

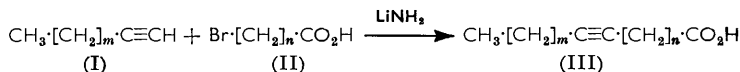
164. Syntheses of Long-chain Acids. Part VI.¹ Acetylenic Acids and *cis,cis*-Docosa-5,13-dienoic Acid.

By D. E. AMES, A. N. COVELL, and T. G. GOODBURN.

Acetylenic acids are prepared by condensation of ω -bromo-acids with lithio-alkynes and the scope of the method is examined. Alk-3-, -4-, and -5-ynoic acids are conveniently prepared by condensation of alkyl halides with the dilithio-derivatives of ω -acetylenic alcohols and oxidation of the resulting alkynols with chromic acid.

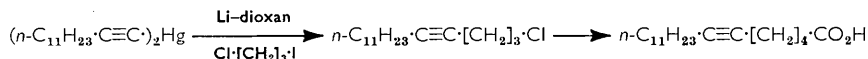
Condensation of the lithio-derivative of *NN*-dimethylhex-5-ynamide with 1-iodohexadec-7-yne gives *NN*-dimethyldocosa-5,13-diynamide which, on hydrolysis and semihydrogenation, yields *cis,cis*-docosa-5,13-dienoic acid.

CONDENSATION of the lithium derivative of an alk-1-yne (I) with an ω -bromo-acid (II) in liquid ammonia-tetrahydrofuran gives the acetylenic acid (III).² The scope of this method has now been examined further and it has been found that no acetylenic acid can be isolated when bromoacetic acid or β -bromopropionic acid is used. Condensation of γ -bromobutyric acid (II; $n = 3$) with hept-1-yne, however, gave undec-5-ynoic acid in low yield



(11%) although with dec-1-yne no acetylenic acid could be isolated. 5-Bromopentanoic acid (II; $n = 4$) with hept-1-yne, however, gave dodec-6-ynoic acid in 90% yield. It has already been shown² that higher bromo-acids (II; $n = 5, 7, \text{ or } 10$) give good yields of acetylenic acids.

Pent-1-yne affords hexadec-12-ynoic acid (III; $m = 2, n = 10$) in high yield on condensation with 11-bromoundecanoic acid. The alkynes (I; $m = 3-7$) also give good yields and the application of the process to higher alkynes has therefore been examined. Taylor and Strong³ showed that the alkynes (I; $m < 10$) could be condensed satisfactorily with ω -chloroalkyl iodides but tridec-1-yne (I; $m = 10$) failed to condense with 1-chloro-4-iodobutane. Lumb and Smith⁴ also failed to alkylate tridec-1-yne with 1-chloro-3-iodopropane in liquid ammonia, even in an autoclave, but they did achieve the following synthesis of tariric acid:



We have now found that tridec-1-yne can be condensed with 5-bromopentanoic acid (II; $n = 4$) in the presence of lithamide in liquid ammonia-tetrahydrofuran at 50° in an

¹ Part V, Ames, Covell, and Goodburn, *J.*, 1963, 5889.

² Ames and Covell, *J.*, 1963, 775.

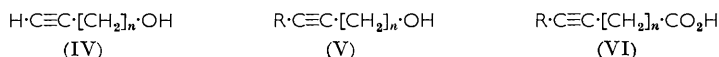
³ Taylor and Strong, *J. Amer. Chem. Soc.*, 1950, **72**, 4263.

⁴ Lumb and Smith, *J.*, 1952, 5032.

autoclave. This direct synthesis gave tariric acid in 49% yield and catalytic semi-hydrogenation furnished petroselinic acid. With 11-bromoundecanoic acid, tridec-1-yne gave tetracos-12-ynoic acid (III; $m = n = 10$) in 71% yield.

Extension of this synthesis to hexadec-1-yne (I; $m = 13$), however, gave less satisfactory results even when the reaction was carried out at 50° in an autoclave; presumably the high melting point and insolubility of the alkyne in liquid ammonia limit the applicability of the method. Under these conditions, hexadec-1-yne gave about 20% of acetylenic acids in condensations with 8-bromo-octanoic acid and with 14-bromotetradecanoic acid. The latter example, giving triacont-15-ynoic acid (I; $m = n = 13$), and thence *cis*-triacont-15-enoic acid, provides the highest acid prepared by this method and appears to be near the limit to which the process can be used effectively.

In view of the failure of ω -bromo-acetic, -propionic, and -butyric acids to condense satisfactorily with alkynes, alternative routes to acids having the acetylenic group near the carboxyl have been examined. The condensation of alkyl halides with the dilithio-derivatives of acetylenic alcohols (IV; $n = 1, 2$, or 3) has been described.¹ High yields are obtained using a 2 : 1 ratio of acetylenic alcohol to alkyl halide (whereas to obtain good yields in the condensation of alkynes with ω -bromo-acids, ratios of 5 : 1 are required).



Oxidation of several alk-3-yn-1-ols (V; $n = 2$) with chromic acid to give the corresponding alk-3-ynoic acids has been reported.⁵ This method has been found to give alk-3-, -4-, and -5-ynoic acids in about 30% yield (some alcohol also being recovered). Oxidation of tetradec- and pentadec-2-yn-1-ols, however, gave unsatisfactory results.

Pentadec-3-ynoic acid (VI; $\text{R} = n\text{-C}_{11}\text{H}_{23}$, $n = 1$), obtained by oxidation of pentadec-3-yn-1-ol (V; $\text{R} = n\text{-C}_{11}\text{H}_{23}$, $n = 2$), was also prepared, less satisfactorily, from tetradec-2-yn-1-ol (V; $\text{R} = n\text{-C}_{11}\text{H}_{23}$, $n = 1$) by conversion into the bromide, treatment with cuprous cyanide, and hydrolysis. Oxidation of hexadec-4-yn-1-ol with chromic acid gave hexadec-4-ynoic acid, previously prepared from tetradec-2-yn-1-ol by malonic ester synthesis.¹

Alkylation of hex-5-yn-1-ol with dodecyl bromide gave octadec-5-yn-1-ol and thence octadec-5-ynoic acid (VI; $\text{R} = n\text{-C}_{12}\text{H}_{25}$, $n = 3$) in 28% overall yield. This acid was also prepared (35% overall yield) by condensation of dodecyl bromide with *NN*-dimethylhex-5-ynamide followed by alkaline hydrolysis.⁶

Synthesis by way of these acetylenic alcohols provides a convenient, direct route to the alk-3-, -4-, and -5-ynoic acids. In the case of alk-5-ynoic acids, however, preparation by way of the dimethylamide furnishes an efficient alternative process. Catalytic semi-hydrogenation⁷ of the acetylenic acids yielded the corresponding *cis*-olefinic acids.

Bagby *et al.*⁸ isolated *cis,cis*-docosa-5,13-dienoic acid from the seed oil of *Limnanthes douglasii*. We examined the synthesis of this interesting acid which is unusual in containing two fully isolated double bonds. 1-Bromohexadec-7-yne (VII; $\text{X} = \text{Br}$) was condensed with but-3-yn-1-ol in presence of lithamide to give eicosa-3,11-diyn-1-ol (VIII). Attempts to convert this alcohol into the bromide or chloride were unsuccessful (cf. the observations of Eglinton and Whiting⁹ on the conversion of but-3-yn-1-ol into halides). Oxidations of the diyne (VIII) with chromic acid gave eicosa-3,11-diynoic acid (IX; $n = 1$, $\text{R} = \text{OH}$) and, by semihydrogenation, *cis,cis*-eicosa-3,11-dienoic acid.

As an alternative route to the higher diacetylenic acid, 1-iodohexadec-7-yne was condensed with *NN*-dimethylhex-5-ynamide in the presence of lithamide to give *NN*-dimethyldocosa-5,13-diynamide (IX; $\text{R} = \text{NMe}_2$, $n = 3$) (62%). Vigorous alkaline

⁵ Jones, Whitham, and Whiting, *J.*, 1954, 3201; Craig and Moyle, *J.*, 1963, 4402.

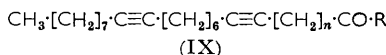
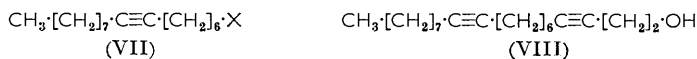
⁶ Cf. Ames and Islip, *J.*, 1963, 4363.

⁷ Cram and Allinger, *J. Amer. Chem. Soc.*, 1956, **78**, 2522.

⁸ Bagby, Smith, Miwa, Lohmar, and Wolff, *J. Org. Chem.*, 1961, **26**, 1261.

⁹ Eglinton and Whiting, *J.*, 1950, 3650.

hydrolysis furnished the parent acid (IX; R = OH, $n = 3$). Catalytic semihydrogenation then gave *cis,cis*-docosa-5,13-dienoic acid which was hydroxylated by the action of



performic acid followed by hydrolysis. The resulting *threo,threo*-5,6,13,14-tetrahydroxydocosanoic acid was identical with the sample prepared from the diene acid of *Limnanthes douglasii*. We are indebted to Dr. I. A. Wolff and Mr. M. Bagby for carrying out the mixed melting point determination.

EXPERIMENTAL

14-Bromotetradecanoic Acid.—14-Hydroxytetradecanoic acid¹ (12.5 g.) was added to a mixture of hydrogen bromide-acetic acid (100 c.c.; d 1.25) and concentrated sulphuric acid (25 c.c.) and left overnight at room temperature. The mixture was heated at 100° for 8 hr., more hydrogen bromide solution (25 c.c.) being added after 3 hr., and poured into ice-water. Filtration and recrystallisation from light petroleum (b. p. 60–80°) gave the bromo-acid (14 g.), m. p. 64–65° (lit.,¹⁰ 63°) (Found: C, 54.2; H, 8.7. Calc. for $\text{C}_{14}\text{H}_{22}\text{BrO}_2$: C, 54.6; H, 8.8%).

Condensation of Alkynes with ω -Bromo-acids.—*Tariric acid.* Tridec-1-yne (30 g.) in tetrahydrofuran (50 c.c.) was added to lithamide [from lithium (1.67 g.)] in liquid ammonia ((300 c.c.)). After 30 min., 5-bromopentanoic acid (6.0 g.) in tetrahydrofuran (100 c.c.) was added and the mixture kept at 40° in an autoclave for 18 hr. Ammonia was allowed to evaporate and dilute hydrochloric acid was added. Isolation with ether gave octadec-6-ynoic acid (tariric acid) (4.6 g.), b. p. 178–180°/0.3 mm., m. p. 49–50° (lit.,⁴ 50–51°) (Found: C, 77.5; H, 11.3. Calc. for $\text{C}_{18}\text{H}_{32}\text{O}_2$: C, 77.1; H, 11.5%). Catalytic hydrogenation over palladised charcoal gave octadecanoic acid, m. p. and mixed m. p. 69–70°.

The following acids were similarly prepared. *Tetracos-12-ynoic acid* (71%) from tridec-1-yne and 11-bromoundecanoic acid. It had m. p. 68–69° [from light petroleum (b. p. 60–80°)] (Found: C, 79.1; H, 11.9. $\text{C}_{24}\text{H}_{44}\text{O}_2$ requires C, 79.1; H, 12.1%). Hydrogenation gave tetracosanoic acid, m. p. 84–85° (from ethanol) (lit.,¹¹ 85–86°). *Tetracos-9-ynoic acid* (22%), from hexadec-1-yne and 8-bromo-octanoic acid, had m. p. 65–66° [from light petroleum (b. p. 60–80°)] (Found: C, 79.4; H, 12.5%). Hydrogenation yielded tetracosanoic acid, m. p. and mixed m. p. 84–85°. *Triacont-15-ynoic acid* (20%), from hexadec-1-yne and 14-bromotetradecanoic acid, had m. p. 76–76.5° (from ethanol) (Found: C, 80.7; H, 12.2. $\text{C}_{30}\text{H}_{56}\text{O}_2$ requires C, 80.3; H, 12.6%). Hydrogenation furnished triacontanoic acid, m. p. 94–95° (from ethanol) (lit.,¹² 93.5–94°).

The following acids were prepared similarly but without use of an autoclave. *Undec-5-ynoic acid* (11%), from hept-1-yne and γ -bromobutyric acid, had b. p. 118–122°/0.15 mm., n_D^{20} 1.4608 (Found: C, 72.1; H, 9.5. $\text{C}_{11}\text{H}_{18}\text{O}_2$ requires C, 72.5; H, 10.0%). Hydrogenation gave undecanoic acid, m. p. and mixed m. p. 27–28°. *Dodec-6-ynoic acid* (90%), from hept-1-yne and 5-bromopentanoic acid, had b. p. 130–135°/0.15 mm., n_D^{25} 1.4612 (Found: C, 72.8; H, 10.3. Calc. for $\text{C}_{12}\text{H}_{20}\text{O}_2$: C, 73.4; H, 10.3%). Rowland, Taylor, and Strong¹³ reported b. p. 112–114°/1 mm., n_D^{25} 1.4462. The discrepancy in refractive index is presumably due to an error. Hydrogenation gave dodecanoic acid, m. p. and mixed m. p. 42–43°. *Hexadec-12-ynoic acid* (82%), from pent-1-yne and 11-bromoundecanoic acid, had b. p. 164–168°/0.2 mm., m. p. 41–42° [from light petroleum (b. p. 40–60°)] (Found: C, 75.7; H, 10.8. $\text{C}_{16}\text{H}_{28}\text{O}_2$ requires C, 76.1; H, 11.2%). Hydrogenation gave hexadecanoic acid, m. p. and mixed m. p. 61–62°.

Alkylation of Acetylenic Alcohols.—The alkynol (0.2 mol.) in tetrahydrofuran (100 c.c.) was added to lithamide [from lithium (0.4 g. atom)] in liquid ammonia (400 c.c.). After the mixture had been stirred for 1 hr., alkyl bromide (0.1 mol.) in tetrahydrofuran (100 c.c.) was added.

¹⁰ Hunsdiecker and Hunsdiecker, *Ber.*, 1942, **75**, 294.

¹¹ Levene and Taylor, *J. Biol. Chem.*, 1924, **59**, 921.

¹² Robinson, *J.*, 1934, 1543.

¹³ Rowland, Taylor, and Strong, *J. Amer. Chem. Soc.*, 1950, **72**, 4263.

The mixture was stirred under reflux for 8 hr. and then allowed to evaporate. Addition of dilute hydrochloric acid and isolation with ether gave the product.

Pentadec-3-yn-1-ol (89%), from but-3-yn-1-ol and undecyl bromide, had m. p. 39–40° [from light petroleum (b. p. 40–60°)] (Found: C, 80.2; H, 12.4. $C_{15}H_{28}O$ requires C, 80.3; H, 12.6%). *Hexadec-4-yn-1-ol* (75%), from pent-4-yn-1-ol and undecyl bromide, had m. p. 34° [from light petroleum (b. p. 40–60°)] (Found: C, 80.1; H, 12.6. $C_{16}H_{30}O$ requires C, 80.6; H, 12.7%). *Octadec-5-yn-1-ol* (75%) from hex-5-yn-1-ol¹⁴ and dodecyl bromide, had m. p. 34°, b. p. 180–185°/2 mm. (Found: C, 80.7; H, 12.7. $C_{18}H_{34}O$ requires C, 81.1; H, 12.9%).

Oxidation of Alkynols to Alkynoic Acids.—*Octadec-5-ynoic Acid.* Octadec-5-yn-1-ol (13.3 g.) in acetone (100 c.c.) was stirred at 15–20° while chromic acid solution¹⁵ (18 c.c.) was added gradually, and then for a further 45 min. Acetone was removed by distillation under reduced pressure (bath 20°) and water (200 c.c.) was added. After extraction with ether, the organic layers were extracted with sodium hydrogen carbonate solution. Acidification gave octadec-5-ynoic acid (5.3 g.), m. p. 50–51° [from light petroleum (b. p. 40–60°)] (lit.,¹⁶ 52.5°).

Pentadec-3-ynoic acid, (29% yield; 37% of alcohol also recovered), had m. p. 68–68.5° [from light petroleum (b. p. 40–60°)] (Found: C, 75.3; H, 11.2. $C_{15}H_{26}O_2$ requires C, 75.6; H 11.0%). Light absorption was of low intensity (ϵ 198 at 205 $m\mu$), indicating absence of conjugated acid.

Hexadec-4-ynoic acid (41%, with 24% of alcohol recovered) had m. p. and mixed¹ m. p. 68–69° [from light petroleum (b. p. 60–80°)].

Pentadec-3-ynoic Acid.—1-Bromotetradec-2-yne¹ (11 g.), cuprous cyanide (4.5 g.), and xylene (10 c.c.) were heated at 160° under reflux for 45 min. After addition of benzene, the filtered solution was distilled to give the crude nitrile, b. p. 115°/0.2 mm. This (6 g.), in methanol (45 c.c.) and water (5 c.c.), was saturated with hydrogen chloride. The solution was refluxed for 1 hr., evaporated under reduced pressure, and the residue refluxed for 2 hr. with potassium hydroxide (5 g.) in water (5 c.c.) and methanol (50 c.c.). Addition of dilute acid and isolation with ether gave the acid (1.0 g.), m. p. and mixed m. p. with sample described above, 64.5–65.5°.

Octadec-5-ynoic Acid.—*NN*-Dimethylhex-5-ynamide⁶ (6.7 g.) in tetrahydrofuran (40 c.c.) was added to a stirred suspension of lithamide [from lithium (0.34 g.)] in liquid ammonia (150 c.c.). After 1 hr., dodecyl bromide (12 g.) in tetrahydrofuran (40 c.c.) was added and the mixture was stirred under reflux for 15 hr. When the ammonia had evaporated, dilute hydrochloric acid was added and the product isolated with ether. *NN*-Dimethyloctadec-5-ynamide (6.9 g.) had b. p. 176–180°/0.2 mm., m. p. 32–34° [from light petroleum (b. p. 40–60°)] (Found: C, 77.8; H, 11.9; N, 4.6. $C_{20}H_{37}NO$ requires C, 78.1; H, 12.1; N, 4.6%). The amide (3.9 g.) and potassium hydroxide (4.7 g.) in water (5 c.c.) and 2-methoxyethanol (50 c.c.) were refluxed for 6 hr., cooled, and poured into dilute hydrochloric acid. Octadec-5-ynoic acid (2.7 g.) had m. p. and mixed m. p. 51–52° [from light petroleum (b. p. 60–80°)] (Found: C, 76.8; H, 11.3. Calc. for $C_{18}H_{32}O_2$: C, 77.1; H, 11.5%).

cis-Olefinic Acids.—Acetylenic acids were semihydrogenated to give the following.²

Petroselinic (*cis*-octadec-6-enoic) acid, b. p. 170–172°/0.5 mm., m. p. and mixed m. p. 28–29°. The benzylamide had m. p. and mixed¹⁷ m. p. 67–68°. *cis-Tetracos-12-enoic acid*, m. p. 50–51° (from ethanol) (Found: C, 78.4; H, 13.0. $C_{24}H_{46}O_2$ requires C, 78.6; H, 12.7%). Treatment with formic acid-hydrogen peroxide and hydrolysis gave threo-12,13-dihydroxy-tetracosanoic acid, m. p. 105–106° (from ethanol) (Found: C, 72.1; H, 12.1. $C_{24}H_{48}O_4$ requires C, 72.0; H, 12.1%). *cis-Tetracos-9-enoic acid*, m. p. 53–54° [from light petroleum (b. p. 60–80°)] (Found: C, 78.9; H, 12.7%). The benzylamide had m. p. 74–75° (from ethanol) (Found: C, 82.0; H, 11.5; N, 2.9. $C_{31}H_{53}NO$ requires C, 81.7; H, 11.7; N, 3.1%). *cis-Triacont-15-enoic acid*, m. p. 65–66° (from methanol) (Found: C, 79.7; H, 12.8. $C_{30}H_{58}O_2$ requires C, 79.9; H, 13.0%). *cis-Hexadec-12-enoic acid*, b. p. 164–166°/0.25 mm., m. p. 24.5–25° (from acetone at –15°) (Found: C, 75.3; H, 12.0. $C_{16}H_{30}O_2$ requires C, 75.5; H, 11.9%). *cis-Pentadec-3-enoic acid*, m. p. 41–42° [from light petroleum (b. p. 40–60°)] (Found: C, 74.9; H, 11.9. $C_{15}H_{28}O_2$ requires C, 75.0; H, 11.7%). The light absorption

¹⁴ Eglinton, Jones, and Whiting, *J.*, 1952, 2873.

¹⁵ Bowers, Halsall, Jones, and Lemin, *J.*, 1953, 2555.

¹⁶ Posternak, *Compt. rend.*, 1916, 162, 944.

¹⁷ Grimwood, Thesis, London, 1963.

data, $\lambda_{\text{inf.}}$ 228 and 240 μ (ϵ 400 and 154), suggested the presence of a trace of conjugated acid but no *trans*-isomer was indicated (band at about 970 cm^{-1} absent). *cis-Octadec-5-enoic acid*, b. p. 160°/0.2 mm., n_D^{24} 1.4582, f. p. 13° (thermometer in liquid) (Found: C, 76.9; H, 11.9. $\text{C}_{18}\text{H}_{34}\text{O}_2$ requires C, 76.5; H, 12.1%). Treatment with formic acid-hydrogen peroxide, followed by alkaline hydrolysis, gave *threo-5,6-dihydroxyoctadecanoic acid*, m. p. 94–95° (from ethanol) (lit.,¹⁶ 94°).

Hexadec-7-yn-1-ol.—Hexadec-7-ynoic acid² (29 g.) in ether (100 c.c.) was added to lithium aluminium hydride (10 g.) in ether (500 c.c.) and the mixture was refluxed for 2 hr. Addition of an excess of 6N-sodium hydroxide solution, isolation with ether, and distillation gave the *alcohol* (23.2 g.), b. p. 138–142°/0.6 mm., n_D^{20} 1.4619 (Found: C, 79.9; H, 12.4. $\text{C}_{16}\text{H}_{30}\text{O}$ requires C, 80.6; H, 12.7%).

1-Bromohexadec-7-yne.—Hexadec-7-yn-1-ol (23 g.) and pyridine (2 c.c.) in ether (100 c.c.) were treated for 30 min. with phosphorus tribromide (5 c.c.) in ether (50 c.c.) below 5°. The mixture was refluxed for 2.5 hr. and poured into water; isolation with ether furnished the *bromide* (13.8 g.), b. p. 136–138°/1 mm., n_D^{21} 1.4759 (Found: C, 63.5; H, 9.8. $\text{C}_{16}\text{H}_{29}\text{Br}$ requires C, 63.8; H, 9.7%).

Eicosa-3,11-diyn-1-ol.—But-3-yn-1-ol (31.8 g.) and 1-bromohexadec-7-yne (13.5 g.) were added successively to lithamide [from lithium (6.3 g.)] in liquid ammonia (500 c.c.) and tetrahydrofuran (250 c.c.). The mixture was refluxed for 20 hr. and then allowed to evaporate; dilute hydrochloric acid was added and the product isolated with ether. Distillation yielded *eicosa-3,11-diyn-1-ol* (4.3 g.; 36%), b. p. 166°/0.2 mm., m. p. 37–39° (Found: C, 82.4; H, 12.0. $\text{C}_{20}\text{H}_{34}\text{O}$ requires C, 82.7; H, 11.8%). 1-Iodo-hexadec-7-yne¹⁸ similarly gave the diynol (81%).

cis,cis-Eicosa-3,11-dienol.—The diynol (10 g.) in ethanol (200 c.c.) was hydrogenated in presence of palladised barium sulphate (1 g.; 5%) and quinoline (1 g.) until 2 mol. of hydrogen had been absorbed. Distillation of the filtered solution gave the *dienol* (8.65 g.), b. p. 152–154°/0.1 mm., n_D^{23} 1.4690 (Found: C, 81.6; H, 13.3. $\text{C}_{20}\text{H}_{38}\text{O}$ requires C, 81.6; H, 13.0%).

Eicosa-3,11-diynoic Acid.—8N-Chromic acid solution¹⁵ was added to the diynol (1.65 g.) in acetone (20 c.c.) until the green-brown colour persisted. After removal of acetone by distillation under reduced pressure, ether and water were added. The ethereal layer was extracted with sodium hydrogen carbonate solution; acidification, isolation with ether, and recrystallisation from light petroleum (b. p. 60–80°) gave the *acid* (0.56 g.; 31%), m. p. 65–66° (Found: C, 78.8; H, 10.5. $\text{C}_{20}\text{H}_{32}\text{O}_2$ requires C, 78.9; H, 10.6%). Hydrogenation in ethanol over palladised charcoal gave eicosanoic acid, m. p. 75–76° (lit.,¹⁹ 75–75.5°).

cis,cis-Eicosa-3,11-dienoic Acid.—Eicosa-3,11-diynoic acid (1.26 g.) in ethanol (60 c.c.) was semihydrogenated in presence of palladised barium sulphate (0.12 g.; 5%) and quinoline (0.12 g.). After evaporation of the filtered solution, the residue, in ether, was washed with 2N-hydrochloric acid and water, dried (Na_2SO_4), and evaporated (finally at 50°/0.1 mm.). The *acid* had m. p. 5–7° (sealed capillary), n_D^{23} 1.4699 (Found: C, 77.2; H, 11.5. $\text{C}_{20}\text{H}_{36}\text{O}_2$ requires C, 77.9; H, 11.8%). The low intensity of ultraviolet absorption at about 220 μ indicated the absence of conjugated acids.

NN-Dimethyldocosa-5,13-diynamide.—*NN*-Dimethylhex-5-ynamide⁶ (10.6 g.) in tetrahydrofuran (40 c.c.) was added to lithamide (from lithium, 0.53 g.) in liquid ammonia (150 c.c.). After the solution had been stirred for 1 hr., 1-iodohexadec-7-yne¹⁸ (26.5 g.) in tetrahydrofuran (40 c.c.) was added. The mixture was refluxed for 18 hr. and then left to evaporate; addition of water and isolation with ether gave the *amide* (16 g.) m. p. 30–32° [from light petroleum (b. p. 40–60°) at –40°] (Found: C, 80.2; H, 11.6; N, 3.8. $\text{C}_{24}\text{H}_{41}\text{NO}$ requires C, 80.2; H, 11.5; N, 3.9%).

Docosa-5,13-diynoic Acid.—The amide (4 g.) in 2-methoxyethanol (50 c.c.) and potassium hydroxide (5 g.) in water (5 c.c.) were refluxed for 6 hr. Water was added to dissolve the potassium salt and the solution was poured into ice-dilute hydrochloric acid. Filtration and recrystallisation from light petroleum (b. p. 40–60°) gave the *acid* (3.1 g.), m. p. 52–54° (Found: C, 79.8; H, 10.8. $\text{C}_{22}\text{H}_{36}\text{O}_2$ requires C, 79.5; H, 10.9%). Hydrogenation in ethanol over palladised charcoal gave docosanoic acid, m. p. 80–81° (from ethanol) (lit.,²⁰ 79.95°).

cis,cis-Docosa-5,13-dienoic Acid.—The diynoic acid (2 g.) in ethanol (100 c.c.) was semihydrogenated over palladised barium sulphate (0.2 g.) and quinoline (0.2 g.). After evaporation

¹⁸ Grimmer and Kracht, *Chem. Ber.*, 1963, **96**, 337.

¹⁹ Adam and Dyer, *J.*, 1925, **127**, 70.

²⁰ Francis and Piper, *J. Amer. Chem. Soc.*, 1939, **61**, 577.

of the filtered solution, the residue, in ether, was washed with 2N-hydrochloric acid and water, and distilled. The *acid* (1.5 g.) had b. p. 183—185°/0.15 mm., n_D^{22} 1.4697, m. p. -4° (sealed capillary) (Found: C, 78.2; H, 11.7. $C_{22}H_{40}O_2$ requires C, 78.5; H, 12.0%). Only a trace of *trans*-isomers was present as indicated by the very weak band at about 970 cm^{-1} .

threo,threo-5,6,13,14-*Tetrahydroxydocosanoic Acid*.—The dienic acid (1 g.), formic acid (9 c.c.; 98%), and hydrogen peroxide (1 c.c.; 30%) were stirred at 20° for 30 min. and then at 30° for 2 hr. Water was added and the product isolated with ether. The residue on evaporation was refluxed for 1 hr. with N-sodium hydroxide (50 c.c.) and the hot solution was poured into ice-dilute hydrochloric acid. Filtration and recrystallisation from ethyl acetate gave the *acid*, m. p. 125—126.5° (Found: C, 64.8; H, 11.0. $C_{22}H_{44}O_6$ requires C, 65.3; H, 11.0%). Mixed m. p. with a sample (m. p. 126—127.5°) prepared from the natural diene acid was 125.5—127° (kindly determined by Dr. I. A. Wolff and Mr. M. Bagby). The m. p. varied slightly with the rate of heating, presumably owing to lactonisation.

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