368. *Unsaturated Fatty Acids. Part I. The Synthesis of Erythrogenic (Isanic) and Other Acetylenic Acids.*

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The structure (II) assigned to erythrogenic (isanic) acid has been confirmed by synthesis.

Oxidative coupling of a mixture of dec-9-ynoic acid (prepared by Barbier–Wieland degradation of undec-10-ynoic acid) and oct-1-en-7-yne (prepared from 6-chlorohex-1-yne) gave the expected three products, one of which, octadec-17-ene-9 : 11-diynoic acid, was isolated and identified with natural erythrogenic acid.

OF the naturally occurring unsaturated fatty acids, those possessing an unsaturated linkage separated from the carboxyl group by a chain of seven methylene groups constitute the main class (cf. Hilditch, *J.*, 1948, 243). The investigations to be described in this series of papers have as their initial objective the synthesis of these fatty acids from easily accessible intermediates of the type $HC{\vdots}C\cdot[CH_2]_7\cdot X$, where X is carboxyl or a group readily converted into carboxyl. The present communication deals chiefly with the confirmation, by total synthesis, of the structure assigned to erythrogenic (isanic) acid.*

The tree *Onguekoa Gore* Engler (syn. *Ongokea klaineana* Pierre; also known by the native names Boleka and Isano), which is indigenous to Equatorial Africa, bears fruits with kernels yielding *ca.* 60% of a viscous oil on extraction. From this Hébert (*Bull. Soc. chim.*, 1896, **15**, 935; *Compt. rend.*, 1896, **122**, 1550) isolated a fatty acid which he believed to belong to the C_{14} series. More recently Steger and van Loon (*Fette u. Seifen*, 1937, **44**, 243) fractionated the ethyl esters of the total fatty acids and found that these contained practically no C_{14} acid fraction, but consisted mainly of acids of the C_{18} series; a monoethylenic, diacetylenic acid was separated by crystallisation and shown to give stearic acid on catalytic reduction. Shortly afterwards the isolation of this unsaturated acid by means of its ether-soluble lead salt was reported by Castille (*Annalen*, 1940, **543**, 104), who ozonised both the acid and its ethyl ester and concluded that the former must have one of the structures (I) and (II) :

(I) $CH_2{:}CH\cdot C{\vdots}C\cdot[CH_2]_4\cdot C{\vdots}C\cdot[CH_2]_7\cdot CO_2H$ $CH_2{:}CH\cdot[CH_2]_4\cdot C{\vdots}C\cdot C{\vdots}C\cdot[CH_2]_7\cdot CO_2H$ (II)

These deductions were confirmed by Steger and van Loon (*Rec. Trav. chim.*, 1940, **59**, 1156; cf. Doucet and Fauve, *Compt. rend.*, 1942, **215**, 533) who favoured the second formula. Subsequent investigations by Castille (*Bull. Acad. Roy. Méd. Belg.*, 1941, **6**, 152) are said to have proved structure (II) correct. Unfortunately full experimental details of these degradative studies have not been published by either the Dutch or the Belgian workers. However, a comparison of the ultra-violet light-absorption properties recorded by Castille (1940) for the natural acid, with those determined later with authentic vinylacetylenes, shows that the structure (I) is inadmissible (Armitage, Cook, Entwistle, Jones, and Whiting, *J.*, 1952, 1998). As was observed by Hébert (*loc. cit.*), this unsaturated fatty acid is readily converted into a bright red insoluble polymer (see below). For this reason Castille proposed the name " erythrogenic acid," but Steger and van Loon refer to the same compound as " isanic acid," the term first introduced by Hébert for his " C_{14} acid."

Many statements have been made that boleka (isano) oil has good drying properties. These claims have, however, been refuted by Steger and van Loon (*Rec. Trav. chim.*, 1941, **60**, 342), and interest in erythrogenic acid therefore centres mainly on its unusual constitution. A few other acetylenic and polyacetylenic compounds have been encountered in Nature (Steger and van Loon, *Rec. Trav. chim.*, 1933, **52**, 593; Anchell, *J. Amer. Chem. Soc.*, 1952, **74**, 1588; Celmer and Solomons, *ibid.*, p. 1870; Ligthelm, Schwartz, and von Holdt, *J.*, 1952, 1088; Anet, Lythgoe, Silk, and Trippett, *Chem. and Ind.*, 1952, 757; Williams, Smirnov, and Gol'mov, *J. Gen. Chem., Moscow*, 1935, **5**, 1195; Sörensen and

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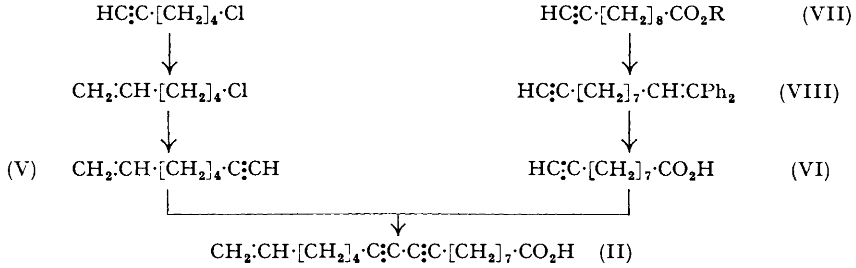
* A preliminary account of this work was given in *Chem. and Ind.*, 1953, 40.

Steen, *Annalen*, 1941, **549**, 80; Stavolt and Sörensen, *Acta Chem. Scand.*, 1950, **4**, 1567; Baalsrud, Stavolt, Holme, Nestvold, Plíva, Sörensen, and Sörensen, *ibid.*, 1952, **6**, 883; Sörensen, *Chem. and Ind.*, 1953, 240), and recently the structures of both tariric acid (III) (Lumb and Smith, *J.*, 1952, 5032) and 8-*cis*-αβ-dihydromatricaria ester (IV) (Christensen and Sörensen, *Acta Chem. Scand.*, 1952, **6**, 893) were substantiated by synthesis.

(III) $CH_3{\cdot}[CH_2]_{10}{\cdot}C{\vdots}C{\cdot}[CH_2]_4{\cdot}CO_2H$ $CH_3{\cdot}CH{:}CH{\cdot}C{\vdots}C{\cdot}C{\vdots}C{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2Me$ (IV)

Conjugated diacetylenes ($R{\cdot}C{\vdots}C{\cdot}C{\vdots}C{\cdot}R$) may be prepared by a variety of methods involving oxidative coupling of a mono-substituted acetylene ($R{\cdot}C{\vdots}CH$) (cf. Jones, *Ann. Reports*, 1944, **41**, 148; Black, Horn, and Weedon, unpublished), and also by alkylation of metal derivatives of diacetylene (Armitage, Jones, and Whiting, *J.*, 1951, 144). The route envisaged for the synthesis of erythrogenic acid consisted of the oxidation, in the presence of cuprous ammonium chloride (cf. Zal'kind and Fundyler, *Ber.*, 1936, **69**, 128), of a mixture of oct-1-en-7-yne (V) and dec-9-ynoic acid (VI), both symmetrical and unsymmetrical coupling of the two components being expected to take place.


$HC{\vdots}C{\cdot}[CH_2]_4{\cdot}Cl \rightarrow CH_2{:}CH{\cdot}[CH_2]_4{\cdot}Cl \rightarrow$ (V) $CH_2{:}CH{\cdot}[CH_2]_4{\cdot}C{\vdots}CH$

(VII) $HC{\vdots}C{\cdot}[CH_2]_8{\cdot}CO_2R \rightarrow$ (VIII) $HC{\vdots}C{\cdot}[CH_2]_7{\cdot}CH{:}CPh_2 \rightarrow$ (VI) $HC{\vdots}C{\cdot}[CH_2]_7{\cdot}CO_2H$

(V) + (VI) $\rightarrow CH_2{:}CH{\cdot}[CH_2]_4{\cdot}C{\vdots}C{\cdot}C{\vdots}C{\cdot}[CH_2]_7{\cdot}CO_2H$ (II)

A convenient route to the decynoic acid (VI) was developed from undec-10-enoic acid, which is readily available commercially, being prepared from ricinoleic acid, and has previously been synthesised (Gaubert, Linstead, and Rydon, *J.*, 1937, 1971). The methods described by earlier workers for converting undecenoic acid into undecynoic acid (VII; R = H), by bromination and subsequent dehydrobromination, were examined, and the overall yield was raised to 60%. Reaction of ethyl undecynoate (VII; R = Et) with phenylmagnesium bromide gave a tertiary alcohol which was dehydrated to the hydrocarbon (VIII) in 70% overall yield. With chromic acid this furnished (58%) the required decynoic acid (VI), oxidation occurring preferentially at the double bond. An analogous series of reactions was carried out starting with ethyl undecynoate and methylmagnesium iodide. Dehydration of the resulting tertiary alcohol gave (56%) a mixture (1 : 2) of 2-methyldodec-1- and -2-en-11-yne, which on oxidation yielded decynoic acid (42%).

Few examples have previously been recorded of similar Barbier–Wieland degradations with unsaturated fatty acids. Oleic acid (Skraup and Schwamberger, *Annalen*, 1928, **462**, 135) and several ω-*cyclo*pent-2′-enyl acids (Buu-Hoï, *Ann. Chim.*, 1944, **19**, 446) give the corresponding lower homologues, but erucic (docos-13-enoic) acid is stated to yield 12 : 13-dihydroxyheneicosanoic acid (Buu-Hoï and Janicaud, *Bull. Soc. chim.*, 1946, 147). It has now been shown that Barbier–Wieland degradation of ethyl undec-10-enoate gives dec-9-enoic acid in 50% yield. This acid occurs naturally in milk fat and in sperm-head oil (Hilditch, " The Chemical Constitution of Natural Fats," Chapman and Hall, London, 1947).

The second component, oct-1-en-7-yne (V), was prepared in the following manner. 6-Chlorohex-1-yne (Newman and Wotiz, *J. Amer. Chem. Soc.*, 1949, **71**, 1292) was partially hydrogenated in the presence of a palladium catalyst to 6-chlorohex-1-ene (90%). This was converted into the corresponding iodide which, without purification, was condensed with sodium acetylide giving the required octenyne (V) in 70% yield (based on chlorohexene).

To establish the conditions for the formation of diacetylenic fatty acids of the required type, preliminary experiments were carried out on the cross-coupling of undec-10-ynoic acid (VII; R = H) with hex-1-yne and oct-1-yne. In both cases the expected mixture of three products was produced, but these were readily separated and under optimum conditions heptadecadiynoic (IX; $n = 3$, $m = 8$) and nonadecadiynoic acid (IX; $n = 5$, $m = 8$) were isolated each in 30% yield (based on undecynoic acid). Similar coupling of oct-1-yne with the decynoic acid (VI) led to dihydroerythrogenic acid (IX; $n = 5$, $m = 7$) which was obtained as a crystalline solid (32%). The preparation of this acid from natural erythrogenic acid has been claimed by Castille (*loc. cit.*) but no physical properties were reported.

$$CH_3\cdot[CH_2]_n\cdot C\vdots C\cdot C\vdots C\cdot[CH_2]_m\cdot CO_2H \quad \text{(IX)}$$

The structures of the diacids (X; $m = 7$) and (X; $m = 8$), formed as by-products in the above reactions by self-coupling of the decynoic and undecynoic acids respectively, were confirmed by catalytic hydrogenation to 1 : 20-eicosane- and 1 : 22-docosane-dioic acid respectively.

$$HO_2C\cdot[CH_2]_m\cdot C\vdots C\cdot C\vdots C\cdot[CH_2]_m\cdot CO_2H \quad \text{(X)}$$

Cross-coupling of the octenyne (V) with the decynoic acid (VI) was next attempted and afforded octadec-17-ene-9 : 11-diynoic acid (II) in 30% yield. Its melting point was identical with that of a specimen of natural erythrogenic acid (for which the authors are greatly indebted to Dr. E. M. Meade), and no depression was observed on admixture (see Table); the identity was confirmed by comparison of the *p*-bromophenacyl esters and 2-hydroxyethylamides. Ozonolysis of the synthetic acid gave formaldehyde (36%).

	Synthetic	Natural	Mixture
Erythrogenic acid	—	39°[1]	—
,, ,,	—	39·5[2]	—
,, ,,	38·4—39·0°	38·5—39·0[3]	38·5—39·0°
2-Hydroxyethylamide	67·0—68·0	67·0—68·0[3]	67·0—68·0
p-Bromophenacyl ester	40·5—41·5	41·0—42·0[4]	40·5—41·5

[1] Steger and van Loon, *Rec. Trav. chim.*, 1940, **59**, 1156. [2] Castille, *Annalen*, 1940, **543**, 104. [3] Determined after repurification of samples supplied by Dr. E. M. Meade. [4] Prepared from Dr. Meade's specimen of the natural acid.

The ultra-violet light absorption properties of the two acids and related compounds are tabulated below. The position and intensity of the absorption maxima of synthetic erythrogenic acid agree well with the corresponding data for heptadeca-10 : 12-, nonadeca-10 : 12-, and octadeca-9 : 11-diynoic acids, and other authentic conjugated diacetylenes. The natural acid, however, exhibits a slightly more complex spectrum; the bands characteristic of the synthetic diyne acids are present, together with others of longer wave-lengths, suggesting that, even after careful purification, the natural acid still contains a small amount (*ca.* 2—3%) of an impurity with an enediyne chromophore. This contaminant has recently been isolated by Meade and named bolekic acid (cf. Jones, Whiting, Armitage,

Light absorption of diacetylenes (*max. in* Å; ε *in parentheses*).

Octa-5 : 7-diyne[1]	2280 (440)	2390 (390)	2540 (240)		
Heptadeca-10 : 12-diynoic acid	2280 (575)	2350 (445)			
Nonadeca-10 : 12-diynoic acid	2270 (470)	2370 (320)			
Octadeca-9 : 11-diynoic acid *	2280 (430)	2360 (320)			
,, 2-hydroxyethylamide †	2270 (550)	2390 (430)	2550 (200)		
Synthetic erythrogenic acid	2270 (370)	2370 (340)	2540 (40)		
Natural ,, ,, ‡	2270 (480)	2400 (480)	2550 (384)	2670 (300)	2800 (260)
,, ,, ,, [2]	2275 (1167)	2400 (870)	2530 (700)	2666 (870)	2820 (700)
Propenyldiacetylene[1]	2300 (2250)	2380 (5000)	2510 (10,000)	2640 (14,000)	2800 (11,000)
2-Hydroxyethylamide of synthetic erythrogenic acid	2270 (640)	2380 (444)	2510 (181)		
2-Hydroxyethylamide of natural erythrogenic acid ‡	2270 (650)	2380 (438)	2510 (228)		
*iso*Butylamide of synthetic erythrogenic acid	2260 (510)	2380 (378)	2510 (214)	2550 (230)	

* Also 2230 Å, ε = 430. † Also 2480 Å, ε = 200. ‡ Determined after repurification of samples supplied by Dr. E. M. Meade.

[1] Armitage, Cook, Entwistle, Jones, and Whiting, *J.*, 1952, 1998. [2] Castille, *Annalen*, 1940, **543**, 104.

Cook, and Entwistle, *Nature*, 1951, **168**, 900). (Castille's light-absorption data for natural erythrogenic acid indicate that his sample contained *ca.* 6% of bolekic acid.) The hydroxyethylamides, which are more readily purified than the parent acids, exhibit almost identical light absorption properties.

Crystals of all the synthetic diacetylenic acids and their derivatives described above exhibit the remarkable photolability observed previously with natural erythrogenic acid (Hébert; Steger and van Loon; Castille; *locc. cit.*) and some other diacetylenes (Jones and Whiting *et al.*, *J.*, 1952, 1998). Natural and synthetic erythrogenic acid both give, on irradiation, even in high vacuum, a vivid red polymer insoluble in the common organic solvents and in alkali. The same effect is observed with the derivatives, though the *p*-bromophenacyl ester is comparatively stable. The natural acid is slightly more sensitive to light than the synthetic, probably owing to contamination with bolekic acid. The polymer has the same composition as the parent acid (Steger and van Loon, and Castille, *locc. cit.*).

On exposure to daylight, the crystal surfaces of the majority of the other diacetylenic acids now reported become blue; this colour changes to red on addition of methanol or other solvents which dissolve the unchanged diacetylenes, but not the polymer. A similar reddening frequently takes place on prolonged exposure to light and, at least in one instance (nonadeca-10 : 12-diynoic acid), a reversible change from blue to red occurs simply on warming from 0° to *ca.* 30°. The formation of the initial colours under the influence of light seems to be accentuated by rise in temperature. All these diacetylenes are quite unaffected by light when in solution; the solid urea complex of erythrogenic acid is also stable.

The structure of these coloured polymers is obscure. It has, however, been suggested that they are formed by cross-linking of poly-yne chains, which in a favourable crystal lattice are perhaps held close together, as a consequence of photochemical activation (Jones, Whiting, *et al.*, *loc. cit.*). It is proposed to examine these phototropic and thermotropic changes in more detail.

This opportunity is taken to report the synthesis of octadec-9-ynoic (stearolic) and heptadec-9-ynoic acid from intermediates developed in the investigations described above. Treatment of the Grignard reagent from the mixture of methyldodecenynes with *n*-octyl and *n*-hexyl toluene-*p*-sulphonate gave, respectively, mixtures of the methyleicosenynes (XI) and (XII), and the corresponding methyloctadecenynes. (Hex-1-yne and oct-1-yne

(XI) $CH_3\cdot[CH_2]_7\cdot C\vdots C\cdot[CH_2]_7\cdot CH{:}CMe_2$ $CH_3\cdot[CH_2]_7\cdot C\vdots C\cdot[CH_2]_8\cdot CMe{:}CH_2$ (XII)

$CH_3\cdot[CH_2]_7\cdot C\vdots C\cdot[CH_2]_7\cdot CO_2H$ (XIII)

were similarly converted into dec-5-yne and tetradec-5-yne in 44 and 34% yield respectively.) Oxidation of these hydrocarbon mixtures with chromic acid led to stearolic (XIII) and hexadec-9-ynoic acid in poor yield. The hydrogenation of stearolic to oleic acid over a lead-poisoned palladium catalyst (Lindlar, *Helv. Chim. Acta*, 1952, **35**, 446) will be described in a later publication.

EXPERIMENTAL

Yields are based on the total amount of acetylenes used.

Light absorptions were determined on alcohol solutions of freshly purified samples.

As far as possible the crystalline diacetylenes were screened from light.

2-Hydroxyethylamides were prepared by the method of Swern, Stutzman, and Roe (*J. Amer. Chem. Soc.*, 1949, **71**, 3017).

Undec-10-ynoic Acid (VII; R = H).—Commercial undec-10-enoic acid was distilled and the fraction, b. p. 155—157°/10 mm., m. p. 24·5—25·0°, was collected. Bromination of the acid in light petroleum (b. p. 60—80°) (previously treated with excess of bromine, and then washed with saturated sodium hydrogen carbonate solution, dried, and distilled) by the method of Myddleton and Barratt (*J. Amer. Chem. Soc.*, 1927, **49**, 2258) gave 10 : 11-dibromoundecanoic acid (70%), m. p. 37—38·5° (*idem, loc. cit.*, give m. p. 38·5°). Dehydrobromination by the procedure of Jeffery and Vogel (*J.*, 1948, 674) gave undec-10-ynoic acid (88%), b. p. 178—184°/15 mm., m. p. 43° (Krafft, *Ber.*, 1896, **29**, 2232, gives m. p. 42·5—43°).

Use of chloroform or carbon tetrachloride (cf. Jeffery and Vogel, *loc. cit.*) for the bromination was unsatisfactory; the crude product solidified slowly and gave poor yields of the acetylenic acid on dehydrobromination.

Ethyl Undec-10-*enoate and Ethyl Undec*-10-*ynoate*.—Esterification of undecenoic acid by Myddleton and Barratt's method (*loc. cit.*) gave the ethyl ester, b. p. 127—130°/10 mm. Ethyl undecynoate, prepared similarly in 83% yield, had b. p. 80—85°/0·1 mm., n_D^{22} 1·4450 (Jeffery and Vogel, *loc. cit.*, give b. p. 142°/13 mm., n_D^{20} 1·4480). The structure of the latter ester was confirmed by hydrolysis with aqueous alkali to undec-10-ynoic acid, m. p. and mixed m. p. 43° (90%).

1 : 1-*Diphenylundec*-10-*yn*-1-*ol and* 1 : 1-*Diphenylundec*-1-*en*-10-*yne* (VIII).—Ethyl undec-10-ynoate (100 g.) in ether (500 c.c.) was added dropwise at 20° to a stirred solution of phenylmagnesium bromide (from 41 g. of magnesium and 260 g. of bromobenzene) in ether (500 c.c.). The mixture was heated under reflux for 2½ hr. The Grignard complex was decomposed by the addition of ice and 2N-sulphuric acid. Isolation in the usual manner gave the alcohol which was dehydrated without purification by heating to 220° for ½ hr. (cf. Skraup and Schwamberger, *Annalen*, 1928, **462**, 135). Distillation gave 1 : 1-*diphenylundec*-1-*en*-10-*yne* (100 g., 70%), b. p. 240—245°/17 mm., 152°/0·02 mm., n_D^{21} 1·5620 (Found : C, 91·2; H, 8·4. $C_{23}H_{26}$ requires C, 91·3; H, 8·7%). Light absorption : max., 2510 Å (ε 18,000). The hydrocarbon gave a precipitate with ammoniacal cuprous chloride.

2-*Methyldodec*-11-*yn*-2-*ol*.—Reaction of ethyl undec-10-ynoate (125 g.) with methylmagnesium iodide (from 50 g. of magnesium) gave the *alcohol* (100 g.), b. p. 77°/0·06 mm., n_D^{19} 1·4601 (Found : C, 79·4; H, 12·6. $C_{13}H_{24}O$ requires C, 79·5; H, 12·3%).

2-*Methyldodec*-2-*en*-11-*yne and* 2-*Methyldodec*-1-*en*-11-*yne*.—A mixture of phosphorus oxychloride (3·2 g.), pyridine (35 c.c.; dried over KOH), and toluene (63 c.c.; dried over Na) was added during 35 min. to a stirred and cooled solution of 2-methyldodec-11-yn-2-ol (10·0 g.) in toluene (48 c.c.). The mixture was heated to 90—95° for 45 min., then cooled and poured on ice. Isolation of the product in the usual manner gave the mixture of hydrocarbons (5·0 g., 56%), b. p. 49°/0·1 mm., n_D^{20} 1·4530 (Found : C, 87·7; H, 12·7. Calc. for $C_{13}H_{22}$: C, 87·5; H, 12·5%). Determination of *iso*propenyl end-groups by the semi-quantitative infra-red method (Barnard, Bateman, Harding, Koch, Sheppard, and Sutherland, *J.*, 1950, 915) showed that the mixture contained *ca.* 30% of 2-methyldodec-1-en-11-yne.

Dehydration with formic acid, as described for the diphenylundecenol below, gave the same yield of hydrocarbons, but the product was contaminated with a small amount of a ketone (2 : 4-dinitrophenylhydrazone) formed, presumably, by hydration of the triple bond.

Dec-9-*ynoic Acid* (VI).—(*a*) A solution of chromium trioxide (17·0 g.) in water (20 c.c.) was added during 2½ hr. to a well stirred, warm (55—60°) solution of 1 : 1-diphenylundec-1-en-10-yne (25·0 g.) in acetic acid (250 c.c.). After the mixture had been stirred overnight at 20°, most of the solvent was evaporated under reduced pressure. The residue was warmed (steam-bath) for 1 hour with 2N-sulphuric acid (400 c.c.), then cooled and diluted with a saturated aqueous solution of sodium chloride (600 c.c.). Isolation of the acidic product in the usual way gave *dec*-9-*ynoic acid* (8·0 g., 58%), b. p. 88°/0·1 mm., n_D^{27} 1·4565, which crystallised in long needles, m. p. 22° (C, 71·5; H, 9·8. $C_{10}H_{16}O_2$ requires C, 71·4; H, 9·6%). The p-*bromophenacyl* ester crystallised from alcohol in plates, m. p. 75° (Found : C, 59·4; H, 6·1. $C_{18}H_{21}O_3Br$ requires C, 59·2; H, 5·8%).

A slightly lower yield of the acid was obtained by oxidising the hydrocarbon in acetone at 20° with chromic acid.

(*b*) Similar oxidation of the mixture of 2-methyldodec-2-en-11-yne and 2-methyldodec-1-en-11-yne in acetic acid gave dec-9-ynoic acid in 42% yield. The *p*-bromophenacyl ester had m. p. and mixed m. p. 75°.

1 : 1-*Diphenylundec*-10-*en*-1-*ol and* 1 : 1-*Diphenylundeca*-1 : 10-*diene*.—Reaction of ethyl undecenate (50·0 g.) with phenylmagnesium bromide (from 14·6 g. of magnesium and 87 g. of bromobenzene), in the manner described for the corresponding acetylene, gave the alcohol as a yellow oil. The crude product was divided into two equal portions which were dehydrated without purification as described below :

(i) (cf. Buu-Hoï, *Ann. Chim.*, 1944, **19**, 446). A mixture of the alcohol and formic acid (98—100%; 70 c.c.) was heated under reflux for 1¼ hr., then cooled and poured into water (400 c.c.). Isolation of the product with benzene and distillation gave 1 : 1-*diphenylundeca*-1 : 10-*diene* (30·0 g., 83% overall), b. p. 228—230°/12—14 mm., n_D^{21} 1·5545 (Found : C, 90·9; H, 9·3. $C_{23}H_{28}$ requires C, 90·8; H, 9·2%). Light absorption : max., 2510 Å (ε 20,000).

(ii) The crude alcohol was heated to 200° for 30 min. and then distilled, giving the hydrocarbon (29·0 g., 80% overall), b. p. 223—225°/10 mm., n_D^{20} 1·5540.

Dec-9-enoic Acid.—(i) A solution of chromium trioxide (19·0 g.) in water (20 c.c.) was added during 1½ hr. with vigorous stirring to a solution of 1 : 1-diphenylundeca-1 : 10-diene (25·0 g.) in glacial acetic acid (250 c.c.) at 35°. After a further ½ hour's stirring acetic acid (*ca.* 70 c.c.) was removed under reduced pressure and 2N-sulphuric acid (500 c.c.) was added to the residue. Extraction of the product with benzene and isolation of the acidic fraction furnished dec-9-enoic acid (8·5 g., 63%), b. p. 158—163°/21 mm., n_D^{21} 1·4485 (Found : C, 70·7; H, 10·6%; equiv., 164. Calc. for $C_{10}H_{18}O_2$: C, 70·6; H, 10·7%; equiv., 170) (Toyama and Tsuchiya, *J. Chem. Soc., Japan*, 1935, **56**, 1313, give b. p. 143—148°/15 mm., n_D^{20} 1·4488, for the natural acid). The *p*-bromophenacyl ester crystallised from aqueous alcohol in plates, m. p. 58° (Found : C, 58·3; H, 6·1. Calc. for $C_{18}H_{23}O_3Br$: C, 58·8; H, 6·3%) (Baudart, *Bull. Soc. chim.*, 1946, 85, gives m. p. 57·5°).

(ii) Oxidation of the hydrocarbon (10·0 g.) in acetone (20 c.c.) (previously treated with excess of $KMnO_4$ and dried over K_2CO_3) by addition (2½ hr.) of a solution of chromium trioxide (7·5 g.) and concentrated sulphuric acid (6·5 c.c.) in water (21 c.c.) gave dec-9-enoic acid (2·5 g., 44%), b. p. 158—165°/16 mm., n_D^{21} 1·4485. The *p*-bromophenacyl ester had m. p. 58°, undepressed on admixture with the specimen described above.

*Heptadeca-*10 : 12-*diynoic Acid* (IX; $n = 3$, $m = 8$).—A solution of hex-1-yne (2·5 g.) and undec-10-ynoic acid (5·0 g.) in alcohol (90 c.c.) was added to a solution of cuprous chloride (6·0 g.) and ammonium chloride (18·0 g.) in hydrochloric acid (90 c.c.; 0·08N) in a 500-c.c. flask. The flask was connected to an oxygen reservoir and shaken until absorption ceased. The resulting light green suspension was treated with 2N-hydrochloric acid (200 c.c.), and then shaken with ether, whereupon two clear layers were obtained. The ethereal layer was washed with water and extracted with 2N-sodium hydroxide. The alkaline extract was acidified with 2N-hydrochloric acid, and the acidic fraction of the product thus liberated was isolated with ether, giving a solid (6·6 g.). Distillation from a short-path still gave (i) a yellow oil (1·0 g.), b. p. 70° (bath-temp.)/10^{-5} mm., which was not examined, and (ii) a solid (2·2 g., 30%), b. p. 110° (bath-temp.)/10^{-5} mm., m. p. 39—41°. Recrystallisation from aqueous alcohol gave *heptadeca-*10 : 12-*diynoic acid* as leaflets, m. p. 40·5—41° (Found : C, 77·9; H, 9·9%; equiv., 266. $C_{17}H_{26}O_2$ requires C, 77·8; H, 10·0%; equiv., 262. Found : hydrogen no. 69, equiv. to 3·8 double bonds). Light absorption : see Table. Crystallisation from alcohol of the solid residue (3·3 g.) from the distillation gave *docosa-*10 : 12-*diynedioic acid* as plates, m. p. 112° (Found : C, 72·85; H, 9·5. $C_{22}H_{34}O_4$ requires C, 72·9; H, 9·5%). Light absorption : max., 2260, 2380, 2510, and 2560 Å (ε 410, 360, 180, and 180 respectively). The *di-*p*-bromophenacyl* ester crystallised from alcohol in plates, m. p. 94° (Found : C, 60·6; H, 6·3. $C_{38}H_{44}O_6Br_2$ requires C, 60·4; H, 5·9%).

From the neutral fraction of the reaction product dodeca-5 : 7-diyne (2·0 g.) was isolated and had b. p. 113°/10 mm., n_D^{19} 1·4890 (Danehy and Nieuwland, *J. Amer. Chem. Soc.*, 1936, **58**, 1609, give b. p. 104°/8 mm.).

The use in the coupling reaction of heterogeneous solutions, or of catalytic amounts of cuprous ammonium chloride, was found unsatisfactory.

Docosanedioic Acid.—A solution of docosa-10 : 12-diynedioic acid (250 mg.) in alcohol (30 c.c.) was shaken with Adams' catalyst (10 mg.) in an atmosphere of hydrogen until absorption was complete (78 c.c. at 22°/765 mm., equiv. to 4·5 double bonds). Removal of catalyst and solvent, and crystallisation of the residue twice from alcohol, gave the saturated diacid as plates, m. p. 126° (Found : C, 71·3; H, 11·4. Calc. for $C_{22}H_{42}O_4$: C, 71·3; H, 11·4%) (Ruzicka, Stoll, and Schinz, *Helv. Chim. Acta*, 1928, **11**, 670, give m. p. 123—124°).

*Nonadeca-*10 : 12-*diynoic Acid* (IX; $n = 5$, $m = 8$).—Oxidation of oct-1-yne (3·5 g.) and undec-10-ynoic acid (5·0 g.) in alcohol (90 c.c.) and hydrochloric acid (90 c.c.; 0·08N), in the presence of cuprous ammonium chloride (from 6 g. of cuprous chloride and 18 g. of ammonium chloride), gave : (i) *Nonadeca-*10 : 12-*diynoic acid* (2·1 g., 32%), b. p. 130° (bath-temp.)/10^{-3} mm., which crystallised from aqueous alcohol in needles, m. p. 42—43° (Found : C, 78·7; H, 10·7. $C_{19}H_{30}O_2$ requires C, 78·6; H, 10·4%. Found : hydrogen no., 81, equiv. to 3·6 double bonds). Light absorption : see Table. The *p*-bromophenacyl ester had m. p. 57°. (ii) Docosa-10 : 12-diynedioic acid (1·0 g.), m. p. and mixed m. p. 112°.

*Octadeca-*9 : 11-*diynoic Acid* (*Dihydroerythrogenic Acid*) (IX; $n = 5$, $m = 7$).—Oxidation in the usual manner of oct-1-yne (3·2 g.) and dec-9-ynoic acid (4·5 g.) in alcohol (75 c.c.) and hydrochloric acid (75 c.c.; 0·08N) containing cuprous ammonium chloride (from 5·5 g. of cuprous chloride and 16·5 g. of ammonium chloride) gave : (i) *Octadec-*9 : 11-*diynoic acid* (2·4 g., 32%), b. p. 145° (bath-temp.)/10^{-4} mm., which crystallised from aqueous alcohol in needles, m. p. 46·0—46·5° (Found : C, 78·5; H, 10·7. $C_{18}H_{28}O_2$ requires C, 78·2; H, 10·2%.

Found : hydrogen no., 71, equiv. to 3·9 double bonds). Light absorption : see Table. The p-*bromophenacyl* ester crystallised from aqueous alcohol in plates, m. p. 58·5° (Found : C, 65·5; H, 6·9. $C_{26}H_{33}O_3Br$ requires C, 65·9; H, 7·0%). The 2-*hydroxyethylamide* crystallised from aqueous acetone in plates, m. p. 70—71° (Found : C, 75·6; H, 10·7. $C_{20}H_{33}O_2N$ requires C, 75·3; H, 10·4%). Light absorption : see Table. (ii) *Eicosa*-9 : 11-*diynedioic acid* (3·0 g.) which crystallised from alcohol in plates (needles from dilute solution), m. p. 120° (Found : C, 71·9; H, 9·1. $C_{20}H_{30}O_4$ requires C, 71·8; H, 9·0%). The *di*-p-*bromophenacyl* ester crystallised from alcohol in plates, m. p. 104° (Found : C, 59·2; H, 5·7. $C_{36}H_{40}O_6Br_2$ requires C, 59·4; H, 5·5%). (iii) Hexadeca-7 : 9-diyne (2·8 g.), b. p. 110°/0·5 mm., n_D^{23} 1·4928.

Stearic Acid.—A solution of octadeca-9 : 11-diynoic acid (250 mg.) in alcohol (20 c.c.) was shaken in hydrogen in the presence of Adams' catalyst (10 mg.) until absorption was complete. Removal of catalyst and solvent and crystallisation of the residue from alcohol gave stearic acid, m. p. 68—69°, undepressed on admixture with an authentic specimen.

Eicosanedioic Acid.—A solution of eicosa-9 : 11-diynedioic acid (0·3 g.) in alcohol (40 c.c.) was shaken with Adams' catalyst (15 mg.) in an atmosphere of hydrogen until absorption was complete (H_2 absorbed, 87 c.c. at 19°/761 mm., equiv. to 4·0 double bonds). Removal of catalyst and solvent and crystallisation of the residue twice from alcohol gave the saturated diacid, m. p. 119·5—120·5° (Found : C, 70·3; H, 11·1. Calc. for $C_{20}H_{38}O_4$: C, 70·2; H, 11·2%) (*idem, loc. cit.*, give m. p. 119—121°).

6-*Chlorohex*-1-*ene.*—A solution of 6-chlorohex-1-yne (40·0 g.) (prepared in 80% yield by the method of Newman and Wotiz, *J. Amer. Chem. Soc.*, 1949, **71**, 1292) in methyl acetate (200 c.c.) was shaken in an atmosphere of hydrogen in the presence of a palladium–calcium carbonate catalyst (4·0 g.; 0·3% of Pd). When 1 mol. of hydrogen had been absorbed (9 l. at 20°/780 mm.), the reaction was interrupted, the catalyst was filtered off, and the solvent was evaporated (through a 12 × 1″ Fenske column). Distillation of the residue in small batches from a Kon flask furnished 6-*chlorohex*-1-*ene* (35 g.), b. p. 128—130°, n_D^{24} 1·4320—1·4330 (Found : C, 60·7; H, 9·5; Cl, 30·2. $C_6H_{11}Cl$ requires C, 60·7; H, 9·4; Cl, 29·9%). The product, unlike the starting material, gave no silver salt. The physical constants were unaltered after fractionation of the chlorohexene through a Stedman column (15 × 2 cm.), but about a third of the material was polymerised in the process.

Oct-1-*en*-7-*yne* (V).—A solution of 6-chlorohex-1-ene (44·0 g.) and sodium iodide (100 g.) in acetone (500 c.c.) was heated under reflux with vigorous stirring overnight. The mixture was then cooled and water was added to dissolve the sodium chloride deposited and to precipitate the 6-iodohex-1-ene. This was isolated with ether in the usual way, and washed thoroughly in pentane solution with water, and the solution was dried ($MgSO_4$) and evaporated. Without further purification the crude 6-iodohexene in ether (100 c.c.) was added during 2½ hr. to a suspension in liquid ammonia (1 l.) of sodium acetylide (prepared from 30·0 g. of sodium *via* sodamide; cf. Vaughn, Vogt, and Nieuwland, *J. Amer. Chem. Soc.*, 1934, **56**, 2120). The mixture was stirred for 3 hr. and then kept overnight, most of the ammonia being allowed to evaporate. Water was added (in an atmosphere of nitrogen) and the product was extracted with ether. The ethereal extract was washed with sulphuric acid (2N) and then water, dried, and evaporated (12 × 1″ Fenske column). Distillation of the residue gave *oct*-1-*en*-7-*yne* (28·0 g.) as a very volatile liquid, b. p. 122°, n_D^{20} 1·4310—1·4325 (Found : C, 88·0; H, 11·0. C_8H_{12} requires C, 88·8; H, 11·2%).

Octadec-17-*ene*-9 : 11-*diynoic Acid* (*Erythrogenic or Isanic Acid*) (II).—Oxidation in the usual manner of oct-1-en-7-yne (6·6 g.) and dec-9-ynoic acid (10·0 g.) in alcohol (100 c.c.) and hydrochloric acid (100 c.c.; 0·08N) containing cuprous ammonium chloride (from 12 g. of cuprous chloride and 36 g. of ammonium chloride) gave a crude product which was separated into neutral and acidic fractions. Distillation of the latter (12·5 g.) from short-path still yielded : (i) A liquid (1·9 g.), b. p. 100° (bath-temp.)/10^{-3} mm., which was not examined. (ii) A liquid (5·1 g.), b. p. 140° (bath-temp.)/10^{-3} mm., which solidified to a wax, m. p. 32—35°. Redistillation gave a solid (4·7 g.), m. p. 37·5—38·5°. Four crystallisations from light petroleum (b. p. 60—80°) yielded octadec-17-ene-9 : 11-diynoic acid as prisms, m. p 38·4—39·0°, unaltered on further crystallisation (Found : C, 79·0; H, 9·7. Calc. for $C_{18}H_{26}O_2$: C, 78·8; H, 9·6%. Hydrogen no., 58, equiv. to 4·7 double bonds). Light absorption : see Table. The p-*bromophenacyl* ester crystallised from aqueous alcohol in leaflets, m. p. 40·5—41·5° (Found : C, 66·2; H, 6·7. $C_{26}H_{31}O_3Br$ requires C, 66·2; H, 6·6%). The 2-*hydroxyethylamide* crystallised from aqueous acetone in leaflets, m. p. 67·0—68·0° (Found : C, 75·7; H, 10·0. $C_{20}H_{31}O_2N$ requires C, 75·7; H, 9·8%). Light absorption : see Table. The iso*butylamide*, prepared *via* the acid chloride, crystallised from acetone in leaflets, m. p. 52—53° (Found :

C, 80·2; H, 10·9. $C_{22}H_{35}ON$ requires C, 80·2; H, 10·7%). Light absorption: see Table. (iii) A residue of eicosa-9 : 11-diynedioic acid (5·3 g.), m. p., and mixed m. p., 120°.

Distillation of the neutral fraction gave a hydrocarbon (3·2 g.), b. p. 80°/10^{-3} mm., n_D^{25} 1·5530.

Ozonolysis of Octadec-17-*ene*-9 : 11-*diynoic Acid*.—A rapid stream of ozonised oxygen was passed for 3 hr. through a solution of synthetic octadec-17-ene-9 : 11-diynoic acid (0·5 g.) in "AnalaR" acetic acid (25 c.c.). Zinc dust (2·0 g.) was then added with cooling and the mixture was steam-distilled into cold water. When 75 c.c. of distillate had been collected, the solution was added to a solution of dimedone (0·55 g.) and sodium acetate (10·6 g.) in water (325 c.c.) and N-hydrochloric acid (75 c.c.), the pH of which had been lowered to 4·6 by the addition of alkali. The buffered solution was kept overnight. The precipitate (195 mg., 36%) was collected and dried. Crystallisation from aqueous methanol gave formaldehyde dimedone derivative, m. p. 189°, undepressed on admixture with an authentic specimen.

Natural Erythrogenic Acid.—The urea complex supplied by Dr. E. M. Meade was treated with water, and the fatty acid thus liberated was isolated by means of ether. Crystallisation from light petroleum (b. p. 60—80°) gave the acid, m. p. 38·5—39·0°, which was characterised (see Table) by formation of the 2-hydroxyethylamide (also supplied by Dr. Meade) and the *p*-bromophenacyl ester (Found: C, 65·8; H, 6·8. Calc. for $C_{26}H_{31}O_3Br$: C, 66·2; H, 6·6%).

Castille states that both permanganate oxidation of the sodium salt of erythrogenic acid (*Annalen*, 1940, **543**, 104), and hydrolysis of the dibromide of the acid (*Bull. Acad. Roy. Méd. Belg.*, 1941, **6**, 152), give "dihydroxyerythrogenic acid," also called "cyanogenic acid," m. p. 92°, by hydroxylation of the terminal double bond. No details of these reactions have been published and the analysis and equivalent weight quoted agree well with a formula $C_{18}H_{32}O_4$ rather than the expected $C_{18}H_{28}O_4$. The homogeneity of the product is therefore doubtful.

Octyl Toluene-p-*sulphonate*.—Toluene-*p*-sulphonyl chloride (134 g.) was added rapidly, in one lot, to a cooled (−5°; ice–salt bath) solution of octan-1-ol (83 g.; freshly distilled) in pyridine (400 c.c.; dried and distilled over solid KOH). The mixture was shaken until dissolution was complete, the temperature being kept below 25°. The mixture was kept at −5° for 2 hr. and the temperature then allowed to rise to 20°. Water was added and the product was extracted with chloroform. The extract was washed thoroughly with water, N-sulphuric acid, and again with water, dried (Na_2SO_4), and evaporated at 20° under reduced pressure. Distillation of the residue from a short-path still, and in the presence of solid potassium hydrogen carbonate, gave the *ester* (144 g., 79%), b. p. 170° (bath-temp.)/10^{-4} mm., n_D^{17} 1·4963 (Found: C, 62·8; H, 8·7. $C_{15}H_{24}O_3S$ requires C, 63·3; H, 8·5%).

The ester decomposed on storage, more rapidly on heating, and was stored at 0° over solid potassium hydrogen carbonate.

Hexyl Toluene-p-*sulphonate*.—Treatment of hexan-1-ol (82 g.) in pyridine (300 c.c.) with toluene-*p*-sulphonyl chloride (169 g.), as described above, gave the ester (166 g., 80%), b. p. 107° (bath-temp.)/10^{-5} mm., n_D^{25} 1·5005 (Found: C, 61·0; H, 7·9. Calc. for $C_{13}H_{20}O_3S$: C, 60·9; H, 7·9%) [Slotta and Behnisch, *Ber.*, 1933, **66**, 360, give b. p. 145—150° (bath-temp.)/ 5×10^{-2} mm.].

Tetradec-5-*yne* (cf. Gilman and Beaber, *J. Amer. Chem. Soc.*, 1923, **45**, 839; Johnson, Schwarz, and Jacobs, *ibid.*, 1938, **60**, 1882).—Hex-1-yne (11·0 g.) was added to ethylmagnesium bromide (from 3·0 g. of magnesium) in ether (100 c.c.). The mixture was heated under reflux for 2½ hr., then cooled, and added during 1/2 hr. to a solution of octyl toluene-*p*-sulphonate (71 g.) in ether (100 c.c.). The resulting white suspension was heated under reflux overnight. Decomposition with ice and 2N-sulphuric acid, and isolation of the product in the usual manner, gave *tetradec*-5-*yne* (7·3 g., 34%), b. p. 94°/15 mm., n_D^{20} 1·4460 (Found: C, 85·8; H, 13·8. $C_{14}H_{26}$ requires C, 86·5; H, 13·5%).

Dodec-5-*yne*.—Repetition of the preceding experiment, but with hexyl toluene-*p*-sulphonate (64 g.), gave *dodec*-5-*yne* (9·0 g., 44%), b. p. 93°/15 mm., n_D^{23} 1·4397 (Found: C, 86·6; H, 13·1. $C_{12}H_{22}$ requires C, 86·7; H, 13·3%).

2-*Methyleicos*-1-*en*-11-*yne and* 2-*Methyleicos*-2-*en*-11-*yne*.—Reaction of the Grignard complex from the mixture (20·0 g.) of 2-methyldodec-1-en-11-yne and 2-methyldodec-2-en-11-yne with octyl toluene-*p*-sulphonate (64 g.) gave a crude product (15·7 g., 50%), b. p. 122—128°/0·1 mm., which could not be separated by distillation from traces of unchanged octyl ester. The latter were removed by treatment with a boiling solution of ethylmagnesium bromide (from 3·0 g. of magnesium) in ether (100 c.c.). Isolation in the usual way gave the mixture of C_{21} hydrocarbons, b. p. 140°/0·3 mm., n_D^{18} 1·4647 (Found: C, 87·0; H, 13·4. Calc. for $C_{21}H_{38}$: C, 86·8; H, 13·2%).

Purification of the crude product was also effected, though less conveniently, by treatment with alcoholic sodium ethoxide at 20° for 3 hr.

2-*Methyloctadec*-1-*en*-11-*yne and* 2-*Methyloctadec*-2-*en*-11-*yne*.—Reaction of the Grignard complex from the mixture (17·8 g.) of 2-methyldodec-1-en-11-yne and 2-methyldodec-2-en-11-yne with hexyl toluene-*p*-sulphonate (52 g.), and isolation and purification of the product as described in the preceding experiment, gave the mixture of hydrocarbons (6·3 g., 24%), b. p. 118°/0·4 mm., n_D^{23} 1·4648 (Found: C, 86·5; H, 13·1. Calc. for $C_{19}H_{34}$: C, 86·9; H, 13·1%).

Octadec-9-*ynoic Acid* (*Stearolic Acid*).—A mixture (3·1 g.) of 2-methyleicos-1-en-11-yne and 2-methyleicos-2-en-11-yne in glacial acetic acid (32 c.c.) was oxidised with a solution of chromium trioxide (2·4 g.) in water (2·5 c.c.) in the usual manner. The resulting mixture was diluted with water and extracted with benzene. The extract was washed with water and treated with excess of 2N-sodium hydroxide. The alkaline aqueous layer and the solid sodium salt which separated as a flocculent precipitate were removed and acidified with 2N-sulphuric acid. Isolation of the product with ether and four crystallisations from aqueous alcohol gave stearolic acid (0·63 g., 21%) as prisms, m. p. 46—47°, undepressed on admixture with an authentic specimen, m. p. 46—47° (Adkins and Burks, *Org. Synth.*, 1947, **27**, 76) (Found: C, 77·2; H, 11·7. Calc. for $C_{18}H_{32}O_2$: C, 77·1; H, 11·5%). The p-*bromophenacyl* ester crystallised from aqueous alcohol in plates, m. p. 54° (Found: C, 65·3; H, 8·1. $C_{26}H_{37}O_3Br$ requires C, 65·3; H, 7·8%).

Hexadec-9-*ynoic Acid*.—Oxidation of a mixture (5·3 g.) of 2-methyloctadec-1-en-11-yne and 2-methyloctadec-2-en-11-yne in glacial acetic acid (55 c.c.) with a solution of chromium trioxide (4·4 g.) in water (5 c.c.), and isolation of the acidic product, gave an oil (3·5 g.) which solidified at 0°. Crystallisation from alcohol and finally from acetic acid yielded the *acid* (0·8 g., 16%) as plates, m. p. 39° (Found: C, 76·4; H, 11·2. $C_{16}H_{28}O_2$ requires C, 76·1; H, 11·2%).

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