Anodic Syntheses. Part XIV.* The Use of Acetylenic Components. A New Synthesis of Oleic Acid.

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[Reprint Order No. 6168.]

The use of (unconjugated) acetylenic acids and half-esters in anodic "crossed" coupling reactions has been examined, and developed into a new synthesis of unsaturated acids.

A study has been made of the partial reduction of acetylenic acids over the Lindlar catalyst.

The electrolysis of a monocarboxylic acid with a half-ester, and hydrolysis of the initial product, provides a convenient synthesis of fatty acids:

$$R{\cdot}CO_2H + HO_2C{\cdot}[CH_2]_n{\cdot}CO_2Me \longrightarrow R{\cdot}[CH_2]_n{\cdot}CO_2Me \longrightarrow R{\cdot}[CH_2]_n{\cdot}CO_2H$$

The extension of this route to the preparation of the important natural ethylenic acids requires the introduction of an unsaturated grouping, either as such or in some protected form, into one of the two components used in the electrolysis. Obvious groupings are double bonds, their dihydroxy-derivatives, and triple bonds. Provided these were separated from the carboxyl group by at least two carbon atoms, they would not be expected to affect markedly the coupling reaction. The required unsaturated acid would then be obtained directly from an ethylenic component, and from a dihydroxy- or acetylenic component by well-known standard reactions on the initial product.

The examination of some of the above possibilities has been reported in previous papers in this series. Thus *cis*- and *trans*-ethylenic acids and their *erythro*- and *threo*-dihydroxy-derivatives have been shown to couple normally with half-esters, the configuration of the

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* Parts IX—XIII, *J.*, 1953, 2393; 1954, 448, 1804, 4219; 1955, 1097.

starting material being fully retained in the product. This provides convenient stereospecific methods for the chain extension of unsaturated fatty acids (Parts IX, X, XII, XIII *).

To complete our initial survey of possible methods for introducing an unsaturated grouping with the monocarboxylic acid component used in the electrolysis, and at the same time to extend our knowledge of the groupings which can be tolerated during coupling reactions of the Kolbe type, we have studied the electrolysis of stearolic (octadec-9-ynoic) acid. Before our work, the behaviour of acetylenic acids at the anode had received very little attention. Only acetylenedicarboxylic acid ($HO_2C{\cdot}C{\vdots}C{\cdot}CO_2H$) and phenylpropiolic acid ($Ph{\cdot}C{\vdots}C{\cdot}CO_2H$) had been examined; as would be expected in view of their αβ-unsaturated structures, neither acid underwent coupling of the Kolbe type (Vanzetti, *Gazzetta*, **1916**, **46**, 49).

When electrolysed in methanol with an excess of methyl hydrogen adipate, stearolic acid (I; X = C⋮C) behaved normally at the anode, giving tetratriaconta-9 : 25-diyne by symmetrical coupling, and, after hydrolysis, behenolic (docos-13-ynoic; II, X = C⋮C) acid in 28% yield by " crossed " coupling with the half-ester. The structure of the acid was confirmed by conversion into erucic acid (see below).

Various anodic chain extensions of the general type,

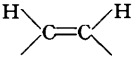
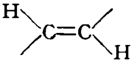
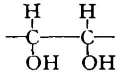
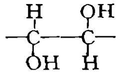
$$\text{(I)}\ CH_3{\cdot}[CH_2]_7{\cdot}X{\cdot}[CH_2]_7{\cdot}CO_2H + HO_2C{\cdot}[CH_2]_4{\cdot}CO_2Me$$

$$\downarrow$$

$$\text{(II)}\ CH_3{\cdot}[CH_2]_7{\cdot}X{\cdot}[CH_2]_{11}{\cdot}CO_2H$$

where X is an unsaturated group or potential unsaturated centre, are compared in Table 1. The nature of the group X has no great influence on the yield of the product of " crossed " coupling. The choice of starting material for the anodic synthesis of any particular unsaturated acid would therefore be governed primarily by such considerations as its availability, and the ease with which both it and the anodic product can be purified. If a suitable natural acid is readily available, this can be used to prepare a *cis*-acid directly, and will normally be the most convenient starting material [cf. synthesis of erucic (docos-*cis*-13-enoic) and nervonic (tetracos-*cis*-15-enoic) acid from oleic acid (Parts IX and X), and of *cis*-vaccenic (octadec-*cis*-11-enoic) acid from palmitoleic (hexadec-*cis*-9-enoic) acid (Part XII)]. If the natural starting material is difficult to purify, or if it is desired to effect a stereomutation during the synthesis to give a *trans*-product, then the anodic chain extension of the dihydroxy-derivative may offer advantages [cf. synthesis of *trans*-vaccenic acid from the *threo*-dihydroxy-derivative of palmitoleic acid (Part XII)]. In the absence of a suitable natural starting material a synthetic acetylenic acid may prove most suitable.

TABLE 1. *Four-carbon anodic chain extension of unsaturated and hydroxy-acids* (I).

C_{18} Acid	X	Mols. of adipic half-ester	Yield (%) of C_{22} acid *
Oleic [1]		4	34
Elaidic [1]		4	42
erythro-9 : 10-Dihydroxystearic [1]	 $-\overset{H}{\underset{OH}{C}}-\overset{H}{\underset{OH}{C}}-$	4·7	34 †
threo-9 : 10-Dihydroxystearic [1]	 $-\overset{H}{\underset{OH}{C}}-\overset{OH}{\underset{H}{C}}-$	5·1	27
Stearolic	—C≡C—	4	28

* Based on unrecovered C_{18} acid. There was retention of configuration in the first four cases.
† Crystalline methyl ester. [1] Bounds, Linstead, and Weedon, *J.*, 1953, 2393.

Turning to methods for the introduction of an unsaturated centre with a dicarboxylic component, attention has so far been directed to the use of acetylenic intermediates of the type (VI). By " crossed " coupling first at one end of the molecule with a monocarboxylic acid, and then at the other with a half-ester, a variety of acetylenic acids, and hence, by partial reduction, the corresponding ethylenic acids, could be prepared from a common intermediate. For the method to have a wide scope the value of n must be small. However, previous investigations on the electrolysis of ethylenic monoacids (see summary by Weedon, *Quart. Rev.*, 1952, **6**, 380) suggest that n must be $\nless 2$ if normal anodic coupling is to occur. The " limiting " diacid (VI; $n = 2$) was rather inaccessible when these investigations began (Johnson, *J.*, 1946, 1011; see, however, an improved synthesis by Jones, Mansfield, and Whiting, *J.*, 1954, 3208) and we selected the then unknown diacids where $n = 3$ and 4 for initial study in order to confirm the validity of the above proposals. Our work with these intermediates can conveniently be divided into three sections : (i) preparation of the diacids, (ii) their use in anodic " crossed " coupling reactions, and (iii) the partial reduction of the resulting acetylenic acids. We have previously reported the preparation of dodec-6-ynedioic acid (VI; $n = 4$) and its use in the synthesis of tariric (octadec-6-ynoic) and petroselinic (octadec-*cis*-6-enoic) acid (Part XI).

Preparation of Intermediates.—The method described in Part XI for the preparation of the dodecynedioic acid (VI; $n = 4$), and indicated in the reaction scheme below, has been

(III) $\mathrm{Cl{\cdot}[CH_2]_n{\cdot}C{\vdots}CH + Br{\cdot}[CH_2]_n{\cdot}Cl \longrightarrow Cl{\cdot}[CH_2]_n{\cdot}C{\vdots}C{\cdot}[CH_2]_n{\cdot}Cl}$ (IV) $\longrightarrow$

(V) $\mathrm{NC{\cdot}[CH_2]_n{\cdot}C{\vdots}C{\cdot}[CH_2]_n{\cdot}CN \longrightarrow HO_2C{\cdot}[CH_2]_n{\cdot}C{\vdots}C{\cdot}[CH_2]_n{\cdot}CO_2H}$ (VI)

examined further. The contaminant of the dichlorodecyne (IV; $n = 4$) is not, as previously suggested, a chlorodecenyne formed by partial dehydrohalogenation, but a chlorododecadiyne (VII) produced in *ca.* 12% yield by self-condensation of the chlorohexyne (III; $n = 4$). The chlorododecadiyne was not isolated, but the crystalline tridecadiynoic acid (VIII) derived from it in the nitrile synthesis was easily separated from the required dodecynedioic acid (VI; $n = 4$). The monoacid was shown by Evans's method (cf. Eglinton and Whiting, *J.*, 1953, 3052) to contain 2 active hydrogen atoms, thus confirming the presence of the ethynyl group ($\mathrm{{\cdot}C{\vdots}CH}$), and on catalytic reduction it absorbed 4 mols. of hydrogen to give tridecanoic acid. When treated under vigorous conditions with alkali it furnished an isomeric acid. By analogy with the rearrangement of other ω-acetylenic acids (Krafft, *Ber.*, 1896, **29**, 2232; Stenhagen, *Arkiv Kemi*, 1949, **1**, 99; Jones, Whitham, and Whiting, *J.*, 1954, 3201), the product is formulated as trideca-6 : 11-diynoic acid (IX).

(VII) $\mathrm{HC{\vdots}C{\cdot}[CH_2]_4{\cdot}C{\vdots}C{\cdot}[CH_2]_4{\cdot}Cl}$ $\mathrm{HC{\vdots}C{\cdot}[CH_2]_4{\cdot}C{\vdots}C{\cdot}[CH_2]_4{\cdot}CO_2H}$ (VIII)

(IX) $\mathrm{CH_3{\cdot}C{\vdots}C{\cdot}[CH_2]_3{\cdot}C{\vdots}C{\cdot}[CH_2]_4{\cdot}CO_2H}$ $\mathrm{HO_2C{\cdot}[CH_2]_4{\cdot}CCl{:}CH{\cdot}[CH_2]_4{\cdot}CO_2H}$ (X)

Hydrolysis of the dinitrile (V; $n = 4$) with methanolic hydrogen chloride led to the hydrogen chloride adduct (X) of the desired acid.

The second intermediate, dec-5-ynedioic acid (VI; $n = 3$), was prepared from trimethylene bromide chloride by the route developed for its higher homologue. However, the yield on each stage was only about half of that in the series where $n = 4$. This suggests that side reactions may be favoured by some steric factor in the trimethylene series. It is perhaps significant that partial hydrolysis occurred during the preparation of the dinitrile (V; $n = 3$), but none during the preparation of the analogue (V; $n = 4$). In view of the unexpectedly low yields in the preparation of dec-5-ynedioic acid alternative methods are being examined.

Anodic Coupling.—To exemplify the route proposed earlier for the synthesis of acetylenic acids from the intermediates (VI) by two successive anodic coupling reactions, syntheses of stearolic acid were undertaken.

Electrolysis of the half-esters (XI) of dodec-6- and dec-5-ynedioic acid with an excess of pentanoic and hexanoic acid respectively, and hydrolysis of the esters formed by " crossed " coupling, gave pentadec-6-ynoic (XII; $n = 4$) and tetradec-5-ynoic acid (XII; $n = 3$) in 25% yield. A very similar yield (23%) of octadec-6-ynoic (tariric) acid was obtained previously by electrolysis of methyl hydrogen dodec-6-ynedioate with octanoic acid (Part XI). The ability of half-esters of the type (XI) to undergo " crossed " coupling thus seems to be well established.

The conversion of the acetylenic acids (XII) into stearolic acid (XIII) required anodic chain extensions similar to that used in the synthesis of behenolic acid. After pentadec-6-ynoic acid had been electrolysed in methanol with an excess of methyl hydrogen glutarate, considerable difficulty was encountered in purifying the product of " crossed " coupling, and stearolic acid was isolated, *via* the lithium salt, only in low yield (6%). The half-ester couples and " cross " couples normally at the anode (cf. Part VIII, Linstead, Lunt, Shephard, and Weedon, *J.*, 1953, 1538; Part X), and we cannot account satisfactorily for the present result. The difficulty may be partly due to some esterification of the pentadecynoic acid with the solvent, accompanying the coupling process and leading to contamination of the product with the starting material. It has recently been shown (Part XIII) that such complications may be avoided by using the benzyl in place of the methyl (or ethyl) hydrogen ester. Chain extension of pentadecynoic acid by means of benzyl hydrogen glutarate might therefore give a better yield of stearolic acid, and will be attempted in due course.

$$\mathrm{CH_3{\cdot}[CH_2]_{7-\mathit{n}}{\cdot}CO_2H + HO_2C{\cdot}[CH_2]_{\mathit{n}}{\cdot}C{\vdots}C{\cdot}[CH_2]_{\mathit{n}}{\cdot}CO_2Me} \quad \mathrm{(XI)}$$

$$\downarrow$$

$$\mathrm{(XII)} \quad \mathrm{CH_3{\cdot}[CH_2]_7{\cdot}C{\vdots}C{\cdot}[CH_2]_{\mathit{n}}{\cdot}CO_2H + HO_2C{\cdot}[CH_2]_{7-\mathit{n}}{\cdot}CO_2Me}$$

$$\downarrow$$

$$\mathrm{(XIII)} \quad \mathrm{CH_3{\cdot}[CH_2]_7{\cdot}C{\vdots}C{\cdot}[CH_2]_7{\cdot}CO_2H}$$

Anodic " crossed " coupling of tetradec-5-ynoic acid with methyl hydrogen adipate took place normally in methanol. After hydrolysis of the initial product, stearolic acid was readily isolated in 24% yield, and identified by direct comparison with an authentic specimen. It yielded stearic acid on complete catalytic hydrogenation.

Partial Reduction of Acetylenic Acids.—The partial reduction of acetylenes has been studied by many previous workers, and widely employed in the synthesis of olefins. Usually chemical methods of reduction give the *trans*-isomer exclusively, whilst catalytic hydrogenation over palladium or nickel gives predominantly the *cis*-isomer (cf. Campbell and Campbell, *Chem. Rev.*, 1942, **31**, 148; Crombie, *Quart. Rev.*, 1952, **6**, 128). In keeping with this generalisation, reduction of stearolic and behenolic acid with zinc and acetic acid is reported to give elaidic (octadec-*trans*-9-enoic) and brassidic (docos-*trans*-13-enoic) acid respectively (Holt, *Ber.*, 1892, **25**, 962; Gonzalez, *Anales Fís. Quím.*, 1926, **24**, 156). Robinson and Robinson (*J.*, 1925, **127**, 175), however, found that treatment of stearolic acid with a mixture of hydrochloric acid, acetic acid, titanous chloride and zinc gave oleic acid; their evidence leaves no doubt that the product had the *cis*-configuration. It is possible that their experiment is related to the recently observed *cis*-reductions of tolane ($\mathrm{Ph{\cdot}C{\vdots}C{\cdot}Ph}$), [$^2H_2$]acetylene, and [1-^{2}H]propyne with metal-promoted zinc reagents (Rabinovitch and Looney, *J. Amer. Chem. Soc.*, 1953, **75**, 2652). Whether or not the *trans*-acids obtained from stearolic and behenolic acid by the earlier workers using zinc and acetic acid were due to an initial *cis*-addition, followed by an inversion of configuration, is debatable.

Numerous catalytic hydrogenations of acetylenic to the corresponding *cis*-ethylenic fatty acids have been recorded. A W6 Raney nickel catalyst has been used in most of the recent work (Strong *et al.*, *ibid.*, 1948, **70**, 1699, 3391; 1950, **72**, 4263; Huber, *ibid.*, 1951, **73**, 2730; Fusari, Greenlee, and Brown, *J. Amer. Oil Chemists' Soc.*, 1951, **28**, 416; cf. Howton and Davis, *J. Org. Chem.*, 1951, **16**, 1405; Lumb and Smith, *J.*, 1952, 5032). In a careful study of the reduction of stearolic acid by this method, Khan (*J. Amer. Oil Chemists' Soc.*, 1953, **30**, 40) found that fractional crystallisation of the crude product after 1 mol. of hydrogen had been absorbed gave 72% of oleic, 16% of stearolic, and 12% of stearic acid, showing that the catalyst is not completely selective. Infrared examination of the crude product revealed the presence of *ca.* 6% of *trans*-olefin, indicating that the reaction is not completely stereospecific. Other authors have also commented on the formation of small amounts of *trans*-olefins and saturated acids during the half-reduction of acetylenic acids over W6 Raney nickel. These impurities can, however, usually be removed by low-temperature crystallisation.

Relatively little use has been made of palladium catalysts for the partial reduction of unconjugated acetylenic fatty acids. Paal and Schiedewitz (*Ber.*, 1930, **63**, 766) found that half-hydrogenation of both stearolic and behenolic acid over 1% palladium–barium sulphate gave a mixture of the *cis*- and the *trans*-isomer of the corresponding ethylenic acid, together with the starting material and the saturated acid. We have noted similar lack of stereospecificity and selectivity in the reduction of stearolic acid over 0·5% palladium–calcium carbonate, although this catalyst was reported by Ames and Bowman (*J.*, 1952, 677) to give high yields of the *cis*-olefin from undec-9-ynoic acid. Hofman and Sax (*J. Biol. Chem.*, 1953, **205**, 55) have recommended 5% palladium–charcoal in an alcohol-pyridine medium for the reduction of octadec-11-ynoic acid to the *cis*-olefin; they claim that much less stearic acid is given by this procedure than by the use of W6 Raney nickel.

The conspicuous success of Lindlar's lead–palladium–calcium carbonate catalyst (*Helv. Chim. Acta*, 1952, **35**, 446) in the synthesis of vitamin A and other polyenes from acetylenic intermediates (cf. Weedon, *Ann. Reports*, 1952, **49**, 137) has led us to examine the use of this catalyst for the half-reduction of acetylenic fatty acids. When authentic stearolic acid was reduced over Lindlar catalyst in ethyl acetate, to which a small amount of quinoline had been added for enhanced selectivity (cf. Lindlar, *loc. cit.*), 1 mol. of hydrogen was rapidly absorbed and the reaction then became extremely slow. Crystallisation of the product following Khan's procedure (*loc. cit.*) gave oleic acid in 74% yield, but no stearic or stearolic acid. Reversed-phase chromatography (cf. Howard and Martin, *Biochem. J.*, 1950, **46**, 532), which provides a much more sensitive method for the analysis of mixtures of saturated, ethylenic, and acetylenic acids (Crombie, unpublished results), also failed to detect any significant quantities of stearic or stearolic acid in the " crude " reduction product. An infrared examination of the latter, after esterification with methanol, indicated the presence of about 5% of *trans*-olefin * (cf. Swern, Knight, Shreve, and Heether, *J. Amer. Oil Chemists' Soc.*, 1950, **27**, 17; Ahlers, Brett, and McTaggart, *J. Appl. Chem.*, 1953, **3**, 433). That no migration of the unsaturated centre had occurred during the reduction (cf. Hilditch and Vidyarthi, *Proc. Roy. Soc.*, 1929, *A*, **122**, 552) was shown by comparing the relative quantities of the diacids produced on ozonolysis of stearolic acid, its " crude " reduction product, and purified natural oleic acid. All three samples gave high yields of azelaic acid (see Table 2). The small amounts of other diacids also obtained may be ascribed to secondary reactions during the ozonolysis and the subsequent decomposition of the ozonide (Ackman, Linstead, and Weedon, unpublished results).

TABLE 2. *Ozonolysis of stearolic and oleic acid.*

Acid ozonised	Total yield (%) of diacids	Composition (%) of diacid mixture : azelaic	suberic	pimelic	other acids
Stearolic	86	96·5	*ca.* 1·5	*ca.* 1·5	Trace
Half-reduction product	71	98·5	*ca.* 1	*ca.* 0·5	Trace
Purified natural oleic	79	96	2·5	*ca.* 1	Trace

The results of the various studies on the partial reduction of stearolic acid are summarised in Table 3. For the preparation of oleic acid, the method with the Lindlar catalyst compares favourably with other procedures, and was used to reduce the anodic sample of stearolic acid, thus completing a new total synthesis of oleic acid. Behenolic acid was similarly converted into erucic acid (88%).

Oleic acid has been known since 1813 (cf. Chevreul, " Recherches chimiques sur les corps gras," Imprimerie Nationale, Paris, 1889), and is recognised as the most widespread and abundant fatty acid in Nature. It is therefore not surprising that its synthesis has attracted considerable attention. The first unambiguous synthesis was by Noller and Bannerot (*J. Amer. Chem. Soc.*, 1934, **56**, 1563). This was not a complete synthesis since one of the starting materials was obtained from natural oleic acid. Two total syntheses were reported by Baudart (*Compt. rend.*, 1943, **217**, 399; 1945, **220**, 404; *Bull. Soc. chim. France*, 1946, **13**, 87), and others by Ames and Bowman (*J.*, 1951, 1079) and by Huber (*J. Amer. Chem. Soc.*, 1951, **73**, 2730). However, all these syntheses, with the exception

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* [*Added in Proof.*]—This has now been reduced to *ca.* 1—2% by doubling the amount of quinoline used in the reduction.

TABLE 3. *Half-reduction of stearolic acid.*

Authors	Method	Main product Structure	M. p.	%	By-product
Gonzalez[1]	Zn–AcOH	Elaidic	—	—	—
Robinson and Robinson[2]	Zn–AcOH–$TiCl_3$	Oleic	—	—	—
Adkins and Billica[3]	H_2–W6-Ni	Elaidic *	42—45°	—	—
Huber[4]	,,	Oleic	10·9—11·5	64	Stearic
Khan[5]	,,	,,	13·0—13·2	65—71	Stearic + *trans*-olefin + stearolic
Paal and Schiedewitz[6] ...	H_2–Pd–$BaSO_4$	Oleic + elaidic	—	—	Stearic + stearolic
Present	H_2–Pd–Pb–$CaCO_3$	Oleic	12·8—13·1	74	*trans*-Olefin

[1] *Anales Fis. Quim.*, 1926, **24**, 156. [2] *J.*, 1925, **127**, 175. [3] *J. Amer. Chem. Soc.*, 1948, **70**, 695. [4] *Ibid.*, 1951, **73**, 2730. [5] *J. Amer. Oil Chemists' Soc.*, 1953, **30**, 40. [6] *Ber.*, 1930, **63**, 766.

* This claim is at variance with the subsequent experience of other workers, all of whom report high yields of *cis*-olefins when reducing acetylenes over Raney nickel. It is noteworthy that Adkins and Billica cite no evidence, apart from m. p., in support of the structure assigned to their product.

of the last, give mixtures of oleic and elaidic acid in which the latter predominates. Only the present synthesis, and that of Huber which shares the same final stage, gives oleic acid by a route which is substantially stereospecific.

EXPERIMENTAL

M. p.s below 35° were determined after solidification of the molten substance in a capillary tube.

Intermediates.—*Acids.* Pentanoic acid was prepared by chromic acid oxidation of pure *n*-pentyl alcohol, and hexanoic acid by catalytic hydrogenation of sorbic acid in alcohol over Adams catalyst. The stearolic acid used in the synthesis of behenolic acid, for comparison with the acids synthesised anodically, and in the pilot reduction studies, was obtained by converting (natural) oleic acid into its dibromide and dehydrobromination of the latter with either alcoholic potassium hydroxide (Adkins and Burks, *Org. Synth.*, 1947, **27**, 76) or sodamide in liquid ammonia (Khan, Deatherage, and Brown, *J. Amer. Oil Chemists' Soc.*, 1951, **28**, 27).

Half-esters. Methyl hydrogen glutarate was prepared from glutaric anhydride (Part VIII, *J.*, 1953, 1538). The anhydride was best obtained by a Michael addition of ethyl malonate to methyl acrylate (Marvel and Stoddard, *J. Org. Chem.*, 1938, **3**, 198), and conversion of the resulting triester into glutaric acid (Bachman, Kushner, and Stevenson, *J. Amer. Chem. Soc.*, 1942, **64**, 977), followed by dehydration of the latter with acetic anhydride (Part VIII). Methyl hydrogen adipate was prepared by the method of Swann, Oehler, and Buswell (*Org. Synth.*, Coll. Vol. II, p. 276), and methyl hydrogen dodec-6-ynedioate as described in Part XI.

1-Chloropent-4-yne was prepared from commercial 1-bromo-3-chloropropane (cf. Henne and Greenlee, *J. Amer. Chem. Soc.*, 1945, **67**, 484). The starting material had b. p. 146°, 35—36°/13 mm., n_D^{19} 1·4870, d_4^{25} 1·589, d_4^{20} 1·597. Its bisthiuronium picrate, formed in 55% yield, had m. p. 229—231° (Levy and Campbell, *J.*, 1939, 1442, give m. p. 229°).

Electrolyses.—The cells " A " and " B," and the general procedure followed, were those described in Part IX (*J.*, 1953, 2393). After each electrolysis any solid which had separated was filtered off, the solution was acidified with a slight excess of 2N-hydrochloric acid and then evaporated under reduced pressure. The residue was extracted with ether and the extracts were washed with 0·5N-sodium hydroxide and dried. Acidification of the alkaline washings gave recovered starting materials, if any. The ethereal solution was evaporated and, unless stated otherwise, the residue was then hydrolysed by boiling it with an excess of aqueous-alcoholic potassium hydroxide (10% w/v) for 2—3 hr. in an atmosphere of nitrogen. Dilution with water, and isolation of the acidic fraction in the usual way, gave a product which was extracted with light petroleum (b. p. 40—60°). Crystallisation of the insoluble portion gave the diacid. Evaporation of the petroleum extracts yielded the monoacid.

Ozonolyses.—The unsaturated acids were ozonised at 0° in acetic acid containing 15% of methyl acetate, and the ozonides were decomposed at 35° in acetic acid with hydrogen peroxide (cf. Klenk and Bongard, *Z. physiol. Chem.*, 1952, **290**, 181). The resulting diacids were analysed by paper chromatography (cf. Cheftel, Munier, and Macheboeuf, *Bull. Soc. Chim. biol.*, 1952, **34**, 380; Reid and Lederer, *Biochem. J.*, 1951, **50**, 60).

Behenolic (*Docos*-13-*ynoic*) *Acid* (II; X = C⋮C).—Stearolic acid (10·0 g.) and methyl hydrogen adipate (17·2 g., 3·0 mols.) in methanol (60 c.c.) were electrolysed in cell " B " (current 0·8—1·0 amp.; faradays passed, *ca.* 1·1 times theor.). More half-ester (5·7 g., 1·0 mol.) was added towards the end of the reaction. After the electrolysis, the solid which had separated was collected and crystallised from methanol–light petroleum, giving *tetratriaconta*-9 : 25-*diyne* (0·7 g., 8%) as plates, m. p. 47·5—48° (Found : C, 86·85; H, 13·35. $C_{34}H_{62}$ requires C, 86·7; H, 13·3%).

The methanolic solution from the cell was acidified and evaporated. The residue was extracted with ether, and the extract was washed with alkali and dried. Acidification of the washings gave stearolic acid (0·8 g.), m. p. 45·5—46·5°, and sebacic acid (0·1 g.), m. p. 130—133°. Evaporation of the ethereal solution and distillation of the residue from a Kon flask gave (i) a fraction (10·15 g.), b. p. 90—121°/0·02 mm., which gave sebacic acid (6·0 g.), m. p. 131—133·5°, on hydrolysis, and (ii) a fraction (3·8 g.), b. p. 130—167°/0·02 mm., n_D^{24} 1·4570—1·4575. The latter, together with the high-boiling residue (2·0 g.), was hydrolysed and the acidic fraction was isolated. Crystallisation from aqueous alcohol and then from light petroleum (b. p. 40—60°) gave behenolic acid (3·1 g.), m. p. 57·5—58° (Found : C, 78·6; H, 11·95%; equiv., 341. Calc. for $C_{22}H_{40}O_2$: C, 78·5; H, 12·0%; equiv., 337) (Haussknecht, *Annalen*, 1867, **143**, 40, gives m. p. 57·5°).

A solution of behenolic acid (17·24 mg.) in acetic acid was shaken with Adams catalyst in hydrogen until absorption was complete (2·184 c.c. at N.T.P., equiv., to 1·9 double bonds). Removal of catalyst and solvent gave docosanoic acid (12 mg.), m. p. 79·5—80° (Francis and Piper, *J. Amer. Chem. Soc.*, 1939, **61**, 577, give m. p. 79·95°).

Dodec-6-ynedioic Acid (VI; $n = 4$) *and Trideca-6 : 12-diynoic Acid* (VIII).—Crude dec-5-yno-1 : 10-dinitrile (96 g.), was prepared and hydrolysed as described in Part XI. Crystallisation of the product from benzene gave dodec-6-ynedioic acid (69·5 g.). The benzene mother-liquors were evaporated and the residue was triturated with light petroleum (b. p. 40—60°). Separation and crystallisation of the insoluble fraction from benzene gave more of the diacid (5·3 g.). Evaporation of the petroleum solution, and crystallisation of the residue (11·4 g.), m. p. 35—38°, from light petroleum (b. p. 40—60°) gave *trideca*-6 : 12-*diynoic acid*, m. p. 39—40° (Found : C, 75·55; H, 8·95%; equiv., 205. $C_{13}H_{18}O_2$ requires C, 75·7; H, 8·8%; equiv., 206). This acid, like undec-10-ynoic acid, gave a colourless precipitate with alcoholic silver nitrate; neither undec-10-enoic nor stearolic acid gave this test which requires an ethynyl group. Determination of active hydrogen by Evans's method (cf. Eglinton and Whiting, *J.*, 1953, 3052) gave a value of 1·95 for both the tridecadiynoic acid and undec-10-ynoic acid (indicating 1 acetylenic hydrogen and 1 carboxyl group), and 1·0 for stearolic acid.

Tridecanoic Acid.—A solution of trideca-6 : 12-diynoic acid (529 mg.) in acetic acid was shaken with Adams catalyst (32 mg.) in hydrogen until absorption was complete (241 c.c. at 18°/762 mm., equiv. to 3·95 double bonds). The solvent and catalyst were removed, and the residue was crystallised from aqueous methanol, giving tridecanoic acid (428 mg.), m. p. 41—42° (Found : C, 72·65; H, 12·1%; equiv., 218. Calc. for $C_{13}H_{26}O_2$: C, 72·85; H, 12·25%; equiv., 214) (De Boer, *Nature*, 1927, **119**, 634, gives m. p. 41·2°). The *p*-bromophenacyl ester, prepared in 68% yield, had m. p. 71·5—72° (Found : C, 61·1; H, 7·8. Calc. for $C_{21}H_{31}O_3Br$: C, 61·3; H, 7·6%) (Moses and Reid, *J. Amer. Chem. Soc.*, 1932, **54**, 2101, give m. p. 75°).

Trideca-6 : 11-*diynoic Acid* (IX).—A solution of trideca-6 : 12-diynoic acid (500 mg.) in 9N-potassium hydroxide–ethylene glycol (5 c.c.) was heated for 1 hr. at 160° (cf. Jones, Whitham, and Whiting, *J.*, 1954, 3201). Isolation of the acidic product in the usual way and crystallisation from light petroleum (b. p. 40—60°) gave *trideca*-6 : 11-*diynoic acid* (151 mg., 30%), m. p. 36—36·5° (Found : C, 75·5; H, 9·05. $C_{13}H_{18}O_2$ requires C, 75·7; H, 8·8%). The acid gave no precipitate with alcoholic silver nitrate. It exhibited no light absorption with $E_{1\,\text{cm.}}^{1\%}$ >15 in the region 210—240 mμ.

6-*Chlorododec*-6-*enedioic Acid* (X).—Dec-5-yno-1 : 10-dinitrile (2·0 g.) was added to cold (0°) saturated methanolic hydrogen chloride (35 c.c.). The resulting solution was kept at 20° overnight, then evaporated under reduced pressure. Water was added and the product was isolated with ether, giving a liquid (2·6 g.; n_D^{23} 1·4659). Hydrolysis for 2 hr. with boiling aqueous-alcoholic potassium hydroxide (10% w/v) led to an acid (2·25 g., 81%), m. p. 62—63°. Crystallisation from ether–light petroleum (b. p. 40—60°) and then from aqueous methanol gave 6-*chlorododec*-6-*enedioic acid*, m. p. 64—65° (Found : C, 54·95; H, 7·55; O, 24·4, 24·35%; equiv., 133. $C_{12}H_{19}O_4Cl$ requires C, 54·85; H, 7·3; O, 24·35%; equiv., 131).

A solution of the diacid (9·991 mg.) in acetic acid was shaken with Adams catalyst in hydrogen until absorption was complete (1·590 c.c. at N.T.P., equiv. to 1·9 mols.). Removal of catalyst and solvent, and crystallisation of the residue from aqueous methanol, gave dodecanedioic acid (5·6 mg., 64%), m. p. 126—127·5°, undepressed on admixture with an authentic specimen (Walker and Lumsden, *J.*, 1901, **79**, 1201, give m. p. 126·5—127°).

1 : 8-*Dichloro-oct-4-yne* (IV; *n* = 3).—A solution of sodamide (from 28·6 g. of sodium; cf. Vaughn, Vogt, and Nieuwland, *J. Amer. Chem. Soc.*, 1934, **56**, 2120) in liquid ammonia (1 l.) was added during 2 hr. to a rapidly stirred solution of 1-chloropent-4-yne (133 g.) (Henne and Greenlee, *ibid.*, 1945, **67**, 484) in liquid ammonia (1 l.). After 20 min., 1-bromo-3-chloropropane (208·5 g.) was added during 2·5 hr., and the mixture was stirred overnight. Ammonium chloride (70 g.) was added, and the ammonia was then evaporated. The residue was extracted thoroughly with ether, and the extract was washed with 2N-hydrochloric acid, then with water and dried ($MgSO_4$). Distillation from a Kon flask and refractionation through a Stedman column (20 × 2 cm.) gave 1 : 8-dichloro-oct-4-yne (43·3 g., 19%), b. p. 111—114°/10 mm., n_D^{20} 1·4853—1·4881. A mixture (83 g.) of the chloropentyne and the bromide chloride was recovered.

Oct-4-yno-1 : 8-dinitrile (V; *n* = 3) *and Dec-5-ynedioic Acid* (VI; *n* = 3).—A mixture of 1 : 8-dichloro-oct-4-yne (41 g.), sodium iodide (85 g.), and dry acetone (600 c.c.) was stirred and heated under reflux for 22 hr. The solid was filtered off and the solution was evaporated under reduced pressure. The residue was extracted with ether, and the extract was washed with aqueous sodium thiosulphate and dried ($MgSO_4$). Evaporation of the solvent gave crude 1 : 8-di-iodo-oct-4-yne (73 g.). A mixture of the latter, potassium cyanide (40 g.), acetone (190 c.c.), and water (85 c.c.) was heated under reflux for 47 hr. Most of the acetone was distilled off and the residue was extracted with ether. The extract was washed with 2N-sodium hydroxide, aqueous sodium thiosulphate, and then water, and dried ($MgSO_4$). Distillation yielded *oct-4-yno-1 : 8-dinitrile* (20 g., 55%), b. p. 97—125°/0·3 mm., n_D^{21} 1·4739 (Found : N, 17·15. $C_{10}H_{12}N_2$ requires N, 17·5%). Acidification of the combined aqueous washings precipitated a solid (1·9 g.) which was collected and had m. p. 103·5—105·5°, undepressed on admixture with the decynedioic acid described below. Acidification of the ether-insoluble portion of the material obtained on evaporation of the acetone gave a nitrogenous acid " Y " (17·5 g.).

A mixture of the dinitrile (18·6 g.), potassium hydroxide (26 g.), water (225 c.c.), and alcohol (120 c.c.) was stirred vigorously, and boiled under reflux for 95 hr. The mixture was cooled and extracted with ether. The aqueous solution was acidified with 6N-hydrochloric acid. The precipitated acid was separated and dried. A further quantity of the crude product was obtained by continuous ether-extraction of the aqueous layer. Crystallisation from benzene gave *dec-5-ynedioic acid* (9·8 g., 43%), m. p. 109—110° (Found : C, 60·75; H, 7·2%; equiv., 102. $C_{10}H_{14}O_4$ requires C, 60·6; H, 7·1%; equiv., 99). Similar alkaline hydrolysis of " Y " also yielded the diacid (4·4 g.). The total yield of decynedioic acid from dichloro-octyne was 30%.

Methyl Dec-5-ynedioate and Methyl Hydrogen Dec-5-ynedioate (XI; *n* = 3).—A mixture of dec-5-ynedioic acid (4·0 g.), absolute methanol (5·0 c.c.), benzene (10 c.c.), and concentrated sulphuric acid (0·6 c.c.) was heated under reflux for 24 hr., and then cooled. Dilution with water and isolation of the neutral product with ether in the usual way gave the *diester* (3·35 g., 79%), b. p. 113—119°/0·5 mm., n_D^{19} 1·4592—1·4615 (Found : C, 63·95; H, 8·15. $C_{12}H_{18}O_4$ requires C, 63·7; H, 8·0%).

A mixture of the diester (3·3 g.), dec-5-ynedioic acid (5·0 g.), *n*-butyl ether (1·0 c.c.), and concentrated hydrochloric acid (0·5 c.c.) was heated at 160°. After 15 min. the temperature was lowered to 130°, methanol (1·0 c.c.) was added, and heating was continued for 4·5 hr., methanol (0·33 c.c.) again being added after 2·5 hr. (cf. Swann, Oehler, and Buswell, *Org. Synth.*, Coll. Vol. II, p. 276). Distillation of the product gave the diester (4·0 g.) and *methyl hydrogen dec-5-ynedioate* (3·3 g.), b. p. 132—142°/0·1 mm., n_D^{20} 1·4682—1·4703 (Found : C, 61·9; H, 7·75. $C_{11}H_{16}O_4$ requires C, 62·25; H, 7·6%).

Pentadec-6-ynoic Acid (XII; *n* = 4).—A solution of pentanoic acid (12·2 g., 3 mols.) and methyl hydrogen dodec-6-ynedioate (9·6 g., 1 mol.) in methanol (60 c.c.) was electrolysed in cell " B " (current 1·2—1·4 amps.; faradays passed, *ca.* 1·3 times theor.). Isolation of the products by the general procedure outlined above, and crystallisation of the diacid fraction (petroleum-insoluble) from aqueous methanol, gave docosa-6 : 16-diynedioic acid (0·35 g., 5%), m. p. 103—103·5°, undepressed on admixture with the sample described in Part XI. (In another experiment the yield of diacid was 9%.) Crystallisation of the monoacid fraction (petroleum-soluble) from aqueous alcohol at 0° gave *pentadec-6-ynoic acid* (1·65 g.), m. p. 25—25·5° (Found : C, 75·75; H, 11·4. $C_{15}H_{26}O_2$ requires C, 75·55; H, 11·0%. Hydrogen no. 128, equiv. to 1·85 double bonds). Distillation of the material recovered from the mother-liquors gave a fraction (1·2 g.), b. p. 90—110° (bath-temp.)/10^{-5} mm., and more of the pentadecynoic acid (0·75 g.; total yield 2·4 g., 25%), b. p. 125—135° (bath-temp.)/10^{-5} mm., m. p. 18—21°.

Redistillation of the combined low-boiling materials from two experiments gave a C_{12} ester fraction, b. p. 123—126°/11 mm., n_D^{20} 1·4603 (Found : C, 73·5; H, 10·1. Calc. for $C_{12}H_{20}O_2$: C, 73·4; H, 10·25%). This probably consists of methyl undec-6-ynoate and methyl undec-10-en-6-ynoate. Analogous mixtures have been obtained previously in couplings with azelaic (Part IV, Linstead, Lunt, and Weedon, *J.*, 1951, 1130) and β-methylglutaric half-esters (Ställberg-Stenhagen, *Arkiv Kemi*, 1950, 2, 95).

Tetradec-5-ynoic Acid (XII; *n* = 3).—Hexanoic acid (10·0 g., 2·95 mols.) and methyl hydrogen dec-5-ynedioate (6·2 g., 1 mol.) in methanol (40 c.c.) were electrolysed in cell " A " (current 1·4—1·5 amp.; faradays passed, *ca.* 1·3 times theor.). Isolation of the products by the general procedure gave : (i) *Octadeca-5 : 13-diynedioic acid* (0·25 g., 6%) which crystallised from aqueous methanol and had m. p. 102—104° (Found : C, 70·85; H, 8·5. $C_{18}H_{26}O_4$ requires C, 70·55; H, 8·55%. Hydrogen no. 81, equiv. to 3·8 double bonds). (ii) *Tetradec-5-ynoic acid* (1·75 g., 27%) which crystallised from aqueous methanol (1 : 3) and had m. p. 33—34° (Found : C, 75·0; H, 10·85. $C_{14}H_{24}O_2$ requires C, 74·95; H, 10·8%). A solution of this acid (11·71 mg.) in acetic acid was shaken with Adams catalyst in hydrogen until absorption was complete (2·226 c.c. at N.T.P., equiv. to 1·9 double bonds). Removal of catalyst and solvent, and crystallisation of the residue from aqueous methanol, gave myristic acid, m. p. and mixed m. p. 53—54·5°.

Stearolic (*Octadec-9-ynoic*) *Acid* (XIII).—(*a*) A solution of pentadec-6-ynoic acid (6·4 g., 1 mol.) and methyl hydrogen glutarate (10·0 g., 2·55 mols.) in methanol (30 c.c.) was electrolysed in cell " A " (current 0·6—0·7 amp.; faradays passed, *ca.* 0·95 times theor.). When the current began to drop, more half-ester (3·35 g., 0·85 mol.) was added. The products were isolated in the usual way, and separated into mono- and di-acid fractions with light petroleum. Crystallisation of the crude diacid (3·6 g.) from water (charcoal) gave suberic acid (2·6 g.), m. p. 138—141°. The monoacid fraction, which was only partly solid, was esterified with methanol. The product was distilled and collected in six fractions, b. p. 85—132°/0·15 mm., which were hydrolysed separately. The acidic products in hot methanol were neutralised with aqueous lithium hydroxide. The solutions were evaporated, and the residues were washed with acetone and then crystallised from water at 0°, giving lithium stearolate as needles, m. p. 190—196° (decomp.). Regeneration of the acid from its salt, isolation with ether, and crystallisation from aqueous alcohol gave stearolic acid (0·44 g., 6%), m. p. and mixed m. p. 45—46°.

(*b*) Tetradec-5-ynoic acid (1·55 g., 1 mol.) and methyl hydrogen adipate (3·3 g., 3 mols.; equiv., 161) in methanol (16 c.c.) were electrolysed in cell " A " (current 1·5—1·6 amps; faradays passed, *ca.* 1·25 times theor.). The products were isolated in the usual way, and separated into mono- and di-acid fractions with light petroleum. Crystallisation of the crude diacid from water gave sebacic acid (0·8 g., 38%), m. p. 131—132·5°. Crystallisation of the crude monoacid from aqueous alcohol gave stearolic acid (467 mg., 24%), m. p. and mixed m. p. 45·5—46·5°, unchanged on further recrystallisation (Found : C, 77·0; H, 11·55. Calc. for $C_{18}H_{32}O_2$: C, 77·1; H, 11·5%). A solution of the stearolic acid (13·78 mg.) in acetic acid was shaken with Adams catalyst in hydrogen until absorption was complete (2·226 c.c. at N.T.P., equiv. to 2·0 double bonds). Removal of catalyst and solvent, and crystallisation of the residue from aqueous alcohol, gave stearic acid (9 mg., 63%), m. p. and mixed m. p. 68·5—69°.

Oleic (*Octadec*-cis-*9-enoic*) *Acid.*—A mixture of Lindlar catalyst (*Helv. Chim. Acta*, 1952, 35, 446), quinoline (1·2 g.), and ethyl acetate (10 c.c.) was shaken in hydrogen until absorption was complete. A solution of stearolic acid (3·0 g.) in ethyl acetate (60 c.c.) was added, and the mixture was shaken until the absorption of hydrogen became very slow. The reaction was then interrupted, and the catalyst was filtered off (kieselguhr). The filtrate was washed with 2N-hydrochloric acid, then with water, dried ($MgSO_4$), and evaporated. The residue (3·0 g.) had m. p. 11·8—12·8°. Reversed-phase chromatography on paraffin from aqueous acetone gave only one band; the sample was shown to contain $<$2·5% of stearolic or stearic acid. Ozonolysis of a portion of the " crude " product gave azelaic acid (see Table 2). A further portion was esterified with methanol, and the product was distilled at 10^{-4} mm. Determination of the intensity of the infrared absorption at 10·35 μ of a sample, in carbon disulphide, of the total distillate indicated the presence of *ca.* 5% of *trans*-olefin.

Crystallisation from acetone at −40° of the product from another preparation, identical with that described above, gave oleic acid (2·25 g.), m. p. and mixed m. p. 12·8—13·1°. Similar reduction of the stearolic acid (301 mg.), synthesised anodically, gave oleic acid (235 mg., 78%), m. p. 11·8—12·8°, raised by one crystallisation from acetone at −50° to m. p. 12·3—13·0°.

Reduction of stearolic acid in ethyl acetate, light petroleum (b. p. 60—80°), or alcohol, with Lindlar catalyst without quinoline, gave products containing stearic acid.

Erucic (*Docos*-cis-*13-enoic*) *Acid.*—Behenolic acid (2·2 g.) in ethyl acetate (80 c.c.) was reduced over Lindlar catalyst (2·2 g.), containing quinoline (0·88 g.), in the manner described for stearolic acid. Isolation of the product and crystallisation from aqueous alcohol gave erucic acid (1·95 g., 88%), m. p. 31·9—33·7°. After one further crystallisation from the same solvent it had m. p. 33·0—33·5° and did not depress the m. p. of a specimen of the natural acid. Performic acid oxidation (cf. Swern, Billen, Findley, and Scanlan, *J. Amer. Chem. Soc.*, **1945**, **67**, 1786) gave *threo*-13 : 14-dihydroxybehenic acid (91%), m. p. and mixed m. p. 100—101° (Dorée and Pepper, *J.*, 1942, 477, give m. p. 101°).

The authors thank Dr. L. Crombie for the reversed-phase chromatogram, Mr. R. G. Ackman for carrying out the ozonolyses, and Mr. M. K. Johnson for assistance during the early stages of the reduction studies. One of the authors (B. C. L. W.) is indebted to the Chemical Society for a grant from the Research Fund, and another (B. W. B.) to the Department of Scientific and Industrial Research for a maintenance grant. Analyses and infrared measurements were carried out in the microanalytical (Mr. F. H. Oliver) and spectrographic (Mr. R. L. Erskine) laboratories of this Department.

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[*Received, February 24th,* 1955.]