Vinyl Epoxides: Reagents for Radical-induced DNA Cleavage

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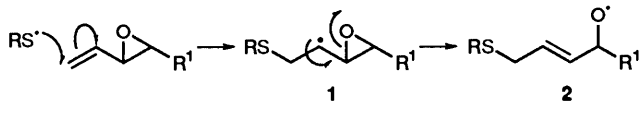
Allyloxyl radicals, formed by addition of thiyl radicals to vinyl epoxides, function as DNA-cleaving agents. Radical-induced damage to DNA is normally caused either by hydrogen-atom abstraction from deoxyribose or addition to the π-bonds of the heterocyclic bases. Model studies showed that allylo · radicals could effect both hydrogen-atom abstraction and addition to simple alkene π-bonds (but ... product of addition to the π-bonds of adenine was observed). Importantly, this model chemistry could be performed in water at room temperature, and using enzymic formation of glutathionyl radicals. An intercalating vinyl epoxide **35** bound to ΦX174 supercoiled DNA caused cleavage when activated by glutathionyl radicals. The potential use of epoxide **35** in reversing the radiation resistance of tumours with a high local concentration of glutathione is discussed.

Ozols has shown that certain tumour cell lines which manifest resistance to radiotherapy have very high intracellular levels of glutathione.[1] Since glutathione (GSH) both quenches harmful reactive entities such as hydroxyl radicals[2] which are produced during radiotherapy by radiolysis of water, and quenches radicals formed on DNA following interaction with these harmful radicals, it suggests that this quenching reaction may be responsible for the resistance. We now propose[3] a method for reversing this protection by allowing the glutathionyl radicals, which are not capable of damaging DNA, to add to a vinyl epoxide located near to DNA.

Thiyl radical addition to a vinyl epoxide gives rise to an epoxycarbinyl radical **1**. The epoxide can then fragment *via* C–O bond cleavage[4] to give an allyloxyl radical **2**. By analogy



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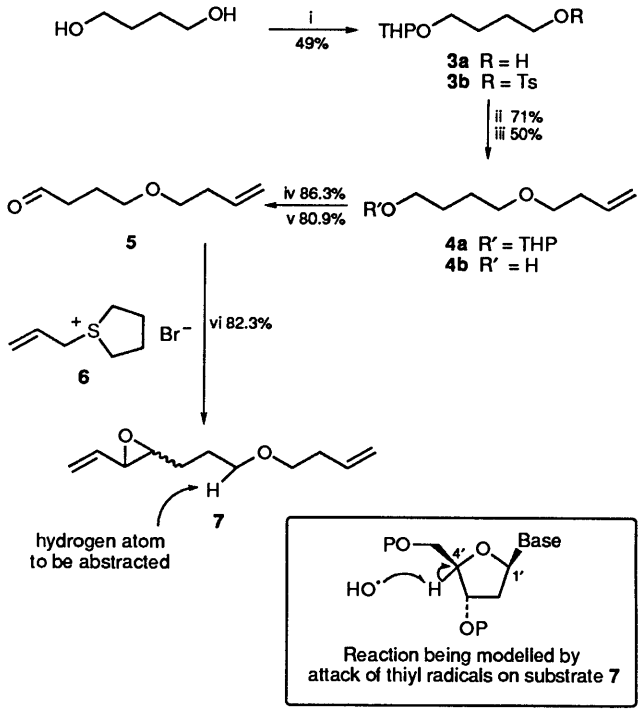
with the hydroxyl radical, such an oxygen-centred radical might be very reactive and capable of damaging DNA. If the vinyl epoxide were attached to a DNA binding agent, then activation by GS· would produce the reactive oxy-radical in the vicinity of DNA, enhancing the possibility of damage to DNA.

Hydroxyl radicals are known to attack DNA in two ways[5]— (a) *via* hydrogen atom abstraction from the deoxyribose sugar ring, eventually leading to cleavage of the DNA backbone,[6] and (b) *via* addition to the π-bonds of the DNA bases.[7] Allyloxyl radicals[4c,8] have alternative reactions available to them not available to hydroxyl radicals, and so studies were first undertaken to probe the ability of allyloxyl radicals to perform the types of reactions which lead to cleavage of DNA.

Modelling of hydrogen atom abstraction from DNA sugars was accomplished by synthesis[9] of a non-cyclic ether analogue **7** of a DNA deoxyribose sugar, in six steps from butane-1,4-diol. After thiyl radical attack on the vinyl epoxide, the resulting oxy-radical is favourably placed to abstract hydrogen from the carbon α to the ether oxygen *via* a six-membered transition state.[10] This mimics hydrogen abstraction from the positions adjacent to an oxygen atom in the deoxyribose of DNA. Photolysis of diphenyl disulfide (giving phenylthiyl radicals) and compound **7** in benzene did indeed, after addition to the epoxide, effect the desired abstraction of hydrogen.

The presence of the resulting radical **8** was confirmed *via* standard 5-*exo* cyclisations A and B onto the two available double bonds to give compounds **10** and **11** as the major products. Cyclisation A followed by a 1,6-H shift, loss of PhS·

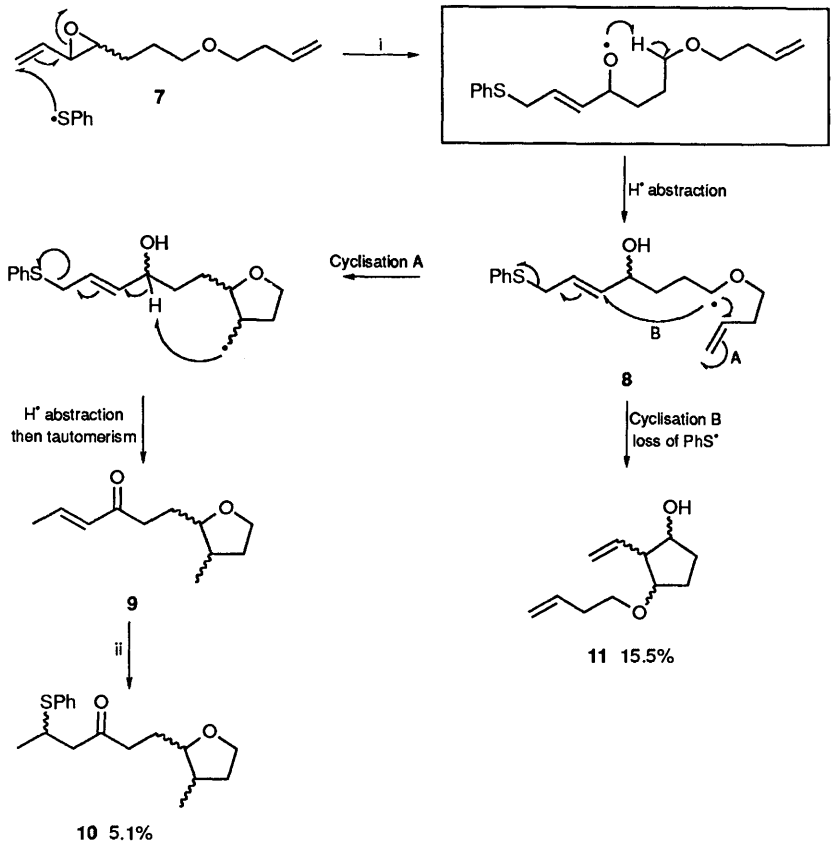


Scheme 1 *Reagents and conditions:* i, diol (10 mol equiv.), dihydropyran, PPTS, CH_2Cl_2, THF, 7 h; ii, TsCl (1.5 mol equiv.), pyridine (2 mol equiv.), $CHCl_3$, 0 °C, 4 h; iii, but-3-en-1-ol (2 mol equiv.), $Bu^t_4NHSO_4$, PhH, 12.5 mol dm^{-3} NaOH, 60 °C, 20 h; iv, Dowex (H^+), MeOH, 60–65 °C, 3 h; v, $(COCl)_2$, DMSO, NEt_3, CH_2Cl_2, −65 to 25 °C, 1 h; vi, $BnEt_3NCl$, 10 mol dm^{-3} NaOH, CH_2Cl_2, −20 to 0 °C, 30 min

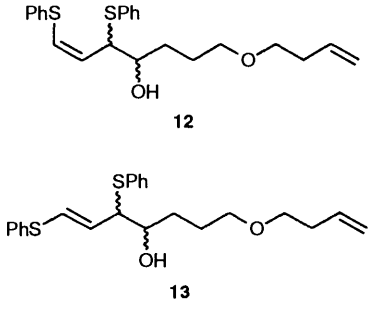
and tautomerism of the enol thus formed gave ketone **9**, observed in trace amounts; addition of thiophenol or PhS· to enone **9** gave ketone **10**. Formation of radical **8** shows that the allyloxy radicals do abstract hydrogen from carbon atoms adjacent to oxygen as in deoxyribose, and hence should be able to effect damage or cleavage of DNA by this mechanism.[11]

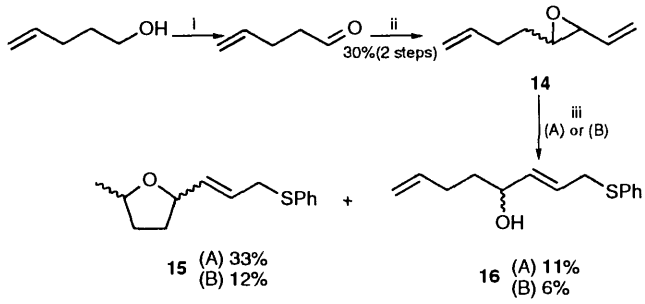
Two by-products of the above reaction were the bisphenylthio compounds **12** and **13**. A possible way in which these compounds could have arisen is shown in Scheme 3.

To model oxy-radical additions onto the π-bonds of DNA bases, compound **14** was synthesized in 2 steps from pent-4-en-1-ol. Addition of allyloxy radicals generated in this way onto the simple double bond[12] proved to be quite easy. Generation of thiyl radicals from thiophenol with (a) azoisobutyronitrile



Scheme 2 *Reagents and conditions:* i, Ph_2S_2 (1 mol equiv.), PhH, *hv* (UV), 80 °C, 2 h; ii, PhSH

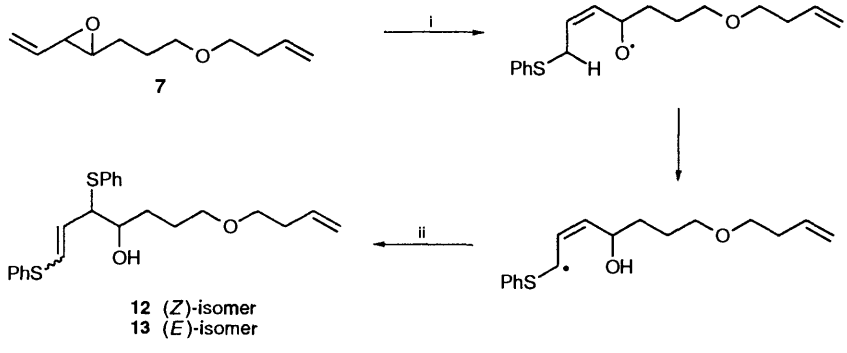




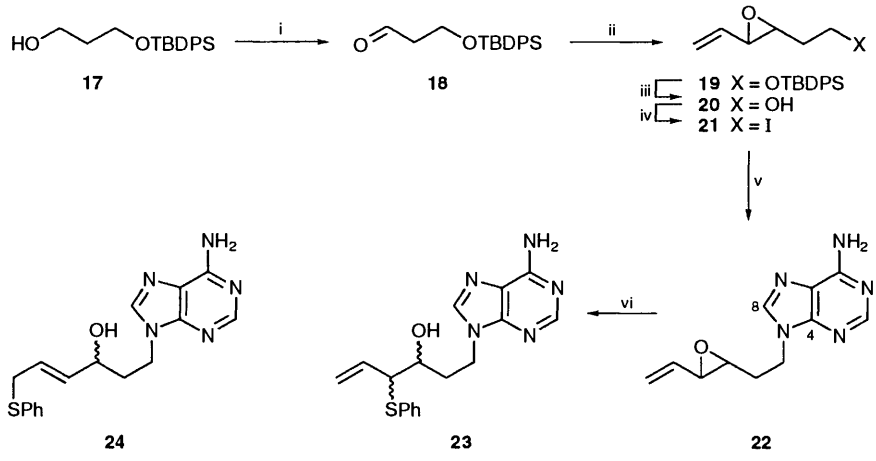
Scheme 4 *Reagents and conditions:* i, PCC, NaOAc, SiO_2, CH_2Cl_2, 2 h; ii, **6**, $BnEt_3NCl$, CH_2Cl_2, 10 mol dm^{-3} NaOH, −25 to 0 °C, 1.5 h; iii, PhS• (A) PhSH, AIBN, THF, 67 °C, 18 h; (B) PhSH, O_2, hexane, 25 °C, 3 days

(AIBN) and heat or (b) oxygen at room temperature, in the presence of epoxide **14**, gave smooth 5-*exo* cyclisation onto the double bond, producing mainly the substituted tetrahydrofuran **15** and some of the quenched alcohol **16**. Thus, quenching of the allyloxyl radical by thiol, a very fast intermolecular reaction, does not suppress the addition to the alkene. Accordingly, provided (i) that the allyloxyl radical can be positioned close to a DNA base, and (ii) that the concentration of free thiol is not very high (as is likely for the *in vivo* case), damage to DNA should result.

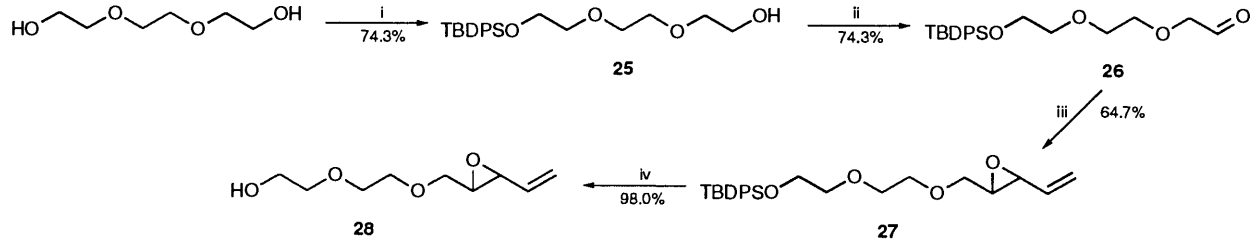
To generate a closer model, the adenine derivative **22** was next synthesized as shown (Scheme 5). Treatment of this molecule with phenylthiyl radicals generated from thermolysis



Scheme 3 *Reagents:* i, PhS•; ii, Ph_2S_2



Scheme 5 *Reagents and conditions:* i, $(COCl)_2$, CH_2Cl_2, DMSO, Pr^iNEt_2, −63 °C; ii, **6**, $BnEt_3NCl$, CH_2Cl_2, 10 mol dm^{-3} NaOH, −20 to 0 °C, 10 min; iii, TBAF, THF, 2 h; iv, imidazole, Ph_3P, I_2, C_6H_6, 5 h; v, adenine, NaH, DMF, 60–70 °C, 1.5 h; vi, PhSH, AIBN, MeCN, MeOH, reflux, 30 h



Scheme 6 *Reagents and conditions:* i, diol (10 mol equiv.), TBDPSCl, imidazole, DMF, 18 h; ii, $(COCl)_2$, DMSO, NEt_3, CH_2Cl_2, −70 to 25 °C, 1 h; iii, **6**, $BnEt_3NCl$, 10 mol dm^{-3} NaOH, CH_2Cl_2, −15 to 0 °C, 20 min; iv, TBAF, THF, 3 h

of AIBN in the presence of thiophenol led to opening of the epoxide ring. However, the products isolated suggested that this ring-opening had occurred to a major extent by nucleophilic attack of the thiol rather than by a radical reaction. No products were detected resulting from attack at C-8 on the imidazole ring of adenine, or from attack on C-4 of the adenine; interestingly, although attack of hydroxyl radical on adenine has a very high rate constant, very low yields of products are *isolated* from this reaction.[5b] (Note: C-4 is the principal site of attack for HO• on adenine, and C-8 is the minor site; however, the product is unstable and readily undergoes cleavage of the C–O bond).[13]

The conditions used in the model reactions so far discussed differ markedly from those required for an *in vivo* study. To be biologically useful the desired radical-induced activation of epoxide must be achievable at ambient temperature and in water. The water-soluble compound **28**, synthesized in four steps from triethylene glycol, was selected as a substrate to test for the addition of thiyl radicals to a vinyl epoxide under these conditions.

Photolysis of bis(2-hydroxyethyl) disulfide in the presence of the alcohol **28** in water gave the oxy-radical **29**, whose formation was established by a characteristic β-cleavage reaction to give diol **30** and aldehydes **31** and **32**, as well as triol **33** formed by hydrolysis of the epoxide (Scheme 7). (Performing the reaction in acetonitrile allowed isolation of sulfides **30** and **31**.) This confirms that simple vinyl epoxides can indeed undergo radical activation by thio radicals at ambient temperature in water. Formation of diol **30** as shown permits a hydroxyethylthio radical to be formed from the corresponding disulfide; the thio radical thus takes part in a chain reaction, although we have not measured the efficiency of this chain.

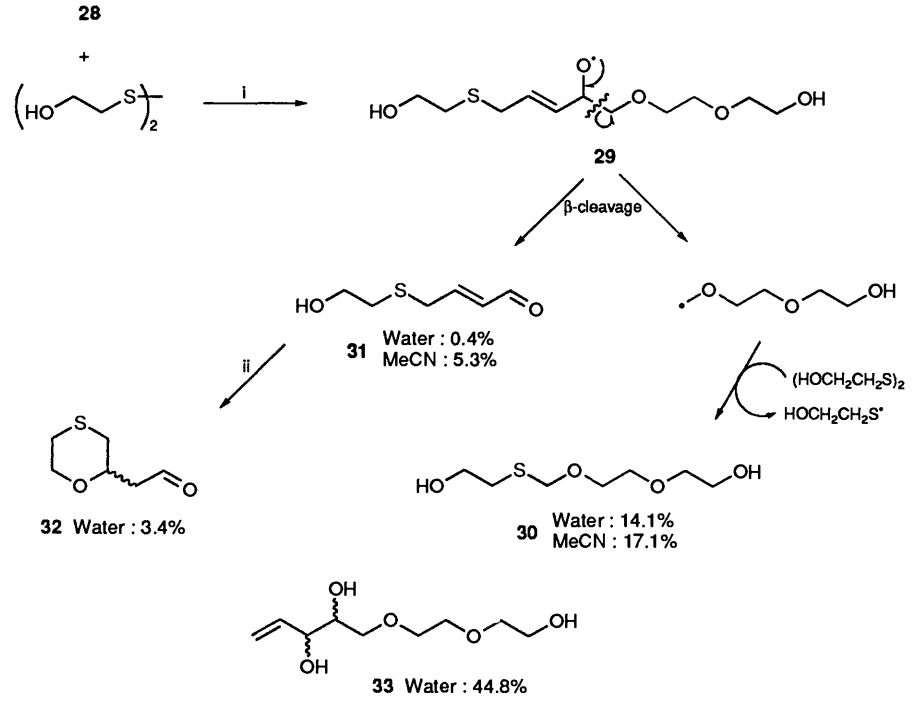
Encouraged by the success of these model studies, we now sought to effect cleavage of DNA with a vinyl epoxide. The compound chosen was the phenanthrolinium salt **35**, which was synthesized from tosyl ester **34**. Phenanthrolinium salts can act as intercalators[14] and the positive charge will lead to attraction to the phosphate ions on the DNA periphery. On activation with a thiyl radical, the oxyl radical **36** should be produced and this oxyl radical should be very slow to add to the phenanthrolinium ring system, since both are electrophilic.

To make the test as biologically relevant as possible, the glutathionyl radical was used as the required thiyl radical and was generated by enzymic[15] means by using horseradish peroxidase (HRP). The incubation with DNA derived from ΦX174 led to the electrophoretogram shown (Fig. 1).

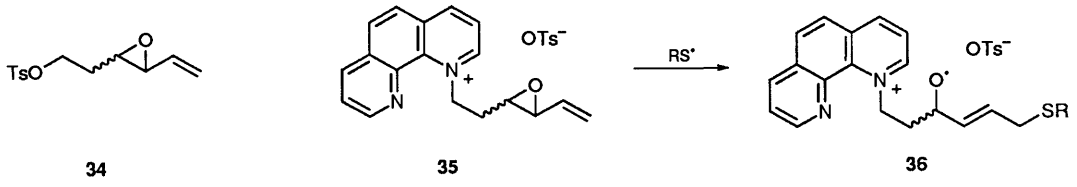
As seen in the electrophoretogram (lane 1), the commercial DNA from ΦX174 exists principally as the supercoiled closed circular duplex of Form I, but with some Form II present. Lane 2 represents a control to show that molecule **35** cannot effect cleavage of DNA on its own under these conditions. It might have been assumed that compound **35** could act as an electrophilic alkylating agent, and that cleavage of DNA would result.[16] Lanes 3 and 4 show that neither glutathione nor hydrogen peroxide can, on their own, effect cleavage of DNA. Lane 5 shows that, under the established conditions for formation of glutathionyl radical with horseradish peroxidase,[15a] but in the absence of compound **35**, no cleavage occurs.

Lanes 6–8 demonstrate that cleavage of DNA to the nicked Form II and to a lesser extent to the linear Form III occurs when the glutathionyl radicals and vinyl epoxide **35** are present. This shows that a combination of vinyl epoxides and thiyl radicals constitutes a novel system for cleavage of DNA. In lanes 9–12, we investigate the exposure of DNA to ten-fold lower concentrations of enzyme, of glutathione, and of hydrogen peroxide. Under these conditions, we cannot see a noticeable difference between the control lane 9 in which no epoxide is present and the lanes 10–12 where the epoxide is present. This means that, at these concentrations, we are not able to detect cleavage of DNA. Cleavage is presumably still occurring but at a slower rate. This is reasonable since the concentrations of enzyme, of hydrogen peroxide, and of glutathione have been dropped substantially, so a significant decrease in radical flux is expected.

In summary, our modelling studies have shown that allyloxyl radicals produced by addition of thio-radical to vinyl epoxides do have the capacity to abstract hydrogen from DNA sugars as



Scheme 7 *Reagents and conditions:* i, MeCN or water, *hv* (UV), 0–40 °C, 7 days; ii, water



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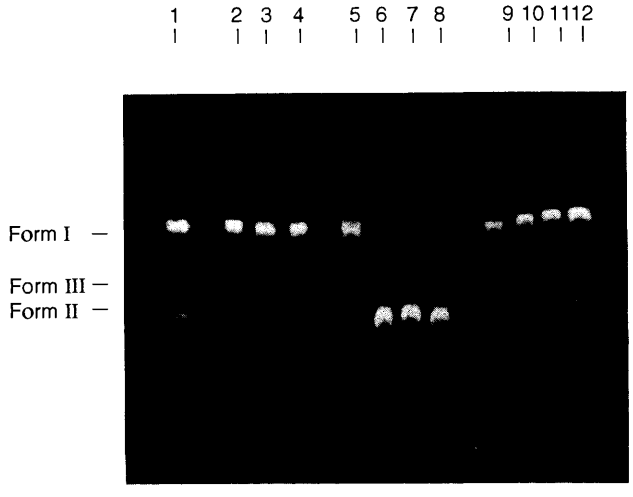

Fig. 1 Lane 1: DNA alone. Lane 2: DNA + 2 mmol dm^{-3} **35**. Lane 3: DNA + 82 mmol dm^{-3} GSH. Lane 4: DNA + 0.82 mmol dm^{-3} H_2O_2. Lane 5: 82 mmol dm^{-3} GSH + 0.82 mmol dm^{-3} H_2O_2 + 0.8 mg cm^{-3} HRP. Lane 6: As Lane 5 plus 2 mmol dm^{-3} **35**. Lane 7: As Lane 5 plus 200 μmol dm^{-3} **35**. Lane 8: As Lane 5 plus 20 μmol dm^{-3} **35**. Lane 9: 8.2 mmol dm^{-3} GSH + 82 μmol dm^{-3} H_2O_2 + 0.08 mg cm^{-3} HRP. Lane 10: As Lane 9 plus 2 mmol dm^{-3} **35**. Lane 11: As Lane 9 plus 200 μmol dm^{-3} **35**. Lane 12: As Lane 9 plus 20μmol dm^{-3} **35**. Loading 0.5 μg DNA per lane (14 nmol dm^{-3}). All reactions were performed in 0.25 mmol dm^{-3} NH_4OAc buffer (10 mm^3; pH 7.05) at 25 °C for 1 h, under oxygen. Electrophoresis was performed on a 0.8% agarose gel at 100 V (3.7 V cm^{-1}) for 3 h (running buffer: 1 × TAE: 40 mmol dm^{-3} Tris Acetate + 1 mmol dm^{-3} EDTA, pH 8.2; ethidium bromide added).

the first step in known reaction pathways to cleavage of the DNA sugar phosphate backbone. We have shown that these radicals can be produced in water at ambient temperature. Further, it has been shown that a vinyl epoxide attached to a DNA intercalator can cleave ΦX174 DNA in the presence of glutathionyl radicals formed in an enzyme reaction. As these radicals are formed at high concentrations when certain cancer cells containing high levels of glutathione are irradiated, it is proposed that compounds of this type may have dual action as antitumour agents, (a) in radiotherapy as described above and (b) in chemotherapy as alkylating agents.[16] Preliminary results have recently indicated promising antitumour activity against various ovarian cancer cell lines.[17]

Experimental

M.p.s were measured on a Kofler hot-stage apparatus unless otherwise indicated. Microanalyses were determined using a Perkin-Elmer 240B elemental analyser. UV spectra were recorded on a Philips PU 8720 spectrometer. IR spectra were recorded on a Perkin-Elmer 1720-X FTIR spectrometer. ^1H NMR (^{13}C NMR) spectra were recorded at 80 MHz on a Bruker WP80SY, at 90 MHz (22.5 MHz) on a JEOL FX90Q, at 250 MHz on a Bruker WM250, at 270 MHz (67.5 MHz) on a JEOL EX270, and at 400 MHz (100 MHz) on a Bruker AM400 spectrometer. For both ^1H and ^{13}C NMR, the solvent used was deuteriochloroform, and with any solvent the internal reference was tetramethylsilane at δ 0.00, unless otherwise indicated. *J*-Values are given in Hz. Mass spectra were recorded on VG Micromass 70E and AEI MS902 spectrometers, or (for accurate FAB and CI spectra) at the SERC mass spectral unit in Swansea.

Column chromatography was performed using Sorbsil C60 'Flash' silica gel (May and Baker) unless otherwise indicated. Also used was Fluka Kieselgel HF254 silica [for preparative TLC (PLC)] and Brockmann Grade I neutral alumina (BDH).

Light petroleum (40–60 °C), pentane, dichloromethane, ethyl acetate and toluene were distilled before use.

HPLC was performed on a Waters 440 machine using (i) a Waters μ-Porasil 7.8 × 300 mm S-15 semi-preparative column, or (ii) a Waters Porasil 19 × 300 mm S-15 preparative column, using distilled solvents.

For reactions, solvents were dried and/or distilled before use where necessary. Tetrahydrofuran (THF) was freshly distilled from sodium–benzophenone. Benzene and diethyl ether were dried over sodium wire. Actonitrile was distilled from phosphoric oxide onto 3 Å molecular sieves and potassium carbonate. Methanol was distilled from magnesium and iodine onto 3 Å sieves. Dichloromethane and chloroform were distilled onto 3 Å sieves.

Pyridine and amines were distilled from calcium hydride onto potassium hydroxide pellets. Dimethyl sulfoxide (DMSO), triethylene glycol, propane-1,3-diol and butane-1,4-diol were distilled from calcium hydride onto 3 Å or 4 Å sieves. Dimethylformamide (DMF) was stirred over calcium hydride overnight, filtered, and distilled onto 3 Å sieves.

Photolysis reactions used a Philips ML'U' 300 W mercury discharge lamp; the strongest UV frequencies are 365.5, 313.0, 302.5, 289.4 and 280.4 nm.

4-(*Tetrahydropyran-2-yloxy*)*butan-1-ol* **3a**.[18]—To a rapidly stirred solution of butane-1,4-diol (477.8 g, 5.30 mol, 10.6 mol equiv.) and pyridinium toluene-*p*-sulfonate (PPTS) (12.57 g, 50 mmol, 0.1 mol equiv.) in dry dichloromethane (900 cm^3) and dry THF (350 cm^3) under nitrogen was added a solution of 2,3-dihydro-4*H*-pyran (42.06 g, 500 mmol, 45.6 cm^3) in dichloromethane (150 cm^3) slowly (dropping funnel) over a period of 2 h. After being stirred for another 5 h, the solution was evaporated to dryness, the residue was taken up in diethyl ether (1.2 dm^3) and extracted with saturated brine (1.2 dm^3) and water (400 cm^3). The aqueous phases were back-extracted with diethyl ether (2 × 600 cm^3) and the combined organic layers were dried ($MgSO_4$), evaporated to dryness, and the residue was chromatographed using dichloromethane–ethyl acetate [4:1 and 2:1 (R_f 0.21)] to give 4-(tetrahydropyran-2-yloxy)-butan-1-ol **3a** as an oil (42.50 g, 243.9 mmol, 48.8%), b.p. 115–120 °C at 0.2–0.3 mmHg (Found: MH^+, 175.1322. Calc. for $C_9H_{19}O_3$: *m/z* 175.1334); ν_{max}(film)/cm^{-1} 3392 and 1024; δ_H(250 MHz) 1.5–1.9 (10 H, m, 5 × CH_2), 1.97 (1 H, s, OH), 3.48 (2 H, m, 1 H of R'OCH_2 and 1 H of ROCH_2), 3.68 (2 H, t, *J* 6.0, HOCH_2), 3.83 (2 H, m, 1 H, of R'OCH_2 and 1 H of ROCH_2) and 4.61 (1 H, t, *J* 3.5, OCHO); δ_C(22.5 MHz) 18.95 (t), 24.97 (t), 25.78 (t), 29.03 (t), 30.17 (t), 61.43 (t), 66.79 (t) and 98.16 (d); *m/z* (FAB) 175 (MH^+, 36%), 173 (9), 101 (47), 85 (100), 73 (86) and 55 (85).

4-(*Tetrahydropyran-2-yloxy*)*butyl Toluene-*p*-sulfonate* **3b**.—To an ice-cooled solution of 4-(tetrahydropyran-2-yloxy)butan-1-ol **3a** (42.50 g, 243.9 mmol) in chloroform (200 cm^3), freshly passed through a long alumina plug to remove all ethanol stabiliser, were added pyridine (39.5 cm^3, 488 mmol, 2 mol equiv.), then tosyl chloride (69.76 g, 366 mmol, 1.5 mol equiv.) in parts over a period of 10 min. The mixture was stirred at 0 °C for 4 h, diluted with dichloromethane (200 cm^3), and extracted with aq. copper sulfate (4%, then 20%) until no further darkening of the aqueous layer occurred. The combined aqueous layers were back-extracted with dichloromethane (2 × 50 cm^3) and the combined organic layers were extracted with water (2 × 100 cm^3), dried ($MgSO_4$), and evaporated to dryness. The green residue was chromatographed using light petroleum–dichloromethane [3:1,1:1 (R_f 0.07) and 1:2] to give 4-(tetrahydropyran-2-yloxy)butyl toluene-*p*-sulfonate **3b** as an oil (56.69 g, 172.6 mmol, 70.8%), ν_{max}(film)/cm^{-1} 1599, 1496, 1359, 1189, 815, 665 and 556; δ_H(250 MHz) 1.5–1.8 (10 H, m, 5 × CH_2), 2.45 (3 H, s, Me), 3.34 (1 H, dt, *J* 9.7 and 6.0, ROCH_2), 3.47 (1 H, m, R'OCH_2), 3.69 (1 H, dt, *J* 9.7 and 6.2, ROCH_2), 3.80 (1 H, m, R'OCH_2), 4.07 (2 H, t, *J* 6.4, TsOCH_2), 4.52 (1 H, br m, OCHO), 7.35 (2 H, d, *J* 8.4, ArH) and 7.79 (2 H, d, *J* 8.3, ArH); δ_C(22.5 MHz) 19.61 (t), 21.51 (q), 25.52 (t), 25.73 (t), 26.11 (t), 30.72 (t), 62.25 (t), 66.47 (t), 70.48 (t), 98.81 (d), 127.85 (d), 129.86 (d), 133.49 (s) and 144.65 (s); *m/z* (EI) 216 (13%), 214 (11), 173 (72), 172 (56.0), 91 (100), 85 (8) and 71 (52).

But-3-enyl-4-(tetrahydropyran-2-yloxy)butyl Ether **4a**.—To a solution of 4-(tetrahydropyran-2-yloxy)butyl toluene-*p*-sulfonate **3b** (16.42 g, 50 mmol), but-3-en-1-ol (7.211 g, 100 mmol, 2 mol equiv.) and tetrabutylammonium hydrogen sulfate (1.698 g, 5 mmol, 10 mol%) in benzene (35 cm^3) was added aq. sodium hydroxide (50%; 100 cm^3) and the mixture was mechanically stirred at 60 °C for 19.5 h. The cooled mixture was diluted with diethyl ether (200 cm^3), the organic layer was extracted with water (4 × 100 cm^3), and the combined aqueous layers were extracted with diethyl ether (50 cm^3). The combined organic layers were dried ($MgSO_4$), evaporated to dryness, and chromatographed using light petroleum–diethyl ether [20:1, 9:1 and 5:1 (R_f 0.28)] to give *but-3-enyl* 4-(*tetrahydropyran-2-yloxy*)*butyl ether* **4a** as a liquid (5.708 g, 25.0 mmol, 50.0%), b.p. 82 °C at 0.5 mmHg (Found: MH^+, 229.1804. $C_{13}H_{25}O_3$ requires *m/z* 229.1804); ν_{max}(film)/cm^{-1} 3078, 1642, 991 and 911; δ_H(250 MHz) 1.5–1.9 (10 H, m, 5 × CH_2), 2.33 (2 H, m, =CHCH_2), 3.4 (1 H, m, OCH_2), 3.47 (4 H, t, *J* 6.8, 2 × OCH_2), 3.5 (1 H, m, OCH_2), 3.76 (1 H, dt, *J* 9.5 and 6.5, OCH_2), 3.86 (1 H, ddd, *J* 11.2, 7.2 and 3.8, OCH_2), 4.59 (1 H, t, *J* 3.4, OCHO), 5.05 (2 H, m, $=CH_2$) and 5.83 (1 H, ddt, *J* 17.1, 10.3 and 6.8, =CH); δ_C(22.5 MHz) 19.67 (t), 25.62 (t), 26.65 (t), 30.83 (t), 34.29 (t), 62.19 (t), 67.34 (t), 70.21 and 70.75 (t), 98.81 (d), 116.20 (t) and 135.44 (d); *m/z* (FAB) 238 (THP^+ + MNBA, 12%), 229 (MH^+, 22), 145 (100), 127 (98), 101 (29), 85 (100), 73 (99) and 55 (89).

4-(*But-3-enyloxy*)*butan-1-ol* **4b**.—To a solution of but-3-enyl 4-(tetrahydropyran-2-yloxy)butyl ether **4a** (10.95 g, 47.96 mmol) in methanol (250 cm^3) was added Dowex 50W-X8(H) acidic resin beads (7.82 g), and the mixture was stirred at 60–65 °C for 3 h. The beads were filtered off and washed well with methanol, then the solution was evaporated to dryness and the residue was chromatographed using light petroleum–diethyl ether (6:1 to 2:3) to give starting material **4a** (0.6749 g, 2.96 mmol, 5.3% recovery) and 4-(*but-3-enyl*)*butan-1-ol* **4b** as a liquid (6.95 g, 48.2 mmol, 86.3%) [(R_f 0.18) 1:1 light petroleum–diethyl ether], b.p. 57 °C at 0.01 mmHg (Found: 2M + H^+, 289.2379. $C_{16}H_{33}O_4$ requires *m/z* 289.237 88); ν_{max}(film)/cm^{-1} 3375, 3078, 1642, 995 and 915; δ_H(250 MHz) 1.68 (4 H, m, 2 × CH_2), 2.35 (2 H, tddd, *J* 6.8, 1.4, 1.4, 1.4, =CHCH_2), 2.57 (1 H, br s, OH), 3.48 (2 H, t, *J* 5.7, OCH_2), 3.50 (2 H, t, *J* 6.8, OCH_2), 3.64 (2 H, t, *J* 5.9, HOCH_2), 5.07 (2 H, m, $=CH_2$) and 5.82 (1 H, ddt, *J* 17.1, 10.2 and 6.8, =CH); δ_C(22.5 MHz) 26.60 (t), 29.96 (t), 34.24 (t), 62.25 (t), 70.32 (t), 70.91 (t), 116.31 (t) and 135.22 (d); *m/z* (FAB) 289 (2M + H^+, 38), 155 (71), 136 (75), 107 (76), 89 (100) and 55 (100).

4-(*But-3-enyloxy*)*butanal* **5**.—To a solution of oxalyl dichloride (6.34 cm^3, 72.7 mmol, 1.1 mol equiv.) in dry dichloromethane (150 cm^3) under nitrogen and cooled to ~ −65 °C was added a solution of dry DMSO (10.32 cm^3, 145.4 mmol, 2.2 mol equiv.) in dichloromethane (30 cm^3) over 9 min (dropping funnel). The solution was stirred for 8 min, then a solution of 4-(but-3-enyloxy)butan-1-ol **4b** (9.53 g, 66.1 mmol) in dichloromethane (65 cm^3) was added during 12 min (dropping funnel) and the solution was stirred for 26 min. Triethylamine (46 cm^3, 331 mmol, 5 mol equiv.) was added (syringe), the white suspension was stirred for 5 min, then was

allowed to warm to room temperature. The mixture was poured onto dichloromethane (200 cm^3) and extracted with water (350 cm^3) and hydrochloric acid (2 mol dm^{-3}; 250 + 100 cm^3). The combined aqueous extracts were back-extracted with dichloromethane (100 cm^3) and the combined organic layers were extracted with water (200 cm^3), dried ($MgSO_4$), evaporated to dryness, and chromatographed using light petroleum–diethyl ether [12:1 and 9:1 (R_f 0.15)] to give 4-(*but*-3-*enyloxy*)*butanal* **5** as a liquid (7.60 g, 53.5 mmol, 80.9%), b.p. 110 °C at 143 mmHg (Found: MH^+, 143.1072. $C_8H_{15}O_2$ requires *m/z* 143.1072); ν_{max}(film)/cm^{-1} 3077, 2723, 1725, 1641, 995 and 916; δ_H(250 MHz) 1.91 (2 H, tt, *J* 6.6 and 6.6, $CH_2CH_2CH_2$), 2.31 (2 H, tddd, *J* 6.7, 1.4, 1.4 and 1.4, =CHCH_2), 2.53 [2 H, td, *J* 7.1 and 1.6, HC(O)CH_2], 3.46 (4 H, t, *J* 6.4, 2 × OCH_2), 5.05 (2 H, m, $=CH_2$), 5.81 (1 H, ddt, *J* 17.1, 10.3 and 6.7, =CH) and 9.78 (1 H, t, *J* 1.6, CHO); δ_C(22.5 MHz) 22.70 (t), 34.18 (t), 40.96 (t), 69.69 (t), 70.26 (t), 116.20 (t), 135.33 (d) and 201.85 (d); *m/z* (FAB) 278 (100), 206 (68), 143 (MH^+, 100), 127 (100) and 101 (51).

1-*Allyltetrahydrothiophenium Bromide* **6**.[9]—To a solution of tetrahydrothiophene (26.46 cm^3, 0.30 mol) in dry methanol (100 cm^3) was added allyl bromide (31.2 cm^3, 0.36 mol, 1.2 mol equiv.; syringe) and the solution was stirred under nitrogen for 22 h at 25 °C. The solvent was removed under reduced pressure, and the solid residue was washed with light petroleum (2 × 100 cm^3), then was evacuated overnight (oil-pump) to give 1-allyltetrahydrothiophenium bromide **6** as light beige, deliquescent crystals (61.83 g, 0.296 mol, 98.5%), m.p. 53–56 °C (sealed tube) [Found: M^+ (cation only), 129.0738. Calc. for $C_7H_{13}S^+$: *m/z* 129.0738]; ν_{max}(film)/cm^{-1} 3436, 3079, 1635, 1435 and 953; δ_H(250 MHz) 2.44 (4 H, m, 3- and 4-H_2), 3.62 (2 H, m, 2- and 5-H), 3.96 (2 H, m, 2- and 5-H), 4.48 (2 H, d, *J* 7.3, =CHCH_2), 5.60 (1 H, d, *J* 10.0, $=CH_2$), 5.71 (1 H, dd, *J* 16.9 and 0.9, $=CH_2$) and 5.93 (1 H, ddt, *J* 17.0, 9.8 and 7.3, =CH); δ_C(22.5 MHz) 29.15 (t), 43.34 (t), 44.86 (t), 125.52 (d) and 127.15 (t); *m/z* (FAB) 339 ($2M^+ + {}^{81}Br^-$, 18.0%), 337 ($2M^+ + {}^{79}Br^-$, 17), 130 (MH^+, 40), 129 [M^+ (cation only), 100] and 87 (83).

But-3-*enyl* 4,5-*Epoxyhept*-6-*enyl Ether* **7**.[9]—A rapidly mechanically stirred solution of 1-allyltetrahydrothiophenium bromide **6** (12.89 g, 61.6 mmol, 1.2 mol equiv.), the aldehyde **5** (7.30 g, 51.3 mmol) and benzyltriethylammonium chloride (1.1694 g, 10 mol%) in dichloromethane (100 cm^3) was cooled to −20 °C and cool (5 °C) aq. sodium hydroxide (10 mol dm^{-3}; 80 cm^3) was added rapidly over a period of 2.5 min (dropping funnel). The vessel was warmed to 0 °C and the mixture was stirred for 30 min before being diluted with dichloromethane (50 cm^3) and water (150 cm^3) and the separated aqueous layer was extracted with dichloromethane (2 × 75 cm^3). The combined organic layers were extracted with water (2 × 150 cm^3), dried ($MgSO_4$), evaporated to dryness, and the residue was chromatographed using light petroleum–diethyl ether (13:1) to give but-3-enyl-4,5-epoxyhept-6-enyl ether **7** as a liquid (7.70 g, 42.3 mmol, 82.3%), present as the *trans* and *cis* epoxide diastereoisomers (58:42%). Partial separation by chromatography yielded a little of each of the two pure diastereoisomers.

But-3-*enyl* trans-4,5-*epoxyhept*-6-*enyl ether* (**7***trans*) as a liquid (0.81 g, 4.44 mmol, 8.7%) [(R_f 0.59) 4:1 light petroleum–diethyl ether], b.p. 100 °C at 0.5 mmHg (Found: C, 72.7; H, 10.3. $C_{11}H_{18}O_2$ requires C, 72.49; H, 9.95%); ν_{max}(film)/cm^{-1} 3079, 1642, 987 and 917; δ_H(250 MHz) 1.7 (4 H, m, 2 × CH_2), 2.33 (2 H, dttdd, *J* 6.7, 6.7, 1.3, 1.3 and 1.3, =CHCH_2), 2.86 [1 H, td, *J* 5.4 and 2.2, CH_2C*H*(O)], 3.10 [1 H, dd, *J* 7.2 and 2.2, =CHC*H*(O)], 3.47 (4 H, t, *J* 6.8, 2 × OCH_2), 5.06 (2 H, m, $=CH_2$), 5.26 (1 H, dd, *J* 9.9 and 2.0, $=CH_2$), 5.45 (1 H, dd, *J* 17.2 and 2.1, $=CH_2$), 5.58 (1 H, ddd, *J* 17.2, 9.9 and 7.3, =CH) and 5.82 (1 H, ddt, *J* 17.2, 10.2 and 6.7, =CH); δ_C(22.5 MHz) 26.11 (t), 28.88 (t), 34.24 (t), 58.29 (d), 59.82 (d), 70.10 (t), 116.04 (t), 118.21 (t), 135.38 (d) and 136.19 (d); *m/z* (FAB) 183 (MH^+, 7.4%), 111 (32), 69 (50) and 55 (100); and *but*-3-*enyl* cis-4,5-*epoxyhept*-6-*enyl ether* (**7***cis*) as a liquid (0.6720 g, 3.69 mmol, 7.2%) [(R_f 0.54) 4:1 light petroleum–diethyl ether], b.p. 100 °C at 0.4 mmHg (Found: MH^+, 183.139. $C_{11}H_{19}O_2$ requires *m/z* 183.138 50); ν_{max}(film)/cm^{-1} 3078, 1640, 987 and 922; δ_H(250 MHz) 1.7 (4 H, m, 2 × CH_2), 2.33 (2 H, dtdd, *J* 6.8, 6.8, 1.3, and 1.3, =CHCH_2), 3.12 [1 H, td, *J* 6.1 and 4.4, CH_2C*H*(O)], 3.41 [1 H, dd, *J* 7.3 and 4.3, =CHC*H*(O)], 3.47 (4 H, t, *J* 6.8, 2 × CH_2O), 5.05 (2 H, m, $=CH_2$), 5.36 (1 H, ddd, *J* 10.6, 1.8 and 0.6, $=CH_2$), 5.48 (1 H, ddd, *J* 17.2, 1.8 and 0.6, $=CH_2$), 5.72 (1 H, ddd, *J* 17.2, 10.3 and 7.1, =CH) and 5.82 (1 H, ddt, *J* 17.1, 10.3 and 6.7, =CH); δ_C(22.5 MHz) 24.70 and 26.65 (t), 34.35 (t), 56.83 (d), 58.18 (d), 70.16 (t), 116.04 (t), 119.78 (t), 133.05 (d) and 135.44 (d): *m/z* (FAB) 183 (MH^+, 47%), 111 (M^+ − but-3-enyloxy, 86), 69 (69) and 55 (91).

Photolytic Addition of Diphenyl Disulfide onto But-3-*enyl* 4,5-*epoxyhept*-6-*enyl Ether* **7** *in Benzene*.—To a solution of but-3-enyl 4,5-epoxyhept-6-enyl ether **7** (0.911 g, 5 mmol), present as the *trans* and *cis* epoxide diastereoisomers (59:41%), in dry deoxygenated benzene (250 cm^3) under nitrogen and irradiated with UV light from a sunlamp was added a solution of diphenyl disulfide (1.201 g, 5.5 mmol, 1.1 mol equiv.) in benzene (20 cm^3) during 1.5 h (syringe pump), during which the solution attained reflux temperature. After another 30 min the solution was evaporated to dryness and repeatedly chromatographed using light petroleum–diethyl ether (4:1 to 1:1), then toluene–diethyl ether (20:1 and 9:1) to give (i) a crude fraction (1) containing 1-(3-methyltetrahydrofuran-2-yl)-5-(phenylthio)hexan-3-one **10** (0.185 g) [(R_f 0.65–0.59), 1:1 light petroleum–diethyl ether; (R_f 0.72–0.58), 4:1 toluene–diethyl ether]; (ii) a crude fraction (2) containing 7-(but-3-enyloxy)-1,3-bis(phenylthio)hept-1-en-4-ol **12** and **13** (0.089 g) [R_f 0.59–0.52), 1:1 light petroleum–diethyl ether; (R_f 0.60–0.53), 4:1 toluene–diethyl ether]; (iii) a crude fraction (3) containing mainly 3-(but-3-enyloxy)-2-vinylcyclopentanol **11** [(R_f 0.48–0.38), 1:1 light petroleum–diethyl ether; (R_f 0.37–0.25), 4:1 toluene–diethyl ether]; and (iv) the major diastereoisomer of 3-(*but*-3-*enyloxy*)-2-*vinylcyclopentanol* **11** as a slightly coloured oil (0.104 g, 0.573 mmol, 11.5%) [(R_f 0.34), 1:1 light petroleum–diethyl ether; (R_f 0.21), 4:1 toluene–diethyl ether] (Found: C, 72.15; H, 10.0. $C_{11}H_{18}O_2$ requires C, 72.49; H, 9.95%); ν_{max}(film)/cm^{-1} 3397, 3079, 1641, 1087, 993 and 914; δ_H(250 MHz) 1.75–2.05 (4 H, m, 4- and 5-H_2), 2.24 (1 H, br s, OH), 2.31 (2 H, qt, *J* 6.7 and 1.3, CH_2CH_2O), 2.61 (1 H, dt, *J* 7.7 and 4.3, 2-H), 3.48 (2 H, t, *J* 6.7, OCH_2), 3.74 (1 H, q, *J* 4.4, 3-H), 3.94 (1 H, dt, *J* 5.7 and 4.6, 1-H), 5.07 (2 H, m, $=CH_2$), 5.12 (2 H, m, $=CH_2$), 5.65 (1 H, ddd, *J* 17.3, 10.2 and 7.7, =CH) and 5.80 (1 H, ddt, *J* 17.2, 10.2 and 6.8, =CH); δ_C(100 MHz) 28.78 and 32.09 (t), 34.44 (t), 57.91 (d), 68.46 (t), 77.07 (d), 84.62 (d), 116.42 (t), 116.61 (t), 135.23 (d) and 137.54 (d); *m/z* (EI) 151 (11%), 110 (M^+ − but-3-enyloxy, 32.4) and 55 ($C_4H_7^+$, 100).

Fraction 1 was purified on a preparative HPLC column (flow rate 8 cm^3 min^{-1}; 45 mg injections) using light petroleum–ethyl acetate (8:1) to give the *minor diastereoisomer* of 1-(3′-*methyltetrahydrofuran*-2-*yl*)-5-(*phenylthio*)*hexan*-3-*one* **10** as a brown oil (13.3 mg, 0.0454 mmol, 0.91%) (t_R 27.5 min) (Found: M^+, 292.1483. $C_{17}H_{24}O_2S$ requires *M*, 292.1497); ν_{max}(film)/cm^{-1} 3058, 1714, 1584, 1477, 1455, 1439, 744 and 693; δ_H(400 MHz) 1.02 (3 H, d, *J* 6.6, 3′-Me), 1.28 (3 H, dd, *J* 6.7 and 1.3, Me), 1.52 (1 H, m, 4′-H), 1.60 (1 H, m, 1-H), 1.78 (1 H, septet, *J* 7.3, 3′-H), 1.93 (1 H, m, 1-H), 2.07 (1 H, m, 4′-H), 2.46 (1 H, m, 1 H, of 2-H), 2.57 (1 H, m, 4-H), 2.60 (1 H, m, 2-H), 2.75 (1 H, m, 4-H), 3.25 (1 H, m, 2′-H), 3.71 (1 H, m, C*H*SPh), 3.77 (2 H, m, 5′-H_2), 7.28 (3 H, m, Ph) and 7.41 (2 H, m, Ph); δ_C(100

MHz) 17.12 (q), 21.08 (q), 27.85 (t), 34.74 (t), 38.36 (d), 39.12 (d), 40.30 (t), 49.66 (t), 66.79 (t), 84.95 (d), 127.25 (d), 129.01 (d), 132.40 (d), 134.46 (s) and 208.68 (s); *m/z* (EI) 292 (M^+, 16%), 194 (72), 179 (3), 151 (19), 141 (59), 137 (100) and 85 (76); and the *major diastereoisomer* of *compound* **10** as an oil (60.7 mg, 0.208 mmol, 4.15%) (t_R 30 min) (Found: M^+, 292.150 57); ν_{max}(film)/cm^{-1} 3058, 1714, 1584, 1479, 1456, 1439, 749 and 694; δ_H(400 MHz) 0.93 (3 H, d, *J* 7.0, 3'-Me), 1.28 (3 H, dd, *J* 6.7 and 2.0, Me), 1.54 (1 H, m, 4'-H), 1.64 (2 H, m, 1-H_2), 2.04 (1 H, m, 4'-H), 2.23 (1 H, septet, *J* 6.7, 3'-H), 2.43 (1 H, m, 2-H), 2.56 (1 H, m, 4-H), 2.59 (1 H, m, 2-H), 2.75 (1 H, dt, *J* 16.9 and 4.8, 4-H), 3.68 (3 H, m, PhSC*H*, 2'- and 5'-H), 3.83 (1 H, m, 5'-H), 7.36 (3 H, m, Ph) and 7.41 (2 H, m, Ph); δ_C(22.5 MHz) 14.19 (q), 21.13 (q), 24.60 (t), 33.80 (t), 35.81 (d), 38.46 (d), 40.63 (t), 49.79 (t), 66.15 (t), 80.72 (d), 127.20 (d), 128.94 (d), 132.40 (d), 134.52 (s) and 208.52 (s); *m/z* (EI) 292 (M^+, 10%), 194 (67), 179 (2), 151 (4), 141 (32), 137 (100) and 85 (61).

Fraction 2 was purified on a semi-preparative HPLC column (flow rate 3 cm^3 min^{-1}; 10 mg injections) using light petroleum–ethyl acetate (8:1) to give four isomers of 7-(but-3-enyloxy)-1,3-bis(phenylthio)hept-1-en-4-ol **12**/**13** (61.6 mg, 0.154 mmol, 3.08%). Two of these isomers were isolated pure: one diastereoisomer of (*Z*)-alcohol **12** as an oil (5.9 mg, 0.0147 mmol, 0.29%) (t_R 14.5 min), λ_{max}(MeCN)/nm 250.4 (ε 8500) and 264.1 (8500); ν_{max}(film)/cm^{-1} 3424, 3074, 3059, 1641, 1583, 1479, 1440, 739 and 691; δ_H(400 MHz) 1.60 (2 H, m), 1.79 (2 H, m), 2.34 (2 H, qt, *J* 6.8 and 1.3), 3.30 (1 H, br s, OH), 3.47 (2 H, t, *J* 5.7, OCH_2), 3.48 (2 H, t, *J* 6.8, OCH_2), 3.71 (1 H, td, *J* 8 and 2.3, C*H*OH), 4.24 (1 H, dd, *J* 10.2 and 7.2, PhSC*H*), 5.07 (2 H, m, =CH_2), 5.73 (1 H, dd, *J* 10.2 and 9.4, C*H*=CH), 5.81 (1 H, ddt, *J* 17.1, 10.3 and 6.7, C*H*=CH_2), 6.28 (1 H, d, *J* 9.3, =C*H*SPh), 7.23 (8 H, m, Ph) and 7.50 (2 H, m, Ph); δ_C(100 MHz) 26.38 (t), 32.01 (t), 34.19 (t), 54.97 (d), 70.32 (t), 70.93 (t), 72.90 (d), 116.56 (t), 126.61 (d), 126.74 (d), 127.54 (d), 128.91 (d), 129.05 (d) and 129.37 (d), 130.30 (d), 2 × 133.32 (s and d), 135.20 (d) and 135.63 (s); *m/z* (FAB) 401 (MH^+, 1%), 400 (M^+, 2), 291 (4), 257 (4), 219 (26), 181 (12) and 55 (100); and one diastereoisomer of (*E*)-alcohol **13** as an oil (4.4 mg, 0.0110 mmol, 0.22%) (t_R 18.3 min), λ_{max}(MeCN)/nm 250.7 (ε 8600) and 264sh (7500); ν_{max}(film)/cm^{-1} 3426, 3074, 3057, 1641, 1583, 1479, 1439, 1109, 741 and 691; δ_H(400 MHz) 1.55–1.84 (5 H, m, 2 × CH_2 and OH), 2.34 (2 H, qt, *J* 6.8 and 1.3, OCH_2CH_2), 3.48 (2 H, t, *J* 5.4, OCH_2), 3.49 (2 H, t, *J* 6.8, OCH_2), 3.71 (2 H, m, C*H*OH and C*H*SPh), 5.07 (2 H, m, =CH_2), 5.79 (1 H, dd, *J* 14.9 and 9.3, C*H*=CH), 5.81 (1 H, ddt, *J* 17.1, 10.3 and 6.7, C*H*=CH_2), 6.02 (1 H, d, *J* 15.0, PhSC*H*=), 7.05 (2 H, m, Ph), 7.25 (6 H, m, Ph) and 7.47 (2 H, m, Ph); δ_C(100 MHz) 26.27 (t), 32.19 (t), 34.18 (t), 60.32 (d), 70.37 (t), 70.93 (t), 72.53 (d), 116.65 (t), 125.44 (d), 126.65 (d), 127.88 (d), 129.04 (d), 129.07 (d), 129.37 (d), 130.90 (d), 133.42 (s), 134.13 (d), 135.13 (d) and 135.23 (s); *m/z* (FAB) 401 (MH^+, 1.1%), 400 (M^+, 1), 291 (9), 257 (6), 219 (30), 181 (25) and 55 (100).

Fraction 3 was purified on a semi-preparative HPLC column (flow rate cm^3 min^{-1}, 10 mg injections) using light petroleum–ethyl acetate (6:1; t_R 13.8 min), then on a preparative HPLC column (flow rate 8 cm^3 min^{-1}) using dichloromethane–ethyl acetate (12:1; t_R 26.5 min), to give the minor diastereoisomer of 3-(but-3-enyloxy)-2-vinylcyclopentanol **11** as an oil (37.2 mg, 0.204 mmol, 4.1%); ν_{max}(film)/cm^{-1} 3372, 3076, 1641, 1086, 996 and 913; δ_H(250 MHz) 1.52 (1 H, ddt, *J* 12.8, 10.3 and 6.5, 5-H), 1.71 (1 H, s, OH), 1.74 (1 H, dddd, *J* 13.8, 9.0, 6.2 and 2.9, 4-H), 2.00 (1 H, ddt, *J* 13.9, 10.3 and 5.6, 4-H), 2.17 (1 H, dddd, *J* 12.8, 9.0, 7.4 and 5.5, 5-H), 2.28 (2 H, qt, *J* 6.8 and 1.4, OCH_2CH_2), 2.32 (1 H, td, *J* 8.5 and 5.4, 2-H), 3.35 (1 H, dt, *J* 9.2 and 6.8, ABX_2 system, 1 H of OCH_2), 3.47 (1 H, dt, *J* 9.2 and 6.8, ABX_2 system, 1 H of OCH_2), 3.87 (1 H, td, *J* 5.5 and 2.9, 3-H), 4.16 (1 H, q, *J* 7.3, 1-H), 5.03 (2 H, m, CH=CH_2), 5.18 (2 H, m, =CH_2), 5.81 (1 H, ddt, *J* 17.2, 10.2 and 6.7, C*H*=CH_2) and 5.98 (1 H, ddd, *J* 17.2, 10.4 and 9.0, C*H*=CH_2); δ_C(100 MHz) 28.90 (t), 31.24 (t), 34.44 (t), 58.01 (d), 68.86 (t), 76.43 (d), 82.08 (d), 116.23 (t) and 117.15 (t), 135.53 (d) and 136.45 (d).

Pent-4-enal.[19,20]—To a solution of dry pent-4-en-1-ol (3.015 g, 35 mmol), Kieselguhr (10 g, 0.17 mol, 5 mol equiv.), Florosil (1 g, 17 mmol, 0.5 mol equiv.), anhydrous sodium acetate (15 g, 0.18 mol, 5 mol equiv.) and crushed activated 3 Å molecular sieves in dry dichloromethane (500 cm^3) was added pyridinium chlorochromate (PCC) (37.7 g, 0.175 mol, 5 mol equiv.) and the brown mixture was stirred for 2 h. Diethyl ether (500 cm^3) was added and the resulting black solid was filtered off through a 6″ column of Florosil. The filtrate was extracted with sodium hydroxide (1 mol dm^{-3}; 2 × 100 cm^3) to remove a carboxylic acid by-product and the aqueous layers were back-extracted with diether ether (100 cm^3). The combined organic layers were extracted with aq. copper sulfate (20%) until no further darkening occurred, then with water (100 cm^3), and were dried ($MgSO_4$) and concentrated to 130 cm^3 by careful, slow distillation through a 1′ Vigreux column, and used in this form in the synthesis of octa-1,3,7-triene 3,4-oxide **14**. Further distillation led to considerable loss of product into the distillate. Chromatography of the residue using dichloromethane (R_f 0.56), however, yielded pent-4-enal as a liquid, b.p. 100 °C; ν_{max}(film)/cm^{-1} 3081, 2726, 1727, 1644 and 919; δ_H(80 MHz) 2.5 (4 H, m, 2- and 3-H_2), 5.00 (1 H, m, 5-H), 5.04 (1 H, m, 5-H), 5.84 (1 H, ddt, *J* 17.2, 9.8 and 6.1, 4-H) and 9.75 (1 H, t, *J* 1.4, 1-H); δ_C(22.5 MHz; $CDCl_3$) 26.07 (t), 42.67 (t), 115.40 (t), 136.42 (d) and 201.38 (d); *m/z* (EI) 85 (MH^+, 66%), 71 (100), 57 (100) and 55 (M^+ − CHO, 68.8).

Octa-1,3,7-triene 3,4-Oxide **14**.[9]—To a solution of pent-4-enal (32 mmol) in dichloromethane (130 cm^3), freshly prepared in the previous experiment, was added 1-allyltetrahydrothiophenium bromide **6** (8 g, 38 mmol) and benzyltriethylammonium chloride (0.85 g, 3.7 mmol), and the solution was cooled to −25 °C. Cool (5 °C) aq. sodium hydroxide (10 mol dm^{-3}; 40 cm^3) was added during 3 min with rapid magnetic stirring of the mixture. After 20 min at −25 °C and 1.5 h at 0 °C the mixture was treated with water (700 cm^3) and the aqueous layer was back-extracted with diethyl ether (2 × 150 cm^3). The combined organic layers were extracted with water (2 × 100 cm^3), dried ($MgSO_4$), carefully evaporated to dryness, and the residue was chromatographed with diethyl ether in pentane [1.5% and 2% (R_f 0.27; iodine best)] to give octa-1,3,7-triene 3,4-oxide **14** as a liquid (1.2981 g, 10.47 mmol, 29.9% over 2 steps from pent-4-en-1-ol) as *trans* and *cis* epoxide diastereoisomers (76:24%), b.p. 125 °C; ν_{max}(film)/cm^{-1} 3081, 1642, 988, 917 and 875; δ_H(250 MHz) 1.67 (2 H, m, 5-H_2), 2.28 (2 H, m, 6-H_2), 2.87 (1 H, td, *J* 5.7 and 2.2, 4-H *trans*), 3.12 (1 H, m, 4-H *cis*), 3.12 (1 H, dd, *J* 7.3 and 2.1, 3-H *trans*), 3.42 (1 H, dd, *J* 7.2 and 4.3, 3-H *cis*), 5.00 (1 H, br d, *J* 10.1, 8-H), 5.07 (1 H, dq, *J* 17.2 and 1.7, 8-H), 5.26 (1 H, dd, *J* 9.8 and 2.0, 1-H *trans*), 5.36 (1 H, ddd, *J* 10.3, 1.7 and 0.6, 1-H *cis*), 5.45 (1 H, dd, *J* 17.2 and 2.2, 1-H *trans*), 5.48 (1 H, ddd, *J* 17.1, 1.7 and 0.6, 1-H *cis*), 5.58 (1 H, ddd, *J* 17.2, 9.9 and 7.3, 2-H *trans*), 5.73 (1 H, ddd, *J* 17.2, 10.2 and 7.1, 2-H *cis*) and 5.84 (1 H, ddt, *J* 17.0, 10.2 and 6.7, 7-H); δ_C(22.5 MHz; $CDCl_3$) 27.41 (t), 30.22 (t), 30.66 (t), 31.58 (t), 57.36 and 58.39 (d), 58.88 (d) and 60.07 (d), 115.44 (t), 118.96 (t), 120.48 (t), 132.83 (d), 136.03 (d) and 137.76 (d); *m/z* (EI) 83 (M^+ − C_3H_5, 55%), 67 (94), 57 (76), 55 (100) and 41 (67).

Radical Addition of Thiophenol to Octa-1,3,7-triene 3,4-Oxide **14** *with AIBN in Refluxing THF.*—A solution of octa-1,3,7-triene 3,4-oxide **14** (0.20 g, 1.6 mmol) in dry THF (30 cm^3) under nitrogen was brought to reflux and solutions of thiophenol (0.26 g, 2.4 mmol, 1.5 mol equiv.) in THF (2 cm^3) and

AIBN (0.22 g, 0.14 mmol, 8 mol%) in THF (2.5 cm^3) were added separately (syringe) during 3 h. After reflux for 18 h, the solution was evaporated to dryness and the residue was chromatographed using light petroleum, light petroleum–dichloromethane (10:1 to 1:1), and dichloromethane, to give starting material **14** (47.3 mg, 0.38 mmol, 24% recovery) (R_f 0.56; dichloromethane); and (E)-2-*methyl*-5-[3-(*phenylthio*)*prop*-1-*enyl*]*tetrahydrofuran* **15**, purified by PLC using 3:1 light petroleum–diethyl ether eluent as a pale yellow oil (0.124 g, 0.529 mmol, 33%) (R_f 0.36; dichloromethane), present as *cis* and *trans* ring diastereoisomers (1:1) (Found: M^+, 234.1072. $C_{14}H_{18}OS$ requires *M*, 234.1078); ν_{max}(film)/cm^{-1} 3060, 1585, 1480, 970, 740 and 690; δ_H(250 MHz) 1.18 (3 H, d, *J* 5.9, 2-Me of one isomer), 1.21 (3 H, d, *J* 5.8, 2-Me of other isomer), 1.45 (2 H, m, 3-H_2), 1.95 (2 H, m, 4-H_2), 3.50 (2 H, d, *J* 6.7, PhSCH_2), 3.95 (1 H, d of quintets, *J* 7.3 and 6.1, 2-H of one isomer), 4.06 (1 H, d of quintets, *J* 7.6 and 6.0, 2-H of other isomer), 4.21 and 4.37 (1 H, q, *J* 6.5, 5-H), 5.51 and 5.54 (1 H, dd, *J* 15.2 and 6.3, C*H*=CHCH$_2$), 5.70 (1 H, dt, *J* 15.3 and 6.9, CH=C*H*CH$_2$), 5.72 (1 H, dt, *J* 15.1 and 6.1, CH=C*H*CH$_2$) and 7.24 (5 H, m, Ph); δ_C(100 MHz) 21.29 (q), 21.31 (q), 32.11 (t), 32.80 (t), 32.89 (t), 33.75 (t), 36.08 (t), 36.11 (t), 75.00 (d), 75.62 (d), 78.38 (d), 79.06 (d), 125.83 (d), 126.23 (d), 126.28 (d), 128.70 (d), 130.17 (d), 130.22 (d), 134.94 (d), 135.02 (d) and 135.91 (s); *m*/*z* (EI) 234 (M^+, 8%), 149 (3), 125 (58), 124 (29), 110 (50), 109 (26), 85 (22.4) and 41 (100); and (E)-1-(*phenylthio*)*octa*-2,7-*dien*-4-*ol* **16**, purified by PLC (2:3 light petroleum–diethyl ether) as a brown oil (40.2 mg, 0.172 mmol, 11%) (R_f 0.22; dichloromethane) (Found: M^+, 234.1076. $C_{14}H_{18}OS$ requires *M*, 234.1078); ν_{max}(film)/cm^{-1} 3380, 3080, 3010, 1645, 1590, 1485, 750 and 700; δ_H(250 MHz), 1.52 (2 H, m, 5-H_2), 1.68 (1 H, br s, OH), 2.00 (2 H, qt, *J* 7.0 and 1.2, 6-H_2), 3.53 (2 H, d, *J* 6.8, 1-H_2), 4.05 (1 H, q, *J* 6.5, 4-H), 4.97 (2 H, m, 8-H_2), 5.51 (1 H, ddt, *J* 15.3, 6.8 and 0.9, 3-H), 5.70 (1 H, dt, *J* 15.3 and 6.9, 2-H), 5.77 (1 H, ddt, *J* 17.1, 10.2 and 6.6, 7-H) and 7.27 (5 H, m, Ph); δ_C(67.5 MHz; $CDCl_3$) 29.45 (t), 35.96 (t), 36.03 (t), 71.74 (d), 114.84 (t), 126.38 (d), 126.47 (d), 128.79 (d), 130.40 (d), 135.42 (s), 136.12 (d) and 138.13 (d); *m*/*z* (EI) 234 (M^+, 3.7%), 217 (6), 135 (18), 124 (4), 123 (61), 110 (100), 109 (18.0), 69 (32.8) and 55 (62.6).

3-(tert-*Butyldiphenylsiloxy*)*propan*-1-*ol* **17**.[21]—To a solution of dry propane-1,3-diol (144 cm^3, 2 mol, 11 mol equiv.) and imidazole (24.77 g, 0.3638 mol, 2 mol equiv.) in dry DMF (450 cm^3) under nitrogen was added *tert*-butylchlorodiphenylsilane (50 g, 47.3 cm^3, 0.1819 mol) dropwise over a period of 3 h (syringe pump). After the mixture had been stirred for 2 days, most of the solvent was removed (50–60 °C; 1–2 mmHg), the residual suspension was poured onto water (250 cm^3), and the precipitated product was taken up in diethyl ether (250 cm^3). The separated aqueous layer was back-extracted with diethyl ether (250 cm^3). The combined organic layers were washed with water (5 × 100 cm^3), dried ($MgSO_4$), evaporated to dryness, and the residue was chromatographed using light petroleum–diethyl ether [40:1 and 3:1 (R_f 0.21)] to give 3-(*tert*-butyldiphenylsiloxy)propan-1-ol **17** as needles (50.03 g, 0.159 mol, 87.5%), m.p. 42–44 °C (lit.,[21] 35–40 °C) (from pentane at −20 °C) (Found: C, 72.6; H, 8.5. Calc. for $C_{19}H_{26}O_2Si$: C, 72.56; H, 8.27%); ν_{max}(KBr)/cm^{-1} 3436, 3071, 3048, 1589, 1470, 1428, 1109, 733 and 702; δ_H(250 MHz) 1.05 (9 H, s, Bu^t), 1.81 (2 H, quintet, *J* 5.6, 2-H_2), 2.11 (1 H, br s, OH), 3.85 (4 H, t, *J* 5.6, 1- and 3-H_2), 7.43 (6 H, m, Ph) and 7.68 (4 H, m, Ph); δ_C(22.5 MHz; $CDCl_3$) 19.17 (s), 26.97 (q), 34.94 (t), 60.56 (t), 62.29 (t), 127.74 (d), 129.74 (d), 133.64 (s) and 135.54 (d); *m*/*z* (FAB) 315 (MH^+, 17%), 257 (16), 237 (13), 199 (81), 179 (64), 137 (71), 135 (100), 117 (82), 77 (19), 75 (59) and 57 (16).

3-(tert-*Butyldiphenylsiloxy*)*propanal* **18**.[22]—To a solution of oxalyl dichloride (15.11 cm^3, 0.1733 mol, 1.1 mol equiv.) in dry dichloromethane (200 cm^3) under nitrogen, mechanically stirred and cooled to −63 °C, was added dropwise (10 min, dropping funnel) a solution of dry DMSO (24.6 cm^3, 0.3465 mol, 2.2 mol equiv.) in dichloromethane (50 cm^3). Then a solution of 3-(*tert*-butyldiphenylsiloxy)propan-1-ol **17** (49.53 g, 0.1575 mol) in dichloromethane (130 cm^3) was added slowly (12 min, dropping funnel). After 1.25 h, dry diisopropylethylamine (137.2 cm^3, 0.7875 mol, 5 mol equiv.) was added (syringe) and the clear mixture was stirred for 10 min at −63 °C. After warming to room temperature, the mixture was poured onto water (100 cm^3), the aqueous layer was back-extracted with dichloromethane (50 cm^3), and the combined organic layers were extracted successively with hydrochloric acid (2 mol dm^{-3}; 400 + 100 cm^3) and water (100 cm^3), dried ($MgSO_4$), and evaporated to dryness. The residue was chromatographed using light petroleum–dichloromethane [(3:1 (R_f 0.22) and 2:1], to give 3-(*tert*-butyldiphenylsiloxy)propanal **18** as crystals (44.67 g, 0.143 mol, 90.8%), m.p. 51–53 °C (from hexane) (Found: C, 72.9; H, 8.0. Calc. for $C_{19}H_{24}O_2Si$: C, 73.03; H, 7.72%); ν_{max}(film)/cm^{-1} 3071, 3050, 2730, 1729, 1590, 1473, 1112 and 704; δ_H(250 MHz)[22] 1.04 (9 H, s, Bu^t), 2.61 (2 H, td, *J* 6.0 and 2.3, 2-H_2), 4.02 (2 H, t, *J* 6.0, 3-H_2), 7.40 (6 H, m, Ph), 7.66 (4 H, m, Ph) and 9.82 (1 H, t, *J* 2.3, 1-H); δ_C(22.5 MHz) 19.12 (s), 26.76 (q), 46.32 (t), 58.29 (t), 127.74 and 129.75 (d), 133.32 (s), 135.49 (d) and 201.10 (d); *m*/*z* (EI) 255 (M^+ − Bu^t, 100%), 225 (70.0), 199 (33), 183 (50), 177 (33) and 117 (42).

6-(tert-*Butyldiphenylsiloxy*)-3,4-*epoxyhex*-1-*ene* **19**.[9]—To a rapidly mechanically stirred solution of 3-(*tert*-butyldiphenylsiloxy)propanal **18** (15.62 g, 50 mmol), 1-allyltetrahydrothiophenium bromide **6** (12.55 g, 60 mmol, 1.2 mol equiv.) and benzyltriethylammonium chloride (1.14 g, 5 mmol, 10 mol%) in dichloromethane (150 cm^3) cooled to −20 °C was added cool (5 °C) aq. sodium hydroxide (10 mol dm^{-3}; 150 cm^3) *via* a dropping funnel over a period of 2 min. The mixture was then adjusted to 0 °C and, after being stirred for another 10 min, was poured onto water (400 cm^3)–dichloromethane (100 cm^3) and the separated aqueous layer was extracted with dichloromethane (2 × 100 cm^3). The combined organic layers were extracted with water (2 × 100 cm^3), dried ($MgSO_4$), evaporated to dryness, and chromatographed using light petroleum–diethyl ether (30:1 and 9:1), to give 6-(*tert*-butyldiphenylsiloxy)-3,4-epoxyhex-1-ene **19** as an oil (7.715 g, 21.9 mmol, 43.8%) [(R_f 0.20), 30:1 light petroleum–diethyl ether], present as *trans* and *cis* epoxide diastereoisomers (69:31%) (Found: C, 74.85; H, 8.3. Calc. for $C_{22}H_{28}O_2Si$: C, 74.95; H, 8.01%); ν_{max}(film)/cm^{-1} 3071, 3050, 1961, 1891, 1829, 1643, 1590, 1568, 1487, 1473, 1111, 926, 882, 824, 739 and 702; δ_H(250 MHz) 1.05 (9 H, s, Bu^t), 1.82 (2 H, q, *J* 6.1, 5-H_2), 3.03 (1 H, td, *J* 5.7 and 2.2, 4-H *trans*), 3.18 (1 H, dd, *J* 7.2 and 2.1, 3-H *trans*), 3.30 (1 H, td, *J* 6.1 and 4.4, 4-H *cis*), 3.42 (1 H, dd, *J* 6.9 and 4.2, 3-H *cis*), 3.80 (2 H, br t, *J* 6, 6-H_2), 5.30 (1 H, m, 1-H, *cis* and *trans*), 5.43 (1 H, ddd, *J* 17.1, 1.8 and 0.7, 1-H *cis*), 5.46 (1 H, dd, *J* 17.3 and 2.1, 1-H *trans*), 5.60 (1 H, ddd, *J* 17.2, 9.8 and 7.3, 2-H *trans*), 5.66 (1 H, ddd, *J* 17.1, 10.2 and 7.0, 2-H *cis*), 7.41 (6 H, m, Ph) and 7.66 (4 H, m, Ph); δ_C(22.5 MHz) 19.18 (s), 26.87 (q), 30.99 (t), 35.21 (t), 56.23 (d), 56.83 (d), 58.13 (d), 58.67 (d), 60.73 (t), 61.27 (t), 118.80 (t), 120.10 (t), 127.64 (d), 129.64 (d), 132.56 (d), 133.65 (s), 135.49 (d) and 135.87 (d); *m*/*z* (FAB) 353 (MH^+, 3%), 295 (51), 275 (21), 199 (41), 197 (47), 137 (34), 135 (100), 77 (13) and 57 (15).

3,4-*Epoxyhex*-5-*en*-1-*ol* **20**.—To a solution of 6-(*tert*-butyldiphenylsiloxy)-3,4-epoxyhex-1-ene **19** (19.20 g, 54.45 mmol) in dry THF (300 cm^3) under nitrogen was added a solution of tetrabutylammonium fluoride (TBAF) (1 mol dm^{-3}; 102 cm^3, 102 mmol, 1.87 mol equiv.) in THF and the dark brown solution

was stirred for 2 h. The solvent was removed under reduced pressure to give a dark brown solid residue, which was chromatographed using dichloromethane and dichloromethane–diethyl ether [(35:1, 20:1 and 4:1 (R_f 0.28)] and distilled (66–74 °C, 0.6 mmHg) to afford 3,4-*epoxyhex*-5-*en*-1-*ol* **20** as a liquid (5.909 g, 51.8 mmol, 95.1%), present as the *trans* and *cis* epoxide diastereoisomers (63:37%) (Found: MH^+, 115.0752. $C_6H_{11}O_2$ requires *m/z* 115.0759); ν_{max}(film)/cm^{-1} 3402, 3089, 1643, 1051, 989, 929 and 877; δ_H(250 MHz) 1.65–1.90 (m, 2-H_2 *cis*, 2-H *trans* and OH), 2.04 (1 H, dtd, *J* 14.6, 6.3 and 4.3, 2-H *trans*), 3.04 (1 H, ddd, *J* 6.5, 4.2 and 2.3, 3-H *trans*), 3.23 (1 H, dd, *J* 6.8 and 2.1, 4-H *trans*), 3.27 (1 H, dt, *J* 7.3 and 5, 3-H *cis*), 3.47 (1 H, dd, *J* 6.9 and 4.2, 4-H *cis*), 3.82 (2 H, br t, *J* 5.9, 1-H_2), 5.27–5.53 (2 H, m, 6-H_2), 5.60 (1 H, ddd, *J* 17.2, 9.5 and 7.0, 5-H *trans*) and 5.74 (1 H, ddd, *J* 17.2, 10.3 and 6.9, 5-H *cis*); δ_C(22.5 MHz) 30.83 and 34.73 (t), 56.40 (d), 56.83 (d), 58.24 (d), 58.45 (d), 59.10 (t), 59.70 (t), 119.18 (t), 120.48 (t), 132.40 (d) and 135.54 (d); *m/z* (FAB) 115 (MH^+, 26%), 95 (30), 83 (39), 69 (72) and 55 (100).

6-*Iodo*-3,4-*epoxyhex*-1-*ene* **21**.—To a solution of imidazole (0.4493 g, 6.6 mmol, 1.1 mol equiv.), triphenylphosphine (1.7311 g, 6.6 mmol, 1.1 mol equiv.) and 3,4-epoxyhex-5-en-1-ol **20** (0.6848 g, 6 mmol) in dry benzene (50 cm^3) under nitrogen was added iodine (1.5989 g, 6.3 mmol, 1.05 mol equiv.) and the reaction stirred was rapidly at 25 °C for 5 h. The mixture was diluted with diethyl ether (25 cm^3) and extracted successively with saturated aq. sodium hydrogen carbonate (40 cm^3), then saturated aq. sodium thiosulfate (40 cm^3) with shaking for a few minutes to discharge any iodine colour remaining, then with water (2 × 20 cm^3). The organic layer was dried ($MgSO_4$) and the solvent was removed to leave wet crystals. These were extracted with cold (−20 °C) diethyl ether (5 × 10 cm^3) and the extracts were filtered, evaporated to dryness, and the residue was chromatographed using pentane–diethyl ether as eluent [80:1 and 50:1 (R_f 0.23)] to give 6-*iodo*-3,4-*epoxyhex*-1-*ene* **21** as a volatile liquid (0.8969 g, 4.00 mmol, 66.7%), present as the *trans* and *cis* epoxide diastereoisomers (68:32) (Found: M^+, 223.970 11. C_6H_9IO requires *M*, 223.969 69); ν_{max}(film)/cm^{-1} 3085, 1642, 987, 924 and 878; δ_H(250 MHz) 2.03–2.27 (2 H, m, 5-H_2), 2.94 (1 H, ddd, *J* 6.3, 4.8 and 2.1, 4-H *trans*), 3.17–3.33 (m, 6-H_2, 3-H *trans* and 4-H *cis*), 3.49 (1 H, dd, *J* 6.7 and 4.3, 3-H *cis*), 5.28–5.41 (m, 1-H_2 *cis* and 1-H *trans*), 5.49 (1 H, dd, *J* 17.2 and 2.3, 1-H *trans*), 5.60 (1 H, ddd, *J* 17.2, 9.3 and 6.7, 2-H *trans*) and 5.72 (1 H, ddd, *J* 17.1, 10.4 and 6.7, 2-H *cis*); δ_C(22.5 MHz) 0.22 (t), 0.65 (t), 31.48 (t), 36.65 (t), 56.45 (d), 58.13 (d), 58.29 (d), 59.81 (d), 119.18 (t), 120.43 (t), 131.91 (d) and 135.00 (d); *m/z* (EI) 224 (M^+, 3%), 183 (27), 155 (37), 128 (7), 127(7), 97 (7), 79 (33), 69 (79) and 41 (100).

9-(3′,4′-*Epoxyhex*-5′-*enyl*)*adenine* **22**.—Sodium hydride (0.1584 g, 6.6 mmol, 2.2 mol equiv.), washed with dry DMF, and adenine (0.8108 g, 6 mmol, 2 mol equiv.) were suspended in DMF (12 cm^3) under nitrogen and heated to 65 °C for 15 min until evolution of hydrogen had subsided. A solution of 6-iodo-3,4-epoxyhex-1-ene **21** (0.6721 g, 3 mmol) in DMF (5 cm^3) was added and the suspension was stirred at 60–70 °C for 1.5 h. After filtration, the solvent was distilled off (80 °C; 3 mmHg) and the residue was chromatographed using 6% methanol in dichloromethane (R_f 0.26) to give 9-(3′,4′-*epoxyhex*-5′-*enyl*)-*adenine* **22** as crystals (0.3676 g, 1.59 mmol, 53.0%), m.p. 137–142 °C (from MeOH–EtOAc), present as *trans* and *cis* epoxide diastereoisomers (70:30) (Found: M^+, 231.1345. $C_{11}H_{13}N_5O$ requires *M*, 231.1120); λ_{max}(EtOH)/nm 208sh (ε 14 000) and 261.0 (9400); ν_{max}(KBr)/cm^{-1} 3365, 3137, 1664, 1601, 1485, 937 and 864; δ_H(250 MHz) 2.01 (1 H, ddt, *J* 14.3, 7.0 and 6.2, 2′-H *trans*), 2.04 (1 H, m, 2′-H *cis*), 2.20 (1 H, m, 2′-H *cis*), 2.35 (1 H, dtd, *J* 14.3, 7.6 and 4.6, 2′-H *trans*), 2.87 (1 H, ddd, *J* 7.2, 4.6 and 2.1, 3′-H *trans*), 3.02 (1 H, dd, *J* 6.9 and 2.1, 4′-H *trans*), 3.12 (1 H, ddd, *J* 7.4, 5.0 and 4.4, 3′-H *cis*), 3.40 (1 H, dd, *J* 6.4 and 4.2, 4′-H *cis*), 4.39 (2 H, dd, *J* 7.8 and 6.6, 1′-H_2), 5.2–5.6 (3 H, m, 5′-H and 6′-H_2), 6.28 (2 H, br s, NH_2), 7.84 (1 H, s, adenine 8-H *cis*), 7.86 (1 H, s, adenine 8-H *trans*), 8.348 (1 H, s, adenine 2-H *trans*) and 8.35 (1 H, s, adenine 2-H *cis*); δ_C(67.5 MHz; CD_3OD) 29.22 (t), 33.46 (t), 41.83 (t), 42.16 (t), 57.20 (d), 57.70 (d), 58.58 (d), 59.21 (d), 119.78 (t), 119.98 (s), 120.81 (t), 132.90 (d), 136.49 (d. 142.62 (d), 150.55 (s), 153.62 (d) and 157.19 (s); *m/z* (EI) 231 (M^+, 85%), 174 (100), 149 (58), 148 (50), 136 (70) and 135 (49).

Addition of Thiophenol to 9-(3,4-*Epoxyhex*-5-*enyl*)*adenine* **22** *in the Presence of Azoisobutyronitrile*.—To a refluxing solution of 9-(3,4-epoxyhex-5-enyl)adenine **22** (58.9 mg, 0.255 mmol) in dry acetonitrile (15 cm^3)–dry methanol (5 cm^3) under nitrogen were added solutions of thiophenol (47.2 mg, 0.428 mmol, 1.68 mol equiv.) in acetonitrile (1.5 cm^3) and AIBN (4.2 mg, 0.026 mmol, 0.1 mol equiv.) in acetonitrile (1 cm^3), slowly over a period of 6 h (syringe). After 24 h at reflux, the solution was evaporated to dryness and the residue was rapidly chromatographed with 6% methanol in dichloromethane as eluent to give 9-[3′-*hydroxy*-4′-(*phenylthio*)-*hex*-5′-*enyl*]*adenine* **23** as a solid (7.9 mg, 0.0231 mmol, 9.1%) [(R_f 0.19), 6% methanol in dichloromethane; UV best], m.p. 80–83 °C, present as *trans* and *cis* diastereoisomers (70:30) (Found: M^+, 341.1230. $C_{17}H_{19}N_5OS$ requires *M*, 341.131 03); λ_{max}(EtOH)/nm 213sh (ε 38 000) and 260.2 (24 000); ν_{max}(KBr)/cm^{-1} 3434, 1644, 1606, 1580, 1479 and 1091; δ_H(250 MHz; CD_3OD) 1.97 (1 H, m, 2′-H), 2.19–2.45 (1 H, m, 2′-H), 3.51–3.66 (2 H, m, 4′-H *trans* and 3′-H), 3.73 (1 H, dd, *J* 8.8 and 5.4, 4′-H *cis*), 4.38 (2 H, t, *J* 7.3, 1′-H_2 *trans*), 4.39 (2 H, t, *J* 7.5, 1′-H_2 *cis*), 4.90–5.06 (2 H, m, 6′-H_2), 5.77 (1 H, ddd, *J* 16.8, 10.4 and 8.9, 5′-H *cis*), 5.81 (1 H, ddd, *J* 17.0, 10.2 and 9.2, 5′-H *trans*), 7.20 (4 H, m, Ph), 7.30 (1 H, m, Ph), 8.09 (1 H, s, adenine 8-H *cis*), 8.10 (1 H, s, adenine 8-H, *trans*) and 8.22 (1 H, s, adenine 2-H); δ_C(100 MHz; $CDCl_3$), 34.86 (t), 35.22 (t) 40.82 (t), 58.94 (d), 59.87 (d), 68.33 (d), 68.60 (d), 117.93 (t), 118.90 (t), 119.49 (s), 127.73 (d), 128.95 (d), 133.17 (d), 133.41 (d), 133.48 (s), 134.10 (d), 134.98 (d), 141.04 (d), 150.15 (s), 152.45 (d) and 155.36 (s); *m/z* (EI) 341 (M^+, 0.5%), 323 (3), 232 (11), 192 (100), 148 (15), 136 (58), 135 (22), 110 (8) and 109 (9); and 9-[3′-*hydroxy*-6′-(*phenylthio*)*hex*-4′-*enyl*]-*adenine* **24** as a solid (3.5 mg, 0.0103 mmol, 4.0%) [(R_f 0.14), 6% methanol in dichloromethane], m.p. 140–147 °C (Found: M^+, 341.1237. $C_{17}H_{19}N_5OS^+$ requires *M*, 341.131 03); λ_{max}(EtOH)/nm 259.0 (ε 18 000); ν_{max}(KBr)/cm^{-1} 3381, 3318, 3124, 1656, 1601, 1578, 1493, 1480, 1065, 966, 798, 750 and 694; δ_H(400 MHz; CD_3OD) 1.92 (2 H, m, 2′-H_2), 3.52 (2 H, d, *J* 6.4, 6′-H_2), 3.97 (1 H, q, *J* 6.0, 3′-H), 4.17 (2 H, t, *J* 7.0, 1′-H_2), 5.53 (1 H, dd, *J* 15.7 and 5.7, 4′-H), 5.70 (1 H, dt, *J* 15.3 and 6.9, 5′-H), 7.12 (1 H, m, Ph), 7.22 (2 H, m, Ph), 7.32 (2 H, m, Ph), 7.96 (1 H, s, adenine 8-H) and 8.22 (1 H, s, adenine 2-H); δ_C(100 MHz; CD_3OD) 36.34 (t), 37.51 (t), 41.47 (t), 69.43 (d), 119.89 (s), 127.10 (d), 127.42 (d), 129.63 (d), 131.02 (d), 136.11 (d), 136.73 (s), 142.49 (d), 150.33 (s), 153.11 (d) and 156.76 (s); *m/z* (EI) 341 (M^+, 2%), 323 (13), 233 (20), 232 (100), 188 (33), 136 (95), 135 (28) and 110 (19).

2-{2-[2-(tert-*Butyldiphenylsiloxy*)*ethoxy*]*ethoxy*}*ethanol* **25**.—To a solution of imidazole (13.62 g 0.2 mol, 2 mol equiv.) and dry triethylene glycol (150 g, 1 mol, 10 mol equiv.) in dry DMF (200 cm^3) under nitrogen was added *tert*-butyldiphenylsilyl chloride (TBDPSCl) (27.49 g, 0.1 mol, 1 mol equiv.) slowly during 4 h (syringe pump) and the reaction mixture was stirred at 25 °C for a further 14 h before being poured onto water (400 cm^3)–diethyl ether (400 cm^3) and the aqueous layer was extracted with more diethyl ether (7 × 150 cm^3). The combined

extracts were dried ($MgSO_4$), evaporated to dryness and the residue was chromatographed using light petroleum–ethyl acetate [4:1 and 2:1 (R_f 0.16)] to give 2-{2-[2-tert-*butyldiphenylsiloxy)ethoxy]ethoxy}ethanol* **25** as an oil (28.86 g, 74.3 mmol, 74.3%) (Found: C, 67.7; H, 8.7. $C_{22}H_{32}O_4Si$ requires C, 68.00; H, 8.30%); ν_{max}(film)/cm^{-1} 3445, 3071, 3050, 1590, 1473, 1428, 1113, 740 and 704; δ_H(250 MHz) 1.05 (9 H, s, Bu^t), 2.22 (1 H, br s, OH), 3.61 (4 H, m, 2 × OCH_2), 3.66 (4 H, s, $ROCH_2CH_2OR'$), 3.72 (2 H, m, $HOCH_2$), 3.81 (2 H, t, *J* 5.2, $TBDPSOCH_2$), 7.40 (6 H, m, Ph) and 7.69 (4 H, m, Ph); δ_C(22.5 MHz) 19.33 (s), 27.03 (q), 61.92 (t), 63.65 (t), 70.64 (t), 70.96 (t), 72.64 (t), 72.75 (t), 127.79 (d), 129.80 (d), 133.86 (s) and 135.75 (d); *m/z* (FAB) 411 ($M + Na^+$, 2%), 253 (13), 199 (40), 197 (44), 165 (96), 135 (100) and 57 (70).

2-{2-[2-(tert-*Butyldiphenylsiloxy)ethoxy]ethoxy}ethanal* **26**.—To a solution of oxalyl dichloride (7.01 cm^3, 80.3 mmol, 1.1 mol equiv.) in dry dichloromethane (175 cm^3) at −65 °C under nitrogen was added a solution of dry DMSO (11.4 cm^3, 161 mmol, 2.2 mol equiv.) in dichloromethane (35 cm^3) over 4 min (dropping funnel). The mixture was mechanically stirred for 24 min, then a solution of 2-{2-[2-(*tert*-butyldiphenylsiloxy)-ethoxy]ethoxy}ethanol **25** (28.37 g, 73.0 mmol) in dichloromethane (150 cm^3) was added during 10 min (funnel), and the mixture was then stirred for a further 22 min. Triethylamine (50.9 cm^3, 0.365 mol, 5 mol equiv.) was added over a period of 2 min and the resulting suspension was stirred for 5 min at −65 °C. After warming to room temperature, the mixture was extracted successively with water (200 cm^3) and hydrochloric acid (2 mol dm^{-3}; 250 cm^3) and the combined aqueous layers were back-extracted with dichloromethane (2 × 100 cm^3). The combined organic extracts were dried ($MgSO_4$), evaporated to dryness, and the residue was chromatographed using 1% ethyl acetate and 0.5% triethylamine in dichloromethane (R_f 0.18) to give 2-{2-[2-(*tert*-butyldiphenylsiloxy)ethoxy]ethoxy}ethanal **26** as an oil (20.98 g, 54.3 mmol, 74.3%), ν_{max}(film)/cm^{-1} 3071, 3050, 2712, 1737, 1590, 1473, 1428, 1113, 740 and 703; δ_H(250 MHz) 1.05 (9 H, s, Bu^t), 3.61 (2 H, t, *J* 5.2, OCH_2), 3.70 (4 H, s, $ROCH_2CH_2OR'$), 3.82 (2 H, t, *J* 5.2, $TBDPSOCH_2$), 4.15 (2 H, d, *J* 0.7, CH_2CHO), 7.39 (6 H, m, Ph), 7.68 (4 H, m, Ph) and 9.69 (1 H, t, *J* 0.7, CHO); δ_C(22.5 MHz) 19.17 (s), 26.87 (q), 63.49 (t), 70.86 (t), 71.29 (t), 72.54 (t), 76.82 (t), 127.64 (d), 129.64 (d), 133.70 (s), 135.60 (d) and 200.61 (d); *m/z* (FAB) 387 (MH^+, 0.2%), 239 (9), 199 (24), 197 (49), 165 (39), 135 (100) and 57 (19).

2-[2-(tert-*Butyldiphenylsiloxy)ethoxy]ethyl* 2,3-*Epoxypent*-4-*enyl Ether* **27**.[9]—To a rapidly mechanically stirred solution of 2-{2-[2-(*tert*-butyldiphenylsiloxy)ethoxy]ethoxy}ethanal **26** (20.65 g, 53.4 mmol), 1-allyltetrahydrothiophenium bromide **6** (13.41 g, 64.1 mmol, 1.2 mol equiv.) and benzyltriethylammonium chloride (1.217 g, 5.34 mmol, 0.1 mol equiv.) in dichloromethane (150 cm^3), cooled to −15 °C, was added cold (5 °C) aq. sodium hydroxide (10 mol dm^{-3}; 150 cm^3) over a period of 2.5 min (dropping funnel). The mixture was adjusted to 0 °C and, after 20 min, was poured onto water (400 cm^3)–dichloromethane (150 cm^3). The aqueous layer was back-extracted with dichloromethane (4 × 150 cm^3) and the combined organic extracts were washed with water (100 cm^3), dried ($MgSO_4$), and evaporated to leave an oil. This was chromatographed using light petroleum–dichloromethane (1:1 and 1:2) and dichloromethane (R_f 0.20) to give 2-[2-(*tert*-butyldiphenylsiloxy)ethoxy]ethyl 2,3-epoxypent-4-enyl ether **27** as an oil (14.75 g, 34.6 mmol, 64.7%), present as *trans* and *cis* epoxide diastereoisomers (90:10) (Found: C, 70.4; H, 8.4. Calc. for $C_{25}H_{34}O_4Si$: C, 70.38; H, 8.03%); ν_{max}(film)/cm^{-1} 3071, 3050, 1645, 1590, 1473, 1428, 1112, 740 and 704; δ_H(250 MHz) 1.05 (9 H, s, Bu^t), 3.07 [1 H, ddd, *J* 5.4, 3.1 and 2.3, CH_2CH(O) *trans*], 3.26 (1 H, dd, *J* 7.0 and 2.1, =CH*CH trans*), 3.32 [1 H, dt, *J* 6.1 and 4.4, CH_2CH(O) *cis*], 3.47 (1 H, dd, *J* 6.7 and 4.4, =CH*CH cis*), 3.52 [1 H, dd, *J* 11.7 and 5.5, OCH_2CH(O)], 3.61 (2 H, t, *J* 5.3, OCH_2), 3.66 (4 H, s, $ROCCH_2CH_2OR'$), 3.78 [1 H, dd, *J* 11.7 and 3.2, OCH_2CH(O)], 3.82 (2 H, t, *J* 5.3, $TBDPSOCH_2$), 5.26–5.50 (2 H, m, $=CH_2$), 5.57 (1 H, ddd, *J* 17.2, 9.5 and 7.0, =CH *trans*), 5.69 (1 H, ddd, *J* 17.2, 10.2 and 6.9, =CH *cis*), 7.40 (6 H, m, Ph) and 7.68 (4 H, m, Ph); δ_C(22.5 MHz) 19.23 (s), 26.87 (q), 2 × 55.85 (d), 56.67 (d), 58.62 (d), 63.55 (t), 68.96 (t), 70.75 (t), 70.91 (t), 71.02 (t), 72.54 (t), 119.35 (t), 120.48 (t), 127.64 (d), 129.59 (d), 131.97 (d), 133.76 (s), 135.04 (d) and 135.60 (d); *m/z* FAB) 239 (9.5%), 209 (28), 199 (22.2), 197 (46), 165 (43), 135 (77), 105 (49), 57 (52) and 55 (100).

2-[2-(2,3-*Epoxypent*-4-*enyloxy)ethoxy]ethanol* **28**.—To a solution of 2-[2-(*tert*-butyldiphenylsiloxy)ethoxy]ethyl 2,3-epoxypent-4-enyl ether **27** (14.52 g, 34.0 mmol) in dry THF (200 cm^3) was added a solution of TBAF (1 mol dm^{-3}; 68 cm^3, 68 mmol, 2 mol equiv.) in THF. The dark red solution was stirred at 25 °C for 2 h, evaporated to dryness, and the residue was chromatographed using dichloromethane–ethyl acetate [3:2 (R_f 0.21)], to give 2-[2-(2,3-*epoxypent*-4-*enyloxy)ethoxy]ethanol* **28** as a slightly coloured oil (6.28 g, 33.4 mmol, 98.0%), present as *trans* and *cis* epoxide diastereoisomers (83:27%) (Found: MH^+, 189.1127. $C_9H_{17}O_4$ requires *m/z* 189.1127); ν_{max}(film)/cm^{-1} 3489, 3090, 1645, 1109, 1070, 991, 934 and 881; δ_H(250 MHz) 2.55 (1 H, br s, OH), 3.11 [1 H, ddd, *J* 5.5, 2.8 and 2.4, OCH_2CH(O) *trans*], 3.29 (1 H, dd, *J* 6.8 and 2.1, =CH*CH trans*), 3.34 [1 H, dt, *J* 6.5 and 4.2, CH_2CH(O) *cis*], 3.50 (1 H, m, =CH*CH cis*), 3.51 [1 H, dd, *J* 11.7 and 5.7, CH_2CH(O)], 3.62 (2 H, t, *J* 4.3, OCH_2CH_2OH), 3.69 (4 H, m, $ROCH_2CH_2OR'$), 3.74 (2 H, m, $HOCH_2$), 3.84 [1 H, dd, *J* 11.7 and 2.9, CH_2CH(O)], 5.30–5.53 (2 H, m, $=CH_2$), 5.60 (1 H, ddd, *J* 17.2, 9.4 and 6.9, =CH *trans*) and 5.71 (1 H, ddd, *J* 17.2, 10.2 and 6.9, =CH *cis*); δ_C(22.5 MHz) 55.64 (d), 55.80 (d), 56.50 (d), 58.45 (d), 61.27 (t), 68.86 (t), 70.21 (t), 70.64 (t), 70.91 (t), 72.59 (t), 119.35 (t), 120.48 (t), 132.19 (d) and 135.22 (d); *m/z* (FAB) 189 (MH^+, 22.0%), 171 (19), 127 (29), 119 (26), 107 (53), 89 (63), 83 (77), and 55 (100).

Photolysis of 2-[2-(2,3-*Epoxypent*-4-*enyloxy)ethoxy]ethanol* **28** *and Bis*-(2-*hydroxyethyl) Disulfide in Acetonitrile*.—A solution of compound **28** (0.3764 g, 2 mmol) and purified bis-(2-hydroxyethyl) disulfide (0.3702 g, 2.4 mmol, 1.2 mol equiv.) in dry deoxygenated acetonitrile (20 cm^3) was irradiated with UV light from a sunlamp at 0–28 °C under nitrogen for 7 days. The solution was evaporated to dryness and the residue was chromatographed using dichloromethane–ethyl acetate (6:1 and 1:1) and then ethyl acetate, to give some remaining starting material **28** (72.5 mg, 0.385 mmol, 19.3% recovery) and the following two products (E)-4-(2-*hydroxyethylthio)but*-2-*enal* **31** as an oil (15.6 mg, 0.107 mmol, 5.3%) [(R_f 0.46), 1:1 dichloromethane–ethyl acetate] (Found: M^+, 146.0397. $C_6H_{10}O_2S$ requires *M*, 146.040 15); λ_{max}(EtOH)/nm 219.3 (ε 4225) and 278.4 (670); ν_{max}(film)/cm^{-1} 3363, 2746, 1682, 1633 and 1051; δ_H(250 MHz; deacidified $CDCl_3$) 1.97 (1 H, br s, OH), 2.69 (2 H, t, *J* 5.9, SCH_2CH_2OH), 3.39 (2 H, dd, *J* 7.3 and 1.2, SCH_2CH=C), 3.76 (2 H, t, *J* 5.8, $HOCH_2$), 6.15 (1 H, ddt, *J* 15.5, 7.7 and 1.2, *CH*CHO), 6.78, (1 H, dt, *J* 15.5 and 7.4, SCH_2CH) and 9.59 (1 H, d, *J* 7.7, HCO); δ_C(67.5 MHz; $CDCl_3$) 32.69 (t), 34.04 (t), 60.59 (t), 133.73 (d), 151.72 (d) and 193.22 (d): *m/z* (EI) 146 (M^+, 23%), 128 (4), 127 (6), 115 (5), 103 (8), 102 (17), 61 (33), 60 (73), 45 (46) and 41 (100); and 2-{[2-(2-*hydroxy ethoxy)ethoxy]methylthio}ethanol* **30** as an oil (67.0 mg, 0.341 mmol, 17.1%) [(R_f 0.23), ethyl acetate] (Found: MH^+, 197.0848. $C_7H_{17}O_4S$ requires *m/z* 197.084 76); ν_{max}(film)/cm^{-1} 3398, 1131, 1068 and 1014; δ_H(250 MHz) 2.85 (2 H, t, *J* 5.0, SCH_2), 3.58 (2 H, m, OCH_2), 3.67 (2 H, m, OCH_2), 3.73 (2 H, m,

OCH_2), 3.79 (2 H, m, $HOCH_2$), 3.79 (2 H, t, *J* 5.0, $HOCH_2$), 3.92 (2 H, br s, 2 × OH) and 4.69 (2 H, s, SCH_2O); δ_C(100 MHz) 37.48 (t), 61.78 (t), 62.50 (t), 67.54 (t), 69.50 (t), 73.18 (t) and 75.04 (t); *m/z* (FAB) 197 (MH^+, 47%), 119 (57), 107 (62), 91 (100), 89 (50), 77 (25) and 45 (77).

Aqueous Photolysis of 2-[2-(2,3-*Epoxypent*-4-*enyloxy*)*ethoxy*]*ethanol* **28** *and Bis*-(2-*hydroxyethyl*) *Disulfide*.—A solution of compound **28** (0.3764 g, 2 mmol) and purified bis(2-hydroxyethyl)disulfide (0.3702 g, 2.4 mmol, 1.2 mol equiv.) in triply deionised deoxygenated water (20 cm^3) was irradiated with UV light from a sunlamp at 25–35 °C under nitrogen for 7 days. The solution was extracted with dichloromethane (6 × 7 cm^3), the organic layers were dried ($MgSO_4$) and evaporated to dryness, and the residue was chromatographed using 4:1 dichloromethane–pentane and then 6:1 dichloromethane–ethyl acetate to give two products: (1,4-*oxathian*-2-*yl*)*acetaldehyde* **32** as an oil (10.0 mg, 0.0684 mmol, 3.4%) [(R_f 0.19), 4:1 dichloromethane–pentane] (Found: M^+, 146.0424. $C_6H_{10}O_2S$ requires *M*, 146.040 15); ν_{max}(film)/cm^{-1} 2732 and 1724; δ_H(250 MHz) 2.27 (1 H, dq, *J* 13.6 and 2.0, 5-H), 2.40 (1 H, br d, *J* 13.4, 3-H), 2.52 (1 H, ddd, *J* 16.5, 4.8 and 1.6, CH_2CHO), 2.65 (1 H, ddd, *J* 16.5, 7.9 and 2.5, CH_2CHO), 2.69 (1 H, br dd, *J* 13.5 and 10.6, 3-H), 2.88 (1 H, br td, *J* 12.7 and 3.1, 5-H), 3.80 (1 H, td, *J* 11.8 and 2.1, 6-H), 4.14 (1 H, dddd, *J* 10.3, 7.8, 4.8 and 2.0, 2-H), 4.20 (1 H, br dt, *J* 11.9 and 2.5, 6-H) and 9.76 (1 H, dd, *J* 2.4 and 1.7, CHO); δ_C(100 MHz; $CDCl_3$) 26.34 (t), 31.20 (t), 49.77 (t), 69.27 (t), 73.28 (d) and 200.09 (d); *m/z* (EI) 146 (M^+, 47.3%), 117 (17), 102 (47), 74 (33) and 46 (100); and (*E*)-4-(2-hydroxyethylthio)but-2-enal **31** as an oil (1.1 mg, 0.0075 mmol, 0.38%). Data were identical with those for product isolated in the previous reaction using acetonitrile.

The remaining aqueous layer was evaporated to dryness and the residue was chromatographed using 2% and then 5% methanol in dichloromethane to give 2-{[2-(2-hydroxyethoxy)-ethoxy]methylthio}ethanol **30** as an oil (55.3 mg, 0.282 mmol, 14.1%) [(R_f 0.41), 5% methanol in dichloromethane]. Data were identical with those for the product isolated in the previous reaction using acetonitrile; and 1-[2-(2-*hydroxyethoxy*)*ethoxy*]*pent*-4-*ene*-2,3-*diol* **33** as an oil (0.1848 g, 0.0896 mmol, 44.8%) [(R_f 0.22), 5% methanol in dichloromethane], present as *trans* and *cis* diol diastereoisomers (10:1) (Found: MH^+, 207.123. $C_9H_{19}O_5$ requires *m/z* 207.123); ν_{max}(film)/cm^{-1} 3384, 1646, 1117 and 1068; δ_H(250 MHz) 3.04 (3 H, br s, 3 × OH), 3.61 (2 H, t, *J* 4, OCH_2), 3.67 (5 H, m, 2 × OCH_2 and 1 H of OCH_2CHOH), 3.75 (2 H, t, *J* 4, $HOCH_2$), 3.72–3.81 (2 H, m, 2-H and 1 H of OCH_2CHOH), 4.17 (1 H, ddt, *J* 6.0, 4.8 and 1.2, =CHC*H*OH isomer 1), 4.28 (1 H, ddt, *J* 5.7, 4.4 and 1.5, =CHC*H*OH isomer 2), 5.24 (1 H, dt, *J* 10.6 and 1.5, $=CH_2$), 5.37 (1 H, dt, *J* 17.3 and 1.5, $=CH_2$) and 5.91 (1 H, ddd, *J* 17.3, 10.5 and 5.7, =CH); δ_C(100 MHz; $CDCl_3$) 61.82 (t), 70.22 (t), 70.90 (t), 72.28 (t), 72.41 (d), 72.74 (t), 73.17 (t), 73.65 (d), 74.63 (d) 116.74 (t), 117.18 (t), 136.76 (d) and 137.10 (d); *m/z* (FAB) 207 (MH^+, 67%), 189 (7), 171 (19), 119 (30), 107 (54), 89 (47), 83 (51) and 45 (100).

3,4-*Epoxyhex*-5-*enyl Toluene*-p-*sulfonate* **34**.—To an ice-cooled solution of 3,4-epoxyhex-5-en-1-ol **20** (0.5707 g, 5 mmol) in dry pyridine (10 cm^3) was added toluene-*p*-sulfonyl chloride (2.38 g, 12.5 mmol, 2.5 mol equiv.) in parts during 3 min. After 1.5 h at 0 °C the mixture was diluted with diethyl ether (20 cm^3) and extracted successively with aq. copper sulfate (2%, then 4%, then 20%) until darkening of the aqueous phase ceased, then with water (20 cm^3). The organic layer was dried ($MgSO_4$), evaporated to dryness, and the residue was chromatographed using light petroleum–ethyl acetate [9:1 and 5:1 (R_f 0.21)] to give 3,4-*epoxyhex*-5-*enyl toluene*-p-*sulfonate* **34** as an oil (1.028 g, 3.83 mmol, 76.6%), present as *trans* and *cis* epoxide diastereoisomers (64:36) (Found: MH^+, 269.0848. $C_{13}H_{17}O_4S$ requires *m/z* 269.084 76); λ_{max}(MeCN)/nm 225.1 (ε 13 000), 261.6 (640) and 272.7 (510); ν_{max}(film)/cm^{-1} 3090, 1644, 1599, 1495, 1359, 1177 and 817; δ_H(250 MHz) 1.78–2.0 (1 H, m, 2-H *cis* and 2-H_2 *trans*), 2.06 (1 H, dtd, *J* 14.8, 7.0 and 4.6, 2-H *trans*), 2.46 (3 H, s, Me), 2.88 (1 H, ddd, *J* 6.5, 4.5 and 2.1, 3-H *trans*), 3.11 (1 H, dd, *J* 6.4 and 2.0), 4-H *trans*), 3.13 (1 H, ddd, *J* 7.0, 5.1 and 4.3, 3-H *cis*), 3.42 (1 H, dd, *J* 6.4 and 4.3, 4-H *cis*), 4.16 (2 H, dd, *J* 7.0 and 5.4, 1-H_2 *trans*), 4.17 (2 H, dd, *J* 6.9 and 5.7, 1-H_2 *cis*), 5.25–5.48 (2 H, m, 6-H_2 *cis* and *trans*), 5.53 (1 H, ddd, *J* 17.1, 9.2 and 6.6, 5-H *trans*), 5.65 (1 H, ddd, *J* 17.2, 10.2 and 6.5, 5-H *cis*), 7.36 (2 H, d, *J* 8.3, ArH) and 7.80 (2 H, d, *J* 8.3, ArH); δ_C(22.5 MHz) 21.56 (q), 27.68 (t), 31.64 (t), 54.85 (d), 56.56 (d), 58.29 (d), 67.07 (t), 67.66 (t), 119.35 (t), 120.59 (t), 127.85 (d), 129.97 (d), 131.75 (d), 135.06 (d), 133.11 (s) and 144.97 (s); *m/z* (FAB) 269 (MH^+, 9%), 227 (6), 155 (30), 97 (100), 91 (53) and 69 (50).

3,4-*Epoxyhex*-5-*enyl*-1,10-*phenanthrolinium Toluene*-p-*sulfonate* **35**.—A solution of 3,4-epoxyhex-5-enyl toluene-*p*-sulfonate **34** (0.1005 g, 0.357 mmol) and anhydrous 1,10-phenanthroline (0.236 g, 1.309 mmol, 3.5 mol equiv.) in dry acetonitrile (2 cm^3) under nitrogen was stirred at 60–70 °C for 3 days. The deep blue solution was evaporated to dryness and the residue was triturated with ethyl acetate (× 2). The residue was taken up in more dry acetonitrile (2–5 cm^3) and the solution was added slowly to rapidly stirred ethyl acetate (50 cm^3) to give a deep blue tar after an initial blue precipitate. After two further precipitations, final traces of phenanthroline were removed by recrystallisation from chloroform–toluene (80 to −60 °C) to give 3,4-*epoxyhex*-5-*enyl*-1,10-*phenanthrolinium toluene*-p-*sulfonate* **35** as a dark blue–green–purple tar (55.7 mg, 0.124 mmol, 33.1%), present as *trans* and *cis* epoxide diastereoisomers (2:1) [Found: M^+ (cation only), 277.1341. $C_{18}H_{17}N_2O^+$ requires *m/z* 277.1341]; λ_{max}(MeCN)/nm 220.2 (ε 97 000), 270.7 (68 000), 308sh (18 000) and 360sh (3100); ν_{max}(film)/3066, 1645, 1629, 1598, 1582, 1530, 1496, 1471, 1217, 1190, 1122, 1035, 1012, 721 and 683; δ_H(250 MHz; CD_3CN) 2.29 (3 H, s, Me), 2.4 (2 H, m, 2-H_2), 3.06 (1 H, dd, *J* 7.0 and 2.0, 4-H *trans*), 3.16 (1 H, ddd, *J* 6.7, 4.8 and 2.0, 3-H *trans*), 3.35 (1 H, dd, *J* 6.8 and 4.5, 4-H *cis*), 3.41 (1 H, td, *J* 6.3 and 4.3, 3-H *cis*), 5.0–5.6 (3 H, m, 5-H and 6-H_2), 6.14 (2 H, m, 1-H_2), 7.11 (2 H, d, *J* 7.9, ArH), 7.58 (2 H, d, *J* 8.0, ArH), 7.96 (1 H, dd, *J* 8.2 and 4.3, ArH), 8.22 (1 H, d, *J* 8.8, ArH), 8.24 (1 H, dd, *J* 8.2 and 5.8, ArH), 8.30 (1 H, d, *J* 8.9, ArH), 8.64 (1 H, dd, *J* 8.2 and 1.7, ArH), 9.19 (1 H, dd, *J* 8.3 and 1.4, ArH), 9.27 (1 H, dd, *J* 4.2 and 1.9, ArH) and 9.32 (1 H, dd, *J* 6.0 and 1.2, ArH); δ_C(67.5 MHz; CD_3CN) 21.29 (q), 30.21 (t), 34.29 (t), 56.37 (d), 57.18 (d), 57.84 (d), 58.65 (d), 62.43 (t), 62.77 (t), 120.29 (t), 121.11 (t), 125.51 (d), 126.41 (d), 126.66 (d), 127.98 (d), 129.34 (d), 131.89 (d), 133.01 (d), 133.12 (d), 134.01 (s), 136.42 (d), 138.15 (s), 138.83 (d), 139.75 (s), 140.93 (s), 146.23 (s), 148.43 (d), 151.00 (d) and 151.98 (d); *m/z* (FAB) 277 [M^+ (cation only), 100%], 194 ($PhenCH_2^+$, 7.7), 181 (Phen + H^+, 49.3), 107 (7.4), 89 (10.8) and 77 (13.2).

DNA Cleavage Experiments

Standard Solutions and Reagents.—*Electrophoresis buffer*: Tris(hydroxymethyl)aminomethane base (242 g, 2 mol), 1 × TAE (Tris acetate)–glacial acetic acid (57.1 cm^3, 1 mol) and ethylenediaminetetraacetic acid disodium salt (18.61 g, 50 mmol) were dissolved in triply deionized water (50 dm^3). Final concentrations were Tris acetate (40 mmol dm^{-3}), EDTA (1 mmol dm^{-3}), EDTA (1 mmol dm^{-3}), pH 8.2. Bromophenol blue gel marker 0.025% w/v solution; a sample (2.5 mg) was dissolved in 10% v/v aq. glycerol (10 cm^3). Ethidium bromide 1% w/v solution; a sample (0.1 g) was dissolved in 1 × Tris

borate–EDTA buffer (10 cm^3) for use as a DNA stain (90 mmol dm^{-3} Tris borate–EDTA).

Reaction buffer: 0.25 mol dm^{-3} ammonium acetate in triply deionized water, pH 7.05.

ΦX174 RF DNA: DNA (0.274 μg mm^{-3}) was dissolved in a 10 mmol dm^{-3} Tris-HCl–5 mmol dm^{-3} NaCl–0.1 mmol dm^{-3} Na_2EDTA buffer, pH 7.4. Relative molecular mass. 3.6×10^6 (5386 bp); therefore concentration of DNA was 7.5×10^{-14} moles DNA mm^{-3} (75 nmol dm^{-3}), or 4.1×10^{-10} moles of base pairs mm^{-3} (0.41 mmol dm^{-3}). The composition of the DNA was 85% Form I and 15% Form II. This DNA, obtained from Bethesda Research Laboratories, was stored at 4 °C.

Preparation of 0.8% *Agarose Gels.*—Agarose (0.8 g) (Sigma Grade A 9539) was added to 1 × TAE buffer (100 cm^3) and the mixture was heated to 90–100 °C until the solution became completely clear. After being degassed carefully for 5–10 min (water-pump), the solution was allowed to cool to 50–60 °C and poured into an exactly horizontal 10 × 10 cm gel mould (complete with an exactly vertical 20-tooth well-comb) to set. The gel was stored under 1 × TAE until ready for use, to prevent dehydration.

Electrophoresis of Agarose Gels.—With the gel submerged in the electrophoresis vessel containing 1 × TAE buffer (850 cm^3), the comb was removed and the DNA mixtures were applied to the relevant wells by using an accurate pipette (Gilson Pipetman). Ethidium bromide solution (85 mm^3) was added to the running buffer and electrophoresis was commenced at 100 V (3.7 V cm^{-1}) for 3 h. The gel was visualised from below with UV light (254 nm) from a transilluminator and was photographed with a Polaroid camera.

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