Natural Acetylenes. Part XL.[1] Syntheses of Polyacetylenic C_{18} and C_{16} Esters with 9-Ene-12,14-diyne Unsaturation, and their Labelling[2,3]

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The esters $R[C{\equiv}C]_2{\cdot}CH_2{\cdot}CH\overset{c}{=}CH{\cdot}[CH_2]_7{\cdot}CO_2Me$ {R = $Me[CH_2]_2$, $MeC{\equiv}C$, *cis*- or *trans*-$MeCH{=}CH$, *trans*-$HO{\cdot}CH_2{\cdot}CH{=}CH$, $HO{\cdot}CH_2{\cdot}C{\equiv}C$, *cis*- or *trans*-$MeO_2C{\cdot}CH{=}CH$, $MeO_2C{\cdot}C{\equiv}C$, $(EtO)_2CH$, OHC, or $H_2N{\cdot}OC$} were prepared from the Wittig salt $Me_3Si{\cdot}C{\equiv}C{\cdot}CH_2{\cdot}CH_2{\cdot}\overset{+}{P}Ph_3I^-$ *via* $IC{\equiv}C{\cdot}CH_2{\cdot}CH\overset{c}{=}CH{\cdot}[CH_2]_7{\cdot}CO_2Me$; several were specifically labelled [at C(9), C(17), and C(18)]. The Wittig salt offers a general route to 1-ene-4,6-diyne and more highly unsaturated skipped en-yne systems.

THE synthesis of labelled methyl crepenynate (II) in which the Wittig reaction between two C_9 fragments represents the last and crucial step has been described.[1] Preliminary experiments utilising an analogous sequence

$$Me[CH_2]_4{\cdot}C{\equiv}C{\cdot}CH_2{\cdot}\overset{-}{C}H{\cdot}\overset{+}{P}Ph_3 + OCH{\cdot}[CH_2]_7{\cdot}CO_2Me \quad (I)$$

$$\longrightarrow Me[CH_2]_4{\cdot}C{\equiv}C{\cdot}CH_2{\cdot}\overset{c}{C}H{=}CH{\cdot}[CH_2]_7{\cdot}CO_2Me \quad (II)$$

of reactions for the synthesis of the more acetylenic C_{18} esters (III) and (IV), postulated to be intermediates in the biogenetic conversion of oleate into some polyacetylenes,[4] were not promising.† Bohlmann *et al.*[5] synthesised these two esters by coupling the C_{13} ethynyl ester (V) with bromopentyne and bromopentadiyne respectively, but an improved route to the C_{13} ester and better yields, especially in the stages likely to involve labelled intermediates, *e.g.* the coupling, were desirable.

† The esters (III) and (XII) have since been prepared by this route by Mr. I. W. Farrell in this laboratory.

[1] Part XXXIX, G. C. Barley, Sir Ewart R. H. Jones, V. Thaller, and R. A. Vere Hodge, *J.C.S. Perkin I*, 1973, 151.

[2] Preliminary communication: A. G. Fallis, Sir Ewart R. H. Jones, and V. Thaller, *Chem. Comm.*, 1969, 924.

[3] A more detailed account of the major part of the work described in this paper is in the D. Phil. Thesis of J. L. Turner, Oxford, 1972.

[4] J. D. Bu'Lock, 'Comparative Phyto-chemistry,' ed. T. Swain, Academic Press, London, 1966, p. 79.

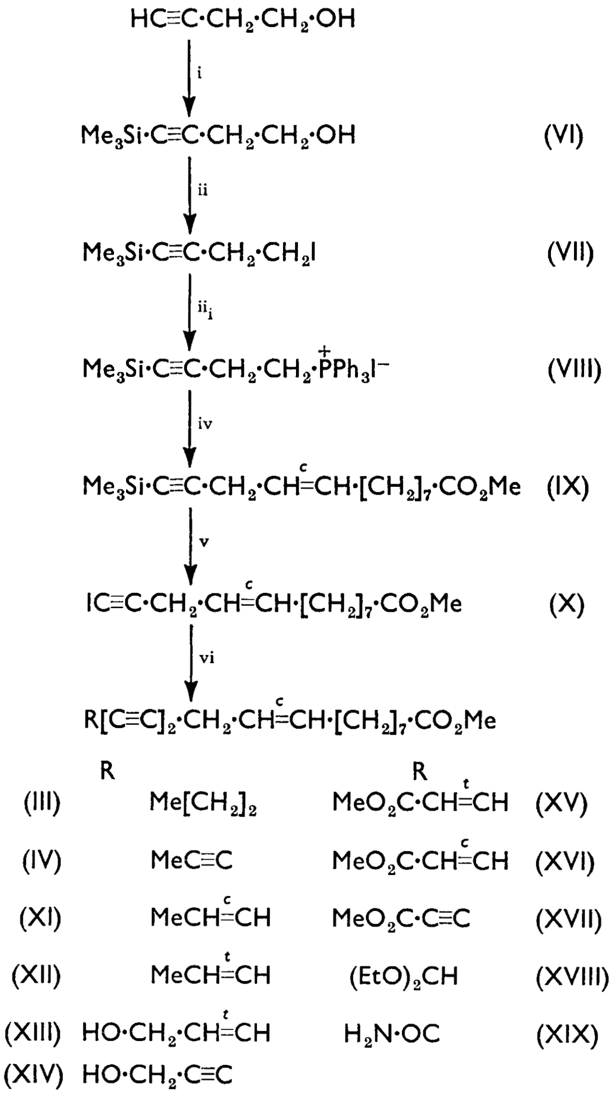
[5] (*a*) F. Bohlmann, R. Jente, W. Lucas, J. Laser, and H. Schulz, *Chem. Ber.*, 1967, **100**, 3183; (*b*) F. Bohlmann, H. C. Hummel, and J. Laser, *ibid.*, 1968, **101**, 3562.

Both aims were achieved through the reaction sequence of Scheme 1. The C_{13} iodo-ester (X) was coupled with the appropriate terminal acetylenes and the C_{18} esters (III), (IV), and (XI)—(XVII) and the C_{16} esters (XVIII) and (XIX) were prepared.

(III) R = $Me[CH_2]_2$ R[C≡C]$_2$·CH_2·CH$\overset{c}{=}$CH·$[CH_2]_7$·CO_2Me R = MeC≡C (IV)

HC≡C·CH_2·CH$\overset{c}{=}$CH·$[CH_2]_7$·CO_2Me (V)

The Wittig salt (VIII) represents a stable intermediate of considerable scope for the synthesis of compounds containing the 1-ene-4,6-diyne and more highly unsaturated chromophores. The crude salt, suitably dried,



i, Reagents: EtMgBr, Me_3SiCl, dil.HCl; ii, $(PhO)_3\overset{+}{P}MeI^-$–$CH_2Cl_2$–$Me_2N$·CHO; iii, Ph_3P–EtOH; iv, NaH–Me_2SO–$[CH_2]_4O$–OCH·$[CH_2]_7$·CO_2Me(I); v, $AgNO_3$, I_2–CH_2Cl_2; vi, RC≡CH–CuCl–NH_2·OH–$EtNH_2$

SCHEME 1

gave satisfactory yields in the Wittig reaction. For this, the salt (VIII), the aldehyde (I) and sodium hydride were stirred together in tetrahydrofuran–dimethyl sulphoxide at 0° (similar reaction conditions were employed to prepare βγ-unsaturated acids [6]) for 20—70 h. The reaction time used depended on the scale of the reaction: better yields (*ca.* 80%) were obtained in smaller scale (less than 1 g Wittig salt) than in larger scale (10 g) reactions. G.l.c. indicated that 95% of the double-bond product was *cis*; incomplete exclusion of moisture adversely affected the favourable *cis–trans* ratio and also resulted in the formation of by-products.

The carbon–silicon bond was cleaved with silver nitrate; [7] the C_{13} ester (V) was isolated but could not be converted with sodium hypobromite into the corresponding bromo-ester. The iodo-ester (X) was obtained, however, in acceptable yields (*ca.* 60%) by the action of iodine in dichloromethane on the silver acetylide, which precipitated during the carbon–silicon bond cleavage. Excess of silver nitrate had to be removed prior to the reaction with iodine to prevent the formation of the nitrate ester (XX) (the addition of iodonium nitrate to

IC≡C·$\overset{c}{C}H_2$·$\overset{b}{C}$HI·$\overset{a}{C}$H(O·NO_2)·$[CH_2]_7$·CO_2Me (XX)

H	τ	J/Hz
a	5·1(m)	
b	5·75(dt)	3·75 and 7·5
c	6·95(d)	7·5

double bonds has been reported before [8]). Although the formation of two iodo-nitrates could be expected, the n.m.r. signals given and the strong peak at *m/e* 305 (33%) assigned to the ion $[IC{\equiv}C{\cdot}CH_2{\cdot}CHI]^+$ favour structure (XX).

The C_{13} ethynyl ester (V) did not couple well with bromoacetylenes (yields of 24 and 14% were observed [5] with bromopentyne and bromopentadiyne, respectively). In contrast, the C_{13} iodo-ester (X) gave acceptable yields with ethynyl compounds. [The use of iodo-acetylenes in Chodkiewicz couplings has not been reported; they were assumed to be too reactive as they act as strong oxidising agents towards the copper(I) ion and favour the secondary self-coupling reaction.[9]] Different conditions were necessary for each of the terminal acetylenes used and yields were often improved (generally to 40—60%) by raising the concentrations of both copper(I) chloride and ethylamine. The iodo-ester (X), contaminated with the C_{13} ethynyl ester (V), was often recovered from the reactions despite the presence of an excess of the ethynyl component in the reaction mixture.

[6] H. S. Corey, jun., J. R. D. McCormick, and W. E. Swensen, *J. Amer. Chem. Soc.*, 1964, **86**, 1884.
[7] H. M. Schmidt and J. F. Arens, *Rec. Trav. chim.*, 1967, **86**, 1138.
[8] L. Birkenbach and J. Gonbeau, *Ber.*, 1934, **67**, 1420; L. J. Morris, *Chem. and Ind.*, 1958, 1291.
[9] P. Cadiot and W. Chodkiewicz, in 'Chemistry of Acetylenes,' ed. H. G. Viehe, M. Dekker, New York, 1969, p. 616.

From the coupling product between the iodo-ester (X) and a mixture of methyl *cis*- and *trans*-pent-2-en-4-ynoate, only the *cis,cis*-diester (XVI) was isolated easily by chromatography. The *cis,trans*-diester (XV) was contaminated with a by-product, also an ester (most likely the C_{26} diester resulting from self-coupling of the iodo-ester), from which it could not be separated. The products from the Wittig reaction between the C_{16} aldehyde ester (XXI) [prepared from the C_{16} acetal ester (XVIII)] and the phosphorane (XXII) on the other

$OCH{\cdot}[C{\equiv}C]_2{\cdot}CH_2{\cdot}CH\overset{c}{=}CH{\cdot}[CH_2]_7{\cdot}CO_2Me$ (XXI)

$MeO_2C{\cdot}\bar{C}H{\cdot}\overset{+}{P}Ph_3$ (XXII)

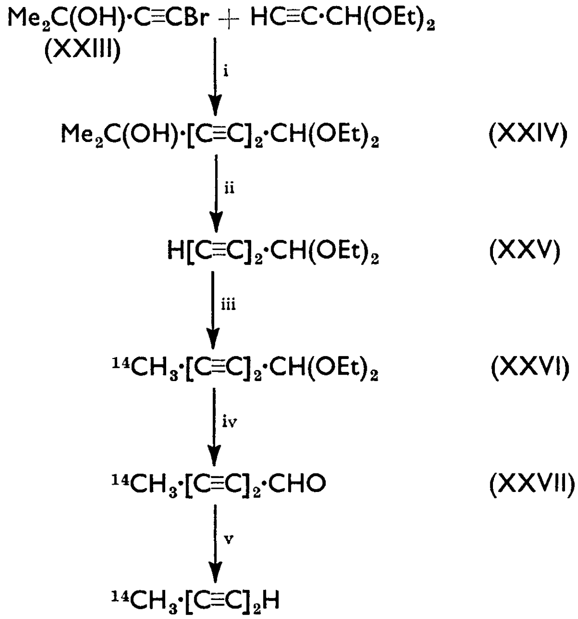
hand were easily separated and the *cis,cis*-diester (XVI) and the *cis,trans*-diester (XV) were obtained in the ratio 1 : 4·1 (a ratio of 1 : 1·7 was obtained in the pentenynoate route). Methyl pent-2-en-4-ynoate was prepared from prop-2-ynal and the phosphorane (XXII) and could be separated by chromatography into the *cis*- and *trans*-isomers.

Propiolamide and the iodo-ester (X) did not couple under normal Chodkiewicz conditions; the iodo-ester was always recovered in high yield from the reaction mixture. The C_{16} amide ester (XIX) was obtained, however, in 20% yield by using the reverse addition procedure for the reactants and a large excess of both catalyst and propiolamide; none of the latter was recovered from the reaction mixture. Propiolamide has been reported [10] to couple normally with some bromoacetylenes and in our hands 4-bromo-2-methylbut-3-yn-2-ol gave a high yield of the expected diyne (the reaction was carried out at 20 and not 0—5° as described [10]).

All the 9-en-12,14-diyne compounds showed a characteristic two proton n.m.r. doublet for the 'skipped' en-yne methylene protons at τ 6·85—7·15 and a multiplet for the vinyl protons of the isolated double bond. Mass spectral molecular ions and strong peaks for fragments arising through loss of $[CH_2]_6{\cdot}CO_2Me$ were obtained in all instances.

Several of the C_{18} and C_{16} compounds were synthesised radioactively labelled, either at C(9) or in the terminal C_5 fragment. For the former, the [9-^{14}C]aldehyde ester, [9-^{14}C]- (1),[1] was used and the C_{18} ester [9-^{14}C]- (IV) and the C_{16} esters [9-^{14}C]- (XVIII), [9-^{14}C]- (XIX), and [9-^{14}C]- (XXI) were prepared.

The labelling of potential precursors in the distal half of the C_{18} esters was of special importance for biosynthetic experiments with C_8 polyacetylenes. The C_{16} aldehyde ester (XXI) and the [2-^{14}C]- and [^{3}H]-labelled phosphorane (XXII) [11] gave the [17-^{3}H]- and [17-^{14}C]-labelled diesters (XV) and (XVI). Sodium butadiynide and [^{14}C]paraformaldehyde gave [1-^{14}C]-penta-2,4-diyn-1-ol which in turn was converted into the labelled hydroxy-ester, [18-^{14}C]- (XIV). The small scale synthesis of penta-1,3-diyne from sodium butadiynide and methyl iodide was not suitable for labelling purposes as the yields were unpredictable and very low. Several alternative routes to penta-1,3-diyne were tried and the one given in Scheme 2 was used to synthesise [5-^{14}C]-penta-1,3-diyne which in turn was converted into the



Reagents: i, CuCl–$NH_2{\cdot}OH$–$EtNH_2$; ii, KOH, 135°; iii, $^{14}CH_3I$–$LiNH_2$; iv, 2N-HCl; v, NaOH–MeOH–H_2O, 50°

SCHEME 2

labelled triyne ester [18-^{14}C]- (IV) (overall activity yield from [^{14}C]iodomethane was 30%).

EXPERIMENTAL

For general techniques see Part XXXIX.[1]

[5-^{14}C]*Penta*-1,3-*diyne*.—1,1-Diethoxyprop-2-yne [12] (6·4 g, 50 mmol) in MeOH (50 ml) containing CuCl (200 mg), $NH_2{\cdot}OH,HCl$ (7 g), and $EtNH_2$ (8 ml) and the bromoacetylene (XXIII) (8·3 g, 50 mmol; prepared from the terminal acetylene and NaOBr in 98% yield) in MeOH (100 ml) were coupled (general procedure for the coupling and work-up given later on). The Et_2O extract was chromatographed [SiO_2 (300 g) column]; elution with petrol–Et_2O (4 : 1) gave first 3,3-diethoxypropyne and then the diynol (XXIV) (7·05 g, 67%), b.p. 123—124° at 0·5 mmHg, n_D^{20} 1·4692 (lit.,[13] b.p. 121—123° at 0·47 mmHg, n_D^{20} 1·4696), $\nu_{max.}$ (CCl_4) 3620 (OH free), 3500 (OH bonded), and 2180 (C≡C) cm^{-1}, τ (CCl_4) 8·8 [t, *J* 7 Hz, $(CH_3{\cdot}CH_2{\cdot}O)_2$], 8·51 [s, $(CH_3)_2COH{\cdot}C{\equiv}C$], 7·78br (OH), 6·41 [m, $(CH_3{\cdot}CH_2{\cdot}O)_2$], and 4·84 [s, $(EtO)_2{\cdot}CH$]. This (1·0 g, 4·8 mmol) was converted [13] into the diyne acetal (XXV) (374 mg, 52%), b.p. 76° at 11 mmHg, n_D^{20} 1·4711 (lit.,[13] 82° at 15 mmHg, n_D^{20} 1·4708), $\nu_{max.}$ (CCl_4) 3320 (C≡CH) and 2100 (C≡C) cm^{-1}, τ (CCl_4) 8·8 [t, *J* 7 Hz, $(CH_3{\cdot}CH_2{\cdot}O)_2$], 7·91 (s, C≡CH), 6·4 [m, $(CH_3{\cdot}CH_2{\cdot}O)_2$], and 4·83 [s, $(EtO)_2CH$].

[10] W. Chodkiewicz, Ph.D. Thesis, Paris, 1957.

[11] G. C. Barley, A. C. Day, U. Graf, Sir Ewart R. H. Jones, I. O'Neill, R. Tachikawa, V. Thaller, and R. A. Vere Hodge, *J. Chem. Soc.* (*C*), 1971, 3308.

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[13] B. P. Gusev and V. F. Kucherov, *Izvest. Akad. Nauk S.S.S.R., Otdel. khim. Nauk*, 1965, **5**, 851.

The acetal (XXV) (160 mg, 1·05 mmol) in Et_2O (1·5 ml) was added at −70° to a stirred suspension of $LiNH_2$ (72 mg, 3·1 mmol) in dry NH_3 (12 ml) and stirring was continued for 0·5 h. [^{14}C]Iodomethane [nominal 500 μCi; 55 mCi $mmol^{-1}$ (Radiochem. Centre, Amersham), diluted with MeI (141 mg)] in Et_2O (3 ml) was then added in portions from a cooled tube (solid CO_2–Me_2CO) connected to the flask by a flexible tube. After stirring for a further 0·5 h at −70° the solution was refluxed for 2·5 h, Et_2O (5 ml) and NH_4Cl were added and NH_3 was allowed to evaporate. The solution was filtered and concentrated, and the residual oil purified, first by shaking with CuCl (0·5 mg) in petrol (50 ml) in the dark for 2 h and then by p.l.c. The band with R_F 0·3 (petrol–Et_2O, 19 : 1) gave the liquid [^{14}C]acetal (XXVI) (500 μCi; 520 μCi $mmol^{-1}$), b.p. 70—72° (block) at 0·5 mmHg, n_D^{20} 1·4825 (lit.,[14] b.p. 72—73° at 0·5 mmHg, n_D^{20} 1·4815; lit.,[13] b.p. 63—64° at 0·6 mmHg, n_D^{20} 1·4838), $\nu_{max.}$ (CCl_4) 2300 and 2200 (C≡C) cm^{-1}, τ (CCl_4) 8·8 [t, *J* 7 Hz, (CH_3·CH_2·O)$_2$], 8·03 (s, CH_3·C≡C), 6·4 [m, (CH_3·CH_2·O)$_2$], and 4·85 [s, (EtO)$_2$·CH]. This and HCl (2N; 5 ml) were shaken for 15 min at 20°. Et_2O (4 ml) was added and the mixture was shaken again. The layers were separated; the aqueous layer was extracted with Et_2O (2 × 6 ml) and the combined Et_2O solutions gave on washing with $NaHCO_3$ (sat.; 3 ml) a solution of hexa-2,4-diynal (XXVII), $\lambda_{max.}$ (Et_2O) 285 (rel. *E* 3·1), 268 (3·9), 255 (2·4), 242·5 (1·15), and 230 (1·0) nm. This was carefully concentrated (below 10°) and the residue was immediately redissolved in MeOH (5 ml) and warmed to 50° under reflux, NaOH (4N; 3 ml) was added down the condenser. Deformylation [15] was complete in 12 min (u.v.) and the mixture was cooled quickly before Et_2O (10 ml) and H_2O (5 ml) were added. The layers were separated, and the aqueous layer was extracted with Et_2O (2 × 5 ml); [5-^{14}C]penta-1,3-diyne (325 μCi; 65%) present in the combined ether layers was used directly in Chodkiewicz reactions.

[1-^{14}C]*Penta*-2,4-*diyn*-1-*ol*.—This was prepared in a small-scale version of the described syntheses.[16] 1,4-Dichlorobut-2-yne (200 mg, 1·6 mmol) in Et_2O (2 ml) was added dropwise to a stirred suspension of $NaNH_2$ in dry liquid NH_3 [from Na (113 mg, 4·9 mmol), $Fe(NO_3)_3$ (1 crystal), and NH_3 (12 ml)] at −70°. Stirring was continued for 5 min, more Et_2O (3 ml) was carefully added and then [^{14}C]paraformaldehyde [0·5 mCi; 230 μCi mg^{-1} (Radiochem. Centre, Amersham), diluted with paraformaldehyde (37 mg)] was introduced in one portion. After 1 h stirring at −50°, first NH_4Cl (400 mg) was added in portions and then Et_2O (5 ml). Evaporation of NH_3, filtration, concentration of the filtrate, and washing of the concentrate with cold petrol (2 × 2 ml) gave [1-^{14}C]pentadiynol (245 μCi; 47%; 380 μCi $mmol^{-1}$), τ ($CDCl_3$) 7·74 (1H, s, C≡CH), 6·82 (1H, s, OH), and 5·65 (2H, s, CH_2·OH). The product was immediately dissolved in MeOH (5 ml) for storage.

Methyl Pent-cis-2-*en*-4-*ynoate and Methyl Pent*-trans-2-*en*-4-*ynoate*.—Prop-2-ynal [17] (300 mg 5·5 mmol) in CH_2Cl_2 (8 ml) was added dropwise to the phosphorane (XXII) [18] (1·68 g, 5 mmol) stirred in CH_2Cl_2 (8 ml) at −15°. Stirring was continued first at −15° for 0·5 h and then for 1 h with slow warming up to 20°. The mixture was transferred directly to a SiO_2 column (30 g) and the products were eluted with petrol–Et_2O (2 : 1). The first 200 ml of eluant, evaporated at 50° gave methyl pent-*trans*-2-en-4-ynoate (230 mg), m.p. 19° (lit.,[19] 19—20°), t_R (80°) 3 min, τ (CCl_4) 6·75 (1H, d, *J* 2·5 Hz, C≡CH), 6·26 (3H, s, CO_2·CH_3), 3·74 (1H, d, *J* 16 Hz, *trans*-CH=*CH*·CO_2Me), and 3·3 (1H, dd, *J* 16 and 2·5 Hz, *trans*-*CH*=CH·CO_2Me). The next 100 ml of eluant contained a mixture of *cis*- and *trans*-isomers, and was followed by 200 ml which contained methyl pent-*cis*-2-en-4-ynoate (110 mg), b.p. 120—124° at 765 mmHg (block) (lit.,[20] 55—60° at 12 mmHg), t_R (80°) 6·5 min. $\lambda_{max.}$ (EtOH) 242·5 (ε 17,750) and 249 (16,500) nm, $\nu_{max.}$ (CCl_4) 3320 (C≡CH), 2125 (C≡C), and 1740 and 1725 (ester CO) cm^{-1}, $\nu_{max.}$ (CS_2) 790 (*cis*-CH=CH) cm^{-1}, τ (CCl_4) 6·55 (1H, d, *J* 2 Hz, HC≡C), 6·25 (3H, s, CO_2·CH_3), 3·97 (1H, dd, *J* 2 and 11·7 Hz, *cis*-CH=*CH*·C≡C), and 3·84 (1H, d, *J* 11·7 Hz, *cis*-CH=*CH*·CO_2Me).

4-*Iodo*-1-*trimethylsilylbut*-1-*yne* (VII).—4-Trimethylsilylbut-3-yn-1-ol (VI) [21] (14 g, 0·1 mmol) in CH_2Cl_2 (25 ml) was added over a few minutes to $(PhO)_3Me\overset{+}{P}I^-$ [22] (53·6 g, 0·13 mol) in CH_2Cl_2 (25 ml)–Me_2N·CHO (10 ml) stirred at 20° in the dark. Stirring was continued for 4 h at 40—45° and the mixture was then left for 14 h at 20°. The solvent was evaporated, the residual oil was triturated with petrol (6 × 150 ml), and the concentrated petrol extracts were purified on a SiO_2 column (500 g); elution with petrol (*ca.* 1 l) and petrol–Et_2O (19 : 1; *ca.* 0·5 l), concentration of the eluate, and distillation of the residue yielded the *iodide* (VII) (17·5 g, 72%), b.p. 82—84° at 8·5 mmHg, n_D^{20} 1·5100 (Found: C, 33·3; H, 5·5; I, 51·0. $C_7H_{13}ISi$ requires C, 33·2; H, 5·2; I, 50·5%), $\nu_{max.}$ (CCl_4) 2175 (C≡C) cm^{-1}, τ (CCl_4) 9·88 [s, $(CH_3)_3Si$], 7·16 (m, CH_2·C≡C), and 6·83 (m, CH_2I).

Triphenyl-(4-*trimethylsilylbut*-3-*ynyl*)*phosphonium Iodide* (VIII).—Ph_3P (19·0 g, 73 mmol) and the iodide (VII) (18·2 g, 72 mmol) in abs. EtOH (200 ml) were heated under reflux for 68 h. After concentration the oily residue crystallised on trituration with Et_2O to give the crude *Wittig salt* (VIII) (35 g, 95%), m.p. 132—133°, which gave cubes (from $[CH_2]_4O$–EtOAc), m.p. 135·5—136·5° (dried at 70° and 0·5 mmHg) (Found: C, 58·6; H, 5·2. $C_{25}H_{28}IPSi$ requires C, 58·4; H, 5·5%). The crude, dried (35° at 0·1 mmHg for 20 h) salt was used in the Wittig reaction.

Methyl 13-*Trimethylsilyltridec*-cis-9-*en*-12-*ynoate* (IX).—The Wittig salt (VIII) (31·2 g, 62 mmol) and methyl 8-formyloctanoate (I) [23] (11·5 g, 62 mmol) in cold (0°) Me_2SO (200 ml; dried over CaH_2 for several days)–$[CH_2]_4O$ (300 ml; freshly distilled from $LiAlH_4$) were added to NaH granules (100%; 1·49 g, 62 mmol) kept in a 1 l flask under N_2 (anhydrous conditions) with stirring and cooling (0°). After 72 h the mixture was poured into Et_2O (1500 ml) and the filtered (Celite) solution was shaken with water (1 l)–HCl (conc.; 1·5 ml). The concentrated organic phase was triturated with boiling petrol (3 × 200 ml); the petrol solution was concentrated (100 ml) and left at 0° for 14 h. The separated solid was filtered off; the filtrate was concentrated and chromatographed on a SiO_2 column (500

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g). Petrol–Et_2O (24 : 1; 4 l) eluted the crude liquid *trimethylsilyl ester* (IX) (9·3 g, 60%), R_F 0·4 (petrol–Et_2O, 9 : 1), t_R (158°) 14·2 min (*ca.* 94% pure *cis*), n_D^{20} 1·472. A sample was distilled at 70° (block) and 0·05 mmHg (Found: C, 69·7; H, 10·5. $C_{17}H_{30}O_2Si$ requires C, 69·3; H, 10·3%), $\nu_{max.}$ (CCl_4) 3020 (CH=CH), 2160 (C≡C), 1740 (ester CO), and 858 [$(Me)_3Si$] cm^{-1}, $\nu_{max.}$ (CS_2) 725 (*cis*-CH=CH) cm^{-1}, τ (CCl_4) 9·86 [s, $(CH_3)_3Si$], 8·16—8·81 (m, CH_2·$[CH_2]_5$·CH_2), 7·91 (m, CH=CH·CH_2·CH_2), 7·75 (t, *J* 7 Hz, CH_2·CH_2·CO_2Me), 7·06 (d, *J* 6 Hz, C≡C·CH_2·CH=CH), 6·35 (s, CO_2·CH_3), and 4·56 (m, *cis*-CH=CH), *m/e* 294 (M^+, 25%), 159 (16), 109 (20·5), 105 (21), 94 (20), 91 (26), 89 (98), and 73 (100).

The Wittig salt (VIII) (200 mg, 0·39 mmol) and methyl 8-formyloctanoate [23] (73 mg, 0·39 mmol) in Me_2SO (4 ml)–$[CH_2]_4O$ (6 ml) were added to NaH (15 mg, 0·63 mmol) as above and stirred for 22 h. Analogous work-up gave the trimethylsilyl ester (IX) (97% pure by g.l.c.) in 83% (95 mg) yield.

Methyl Tridec-cis-9-*en*-12-*ynoate* (V).—$AgNO_3$ (540 mg) in H_2O (10 ml) was added dropwise to the trimethylsilyl ester (IX) (350 mg) stirred in EtOH (30 ml). After 0·5 h KCN (1·0 g) in H_2O (10 ml) was added to the suspension, which was stirred until homogeneous. H_2O (50 ml) was added and the product was isolated with Et_2O and purified by p.l.c. (petrol–Et_2O, 9 : 1) yielding the liquid ethynyl ester (V) [5a] (183 mg, 70%), $\nu_{max.}$ (CCl_4) 3330 (C≡CH), 2120 (C≡C), 1745 (ester CO), and 1665 (CH=CH) cm^{-1}, $\nu_{max.}$ (CS_2) 725 (*cis*-CH=CH) cm^{-1}, τ (CCl_4) 8·2—8·9 (10H, m, CH_2·$[CH_2]_5$·CH_2·CO_2Me), 7·8—8·1 (2H, m, CH=CH·CH_2·CH_2), 7·78 (2H, t, *J* 7 Hz, CH_2·CH_2·CO_2Me), 7·11 (2H, m, C≡C·CH_2·CH=CH), 8·2 (1H, t, *J* 2 Hz, HC≡C), 6·4 (3H, s, CO_2·CH_3), and 4·5—4·7 (2H, m, CH=CH).

Methyl 13-*Iodotridec*-cis-9-*en*-12-*ynoate* (X).—$AgNO_3$ (1·2 g, 7 mmol) in EtOH (12 ml)–H_2O (12 ml) was added dropwise to the trimethylsilyl ester (IX) (1·0 g, 3·4 mmol) in EtOH (60 ml) stirred at 20° (under N_2 in the dark). After 0·5 h the mixture was cooled to 0° for 10 min and centrifuged, the liquid was decanted, and the Ag acetylide was immediately dissolved in CH_2Cl_2 (120 ml; decanted from anh. K_2CO_3). This solution was shaken thoroughly with H_2O (25 ml)–NH_3 aq. (35%; 0·1 ml); the layers were separated, and I_2 in CH_2Cl_2 was added dropwise to the dark, moist, organic phase stirred under N_2 (gradual lightening in colour and precipitation of AgI occurred) until a faint pink colouration was obtained. Stirring was continued for 0·75 h, the mixture was filtered (Celite; removal of AgI), washed with $Na_2S_2O_3$–H_2O (10%; 10 ml), dried, and concentrated to a sweet-smelling oil (1·2 g) which on p.l.c. (petrol–Et_2O, 19 : 1; 2 elutions) yielded the liquid *iodo-ester* (X) (635 mg, 54%), R_F 0·4, b.p. 100—110° (block) at 2·27 × 10^{-5} mmHg (Found: C, 47·9; H, 6·2; I, 36·25. $C_{14}H_{21}IO_2$ requires C, 48·3; H, 6·1; I, 36·4%), $\nu_{max.}$ (CCl_4) 3020 (CH=CH) and 1740 (ester CO) cm^{-1}, τ (CCl_4) 8·2—8·9 (m, CH_2·$[CH_2]_5$·CH_2), 7·8—8·1 (m, CH=CH·CH_2·CH_2), 7·86 (t, *J* 7 Hz, CH_2·CH_2·CO_2Me), 6·93 (d, *J* 6·5 Hz, C≡C·CH_2·CH=CH), 6·38 (s, CO_2·CH_3), and 4·3—4·8 (m, CH_2·CH=CH·CH_2).

Methyl 10,13-*di-iodo*-9-*nitro-oxytridec*-12-*ynoate* (XX). P.l.c. (petrol–Et_2O, 19 : 1; 2 elutions) of the crude iodo-ester (X) (R_F 0·4) gave a second band (R_F 0·3) most likely due to the *nitrate ester* (XX), $\nu_{max.}$ (CCl_4) 2200 (C=C), 1735 (ester CO), and 1640 and 1270 ($O·NO_2$) cm^{-1}, τ (CCl_4) 8·0—8·88 (12H, m, $[CH_2]_6$·CH_2·CO_2Me), 7·76 (2H, t, *J* 7 Hz CH_2·CH_2·CO_2Me), 6·95 (2H, d, *J* 7·5 Hz, C≡C·CH_2·CHI), 6·38 (3H, s, CO_2·CH_3), 5·77 (1H, dt, *J* 3·75 and 7·5 Hz, CHI), and 5·1 (1H, dt, *J* 3·75 and 6·7 Hz, ·CH·O·NO_2), *m/e* 537 (M^+, *ca.* 1%), 491 (27), 364 (20), 305 (33), 237 (36), 219 (45), 178 (100), 165 (76), and 145 (48).

[9-^{14}C]*Methyl* 13-*Iodotridec*-cis-9-*en*-12-*ynoate*, [9-^{14}C]-(X).—[9-^{14}C]Methyl 8-formyloctanoate [9-^{4}C]- (1) [1] (61 mg; 1 mCi; 3·07 mCi $mmol^{-1}$) and the Wittig salt (VIII) gave the [9-^{14}C]trimethylsilyl ester [9-^{14}C]- (IX) (76·5 mg; 791 μCi; 79%) and this yielded (1/13th scale of the 'cold' synthesis) the [9-^{14}C]iodo-ester [9-^{14}C]- (X) (383 μCi; 48%; 3·07 mCi $mmol^{-1}$).

General Reaction Procedure for the Chodkiewicz Coupling.—Unless stated otherwise the following procedure was used (solvent and quantities are stated for each reaction). To a solution of CuCl, NH_2·OH,HCl, and $EtNH_2$–H_2O (40%) stirred vigorously under N_2 at 20°, a solution of the terminal acetylene component and then after 5 min a solution of the halogenated acetylene were added dropwise. Stirring was continued for 1 h and KCN (*ca.* 0·1 g)–H_2O–ice and Et_2O were added. The product was isolated with Et_2O and purified as stated for each compound.

Methyl Octadec-cis-9-*ene*-12,14-*diynoate* (III).—Pent-1-yne (68 mg, 1 mmol) in MeOH (5 ml) containing CuCl (12 mg), NH_2·OH,HCl (120 mg), and $EtNH_2$ (0·5 ml) and the iodo-ester (X) (250 mg, 0·71 mmol) in MeOH (5 ml) were coupled. The Et_2O extract was dissolved in EtOH (10 ml) and added dropwise to $AgNO_3$ (250 mg, 1·5 mmol) stirred in EtOH (2 ml)–H_2O (2 ml)–NH_3 (35%; 0·2 ml). After 0·5 h the mixture was centrifuged and the liquid was decanted. It was extracted with Et_2O and the concentrated Et_2O extract was purified by repeated p.l.c. (petrol–Et_2O, 19 : 1, 3 elutions); the band with R_F 0·6 yielded the diyne ester (III) [5a] (67 mg, 32·5%), R_F 0·4 (petrol–CH_2Cl_2, 3 : 2), $\lambda_{max.}$ 254 and 235 nm, $\nu_{max.}$ (CS_2) 1750 (ester CO) and 735 (*cis*-CH=CH) cm^{-1}, τ (CCl_4) 9·0 (t, *J* 6 Hz, CH_3·CH_2), 8·55 (m, $[CH_2]_5$ and CH_3·CH_2), 7·65—8·15 (m, CH_2·CH_2·C≡C, CH=CH·CH_2·CH_2, and CH_2·CO_2·CH_3), 7·05 (d, *J* 5 Hz, C≡C·CH_2·CH=CH), 6·4 (s, O·CH_3), and 4·4—4·8 (m, CH_2·CH=CH·CH_2), *m/e* 288 (M^+, 2%), 257 (5), 145 (40), 131 (40), 117 (100), and 91 (60).

Methyl Octadec-cis-9-*ene*-12,14,16-*triynoate* (IV).—Penta-1,3-diyne (38 mg, 0·6 mmol) in MeOH (6 ml)–Me_2N·CHO (0·25 ml) containing $EtNH_2$ (0·5 ml), CuCl (9 mg), and NH_2·OH,HCl (50 mg) was coupled with the iodo-ester (X) (168 mg, 0·48 mmol) in MeOH (6 ml) in a closed system. P.l.c. of the Et_2O extract (petrol–Et_2O, 19 : 1; 3 elutions) gave the liquid triyne ester (IV) [5b] (61 mg, 45%), R_F 0·5, needles (from petrol at −40°), m.p. *ca.* 10°, b.p. 140—145° (block) at 2·3 × 10^{-5} mmHg, R_F 0·35 (petrol–EtOAc, 9 : 1), 0·5 (CH_2Cl_2), and 0·4 (petrol–MeOH, 97 : 3) (M^+, 284·1786. Calc. for $C_{19}H_{24}O_2$: *M*, 284·1776), $\lambda_{max.}$ (EtOH) 211 (ε 129,000) nm, $\nu_{max.}$ (CCl_4) 3020 (CH=CH), 2220 and 2030 (C≡C), 1740 (ester CO), and 1650 (CH=CH) cm^{-1}, $\nu_{max.}$ (CS_2) 710 (*cis*-CH=CH) cm^{-1}, τ (CCl_4) 8·2—8·9 (m, CH_2·$[CH_2]_5$·CH_2), 7·3—8·15 (m, CH=CH·CH_2·CH_2), 7·26 (t, *J* 7 Hz, CH_2·CH_2·CO_2Me), 6·99 (d, *J* 6 Hz, C≡C·CH_2·CH=CH), 6·37 (s, CO_2·CH_3), and 4·55 (m, *cis*-CH_2·CH=CH·CH_2), *m/e* 284 (M^+, 3%), 189 (9), 169 (27), 155 (63), 141 (100), and 128 (32).

[9-^{14}C]*Methyl Octadec*-cis-9-*ene*-12,14,16-*triynoate*, [9-^{14}C]-(IV).—[9-^{14}C]Iodo-ester [9-^{14}C]- (X) (100 μCi; 11·2 mg, 0·033 mmol) was coupled with penta-1,3-diyne (3·2 mg, 0·05 mmol) as described above and gave [9-^{14}C]- (IV) (53

[23] E. H. Pryde, D. E. Anders, H. M. Teeter, and J. C. Cowan, *J. Org. Chem.*, 1960, **25**, 618.

μCi; 3·07 mCi mmol^{-1}; 53%). Unchanged iodo-ester [9-^{14}C]- (X) (9·1 μCi) was recovered during the purification of the product.

[18-^{14}C]*Methyl Octadec*-cis-9-*ene*-12,14,16-*triynoate*, [18-^{14}C]- (IV).—[5-^{14}C]Penta-1,3-diyne (325 μCi) was coupled with the iodo-ester (X) (348 mg, 1 mmol) as described above and gave [18-^{14}C]methyl octadec-9-*cis*-ene-12,14,16-triynoate [18-^{14}C]- (IV) (154 μCi; 0·52 mCi mmol^{-1}; 30% overall yield from $^{14}CH_3I$).

Methyl Octadeca-cis-9,cis-16-*diene*-12,14-*diynoate* (XI).—*cis*-Pent-3-ene-1-yne [24] (35 mg, 0·53 mmol) in MeOH (5 ml)–Et_2O (5 ml) containing NH_2·OH,HCl (100 mg), CuCl (8 mg), and $EtNH_2$ (1 ml) was coupled with the iodo-ester (X) (150 mg, 0·43 mmol) in MeOH (10 ml) in a closed system. The concentrated Et_2O extract, an oil (110 mg), was dissolved in EtOH (10 ml) and treated with $AgNO_3$ (150 mg) in H_2O (10 ml)–EtOH (10 ml)–NH_3 (35%; 1 drop). After 0·5 h with occasional swirling the acetylide was filtered off (Celite); the filtrate was concentrated to 15 ml, and diluted with H_2O (50 ml). Et_2O extraction and p.l.c., first with petrol–Et_2O (4 : 1; 1 elution) then with petrol–Et_2O (9 : 1; 2 elutions; R_F 0·5) gave the liquid cis,cis-*dienediyne ester* (XI) (53 mg, 44%), which crystallised from petrol at −70°, m.p. below 0° (M^+, 286·1932. $C_{19}H_{26}O_2$ requires *M*, 286·1933), $\lambda_{max.}$ (EtOH) 281·5 (ε 11,750), 266 (15,000), 251·5 (10,250), 239 (5750), 227·5 (3250), and 213 (56,500) nm, $\nu_{max.}$ (CCl_4) 3025 (CH=CH), 2220 and 2180 (C≡C), and 1745 (ester CO) cm^{-1}, $\nu_{max.}$ (CS_2) 705 (*cis*-CH=CH) cm^{-1}, τ (CCl_4) 8·85—7·8 (m, [CH_2]$_6$·CH_2·CO_2Me), 8·1 (d, *J* 6·4 Hz, CH_3·CH=), 7·78 (t, *J* 7 Hz, CH_2·CH_2·CO_2Me), 6·96 (d, *J* 5·5 Hz, C≡C·CH_2·CH=CH), 6·39 (s, CO_2·CH_3), 4·56 (m, CH_2·*CH*=*CH*·CH_2), 4·54 (d, *J* 10·4 Hz, *cis*-CH_3·CH=*CH*), and 3·94 (dq, *J* 10·4 and 6·4 Hz, *cis*-CH_3·*CH*=CH), *m/e* 286 (M^+, 3%), 157 (38), 143 (98), 129 (98), 128 (100), 115 (43), 91 (42), 87 (32), and 79 (50).

Methyl Octadeca-cis-9,trans-16-*diene*-12,14-*diynoate* (XII).—*trans*-Pent-3-en-1-yne [24] (50 mg, 0·75 mmol) similarly gave the cis,trans-*dienediyne ester* (XII) (74 mg, 50%) which crystallised from petrol at −40°, m.p. below 0°, $\lambda_{max.}$ (EtOH) 282 (ε 17,000), 266·5 (22,500), 252·5 (15,250), 239·5 (7250), 228 (4000), and 213·5 (57,250) nm, $\nu_{max.}$ (CCl_4) 3030 (CH=CH), 2235 (C≡C), and 1745 (ester (CO) cm^{-1}, $\nu_{max.}$ (CS_2) 945 (*trans*-CH=CH) cm^{-1}, τ (CCl_4) 8·85—7·90 (m, [CH_2]$_6$·CH_2·CO_2Me), 8·18 (d, *J* 6·8 Hz, CH_3·CH=), 7·78 (t, *J* 7 Hz, CH_2·CH_2·CO_2·CH_3), 6·98 (d, *J* 5·5 Hz, C≡C·CH_2·CH=CH), 6·40 (s, CO_2·CH_3), 4·58 (m, CH_2·*CH*=*CH*·CH_2), 4·48 (d, *J* 15·7 Hz, *trans*-CH_3·CH=*CH*), and 3·80 (dq, *J* 15·7 and 6·8 Hz, *trans*-CH_3·*CH*=CH), *m/e* 286 (M^+, 3%), 157 (27), 143 (63), 129 (88), 128 (100), 115 (60), 91 (41), 87 (21), and 79 (48).

Methyl 18-Hydroxyoctadeca-cis-9,trans-16-*diene*-12,14-*diynoate* (XIII).—*trans*-Pent-2-en-4-yn-1-ol [19] (30 mg, 0·37 mmol) in MeOH (6 ml) containing NH_2OH,HCl (35 mg), CuCl (3 mg), and $EtNH_2$ (0·14 ml) was coupled with the iodo-ester (X) (105 mg, 0·302 mmol) in MeOH (4 ml). Repeated p.l.c. of the Et_2O extract (R_F 0·35 in petrol–Et_2O, 1 : 1; R_F 0·2 in CH_2Cl_2, 3 elutions; R_F 0·35 in $CHCl_3$) gave the liquid *hydroxy-ester* (XIII) (46 mg, 48%), b.p. 160—170° (block) at 10^{-5} mmHg (Found: C, 75·3; H, 8·75. $C_{19}H_{26}O_3$ requires C, 75·5; H, 8·7%), $\lambda_{max.}$ (EtOH) 283 (ε 15,750), 266 (19,500), 252 (13,500), 239 (4500), and 227·5 (3000) nm, $\nu_{max.}$ (CCl_4) 3620 (OH free), 3490 (OH bonded), 3010 (CH=CH), 2240 (C≡C), 1745 (ester CO), 1650 (CH=CH), and 950 (*trans*-CH=CH) cm^{-1}, τ ($CDCl_3$) 8·13br (OH), 7·8—8·9 (m, CH=CH·[CH_2]$_6$·CH_2), 7·68 (t, *J* 7 Hz, CH_2·CH_2·CO_2-Me), 6·94 (d, *J* 6 Hz, CH=CH·CH_2·C≡C), 6·33 (s, CO_2·CH_3), 5·77 (dd, *J* 5·5 and 2 Hz, CH=CH·CH_2·OH), 4·53 (m, *cis*-CH_2·*CH*=*CH*·CH_2), 4·19 (dm, *J* 16 and *ca.* 1 Hz, *trans*-*CH*=CH·CH_2·OH), and 3·59 (dt, *J* 16 and 5·5 Hz, *trans*-CH=*CH*·CH_2·OH), *m/e* 302 (M^+, 1%), 284 (2·8), 171 (24), 152 (64), 149 (24), 124 (20), 111 (37), 97 (34), 83 (57), and 74 (100).

Methyl 18-Hydroxyoctadec-cis-9-*ene*-12,14,16-*triynoate* (XIV).—Penta-2,4-diyn-1-ol [16] (52 mg, 0·64 mmol) in MeOH (7 ml)–Me_2N·CHO (0·2 ml) containing CuCl (6 mg), NH_2OH,HCl (60 mg), and $EtNH_2$ (0·3 ml) and the iodo-ester (X) (160 mg, 0·46 mmol) in MeOH (6 ml) were coupled. P.l.c. of the Et_2O extract (petrol–Et_2O, 1 : 1; 2 elutions) gave the liquid *hydroxy-ester* (XIV) (102 mg), R_F 0·5, plates (from Et_2O–hexane) (72 mg, 52%), m.p. 43° (Found: C, 76·2; H, 8·0. $C_{19}H_{24}O_3$ requires C, 76·0; H, 8·05%), $\lambda_{max.}$ (EtOH) 213 (ε 141,000) nm, $\nu_{max.}$ (CCl_4) 3660 (OH free), 3478 (OH bonded), 3020 (CH=CH), 2220 and 2100 (C≡C), and 1745 (ester CO) cm^{-1}, $\nu_{max.}$ (CS_2) 725 (*cis*-CH=CH) cm^{-1}, τ (CCl_4) 8·2—8·9 (m, CH_2·[CH_2]$_5$·CH_2), 7·55—8·2 (m, CH_2·[CH_2]$_5$·CH_2), 7·23br (OH), 6·97 (d, *J* 6 Hz, C≡C·CH_2·CH=CH), 6·35 (s, CO_2·CH_3), 5·75 (s, CH_2·OH), and 4·3—4·8 (m, *cis*-CH_2·*CH*=*CH*·CH_2), *m/e* 300 (M^+, 5%), 282 (15), 167 (70), 153 (67), 141 (45), 129 (52), 128 (100), and 127 (55).

[18-^{14}C]*Methyl 18-Hydroxyoctadec*-cis-9-*ene*-12,14,16-*triynoate*, [18-^{14}C]- (XIV).—[1-^{14}C]Penta-2,4-diyn-1-ol (245 μCi, 380 μCi mmol^{-1}) was converted into the [18-^{14}C]hydroxy-ester [18-^{14}C]- (XIV) (91 μCi; 380 μCi mmol^{-1}) as described above.

Methyl 16,16-Diethoxyhexadec-cis-9-*ene*-,12,14-*diynoate* (XVIII).—3,3-Diethoxypropyne [12] (185 mg, 1·45 mmol) in MeOH (12 ml) containing $EtNH_2$ (2 ml), NH_2OH,HCl (120 mg), and CuCl (8 mg) was coupled with the iodo-ester (X) (420 mg, 1·2 mmol) in MeOH (8 ml). Repeated p.l.c. of the Et_2O extract (R_F 0·5; petrol–Et_2O, 19 : 1; 2 elutions) gave the liquid *acetal ester* (XVIII) (243 mg, 58%), $\nu_{max.}$ (CCl_4) 3020 (CH=CH), 2280 and 2180 (C≡C), and 1750 (ester CO) cm^{-1}, $\nu_{max.}$ (CS_2) 725 (*cis*-CH=CH) cm^{-1}, τ (CCl_4) 8·82 [6H, t, *J* 7 Hz, (CH_3·CH_2·O)$_2$], 8·2—8·9 (10H, m, CH_2·[CH_2]$_5$·CH_2), 7·8—8·2 (2H, m, CH=CH·CH_2·CH_2), 7·79 (2H, t, *J* 7 Hz, CH_2·CH_2·CO_2Me), 6·92 (2H, d, *J* 7 Hz, C≡C·CH_2·CH=CH), 6·42 (3H, s, CO_2·CH_3), 6·44 [4H, m, (CH_3·CH_2·O)$_2$], 4·86 [1H, s, (EtO)$_2$CH], and 4·59 (2H, m, CH_2·*CH*=*CH*·CH_2), *m/e* 348 (M^+, 10%), 303 (98), 302 (73), 215 (35), 159 (45), 145 (38), 131 (72), 117 (53), 115 (50), 103 (71), and 91 (100).

Methyl 15-Formylpentadec-cis-9-*ene*-12,14-*diynoate* (XXI).—The acetal ester (XVIII) (348 mg, 1 mmol) was kept in Me_2CO (10 ml)–HCl (conc., 1 ml) for 0·5 h. H_2O (20 ml)–$NaHCO_3$ addition (pH *ca.* 8), ether extraction, and p.l.c. (R_F 0·35; petrol–Et_2O, 19 : 1) gave the liquid *aldehyde ester* (XXI) (249 mg, 90%), $\lambda_{max.}$ (EtOH) 288 (ε 5750), 272 (6925), 257 (4575), 244 (2475), and 232 (1825) nm, $\nu_{max.}$ (CCl_4) 3020 (CH=CH), 2730 (CHO), 2230 and 2130 (C≡C), 1745 (ester CO), and 1665 (aldehyde CO) cm^{-1}, $\nu_{max.}$ (CS_2) 740 (*cis*-CH=CH) cm^{-1}, τ (CCl_4) 7·8—8·9 (12H, m, CH=CH·[CH_2]$_6$·CH_2), 7·78 (2H, t, *J* 7 Hz, CH_2·CH_2·CO_2Me), 6·89 (2H, d, *J* 6 Hz, CH=CH·CH_2·C≡C), 6·4 (3H, s, CO_2·CH_3), 4·3—4·8 (2H, m, CH_2·*CH*=*CH*·CH_2), and 0·88 (1H, s, CHO), *m/e* 274 (7%), 215 (32), 214 (36), 157 (62), 145 (78), 85 (18), 157 (62), 145 (78), 131 (98), 117 (98), 103 (86), 91 (78), and 77 (100).

[9-^{14}C]*Methyl 15-Formylpentadec*-cis-9-*ene*-12,14-*diynoate*, [9-^{14}C]- (XXI).—3,3-Diethoxypropyne (5·5 mg, 0·0425 mmol) and the [9-^{14}C]iodo-ester [9-^{14}C]- (X) (100 μCi; 11·3

[24] J. L. H. Allan and M. C. Whiting, *J. Chem. Soc.*, 1953, 3314.

mg; 3·07 μCi mmol^{-1}) gave the [9-^{14}C]acetal ester [9-^{14}C]-(XVIII) [38·6 μCi; 39% label conversion; iodo-ester (29·3 μCi) was recovered, increasing thus the label yield to 55%]. This (10 μCi) was converted into the aldehyde ester [9-^{14}C]- (XXI) (9·1 μCi; 3·07 mCi mmol^{-1}; 91%).

Dimethyl Octadeca-trans-2,cis-9-*diene*-4,6-*diynedioate* (XV) *and Dimethyl Octadeca*-cis-2,cis-9-*diene*-4,6-*diynedioate* (XVI).—(*a*) The aldehyde ester (XXI) (137 mg, 0·5 mmol) in CH_2Cl_2 (6 ml) was added dropwise to the phosphorane (XXII) (184 mg, 0·55 mmol) stirred rapidly in CH_2Cl_2 (6 ml) at −10°. After 0·5 h at −10° the mixture was allowed to warm to 20° over 0·5 h. Transfer into Et_2O (10 ml), filtration, and p.l.c. (petrol–Et_2O, 2 : 1; 2 elutions) gave bands A (R_F 0·55) and B (R_F 0·4). On rechromatography (same solvent system), band A gave the liquid trans,-cis-*dimethyl ester* (XV) (98 mg), plates (from petrol at −70°), m.p. *ca.* 18° (Found: C, 73·0; H, 7·8. $C_{20}H_{26}O_4$ requires C, 72·7; H, 7·9%), $\lambda_{max.}$ (EtOH) 304·5 (ε 19,250), 286·5 (19,500), 271 (10,500), 257 infl (5150), 223 (35,000), and 215 (28,750) nm, $\nu_{max.}$ (CCl_4) 3025 (CH=CH), 2218 and 2120 (C≡C), 1745 (nonconj. ester CO), 1730 (conj. ester CO), 1617 (CH=CH), and 957 (*trans*-CH=CH) cm^{-1}, $\nu_{max.}$ (CS_2) 715 (*cis*-CH=CH) cm^{-1}, τ (CCl_4) 8·23—8·87 (m, CH_2·[CH_2]$_5$·CH_2·CO_2Me), 7·95 (m, CH=CH·CH_2·CH_2), 7·78 (t, *J* 7 Hz, CH_2·CH_2·CO_2Me), 6·92 (d, *J* 6 Hz, C≡C·CH_2·CH=CH), 6·4 (s, CO_2·CH_3), 6·27 (s, CH=CH·CO_2·CH_3), 4·31—4·77 (m, *cis*-CH_2·*CH*=*CH*·CH_2), 3·75 (d, *J* 17 Hz, *trans*-CH=*CH*·CO_2Me), and 3·26 (d, *J* 17 Hz, *trans*-*CH*=CH·CO_2Me), *m/e* 330 (M^+, 13%), 299 (35), 289 (100), 201 (16), 188 (15), 187 (55), 155 (50), 129 (26), and 97 (18). Band B gave the liquid cis,cis-*dimethyl ester* (XVI) (24 mg) (plates from petrol at −70°, m.p. below 0°), $\lambda_{max.}$ (EtOH) 307 (ε 14,000), 289 (15,000), 274·5 (9250), 225 (29,000), and 216·5 (25,000) nm, $\nu_{max.}$ (CCl_4) 3025 (CH=CH), 2216 and 2120 (C≡C), 1740—1720 (nonconj. and conj. ester CO), and 1608 (CH=CH) cm^{-1}, $\nu_{max.}$ (CS_2) 805 (conj. *cis*-CH=CH) and 720 (nonconj. *cis*-CH=CH) cm^{-1}, τ (CCl_4) 8·26—8·87 (10H, m, CH_2·[CH_2]$_5$·CH_2), 7·94 (2H, m, CH=CH·CH_2·CH_2), 7·78 (2H, m, CH_2·CH_2·CO_2Me), 6·91 (2H, d, *J* 5·4 Hz, C≡C·CH_2·CH=CH), 6·4 (3H, s, CH_2·CO_2·CH_3), 6·27 (3H, s, CH=CH·CO_2·CH_3), 4·41—4·71 (2H, m, *cis*-CH_2·*CH*=*CH*·CH_2), and 3·9 (2H, s, *cis*-*CH*=*CH*·CO_2Me), *m/e* 330 (M^+, 15%), 299 (55), 200 (25), 187 (100), 175 (10), 155 (30), 125 (26), and 97 (55). Combined yield of the two isomers 75%; ratio of *cis,trans* to *cis,cis* was 4·1 : 1.

(*b*) Prop-2-ynal (30 mg ,0·56 mmol) in CH_2Cl_2 (4 ml) was treated with the phosphorane (XXII) (150 mg, 0·44 mmol) in CH_2Cl_2 (4 ml). The mixture was added to CuCl (6 mg), NH_2·OH,HCl (100 mg), and $EtNH_2$ (0·4 ml) stirred in MeOH (8 ml), and to this was added dropwise the iodo-ester (X) (150 mg, 0·44 mmol) in MeOH (15 ml). Usual work-up and p.l.c. (see above) gave the slightly contaminated *trans,cis*-diester (XV) (40 mg) (n.m.r. indicated the presence of a second ester which could not be removed by p.l.c. in several solvent systems), and the *cis,cis*-diester (XVI) (24 mg). Combined yield of the two isomers was 43%; the ratio of *cis,trans* to *cis,cis* was 1·7 : 1.

[2-^{3}H]*Dimethyl Octadeca*-trans-2,cis-9-*diene*-4,6-*diynedioate*, [2-^{3}H]- (XV), *and* [2-^{3}H]*Dimethyl Octadeca*-cis-2,cis-9-*diene*-4,6-*diynedioate*, [2-^{3}H]- (XVI).—[2-^{3}H]Phosphorane (XXII) (318 μCi; 5·3 mCi mmol^{-1}; 0·06 mmol) and the aldehyde (XXI) (19·2 mg, 0·07 mmol) gave the [2-^{3}H]-*trans,cis*-diester [2-^{3}H]- (XV) (190 μCi; 5·3 mCi mmol^{-1}) and the [2-^{3}H]-*cis,cis*-diester [2-^{3}H]- (XVI) (40·3 μCi; 5·3 mCi mmol^{-1}). Combined tritium yield was 74%.

[2-^{14}C]*Dimethyl Octadeca*-trans-2,cis-9-*diene*-4,6-*diynedioate*, [2-^{14}C]- (XV), *and* [2-^{14}C]*Dimethyl Octadeca*-cis-2,cis-9-*diene*-4,6-*diynedioate*, [2-^{14}C]- (XVI).—[2-^{14}C]Phosphorane (XXII) (164·4 μCi; 1·37 mCi mmol^{-1}, 0·12 mmol) and the aldehyde (XXI) (32·9 mg, 0·12 mmol) gave the [2-^{14}C]-*trans,cis*-diester [2-^{14}C]- (XV) (111·4 μCi; 1·37 mCi mmol^{-1}) and the [2-^{14}C]-*cis,cis*-diester [2-^{14}C]- (XVI) (25·7 μCi; 1·37 mCi mmol^{-1}). Combined ^{14}C yield was 83%.

Dimethyl Octadeca-cis-9-*ene*-2,4,6-*triynedioate* (XVII).—Methyl penta-2,4-diynoate [25] (55 mg, 0·51 mmol) in MeOH (8 ml) containing CuCl (8 mg), NH_2OH,HCl (75 mg), and $EtNH_2$ (0·25 ml) and the iodo-ester (X) (139·6 mg, 0·37 mmol) in MeOH (5 ml) were coupled. P.l.c. of the Et_2O extract (petrol–Et_2O, 9 : 1; 4 elutions) yielded the liquid diester (XVII) (52·5 mg, 43%), R_F 0·4, needles (from petrol at −70°), m.p. *ca.* 0° (M^+, 328·1674. $C_{20}H_{24}O_4$ requires *M*, 328·1674), $\lambda_{max.}$ (EtOH) 328·5 (ε 3800), 307·5 (5700), 288·5 (4300), 272 (1900), 257·5 (1100), 227·5 (115,000), 218·5 (102·000), and 210infl (75,000) nm, $\nu_{max.}$ (CCl_4) 3030 (CH=CH), 2205 and 2120 (C≡C), and 1745—1720 (nonconj. and conj. ester CO) cm^{-1}, τ (CCl_4) 7·9—8·8 (m, [CH_2]$_6$·CH_2·CO_2Me), 7·77 (t, *J* 7 Hz, CH_2·CO_2Me), 6·92 (d, *J* 5 Hz, C≡C·CH_2·CH=CH), 6·40 (s, CH_2·CO_2·CH_3), 6·25 (s, C≡C·CO_2·CH_3), and 4·6 (m, CH=CH).

Methyl 15-Carbamoylpentadec-cis-9-*ene*-12,14-*diynoate* (XIX).—The iodo-ester (X) (100 mg, 0·29 mmol) in MeOH (3 ml) was added to CuCl (30 mg), NH_2·OH,HCl (15 mg), and $EtNH_2$ (1 ml) stirred in MeOH (1 ml)–Me_2N·CHO (1 ml) under N_2, and then, after 1 min, propiolamide [26] (50 mg, 0·72 mmol) in Et_2O (25 ml) was added dropwise over 15 min to the vigorously stirred mixture. Usual work-up, isolation with Et_2O, p.l.c. (Et_2O; R_F 0·5), and crystallisation (CS_2) gave plates of the *amide ester* (XIX) (20 mg, 24%), m.p. 56—58° (Found: C, 70·6; H, 8·1; N, 4·7. $C_{17}H_{23}NO_3$ requires C, 70·6; H, 8·0; N, 4·8%), $\lambda_{max.}$ (EtOH) 274 (ε 3850), 259 (5850), 245 (4950), 232 (5150), and 221infl (6900) nm, $\nu_{max.}$ (CCl_4) 3520, 3480, and 3390 (NH free), 3330 and 3170 (NH bonded), 3020 (CH=CH), 2230 and 2150 (C≡C), 1745 (ester CO), and 1680 (amide CO) cm^{-1}, $\nu_{max.}$ (CS_2) 735 (*cis*-CH=CH) cm^{-1}, τ (CS_2) 8·2—8·9 (m, CH_2·[CH_2]$_5$·CH_2), 7·8—8·2 (m, CH=CH·CH_2·CH_2), 7·89 (t, *J* 7 Hz, CH_2·CH_2·CO_2Me), 6·95 (d, *J* 7 Hz, C≡C·CH_2·CH=CH), 6·43 (s, CO_2·CH_3), 4·3—4·9 (m, CH_2·*CH*=*CH*·CH_2), and 4·0br and 3·2br (NH_2), *m/e* 289 (M^+, 7%), 272 (28), 147 (58), 146 (48), 129 (100), 117 (46), 115 (45), 103 (42), 91 (47), and 78 (84).

[9-^{14}C]*Methyl 15-Carbamoylpentadec*-cis-9-*ene*-12,14-*diynoate*, [9-^{14}C]- (XIX).—[9-^{14}C]Iodo-ester [9-^{14}C]- (X) (100 μCi; 3·07 mCi mmol^{-1}, 0·033 mmol) and propiolamide (7·5 mg, 0·108 mmol) gave, by the above procedure, the [9-^{14}C]amide [9-^{14}C]- (XIX) (12·6 μCi; 3·07 mCi mmol^{-1}). Unchanged [9-^{14}C]iodo-ester [9-^{14}C]- (X) (68 μCi) was recovered during the p.l.c. purification.

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