane gave the solid isomer (128 g.) as needles, m. p. 58° [Milas *et al.*, *J. Amer. Chem. Soc.*, 1948, **70**, 1829, give m. p. 61—61·5° (corr.)]. The pentane solution, after removal of the solid, was evaporated and the residue distilled yielding the liquid isomer (431 g.), b. p. 74—77°/14 mm., n_D^{20} 1·4693 (Milas *et al.* give b. p. 84°/17 mm.).

2-*Methyl*-1-*ethynyl*cyclo*hex*-1-*ene* (II; R_1 = H, R_2 = Me).—The above carbinol (100 g.; liquid isomer) was distilled slowly (*ca.* 50 g./hr.) at 50 mm. through a hard-glass tube (60 × 2 cm.) containing a supported aluminium phosphate catalyst (for preparation see Heilbron, Jones, and Richardson, this vol., p. 287) maintained at 300—320°. The emergent gases were cooled and the liquid product was collected in a receiver cooled in ice–salt. After being shaken with a saturated solution of potassium chloride (100 c.c.) the organic layer was separated and dried ($CaCl_2$). Fractional distillation through a 40-cm. vacuum-jacketed Fenske column, at a reflux ratio of 20 : 1, gave 2-methyl-1-ethynyl*cyclo*hex-1-ene (47 g.), b. p. 67—69°/35 mm., n_D^{23} 1·4890 (Found: C, 89·6; H, 10·0. Calc. for C_9H_{12}: C, 90·0; H, 10·0%). Light absorption: Maximum, 2240 A.; $E_{1\,cm.}^{1\%}$, 520. A small portion (6 g.) of the hydrocarbon was added to an ammoniacal solution of silver nitrate (20 g.) in aqueous alcohol (95%; 400 c.c.), and the mixture was set aside at 20° for 30 minutes. The solid deposited was filtered, washed with water, alcohol, and ether, and dried under reduced pressure. The silver complex (4·7 g.) was added to a solution of potassium cyanide (20 g.) in water (30 c.c.), and the mixture was boiled under reflux until all the solid had disappeared (1 hour). After the mixture had cooled, the pure enyne (1·5 g.) was isolated by means of ether and distilled; b. p. 70°/35 mm., n_D^{15} 1·4937. Active hydrogen (Zerewitinoff): the hydrocarbon (75 mg.) evolved 15·5 c.c. of methane at 18°/769 mm., equivalent to 1·05 atom of active hydrogen per mole. Light absorption: Maxima, 2230 and 2270 A.; $E_{1\,cm.}^{1\%}$ 1000 and 1000; ε, 12,000. (Milas *et al.*, *loc. cit.*, give b. p. 63—65°/30 mm., n_D^{25} 1·4895; light absorption: Maximum, 2290 A.; ε, 10,000.)

Dehydration of 2-methyl-1-ethynyl*cyclo*hexanol (110 g.; solid isomer), in the manner described above, gave the hydrocarbon (45 g.), b. p. 85—88°/55 mm., n_D^{25} 1·4961. Light absorption: Maximum, 227 A.; $E_{1\,cm.}^{1\%}$, 625. A small portion (3 g.) of the product was converted into the silver complex (3·2 g.) and regenerated, in the manner described above, yielding the enyne (0·9 g.), b. p. 42—45°/9 mm., n_D^{17} 1·4945. Active hydrogen (Zerewitinoff): the hydrocarbon (78 mg.) evolved 13·8 c.c. of methane at 18°/770 mm., equivalent to 0·9 atom of active hydrogen per mole. Light absorption: Maximum, 2270 A.; $E_{1\,cm.}^{1\%}$, 100; ε, 12,000. (Milas *et al.*, *loc. cit.*, give b. p. 63·5—64°/30 mm., n_D^{25} 1·4883; light absorption: Maximum, 2290 A., ε, 11,500.)

Ozonolysis of 2-*Methyl*-1-*ethynyl*cyclo*hex*-1-*ene* (cf. Strain, *J. Biol. Chem.*, 1933, **102**, 137).—(*a*) A solution of the hydrocarbon (1·0 g.; from the liquid carbinol) in carbon tetrachloride (30 c.c.) was treated with ozonised oxygen for 5 hours. Glacial acetic acid (40 c.c.) was then added and the ozonolysis continued for a further 5 hours. Hydrogen peroxide (3 c.c. of 100-vol. solution) was added and the solution was kept for 14 hours. After removal of the acetic acid and carbon tetrachloride by steam-distillation, the residue was treated with a solution of 2 : 4-dinitrophenylhydrazine (1 g.) in sulphuric acid (10 c.c.; 30% w/v). The product was extracted with benzene, and the extract was washed with sulphuric acid (10% w/v) and water, dried, and evaporated, giving a red viscous liquid (0·89 g.). Trituration with methanol yielded a solid which crystallised from acetic acid–methanol in yellow plates (0·28 g.), m. p. 132° [Milas *et al.*, *loc. cit.*, give m. p. 132·6—133·1° (corr.) for the 2 : 4-dinitrophenylhydrazone of hexan-5-one-1-carboxylic acid] (Found: N, 17·45. Calc. for $C_{13}H_{16}O_6N_4$: N, 17·3%).

(*b*) Ozonolysis of the hydrocarbon (1·0 g.; from the solid carbinol), and treatment of the crude product with a solution of 2 : 4-dinitrophenylhydrazine in sulphuric acid in the manner described above, led to a red viscous oil (0·43 g.) which partly solidified. Recrystallisation of the solid from methanol gave the 2 : 4-dinitrophenylhydrazone (40 mg.), m. p. 131° undepressed on admixture with a specimen from (*a*).

1-*Acetyl*-2-*methyl*cyclo*hexene*.—(*a*) A mixture of 2-methyl-1-ethynyl*cyclo*hexene (2 g.; from the liquid carbinol), mercuric acetate (0·5 g.), glacial acetic acid (15 c.c.), ethanol (15 c.c.) and water (5 c.c.) was heated under reflux for 30 minutes. After cooling, the mixture was poured into water (100 c.c.), and the product was extracted with light petroleum (50 c.c.; b. p. 40—60°). The petroleum solution was washed with sodium hydrogen carbonate solution and water, dried, and evaporated. The residue (2 g.) was divided into 2 portions.

The first portion (0·5 g.) was treated with a solution of 2 : 4-dinitrophenylhydrazine (2 g.) and concentrated sulphuric acid (2 g.) in methanol (20 c.c.), the mixture was set aside for 2 hours at 20° and then poured into water (100 c.c.). The derivative was extracted with benzene and the extract was washed with dilute sulphuric acid (10% w/v) and water. After drying, the benzene solution was poured on a column of alumina, yielding one band. Elution of the latter with benzene, evaporation of the benzene solution, and crystallisation of the residue from ethyl acetate gave the 2 : 4-dinitrophenylhydrazone of 1-acetyl-2-methyl*cyclo*hexene (0·75 g.) as scarlet plates, m. p. 124°, undepressed on admixture with an authentic specimen (Braude, Jones, Sondheimer, and Toogood, this vol., p. 607, give m. p. 124—125°).

The second portion (1·5 g.) of the crude hydration product was treated with an excess of semicarbazide acetate in aqueous methanol (80%), the solution was warmed to 60° and set aside at 20° for 12 hours and at 0° for 16 hours. The solid deposited was recrystallised from methanol giving the semicarbazone of 1-acetyl-2-methyl*cyclo*hexene (1·4 g.) as plates, m. p. 215°, undepressed on admixture with an authentic specimen (Braude, Jones, Koch, Richardson, and Sondheimer, this vol., p. 1890, give m. p. 213°).

(*b*) The enyne (2 g.; prepared from the solid carbinol) was hydrated in the manner described above, and the product treated with an excess of semicarbazide acetate in aqueous methanol. The crude derivative (1·7 g.) on fractional crystallisation from methanol gave the semicarbazone of 1-acetyl-2-methyl*cyclo*hexene (1·2 g.), m. p. and mixed m. p. with an authentic specimen, 215°.

(*c*) The enyne (1 g.; prepared from the solid carbinol) was hydrated in the usual manner, and the product treated with methanolic 2 : 4-dinitrophenylhydrazine sulphate. The crude derivative (1·6 g.) was shown, by chromatographic separation on alumina, to contain *ca.* 80% of the 2 : 4-dinitrophenylhydrazone of 1-acetyl-2-methyl*cyclo*hexene and *ca.* 20% of an *isomer* which crystallised from methanol in orange plates, m. p. 113° (Found : N, 17·6. $C_{15}H_{18}O_4N_4$ requires N, 17·6%). Light absorption in chloroform (main band only) : Maximum, 3710 A.; ε, 23,500. Admixture of the two derivatives caused a marked depression of the m. p.

2 : 2-*Dimethyl*-1-*ethynyl*cyclo*hexanol* (I; R_1 = Me, R_2 = H).—2 : 2-Dimethyl*cyclo*hexanone (126 g.; regenerated from the semicarbazone, m. p. 200°) was condensed with sodium acetylide (from 25 g. of sodium) in liquid ammonia (1 l.) by the procedure described above. Distillation of the product gave the carbinol (128 g.), b. p. 86—89°/20 mm., n_D^{23} 1·4787 (Chanley, *J. Amer. Chem. Soc.*, 1948, **70**, 244, gives b. p. 113—113·5°/49 mm., n_D^{25} 1·4790) (Found : C, 79·0; H, 10·5. Calc. for $C_{10}H_{16}O$: C, 78·9; H, 10·6%). The 3 : 5-*dinitrobenzoate* crystallised from light petroleum (b. p. 40—60°) in needles, m. p. 115° (Found : N, 8·4. $C_{17}H_{18}O_6N_2$ requires N, 8·1%).

6 : 6-*Dimethyl*-1-*ethynyl*cyclo*hex*-1-*ene* (II; R_1 = Me, R_2 = H).—The above carbinol (128 g.) was slowly distilled (*ca.* 40 g. per hour) at 60 mm. through a supported aluminium phosphate catalyst maintained at 300—320°. Isolation of the product in the usual way and distillation gave 6 : 6-*dimethyl*-1-*ethynyl*cyclo*hex*-1-*ene* (73 g.), b. p. 77—84°/35 mm., n_D^{29} 1·4792 (Found : C, 89·1; H, 10·85. $C_{10}H_{14}$ requires C, 89·5; H, 10·5%). Light adsorption : Maximum, 2240 A.; $E_{1\text{ cm.}}^{1\%}$, 610. A small portion (4 g.) was converted into the silver complex (4·9 g.), and the enyne regenerated in the usual way giving an oil (1·3 g.), b. p. 86—88°/60 mm., n_D^{15} 1·4873. Active hydrogen (Zerewitinoff) : the enyne (72 mg.) evolved 13·4 c.c. of methane at 18°/769 mm., equivalent to 1·05 atoms of active hydrogen per mole. Light absorption : Maxima, 2230 and 2280 A.; $E_{1\text{ cm.}}^{1\%}$, 680 and 680; ε, 9000.

1-*Acetyl*-6 : 6-*dimethyl*cyclo*hexene*.—A solution of the above hydrocarbon (0·6 g.) and mercuric acetate (0·25 g.) in a mixture of glacial acetic acid (7·5 c.c.), ethanol (7·5 c.c.), and water (2·5 c.c.) was heated under reflux for 30 minutes. After cooling, the mixture was poured into dilute sulphuric acid (10% w/v). The product was isolated in the usual manner with light petroleum (b. p. 40—60°) and converted into the semicarbazone which crystallised from methanol in plates (0·35 g.), m. p. 201°, undepressed on admixture with an authentic specimen of 1-acetyl-6 : 6-dimethyl*cyclo*hexene semicarbazone (Chanley, *loc. cit.*, gives m. p. 201—201·5°).

1-(2′-*Methyl*cyclo*hex*-1′-*enyl*)-3-*methylocta*-4 : 6-*dien*-1-*yn*-3-*ol* (III; R_1 = H, R_2 = Me).—2-Methyl-1-ethynyl*cyclo*hex-1-ene (20 g.) in ether (20 c.c.) was added dropwise to a solution of ethylmagnesium bromide (prepared from 4 g. of magnesium) in ether (150 c.c.). After the addition was complete, the mixture was boiled under reflux for 1½ hours and then cooled and diluted with ether (600 c.c.). Crotonylideneacetone (18·2 g.) in ether (25 c.c.) was added dropwise to the stirred Grignard reagent at 0° during 1 hour, and the mixture was stirred for a further 45 minutes at 20°. The complex was decomposed by addition of ice and ammonium chloride (25 g.), and the product was isolated by means of ether in the usual way. Distillation from a short-path still gave 1-(2′-*methyl*cyclo*hex*-1′-*enyl*)-3-*methylocta*-4 : 6-*dien*-1-*yn*-3-*ol* (17·6 g.) as a pale yellow viscous liquid, b. p. 80—90° (bath temp.)/10^{-5} mm., n_D^{18} 1·5400 (Found : C, 82·8; H, 9·85. $C_{16}H_{22}O$ requires C, 83·5; H, 9·6%). Light absorption : see Table.

8-(2′-*Methyl*cyclo*hex*-1′-*enyl*)-6-*methylocta*-3 : 5-*dien*-7-*yn*-2-*ol* (IV; R_1 = H, R_2 = Me).—A solution of the above carbinol (16 g.), and a trace of quinol, in ether (100 c.c.) was shaken for 16 hours with dilute sulphuric acid (500 c.c.; 1% w/v). Isolation of the product with ether in the usual way gave the crude carbinol (15·5 g.) as a viscous yellow oil. Distillation of a small portion yielded 8-(2′-*methyl*cyclo*hex*-1′-*enyl*)-6-*methylocta*-3 : 5-*dien*-7-*yn*-2-*ol*, b. p. 75—85° (bath temp.)/10^{-5} mm., n_D^{20} 1·5696 (Found : C, 83·2; H, 9·75. $C_{16}H_{22}O$ requires C, 83·5; H, 9·6%). Light absorption : see Table.

8-(2′-*Methyl*cyclo*hex*-1′-*enyl*)-6-*methylocta*-3 : 5-*dien*-7-*yn*-2-*one* (V; R_1 = H, R_2 = Me).—A solution of the rearranged carbinol (12 g.; crude) and aluminium *tert.*-butoxide (30 g.) in dry acetone (500 c.c.) and dry benzene (750 c.c.) was boiled under reflux for 48 hours. After cooling, the mixture was poured into dilute sulphuric acid (4 l.; 2·5% w/v), and the organic layer separated. The aqueous solution was extracted with ether, and the combined ethereal extracts and benzene layer were washed with sodium hydrogen carbonate solution and water and dried. The solvents were evaporated, and the residue was dissolved in methanol and added to an excess of semicarbazide acetate in aqueous methanol (80%). The solution was warmed to 60° and then set aside for 24 hours at 20° and finally for 24 hours at 0°. The product which separated was recrystallised from methanol to give the *semicarbazone* (4·9 g.) as pale yellow plates, m. p. 186° (Found : N, 14·35. $C_{17}H_{23}ON_3$ requires N, 14·7%). Light absorption : Maximum, 3330 A.; ε, 40,000. Inflexion, 3480 A.; ε, 33,500.

The semicarbazone (4·4 g.; m. p. 186°) was suspended in light petroleum (200 c.c.; b. p. 80—100°) and dilute sulphuric acid (200 c.c.; 10% w/v), and the mixture was heated under reflux with vigorous stirring until all the solid had disappeared (3 hours). The product was isolated from the petroleum layer in the usual way and distilled, giving the *ketone* (2·9 g.) as a pale yellow oil, b. p. 80—90° (bath temp.)/10^{-5} mm., n_D^{18} 1·5945 (Found : C, 83·75; H, 9·3. $C_{16}H_{20}O$ requires C, 84·2; H, 8·8%). Light absorption : see Table.

The 2 : 4-*dinitrophenylhydrazone* was purified by adsorption on a column of alumina from benzene solution and crystallised from ethyl acetate–ethanol in purple needles, m. p. 175° (Found : N, 13·6. $C_{22}H_{24}O_4N_4$ requires N, 13·7%). Light absorption in chloroform (main band only) : Maximum 4110 A.; ε, 39,000.

Ozonolysis of the C_{16} *Ketone* (V; R_1 = H; R_2 = Me).—A solution of the regenerated ketone (237 mg.) in carbon tetrachloride (10 c.c.) was treated with ozonised oxygen for 2 hours; glacial acetic acid (10 c.c.) was added and the ozonolysis was continued for a further 2 hours. The crude product was converted into the 2 : 4-dinitrophenylhydrazone, which was isolated in the manner described above. Crystallisation from methanol gave the 2 : 4-dinitrophenylhydrazone of hexan-5-one-1-carboxylic acid as yellow plates (25 mg.), m. p. 131°, undepressed on admixture with the specimen described above.

8-(2′-*Methyl*cyclo*hexyl*)-6-*methyloctan*-2-*one*.—A solution of the above C_{16} ketone (265 mg.) in ethyl

acetate was shaken in hydrogen in the presence of platinic oxide (10 mg.) until absorption was complete (132 c.c. at 18°/773 mm., equivalent to 4·9 double bonds). After removal of the catalyst and solvent, distillation of the residue gave the saturated *ketone*, b. p. 110—115°/0·1 mm., n_D^{23} 1·4695 (Found : C, 80·65; H, 12·4. $C_{16}H_{30}O$ requires C, 80·7; H, 12·6%). The 2 : 4-*dinitrophenylhydrazone* crystallised from methanol in yellow plates, m. p. 39° (Found : N, 13·5. $C_{22}H_{34}O_4N_4$ requires N, 13·4%).

8-(2′-*Methyl*cyclo*hex*-1′-*enyl*)-2 : 6-*dimethylocta*-1 : 3 : 5-*trien*-7-*yne*-1-*carboxylic Acid* (VI; R_1 = H, R_2 = Me).—A mixture of the regenerated ketone (V; R_1 = H, R_2 = Me) (2·9 g.), methyl bromoacetate (2·3 g.), activated zinc turnings (1 g.), mercuric chloride (0·1 g.), and dry benzene (15 c.c.) was heated under reflux for 1¼ hours, during which time most of the zinc dissolved. The reaction mixture was then cooled, decanted from unchanged zinc, and shaken with dilute acetic acid (200 c.c.; 5% w/v). The benzene layer was separated, washed free from acid, dried, and evaporated. The residual orange-red oil (3·2 g.) was added to anhydrous oxalic acid (5 g.), and the mixture was heated at 95—100°/0·1 mm. for 2 hours. After the mixture had cooled, the crude unsaturated ester (1·7 g.) was isolated by extraction with light petroleum (b. p. 40—60°).

The ester was dissolved in methanolic potassium hydroxide (250 c.c.; 10% w/v) and kept for 48 hours at 20°. The solution was poured into water (2 l.), the non-saponifiable material was extracted with ether, and the aqueous layer was acidified with dilute phosphoric acid (150 c.c.; 50% w/v). The liberated acid was extracted with ether, and the ethereal solution was washed with water, dried, and evaporated. The residue, a viscous orange gum (0·9 g.), crystallised partly on trituration with methanol. Recrystallisation from the same solvent gave the *acid* (275 mg.) as pale yellow needles, m. p. 167° (Found : C, 80·25; H, 8·4. $C_{18}H_{22}O_2$ requires C, 80·0; H, 8·2%). Light absorption : see Table.

1-(6′ : 6′-*Dimethyl*cyclo*hex*-1′-*enyl*)-3-*methylocta*-4 : 6-*dien*-1-*yn*-3-*ol* (III; R_1 = Me, R_2 = H).—A solution of crotonylideneacetone (41 g.) in ether (50 c.c.) was added slowly to 6 : 6-dimethyl-1-ethynyl-*cyclo*hexenylmagnesium bromide (prepared from 10 g. of magnesium and 50 g. of 6 : 6-dimethyl-1-ethynyl*cyclo*hex-1-ene) in ether (1,250 c.c.). The condensation and isolation of the product were effected by the procedure described above. The *carbinol* (63 g.) was obtained as a pale yellow oil, b. p. 80—90° (bath temp.)/10^{-5} mm., n_D^{21} 1·5232 (Found : C, 83·05; H, 10·2. $C_{17}H_{24}O$ requires C, 83·6; H, 9·8%). Light absorption : see Table.

8-(6′ : 6′-*Dimethyl*cyclo*hex*-1′-*enyl*)-6-*methylocta*-3 : 5-*dien*-7-*yn*-2-*ol* (IV; R_1 = Me, R_2 = H).—The above carbinol (60 g.), and a trace of quinol, in ether (200 c.c.) were shaken with dilute sulphuric acid (1·5 l.; 1% w/v) for 20 hours. Isolation of the product in the usual way gave the crude carbinol (58 g.) as a viscous oil. A small portion was distilled, yielding 8-(6′ : 6′-*dimethyl*cyclo*hex*-1′-*enyl*)-6-*methylocta*-3 : 5-*dien*-7-*yn*-2-*ol*, b. p. 85—95° (bath temp.)/10^{-5} mm., n_D^{21} 1·5432 (Found : C, 82·6; H, 10·1. $C_{17}H_{24}O$ requires C, 83·6; H, 9·8%). Light absorption : see Table.

8-(6′ : 6′-*Dimethyl*cyclo*hex*-1′-*enyl*)-6-*methylocta*-3 : 5-*dien*-7-*yn*-2-*one* (V; R_1 = Me, R_2 = H).—A solution of the preceding rearranged carbinol (55 g.; crude) and aluminium *tert.*-butoxide (100 g.) in benzene (2·5 l.) and acetone (1·65 l.) was heated under reflux for 48 hours. The crude product was isolated and treated with an excess of semicarbazide acetate in aqueous methanol (80%) in the usual manner. The solid deposited was recrystallised from methanol giving the *semicarbazone* (23 g.) as pale yellow plates, m. p. 187° (Found : N, 14·0. $C_{18}H_{25}ON_3$ requires N, 14·05%). Light absorption : Maximum, 3360 A.; ε, 42,500. Inflexion, 3470 A.; ε, 36,000.

Regeneration from the semicarbazone (15 g.; m. p. 187°) by the procedure described above gave the *ketone* (9 g.) as a pale yellow oil, b. p. 80° (bath temp.)/10^{-5} mm., n_D^{20} 1·5937 (Found : C, 84·5; H, 9·45. $C_{17}H_{22}O$ requires C, 84·3; H, 9·1%). Light absorption : see Table. The 2 : 4-*dinitrophenylhydrazone* was purified by adsorption on alumina from benzene solution and crystallised from ethyl acetate in dark red leaflets, m. p. 187° (Found : N, 13·35. $C_{23}H_{26}O_4N_4$ requires N, 13·3%). Light absorption in chloroform (main band only) : Maximum, 4110 A.; ε, 42,000.

8-(2′ : 2′-*Dimethyl*cyclo*hexyl*)-6-*methyloctan*-2-*one*.—A solution of the above ketone (2·1 g.) in ethyl acetate (25 c.c.) was shaken in hydrogen in the presence of platinic oxide (0·1 g.) until absorption was complete (932 c.c. at 14°/765 mm.; equivalent to 4·8 double bonds). After removal of the catalyst and solvent, distillation of the residue gave the saturated *ketone* (1·9 g.), b. p. 106—108°/0·1 mm., n_D^{20} 1·4913 (Found : C, 80·9; H, 12·3. $C_{17}H_{32}O$ requires C, 81·0; H, 12·7%). The 2 : 4-*dinitrophenylsemicarbazone* crystallised from alcohol in yellow needles, m. p. 171° (Found : N, 14·65. $C_{24}H_{37}O_5N_5$ requires N, 14·75%).

8-(6′ : 6′-*Dimethyl*cyclo*hex*-1′-*enyl*)-2 : 6-*dimethylocta*-1 : 3 : 5-*trien*-7-*yne*-1-*carboxylic Acid* (VI; R_1 = Me, R_2 = H).—The regenerated ketone (V; R_1 = Me, R_2 = H) (7·5 g.) was condensed with methyl bromoacetate (6 g.) and zinc (2·5 g.) in benzene (75 c.c.), and the resulting crude hydroxy-ester was dehydrated and hydrolysed in the usual manner, giving the crude acid (3·4 g.) as a viscous orange gum which partly solidified on trituration with light petroleum (b. p. 40—60°). Recrystallisation of the solid from methanol yielded the *acid* (1·72 g.) as pale yellow prisms, m. p. 171° (Found : C, 80·15; H, 8·4. $C_{19}H_{24}O_2$ requires C, 80·3; H, 8·4%). Light absorption : see Table.

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IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY,
LONDON, S.W.7.

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