

Lipids. Part II. Total Synthesis of Ricinoleic Acid.*

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(±)-12-Hydroxyoctadec-9-ynoic acid (ricinostearolic acid) (VII) is synthesised by a method which employs the bifunctional properties of propargyl bromide : in this way an yn-β-ol system is built up in the centre of a long chain. The acid is semihydrogenated to (±)-12-hydroxyoctadec-*cis*-9-enoic acid (I). Comparison of the infrared spectrum of its methyl ester with that of natural methyl (+)-ricinoleate shows that the two compounds are structurally identical.

Natural (+)-ricinoleic acid is degraded into 12-oxo-octadec-9-ynoic acid (IX), and conditions established for its borohydride reduction to (±)-12-hydroxyoctadec-9-ynoic acid which is shown to be identical with the entirely synthetic specimen. The oxo-acetylenic acid (IX) is extremely easily isomerised by alkali to the allenic 12-oxo-octadec-9 : 10-dienoic acid (XI). The latter gives (±)-12-hydroxy-10-oxo-octadecanoic acid when treated with potassium borohydride. This is shown to differ from (±)-12-hydroxy-9-oxo-octadecanoic acid, isolated by hydration of (VII) under the usual acidic conditions, and an explanation for its formation is proposed.

Since ricinostearolic acid can be converted into ximenynic acid, a total synthesis of the latter is also achieved.

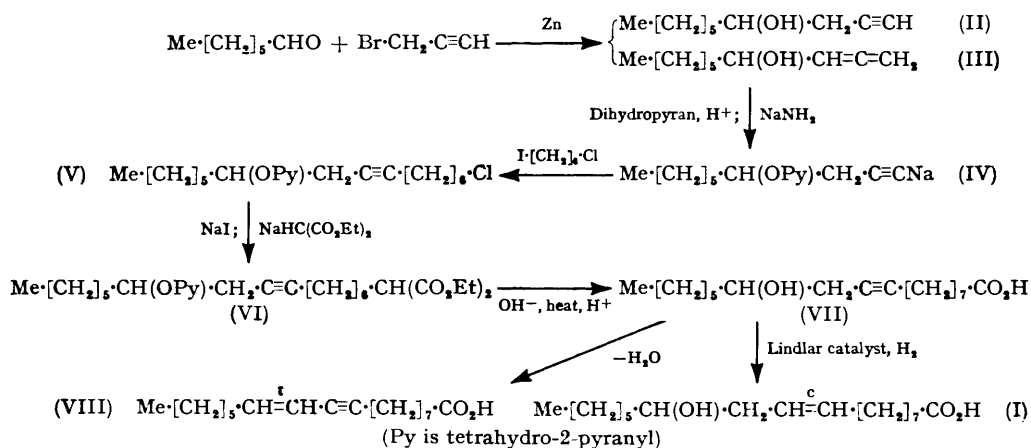
(+)-RICINOLEIC ACID (I) is the main fatty acid in castor oil, which is obtained from the seeds of *Ricinus communis* (family Euphorbiaceae). A recent report (Hilditch and Riley, *J. Sci. Food Agric.*, 1951, **2**, 245) states that on hydrolysis the glycerides yield 91.4—94.9% of this, together with 4.5—5.0% of linoleic acid and small amounts of oleic, saturated, and dihydroxy-acids. The natural occurrence of the acid is discussed by Hilditch ("Chemical Constitution of Natural Fats," Chapman and Hall, London, 1947, p. 170), Ralston ("Fatty Acids and Their Derivatives," Wiley, New York, 1948, p. 188), and Eckey ("Vegetable Fats and Oils," Reinhold, New York, 1954, p. 587). Saalmuller (*Annalen*, 1847, **64**, 108) appears to have been the first to isolate ricinoleic acid in moderately pure form and after Krafft's proposal (*Ber.*, 1888, **21**, 2730) that it was 12-hydroxyoctadec-10-enoic acid, the correct structure was shown to be 12-hydroxyoctadec-9-enoic acid by Goldsobel (*Ber.*, 1894, **27**, 3121; cf. Baruch, *Ber.*, 1893, **26**, 1867; 1894, **27**, 172, 176; Holt and Baruch, *Ber.*, 1893, **26**, 838). Goldsobel's structure is supported by a considerable body of later evidence. The present communication reports the first total synthesis of (±)-ricinoleic acid (for a summary see *Chem. and Ind.*, 1954, 1197).

n-Heptaldehyde was converted, either by a Reformatski reaction employing zinc and propargyl bromide (cf. Ziele and Meyer, *Ber.*, 1942, **75**, 356; Henbest, Jones, and Walls,

* The paper by Crombie and Taylor (*J.*, 1954, 2816) is considered to be Part I of this series.

J., 1949, 2696; Crombie, *J.*, 1955, 1007) or, less well, by a Grignard reaction with propargyl-magnesium bromide (Golse and Le-Van-Thoi, *Compt. rend.*, 1950, 230, 210; Prevost, Gaudemar, and Honigberg, *ibid.*, 1950, 230, 1186; Gaudemar, *ibid.*, 1951, 233, 64) into (\pm)-4-hydroxydec-1-yne (II). In view of reports (Wotiz, *J. Amer. Chem. Soc.*, 1951, 73, 693; Celmer and Solomons, *ibid.*, 1953, 75, 3430) it seemed likely that the dec-1-yne (II) would be contaminated by the allene (III) and presence of the latter was demonstrated in the product from the Reformatski reaction by the characteristic infrared absorption at *ca.* 1970 cm^{-1} (Sheppard and Simpson, *Quart. Rev.*, 1952, 6, 1; Wotiz and Celmer, *J. Amer. Chem. Soc.*, 1952, 74, 1860). The allene does not interfere with subsequent stages in the synthesis because, when the mixture is converted into the tetrahydropyranyl ether (Parham and Anderson, *ibid.*, 1948, 70, 4187) and then treated with sodamide in liquid ammonia, only the decyne (II) gives a sodio-derivative (IV). It is conceivable that isomerisation of the allene to the acetylene proceeds under the influence of sodamide but we have no experimental evidence on this point: Bouis [*Ann. Chim. (France)*, 1928, 9, 459] describes such rearrangements under more drastic conditions.

The sodio-derivative of (\pm)-4-(tetrahydropyranyloxy)dec-1-yne was treated with 1-chloro-6-iodohexane according to a general method due to Strong (Ahmad, Bumpus, and Strong, *J. Amer. Chem. Soc.*, 1948, 70, 3391; Taylor and Strong, *ibid.*, 1950, 72, 4263), to give (\pm)-1-chloro-10-(tetrahydropyranyloxy)hexadec-7-yne (V). This was heated under reflux with sodium iodide in acetone and the 1-iodo-compound, formed by metathesis, was treated with sodiomalonic ester. Hydrolysis with alkali, thermal decarboxylation,

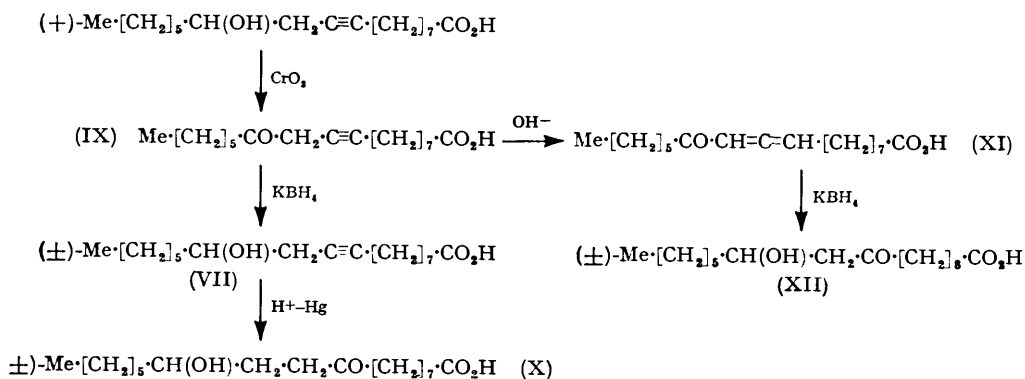


and destruction of the pyranlyl residue in acid produced (\pm)-12-hydroxyoctadec-9-ynoic acid [(\pm)-ricinostearic acid (VII)]. This was obtained crystalline, m. p. 53—53.5°, and characterised as its *p*-bromophenacyl ester.

Before proceeding further it seemed desirable to degrade natural (+)-ricinoleic acid to (\pm)-ricinostearic acid and rigidly confirm the identity of the synthetic specimen by direct comparison. Natural (+)-ricinoleic acid was brominated and dehydrobrominated to give (+)-ricinostearic acid (Ulrich, *Z. fur Chemie*, 1867, 3, 545; Grün and Woldenburg, *J. Amer. Chem. Soc.*, 1909, 31, 490). Oxidation with chromic acid at 0° then gave 12-oxo-octadec-9-ynoic acid (IX) in satisfactory yield, hydrogenated to 12-oxo-octadecanoic acid as expected (mixed m. p.). It is important that no trace of alkali is used during the working up of the oxo-acetylenic acid for reasons discussed below. When the acid (IX) was reduced with an excess of potassium borohydride in 90% methanol at 0° and then decomposed with dilute sodium hydroxide at 45°, the required (\pm)-12-hydroxyoctadec-9-ynoic acid (VII) was obtained in 85% yield. It was identical in all respects with the acid produced by total synthesis.

The correct conditions for reduction of the acetylenic ketone (IX) to the acetylenic alcohol (VII) were only arrived at after considerable experimentation. 12-Oxo-octadec-9-ynoic acid,

when neutralised to phenolphthalein and then treated, in aqueous solution, with potassium borohydride, gave oils. Reduction in methanol or methanol containing a little water gave a crystalline substance, m. p. 82°, in yields of up to 40%, after the product had been decomposed with alkali in the usual way : this was different from (\pm)-12-hydroxyoctadec-9-ynoic acid ; its empirical formula was $C_{18}H_{34}O_4$ and it yielded a *p*-bromophenacyl ester, a semicarbazone, and a 1-naphthylurethane, all crystalline. This utilises the four oxygen

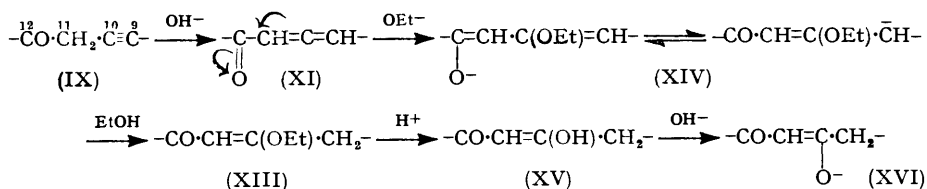


atoms in functional groupings—hydroxyl, oxo, and carboxylic acid—and the structure was readily demonstrated by Schmidt degradation to sebacic acid. The compound must therefore be (\pm)-12-hydroxy-10-oxo-octadecanoic acid (XII) formed by the reduction of the 12-oxo-grouping of 12-oxo-octadec-9-ynoic acid and the formal hydration of the acetylene linkage. In agreement, its oxidation product showed the typical spectroscopic properties, in alkaline and neutral solution, of a 1 : 3-diketone. The hydration is abnormal on two counts. First, the reaction conditions were such that hydration of a triple bond would not normally be expected and, secondly, the direction of the hydration is abnormal. Thus when (+)-12-hydroxyoctadec-9-ynoic acid is treated with sulphuric acid and a mercury catalyst (Goldsobel, *loc. cit.*; Mangold, *Monatsh.*, 1894, 15, 307) it is (+)-12-hydroxy-9-oxo-octadecanoic acid (X) which is produced. This has been firmly established by Beckmann degradation of its ketoxime and isolation of azelaic acid. The preparation of (\pm)-12-hydroxy-9-oxo-octadecanoic acid by such a method is described in the Experimental section. The melting points of the (\pm)-12-hydroxy-9- and -10-oxo-acids are markedly depressed on admixture.

The reason for the abnormal hydration was made clearer by the observation that 12-oxo-octadec-9-ynoic acid is remarkably unstable to alkali. Thus, although this compound showed no significant high-intensity ultraviolet absorption in neutral or acidic medium, when dissolved in 0.64% sodium hydrogen carbonate solution it had maximal absorption, after one hour, at 226 $m\mu$ (ϵ 11,450). Alcoholic potassium hydroxide (N/1000) gave a solution with maximum absorption at 223 $m\mu$ (ϵ 11,550) three minutes after dissolution of the keto-acetylene. This absorption then began to decline and a new maximum eventually appeared at 263 $m\mu$. Absorption at 223—226 $m\mu$ is consistent with the presence of an α -unsaturated ketone grouping and strongly suggests that an allenic $\alpha\beta$ -diunsaturated ketone is responsible since the β -double bond, being at right angles to the α -bond, is chromophorically ineffective (Celmer and Solomons, *J. Amer. Chem. Soc.*, 1953, 75, 1372; Jones, Shaw, and Whiting, *J.*, 1954, 3212). The presence of this chromophore was fully established by isolation of the crude allene, m. p. 28—31° : it showed the infrared absorption characteristic of the $\text{CO}\cdot\text{CH}=\text{C}=\text{CH}$ grouping. When its sodium salt was treated with potassium borohydride in methanol, working up under mild conditions without the addition of alkali gave a hydroxy-acid whose infrared spectrum indicated removal of the allene grouping. The initiating step in the abnormal hydration is thus allene formation and this is followed by attack at $C_{(10)}$. Very recently, a similar ready isomerisation of a β -acetylenic acid (but-3-ynoic acid) to an α -allenic acid has been reported as proceeding under mild alkaline

conditions (Eglinton, Jones, Mansfield, and Whiting, *J.*, 1954, 3197). Dr. M. C. Whiting has also informed us that the reaction $R\cdot C\equiv C\cdot CHMe\cdot CHO \rightarrow R\cdot CH:C:CMe\cdot CHO$ can be effected by shaking with sodium hydrogen carbonate solution.

It was mentioned above that in ethanolic 0.001N-alkali, a new absorption at 263 $m\mu$ gradually replaces that due to conjugated oxo-allene. In ethanolic 0.01N-potassium hydroxide, maximum intensity (see Table) is reached in 30 min. and the absorption is ascribed to the enol ether (XIII). Formation of the latter may be represented as attack of OEt^- at $C_{(10)}$ to give the resonating anion (XIV) which acquires a proton at $C_{(9)}$ by reaction with the solvent. When the solution is acidified (to 0.12N with hydrochloric acid), there is no sudden change in light absorption: this suggests that the absorption in alkaline solution was due to (XIII) rather than (XIV). However, there is a small drop in intensity and maximal absorption moves to longer wavelength, becoming stationary after 1 hr. This is interpreted as being due to acidic cleavage of the enol ether to the 1:3-diketone (XV) since, if the solution is now made alkaline, the maximum shifts to a position characteristic of the enolate ion (XVI), intensity being greatly increased. The crude product from these reactions was isolated and had a strong infrared band at 1579 cm^{-1} as expected for a 1:3-diketone (Bellamy, "The Infra-Red Spectra of Complex Molecules," Methuen, London, 1954, p. 114, gives 1540—1640 cm^{-1}). The sequence of changes may be summarised:



this suggests that the product from the reaction of the allene (XI) with potassium borohydride in methanol is an enol ether, the 12-oxo-function then being reduced in the usual way. Such enol ethers are known to be readily hydrolysed by acid and the 10-oxo-grouping probably appears during working up with mineral acid.

	$\lambda_{max.}$	ϵ
$Me\cdot[CH_2]_8\cdot CO\cdot CH:C(OEt)\cdot[CH_2]_8\cdot CO_2H$ (XIII) ¹	263	11,900
$Me\cdot[CH_2]_8\cdot CO\cdot CH:C(OH)\cdot[CH_2]_8\cdot CO_2H$ (XV) ¹	275	11,300 ^{8a}
$Me\cdot[CH_2]_8\cdot CO\cdot CH:C(O^-)\cdot[CH_2]_8\cdot CO_2H$ (XVI) ¹	297	24,000
$Me\cdot C(OMe):CH\cdot COMe$ ^{2,4}	257	13,600
$Me\cdot C(O^-):CH\cdot COMe$ ^{2,5}	293	21,800
$Me\cdot[CH_2]_7\cdot CO\cdot CH:C(OH)\cdot[CH_2]_7\cdot CO_2H$ ^{3,6}	275	10,500 ^{8b}
	276	15,900 ^{8c}
$Me\cdot[CH_2]_7\cdot CO\cdot CH:C(O^-)\cdot[CH_2]_7\cdot CO_2H$ ^{3,7}	296	22,800

For conciseness, tautomeric forms and resonance possibilities are not illustrated.

¹ For conditions of measurement see text. ² Eistert, Merkel, and Reiss, *Chem. Ber.*, 1954, **87**, 1513. ³ Nunn, *J.*, 1952, 313. ⁴ In hexane. ⁵ In 5N-sodium hydroxide. ⁶ In ethanol. ⁷ In ethanolic sodium hydroxide. ⁸ The ϵ for 1:3-diketones is concentration-dependent because of their tautomeric character: (a) c , 0.00013, (b) c , 0.0001, (c) c , 0.000014 mole/l.

The total synthesis of (\pm)-ricinoleic acid was completed by semihydrogenation of (\pm)-12-hydroxyoctadec-9-ynoic acid (which was now available in quantity *via* the degradation procedure) with a palladium catalyst poisoned by lead and quinoline (Lindlar, *Helv. Chim. Acta*, 1952, **35**, 446). Trial experiments, differing from the above only in that the quinoline was omitted, had shown that this reduction proceeded selectively and stereospecifically in the (+)-series to give partially synthetic (+)-ricinoleic acid, but the semihydrogenation procedure was much less satisfactory in the case of 12-oxo-octadec-9-ynoic acid because of unselectivity. The totally synthetic (\pm)-ricinoleic acid was purified by low-temperature crystallisation and had m. p. 23—24°. It was characterised as its *p*-bromophenacyl ester. The infrared spectrum of its methyl ester (liquid film) was indistinguishable from that of natural methyl (+)-ricinoleate.

Ricinstearolic acid is closely related in structure to ximenynic acid (octadec-*trans*-11-en-9-ynoic acid) which occurs in the seed fats of three species of the genus *Ximenia* (family

Olacaceae) (Ligthelm and Schwartz, *J. Amer. Chem. Soc.*, 1950, **72**, 1868; Ligthelm, Schwartz, and von Holdt, *J.*, 1952, 1088), and two of the *Santalum* genus (family Santalaceae) (Hatt and Szumer, *Chem. and Ind.*, 1954, 962). Hatt and Szumer also consider that santalbic acid (from the seeds of *Santalum album* Linn., the sandalwood tree; see Madhuranath and Munjanath, *J. Indian Chem. Soc.*, 1938, **15**, 389) is identical with ximenynic acid and this has been confirmed by Gunstone and McGee (*Chem. and Ind.*, 1954, 1112). As methyl ximenynate should be obtainable from methyl ricinostearolate merely by direct dehydration, the latter was treated with phosphorus oxychloride in pyridine but the product was a mixture of enyne and methyl 12-chloro-octadec-9-ynoate. Dehydrohalogenation was completed by heating under reflux with quinoline, and the product had the correct analysis for methyl ximenynate though its ultraviolet absorption indicated that it was as yet only 76% pure. Experiments aimed at its purification were discontinued when Grigor, MacInnes, and McLean (*Chem. and Ind.*, 1954, 1112) reported that methyl ricinostearolate had been converted into its chloro-compound and dehydrohalogenated with methanolic potassium hydroxide to octadec-*trans*-11-en-9-ynoic acid which was identical with ximenynic acid. Our synthesis of (\pm)-ricinostearolic acid therefore embraces a total synthesis of ximenynic acid [with the reservation that (+)-acid is used for the interconversion step].

Soon after the appearance of our preliminary communication (*loc. cit.*), Kendall, Lumb, and Smith (*ibid.*, p. 1228) notified a second and different synthesis of (\pm)-ricinoleic acid. As they state that the synthesis is being repeated on a larger scale to obtain more material, detailed comment is unwarranted, but they report m. p. of only +3° for their (\pm)-ricinoleic acid whereas the value obtained in two experiments in the present work was 23–24°. During the distillation of their acid, diene was found in the first distillate and it seems possible that their main product was also contaminated with this. A very refined distillation technique would be required to separate the two components on so small a quantity (240 mg.). Nevertheless the spectrum of their acid in the infrared was closely similar to that of (+)-ricinoleic acid, though their implied criteria of identity, involving melting points of active and inactive forms, require reconsideration.

EXPERIMENTAL

Analyses were carried out in the Microanalytical Laboratory (Mr. F. H. Oliver) of this Department. The ultraviolet light absorptions were measured in pure ethanol with a Unicam instrument.

Dec-1-yn-4-ol (II).—Propargyl bromide, b. p. 32°/75 mm., n_D^{25} 1.4937, was prepared by Kirrman's method (*Bull. Soc. chim. France*, 1926, **39**, 698) in 77–80% yields.

(a) *Grignard method*. Magnesium (4.0 g.) was covered with ether (dried over sodium), and propargyl bromide (20.0 g.) in ether (20 ml.) was added dropwise. Mercuric chloride (50 mg.) was used to initiate the vigorous reaction. When addition was complete the product was heated under reflux for 10 min., then cooled, and heptaldehyde (21.0 g.) in ether (20 ml.) added at such a rate that the ether refluxed gently. The product was heated under reflux for 1 hr., set aside overnight, and finally poured into ice and dilute sulphuric acid. The ether layer was separated, dried (K_2CO_3), and distilled to give *dec-1-yn-4-ol* (6.0 g., 23%), b. p. 57°/0.06 mm., n_D^{25} 1.4490 (Found: C, 77.6; H, 11.85. $C_{10}H_{18}O$ requires C, 77.85; H, 11.75%). In a second experiment the yield was 4.4 g. (17%).

(b) *Reformatski method*. Zinc wool (37 g.), etched with dilute hydrochloric acid, was washed with water, methanol, and dry ether. Tetrahydrofuran (50 ml.; dried over sodium) was added, together with mercuric chloride (50 mg.). Heptaldehyde (61 g.) and propargyl bromide (51 g.) were mixed with tetrahydrofuran (100 ml.) and added to the zinc with shaking, at such a rate that gentle refluxing was maintained. Finally the mixture was heated under reflux for 30 min. and poured into ice-cold dilute acetic acid. The upper layer was united with two ethereal extracts of the aqueous phase (previously saturated with salt). Drying (Na_2SO_4), evaporation, and distillation yielded *dec-1-yn-4-ol* (55.4% in the best experiment). In other cases the yield was 46–50%. Absorption at 1953 cm^{-1} (C:C), as well as at 2146 and 3262 cm^{-1} (C:CH), showed that the allene (III) was also present.

(±)-4-(*Tetrahydro-2-pyranyloxy*)*dec-1-yne*.—Dec-1-yn-4-ol (56 g.) was mixed with dihydropyran (32 g.). On the addition of two drops of concentrated hydrochloric acid, the mixture became warm, and after ice-cooling was set aside overnight. Solid potassium hydroxide was added and the liquid decanted. A few cg. of potassium carbonate were added and on distillation 4-(*tetrahydro-2-pyranyloxy*)*dec-1-yne* (73 g., 84%), b. p. 84°/10⁻³ mm., n_D^{23} 1.4588, was isolated (Found: C, 75.25; H, 11.05. C₁₅H₂₆O₂ requires C, 75.55; H, 11.0%).

1-Chloro-6-iodohexane.—This was prepared according to the directions of Raphael and Sondheimer (*J.*, 1950, 2100). 1:6-Hexanediol was first converted into 1:6-dichlorohexane, b. p. 92–93°/13 mm., n_D^{23} 1.4595, in 88.5% yield. Dichlorohexane (245 g.) in acetone (1.5 l.) when treated with sodium iodide (245 g.) gave a fraction, b. p. 45–59°/0.5 mm., n_D^{21} 1.4719 (88 g., mainly recovered dichlorohexane), and one of b. p. 66–69°/0.5 mm., n_D^{21} 1.5234–1.5245 (145 g., the required iodochloride).

(±)-1-Chloro-10-(*tetrahydro-2-pyranyloxy*)*hexadec-7-yne* (V).—Sodamide was prepared in liquid ammonia (500 ml.) from sodium (2.0 g.), 4-(*tetrahydro-2-pyranyloxy*)*dec-1-yne* (9.0 g.) added, and the solution stirred for 90 min. 1-Chloro-6-iodohexane (9.0 g.) was then added dropwise and the solution stirred overnight. The ammonia was allowed to evaporate and water (100 ml.) added cautiously. The residue, after extraction with ether, drying, and evaporation, was distilled, to yield 1-chloro-10-(*tetrahydro-2-pyranyloxy*)*hexadec-7-yne* (5.6 g., 42%), b. p. 164°/10⁻⁶ mm., n_D^{23} 1.4772 (Found: Cl, 10.05. C₂₁H₃₇O₂Cl requires Cl, 9.95%). The fractions which boiled at higher temperatures than the starting materials but below the above product gave higher chlorine analyses than expected for the above formula and probably represent material from which the tetrahydropyranyl grouping has been eliminated.

(±)-12-Hydroxyoctadec-9-ynoic acid (VII).—1-Chloro-10-(*tetrahydro-2-pyranyloxy*)*hexadec-7-yne* (3.99 g.) was heated under reflux with sodium iodide (3.5 g.) in acetone (50 ml.) for 7 hr.; sodium chloride was precipitated. After pouring into water and extraction with ether, the extracts were dried and evaporated to yield crude 1-iodo-10-(*tetrahydro-2-pyranyloxy*)*hexadec-7-yne*. This was added to a solution of diethyl sodiomalonate prepared from diethyl malonate (1.96 g.), sodium (0.28 g.), and ethanol (20 ml.), and the mixture heated under reflux for 17 hr., then cooled. Potassium hydroxide (4.0 g.) in methanol (40 ml.) and water (2 ml.) was added and hydrolysis allowed to proceed at 25° for 44 hr. The product was poured into water and extracted with ether to eliminate non-acidic materials (0.8 g.). Acidification (sulphuric acid) of the aqueous phase, followed by ether-extraction, produced the oily malonic acid (2.22 g.). This was heated at 10⁻⁶ mm. with a jacket-temperature of 140° for 2 hr. during which the majority distilled. This distillate was then heated under reflux for 30 min. with 2*N*-sulphuric acid and extracted with ether. Extraction of the latter phase with dilute aqueous sodium hydroxide, followed by acidification and isolation with ether in the usual way, yielded (±)-12-hydroxyoctadec-9-ynoic acid [(±)-ricinostearolic acid], m. p. 51–52°. This was twice crystallised from light petroleum (b. p. 80–100°) to yield the pure acid (255 mg., 7.7%), m. p. 53.0–53.5° (Found: C, 72.5; H, 10.8. C₁₈H₃₂O₃ requires C, 72.9; H, 10.9%). The *p*-bromophenacyl ester crystallised from ethanol in plates, m. p. 82° (Found: C, 62.85; H, 7.65. C₂₆H₃₇O₄Br requires C, 63.25; H, 7.55%). The m. p.s of the acid and its derivative were not depressed when appropriately mixed with (±)-ricinostearolic acid and its *p*-bromophenacyl ester prepared from natural (+)-ricinoleic acid.

(+)-12-Hydroxyoctadec-9-ynoic Acid [(+)-Ricinostearolic Acid].—Methyl (+)-ricinoleate was isolated from castor oil by the procedure given in "Biochemical Preparations," Vol. II, and distilled at low pressure through a 12" vacuum-jacketed column, packed with glass helices. Attempts to distil at 0.2 mm. through a high-efficiency electrically heated column with Stedman gauze packing caused considerable decomposition and formation of water and heptaldehyde. Castor oil (B.P.) (235 g.) yielded methyl ricinoleate (133.5 g.), b. p. 181–182°/0.15 mm., n_D^{22} 1.4620, m. p. –6°, $[\alpha]_D^{22}$ 5.10° (homogeneous). Recorded data (*op. cit.*; Brown and Green, *J. Amer. Chem. Soc.*, 1940, 62, 738; Walden, *Ber.*, 1903, 36, 782): b. p. 185–187°/2.0 mm., n_D^{20} 1.4629, m. p. –4°, $[\alpha]_D^{20}$ 5.05°.

Methyl ricinoleate (135 g.) was suspended in water (450 ml.), and bromine (90 g.) added with continuous shaking. A heavy oil separated. This was taken up in ether, separated, and washed with water and dilute sodium carbonate solution. After drying and evaporation, the residual crude dibromide was heated under reflux with excess of 10% ethanolic potassium hydroxide for 20 hr. Water was added and the acidified solution extracted with ether. The extracts were dried and evaporated; a thick oil remained which solidified on cooling. After several crystallisations from light petroleum (b. p. 60–80°) it melted at 52°. The yield of (+)-ricinostearolic acid was 50.5 g. (39%), $[\alpha]_D^{22}$ 13.2° (*c* 53% in acetone). Iyer, Sudborough,

and Ayyer (*J. Indian Inst. Sci.*, 1925, 8, A, 29) give $[\alpha]_D$ 13.67° (in acetone). The *p*-bromophenacyl ester crystallised from ethanol in plates, m. p. 63° (Found: C, 63.2; H, 7.7; Br, 16.45. $C_{26}H_{37}O_4Br$ requires C, 63.3; H, 7.55; Br, 16.2%). The 3:5-dinitrobenzoate and α -naphthylurethane were obtained as oils; the *S*-benzylthiuronium salt melted at 125° but its tendency to give unsharp values, dependent on the rate of heating (cf. Berger, *Acta Chem. Scand.*, 1954, 8, 427), renders it an unsuitable derivative. When (+)-ricinostearic acid was admixed with the (\pm)-acid, its m. p. was depressed to 49°. The preparative method used above is based on the directions of Grün and Woldenburg (*loc. cit.*).

12-Oxo-octadec-9-ynoic acid (IX).—To (+)-ricinostearic acid (28.5 g.) in acetone (360 ml.) chromic acid (6.6 g.) in concentrated sulphuric acid (10.6 g.) and water (made up to 33 ml.) was added slowly at 0° (thermometer in liquid), with vigorous stirring. The mixture was stirred at 0° for a further hour, water (1 l.) added, and the solution extracted three times with ether. After drying (Na_2SO_4), the extracts were evaporated *in vacuo* and the pale yellow solid which remained crystallised from ethanol, to give 12-oxo-octadec-9-ynoic acid as waxy plates, m. p. 62—64° (15.5 g., 55%). Further crystallisation raised the m. p. to 64—64.5° (Found: C, 73.3; H, 10.45. $C_{18}H_{30}O_3$ requires C, 73.4; H, 10.25%). The substance deteriorates slowly.

Complete hydrogenation in the presence of 3% palladium-calcium carbonate gave 12-oxostearic acid, m. p. 82° after crystallisation from methanol (Found: C, 72.25; H, 11.45. $C_{18}H_{34}O_3$ requires C, 72.45; H, 11.5%). As the m. p. differences among the oxostearic acids are small, 12-oxostearic acid was prepared by oxidation of (+)-12-hydroxystearic acid (0.78 g.) with chromic acid (0.19 g.) in glacial acetic acid (10 ml.) at 100° for 10 min. Under these conditions the oxidation was not complete, so the product was oxidised further with chromic acid (0.093 g.) in glacial acetic acid (10 ml.) for 10 min. The product was poured into water, and the solid removed and recrystallised from methanol as white plates, m. p. 82° (0.60 g.) (Bergström, Aulin-Erdtman, Rolander, Stenhagen, and Östling, *Acta Chem. Scand.*, 1952, 6, 1157, give m. p. 81.5—81.9°). On admixture with the above specimen there was no depression of m. p.

Partial Hydrogenation of 12-Oxo-octadec-9-ynoic Acid.—The acid (0.26 g.) was dissolved in methanol (5 ml.) and hydrogenated in the presence of Lindlar catalyst (*loc. cit.*; 100 mg.). When hydrogen (21 ml. at 19°/760 mm.) had been absorbed (calc. for semihydrogenation, 21 ml.), the reaction was discontinued and the catalyst removed. Evaporation, and crystallisation from methanol, yielded white crystals (100 mg.), m. p. 72—75°, which after three further crystallisations gave 12-oxostearic acid, m. p. 81—82° undepressed with the specimen prepared as above. This demonstrates that the hydrogenation was not fully selective. From the mother-liquors a small amount of solid, m. p. 34—35°, was isolated. A second hydrogenation with the oxoacetylenic acid (0.82 g.), ethyl acetate (10 ml.), and Lindlar catalyst (0.40 g.) was carried out, absorption of 68 ml. of hydrogen (19°/760 mm.) being permitted (Calc. for semihydrogenation 66.8 ml.). The product was worked up and higher-melting material eliminated by crystallisation, attention being concentrated on the mother-liquors. Crystallisation of the product from these from 80% ethanol and then light petroleum (b. p. 40—60°) gave a material, m. p. 38—39.5°, which was unstable and is probably the expected 12-oxo-oleic acid. This was described by Ellis (*J.*, 1950, 9), who records its m. p. as 39°.

(\pm)-12-Hydroxyoctadec-9-ynoic acid (VII).—To 12-oxo-octadec-9-ynoic acid (3.13 g.) in methanol (140 ml.) a solution of potassium borohydride (0.95 g., 7 equivs.) in water (10 ml.) was added. The mixture was set aside for 16 hr. at 0°, 10% aqueous sodium hydroxide (60 ml.) added, and the solution heated at 45° for 15 min. Water and dilute hydrochloric acid were added. Ether-extraction, drying, and evaporation gave a white solid, m. p. 50—51°. Recrystallisation from acetone at low temperature yielded (\pm)-12-hydroxyoctadec-9-ynoic acid (2.65 g., 85%), m. p. 53—53.5° (Found: C, 72.7; H, 10.85; microhydrogenation, 1.8H₂. $C_{18}H_{32}O_3$ requires C, 72.9; H, 10.9%). Its *p*-bromophenacyl ester had m. p. 82° Meerwein-Ponndorf reduction of the methyl ester of (IX) gave only oils.

(\pm)-12-Hydroxy-10-oxo-octadecanoic acid (XII).—12-Oxo-octadec-9-ynoic acid (0.42 g.) was neutralised in methanol (10 ml.) with a solution of sodium methoxide in methanol. Potassium borohydride (47.4 mg., 2 equivs.) was added in water (1.0 ml.), and the solution heated at 50° for 1 hr. 2*N*-Sodium hydroxide was then added and heating continued for 15 min. The mixture was made well acid with dilute mineral acid to give (\pm)-12-hydroxy-10-oxo-octadecanoic acid (178 mg., 40%), m. p. 77—79°, raised by recrystallisation from acetone to 82—82.5° (Found: C, 68.85; H, 11.1; microhydrogenation 0.65H₂. $C_{18}H_{34}O_4$ requires C, 68.75; H, 10.9%; microhydrogenation, 1.0H₂ for complete reduction of an oxo grouping, which proceeds slowly with Adams catalyst in glacial acetic acid, under the conditions employed). The infrared

spectrum showed the presence of hydroxylic (3195 and 3290 cm^{-1}), carbonyl (1687 cm^{-1}), and carboxylic (1702 cm^{-1}) absorption. The *p*-bromophenacyl ester, crystallised from ethanol, had m. p. 90—90.5° (Found: C, 60.95; H, 7.75. $\text{C}_{26}\text{H}_{39}\text{O}_5\text{Br}$ requires C, 61.05; H, 7.7%). A semicarbazone was obtained as plates, m. p. 108.5—109.5°, from ethanol (Found: C, 61.1; H, 9.9; N, 11.15. $\text{C}_{19}\text{H}_{37}\text{O}_4\text{N}_3$ requires C, 61.4; H, 10.05; N, 11.3%). The α -naphthylurethane formed plates, m. p. 48°, from light petroleum (b. p. 100—120°).

The keto-alcohol (XII) (77 mg.) was dissolved in acetone (2.0 ml.), and chromic acid (17.2 mg., in 0.5 ml. of water containing a drop of sulphuric acid) was added. After 3 hr. the solution was extracted with ether and worked up in the usual way. Light-absorption data for the crude product, which had only partially oxidised, were λ_{max} , 275 μ (ϵ 1480 in neutral ethanol), changed to λ_{max} , 298 μ (ϵ 3530) on the addition of alkali. The absorption, which is characteristic of a 1:3-dioxo-compound, is due to 10:12-dioxo-octadecanoic acid. Nunn (*J.*, 1952, 313) records that 9:11-dioxononadecanoic acid has maximal absorption at 275 μ : in alkaline solution this shifts to 296 μ and the ϵ of the compound, which is concentration-dependent, is increased 2.17-fold.

A series of experiments was carried out on the conditions of the borohydride reduction. If the acid was neutralised before reduction, with sodium hydroxide or sodium methoxide, either (\pm)-12-hydroxy-10-oxo-octadecanoic acid or intractable oils were obtained, although very occasionally small amounts of (\pm)-12-hydroxyoctadec-9-ynoic acid were formed. Water or methanol containing considerable amounts of water tended to give oils when used as the solvent. Only when the borohydride was added to the free acid was (\pm)-12-hydroxyoctadec-9-ynoic acid obtained in good yield.

(\pm)-12-Hydroxy-9-oxo-octadecanoic acid (X).—(\pm)-12-Hydroxyoctadec-9-ynoic acid (130 mg.) was hydrated with sulphuric acid and a mercury catalyst in the usual way, to give (\pm)-12-hydroxy-9-oxo-octadecanoic acid (24 mg.), m. p. 83.5° (Found: C, 68.5; H, 11.0. $\text{C}_{18}\text{H}_{34}\text{O}_4$ requires C, 68.75; H, 10.9%). On admixture of this with the 10-keto-isomer of m. p. 82°, the m. p. was 70—76°.

Schmidt Degradation of (\pm)-12-Hydroxy-10-oxo-octadecanoic Acid.—The hydroxy-keto acid (310 mg.) was added to chloroform (1.6 ml.) and concentrated sulphuric acid (0.8 ml.), and then cooled in ice. Sodium azide (65.2 mg.) was added in small portions to the stirred solution. After 15 min. the solution was poured into ice-water and extracted with chloroform. The extracts were dried and evaporated and the partly solid product was heated for 3½ hr. in a sealed tube at 100° with concentrated hydrochloric acid (1.5 ml.). The solution was made alkaline, neutral material removed with ether, and the acid liberated and collected in the usual way. The oily acid was dissolved in hot water and filtered through kieselguhr to remove oil, and the filtrate was cooled. A colourless acid, m. p. 127°, crystallised. This m. p. was raised to 131° (20 mg.) by another crystallisation. The m. p. was undepressed by admixture with sebacic acid, m. p. 133°.

Action of Alkali on 12-Oxo-octadec-9-ynoic Acid (IX).—The acid (269 mg.) was dissolved in ethanol (25 ml.) containing *N*-potassium hydroxide (1 ml.; 0.92 ml. is required for neutralisation of the acid). The ultraviolet light absorption, three minutes after dissolution, was λ_{max} , 223 μ (ϵ 14,200). The mixture was at once added to a solution containing *N*-hydrochloric acid (1.1 ml.) and extracted with ether. Evaporation of the dried extract yielded a pale yellow oil which at 0° set to a solid, m. p. 28—31° (XI). It was not further purified. The infrared spectrum (paraffin mull) showed strong absorption at 1952 (allene), 1706 (carboxyl), and 1678 cm^{-1} (α -unsaturated ketone). There was no significant absorption in the olefinic CH out-of-plane deformation region (950—1010 cm^{-1}).

Action of Potassium Borohydride on the Oxo-allene (XI).—Crude allene (m. p. 28—31°; 93 mg.) was dissolved in methanol (4 ml.), cooled in ice-salt, and neutralised to phenolphthalein with 0.2*N*-sodium hydroxide. Potassium borohydride (14.8 mg.) was added and the solution set aside at 0° for 12 hr. It was poured into dilute acid, and the oily product isolated with ether. This showed absorption at 3390 cm^{-1} (hydroxyl) (liquid film) but there was no absorption in the allenic or acetylenic region, or between 950 and 1010 cm^{-1} .

Dehydration of Methyl Ricinastearolate.—Ricinastearic acid (5.0 g.) in ether was titrated with ethereal diazomethane to a permanent yellow colour. The solvent was evaporated under reduced pressure, leaving crude methyl ricinastearolate which was dissolved in dry pyridine (10 ml.) and treated slowly with phosphorus oxychloride (5.0 g.) in pyridine (10 ml.). The reactants were stirred for 2 hr. and then heated on a steam-bath for 30 min. Dilute sulphuric acid was added at 0° and the solution extracted with ether. The extracts were washed, dried, evaporated, and distilled, to give methyl 12-chlororicinastearolate (2.7 g., 54%), b. p. 148—149°/10⁻² mm.,

n_D^{20} 1.4682 (Found: C, 70.9; H, 10.3; Cl, 8.95; microhydrogenation $2.1H_2$. $C_{19}H_{33}O_2Cl$ requires C, 69.4; H, 10.1; Cl, 10.8%). The analytical results and the ultraviolet light absorption (λ_{max} 227 $m\mu$; ϵ 1950) demonstrate contamination with methyl ximenynate. Ligthelm, Schwartz, and von Holdt (*loc. cit.*) give λ_{max} 229 $m\mu$ (ϵ 16,030) for pure methyl ximenynate.

The above 12-chlororicinoleic ester (5.4 g.) was heated under reflux with quinoline (9.6 g.) for 1 hr. in a nitrogen atmosphere. The cooled solution was poured into dilute sulphuric acid at 0° , extracted, and worked up in the usual manner. The product had b. p. 143—144°/0.05 mm., n_D^{21} 1.4717, λ_{max} 226 $m\mu$ (ϵ 10,510) (Found: C, 77.85; H, 11.0. $C_{19}H_{32}O_2$ requires C, 78.0; H, 11.05%). Ligthelm *et al.* give n_D^{25} 1.4700. In a second experiment the light absorption was λ_{max} 228 $m\mu$ (ϵ 12,260), *i.e.*, the substance was approx. 76% pure.

Methyl (+)-Ricinoleate (Partially Synthetic).—(+)-12-Hydroxyoctadec-9-ynoic acid (1.00 g.; derived from the degradation of natural material, see above) was hydrogenated in methanol (12 ml.) with Lindlar catalyst (1.0 g.), absorption being interrupted just before uptake of 1 mol. of hydrogen. The catalyst was removed, the methanol evaporated, and the oil treated with diazomethane in ether and distilled. Methyl (+)-ricinoleate (0.89 g.), b. p. 167°/0.15 mm., n_D^{20} 1.4629, $[\alpha]_D^{25}$ $5.0^\circ \pm 0.2^\circ$ (c 10% in EtOH) was obtained. After hydrolysis a *p*-bromophenacyl ester was prepared which crystallised from ethanol in plates, m. p. 58° (Found: C, 62.85; H, 8.15. $C_{26}H_{39}O_4Br$ requires C, 63.0; H, 7.95%). The hydroxamic acid was prepared by adding methyl (+)-ricinoleate (3.14 g.) in ethanol (30 ml.) to hydroxylamine hydrochloride (0.84 g.) in methanol (6 ml.). The solution was treated slowly with sodium (0.50 g.) in ethanol (20 ml.), and the resulting solution set aside at 20° for 3 days. Sodium chloride was removed by filtration and the product neutralised with ice-cold dilute hydrochloric acid. Water was added and the product filtered off and recrystallised from ethyl acetate as waxy plates, m. p. 63° (1.85 g.) (Found: C, 69.25; H, 11.3. $C_{18}H_{35}O_3N$ requires C, 69.0; H, 11.25%). Yukawa and Inoue (*J. Agric. Chem. Soc. Japan*, 1942, 18, 875; *Bull. Agric. Chem. Soc. Japan*, 1942, 18, 72; cf. *Chem. Abs.*, 1951, 45, 8449) give m. p. 65.5°.

(±)-Ricinoleic Acid.—(±)-12-Hydroxyoctadec-9-ynoic acid (1.06 g.) in methanol (10 ml.) containing Lindlar catalyst (0.5 g.) and quinoline (5 drops) was hydrogenated. When hydrogen (83.2 ml.) had been absorbed at $29^\circ/766$ mm. (required for semihydrogenation 83.1 ml.), the reaction was interrupted and the catalyst filtered off. Dilute hydrochloric acid was added to the filtrate and the mixture extracted with ether. The extract was washed with dilute hydrochloric acid, then water, and dried and evaporated. The residual oil was crystallised from acetone at -70° to give totally synthetic (±)-ricinoleic acid (0.80 g.), m. p. 23—24°, n_D^{19} 1.4723 (supercooled) (Found: C, 72.15; H, 11.6. $C_{18}H_{34}O_3$ requires C, 72.45; H, 11.5%). Hawke (*J. S. African Chem. Inst.*, 1949, 2, 125) gives n_D^{25} 1.4703 for pure natural (+)-ricinoleic acid. The *p*-bromophenacyl ester had m. p. 62—63° and crystallised from ethanol in plates (Found: C, 62.95; H, 8.0. $C_{26}H_{39}O_4Br$ requires C, 63.0; H, 7.95%). (±)-Ricinoleic acid (410 mg.) with diazomethane gave the methyl ester (260 mg.), b. p. 178°/1 mm., n_D^{16} 1.4638 (Found: C, 73.1; H, 11.75; microhydrogenation, $0.95H_2$. $C_{19}H_{36}O_3$ requires C, 73.05; H, 11.6%). Its infrared spectrum (liquid film) was not distinguishable from that of natural methyl (+)-ricinoleate.

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