ELECTRONIC SUPPORTING INFORMATION

The Stereochemical Course of Bromoetherification of Enynes

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Contents

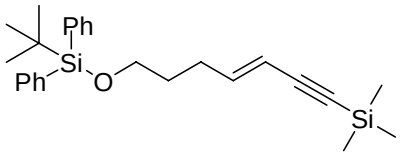
General. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance 400 spectrometer (at 400 and 100 MHz respectively) or on a Jeol GSK-270 spectrometer (at 270 and 68 MHz respectively) in $CDCl_3$ using the residual solvent signal as the internal standard. Chemical shifts (δ) are given in parts per million and coupling constants (J) in Hz. All the following ^{1}H NMR data use the abbreviations as follows: singlet (s), broad singlet (br s), doublet (d), broad doublet (br d), doublet of doublets (dd), doublet of triplets (dt), triplet (t), apparent quartet (app. q), multiplet (m), broad multiplet (br m) and aromatic (Ar). In certain instances structural assignments of the ^{1}H and ^{13}C NMR spectra were elucidated with the aid of COSY, HMQC and PENDANT experiments. AA'BB' systems (protons chemically but not magnetically equivalent) in *para* substituted benzene rings are reported as doublets.

Infrared spectra were recorded on a Perkin Elmer Spectrum RX FT-IR system with internal background calibration in the range 600-4000 cm^{-1}, or a Mattson 500 FTIR spectrometer using thin films on NaCl plates (thin film). Absorption maxima are recorded in wavenumbers (cm^{-1}). Mass spectra including high resolution spectra were recorded by the Imperial College Department of Chemistry Mass Spectrometry Service using chemical ionisation (CI). All analyses were performed in positive ionisation mode using ammonia as the CI reagent gas compound. Elemental analyses were performed by the London Metropolitan University Analytical Service.

Materials. All solvents were reagent grade. Water was distilled. Where anhydrous solvents were required, they were freshly distilled under nitrogen prior to use. CH_2Cl_2 was distilled from calcium hydride, whilst THF and Et_2O were distilled from potassium and sodium wire respectively, in the presence of benzophenone. Solvents and reagents were deoxygenated where necessary by purging with nitrogen. Petroleum ether refers to light petroleum, the fraction of petroleum ether boiling in the range of 40-60 ºC. All reagents were used as supplied without prior purification unless otherwise stated, and obtained from Acros Organics Ltd and Sigma-Aldrich Chemical Co Ltd. Thin layer chromatography was performed using commercially available Merck Kieselgel aluminium backed plates coated with a 0.20 mm layer of silica gel 60 with fluorescent indicator UV_{254}. These plates were visualised using either ultraviolet light of 254 nm

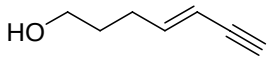
wavelength, or by staining the plates with potassium permanganate or vanillin solution followed by gentle warming. Flash column chromatography was carried out using BDH 33-70 μm grade silica gel. Reactions requiring anhydrous conditions were performed under nitrogen in oven dried glassware.

(*E*)-7-(*tert*-Butyldiphenylsilanyloxy)-1-trimethylsilanylhept-3-en-1-yne (**11**)



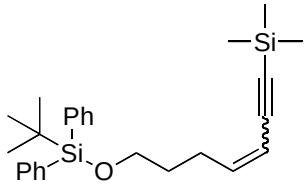
To a stirred suspension of phosphonium bromide **10** (431 mg, 0.95 mmol) in anhydrous THF (25 mL) was added dropwise NaHMDS in THF (1.0 M, 0.92 mL, 0.92 mmol) at 0 ^{o}C. The reaction mixture was allowed to warm to room temperature and stirred for 40 min. The mixture was cooled to -78 ^{o}C and aldehyde **9** (209 mg, 0.64 mmol) in THF (2 mL) was added dropwise. After complete addition the reaction was allowed to warm to room temperature over 12 h. The reaction mixture was poured into H_2O (80 mL) and extracted with Et_2O (2 × 80 mL). The combined organics were washed with brine (1 × 80 mL), dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The residue was chromatographed (petroleum ether : CH_2Cl_2 90 : 10) to yield (*E*)-enyne **11** (111 mg, 0.26 mmol, 45%) as a colourless oil: R_f 0.34 (petroleum ether : CH_2Cl_2 80 : 20); IR (thin film) 2176, 2138 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.64-7.63 (4H, m, PhH), 7.46-7.34 (6H, m, PhH), 6.22 (1H, dt, *J* = 15.9, 6.8 Hz, -C≡C-CH=CH-), 5.52 (1H, d, *J* = 15.9 Hz, -C≡C-CH=CH-), 3.68 (2H, t, *J* = 6.2 Hz, -CH$_2$-O-Si-), 2.28-2.15 (2H, m, -CH=CH-CH$_2$-CH$_2$-), 1.63 (2H, m, -CH=CH-CH$_2$-), 1.07 (9H, s, -Si-C(CH$_3$)$_3$), 0.21 (9H, s, -Si(CH$_3$)$_3$); ^{13}C NMR (68 MHz, $CDCl_3$) δ 145.8, 135.6, 134.0 (PhC-*ipso*), 129.7, 127.0, 110.1, 104.2 (-Si-C≡C-), 92.7 (-Si-C≡C-), 63.0 (-CH$_2$-O-Si-), 31.6, 29.6, 26.9 (-Si-C(CH$_3$)$_3$), 19.3 (-Si-C(CH$_3$)$_3$), 0.1 (-Si(CH$_3$)$_3$); MS (CI$^+$, NH_3) *m/z* 438 $(M + NH_4)^+$, 421 $(M + H)^+$, 165 (M - OTBDPS)$^+$; HRMS (CI$^+$, NH_3) *m/z* calcd for $C_{26}H_{37}OSi_2$ $(M + H)^+$ 421.2383, found 421.2367; Anal. calcd for $C_{26}H_{36}OSi_2$: C, 74.22; H, 8.62. Found: C, 74.12; H, 8.54%.

(*E*)-Hept-4-en-6-yn-1-ol (**5**)



To a stirred solution of enyne **11** (237 mg, 0.56 mmol) in anhydrous THF (5 mL) was added TBAF in THF (1.0 M, 2.0 mL, 2.0 mmol) at 0 ^{o}C and the reaction mixture was allowed to stir at this temperature for 3 h. The mixture was diluted with Et_2O (30 mL) and washed with a saturated aqueous solution of $NaHCO_3$ (1 × 30 mL). The aqueous layer was extracted with Et_2O (2 × 30 mL) and the combined organics were dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The residue was chromatographed (petroleum ether : Et_2O 30 : 70) to yield enyne alcohol **5** (53 mg, 0.48 mmol, 86%) as a yellow oil: R_f 0.50 (petroleum ether : Et_2O 30 : 70); IR (thin film) 3600-3200, 3293, 2102 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 6.24 (1H, dt, *J* = 15.9, 7.0 Hz, HC≡C-CH=C<u>H</u>-), 5.47 (1H, br d, *J* = 15.9 Hz, HC≡C-C<u>H</u>=CH-), 3.65 (2H, t, *J* = 6.4 Hz, -C<u>H</u>$_2$-OH), 2.78 (1H, br s, <u>H</u>C≡C-), 2.24-2.14 (2H, m, -CH=CH-CH$_2$-C<u>H</u>$_2$-), 1.65 (2H, td, *J* = 7.0, 14.1 Hz, -CH=CH-C<u>H</u>$_2$-); ^{13}C NMR (68 MHz, $CDCl_3$) δ 145.9 (HC≡C-<u>C</u>H=CH- or HC≡C-CH=<u>C</u>H-), 109.2 (HC≡C-<u>C</u>H=CH- or HC≡C-CH=<u>C</u>H-), 82.4 (HC≡<u>C</u>-), 76.0 (H<u>C</u>≡C-), 62.1, 31.5, 29.4; MS (CI$^+$, NH_3) *m/z* 128 $(M + NH_4)^+$, 111 $(M + H)^+$; HRMS (CI$^+$, NH_3) *m/z* calcd for $C_7H_{14}NO$ $(M + NH_4)^+$ 128.1075, found 128.1076.

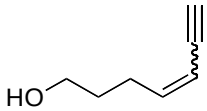
(Z)-7-(*tert*-Butyldiphenylsilanyloxy)-1-trimethylsilanylhept-3-en-1-yne (**15**)



To a stirred suspension of phosphonium iodide **13** (119 mg, 0.17 mmol) in anhydrous THF (5 mL) was added dropwise NaHMDS in THF (1.0 M, 160 μL, 0.16 mmol) at 0 ^{o}C. The reaction mixture was allowed to warm to room temperature and stirred for 40 min. The mixture was cooled to -78 ^{o}C and propargyl aldehyde **14** (14 mg, 0.11 mmol) in THF

(0.5 mL) was added dropwise. After complete addition the reaction mixture was allowed to warm to room temperature over 5 h. The mixture was poured into H_2O (10 mL) and extracted with Et_2O (2 × 10 mL). The combined organics were washed with brine (1 × 10 mL), dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The residue was chromatographed (petroleum ether : CH_2Cl_2 90 : 10) to yield a mixture of (*E*)-**11** and (*Z*)-**15** enynes (28 mg, 67 μmol, 58%) as a colourless oil in a 1 : 1.6 ratio in favour of the (*Z*)-enyne. (*Z*)-Enyne **15**: R_f 0.34 (petroleum ether : CH_2Cl_2 80 : 20); IR (thin film) 2175, 2141 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.72-7.61 (4H, m, PhH), 7.48-7.33 (6H, m, PhH), 5.91 (1H, dt, *J* = 10.8, 7.2 Hz, -C≡C=CH=CH-), 5.46 (1H, br d, *J* = 10.8 Hz, -C≡C-CH=CH-), 3.65 (2H, t, *J* = 6.2 Hz, -CH_2-O-Si-), 2.49-2.38 (2H, m, -CH=CH-CH_2-CH_2-), 1.73-1.54 (2H, m, -CH=CH-CH_2-), 1.08 (9H, s, -Si-C(CH_3)$_3$), 0.20 (9H, s, -Si(CH_3)$_3$); ^{13}C NMR (68 MHz, $CDCl_3$) δ 145.1, 135.7, 133.9 (PhC-*ipso*), 129.6, 127.7, 109.4, 104.2 (-Si-C≡C-), 92.7 (-Si-C≡C-), 63.5 (-CH_2-O-Si-), 31.8, 29.5, 27.0 (-Si-C(CH_3)$_3$), 19.3 (-Si-C(CH_3)$_3$), 0.1 (-Si(CH_3)$_3$); MS (CI^+, NH_3) *m/z* 438 $(M + NH_4)^+$, 421 $(M + H)^+$, 165 $(M - OTBDPS)^+$; HRMS (CI^+, NH_3) *m/z* calcd for $C_{26}H_{37}OSi_2$ $(M + H)^+$ 421.2383, found 421.2367.

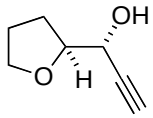
(*Z*)-Hept-4-en-6-yn-1-ol (**6**)



To a stirred solution of (*E*)-**11** and (*Z*)-**15** enynes (1 : 1.6 mixture) (80 mg, 0.19 mmol) in anhydrous THF (2 mL) was added TBAF in THF (1.0 M, 670 μL, 0.67 mmol) at 0 °C and the reaction mixture was allowed to stir at this temperature for 3 h. The mixture was diluted with Et_2O (30 mL) and washed with a saturated aqueous solution of $NaHCO_3$ (1 × 30 mL). The aqueous layer was extracted with Et_2O (2 × 30 mL) and the combined organics were dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The residue was chromatographed (petroleum ether : Et_2O 30 : 70) to yield (*E*)-**5** and (*Z*)-**6** enyne alcohols (13 mg, 0.12 mmol, 62%) as a yellow oil in a 1 : 1.6 ratio in favour of the (*Z*)-enyne alcohol **6**. (*Z*)-Enyne alcohol **6**: R_f 0.50 (petroleum ether : Et_2O 30 : 70); IR

(thin film) 3600-3200, 2102 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 6.02 (1H, dt, *J* = 10.8, 7.6 Hz, HC≡C-CH=C<u>H</u>-), 5.53-5.44 (1H, m, HC≡C-C<u>H</u>=CH-), 3.63 (2H, t, *J* = 6.5 Hz, -C<u>H</u>$_2$-OH), 3.08 (1H, br s, <u>H</u>C≡C-), 2.47-2.38 (2H, m, -CH=CH-CH$_2$-C<u>H</u>$_2$-), 1.70-1.58 (2H, -CH=CH-C<u>H</u>$_2$-); ^{13}C NMR (68 MHz, $CDCl_3$) δ 145.1 (HC≡C-<u>C</u>H=CH- or HC≡C-CH=<u>C</u>H-), 109.0 (HC≡C-<u>C</u>H=CH- or HC≡C-CH=<u>C</u>H-), 81.8 (HC≡<u>C</u>-), 76.0 (H<u>C</u>≡C-), 62.09 (-<u>C</u>H$_2$-OH), 31.4, 29.4.

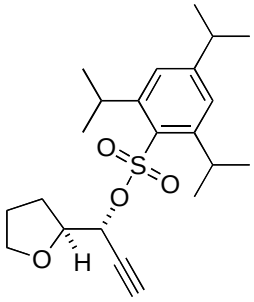
(*R**)-1-((*S**)-Tetrahydrofuran-2-yl)prop-2-yn-1-ol (**16**)



To a stirred solution of enyne **5** (110 mg, 1.0 mmol) in dichloromethane (8.0 mL) at 0°C was added *m*-chloroperbenzoic acid (70%, 49 mg, 2.0 mmol). The mixture was stirred at r.t. for 24 h, and a further portion *m*-chloroperbenzoic acid (25 mg, 1.0 mmol) was added. The mixture was stirred for 16 h, diluted with dichloromethane (15 mL), and the solution was washed successively with saturated sodium hydrogen carbonate solution (5 mL), saturated sodium sulfite solution (5 mL), and brine (5 mL). The organic phase was dried over anhydrous magnesium sulfate, and the solvent was removed *in vacuo*. The residue was purified by silica gel column chromatography (petroleum ether : Et_2O 33 : 67) to give 3-((2*R**,3*R**)-3-ethynyloxiran-2-yl)propan-1-ol (Mukai, C.; Sugimoto, Y.-i.; Ikeda Y.; Hanaoka, M. *Tetrahedron Lett.* **1994**, *35*, 2183-2186) as a colourless oil (57 mg, 45% yield). To a stirred solution of this epoxide (27 mg, 0.21 mmol) in anhydrous dichloromethane (4.0 mL) at –40°C was added (1*S*)-(+)-camphor-10-sulfonic acid (5 mg). The mixture was allowed to warm to r.t. over 4 h, after which time the reaction was quenched by the addition of 2 drops of triethylamine. The solvent was removed *in vacuo* and the residue was purified by column chromatography to give the title compound **16** (21 mg, 78% yield) as a colourless oil. R_f 0.5 (petroleum ether : Et_2O 30 : 70); IR (thin film) 3409 (br), 3289, 2115 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.44 (1H, m), 4.07 (1H, m), 3.94 (1H, m), 3.85 (1H, m), 2.68 (1H, br s), 2.43 (1H, s), 1.85-2.10 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 81.9, 81.1, 73.9, 69.4, 64.4, 26.5, 26.0; MS (CI^+, NH_3) *m/z* 144 $(M + NH_4)^+$; HRMS (CI^+, NH_3) *m/z* calcd for $C_7H_{14}NO_2$ $(M + NH_4)^+$ 144.1025,

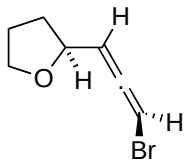
found 144.1027. The corresponding *R**,*R**-diastereomer was present as ca 15% of the mixture.

(*R**)-1-((*S**)-Tetrahydrofuran-2-yl)prop-2-ynyl 2,4,6-triisopropylbenzenesulfonate (**17**)



To a stirred solution of alcohol **16** (21 mg, 0.17 mmol) in anhydrous dichloromethane (3 mL) was added 2,4,6-triisopropylbenzenesulfonyl chloride (84 mg, 0.27 mmol) and 4-dimethylaminopyridine (47 mg, 0.39 mmol). The mixture was heated to 40°C for 1.5 h. The cooled mixture was dilute with diethyl ether (10 mL) and filtered through celite. The solvent was removed *in vacuo* and the residue was purified by column chromatography (petroleum ether : Et_2O 75 : 25) to give the title compound **17** (45 mg, 69% yield) as a colourless oil. R_f 0.35 (petroleum ether : Et_2O 75 : 25); IR (thin film) 3282, 2125 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.15 (2H, s), 5.13 (1H, br m),4.25-4.14 (3H, m), 3.95 (1H, m), 3.85 (1H, m), 2.92 (1H, m), 2.29 (1H, s), 2.18-1.82 (4H, m), 1.30-1.20 (15H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.6, 150.6, 130.5, 123.4, 79.5, 76.6, 77.2, 71.2, 69.4, 34.1, 29.5, 27.4, 25,5, 24.6, 24.4, 23.5; MS (CI^+, NH_3) *m/z* 410 $(M + NH_4)^+$; HRMS (CI^+, NH_3) *m/z* calcd for $C_{22}H_{36}NO_4S$ $(M + NH_4)^+$ 410.2365, found 410.2366.

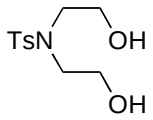
(*S**)-2-((*R**)-3-Bromopropa-1,2-dienyl)tetrahydrofuran (**7a**)



To a stirred solution of trisylate **17** (30 mg, 0.08 mmol) in anhydrous tetrahydrofuran (2 mL) was added lithium(I) bromide (26 mg, 0.30 mmol) and copper(I) bromide (44 mg, 0.30 mmol). The mixture was heated to 60°C for 20 h. The mixture was cooled to r.t.

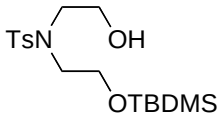
and diluted with diethyl ether (10 mL). The organic phase was washed successively with saturated ammonium chloride solution and brine, and dried over anhydrous magnesium sulfate. The solvent was removed *in vacuo* and the residue was purified by column chromatography (3:1 petroleum ether:diethyl ether, R_f = 0.35) to give the title compound **7a** as a colourless oil (4 mg, 28% yield). This compound proved to be identical to the major diastereoisomer from the bromoetherification of *E*-enyne **5** (see footnote ‡ in main text of paper).

N,*N*-Bis-(2-hydroxyethyl)-4-methyl-benzenesulfonamide (**19**)



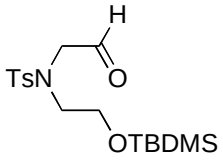
To a three-necked flask equipped with a thermometer and a reflux condenser were successively added H_2O (29 mL), K_2CO_3 (3.75 g, 27.1 mmol) and diethanolamine (**18**) (5.00 g, 47.6 mmol). The mixture was then heated to 70 °C and *p*-toluenesulfonyl chloride (8.93 g, 46.9 mmol) added portionwise over 10 minutes such that the temperature of the reaction did not rise. The mixture was then heated to 100 °C for 1 h after which all the *p*-toluenesulfonyl chloride had been dissolved. The reaction mixture was then slowly allowed to cool down to room temperature and subsequently cooled to 0 °C after which a small amount of white solid appeared. The solid was removed by filtration and the filtrate placed in the freezer overnight after which a white solid precipitated. The solid was collected by filtration, washed repeatedly with ice water, and dried under vacuum over P_2O_5 to give the *N*-tosyl diol **19** (7.66 g, 63%) as a white solid: ^{1}H NMR (400 MHz; $CDCl_3$) 7.71 (2H, d, *J* = 8.4 Hz, Ar<u>H</u>), 7.34 (2H, d, *J* = 8.0 Hz, Ar<u>H</u>), 3.95 (2H, t, *J* = 5.2 Hz, 2 × -CH_2O<u>H</u>), 3.88 (4H, app. q, *J* = 4.6 Hz, 2 × -NCH_2C<u>H_2</u>OH), 3.28 (4H, t, *J* = 4.8 Hz, 2 × -NC<u>H_2</u>CH_2OH), 2.45 (3H, s, -C_6H_4C<u>H_3</u>); ^{13}C NMR (100 MHz; $CDCl_3$) 143.8, 135.2, 129.9, 127.3, 62.3 (-NCH_2<u>C</u>H_2OH), 53.0 (-N<u>C</u>H_2CH_2OH), 21.6 (-C_6H_4<u>C</u>H_3). This data is in agreement with that previously reported in the literature (reference 17 in manuscript).

N-[2-(*tert*-Butyldimethylsilanyloxy)ethyl]-*N*-(2-hydroxyethyl)-4-methyl-benzenesulfonamide (**20**)



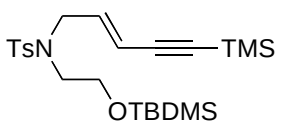
To a stirred suspension of diol **19** (1.94 g, 7.5 mmol) in anhydrous CH_2Cl_2 (15.5 mL) were added sequentially NEt_3 (1.09 mL, 7.85 mmol), DMAP (46 mg, 0.37 mmol) and *tert*-butyldimethylsilyl chloride (1.13 g, 7.5 mmol). The reaction mixture was stirred at room temperature for 21.5 h, after which it was diluted with CH_2Cl_2 (30 mL), washed with H_2O (2 × 30 mL) and a saturated aqueous solution of NH_4Cl (2 × 23 mL), dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The residue was pre-absorbed onto silica and chromatographed (petroleum ether : Et_2O 50 : 50) to give monoalcohol **20** (1.140 g, 41%) as a colourless oil: R_f 0.20 (petroleum ether : Et_2O 50 : 50); IR (thin film) 3600-3300 cm^{-1}; ^1H NMR (400 MHz; $CDCl_3$) 7.71 (2H, d, *J* = 8.4 Hz, Ar<u>H</u>), 7.33 (2H, d, *J* = 8.0 Hz, Ar<u>H</u>), 3.91 (2H, t, *J* = 5.2 Hz, -$NCH_2C\underline{H}_2OSi$-), 3.78 (2H, br t, *J* = 4.6 Hz, -$NCH_2C\underline{H}_2OH$), 3.67 (1H, br s, -$CH_2O\underline{H}$), 3.30 (2H, t, *J* = 5.2 Hz), 3.27 (2H, t, *J* = 4.8 Hz), 2.44 (3H, s, -$C_6H_4C\underline{H}_3$), 0.92 (9H, s, -$Si(CH_3)_2C(C\underline{H}_3)_3$), 0.12 (6H, s, -$Si(C\underline{H}_3)_2C(CH_3)_3$); ^{13}C NMR (100 MHz; $CDCl_3$) 143.6, 135.8, 129.8, 127.3, 63.8, 62.3, 53.4, 52.4, 25.9 (-$Si(CH_3)_2C(\underline{C}H_3)_3$), 21.6 (-$C_6H_4\underline{C}H_3$), 18.4 (-$Si(CH_3)_2\underline{C}(CH_3)_3$), −5.5 (-$Si(\underline{C}H_3)_2C(CH_3)_3$); MS ($CI^+$, NH_3) *m/z* 391 $(M + NH_4)^+$, 374 $(M + H)^+$; HRMS (CI^+, NH_3) *m/z* calcd for $C_{17}H_{32}NO_4SSi$ $(M + H)^+$ 374.1821, found 374.1831; Anal. calcd for $C_{17}H_{31}NO_4SSi$: C, 54.66; H, 8.36; N, 3.75. Found: C, 54.57; H, 8.38; N, 3.65%.

N-[2-(*tert*-Butyldimethylsilanyloxy)ethyl]-4-methyl-*N*-(2-oxo-ethyl)benzenesulfonamide (**21**)



To a stirred suspension of Dess-Martin periodinane (4.11 g, 9.7 mmol) in $CDCl_3$ (30 mL) under a nitrogen atmosphere was added dropwise a solution of alcohol **20** (2.12 g, 5.7 mmol) in $CDCl_3$ (11 mL, 6.5 mL rinse) at 0 °C. The reaction mixture was stirred at 0 °C for 1 h and subsequently allowed to warm to room temperature and stirred for a further 1.5 h at this temperature. The reaction mixture was diluted with Et_2O (130 mL) and the suspension obtained poured into a 1.0 N aqueous solution of NaOH (100 mL). The mixture was stirred for 10 minutes after which the two phases were separated. The ether layer was washed with a 1.0 N aqueous solution of NaOH (1 × 100 mL) and H_2O (1 × 130 mL), dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo* to give aldehyde **21** (1.99 g, 94%) as a colourless oil that solidified to give a white crystalline solid upon standing: R_f 0.35 (petroleum ether : Et_2O 50 : 50); IR (thin film) 1736 cm^{-1}; ^1H NMR (400 MHz; $CDCl_3$) 9.64 (1H, t, *J* = 1.2 Hz, -C<u>H</u>O), 7.70 (2H, d, *J* = 8.4 Hz, Ar<u>H</u>), 7.33 (2H, d, *J* = 8.0 Hz, Ar<u>H</u>), 3.96 (2H, d, *J* = 1.2 Hz, -NC<u>H</u>$_2$CHO), 3.82 (2H, t, *J* = 5.0 Hz, -NCH$_2$C<u>H</u>$_2$OSi-), 3.33 (2H, t, *J* = 5.0 Hz, -NC<u>H</u>$_2$CH$_2$OSi-), 2.44 (3H, s, -C$_6$H$_4$C<u>H</u>$_3$), 0.85 (9H, s, -Si(CH$_3$)$_2$C(C<u>H</u>$_3$)$_3$), 0.03 (6H, s, -Si(C<u>H</u>$_3$)$_2$C(CH$_3$)$_3$); ^{13}C NMR (100 MHz; $CDCl_3$) 199.1 (-<u>C</u>HO), 143.9, 136.0, 129.9, 127.2, 63.5 (-NCH$_2$<u>C</u>H$_2$OSi-), 58.8 (-N<u>C</u>H$_2$CHO), 52.0 (-N<u>C</u>H$_2$CH$_2$OSi-), 25.8 (-Si(CH$_3$)$_2$C(<u>C</u>H$_3$)$_3$), 21.5 (-C$_6$H$_4$<u>C</u>H$_3$), 18.2 (-Si(CH$_3$)$_2$<u>C</u>(CH$_3$)$_3$), −5.5 (-Si(<u>C</u>H$_3$)$_2$C(CH$_3$)$_3$); MS (CI^+, NH_3) *m/z* 389 $(M + NH_4)^+$, 372 $(M + H)^+$; HRMS (CI^+, NH_3) *m/z* calcd for $C_{17}H_{30}NO_4SSi$ $(M + H)^+$ 372.1665, found 372.1658.

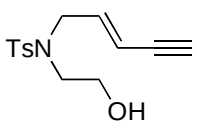
N-[2-(*tert*-Butyldimethylsilanyloxy)ethyl]-4-methyl-*N*-((*E*)-5-trimethylsilanyl-pent-2-en-4-ynyl)benzenesulfonamide (**22**).



To a stirred suspension of phosphonium bromide **10** (3.56 g, 7.86 mmol) in anhydrous THF (120 mL) at 0 °C was added dropwise NaHMDS in THF (1.0 M, 7.27 mL, 7.27

mmol). The reaction mixture was allowed to warm to room temperature and stirred for 40 min. The mixture was then cooled to −78 °C and a solution of aldehyde **21** (1.96 g, 5.27 mmol) in THF (30 mL, 6 mL rinse) added dropwise. After complete addition the reaction was allowed to slowly warm to room temperature over 15.33 h. The reaction mixture was poured into a saturated aqueous solution of NH_4Cl (300 mL) and extracted with Et_2O (2 × 450 mL). The combined organic extracts were washed with brine (1 × 450 mL), dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The residue obtained was pre-absorbed onto silica and chromatographed (petroleum ether : Et_2O 90 : 10) to give *E*-enyne **22** (1.67 g, 68%) as the major component in a *E*:*Z* mixture (see footnote ¶ in main text of paper) as a mixture of a colourless oil and a white crystalline solid. *E*-enyne: R_f 0.73 (petroleum ether : Et_2O 30 : 70); IR (thin film) 2174, 2135 cm^{-1}; ^1H NMR (400 MHz; $CDCl_3$) 7.68 (2H, d, *J* = 8.4 Hz, Ar<u>H</u>), 7.28 (2H, d, *J* = 8.0 Hz, Ar<u>H</u>), 5.99 (1H, dt, *J* = 16.0, 6.4 Hz, -NCH$_2$C<u>H</u>=CH-), 5.60 (1H, d, *J* = 16.0 Hz, -CH=C<u>H</u>C≡), 3.91 (2H, d, *J* = 6.4 Hz, -NC<u>H</u>$_2$CH=CH-), 3.71 (2H, t, *J* = 6.0 Hz, -NCH$_2$C<u>H</u>$_2$OSi-), 3.20 (2H, t, *J* = 6.2 Hz, -NC<u>H</u>$_2$CH$_2$OSi-), 2.40 (3H, s, -C$_6$H$_4$C<u>H</u>$_3$), 0.86 (9H, s, -Si(CH$_3$)$_2$C(C<u>H</u>$_3$)$_3$), 0.16 (9H, s, -Si(C<u>H</u>$_3$)$_3$), 0.02 (6H, s, -Si(C<u>H</u>$_3$)$_2$C(CH$_3$)$_3$); ^{13}C NMR (100 MHz; $CDCl_3$) 143.3, 139.0, 137.0, 129.7, 127.2, 113.5, 102.4 (-<u>C</u>≡CSi-), 95.6 (-C≡<u>C</u>Si-), 62.4 (-NCH$_2$<u>C</u>H$_2$OSi-), 51.0, 49.3, 25.9 (-Si(CH$_3$)$_2$C(<u>C</u>H$_3$)$_3$), 21.5 (-C$_6$H$_4$<u>C</u>H$_3$), 18.2 (-Si(CH$_3$)$_2$<u>C</u>(CH$_3$)$_3$), −0.2 (-Si(<u>C</u>H$_3$)$_3$), −5.4 (-Si(<u>C</u>H$_3$)$_2$C(CH$_3$)$_3$); MS (CI^+, NH_3) *m/z* 483 $(M + NH_4)^+$, 466 $(M + H)^+$; HRMS (CI^+, NH_3) *m/z* calcd for $C_{23}H_{39}NO_3SSi_2$ $(M + H)^+$ 466.2267, found 466.2272; Anal. calcd for $C_{23}H_{40}NO_3SSi_2$: C, 59.31; H, 8.44; N, 3.01. Found: C, 59.25; H, 8.38; N, 2.96%.

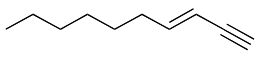
N-(2-Hydroxyethyl)-4-methyl-*N*-((*E*)-pent-2-en-4-ynyl)benzenesulfonamide **23**



To a stirred solution of enyne **22** (185 mg, 0.40 mmol, 19:1 *E*:*Z*) and acetic acid (0.11 mL, 1.98 mmol) in anhydrous THF (16.5 mL) at 0 °C was added dropwise TBAF in THF

(1.0 M, 1.15 mL, 1.15 mmol) and the reaction mixture allowed to stir at 0 °C for 1 h and at room temperature for 3 h. After this time more acetic acid (0.11 mL, 1.98 mmol) was added at room temperature after which the reaction mixture was cooled to 0 °C. TBAF in THF (1.0 M, 1.15 mL, 1.15 mmol) was added dropwise and the reaction mixture stirred at 0 °C for 1 h and at room temperature for 2.5 h. The reaction mixture was diluted with Et_2O (35 mL) and washed with a saturated aqueous solution of $NaHCO_3$ (1 × 35 mL) and brine (1 × 35 mL). The aqueous washes were extracted with Et_2O (2 × 35 mL), and the combined organic extracts dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The residue obtained was pre-absorbed onto silica and chromatographed (petroleum ether : Et_2O 30 : 70) to give the title compound **23** (98 mg, 88%) as a colourless oil. ^{1}H NMR analysis of this oil showed it to be a 21:1 mixture of *E*:*Z* enynes. R_f 0.25 (petroleum ether : Et_2O 30 : 70); IR (thin film) 3600-3200, 3284, 2100 cm^{-1}; ^{1}H NMR (400 MHz; $CDCl_3$) 7.71 (2H, d, *J* = 8.4 Hz, Ar<u>H</u>), 7.33 (2H, d, *J* = 8.0 Hz, Ar<u>H</u>), 6.02 (1H, dt, *J* = 15.9, 6.5 Hz, -NCH$_2$C<u>H</u>=CH-), 5.61 (1H, dd, *J* = 15.6, 1.6 Hz -CH=C<u>H</u>C≡), 3.92 (2H, d, *J* = 6.4 Hz, -NC<u>H</u>$_2$CH=CH-), 3.73 (2H, br s, -NCH$_2$C<u>H</u>$_2$OH), 3.24 (2H, t, *J* = 5.6 Hz, -NC<u>H</u>$_2$CH$_2$OH), 2.91 (1H, d, *J* = 2.0 Hz, -C≡C<u>H</u>), 2.55 (1H, br s, -O<u>H</u>), 2.44 (3H, s, -C$_6$H$_4$C<u>H</u>$_3$); ^{13}C NMR (100 MHz; $CDCl_3$) 143.8, 139.4, 136.1, 129.9, 127.3, 112.9, 80.9 (-<u>C</u>≡CH), 78.7 (-C≡<u>C</u>H), 61.0 (-NCH$_2$<u>C</u>H$_2$OH), 50.9, 49.9, 21.5 (-C$_6$H$_4$<u>C</u>H$_3$); MS (CI$^+$, NH_3) *m/z* 297 $(M + NH_4)^+$, 280 $(M + H)^+$; HRMS (CI$^+$, NH_3) *m/z* calcd for $C_{14}H_{18}NO_3S$ $(M + H)^+$ 280.1007, found 280.1001; Anal. calcd for $C_{14}H_{17}NO_3S$: C, 60.19; H, 6.13; N, 5.01. Found: C, 60.21; H, 5.96; N, 5.09%.

(E)-Dec-3-en-1-yne (**25**)

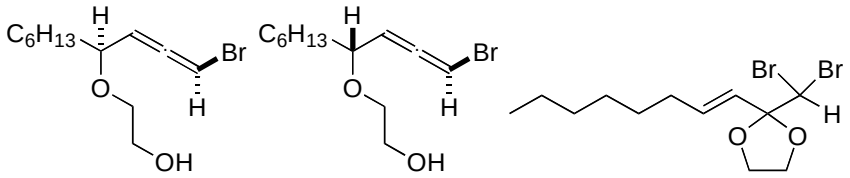


To a stirred suspension of phosphonium bromide **10** (16.1 g, 35.5 mmol) in anhydrous THF (500 mL) was added dropwise NaHMDS in THF (1.0 M, 34.6 mL) at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 40 min. The mixture was cooled to -78 °C and freshly distilled heptaldehyde (3.35 mL, 24 mmol) was added dropwise. After complete addition the reaction was allowed to warm to room

temperature over 18h. The mixture was poured into H_2O (200 mL) and extracted with Et_2O (4 x 90 mL). The combined organics were washed with brine (2 x 80 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was chromatographed (neat petroleum ether) to afford *(E)*-dec-3-en-1-ynyl-trimethylsilane (2.16 g, 43%) as a colourless oil. R_f 0.47 (neat petroleum ether); IR (thin film) 2957, 2927, 2857, 2176, 2145, 1460, 1249, 843; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.21 (1H, td, *J* = 6.9, 15.9 Hz, -C≡C-CH=C<u>H</u>-), 5.49 (1H, d, *J* = 15.9 Hz, -C≡C-C<u>H</u>=CH-), 2.09 (2H, q, *J* = 1.2, 6.9 Hz, CH=CH-C<u>H</u>$_2$-), 1.32-1.41 (2H, m, CH=CH-CH$_2$-C<u>H</u>$_2$-), 1.20-1.31 (6H, m,-C<u>H</u>$_2$-), 0.88 (3H, t, *J* = 7.1 Hz, -C<u>H</u>$_3$), 0.18 (9H, s, -Si(C<u>H</u>$_3$)$_3$; ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.4, 109.5, 104.2, 92.4, 33.1, 31.7, 28.9, 28.5, 22.6, 14.1, 0.3. MS (EI) *m/z* 208 (M^+); HRMS (EI) *m/z* calcd for $C_{13}H_{24}Si$ 208.1647, found 208.1646.

To a stirred solution of *(E)*-dec-3-en-1-ynyl-trimethylsilane (2.16 g, 10.4 mmol) in anhydrous THF (25 mL) was added dropwise TBAF in THF (1.0 M, 36.4 mL) at 0 °C. The reaction mixture was allowed gradually to warm to room temperature and stirred for 12 h. The mixture was diluted with Et_2O (20 mL) and washed with a saturated aqueous solution of $NaHCO_3$ (1 x 30 mL). The aqueous layer was extracted with Et_2O (4 x 20 mL) and the combined organics were dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was chromatographed (neat petroleum ether) to afford *(E)*-enyne **25** (1.3 g, 92%) as a colourless oil. R_f 0.64 (petroleum ether : Et_2O, 1 : 1); IR (thin film) 2921, 2851, 1657, 1632, 1468, 1424, 1042; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.25 (1H, td, *J* = 7.1, 15.9 Hz, -C≡C-CH=C<u>H</u>-), 5.45 (1H, d, *J* = 15.9 Hz, -C≡C-C<u>H</u>=CH-), 2.77 (1H, s, -C≡C<u>H</u>) 2.10 (2H, q, *J* = 1.4, 7.1 Hz, CH=CH-C<u>H</u>$_2$-), 1.34-1.43 (2H, m, CH=CH-CH$_2$-C<u>H</u>$_2$-), 1.21-1.34 (6H, m, -C<u>H</u>$_2$-), 0.88 (3H, t, *J* = 7.0 Hz, -C<u>H</u>$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.0, 108.4, 82.6, 75.5, 33.0, 31.6, 28.8, 28.5, 22.6, 14.1. MS (CI) *m/z* 137 $(M + H)^+$.

2-((2*R**,4*S**)-1-bromodeca-1,2-dien-4-yloxy)ethanol (**26**), 2-((2*R**,4*R**)-1-bromodeca-1,2-dien-4-yloxy)ethanol (**27**) and (*E*)-2-(dibromomethyl)-2-(oct-1-enyl)-1,3-dioxolane (**28**).



To a stirred suspension of enyne **25** (1.3 g, 9.5 mmol) in ethylene glycol (160 mL, 300 equivalents) was added NBS (1.7 g, 9.5 mmol) at -10 °C. The reaction mixture was allowed gradually to warm to room temperature and stirred for 14 h. The mixture was diluted with Et_2O (50 mL) and washed with H_2O (1 x 30 mL). The aqueous layer was extracted with Et_2O (5 x 15 mL) and the combined organics were dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was chromatographed (petroleum ether : Et_2O, 8 : 2) to give first dioxolane **28** (326 mg, 10%) as a colourless oil. R_f 0.64 (petroleum ether : Et_2O, 6 : 4); IR (thin film) 2956, 2924, 2855, 1688, 1466, 1192, 1144, 1104, 1037; ^{1}H NMR (400 MHz, $CDCl_3$) δ ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.2, 123.9, 107.3, 66.2, 49.2, 31.6, 28.6, 22.4, 13.9. MS (CI) *m/z* 354 $(M + H)^+$; HRMS (CI) *m/z* calcd for $C_{12}H_{21}Br_2O_2$ 354.9908, found 354.9908; second bromoallene **26** (185 mg, 7%) as a colourless oil. R_f 0.25 (petroleum ether : Et_2O, 6 : 4); IR (thin film) 3413 (br), 2928, 2858, 1460, 1378, 1193, 1107, 1054; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.96 (1H, d, *J* = 5.8 Hz, C<u>H</u>(Br)C=CH-), 5.20 (1H, dd, *J* = 5.8, 2.1 Hz, CH(Br)C=C<u>H</u>-), 3.79-3.87 (1H, m), 3.60-3.70 (3H, m), 3.37-3.44 (1H, m), 2.56 (1H, s, O<u>H</u>), 1.59-1.67 (1H, m, -C<u>H</u>$_2$-CH-OCH_2-), 1.45-1.53 (1H, m, -C<u>H</u>$_2$-CH-OCH_2-), 1.20-1.35 (8H, m, -C<u>H</u>$_2$-), 0.82 (3H, t, *J* = 6.5 Hz, -C<u>H</u>$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.1, 100.7, 77.7, 73.2, 70.2, 61.6, 35.2, 31.6, 28.9, 26.8, 25.1, 22.4, 13.9. MS (CI) *m/z* 294 $(M + NH_3)^+$; HRMS (CI) *m/z* calcd for $C_{12}H_{25}NBrO_2$ 294.1069, found 294.1071; and third bromoallene **27** (160 mg, 6%) as a colourless oil. R_f 0.19 (petroleum ether : Et_2O, 6 : 4); IR (thin film) 3413 (br), 2928, 2858, 1460, 1378, 1193, 1108, 1053; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.00 (1H, d, *J* = 5.8 Hz, C<u>H</u>(Br)C=CH-), 5.23 (1H, dd, *J* = 5.8, 2.1 Hz, CH(Br)C=C<u>H</u>-), 3.83-3.89 (1H, m), 3.59-3.71 (3H, m), 3.38-3.43 (1H, m), 2.53 (1H, s, O<u>H</u>), 1.62-1.70 (1H, m, -C<u>H</u>$_2$-CH-OCH_2-), 1.46-1.56 (1H, m, -C<u>H</u>$_2$-CH-OCH_2-), 1.16-1.39 (8H, m, -C<u>H</u>$_2$-), 0.83 (3H, t, *J* = 6.5 Hz, -C<u>H</u>$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.5, 101.4, 77.8, 74.0, 72.7, 61.6, 35.4,

31.6, 28.9, 26.8, 25.0, 22.3, 13.9. MS (CI) *m/z* 294 $(M + NH_3)^+$; HRMS (CI) *m/z* calcd for $C_{12}H_{25}NBrO_2$ 294.1069, found 294.1071.

X-Ray crystallography

Single crystal X-ray analysis of **24** revealed disorder in the bromoallene group comprised of C(7), C(8) and Br. Three separate orientations (**I**, **II** and **III**) were identified of *ca.* 71, 15 and 14% occupancy respectively (see Figs. S1, S2 and S3 respectively). Whilst orientation **I** and **II** clearly represent different diastereoisomers, some explanation is required for orientation **III**. Orientations **I** and **II** were relatively easy to identify from Δ*F* maps, but for orientation **III** only the bromine site was easily identified; the corresponding carbons atoms were not located. In cases of multiple overlapping partial-occupancy orientations such as this, it is the heavier atoms that will stand out most clearly (*i.e.* the bromine). It is, however, worth stressing that the carbons atoms for the 15% occupancy orientation **II** were found from Δ*F* maps whilst those for the virtually identical occupancy orientation **III** (14% occupancy) were not, strongly suggesting that the carbon atoms for orientation **III** were at similar positions to those of either orientation **I** or orientation **II**. Given this, it was possible to infer the positions of the carbon atoms for orientation **III** had to be similar to those for orientation **I** as the only other possible pathways from C(7) to Br" would involve carbons atoms well removed from those of orientations **I** and **II** and so they should have been visible from a Δ*F* map. This makes orientation **III** the same diastereoisomer as orientation **I**, giving a *ca.* 85:15 or 5.7:1 diastereomeric ratio. Having said this, the possibility that the carbon atoms for orientation **III** are actually in a different location that would make it the same diastereoisomer as orientation **II** cannot be entirely discounted, though we feel that it is unlikely.

Once positioned, the carbon atoms of orientation **III** were treated in a similar fashion to their counterparts in orientations **I** and **II**. The bond lengths and angles within the three orientations were tied together using SADI restraints, and the thermal parameters were likewise linked using SIMU commands; the occupancies were allowed to vary subject to their totalling unity. Though the bromine centres of all three orientations were refined anisotropically, only for the major occupancy orientation **I** were the carbon atoms C(8) and C(9) allowed to refine anisotropically.

The C_4NO six-membered ring has a chair conformation, {C(2),C(3),C(5),C(6)} being coplanar to better than 0.01 Å with O(1) and N(4) each lying *ca.* 0.66 Å out of this plane

on opposite sides. The tosyl and bromoallene substituents are both in equatorial positions, the N(4) centre being pyramidal (the nitrogen lies *ca.* 0.36 Å out of the plane of its substituents).

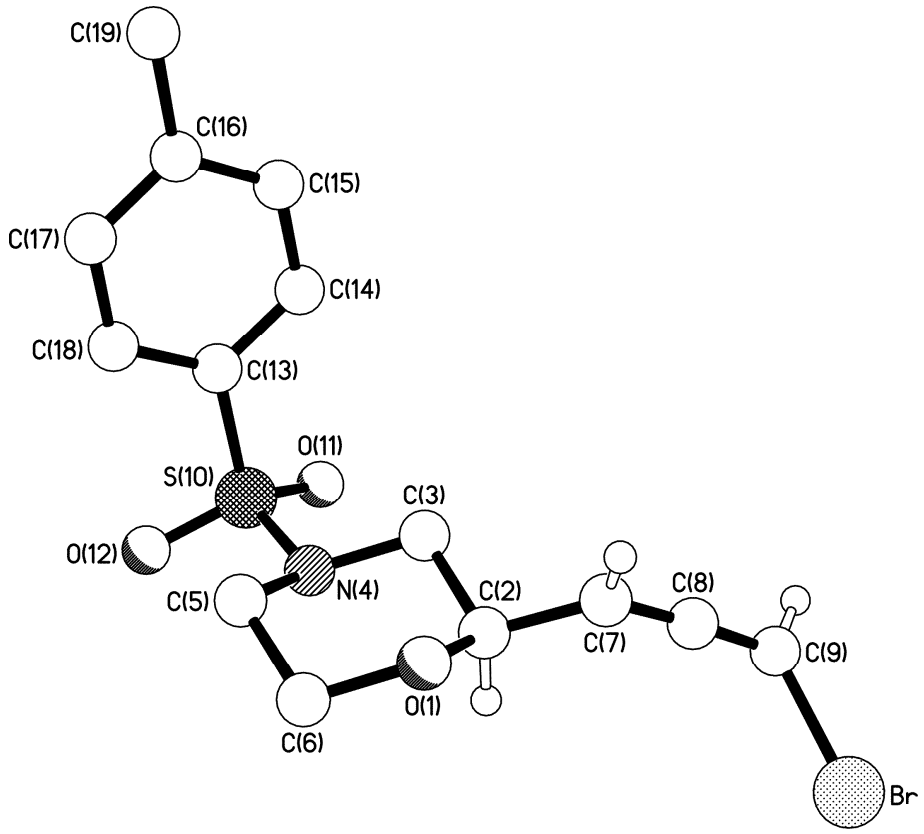


Figure S1 The molecular structure of **24** showing the major occupancy orientation (**I**, *ca.* 71% occupancy) for the bromoallene group C(8), C(9) and Br.

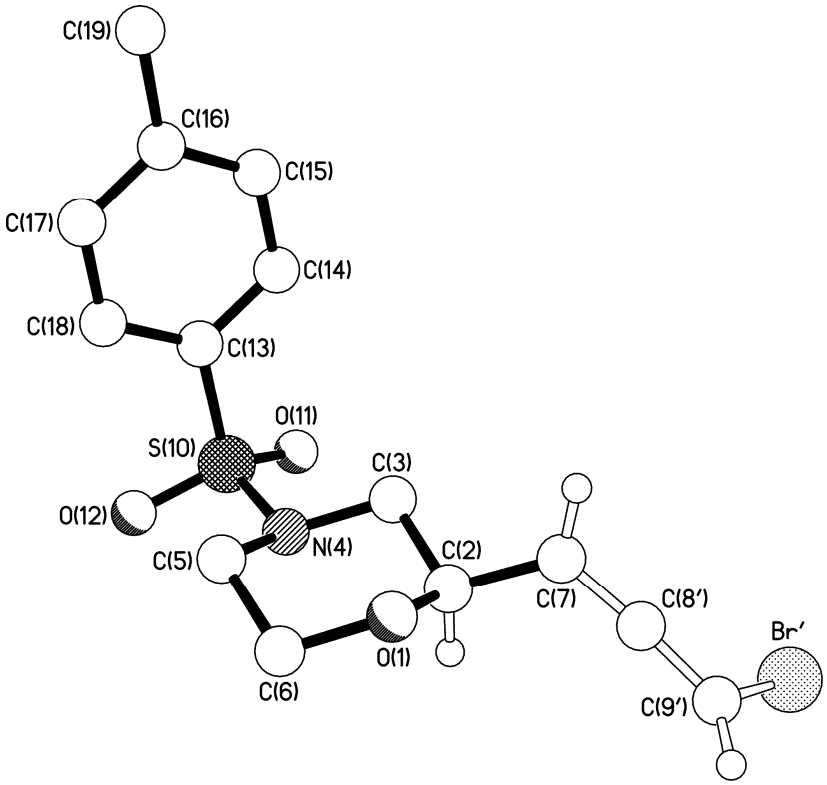


Figure S2 The molecular structure of **24** showing the second orientation (**II**, *ca.* 15% occupancy) for the bromoallene group C(8)', C(9)' and Br'.

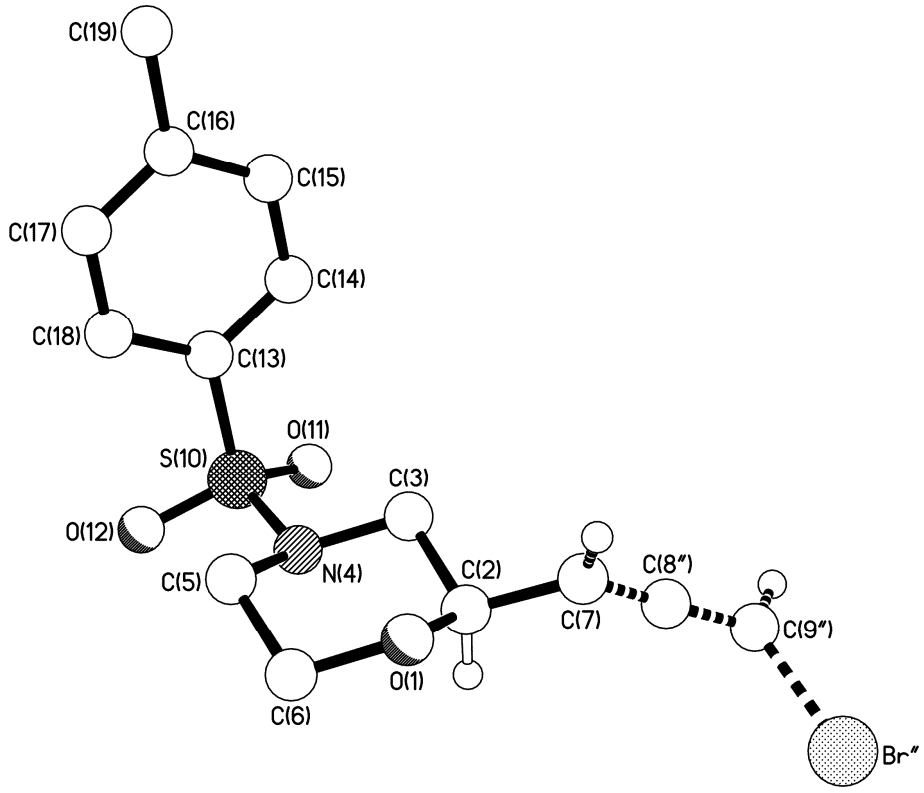


Figure S3 The molecular structure of **24** showing the lowest occupancy orientation (**III**, *ca.* 14%) for the bromoallene group C(8)", C(9)" and Br".

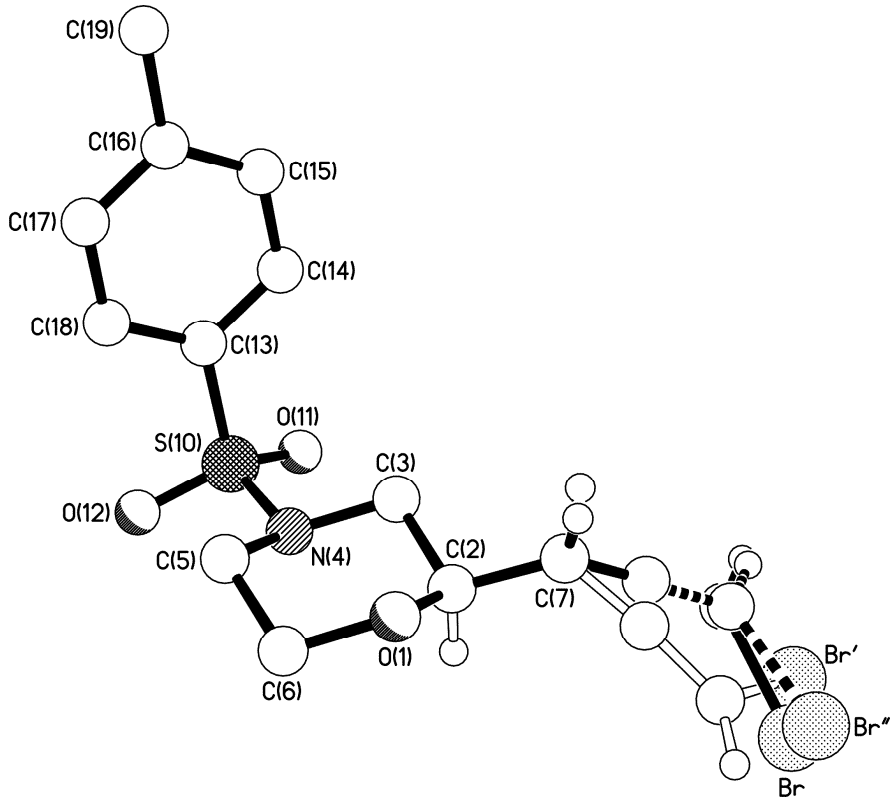


Figure S4 Overlay of all three orientations for the bromoallene group in the crystal structure of **24**. Orientation **I** (*ca.* 71% occupancy) is shown with dark bonds, orientation **II** (*ca.* 15% occupancy) with open bonds, and orientation **III** (*ca.* 14% occupancy) with dashed dark bonds.

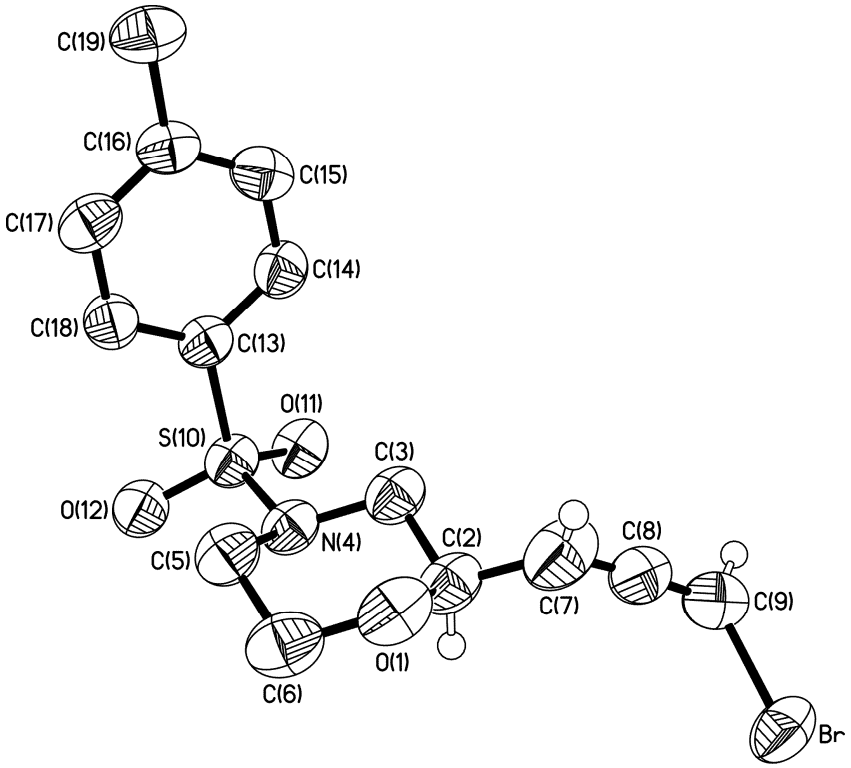


Figure S5 The molecular structure of **24** (major occupancy orientation, 50% probability ellipsoids).

Notes ‡, §, ¶, ††, **, ¶¶, ‡‡, ***

‡ Bromoallene **7a**: R_f 0.53 (petroleum ether : Et_2O; 70 : 30); ^1H NMR (270 MHz, $CDCl_3$) δ 6.04 (1H, dd, *J* = 1.6, 5.7 Hz, C<u>H</u>(Br)=C=CH-), 5.42 (1H, dd, *J* = 5.4, 5.7 Hz, CH(Br)=C=C<u>H</u>-), 4.61-4.50 (1H, m, -C<u>H</u>(O-)-CH=C=C-), 3.96-3.75 (2H, m, -O-C<u>H$_2$</u>-), 2.21-1.65 (4H, m, -O-CH$_2$-C<u>H$_2$</u>-C<u>H$_2$</u>-); ^{13}C NMR (68 MHz, $CDCl_3$) δ 201.1 (-C=<u>C</u>=C-), 102.8 (CH(Br)=C=<u>C</u>H-), 75.1, 73.9, 68.3, 31.4, 25.3. Bromoallene **7b**: R_f 0.53 (petroleum ether : Et_2O 70 : 30); ^1H NMR (270 MHz, $CDCl_3$) δ 6.03 (1H, dd, *J* = 1.9, 5.7 Hz, C<u>H</u>(Br)=C=CH-), 5.40 (1H, dd, *J* = 5.7, 5.9 Hz, CH(Br)=C=C<u>H</u>-), 4.58-4.49 (1H, m, C<u>H</u>(O-)-CH=C=C-), 3.94-3.74 (2H, m, -O-C<u>H$_2$</u>-), 2.15-1.72 (4H, m, -O-CH$_2$-C<u>H$_2$</u>-C<u>H$_2$</u>-); ^{13}C NMR (68 MHz, $CDCl_3$) δ 201.3 (-C=<u>C</u>=C-), 102.3 (CH(Br)=C=<u>C</u>H-), 75.6, 73.7, 68.2, 31.4, 25.5.

§ The reaction of the 1:1.6 mixture of enyne alcohols **5**:**6** with NBS gave a 1:1.5 diastereomeric mixture of the two bromoallenes **7a** and **7b**, and pure **5** gave a 6:1 mixture. This allows the estimation of a pure sample of *Z*-enyne **6** to give a 1:7 mixture of the two diastereoisomers.

¶ Enyne **22** was obtained in an approximately 5.9:1 *E*:*Z* mixture as indicated by ^1H NMR spectroscopic analysis of the crude reaction mixture. Careful chromatographic purification (petroleum ether : Et_2O; 90 : 10) resulted in different fractions containing different ratios of *E*- and *Z*-enyne, with the *Z*-enyne being the first of the two products eluting from the column. Fractions with an *E*:*Z* ratio as high as 18.9:1 were obtained representing a 15% yield. The main bulk of the material obtained had a *E*:*Z* ratio of approximately 4.5:1 and corresponded to a 37% yield. An initial fraction with an *E*:*Z* ratio of 1.4:1 represented a 6% yield and another fraction with a 13.1:1 *E*:*Z* ratio corresponded to a 10% yield. Thus, the overall amount of pure protected enyne formed corresponded to 68% yield.

†† After deprotection of a *ca.* 19:1 *E*:*Z* mixture of protected enyne **22**, the enyne **23** was obtained in >20:1 *E*:*Z* ratio.

** To a stirred solution of *E*-enyne **23** (98 mg, 0.35 mmol) in anhydrous CH_2Cl_2 (4 mL) was added NBS (187 mg, 1.05 mmol) at −40 °C and the reaction mixture allowed to warm to room temperature over 14.5 hours. The reaction mixture was diluted with

CH_2Cl_2 (19 mL) and washed with a saturated aqueous solution of sodium sulfite (2 × 19 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The residue obtained was pre-absorbed onto silica and chromatographed (petroleum ether : Et_2O; 40 : 60) to give bromoallene **24** (83 mg, 66%) as a colourless oil which solidified upon standing at 0 °C. R_f 0.40 (petroleum ether : Et_2O; 30 : 70); ^{1}H NMR (major diastereoisomer resonances only) (400 MHz; $CDCl_3$) 7.64 (2H, d, J = 8.4 Hz, ArH), 7.36 (2H, d, J = 8.4 Hz, ArH), 6.12 (1H, dd, J = 6.0, 2.0 Hz, -CH(Br)=C=CH-), 5.35 (1H, t, J = 5.6 Hz, -CH(Br)=C=CH-), 4.27-4.22 (1H, m, -NCH_2CH-), 3.96 (1H, dt, J = 11.7, 2.7 Hz, -$NCH_2CH_AH_BO$-), 3.72 (1H, td, J = 11.3, 2.7 Hz, -$NCH_2CH_AH_BO$-), 3.59 (1H, br d, J = 11.2 Hz, -NCH_AH_BCH-), 3.47 (1H, br d, J = 11.6 Hz, -$NCH_AH_BCH_2O$-), 2.50 (1H, dt, J = 11.3, 3.3 Hz, -$NCH_AH_BCH_2O$-), 2.45 (3H, s, -$C_6H_4CH_3$), 2.31 (1H, dd, J = 11.2, 9.6 Hz, -NCH_AH_BCH-); ^{13}C NMR (major diastereoisomer resonances only) (100 MHz; $CDCl_3$) 202.0 (-C=C=C-), 144.2, 132.0, 129.9, 127.8, 98.2 (CH(Br)=C=CH-), 74.9 (-CH(Br)=C=CH-), 71.6 (-NCH_2CH-), 65.8 (-NCH_2CH_2O-), 49.5 (-NCH_2CH-), 45.3 (-NCH_2CH_2O-), 21.6 (-$C_6H_4CH_3$); MS (CI^+, NH_3) *m/z* 377 and 375 $(M + NH_4)^+$, 360 and 358 $(M + H)^+$; HRMS (CI^+, NH_3) *m/z* calcd for $C_{14}H_{20}{}^{81}BrN_2O_3S$ $(M + NH_4)^+$ 377.0358, found 377.0359; calcd for $C_{14}H_{20}{}^{79}BrN_2O_3S$ $(M + NH_4)^+$ 375.0378, found 375.0383; Anal. calcd for $C_{14}H_{16}BrNO_3S$: C, 46.94; H, 4.50; N, 3.91. Found: C, 46.84; H, 4.48; N, 3.73%. Bromoallene **24** was recrystallised from hexane. *Crystal data for* **24**: $C_{14}H_{16}BrNO_3S$, M = 358.25, monoclinic, $P2_1/c$ (no.14), a = 17.481(2), b = 10.1393(16), c = 8.799(2) Å, β = 98.488(13)°, V = 1542.5(5) Å^3, Z = 4, D_c = 1.543 g cm^{-3}, μ(Cu-Kα) = 4.959 mm^{-1}, T = 173 K, colourless needles, Oxford Diffraction Xcalibur PX Ultra diffractometer; 2968 independent measured reflections, F^2 refinement, R_1 = 0.059, wR_2 = 0.141, 2449 independent observed absorption-corrected reflections [$|F_o| > 4\sigma(|F_o|)$, $2\theta_{max}$ = 142°], 220 parameters. CCDC 625183.

¶¶ The corresponding *Z*-enyne was prepared from aldehyde **21**. However, on attempted cyclisation with NBS, significant decomposition occurred and no bromoallenes were detected.

‡‡ The solid state structure revealed disorder in the bromoallene unit with three separate orientations (denoted **I**, **II** and **III**) of two different diastereoisomers being identified. The three orientations for the bromoallene group (**I**, **II** and **III**) have

occupancies of *ca.* 71, 15 and 14% respectively, with orientations **I** and **III** representing the major diastereoisomer (overall occupancy *ca*. 85%), and orientation **II** the minor. For orientation **III** only the bromine atom was clearly located, the carbon atoms being inferred, so it is possible, though unlikely, that it could have been modelled as the other diastereoisomer (See pages S16-S22).

*** Due to their very similar chemical shifts, the definitive assignment of the stereochemistries of these two bromoallenes by NMR methods was not possible. For an interesting discussion of the nature of this problem see reference 14 of the main manuscript.