Conjugate, Homoconjugate, and 1,2-Additions of Acetylene Nucleophiles and their Application to Prostaglandin Synthesis

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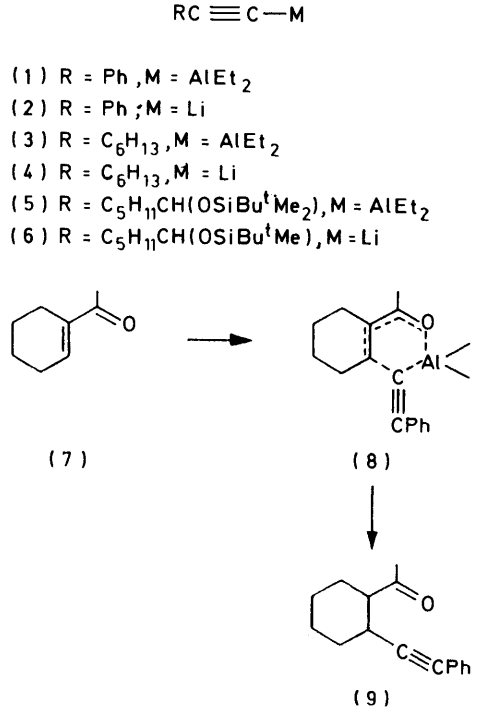
1-Acylcyclopent-1-enes (10) and (11) undergo 1,4- and 1,2-addition reactions with various alkynylalane reagents at ambient temperatures. Homoconjugate additions of alkynylalanes to *endo*-3-t-butyldimethylsilyloxytricyclo-[3.2.0.0^{2,7}]heptan-6-one (12) occur to give 7-*anti*-alkynylbicyclo[2.2.1]heptanones (24) and (25). 1-Lithioalk-1-ynes can undergo conjugate additions when the reagent is solvated with hexamethylphosphoric triamide.

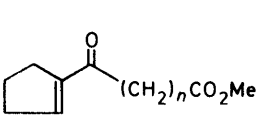
These reactions, designed to provide an approach to prostanoic acid derivatives and their intermediates, avoid the use of low temperatures for conjugate additions.

RECENTLY the scope of nucleophilic addition reactions of acetylides has been extended by the observation that diethylalkynylalane reagents, *e.g.* (1), undergo 1,4-addition reactions with α,β-unsaturated ketones, *e.g.* (7),[1] to give γ,δ alkynylketones, *e.g.* (9). It was suggested that the reaction is restricted to ketones which are able to adopt a cisoid conformation to allow delivery of the alkynyl

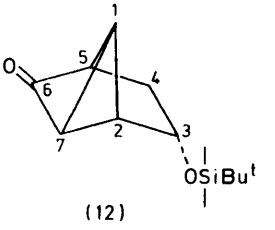


SCHEME 1

group through a six-membered transition state (8) (Scheme 1).[1] In contrast the alkali-metal acetylides, or their Grignard reagents, undergo 1,2-addition reactions to give the corresponding carbinol derivative.[2] Conjugated enones which are rigidly constrained to a transoid geometry, as in cyclohex-2-enones, are postulated to give only 1,2-adducts with diethylalkynylalanes.[1] We have studied the reactions of diethylalkynylalanes and 1-lithioalk-1-ynes with 1-acylcyclopent-1-ene derivatives (10) and (11) and *endo*-3-t-butyldimethylsilyloxytricyclo[3.2.0.0.^{2,7}]heptan-6-one (12)[3] as an approach to modified prostanoids. These reactions can be carried out at ambient temperatures whereas the homoconjugate addition reactions of the less-stable mixed organocuprate (23) with the tricycloheptanone (12) require low reaction temperatures (*e.g.* −78 °C).[3] Thus the availability of a more thermally stable Ω-side-chain reagent would simplify and therefore



(10) *n* = 4
(11) *n* = 5

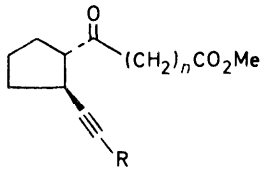


(12)

reduce the costs of the large-scale synthesis of prostanoids.

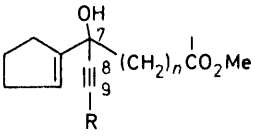
As a model reaction, conditions favouring the conjugate addition of phenylacetylide derivatives (1) and (2) to 1-(1-oxo-6-methoxycarbonylhexyl)cyclopent-1-ene (11) were examined. The alane addition reaction was also carried out with the lower homologue, 1-(1-oxo-5-methoxycarbonylpentyl)cyclopent-1-ene (10). The cyclopentene derivatives (10) and (11) were readily obtained from a Friedel-Crafts reaction involving cyclopentene[4] and 5-methoxycarbonylpentanoyl and 6-methoxycarbonylhexanoyl chloride respectively in the presence of aluminium chloride. Monomethyl adipate and pimelate were prepared by disproportionation of the dimethyl ester in the presence of its dicarboxylic acid.

Reaction of the 1-acylcyclopentene derivative (11) with diethylalanyl(phenyl)acetylene (1) in a solution of ether–hexane at 0—25 °C gave approximately 80% conversion into addition products. Separation by medium-pressure [6] chromatography showed that 1,4-

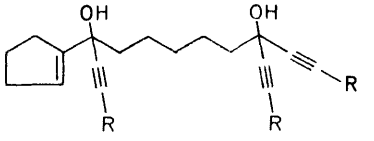


(13) $n = 5$, R = Ph
(14) $n = 5$, R = C_6H_{13}
(15) $n = 5$, R = $C_5H_{11}CH(OSiBu^tMe_2)$
(16) $n = 4$, R = Ph
(17) $n = 4$; R = $C_5H_{11}(OSiBu^tMe_2)$

and 1,2-addition to the α,β-unsaturated carbonyl system had occurred in the ratio of 1 : 1 to give the ketone (13) and the alcohol (18). The structures were elucidated by spectroscopic methods with the ^1H, ^{13}C n.m.r., and i.r. spectra being particularly diagnostic with respect to the carbonyl and olefin absorptions. Similar results were obtained from reaction of 1-acylcyclopentene (11) with the diethylalanyl derivatives of oct-1-yne (3) and 3-t-butyldimethylsilyloxyoct-1-yne (5) when 1,2- (19) and (20) and 1,4-adducts (14) and (15)

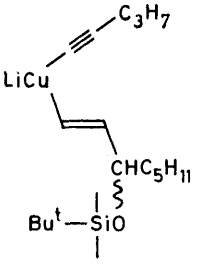


(18) $n = 5$, R = Ph
(19) $n = 5$, R = C_6H_{13}
(20) $n = 5$, R = $C_5H_{11}CH(OSiBu^tMe_2)$



(21) R = Ph
(22) R = C_6H_{13}

were again isolated in a 1 : 1 ratio. The lower homologue 1-(1-oxo-5-methoxycarbonylpentyl)cyclopent-1-ene (10) also gave similar results but only the 1,4-adducts (16) and (17) were isolated for further work.



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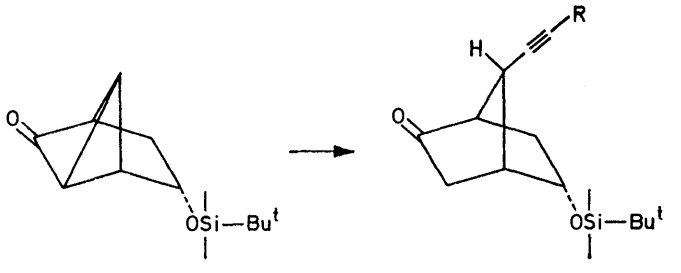

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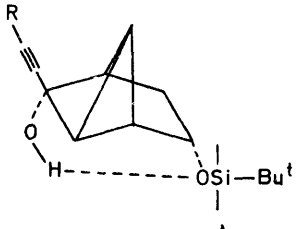
(24) R = Ph
(25) R = $C_5H_{11}CH(OSiBu^tMe_2)$



(26) R = $C_5H_{11}CH(OSiBu^tMe_2)$

Although no attempts were made to optimise the reaction conditions to favour the 1,4-addition of the alkynylalanes our results are in contrast to the observations of Hooz and Layton [1] who found that with 1-acetylcyclohexene the 1,4-adducts are the major products. With mesityl oxide, however, a mixture of 1,2- and 1,4-adducts are obtained.[1]

The reactions of 1-lithioalk-1-ynes (2) and (4) were also studied and found to give exclusively the 1,2-adducts (18) and (19) on reaction with 1-(1-oxo-6-methoxycarbonylhexyl)cyclopent-1-ene. In addition the ester functions were also attacked under the reaction conditions to give the diols (21) and (22).

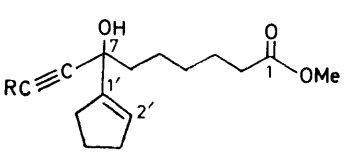
The key step in a recent synthesis of PG-$F_{2\alpha}$ involves a homoconjugate addition reaction of a mixed organocuprate reagent (23), derived from a protected 3-hydroxyoct-1-enyl unit with 3-t-butyldimethylsilyloxytricyclo[3.2.0.0.^{2,7}]heptan-6-one (12) at −78 °C.[3] We investigated reactions of alkynylalanes at room temperature to establish whether similar stereoselective ring openings could be achieved although in this case the alane reagent could not attain a six-membered transition state of the type (8) previously postulated for delivery of the alkynyl group. Reaction of the organoalane derived from phenylacetylene (1) with the tricyclic ketone (12) gave the bicyclo[2.2.1]heptanone (24) in 70% yield clearly demonstrating that homoconjugate addition occurs on the side remote from the carbonyl group. A similar reaction using the 3-t-butyldimethylsilyloxyoct-1-ynylalane (5) gave the bicyclo[2.2.1]-heptanone (25) but only in 15% yield. In contrast the reaction of (12) in diethyl ether or tetrahydrofuran with the 1-lithio-3-hydroxyoct-1-ynyl derivative (6) gave predominantly the alkynylcarbinol (26) (75%), and, the cyclopropane ring which is usually very susceptible to nucleophilic attack, was left largely intact.[3,7] However, by addition of hexamethylphosphoric triamide [7] as co-solvent homoconjugate addition could be enhanced and a 45% yield of the bicyclo[2.2.1]heptanone (25) was obtained.

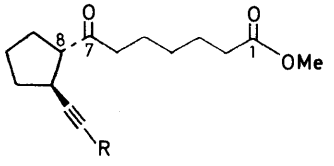
Our results demonstrate that alkynylalane reagents are useful for 1,4-addition reactions to 1-acylcyclopent-1-enes, but that 1,2-addition also occurs. The six-membered transition state postulated as a requirement for conjugate addition cannot be involved in the homoconjugate addition to the tricyclic ketone (12), and the carbonyl oxygen is too remote from the side of nucleophilic attack to be involved in a transition state for intramolecular transfer of the acetylene moiety. 1-Lithioalk-1-ynes in hexamethylphosphoric triamide [8] may be used with advantage for homoconjugate additions as an alternative to alkynylalane reagents, but the solvated lithioalk-1-yne is more reactive and ester groups may also be attacked.

EXPERIMENTAL

I.r. spectra were recorded on a Perkin-Elmer 297 grating spectrophotometer and ^{1}H n.m.r. spectra with a Perkin-Elmer R32 (90 MHz) instrument. ^{13}C N.m.r. spectra were recorded on a Varian CFT-20 instrument. Low-resolution mass spectra were determined on a A.E.I. MS 12 single focusing spectrometer and accurate mass measurements on a A.E.I. MS902S instrument. T.l.c. was carried out with Camlab ' Polygram ' pre-coated silica-gel plates. Short-path column chromatography used Merck Kieselgel G and all solvents for chromatography were distilled before use.

Diagnostic ^{13}C n.m.r. data for products from addition of diethylalkynylalane to 1-(1′-oxo-6′-methoxycarbonylhexyl)cyclopent-1-ene





R \ Atom	C-7	C-1′	C-2′	C-1	C-1	C-7	C-8
Ph	70.73 s	146.73 s	124.96 d	173.76 s	173 32 s	209.57 s	54.87 d
C_6H_{13}	70.21 s	147.12 s	125.60 d	173.60 s	173.27 s	209.57 s	54.94 d
C_5H_{11}(CHOSiBu^{t}Me$_2$)	70.51 s	146.80 s	126.21 d	173.80 s	173.48 s	209.27 s	55.19 d

Preparation of 5-Methoxycarbonylpentanoic and 6-Methoxycarbonylhexanoic Acids.—Equimolar quantities of the dicarboxylic acid and its dimethyl ester were refluxed together for 24 h. The reaction mixture was allowed to cool and shaken with cold solvent (benzene or ethyl acetate). The insoluble dicarboxylic acid was filtered off and the mono- and di-methyl esters isolated by distillation.

For 5-methoxycarbonylpentanoic acid, hexanedioic acid (36.5 g, 0.25 mol) and its dimethyl ester (43.5 g, 0.25 mol) were used and the reaction mixture worked up using ethyl acetate. Distillation gave dimethyl adipate (20 g, 0.12 mol), b.p. 106 °C at 0.15 mmHg (lit.,[9] 115 °C at 13 mmHg), and 5-methoxycarbonylpentanoic acid (35.3 g, 0.22 mol), b.p. 116 °C at 0.15 mmHg (lit.,[10] 176—180 °C at 30 mmHg). Hexanedioic acid was also recovered (20 g, 0.14 mol), m.p. 152° (lit.,[9] m.p. 153 °C).

For 6-methoxycarbonylhexanoic acid, heptanedioic acid (30.5, 0.19) and its dimethyl ester (35.8 g, 0.19 mol) were used and the reaction mixture was worked up using benzene. Distillation gave dimethyl pimelate (18 g, 0.1 mol), b.p. 78 °C at 0.15 mmHg (lit.,[9] b.p. 80 °C at 1 mmHg), and 6-methoxycarbonylhexanoic acid (30 g, 0.17 mol), b.p. 118 °C at 0.15 mmHg (lit.,[9] b.p. 160 °C at 4 mmHg). Heptanedioic acid was also recovered (15 g, 0.1 mol), m.p. 105 °C (lit.,[9] m.p. 106 °C).

Preparation of 5-Methoxycarbonylpentanoyl and 6-Methoxycarbonylhexanoyl Chlorides.—Equimolar quantities of thionyl chloride were allowed to react with either 5-methoxycarbonylpentanoic acid (65.7 g, 0.41 mol) or 6-methoxycarbonylhexanoic acid (34.8 g, 0.2 mol) by stirring for 3 h at room temperature and 3 h at 40 °C until evolution of hydrogen chloride ceased. Distillation of the pale yellow liquids gave 5-methoxycarbonylpentanoyl chloride (66.5 g, 90%), b.p. 48 °C at 0.01 mmHg (lit.,[10] 141 °C at 36 mmHg), $\nu_{max.}$ (film) 2 950, 1 800, 1 740, and 1 200 cm^{-1}; and 6-methoxycarbonylhexanoyl chloride (36.7 g, 96%) b.p. 54 °C at 0.02 mmHg, $\nu_{max.}$ (film) 2 950, 1 800, 1 740, and 1 200 cm^{-1} respectively. Both acid chlorides were used in the following Friedel-Crafts reactions without further purification.

Preparation of 1-(1′-Oxo-5′-methoxycarbonylpentyl)cyclopent-1-ene and 1-(1′-Oxo-6′-methoxycarbonylhexyl)cyclopent-1-ene.—The acid chloride (1 mol equiv.) was added to a suspension of finely divided aluminium chloride (1.5 mol equiv.) in dichloromethane (100 ml per 0.1 to 0.2 mol of reactant). The resulting complex was filtered through a sinter (No. 3) into a cooled beaker. Cyclopentene (1 mol equiv.) in dichloromethane (30 ml per 0.1 to 0.2 mol of reactant) was added dropwise, with stirring, at a rate such as to maintain the temperature at 0 °C. The mixture was kept at 0 °C for 5 min and then poured into dilute hydrochloric acid and ice. The organic layer was separated and washed with water and 10% sodium carbonate solution and then dried ($MgSO_4$). Solvent was removed and the residue distilled from anhydrous sodium carbonate.

From 6-methoxycarbonylhexanoyl chloride (34 g, 0.18 mol), aluminium chloride (35.3 g, 0.27 mol), and cyclopentene (12 g, 0.18 mol), 1-(1-oxo-6′-methoxycarbonylhexyl)cyclopent-1-ene (21.43 g, 54%), b.p. 132 °C at 0.05 mmHg was obtained: $\nu_{max.}$ (film) 2 950, 2 850, 1 740, 1 665, 1 618, and 1 170 cm^{-1}; δ_H ($CDCl_3$) 6.75 (1 H, t, olefinic), 3.66 (3 H, s, CO_2CH_3), 2.55 (4 H, m, methylene), 2.32 (4 H, m, methylene), and 1.66 (8 H, m, methylene); δ_C ($CDCl_3$), 198.46 (s, C-1), 173.57 (s, C-7), 145.62 (s, C-1), 142.31 (d, C-2), 51.000 (q, C-8′), 38.47 (t, C-3), 33.58 (t, C-3′ and 5′), 30.51 (t, C-5), 28.57 (t, C-4′), 24.52 (t, C-2′), 23.91 (t, C.6 and 22.57 (t, C-4) (Found: C, 69.95; H, 8.75%. $C_{13}H_{20}O_3$ requires C, 69.65; H, 8.9%).

From 5-methoxycarbonylpentanoyl chloride (17.85 g, 0.1 mol), aluminium chloride (19.9 g, 0.15 mol), and cyclopentene (6.8 g, 0.1 mol), 1-(1′-oxo-5′-methoxycarbonylpentyl)cyclopent-1-ene (10 g, 50%), b.p. 112 °C at 0.05 mmHg was obtained; $\nu_{max.}$ (film) 2 950, 2 850, 1 740, 1 665, 1 618, and 1 170 cm^{-1}; δ_H ($CDCl_3$) 6.75 (1 H, t, olefinic), 3.65 (3 H, s, $-CO_2CH_3$), 2.55 (4 H, m, methylene), 2.32 (4 H, m, methylene), and 1.65 (6 H, m, methylene); δ_C ($CDCl_3$) 197.98 (s, C-1′), 173.31 (s, C-6′), 145.57 (s, C-1), 142.31 (d, C-2), 50.96 (q, C-7′), 38.31 (t, C-3), 33.56 (t, C-3′ and 4′), 30.50 (t, C-5), 24.39 (t, C-2′), 23.78 (t, C-5′), and 22.56 (t, C-4) (Found: C, 68.7; H, 8.7%. $C_{12}H_{18}O$ requires C, 68.57; H, 8.57%).

Preparation of Alkynylalane Reagents: General Procedures.—To a cooled, ice–water, stirred solution of terminal acetylene (1 equiv.) in dry ether was added a solution of n-butyl-lithium (1 equiv.) in hexane under argon. After the mixture had been stirred for a further 15 min a solution of diethylaluminium chloride (1 equiv.) in hexane was added to it. A precipitate of lithium chloride was observed and the mixture was stirred for a further 15 min at room temperature.

Addition Reactions of Alkynylalane Reagents with Cyclopentenones: General Procedure.—To a stirred solution of alkynylalane (1.5 equiv.) was added a solution of cyclopentenone (1 equiv.) in dry diethyl ether at room temperature under argon. After being stirred for 3 h, the reaction mixture was poured into a mixture of ice–concentrated hydrochloric acid. The aqueous phase was separated and extracted with diethyl ether (3 × 50 ml). The organic phase and ether extracts were combined and washed with water (3 × 50 ml) and saturated aqueous sodium chloride (1 × 50 ml) and dried ($MgSO_4$). After evaporation of solvent the residue was chromatographed using short-path column chromatography.

Reaction of Diethyl(2-phenylethynyl)alane (1) with 1-(1′-Oxo-6′-methoxycarbonylhexyl)cyclopent-1-ene (11).—A solution of 1-(1′-oxo-6′-methoxycarbonylhexyl)cyclopent-1-ene (11) (2.24 g, 10 mmol) in dry ether was treated with diethyl(2-phenylethynyl)alane (1) (15 mmol). The reaction was worked up as usual and chromatography on silica gel (200 g) gave on elution with 95% toluene–ethyl acetate the following (in order of elution): methyl 14-phenyl-15,16,17,18,19,20-hexanorprostanoate (13) (0.78 g, 39%) as a colourless oil, $\nu_{max.}$ (film) 2 925, 2 850, 1 740, 1 710, 1 250, and 835 cm^{-1}; δ_H ($CDCl_3$) 7.25 (5 H, m, aromatic), 3.60 (3 H, s, CO_2CH_3), 3.4—3.0 (2 H, m, H-8 and H-12), and 3.0—1.1 (16 H, m, methylene); δ_C ($CDCl_3$) 209.57 (s, C-7), 173.32 (s, C-1), 130.98 (d, C-16 and C-20), 127.67 (d, C-17 and C-19), 127.31 (d, C-18), 123.04 (s, C-15), 89.71 (s, C-14), 82.88 (s, C-13), 54.87 (d, C-8), 50.76 (q, CO_2CH_3), 42.33 (t, C-9), 33.91 (d, C-12), 33.21 (t, C-2 and C-6), 28.31 (t, C-4), 25.38 (t, C-11), 24.28 (t, C-5), 23.43 (t, C-3), and 22.58 (t, C-10);

Accurate mass		Found	Calc.
$M^{+\cdot}$	$C_{21}H_{26}O_3^{+\cdot}$	326.1881	326.1881
$[M - OMe]^+$	$C_{20}H_{23}O_2^+$	295.1697	295.1697
$[M - (CH_2)_5CO_2Me]^+$	$C_{14}H_{13}O^+$	197.0966	197.0966

and methyl 7-cyclopent-1-enyl-7-hydroxy-9-phenylnona-8-ynoate (18) (0.75 g, 38%) as a colourless oil, $\nu_{max.}$ (film) 3 475, 2 925, 2 850, 1 740, 1 250, and 835 cm^{-1}; δ_H ($CDCl_3$) 7.30 (5 H, m, aromatic), 5.9 (1 H, t, olefinic), 3.65 (3 H, s, $-CO_2CH_3$), 2.7—1.2 (17 H, m, 16 × CH_2 and 1 × OH); δ_C ($CDCl_3$) 173.76 (s, C-1), 146.53 (s, C-1′), 131.29 (d, C-2″ and C-6″), 127.87 (d, C-3″ and C-5″), 126.40 (d, C-4″), 124.96 (d, C-2′), (s, C-1″), 91.36 (s, C-9), 84.16 (s, C-8), 70.73 (s, C-7), 51.01 (q, $-CO_2CH_3$), 40.27 (t, C-5′), 33.65 (t, C-2), 31.95 (t, C-6), 30.83 (t, C-3′), 28.86 (t, C-4), 24.57 (t, C-5), 23.82 (t, C-3), and 23.48 (t, C-4′),

Accurate mass		Found	Calc.
$M^{+\cdot}$	$C_{21}H_{26}O_3^{+\cdot}$	326.1881	326.1881
$[M - OMe]^+$	$C_{20}H_{23}O_2^+$	295.1684	295.1697
$[M - (CH_2)_5CO_2Me]^+$	$C_{14}H_{13}O^+$	197.0965	197.0966
	C_6H_5	77.0391	77.0391

Reaction of Diethyl(oct-1-ynyl)alane (3) with 1-(1′-Oxo-6′-methoxycarbonylhexyl)cyclopent-1-ene (11).—A solution of 1-(1′-oxo-6′-methoxycarbonylhexyl)cyclopent-1-ene (11) (2.24 g, 10 mmol) in dry diethyl ether (10 ml) was treated with a stirred solution of diethyl(oct-1-ynyl)alane (3) (15 mmol). The reaction was worked up in the usual manner to give, after short-column chromatography on silica gel (200 g) and elution with 95% toluene–ethyl acetate, the following (in order of elution): methyl 7-oxaprost-13-ynoate (14) (0.7 g, 36%) as a colourless oil, $\nu_{max.}$ (film) 2 925, 2 850, 1 740, 1 710, and 1 710 cm^{-1}; δ_H ($CDCl_3$) 3.65 (3 H, s, CO_2CH_3), 3.1—2.8 (2 H, m, H-8 and H-12), 2.7—1.1 (26 H, m, methylene), 0.87 (3 H, t, CH_3); δ_C ($CDCl_3$) 209.57 (s, C-7), 173.27 (a, C-1), 82.74 (s, C-14), 79.69 (s, C-13),

54.94 (d, C-8), 50.74 (q, $-CO_2CH_3$), 42.10 (t, C-9), 33.42 (t, C-2 and C-6), 30.88 (t, C-18), 28.33, 27.95, 24.96, 24.30, 23.17, 22.58, and 22.06 (overlapping signals, C-3, C-4, C-5, C-10, C-11, C-12, C-16, C-17, and C-19), 18.18 (t, C-15), and 13.42 (q, C-20); and 7-cyclopent-1-enyl-7-hydroxy-

Accurate Mass		Found	Calc.
$M^{+\cdot}$	$C_{21}H_{34}O_3^{+\cdot}$	334.2522	334.2506
$[M - OMe]^+$	$C_{20}H_{31}O_2^+$	303.2323	303.2322
$[M - (CH_2)_5CO_2Me]^+$	$C_{14}H_{21}O^+$	205.1591	205.1591

pentadeca-8-ynoate (19) (0.72 g, 25%) as a colourless oil, $\nu_{max.}$ (film) 3 475, 2 925, 2 850, 1 740, and 1 170 cm^{-1}; δ_H (*CDCl*$_3$) *5.83* (1 H, t, olefinic), 3.65 (3 H, s, CO_2CH_3), 2.32—1.90 (29 H, m, 28 × CH_2 and 1 × OH), 0.9 (3 H,t, CH_3); δ_C ($CDCl_3$) 173.60 (s, C-1), 147.12 (s, C-1′), 125.60 (d, C-2′), 84.26 (s, C-9), 82.17 (s, C-8), 70.20 (s, C-7), 50.81 (q, $-CO_2CH_3$), 40.30 (t, C-5′), 33.50, 31.76, 30.69, 28.72, 28.10, 24.43, 23.68, 23.35, and 22.10 (overlapping signals, C-2, C-3, C-4, C-5, C-6, C-11, C-12, C-13, C-14, C-3′ and C-4′), 18.20 (t, C-10), and 13.45 (q, C-15).

Accurate mass		Found	Calc.
$M^{+\cdot}$	$C_{21}H_{34}O_3^{+\cdot}$	334.2524	334.2506
$[M - OMe]^+$	$C_{20}H_{31}O_2^+$	303.2323	403.2322
$[M - (CH_2)_5CO_2Me]^+$	$C_{14}H_{21}O^+$	205.1585	205.1591

The *trans*-stereochemistry of the side-chains in product (14) was confirmed by the fact that no isomerisation occurred when (14) was boiled in methanolic sodium acetate.

Reaction of 3-*t-Butyldimethylsilyloxyoct*-1-*ynyldiethylalane* (5) *with* 1-(1′-*Oxo*-6′-*methoxycarbonylhexyl*)*cyclopent*-1-*ene* (11).—A solution of 1-(1′-oxo-6′-methoxycarbonylhexyl)-cyclopent-1-ene (11) (1.12 g, 5 mmol) in dry diethyl ether (10 ml) was treated with stirred solution of 3-t-butyldimethylsilyloxyoct-1-ynyldiethylalane (5) (7.5 mmol). The reaction was worked up in the usual manner to give, after short-column chromatography on silica gel (200 g) and elution with 95% toluene–ethyl acetate, the following (in order of elution): methyl 15-t-butyldimethylsilyloxy-methyl-7-oxoprost-13-ynoate (15) (0.67 g, 29%) as a colourless oil, $\nu_{max.}$ (film) 2 925, 2 850, 1 740, 1 710, 1 250, and 835 cm^{-1}; δ_H ($CDCl_3$) 4.27 (1 H, t, SiO·C*H*·CH_2), 3.65 (3 H, s, CO_2CH_3), 3.0—2.6 (2 H, m, H-8 and H-12), 2.5—1.0 (24 H, m, methylene), 0.9 [12 H, s, $SiC(CH_3)_3$ and 1 × CH_3], and 0.1 [6 H, s, $Si(CH_3)_2$]; δ_C ($CDCl_3$) 209.27 (s, C-7), 173.48 (s, C-1), 84.75 (s, C-14), 83.75 (s, C-13), 62.76 (d, C-15), 55.19 (d, C-8), 50.91 (q, $-CO_2CH_3$), 42.29 (t, C-9), 38.59, 33.55, 33.23, 31.14, 28.53, 25.17, 24.54, 23.11, 22.84, and 22.23 (overlapping signals, C-2, C-3, C-4, C-5, C-6, C-10, C-11, C-12, C-16, C-17, C-18, and C-19), 17.83 [s, *C*$(CH_3)_3$], 13.57 (q, C-20), −4.83 and −5.34 [overlapping q, $-Si(CH_3)_2$], and 25.51 [q, $-SiC(CH_3)_3$]; and methyl (10-t-

Accurate Mass		Found	Calc.
$M^{+\cdot}$	$C_{27}H_{48}O_4Si^{+\cdot}$	464.3316	464.3319
$[M - 57]^+$	$C_{23}H_{39}O_4Si^+$	407.2616	407.2615

butyldimethylsilyloxy-7-cyclopent-1-enyl-7-hydroxy-pentadeca-8-ynoate (20) (0.65 g, 28%) as a colourless oil, $\nu_{max.}$ (film) 3 475, 2 925, 2 850, 1 740, 1 250, and 835 cm^{-1}; δ_H ($CDCl_3$) 5.8 (1 H, t, olefinic), 4.38 (1 H, t, SiOC*H*·CH_2), 3.65 (3 H, s, CO_2CH_3), 2.5—1.1 (25 m, H, 24 × CH_2 and 1 × OH), 0.9 [12 H, s, $SiC(CH_3)_3$ and CH_3], 0.1 [6 H, s, $Si(CH_3)_2$]; δ_C ($CDCl_3$) 173.80 (s, C-1), 146.80 (s, C-1′), 126.21 (d, C-2′), 86.15 and 85.91 (2 × s, C-8 and C-9), 70.51 (s, C-7), 62.85 (d, C-10), 51.12 (q, CO_2CH_3), 40.38, 38.60, 33.80, 32.07, 31.22, 31.00 29.03, 24.75, 23.90, 23.55, and 22.33 (overlapping signals, C-2, C-3, C-4, C-5, C-6, C-11, C-12, C-13, and C-14), 18.02 [s, Si*C*$(CH_3)_3$], 13.67 (q, C-15), −4.65 and −5.14 [overlapping q, $-Si(CH_3)_2$], and 25.61 [q, $-SiC(CH_3)_3$].

Accurate Mass		Found	Calc.
$M^{+\cdot}$	$C_{27}H_{48}O_4Si^{+\cdot}$	464.3316	464.3319
$[M - 57]^+$	$C^{23}H^{29}O^4Si^+$	407.2616	407.2615

Preparation of 3-endo-*t-Butyldimethylsilyloxytricyclo*-[3.2.0.0^{2,7}]*heptan*-6-*one* (12).—To a cooled, −65 °C, stirred solution of potassium t-butoxide (1.8 g, 16 mmol) in dry tetrahydrofuran (THF) (50 ml) was added a solution of 2-*exo*-bromo-3-*endo*-t-butyldimethylsilyloxybicyclo[3.2.0]-heptan-6-one (3.2 g, 10 mmol) in dry tetrahydrofuran (25 ml) under argon. The resulting white suspension was stirred at −60 °C for 45 min. Glacial acetic acid (0.36 g, 6 mmol) in dry diethyl ether (12 ml) was added and the mixture was poured into dry diethyl ether (200 ml) containing Hyflo at −70 °C under argon. The resulting mixture was filtered through a bed of Hyflo under argon and the filtrate evaporated at room temperature under reduced pressure to give 3-*endo*-t-butyldimethylsilyloxytricyclo[3.2.0.0^{2,7}]heptan-6-one (12) as a colourless oil which became crystalline on standing (2.3 g, 100%), $\nu_{max.}$ and δ_H see lit.[3]; δ_C ($CDCl_3$) 188.96 (s, C-1), 71.29 (d, C-3), 56.88, 46.01, 41.97, 29.29 (4 × d, C-5, C-7, C-2 and C-1), 41.62 (t, C-4), 25.15 (q, Si*C*Me_3), 17.33 (s, Si*C*Me_3), and −5.40 (q, Si*Me*$_2$).

Reaction of Diethyl(2-*phenylethynyl*)*alane* (1) *with* 3-endo-*t-Butyldimethylsilyloxytricyclo*[3.2.0.0^{2,7}]*heptan*-6-*one* (12).—A solution of 3-*endo*-t-butyldimethylsilyloxy-tricyclo[3.2.0.0.^{2,7}]heptan-6-one (12) (0.95 g, 4 mmol) in dry diethyl ether (10 ml) was added to a stirred solution of 2-phenylethynylalane (1) (10 mmol) at room temperature under argon. The reaction mixture was stirred for 2 h at room temperature and poured onto ice–concentrated hydrochloric acid. The aqueous layer was extracted with diethyl ether (3 × 50 ml). The organic layer and ether extracts were combined, washed with water (3 × 50 ml) and saturated sodium chloride solution (1 × 50 ml), and dried ($MgSO_4$). After evaporation of solvent and short-column chromatography on silica gel (100 g) and elution with toluene gave 7-*anti*-(2-phenylethynyl)-5-*endo*-t-butyl-dimethylsilyloxybicyclo[2.2.1]heptan-2-one (24) as a colourless oil which solidified on standing (1.0 g, 74%), m.p. 74%), m.p. 68 °C, $\nu_{max.}$ (Nujol) 1 760, 1 250, 1 050, and 835 cm^{-1}; δ_H ($CDCl_3$) 7.35 (5 H, m, aromatic), 4.85 (1 H, m, H-5 *exo*), 3.05 (1 H, bs, H-7), 2.9—2.5 (4 H, m, H-1, H-4, H-6 *exo*, H-3 *endo*), 2.0 (1 H, dd, H-3 *exo*), 1.4 (1 H, m, H-6 *endo*) 0.9 [9 H, s, $SiC(CH_3)_3$], and 0.1 [6 H, s, $Si(CH_3)_2$] (Found: C, 74.35; H, 8.25. $C_{21}H_{28}O_2Si$ requires C, 74.12; H, 8.24%).

Reaction of 3-*t-Butyldimethyloxyoct*-1-*ynyldiethylalane* (5) *with* 3-endo-*t-Butyldimethylsilyloxytricyclo*[3.2.0.0.^{2,7}]*heptan*-6-*one* (12).—A solution of 3-*endo*-t-butyldimethylsilyloxy-tricyclo[3.2.0.0^{2,7}]heptan-6-one (12) (2.3 g, 10 mmol) in dry diethyl ether (10 ml) was added to a stirred solution of 3-t-butyldimethylsilyloxyoct-1-ynyldiethylalane (5) (15 mmol) at room temperature under argon. The reaction mixture was stirred for 2 h at room temperature and poured into ice–water. After neutralisation with dilute hydrochloric acid the aqueous layer was extracted with diethyl ether (3 × 50 ml). The organic phase and ether extracts were combined, washed with water (2 × 50 ml) and saturated sodium chloride solution (1 × 50 ml), and dried ($MgSO_4$). After evaporation of solvent and separation using short-column chromatography on silica gel (200 g) elution with 95% light petroleum (b.p. 60—80 °C)–ethyl acetate gave 7-*anti*-(3-t-butyldimethylsilyloxyoct-1-ynyl) 5-*endo*-t-butyldimethylsilyloxybicyclo[2.2.1]heptan-2-one

(25) (0.69 g, 15%) as a colourless oil, $\nu_{max.}$ (film) 2 940, 2 850, 1 760, 1 250, 1 070, and 835 cm^{-1}; δ_H ($CDCl_3$) 4.72 (1 H, m, H-5 *exo*), 4.33 (1 H, dt, H-3′), 2.82 (1 H, brs, H-7), 2.75—2.3 (4 H, m, H-1, H-4, H-6 *exo* and H-3 *endo*), 1.9 (1 H, dd, H-3 *exo*), 1.7—1.1 (9 H, m, H-6 *endo*, 2 × H-4′, 2 × H-5′, 2 × H-6′, 2 × H-7′), 0.9 (21 H, s, 2 × Bu^t, 3 × H-8′), and 0.1 [12 H, s, 2 × $Si(CH_3)_2$].

Accurate mass		Found	Calc.
$[M - 57]^+$	$C_{23}H_{41}O_3Si_2^+$	421.2598	421.2595

Reaction of 3-*t-Butyldimethylsilyloxy*-1-*lithio-oct*-1-*yne*(6) *with* 3-endo-*t-Butyldimethylsilyloxytricyclo*[3.2.0.0^{2,7}]*heptan*-6-*one* (12).—A solution of 3-*endo*-t-butyldimethylsilyloxytricyclo[3.2.0.0.^{2,7}]heptan-6-one (12) (0.43 g, 1.87 mmol) in dry diethyl ether (10 ml) was added to a stirred solution of 3-t-butyldimethylsilyloxy-1-lithio-oct-1-yne (6) (3 mmol) at room temperature under argon. The reaction mixture was stirred for 2 h at room temperature and poured onto ice–water. After neutralisation with dilute hydrochloric acid the aqueous layer was extracted with diethyl ether (3 × 50 ml). The organic layer and ether extracts were combined, washed with water (2 × 50 ml) and saturated sodium chloride solution (1 × 50 ml), and dried ($MgSO_4$). After evaporation of solvent and short-column chromatography on silica gel (200 g) elution with 95% light petroleum (b.p. 60—80 °C)–ethyl acetate gave 3-*endo*-t-butyldimethylsilyloxy-6-*endo*-hydroxy-6-*exo*-3′-t-butyldimethylsilyloxyoct-1′-ynyltricyclo[3.2.0.0^{2,7}]heptane (26) (0.67 g, 75%) as a colourless oil, $\nu_{max.}$ (film) 3 400, 1 250, 1 050, and 835 cm^{-1}; δ_H ($CDCl_3$) 4.75 (1 H, dd, H-3), 4.42 (1 H, dd, H-3), 2.80 (1 H, bs, H-5), 2.5—1.1 (14 H, m, H-1, H-2, H-4 *exo* and *endo* H-7, 8 × CH_2 and 1 × OH), 0.9 [21 H, s, 2 × SiC-$(CH_3)_3$ and CH_3], and 0.1 [12 H, s, 2 × $Si(CH_3)_2$]; δ_C ($CDCl_3$)

Accurate Mass		Found	Calc.
$[M - 57]^+$	$C_{23}H_{41}O_3Si_2^+$	421.2594	421.2595
$[M - 57 - 132]^+$	$C_{17}H_{25}O_2Si^+$	289.1615	289.1623

87.03 (s, C-2′), 81.68 (s, C-1′), 62.50 (d, C-3′), 38.81 * (t, C-4′), 24.41 (t, C-5′), 31.00 † (t, C-6′), 22.07 (t, C-7′), 13.44 (q, C-8′), 73.24 (s, C-3), 62.86 (s, C-6), 51.76, 31.73,† and 30.03 (3 × d, C-5, C-1, C-2 or C-7), 38.21 * (t, C-4), 25.28 (q, SiC*Me*$_3$), 17.46 (s, Si*C*Me$_3$), and −5.26 and −5.60 (q, Si*Me*).

Reaction of 3-*t-Butyldimethylsilyloxy*-1-*lithio-oct*-1-*yne* (6) *with* 3-endo-*t-Butyldimethylsilyloxytricyclo*[3.2.0.0^{2,7}]*heptan*-6-*one* (12) *in the Presence of Hexamethylphosphoric Triamide* (*HMPA*).—To a stirred solution of 3-t-butyldimethylsilyloxy-1-lithio-oct-1-yne (6) (5 mmol) in tetrahydrofuran (THF) (30 ml) under argon was added dry HMPA (10 ml). The resulting red solution was stirred for 15 min and to it was added a solution of 3-*endo*-t-butyldimethylsilyloxytricyclo[3.2.0.0.^{2,7}]heptan-6-one (12) (0.59 g, 2.5 mmol) in dry THF (10 ml) at room temperature. After the mixture had been stirred for a further 2 h the reaction mixture was poured onto ice–water and neutralised with dilute hydrochloric acid. The aqueous phase was extracted with diethyl ether (3 × 50 ml) and the organic phase and ether extracts were combined, washed with water (2 × 50 ml) and saturated sodium chloride (1 × 50 ml), and dried ($MgSO_4$). After evaporation of solvent short-column chromatography on silica gel (200 g) and elution with 95% light petroleum (b.p. 60—80 °C)–ethyl acetate gave 7-*anti*-(3-t-butyldimethylsilyloxyoct-1-ynyl)-5-*endo*-t-butyldimethylsilyloxybicyclo[2.2.1]heptan-2-one (25) (0.53 g, 45%) and 3-*endo*-t-butyldimethylsilyloxy-6-*endo*-hydroxy-6-*exo*-3′-t-butyldimethylsilyloxyoct-1′-ynyltricyclo[3.2.0.0.^{2,7}]heptane (26) (0.15 g, 13%). The spectral data of the above two compounds were in complete agreement with those previously isolated.

Reaction of 1-*Lithio-oct*-1-*yne* (4) *with* 1-(1′-*Oxo*-6′-*methoxycarbonylhexyl*)*cyclopent*-1-*ene* (11).—A solution of 1-(1′-oxo-6′-methoxycarbonylhexyl)cyclopent-1-ene (11) (1.65 g, 7.3 mmol) in dry THF (10 ml) was added to a stirred solution of 1-lithio-oct-1-yne (10 mmol) in dry THF (30 ml) under argon. The reaction was stirred for 3 h at room temperature and then poured onto ice–concentrated hydrochloric acid. The aqueous layer was extracted with diethyl ether (3 × 50 ml). The organic layer and ether extracts were combined, washed with water (3 × 50 ml) and saturated sodium chloride solution (1 × 50 ml), and dried ($MgSO_4$). Evaporation of solvent and short-column chromatography on silica gel (200 g) and elution with 95% toluene–ethyl acetate gave (in order of elution): 9-cyclopent-1-enyl-15-oct-1-ynyltricosa-7,16-diyne-9,15-diol (22) (0.48 g, 12.5%) as a colourless oil, $\nu_{max.}$ (film) 3 425, 2 925, 2 850, 1 450, and 725 cm^{-1}; δ_H ($CDCl_3$) 5.82 (1 H, t, olefinic), 0.9 (9 H, t, 3 × Me), and 2.5—1.2 (48 H, bm, 23 × CH_2 and 2 × OH), and 7-cyclopent-1-enyl-7-hydroxypentadeca-8-ynoate (19) (1.1 g, 44%) identical with a sample isolated previously.

Accurate mass		Found	Calc.
$[M - 18]^+$	$C_{36}H_{56}O^+$	504.4324	504.4328
$[M - 36]^+$	$C_{36}H_{54}^+$	486.4232	486.4223

Reaction of 1-*Lithio*-2-*phenylethyne* (2) *with* 1-(1′-*Oxo*-6′-*methoxycarbonylhexyl*)*cyclopent*-1-*ene* (11).—A solution of 1-(1′-oxo-6′-methoxycarbonylhexyl)cyclopent-1-ene (11) (1.12 g, 5 mmol) in dry THF (10 ml) was added to a stirred solution of 1-lithio-2-phenylethyne (2) (7.5 mmol) in dry THF (30 ml) under argon. The reaction was stirred for 3 h at room temperature and then poured onto ice–concentrated hydrochloric acid. The aqueous layer was extracted with diethyl ether (3 × 50 ml). The organic layer and ether extracts were combined, washed with water (3 × 50 ml) and saturated sodium chloride solution (1 × 50 ml), and dried ($MgSO_4$). Evaporation of solvent and short-column chromatography on silica gel (200 g) and elution with 95% toluene–ethyl acetate gave (in order of elution): 3-cyclopent-1-enyl-1,11-diphenyl-9-phenylethynylundec-1,10-diyne-3,9-diol (21) (0.42 g, 15%) as a colourless viscous oil, $\nu_{max.}$ (film) 3 400, 2 950, 2 850, 1 600, 690, and 750 cm^{-1}; δ_H ($CDCl_3$) 7.5—7.2 (15 H, m, aromatic), 5.95 (1 H, t, olefinic), 3.2—1.2 (18 H, bm, 8 × CH_2 and 2 × OH), and

Accurate mass		Found	Calc.
$[M - 18]^+$	$C_{36}H_{32}O^+$	480.2449	480.2451
$[M - 36]^+$	$C_{36}H_{30}^+$	462.2346	462.2347

7-cyclopent-1-enyl-7-hydroxy-9-phenylnona-8-ynoate (18) (0.56 g, 33%) identical with product previously isolated.

*·† These assignments may be interchanged.

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