Tetrahedron Vol. 48, No. 16, pp. 3413-3428, 1992
Printed in Great Britain

0040-4020/92 $5.00+.00

Free Radical Macrocyclisation *via* Propiolate Esters.

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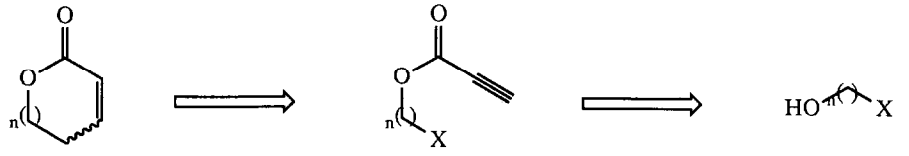
(*Received in UK* 18 *February* 1992)

Key Words: Radical; macrocyclisation; propiolate ester; macrocyclic unsaturated lactone; high dilution

Abstract: *Intramolecular free-radical addition to propiolate esters has provided a new and a stereoselective route to 14-16 membered trans- α,β-unsaturated macrocyclic lactones from their corresponding ω-iodoalkyl-propiolate esters under triphenyltin hydride/AIBN mediated conditions. Attempts to synthesise analogous 10-13 membered lactones proved unsuccessful, resulting in acyclic products derived from direct reduction at the radical centre.*

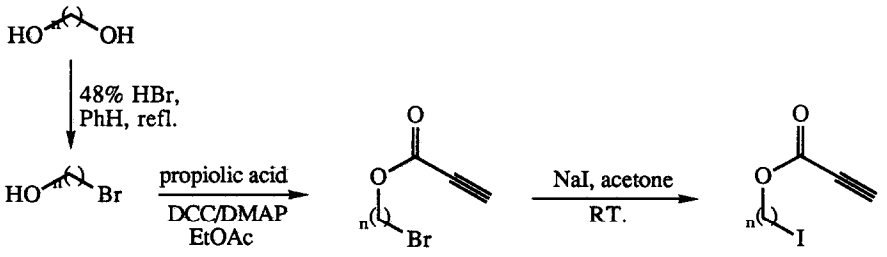
Giese's studies[1] have provided quantitative information about how the nature of alkene substituents can influence the rate of radical addition to double bonds. In particular carbon centred radicals are generally regarded as being of a nucleophilic nature and hence electron withdrawing groups on a double bond enhance the rate of addition[2]. With this in mind we reasoned that a propiolate moiety[3] (Scheme 1) should be a good radicalphile under the macrocyclisation conditions pioneered by Porter[4], and should provide a facile route to large ring α,β-unsaturated lactones[5], a structural feature common to several naturally occurring macrolides[6].



X=Br, I, SePh

Scheme 1

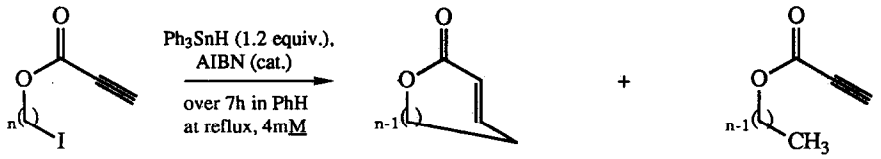
A general approach to the desired radical substrates involved esterification of a suitably functionalised ω-alcohol bearing a radical precursor (Br, I, SePh) with propiolic acid. ω-Bromoalkanols **1a-1g** of different chain lengths (n=6-12) prepared from their respective diols and 48% HBr according to the procedure of Kang[7], were esterified by slow addition of propiolic acid[8] over 4h to a dilute solution of the desired alcohol, DCC and catalytic DMAP in ethyl acetate. These bromides **2a-2g** were smoothly converted to their corresponding iodides **3a-3g** in almost quantitative yield by stirring overnight with excess sodium iodide in acetone[9] (Scheme 2).



n=6, **1a**, 85%	**2a**, 63%	**3a**, 97%
n=7, **1b**, 69%	**2b**, 60%	**3b**, 97%
n=8, **1c**, 73%	**2c**, 68%	**3c**, 98%
n=9, **1d**, 80%	**2d**, 65%	**3d**, 98%
n=10, **1e**, 85%	**2e**, 65%	**3e**, 92%
n=11, **1f**, Aldrich	**2f**, 70%	**3f**, 97%
n=12, **1g**, 88%	**2g**, 63%	**3g**, 98%

Scheme 2

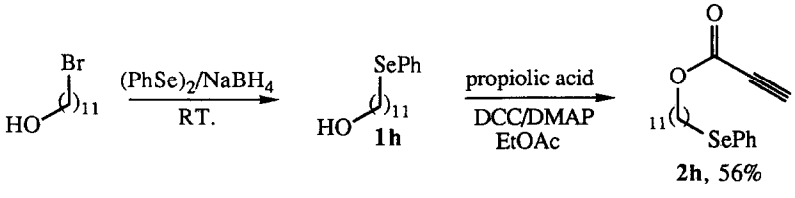
The optimum conditions that effected radical macrocyclisation involved slow addition of triphenyltin hydride (1.2 equiv.) and catalytic AIBN *via* a syringe pump over 7h to a 4mM solution of the radical substrate **3a-3g** at reflux in benzene. At low substrate concentration (10^{-1} and 10^{-2} M) intra- and intermolecular reactions are known to compete in large ring formation[10] and Porter[4] has demonstrated that radicals that propagate at or below such dilutions, e.g. 5mM, are effective in the synthesis of 12-16 membered macrocyclic enones and ketones. With the substrates **3a-3g** at concentrations >25mM we found that in addition to reduction at the radical centre, hydrostannation of the acetylenic bond[11] was a competing pathway whilst very dilute substrate concentrations (<2mM) were too low for effective propagation of the radical chain process. Slow addition[12] of triphenyltin hydride (low effective tin hydride concentration) *via* a syringe pump to the substrate (4mM) at reflux encouraged cyclisation at the expense of reduction at the radical centre and hydrostannation of the acetylenic bond, with the best yields being obtained over an addition period of 7h. A longer addition time (24h) did reduce the amount of acyclic directly reduced product but showed no improvement on the overall yield of the cyclised product. The results of macrocyclisation of substrates **3a-3g** under the optimised conditions are illustrated in Scheme 3. Prior to column chromatography, the crude product was dissolved in ether and subjected to a 10% (w/v) aqueous potassium fluoride wash[13], resulting in a white polymeric suspension of triphenyltin fluoride which was easily removed by filtration through a pad of Celite®; this aided purification of the reduced acyclic and macrocyclic products.



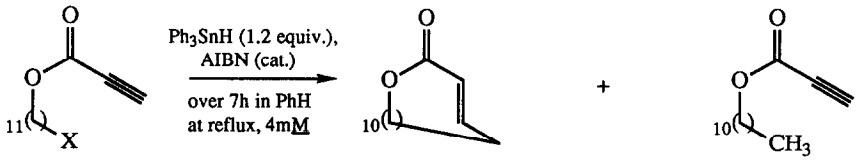
substrate	cyclised	reduced
n=6, **3a**	--	**5a**, 87%
n=7, **3b**	--	**5b**, 84%
n=8, **3c**	--	**5c**, 78%
n=9, **3d**	traces	**5d**, 76%
n=10, **3e**	**4e**, 48% (14-membered ring)	**5e**, 37%
n=11, **3f**	**4f**, 60% (15-membered ring)	**5f**, 31%
n=12, **3g**	**4g**, 55% (16-membered ring)	**5g**, 29%

Scheme 3

Large 14-, 15-, and 16-membered *trans*- unsaturated lactones were easily formed in good yield (Scheme 3). Cyclisation was both regio- and stereospecific as only the *trans*- isomer resulting from preferential *endo*- attack was observed. This can be rationalised by the alkyl radical species attacking the carbon atom with the largest LUMO coefficient resulting in a *transoid* orientation of the newly formed radical orbital which on hydrogen abstraction would give the kinetically favoured *cis*- cyclised product. Due to slow hydrogen abstraction from the tin hydride under the reaction conditions however, the cyclised radical intermediate inverts producing after reduction the thermodynamically favoured *trans*- cyclised product. The synthesis of smaller rings was found to be unsuccessful resulting in high yields of the reduced products **5a-5d**. It is worth noting that no intermolecular radical addition, as previously reported by Barth and O.-Yang[14] to yield dimers in the small ring region was observed. The choice of substrate[15] did influence the outcome of the reaction as the iodide **3f** was found to be superior to the bromide **2f**. The selenide **2h** (Scheme 4) was found to be the poorest substrate[16] as even under the optimised macrocyclisation conditions tin adducts derived from hydrostannation of the acetylenic bond was observed on ^{1}H n.m.r. analysis of the crude reaction mixture.



Scheme 4

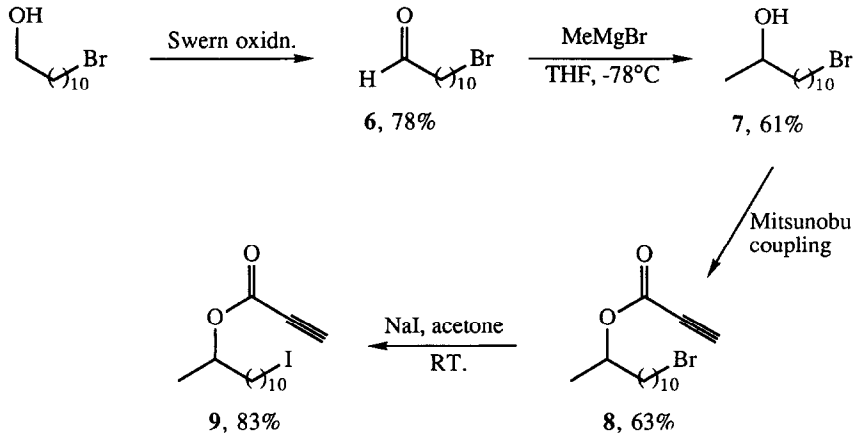


4f **5f**

substrate	cyclised	reduced
2f, X=Br	46%	40%
2h, X=SePh	41%	32%
3f, X=I	60%	31%

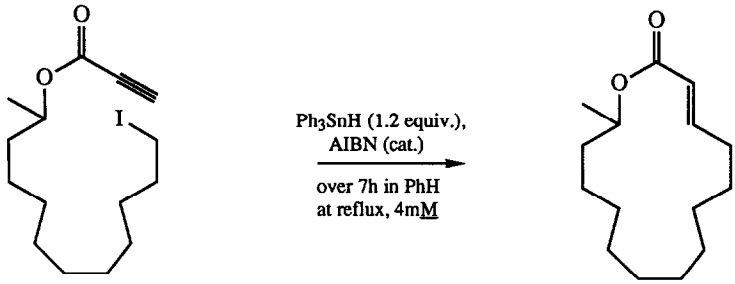
Scheme 4 (cont.)

In the synthesis of a secondary propiolate precursor **9** (Scheme 5) esterification of the secondary alcohol **7** under the DCC/DMAP mediated conditions previously used for primary propiolates was unsuccessful. This was presumably due to the slower rate of esterification with the relatively hindered secondary alcohol thus facilating polymerisation of the propiolic acid. Successful coupling was however achieved using a modified version of the Mitsunobu reaction[17]. It was found that coupling under the standard Mitsunobu conditions[18] resulted in a complex mixture from which no desired product **8** could be isolated, however dropwise addition of a mixture of the alcohol (1 equiv.) and triphenylphosphine (2 equiv.) to a solution of propiolic acid (2 equiv.) and DEAD (2 equiv.) at room temperature afforded **8** in good yield (63%). Presumably the low concentration of the activated alcohol/phosphonium intermediate formed under these reaction conditions can be driven to the propiolate ester product by the high concentration of propiolic acid present in the reaction mixture. Consequently two equivalents of acid were needed to drive the reaction to completion.



Scheme 5

Radical reaction of **9** under the standard conditions led to the *trans*- 15-membered cyclised product **10** (Scheme 6) in 63% yield with a coproduced acyclic reduced material in significantly lower yield than for the analogous formation **5f** from **3f** (on the basis of crude ^{1}H n.m.r. analysis).



9 **10**, 63%

Scheme 6

In summary radical macrocyclisation of ω-iodoalkylpropiolates has provided a new and stereoselective route to 14-16 membered *trans*- α,β-unsaturated lactones. Smaller ring lactones cannot be made in this fashion due to reduction at the radical centre without cyclisation being the dominant pathway.

EXPERIMENTAL SECTION

Infrared (IR) spectra were recorded on a Perkin-Elmer 681 spectrometer with only selected absorptions being recorded. Absorption maxima were recorded in cm^{-1}. Nuclear magnetic resonance (NMR) spectra were recorded on a Varian Gemini-200 spectrometer. Spectra were taken using $CDCl_3$ as solvent with chemical shifts quoted in parts per million (δ p.p.m.) using the residual solvent peak as an internal reference. Coupling constants (*J*) are quoted to the nearest 0.5Hz. ^{13}C spectra were recorded on a Varian Gemini-200 spectrometer, using DEPT editing where indicated; quaternary carbons were assigned from a broad band proton decoupled analysis used in combination with the DEPT programme. Mass spectra were recorded on a V.G. Micromass ZAB 1F (IBEI/EI/DCI), a V.G. 20-250 (DCI/CI) or V.G. TRIO 1 (GCMS) spectrometer, with only the major isotope peaks for selenides being assigned. Bulb to bulb distillation refers to distillation at reduced pressure using a horizontal Kugelrohr apparatus, the temperature quoted being that of the heating bath. Melting points were obtained using a Buchi 510 capillary melting point apparatus and are uncorrected. Microanalyses were performed in the Dyson Perrins Laboratory.

Flash chromatography was performed on silica gel (Merck-Kieselgel $60GF_{254}$ 230-400mesh). Preparative plate (p.l.c.) chromatography was carried out on glass plates (20cm x 20cm) coated with silica gel (Blend 41) and with a Kieselgel band and were pre-eluted with dichloromethane before use. Thin layer chromatography was performed on aluminium sheets pre-coated with Merck DC-Alufolien 60 F_{254} plates being visualised by either the quenching of u.v. fluorescence (λ_{max}=254nm) or by staining with 5% (w/v) potassium permanganate and 0.5% (w/v) potassium carbonate solution or 10% (w/v) ammonium molybdate in 2M sulphuric acid followed by heating.

All solvents were distilled before use; tetrahydrofuran (THF) was obtained dry and oxygen free by distillation from sodium/benzophenone ketyl. 'Petrol' refers to the fraction of light petroleum ether boiling between 40-60°C. Solvents were evaporated at 35°C or below on a Buchi R110 Rotavapor. The purity of triphenyltin hydride was regularly ascertained by comparison of the ^1H n.m.r. integration of the tin hydride and the aryl resonances. All other reagents were used as obtained from commercial sources.

6-Bromohexanol **1a**. The literature procedure[7] was followed using 1,6-heptanediol (11.8g, 100mmol) for 28h to afford **1a** (15.9g, 85%) as a colourless oil. $\nu_{max.}$ (thin film) 3690-3010 (br), 2938 (vs), 2860 (vs), 1460 (s), 1440 (m), 1052 (s), and 642 (s); δ_H (200MHz) 1.20-1.58 (6H, m, ($HOCH_2(C\underline{H}_2)_3C_2H_4Br$), 1.70-1.90 (2H, m, $C\underline{H}_2CH_2Br$), 3.35 (2H, t, *J* 7.0Hz, CH_2Br), and 3.53 (2H, t, *J* 7.0Hz, CH_2OH); δ_C (50.4MHz, DEPT) 62.32 (CH_2OH), 33.81 (CH_2Br), 32.54, 32.22, 27.75, 24.75 (CH_2); *m/z* (C.I., NH_3) 200 (MNH_4^+, ^{81}Br, 14%), 198 (MNH_4^+, ^{79}Br, 15), 164 (5), 162 (6), 151 (3), 134 (8), 100 (15), 98 (8), 83 (95), 82 (100), 81 (33), 72 (20), 69 (22), 67 (35), 58 (58), 55 (60).

7-Bromoheptanol **1b**. The literature procedure[7] was followed using 1,7-heptanediol (13.2g, 100mmol) for 20h to afford **1b** (13.5g, 69%) as a colourless oil. $\nu_{max.}$ (thin film) 3700-3010 (br), 2938 (vs), 2860 (vs), 1462 (m), 1440 (w), 1055 (s), and 642 (s); δ_H (200MHz) 1.15-1.60 (8H, m, ($HOCH_2(C\underline{H}_2)_4C_2H_4Br$), 1.72-1.90 (2H, m,$C\underline{H}_2CH_2Br$), 3.38 (2H, t, *J* 7.0Hz, CH_2Br), and 3.57 (2H, t, *J* 7.0Hz, $C\underline{H}_2OH$); δ_C (50.4MHz, DEPT) 62.57 (CH_2OH), 33.87 (CH_2Br), 32.54, 32.39, 28.39, 27.93, 25.41 (CH_2); *m/z* (C.I., NH_3) 214 (MNH_4^+, ^{81}Br, 76%), 212 (MNH_4^+, ^{79}Br, 76), 168 (12), 150 (22), 148 (22), 114 (11), 97 (34), 96 (51), 86 (24), 81 (42), 71 (20), 69 (40), 58 (38), 67 (18) 58 (100).

8-Bromooctanol **1c**. The literature procedure[7] was followed using 1,8-octanediol (14.6g, 100mmol) for 18h to afford **1c** (15.1g, 73%) as a colourless oil. $\nu_{max.}$ (thin film) 3700-3010 (br), 2930 (vs), 2860 (vs), 1465 (s), 1440 (s), 1246 (w), 1053 (s); δ_H (200MHz) 1.28 (8H, br, s, ($HOC_2H_4(C\underline{H}_2)_4C_2H_4Br$), 1.30-1.58 (2H, m, $C\underline{H}_2CH_2OH$), 1.70-1.88 (2H, m, $C\underline{H}_2CH_2Br$), 3.36 (2H, t, *J* 7.0Hz, CH_2Br), and 3.55 (2H, t, *J* 7.0Hz, CH_2OH); δ_C (50.4MHz, DEPT) 62.56 ($C\underline{H}_2OH$), 33.89 (CH_2Br), 32.60, 32.44, 29.05, 28.54, 27.91, 25.48 (CH_2); *m/z* (C.I., NH_3) 228 (MNH_4^+, ^{81}Br, 92%), 226 (MNH_4^+, ^{79}Br, 90), 182 (22), 164 (11), 162 (10), 148 (14), 146 (12), 137 (10), 135 (10), 82 (46), 81 (43), 72 (16), 71 (22), 69 (48), 68 (25), 67 (22), 58 (100).

9-Bromononanol **1d**. The literature procedure[7] was followed using 1,9-nonanediol (16.2g, 100mmol) for 24h to afford **1d** (17.7g, 80%) as a colourless oil. $\nu_{max.}$ (thin film) 3700-3030 (br), 2930 (vs), 2860 (vs), 1465 (m), 1440 (s), 1250 (w), 1058 (s), 724 (s); δ_H (200MHz) 1.26 (10H, br, s, ($HOC_2H_4(C\underline{H}_2)_5C_2H_4Br$), 1.35-1.54 (2H, m, $C\underline{H}_2CH_2OH$), 1.70-1.88 (2H, m, $C\underline{H}_2CH_2Br$), 3.36 (2H, t, *J* 7.0Hz, CH_2Br), and 3.55 (2H, t, *J* 7.0Hz, CH_2OH); δ_C (50.4MHz, DEPT) 62.6 ($C\underline{H}_2OH$), 33.89 (CH_2Br), 32.61, 32.48, 32.13, 29.16, 28.51, 27.95, 25.53 (CH_2); *m/z* (C.I., NH_3) 242 (MNH_4^+, ^{81}Br, 80%), 240 (MNH_4^+, ^{79}Br, 80), 196 (37), 148 (25), 137 (85), 135 (80), 114 (58), 100 (39), 95 (38), 81 (42), 69 (48), 58 (100).

10-Bromodecanol **1e**. The literature procedure[7] was followed using 1,10-decanediol (11.8g, 100mmol) for 28h to afford **1e** (15.2g, 85%) as a colourless waxy solid. $\nu_{max.}$ (thin film) 3640-3060 (br), 2925 (vs), 2855 (vs), 1462 (m), 1436 (w), 1255 (w), 1058 (s); δ_H (200MHz) 1.23 (12H, br, s, ($HOC_2H_4(C\underline{H}_2)_6C_2H_4Br$), 1.38-1.54 (2H, m, $C\underline{H}_2CH_2OH$), 1.70-1.87 (2H, m, $C\underline{H}_2CH_2Br$), 3.34 (2H, t, *J* 7.0Hz, CH_2Br), and 3.53 (2H, t, *J* 7.0Hz, CH_2OH); δ_C (50.4MHz, DEPT) 62.52 ($C\underline{H}_2OH$), 33.83 (CH_2Br), 32.64, 32.47, 32.13, 29.51, 29.22, 28.57, 27.95, 25.53 (CH_2); *m/z* (C.I., NH_3) 256 (MNH_4^+, ^{81}Br, 5%), 254 (MNH_4^+, ^{79}Br, 6%), 210 (18), 174 (20), 110 (22), 109 (32), 97 (10), 96 (36), 95 (80), 83 (22), 82 (60), 81 (100), 72 (18), 71 (31), 69 (38), 68 (56), 67 (42), 58 (92).

12-Bromododecanol **1g**. The literature procedure[7] was followed using 1,12-dodecanediol (20.2g, 100mmol) for 28h to afford **1g** (23.3g, 88%) as a white waxy solid. $\nu_{max.}$ ($CHCl_3$) 3640-3100 (br), 2922 (vs), 2858 (s), 1462 (m), 1365 (m), 1050 (br, m), 980 (m); δ_H (200MHz) 1.28 (16H, br, s, $HOC_2H_4(C\underline{H}_2)_8C_2H_4Br$), 1.50-1.68 (2H, m, $C\underline{H}_2CH_2OH$), 1.75-1.92 (2H, m, $C\underline{H}_2CH_2Br$), 3.41 (2H, t, *J* 7.0Hz, CH_2Br) and 3.64 (2H, t, *J* 7.0Hz, CH_2OH); δ_C (50.4MHz, DEPT) 63.05 ($C\underline{H}_2OH$), 34.00 (CH_2Br), 32.71, 29.42, 29.31, 28.62, 28.06, 25.61 (CH_2); *m/z* (C.I., NH_3) 284 (MNH_4^+, ^{81}Br, 94%), 282 (MNH_4^+, ^{79}Br, 100%), 240 (22), 238 (65), 220 (12), 148 (10), 137 (15), 123 (10), 114 (18), 100 (32), 95 (23), 83 (29), 82 (29), 71 (15), 69 (38), 68 (15), 58 (84) and 55 (28).

11-Phenylselenoundecanol **1h**. Sodium borohydride (1.1equiv.) was added in portions to a stirred solution of diphenyl diselenide (0.5 equiv.) in ethanol (≈4ml/mmol of diphenyl diselenide) at 0°C. To the resulting colourless solution was added a solution of 11-bromo-undecanol **1f** (2.0g, 7.96mmol) dissolved in the minimum quantity of ethanol. The mixture was stirred overnight then the ethanol removed *in vacuo*, and the residue dissolved in equal volumes of 10% (w/v) sodium carbonate and ether. The aqueous layer was thoroughly extracted with ether and the combined organic portions washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. Column chromatography (SiO_2; 5%, ether/petrol) afforded the title compound **1h** as a pale yellow solid (2.52g, 97%) (m.p. 54-55°C). $\nu_{max.}$ ($CHCl_3$) 3628 (m), 3580-3100 (br), 3078 (w), 3010 (s), 2934 (vs), 2860 (vs), 1582 (m), 1480 (s), 1440 (s), 1024 (s) and 691 (s); δ_H (200MHz) 1.28 (14H, br, s, $PhSeC_2H_4(C\underline{H}_2)_7C_2H_4OH$), 1.50-1.81 (4H, m, $PhSeCH_2C\underline{H}_2(CH_2)_7C\underline{H}_2CH_2$-OH), 2.92 (2H, t, *J* 7.5Hz, $C\underline{H}_2SePh$), 3.66 (2H, t, *J* 6.5Hz, $C\underline{H}_2OH$), 7.20-7.32 (3H, m, Ph-H), and 7.45-7.58 (2H, m, Ph-H); δ_C (50.4MHz, DEPT) 130.84 (*i*CSe), 132.45, 129.10, 126.7 (aromatic CH), 62.91 (CH_2OH), 32.64 ($\underline{C}H_2SePh$), 30.00, 29.70, 29.34, 28.94, 27.80, 25.61 (CH_2) *m/z* (C.I.,NH_3) 348 (20%), 347 (20), 346 (MNH_4^+, ^{80}Se, 96), 344 (MNH_4^+, ^{78}Se, 54), 343 (26), 342 (22), 330 (29), 329 (MH^+, ^{80}Se, 74), 328 (100), 327 (43), 326 (63), 325 (34), 324 (21), 311 (30) and 272 (27).

General procedure for the preparation of ω-bromoalkylpropiolates **2a-2g** *and ω-phenylselenoalkylpropiolate* **2h**. To a mixture of the desired ω-bromoalkanol or ω-phenylselenoalkanol (1.0 equiv.), DCC (1.05 equiv.) and DMAP (0.1 equiv.) stirring in dry ethyl acetate (≈10ml/mmol of alcohol) at 0°C under an argon atmosphere was added a solution of propiolic acid (1.1 equiv.) in dry ethyl acetate (≈2ml/mmol of acid), dropwise over 4h *via* a syringe pump. After stirring overnight at room temperature, a resulting white precipitate of DCU was filtered off, thoroughly washed with ether and the collected filtrate washed with saturated aqueous sodium bicarbonate and brine. The solvent was subsequently removed *in vacuo* to yield reddish-brown oils which were purified by flash chromatography (SiO_2; 10% ether/petrol as eluant) to afford spectroscopically and/or analytically pure propiolate esters

6-Bromohexylpropiolate **2a**. The standard procedure afforded **2a** as a colourless oil (4.08g, 63%) from 6-bromohexanol **1a** (5.0g, 27.9mmol) and propiolic acid (2.15g, 30.6mmol). (Found: C, 46.83; H, 5.80. $C_9H_{13}O_2Br$ requires C, 46.37; H, 5.62%); $\nu_{max.}$ (thin film) 3280 (s), 2940 (vs), 2864 (vs), 2120 (s), 1715 (vs), 1466 (s), 1440 (m), 1270-1210 (br, vs), 1040 (m), 970 (m) and 758 (s); δ_H (200MHz) 1.25-1.53 (4H, m, $BrC_2H_4(C\underline{H}_2)_2$), 1.53-1.72 (2H, m, $OCH_2C\underline{H}_2$), 1.72-1.89 (2H, m, $C\underline{H}_2CH_2Br$), 2.90 (1H, s, CCH), 3.33 (2H, t, *J* 7.0Hz, CH_2Br), 4.12 (2H, t, *J* 7.0Hz, CH_2O); δ_C (50.4MHz, DEPT) 152.88 (C=O), 74.73 ($C\underline{C}H$),

74.40 (CCH), 66.06 (OCH_2), 33.53, 32.35, 27.95, 27.49, 24.77 (CH_2); *m/z* (C.I., NH_3) 254 (7%), 251 (10), 252 (MNH_4^+, ^{81}Br, 100), 250 (MNH_4^+, ^{79}Br, 98), 178 (12), 163 (13), 153 (11), 107 (10), 100 (28), 87 (30), 83 (62), 82 (55), 81 (37), 70 (20), 67 (19), 58 (55), 55 (48), 53 (85).

7-Bromoheptylpropiolate **2b**. The standard procedure afforded **2b** as a colourless oil (3.75g, 60%) from 7-bromoheptanol **1b** (5.0g, 25.7mmol) and propiolic acid (1.98g, 28.3mmol). (Found: C, 48.36; H, 6.23. $C_{10}H_{15}O_2Br$ requires C, 48.60; H, 6.12%); $\nu_{max.}$ (thin film) 3280 (s), 2920 (vs), 2862 (vs), 2120 (s), 1712 (vs), 1468 (s), 1440 (m), 1270-1210 (br, vs), 975 (m), 758 (s) and 728 (m); δ_H (200MHz) 1.28 (6H, br, s, $BrC_2H_4(CH_2)_3$), 1.60-1.70 (2H, m, OCH_2CH_2), 1.70-1.88 (2H, m, CH_2CH_2Br), 2.90 (1H, s, CCH), 3.32 (2H, t, *J* 7.0Hz, CH_2Br), 4.12 (2H, t, *J* 7.0Hz, CH_2O); δ_C (50.4MHz, DEPT) 152.40 (C=O), 74.70 (CCH), 66.18 (OCH_2), 33.74, 32.44, 28.10, 27.99, 27.77, 25.40 (CH_2); *m/z* (C.I., NH_3) 268 (12%), 267 (11), 266 (MNH_4^+, ^{81}Br, 100), 264 (MNH_4^+, ^{79}Br, 93), 222 (20), 220 (19), 199 (12), 186 (22), 184 (16), 169 (12), 114 (12), 97 (23), 87 (12), 90 (12), 58 (23).

8-Bromooctylpropiolate **2c**. The standard procedure afforded **2c** as a colourless oil (4.25g, 68%) from 8-bromooctanol **1c** (5.0g, 24.0mmol) and propiolic acid (1.95g, 27.7mmol). $\nu_{max.}$ (thin film) 3280 (s), 2925 (vs), 2858 (vs), 2120 (s), 1715 (vs), 1465 (s), 1270-1210 (br, vs), 978 (m), 752 (s) and 722 (m); δ_H (200MHz) 1.28 (8H, br, s, $BrC_2H_4(CH_2)_4$), 1.53-1.72 (2H, m, OCH_2CH_2), 1.72-1.89 (2H, m, CH_2CH_2Br), 2.89 (1H, s, CCH), 3.36 (2H, t, *J* 7.0Hz, CH_2Br), 4.12 (2H, t, *J* 7.0Hz, CH_2O); δ_C (50.4MHz, DEPT) 152.94 (C=O), 74.59 (CCH), 66.28 (OCH_2), 33.83, 32.54, 28.76, 28.39, 28.07, 27.68, 25.73 (CH_2); *m/z* (C.I., NH_3) 281 (12%), 280 (MNH_4^+, ^{81}Br, 100), 278 (MNH_4^+, ^{79}Br, 98), 191 (6), 148 (5), 135 (7), 111 (22), 100 (14), 95 (10), 87 (16), 81 (19), 69 (26), 58 (22), 53 (37).

9-Bromononylpropiolate **2d**. The standard procedure afforded **2d** as a colourless oil (4.01g, 65%) from 9-bromononanol **1d** (5.0g, 22.5mmol) and propiolic acid (1.73g, 24.7mmol). (Found: C, 52.21; H, 7.13. $C_{12}H_{19}O_2Br$ requires C, 52.38; H, 6.96%); $\nu_{max.}$ (thin film) 3278 (m), 2925 (vs), 2858 (vs), 2120 (s), 1712 (vs), 1465 (s), 1230 (br, vs) and 755 (m); δ_H (200MHz) 1.33 (10H, br, s, $BrC_2H_4(CH_2)_5$), 1.55-1.78 (2H, m, OCH_2CH_2), 1.78-1.94 (2H, m, CH_2CH_2Br), 2.89 (1H, s, CCH), 3.42 (2H, t, *J* 7.0Hz, CH_2Br), 4.13 (2H, t, *J* 7.0Hz, CH_2O); δ_C (50.4MHz, DEPT) 153.00 (C=O), 74.76 (CCH), 74.43 (CCH), 66.40 (OCH_2), 33.89, 32.64, 29.09, 28.88, 28.50, 28.14, 27.96, 25.55 (CH_2); *m/z* (C.I., NH_3) 295 (12%), 294 (MNH_4^+, ^{81}Br, 100), 292 (MNH_4^+, ^{79}Br, 98), 248 (6), 135 (12), 125 (8), 100 (12), 95 (14), 83 (15), 81 (25), 69 (23), 55 (26), 53 (40).

10-Bromodecylpropiolate **2e**. The standard procedure afforded **2e** as a colourless oil (4.20g, 65%) from 10-bromodecanol **1e** (5.31g, 22.5mmol) and propiolic acid (1.73g, 24.7mmol). (Found: C, 53.79; H, 7.42. $C_{13}H_{21}O_2Br$ requires C, 53.99; H, 7.32%); $\nu_{max.}$ (thin film) 3278 (m), 2922 (vs), 2858 (s), 2120 (s), 1712 (vs), 1230 (br, vs) and 758 (m); δ_H (200MHz) 1.28 (12H, br, s, $BrC_2H_4(CH_2)_6$), 1.55-1.74 (2H, m, OCH_2CH_2), 1.74-1.92 (2H, m, CH_2CH_2Br), 2.89 (1H, s, CCH), 3.38 (2H, t, *J* 7.0Hz, CH_2Br), 4.18 (2H, t, *J* 7.0Hz, CH_2O); δ_C (50.4MHz, DEPT) 153.02 (C=O), 74.76 (CCH), 74.45 (CCH), 66.41 (OCH_2), 33.93, 32.65, 29.15, 28.94, 28.54, 28.13, 27.97, 25.56 (CH_2); *m/z* (C.I., NH_3) 309 (12%), 308 (MNH_4^+, ^{81}Br, 100), 306 (MNH_4^+, ^{79}Br, 92), 262 (11), 228 (13), 156 (6), 95 (6), 81 (8), 70 (7), 55 (22).

11-Bromoundecylpropiolate **2f**. The standard procedure afforded **2f** as a colourless oil (2.55g, 70%) from 11-bromoundecanol **1f** (3.0g, 12mmol) and propiolic acid (924mg, 13.2mmol). (Found: C, 55.58; H, 7.81. $C_{14}H_{23}O_2Br$ requires C, 55.45; H, 7.65%); $\nu_{max.}$ (thin film) 3280 (m), 2925 (vs), 2858 (s), 2120 (s), 1712 (vs), 1438 (w), 1232 (br, vs), 970 (w) and 758 (m); δ_H (200MHz) 1.28 (14H, br, s, $BrC_2H_4(C\underline{H}_2)_7$), 1.55-1.76 (2H, m, $OCH_2C\underline{H}_2$), 1.76-1.94 (2H, m, $C\underline{H}_2CH_2Br$), 2.89 (1H, s, CCH), 3.40 (2H, t, *J* 7.0Hz, CH_2Br), 4.18 (2H, t, *J* 7.0Hz, CH_2O); δ_C (50.4MHz, DEPT) 153.00 (C=O), 74.63 ($C\underline{C}H$), 66.41 (OCH_2), 33.92, 32.66, 29.23, 28.96, 28.58, 28.14, 27.99, 25.55 (CH_2); *m/z* (C.I., NH_3) 338 (6%), 322 (MNH_4^+, ^{81}Br, 21), 320 (MNH_4^+, ^{79}Br, 19), 278 (12), 255 (23), 244 (52), 242 (100), 225 (80), 170 (15), 152 (11), 109 (13), 95 (21), 81 (22), 71 (18), 58 (62).

12-Bromododecylpropiolate **2g**. The standard procedure afforded **2g** as a colourless oil (3.77g, 63%) from 12-bromododecanol **1g** (5.0g, 18.86mmol) and propiolic acid (1.45g, 20.75mmol). $\nu_{max.}$ (thin film) 3275 (s), 2924 (vs), 2858 (vs), 2120 (s), 1712 (vs), 1465 (m), 1232 (br, vs), 910 (w), 756 (s) and 735 (s); δ_H (200MHz) 1.28 (16H, br, s, $BrC_2H_4(C\underline{H}_2)_8$), 1.58-1.77 (2H, m, $OCH_2C\underline{H}_2$), 1.77-1.94 (2H, m, $C\underline{H}_2CH_2Br$), 2.89 (1H, s, CCH), 3.42 (2H, t, *J* 7.0Hz, CH_2Br), 4.20 (2H, t, *J* 7.0Hz, CH_2O); δ_C (50.4MHz, DEPT) 153.04 (C=O), 74.76 ($\underline{C}CH$), 74.40 ($C\underline{C}H$), 66.46 (OCH_2), 33.96, 32.69, 29.28, 28.98, 28.61, 28.14, 28.01, 25.57 (CH_2); *m/z* (C.I., NH_3) 337 (10%), 336 (MNH_4^+, ^{81}Br, 55), 334 (MNH_4^+, ^{79}Br, 54), 292 (7), 269 (15), 258 (53), 256 (100), 239 (75), 199 (10), 184 (13), 123 (90), 108 (12), 95 (25), 82 (18), 81 (21), 72 (21), 58 (69).

11-Phenylselenoundecylpropiolate **2h**. The standard procedure afforded **2h** as a colourless oil (982mg, 56%) from 12-phenylselenoundecanol **1h** (1.5g, 4.58mmol) and propiolic acid (353mg, 5.04mmol). (Found: C, 63.12; H, 7.43. $C_{20}H_{28}O_2Se$ requires C, 63.32; H, 7.44%); $\nu_{max.}$ (thin film) 3270 (m), 3065 (w), 2920 (vs), 2850 (s), 2120 (s), 1712 (vs), 1579 (m), 1478 (s), 1438 (s), 1230 (br, vs), 1022 (m), 755 (s), 735 (s) and 690 (s); δ_H (200MHz) 1.28 (14H, br, s, $PhSeC_2H_4(C\underline{H}_2)_7$), 1.54-1.81 (4H, m, $PhSeCH_2C\underline{H}_2(CH_2)_7C\underline{H}_2$), 2.89 (1H, s, CCH), 2.93 (2H, t, *J* 7.0Hz, $C\underline{H}_2SePh$), 4.21 (2H, t, *J* 7.0Hz, CH_2O), 7.20-7.32 (3H, m, Ph-H), 7.44-7.55 (2H, m, Ph-H); δ_C (50.4MHz, DEPT) 153.00 (C=O), 130.88 (*i*CSe), 132.44, 129.10, 126.67 (aromatic CH), 74.80 ($\underline{C}CH$), 74.56 ($C\underline{C}H$), 66.41 (OCH_2), 29.99, 29.67, 29.30, 28.83, 28.17, 27.74, 25.60 (CH_2); *m/z* (C.I., NH_3) 398 (MNH_4^+, ^{80}Se, 85%), 396 (MNH_4^+, ^{78}Se, 42), 381 (MH^+, ^{80}Se, 100), 379 (MH^+, ^{78}Se, 63), 311 (32), 226 (10), 157 (17), 109 (7), 97 (15), 91 (12), 83 (13), 78 (16), 69 (16).

General procedure for the preparation of ω-Iodoalkylpropiolates **3a-3g**. Sodium iodide (3 equiv.) dissolved in the minimum quantity of acetone (≈10ml) was added to a stirred solution of bromide (1 equiv.) in acetone (≈1ml/mmol) at room temperature. The slightly yellow solution was stirred at ambient temperature overnight, then filtered into ether (50ml) and washed with aqueous sodium thiosulphate (0.5M, 15ml), brine, dried ($MgSO_4$) and filtered. Removal of solvent *in vacuo* gave yellow oils which were purified by column chromatography (SiO_2; 20% ether/petrol).

6-Iodohexylpropiolate **3a**. The standard procedure afforded **3a** as a colourless oil (4.08g, 97%) from 6-bromohexylpropiolate **2a** (3.5g, 15.1mmol) and sodium iodide (6.81g, 45.4mmol). (Found: C, 38.41; H, 4.96. $C_9H_{13}O_2I$ requires C, 38.59; H, 4.68%); $\nu_{max.}$ (thin film) 3275 (s), 2930 (vs), 2859 (s), 2120 (vs),

1712 (vs), 1462 (s), 1230 (br, vs), 1170 (m), 910 (m), 752 (s) and 732 (s); δ_H (200MHz) 1.30-1.52 (4H, m, $IC_2H_4(C\underline{H}_2)_2$), 1.58-1.75 (2H, m, $OCH_2C\underline{H}_2$), 1.75-1.90 (2H, m, $C\underline{H}_2CH_2I$), 2.90 (1H, s, CCH), 3.17 (2H, t, *J* 7.0Hz, CH_2I), 4.18 (2H, t, *J* 7.0Hz, CH_2O); δ_C (50.4MHz, DEPT) 152.94 (C=O), 74.65 (C$\underline{C}$H), 66.10 (OCH_2), 33.09, 29.85, 27.96, 24.61 (CH_2), 6.67 (CH_2I); *m/z* (C.I., NH_3) 300 (2%), 299 (14), 298 (MNH_4^+, 100), 211 (41), 153 (15), 100 (20), 83 (43), 80 (5), 70 (6), 59 (13), 53 (35).

7-Iodoheptylpropiolate **3b**. The standard procedure afforded **3b** as a colourless oil (4.01g, 97%) from 7-bromoheptylpropiolate **2b** (3.5g, 13.7mmol) and sodium iodide (6.16g, 41.1mmol). (Found: C, 40.76; H, 5.40. $C_{10}H_{15}O_2I$ requires C, 40.84; H, 5.14%); $\nu_{max.}$ (thin film) 3275 (s), 2920 (vs), 2858 (s), 2120 (s), 1712 (vs), 1462 (m), 1232 (br, vs), 1168 (m), 970 (m) and 752 (s); δ_H (200MHz) 1.35 (6H, br, s, $IC_2H_4(C\underline{H}_2)_3$), 1.58-1.75 (2H, m, $OCH_2C\underline{H}_2$), 1.75-1.89 (2H, m, $C\underline{H}_2CH_2I$), 2.90 (1H, s, CCH), 3.17 (2H, t, *J* 7.0Hz, CH_2I), 4.17 (2H, t, *J* 7.0Hz, CH_2O); δ_C (50.4MHz, DEPT) 152.94 (C=O), 74.55 (C$\underline{C}$H), 66.24 (OCH_2), 33.17, 30.14, 28.03, 27.92, 25.41 (CH_2), 6.92 (CH_2I); *m/z* (C.I., NH_3) 314 (2%), 313 (17), 312 (MNH_4^+, 100), 225 (18), 167 (7), 97 (16), 55 (7), 63 (14).

8-Iodooctylpropiolate **3c**. The standard procedure afforded **3c** as a colourless oil (4.09g, 98%) from 8-bromooctylpropiolate **2c** (3.5g, 13.46mmol) and sodium iodide (6.05g, 40.88mmol). (Found: C, 42.94; H, 5.77. $C_{11}H_{17}O_2I$ requires C, 42.87; H, 5.56%); $\nu_{max.}$ (thin film) 3280 (s), 2925 (vs), 2858 (vs), 2120 (s), 1712 (vs), 1465 (m), 1230 (br, vs), 1165 (m) and 752 (s); δ_H (200MHz) 1.32 (8H, br, s, $IC_2H_4(C\underline{H}_2)_4$), 1.57-1.75 (2H, m, $OCH_2C\underline{H}_2$), 1.75-1.89 (2H, m, $C\underline{H}_2CH_2I$), 2.89 (1H, s, CCH), 3.17 (2H, t, *J* 7.0Hz, CH_2I), 4.17 (2H, t, *J* 7.0Hz, CH_2O); δ_C (50.4MHz, DEPT) 152.96 (C=O), 74.73 (C$\underline{C}$H), 74.54 (C$\underline{C}$H), 66.32 (OCH_2), 33.27, 30.19, 28.76, 28.18, 28.09, 25.48 (CH_2), 7.05 (CH_2I); *m/z* (C.I., NH_3) 328 (3%), 327 (21), 326 (MNH_4^+, 100), 239 (7), 181 (7), 111 (9), 69 (12), 58 (13), 53 (14).

9-Iodononylpropiolate **3d**. The standard procedure afforded **3d** as a colourless oil (4.04g, 98%) from 9-bromononylpropiolate **2d** (3.5g, 12.76mmol) and sodium iodide (5.74g, 38.28mmol). (Found: C, 45.05; H, 6.27. $C_{12}H_{19}O_2I$ requires C, 44.74; H, 5.94%); $\nu_{max.}$ (thin film) 3278 (m), 2922 (vs), 2858 (vs), 2120 (s), 1712 (vs), 1230 (br, vs) and 752 (m); δ_H (200MHz) 1.31 (10H, br, s, $IC_2H_4(C\underline{H}_2)_5$), 1.58-1.75 (2H, m, $OCH_2C\underline{H}_2$), 1.75-1.91 (2H, m, $C\underline{H}_2CH_2I$), 2.89 (1H, s, CCH), 3.18 (2H, t, *J* 7.0Hz, CH_2I), 4.18 (2H, t, *J* 7.0Hz, CH_2O); δ_C (50.4MHz, DEPT) 152.98 (C=O), 74.76 (C$\underline{C}$H), 74.47 (C$\underline{C}$H), 66.36 (OCH_2), 33.40, 30.28, 29.05, 28.87, 28.24, 28.11, 25.52 (CH_2), 7.10 (CH_2I); *m/z* (C.I., NH_3) 341 (17%), 340 (MNH_4^+, 100), 253 (16), 225 (7), 125 (13), 83 (12), 69 (14), 58 (13), 53 (25).

10-Iododecylpropiolate **3e**. The standard procedure afforded **3e** as a colourless oil (4.80g, 92%) from 10-bromodecylpropiolate **2e** (4.13g, 14.3mmol) and sodium iodide (6.45g, 43mmol). (Found: C, 46.22; H, 6.37. $C_{13}H_{21}O_2I$ requires C, 46.44; H, 6.30%); $\nu_{max.}$ (thin film) 3280 (s), 2925 (vs), 2858 (s), 2120 (s), 1715 (vs), 1465 (m), 1230 (br, vs) and 758 (m); δ_H (200MHz) 1.30 (12H, br, s, $IC_2H_4(C\underline{H}_2)_6$), 1.58-1.78 (2H, m, $OCH_2C\underline{H}_2$), 1.78-1.92 (2H, m, $C\underline{H}_2CH_2I$), 2.88 (1H, s, CCH), 3.19 (2H, t, *J* 7.0Hz, CH_2I), 4.19 (2H, t, *J* 7.0Hz, CH_2O); δ_C (50.4MHz, DEPT) 152.99 (C=O), 74.76 (C$\underline{C}$H), 74.50 (C$\underline{C}$H), 66.39 (OCH_2), 33.37, 30.32, 29.14, 28.94, 28.32, 28.13, 25.56 (CH_2), 7.20 (CH_2I); *m/z* (C.I., NH_3) 355 (15%), 354 (MNH_4^+, 100), 228 (22), 170 (11), 156 (10), 116 (10), 58 (12).

11-Iodoundecylpropiolate **3f**. The standard procedure afforded **3f** as a colourless oil (2.59g, 97%) from 11-bromoundecylpropiolate **2f** (2.3g, 7.62mmol) and sodium iodide (3.43g, 22.86mmol). (Found: C, 48.15; H, 7.06. $C_{14}H_{23}O_2I$ requires C, 48.01; H, 6.62%); $\nu_{max.}$ (thin film) 3275 (m), 2922 (vs), 2850 (s), 2120 (s), 1712 (vs), 1463 (m), 1230 (br, vs) and 751 (m); δ_H (200MHz) 1.28 (14H, br, s, $IC_2H_4(C\underline{H}_2)_7$), 1.57-1.76 (2H, m, $OCH_2C\underline{H}_2$), 1.76-1.91 (2H, m, $C\underline{H}_2CH_2I$), 2.88 (1H, s, CCH), 3.18 (2H, t, *J* 7.0Hz, CH_2I), 4.18 (2H, t, *J* 7.0Hz, CH_2O); δ_C (50.4MHz, DEPT) 153.00 (C=O), 74.77 (C$\underline{C}$H), 74.40 (C$\underline{C}$H), 66.43 (OCH_2), 33.39, 30.32, 29.22, 28.97, 28.36, 28.14, 25.56 (CH_2), 7.17 (CH_2I); *m/z* (C.I., NH_3) 369 (22%), 368 (MNH_4^+, 100), 281 (17), 239 (9), 223 (8), 153 (6), 111 (6), 97 (19), 83 (11), 58 (11), 53 (20).

12-Iododecylpropiolate **3g**. The standard procedure afforded **3g** as a colourless oil (3.92g, 98%) from 12-bromododecylpropiolate **2g** (3.5g, 11mmol) and sodium iodide (4.88g, 33mmol). (Found: C, 49.14; H, 6.68. $C_{15}H_{25}O_2I$ requires C, 49.46; H, 6.92%); $\nu_{max.}$ (thin film) 3280 (w), 2925 (vs), 2858 (vs), 2120 (s), 1715 (vs), 1465 (m), 1230 (br, vs) and 752 (m); δ_H (200MHz) 1.28 (16H, br, s, $IC_2H_4(C\underline{H}_2)_8$), 1.58-1.72 (2H, m, $OCH_2C\underline{H}_2$), 1.72-1.89 (2H, m, $C\underline{H}_2CH_2I$), 2.88 (1H, s, CCH), 3.17 (2H, t, *J* 7.0Hz, CH_2I), 4.18 (2H, t, *J* 7.0Hz, CH_2O); δ_C (50.4MHz, DEPT) 153.01 (C=O), 74.76 (C$\underline{C}$H), 74.40 (C$\underline{C}$H), 66.43 (OCH_2), 33.41, 30.35, 29.30, 28.98, 28.36, 28.14, 25.56 (CH_2), 7.18 (CH_2I); *m/z* (C.I., NH_3) 383 (22%), 382 (MNH_4^+, 100), 295 (15), 237 (8), 111 (6), 97 (6), 53 (6).

Radical reactions on propiolates **3a-3g** and **9**. To a degassed solution of the desired propiolate substrate (1.0 equiv.) in benzene (4m$\underline{M}$ solution) at reflux under argon was added slowly, *via* a syringe pump over 7h, a mixture of triphenyltin hydride (1.2 equiv.) and AIBN (0.1 equiv.) in benzene. The mixture was heated at reflux for a further 14h, then cooled, and the solvent removed *in vacuo*. The residue formed was dissolved in ether (20ml) and treated with 10% (w/v) aqueous potassium fluoride (20ml), then stirred vigorously at room temperature over 1h. The white suspension formed was filtered through Celite®, the organics washed with brine, dried ($MgSO_4$) and solvent removed *in vacuo* to yield viscous yellow oils. Flash chromatography (SiO_2; 10% ether/petrol as eluant) afforded cyclised and reduced products which at this stage were contaminated with small amounts of stannane impurities. Subsequent purification by p.l.c. (SiO_2; 5% ether/petrol) yielded spectroscopically and/or analytically pure products as colourless oils.

Attempted radical cyclisation of 6-Iodohexylpropiolate **3a**. The standard procedure using **3a** (210mg, 0.75mmol) and triphenyltin hydride (316mg, 0.9mmol) afforded the reduced product *n-hexylpropiolate* **5a** (100mg, 87%) as a colourless oil. $\nu_{max.}$ (thin film) 3280 (m), 2960 (vs), 2930 (vs), 2860 (s), 2120 (s), 1715 (vs), 1465 (m), 1230 (br, vs) and 755 (m); δ_H (200MHz) 0.90 (3H, ca. t, *J* 6.0Hz, CH_3), 1.15-1.48 (6H, br, s, $OC_2H_4(C\underline{H}_2)_3$), 1.58-1.88 (2H, m, $OCH_2C\underline{H}_2$), 2.88 (1H, s, CCH), 4.20 (2H, t, *J* 7.0Hz, OCH_2); δ_C (50.4MHz) 153.10 (C=O), 74.37 (C$\underline{C}$H), 66.46 (OCH_2), 31.19, 28.11, 25.26, 22.32 (CH_2), 13.78 (CH_3); *m/z* (C.I., NH_3) 174 (10%), 173 (18), 172 (MNH_4^+, 100), 111 (6), 100 (15), 97 (5), 87 (18), 83 (19), 81 (8), 70 (17) and 58 (20).

Attempted radical cyclisation of 7-Iodoheptylpropiolate **3b**. The standard procedure using **3b** (220mg, 0.75mmol) and triphenyltin hydride (316mg, 0.9mmol) afforded the reduced product *n-heptylpropiolate* **5b** (105mg, 84%) as a colourless oil. $\nu_{max.}$ (thin film) 3280 (m), 2960 (vs), 2930 (vs), 2860 (s), 2120 (s), 1715

(vs), 1462 (m), 1230 (br, vs) and 755 (m); δ_H (200MHz) 0.89 (3H, ca. t, *J* 6.0Hz, CH_3), 1.00-1.48 (8H, br, s, $OC_2H_4(CH_2)_4$), 1.50-1.75 (2H, m, OCH_2CH_2), 2.89 (1H, s, CCH), 4.20 (2H, t, *J* 7.0Hz, OCH_2); δ_C (50.4MHz) 153.02 (C=O), 74.76 (CCH), 74.38 (CCH), 66.46 (OCH_2), 31.50, 28.65, 28.14, 25.54, 22.38 (CH_2), 13.84 (CH_3); *m/z* (C.I., NH_3) 187 (15%), 186 (MNH_4^+, 100), 111 (6), 97 (10), 87 (15), 70 (15), 58 (20) and 53 (23).

Attempted radical cyclisation of 8-Iodooctylpropiolate **3c**. The standard procedure using **3c** (231mg, 0.75mmol) and triphenyltin hydride (316mg, 0.9mmol) afforded the reduced product *n-octylpropiolate* **5c** (106mg, 78%) as a colourless oil. (Found: C, 72.20; H, 9.75. $C_{11}H_{18}O_2$ requires C, 72.49; H, 9.95%); $\nu_{max.}$ (thin film) 3280 (w), 2958 (s), 2925 (s), 2858 (s), 2120 (s), 1715 (vs), 1465 (m), 1230 (br, vs) and 758 (m); δ_H (200MHz) 0.88 (3H, ca. t, *J* 7.0Hz, CH_3), 1.28 (10H, br, s, $OC_2H_4(CH_2)_5$), 1.56-1.75 (2H, m, OCH_2CH_2), 2.89 (1H, s, CCH), 4.19 (2H, t, *J* 7.0Hz, OCH_2); δ_C (50.4MHz) 153.02 (C=O), 74.76 (CCH), 74.40 (CCH), 66.44 (OCH_2), 31.40, 28.97, 28.14, 25.58, 22.45 (CH_2), 13.87 (CH_3); *m/z* (C.I., NH_3) 202 (6%), 201 (12), 200 (MNH_4^+, 100), 87 (10), 84 (10), 83 (10), 70 (15), 69 (14), 58 (10), 56 (16), 55 (15) and 53 (12).

Attempted radical cyclisation of 9-Iodononylpropiolate **3d**. The standard procedure using **3d** (242mg, 0.75mmol) and triphenyltin hydride (316mg, 0.9mmol) afforded the reduced material *n-nonylpropiolate* **5d** (112mg, 76%) as a colourless oil. $\nu_{max.}$ (thin film) 3280 (w), 2958 (s), 2922 (s), 2856 (s), 2120 (s), 1716 (vs), 1468 (m), 1230 (br, vs) and 755 (m); δ_H (200MHz) 0.89 (3H, ca. t, *J* 7.0Hz, CH_3), 1.28 (12H, br, s, $OC_2H_4(CH_2)_6$), 1.58-1.77 (2H, m, OCH_2CH_2), 2.89 (1H, CCH), 4.19 (2H, t, *J* 7.0Hz, OCH_2); δ_C (50.4MHz) 153.02 (C=O), 74.77 (CCH), 74.39 (CCH), 66.46 (OCH_2), 31.70, 29.27, 29.03, 28.03, 28.14, 25.59, 22.49 (CH_2), 13.91 (CH_3); *m/z* (C.I., NH_3) 229 (16%), 216 (24), 214 (MNH_4^+, 100), 204 (7), 160 (8), 109 (5), 95 (5), 87 (5), 80 (50), 70 (9) and 58 (24).

E-Tridec-2-ene-13-olide **4e**. The standard procedure using 10-iododecylpropiolate **3e** (251mg, 0.75mmol) and triphenyltin hydride (316mg, 0.9mmol) afforded the title compound **4e** (75mg, 48%), and reduced material *n-decylpropiolate* **5e** (59mg, 37%) as colourless oils. Data for **4e** (Found: C, 74.05; H, 10.68. $C_{13}H_{22}O_2$ requires C, 74.24; H, 10.54%); $\nu_{max.}$ (thin film) 3026 (m), 2933 (vs), 2859 (s), 1708 (vs), 1263 (vs), 1098 (br, m), 1015 (br, m), 790 (s) and 726 (s); δ_H (200MHz) 1.15-1.75 (16H, m, C5-C12-$(H_2)_8$), 2.20-2.32 (2H, m, C4-H_2), 4.25 (2H, t, *J* 7.0Hz, C13-H_2), 5.83 (1H, d, *J* 16.0Hz, =C2-H), 7.03 (1H, dt, *J* 16.0, 7.5Hz, =C3-H); δ_C (50.4MHz) 166.85 (C=O), 150.99, 122.27 (COCH=CH), 64.25 (OCH_2), 26.79, 26.70, 26.53, 26.23, 25.81, 24.90 (CH_2); *m/z* (C.I., NH_3) 228 (MNH_4^+, 16%), 212 (15), 211 (MH^+, 100), 95 (6), 81 (12), 68 (10) and 55 (7). Data for **5e**: (Found: C, 74.49; H, 10.60. $C_{13}H_{22}O_2$ requires C, 74.24; H, 10.54%); $\nu_{max.}$ (thin film) 3280 (w), 2958 (s), 2920 (s), 2858 (s), 2120 (s), 1715 (vs), 1465 (m), 1230 (br, vs), and 756 (m); δ_H (200MHz) 0.86 (3H, ca. t, *J* 7.0Hz, CH_3), 1.25 (14H, br, s, $OC_2H_4(CH_2)_7$), 1.56-1.75 (2H, m, OCH_2CH_2), 2.88 (1H, s, CCH), 4.17 (2H, t, *J* 7.0Hz, OCH_2); δ_C (50.4MHz) 152.98 (C=O), 74.74 (CCH), 74.40 (CCH), 66.39 (OCH_2), 31.71, 29.31, 29.12, 28.99, 28.13, 25.56, 22.49 (CH_2), 13.87 (CH_3); *m/z* (C.I., NH_3) 230 (30%), 228 (MNH_4^+, 100), 218 (8), 156 (6), 95 (7), 81 (7), 70 (8) and 58 (23).

E-Tetradec-2-ene-14-olide **4f**. The standard procedure using 11-iodoundecylpropiolate **3f** (262mg, 0.75mmol) and triphenyltin hydride (316mg, 0.9mmol) afforded the title compound **4f** (100mg, 60%), and reduced material *n-undecylpropiolate* **5f** (52mg, 31%) as colourless oils. Data for **4f**: (Found: C, 74.87; H, 10.78. $C_{14}H_{24}O_2$ requires C, 74.95; H, 10.78%); $\nu_{max.}$ (thin film) 2922 (vs), 2850 (s), 1718 (vs), 1650 (w), 1250 (br, s), 1158 (m), 1040 (m), 990 (m) and 726 (s); δ_H (200MHz) 1.20-1.75 (18H, m, C5-C13-$(H_2)_9$), 2.20-2.32 (2H, m, C4-H_2), 4.25 (2H, t, *J* 7.0Hz, C14-H_2), 5.82 (1H, d, *J* 16.0Hz, =C2-H), 6.98 (1H, dt, *J* 16.0, 7.5Hz, =C3-H); δ_C (50.4MHz) 166.80 (C=O), 150.97, 122.26 (CO<u>C</u>H=<u>C</u>H), 64.25 (OCH_2), 32.11, 31.92, 27.88, 27.10, 26.79, 26.40, 26.23, 25.81, 24.91 (CH_2); *m/z* (C.I., NH_3) 243 (5%), 242 (MNH_4^+, 32), 226 (15), 225 (MH^+, 100); Data for **5f**: (Found: C, 74.82; H, 11.07. $C_{14}H_{24}O_2$ requires C, 74.95; H, 10.78%); $\nu_{max.}$ (thin film) 3280 (m), 2950 (s), 2920 (vs), 2850 (s), 2120 (s), 1715 (vs), 1465 (m), 1230 (br, vs), and 755 (m); δ_H (200MHz) 0.86 (3H, <u>ca</u>. t, *J* 7.0Hz, CH_3), 1.24 (16H, br, s, $OC_2H_4(C\underline{H}_2)_8$), 1.55-1.73 (2H, m, $OCH_2C\underline{H}_2$), 2.88 (1H, s, CCH), 4.16 (2H, t, *J* 7.0Hz, OCH_2); δ_C (50.4MHz) 152.94 (C=O), 74.73 (<u>C</u>CH), 74.37 (C<u>C</u>H), 66.35 (OCH_2), 31.73, 29.39, 29.28, 29.15, 28.98, 28.13, 25.56, 22.47 (CH_2), 13.87 (CH_3); *m/z* (C.I., NH_3) 244 (22%), 242 (MNH_4^+, 100), 227 (2), 170 (2), 125(2), 109 (3), 95 (4), 70 (4) and 58 (22).

E-Pentadec-2-ene-15-olide **4g**. The standard procedure using 12-iodododecylpropiolate **3g** (272mg, 0.75mmol) and triphenyltin hydride (316mg, 0.9mmol) afforded the title compound **4g** (98mg, 55%), and reduced material *n-dodecylpropiolate* **5g** (52mg, 29%) as colourless oils. Data for **4g**: (Found: C, 75.64; H, 11.31. $C_{15}H_{26}O_2$ requires C, 75.58; H, 10.99%); $\nu_{max.}$ (thin film) 3029 (s), 2933 (vs), 2859 (s), 1709 (vs), 1213 (br, s), 1097 (s), 1016 (s), 809 (s), 772 (s) and 729 (s); δ_H (200MHz) 1.05-1.85 (20H, m, C5-C14-$(H_2)_{10}$), 2.18-2.32 (2H, m, C4-H_2), 4.22 (2H, t, *J* 7.0Hz, C15-H_2), 5.82 (1H, d, *J* 16.0Hz, =C2-H), 6.93 (1H, dt, *J* 16.0, 7.5Hz, =C3-H); δ_C (50.4MHz) 166.86 (C=O), 149.88, 122.70 (CO<u>C</u>H=<u>C</u>H), 64.37 (OCH_2), 31.03, 27.98, 27.13, 26.83, 26.47, 26.03, 25.39, 25.20 (CH_2); *m/z* (C.I., NH_3) 257 (3%), 256 (MNH_4^+, 20), 226 (15), 239 (MH^+, 100), 109 (6), 95 (10), 84 (14), 68 (8) and 55 (80); Data for **5g**: (Found: C, 75.22; H, 11.12. $C_{15}H_{26}O_2$ requires C, 75.58; H, 10.99%); $\nu_{max.}$ (thin film) 3280 (m), 2920 (vs), 2856 (s), 2120 (s), 1716 (vs), 1465 (m), 1230 (br, vs), and 758 (m); δ_H (200MHz) 0.88 (3H, <u>ca</u>. t, *J* 7.0Hz, CH_3), 1.24 (18H, br, s, $OC_2H_4(C\underline{H}_2)_9$), 1.56-1.77 (2H, m, $OCH_2C\underline{H}_2$), 2.88 (1H, CCH), 4.19 (2H, t, *J* 7.0Hz, OCH_2); δ_C (50.4MHz) 153.02 (C=O), 74.70 (<u>C</u>CH), 74.36 (C<u>C</u>H), 66.46 (OCH_2), 31.78, 29.48, 29.31, 29.19, 29.01, 28.14, 25.59, 22.53 (CH_2), 13.93 (CH_3); *m/z* (C.I., NH_3) 258 (54%), 256 (MNH_4^+, 100), 241 (12), 202 (5), 125 (5), 107 (8), 95 (10), 81 (12), 69 (14), 58 (28) and 55 (43).

11-Bromoundecanal **6**. To a sirred solution of oxalyl chloride (1.92ml, 22mmol) in dry dichloromethane (50ml) at -60°C under argon was added slowly, over 5min, a solution of dimethylsulphoxide (3.41ml, 48mmol) in dichloromethane (10ml). The mixture was stirred for 10min, then 11-bromoundecanol **1f** (5.02g, 20mmol) dissolved in dichloromethane (20ml) was added dropwise, over 10min, and stirred for a further 45min. Triethylamine (14ml, 100mmol) was carefully added and the white precipitate allowed to warm up to room temperature and stirred for 10min. Water (50ml) was added, the layers separated and the aqueous phase extracted with dichloromethane (3x100ml). The combined organic portions were washed with brine then dried ($MgSO_4$), filtered and concentrated to yield 11-bromoundecanal **6** (3.9g, 78%) after flash chromatography (SiO_2; 10% ether/petrol); $\nu_{max.}$ (thin film) 2930 (vs), 2860 (s), 2720 (s), 1730 (s), 1465 (w), 1255 (w) and 720

(w); δ_H (200MHz) 1.15-1.45 (12H, m, $BrC_2H_4(C\underline{H}_2)_6$), 1.45-1.68 (2H, m, $OCCH_2C\underline{H}_2$), 1.70-1.90 (2H, m, $C\underline{H}_2CH_2Br$), 2.37 (2H, ca. t, *J* 7.0Hz, CH_2CO), 3.35 (2H, t, *J* 7.0Hz, CH_2Br), 9.71 (1H, br, s, CHO); δ_C (50.4MHz, DEPT) 43.72, 33.82, 32.62, 29.09, 28.92, 28.51, 27.93, 21.83 (CH_2); *m/z* (C.I., NH_3) 268 (MNH_4^+, ^{81}Br, 90%), 266 (MNH_4^+, ^{79}Br, 100), 218 (7), 202 (10), 175 (28), 151 (18), 108 (10), 95 (22), 81 (16).

12-Bromododecan-2-ol **7**. A solution of 11-bromoundecanal **6** (2.5g, 10mmol) at -78°C in dry THF (100ml) was treated with methylmagnesium bromide (8ml of a 1.5M solution in THF) dropwise, over 5 minutes. The cloudy mixture formed was stirred at -78°C for 1h and then quenched with saturated aqueous ammonium chloride solution. The biphasic mixture was extracted with ethyl acetate, and the combined organic extracts were dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (SiO_2; 20%, ether/petrol) to afford **7** (1.62g, 61%) as a colourless oil. $\nu_{max.}$ (thin film) 3650-3100 (br), 2970 (m), 2930 (vs), 2860 (s), 1468 (m), 1375 (w), 1255 (w), 1125 (w), 1060 (w) and 720 (w); δ_H (200MHz) 1.17 (3H, d, *J* 6.0Hz, CH_3), 1.20-1.50 (16H, m, $BrC_2H_4(C\underline{H}_2)_8$), 1.84-1.92 (2H, m, $BrCH_2C\underline{H}_2$), 3.39 (2H, t, *J* 7.0Hz, CH_2Br), 3.78 (1H, m, CHOH); δ_C (50.4MHz, DEPT) 68.07 (CHOH), 39.20, 33.92, 32.68, 29.44, 29.30, 28.58, 27.99, 25.59 (CH_2), 23.30 (CH_3); *m/z* (C.I., NH_3) 285 (12%), 284 (MNH_4^+, ^{81}Br, 85%), 282 (MNH_4^+, ^{79}Br, 100), 238 (12), 202 (20), 137 (7), 109 (11), 95 (18), 68 (5), 58 (28).

12-Bromododecyl-2-propiolate **8**. A mixture of alcohol **7** (1.56g, 5.84mmol) and triphenylphosphine (3.06g, 11.67mmol) in dry THF (20ml) was added dropwise, over 0.5h, to a stirred solution of propiolic acid (817mg, 11.67mmol) and DEAD (2.03g, 11.67mmol) in the same amount of solvent under argon at room temperature. The reaction mixture was stirred overnight then concentrated under reduced pressure. The reddish brown residue was purified by flash column chromatography (SiO_2; 10%, ether/petrol) to give the title compound **8** (1.16g, 63%) as a colourless oil. $\nu_{max.}$ (thin film) 3290 (m), 2982 (m), 2930 (vs), 2860 (s), 2120 (s), 1715 (vs), 1465 (m), 1380 (w), 1240 (br, vs), 1130 (m) and 755 (s); δ_H (200MHz) 1.20-1.75 (19H, m, $BrC_2H_4(C\underline{H}_2)_8$ and $C\underline{H}_3$), 1.75-1.92 (2H, m, $BrCH_2C\underline{H}_2$), 2.87 (1H, s, CCH), 3.41 (2H, t, *J* 7.0Hz, CH_2Br), 5.01 (1H, m, OCH); δ_C (50.4MHz, DEPT) 75.10 (OCH), 74.03 ($\underline{C}CH$), 73.85 ($C\underline{C}H$), 35.49, 33.93, 32.67, 29.23, 29.16, 28.58, 27.99, 25.08 (CH_2), 19.55 (CH_3); *m/z* (C.I., NH_3) 337 (12%), 336 (MNH_4^+, ^{81}Br, 100%), 334 (MNH_4^+, ^{79}Br, 98), 290 (12), 254 (15), 147 (8), 137 (4), 109 (8), 95 (12), 81 (11), 70 (9), 58 (25).

12-Iodododecyl-2-propiolate **9**. The standard procedure afforded **9** as a colourless oil (936mg, 83%) from bromide **8** (1.0g, 3.13mmol) and sodium iodide (1.38g, 9.39mmol). (Found: C, 49.61; H, 7.05. $C_{15}H_{25}O_2I$ requires C, 49.46; H, 6.92%); $\nu_{max.}$ (thin film) 3280 (w), 2982 (w), 2930 (vs), 2860 (s), 2120 (s), 1715 (vs), 1465 (m), 1380 (w), 1240 (br, vs), 1130 (m), 970 (w) and 760 (s); δ_H (200MHz) 1.20-1.75 (19H, m, $IC_2H_4(C\underline{H}_2)_8$ and $C\underline{H}_3$), 1.75-1.92 (2H, m, $ICH_2C\underline{H}_2$), 2.87 (1H, s, CCH), 3.19 (2H, t, *J* 7.0Hz, CH_2I), 5.02 (1H, m, OCH); δ_C (50.4MHz, DEPT) 152.61 (C=O), 75.09 (OCH), 74.04 ($\underline{C}CH$), 73.85 ($C\underline{C}H$), 35.49, 33.40, 30.33, 29.23, 28.99, 28.35, 25.09, 19.59 (CH_2), 7.17 (CH_2I), 19.58 (CH_3); *m/z* (C.I., NH_3) 384 (8%), 383 (15), 382 (MNH_4^+, 100%), 295 (28), 256 (18), 239 (11), 184 (6), 95 (7), 81 (8), 69 (9), 58 (16).

E-Pentadec-2-ene-14-olide **10**. Application of the standard procedure for radical cyclisation using **9** (275mg, 0.75mmol) and triphenyltin hydride (316mg, 0.9mmol) afforded the title compound **10** (112mg, 63%) as a colourless oil. (Found: C, 75.82 H, 11.20. $C_{15}H_{26}O_2$ requires C, 75.58; H, 10.99%); $\nu_{max.}$ (thin film) 2978 (s), 2930 (vs), 2860 (s), 1715 (vs), 1650 (w), 1460 (m), 1448 (m), 1355 (m), 1205 (m), 1180 (m), 1128 (m) and 985 (m); δ_H (200MHz) 1.00-1.80 (19H, br, m, C5-C12-$(H_2)_8$ and C15-H_3), 2.05-2.35 (4H, m, C4-H_2 and C13-H_2), 5.02 (1H, m, C14-H), 5.79 (1H, d, *J* 16.0Hz, =C2-H), 5.89 (1H, m, =C3-H); δ_C (50.4MHz) 166.44 (C=O), 150.07, 122.88 (COCH=CH), 71.16 (OCH), 34.59, 31.97, 27.71, 27.23, 27.09, 26.87, 26.22, 25.77, 23.81 (CH_2) and 20.27 (CH_3); *m/z* (C.I., NH_3) 257 (3%), 256 (MNH_4^+, 22), 239 (MH^+, 100), 221 (15), 194 (120, 109 (10), 95 (11), 81 (19), 68 (10) and 55 (12).

Acknowledgments.

We thank the Vice Chancellors and Principals for an ORS Award to S.H.R. and Imperial Chemical Industries and Merck, Sharp and Dohme for financial support.

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