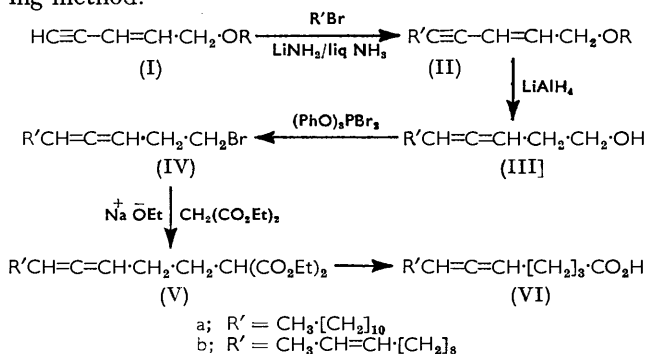# Allenes. Part XXII.[1] The Synthesis and Absolute Configuration of Laballenic and Lamenallenic acids

By **J. S. Cowie, Phyllis D. Landor, S. R. Landor***† and **N. Punja**, Fourah Bay College, University of Sierra Leone, Woolwich Polytechnic, London S.E. 18, and Makerere University, Kampala

The synthesis of two naturally occurring allenic acids (−)-octadeca-5,6-dienoic acid (laballenic acid) and (−)-octadeca-5,6-*trans*-16-trienoic acid (lamenallenic acid) is described and both are shown to have the *R*-configuration

In recent years, three allenic acids [2-4] have been isolated from the seed oils of higher plants and were found to differ from the conjugated allenediynes, elaborated by fungi, in having an isolated allene group. We now report the synthesis of two of these natural allenes, (−)-octadeca-5,6-dienoic acid (laballenic acid) [2,5] (VIa) and (−)-octadeca-5,6-*trans*-16-trienoic acid (lamenallenic acid) [4] (VIb) and their methyl esters, by the following method.

a; R′ = CH₃·[CH₂]₁₀
b; R′ = CH₃·CH=CH·[CH₂]₈

The key allenic alcohol (IIIa) was prepared from 1-tetrahydropyran-2-yloxypent-*trans*-2-en-4-yne (I; R = Thp), lithamide in liquid ammonia and n-undecyl bromide to give 1-tetrahydropyran-2-yloxyhexadec-*trans*-2-en-4-yne (IIa; R = Thp), followed by hydrolysis to the alcohol and reduction with lithium aluminium hydride. The alcohol (IIIa) was then converted by a standard homologation procedure *via* the bromide (IVa) and reaction with diethyl malonate, followed by hydrolysis and decarboxylation to octadeca-5,6-dienoic acid (±)-laballenic acid, (VIa), $\nu_{max.}$ 1960 (C=C=C) and 1730 cm⁻¹

[1] Part XXI, P. M. Greaves, M. Kalli, P. D. Landor, and S. R. Landor, *J. Chem. Soc. (C)*, 1971, 667.

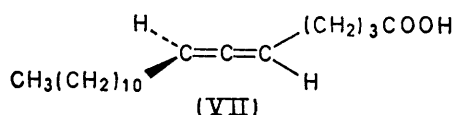[2] M. O. Bagby, C. R. Smith, and I. A. Wolff, *J. Org. Chem.*, 1965, **30**, 4227.

[3] H. W. Sprecher, R. Maier, M. Barber, and R. T. Holman, *Biochemistry*, 1965, **4**, 1856.

[4] K. L. Mikolajczak, M. F. Rogers, C. R. Smith, and I. A. Wolff, *Biochem. J.*, 1967, **105**, 1245.

[5] For a preliminary report of the synthesis see *Tetrahedron Letters*, 1966, 4905.
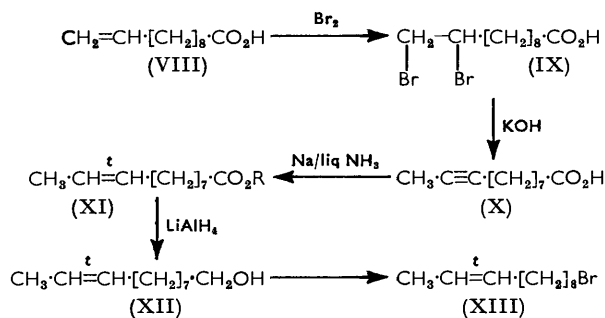
(C=O). The acid was characterised as the *p*-bromophenacyl ester, m.p. 46—46·5°, in close agreement with that reported by Bagley, Smith and Wolff,[2] and as the methyl ester, b.p. 144—146°/5 × 10⁻² mm, $v_{max.}$ 1960 (C=C=C) and 1750 cm⁻¹ (C=O), which was shown to be pure by g.l.c., elemental analysis and by hydrogenation to methyl stearate.

When (IIa; R = H) was reduced with the lithium aluminium hydride-3-*O*-benzyl-1,2-*O*-cyclohexylidene-α-D-glucofuranose[6] complex it gave (—)hexadeca-3,4-dien-1-ol, $[\alpha]_D^{20}$ —4·4°. We have already shown[7] that reduction of 2-en-4-yn-1-ols with this complex gives allenic alcohols of the (*R*)-configuration and therefore (—)-hexadeca-3,4-dien-1-ol must have the (*R*)-configuration. Conversion of the (—)-allenic alcohol, *via* the bromide, the malonic ester (Va), and hydrolysis and decarboxylation to (—)-laballenic acid $[\alpha]_D^{20}$ —3·0° by reactions remote from the allenic group, establishes that the naturally occurring acid has the (*R*)-configuration (VII). This conclusion is supported by a theoretical deduction based on an extension of Brewster's theory[8,9] which predicts on the basis of polarisabilities of substituents, that (VII) should have a negative rotation. (—)-Laballenic acid has also been isolated by Bohlmann from the leaves and roots of a Compositae.[10]

Octadeca-5,6-*trans*-16-trienoic acid (lamenallenic acid), (VIb) was prepared by a similar synthesis. 1-Bromoundec-*trans*-9-ene (XIII), required to alkylate the 1-tetrahydropyran-2-yloxypent-*trans*-2-en-4-yne (I; R = Thp), was first synthesised by the following method.

what longer three-step procedure of Ames and Bowman[13] and characterised as the methyl ester (XI; R = Me) which gave a single peak on g.l.c., $v_{max.}$ 970 cm⁻¹ (C=C, trans) and τ 4·6 (2H, m, CH=CH). The methyl ester was reduced to the corresponding alcohol (XII) and converted into the bromide (XIII) by means of triphenylphosphite dibromide and gave $v_{max.}$ 965 (C=C, trans) and τ 4·58 (2H, m, CH=CH). The bromide (XIII) was then used to alkylate the tetrahydropyranyloxypentenynol (I; R = Thp), and the product was converted into the allenol (IIIb), the bromide (IVb), and the dicarboxylic acid ester (Vb). However, hydrolysis and attempted decarboxylation by the method described previously, followed by esterification gave a mixture of methyl lamenallenate (VIb; H = Me) and methyl 2-carbomethoxylamenallenate. Almost complete decarboxylation was subsequently achieved by heating the ester with a trace of hydrochloric acid at 160°. The methyl lamenallenate was characterised by $v_{max.}$ 1965 (C=C=C), 1740 (C=O), and 965 (C=C, trans), τ 5·0 (2H, m, CH=C=CH), 4·65 (2H, m, CH=CH), one spot on t.l.c. (R_F 0·73), elemental analysis and *p*-bromophenacyl ester, m.p. 39·5—40°; all the data is in close agreement with that published for the natural product by the previous workers.[4] The alcohol (IIb) was reduced with the lithium aluminium hydride-3-*O*-benzyl-1,2-*O*-cyclohexylidene-α-D-glucofuranose complex to give (—)-hexadeca-3,4-*trans*-14-trien-1-ol, $[\alpha]_D^{20}$ —8·34°. Using the conditions described for the racemate, the allenic alcohol was converted into (—)-octadeca-5,6-*trans*-16-trienoic acid, $[\alpha]_D^{20}$ —6·21°, which, by the arguments already advanced for laballenic acid must therefore have the (*R*)-configuration.

(VII)

CH₃(CH₂)₁₀ ... H ... C=C=C ... (CH₂)₃COOH ... H

CH₂=CH·[CH₂]₈·CO₂H →(Br₂)→ CH₂—CH·[CH₂]₈·CO₂H
(VIII) |Br |Br   (IX)

↓KOH

CH₃·CH=CH·[CH₂]₇·CO₂R ←(Na/liq NH₃)— CH₃·C≡C·[CH₂]₇·CO₂H
(XI)   (X)

↓LiAlH₄

CH₃·CH=CH·[CH₂]₇·CH₂OH → CH₃·CH=CH·[CH₂]₈Br
(XII)   (XIII)

Undec-9-ynoic acid (X) was prepared from undec-10-enoic acid (VIII) by bromination and dehydrobromination using the Krafte procedure.[11] The acetylenic acid was reduced to undec-*trans*-9-enoic (XI; R = H) with sodium metal in liquid ammonia[12] to avoid the some-

EXPERIMENTAL

I.r. spectra were determined for liquid films (0·025-mm cell) and for 5% solutions in chloroform, with Perkin-Elmer 237 and 337 spectrophotometers. U.v. spectra were obtained for ethanolic solutions with a Bausch and Lomb Spectronic 505 spectrometer. N.m.r. spectra were determined with Perkin-Elmer R10 and Varian A60 spectrometers for *ca.* 20% solutions in deuteriochloroform or carbon tetrachloride, with tetramethylsilane as internal standard. G.l.c. was carried out with a Griffin and George instrument using 6 ft glass columns with nitrogen as carrier gas at a flow rate of 2 l/h (laballenic acid synthesis) or with a Pye 104 instrument using 5 ft glass columns with nitrogen at 2·5 l/h (lamenallenic acid synthesis). Columns were packed with 10% silicone oil SE-30 or 20% Carbowax 20M on Chromosorb W throughout. Solutions in organic solvents were dried with anhydrous magnesium sulphate, except where stated otherwise.

1-*Tetrahydropyranyl-2-yloxypent*-trans-2-*en*-4-*yne*.—
Toluene-*p*-sulphonic acid (0·5 g) was added to a mixture of

[6] S. R. Landor, B. J. Miller, and A. R. Tatchell, *J. Chem. Soc.* (C), 1966, 1822.

[7] (a) R. J. D. Evans, S. R. Landor, and J. P. Regan, *Chem. Comm.*, 1965, 397; (b) S. R. Landor, R. J. Miller, J. P. Regan, and A. R. Tatchell, *Chem. Comm.*, 1966, 585.

[8] J. H. Brewster, *J. Amer. Chem. Soc.*, 1959, 81, 5475.

[9] G. Lowe, *Chem. Comm.*, 1965, 441.

[10] F. Bohlmann, K. M. Rode, and M. Grenz, *Chem. Ber.*, 1967, 100, 3201.

[11] K. Krafte, *Chem. Ber.*, 1896, 29, 2234.

[12] D. R. Howton and R. H. Davis, *J. Org. Chem.*, 1951, 16, 1405.

[13] D. E. Ames and R. E. Bowman, *J. Chem. Soc.*, 1952, 677.

2,3-dihydropyran (63·0 g, 0·75 mol) and pent-*trans*-2-en-4-yn-1-ol (41·0 g, 0·5 mol) with slight cooling. The reaction mixture was shaken for 30 min and then set aside for 1 h; anhydrous sodium carbonate (5 g) was then added and the mixture was filtered and distilled to give 1-tetrahydropyranyl-2-yloxy-pent-*trans*-2-en-4-yne (80·0 g, 97%), b.p. 78—80°/3 mm; $\nu_{max.}$ 3300 (≡CH), 2120 (C≡CH), and 1630 cm^{-1} (C=C) and characteristic bands for the tetrahydropyranyl-2-yloxy-group, $\lambda_{max.}$ 227 (ε 13,000) and λ_{sh} 234 nm (ε 10,700), and one peak on g.l.c., R_t 23 min (silicone oil; 176°).

n-Undecyl Bromide.[14]—Silver nitrate solution (85·0 g, 0·5 mol) in water (250 ml) was added during 15 min to a well stirred solution of lauric acid (93·0 g, 0·5 mol) in 1·5N-potassium hydroxide at 60—70°, and the mixture was stirred for a further 15 min. The silver salt was filtered off, washed with methanol, and dried *in vacuo* at 70°. A solution of bromine (80 g, 0·5 mol) in carbon tetrachloride (200 ml) was added during 1 h to a well stirred suspension of the dry silver laurate in 1 l of carbon tetrachloride (freshly distilled from phosphorus pentoxide) at 0°. The reaction mixture was slowly heated to reflux temperature until the liberation of carbon dioxide was complete (*ca.* 2 h); silver bromide was filtered off and the filtrate was washed with sodium hydroxide and water, dried, and distilled to give n-undecyl bromide (96·5 g, 82%), b.p. 135—138°/15 mm, and one peak on g.l.c., R_t 14 min (silicone oil; 176°).

1-Tetrahydropyran-2-yloxyhexadec-trans-2-en-4-yne.— 1-Tetrahydropyran-2-yloxypent-*trans*-2-en-4-yne (56·4 g, 0·4 mol) was added dropwise during 1 h, to lithamide (from 3·0 g, 0·45 g-atom of lithium) in liquid ammonia with a catalytic amount of ferric nitrate; the reaction mixture was stirred for 4 h, when n-undecyl bromide (94·0 g, 0·4 mol) was added during 1 h and stirring was continued for a further 4 h. After being set aside overnight, the mixture was decomposed with ammonium chloride, extracted into ether, dried, and distilled to give, after a forerun of starting materials, 1-tetrahydropyranyl-2-yloxyhexadec-*trans*-2-en-4-yne (69 g, 57%), b.p. 140—145°/1 × 10^{-3} mm (Found: C, 78·7; H, 11·3. $C_{21}H_{36}O_2$ requires C, 76·8; H, 11·3%), $\nu_{max.}$ 2210 (C≡C), 1640 (C=C), and 960 cm^{-1} (C=C, *trans*) and the characteristic tetrahydropyran-2-yl ether bands, $\lambda_{max.}$ 228 (ε 13,200) and λ_{sh} 236 nm (ε 11,200), and one peak on g.l.c., R_t 45 min (silicone oil; 178°).

Hexadec-trans-2-en-4-yn-1-ol.— 1-Tetrahydropyranyl-2-yloxyhexadec-*trans*-2-en-4-yne (64·8 g, 0·2 mol) was dissolved in methanol (250 ml) and concentrated hydrochloric acid (10 ml) and heated under reflux for 4 h. After cooling, the solution was neutralised with an excess of aqueous sodium hydrogen carbonate and extracted into ether; the extract was washed with water, dried, and distilled, to give hexadec-*trans*-2-en-4-yn-1-ol (39·2 g, 83%), b.p. 136—140°/2 mm (Found: C, 81·3; H, 11·0. $C_{16}H_{28}O$ requires C, 80·8; H, 11·7%), $\nu_{max.}$ 3400 (OH), 2210 (C≡C), 1640 (C=C), and 960 cm^{-1} (C=C, *trans*); g.l.c., R_t 25 min (silicone oil; 176°).

Hexadeca-3,4-dien-1-ol.— Hexadec-*trans*-2-en-4-yn-1-ol (31·0 g, 0·13 mol) in dry ether (100 ml) was added dropwise during 2 h to lithium aluminium hydride (10·0 g, 0·26 mol) in dry ether (500 ml) and the reaction mixture was heated under reflux for 2 h. An excess of lithium aluminium hydride was decomposed with water, 10% hydrochloric acid was added to lower the pH to 2, and the product was separated with ether, dried, and distilled to give hexadeca-3,4-dien-1-ol (19·4 g, 63%), b.p. 120—124°/0·1 mm (Found: C, 80·8; H, 11·7. $C_{16}H_{30}O$ requires C, 80·6; H, 11·7%),

$\nu_{max.}$ 3400 (OH) and 1950 cm^{-1} (C=C=C); g.l.c. R_t 62 min (silicone oil, 176°).

1-Bromohexadeca-3,4-diene.—Hexadeca-3,4-dien-1-ol (17·6 g, 0·075 mol) dissolved in dry pyridine (6·4 g, 0·08 mol) was added dropwise during 15 min, to well-stirred triphenylphosphite dibromide [15] (prepared from 31·0 g of triphenyl phosphite) in dry ether (50 ml) at 0°. The reaction mixture was stirred for 30 min at 0° and 1 h at room temperature; water was then added and the product was separated with ether. The extract was washed with 20% hydrochloric acid and water, dried, and distilled to give 1-bromohexadeca-3,4-diene (11·5 g, 52%), b.p. 138—146°/2 mm, $\nu_{max.}$ 1960 cm^{-1} (C=C=C), g.l.c. gave one main peak (80%); R_t 80 min (silicone oil, 176°).

Methyl Octadeca-5,6-dienoate [(±)-*Methyl Laballenate*].— Sodium (1·0 g, 0·045 g-atom) was added to dry ethanol (225 ml); when all the sodium had reacted diethyl malonate (0·7 g, 0·045 mol) was added to the reaction mixture which was then stirred for 1 h. Then, 1-bromohexadeca-3,4-diene (11·4 g, 0·037 mol) was added during 15 min and the mixture was heated under reflux for 1 h and left overnight at room temperature. The product was separated with ether, dried, and evaporated to give the crude substituted malonate ester (10 g), which was hydrolysed in ethanol–20% aqueous sodium hydroxide (20 ml) at reflux temperature for 1 h; the mixture was acidified with concentrated hydrochloric acid (25 ml) and again heated at reflux temperature for 3 h. The product was isolated with ether, evaporated, finally on a rotatory evaporator at 90—100°/15 mm for 2 h to give octadeca-5,6-dienoic acid (5·0 g), $\nu_{max.}$ 3400—2600 (CO$_2$H), 1960 (C=C=C), and 1700 cm^{-1} (C=O).

Octadeca-5,6-dienoic acid (4·2 g, 0·015 mol) in methanol (10 ml) was added to hydrogen chloride (1·5 g)–methanol (25 ml) with shaking and then left at room temperature overnight. The product was isolated with ether, washed with saturated aqueous sodium hydrogen carbonate and water, and then dried and distilled to give methyl octadeca-5,6-dienoate (2·5 g, 56%), b.p. 144—146°/5 × 10^{-2} mm (Found: C, 77·3; H, 11·7. $C_{19}H_{34}O_2$ requires C, 77·5; H, 11·6%), $\nu_{max.}$ 1960 (C=C=C) and 1750 cm^{-1} (C=O); g.l.c. gave one peak, R_t 74 min (silicone oil, 176°). *p*-Bromophenacyl laballenate had m.p. 46—46·5° (lit.,[2] 47—47·5°) (Found: C, 65·1; H, 8·0. $C_{26}H_{37}BrO_3$ requires C, 65·4; H, 7·8%). The ester (0·3 g, 0·001 mol) in ethyl acetate (50 ml) with platinum oxide (0·1 g) absorbed hydrogen (48 ml, 0·0011 mol) and gave methyl stearate, m.p. 40°, identical with an authentic specimen.

(−)-*Hexadeca-3,4-dien-1-ol*.— 3-*O*-Benzyl-1,2-*O*-cyclohexylidene-α-D-glucofuranose [6] (49·1 g, 0·30 mol) dissolved in dry ether (200 ml) was added during 1 h to a slurry of lithium aluminium hydride (6·0 g, 0·31 mol) in dry ether (500 ml). The reaction mixture was heated for 2 h under reflux, cooled to room temperature, and then hexadec-2-en-4-yn-1-ol (17·7 g, 0·075 mol) in dry ether (100 ml) was added to it during 1 h. Hydrochloric acid (10%) was added to attain pH 2 and the product was separated with ether, dried, and distilled to give (−)-hexadeca-3,4-dien-1-ol (7·8 g, 44%), b.p. 120—124°/0·1 mm, $[\alpha]_D^{20}$ −4·4° (neat), i.r. and g.l.c. were identical to those of the racemic form.

(−)-*Methyl Octadeca-5,6-dienoate* [(−)-*Methyl Laballenate*].—(−)-Hexadeca-3,4-dien-1-ol (7·1 g, 0·03 mol) gave, by a similar method to the racemic form, (−)-octadeca-5,6-dienoic acid (2·6 g) $[\alpha]_D^{20}$ −3·0° (*c* 25 in ethanol) with i.r.

[14] A. Luttringhaus and D. Schade, *Ber.*, 1941, **24**, 1565.

identical to the racemic acid. The allenic acid (2·1 g, 0·0075 mol) gave (−)-methyl octadeca-5,6-dienoate (2·0 g) $[\alpha]_D^{20}$ −3·0° (c, 45 in ethanol) [lit.,[2] $[\alpha]_D^{26}$ −47·3 (c, 1·8, in ethanol) i.r. identical to the racemic ester.

Undec-9-ynoic Acid.—Bromine (106 g, 0·66 mol) was added dropwise with stirring to undec-10-enoic acid (120 g, 0·65 mol) in carbon tetrachloride (400 ml) at 0°; the reaction mixture was stirred for 0·5 h at room temperature after which the solvent was removed. The crude 10,11-dibromo-undecanoic acid so obtained was added to potassium hydroxide (270 g) in water (160 ml). The reaction mixture was heated to 180° for 0·5 h, cooled, diluted with water (600 ml), and acidified with concentrated hydrochloric acid. The product was isolated with ethyl acetate, dried, and distilled to give undec-9-ynoic acid (75·3 g, 63%), b.p. 120—126°/0·2 mm (lit.,[11] 134—138°/0·7 mm) as a white waxy solid $\nu_{max.}$ 3500—2500 (CO₂H), 1690 cm⁻¹ (C=O); τ 8·92 [10H, s, (CH₂)₅], 8·25 (3H, t, CH₃–C≡C, J 2·5 Hz), 8·08 (2H, m, CH₂–C≡C, J 2·5 Hz), 7·68 (2H, t, CH₂CO₂H), and 0·26 (1H, s, CO₂H); the methyl ester had b.p. 88—89°/0·25 mm, $\nu_{max.}$ 1740 (C=O), and one peak on g.l.c., R_t 13·5 min (silicone oil; 150°) and R_t 10·5 min (Carbowax 20M; 160°).

Undec-trans-9-enoic acid.—Undec-9-ynoic acid (53·5 g, 0·295 mol) was dissolved in liquid ammonia (2 l) and sodium (27·6 g, 1·2 g-atom) was added to it during 1 h. The reaction mixture was stirred 15 min and then the excess of ammonia was evaporated; methanol (200 ml) was added cautiously to the residue followed by hydrochloric acid. The product was extracted with light petroleum; the extract was dried and evaporated to give undec-trans-9-enoic acid (40·6 g, 75%), b.p. 137—140°/1 mm (lit.,[13] 121—123°/0·7 mm) $\nu_{max.}$ 3500—2400 (CO₂H), 1700 (C=O), and 695 cm⁻¹ (C=C, trans); τ 8·75 (10H, s, (CH₂)₅), 8·25 (3H, d of d, CH₃CH=), 8·1 (2H, m, C=CH–CH₂–), 7·6 (2H, t, –CH₂CO₂H), 4·6 (2H, m, –CH=CH–), and 1·5 (1H, s, CO₂H).

Methyl Undec-trans-9-enoate.—Methanol (6·7 g, 0·21 mol) and concentrated sulphuric acid (0·6 ml) was added to undec-trans-9-enoic acid (34 g, 0·19 mol) in methylene chloride (62 ml) and the reaction mixture was heated under reflux for 12 h. The product was isolated by the addition of water, extraction into methylene chloride, and distillation to give methylundec-trans-9-enoate (28·6 g, 78%), b.p. 84—86°/0·2 mm, $\nu_{max.}$ 1740 (C=O) and 970 cm⁻¹ (C=C, trans), and one peak on g.l.c., R_t 12 min (silicone oil; 140°).

Undec-trans-9-en-1-ol.— Methyl undec-trans-9-enoate (27·8 g, 0·14 mol) in dry ether (50 ml) was added dropwise with vigorous stirring to lithium aluminium hydride (3·5 g, 0·09 mol) in dry ether (200 ml) and the mixture was heated under reflux for 1 h. The excess of lithium aluminium hydride was decomposed with the minimum volume of water and the product was isolated with ether; the dried extract was distilled to give undec-trans-9-en-1-ol (22·1 g, 93%), b.p. 84—86°/0·1 mm (Found: C, 77·8; H, 12·8. C₁₁H₂₂O requires C, 77·6; H, 13·0%), $\nu_{max.}$ 3350 (OH), 1640 (C=C) and 965 cm⁻¹ (C=C, trans); τ 8·7 [12H, s, (CH₂)₆], 8·35 (3H, dd, CH₃), 8·20 (1H, s, OH), 8·05 (2H, m, C=CH–CH₂–), 6·40 (2H, t, CH₂OH), and 4·6 (2H, m, CH=CH), and one peak on g.l.c.; R_t 49 min (Carbowax 20M; 120°).

1-Bromondec-trans-9-ene.—Undec-trans-9-en-1-ol (54 g, 0·318 mol) in dry ether (100 ml) and dry pyridine (29·5 g, 0·364 mol) was added during 1 h with vigorous stirring to triphenylphosphite dibromide [15] (prepared from 112 g of triphenyl phosphite) in dry ether (200 ml) at 0°. The reaction mixture was stirred for 1 h at room temperature,

water was added and the product was separated with ether; the extract was washed with dilute hydrochloric acid, water, and dilute sodium hydroxide, and then dried and distilled to give 1-bromoundec-trans-9-ene (45 g, 61%), b.p. 84—86°/0·7 mm (Found: C, 56·65; H, 8·95; Br, 34·45. C₁₁H₂₁Br requires C, 56·65; H, 9·1; Br, 34·25%), $\nu_{max.}$ 1640 (C=C) and 965 cm⁻¹ (C=C, trans); τ 8·70 [10H, s, (CH₂)₅], 8·37 (3H, dd, CH₃), 7·8 (4H, m, C=CH–CH₂ and CH₂CH₃Br), 6·59 (2H, t, CH₂Br), 4·58 (2H, m, CH=CH), and one peak on g.l.c., R_t = 27·5 min (silicone oil; 120°) but g.l.c. on Carbowax 20M at 120° showed that 2% of 1-bromo-undec-cis-9-ene was present.

1-Tetrahydropyran-2-yloxyhexadeca-trans-2-trans-14-dien-4-yne.— 1-Tetrahydropyran-2-yloxypent-trans-2-en-4-yne (33·2 g, 0·2 mol) was added during 1 h to lithamide (from 1·4 g, 0·2 g-atom of lithium) in liquid ammonia (2 l) with a catalytic amount of ferric nitrate; the reaction mixture was stirred for 5 h after which 1-bromoundec-trans-9-ene (38 g, 0·165 mol) was added during 0·5 h. Stirring was continued for ca. 13 h. Work-up gave 1-tetrahydropyran-2-yloxyhexadeca-trans-2-trans-14-dien-4-yne (31·6 g, 61%), b.p. 170—175°/2 × 10⁻³ mm (Found: C, 78·8; H, 11·1 C₂₁H₃₄O₂ requires C, 79·1; H, 10·8%), $\nu_{max.}$ 2220 (C≡C), 1640 (C=C), 970—955 (unresolved C=C and –C≡C–CH=CH) and the characteristic tetrahydropyran-2-yl ether bands, $\lambda_{max.}$ 227 (ε 16,300) and λ_{sh} 236 nm (ε 13,900); τ 8·65—7·50 (25H, m, –O·CH[CH₂]₃·CH₂O, (CH₂)₆, CH₃CH=CH, CH₂–C≡C, CH₃CH=CHCH₂), 6·68—5·92 (2H, m, –O·CH·[CH₂]₃·CH₂O 5·80 (2H, dd, CH₂OThp), 5·34 (1H, t, O·[CH₂]₄·CH·O·), 4·55 (2H, m, CH₃CH=CH), 4·27 (1H, dtt, CH=CHCH₂O), and 3·80 (1H, dt, C=CHCH₂O).

Hexadeca-trans-2-trans-14-dien-4-yn-1-ol.— Tetrahydropyran-2-yloxyhexadeca-trans-2-trans-14-dien-4-yne (14 g, 0·044 mol) was added to methanol (60 ml) and concentrated hydrochloric acid (2 ml) and heated under reflux for 4 h. An excess of sodium hydrogen carbonate (solid) was added to the mixture and the product was worked up with ether and pentane to give hexadeca-trans-2-trans-14-dien-4-yn-1-ol (8·6 g, 83%), b.p. 152—156°/0·7 mm (Found: C, 81·8; H, 11·0. C₁₆H₂₆O requires C, 82·0; H, 11·2) $\nu_{max.}$ 3350 (OH), 2210 (C≡C), 1640 (C=C), and 970—955 cm⁻¹ (unresolved C=C and –C≡C–CH=CH), τ 8·70—7·58 [20H, m, (CH₂)₆, CH₃CH=CH, OH, C=CHCH₂ and CH₂C≡C], 5·82 (2H, d, CH₂OH) 4·56 (2H, m, CH₃CH=CH), 4·28 (1H, dtt, CH=CHCH₂OH), 3·78 (1H, dt, C=CHCH₂OH); and one peak on g.l.c., R_t 57 min (silicone oil, 178°).

Hexadeca-3,4-trans-14-trien-1-ol.— Hexadeca-trans-2-trans-14-dien-4-yn-1-ol (8·3 g, 0·036 mol) in dry ether (15 ml) was added dropwise with stirring to lithium aluminium hydride (6 g, 0·158 mol) in dry ether (200 ml) and the reaction mixture was heated under reflux for 5 h. The minimum amount of water was added to the reaction mixture which was worked up with ether to give hexadeca-3,4-trans-14-trien-1-ol (6·8 g, 81%), b.p. 146—149°/0·4 mm (Found: C, 81·1; H, 11·9. C₁₆H₂₈O requires C, 81·3; H, 11·9), $\nu_{max.}$ 3350 (OH), 1960 (C=C=C), 1645 (C=C), 970 (C=C), and 870 cm⁻¹ (C=C=C); τ 8·70—7·58 [22H, m, (CH₂)₆, CH₃CH=, OH, CH=CHCH₂, CH₂CH=C=CHCH₂] 4·85

[15] D. K. Black, S. R. Landor, A. N. Patel, and P. F. Whiter, J. Chem. Soc. (C), 1967, 2260.

(2H, dtt, CH=C=CH), 4·56 (2H, m, CH=CH); g.l.c., R_t 32 min (silicone oil, 185°).

1-*Bromohexadeca*-3,4-trans-14-*triene*.— Hexadeca-3,4-*trans*-14-trien-1-ol (6·8 g, 0·029 mol) dissolved in dry pyridine (2·76 g, 0·033 mol) was added dropwise to well stirred triphenyl phosphite dibromide [15] (prepared from triphenyl phosphite, 12 g, 0·0386 mol) in dry ether (100 ml) at 0°. After 1 h at room temperature, the product was worked up as described previously to give 1-bromohexadeca-3,4-*trans*-14-triene (5 g, 58%), b.p. 134—136°/0·2 mm, $\nu_{max.}$ 1965 (C=C=C), 1640 (C=C), 970 (C=C, *trans*), and 870 cm^{-1} (C=C=C); τ 8·72 [12H, s, (CH$_2$)$_6$], 8·38 (3H, m, CH_3), 8·02 (4H, t, CH_2CH=C=CHCH_2), 7·50 (2H, m, CH=CHCH_2), 6·65 (2H, t, CH_2Br), 4·88 (2H, m, CH=C=CH), and 4·60 (2H, m, CH=CH).

Methyl Octadeca-5,6-trans-16-*trienoate*[(±) *Methyl Lamenallenate*].—Sodium (0·46 g, 0·02 g-atom) was added to dry ethanol (100 ml), and when all the sodium had reacted, diethyl malonate (3·5, 0·022 mol) was added to the reaction mixture which was then stirred for 1 h. 1-Bromohexadeca-3,4-*trans*-14-triene (5 g, 0·0168 mol) was added to the mixture which was stirred for 8 h under reflux. Half of the ethanol was distilled off and the product was separated with ether; the extract was dried and evaporated to give the crude diester (8 g) which was hydrolysed by sodium hydroxide (45 ml, 10%) and ethanol (18 ml) at reflux for 2 h and decarboxylated by acidification with concentrated hydrochloric acid (20 ml) and heating under reflux for 4 h. The product was isolated with ether, and evaporated to give octadeca-5,6-*trans*-16-trienoic acid (5·3 g), $\nu_{max.}$ 3500—2500 (COOH), 1960 (C=C=C), 1760—1710 (C=O), 1640 (C=C), 970 (C=C, *trans*), and 875 cm^{-1} (C=C=C). The crude acid was added to hydrogen chloride (1·5 g) in methanol (25 ml) and the mixture was shaken for 0·5 h; it was then left overnight. The product was isolated with ether, washed with saturated aqueous sodium hydrogen carbonate and water, and then dried and distilled to give crude methyl octadeca-5,6-*trans*-16-trienoate (3·4 g, 53%), b.p. 136—140°/-1·5 × 10^{-3} mm; $\nu_{max.}$ 1965 (C=C=C), 1740 (C=O), 1640 (C=C), 965 (C=C, *trans*), and 875 cm^{-1} (C=C=C). T.l.c. on silica gel 'G', developed in methylene chloride showed two peaks (R_F 0·65 and 0·73).

Separation of these components was effected by silica-gel dry-column chromatography [16] developed by methylene chloride to give (1) methyl 2-carbomethoxyoctadeca-5,6-*trans*-16-trienoate (2·45 g, 72%); t.l.c. showed one spot R_F 0·65 (Found: C, 71·7; H, 9·9. C$_{21}$H$_{34}$O$_4$ requires C, 71·9; H, 9·8%); τ 8·72 [14 H, s, (CH$_2$)$_6$, CH_2CH$<$] 8·48 (3H, m, CH$_3$CH), 8·08—8·25 [7H, m, CH_2CH= and CH(CO$_2$Me)$_2$], 6·28 [6H, s, (CO$_2$Me)$_2$], 4·93 (2H, m, CH=C=CH), and 4·60 (2H, m, −CH=CH−).

(ii) Methyl octadeca-5,6-*trans*-16-trienoate [(±)-methyl lamenallenate] (0·95 g, 28%), t.l.c. showed one spot, R_F 0·73 (Found: C, 77·9; H, 10·7. C$_{19}$H$_{32}$O$_2$ requires C, 78·0; H, 11·0%); τ 8·73 (14H, s, (CH$_2$)$_6$ and CH_2CH$_2$CO$_2$Me], 8·42 (3H, m, CH_3CH=CH), 8·06—8·26 (6H, m, CH$_2$CH=C=CHCH_2 and CH=CH−CH_2), 7·74 (2H, t, CH_2CO$_2$Me), 6·42 (3H, s, CO$_2$Me), 5·0 (2H, m, CH=C=CH), and 4·65 (2H, m, CH=CH).

A further sample of (±)methyl lamenallenate was obtained by taking a crude mixture of mono- and di-carboxylic acids (0·8 g) and heating them with concentrated hydrochloric acid (1 drop) at 160° for 1 h. After esterification, (±)methyl lamenallenate (0·7 g) was isolated by silica-gel dry-column chromatography developed by methylene chloride. T.l.c. gave a single spot R_F 0·73; i.r. and n.m.r. spectra were identical with those above.

(−)-*Hexadeca*-3,4-trans-14-*trien-1-ol*.—3-*O*-Benzyl-1,2-*O*-cyclohexylidene-α-D-glucofuranose (60·4 g, 0·173 mol) in dry ether (150 ml) was added with stirring to a slurry of lithium aluminium hydride (9·0 g, 0·237 mol) in dry ether (200 ml). The reaction mixture was heated for 1·5 h under reflux and was then cooled to room temperature; hexadeca-*trans*-2-*trans*-14-dien-4-yn-1-ol (10 g, 0·043 mol) in dry ether (50 ml) was added dropwise to it with vigorous stirring; refluxing was then continued for 7 h. Work-up gave (−)-hexadeca-3,4-*trans*-14-trien-1-ol (7·52 g, 75%), b.p. 126—128°/0·2 mm, $[\alpha]_D^{20}$ 8·34° (*c* 6·2 in ethanol); i.r. and g.l.c. were identical to those of the racemic form.

(−)-*Methyl Octadeca*-5,6-trans-16-*trienoate* [(−)-*Methyl Lamenallenate*].—(−)-Hexadeca-3,4-*trans*-14-trien-1-ol (4·7 g, 0·02 mol) gave by a similar method to that used to prepare the racemic form, (−)-octadeca-5,6-*trans*-16-trienoic acid (2·5 g) $[\alpha]_D^{20}$ −6·21° (*c* 3·6 in ethanol); its i.r. spectrum was identical to that of the racemic acid; it gave a *p*-bromophenacyl ester, m.p. 39·5—40° (lit.,[4] 40·5—41·5), t.l.c. on silica gel 'G' developed with methylene chloride gave a single spot R_F 0·87. The allenic acid (1·7 g) gave (−)-methyl octadeca-5,6-*trans*-16-trienoate [(−)-methyl lamenallenate] (0·9 g, 46%) $[\alpha]_D^{20}$ −5·8° (*c* 5·6 in ethanol) [lit.,[4] $[\alpha]_D^{25}$ −50° (*c*, 0·82 ethanol)]; its i.r. and n.m.r. spectra were identical with those of the racemic form, and t.l.c. gave a single spot R_F 0·73.

[16] B. Loev and M. M. Goodman, *Chem. and Ind.*, 1967, 2026.