Intramolecular termination of radical-polar crossover reactions

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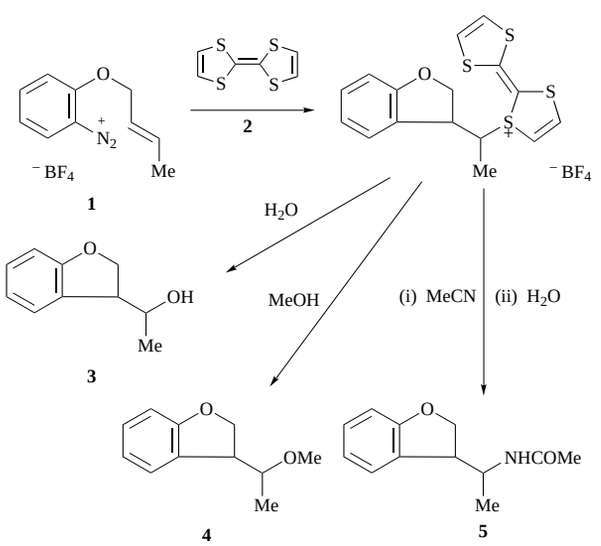
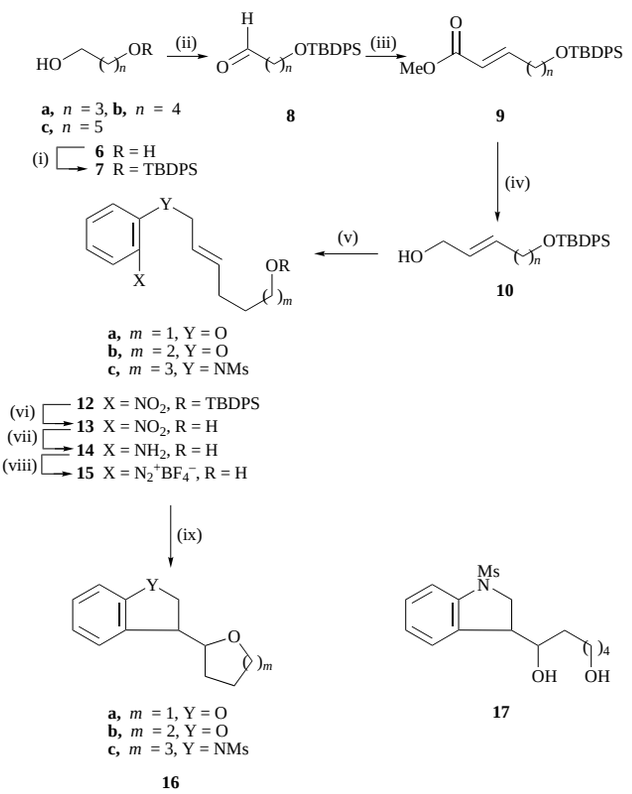
Cyclic ethers result from intramolecular trapping of cations formed through the radical-polar crossover process.

Tributyltin hydride has been an extremely useful reagent which has led to a deeper knowledge of radical processes in solution. However, the neurotoxicity of trialkyltin products and the frequently cited problems associated with separation of organotin residues from reaction products, has led the pharmaceutical industry to shun radical chemistry pending the development of alternative and better methodology. Whereas polymer-bound tin reagents might be thought to overcome the problems, this appears not to be the case.[1] An attractive alternative to the tin reagents, at least for the generation of aryl radicals, is the catalytic 'radical-polar crossover' reaction. This reaction has the added benefit of permitting functionalisation of the site of the final radical by carbon–heteroatom bond formation and we have shown that alcohols **3**, ethers **4** and amides **5** result from this chemistry when a diazonium salt **1** is treated with tetrathiafulvalene (TTF) **2** in moist acetone, alcohol or nitrile solvents (Scheme 1).[2,3] Convinced that the synthetic scope of the reaction could be increased by developing intramolecular termination of such reactions, we launched a series of experiments to determine whether intramolecular alcohols could act as the ultimate nucleophiles in these reactions and now report our results.



Scheme 1

Initial synthetic targets were the diazonium salts **15a–c**, which were prepared as follows (Scheme 2). Protection of butane-1,4-diol **6a**, pentane-1,5-diol **6b** or hexane-1,6-diol **6c** as the *tert*-butyldiphenylsilyl ether proceeded smoothly to afford **7a**, **7b** and **7c** respectively, the products being clear, viscous oils. Swern oxidation led to aldehydes **8a–c** which could now be elaborated to incorporate the double bond in the desired position by Wadsworth–Emmons reaction furnishing **9a–c** as a mixture of *cis* and *trans* isomers. Although separation of the two isomers by column chromatography was possible, this was unnecessary for our purposes as the final radical reaction should proceed well irrespective of the geometry about the C=C bond.



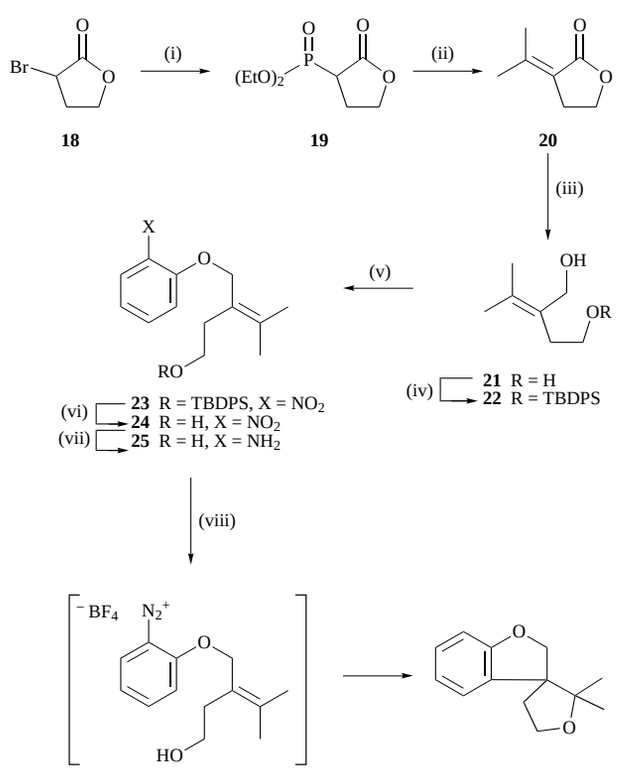
Scheme 2 *Reagents and conditions*: (i) TBDPSCl, imidazole, DMF, 8 h; (**a**) 87%; (**b**) 86%; (**c**) 66%; (ii) $(COCl)_2$, DMSO, NEt_3. −70 °C, 2 h; (**a**) 95%; (**b**) 85%; (**c**) 89%; (iii) NaH, $(MeO)_2P(O)CH_2CO_2Me$, THF; (**a**) 91%; (**b**) 92%; (**c**) 77%; (iv) DIBALH, THF, −78 °C, 20 min; (**a**) 96%; (**b**) 89%; (**c**) 88%; (v) 2-nitrophenol, DEAD, PPh_3, THF, 0 °C→rt, 16 h; (**a**) 94%; (**b**) 94%; 2-nitro-*N*-methylsulfonylaniline, DEAD, PPh_3, THF, 0 °C→rt, 17 h; (**c**) 88%; (vi) TBAF, THF, 1 h; (**a**) 98%; (**b**) 96%; (**c**) 88%; (vii) $Cu(acac)_2$, $NaBH_4$, EtOH, 3 h; (**a**) 96%; (**b**) 96%; (**c**) 89%; (viii) $NOBF_4$, CH_2Cl_2, 0 °C; (ix) TTF, acetone, rt; (**a**) 42%; (**b**) 38%; (**c**) 4% (from **14a–c**)

Reduction of each of the compounds **9a–c** to afford **10a–c** was effected using diisobutylaluminium hydride. Surprisingly, the ester **9a** afforded a 1:1 mixture of **10a** and the silane[4] Ph_2Bu^tSiH **11**. The ^1H NMR spectrum clearly showed the Si–H proton as a singlet at 4.63 ppm and an infrared absorption at 2114 cm^{-1} was also attributable to this functionality.

Mitsunobu reaction of **10a–b** with 2-nitrophenol and coupling of alcohol **10c** with 2-nitro-*N*-methylsulfonylaniline furnished the respective coupled products **12a–c**, which were deprotected with tetra-*n*-butylammonium fluoride (TBAF) to reveal the hydroxy functionality in **13a–c**. Reduction to **14a–c**[5] was followed by diazotisation. This was effected with nitrosonium tetrafluoroborate to give diazonium salts **15a–c** as dark red oils, which were reacted immediately with TTF in acetone.

The ^1H NMR spectra of the organic constituents of the crude reaction mixtures from **15a,b** showed only one product in each case, and purification afforded the bis-ethers **16a,b** in moderate yield. As a result, a mild procedure for the construction of heterocycles in a tandem carbon–carbon and carbon–oxygen bond forming sequence had been demonstrated. Attempts to extend this to the more difficult seven-membered ring formation were not so easy and the best yield of the cyclic ether **16c** formed was 4%. Repeating the reaction under different conditions led to the diol **17**, as a diastereoisomeric mixture, isolated in 45% yield.

Our attention then turned to a more complex substrate **26**, which would lead to the spirobicyclic product **27**. This was of particular interest because of the abundance of spirobicyclic natural products. This diazonium salt was prepared as shown in Scheme 3. The α-bromolactone **18** was treated under Michaelis–



Scheme 3 *Reagents and conditions*: (i) $P(OEt)_3$, 71%; (ii) NaH, Me_2CO, THF, 58%; (iii) LAH, Et_2O, 94%; (iv) TBDPSCl, imidazole, DMF, 69%; (v) 2-nitrophenol, PPh_3, DEAD, THF, 71%; (vi) TBAF, THF, 99%; (vii) $NaBH_4$, $Cu(acac)_2$, EtOH, 71%; (viii) $NOBF_4$, acetone; (ix) TTF, acetone, 57% (from amine **25**)

Arbuzov conditions to give the corresponding phosphonate **19** which after a Wadsworth–Emmons reaction gave the isopropylidenelactone **20**. This was reduced to afford the diol **21**. Selective protection with *tert*-butyldiphenylsilyl chloride and imidazole gave almost exclusively the monoprotected alcohol **22**, which was then coupled to *o*-nitrophenol using a Mitsunobu reaction to yield the nitroarene **23**. Deprotection of the silyl ether afforded **24** and reduction to the aromatic amine **25** was followed by diazotisation. This diazonium salt refused to crystallise or solidify, and so was used *in situ* and afforded the desired spiro product **27** in 57% yield (from amine **25**).

These experiments clearly demonstrate that intramolecular nucleophiles can be used to terminate the radical-polar crossover cycle, and the formation of the spiro bis-ether **27** suggests that the method may be of use in organic synthesis of natural compounds.

Experimental

Melting points were determined on a Kofler hot stage apparatus and are uncorrected. Microanalyses were determined using a Perkin-Elmer 240B elemental analyser. Infrared spectra were obtained on a Perkin-Elmer 1720-X FTIR or a Pye-Unicam SP3-100 spectrometer. Ultraviolet spectra were recorded on a Philips PU8700 series instrument. ^1H NMR spectra were recorded at 250 MHz on a Bruker WM250, at 270 MHz on a JEOL EX270 or at 400 MHz on a Bruker AM400 spectrometer. ^{13}C NMR spectra were recorded at 67.5 MHz on a JEOL EX270 or at 100 MHz on a Bruker AM400 spectrometer. NMR experiments were carried out in deuterochloroform, [$^2H_4$]methanol, [$^2H_6$]acetone, [$^2H_3$]acetonitrile or [$^2H_6$]dimethyl sulfoxide with tetramethylsilane as an internal reference. Chemical shifts are quoted in parts per million (ppm). The following abbreviations are used for multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Coupling constants are reported in hertz (Hz). In cases where superimposition of the signals of two, or more, isomers occurred, the signals have been reported as multiplets (m), unless the coupling constants of each isomer could be ascertained. In compounds present as a mixture of diastereoisomers, 'minor' refers to signals assigned to a minor isomer. Mass spectra were recorded on a VG Micromass 7070E or an AEI MS902 instrument. High resolution FAB or CI spectra were recorded at the EPSRC Mass Spectrometery Service Centre, Swansea.

Where necessary, solvents were dried and/or distilled before use. Tetrahydrofuran was distilled from sodium–benzophenone. Acetonitrile was distilled from phosphorus(v) oxide. Dichloromethane was distilled from calcium hydride. Diethyl ether, toluene and benzene were dried over sodium wire. Unless otherwise stated, all petrol was of boiling range 40–60 °C and was distilled before use. Chromatography was performed using Sorbsil C60 (May and Baker), Kieselgel 60 (Art 9385) or Kieselgel HF254 silica gels.

4-(*tert*-Butyldiphenylsilyloxy)butanol 7a

tert-Butyldiphenylsilyl chloride (12 ml, 46 mmol) was added to a mechanically stirred solution of butane-1,4-diol (50 ml, 50.85 g, 0.57 mmol) and imidazole (7.85 g, 0.12 mmol) in dry *N*,*N*-dimethylformamide (300 ml), *via* a syringe pump over a period of 5 h after which the *N*,*N*-dimethylformamide was removed by distillation (bp 65–70 °C at 10 mmHg). Water (600 ml) was added to the residue leading to the formation of a white suspension which was extracted with diethyl ether (3 × 600 ml); the aqueous layer was back washed with diethyl ether (3 × 600 ml). The combined organic phase was dried and evaporated under reduced pressure leading to a yellow oil (17.6 g). This was chromatographed on silica gel using dichloromethane–ethyl acetate (98:2 then 50:50) as the eluting solvent to afford 4-(*tert*-butyldiphenylsilyloxy)butanol[6] **7a** as a clear oil (13.18 g, 40.2 mmol, 87%) (Found: C, 73.30; H, 8.89; MH^+, 329.1946. $C_{20}H_{28}O_2Si$ requires C, 73.12; H, 8.59%; *MH*, 329.1937); ν_{max}(film)/cm^{-1} 3343, 3071, 3050, 2999, 2932, 1590, 1112, 741, 703; δ_H(250 MHz) 1.05 (9H, s, 3 × CH_3), 1.66 (4H, m, 2 × CH_2), 3.67 (4H, m, 2 × OCH_2), 7.40 (6H, m, ArH), 7.68 (4H, m, ArH); δ_C(67.5 MHz) 15.1 (C), 26.8 (CH_3), 29.1 (CH_2), 29.4

(CH_2), 62.3 (CH_2), 63.9 (CH_2), 127.6 (CH), 129.6 (CH), 133.6 (C), 135.5 (CH); *m/z* (FAB) 329 [(MH^+), 20%], 199 (100), 105 (29), 75 (51).

5-(*tert*-Butyldiphenylsilyloxy)pentanol 7b

The procedure was performed as described for obtaining **7a**, using pentane-1,5-diol (85 ml, 0.81 mol), imidazole (10.2 g, 0.15 mol), *tert*-butyldiphenylsilyl chloride (20.08 g, 73 mmol) in *N*,*N*-dimethylformamide (400 ml). Chromatography on silica gel using dichloromethane–ethyl acetate (97 : 3 and then 80 : 20) furnished 5-(*tert*-butyldiphenylsilyloxy)pentanol **7b**[7] as a clear oil (21.48 g, 63 mmol, 86%) (Found: C, 73.76; H, 8.96; MH^+, 343.2086. $C_{21}H_{30}O_2Si$ requires C, 73.63; H, 8.83%; *MH*, 343.2093); ν_{max}(film)/cm^{-1} 3338, 3071, 2932, 2859, 1590, 1390, 1263, 1112, 738, 702; δ_H(270 MHz) 1.05 (9H, s, 3 × CH_3), 1.33–1.64 (6H, m, 3 × CH_2), 3.61 (2H, t, *J* 6.3, OCH_2), 3.66 (2H, t, *J* 6.3, OCH_2), 7.38 (6H, m, ArH), 7.65 (4H, m, ArH); δ_C(67.8 MHz) 19.1 (C), 21.9 (CH_2), 26.8 (CH_3), 32.2 (CH_2), 33.3 (CH_2), 62.8 (CH_2), 63.7 (CH_2), 127.5 (CH), 129.5 (CH), 134.0 (C), 135.5 (CH); *m/z* (FAB) 343 [(MH^+), 11%], 199 (84), 135 (74), 69 (100).

6-(*tert*-Butyldiphenylsilyloxy)hexanol 7c

A solution of hexane-1,6-diol (38.9 g, 330 mmol, 11 equiv.) and imidazole (22.5 g, 330 mmol, 11 equiv.) in dry DMF (95 ml) was stirred under N_2 at room temperature. *tert*-Butyldiphenylsilyl chloride (7.8 ml, 8.3 g, 30 mmol, 1 equiv.) in DMF (15 ml) was added dropwise over 2 h *via* a syringe pump, and the resultant solution was stirred for a further 48 h. The majority of the solvent was removed *in vacuo*, and the material was partitioned between water (500 ml) and ethyl acetate (200 ml). The aqueous layer was extracted with ethyl acetate (2 × 100 ml), and the combined organic portions were washed with water (5 × 100 ml) and dried over $MgSO_4$. Removal of solvent *in vacuo* gave a yellow oil (7.17 g), which was purified on silica gel using dichloromethane as the eluent to give 6-(*tert*-butyldiphenylsilyloxy)hexanol **7c**[8] as a yellow oil (7.07 g, 66%); ν_{max}(film)/cm^{-1} 3351, 3074, 2931, 2858; δ_H($CDCl_3$, 250 MHz) 1.06 (9H, s, Bu^t), 1.35–1.45 (5H, m, 2 × CH_2, OH), 1.54–1.62 (4H, m, 2 × CH_2), 3.63 (2H, t, *J* 6.6, CH_2O), 3.67 (2H, t, *J* 6.3, CH_2O), 7.36–7.44 (6H, m, 6 × ArH), 7.68–7.74 (4H, m, ArH); δ_C($CDCl_3$, 67.8 MHz) 19.4 (C), 25.6 (CH_2), 25.7 (CH_2), 27.0 (CH_3), 32.7 (CH_2), 32.8 (CH_2), 62.9 (CH_2), 64.0 (CH_2), 127.7 (CH), 129.7 (CH), 134.3 (C), 135.7 (CH).

4-(*tert*-Butyldiphenylsilyloxy)butanal 8a

Dimethyl sulfoxide (6.4 ml, 2.91 g, 37 mmol) was added over 5 min to a mechanically stirred solution of oxalyl chloride (3.9 ml, 5.6 g, 17 mmol) in dry dichloromethane (600 ml) at −78 °C and effervescence was observed. The mixture was stirred for 10 min leading to the formation of a white suspension. 4-(*tert*-Butyldiphenylsilyloxy)butanol **7a** (13.18 g, 40 mmol) was added as a solution in dichloromethane (100 ml) over 30 min. The mixture was stirred for 20 min before addition of triethylamine (28 ml, 20.5 g, 200 mmol) and then warmed to room temperature. The organic phase was washed with water (3 × 800 ml) and hydrochloric acid (2 M, 3 × 800 ml). The combined organic extracts were dried and concentrated *in vacuo* to afford a pale yellow oil (13.5 g). This was chromatographed on silica eluting firstly with petrol–dichloromethane (50 : 50) and then with dichloromethane–ethyl acetate (95 : 5) to afford 4-(*tert*-butyldiphenylsilyloxy)butanal **8a**[9] (12.46 g, 38 mmol, 95%) as a pale yellow oil (Found: C, 73.33; H, 8.43. $C_{20}H_{26}O_2Si$ requires C, 73.57; H, 8.03%); ν_{max}(film)/cm^{-1} 3072, 2933, 2857, 2722, 1727, 1111, 741, 706; δ_H(400 MHz) 1.04 (9H, s, CH_3), 1.89 (2H, m, CH_2), 2.54 (2H, td, *J* 6.3, 1.8, CH_2CHO), 3.70 (2H, t, *J* 6.3, CH_2OSi), 7.39 (6H, m, ArH), 7.65 (4H, m, ArH), 9.78 (1H, t, *J* 1.8, CHO); δ_C(100 MHz) 19.2 (C), 25.3 (CH_2), 26.8 (CH_3), 40.7 (CH_2), 62.9 (CH_2), 127.7 (CH), 129.7 (CH), 133.6 (C), 135.5 (CH), 202.3 (CH); *m/z* (FAB) 325 [($M - H)^+$, 8%], 207 (15), 199 (56), 183 (16), 105 (28).

5-(*tert*-Butyldiphenylsilyloxy)pentanal 8b

Using the same procedure as in the preparation of **8a**, oxalyl chloride (2.2 ml, 25 mmol), dimethyl sulfoxide (3 ml, 42.3 mmol), 5-(*tert*-butyldiphenylsilyloxy)pentanol **7b** (6.06 g, 17.7 mol) and triethylamine (13 ml, 94 mmol) in dichloromethane (300 ml) were reacted. The crude product was chromatographed on silica gel using dichloromethane (100%) as eluting solvent to afford 5-(*tert*-butyldiphenylsilyloxy)pentanal **8b**[10] (5.14 g, 15 mmol, 85%) as a pale yellow oil (Found: M^+, 340.1811. $C_{21}H_{28}O_2Si$ requires *M*, 340.1859); ν_{max}(film)/cm^{-1} 3070, 3050, 3014, 2990, 2929, 2857, 2713, 1728, 1589, 1112, 735, 702; δ_H(270 MHz) 1.05 (9H, s, 3 × CH_3), 1.57 (2H, m, CH_2), 1.75 (2H, tt, *J* 8, 8, CH_2), 2.40 (2H, td, *J* 7.2, 2, CH_2CHO), 3.67 (2H, t, *J* 6, $SiOCH_2$), 7.34–7.45 (6H, m, ArH), 7.65 (4H, m, ArH), 9.73 (1H, t, *J* 2, CHO); δ_C(67.8 MHz) 18.9 (C), 19.6 (CH_2), 27.3 (CH_3), 32.2 (CH_2), 43.9 (CH_2), 63.7 (CH_2), 128.1 (CH), 123.0 (CH), 134.3 (C), 135.9 (CH), 202.8 (CH).

6-(*tert*-Butyldiphenylsilyloxy)hexanal 8c

A solution of oxalyl chloride (2.0 ml, 2.66 g, 21 mmol, 1.1 equiv.) in dry dichloromethane was stirred under N_2 and cooled to −78 °C. Dry dimethyl sulfoxide (2.9 ml, 42 mmol, 2.2 equiv.) in dichloromethane (10 ml) was added over 15 min, and the resulting solution was stirred for 30 min. 6-(*tert*-Butyldiphenylsilyloxy)hexanol **7c** (6.9 g, 19 mmol, 1 equiv.) in dichloromethane (50 ml) was added over 15 min and the resulting solution was stirred for a further 20 min. Triethylamine (5.8 ml, 4.25 g, 42 mmol, 2.2 equiv.) was then added over 10 min, the mixture was stirred for a further 10 min at −78 °C, before being allowed to warm to room temperature and stirred for 15 h. The solution was washed with water (50 ml), and the aqueous phase was extracted with dichloromethane (2 × 50 ml). The combined organic portions were washed with HCl (2 M, 2 × 100 ml), water (100 ml) and brine (100 ml), dried over $MgSO_4$ and the solvent was removed *in vacuo* to give a yellow oil (7.14 g). The material was purified by chromatography on silica gel using 50 : 50 hexane–dichloromethane as the eluent, to give 6-(*tert*-butyldiphenylsilyloxy)hexanal **8c**[11] as a pale yellow oil (5.97 g, 89%); ν_{max}(film)/cm^{-1} 3069, 2929, 2857, 1724; δ_H($CDCl_3$, 250 MHz), 1.06 (9H, s, Bu^t), 1.27–1.69 (6H, m, 3 × CH_2), 2.42 (2H, td, *J* 7.1, 1.8, CH_2CHO), 3.69 (2H, t, *J* 6.2, CH_2O), 7.37–7.45 (6H, m, 6 × ArH), 7.67–7.71 (4H, m, 4 × ArH), 9.76 (1H, t, *J* 1.8, CHO); δ_C($CDCl_3$, 67.8 MHz) 19.4 (C), 22.0 (CH_2), 25.6 (CH_2), 27.1 (CH_3), 32.4 (CH_2), 44.0 (CH_2), 63.7 (CH_2), 127.8 (CH), 129.7 (CH), 134.2 (C), 135.7 (CH), 202.6 (CH).

Methyl 6-(*tert*-butyldiphenylsilyloxy)hex-2-enoate 9a

To a mechanically stirred slurry of washed sodium hydride (1.88 g, 49 mmol, 60% suspension in mineral oil) in tetrahydrofuran (500 ml) at 0 °C was added trimethyl phosphonoacetate (6.8 ml, 42 mmol) over a period of 15 min and stirring was continued for 4 h leading to a white, gelatinous suspension. 4-(*tert*-Butyldiphenylsilyloxy)butanal **8a** (12.01 g, 37 mmol) was then added at room temperature and the mixture stirred for a further 16 h, after which the tetrahydrofuran was removed under reduced pressure. Diethyl ether (500 ml) was added to the residue and the organic phase washed with water (3 × 500 ml), then dried and concentrated to afford a pale yellow oil. This was further purified by chromatography on silica gel eluting with dichloromethane. Methyl (6-*tert*-butyldiphenylsilyloxy)-hex-2-enoate **9a** was obtained as a pale yellow oil (12.71 g, 32 mmol, 91%) as a mixture of geometric isomers (90 : 10). A small sample of methyl 6-(*tert*-butyldiphenylsilyloxy)hex-2-enoate (513 mg) was chromatographed on silica gel using petrol–dichloromethane (50 : 50) as eluting solvent in order to separate the two *E*/*Z* isomers. The major isomer was assigned to be the *E* isomer and the minor to be the *Z* isomer.

(E)-*Methyl* 6-(tert-*butyldiphenylsilyloxy*)*hex*-2-*enoate* (200 mg, 0.52 mmol, 34%) (Found: C, 71.91; H, 7.93; MNa^+, 405.1856. $C_{23}H_{30}O_3Si$ requires C, 72.21; H, 7.90%; *MNa*, 405.1862); ν_{max}(film)/cm^{-1} 3077, 2934, 1726, 1659, 1591, 1110, 740, 706; δ_H(250 MHz) 1.06 (9H, s, 3 × CH_3), 1.71 (2H, tt, *J* 6, 6, CH_2), 2.35 (2H, td, *J* 6.5, 6.5, HCCH_2), 3.68 (2H, t, *J* 6, $SiOCH_2$), 3.74 (3H, s, OCH_3), 5.85 (1H, dt, *J* 15, 1.5, HCCO), 6.98 (1H, dt, *J* 15, 7, *H*CCH_2), 7.35–7.47 (6H, m, ArH), 7.66 (4H, m, ArH); δ_C(67.8 MHz) 19.2 (C), 26.8 (CH_3), 28.6 (CH_2), 30.8 (CH_2), 51.3 (CH_3), 62.8 (CH_2), 121.0 (CH), 127.6 (CH), 129.7 (CH), 133.7 (C), 135.5 (CH), 149.2 (CH), 167.0 (C); *m*/*z* 405 [(MNa^+), 65%].

(Z)-*Methyl* 6-(tert-*butyldiphenylsilyloxy*)*hex*-2-*enoate* (28 mg, 0.07 mmol, 5%); ν_{max}(film)/cm^{-1} 3072, 2933, 2860, 1725, 1647, 1591, 1111, 1002, 740, 705; δ_H(250 MHz) 1.05 (9H, s, CH_3), 1.68 (2H, tt, *J* 7, 7, CH_2), 2.73 (2H, td, *J* 7.3, 7.3, CH_2CH), 3.69 (5H, m, CH_2OSi, OCH_2), 5.73 (1H, d, *J* 11.7, HCCO), 6.22 (1H, dt, *J* 11.5, 7.4, *H*CCH_2), 7.37 (6H, m, ArH), 7.65 (4H, m, ArH); δ_C(67.8 MHz) 19.2 (C), 25.7 (CH_2), 29.8 (CH_3), 31.9 (CH_2), 51.0 (CH_3), 63.4 (CH_2), 119.4 (CH), 127.6 (CH), 129.5 (CH), 133.9 (C), 135.5 (CH), 150.3 (CH), 166.3 (C); *m*/*z* (FAB) 325 [(M − Bu′), 60%], 305 (33), 213 (35), 197 (25), 95 (78).

Methyl 7-(*tert*-butyldiphenylsilyloxy)hept-2-enoate 9b

Using the same procedure as described for obtaining **9a**, trimethyl phosphonoacetate (1.45 ml, 1.63 g, 8.95 mmol), sodium hydride (483 mg, 12.5 mmol, 60% suspension in mineral oil) and 5-(*tert*-butyldiphenylsilyloxy)pentanal **8b** (2.77 g, 8.14 mmol) in tetrahydrofuran (250 ml) were reacted. Column chromatography of the crude compound on silica gel using dichloromethane as eluting solvent led to *methyl* (7-tert-*butyldiphenylsilyloxy*)*hept*-2-*enoate* (2.96 g, 7.5 mmol, 92%) as a pale yellow oil (Found: M^+, 396.2124. $C_{24}H_{32}O_3Si$ requires *M*, 396.2121); ν_{max}(film)/cm^{-1} 3071, 3050, 2932, 2858, 1728, 1657, 1590, 1112, 742, 703; δ_H(250 MHz) 1.05 (9H, s, 3 × CH_3), 1.28–1.58 (4H, m, 2 × CH_2), 2.19 (2H, m, CH_2CH), 3.68 (2H, br t, *J* 5.6, $SiOCH_2$), 3.73 (3H, s, OCH_3), 5.83 (1H, dt, *J* 15.6, 2, HCCO), 6.96 (1H, dt, *J* 15.6, 7.1, HCCH_2), 7.40 (6H, m, ArH), 7.65 (4H, m, ArH); δ_C(67.8 MHz) 19.6 (C), 24.7 (CH_2), 27.2 (CH_3), 32.5 ($2CH_2$), 51.7 (CH_3), 63.8 (CH_2), 121.4 (CH), 128.0 (CH), 129.9 (CH), 134.3 (C), 135.9 (CH), 149.8 (CH), 167.4 (C).

Methyl 8-(*tert*-butyldiphenylsilyloxy)oct-2-enoate 9c

Sodium hydride (60% dispersion in oil, 1.0 g, 19.6 mmol, 1.15 equiv.) was washed with dry THF, and was then stirred in THF (400 ml) under N_2 at 0 °C. Trimethyl phosphonoacetate (4.1 ml, 3.40 g, 18.7 mmol, 1.1 equiv.) in THF (50 ml) was added over 30 min, and the resulting mixture was stirred for 1 h. 6-(*tert*-Butyldiphenylsilyloxy)hexanal **8c** (5.9 g, 17 mmol, 1 equiv.) in THF (50 ml) was added over 20 min, and the mixture was allowed to warm to room temperature and stirred for a further 24 h. Water (100 ml) was added and the solvent was removed *in vacuo*. The solution was extracted with ethyl acetate (3 × 50 ml), and the combined organic portions were washed with water (3 × 50 ml), dried over $MgSO_4$ and the solvent was removed *in vacuo* to give a pale yellow oil (6.06 g). The material was purified by chromatography on silica gel (30 : 70, hexane–dichloromethane) to give *methyl* 8-(tert-*butyldiphenylsilyloxy*)-*oct*-2-*enoate* **9c** as a 6 : 1 mixture of the *E* and *Z* isomers, as a yellow oil (5.38 g, 77%) (Found: MNH_4^+, 428.2621. $C_{25}H_{34}NO_3Si$ requires *MNH*$_4$, 428.2621); ν_{max}(film)/cm^{-1} 3069, 2929, 2857, 1724, 1657; δ_H($CDCl_3$, 250 MHz) 1.09 (9H, s, Bu′), 1.38–1.45 (4H, m, 2 × CH_2), 1.53–1.63 (2H, m, CH_2), 2.16–2.21 (2H, m, CH_2CH=), 2.60–2.73 (2H, m, CH_2 minor), 3.67 (2H, t, *J* 6.4, CH_2O), 3.72 (3H minor, s, CH_3O minor), 3.74 (3H, s, CH_3O), 5.72–5.82 (1H, m, CH= minor), 5.81 (1H, dt, *J* 15.6, 1.6, MeO_2CCH=), 6.12–6.26 (1H, m, CH= minor), 6.96 (1H, dt, *J* 15.6, 7.0, =CHCH_2), 7.35–7.44 (6H, m, 6 × ArH), 7.65–7.69 (4H, m, 4 × ArH); δ_C($CDCl_3$, 67.8 MHz) 19.2 (C), 25.2 (CH_2), 25.5 (CH_2), 26.9 (CH_3), 27.7 (CH_2), 28.7 (CH_2), 28.9 (CH_2), 32.1 (CH_2), 32.3 (CH_2), 50.8 (CH_3), 51.2 (CH_3), 63.7 (CH_2), 63.8 (CH_2), 119.3 (CH), 121.0 (CH), 127.7 (CH), 129.6 (CH), 134.0 (C), 135.6 (CH), 149.4 (CH), 150.7 (CH), 166.7 (C), 166.9 (C); *m*/*z* (CI) 428 (MNH_4^+, 100%), 411 (MH^+, 5), 353 (8), 333 (21).

6-(*tert*-Butyldiphenylsilyloxy)hex-2-enol 10a

To a well stirred solution of methyl (6-*tert*-butyldiphenylsilyloxy)hex-2-enoate **9a** (9.99 g, 25 mmol) in dry toluene (350 ml) at −70 °C was added diisobutylaluminium hydride (35 ml, 52.5 mmol, 1.5 M as solution in toluene) dropwise over a period of 0.5 h under a steady stream of nitrogen whilst maintaining the temperature. The mixture was stirred for 10 min, quenched with methanol (200 ml, cooled to −60 °C) and then warmed to room temperature leading to a white suspension. Toluene was removed under reduced pressure and the colourless residue dissolved in hydrochloric acid (1 M, 600 ml). The aqueous layer was extracted with dichloromethane (3 × 800 ml), the combined organic phases dried and concentrated by rotary evaporation leading to the crude compound (9.16 g) which was chromatographed on silica gel using dichloromethane–ethyl acetate (99 : 1) as eluting solvent to furnish two compounds, 6-(*tert*-butyldiphenylsilyloxy)hex-2-enol[12] **10a** and *tert*-butyldiphenylsilane **11**. 6-(*tert*-Butyldiphenylsilyloxy)hex-2-enol **10a** (8.5 g, 24 mmol, 96%) was obtained as a pale yellow oil (Found: C, 74.48; H, 8.48. $C_{22}H_{30}O_2Si$ requires C, 74.53; H, 8.53%); ν_{max}(film)/cm^{-1} 3339, 3071, 3050, 3015, 2932, 2858, 1670, 1112, 1007, 970, 741, 703; δ_H(250 MHz) 1.04 (9H, s, 3 × CH_3), 1.39 (1H, br s, OH), 1.64 (2H, tt, *J* 7, 7, HCH_2CCH_2), 2.16 (2H, m, HCCH_2), 3.66 (2H, t, *J* 6.3, $SiOCH_2$), 4.04 (2H, d, *J* 6.5, H_2COH), 5.64 (2H, m, HC=CH), 7.35–7.45 (6H, m, ArH), 7.65 (4H, dd, *J* 8, 2, ArH); δ_C(67.5 MHz) 19.1 (C), 26.7 (CH_3), 28.32 (CH_2), 31.84 (CH_2), 32.17 (CH_2 minor), 63.04 (CH_2), 63.29 (CH_2), 126.7 (CH), 127.0 (CH), 127.5 (CH), 131.8 (CH minor), 132.2 (CH), 133.8 (C), 135.4 (CH); *m*/*z* (FAB) 337 [(M^+ − H_2O), 6%], 199 (55), 181 (150).

tert-Butyldiphenylsilane **11** (100 mg, 0.42 mmol, 2.3%) was also isolated as a clear oil; ν_{max}(film)/cm^{-1} 3070, 3051, 3013, 2999, 2955, 2927, 2893, 2856, 2114, 1589, 734, 700; δ_H(250 MHz) 1.04 (9H, s, 3 × CH_3), 4.63 (1H, s, SiH), 7.37 (6H, m, ArH), 7.66 (4H, m, ArH); δ_C(100 MHz) 17.9 (C), 27.9 (CH_3), 127.9 (CH), 129.1 (CH), 134.0 (C), 135.6 (CH).

7-(*tert*-Butyldiphenylsilyloxy)hept-2-enol 10b

Using the same procedure as described for obtaining **10a**, methyl 7-(*tert*-butyldiphenylsilyloxy)hept-2-enoate **9b** (4.99 g, 12.6 mmol) and diisobutylaluminium hydride (18 ml, 27 mmol, 1.5 M as a solution in toluene) in dry toluene (200 ml) were reacted. Flash chromatography on silica gel using dichloromethane–ethyl acetate (99 : 1) as eluting solvent furnished 7-(tert-*butyldiphenylsilyloxy*)*hept*-2-*enol* **10b** (4.15 g, 11.3 mmol, 89%) as a pale oil (Found: C, 74.94; H, 9.00. $C_{23}H_{32}O_2Si$ requires C, 74.95; H, 8.75%); ν_{max}(film)/cm^{-1} 3338, 3071, 3049, 2932, 2858, 1680, 1590, 1112, 999, 762, 702; δ_H(250 MHz) 1.05 (9H, s, 3 × CH_3), 1.43–1.59 (5H, br m, OH, 2 × CH_2), 2.04 (2H, m, HCCH_2), 3.65 (2H, t, *J* 6, $SiOCH_2$), 4.06 (2H, d, *J* 5.5, $HOCH_2$), 5.65 (2H, m, HC=CH), 7.40 (6H, m, ArH), 7.67 (4H, m, ArH); δ_C(67.5 MHz) 19.1 (C), 25.3 (CH_2), 26.8 (CH_3), 31.8 (CH_2), 31.9 (CH_2), 63.6 (CH_2), 63.7 (CH_2), 127.5 (CH), 129.0 (CH), 129.5 (CH), 133.0 (CH), 134.0 (C), 135.5 (CH); *m*/*z* (FAB) 351 [(M^+ − H_2O), 9%], 199 (99), 181 (27), 105 (44), 95 (52), 67 (47), 55 (47).

8-(*tert*-Butyldiphenylsilyloxy)oct-2-enol 10c

A solution of methyl 8-(*tert*-butyldiphenylsilyloxy)oct-2-enoate **9c** (5.2 g, 12.7 mmol, 1 equiv.) in dry toluene (60 ml) was cooled to −78 °C under N_2. Diisobutylaluminium hydride (1.5 M solution in toluene, 17.8 ml, 26.7 mmol, 2.1 equiv.) was added over 35 min, and the resulting solution was stirred for a further 30 min at −78 °C. Quenching with methanol (15 ml) and removal

of solvent *in vacuo* gave a clear gel, which was partitioned between dichloromethane (100 ml) and hydrochloric acid (2 M, 200 ml). The aqueous layer was extracted with dichloromethane (2 × 25 ml), and the combined organic portions were washed with hydrochloric acid (2 M, 2 × 25 ml), dried over $MgSO_4$ and the solvent removed *in vacuo* to give a cream oil (4.76 g). Column chromatography on silica gel (1:20, diethyl ether–dichloromethane) gave 8-(tert-*butyldiphenylsilyloxy*)*oct*-2-*enol* **10c** as a 6:1 mixture of the *E* and *Z* isomers and as a yellow oil (4.1 g, 88%) (Found: M^+, 382.2359. $C_{24}H_{34}O_2Si$ requires *M*, 382.2328); ν_{max}(film)/cm^{-1} 3333, 3074, 2929, 2857; δ_H($CDCl_3$, 250 MHz) 1.06 (9H, s, Bu^t), 1.34–1.53 (5H, m, 2 × CH_2, OH), 1.54–1.60 (2H, m, CH_2), 2.03–2.05 (2H, m, CH_2CH=), 3.66 (2H, t, *J* 6.4, CH_2O), 4.09 (2H, d, *J* 4.0, $HOCH_2$), 4.19 (2H, d, *J* 6.0, $HOCH_2$ minor), 5.52–5.79 (2H, m, CH=CH), 7.35–7.47 (6H, m, 6 × ArH), 7.66–7.70 (4H, m, 4 × ArH); δ_C($CDCl_3$, 67 MHz) 19.2 (C), 25.3 (CH_2), 26.9 (CH_3), 27.4 (CH_2), 28.9 (CH_2), 29.3 (CH_2), 32.2 (CH_2), 32.4 (CH_2), 58.2 (CH_2), 63.2 (CH_2), 63.9 (CH_2), 127.6 (CH), 128.9 (CH), 129.2 (CH), 129.5 (CH), 132.0 (CH), 132.5 (CH), 134.0 (C), 135.5 (CH); *m*/*z* (EI) 382 (M^+, 1%), 365, 325, 307 (21), 200, 199, 139, 109.

tert-Butyl[6-(2-nitrophenoxy)hex-4-enyloxy]diphenylsilane 12a

Diethyl azodicarboxylate (4.2 ml, 3.8 g, 27 mmol) in tetrahydrofuran (100 ml) was added to 2-nitrophenol (3.77 g, 27 mmol), 6-(*tert*-butyldiphenylsilyloxy)hex-2-enol **10a** (5.76 g, 16.3 mmol) and triphenylphosphine (7.02 g, 27 mmol) and the mixture was stirred together in dry tetrahydrofuran (400 ml) at −5 °C for 30 min and then at room temperature for 12 h. The tetrahydrofuran was removed *in vacuo*, and the residue was dissolved in dichloromethane (400 ml). The organic phase was washed with aqueous sodium hydroxide (2 M, 3 × 500 ml), aqueous hydrochloric acid (2 M, 3 × 500 ml), aqueous sodium hydrogen carbonate (2 M, 3 × 500 ml) and brine (2 M, 2 × 500 ml). The organic layer was then dried and evaporated. The residue was adsorbed onto silica gel (from dichloromethane) and further purified by flash chromatography on silica gel firstly eluting with petrol–dichloromethane (50:50) and then with dichloromethane (100%) to afford tert-*butyl*[6-(2-*nitrophenoxy*)-*hex*-4-*enyloxy*]*diphenylsilane* **12a** (7.24 g, 15.2 mmol, 94%) as a yellow gum (Found: C, 70.71; H, 7.18; N, 2.90. $C_{28}H_{33}NO_4Si$ requires C, 70.70; H, 6.99; N, 2.94%); ν_{max}(film)/cm^{-1} 3069, 3048, 2997, 2930, 2891, 2856, 1607, 1583, 1387, 1111, 940, 771, 735, 703; δ_H(250 MHz) 1.05 (9H, s, CH_3), 1.65 (2H, tt, *J* 6, 6, CH_2), 2.18 (2H, td, *J* 7, 7, $HCCH_2$), 3.66 (2H, t, *J* 7, $SiOCH_2$), 4.58 (2H, d, *J* 6.4, OCH_2), 4.71 (d, *J* 4, OCH_2 minor), 5.61–5.88 (2H, m, HC=CH), 6.96 (2H, m, ArH), 7.33–7.49 (7H, m, ArH), 7.65 (4H, dd, *J* 8, 2, ArH), 7.80 (1H, dd, *J* 8, 2, ArH); δ_C(67.5 MHz) 19.2 (C), 26.8 (CH_3), 28.6 (CH_2), 31.7 (CH_2), 63.1 (CH_2), 70.1 (CH_2), 114.9 (CH), 120.1 (CH), 123.6 (CH), 125.4 (CH), 127.5 (CH), 129.4 (CH), 133.7 (CH), 133.8 (C), 135.5 (CH), 135.4 (CH), 140.2 (C), 152.0 (C).

tert-Butyl[7-(2-nitrophenoxy)hept-5-enyloxy]diphenylsilane 12b

Diethyl azodicarboxylate (2.6 ml, 16.3 mmol) in tetrahydrofuran (60 ml) was added to 2-nitrophenol (2.28 g, 16.4 mmol), 7-(*tert*-butyldiphenylsilyloxy)hept-2-enol **10b** (3.87 g, 10.5 mmol) and triphenylphosphine (4.55 g, 17.4 mmol) in dry tetrahydrofuran (300 ml) at −5 °C. The mixture was stirred at room temperature for 12 h, the tetrahydrofuran was removed *in vacuo* and then the residue was dissolved in dichloromethane (400 ml). The organic phase was washed with aqueous sodium hydroxide (2 M, 3 × 500 ml) hydrochloric acid (2 M, 3 × 300 ml), aqueous sodium hydrogen carbonate (2 M, 3 × 300 ml) and brine (2 M, 2 × 300 ml). The organic layer was then dried and evaporated. The residue was adsorbed onto silica gel (from dichloromethane) and further purified by flash chromatography on silica gel firstly eluting with petrol–dichloromethane (66:34) and then with dichloromethane (100%) to afford tert-*butyl*[7-(2-*nitrophenoxy*)*hept*-5-*enyloxy*]*diphenylsilane* **12b** (4.04 g, 8.3 mmol, 94%) as a yellow gum (Found: C, 71.46; H, 7.28; N, 2.77. $C_{29}H_{35}NO_4Si$ requires C, 71.13; H, 7.28; N, 2.86%); ν_{max}(film)/cm^{-1} 3070, 3048, 2998, 2931, 2891, 2857, 1607, 1583, 1353, 1111, 973, 771, 743, 703; δ_H(250 MHz) 1.04 (9H, s, 3 × CH_3), 1.49 (4H, m, 2 × CH_2), 2.05 (2H, td, *J* 6.3, 6.3, $HCCH_2$), 3.65 (2H, t, *J* 6, $SiOCH_2$), 4.60 (2H, d, *J* 5.5, OCH_2), 4.69 (d, *J* 3.6, OCH_2 minor), 5.52–5.91 (2H, m, HC=CH), 7.00 (1H, dd, *J* 8, 8, ArH), 7.04 (1H, d, *J* 8.5, ArH), 7.35–7.51 (7H, m, ArH), 7.64 (4H, dd, *J* 8, 2, ArH), 7.80 (1H, d, *J* 8, ArH); δ_C(67.5 MHz) 19.1 (C), 25.0 (CH_2), 26.8 (CH_3), 31.9 ($2CH_2$), 63.6 (CH_2), 70.1 (CH_2), 115.0 (CH), 120.2 (CH), 123.6 (CH), 125.4 (CH), 127.5 (CH), 129.4 (CH), 133.8 (CH), 133.9 (C), 135.5 (CH), 136.0 (CH), 140.1 (C), 151.9 (C).

N-[8-(*tert*-Butyldiphenylsilyloxy)oct-2-enyl]-*N*-(2-nitrophenyl)-methanesulfonamide 12c

A solution of 2-nitro-*N*-methylsulfonylaniline (2.59 g, 12 mmol, 1.5 equiv.) and triphenylphosphine (3.14 g, 12 mmol, 1.5 equiv.) in dry THF (60 ml) was cooled to 0 °C under nitrogen. 8-(*tert*-Butyldiphenylsilyloxy)oct-2-enol **10c** (3.06 g, 8 mmol, 1 equiv.) was added followed by diethyl azodicarboxylate (1.9 ml, 2.09 g, 12 mmol, 1.5 equiv.), and the resulting solution was stirred for 17 h. The solvent was removed *in vacuo*, giving an orange material, which was dissolved in ethyl acetate (50 ml) and washed with aqueous sodium hydroxide (2 M, 5 × 25 ml), aqueous hydrochloric acid (2 M, 2 × 25 ml) and water (2 × 25 ml), dried over $MgSO_4$ and the solvent was removed *in vacuo* to give a brown oil. The bulk of the triphenylphosphine oxide was removed by precipitation from the reaction solution. The material was then purified by column chromatography on silica gel eluting with hexane–dichloromethane (10:90) to give N-[8-(tert-*butyldiphenylsilyloxy*)*oct*-2-*enyl*]-N-(2-*nitrophenyl*)-*methanesulfonamide* **12c** as a 6:1 mixture of the *E* and *Z* isomers and as a clear oil (4.1 g, 88%) (Found: MNH_4^+, 598.2770. $C_{31}H_{40}N_2O_5SSi$ requires *MNH*$_4$, 598.2771); ν_{max}(film)/cm^{-1} 3070, 2931, 2857, 1605, 1538; δ_H($CDCl_3$, 400 MHz) 1.05 (9H, s, Bu^t), 1.12–1.34 (4H, m, 2 × CH_2), 1.48–1.55 (2H, m, CH_2), 1.73–1.99 (2H, m, CH_2), 3.04 (3H, s, SO_2CH_3), 3.63 (2H, t, *J* 6.6, CH_2O), 4.12–4.14 (2H, br m, NCH_2CH), 5.46–5.54 (2H, m, CH=CH), 7.38–7.61 (9H, m, 9 × ArH), 7.67–7.71 (4H, m, 4 × ArH), 7.83–7.87 (1H, m, ArH); δ_C($CDCl_3$, 63 MHz) 19.2 (C), 25.1 (CH_2), 25.3 (CH_2), 26.9 (CH_3), 28.5 (CH_2), 29.0 (CH_2), 32.0 (CH_2), 32.3 (CH_2), 40.2 (CH_3), 40.3 (CH_3), 48.1 (CH_2), 53.7 (CH_2), 63.9 (CH_2), 123.0 (CH), 123.7 (CH), 125.1 (CH), 127.7 (CH), 129.3 (CH), 129.4 (CH), 129.6 (CH), 132.0 (C), 132.1 (C), 133.1 (CH), 133.2 (CH), 133.4 (CH), 133.5 (CH), 134.1 (C), 135.6 (CH), 135.9 (CH), 137.7 (CH), 148.8 (C); *m*/*z* (CI) 598 (M^+, 100%), 581 (3), 551 (75), 471 (22).

6-(2-Nitrophenoxy)hex-4-enol 13a

Tetra-*n*-butylammonium fluoride (1 M in tetrahydrofuran, 40 ml, 40 mmol) was added dropwise to a solution of the *tert*-butyl[6-(2-nitrophenoxy)hex-4-enyloxy]diphenylsilane **12a** (9.1 g, 19.2 mmol) in tetrahydrofuran (20 ml) and the mixture stirred for 1 h after which the excess tetrahydrofuran was evaporated *in vacuo*. The resultant brown oil was partitioned between dichloromethane–water (400 ml, 50:50 v/v) and the aqueous phase was further extracted with dichloromethane (2 × 200 ml). The combined organic extracts were dried and evaporated under reduced pressure to give a crude yellow oil. This was adsorbed onto silica gel (from dichloromethane) and further purified by chromatography on silica gel eluting firstly with dichloromethane (100%) and then dichloromethane–ethyl acetate (90:10) to yield 6-(2-*nitrophenoxy*)*hex*-4-*enol* **13a** (4.46 g, 18.8 mmol, 98%) as a yellow oil (Found: C, 60.90; H, 6.65; N, 5.65. $C_{12}H_{15}NO_4$ requires C, 60.75; H, 6.37; N, 5.90%); ν_{max}(film)/cm^{-1} 3368, 2936, 2931, 1608, 1583, 1526, 1353, 974, 780, 746; δ_H(400 MHz) 1.52 (1H, br s, OH), 1.68 (2H, tt, *J* 7, 7, CH_2), 2.18 (2H, td, *J* 7, 7, $HCCH_2$), 3.65 (2H, t, *J* 6.5, $HOCH_2$), 4.62 (2H, dd, *J* 6.4, 1, OCH_2), 4.74 (br d, *J* 4.6, OCH_2 minor),

5.68–5.75 (1H, m, HC=CH), 5.87–5.93 (1H, m, HC=CH), 6.99 (1H, ddd, *J* 8, 8, 1, ArH), 7.06 (1H, dd, *J* 8, 1, ArH), 7.50 (1H, ddd, *J* 8, 8, 1.7, ArH), 7.81 (1H, dd, *J* 8, 1.7, ArH); δ_C(67.8 MHz) 23.9 (CH_2), 28.4 (CH_2), 31.5 (CH_2), 31.7 (CH_2), 61.5 (CH_2), 61.8 (CH_2), 65.4 (CH_2), 69.9 (CH_2), 115.0 (CH), 120.2 (CH), 123.2 (CH), 125.4 (CH), 133.9 (CH), 135.2 (CH), 139.9 (C), 151.8 (C).

7-(2-Nitrophenoxy)hept-5-enol 13b

In a procedure analogous to that for obtaining **13a**, *tert*-butyl-[7-(2-nitrophenoxy)hept-5-enyloxy]diphenylsilane **12b** (3.89 g, 8 mmol) was exposed to tetra-*n*-butylammonium fluoride (1 M in tetrahydrofuran, 16 ml, 16 mmol). The crude yellow oil was adsorbed onto silica (from dichloromethane) and further purified by chromatography on silica gel eluting firstly with dichloromethane (100%) and then dichloromethane–ethyl acetate (75:25) to yield 7-(2-*nitrophenoxy*)*hept*-5-*enol* **13b** (1.92 g, 7.65 mmol, 96%) as a yellow oil (Found: C, 62.09; H, 7.11; N, 5.21. $C_{13}H_{17}NO_4$ requires C, 62.14; H, 6.82; N, 5.57%); ν_{max}(film)/cm^{-1} 3369, 2935, 2862, 1608, 1583, 1353, 974, 746; δ_H(400 MHz) 1.46–1.61 (5H, m, 2 × CH_2, OH), 2.12 (2H, td, *J* 6.7, 6.7, HCCH_2), 3.64 (2H, t, *J* 6.5, HOCH_2), 4.62 (2H, dd, *J* 5.7, 1, ArOCH_2), 4.72 (d, *J* 6, ArOCH_2 minor), 5.69 (1H, m, HC=CH), 5.87 (1H, m, HC=CH), 7.01 (1H, ddd, *J* 8, 8, 1, ArH), 7.04 (1H, d, *J* 8, ArH), 7.50 (1H, ddd, *J* 8, 8, 2, ArH), 7.81 (1H, dd, *J* 8, 1.7, ArH); δ_C(67.8 MHz) 24.6 (CH_2), 31.6 (CH_2), 31.7 (CH_2), 61.9 (CH_2), 69.7 (CH_2), 114.8 (CH), 119.9 (CH), 123.3 (CH), 125.1 (CH), 133.8 (CH), 135.5 (CH), 139.6 (C), 151.6 (C); *m*/*z* (EI) 219 (10%), 151 (23), 139 (52), 67 (100).

***N*-(8-Hydroxyoct-2-enyl)-*N*-(2-nitrophenyl)methanesulfonamide 13c**

A solution of *N*-[8-(*tert*-butyldiphenylsilyloxy)oct-2-enyl]-*N*-(2-nitrophenyl)methanesulfonamide **12c** (2.32 g, 4 mmol, 1 equiv.) and tetrabutylammonium fluoride (1 M in THF, 8 ml, 8 mmol, 2 equiv.) in dry THF (20 ml) was stirred under nitrogen for 16 h. The solvent was removed *in vacuo* to give red material, which was partitioned between dichloromethane (25 ml) and water (25 ml). The aqueous phase was extracted with dichloromethane (2 × 25 ml) and the combined organic portions were washed with water (2 × 25 ml), dried over $MgSO_4$ and the solvent removed *in vacuo* to give an oil. Column chromatography on silica gel and eluting with diethyl ether gave N-(8-*hydroxyoct*-2-*enyl*)-N-(2-*nitrophenyl*)*methanesulfonamide* **13c** as a 6:1 mixture of the *E* and *Z* isomers, as a yellow oil (1.2 g, 88%) (Found: MNH_4^+, 360.1593. $C_{15}H_{22}N_2O_5S$ requires MNH_4, 360.1593); ν_{max}(film)/cm^{-1} 3398, 3350, 2932, 2858, 1604, 1533; δ_H($CDCl_3$, 250 MHz) 1.18–1.28 (4H, m, 2 × CH_2), 1.41–1.51 (2H, m, CH_2), 1.75 (1H, br s, OH), 1.82–1.98 (2H, m, CH_2), 3.01 (3H major, s, SO_2CH_3 major), 3.02 (3H, minor, s, SO_2CH_3 minor), 3.56 (2H, t, CH_2OH), 4.00–4.44 (2H, br m, NCH_2CH), 5.36–5.58 (2H, m, CH=CH), 7.45–7.52 (2H, m, 2 × ArH), 7.62 (1H, ddd, *J* 7.6, 7.6, 1.6, ArH), 7.87 (1H, dd, *J* 7.6, 1.6, ArH); δ_C($CDCl_3$, 67.8 MHz) 24.8 (CH_2), 25.0 (CH_2 minor), 26.7 (CH_2 minor), 28.3 (CH_2), 28.7 (CH_2 minor), 31.7 (CH_2), 32.1 (CH_2), 39.5 (CH_3), 47.8 (CH_2 minor), 53.4 (CH_2), 62.1 (CH_2), 122.7 (CH minor), 123.4 (CH), 124.9 (CH), 129.2 (CH), 129.3 (CH minor), 131.7 (C), 131.8 (C minor), 132.2 (CH minor), 132.4 (CH), 133.2 (CH), 133.3 (CH minor), 135.5 (CH minor), 137.4 (CH), 148.8 (C).

6-(2-Aminophenoxy)hex-4-enol 14a

Sodium borohydride (250 mg, 6.6 mmol) was added to a rapidly stirred solution of copper(II) acetylacetonate (140 mg, 0.5 mmol) in ethanol (60 ml) under nitrogen leading to the formation of a brown suspension. Stirring was contained until a dark 'clumpy' solid precipitated and the supernatant turned clear. 6-(2-*Nitrophenoxy*)*hex*-4-*enol* **13a** (500 mg, 2 mmol) was added in ethanol (10 ml) over 10 min and the mixture was allowed to react for 1.5 h. After quenching with water (200 ml) and concentrating to low volume, the aqueous phase was saturated with solid sodium hydrogen carbonate (1 g), stirred for 1 h and then extracted with dichloromethane (3 × 300 ml). The combined organic phase was washed with brine (2 × 300 ml), aqueous ammonia (35% w/v, 3 × 300 ml) and water (3 × 400 ml), dried and then evaporated under reduced pressure to yield 6-(2-*aminophenoxy*)*hex*-4-*enol* **14a** (418 mg, 2 mmol, 96%) as an orange oil (Found: M^+, 207.1259. $C_{12}H_{17}NO_2$ requires *M*, 207.1259); ν_{max}(film)/cm^{-1} 3354, 2933, 1614, 1504, 739; δ_H(400 MHz) 1.66 (2H, tt, *J* 7, 7, CH_2), 2.18 (2H, td, *J* 7, 7, HCCH_2), 2.98 (2H, br s, NH_2), 3.63 (2H, t, *J* 7, HOCH_2), 4.48 (2H, d, *J* 5.3, OCH_2), 4.60 (d, *J* 6, OCH_2 minor), 5.28 (2H, m, HC=CH), 6.67–6.80 (4H, m, ArH); δ_C(67.5 MHz) 23.8 (CH_2), 28.3 (CH_2), 31.5 (CH_2), 31.8 (CH_2), 61.3 (CH_2), 61.5 (CH_2), 64.0 (CH_2), 68.5 (CH_2), 112.0 (CH), 115.1 (CH), 118.3 (CH), 121.0 (CH), 125.3 (CH), 134.2 (CH), 136.0 (C), 146.2 (C); *m*/*z* (EI) 207 (M^+, 6%), 109 (100), 80 (35), 53 (18).

7-(2-Aminophenoxy)hept-5-enol 14b

In a procedure analogous to that for obtaining **14a**, 7-(2-nitrophenoxy)hept-5-enol **13b** (501 mg, 2 mmol) copper(II) acetylacetonate (131 mg, 0.5 mmol) and sodium borohydride (224 mg, 5.9 mmol) in ethanol (50 ml) were reacted for 1.5 h to give 7-(2-*aminophenoxy*)*hept*-5-*enol* **14b** (425 mg, 1.92 mmol, 96%) as an orange oil (Found: M^+, 221.1434. $C_{13}H_{19}NO_2$ requires *M*, 221.1416); ν_{max}(film)/cm^{-1} 3384, 2933, 1613, 738; δ_H(400 MHz) 1.48 (2H, tt, *J* 7, 7, CH_2), 1.55 (2H, tt, *J* 7, 7, CH_2), 2.11 (2H, td, *J* 7, 7, HCCH_2), 3.04 (3H, br s, OH, NH_2), 3.62 (2H, t, *J* 6.5, HOCH_2), 4.50 (2H, d, *J* 5.5, OCH_2), 4.58 (d, *J* 6, OCH_2 minor), 5.29–5.85 (2H, m, HC=CH), 6.68–6.80 (4H, m, ArH); δ_C(67.5 MHz) 24.7 (CH_2), 31.6 (CH_2), 31.6 (CH_2), 61.7 (CH_2), 68.7 (CH_2), 111.8 (CH), 115.0 (CH), 118.0 (CH), 120.8 (CH), 124.9 (CH), 134.5 (CH), 136.0 (C), 146.0 (C); *m*/*z* (EI) 221 (M^+, 13%), 109 (100), 95 (10), 80 (24).

***N*-(2-Aminophenyl)-*N*-(8-hydroxyoct-2-enyl)methanesulfonamide 14c**

To a stirred solution of copper(II) acetylacetonate (0.11 g, 0.42 mmol, 0.2 equiv.) in ethanol (30 ml) under nitrogen, was added sodium borohydride (0.08 g, 2.1 mmol, 1 equiv.). The resulting mixture was stirred for 30 min, during which time a 'clumpy' black solid formed and the solution became clear. *N*-(8-Hydroxyoct-2-enyl)-*N*-(2-nitrophenyl)methanesulfonamide **13c** (0.72 g, 2.1 mmol, 1 equiv.) in ethanol (10 ml) was added, followed by sodium borohydride (0.16 g, 4.2 mmol, 2 equiv.). The resulting solution was stirred for a further 3 h, and then quenched with water (60 ml). The copper reagent was removed by filtration, and the solvent was removed *in vacuo*. The resulting material was partitioned between dichloromethane (25 ml) and water (25 ml). The aqueous phase was extracted with dichloromethane (2 × 25 ml), and the combined organic portions were washed with water (2 × 15 ml), dried over $MgSO_4$ and the solvent removed *in vacuo* to give an oil (0.64 g). Column chromatography using ~20 g of silica and diethyl ether as the eluent, gave N-(2-*aminophenyl*)-N-(8-*hydroxyoct*-2-*enyl*)*methanesulfonamide* **14c** as a yellow oil (0.58 g, 89%) (Found: MH^+, 313.1586. $C_{15}H_{24}N_2O_3S$ requires *MH*, 313.1586); ν_{max}(film)/cm^{-1} 3477, 3415, 3381, 2931, 2852, 1621; δ_H($CDCl_3$, 250 MHz) 1.20–1.34 (4H, m, 2 × CH_2), 1.43–1.54 (2H, m, CH_2), 1.93–2.01 (2H, m, CH_2), 2.55–2.94 (3H, br s, NH_2, OH), 2.98 (3H, s, SO_2CH_3), 2.99 (3H, s, SO_2CH_3 minor), 3.60 (2H, t, *J* 6.5, CH_2OH), 4.02–4.24 (2H, br m, NCH_2), 5.41–5.59 (2H, m, CH=CH), 6.69–6.81 (2H, m, ArH), 7.05–7.17 (2H, m, ArH); δ_C($CDCl_3$, 63 MHz) 24.8 (CH_2), 25.0 (CH_2), 26.8 (CH_2), 28.3 (CH_2), 28.8 (CH_2), 31.6 (CH_2), 32.2 (CH_2), 38.4 (CH_3), 47.2 (CH_2), 52.7 (CH_2), 62.1 (CH_2), 116.5 (CH), 117.7 (CH), 117.8 (CH), 123.4 (CH), 124.0 (CH), 124.4 (C), 128.9 (CH), 129.0 (CH), 129.2 (CH), 134.4 (CH), 136.2 (CH), 146.4 (C); *m*/*z* (CI) 313 (MH^+, 10%), 235 (5), 109 (100).

2-(6-Hydroxyhex-2-enyloxy)benzenediazonium tetrafluoroborate 15a

6-(2-Aminophenoxy)hex-4-enol **14a** (400 mg, 1.93 mmol) was added dropwise to a solution of nitrosonium tetrafluoroborate (256 mg, 2.2 mmol) in dichloromethane (5 ml) at 0 °C and stirring was continued for 10 min after which the dichloromethane was evaporated under an atmosphere of nitrogen to afford 2-(6-*hydroxyhex*-2-*enyloxy*)*benzenediazonium tetrafluoroborate* **15a** as a red oil. This was forwarded immediately for reaction with TTF without further purification, and spectroscopic data were determined on a small sample; ν_{max}(film)/cm^{-1} 3335, 3110, 2943, 2250, 1592, 735; δ_H(CD_3COCD_3, 400 MHz) 1.67 (2H, tt, *J* 7, 7, CH_2), 2.15 (2H, td, *J* 7, 7, HCCH_2), 3.56 (2H, t, *J* 6, HOCH_2), 5.06 (2H, d, *J* 6, OCH_2), 5.18 (d, *J* 6.2, OCH_2 minor), 5.75–5.90 (1H, m, HC=CHCH_2), 6.09–6.16 (1H, m, HC=CHCH_2), 7.47 (1H, dd, *J* 8, 8, ArH), 7.73 (1H, d, *J* 8, ArH), 8.26 (1H, ddd, *J* 8, 8, 1.5, ArH), 8.55 (1H, dd, *J* 8, 1.5, ArH); δ_C(CD_3COCD_3, 67.5 MHz) 29.0 (CH_2), 32.5 (CH_2), 61.7 (CH_2), 73.3 (CH_2), 102.7 (C), 116.7 (CH), 123.8 (CH), 123.9 (CH), 133.2 (CH), 139.2 (CH), 145.1 (CH), 163.4 (C).

2-(7-Hydroxyhept-2-enyloxy)benzenediazonium tetrafluoroborate 15b

In a procedure analogous to that for obtaining **15a**, 7-(2-aminophenoxy)hept-5-enol **14b** (400 mg, 1.81 mmol) and nitrosonium tetrafluoroborate (233 mg, 2 mmol) in dichloromethane (5 ml) were reacted to afford 2-(7-*hydroxyhept*-2-*enyloxy*)*benzenediazonium tetrafluoroborate* **15b** as a red oil. This was reacted immediately with TTF without further purification. The following data were obtained on a small sample of retained material: ν_{max}(film)/cm^{-1} 3339, 3112, 2938, 2864, 2262, 1671, 1594, 975, 762; δ_H(CD_3COCD_3, 400 MHz) 1.50 (4H, m, 2 × CH_2), 2.28 (2H, td, *J* 6.6, 6.6, HCCH_2), 3.54 (2H, t, *J* 6, HOCH_2), 5.07 (2H, d, *J* 6.3, OCH_2), 5.13 (d, *J* 6.6, OCH_2 minor), 5.78–5.90 (1H, m, HC=CH), 6.07–6.15 (1H, m, HC=CH), 7.48 (1H, dd, *J* 8, 8, ArH), 7.76 (1H, d, *J* 8, ArH), 8.27 (1H, ddd, *J* 8, 8, 1.5, ArH), 8.56 (1H, dd, *J* 8, 1.5, ArH); δ_C(CD_3COCD_3, 67.5 MHz) 25.8 (CH_2), 32.7 (CH_2), 32.9 (CH_2), 62.2 (CH_2), 73.3 (CH_2), 102.7 (C), 116.7 (CH), 123.3 (CH), 123.9 (CH), 133.2 (CH), 139.5 (CH), 145.1 (CH), 163.4 (C).

2-[*N*-(8-Hydroxyoct-2-enyl)-*N*-(methylsulfonyl)amino]benzenediazonium tetrafluoroborate 15c

A solution of *N*-(2-aminophenyl)-*N*-(8-hydroxyoct-2-enyl)-methanesulfonamide **14c** (156 mg, 0.5 mmol, 1 equiv.) in dichloromethane (2.5 ml) was cooled to 0 °C under nitrogen. Nitrosonium tetrafluoroborate (70 mg, 0.6 mmol, 1.1 equiv.) and dichloromethane (2.5 ml) were added, and the mixture was stirred for 30 min. Removal of solvent *in vacuo* gave the 2-[N-(8-*hydroxyoct*-2-*enyl*)-N-(*methylsulfonyl*)*amino*]*benzenediazonium tetrafluoroborate* **15c** as a crude red oil. In order to gain material for compilation of spectroscopic data, purification was attempted. The unstable oil was dissolved in acetone (3 ml) and the solution was added to vigorously stirred diethyl ether (50 ml), causing oil formation round the flask. The bulk of the solvent was decanted off, and the remainder was removed *in vacuo* to leave the diazonium salt as a red oil; ν_{max}(film)/cm^{-1} 3100, 2934, 2862, 2283; δ_H($CDCl_3$, 250 MHz) 1.11–1.56 (6H, m, 3 × CH_3), 1.92–1.98 (2H, m, =CHCH_2), 3.30 (3H, s, SO_2CH_3), 3.45 (2H, t, *J* 7.5, CH_2OH), 4.62 (2H, d, *J* 6.8, NCH_2CH=), 5.52–5.80 (2H, m, CH=CH), 8.10 (1H, ddd, *J* 7.8, 7.8, 1.0, ArH), 8.38 (1H, dd, *J* 8.0, 1.0, ArH), 8.52 (1H, ddd, *J* 7.5, 7.5, 1.5, ArH), 8.95 (1H, dd, *J* 8.2, 1.2, ArH).

3-(Tetrahydrofuran-2-yl)-2,3-dihydrobenzofuran 16a

Tetrathiafulvalene (367 mg, 1.8 mmol) was added to a solution of crude 2-(6-hydroxyhex-2-enyloxy)benzenediazonium tetrafluoroborate **15a** (514 mg, 1.68 mmol) in degassed acetone (5 ml). The acetone was evaporated and the crude residue was adsorbed onto silica gel and purified by column chromatography on silica gel eluting with petrol–ethyl acetate (94 : 6) to afford 3-(*tetrahydrofuran*-2-*yl*)-2,3-*dihydrobenzofuran* **16a** (134 mg, 0.71 mmol, 42% from **14a**) as a pale oil (Found: M$^+$, 190.0995. $C_{12}H_{14}O_2$ requires *M*, 190.0994); ν_{max}(film)/cm^{-1} 3047, 2972, 2872, 1610, 1595, 752; δ_H(400 MHz) spectrum showed this compound to be a 3 : 1 diastereoisomeric mixture and assignments were made from ^{1}H–^{1}H and ^{1}H–^{13}C-2D shift correlation experiments: 1.50–2.07 (4H, m, CH_2CH_2), 3.55 and 3.67 (1H, 2 × m, HCAr), 3.77 (1H, m, H_2CO), 3.86 (ddd, *J* 7, 7, 7, HCO minor), 3.94 (1H, ddd, *J* 7, 7, 7, H_2CO), 4.03 (1H, ddd, *J* 7, 7, 7, HCO), 4.36 and 4.57 (2H, 2 × m, H_2COAr), 6.77–6.86 (2H, m, ArH), 7.10 (1H, m, ArH), 7.21 (dd, *J* 7.4, 0.7, ArH minor), 7.30 (1H, dd, *J* 7.4, 0.7, ArH); δ_C(100 MHz) 25.5 (CH_2), 25.8 (CH_2), 28.1 (CH_2), 29.2 (CH_2), 46.1 (CH), 47.0 (CH), 67.9 (CH_2), 68.2 (CH_2), 72.5 (CH_2), 74.1 (CH_2), 81.0 (CH), 81.2 (CH), 109.3 (CH), 109.5 (CH), 120.1 (CH), 120.2 (CH), 125.1 (CH), 125.3 (CH), 128.2 (C), 128.4 (CH), 128.5 (CH), 160.1 (C), 160.6 (C).

3-(Tetrahydropyran-2-yl)-2,3-dihydrobenzofuran 16b

Tetrathiafulvalene (250 mg, 1.3 mmol) was added to a solution of crude 2-(7-hydroxyhept-2-enyloxy)benzenediazonium tetrafluoroborate **15b** (502 mg, 1.57 mmol) in degassed acetone (5 ml). The acetone was evaporated and the crude residue was adsorbed onto silica gel and purified by column chromatography on silica gel eluting with petrol–ethyl acetate (94 : 6) to afford 3-(*tetrahydropyran*-2-*yl*)-2,3-*dihydrobenzofuran* **16b** (119 mg, 0.58 mmol, 38% from **14b**) as a pale oil (Found: M$^+$, 204.1149. $C_{13}H_{16}O_2$ requires *M*, 204.1150); ν_{max}(film)/cm^{-1} 2936, 2848, 1610, 1595, 752; δ_H(400 MHz) spectrum showed this compound to be an approximately 1 : 1 diastereoisomeric mixture and assignments were made from ^{1}H–^{1}H and ^{1}H–^{13}C-2D shift correlation experiments: 1.28–1.58 (4H, m, 2 × CH_2), 1.80 (2H, m, OCCH_2), 3.30–3.56 (3H, m, HCAr, HCO, H_2CO overlapping), 4.01 (1H, m, H_2CO), 4.45–4.60 (2H, m, H_2COAr), 6.75–6.84 (2H, m, ArH), 7.09–7.19 (1H, m, ArH), 7.21, 7.28 (1H, 2 × d, *J* 7.2, ArH); δ_C(100 MHz) 23.2 (CH_2), 25.9 (CH_2), 26.0 (CH_2), 27.1 (CH_2), 29.0 (CH_2), 47.0 (CH), 47.9 (CH), 68.6 (CH_2), 72.4 (CH_2), 73.8 (CH_2), 79.1 (CH), 79.7 (CH), 109.3 (CH), 109.5 (CH), 119.9 (CH), 120.1 (CH), 125.6 (CH), 125.7 (CH), 127.1 (C), 127.6 (C), 128.4 (CH), 128.5 (CH), 160.3 (C), 160.6 (C).

***N*-Methylsulfonyl-3-oxepan-2-yl-2,3-dihydro-1*H*-indole 16c**

A solution of *N*-(2-aminophenyl)-*N*-(8-hydroxyoct-2-enyl)-methanesulfonamide **14c** (468 mg, 1.5 mmol, 1 equiv.) in dichloromethane (5 ml) was cooled to 0 °C under nitrogen. Nitrosonium tetrafluoroborate (211 mg, 1.8 mmol, 1.1 equiv.) and dichloromethane (5 ml) were added, and the mixture was stirred for 60 min. The solvent was removed *in vacuo*, and then the crude material was dissolved in dry acetonitrile (10 ml) and stirred under N_2 at 0 °C. Tetrathiafulvalene (306 mg, 1.5 mmol, 1 equiv.) was added, and the mixture was stirred for 24 h. Removal of solvent *in vacuo* gave a black material, which was partitioned between dichloromethane (30 ml) and water (20 ml). The aqueous phase was extracted with dichloromethane (2 × 10 ml), and the combined organic portions were washed with water (3 × 20 ml) and dried over $MgSO_4$. Removal of solvent *in vacuo* gave a crude brown oil (190 mg). Gradient elution column chromatography on silica gel (hexane–ethyl acetate) gave impure ether. Repeated column chromatography gave N-*methylsulfonyl*-3-*oxepan*-2-*yl*-2,3-*dihydro*-1H-*indole* **16c** as a 7 : 9 mixture of two diastereomers (17.8 mg, 4.0% from **14c**) (Found: M$^+$, 295.1237. $C_{15}H_{21}NO_3S$ requires *M*, 295.1242); ν_{max}(film)/cm^{-1} 2929, 2859, 1598; δ_H($CDCl_3$, 250 MHz) 1.48–1.85 (8H, m, 4 × CH_2), 2.89, 2.87 (3H, s, SO_2CH_3), 3.34–3.62 (3H, m, NCH_2CH, CH_2OR), 3.76–4.15 (3H, m, NCH_2, CHOR), 7.01–7.07 (1H, m, ArH), 7.19–7.27 (1.5H, m, ArH), 7.39–7.45 (1.5H, m, ArH); δ_C($CDCl_3$, 63 MHz) 25.7 (CH_2), 26.1 (CH_2), 26.5 (CH_2), 30.6 (CH_2), 30.8 (CH_2), 32.7 (CH_2), 33.9 (CH_2), 34.6

(CH_3), 45.6 (CH), 46.6 (CH), 52.2 (CH_2), 52.9 (CH_2), 69.7 (CH_2), 70.1 (CH_2), 80.7 (CH), 81.7 (CH), 113.4 (CH), 113.7 (CH), 123.5 (CH), 123.6 (CH), 125.3 (CH), 126.6 (CH), 128.5 (CH), 132.5 (C), 132.7 (C), 142.3 (C), 142.7 (C); *m*/*z* (EI) 295 (M^+, 35%), 196 (42), 117 (100), 99 (100).

3-(1,6-Dihydroxyhexyl)-*N*-methylsulfonyl-2,3-dihydro-1*H*-indole 17

A solution of *N*-(2-aminophenyl)-*N*-(8-hydroxyoct-2-enyl)-methylsulfonamide **14c** (156 mg, 0.5 mmol, 1 equiv.) in dichloromethane (2.5 ml) was cooled to 0 °C under N_2. Nitrosonium tetrafluoroborate (70 mg, 0.6 mmol, 1.1 equiv.) and dichloromethane (2.5 ml) were added, and the mixture was stirred for 30 min. The solvent was removed *in vacuo*, and then the crude material was dissolved in acetone (5 ml) and stirred under N_2 at 0 °C. Tetrathiafulvalene (102 mg, 0.5 mmol, 1 equiv.) was added, and the mixture was stirred under nitrogen at room temperature for 2 h. Removal of solvent *in vacuo* gave a black material, which was partitioned between dichloromethane (30 ml) and water (20 ml). The aqueous phase was extracted with dichloromethane (2 × 10 ml), and the combined organic portions were washed with water (3 × 20 ml) and dried over $MgSO_4$. Removal of solvent *in vacuo* gave a crude brown oil (190 mg). Gradient elution column chromatography using ~3 g of silica and hexane–ethyl acetate as the eluent, gave impure diol (80 mg). Column chromatography using ~2.5 g of silica and 50% hexane–50% ethyl acetate, gave 3-(1,6-*dihydroxyhexyl*)-N-*methylsulfonyl*-2,3-*dihydro*-1H-*indole* **17** as a 1:1 mixture of two diastereoisomers, as a yellow oil (71 mg, 45%) (Found: MNH_4^+, 331.1692. $C_{15}H_{23}NO_4S$ requires MNH_4, 331.1692); ν_{max}(film)/cm^{-1} 3520, 3382, 2933, 2859; δ_H($CDCl_3$, 250 MHz) 1.25–1.59 (8H, m, 4 × CH_2), 2.13 (2H, br s, 2 × OH), 2.86, 2.88 (3H, s, SO_2CH_3), 3.38–3.45 (1H, m, NCH_2CH), 3.62–3.74 and 3.89–4.08 (5H, m, CH_2OH, CHOH, NCH_2), 7.01–7.09 (1H, m, ArH), 7.22–7.34 (2H, m, ArH), 7.40–7.45 (1H, m, ArH); δ_C($CDCl_3$, 67.8 MHz) 25.7 (CH_2), 25.7 (CH_2), 25.8 (CH_2), 25.8 (CH_2), 32.5 (CH_2), 32.6 (CH_2), 33.9 (CH_2), 34.6 (CH_2), 34.7 (CH_3), 34.8 (CH_3), 46.0 (CH), 46.1 (CH), 50.8 (CH_2), 53.2 (CH_2), 62.7 (CH_2), 62.7 (CH_2), 72.3 (CH), 73.9 (CH), 113.5 (CH), 113.8 (CH), 123.6 (CH), 123.9 (CH), 125.1 (CH), 126.6 (CH), 128.9 (CH), 131.4 (CH), 132.2 (C), 142.7 (CH), 143.0 (C); *m*/*z* (EI) 313 (M^+, 21%), 234 (14), 196 (100), 117 (100).

Diethyl (2-oxotetrahydrofuran-3-yl)phosphonate 19

A mixture of triethyl phosphite (5.0 g, 30 mmol, 1.0 equiv.) and α-bromo-γ-butyrolactone **18** (4.95 g, 30 mmol, 1.0 equiv.) was heated to reflux. After 4 h the mixture was allowed to cool and then rotary evaporated (to remove ethyl bromide). The resulting mixture was then purified by distillation to give diethyl (2-oxotetrahydrofuran-3-yl)phosphonate[13] **19** in the third fraction (bp 120–122 °C at 0.05 mmHg) as a clear liquid (4.7 g, 21.2 mmol, 71%) (Found: M^+, 222.0634. $C_8H_{15}O_5P$ requires *M*, 222.0657); ν_{max}(film)/cm^{-1} 2986, 2914, 1773, 1255, 1028; δ_H(250 MHz, $CDCl_3$) 1.37 (6H, dt, *J* 7.1, 2.0, CH_3CH_2OP), 2.62 (2H, m, CH_2CH), 3.09 (1H, ddd, *J* 24.0, 9.1, 6.9, CH_2CH), 4.15–4.5 (6H, m, CH_2OP, 2 × CH_2OCO); δ_C(67.8 MHz, $CDCl_3$) 16.0 (CH_3), 24.4 (CH_2), 38.3 (CH, J_{C-P} 144), 62.8 (CH_2, J_{C-P} 35), 67.4 (CH_2, J_{C-P} 4.9), 171.9 (C, J_{C-P} 3.6); *m*/*z* (EI^+) 222 (M^+, 13%), 195 (83), 179 (34), 167 (96), 148 (60), 138 (92), 86 (100).

3-Isopropylidenetetrahydrofuran-2-one 20

To a slurry of tetrahydrofuran-washed sodium hydride (0.27 g, 6.77 mmol, 1.0 equiv.) was added diethyl (2-oxotetrahydrofuran-3-yl)phosphonate **19** (1.5 g, 6.77 mmol, 1.0 equiv.) as a solution in dry tetrahydrofuran (100 ml) dropwise over 20 min at 0 °C. The mixture was stirred for 30 min before the addition of dry acetone (0.39 g, 6.77 mmol, 1.0 equiv.) as a solution in tetrahydrofuran (50 ml). The mixture was then stirred for 36 h before the addition of diethyl ether (20 ml) followed by water (50 ml). The tetrahydrofuran was then removed under reduced pressure and the aqueous residue extracted with chloroform (3 × 100 ml) which was then washed with water (2 × 100 ml) and dried ($MgSO_4$) before evaporating to dryness to give a yellow oil that was purified by column chromatography on silica gel (1:4, diethyl ether–petrol) to give 3-isopropylidenetetrahydrofuran-2-one[14] **20** as a colourless oil (498 mg, 3.94 mmol, 58%) (Found: M^+, 126.0692. $C_7H_{10}O_2$ requires *M*, 126.0681); ν_{max}(film)/cm^{-1} 2987, 2915, 1746, 1668; δ_H(250 MHz, $CDCl_3$) 2.10 (3H, s, Me), 2.46 (3H, t, *J* 2.0, Me), 2.75 (2H, m, CCH_2), 4.24 (2H, t, *J* 8.0, CH_2O); δ_C(67.8 MHz, $CDCl_3$) 19.1 (CH_3), 24.1 (CH_3), 27.2 (CH_2), 63.8 (CH_2), 118.1 (C), 149.6 (C), 170.2 (C); *m*/*z* (EI^+) 126 (M^+, 100%), 97 (18), 67 (31).

2-Isopropylidene-1,4-diol 21

To a solution of 3-isopropylidenetetrahydrofuran-2-one **20** (0.9 g, 7.1 mmol, 1.0 equiv.) in diethyl ether (5 ml) was added lithium aluminium hydride (1.08 g, 28.4 mmol, 4.0 equiv.) and the mixture stirred at reflux for 1 h. Water (5 ml) followed by sodium hydroxide (2 M, 5 ml) were added slowly with cooling and the resulting mixture extracted with diethyl ether (5 × 50 ml). The combined diethyl ether phase was dried ($MgSO_4$), evaporated to dryness and purified by column chromatography on silica gel (1:1, diethyl ether–petrol) to give 2-isopropylidenebutane-1,4-diol[15] **21** as a clear colourless oil (0.86 g, 6.67 mmol, 94%) (Found: M^+, 130.0974. $C_7H_{14}O_2$ requires *M*, 130.0994); ν_{max}(film)/cm^{-1} 3313, 2926, 2875, 2731, 1661, 1445, 1373, 1041; δ_H(250 MHz, $CDCl_3$) 1.71 (3H, s, Me), 1.77 (3H, s, Me), 2.42 (2H, t, *J* 5.8, CH_2CH_2OH), 3.66 (2H, t, *J* 5.9, CH_2CH_2OH), 4.11 (2H, s, CCH_2OH); δ_C(67.8 MHz, $CDCl_3$) 20.2 (CH_3), 20.5 (CH_3), 34.8 (CH_2), 61.6 (CH_2), 62.4 (CH_2), 129.2 (C), 132.1 (C); *m*/*z* (EI^+) 130 (M^+, 18%), 115 (14), 99 (20), 97 (97), 83 (63).

4-(*tert*-Butyldiphenylsilyloxy)-2-isopropylidenebutanol 22

To a solution of 2-isopropylidenebutane-1,4-diol **21** (384 mg, 2.95 mmol, 1.0 equiv.) and imidazole (402 mg, 5.9 mmol, 2.0 equiv.) in dry dimethylformamide (50 ml) was added *tert*-butyldiphenylsilyl chloride (0.81 g, 2.95 mmol, 1.0 equiv.) and the mixture stirred for 16 h. The mixture was evaporated to dryness and then water (20 ml) added causing the formation of a white suspension that was extracted with diethyl ether (5 × 50 ml). The organic extract was then dried ($MgSO_4$) and evaporated to dryness to give a yellow oil which was purified by column chromatography (20% diethyl ether–petrol) to give 4-(tert-*butyldiphenylsilyloxy*)-2-*isopropylidenebutandiol* **22** as a clear colourless oil (745 mg, 2.02 mmol, 69%) (Found: MNH_4^+, 386.2515. $C_{23}H_{32}O_2Si$ requires MNH_4, 386.2515); ν_{max}(film)/cm^{-1} 3393, 3070, 3049, 2930, 2857, 1589, 1471, 1111, 1082, 739, 702; δ_H(400 MHz, $CDCl_3$) 1.05 (9H, s, Bu^t), 1.59 (3H, s, Me), 1.75 (3H, s, Me), 2.45 (2H, t, *J* 6.2, CH_2CH_2O), 3.69 (2H, t, *J* 6.3, CH_2CH_2O), 4.12 (2H, s, CH_2OH), 7.35–7.41 (6H, m, ArH), 7.66–7.71 (4H, m, ArH); δ_C(67.8 MHz, $CDCl_3$) 18.9 (C), 20.1 (CH_3), 20.5 (CH_3), 26.7 (CH_3), 33.9 (CH_2), 62.8 (CH_2), 63.5 (CH_2), 127.7 (CH), 129.5 (C), 129.7 (CH), 131.1 (C), 133.0 (C), 135.6 (CH); *m*/*z* (FAB) 353 [(M − Me^+), 6%], 351 (22), 311 (5), 131 (6).

***tert*-Butyl[4-methyl-3-(2-nitrophenoxymethyl)pent-3-enyloxy]-diphenylsilane 23**

2-Nitrophenol (192 mg, 1.38 mmol, 1.0 equiv.) and triphenylphosphine (362 mg, 1.38 mmol, 1.0 equiv.) were dissolved in dry tetrahydrofuran (20 ml). 4-(*tert*-Butyldiphenylsilyloxy)-2-isopropylidenebutanol **22** (508 mg, 1.38 mmol, 1.0 equiv.) was added and the mixture cooled to 0 °C. Diethyl azodicarboxylate (240 mg, 0.21 ml, 1.38 mmol, 1.0 equiv.) was added dropwise over 15 min. The mixture was stirred for 2 h and then more diethyl azodicarboxylate (120 mg, 0.1 ml, 0.69 mmol, 0.5 equiv.) was added before stirring for 12 h. The reaction mixture was evaporated to dryness, dissolved in ethyl acetate (50 ml) and washed with water (50 ml), aqueous sodium hydroxide (2 M,

3 × 50 ml) and aqueous hydrochloric acid (2 M, 50 ml). The organic phase was then dried ($MgSO_4$) and evaporated to dryness before purifying by column chromatography (2% diethyl ether in petrol) to give tert-*butyl*[4-*methyl*-3-(2-*nitrophenoxymethyl*)*pent*-3-*enyloxy*]*diphenylsilane* **23** as a clear yellow oil (480 mg, 0.98 mmol, 71%) [Found: MNH_4^+, 507.268. $C_{29}H_{35}NO_4Si$ requires *MNH*$_4$, 507.2679]; ν_{max}(film)/cm^{-1} 3071, 3048, 2930, 2857, 1606, 1582, 1524, 1485, 1471, 1353, 1111, 1086, 742, 702; δ_H(250 MHz, $CDCl_3$) 1.03 (9H, s, Bu^t), 1.65 (3H, s, Me), 1.74 (3H, s, Me), 2.51 (2H, t, *J* 6.9, C*H*$_2$CH$_2$O), 3.72 (2H, t, *J* 7.0, CH$_2$C*H*$_2$O), 4.51 (2H, s, ArOCH$_2$), 6.96 (1H, d, *J* 8.0, ArH), 6.98 (1H, dd, *J* 8.0, 8.0, ArH), 7.31–7.38 (6H, m, PhH), 7.45 (1H, dd, *J* 8.1, 8.1, ArH), 7.63–7.67 (4H, m, ArH), 7.79 (1H, d, *J* 7.8, ArH); δ_C(67.8 MHz, $CDCl_3$) 19.5 (C), 20.9 (CH_3), 21.2 (CH_3), 27.2 (CH_3), 34.0 (CH_2), 63.1 (CH_2), 70.0 (CH_2), 115.3 (CH), 120.4 (CH), 124.6 (C), 125.8 (CH), 127.9 (CH), 128.0 (C), 129.9 (CH), 134.2 (CH), 135.3 (C), 135.9 (CH), 140.5 (C), 152.8 (C); *m*/*z* (FAB) 251 (4.2%), 139 (16), 135 (100), 131 (6), 122 (9).

4-Methyl-3-(2-nitrophenoxymethyl)pent-3-enol 24

To *tert*-butyl[4-methyl-3-(2-nitrophenoxymethyl)pent-3-enyloxy]diphenylsilane **23** (356 mg, 7.46 × 10^{-4} mol, 1.0 equiv.) was added a solution of tetrabutylammonium fluoride (1 M, 1.5 ml, 1.5 mmol, 2.0 equiv.) and the mixture stirred for 4 h. Water (5 ml) was then added and the mixture extracted with diethyl ether (3 × 20 ml). The organic phase was dried ($MgSO_4$), evaporated to dryness and purified by column chromatography (60 : 40, diethyl ether–petrol) to give 4-*methyl*-3-(2-*nitrophenoxymethyl*)-*pent*-3-*enol* **24** as a clear yellow oil (185 mg, 7.37 × 10^{-4} mol, 99%); ν_{max}(film)/cm^{-1} 3374, 3078, 2932, 1606, 1582, 1518, 1485, 1351, 745; δ_H(250 MHz, $CDCl_3$) 1.79 (3H, s, Me), 1.81 (3H, s, Me), 2.29 (1H, br s, OH), 2.52 (2H, t, *J* 6.6, C*H*$_2$CH$_2$OH), 3.73 (2H, t, *J* 6.5, CH$_2$OH), 4.67 (2H, s, ArOCH$_2$), 7.02 (1H, dd, *J* 8, 8, ArH), 7.13 (1H, d, *J* 8, ArH), 7.54 (1H, dd, *J* 8, 8, ArH), 7.84 (1H, d, *J* 8, ArH); δ_C(100 MHz, $CDCl_3$) 20.6 (CH_3), 20.9 (CH_3), 34.6 (CH_2), 61.3 (CH_2), 69.8 (CH_2), 114.7 (CH), 120.2 (CH), 123.7 (C), 125.6 (CH), 134.3 (CH), 136.1 (C), 139.8 (C), 152.3 (C); *m*/*z* (FAB) 252 [(M + H)$^+$, 1.4%], 207 (3), 138 (6), 123 (14), 122 (14), 113 (48), 77 (32) [Found: $(MNH_4)^+$, 269.1501. $C_{13}H_{17}NO_4$ requires *MNH*$_4$, 269.1501].

3-(2-Aminophenoxymethyl)-4-methylpent-3-enol 25

An analogous procedure as used in the preparation of **14a** was used here with copper(II) acetylacetonate (40 mg, 0.15 mmol, 0.2 equiv.) sodium borohydride (0.43 g, 11.4 mmol, 15 equiv.) and 4-methyl-3-(2-nitrophenoxymethyl)pent-3-enol **24** to give 3-(2-*aminophenoxymethyl*)-4-*methylpent*-3-*enol* **25** as a yellow oil which crystallised on standing to give a cream coloured solid (119 mg, 0.54 mmol, 71%), mp 71–73 °C [Found: MH$^+$, 222.1494. $C_{13}H_{19}NO_2$ requires *MH*, 222.1494]; ν_{max}(disc)/cm^{-1} 3386, 3288, 3200, 2997, 2943, 2872, 1600, 1507, 744; δ_H(250 MHz, $CDCl_3$) 1.79 (3H, s, Me), 1.80 (3H, s, Me), 2.50 (2H, t, *J* 6.6, C*H*$_2$CH$_2$OH), 3.68 (2H, t, *J* 6.6, C*H*$_2$OH), 4.51 (2H, s, ArOCH$_2$), 6.71–6.83 (4H, m, ArH); δ_C(67.8 MHz, $CDCl_3$) 20.5 (CH_3), 20.8 (CH_3), 34.7 (CH_2), 61.3 (CH_2), 68.5 (CH_2), 112.1 (CH), 115.2 (CH), 118.4 (CH), 121.3 (CH), 124.7 (C), 135.0 (C), 136.3 (C), 146.5 (C); *m*/*z* (FAB) 222 [(M + H)$^+$, 4%], 129 (5), 109 (41), 93 (20).

Formation of diazonium salt from 3-(2-aminophenoxymethyl)-4-methylpent-3-enol 25 and reaction with tetrathiafulvalene

To a solution of 3-(2-aminophenoxymethyl)-4-methylpent-3-enol **25** (119 mg, 0.54 mmol, 1.0 equiv.) in dichloromethane (3 ml) at 0 °C was added nitrosonium tetrafluoroborate (63 mg, 0.54 mmol, 1.0 equiv.) and the mixture stirred for 5 min before evaporating the solvent under a strong stream of nitrogen at 0 °C to leave a red oil. Dry acetone (2 ml) was added followed by tetrathiafulvalene (109 mg, 0.54 mmol, 1.0 equiv.) and the mixture stirred for 30 min. The reaction mixture was poured into diethyl ether causing the precipitation of a black solid. The filtrate was evaporated to dryness and purified by column chromatography (1 : 4, diethyl ether–petrol) to give 2′,2′-*dimethylspiro*[2,3-*dihydrobenzofuran*-3,3′-*tetrahydrofuran*] **27** as yellow plates (62 mg, 0.3 mmol, 57%), mp 44–46 °C [Found: MH$^+$, 204.118. $C_{13}H_{16}O_2$ requires *MH*, 204.115]; ν_{max}(disc)/cm^{-1} 2980, 2926, 2876, 1607, 1594, 1478, 1455, 753; δ_H(250 MHz, $CDCl_3$) 1.16 (3H, s, CH_3), 1.27 (3H, s, CH_3), 2.31 (1H, ddd, *J* 12.8, 9.1, 6.8, CC*H*$_2$CH$_2$O), 2.53 (1H, ddd, *J* 12.8, 9.1, 6.7, CC*H*$_2$CH$_2$O), 4.00–4.18 (2H, m, CH$_2$O), 4.35 (1H, d, *J* 9.2, ArOCH$_2$), 4.62 (1H, d, *J* 9.2, ArOCH$_2$), 6.88 (1H, d, *J* 7.9, ArH), 6.94 (1H, dd, *J* 7.5, 7.5, ArH), 7.22 (1H, d, *J* 7.6, ArH), 7.30 (1H, dd, *J* 7.9, 7.9, ArH); δ_C(67.8 MHz, $CDCl_3$) 23.0 (CH_3), 23.1 (CH_3), 38.5 (CH_2), 57.7 (C), 63.2 (CH_2), 78.2 (CH_2), 109.7 (CH), 120.6 (CH), 124.9 (CH), 128.5 (CH), 130.8 (C), 159.7 (C).

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