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Transannular, decarboxylative Claisen rearrangement reactions for the synthesis of sulfur-substituted vinylcyclopropanes

Donald Craig, Sophie J. Gore, Mark I. Lansdell, Simon E. Lewis, Alexander V. W. Mayweg and Andrew J. P. White.

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1. General Experimental:

All reactions were performed under nitrogen unless otherwise stated. Melting points were determined using Stuart Scientific SMP1 melting point apparatus and are uncorrected. Infrared spectra were recorded on Mattson 5000 FTIR and Perkin-Elmer Spectrum RX FT-IR System spectrometers. Proton nuclear magnetic resonance (^1H NMR) and carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded in CDCl_3 unless otherwise stated on a Jeol GX-270, Brüker DRX-300, Brüker AV-400 or Brüker AV-500 spectrometer. Chemical shifts are in parts per million (ppm) and are referenced relative to the residual proton-containing solvent (^1H NMR: 7.26 ppm for CDCl_3 ; ^{13}C NMR: 77.0 ppm for CDCl_3). Mass spectra (CI, EI and FAB) were recorded using Micromass AutoSpec-Q, Micromass Platform II or Micromass AutoSpec Premier instruments. Elemental analyses were performed at the microanalytical laboratories of the London Metropolitan University. Optical rotations were measured on an Optical Activity Ltd. instrument. Analytical thin layer chromatography (TLC) was performed on pre-coated Aluminium-backed Merck Kieselgel 60 F_{254} plates. Visualisation was effected with ultraviolet light, potassium permanganate or vanillin as appropriate. Flash chromatography was performed using BDH (40–63 μm) silica gel unless otherwise stated. Standard solvents were distilled under nitrogen prior to use; Et_2O and THF from sodium-benzophenone ketyl, CH_2Cl_2 from CaH_2 and toluene from sodium. All other solvents were reagent grade. Petrol refers to petroleum ether of the fraction bp 40–60 °C. All liquid reagents were distilled prior to use. BSA was purchased from Alfa Aesar Lancaster and distilled prior to use. Potassium acetate was oven-dried at 120 °C for several days prior to use. Microwave reactions were performed in a Biotage initiator.

2. General Procedures

General Procedure A: preparation of cyclic orthoesters from 1,4-diols

To a solution of the diol (1.0 equiv.) in CH_2Cl_2 was added CSA (1 mol%) and trimethylorthoformate (2.0 equiv.). The reaction mixture was stirred at rt for 1 h before addition of NEt_3 . The mixture was concentrated under reduced pressure and purified by chromatography to give the desired orthoester.

General Procedure B: preparation of allylic alcohols from cyclic orthoesters

To a solution of the orthoester (1.0 equiv.) in PhMe at $-78\text{ }^\circ\text{C}$ was added DIBAL-H (1.3 equiv.) dropwise. The reaction mixture was allowed to warm to rt and stirred for 16 h. The reaction mixture was again cooled to $0\text{ }^\circ\text{C}$, carefully quenched with sat. Na/K tartrate soln. and the mixture stirred for a further 1 h. The aqueous layer was then extracted with EtOAc and the combined organic layers washed with sat. aq. NaCl ($\times 2$) and H_2O , dried (MgSO_4) and concentrated under reduced pressure. Purification by chromatography gave the desired alkene.

General Procedure C: preparation of mesylates from allylic alcohols

To a solution of alcohol (1.0 equiv.) in CH_2Cl_2 at $0\text{ }^\circ\text{C}$ was added NEt_3 (3.0 equiv.). The reaction mixture was stirred at $0\text{ }^\circ\text{C}$ for 15 min, and methanesulfonyl chloride (2.0 equiv.) was added dropwise. The reaction was stirred at $0\text{ }^\circ\text{C}$ for 30 min, washed with 2 M aq. HCl ($\times 2$) and sat. aq. NaHCO_3 ($\times 2$). The organic phase was dried (MgSO_4) and concentrated under reduced pressure to give the desired methane sulfonate

General Procedure D: alkylation of sulfone- and sulfoximine-substituted acetates

To a suspension of sodium hydride (60% dispersion in mineral oil, washed with hexane; 1.1 equiv.) in THF or DMF at $0\text{ }^\circ\text{C}$, was added dropwise a solution of the ester (1.0 equiv.) in THF or DMF. The reaction mixture was stirred at $0\text{ }^\circ\text{C}$ for 30 min and a solution of the methane sulfonate or iodide (1.0 equiv.) in THF or DMF was added dropwise. The reaction mixture was stirred at $0\text{ }^\circ\text{C}$ for a further 30 min, then at rt for 16 h. The solution was concentrated under reduced pressure and the crude product suspended in EtOAc, washed with sat. aq. NH_4Cl , H_2O and sat. aq. NH_4Cl

The organic phase was dried (MgSO_4), concentrated under reduced pressure and purified by chromatography to give the desired alkylated ester.

General Procedure E: hydrolysis of MOM ethers/*tert*-butyl esters

To a solution of the ester (1.0 equiv.) in MeCN was added 2 M aq. HCl. The reaction mixture was heated under reflux for 2 h, cooled, and partitioned between CH_2Cl_2 and H_2O . The aqueous phase was washed with CH_2Cl_2 ($\times 5$). The combined organic washings were dried (MgSO_4), concentrated under reduced pressure, and purified by chromatography to give the desired alcohol/hydroxyacid.

General Procedure F: hydrolysis of methyl esters

To a solution of the ester (1.0 equiv.) in THF was added 2 M aq. LiOH (5.0 equiv.). The reaction was stirred at rt for 1 h, then partitioned between Et_2O and H_2O and the aqueous layer acidified to pH 1 with 2 M aq. HCl. The aqueous layer was then extracted with Et_2O ($\times 3$) and the organic layers combined, dried (MgSO_4) and concentrated under reduced pressure to give, without further purification, the desired acid.

General Procedure G: cyclisation of hydroxyacids to give unsaturated ϵ -lactones

To a solution of the hydroxyacid (1.0 equiv.) in CH_2Cl_2 at 0 °C was added EDCI (1.1 equiv.) portionwise. The reaction mixture was allowed to warm to rt and left to stir for 16 h. The reaction mixture was partitioned between H_2O and CH_2Cl_2 , the organic layer washed with sat. aq. NH_4Cl and H_2O , dried (MgSO_4) and concentrated under reduced pressure. The product was purified by chromatography to give the desired lactone.

General Procedure H: dCr reaction of unsaturated ϵ -lactones

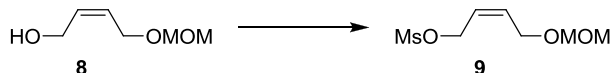
A solution of lactone (1.0 equiv.), BSA (1.0 equiv.) and KOAc (0.1 equiv.) in DMF was subjected to microwave irradiation at 160 °C for 10 min. The reaction mixture was diluted with EtOAc, washed with sat. aq. NaCl ($\times 3$) and H_2O , dried (MgSO_4) and concentrated under reduced pressure to give the desired cyclopropane.

General Procedure I: preparation of 1,4-diols from furan-2(5*H*)-ones

To a solution of furan-2(5*H*)-one (1.0 equiv.) in PhMe at $-78\text{ }^{\circ}\text{C}$ was added DIBAL-H (2.2 equiv.) dropwise. The reaction mixture was allowed to stir at $-78\text{ }^{\circ}\text{C}$ for 2 h, then warmed to rt and stirred for a further 2 h. The reaction mixture was again cooled to $0\text{ }^{\circ}\text{C}$ and carefully quenched with sat. Na/K tartrate soln. and the mixture stirred for a further 1 h. The aqueous layer was then extracted with EtOAc and the combined organic layers washed with sat. aq. NaCl ($\times 2$) and H_2O , dried (Na_2SO_4) and concentrated under reduced pressure. Purification by chromatography gave the desired 1,4-diol.

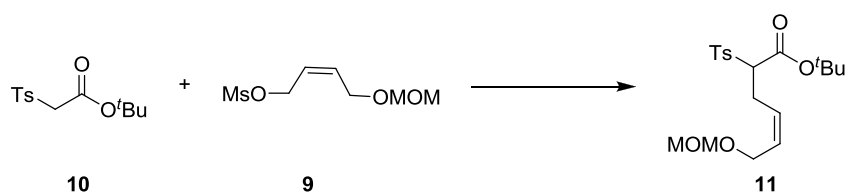
3. Synthesis and reactions of lactone 13

Methanesulfonic acid (*Z*)-4-(methoxymethoxy)but-2-enyl ester **9**



According to general procedure **C**, alcohol **8**¹ (1.72 g, 13.0 mmol, 1.0 equiv.) in CH₂Cl₂ (65 mL) was reacted with NEt₃ (5.44 mL, 39.0 mmol, 3.0 equiv.) and methanesulfonyl chloride (2.01 mL, 26.0 mmol, 2.0 equiv.) to give methanesulfonic acid (*Z*)-4-(methoxymethoxy)but-2-enyl ester **9** as an orange oil, which was used crude in the next step; R_f 0.17 (50% EtOAc–petrol); δ_H (270 MHz, CDCl₃) [5.94–5.85, 5.82–5.71] (2H, 2 × m, CH=CH), 4.84 (2H, d, *J* 6.5 Hz, CHCH₂OS), 4.62 (2H, s, OCH₂O), 4.17 (2H, d, *J* 6.5 Hz, CHCH₂OMOM), 3.37 (3H, s, OCH₃), 3.01 (3H, s, SCH₃); δ_C (67.5 MHz, CDCl₃) 132.6 (CHCH₂OMOM), 124.9 (CHCH₂OMs), 95.8 (OCH₂O), 65.3 (CH₂OS), 62.7 (=CH-CH₂O), 55.5 (OCH₃), 38.1 (SCH₃).

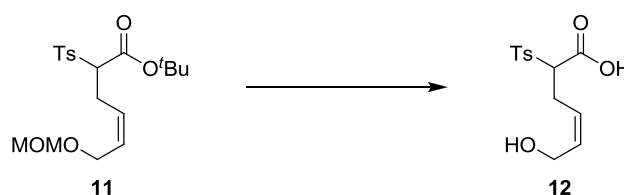
(*Z*)-*tert*-Butyl 6-(methoxymethoxy)-2-tosylhex-4-enoate **11**



According to general procedure **D**, a suspension of sodium hydride (766 mg, 31.9 mmol, 1.1 equiv.) in THF (50 mL) was treated with a solution of ester **10**² (7.84 g, 29.0 mmol, 1.0 equiv.) in THF (50 mL) followed by a solution of methanesulfonic acid (*Z*)-4-(methoxymethoxy)but-2-enyl ester **9** (29.0 mmol, 1.0 equiv.) in THF (40 mL). Purification by chromatography (20% EtOAc–petrol) gave (*Z*)-*tert*-butyl 6-(methoxymethoxy)-2-tosylhex-4-enoate **11** (6.95 g, 57% over two steps) as a yellow oil; R_f 0.32 (35% EtOAc–petrol); ν_{max} (film) 1732, 1699, 1597, 1456, 1396, 1369, 1327, 1306, 1292, 1246, 1213, 1147, 1105, 1086, 1047, 993, 947, 920, 883, 837, 816, 760, 714, 667 cm⁻¹; δ_H (500 MHz, CDCl₃) 7.74 (2H, d, *J* 8.5 Hz, *o*-SO₂Ar), 7.33 (2H, d, *J* 8.5 Hz, *m*-SO₂Ar), [5.68–5.63, 5.44–5.39] (2H, m, -CH=CH-), 4.58 (2H, s, -OCH₂O-), [4.10, 4.01] (2 × 1H, dd, *J* 12.5, 6.5 Hz, =CH-CH₂O-), 3.84 (1H, dd, *J* 10.5, 4.5 Hz, Ts-CH<), 3.32 (3H, s, -OCH₃), 2.75–2.70 (2H, m, Ts-CH-CH₂-CH=), 2.43 (3H, s, Ts-CH₃), 1.31 (9H, s, -C(CH₃)₃); δ_C (75 MHz, CDCl₃) 164.4 (C=O), 145.3

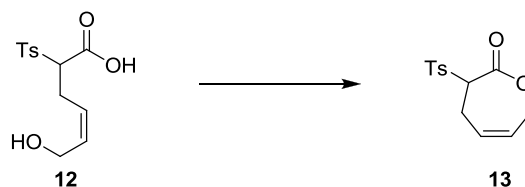
(4°), 134.4 (4°), 130.2 (3°), 129.6 (3°), 129.4 (3°), 126.2 (3°), 95.8 (-OCH₂O-), 83.3 (-C(CH₃)₃), 70.6 (Ts-CH-COO-), 62.8 (-OCH₂-CH=), 55.3 (-OCH₃), 27.6 (-C(CH₃)₃), 25.3 (Ts-CH-CH₂-CH=), 21.7 (Ts-CH₃); *m/z* (CI) 402 [M+NH₄]⁺, 358 [M+NH₄-CH₂OCH₃]⁺, 346, 323, 314, 302, 288, 284, 232, 197, 192, 174, 139 (Found: [M+NH₄]⁺, 402.1948. C₁₉H₂₈O₆S requires [M+NH₄]⁺, 402.1950) (Found: C, 59.21; H, 7.37. C₁₉H₂₈O₆S requires C, 59.35; H, 7.34%).

(Z)-6-Hydroxy-2-tosylhex-4-enoic acid **12**



According to general procedure **E**, ester **11** (882 mg, 2.29 mmol, 1.0 equiv.) was heated under reflux in MeCN (25 mL) and 2 M aq. HCl (5 mL). Purification by recrystallisation from CHCl₃–petrol gave *(Z)*-6-hydroxy-2-tosylhex-4-enoic acid **12** (577 mg, 81%) as a colourless crystalline solid; mp 124–126 °C; ν_{max} (film) 3480, 3029, 1732, 1597, 1444, 1401, 1383, 1319, 1303, 1292, 1246, 1146, 1084, 1016, 815, 711, 663 cm⁻¹; δ_{H} (300 MHz, DMSO-*d*₆) 7.75 (2H, d, *J* 7.0 Hz, *o*-SO₂Ar), 7.47 (2H, d, *J* 7.0 Hz, *m*-SO₂Ar), [5.60-5.53, 5.30-5.22] (2H, m, -CH=CH-), 4.20 (1H, dd, *J* 7.5, 3.5 Hz, Ts-CH<), 3.99-3.83 (2H, m, HO-CH₂-), 2.56-2.50 (2H, m, Ts-CH-CH₂-CH=), 2.42 (3H, s, Ts-CH₃); δ_{C} (75 MHz, DMSO-*d*₆) 166.8 (C=O), 145.5, 134.8, 134.6, 130.2, 129.4, 123.9, 69.6, 57.2, 25.4, 21.6; *m/z* (CI) 284 [M+NH₄-H₂O]⁺, 258, 240, 223, 174, 156, 139, 130 (Found: [M+NH₄-H₂O]⁺, 284.0968. C₁₃H₁₆O₅S requires [M+NH₄-H₂O]⁺, 284.0957) (Found: C, 54.76; H, 5.49. C₁₃H₁₆O₅S requires C, 54.92; H, 5.67%).

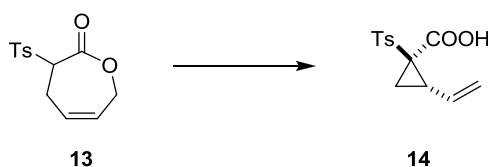
3-Tosyl-3,4-dihydrooxepin-2(7H)-one **13**



According to general procedure **G**, *(Z)*-6-hydroxy-2-tosylhex-4-enoic acid **12** (2.50 g, 8.80 mmol, 1.0 equiv.) in CH₂Cl₂ (150 mL) was treated with *N,N'*-diisopropylcarbodiimide (1.51 mL, 9.67 mmol, 1.1 equiv.). Purification by chromatography (30% EtOAc–petrol) gave 3-tosyl-4,7-dihydrooxepin-2(3*H*)-one **13**

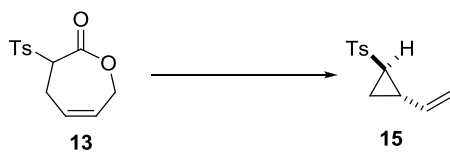
(1.83 g, 78%) as a colourless powder; mp 144–146 °C; R_f 0.56 (50% EtOAc–petrol); ν_{\max} (film) 3041, 1745, 1597, 1471, 1435, 1400, 1387, 1352, 1321, 1257, 1225, 1176, 1146, 1084, 1049, 1016, 943, 912, 879, 816, 800, 766, 729, 706, 660 cm^{-1} ; δ_{H} (500 MHz, CDCl_3) 7.98 (2H, d, J 8.0 Hz, *o*- SO_2Ar), 7.38 (2H, d, J 8.0 Hz, *m*- SO_2Ar), [5.92–5.88, 5.86–5.82] (2H, m, $-\text{CH}=\text{CH}-$), [4.91 (app d quint, J 15.5, 3.0 Hz), 4.46 (ddd, J 15.0, 7.0, 1.0 Hz)], (2H, $-\text{OCH}_2-$), 4.70 (1H, dd, J 13.0, 4.0 Hz, Ts-CH<), [3.16–3.10, 2.69–2.61], (2H, m, Ts-CH- CH_2 -CH=), 2.45 (3H, s, Ts- CH_3); δ_{C} (67.5 MHz, CDCl_3) 166.7 (C=O), 145.7 (4°), 133.6 (4°), 130.6 (3°), 129.7 (3°), 129.5 (3°), 124.3 (3°), 64.3 (Ts-CH<), 64.0 ($-\text{OCH}_2-$), 27.1 (Ts-CH- CH_2 -CH=), 21.8 (Ts- CH_3); m/z (CI) 284 $[\text{M}+\text{NH}_4]^+$, 189, 174, 130, 77 (Found: $[\text{M}+\text{NH}_4]^+$, 284.0957). $\text{C}_{13}\text{H}_{14}\text{O}_4\text{S}$ requires $[\text{M}+\text{NH}_4]^+$, 284.0957) (Found: C, 58.51; H, 5.47. $\text{C}_{13}\text{H}_{14}\text{O}_4\text{S}$ requires C, 58.63; H, 5.30%).

(1R,2S*)-1-Tosyl-2-vinylcyclopropanecarboxylic acid 14*



A solution of lactone **13** (150 mg, 560 μmol , 1.0 equiv.) in CH_2Cl_2 (6 mL) was treated with KOAc (5.5 mg, 56.0 μmol , 0.1 equiv.) and BSA (140 μl , 560 μmol , 1.0 equiv.). The reaction mixture was stirred at rt for 16 h, then diluted with CH_2Cl_2 , washed with 2 M aq. HCl and H_2O , dried (MgSO_4) and concentrated under reduced pressure to give *(1R*,2S*)-1-tosyl-2-vinylcyclopropanecarboxylic acid 14* (150 mg, 100%) as a colourless solid; mp 118–120 °C; ν_{\max} (nujol) 3339, 2717, 2590, 1694, 1596, 1318, 1289, 1145, 1084, 929, 817, 726, 665 cm^{-1} ; δ_{H} (270 MHz, $\text{DMSO}-d_6$) 7.78 (2H, d, J 8.0 Hz, *o*- SO_2Ar), 7.33 (2H, d, J 8.0 Hz, *m*- SO_2Ar), 5.58 (1H, ddd, J 17.0, 10.0, 8.5 Hz, $\text{CH}=\text{CH}_2$), 5.39 (1H, dd, J 17.0, 1.5 Hz, $\text{CH}=\text{CH}_2$ *cis*), 5.22 (1H, dd, J 10.0, 1.5 Hz, $\text{CH}=\text{CH}_2$ *trans*), 3.02 (1H, m, SCCH), 2.44 (3H, s, ArCH_3), 2.16 (1H, dd, J 10.0, 5.5 Hz, SCCH $_2$), 1.96 (1H, dd, J 8.5, 5.5 Hz, SCCH $_2$); δ_{C} (100 MHz, $\text{DMSO}-d_6$) 168.0 (C=O), 145.2, 136.0 (4°), 130.6, 129.8, 128.8 (3°), 121.2 ($\text{CH}=\text{CH}_2$), 50.5 (SC), 33.0 (SCCH), 21.7 (ArCH_3), 20.3 (SCCH $_2$); m/z (CI) 284 $[\text{M}+\text{NH}_4]^+$, 242, 240, 174, 162, 145, 102, 85 (Found: $[\text{M}+\text{NH}_4]^+$, 284.0964). $\text{C}_{13}\text{H}_{14}\text{O}_4\text{S}$ requires $[\text{M}+\text{NH}_4]^+$, 284.0957).

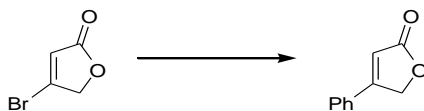
p-Tolyl (1*R**,2*S**)-2-vinylcyclopropyl sulfone **15**



According to general procedure **H**, lactone **13** (150 mg, 560 μmol , 1.0 equiv.) in DMF (mL) was treated with BSA (140 μl , 560 μmol , 1.0 equiv.) and KOAc (5.53 mg, 56.0 μmol , 0.1 equiv.) to give *p*-tolyl (1*R**,2*S**)-2-vinylcyclopropyl sulfone **15** (110 mg, 88%) as a yellow oil; R_f 0.59 (50% EtOAc–petrol); ν_{max} (film) 3086, 3041, 2925, 1639, 1598, 1495, 1444, 1402, 1343, 1313, 1147, 1089, 942, 914, 858, 816, 743, 666, 646 cm^{-1} ; δ_{H} (400 MHz, DMSO- d_6) 7.76 (2H, d, J 8.0 Hz, *o*-SO₂Ar), 7.44 (2H, d, J 8.0 Hz, *m*-SO₂Ar), 5.38 (1H, ddd, J 17.0, 10.0, 8.5 Hz, CH=CH₂), 5.22 (1H, d, J 17.0 Hz, CH=CH₂ *cis*), 4.97 (1H, d, J 10.0 Hz, CH=CH₂ *trans*), 2.95 (1H, m, SCH), 2.40 (3H, s, ArCH₃), 2.24 (1H, m, SCHCH), [1.44, 1.17] (2H, 2 \times m, SCHCH₂); δ_{C} (100 MHz, DMSO- d_6) 144.0, 137.6 (4 $^\circ$), 136.1, 129.9, 127.1 (3 $^\circ$), 116.1 (CH=CH₂), 38.7 (SCH), 22.3 (SCHCH), 21.0 (ArCH₃), 12.3 (SCHCH₂); m/z (CI) 240 [M+NH₄]⁺, 223, 84, 67 (Found [M+NH₄]⁺, 240.1067. C₁₂H₁₄O₂S requires [M+NH₄]⁺, 240.1058).

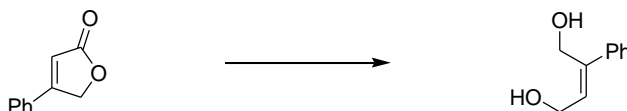
4. Synthesis of aryl-substituted substrate precursors

4-Phenylfuran-2(5H)-one



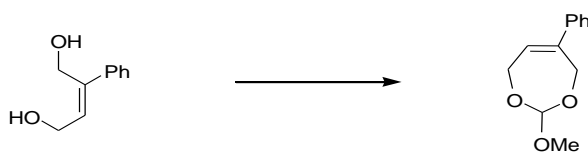
Phenylboronic acid (76 mg, 0.62 mmol, 1.0 equiv.), 4-bromofuran-2(5H)-one³ (100 mg, 0.62 mmol, 1.0 equiv.) and PdCl₂(PPh₃)₂ (8.7 mg, 2.0 mol%) in 2 M aq. KF (2 mL) and THF (2 mL) were heated under reflux for 5 h. After cooling to rt the layers were separated and the aqueous layer further extracted with EtOAc (×3). The combined organic extracts were washed with sat. aq. NaCl, dried (MgSO₄) and concentrated under reduced pressure to give 4-phenylfuran-2(5H)-one as a colourless solid; R_f 0.57 (1% AcOH–EtOAc); ν_{max} (film) 3111, 2929, 1793, 1734, 1621, 1450, 1331, 1167, 1048, 894, 862, 771, 684 cm⁻¹; δ_H (400 MHz) 7.50 (5H, m, Ph), 6.38 (1H, t, *J* 1.5 Hz, CH), 5.23 (2H, d, *J* 1.5 Hz, CH₂); δ_C (100 MHz) 173.9 (C=O), 163.9, 131.8 (4°), 129.7, 129.3, 126.4 (3°), 113.1 (CH), 71.0 (CH₂); *m/z* (CI) 178 [M+NH₄]⁺; data were in accordance with those previously reported.⁴

(Z)-2-Phenylbut-2-ene-1,4-diol



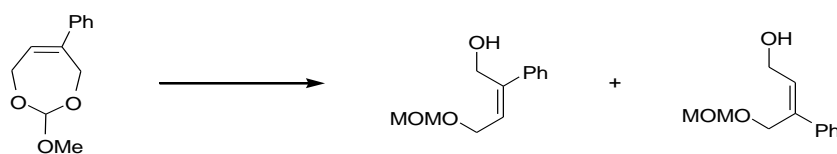
According to general procedure I, a solution of 4-phenylfuran-2(5H)-one (950 mg, 5.93 mmol, 1.0 equiv.) in PhMe (10 mL) was treated with DIBAL-H (1.7 M in PhMe; 7.68 mL, 13.0 mmol, 2.2 equiv.). Purification by chromatography (50–70% EtOAc–petrol) gave (Z)-2-phenylbut-2-ene-1,4-diol (793 mg, 81%) as a colourless oil; R_f 0.08 (50% EtOAc–petrol); ν_{max} (film) 3298, 2885, 1685, 1598, 1493, 1445, 1000, 758, 697 cm⁻¹; δ_H (300 MHz) 7.45 (2H, m, *m*-Ph), 7.35 (3H, m, *o*-/*p*-Ph), 6.12 (1H, t, *J* 7.0 Hz, CH), 4.59 (2H, s, CCH₂OH), 4.42 (2H, d, *J* 7.0 Hz, CHCH₂), 2.04 (2H, s, OH); δ_C (75 MHz) 142.9, 140.4 (4°), 129.8, 128.6, 127.8, 126.4 (3°), 60.4 (CCH₂OH), 59.0 (CHCH₂OH); *m/z* (CI) 182 [M+NH₄]⁺, 164, 146, 118, 103, 91, 78; (Found [M+NH₄]⁺, 182.1175. C₁₀H₁₂O₂ requires [M+NH₄]⁺, 182.1176) (Found: C, 73.15; H, 7.37. C₁₀H₁₂O₂ requires C, 73.21; H, 7.40); data were in accordance with those previously reported.⁵

2-Methoxy-5-phenyl-4,7-dihydro-1,3-dioxepine



According to general procedure **A**, a solution of (*Z*)-2-phenylbut-2-ene-1,4-diol (3.67 g, 22.6 mmol, 1.0 equiv.) in CH₂Cl₂ (60 mL) was treated with CSA (52.5 mg, 0.23 mmol, 1 mol%) and trimethyl orthoformate (4.96 mL, 45.3 mmol, 2.0 equiv.). Purification by chromatography (20–40% EtOAc–petrol) gave 2-methoxy-5-phenyl-4,7-dihydro-1,3-dioxepine (3.64 g, 78%) as a colourless oil; *R_f* 0.59 (50% EtOAc–petrol); *v*_{max} (film) 2940, 2869, 2842, 1599, 1494, 1446, 1344, 1279, 1209, 1133, 1102, 1088, 1034, 753, 701 cm⁻¹; δ_{H} (300 MHz) 7.29 (5H, m, Ph), 5.88 (1H, tt, *J* 4.0, 1.0 Hz, CHCH₂), 5.47 (1H, s, OCH), 4.88 (1H, dd, *J* 15.5, 2.0 Hz, CCH₂), 4.61 (1H, dddd *J* 16.0, 4.0, 2.0, 2.0 Hz, CHCH₂), 4.50 (1H, ddd, *J* 16.0, 3.5, 1.5 Hz, CCH₂), 4.28 (1H, dddd, *J* 16.0, 4.0, 2.0, 2.0 Hz, CHCH₂), 3.45 (3H, s, CH₃); δ_{C} (75 MHz) 141.1, 139.5 (4°), 128.5, 127.5, 126.3, 126.1 (3°), 113.8 (CHO), 64.0 (CCH₂O), 61.3 (CHCH₂O), 53.6 (CH₃); *m/z* (ESI) 229 [M+Na]⁺, 206, 147, 129, 115, 91, 78 (Found [M+Na]⁺, 229.0835. C₁₂H₁₄O₃ requires [M+Na]⁺, 229.0835) (Found: C, 69.79; H, 6.90. C₁₂H₁₄O₃ requires C, 69.88; H, 6.84).

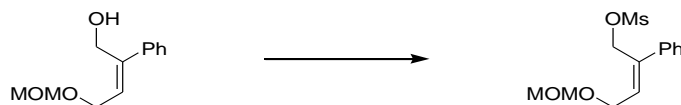
(Z)-4-Methoxymethoxy-2-phenylbut-2-en-1-ol and *(Z)*-4-methoxymethoxy-3-phenylbut-2-en-1-ol



According to general procedure **B**, a solution of 2-methoxy-5-phenyl-4,7-dihydro-1,3-dioxepine (4.64 g, 22.5 mmol, 1.0 equiv.) in PhMe (4.0 mL) was treated with DIBAL-H (1.2 M in PhMe; 41.2 mL, 49.5 mmol, 1.3 equiv.) Purification by chromatography (25% EtOAc–petrol) gave (*Z*)-4-methoxymethoxy-2-phenylbut-2-en-1-ol and (*Z*)-4-methoxymethoxy-3-phenylbut-2-en-1-ol (3.73 g, 80%; ratio 69:31; separable by chromatography) as colourless oils; (*Z*)-4-methoxymethoxy-2-phenylbut-2-en-1-ol: *R_f* 0.28 (50% EtOAc–heptane); *v*_{max} (film) 3411, 2934, 2884, 1493, 1445, 1377, 1149, 1089, 1033, 1013, 945, 917, 766, 697 cm⁻¹; δ_{H} (300 MHz) 7.49 (2H, m, *m*-Ph), 7.39–

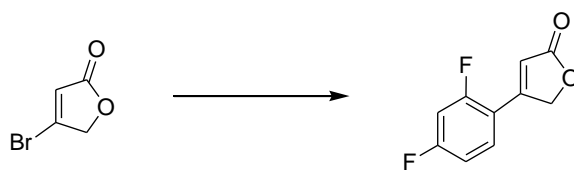
7.29 (3H, m, *o*-/*p*-Ph), 6.04 (1H, t, *J* 7.0 Hz, CH), 4.71 (2H, s, OCH₂O), 4.55 (2H, d, *J* 6.5 Hz, CCH₂OH), 4.35 (2H, d, *J* 7.0 Hz, CHCH₂), 3.42 (3H, s, CH₃), 2.37 (1H, t, *J* 6.5 Hz, OH); δ_C (75 MHz) 144.1, 140.5 (4°), 128.5, 127.8, 126.5, 126.4 (3°), 95.3 (OCH₂O), 63.2 (CH₂OH), 60.2 (CHCH₂), 55.4 (OCH₃); *m/z* (CI) 226 [M+NH₄]⁺, 129 (Found [M+NH₄]⁺, 226.1438. C₁₂H₁₆O₃ requires [M+NH₄]⁺, 226.1438) (Found: C, 69.29; H, 7.72. C₁₂H₁₆O₃ requires C, 69.21; H, 7.74); (*Z*)-4-methoxymethoxy-3-phenylbut-2-en-1-ol: *R_f* 0.22 (50% EtOAc–heptane); ν_{\max} (film) 3388, 2932, 2883, 1494, 1446, 1384, 1210, 1147, 1097, 1034, 945, 920, 757, 699 cm⁻¹; δ_H (300 MHz) 7.48 (2H, m, *m*-Ph), 7.32 (3H, m, *o*-/*p*-Ph), 6.27 (1H, t, *J* 7.0 Hz, CH), 4.66 (2H, s, OCH₂O), 4.56 (2H, s, CCH₂), 4.38 (2H, d, *J* 6.5 Hz, CH₂OH), 3.38 (3H, s, CH₃); δ_C (100 MHz) 140.5, 138.4 (4°), 131.8, 128.5, 127.7, 126.3 (3°), 95.1 (OCH₂O), 63.7 (CH₂OH), 58.9 (CHCH₂), 55.5 (OCH₃); *m/z* (CI) 226 [M+NH₄]⁺, 191, 161, 159, 131, 129 (Found [M+NH₄]⁺, 226.1438. C₁₂H₁₆O₃ requires [M+NH₄]⁺, 226.1438) (Found: C, 69.27; H, 7.80. C₁₂H₁₆O₃ requires C, 69.21; H, 7.74).

Methanesulfonic acid (Z)-4-methoxymethoxy-2-phenylbut-2-enyl ester



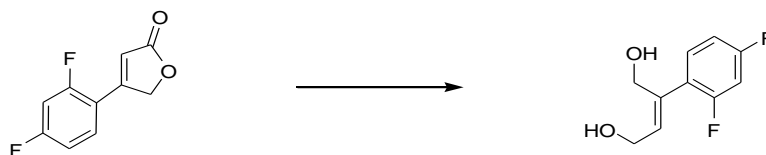
According to general procedure C, a solution of (*Z*)-4-methoxymethoxy-2-phenylbut-2-en-1-ol (122 mg, 0.59 mmol, 1.0 equiv.) in CH₂Cl₂ (2 mL) was treated with NEt₃ (245 μ L, 1.76 mmol, 3.0 equiv.) and MsCl (90.7 μ L, 1.17 mmol, 2.0 equiv.) to give methanesulfonic acid (*Z*)-4-methoxymethoxy-2-phenylbut-2-enyl ester (162 mg, 96%) as a colourless oil which was without further purification; *R_f* 0.34 (50% EtOAc–heptane); ν_{\max} (film) 3025, 2937, 2888, 1447, 1354, 1174, 1150, 1103, 1037, 929, 845, 772, 699 cm⁻¹; δ_H (400 MHz) 7.43 (2H, m, *o*-Ph), 7.35 (3H, m, *m*-/*p*-Ph), 6.26 (1H, t, *J* 6.5 Hz, CH), 5.21 (2H, s, CCH₂), 4.70 (2H, s, OCH₂O), 4.39 (2H, d, *J* 6.5 Hz, CHCH₂), 3.41 (3H, s, OCH₃), 2.90 (3H, s, SCH₃); δ_C (100 MHz) 138.6, 135.6 (4°), 132.0, 128.6, 128.3, 126.3 (3°), 96.0 (OCH₂O), 65.8 (CH₂OS), 63.3 (CHCH₂), 55.5 (OCH₃), 38.2 (SO₂CH₃); *m/z* (CI) 304 [M+NH₄]⁺ (Found [M+NH₄]⁺, 304.1226. C₁₃H₁₈O₅S requires [M+NH₄]⁺, 304.1219).

4-(2,4-Difluorophenyl)furan-2(5H)-one



To 4-bromofuran-2(5H)-one (2.0 g, 12.3 mmol, 1.0 equiv.) and PdCl₂(PPh₃)₂ (172 mg, 0.25 mmol, 2 mol%) in 2 M aq. KF (40 mL) and THF (40 mL) was added 2,4-difluorophenylboronic acid (1.94 g, 12.3 mmol, 1.0 equiv.) and the mixture heated under reflux for 5 h. After cooling to rt the layers were separated and the aqueous layer extracted with EtOAc (×3). The combined organic phases were washed with sat. aq. NaCl, dried (Na₂SO₄) and concentrated under reduced pressure. Purification by chromatography (20–40% EtOAc–petrol) gave 4-(2,4-difluorophenyl)furan-2(5H)-one (2.39 g, 99%) as a colourless solid; R_f 0.40 (50% EtOAc–petrol); ν_{max} (film) 3118, 3059, 1799, 1735, 1618, 1609, 1585, 1508, 1490, 1456, 1425, 1333, 1266, 1163, 1148, 1106, 1049, 996, 961, 897, 888, 872, 809, 734 cm⁻¹; δ_H (300 MHz) 7.48 (1H, m, *o*-ArF), 6.99 (2H, m, *m*-ArF), 6.49 (1H, t, *J* 2.0 Hz, CH), 5.24 (2H, d, *J* 2.0 Hz, CH₂); δ_C (75 MHz) 173.4 (C=O), 166.5, 166.4, 163.3, 163.2, 163.1, 162.9, 159.9, 159.7, (CF), 157.3 (4°), 129.5, 129.4 (3°), 115.9, 115.9, 115.8, 115.8 (CFCHCH), 114.7, 114.6, 114.5 (CCF), 112.9, 112.8, 112.6, 112.6 (CFCHCH), 105.8, 105.4, 105.1 (CFCHCF) 71.7 (CH₂); *m/z* (EI) 214 [M+NH₄]⁺, 197 (Found [M+H]⁺, 197.0409. C₁₀H₆F₂O₂ requires [M+H]⁺, 197.0409) (Found: C, 61.29; H, 3.06. C₁₀H₆F₂O₂ requires C, 61.23; H, 3.08); data were in accordance with those previously reported.⁶

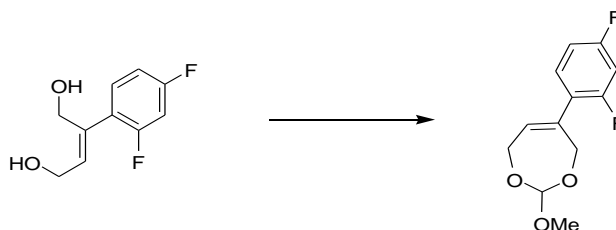
(Z)-2-(2,4-Difluorophenyl)but-2-ene-1,4-diol



According to general procedure I, a solution of 4-(2,4-difluorophenyl)furan-2(5H)-one (602 mg, 3.07 mmol, 1.0 equiv.) in PhMe (5 mL) was treated with DIBAL-H (1.7 M in PhMe; 3.97 mL, 6.75 mmol, 2.2 equiv.). Purification by chromatography (50–70% EtOAc–petrol) gave (Z)-2-(2,4-difluorophenyl)but-2-ene-1,4-diol (262 mg, 42%) as a colourless oil; R_f 0.10 (50% EtOAc–petrol); ν_{max} (film) 3305, 2884, 1613, 1592,

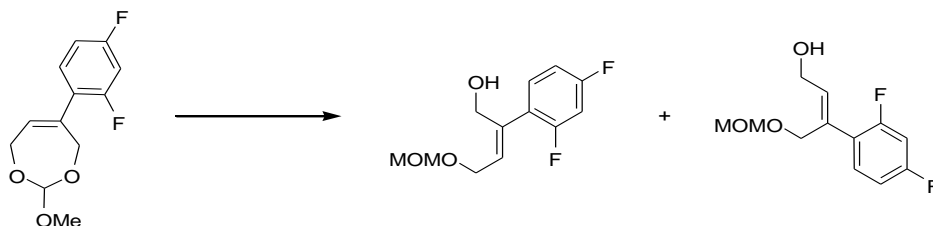
1500, 1421, 1265, 1138, 1095, 997, 965, 847, 811, 723 cm^{-1} ; δ_{H} (400 MHz) 7.28 (1H, m, *o*-ArF), 6.84 (2H, m, *m*-ArF), 6.00 (1H, t, *J* 6.5 Hz, CH), 4.49 (2H, s, CCH_2OH), 4.40 (2H, d, *J* 6.5 Hz, CHCH_2), 2.22 (2H, br s, OH); δ_{C} (100 MHz) 163.7, 163.6, 161.2, 161.1, 160.9, 160.8, 158.7, 158.6 (CF), 138.2 (4°), 133.4 (3°), 131.1, 131.0 (CFCHCH), 128.6, 128.5 (CCF), 111.6, 111.5, 111.4, 111.3 (CFCHCH), 104.3, 104.1, 103.8 (CFCHCF), 61.1 (CCH_2), 58.8 (CHCH_2); *m/z* (CI) 218 [$\text{M}+\text{NH}_4$] $^+$, 182; (Found: C, 60.08; H, 5.00. $\text{C}_{10}\text{H}_{10}\text{F}_2\text{O}_2$ requires C, 60.00; H, 5.04).

5-(2,4-Difluorophenyl)-2-methoxy-4,7-dihydro-1,3-dioxepine



According to general procedure **A**, a solution of (*Z*)-2-(2,4-difluorophenyl)but-2-ene-1,4-diol (250 mg, 1.24 mmol, 1.0 equiv.) in CH_2Cl_2 (5 mL) was treated with CSA (14.5 mg, 0.062 mmol, 5 mol%) and trimethyl orthoformate (545 μL , 4.98 mmol, 4.0 equiv.). Purification by chromatography (20–50% EtOAc–petrol) gave 5-(2,4-difluorophenyl)-2-methoxy-4,7-dihydro-1,3-dioxepine (300 mg, 100%) as a colourless solid; mp 39–41 $^\circ\text{C}$; R_f 0.54 (50% EtOAc–heptane); ν_{max} (film) 2942, 2845, 1614, 1591, 1500, 1424, 1266, 1134, 1097, 1068, 1023, 966, 847, 798, 733 cm^{-1} ; δ_{H} (300 MHz) 7.18 (1H, m, *o*-ArF), 6.80 (2H, m, *m*-ArF), 5.80 (1H, t, *J* 4.0 Hz, CHCH_2), 5.45 (1H, s, OCH), 4.74 (1H, ddd, *J* 15.5, 2.0, 2.0 Hz, CCH_2), 4.59 (1H, dddd *J* 16.5, 4.0, 2.0, 2.0 Hz, CHCH_2), 4.39 (1H, dddd, *J* 15.5, 3.5, 2.0, 2.0 Hz, CCH_2), 4.26 (1H, dddd, *J* 16.5, 4.0, 2.0, 2.0 Hz, CHCH_2), 3.43 (CH_3); δ_{C} (75 MHz) 164.1, 164.0, 161.5, 161.3, 160.8, 160.7, 158.2, 158.0 (CF), 136.5, (4°), 130.5, 130.3 (CFCHCH), 129.5, (3°), 124.0, 123.9, 123.8, 123.7 (CCF), 113.8 (CHO), 111.6, 111.5, 111.3, 111.2 (CFCHCH), 104.5, 104.1, 103.8 (CFCHCF), 63.9, 63.8 (CCH_2O), 61.1 (CHCH_2O), 53.7 (CH_3); *m/z* (ESI) 265 [$\text{M}+\text{Na}$] $^+$, 183, 165, 151, 127 (Found [$\text{M}+\text{Na}$] $^+$, 265.0646. $\text{C}_{12}\text{H}_{12}\text{F}_2\text{O}_3$ requires [$\text{M}+\text{Na}$] $^+$, 265.0647) (Found: C, 59.59; H, 4.89. $\text{C}_{12}\text{H}_{12}\text{F}_2\text{O}_3$ requires C, 59.50; H, 4.99).

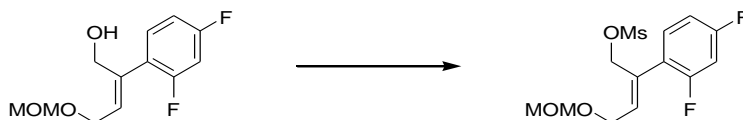
(*Z*)-2-(2,4-Difluorophenyl)-4-(methoxymethoxy)but-2-en-1-ol and (*Z*)-3-(2,4-difluorophenyl)-4-(methoxymethoxy)but-2-en-1-ol



According to general procedure **B**, to a solution of 5-(2,4-difluorophenyl)-2-methoxy-4,7-dihydro-1,3-dioxepine (781 mg, 3.22 mmol, 1.0 equiv.) in PhMe (8.3 mL) was treated with DIBAL-H (1.7 M in PhMe; 2.47 mL, 4.19 mmol, 1.3 equiv.). Purification by chromatography (20% EtOAc–petrol) gave (*Z*)-2-(2,4-difluorophenyl)-4-(methoxymethoxy)but-2-en-1-ol and (*Z*)-3-(2,4-difluorophenyl)-4-(methoxymethoxy)but-2-en-1-ol (739 mg, 94%; ratio 68:32; separable by chromatography) as colourless oils; (*Z*)-2-(2,4-difluorophenyl)-4-(methoxymethoxy)but-2-en-1-ol: R_f 0.25 (50% EtOAc–petrol); ν_{\max} (film) 3394, 2939, 2886, 1616, 1592, 1501, 1422, 1266, 1139, 1097, 967, 850, 815 cm^{-1} ; δ_{H} (300 MHz) 7.30 (1H, m, *o*-ArF), 6.83 (2H, m, *m*-ArF), 5.90 (1H, t, J 7.0 Hz, CH), 4.71 (2H, s, OCH₂O), 4.47 (2H, d, J 5.5 Hz, CCH₂OH), 4.34 (2H, d, J 7.0 Hz, CHCH₂), 3.41 (3H, s, CH₃), 2.22 (1H, t, J 6.0 Hz, OH); δ_{C} (100 MHz) 163.7, 163.5, 161.2, 161.1, 158.5, 158.6 (CF), 138.9 (4°), 131.1, 131.0 (CFCHCH), 130.2 (3°), 125.1, 124.9 (CCF), 111.5, 111.4, 111.3, 111.2 (CFCHCH), 104.3, 104.1, 103.8 (CFCHCF), 95.6 (OCH₂O), 63.0 (CH₂OH), 60.7, 60.6 (CHCH₂O), 55.4 (CH₃); m/z (CI) 262 [M+NH₄]⁺, 227, 183 (Found [M+NH₄]⁺, 262.1249. C₁₂H₁₄F₂O₃ requires [M+NH₄]⁺, 262.1249) (Found: C, 58.92; H, 5.69. C₁₂H₁₄F₂O₃ requires C, 59.01; H, 5.78); (*Z*)-3-(2,4-difluorophenyl)-4-(methoxymethoxy)but-2-en-1-ol: R_f 0.19 (50% EtOAc–petrol); ν_{\max} (film) 3404, 2945, 2887, 1616, 1593, 1501, 1422, 1266, 1140, 1097, 1039, 1007, 966, 919, 850, 815 cm^{-1} ; δ_{H} (300 MHz) 7.29 (1H, m, *o*-ArF), 6.83 (2H, m, *m*-ArF), 6.07 (1H, t, J 7.0 Hz, CH), 4.62 (2H, s, OCH₂O), 4.47 (2H, s, CCH₂), 4.37 (2H, t, J 6.0 Hz, CH₂OH), 3.34 (3H, s, CH₃) 2.14 (1H, t, J 6.0 Hz, OH); δ_{C} (75 MHz) 164.0, 163.9, 161.7, 161.5, 160.7, 160.6, 158.4, 158.3 (CF), 134.9 (3°), 134.1(4°), 131.0, 130.9, 130.9, 130.8, (CFCHCH), 125.2, 125.1, 125.0, 124.9 (CCF), 111.4, 111.4, 111.2, 111.1 (CFCHCH), 104.4, 104.0, 103.7 (CFCHCF), 95.4 (OCH₂O), 64.4 (CH₂OH), 58.7 (CCH₂) 55.5 (CH₃); m/z (EI) 262 [M+NH₄]⁺, 227, 197, 167 (Found [M+NH₄]⁺,

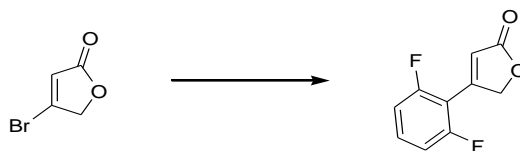
262.1249. C₁₂H₁₄F₂O₃ requires [M+NH₄]⁺, 262.1249) (Found: C, 59.14; H, 5.67. C₁₂H₁₄F₂O₃ requires C, 59.01; H, 5.78).

Methanesulfonic acid (Z)-2-(2,4-difluorophenyl)-4-(methoxymethoxy)but-2-enyl ester



According to general procedure C, to a solution of (Z)-2-(2,4-difluorophenyl)-4-(methoxymethoxy)but-2-en-1-ol (68 mg, 0.28 mmol, 1.0 equiv.) in CH₂Cl₂ (1 mL) was treated with NEt₃ (116 μL, 0.84 mmol, 3.0 equiv.) and MsCl (43.1 μL, 0.56 mmol, 2.0 equiv.) to give methanesulfonic acid (Z)-2-(2,4-difluorophenyl)-4-(methoxymethoxy)but-2-enyl ester (84 mg, 93%) as a colourless oil, which was used without further purification; R_f 0.35 (50% EtOAc–petrol); ν_{max} (film) 2942, 1615, 1592, 1502, 1353, 1267, 1172, 1141, 1099, 1048, 1030, 920, 846, 807 cm⁻¹; δ_H (400 MHz) 7.28 (1H, m, *o*-ArF), 6.86 (2H, m, *m*-ArF), 6.07 (1H, t, *J* 6.5 Hz, CH), 5.13 (2H, s, CCH₂), 4.69 (2H, s, OCH₂O), 4.36 (2H, d, *J* 6.5 Hz, CHCH₂), 3.41 (3H, s, OCH₃), 2.92 (3H, s, SCH₃); δ_C (100 MHz) 164.0, 163.9, 161.5, 161.4, 161.2, 161.1, 158.7, 158.6 (CF), 134.8 (4°), 134.8 (3°), 131.3, 131.3, 131.2, 131.2 (CFCHCH), 123.1, 123.1, 123.0, 123.0 (CCF), 111.8, 111.8, 111.6, 111.5 (CFCHCH), 104.5, 104.2, 104.0 (CFCHCF), 96.0 (OCH₂O), 66.3, 66.3 (CHCH₂), 63.0 (CCH₂), 55.5 (OCH₃), 37.7 (SCH₃); *m/z* (CI) 340 [M+NH₄]⁺, 165 (Found [M+NH₄]⁺, 340.1025. C₁₁H₁₆F₂O₅S requires [M+NH₄]⁺, 340.1025).

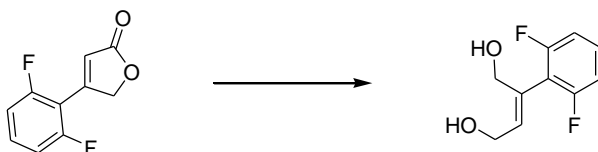
4-(2,6-Difluorophenyl)furan-2(5H)-one



To 4-bromofuran-2(5H)-one (4.25 g, 26.1 mmol, 1.0 equiv.) and PdCl₂(PPh₃)₂ (366 mg, 0.52 mmol, 2 mol%) in 2 M aq. KF (87 mL) and THF (87 mL) was added 2,6-difluorophenylboronic acid (4.12 g, 26.1 mmol, 1.0 equiv.) and the mixture heated under reflux for 5 h. After cooling to rt the layers were separated and the aqueous layer further extracted with EtOAc (×3). The combined organic phases were washed with sat. aq. NaCl, dried (MgSO₄) and concentrated under reduced pressure.

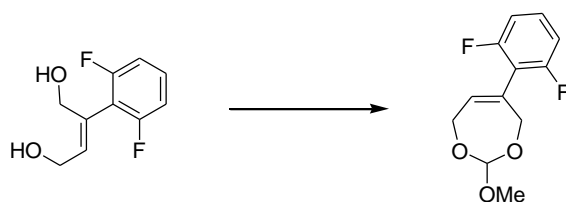
Purification by chromatography (30–50% EtOAc–petrol) gave 4-(2,6-difluorophenyl)furan-2(5*H*)-one (4.40 g, 86%) as a colourless solid; R_f 0.52 (50% EtOAc–petrol); ν_{\max} (film) 3055, 2987, 1758, 1626, 1466, 1265, 1167, 1071, 1053, 1017, 896, 868, 791, 741, 704 cm^{-1} ; δ_{H} (400 MHz) 7.45 (1H, tt, J 8.5, 6.5 Hz, *p*-ArF), 7.04 (2H, dd, J 9.5, 8.5 Hz, *m*-ArF), 6.68 (1H, s, CH), 5.29 (2H, s, CH₂); δ_{C} (100 MHz) 173.3 (C=O), 162.5, 162.4, 160.0, 159.9 (CF), 153.3 (CCH), 133.0, 132.9, 132.8 (CFCHCH), 119.4, 119.3, 119.2 (CCH), 112.7, 112.4 (CHCF), 108.5, 108.4, 108.2 (CCF), 73.1, 73.0 (CH₂); m/z (CI) 197 [M+H]⁺, 410, 214 (Found [M+H]⁺, 197.0421. C₁₀H₆F₂O₂ requires [M+H]⁺, 197.0414) (Found: C, 61.18; H, 2.99. C₁₀H₆F₂O₂ requires C, 61.23; H, 3.08).

(Z)-2-(2,6-Difluorophenyl)but-2-ene-1,4-diol



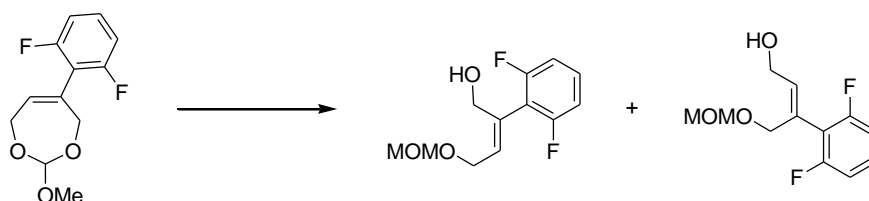
According to general procedure **I**, 4-(2,6-difluorophenyl)furan-2(5*H*)-one (4.32 g, 22.0 mmol, 1.0 equiv.) in PhMe (70 mL) was treated with DIBAL-H (1.2 M in PhMe; 40.4 mL, 48.5 mmol, 2.2 equiv.). Purification by chromatography (50% EtOAc–petrol) gave *(Z)*-2-(2,6-difluorophenyl)but-2-ene-1,4-diol (2.61 g, 60%) as a colourless oil; R_f 0.15 (50% EtOAc–petrol); ν_{\max} (film) 3338, 2886, 1622, 1586, 1462, 1269, 1231, 1000, 788 cm^{-1} ; δ_{H} (400 MHz) 7.22 (1H, tt, J 8.5, 6.5 Hz, *p*-ArF), 6.90 (2H, t, J 8.0 Hz, *m*-ArF), 6.00 (1H, t, J 6.5 Hz, CCH), 4.46 (2H, s, CCH₂), 4.45 (2H, d, J 7.0 Hz, CHCH₂), 2.14 (2H, br s, OH); δ_{C} (100 MHz) 161.6, 161.5, 159.1, 159.1 (CF) 136.0 (CHCH₂OH), 131.3 (CCH₂), 128.9, 128.8 (CFCHCH), 118.1 (CCF), 111.6, 111.5, 111.4, 111.3 (CFCH), 61.3 (CCH₂), 58.9 (CHCH₂); m/z (CI) 218 [M+NH₄]⁺, 200 (Found [M+NH₄]⁺, 218.0999. C₁₀H₁₀F₂O₂ requires [M+NH₄]⁺, 218.0993) (Found: C, 59.97; H, 5.01. C₁₀H₁₀F₂O₂ requires C, 60.00; H, 5.04).

5-(2,6-Difluorophenyl)-2-methoxy-4,7-dihydro-1,3-dioxepine



According to general procedure **A**, (Z)-2-(2,6-difluorophenyl)but-2-ene-1,4-diol (1.60 g, 7.99 mmol, 1.0 equiv.) in CH_2Cl_2 (20 mL) was treated with CSA (18.6 mg, 0.08 mmol, 1 mol%) and trimethyl orthoformate (1.75 mL, 16.0 mmol, 2.0 equiv.). Purification by chromatography (20→50% EtOAc–petrol) gave 5-(2,6-difluorophenyl)-2-methoxy-4,7-dihydro-1,3-dioxepine (1.77 mg, 91%) as a yellow liquid; R_f 0.67 (50% EtOAc–petrol); ν_{max} (film) 2945, 2874, 2846, 1621, 1583, 1567, 1463, 1388, 1344, 1270, 1230, 1212, 1136, 1035, 998, 915, 814, 784, 722 cm^{-1} ; δ_{H} (400 MHz) 7.22 (1H, tt, J 8.5, 6.5 Hz, p -ArF), 6.91 (2H, t, J 8.0 Hz, m -ArF), 5.92 (1H, t, J 3.5 Hz, CHCH_2), 5.49 (1H, s, OCH), 4.69 (2H, m, CCH_2), 4.38 (2H, m, CHCH_2), 3.47 (3H, s, CH_3); δ_{C} (100 MHz) 161.4, 161.3, 158.9, 158.8 (CF) 132.3 (CCH_2), 129.7 (CHCH_2), 128.9, 128.8, 128.7 (CFCHCH), 116.7 (CCF), 113.7 (CHO), 111.7, 111.6, 111.5, 111.4 (CFCH), 63.9 (CCH_2), 61.3 (CHCH_2), 53.7 (CH_3); m/z (CI) 143 $[\text{M}+\text{H}]^+$, 502, 260, 228, 211, 200, 182 (Found $[\text{M}+\text{H}]^+$, 243.0841. $\text{C}_{12}\text{H}_{12}\text{F}_2\text{O}_3$ requires $[\text{M}+\text{H}]^+$, 243.0833) (Found: C, 59.58; H, 5.05. $\text{C}_{12}\text{H}_{12}\text{F}_2\text{O}_3$ requires C, 59.50; H, 4.99).

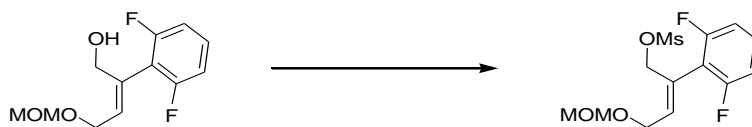
(Z)-2-(2,6-Difluorophenyl)-4-(methoxymethoxy)but-2-en-1-ol and (Z)-3-(2,6-difluorophenyl)-4-(methoxymethoxy)but-2-en-1-ol



According to general procedure **B**, 5-(2,6-difluorophenyl)-2-methoxy-4,7-dihydro-1,3-dioxepine (2.78 g, 11.48 mmol, 1.0 equiv.) in PhMe (36.4 mL) was treated with DIBAL-H (1.2 M in PhMe; 21.0 mL, 25.3 mmol, 2.2 equiv.). Purification by chromatography (5→10% $\text{Et}_2\text{O}-\text{CH}_2\text{Cl}_2$) gave (Z)-2-(2,6-difluorophenyl)-4-(methoxymethoxy)but-2-en-1-ol and (Z)-3-(2,6-difluorophenyl)-4-methoxymethoxybut-2-en-1-ol (2.32 g, 82%; ratio 66:34; separable by chromatography) as colourless

oils; (Z)-2-(2,6-difluorophenyl)-4-(methoxymethoxy)but-2-en-1-ol: R_f 0.39 (20% Et₂O–CH₂Cl₂); ν_{\max} (film) 3433, 2939, 1622, 1585, 1462, 1268, 1231, 1150, 1101, 1043, 996, 788 cm⁻¹; δ_H (400 MHz) 7.21 (1H, tt, J 8.5, 6.5 Hz, p -ArF), 6.90 (2H, t, J 8.0 Hz, m -ArF), 5.87 (1H, t, J 7.0 Hz, CH), 4.73 (2H, s, OCH₂O), 4.42 (2H, s, CCH₂OH), 4.37 (2H, d, J 7.0 Hz, CHCH₂), 3.42 (3H, s, CH₃), 2.16 (1H, br s, OH); δ_C (100 MHz) 161.7, 161.6, 159.2, 159.1 (CF), 132.9 (CCH₂), 132.4 (CHCH₂), 129.0, 128.9, 128.8 (CFCHCH), 118.3, 118.1, 117.9 (CCF), 111.5, 111.5, 111.4, 111.3 (CFCH), 95.3 (OCH₂O), 62.5 (CH₂OH), 60.8 (CHCH₂), 55.5 (CH₃); m/z (CI) 262 [M+NH₄]⁺, 506, 230 (Found [M+NH₄]⁺, 262.1265). C₁₂H₁₄F₂O₃ requires [M+NH₄]⁺, 262.1255) (Found: C, 59.01; H, 5.78. C₁₂H₁₄F₂O₃ requires C, 59.06; H, 5.78); (Z)-3-(2,6-difluorophenyl)-4-(methoxymethoxy)but-2-en-1-ol: R_f 0.31 (20% Et₂O–CH₂Cl₂); ν_{\max} (film) 3412, 2932, 1623, 1463, 1268, 1231, 1150, 1101, 1053, 995, 790 cm⁻¹; δ_H (400 MHz) 7.24 (1H, tt, J 8.5, 6.5 Hz, p -ArF), 6.92 (2H, t, J 8.0 Hz, m -ArF), 6.08 (1H, t, J 7.0 Hz, CH), 4.65 (2H, s, OCH₂O), 4.46 (2H, s, CCH₂), 4.42 (2H, d, J 7.0 Hz, CH₂OH), 3.35 (3H, s, CH₃) 2.11 (1H, br s, OH); δ_C (100 MHz) 161.7, 161.6, 159.2, 159.2 (CF) 137.2 (CHCH₂), 128.9, 128.8, 128.7 (CFCHCH), 127.8 (CCH₂), 118.2, 118.0, 117.8 (CCF), 111.5, 111.4, 111.3 (CFCH), 95.0 (OCH₂O), 64.1 (CH₂OH), 58.7 (CCH₂) 55.4 (CH₃); m/z (CI) 262 [M+NH₄]⁺, 506, 230 (Found [M+NH₄]⁺, 262.1263). C₁₂H₁₄F₂O₃ requires [M+NH₄]⁺, 262.1255) (Found: C, 59.12; H, 5.69. C₁₂H₁₄F₂O₃ requires C, 59.01; H, 5.78).

Methanesulfonic acid (Z)-2-(2,6-difluorophenyl)-4-(methoxymethoxy)but-2-enyl ester

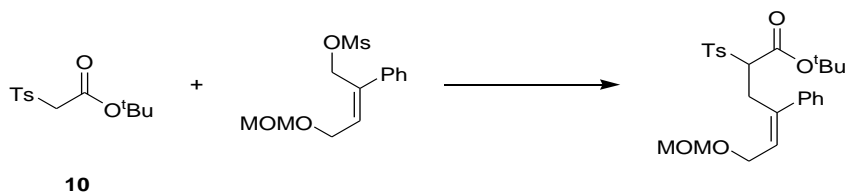


According to general procedure C, (Z)-2-(2,6-difluorophenyl)-4-(methoxymethoxy)but-2-en-1-ol (349 mg, 1.43 mmol, 1.0 equiv.) in CH₂Cl₂ (7.2 mL) was treated with NEt₃ (597 μ L, 4.29 mmol, 3.0 equiv.) and MsCl (221 μ L, 2.86 mmol, 2.0 equiv.) to give methanesulfonic acid (Z)-2-(2,6-difluorophenyl)-4-(methoxymethoxy)but-2-enyl ester as a colourless oil, used crude in the next step; R_f 0.64 (50% EtOAc–petrol); ν_{\max} (film) 3436, 3004, 2934, 2887, 1622, 1586, 1464, 1360, 1329, 1271, 1254, 1196, 1151, 1104, 1047, 999, 789, 735 cm⁻¹; δ_H (400 MHz) 7.28 (1H, tt, J 8.5, 6.5 Hz, o -ArF), 6.93 (2H, t, J 8.0 Hz, m -ArF), 6.08 (1H, t, J 6.5 Hz,

CH), 5.11 (2H, s, CCH₂), 4.69 (2H, s, OCH₂O), 4.38 (2H, d, *J* 6.5 Hz, CHCH₂), 3.40 (3H, s, OCH₃), 2.93 (3H, s, SCH₃); δ_C (100 MHz) 161.6, 161.5, 159.1, 159.1 (CF), 137.3 (CCH₂), 129.8, 129.7, 129.6 (CFCHCH), 125.1 (CHCH₂), 116.2, 116.1, 115.9 (CCF), 111.7, 111.7, 111.5, 111.5 (CFCHCH), 95.9 (OCH₂O), 66.6 (CHCH₂), 62.8 (CCH₂), 55.5 (OCH₃), 37.9 (SCH₃); *m/z* (CI) 340 [M+NH₄]⁺, 102 (Found [M+NH₄]⁺, 340.1020. C₁₁H₁₆F₂O₅S requires [M+NH₄]⁺, 340.1030).

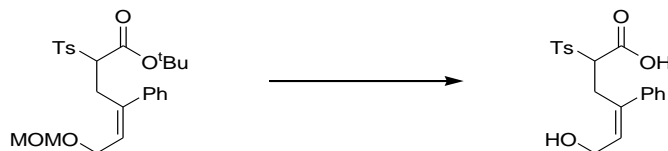
5. Synthesis and reactions of γ -aryl-substituted lactones 16a–c

tert-Butyl (*E*)-6-Methoxymethoxy-4-phenyl-2-tosylhex-4-enoate



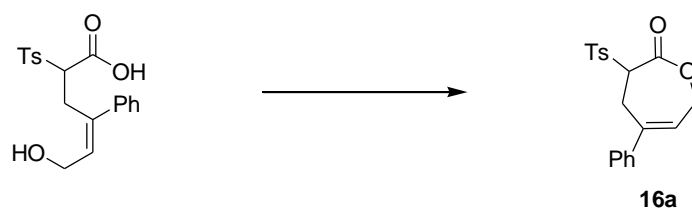
According to general procedure **D**, a suspension of sodium hydride (25 mg, 0.62 mmol, 1.1 equiv.) in THF (0.3 mL) at 0 °C was treated with *tert*-butyl 2-tosylacetate **10**² (153 mg, 0.57 mmol, 1.0 equiv.) in THF (0.4 mL) and methanesulfonic acid (*Z*)-4-methoxymethoxy-2-phenylbut-2-enyl ester (162 mg, 0.57 mmol, 1.0 equiv.) in THF (0.3 mL) to give *tert*-butyl (*E*)-6-methoxymethoxy-4-phenyl-2-tosylhex-4-enoate which was used without further purification; R_f 0.48 (50% EtOAc–heptane); ν_{\max} (film) 2980, 2933, 1732, 1597, 1493, 1446, 1370, 1327, 1151, 1084, 1047, 919, 836, 816, 766, 714, 699, 566 cm^{-1} ; δ_{H} (400 MHz) 7.77 (2H, d, J 8.0 Hz, *o*-SO₂Ar), 7.37 (2H, d, J 8.0 Hz, *m*-SO₂Ar), 7.29 (5H, m, Ph), 5.91 (1H, t, J 6.5 Hz, CHCH₂OH), 4.66 (2H, s, OCH₂O), 4.32 (1H, dd, J 13.0, 7.0 Hz, CHCH₂O), 4.18 (1H, dd, J 13.0, 6.0 Hz, CHCH₂O), 3.82 (1H, dd, J 4.5, 1.0 Hz, SCH), 3.39 (3H, s, OCH₃), 3.25 (2H, m, CHCH₂O), 2.48 (3H, s, ArCH₃), 1.23 (9H, s, C(CH₃)₃); δ_{C} (100 MHz) 164.3 (C=O), 145.3, 139.9, 137.6, 134.3 (4°), 129.6, 129.4, 128.7, 128.6, 127.9, 126.5 (3°), 95.9 (OCH₂O), 83.1 (C(CH₃)₃), 69.4 (SCH), 64.0 (OCH₂CH), 55.3 (OCH₃), 27.5 (C(CH₃)₃), 27.2 (SCHCH₂), 21.7 (ArCH₃); m/z (CI) 478 [M+NH₄]⁺ (Found [M+NH₄]⁺, 478.2260. C₂₅H₃₂O₆S requires [M+NH₄]⁺, 478.2263) (Found: C, 65.19; H, 7.00. C₂₅H₃₂O₆S requires C, 65.17; H, 6.97).

(*E*)-6-Hydroxy-4-phenyl-2-tosylhex-4-enoic acid



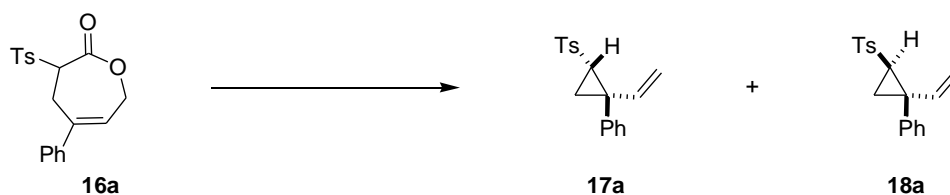
According to general procedure **E**, a solution *tert*-butyl (*E*)-6-methoxymethoxy-4-phenyl-2-tosylhex-4-enoate (218 mg, 0.47 mmol, 1.0 equiv.) in MeCN (4.5 mL) was treated with 2 M aq. HCl (0.9 mL) to give (*E*)-6-hydroxy-4-phenyl-2-tosylhex-4-enoic acid, which was used without further purification.

5-Phenyl-3-tosyl-4,7-dihydrooxepin-2(3H)-one **16a**



According to general procedure **G**, a solution of (*E*)-6-hydroxy-4-phenyl-2-tosylhex-4-enoic acid, (109 mg, 0.30 mmol, 1.0 equiv.) in CH₂Cl₂ (0.75 mL) was treated with EDCI (63 mg, 0.33 mmol, 1.1 equiv.). Purification by chromatography (30% EtOAc–petrol) gave 5-phenyl-3-tosyl-4,7-dihydrooxepin-2(3*H*)-one **16a** (69 mg, 35% over three steps) as a colourless solid; *R_f* 0.40 (50% EtOAc–petrol); *v*_{max} (film) 2925, 1739, 1596, 1324, 1269, 1158, 1143, 1087, 1056, 1019, 815, 746, 692, 662 cm⁻¹; δ_{H} (300 MHz) 7.99 (2H, d, *J* 8.5 Hz, *o*-SO₂Ar), 7.39–7.29 (7H, m, *m*-SO₂Ar and Ph), 6.07 (1H, m, CHCH₂O), [5.06, 5.00] (1H, 2 × dd, *J* 3.5, 3.5 Hz, SCH), [4.86, 4.82] (1H, 2 × d, *J* 4.0 Hz, OCH₂), [4.68, 4.62] (1H, 2 × d, *J* 7.5 Hz, OCH₂), [3.57, 3.51] (1H, 2 × m, SCHCH₂), 3.03 (1H, m, SCHCH₂), 2.45 (3H, s, CH₃); δ_{C} (75 MHz) 166.6 (C=O), 145.8, 141.4, 140.2, 133.5 (4°), 130.5, 129.7, 128.7, 125.9 (3°), 121.3 (CHCH₂O), 64.3 (SCH), 64.0 (OCH₂), 29.7, 29.5 (SCHCH₂), 21.8 (ArCH₃); *m/z* (CI) 360 [M+NH₄]⁺, 187 (Found [M+NH₄]⁺, 360.1263. C₁₉H₁₈O₄S requires [M+NH₄]⁺, 360.1264) (Found: C, 66.63; H, 5.30. C₁₉H₁₈O₄S requires C, 66.65; H, 5.30).

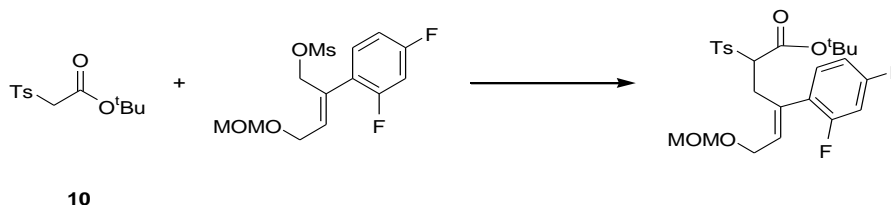
((1*R**,2*R**)-2-Phenyl-2-vinylcyclopropyl) *p*-tolyl sulfone **17a** and ((1*R**,2*S**)-2-phenyl-2-vinylcyclopropyl) *p*-tolyl sulfone **18a**



According to general procedure **H**, a solution of lactone **16a** (27 mg, 0.08 mmol, 1.0 equiv.) in DMF (0.4 mL) was treated with KOAc (0.8 mg, 0.008 mmol, 0.1 equiv.) and BSA (19.1 μ L, 0.08 mmol, 1.0 equiv.) to give a diastereomeric mixture (3:2) of ((1*R**,2*R**)-2-phenyl-2-vinylcyclopropyl) *p*-tolyl sulfone **17a** and ((1*R**,2*S**)-2-phenyl-2-vinylcyclopropyl) *p*-tolyl sulfone **18a** (20 mg, 87%), which were separable by chromatography (20% EtOAc–petrol) as colourless oils; **17a**: *R_f* 0.57 (50% EtOAc–petrol); *v*_{max} (film) 2924, 1633, 1598, 1446, 1403, 1318, 1266, 1148, 1088,

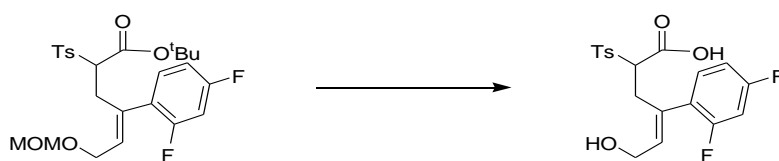
738, 701 cm^{-1} ; δ_{H} (400 Hz) 7.86 (2H, d, J 8.0 Hz, o -SO₂Ar), 7.37 (2H, d, J 8.0 Hz, m -SO₂Ar), 7.24 (3H, m, o -/ p -Ph), 7.04 (2H, dd, J 7.5, 1.5 Hz, m -Ph), 6.45 (1H, dd, J 17.0, 10.5 Hz, CH=CH₂), 5.18 (1H, dd, J 10.5, 1.0 Hz, CH=CH₂ *trans*), 4.57 (1H, dd, J 17.0, 1.0 Hz, CH=CH₂ *cis*), 2.89 (1H, dd, J 9.0, 6.0 Hz, SCH), 2.47 (3H, s, ArCH₃), 2.13 (1H, dd, J 6.0, 6.0 Hz, SCHCH₂), 1.83 (1H, dd, J 9.0, 5.5 Hz, SCHCH₂); δ_{C} (100 Hz) 144.4, 140.0, 138.2, 137.2 (4°), 129.7, 129.5, 128.5, 127.6, 127.5 (3°), 118.3 (CH=CH₂), 46.9 (SCH), 38.6 (SCHC), 21.7 (ArCH₃), 19.4 (SCHCH₂); m/z (CI) 316 [M+NH₄]⁺, 143 (Found [M+NH₄]⁺, 316.1382. C₁₈H₁₈O₂S requires [M+NH₄]⁺, 316.1371); **18a**: R_f 0.50 (50% EtOAc–petrol); ν_{max} (film) 3059, 2925, 1633, 1598, 1495, 1446, 1323, 1298, 1266, 1149, 1087, 914, 737, 702 cm^{-1} ; δ_{H} (400 Hz) 7.56 (2H, d, J 8.0 Hz, o -SO₂Ar), 7.33–7.26 (7H, m, m -SO₂Ar and Ph), 5.64 (1H, dd, J 17.0, 10.5 Hz, CH=CH₂), 5.02 (1H, dd, J 10.5, 0.5 Hz, CH=CH₂ *trans*), 4.75 (1H, dd, J 17.0, 0.5 Hz, CH=CH₂ *cis*), 2.84 (1H, dd, J 8.5, 6.0 Hz, SCH), 2.43 (3H, s, ArCH₃), 2.25 (1H, dd, J 6.0, 5.5 Hz, SCHCH₂), 1.49 (1H, dd, J 8.5, 5.5 Hz, SCHCH₂); δ_{C} (100 Hz) 144.1, 141.7, 138.2, 134.8 (4°), 130.6, 129.6, 128.1, 127.7, 127.6 (3°), 115.3 (CH=CH₂), 45.8 (SCH), 38.3 (SCHC), 21.6 (ArCH₃), 18.0 (SCHCH₂); m/z (CI) 316 [M+NH₄]⁺ (Found [M+NH₄]⁺, 316.1380. C₁₈H₁₈O₂S requires [M+NH₄]⁺, 316.1371).

tert-Butyl (*E*)-4-(2,4-Difluorophenyl)-6-methoxymethoxy-2-tosylhex-4-enoate



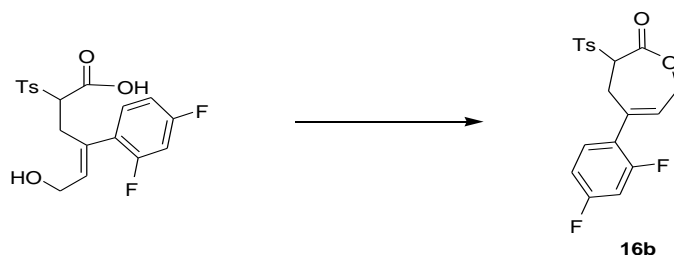
According to general procedure **D**, a suspension of sodium hydride (11.5 mg, 0.29 mmol, 1.1 equiv.) in THF (0.3 mL) was treated with *tert*-butyl 2-tosylacetate **10** (71 mg, 0.26 mmol, 1.0 equiv.) in THF (0.4 mL) followed by methanesulfonic acid (*Z*)-2-(2,4-difluorophenyl)-4-(methoxymethoxy)but-2-enyl ester (84 mg, 0.26 mmol, 1.0 equiv.) in THF (0.3 mL) to give *tert*-butyl (*E*)-4-(2,4-difluorophenyl)-6-methoxymethoxy-2-tosylhex-4-enoate, which was used without further purification; R_f 0.49 (50% EtOAc–heptane).

(E)-4-(2,4-Difluorophenyl)-6-hydroxy-2-tosylhex-4-enoic acid



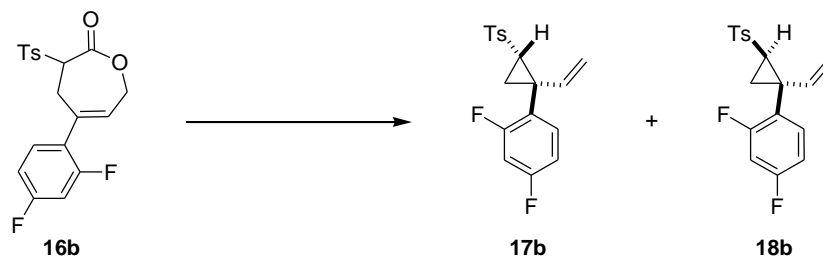
According to general procedure **E**, a solution of *tert*-butyl (*E*)-4-(2,4-difluorophenyl)-6-methoxymethoxy-2-tosylhex-4-enoate (85 mg, 0.17 mmol, 1.0 equiv.) in MeCN (1.5 mL) was treated with 2 M aq. HCl (0.3 mL) to give (*E*)-4-(2,4-difluorophenyl)-6-hydroxy-2-tosylhex-4-enoic acid as a colourless gum, which was used without further purification.

5-(2,4-Difluorophenyl)-3-tosyl-4,7-dihydro-3H-oxepin-2-one **16b**



According to general procedure **G**, a solution of (*E*)-4-(2,4-difluorophenyl)-6-hydroxy-2-tosylhex-4-enoic acid (77 mg, 0.19 mmol, 1.0 equiv.) in CH₂Cl₂ (0.5 mL) was treated with EDCI (41 mg, 0.21 mmol, 1.1 equiv.). Purification by chromatography (40% EtOAc–petrol) gave 5-(2,4-difluorophenyl)-3-tosyl-4,7-dihydrooxepin-2(3*H*)-one **16b** (73 mg, 74% over three steps) as a colourless solid; *R*_f 0.36 (50% EtOAc–petrol); *v*_{max} (film) 1745, 1594, 1501, 1321, 1305, 1291, 1265, 1139, 1084, 972, 850, 813, 670 cm⁻¹; δ_{H} (400 MHz) 7.95 (2H, d, *J* 8.5 Hz, *o*-SO₂Ar), 7.36 (2H, d *J* 8.0 Hz, *m*-SO₂Ar), 7.17 (1H, td, *J* 8.5, 6.5 Hz, *o*-ArF), 6.90–6.79 (2H, m, *m*-ArF), 5.95 (1H, m, CHCH₂O), [5.04, 4.99] (1H, 2 × dd, *J* 6.5, 3.5 Hz, SCH), [4.86, 4.81] (1H, 2 × d, *J* 4.0 Hz, OCH₂), [4.67, 4.62] (1H, 2 × d, *J* 7.5 Hz, OCH₂), [3.43, 3.37] (1H, 2 × m, SCHCH₂), 3.01 (1H, m, SCHCH₂), 2.45 (3H, s, CH₃); δ_{C} (75 MHz) 166.3 (C=O), 164.6, 164.4, 161.3, 161.2, 161.2, 161.1, 158.1, 157.9 (CF), 145.8, 136.8, 133.6 (4°), 130.4, 130.3, 130.3, 129.9 (CFCHCH), 130.5, 129.7, 125.1, (3°), 124.8, 124.7, 124.6, 124.5 (CCF), 111.9, 111.8, 111.6, 111.6 (CFCHCH), 104.9, 104.5, 104.2 (CFCHCF), 64.4, 63.6 (OCH₂), 63.7 (SCH), 30.0, 29.9 (SCHCH₂), 21.7 (CH₃); *m/z* (CI) 396 [M+NH₄]⁺ (Found [M+NH₄]⁺, 396.1075. C₁₉H₁₆F₂O₄S requires [M+NH₄]⁺, 396.1076).

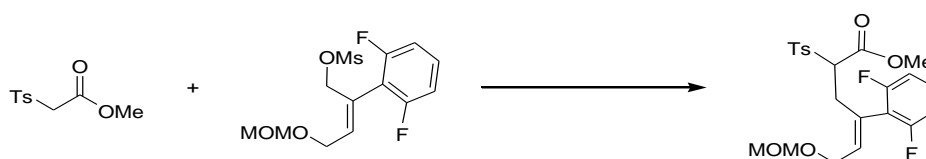
((1*R**,2*R**)-2-(2,4-Difluorophenyl)-2-vinylcyclopropyl) *p*-tolyl sulfone **17b** and ((1*R**,2*S**)-2-(2,4-difluorophenyl)-2-vinylcyclopropyl) *p*-tolyl sulfone **18b**



According to general procedure **H**, lactone **16b** (70.0 mg, 0.20 mmol, 1.0 equiv.) in DMF (1.0 mL) was treated with KOAc (pinch) and BSA (46.0 μ L, 0.20 mmol, 1.0 equiv.) to give a diastereomeric mixture (3:2) of ((1*R**,2*R**)-2-(2,4-difluorophenyl)-2-vinylcyclopropyl) *p*-tolyl sulfone **17b** and ((1*R**,2*S**)-2-(2,4-difluorophenyl)-2-vinylcyclopropyl) *p*-tolyl sulfone **18b** (46 mg, 75%) as a colourless gum, separable by chromatography (10–20% EtOAc–petrol); **17b**: R_f 0.55 v_{max} (film) 3056, 2926, 1618, 1508, 1426, 1266, 1148, 1090, 738 cm^{-1} ; δ_H (500 MHz) 7.84 (2H, d, J 8.0 Hz, *o*-SO₂Ar), 7.36 (2H, d, J 8.0 Hz, *m*-SO₂Ar), 7.01 (1H, ddd, J 8.5, 8.5, 6.5 Hz, CFCHCH), 6.80 (1H, dddd, J 8.0, 8.0, 2.5, 1.0 Hz, CFCHCH), 6.72 (1H, ddd, J 10.0, 9.0, 2.5 Hz, CFCHCF), 6.39 (1H, dd, J 17.0, 10.5 Hz, CH=CH₂), 5.18 (1H, d, J 10.5 Hz, CH=CH₂ *trans*), 4.56 (1H, d, J 17.0 Hz, CH=CH₂ *cis*), 2.84 (1H, dd, J 9.0, 6.5 Hz, SCH), 2.47 (3H, s, ArCH₃), 2.19 (1H, dd, J 6.0, 6.0 Hz, SCHCH₂), 1.79 (1H, dd, J 9.0, 6.0 Hz, SCHCH₂); δ_C (100 MHz) 163.7, 163.6, 162.9, 162.8, 161.8, 161.7, 160.9, 160.8 (CF), 144.4, 138.0 (4°), 139.9, 129.7, 127.6 (3°), 133.5 (CCF), 118.7 (CFCHCH), 115.4 (CH=CH₂), 111.2, 111.1, 111.0 (CFCHCH), 104.3, 104.1, 103.9 (CFCHCF), 45.4 (SCH), 29.7 (SCHC), 21.6 (ArCH₃), 18.7 (SCHCH₂); δ_F (376 MHz) –109.3 (1F, ddd, J 16.5, 8.0, 6.5 Hz, *p*-CF); m/z (CI) 352 [M+NH₄]⁺, 316 (Found [M+NH₄]⁺, 352.1198. C₁₈H₁₆F₂O₂S requires [M+NH₄]⁺, 352.1183); **18b**: R_f 0.59 (50% EtOAc–petrol); v_{max} (film) 3923, 1598, 1505, 1425, 1321, 1290, 1148, 1088, 967, 851, 741, 659 cm^{-1} ; δ_H (400 MHz) 7.66 (2H, d, J 8.0 Hz, *o*-SO₂Ar), 7.45 (1H, dd, J 15.0, 8.5 Hz, CFCHCH), 7.32 (2H, d, J 8.0 Hz, *m*-SO₂Ar), 6.90 (1H, dddd, J 9.0, 9.0, 2.5, 1.0 Hz, CFCHCH), 6.80 (1H, ddd, J 10.5, 9.0, 2.5 Hz, CFCHCF), 5.55 (1H, dd, J 17.0, 10.5 Hz, CH=CH₂), 5.04 (1H, d, J 10.5 Hz, CH=CH₂ *trans*), 4.74 (1H, d, J 17.0 Hz, CH=CH₂ *cis*), 2.82 (1H, dd, J 8.5, 6.5 Hz, SCH), 2.45 (3H, s, ArCH₃), 2.17 (1H, dd, J 6.0, 6.0 Hz, SCHCH₂), 1.64 (1H, dd, J 8.5, 6.0 Hz, SCHCH₂); δ_C (100 MHz) 163.8, 163.6, 162.6, 162.4, 161.3, 161.2, 160.2, 160.0 (CF), 144.5, 137.7 (4°),

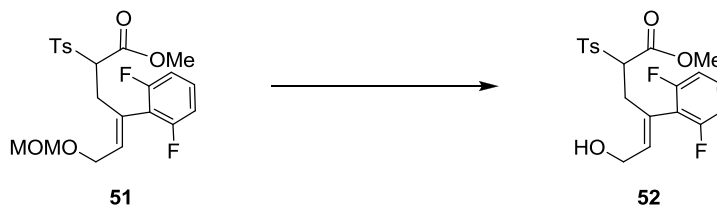
132.4, 132.3, 132.3, 132.2 (CCF), 135.5, 129.7, 127.6 (3°), 123.1, 123.0 (CFCHCH), 117.6 (CH=CH₂), 111.6, 111.6, 111.4, 111.4 (CFCHCH), 104.5, 104.2, 104.0 (CFCHCF), 46.7 (SCH), 29.7 (SCHCH), 21.7 (ArCH₃), 19.4 (SCHCH₂); δ_F (376 MHz) -108.8 (1F, ddd, *J* 16.5, 8.5, 6.5 Hz, *o*-CF), -109.4 (1F, dd, *J* 17.5, 8.5 Hz, *p*-CF); *m/z* (CI) 352 [M+NH₄]⁺, 316, 298 (Found [M+NH₄]⁺, 352.1198. C₁₈H₁₆F₂O₂S requires [M+NH₄]⁺, 352.1183);

Methyl (E)-4-(2,6-difluorophenyl)-6-methoxymethoxy-2-tosylhex-4-enoate



According to general procedure **D**, sodium hydride (40.2 mg, 1.00 mmol, 1.2 equiv.) in DMF (1.5 mL) was treated with methyl 2-tosylacetate^{Error! Bookmark not defined.} (191 mg, 0.84 mmol, 1.0 equiv.) in DMF (1.5 mL) and methanesulfonic acid (Z)-2-(2,6-difluorophenyl)-4-(methoxymethoxy)but-2-enyl ester (0.84 mmol, 1.0 equiv.) in THF (1.2 mL) to give methyl (*E*)-4-(2,6-difluorophenyl)-6-methoxymethoxy-2-tosylhex-4-enoate, which was used without further purification; *R_f* 0.64 (50% EtOAc–petrol).

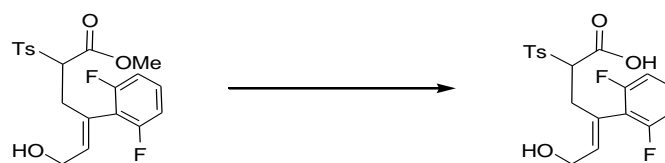
(E)-Methyl 4-(2,6-difluorophenyl)-6-hydroxy-2-tosylhex-4-enoate



According to general procedure **E**, methyl (*E*)-4-(2,6-difluorophenyl)-6-methoxymethoxy-2-tosylhex-4-enoate (0.84 mmol, 1.0 equiv.) in MeCN (8.4 mL) was treated with 2 M aq. HCl (1.68 mL). Purification by chromatography (20→40% EtOAc–petrol) gave (*E*)-methyl 4-(2,6-difluorophenyl)-6-hydroxy-2-tosylhex-4-enoate (277 mg, 80% over three steps) as a colourless gum; *R_f* 0.33 (50% EtOAc–petrol); ν_{\max} (film) 3055, 2986, 1741, 1620, 1463, 1423, 1265, 1149, 1085, 895, 738 cm⁻¹; δ_H (400 MHz) 7.70 (2H, d, *J* 8.0 Hz, *o*-SO₂Ar), 7.35 (2H, d, *J* 8.0 Hz, *m*-SO₂Ar), 7.23 (1H, tt, *J* 8.5, 6.5 Hz, *p*-ArF), 6.87 (2H, t, *J* 8.0 Hz, *m*-ArF), 5.83 (1H, t, *J* 7.0 Hz, CHCH₂OH), 4.36 (1H, dd, *J* 13.5, 7.5 Hz, CH₂OH), 4.18 (1H, dd, *J* 13.5, 6.5 Hz, CH₂OH), 3.84 (1H, dd, *J* 12.0, 3.5 Hz, SCH), 3.59 (3H, s, OCH₃), 3.29 (1H,

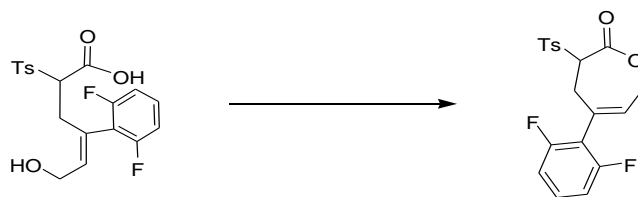
dd, J 14.0, 12.0 Hz, SCHCH₂), 3.02 (1H, dd, J 14.0, 2.5 Hz, SCHCH₂), 2.47 (3H, s, ArCH₃); δ_C (100 MHz) 166.3 (C=O), 161.5, 161.4, 159.0, 158.9 (CF), 145.7, 136.9, 133.6 (4°), 129.8, 129.2 (3°), 129.6, 129.5, 129.4 (CFCHCH), 125.0 (CHCH₂OH), 117.2 (CCF), 111.7, 111.6, 111.5, 111.4 (CFCH), 69.0 (SCH), 58.6 (CH₂OH), 53.1 (OCH₃), 28.0 (SCHCH₂), 21.7 (ArCH₃); m/z (CI) 428 [M+NH₄]⁺, 410, 393, 272, 174; (Found [M+NH₄]⁺, 428.1325. C₂₀H₂₀F₂O₅S requires [M+NH₄]⁺, 428.1343).

(E)-4-(2,6-Difluorophenyl)-6-hydroxy-2-tosylhex-4-enoic acid



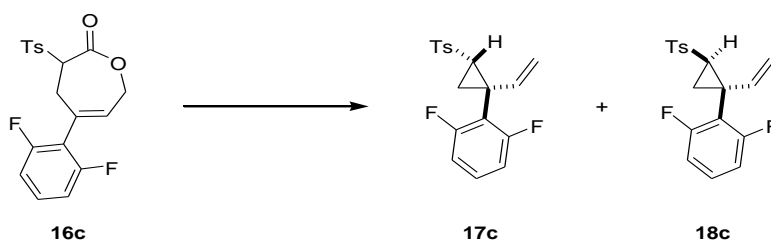
According to general procedure **F**, (*E*)-methyl 4-(2,6-difluorophenyl)-6-hydroxy-2-tosylhex-4-enoate (270 mg, 0.66 mmol, 1.0 equiv.) in THF (1.65 mL) was treated with 2 M aq. LiOH (1.65 mL) to give (*E*)-4-(2,6-difluorophenyl)-6-hydroxy-2-tosylhex-4-enoic acid (214 mg, 82%), which was used without further purification; ν_{\max} (film) 3416, 3055, 2986, 1731, 1622, 1464, 1324, 1265, 1232, 1149, 1084, 1001, 815, 789, 738, 704 cm⁻¹; δ_H (400 MHz) 7.71 (2H, d, J 8.5 Hz, *o*-SO₂Ar), 7.33 (2H, d, J 8.5, 0.5 Hz, *m*-SO₂Ar), 7.23 (1H, tt, J 8.5, 6.5 Hz, *p*-ArF), 6.83 (2H, dd, J 8.5, 7.5 Hz, *m*-ArF), 5.82 (1H, dd, J 7.5, 6.5 Hz, CHCH₂OH), 4.42 (1H, dd, J 13.0, 8.5 Hz, CH₂OH), 4.12 (1H, dd, J 13.0, 6.0 Hz, CH₂OH), 3.81 (1H, dd, J 12.0, 3.0 Hz, SCH), 3.30 (1H, dd, J 14.0, 12.0 Hz, SCHCH₂), 2.96 (1H, dd, J 14.0, 2.0 Hz, SCHCH₂), 2.44 (3H, s, ArCH₃); δ_C (100 MHz) 168.2 (C=O), 161.5, 161.4, 159.0, 159.0 (CF), 145.8, 135.9, 133.5 (4°), 129.9, 129.3 (3°), 129.8, 129.6, 129.5 (CFCHCH), 125.9 (CHCH₂OH), 117.3, 117.1, 116.9 (CCF), 111.8, 111.7, 111.6, 111.5 (CFCH), 68.7 (SCH), 58.4 (CH₂OH), 28.2 (SCHCH₂), 21.8 (ArCH₃); m/z (CI) 370 [M-CO₂+NH₄]⁺, 412, 396, 352, 335, 174 (Found [M+NH₄]⁺, 414.1185. C₁₉H₁₈F₂O₅S requires [M+NH₄]⁺, 414.1187) (Found: C, 57.62; H, 4.49. C₁₉H₁₈F₂O₅S requires C, 57.57; H, 4.58).

5-(2,6-Difluorophenyl)-3-tosyl-4,7-dihydrooxepin-2(3H)-one **16c**



According to general procedure **G**, (*E*)-4-(2,6-difluorophenyl)-6-hydroxy-2-tosylhex-4-enoic acid (98 mg, 0.25 mmol, 1.0 equiv.) in CH₂Cl₂ (1.25 mL) was treated with EDCI (52.7 mg, 0.28 mmol, 1.1 equiv.). Purification by chromatography (30% EtOAc–petrol) gave 5-(2,6-difluorophenyl)-3-tosyl-4,7-dihydrooxepin-2(3*H*)-one **16c** (73 mg, 74% over three steps) as a colourless solid; *R_f* 0.60 (50% EtOAc–petrol); ν_{max} (film) 3139, 1748, 1622, 1463, 1398, 1321, 1267, 1231, 1144, 1084, 1002, 781, 735, 666 cm⁻¹; δ_{H} (400 MHz) 7.95 (2H, d, *J* 8.5 Hz, *o*-SO₂Ar), 7.36 (2H, d *J* 8.0 Hz, *m*-SO₂Ar), 7.28 (1H, td, *J* 8.5, 6.5 Hz, *o*-ArF), 6.92 (2H, dd, *J* 8.0, 8.0 Hz, *m*-ArF), 5.96 (1H, m, CHCH₂O), [5.06, 5.02] (1H, 2 × dd, *J* 3.5, 3.5 Hz, SCH), [4.87, 4.83] (1H, 2 × d, *J* 4.0 Hz, OCH₂), [4.68, 4.64] (1H, 2 × d, *J* 7.5 Hz, OCH₂), 3.29 (1H, d, *J* 17.5 Hz, SCHCH₂), 3.02 (1H, m, SCHCH₂), 2.45 (3H, s, CH₃); δ_{C} (100 MHz) 166.2 (C=O), 161.0, 160.9, 158.5, 158.4 (CF), 145.7, 133.6, 130.6 (4°), 130.4, 129.6, (3°), 130.0, 129.9, 129.8 (CFCHCH), 127.5 (CHCH₂OH), 117.6 (CCF), 111.9, 111.8, 111.7, 111.6 (CFCHCH), 64.4 (OCH₂), 63.6 (SCH), 29.8 (SCHCH₂), 21.7 (CH₃); *m/z* (CI) 396 [M+NH₄]⁺, 254, 242, 174 (Found [M+NH₄]⁺, 396.1085. C₁₉H₁₆F₂O₄S requires [M+NH₄]⁺, 396.1081) (Found: C, 60.38; H, 4.19. C₁₉H₁₆F₂O₄S requires C, 60.31; H, 4.26).

((1*R**,2*R**)-2-(2,6-Difluorophenyl)-2-vinylcyclopropyl) *p*-tolyl sulfone **17c** and ((1*R**,2*S**)-2-(2,6-difluorophenyl)-2-vinylcyclopropyl) *p*-tolyl sulfone **18c**

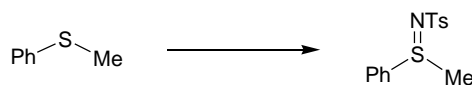


According to general procedure **I**, lactone **16c** (63 mg, 0.17 mmol, 1.0 equiv.) in DMF (0.85 mL) was treated with KOAc (0.85 mg, 0.017 mmol, 0.1 equiv.) and BSA (41 μ L, 0.17 mmol, 1.0 equiv.) to give a diastereomeric mixture (2:3) of ((1*R**,2*R**)-2-(2,6-difluorophenyl)-2-vinylcyclopropyl) *p*-tolyl sulfone **17c** and ((1*R**,2*S**)-2-(2,6-

difluorophenyl)-2-vinylcyclopropyl) *p*-tolyl sulfone **18c** (47 mg, 82%) as a colourless oil, separable by chromatography (10% Et₂O–petrol); **17c**: R_f 0.34 (50% Et₂O–petrol); ν_{max} (film) 3054, 1625, 1467, 1321, 1265, 1151, 1090, 1008, 790, 738, 704, 653 cm⁻¹; δ_H (400 MHz) 7.84 (2H, d, *J* 8.0 Hz, *o*-SO₂Ar), 7.34 (2H, d, *J* 8.0 Hz, *m*-SO₂Ar), 7.21 (1H, tt, *J* 8.5, 6.5 Hz, *p*-ArF), 6.80 (2H, t, *J* 8.0 Hz, *m*-ArF), 6.35 (1H, dd, *J* 17.0, 10.5 Hz, CH=CH₂), 5.17 (1H, d, *J* 10.5 Hz, CH=CH₂ *trans*), 4.62 (1H, d, *J* 17.0 Hz, CH=CH₂ *cis*), 2.91 (1H, dd, *J* 9.0, 6.5 Hz, SCHCH₂), 2.46 (3H, s, ArCH₃), 2.30 (1H, dd, *J* 6.5, 6.5 Hz, SCHCH₂), 1.8 (1H, dd, *J* 9.0, 6.0 Hz, SCHCH₂); δ_C (100 MHz) 162.9, 162.8, 160.4, 160.3 (CF), 144.4, 137.5 (4°), 134.5 (CH=CH₂), 129.9, 129.8, 129.7 (CFCHCH), 129.5, 128.1 (3°), 117.2 (CH=CH₂), 111.8, 111.5 (CFCH), 46.6 (SCH), 27.9 (SCHC), 21.7 (ArCH₃), 19.8 (CH₂); *m/z* (CI) 352 [M+NH₄]⁺ (Found [M+NH₄]⁺, 352.1183. C₁₈H₁₆F₂O₂S requires [M+NH₄]⁺, 352.1183) (Found: C, 64.69; H, 4.75. C₁₈H₁₆F₂O₂S requires C, 64.65; H, 4.82); **18c**: R_f 0.27 (50% Et₂O–petrol); ν_{max} (film) 1628, 1466, 1325, 1298, 1234, 1150, 1088, 1004, 910, 734 cm⁻¹; δ_H (400 MHz) 7.68 (2H, d, *J* 8.0 Hz, *o*-SO₂Ar), 7.32 (2H, d, *J* 8.0 Hz, *m*-SO₂Ar), 7.30 (1H, tt, *J* 8.5, 6.5 Hz, *p*-ArF), 6.92 (2H, dd, *J* 17.0, 8.5 Hz, *m*-ArF), 5.56 (1H, dd, *J* 17.0, 10.5 Hz, CH=CH₂), 5.06 (1H, d, *J* 10.5 Hz, CH=CH₂ *trans*), 4.82 (1H, d, *J* 17.0 Hz, CH=CH₂ *cis*), 2.85 (1H, ddd, *J* 8.5, 6.5, 2.0 Hz, SCHCH₂), 2.44 (3H, s, ArCH₃), 2.23 (1H, ddd, *J* 6.5, 6.5, 2.5 Hz, SCHCH₂), 1.71 (1H, dd, *J* 9.0, 6.0 Hz, SCHCH₂); δ_C (125 MHz) 163.5, 163.5, 162.8, 162.7, 161.5, 161.5, 160.8, 160.8 (CF), 144.3, 138.6, 138.1 (4°), 134.5 (CH=CH₂), 129.5, 129.6, 129.7 (CFCHCH), 129.7, 127.7 (3°), 115.2 (CH=CH₂), 112.4, 112.2, 112.2, 112.1 (CFCHCF), 111.8, 111.8, 111.7, 111.6, 111.4, 111.4, 111.3, 111.2 (CFCH), 44.9 (SCH), 29.1 (SCHC), 21.6 (ArCH₃), 18.9 (CH₂); *m/z* (CI) 352 [M+NH₄]⁺ (Found [M+NH₄]⁺, 352.1197. C₁₈H₁₆F₂O₂S requires [M+NH₄]⁺, 352.1183) (Found: C, 64.77; H, 4.73. C₁₈H₁₆F₂O₂S requires C, 64.65; H, 4.82).

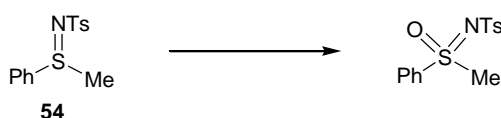
6. Synthesis and reactions of sulfoximinyl lactones 19 and 20

(±)-*S*-Methyl-*S*-phenyl-*N*-tosylsulfilimine



Thioanisole (5.87 mL, 50.0 mmol, 1.0 equiv.) and tetrabutylammonium bromide (0.81 g, 2.50 mmol, 5.0 mol%) were dissolved in CH₂Cl₂ (100 mL). Solid chloramine-T trihydrate (dried under vacuum over P₂O₅; 15.5 g, 55.0 mmol, 1.1 equiv.) was slowly added with stirring and cooling in a water bath. After addition was complete the water bath was removed and stirring continued for 2 h. The reaction mixture was washed with cold 5% aq. NaOH and H₂O (×2), the organic layer dried (MgSO₄) and concentrated under reduced pressure. The crude sulfilimine was recrystallised from methanol–water (9:1) to give (±)-*S*-methyl-*S*-phenyl-*N*-tosylsulfilimine (13.9 g, 95%) as colourless needles; mp 130 °C; R_f 0.07 (20% EtOAc–petrol); ν_{max} (nujol) 1593, 1295, 1279, 1142, 1086, 1021, 989, 932, 826, 766, 746, 689, 652 cm⁻¹; δ_H (270 MHz) 7.68 (4H, m, *o*-Ph, *o*-SO₂Ar), 7.49 (3H, m, *m*-/*p*-Ph), 7.14 (2H, d, *J* 8.0 Hz, *m*-SO₂Ar), 2.82 (3H, s, SCH₃), 2.33 (3H, s, ArCH₃); δ_C (100 MHz) 141.7, 141.2, 136.1 (4°), 132.4, 129.9, 129.2, 126.2, 125.8 (3°), 39.1 (SCH₃), 21.3 (ArCH₃); *m/z* (CI) 294 [M+H]⁺, 206, 189; data were in accordance with those previously reported.⁷

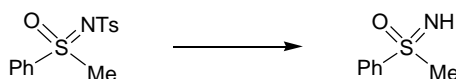
(±)-*S*-Methyl-*S*-phenyl-*N*-tosylsulfoximine



To a solution of the (±)-*S*-methyl-*S*-phenyl-*N*-tosylsulfilimine (13.5 g, 46.0 mmol, 1.0 equiv.) in CCl₄ (100 mL) and MeCN (100 mL) was added RuO₂·xH₂O (12.2 mg, 0.92 mmol, 2.0 mol%). A solution of NaIO₄ (19.7 g, 92.0 mmol, 2.0 equiv.) in H₂O (200 mL) was then added slowly (~30 min) and the reaction stirred for 90 min. The phases were separated and the aqueous layer extracted with CH₂Cl₂. The organic layers were combined and *i*PrOH (4.5 mL) added and the reaction mixture stirred for a further 1 h, then filtered over celite, dried (MgSO₄), and concentrated under reduced pressure. The yellow/green crystals were washed with EtOH to give the (±)-*S*-methyl-*S*-phenyl-*N*-tosylsulfoximine (11.8 g, 83%) as colourless crystals; mp 102 °C; ν_{max} (nujol) 1597, 1580, 1327, 1314, 1230, 1146, 1090, 1067, 982, 811, 754, 740, 689, 653 cm⁻¹; δ_H (270

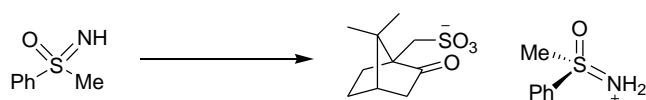
MHz) 8.00 (2H, d, J 7.5 Hz, *o*-Ph), 7.84 (2H, d, J 8.5 Hz, *o*-SO₂Ar), 7.72–7.56 (3H, m, *m*-/*p*-Ph), 7.24 (2H, d, J 8.5 Hz, *m*-SO₂Ar), 3.41 (3H, s, SCH₃), 2.38 (3H, s, ArCH₃); δ_C (67.5 MHz) 142.9, 140.7, 138.6 (4°), 134.5, 129.8, 129.4, 127.6, 126.7 (3°), 46.7 (SCH₃), 21.6 (ArCH₃); m/z (CI) 327 [M+NH₄]⁺, 294, 189, 52; data were in accordance with those previously reported.⁸

(±)-*S*-Methyl-*S*-phenylsulfoximine



A solution of (±)-*S*-methyl-*S*-phenyl-*N*-tosylsulfoximine (11.8 g, 38.1 mmol, 1.0 equiv.) was heated in conc. H₂SO₄ (20 mL) for 25 min at 120 °C. The reaction was cooled to rt, then poured into ice and neutralised using 2 M aq. NaOH. The reaction mixture was extracted with CH₂Cl₂ (×2), and the organic layer dried (MgSO₄) and concentrated under reduced pressure to give (±)-*S*-methyl-*S*-phenylsulfoximine (5.83 g, 99%) as a colourless oil; ν_{\max} (film) 3268, 3191, 3091, 3062, 3018, 1446, 1409, 1320, 1222, 1097, 1070, 1029, 1010, 950, 769, 742, 690 cm⁻¹; δ_H (270 MHz) 7.99 (2H, d, J 8.0 Hz, *o*-Ph), 7.64–7.50 (3H, m, *m*-/*p*-Ph), 3.07 (3H, s, SCH₃); δ_C (67.5 MHz) 143.4 (4°), 133.2, 129.4, 127.8 (3°), 46.2 (SCH₃); m/z (CI) 156 [M+H]⁺; data were in accordance with those previously reported.⁹

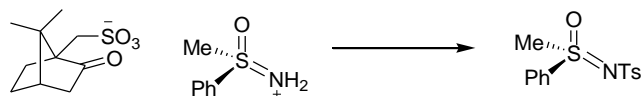
(-)-(R_S)-*S*-Methyl-*S*-phenylsulfoximine-(-)-camphorsulfonic acid



A solution of (-)-(*R*_S)-camphorsulfonic acid (4.28 g, 18.4 mmol, 0.5 equiv.) in dry acetone (distilled over P₂O₅; 30 mL) was added to a solution of (±)-*S*-methyl-*S*-phenylsulfoximine (5.72 g, 36.9 mmol, 1.0 equiv.) in dry acetone (20 mL) at rt and stirred for 16 h. The precipitate was then filtered and washed with dry acetone (×3) to give (-)-(*R*_S)-*S*-methyl-*S*-phenylsulfoximine-(-)-camphorsulfonic acid (5.40 g, 40% from a possible 50%) as a colourless powder; mp 172–174 °C; ν_{\max} (nujol) 1728, 1580, 1415, 1253, 1231, 1190, 1140, 1038, 669, 748 cm⁻¹; δ_H (270 MHz) 8.17 (2H, d, J 8.0 Hz, *o*-Ph), 7.82–7.67 (3H, m, *m*-/*p*-Ph), 3.84 (3H, s, SCH₃), [3.11 and 2.62] (2H, 2 × d, J 15.0 Hz, SCH₂), [2.42, 2.24] (2H, 2 × m, SCH₂CCH₂), 1.96 (1H, dd, J 4.0, 4.0

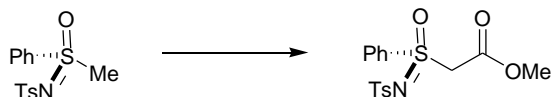
Hz, CHCH₂CO), 1.89 (1H, dd, *J* 8.0, 4.0 Hz, CHCH₂CO), 1.80 (1H, d, *J* 18.5 Hz, CHCH₂CO), 1.48 (1H, ddd, *J* 13.0, 9.5, 4.0 Hz, CHCH₂CH₂), 1.28 (1H, ddd, *J* 13.0, 9.5, 4.0 Hz, CHCH₂CH₂), [0.95, 0.73] (6H, 2 × s, CSA⁻CH₃); δ_C (125 MHz, DMSO-d₆) 215.9 (C=O), 137.9 (4°), 130.2, 128.2, 125.5 (3°), 58.0 (SO₂CH₂C), 47.1 (C(CH₃)₂), 46.9 (SO₂CH₂), 43.5 (SCH₃), 42.2 (CH₂CO), 42.1 (CHCO), 26.3 (SO₂CH₂CCH₂), 24.1 (CH₂CCO), 19.9, 19.5 (C(CH₃)₂); *m/z* (CI) 156; data were in accordance with those previously reported.¹⁰

(-)-(R_S)-S-Methyl-S-phenyl-N-tosylsulfoximine



(-)-(R_S)-S-Methyl-S-phenylsulfoximine(-)-camphorsulfonic acid (8.2 g, 22.2 mmol, 1.0 equiv.) was dissolved in dry pyridine (15 mL). Tosyl chloride (4.23 g, 22.2 mmol, 1.0 equiv.) was added slowly and the reaction was stirred for 16 h. The reaction mixture was then poured onto H₂O and extracted with CH₂Cl₂. The organic layers were combined, washed with 2 M aq. HCl (×2) and H₂O, dried (MgSO₄) and concentrated under reduced pressure to give (-)-(R_S)-S-methyl-S-phenyl-N-tosylsulfoximine (6.07 g, 88%) as a colourless crystalline solid; mp 106–107 °C; [α]_D²² -40.0 (*c* 5.0, CH₂Cl₂); ν_{max} (nujol) 2361, 1735, 1312, 1239, 1061, 965, 805, 685, 651 cm⁻¹; δ_H (270 MHz) 7.99 (2H, d, *J* 8.0 Hz, *o*-Ph), 7.82 (2H, d, *J* 8.0 Hz, *o*-SO₂Ar), 7.72–7.55 (3H, m, *m*/*p*-Ph), 7.23 (2H, d, *J* 8.0 Hz, *m*-SO₂Ar), 3.41 (3H, s, SCH₃), 2.38 (3H, s, ArCH₃); δ_C (67.5 MHz) 143.0, 140.7, 138.6 (4°), 134.5, 129.8, 129.4, 127.6, 126.7 (3°), 46.7 (SCH₃), 21.6 (ArCH₃); data were in accordance with those previously reported.¹¹

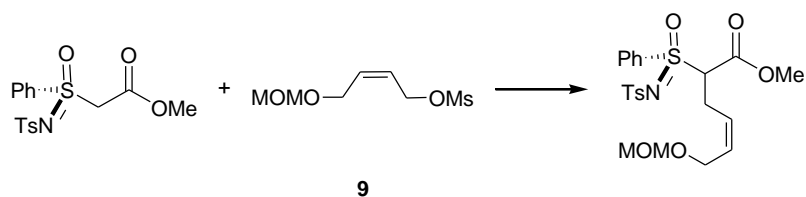
Methyl (R_S)-2-(N-tosylphenylsulfonimidoyl)acetate



To a suspension of sodium hydride (60% dispersion in mineral oil, washed in hexane; 430 mg, 10.7 mmol, 2.2 equiv.) in THF (10 mL) was added dimethyl carbonate (8.50 mL, >20 equiv.) and the reaction mixture stirred at reflux whilst a solution of (-)-(R_S)-S-methyl-S-phenyl-N-tosylsulfoximine (1.50 g, 4.85 mmol, 1.0 equiv.) in THF (15 mL) was added dropwise. The stirred reaction mixture was heated under reflux

overnight, cooled on ice and then quenched with MeOH–AcOH (2:1, 15 mL). The solution was poured onto H₂O and the product extracted with Et₂O (×5). The combined organic layers were washed with sat. aq. NaHCO₃ and H₂O, dried (MgSO₄) and concentrated under reduced pressure. The yellow oil was then treated with EtOH to give methyl (*R*_S)-2-(*N*-tosylphenylsulfonimidoyl)acetate (1.39 g, 78%) as a colourless solid; mp 76–77 °C; [α]_D²² –32.2 (*c* 5.0, CH₂Cl₂); R_f 0.43 (50% EtOAc–petrol); ν_{max} (film) 1742, 1643, 1496, 1447, 1318, 1153, 814, 666 cm⁻¹; δ_H (270 MHz) 7.99 (2H, d, *J* 7.5 Hz, *o*-Ph), 7.86 (2H, d, *J* 8.5 Hz, *o*-SO₂Ar), 7.70 (1H, m, *p*-Ph), 7.58 (2H, m, *m*-Ph), 7.25 (2H, d, *J* 8.5 Hz, *m*-SO₂Ar), [4.79, 4.58] (2H, AB doublet, *J* 14.5 Hz, CH₂), 3.64 (3H, s, OCH₃), 2.38 (3H, s, ArCH₃); δ_C (67.5 MHz) 162.2 (C=O), 143.3, 140.4, 135.9 (4°), 135.0, 129.5, 129.4, 128.7, 126.8 (3°), 61.4 (CH₂), 53.4 (OCH₃), 21.6 (ArCH₃); *m/z* (CI) 385 [M+NH₄]⁺, 279, 208, 189; data were in accordance with those previously reported.¹²

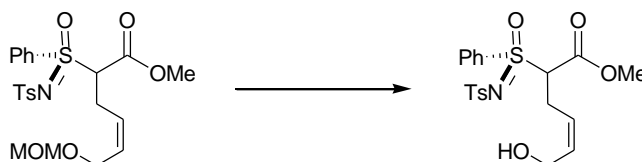
Methyl (R_S,Z)-6-(methoxymethoxy)-2-(N-tosylphenylsulfonimidoyl)hex-4-enoate



According to general procedure **D**, a suspension of sodium hydride (0.42 g, 10.5 mmol, 1.1 equiv.) in THF (10 mL) was treated with methyl (*R*_S)-2-(*N*-tosylphenylsulfon-imidoyl)acetate (3.49 g, 9.5 mmol, 1.0 equiv.) in THF (25 mL), followed by mesylate **9** (2.00 g, 9.50 mmol, 1.0 equiv.) in THF (15 mL). Purification by chromatography (20→40% EtOAc–petrol) gave a diastereomeric mixture (1:1) of methyl (*R*_S,*Z*)-6-(methoxymethoxy)-2-(*N*-tosylphenylsulfonimidoyl)hex-4-enoate (3.68 g, 80%) as a colourless gum; R_f 0.42 (50% EtOAc–petrol); ν_{max} (film) 2952, 1746, 1598, 1447, 1321, 1245, 1152, 1087, 1061, 1018, 997, 815, 765, 685, 666 cm⁻¹; δ_H (500 MHz) 7.96 (2H, m, *o*-Ph), 7.88 (2H, m, *o*-SO₂Ar), 7.76 (1H, m, *p*-Ph), 7.63 (2H, m, *m*-Ph), 7.28 (2H, m, *m*-SO₂Ar), 5.71 (1H, dt, *J* 11.0, 6.5 Hz, OCH₂CH), 5.40 (1H, m, SCHCH₂CH), [4.89, 4.64] (1H, dd, *J* 11.0, 3.5 Hz, SCH), [4.59, 4.57] (2H, 2 × s, OCH₂O), 4.08–3.98 (2H, m, CHCH₂O), [3.74, 3.69] (3H, 2 × s, CO₂CH₃), [3.35, 3.33] (3H, 2 × s, CH₂OCH₃), [2.91–2.84, 2.72–2.54] (2H, 2 × m, SCHCH₂), 2.42 (3H, s, ArCH₃); δ_C (125 MHz) 165.2, 164.0 (C=O), 143.1, 143.0, 140.7, 140.5, 134.4, 133.8 (4°), 135.0, 135.0, 131.3, 131.2, 129.8, 129.7, 129.3, 126.7, 126.7, 124.7 (3°),

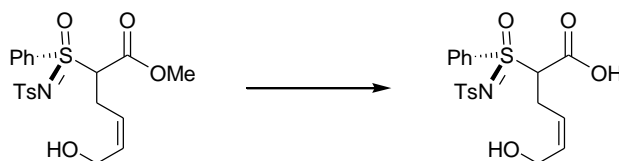
95.8 (OCH₂O), 71.1, 70.4 (SCH), 62.6 (OCH₂CH), 55.3 (CH₂OCH₃), 53.4, 53.3 (CO₂CH₃), 26.4, 25.1 (SCHCH₂), 21.6 (ArCH₃); *m/z* (CI) 499 [M+NH₄]⁺, 455, 450, 420, 385, 313, 189 (Found [M+NH₄]⁺, 499.1591. C₂₂H₂₇NO₇S₂ requires [M+NH₄]⁺, 499.1573) (Found: C, 54.89; H, 5.63; N, 2.92. C₂₂H₂₇NO₇S₂ requires C, 54.87; H, 5.65; N, 2.91).

Methyl (R_S,Z)-6-hydroxy-2-(N-tosylphenylsulfonimidoyl)hex-4-enoate



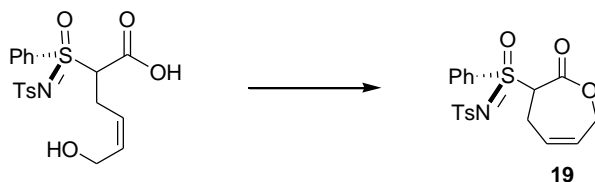
According to general procedure **E**, methyl (*R_S,Z*)-6-(methoxymethoxy)-2-(*N*-tosylphenylsulfonimidoyl)hex-4-enoate (1.40 g, 2.90 mmol, 1.0 equiv.) was heated under reflux in MeCN (30 mL) and 2 M aq. HCl (6 mL) to give methyl (*R_S,Z*)-6-hydroxy-2-(*N*-tosylphenylsulfonimidoyl)hex-4-enoate (1.13 g, 89%) as a viscous, colourless oil; *R_f* 0.13 (50% EtOAc–petrol); *v*_{max} (film) 3525, 2954, 1744, 1598, 1447, 1318, 1242, 1153, 1088, 1062, 998, 815, 754, 685. 665 cm⁻¹; *δ*_H (400 MHz) 7.94 (2H, d, *J* 8.5 Hz, *o*-Ph), 7.87 (2H, m, *o*-SO₂Ar), 7.76 (1H, m, *p*-Ph), 7.62 (2H, m, *m*-Ph), 7.28 (2H, m, *m*-SO₂Ar), 5.77 (1H, m, CHCH₂OH), 5.35 (1H, m, SCHCH₂CH), [4.99, 4.67] (1H, dd, *J* 11.5, 3.5 Hz, SCH), 4.16–4.05 (2H, m, CH₂OH), [3.76, 3.61] (3H, 2 × s, OCH₃), 2.96–2.84 (1H, m, SCHCH₂), [2.77, 2.69] (1H, m, SCHCH₂), 2.41 (3H, s, ArCH₃); *δ*_C (100 MHz) 165.6, 165.3 (C=O), 143.2, 143.0, 140.6, 140.4, 134.4, 133.3 (4°), 135.2, 135.0, 133.9, 133.8, 129.8, 129.6, 129.4, 129.3, 124.0, 123.8 (3°), 71.2, 70.5 (SCH), 58.1, 58.0 (CH₂OH), 53.5, 53.4 (OCH₃), 26.4, 25.0 (SCHCH₂), 21.6 (ArCH₃); *m/z* (CI) 455 [M+NH₄]⁺, 300, 189, 160 (Found [M+NH₄]⁺, 455.1295. C₂₀H₂₃NO₆S₂ requires [M+NH₄]⁺, 455.1311) (Found: C, 55.02; H, 5.27; N, 3.09. C₂₀H₂₃NO₆S₂ requires C, 54.90; H, 5.30; N, 3.20).

(R_S,Z)-6-Hydroxy-2-(*N*-tosylphenylsulfonimidoyl)hex-4-enoic acid



According to procedure **F**, methyl (*R_S,Z*)-6-hydroxy-2-(*N*-tosylphenylsulfonimidoyl)hex-4-enoate (1.10 g, 2.51 mmol, 1.0 equiv.) in THF (6.3 mL) was treated with 2 M aq. LiOH (6.3 mL, 2.00 mmol, 5.0 equiv.) to give (*R_S,Z*)-6-hydroxy-2-(*N*-tosylphenylsulfonimidoyl)hex-4-enoic acid (860 mg, 81%) as a colourless solid, which was used without further purification; mp 149–151 °C; δ_{H} (400 MHz, DMSO-*d*₆); 7.91–7.88 (2H, m, *o*-Ph), 7.85–7.79 (1H, m, *p*-Ph), 7.72–7.63 (4H, m, *o*-SO₂Ar and *m*-Ph), 7.35–7.31 (2H, m, *m*-SO₂Ar), 5.82–5.75 (1H, m, CHCH₂OH), 5.48–5.41 (1H, m, SCHCH₂CH), 4.90 (1H, dd, *J* 11.5, 3.0 Hz, SCH), 4.10 (2H, ddd, *J* 19.0, 13.0, 7.0 Hz, CH₂OH), [2.82–2.80, 2.69–2.61] (2H, 2 × m, SCHCH₂), 2.41 (3H, s, ArCH₃); δ_{C} (100 MHz, DMSO-*d*₆) 165.6, 165.5 (C=O), 143.1, 143.0, 142.9, 141.1, 136.6, 135.1 (4°), 135.4, 135.2, 134.9, 133.6, 130.1, 130.0, 129.8, 129.8, 129.8, 128.5, 126.4, 125.0, 122.9, 122.4 (3°) 70.3, 70.1 (SCH), 57.1, 57.1 (CH₂OH), 25.4, 24.7 (SCHCH₂), 21.4 (ArCH₃); *m/z* (FAB⁺) 424 [M+H]⁺, 406, 392, 296, 167, 125, 89, 77 (Found [M+H]⁺, 424.0887. C₁₉H₂₁NO₆S₂ requires [M+H]⁺, 424.0889) (Found: C, 53.91; H, 4.94; N, 3.24. C₁₉H₂₁NO₆S₂ requires C, 53.88; H, 5.00; N, 3.31).

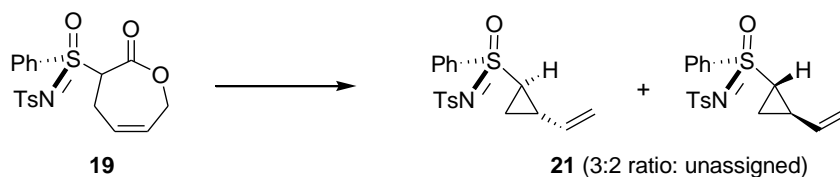
(R_S)-3-(N-Tosylphenylsulfonimidoyl)-4,7-dihydrooxepin-2(3H)-one **19**



According to general procedure **G**, (*R_S,Z*)-6-hydroxy-2-(*N*-tosylphenylsulfonimidoyl)hex-4-enoic acid (0.84 g, 1.99 mmol, 1.0 equiv.) in CH₂Cl₂ (5 mL) was treated with EDCI (0.42 g, 2.19 mmol, 1.1 equiv.). The product was purified by chromatography (20→50% EtOAc–petrol) to give (*R_S*)-3-(*N*-tosylphenylsulfonimidoyl)-4,7-dihydrooxepin-2(3H)-one **19** (0.68 g, 84%) as a colourless crystalline solid; mp 74–76 °C; *R_f* 0.26 (50% EtOAc–petrol); ν_{max} (film)

3441 (br), 3056, 1748, 1598, 1448, 1386, 1316, 1265, 1151, 1087, 736 cm^{-1} ; δ_{H} (500 MHz) 8.14 (2H, d, J 7.5 Hz, *o*-Ph), 7.87 (2H, d, J 8.5 Hz, *o*-SO₂Ar), 7.70 (1H, m, *p*-Ph), 7.58 (2H, dt, J 7.5, 7.5 Hz, *m*-Ph), 7.28 (2H, m, *m*-SO₂Ar), [6.03, 5.78] (1H, dd, J 13.0, 4.0 Hz, SCH), 5.88 (2H, d, J 4.0 Hz, HC=CH), [5.11, 4.51] (2H, m, OCH₂), [3.31, 3.15] (1H, dd, J 17.5, 3.5 Hz, SCHCH₂), 2.45–2.36 (1H, m, SCHCH₂), 2.40 (3H, s, ArCH₃); δ_{C} (125 MHz) 166.4 (C=O), 143.2, 143.2, 140.40, 140.2, 133.0, 132.8, (4°), 134.9, 131.1, 131.0, 129.3, 129.0, 128.9, 128.6, 126.7, 126.7, 124.9, 124.5, (3°), 65.4, 65.3 (SCH), 64.2, 64.1 (OCH₂), 28.9, 27.5 (SCHCH₂), 21.5 (ArCH₃); m/z (CI) 423 [M+NH₄]⁺, 379, 189, 128 (Found [M+NH₄]⁺, 423.1055. C₁₉H₁₉NO₅S₂ requires [M+NH₄]⁺, 423.1048) (Found: C, 56.21; H, 4.80; N, 3.52. C₁₉H₁₉NO₅S₂ requires C, 56.28; H, 4.72; N, 3.45).

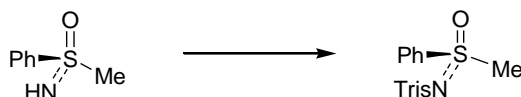
(*R_S,1R,2S*)-*S*-Phenyl-*S*-(2-vinylcyclopropyl)-*N*-tosylsulfoximine and (*R_S,1S,2R*)-*S*-Phenyl-*S*-(2-vinylcyclopropyl)-*N*-tosylsulfoximine **21**



According to general procedure **H**, lactone **19** (50.0 mg, 120 μmol , 1.0 equiv.), was treated with BSA (30.5 μl , 120 μmol , 1.0 equiv.) and KOAc (1.2 mg, 12.0 μmol , 0.1 equiv.) in DMF (0.6 mL) to give a diastereomeric mixture (3:2, unassigned) of (*R_S,1R,2S*)-*S*-phenyl-*S*-(2-vinylcyclopropyl)-*N*-tosylsulfoximine and (*R_S,1S,2R*)-*S*-phenyl-*S*-(2-vinylcyclopropyl)-*N*-tosylsulfoximine **21** (28.0 mg, 65%) as a colourless oil; R_f 0.50 (50% EtOAc–petrol); ν_{max} (film) 3052, 2985, 2923, 2852, 1640, 1598, 1447, 1421, 1316, 1264, 1151, 1070 cm^{-1} ; δ_{H} (400 MHz) 7.96 (2H, m, *o*-Ph), 7.83 (2H, d, J 8.0 Hz, *o*-SO₂Ar), 7.70 (1H, t, J 7.5 Hz, *p*-Ph), 7.60 (2H, t, J 7.5 Hz, *m*-Ph), 7.26 (2H, d, J 8.0 Hz, *m*-SO₂Ar), 5.55 (1H, ddd, J 17.5, 10.0, 7.5 Hz, CH=CH₂ minor), 5.35 (1H, ddd, J 17.5, 10.0, 7.5 Hz, CH=CH₂ major), 5.28 (1H, d, J 17.5 Hz, CH=CH₂ *cis* minor), 5.15 (1H, d, J 10.0 Hz, CH=CH₂ *trans* minor), 5.07 (1H, d, J 17.0 Hz, CH=CH₂ *cis* major), 5.01 (1H, d, J 10.0 Hz, CH=CH₂ *trans* major), 2.70 (1H, m, SCH major and minor), 2.63 (1H, m, SCHCH minor), 2.42 (3H, s, ArCH₃), 2.23 (1H, m, SCHCH major), 1.95 (1H, dt, J 10.0, 5.5 Hz, SCHCH₂ major), 1.42 (1H, dt, J 8.0, 6.5 Hz, SCHCH₂ major), 1.53 (1H, dt, J 10.0, 5.5 Hz, SCHCH₂ minor), 1.16 (1H, dt, J 8.0, 6.5 Hz, SCHCH₂ minor); δ_{C} (100 MHz) 142.8, 140.8, 138.7 (4°), 134.2,

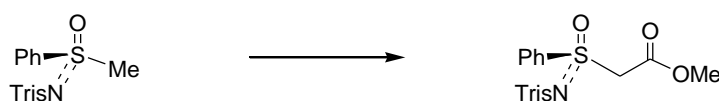
134.1, 134.0, 129.6, 129.2, 127.7, 127.6, 126.6 (3°), 117.7, 117.4 (CH=CH₂), 41.7, 41.6 (SCH), 24.1, 23.3 (SCHCH), 21.5 (ArCH₃), 14.4, 12.7 (SCHCH₂); *m/z* (CI) 362 [M+H]⁺, 379, 189, 52 (Found [M+H]⁺, 362.0888. C₁₈H₁₉NO₃S₂ requires [M+H]⁺, 362.0885) (Found: C, 59.81; H, 5.26; N, 3.89. C₁₈H₁₉NO₃S₂ requires C, 59.81; H, 5.30; N, 3.87).

(+)-(S_S)-S-Methyl-S-phenyl-N-(2,4,6-triisopropylphenylsulfonyl)sulfoximine



To a solution of (+)-(S_S)-S-methyl-S-phenylsulfoximine (8.40 g, 54.0 mmol, 1.0 equiv.) in pyridine (45 mL) at -5 °C, was added DMAP (30 mg) and 2,4,6-triisopropylphenylsulfonyl chloride (16.4 g, 54.0 mmol, 1.0 equiv.) to give a yellow solution. The reaction was heated at 60 °C for 2 h. The reaction was cooled to rt, poured into cold H₂O and 2 M aq. HCl added. The organic layer was extracted with CH₂Cl₂, and then washed with 2 M aq. HCl and H₂O, until pH 8 was achieved. The organic layer was dried (MgSO₄) and concentrated under reduced pressure. The orange oil was treated with EtOH to give (+)-(S_S)-S-methyl-S-phenyl-N-(2,4,6-triisopropylphenylsulfonyl)sulfoximine (14.15 g, 59%) as a colourless solid; *R_f* 0.60 (50% EtOAc–petrol); mp 139–141 °C; [α]_D²⁰ +20.0 (*c* 5.0, CH₂Cl₂); *v*_{max} (film) 3055, 2963, 2870, 1599, 1463, 1448, 1423, 1312, 1294, 1265, 1238, 1148, 1100, 1069, 741, 704 cm⁻¹; δ_H (400 MHz) 8.02 (2H, d, *J* 8.0 Hz, *o*-Ph) 7.71 (1H, t, *J* 7.5 Hz, *p*-Ph) 7.61 (2H, t, *J* 8.0 Hz, *m*-Ph), 7.14 (2H, s, *m*-SO₂Ar), 4.40 (2H, sept, *J* 6.5 Hz, *o*-ArCH), 3.44 (3H, s, SCH₃), 2.90 (1H, sept, *J* 7.0 Hz, *p*-ArCH), 1.29–1.24 (18H, m, CH(CH₃)₂); δ_C (100 MHz) 152.0, 149.0, 138.8, 137.2 (4°), 134.3, 129.6, 127.5, 123.4 (3°), 47.0 (SCH₃), 34.1 (*p*-ArCH), 29.3 (*o*-ArCH), 24.7, 24.6 (*o*-ArCH(CH₃)₂), 23.7 (*p*-ArCH(CH₃)₂); *m/z* (CI) 439 [M+NH₄]⁺, 422, 299, 208, 156, 141, 80; data were in accordance with those previously reported.¹³

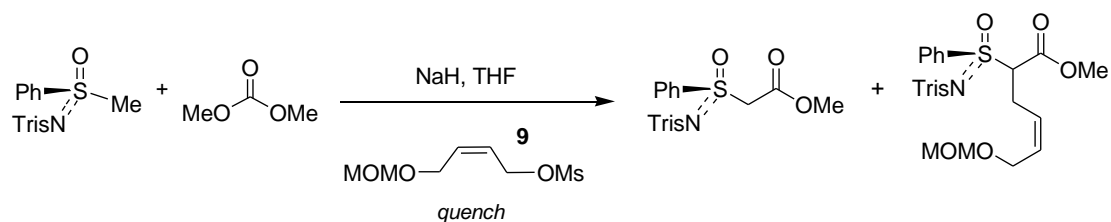
(+)-Methyl (S_S)-2-(N-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)acetate



To sodium hydride (60% dispersion in mineral oil, washed with hexane; 68.0 mg, 2.82 mmol, 2.5 equiv.) suspended in THF (2 mL) was added dimethyl carbonate (2

mL) and the reaction mixture stirred at reflux whilst a solution of (+)-(*S_S*)-*S*-methyl-*S*-phenyl-*N*-(2,4,6-triisopropylphenylsulfonyl)sulfoximine (500 mg, 1.13 mmol, 1.0 equiv.) in THF (3 mL) was added dropwise. The stirred reaction was heated under reflux for 16 h, cooled on ice and quenched with MeOH–AcOH (2:1; 2 mL). The solution was poured on to H₂O and the product extracted with Et₂O (×5). The combined organic layers were washed with sat. aq. NaHCO₃ and H₂O, dried (MgSO₄) and concentrated under reduced pressure. The yellow oil was then crystallised from EtOH to give (+)-methyl (*S_S*)-2-(*N*-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)acetate (0.29 g, 75%) as a colourless solid; mp 111–112 °C; *R_f* 0.40 (100% CH₂Cl₂); [α]_D²⁰ +11.0 (*c* 5.0, CH₂Cl₂); *v*_{max} (film) 3055, 2960, 1749, 1599, 1265, 1149, 1095, 1065, 738, 704 cm⁻¹; δ_H (400 MHz) 8.04 (2H, d, *J* 7.5 Hz, *o*-Ph), 7.74 (1H, t, *J* 7.5 Hz, *p*-Ph) 7.62 (2H, t, *J* 8.0 Hz, *m*-Ph), 7.14 (2H, s, *m*-SO₂Ar), [4.76, 4.62] (2H, AB doublet, *J* 14.5 Hz, CH₂), 4.40 (2H, sept, *J* 6.5 Hz, *o*-ArCH), 3.68 (3H, s, OCH₃), 2.90 (1H, sept, *J* 7.0 Hz, *p*-ArCH), 1.29–1.21 (18H, m, CH(CH₃)₂); δ_C (100 MHz) 162.2, (C=O), 152.2, 149.1, 137.0, 136.5 (4°), 134.8, 129.4, 128.6, 123.5 (3°), 61.8 (OCH₃), 53.2 (CH₂), 34.1 (*p*-ArCH), 29.3 (*o*-ArCH), 24.7, 24.6 (*o*-ArCH(CH₃)₂), 23.6 (*p*-ArCH(CH₃)₂); *m/z* (CI) 497 [M+NH₄]⁺, 301, 208 (Found [M+NH₄]⁺, 497.2141. C₂₄H₃₃NO₅S₂ requires [M+NH₄]⁺, 497.2144).

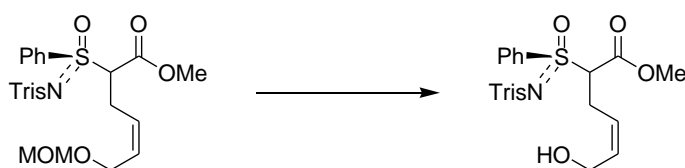
Methyl (S_S,Z)-6-(methoxymethoxy)-2-(N-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)hex-4-enoate



To a suspension of sodium hydride (60% dispersion in mineral oil, washed with hexane; 1.19 g, 29.7 mmol, 2.5 equiv.) in THF (30 mL) was added dimethyl carbonate (20 mL) and the reaction mixture was stirred at reflux whilst a solution of (+)-methyl (*S_S*)-2-(*N*-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)acetate (5.00 g, 11.9 mmol, 1.0 equiv.) in THF (30 mL) was added dropwise. The stirred reaction was heated under reflux overnight, cooled in ice and quenched with mesylate **9** (2.49 g, 11.9 mmol, 1.0 equiv.), followed by MeOH–AcOH (2:1; 10 mL). The solution was poured on to water and the product extracted with Et₂O (×5). The combined organic

layers were washed with sat. aq. NaHCO₃ and H₂O, dried (MgSO₄) and concentrated under reduced pressure. The yellow oil was purified by chromatography (100% CH₂Cl₂) to give recovered (+)-methyl (S_S)-2-(N-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)acetate (2.06 g, 36%) as a colourless solid, and methyl (S_S,Z)-6-(methoxymethoxy)-2-(N-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)hex-4-enoate (3.01 g, 47%) as a yellow oil; R_f 0.17 (100% CH₂Cl₂); ν_{max} (film) 2958, 1747, 1600, 1448, 1362, 1317, 1244, 1196, 1150, 1094, 1048, 998, 940, 922, 844, 768, 749, 685, 665 cm⁻¹; δ_H (400 MHz) 7.95 (2H, d, *J* 8.0 Hz, *o*-Ph), 7.73 (1H, tt, *J* 7.5, 1.0 Hz, *p*-Ph), 7.59 (2H, td, *J* 8.0, 3.0 Hz, *m*-Ph), 7.13 (2H, s, *m*-SO₂Ar), 5.70 (1H, dt, *J* 11.0, 6.5 Hz, OCH₂CH), 5.39 (1H, dd, *J* 11.0, 7.0 Hz, SCHCH₂CH), [4.57, 4.56] (2H, 2 × s, CH₂OCH₃), 4.06–3.95, (2H, m, *o*-ArCH), [3.72, 3.62] (3H, 2 × s, CO₂CH₃), [3.32, 3.31] (3H, 2 × s, CH₂OCH₃), 2.88 (1H, sept, *J* 7.0 Hz, *p*-ArCH), 1.28–1.19 (18H, m, CH(CH₃)₂); δ_C (100 MHz) 165.3, 165.1 (C=O), 152.2, 152.1, 149.2, 149.1, 137.3, 137.0, 134.2, 132.3, 131.1, 124.9 (4°), 134.9, 134.8, 132.6, 131.2, 129.8, 129.2, 124.9, 123.5 (3°), 95.8 (OCH₂O), 71.4, 70.7 (SCH), 62.6, 62.6 (OCH₂OCH₂), 55.4, 55.3 (CH₂OCH₃), 53.3, 53.2 (CO₂CH₃), 34.1, (*p*-ArCH), 29.3, 29.3 (*o*-ArCH), 26.5, 25.2 (SCHCH₂), 24.7, 24.6 (*o*-ArCH(CH₃)₂), 23.6, (*p*-ArCH(CH₃)₂); *m/z* (CI) 611 [M+NH₄]⁺, 567, 532, 497, 425, 301 (Found [M+NH₄]⁺, 611.2388. C₃₀H₄₃NO₇S₂ requires [M+NH₄]⁺, 611.2825) (Found: C, 60.59; H, 7.18; N, 2.26. C₃₀H₄₃NO₇S₂ requires C, 60.68; H, 7.30; N, 2.36).

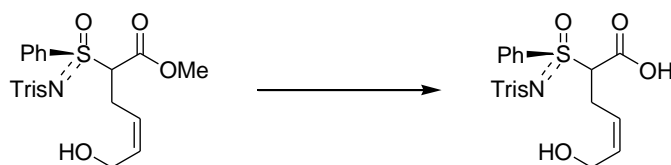
Methyl (S_S,Z)-6-hydroxy-2-(N-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)hex-4-enoate



According to general procedure **E**, a solution of methyl (S_S,Z)-6-(methoxymethoxy)-2-(N-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)hex-4-enoate (2.50 mg, 4.20 mmol) in MeCN (42 mL) was treated with 2 M aq. HCl (8.5 mL) to give methyl (S_S,Z)-6-hydroxy-2-(N-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)hex-4-enoate (2.14 g, 93%) as a yellow oil; R_f 0.24 (50% EtOAc–petrol); ν_{max} (film) 3425, 2960, 1743, 1643, 1600, 1448, 1314, 1245, 1149, 1093, 1054 cm⁻¹; δ_H (400 MHz) 7.95 (2H, d, *J* 8.0 Hz, *o*-Ph), 7.76 (1H, dt, *J* 7.5, 7.5 Hz, *p*-Ph), 7.62 (2H, dt, *J* 8.0, 7.5

Hz, *m*-Ph), 7.14 (2H, s, *m*-SO₂Ar), 5.79 (1H, dt, *J* 13.0, 6.5 Hz, CHCH₂OH), 5.37 (1H, dt, *J* 18.0, 8.0 Hz, SCHCH₂CH), [4.99, 4.59] (1H, 2 × dd, *J* 11.5, 3.5 Hz, SCH), 4.37 (2H, 2 × sept, *J* 6.5 Hz, *o*-ArCH), 4.18–4.06 (2H, m, CH₂OH), [3.77, 3.63] (3H, 2 × s, OCH₃), 3.00–2.87 (2H, m, *p*-ArCH and 1 × SCHCH₂), [2.80–2.71, 2.59–2.51] (1H, 2 × m, 1 × SCHCH₂), 1.30–1.18 (18H, m, CH(CH₃)₂); δ_C (100 MHz) 165.8, 165.5 (C=O), 152.3, 152.1, 149.2, 149.1, 137.9, 137.2, 136.9, 134.9, 133.8, 128.2, 124.0 (4°), 135.0, 133.8, 129.7, 129.7, 129.2, 129.1, 125.3, 124.7, 123.5, 123.5 (3°), 71.5, 70.8 (SCH), 58.1, 58.0 (CH₂OH), 53.4, 53.3 (CO₂CH₃), 34.1, (*p*-ArCH), 29.4, 29.3 (*o*-ArCH), 26.4, 25.1 (SCHCH₂), 24.7, 24.6 (*o*-ArCH(CH₃)₂), 23.6, (*p*-ArCH(CH₃)₂); *m/z* (CI) 567 [M+NH₄]⁺, 425, 301, 284, 194 (Found [M+NH₄]⁺, 567.2579. C₂₈H₃₉NO₆S₂ requires [M+NH₄]⁺, 567.2563).

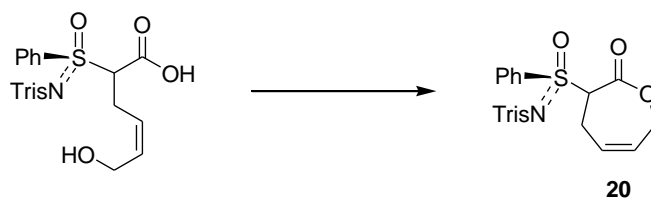
(S_S,Z)-6-Hydroxy-2-(*N*-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)hex-4-enoic acid



According to general procedure **F**, a solution of methyl (*S_S,Z*)-6-hydroxy-2-(*N*-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)hex-4-enoate (2.14 g, 3.89 mmol, 1.0 equiv.) in THF (10 mL) was treated with 2 M aq. LiOH (10.0 mL, 20.0 mmol, 5.0 equiv.) to give (*S_S,Z*)-6-hydroxy-2-(*N*-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)hex-4-enoic acid (1.84 g, 88%) as a colourless crystalline solid; mp 58–60 °C; ν_{max} (film) 3445 (br), 2963, 1645, 1600, 1448, 1265, 1147, 1094, 1063, 738 cm⁻¹; δ_H (400 MHz) 7.95, (2H, d, *J* 7.5 Hz, *o*-Ph), 7.73 (1H, m, *p*-Ph), 7.59 (2H, dt, *J* 7.5, 7.5 Hz, *m*-Ph), 7.13 (2H, s, *m*-SO₂Ar), 5.76 (1H, dd, *J* 17.5, 7.0 Hz, CHCH₂OH), 5.58 (1H, br s, CO₂H), 5.42 (1H, dd, *J* 16.0, 10.0 Hz, SCHCH₂CH), [4.83, 4.58] (1H, 2 × dd, *J* 11.5, 3.0 Hz, SCH), 4.32 (2H, sept, *J* 6.5 Hz, *o*-ArCH), [4.12, 4.01] (2H, 2 × d, *J* 6.5 Hz, CH₂OH), 2.95–2.56 (3H, m, *p*-ArCH and SCHCH₂), 1.29–1.20 (18H, m, CH(CH₃)₂); δ_C (100 MHz) 166.7, 166.2 (C=O), 152.4, 149.2, 136.8, 134.3, 133.9, 124.2 (4°), 135.0, 133.0, 132.8, 129.7, 129.3, 124.9, 124.7, 123.5 (3°), 71.4, 70.9 (SCH), 58.5, 57.8 (CH₂OH), 34.2 (*p*-ArCH), 29.3 (*o*-ArCH), 26.2, 25.1 (SCHCH₂), 24.7, 24.7, 24.6, 24.6 (*o*-ArCH(CH₃)₂), 23.6 (*p*-ArCH(CH₃)₂); *m/z* (FAB) 536 [M+NH₄]⁺, 538, 518, 446, 282, 267, 203, 125, 93 (Found [M+NH₄]⁺, 536.2122).

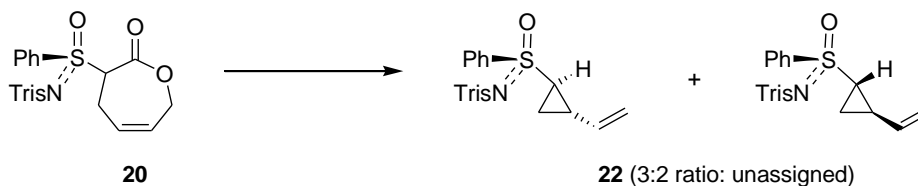
$C_{27}H_{37}NO_6S_2$ requires $[M+NH_4]^+$, 536.2141) (Found: C, 60.55; H, 6.91; N, 2.63. $C_{27}H_{37}NO_6S_2$ requires C, 60.53; H, 6.96; N, 2.61).

(*S_S*)-3-(*N*-(2,4,6-Triisopropylphenylsulfonyl)phenylsulfonylimidoyl)-4,7-dihydrooxepin-2(3*H*)-one **20**



According to general procedure **G**, a solution of (*S_S*,*Z*)-6-hydroxy-2-(*N*-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonylimidoyl)hex-4-enoic acid (1.00 g, 1.87 mmol, 1.0 equiv.) in CH_2Cl_2 (10 mL) was treated with EDCI (0.39 g, 2.05 mmol, 1.1 equiv.) and purified by chromatography (50% EtOAc–petrol) to give (*S_S*)-3-(*N*-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonylimidoyl)-4,7-dihydrooxepin-2(3*H*)-one **20** (0.87 g, 90%) as a colourless crystalline solid; mp 77–79 °C; R_f 0.63 (50% EtOAc–petrol); ν_{max} (film) 3442 (br), 3055, 1752, 1638, 1600, 1422, 1265, 1148, 1093, 1054, 895, 735 cm^{-1} ; δ_H (500 MHz) 8.14 (2H, 2 × dt, J 7.0, 1.5 Hz, *o*-Ph), 7.69 (1H, m, *p*-Ph), 7.57 (2H, m, *m*-Ph), [7.11, 7.10] (2H, 2 × s, *m*-SO₂Ar), [6.00, 5.73] (1H, dd, J 13.0, 3.5 Hz, SCH), 5.88 (2H, br d, J 3.5 Hz, HC=CH), [5.12, 4.51] (2H, m, OCH₂), 4.37 (2H, sept, *o*-ArCH), [3.40, 3.21] (1H, dd, J 17.5, 3.0 Hz, SCHCH₂), 2.87 (1H, sept, *p*-ArCH), 2.41 (1H, td, J 16.0, 2.5 Hz, SCHCH₂), 1.27–1.14 (18H, m, CH(CH₃)₂); δ_C (125 MHz) 166.3 (C=O), 152.2, 149.2, 149.0, 137.0, 136.7, 133.5, 133.1 (4°), 134.8, 134.8, 131.1, 130.9, 128.8, 128.7, 124.8, 124.4, 123.5, 123.4 (3°), 66.0, 65.8 (SCH), 64.2, 64.0 (OCH₂), 34.1 (*p*-ArCH), 29.3, 29.2 (*o*-ArCH), 28.9, 27.6 (SCHCH₂), 24.7, 24.7, 24.6, 24.5 (*o*-ArCH(CH₃)₂), 23.6 (*p*-ArCH(CH₃)₂); m/z (CI) 535 $[M+NH_4]^+$, 491, 425, 301 (Found $[M+NH_4]^+$, 535.2300. $C_{27}H_{35}NO_5S_2$ requires $[M+NH_4]^+$, 535.2300) (Found: C, 62.54; H, 6.71; N, 2.87. $C_{27}H_{35}NO_5S_2$ requires C, 62.64; H, 6.81; N, 2.71).

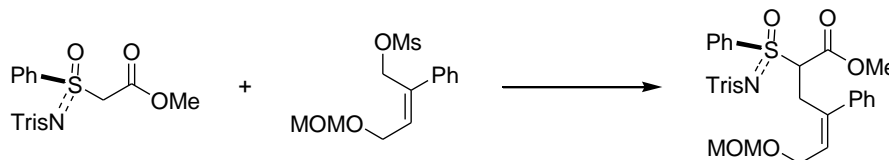
(*S_S,1R,2S*)-*S*-Phenyl-*S*-(2-vinylcyclopropyl)-*N*-tosylsulfoximine and (*S_S,1S,2R*)-*S*-Phenyl-*S*-(2-vinylcyclopropyl)-*N*-tosylsulfoximine **22**



According to general procedure **H**, a solution of lactone **20** (50.0 mg, 97.0 μmol , 1.0 equiv.) was treated with BSA (23.9 μl , 97.0 μmol , 1.0 equiv.) and KOAc (1.0 mg, 9.70 μmol , 0.1 equiv.) in DMF (1 mL) to give a diastereomeric mixture (3:2, unassigned) of (*S_S,1R,2S*)-*S*-phenyl-*S*-(2-vinylcyclopropyl)-*N*-tosylsulfoximine and (*S_S,1S,2R*)-*S*-phenyl-*S*-(2-vinylcyclopropyl)-*N*-tosylsulfoximine **22** (32 mg, 69%) as a brown oil; R_f 0.80 (50% EtOAc–petrol); ν_{max} (film) 3449 (br), 3057, 1639, 1421, 1264, 1148, 1100, 895, 737 cm^{-1} ; δ_{H} (500 MHz) 7.94 (2H, dt, J 8.0, 1.5 Hz, *o*-Ph), 7.66 (1H, m, *p*-Ph), 7.56 (2H, td, J 8.0, 1.5 Hz, *m*-Ph), 7.11 (1H, s, *m*-SO₂Ar major), 7.10 (1H, s, *m*-SO₂Ar minor), 5.50 (1H, ddd, J 17.0, 10.0, 7.5 Hz, CH=CH₂ minor), 5.32 (1H, ddd, J 17.0, 10.0, 7.5 Hz, CH=CH₂ major), 5.23 (1H, d, J 17.0 Hz, CH=CH₂ *cis* minor), 5.11 (1H, d, J 10.0 Hz, CH=CH₂ *trans* minor), 5.04 (1H, d, J 17.0 Hz, CH=CH₂ *cis* major), 4.98 (1H, d, J 10.0 Hz, CH=CH₂ *trans* major), 4.35 (2H, 2 \times sept, J 7.0 Hz, *o*-ArCH), 2.88 (1H, sept, J 7.0 Hz, *p*-ArCH), 2.67 (1H, m, SCH major), 2.65 (1H, m, SCH minor), 2.61 (1H, m, SCHCH minor), 2.23 (1H, m, SCHCH major), [1.92, 1.37] (2H, 2 \times m, SCHCH₂ major), [1.50, 1.10] (2H, 2 \times m, SCHCH₂ minor), 1.28–1.20 (18H, m, CH(CH₃)₂); δ_{C} (125 MHz) 151.9, 151.8, 149.1, 139.2, 139.2, 137.3 (4 $^\circ$), 134.3, 133.9, 129.4, 127.7, 127.6, 123.3 (3 $^\circ$), 134.2, 133.8 (CH=CH₂), 117.5, 117.2 (CH=CH₂), 42.0 (SCH), 34.1 (*p*-ArCH), 29.2, 29.2 (*o*-ArCH), 24.7, 24.7, 24.6, 24.6 (*o*-ArCH(CH₃)₂), 23.7, 23.2 (SCHCH), 23.6 (*p*-ArCH(CH₃)₂), 14.2, 12.4 (SCHCH₂); m/z (CI) 491 [M+NH₄]⁺, 474 [M+H]⁺, 301, 52 (Found [M+H]⁺, 474.2157. C₂₆H₃₅NO₃S₂ requires [M+H]⁺, 474.2137) (Found: C, 66.00; H, 7.44; N, 2.80. C₂₆H₃₅NO₃S₂ requires C, 65.92; H, 7.45; N, 2.96).

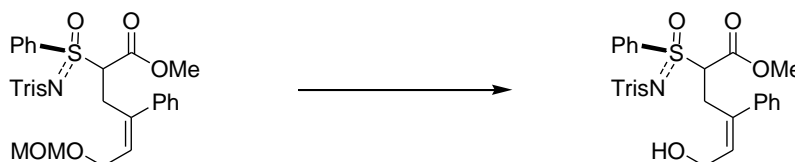
7. Synthesis and reactions of sulfoximinyl γ -aryl lactones 23a–c

(\pm)-Methyl (Z)-6-methoxymethoxy-4-phenyl-2-(N-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)hex-4-enoate



According to general procedure **D**, a suspension of sodium hydride (13.7 mg, 0.57 mmol, 1.2 equiv.) in THF (0.75 mL) was treated with (\pm)-methyl 2-(N-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)acetate (228 mg, 0.48 mmol, 1.0 equiv.) in THF (1.0 mL) and methanesulfonic acid (Z)-4-methoxymethoxy-2-phenylbut-2-enyl ester (136 mg, 0.48 mmol, 1.0 equiv.) in THF (0.75 mL) to give (\pm)-methyl (Z)-6-methoxymethoxy-4-phenyl-2-(N-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)hex-4-enoate, which was used without further purification; R_f 0.40 (50% EtOAc–petrol).

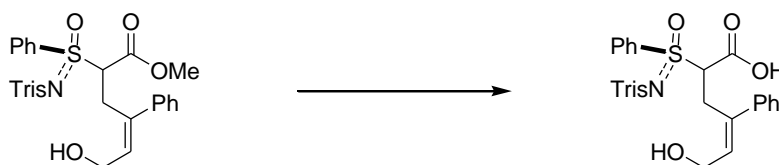
(\pm)-Methyl (Z)-6-hydroxy-4-phenyl-2-(N-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)hex-4-enoate



According to general procedure **E**, a solution of (Z)-6-methoxymethoxy-4-phenyl-2-(N-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)hex-4-enoate (276 mg, 0.41 mmol, 1.0 equiv.) in MeCN (4 mL) was treated with 2 M aq. HCl (0.8 mL). Purification by chromatography (20→50% EtOAc–petrol) gave (\pm)-methyl (Z)-6-hydroxy-4-phenyl-2-(N-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)hex-4-enoate as a colourless oil; R_f 0.16 (50% EtOAc–petrol); ν_{\max} (film) 2957, 2869, 1743, 1599, 1447, 1313, 1296, 1243, 1195, 1147, 1091, 1048, 1021, 997, 764, 683 cm^{-1} ; δ_{H} (400 MHz) 7.93 (2H, dd, J 8.0, 8.0 Hz, *o*-SPh), 7.74 (1H, m, *p*-SPh), 7.59 (2H, m, *m*-SPh), 7.32–7.17 (5H, m, Ph), 7.10 (2H, s, *m*-SO₂Ar), 5.97 (1H, 2 \times t, J 6.5 Hz, CHCH₂OH), [4.63, 4.41] (1H, 2 \times dd, J 11.5, 3.5 Hz, SCH), 4.30 (2H, sept, J 7.0 Hz, *o*-ArCH), 4.20 (2H, m, CH₂OH), [3.48, 3.41] (3H, 2 \times s, OCH₃), 3.17 (2H, m, SCHCH₂), 2.87 (1H, 2 \times sept, J 7.0 Hz, *p*-ArCH), [2.04, 1.84] (1H, 2 \times dd, J 7.0, 5.0

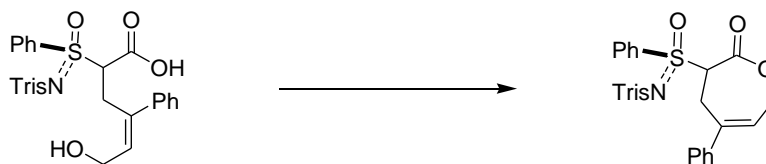
Hz, SCHCH₂), 1.27–1.18 (18H, m, CH(CH₃)₂); δ_C (100 MHz) 165.5, 165.4 (C=O), 152.2, 152.1, 149.2, 149.1, 139.4, 139.3, 137.1, 137.0, 134.8, 134.6, (4°), 136.1, 135.8, 135.2, 134.9, 129.7, 129.6, 129.2, 128.8, 128.6, 128.2, 128.1, 126.6, 126.4 (3°), 123.4, 123.4 (*m*-SO₂Ar), 70.6, 70.4 (SCH), 58.9, 58.8 (CH₂OH), 53.1, 53.1 (OCH₃), 34.1 (*p*-ArCH), 29.3 (*o*-ArCH), 27.8, 26.7, (SCHCH₂), 24.7, 24.6 (*o*-ArCH(CH₃)₂), 23.6 (*p*-ArCH(CH₃)₂); *m/z* (CI) 643 [M+NH₄]⁺ (Found [M+NH₄]⁺, 643.2873. C₃₄H₄₃NO₆S₂ requires [M+NH₄]⁺, 643.2870) (Found: C, 65.29; H, 6.93; N, 2.24. C₃₄H₄₃NO₆S₂ requires C, 65.25; H, 6.93; N, 2.24.).

(±)-(Z)-6-Hydroxy-4-phenyl-2-(N-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)hex-4-enoic acid



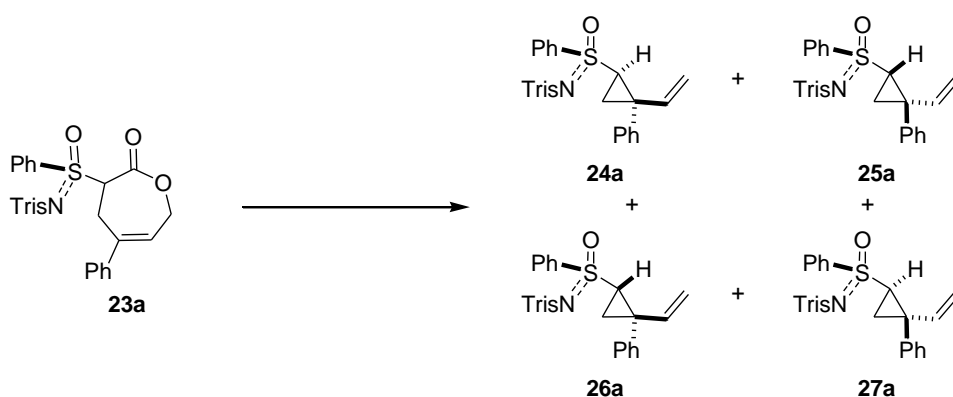
According to general procedure F, a solution of (±)-methyl (Z)-6-hydroxy-4-phenyl-2-(N-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)hex-4-enoate (117 mg, 0.19 mmol, 1.0 equiv.) in THF (0.5 mL) was treated with 2 M aq. LiOH (0.5 mL) to give (±)-(Z)-6-hydroxy-4-phenyl-2-(N-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)hex-4-enoic acid as a colourless foam, which was used without further purification; ν_{max} (film) 3420, 2959, 1738, 1599, 1447, 1311, 1295, 1244, 1147, 1092, 1049, 1021, 997, 764, 753, 743, 684 cm⁻¹; δ_H (300 MHz; CD₃OD) 7.87 (2H, d, *J* 8.0 Hz, *o*-SPh), 7.79 (1H, 2 × t, *J* 7.5 Hz, *p*-SPh), 7.61 (2H, 2 × t, *J* 8.0 Hz, *m*-SPh), 7.31 (2H, s, *m*-SO₂Ar), 7.25–7.09 (5H, m, Ph), [5.93, 5.87] (1H, 2 × t, *J* 6.5 Hz, CHCH₂OH), 4.20 (2H, 2 × sept, *J* 6.5 Hz, *o*-ArCH), 4.29–4.04 (3H, m, SCH and CH₂OH), 3.40–3.06 (2H, m, SCHCH₂), 2.90 (1H, 2 × sept, *J* 6.5 Hz, *p*-ArCH), 1.26–1.12 (18H, m, CH(CH₃)₂); δ_C (75 MHz; CD₃OD) 166.7, 166.6 (C=O), 153.8, 153.8, 150.6, 150.6, 141.2, 141.0, 138.5, 138.5, 136.2, 136.1, 133.4, 133.3 (4°), 136.5, 136.4, 130.9, 130.9, 130.6, 130.4, 129.8, 129.7, 129.1, 129.1, 127.7, 127.6, 124.6 (3°), 72.0, 71.5 (SCH), 59.7, 59.7 (CH₂OH), 35.4 (*p*-ArCH), 30.5, 30.5 (*o*-ArCH), 28.6, 28.0 (SCHCH₂), 25.1, 25.1 (*o*-ArCH(CH₃)₂), 24.1 (*p*-ArCH(CH₃)₂); *m/z* (CI) 629 [M+NH₄]⁺, 594, 550 (Found [M+NH₄]⁺, 629.2717. C₃₃H₄₁NO₆S₂ requires [M+NH₄]⁺, 629.2714).

(±)-5-Phenyl-3-(*N*-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)-4,7-dihydrooxepin-2(3*H*)-one **23a**



According to general procedure **G**, a solution of (±)-(*Z*)-6-hydroxy-4-phenyl-2-(*N*-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)hex-4-enoic acid (109 mg, 0.18 mmol, 1.0 equiv.) in CH₂Cl₂ (1.0 mL) was treated with EDCI (41 mg, 0.21 mmol, 1.2 equiv.). Purification by chromatography (30% EtOAc–petrol) gave (±)-5-phenyl-3-(*N*-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)-4,7-dihydrooxepin-2(3*H*)-one **23a** (103 mg, 36% over four steps) as a colourless solid; *R*_f 0.45 (50% EtOAc–petrol); ν_{\max} (film) 2958, 1753, 1599, 1446, 1311, 1246, 1148, 1093, 1057 cm⁻¹; δ_{H} (400 MHz) 8.17 (2H, m, *o*-SPh), 7.70 (1H, td, *J* 7.5, 1.5 Hz, *p*-SPh), 7.58 (2H, m, *m*-SPh), 7.37–7.31 (4H, m, *o*-/*m*-Ph), 7.27 (1H, m, *p*-Ph), [7.12, 7.11] (2H, 2 × s, *m*-SO₂Ar), [6.15, 5.91] (1H, dd, *J* 13.0, 3.5 Hz, SCH), 6.05 (1H, dtd, *J* 9.5, 5.5, 3.5, 2.0 Hz, OCH₂CH), 5.26 (1H, ddd, *J* 16.0, 12.5, 3.5 Hz, OCH₂), 4.67 (1H, dd, *J* 16.0, 7.5 Hz, OCH₂), 4.39 (2H, 2 × sept, *J* 7.0 Hz, *o*-ArCH), [3.82, 3.61] (1H, d, *J* 17.5 Hz, SCHCH₂), 2.87 (1H, 2 × sept, *J* 7.0 Hz, *p*-ArCH), 2.75 (1H, 2 × d, *J* 13.5 Hz, SCHCH₂), 1.28–1.20 (18H, m, CH(CH₃)₂); δ_{C} (100 MHz) 166.3 (C=O), 152.3, 149.3, 149.0, 141.0, 140.8, 140.4, 140.3, 137.0, 136.6, 133.6, 133.2 (4°), 134.9, 131.1, 131.0, 128.9, 128.8, 128.7, 128.7, 126.3, 126.0, 123.5, 123.5, 121.9, 121.6 (3°), 66.0, 65.7 (SCH), 64.4, 64.2 (OCH₂), 34.1 (*p*-ArCH), 31.9, 30.4 (SCHCH₂), 29.4, 29.3 (*o*-ArCH), 24.7, 24.7, 24.6, 24.5 (*o*-ArCH(CH₃)₂), 23.6 (*p*-ArCH(CH₃)₂); *m/z* (CI) 611 [M+NH₄]⁺, 425, 301, 251, 206, 156, 132 (Found [M+NH₄]⁺, 611.2623. C₃₃H₃₉NO₅S₂ requires [M+NH₄]⁺, 611.2613) (Found: C, 66.66; H, 6.53; N, 2.27. C₃₃H₃₉NO₅S₂ requires C, 66.75; H, 6.62; N, 2.36.).

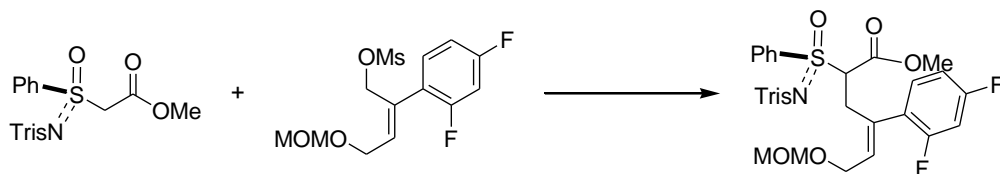
(*S**_s,1*R*,2*R*)-*S*-Phenyl-*S*-(2-phenyl-2-vinylcyclopropyl)-*N*-(2,4,6-triisopropylphenylsulfonyl)sulfoximine **24a**, (*S**_s,1*S*,2*S*)-*S*-phenyl-*S*-(2-phenyl-2-vinylcyclopropyl)-*N*-(2,4,6-triisopropylphenylsulfonyl)sulfoximine **25a**, (*S**_s,1*S*,2*R*)-*S*-phenyl-*S*-(2-phenyl-2-vinylcyclopropyl)-*N*-(2,4,6-triisopropylphenylsulfonyl)sulfoximine **26a**, and (*S**_s,1*R*,2*S*)-*S*-phenyl-*S*-(2-phenyl-2-vinylcyclopropyl)-*N*-(2,4,6-triisopropylphenylsulfonyl)sulfoximine **27a**



According to general procedure **H**, a solution of lactone **23a** (50 mg, 0.08 mmol, 1.0 equiv.) in DMF (0.4 mL) was treated with KOAc (0.8 mg, 0.008 mmol, 0.1 equiv.) and BSA (20.8 μ L, 0.08 mmol, 1.0 equiv.) to give the sulfoximines **24a–27a** as a colourless gum (34 mg, 78%) as a mixture of diastereomers (ratio **24a:25a:26a:27a** = 44:22:26:7) which were separable by chromatography (10% EtOAc–petrol); **25a** (isolated as a single diastereoisomer): R_f 0.44 (50% EtOAc–petrol); ν_{\max} (film) 2960, 1600, 1447, 1423, 1311, 1265, 1148, 1099, 1068, 998, 737, 702 cm^{-1} ; δ_H (400 Hz) 8.03 (2H, d, J 7.5 Hz, *o*-Ph), 7.70 (1H, tt, J 7.5, 1.5 Hz, *p*-Ph), 7.60 (2H, t, J 7.5 Hz, *m*-Ph), 7.21 (3H, m, Ph), 7.11 (2H, s, *m*-SO₂Ar), 6.82 (2H, m, Ph), 6.12 (1H, dd, J 17.0, 10.5 Hz, CH=CH₂), 5.04 (1H, dd, J 10.5, 1.0 Hz, CH=CH₂ *trans*), 4.42 (1H, d, J 17.0 Hz, CH=CH₂ *cis*), 4.39 (2H, sept, J 7.0 Hz, *o*-ArCH), 3.33 (1H, dd, J 9.0, 6.0 Hz, SCH), 2.88 (1H, sept, J 7.0 Hz, *p*-ArCH), 2.30 (1H, dd, J 6.0, 6.0 Hz, SCHCH₂), 2.07 (1H, dd, J 9.0, 6.0 Hz, SCHCH₂), 1.24 (18H, m, CH₃); δ_C (100 MHz) 151.9, 149.1, 139.2, 139.1, 137.3 (4°), 138.8 (CH=CH₂), 134.0, 129.2, 128.6, 127.8, 127.7, 123.3 (3°), 119.0 (CH=CH₂), 48.4 (SCH), 39.4 (SCHC), 34.1 (*p*-ArCH), 29.2 (*o*-ArCH), 24.7, 24.6, 23.7, 23.6 (CH(CH₃)₂), 20.0 (SCHCH₂); m/z (CI) 550 [M+H]⁺, 567, 425, 301 (Found [M+H]⁺, 550.2457. C₃₂H₃₉NO₃S₂ requires [M+H]⁺, 550.2450); **24a** (isolated as a single diastereoisomer): R_f 0.41 (50% EtOAc–petrol); ν_{\max} (film) 2961, 2929, 1600, 1463, 1447, 1423, 1311, 1265, 1149, 1097, 1051, 739, 703 cm^{-1} ; δ_H (400 Hz) 8.04 (2H, d, J 7.5 Hz, *o*-Ph), 7.68 (1H, t, J 7.5 Hz, *p*-Ph), 7.58 (2H, t, J 7.5 Hz, *m*-

Ph), 7.29 (5H, m, Ph), 7.12 (2H, s, *m*-SO₂Ar), 6.43 (1H, dd, *J* 17.0, 10.5 Hz, CH=CH₂), 5.12 (1H, d, *J* 10.5 Hz, CH=CH₂ *trans*), 4.65 (1H, dd, *J* 17.0, 0.5 Hz, CH=CH₂ *cis*), 4.39 (2H, sept, *J* 7.0 Hz, *o*-ArCH), 3.03 (1H, dd, *J* 8.5, 6.5 Hz, SCH), 2.90 (1H, sept, *J* 7.0 Hz, *p*-ArCH), 2.03 (1H, dd, *J* 6.0, 6.0 Hz, SCHCH₂), 1.75 (1H, dd, *J* 8.5, 6.0 Hz, SCHCH₂), 1.28 (18H, m, CH₃); δ_C (125 MHz) 151.8, 149.2, 140.3, 139.7, 137.5 (4°), 136.1, 133.8, 129.5, 129.4, 128.6, 127.9, 127.7, 123.2 (3°), 118.8 (CH=CH₂), 49.0 (SCH), 41.1 (SCHC), 34.1 (*p*-ArCH), 29.3 (*o*-ArCH), 24.8, 24.7, 23.7, 23.6 (CH(CH₃)₂), 19.1 (SCHCH₂); *m/z* (CI) 550 [M+H]⁺, 567, 425, 301 (Found [M+H]⁺, 550.2465. C₃₂H₃₉NO₃S₂ requires [M+H]⁺, 550.2450); **26a** (isolated as a single diastereoisomer): R_f 0.38 (50% EtOAc–petrol); ν_{max} (film) 2960, 2928, 1600, 1463, 1448, 1311, 1295, 1265, 1244, 1148, 1098, 1068, 1030, 738, 702 cm⁻¹; δ_H (400 Hz) 7.61 (1H, m, Ph), 7.43 (4H, m, Ph), 7.21 (1H, m, Ph), 7.10 (2H, m, Ph), 7.08 (2H, s, *m*-SO₂Ar), 6.79 (2H, d, *J* 7.5 Hz, Ph), 5.72 (1H, dd, *J* 17.0, 10.5 Hz, CH=CH₂), 5.05 (1H, d, *J* 10.5 Hz, CH=CH₂ *trans*), 4.82 (1H, d, *J* 17.0 Hz, CH=CH₂ *cis*), 4.33 (2H, sept, *J* 6.5 Hz, *o*-ArCH), 3.51 (1H, dd, *J* 9.0, 5.5 Hz, SCH), 2.87 (1H, sept, *J* 7.0 Hz, *p*-ArCH), 2.63 (1H, dd, *J* 6.0, 6.0 Hz, SCHCH₂), 1.89 (1H, dd, *J* 9.0, 6.0 Hz, SCHCH₂), 1.25 (18H, m, CH₃); □ δ_C (100 MHz) 151.7, 149.0, 140.3, 137.8, 137.2 (4°), 133.5, 132.4, 130.3, 129.4, 128.7, 128.0, 127.6, 123.2 (3°), 115.6 (CHCH₂), 46.8 (SCH), 38.2 (SCHC), 34.1 (*p*-ArCH), 29.1 (*o*-ArCH), 24.7, 24.6, 23.7, 23.6 (CH(CH₃)₂), 17.4 (SCHCH₂); *m/z* (CI) 550 [M+H]⁺, 567, 425, 301, 272, 254, 237 (Found [M+H]⁺, 550.2435. C₃₂H₃₉NO₃S₂ requires [M+H]⁺, 550.2450).

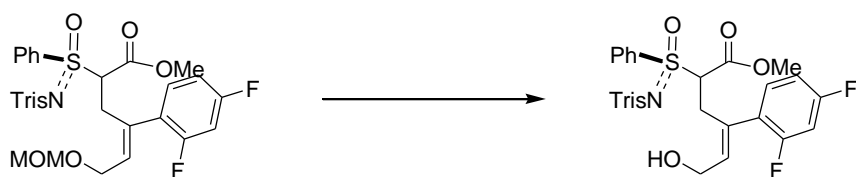
(±)-Methyl (E)-4-(2,4-difluorophenyl)-6-(methoxymethoxy)-2-(N-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)hex-4-enoate



According to general procedure **D**, a suspension of sodium hydride (54 mg, 1.35 mmol, 1.1 equiv.) in THF (1.5 mL) was treated with (±)-methyl 2-(N-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)acetate (589 mg, 1.23 mmol, 1.0 equiv.) in THF (2 mL) and methanesulfonic acid (Z)-2-(2,4-difluorophenyl)-4-(methoxymethoxy)but-2-enyl ester (396 mg, 1.23 mmol, 1.0 equiv.) in THF (1.5 mL) to give (±)-methyl (E)-4-(2,4-difluorophenyl)-6-(methoxymethoxy)-2-(N-(2,4,6-

triisopropylphenylsulfonyl)phenylsulfonimidoyl)hex-4-enoate as a colourless gum, which was used without further purification; R_f 0.44 (50% EtOAc–petrol); ν_{\max} (film) 2955, 2925, 1744, 1599, 1501, 1315, 1243, 1148, 1091, 1039, 1022, 997, 961, 845, 684 cm^{-1} ; δ_{H} (300 MHz) 7.92 (2H, d, J 7.5 Hz, *o*-Ph), 7.74 (1H, t, J 7.5 Hz, *p*-Ph), 7.59 (2H, t, J 8.0 Hz, *m*-Ph), 7.08 (2H, *m*-SO₂Ar), 7.13–7.03 (1H, m, ArF), 6.85–6.70 (2H, m, ArF), 5.76 (1H, t, J 6.5 Hz, CHCH₂O), 4.58 (2H, s, OCH₂O), 4.47 (1H, dd, J 12.0, 3.0 Hz, SCH), 4.27 (2H, sept, J 7.0 Hz, *o*-ArCH), 4.10 (2H, dd, J 6.5, 3.0 Hz, OCH₂CH), 3.54 (3H, s, CO₂CH₃), 3.34 (3H, s, CH₂OCH₃), [3.21, 3.17] (1H, 2 × m, SCHCH₂), 3.00 (1H, 2 × d, J 12.0 Hz, SCHCH₂), 2.86 (1H, sept, J 7.0 Hz, *p*-ArCH), 1.25–1.16 (18H, m, CH(CH₃)₂); δ_{C} (75 MHz) 164.8 (C=O), 164.3, 164.0, 161.6, 161.5, 161.0, 160.8, 158.3, 158.2 (CF), 152.1, 149.2, 137.0, 133.0 (4°), 134.8, 134.7, 129.7, 129.2, 123.4 (3°), 131.3, 131.2, 131.2, 131.1 (CFCHCH), 124.0, 123.9, 123.8, 123.7 (CCF), 111.5, 111.5, 111.3, 111.2 (CFCHCH), 104.6, 104.2, 103.9 (CFCHCF), 95.9 (OCH₂O), 70.1 (SCH), 63.3 (CHCH₂O), 55.4 (CH₂OCH₃), 53.1 (CO₂CH₃), 34.1 (*p*-ArCH), 29.7, 29.0 (SCHCH₂), 29.3 (*o*-ArCH), 24.7 (*o*-ArCH(CH₃)₂), 23.6 (*p*-ArCH(CH₃)₂); m/z (EI) 723 [M+NH₄]⁺ (Found [M+NH₄]⁺, 723.2943. C₃₆H₄₅F₂NO₇S₂ requires [M+NH₄]⁺, 723.2944) (Found: C, 61.23; H, 6.42; N, 1.95. C₃₆H₄₅F₂NO₇S₂ requires C, 61.26; H, 6.43; N, 1.98.).

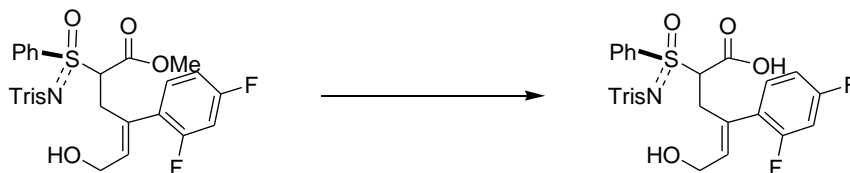
(±)-Methyl (E)-4-(2,4-difluorophenyl)-6-hydroxy-2-(N-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)hex-4-enoate



According to general procedure **E**, (±)-methyl (E)-4-(2,4-difluorophenyl)-6-(methoxymethoxy)-2-(N-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)hex-4-enoate (433 mg, 0.61 mmol, 1.0 equiv.) in MeCN (6 mL) was treated with 2 M aq. HCl (1.2 mL). Purification by chromatography (20→40% EtOAc–petrol) gave (±)-methyl (E)-4-(2,4-difluorophenyl)-6-hydroxy-2-(N-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)hex-4-enoate (331 mg, 41% over two steps) as a colourless gum; R_f 0.21 (50% EtOAc–petrol); ν_{\max} (film) 2958, 1743, 1599, 1501, 1447, 1423, 1312, 1295, 1242, 1147, 1091, 1048, 1021, 997, 966, 846, 769, 740, 684 cm^{-1} ; δ_{H} (500 MHz) 7.90 (2H, m, *o*-Ph), 7.73 (1H, m, *p*-Ph), 7.58 (2H, m, *m*-Ph), 7.09

(1H, m, *o*-ArF), 7.09 (2H, s, *m*-SO₂Ar), 6.79 (2H, m, *m*-ArF), 5.84 (1H, 2 × t, *J* 6.5 Hz, CHCH₂OH), [4.69, 4.38] (1H, 2 × dd, *J* 11.5, 3.5 Hz, CHCH₂OH), 4.30 (2H, m, CH₂OH), 4.24 (2H, m, *o*-ArCH), [3.53, 3.46] (3H, 2 × s, OCH₃), [3.33, 3.25] (1H, 2 × dd, *J* 14.0, 3.5 Hz, SCHCH₂), [3.16, 2.97] (1H, 2 × dd, *J* 14.0, 11.5 Hz, SCHCH₂), 2.86 (1H, 2 × sept, *J* 7.0 Hz, *p*-ArCH), [2.14, 1.85] (1H, t, *J* 6.0 Hz, OH), 1.21 (18H, m, CH(CH₃)₂); δ_C (125 MHz) 165.6, 165.4 (C=O), 163.6, 163.5, 161.6, 161.5, 161.0, 160.9, 159.0, 158.9 (CF), 152.2, 152.2, 149.2, 149.1, 137.1, 136.9, 134.0, 130.8, 130.7 (4°), 124.1, 124.0, 124.0, 123.9 (CCF), 135.3, 135.1, 135.0, 134.9, 129.7, 129.6, 129.2, 123.5, 123.4 (3°), 131.3, 131.3, 131.2, 131.2, 131.1, 131.1, 131.0, 131.0 (CFCHCH), 111.7, 111.5, 111.3 (CFCHCH), 104.6, 104.4, 104.2, 104.0 (CFCHCF), 70.7, 70.3 (SCH), 58.7, 58.5 (CH₂OH), 53.2, 53.2 (OCH₃), 34.1 (*p*-ArCH), 29.3, 29.3 (*o*-ArCH), 28.9, 27.8 (SCHCH₂), 24.7, 24.6 (*o*-ArCH(CH₃)₂), 23.6 (*p*-ArCH(CH₃)₂); δ_F (376 MHz) [-108.8, -109.0] (1F, 2 × qd, *J* 8.0, 6.5 Hz, *o*-CF), -109.8 (1F, m, *p*-CF); *m/z* (EI) 679 [M+NH₄]⁺, 644, 408 (Found [M+NH₄]⁺, 679.2680. C₃₄H₄₁F₂NO₆S₂ requires [M+NH₄]⁺, 679.2682) (Found: C, 61.80; H, 6.32; N, 2.18. C₃₄H₄₁F₂NO₆S₂ requires C, 61.70; H, 6.24; N, 2.12).

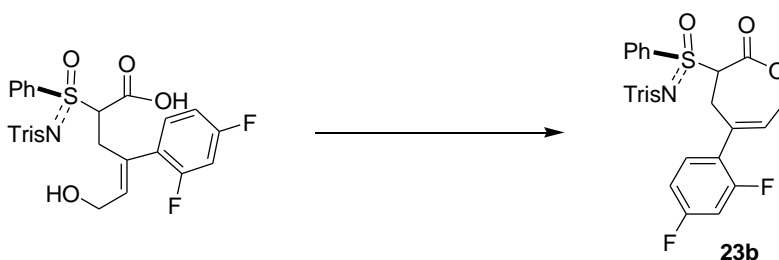
(±)-(E)-4-(2,4-Difluorophenyl)-6-hydroxy-2-(N-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)hex-4-enoic acid



According to general procedure **F**, a solution of (±)-methyl (*E*)-4-(2,4-difluorophenyl)-6-hydroxy-2-(*N*-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)hex-4-enoate (326 mg, 0.49 mmol, 1.0 equiv.) in THF (1.25 mL) was treated with 2 M aq. LiOH (1.25 mL) to give (±)-(*E*)-4-(2,4-difluorophenyl)-6-hydroxy-2-(*N*-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)hex-4-enoic acid (290 mg, 91%) as a colourless foam, which was used without further purification; ν_{max} (film) 2958, 2556, 1731, 1599, 1501, 1448, 1423, 1293, 1244, 1141, 1091, 1049, 1021, 997, 966, 848, 765, 741, 684 cm⁻¹; δ_H (300 MHz; CD₃OD) 7.86 (2H, d, *J* 8.0 Hz, *o*-Ph), 7.78 (1H, m, *p*-Ph), 7.60 (2H, m, *m*-Ph), 7.24–7.09 (1H, m, *o*-ArF), 7.15 (2H, s, *m*-SO₂Ar), 6.96–6.81 (2H, m, *m*-ArF), 5.77 (1H, 2 × t, *J* 6.5 Hz, CHCH₂OH), 4.29–4.03 (3H, m, SCH and CH₂OH), 4.17 (2H, 2 × sept, *J* 6.5 Hz, *o*-ArCH), 3.28–3.05 (2H, m,

SCHCH₂), 2.90 (1H, 2 × sept, *J* 7.0 Hz, *p*-ArCH), 1.26–1.12 (18H, m, CH(CH₃)₂); δ_C (75 MHz; CD₃OD) 166.0 (C=O), 165.9, 165.7, 163.2, 163.0, 162.6, 162.4, 159.9, 159.7 (CF), 153.8, 150.6, 150.6, 138.5, 138.4, 137.2, 137.0, 136.3, 136.2 (4°), 126.0, 126.0, 125.8, 125.6 (CCF), 133.2, 133.1, 133.0, 133.0, 131.5, 131.4, 124.5 (3°), 130.9, 130.8, 130.6, 130.4 (CFCHCH), 112.7, 112.4, 112.3 (CFCHCH), 105.4, 105.0, 104.7 (CFCHCF) 72.0, 71.4 (SCH), 59.3, 59.2 (CH₂OH), 35.4 (*p*-ArCH), 30.5 (*o*-ArCH), 29.7, 29.0 (SCHCH₂) 25.1, 25.1, 25.0 (*o*-ArCH(CH₃)₂), 24.1 (*p*-ArCH(CH₃)₂); *m/z* (EI) 665 [M+NH₄]⁺, 630 (Found [M+NH₄]⁺, 665.2524. C₃₃H₃₉F₂NO₆S₂ requires [M+NH₄]⁺, 665.2525) (Found: C, 61.06; H, 5.99; N, 2.09. C₃₃H₃₉F₂NO₆S₂ requires C, 61.19; H, 6.07; N, 2.16).

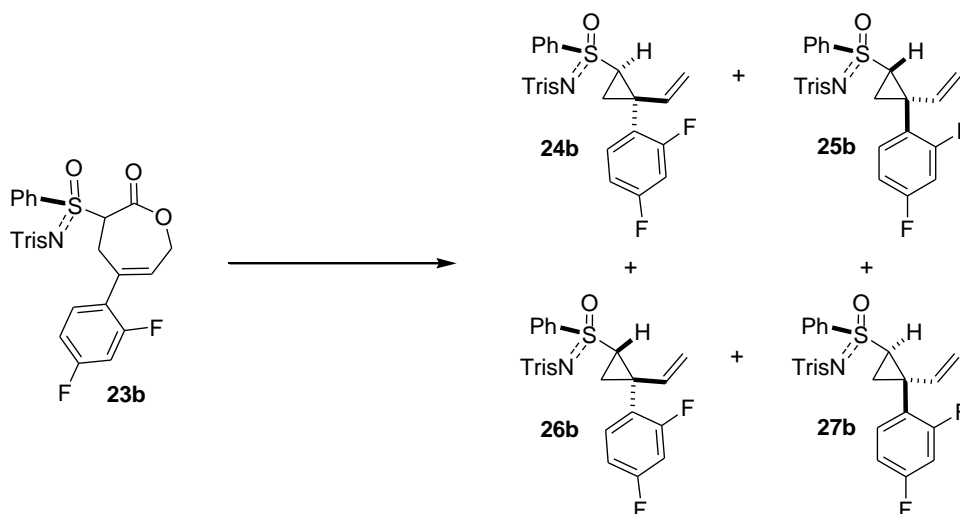
(±)-5-(2,4-Difluorophenyl)-3-(*N*-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)-4,7-dihydrooxepin-2(3*H*)-one **23b**



According to general procedure **G**, (±)-(*E*)-4-(2,4-difluorophenyl)-6-hydroxy-2-(*N*-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)hex-4-enoic acid (260 mg, 0.40 mmol, 1.0 equiv.) in CH₂Cl₂ (1.0 mL) at 0 °C was treated with EDCI (85 mg, 0.44 mmol, 1.1 equiv.). Purification by chromatography (40% EtOAc–petrol) gave (±)-5-(2,4-difluorophenyl)-3-(*N*-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)-4,7-dihydrooxepin-2(3*H*)-one **23b** (89 mg, 35%) as a colourless solid; mp 86–87 °C; *R_f* 0.48 (50% EtOAc–petrol); ν_{max} (film) 2959, 1754, 1502, 1231, 1141, 1090, 1048, 1022, 998, 972, 847, 733, 682 cm⁻¹; δ_H (400 MHz) 8.13 (2H, 2 × d, *J* 7.0 Hz, *o*-Ph), 7.70 (1H, t, *J* 7.5 Hz, *p*-Ph), 7.57 (2H, t, *J* 7.5 Hz, *m*-Ph), 7.30–7.12 (1H, m, *o*-ArF), [7.12, 7.10] (2H, 2 × s, *m*-SO₂Ar), 6.92–6.79 (2H, m, *m*-ArF), [6.08, 5.89] (1H, 2 × dd, *J* 13.0, 3.5 Hz, SCH), 5.96 (1H, m, CHCH₂O), 5.23 (1H, ddd, *J* 16.0, 13.0, 3.5 Hz, OCH₂), 4.68 (1H, ddd, *J* 16.0, 7.5, 4.0 Hz, OCH₂), 4.37 (2H, sept, *J* 6.5 Hz, *o*-ArCH), [3.66, 3.47] (1H, 2 × d, *J* 17.5 Hz, SCHCH₂), 2.88 (1H, sept, *J* 6.5 Hz, *p*-ArCH), 2.78 (1H, m, SCHCH₂) 1.27–1.12 (18H, m, CH(CH₃)₂); δ_C (125 MHz) 166.1, 166.0 (C=O), 163.8, 163.8, 161.9, 161.8, 160.6, 160.5, 158.6, 158.5 (CF),

152.3, 152.2, 149.2, 149.0, 136.9, 136.5, 135.9, 135.7, 134.9, 134.9, 133.5, 133.2 (4°), 131.0, 130.9, 128.9, 128.8, 125.5, 125.1, 123.5, 123.4 (3°), 130.6, 130.6, 130.5, 130.5, 130.4, 130.4, 130.3, 130.3 (CFCHCH), 124.7, 124.7, 124.6, 124.5 (CCF), 111.9, 111.8, 111.8, 111.7, 111.7, 111.6, 111.6 (CFCHCH), 104.7, 104.5, 104.3 (CFCHCF), 65.8, 65.4 (SCH), 64.0, 63.8 (OCH₂), 34.1, 34.1 (*p*-ArCH), 32.0, 30.6 (SCHCH₂), 29.3, 29.3 (*o*-ArCH), 24.7, 24.6, 24.4 (*o*-ArCH(CH₃)₂), 23.6 (*p*-ArCH(CH₃)₂); *m/z* (EI) 647 [M+NH₄]⁺, 630 [M+H]⁺ (Found [M+H]⁺, 630.2156. C₃₃H₃₇F₂NO₅S₂ requires [M+H]⁺, 630.2154) (Found: C, 63.07; H, 5.97; N, 2.18. C₃₃H₃₇F₂NO₅S₂ requires C, 62.94; H, 5.92; N, 2.22).

(S*_s,1R,2R)-S-(2-(2,4-Difluorophenyl)-2-vinylcyclopropyl)-S-phenyl-N-(2,4,6-triisopropylphenylsulfonyl)sulfoximine **24b**, (S*_s,1S,2S)-S-(2-(2,4-difluorophenyl)-2-vinylcyclopropyl)-S-phenyl-N-(2,4,6-triisopropylphenylsulfonyl)sulfoximine **25b**, (S*_s,1S,2R)-S-(2-(2,4-difluorophenyl)-2-vinylcyclopropyl)-S-phenyl-N-(2,4,6-triisopropylphenylsulfonyl)sulfoximine **26b**, and (S*_s,1R,2S)-S-(2-(2,4-difluorophenyl)-2-vinylcyclopropyl)-S-phenyl-N-(2,4,6-triisopropylphenylsulfonyl)sulfoximine **27b**

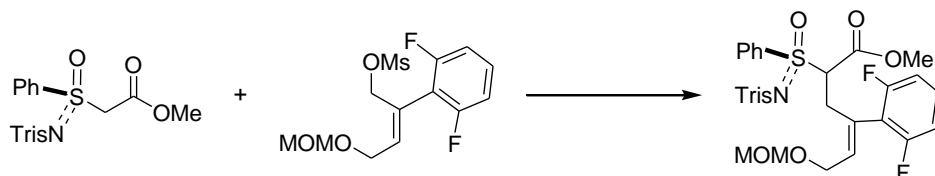


According to general procedure **H**, lactone **23b** (7.0 mg, 0.02 mmol, 1.0 equiv.) in DMF (0.1 mL) was treated with KOAc (pinch) and BSA (4.6 μL, 0.02 mmol, 1.0 equiv.) to give the sulfoximines **24b–27b** as a colourless gum (5 mg, 70%) as a mixture of diastereoisomers (ratio **24b:25b:26b:27b** = 44:16:33:7) which were partially separable by chromatography (10→40% EtOAc–petrol); **25b** (isolated as a single diastereoisomer): *R_f* 0.60 (50% EtOAc–petrol); *v*_{max} (film) 2985, 1740, 1447, 1374, 1240, 1047, 938, 847, 737, 634, 608 cm⁻¹; δ_H (500 MHz) 8.00 (2H, dd, *J* 8.5,

1.0 Hz, *o*-Ph), 7.69 (1H, tt, *J* 7.5, 1.5 Hz, *p*-Ph), 7.57 (2H, t, *J* 8.0 Hz, *m*-Ph), 7.12 (2H, s, *m*-SO₂Ar), 6.89 (1H, dt, *J* 8.5, 6.5 Hz, CFCHCH) 6.78 (1H, t, *J* 8.0, Hz, CFCHCH) 6.67 (1H, ddd, *J* 10.0, 9.0, 2.5 Hz, CFCHCF) 6.11 (1H, dd, *J* 17.0, 10.5 Hz, CH=CH₂), 5.06 (1H, dd, *J* 10.5, 1.0 Hz, CH=CH₂ *trans*) 4.44 (1H, d, *J* 17.0 Hz, CH=CH₂ *cis*) 4.40 (2H, sept, *J* 7.0 Hz, *o*-ArCH) 3.29 (1H, dd, *J* 9.0, 6.0 Hz, SCH) 2.88 (1H, sept, *J* 7.0 Hz, *p*-ArCH) 2.39 (1H, dd, *J* 6.5, 6.5 Hz, SCHCH₂) 2.06 (1H, dd, *J* 9.0, 6.5 Hz, SCHCH₂), 1.22–1.25 (18H, m, CH(CH₃)₂); δ_C (125 MHz) 163.6, 163.5, 162.3, 162.2, 160.2, 160.1 (CF), 152.0, 149.1, 138.2, 137.1 (4°), 134.2 (CH=CH₂), 134.1 (*p*-Ph), 132.0, 131.9, 131.9 (CFCHCH), 129.0 (*m*-Ph), 128.1 (*o*-Ph), 123.3 (*m*-SO₂Ar), 122.3, 122.2 (CCF), 118.4 (CH=CH₂), 111.7, 111.6 (CFCHCH), 104.5, 104.3, 104.1 (CFCHCF), 48.0 (SCH), 34.1 (SCHC), 34.1 (*p*-ArCH), 29.2 (*o*-ArCH), 24.7, 24.6, 23.7, 23.6 (CH(CH₃)₂), 20.3 (SCHCH₂); *m/z* (CI) 603 [M+NH₄]⁺, 586, 301 (Found [M+H]⁺, 586.2257. requires [M+H]⁺, 586.2261); **24b** and **26b** (isolated as a mixture of the two diastereoisomers): R_f 0.67 (50% EtOAc–petrol); ν_{max} (film) 2985, 1740, 1447, 1374, 1240, 1094, 1047, 938, 847, 737, 634, 608 cm⁻¹; δ_H (500 MHz) 8.03 (2H, dd, *J* 8.5, 1.0 Hz, *o*-Ph **24b**) 7.66 (2H, m, Ph) 7.57 (3H, m, Ph) 7.47 (2H, dd, *J* 8.5, 7.5 Hz, *m*-Ph minor) 7.32 (1H, dt, *J* 8.5, 6.5 Hz, *p*-Ph **24b**), 7.11 (2H, s, *m*-SO₂Ar **24b**), 7.06 (2H, s, *m*-SO₂Ar **26b**), 6.85 (1H, m, ArF), 6.74 (1H, m, ArF), 6.50 (1H, m, ArF), 6.36 (1H, dd, *J* 17.0, 10.5 Hz, CH=CH₂ **24b**), 5.60 (1H, dd, *J* 17.0, 10.5 Hz, CH=CH₂ **26b**), 5.11 (1H, dd, *J* 10.5, 1.0 Hz, CH=CH₂ *trans* **24b**), 5.02 (1H, d, *J* 10.5 Hz, CH=CH₂ *trans* **26b**), 4.74 (1H, dd, *J* 17.0, 1.5 Hz, CH=CH₂ *cis* **26b**), 4.64 (1H, d, *J* 17.0 Hz, CH=CH₂ *cis* **24b**), 4.35 (2H, sept, *J* 6.5 Hz, *o*-ArCH **24b**), 4.27 (2H, sept, *J* 6.5 Hz, *o*-ArCH **26b**), 3.43 (1H, dd, *J* 9.0, 5.5 Hz, SCH **26b**), 2.98 (1H, dd, *J* 9.0, 6.5 Hz, SCH **24b**), 2.88 (1H, sept, *J* 6.5 Hz, *p*-ArCH **24b**), 2.85 (1H, sept, *J* 6.5 Hz, *p*-ArCH **26b**), 2.61 (1H, dd, *J* 6.0, 6.0 Hz, SCHCH₂ **26b**), 2.13 (1H, dd, *J* 6.5 Hz, SCHCH₂ **24b**), 1.96 (1H, dd, *J* 9.0, 6.5 Hz, SCHCH₂ **26b**), 1.71 (1H, dd, *J* 9.0, 6.0 Hz, SCHCH₂ **24b**), 1.30–1.17 (18H, m, CH(CH₃)₂); δ_C (125 MHz) 163.7, 163.6, 163.5, 162.8, 162.1, 162.1, 161.7, 161.6, 161.5, 160.8, 160.7, 160.1, 160.0 (CF), 151.9, 149.2, 149.0, 137.6, 137.4, 137.0 (4°), 138.5, 134.5 (CH=CH₂), 134.0, 133.9, 129.4, 129.0, 128.0, 127.6 (3°), 132.9, 132.9, 132.8, 132.8 (CFCHCH), 123.3, 122.8, 122.8, 122.7, 122.6 (CCF), 118.3, 115.6 (CH=CH₂), 117.0, 117.0, 111.7, 111.7, 111.5, 111.5, 111.2, 111.0 (CFCHCH), 104.4, 104.2, 104.1, 104.0, 103.9, 103.7 (CFCHCF), 48.9, 46.7 (SCH), 35.5, 34.1, 33.9 (*p*-ArCH), 29.7, 29.3, 29.1 (*o*-ArCH), 24.8, 24.8, 24.6, 24.6, 23.7, 23.6, 23.6 (CH(CH₃)₂), 19.7, 17.7

(SCHCH₂); *m/z* (CI) 603 [M+NH₄]⁺, 586, 425 (Found [M+H]⁺, 586.2258. requires [M+H]⁺, 586.2261).

(±)-Methyl (E)-4-(2,6-difluorophenyl)-6-(methoxymethoxy)-2-(N-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)hex-4-enoate



According to general procedure **D**, sodium hydride (102 mg, 2.55 mmol, 1.2 equiv.) in DMF (3.5 mL) was treated with (±)-methyl 2-(N-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)acetate (1.02 g, 2.13 mmol, 1.0 equiv.) in DMF (3.5 mL) and methanesulfonic acid (Z)-2-(2,6-difluorophenyl)-4-(methoxymethoxy)but-2-enyl ester (2.13 mmol, 1.0 equiv.) in DMF (3.5 mL) to give (±)-methyl (E)-4-(2,6-difluorophenyl)-6-(methoxymethoxy)-2-(N-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)hex-4-enoate as a colourless gum, which was used without further purification; *R_f* 0.71 (50% EtOAc–heptane).

(±)-Methyl (E)-4-(2,6-difluorophenyl)-6-hydroxy-2-(N-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)hex-4-enoate



According to general procedure **E**, (±)-methyl (E)-4-(2,6-difluorophenyl)-6-(methoxymethoxy)-2-(N-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)hex-4-enoate (2.13 mmol, 1.0 equiv.) in MeCN (22 mL) was treated with 2 M aq. HCl (4.5 mL). Purification by chromatography (20→40% EtOAc–petrol) gave (±)-methyl (E)-4-(2,6-difluorophenyl)-6-hydroxy-2-(N-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)hex-4-enoate (491 mg, 33% over two steps) as a colourless gum; *R_f* 0.36 (50% EtOAc–heptane); *v*_{max} (film) 2958, 1744, 1621, 1462, 1316, 1237, 1150, 1095, 1057 cm⁻¹; *δ*_H (400 MHz) 7.90 (2H, d, *J* 8.0 Hz, *o*-Ph), 7.72 (1H, m, *p*-Ph), 7.58 (2H, m, *m*-Ph), 7.22 (1H, m, *o*-ArF), 7.09 (2H, s, *m*-SO₂Ar), 6.86 (2H, 2 × t, *J* 8.0 Hz, *m*-ArF), 5.84 (1H, 2 × t, *J* 6.5 Hz, CHCH₂OH), 4.64 (1H, dd, *J* 12.0, 3.0 Hz, SCH), 4.37

(1H, dd, *J* 11.0, 4.5 Hz, SCH), 4.29 (2H, m, CH₂OH), 4.25 (2H, m, *o*-ArCH), [3.58, 3.47] (3H, 2 × s, OCH₃), [3.25, 3.18] (1H, 2 × dd, *J* 13.5, 2.0 Hz, SCHCH₂), [3.15, 3.00] (1H, 2 × d, *J* 12.0 Hz, SCHCH₂), 2.86 (1H, 2 × sept, *J* 7.0 Hz, *p*-ArCH), 2.05 (1H, br s, OH), 1.20 (18H, m, CH(CH₃)₂); δ_C (100 MHz) 165.5, 165.3 (C=O), 161.4, 158.9 (CF), 152.2, 152.1, 149.2, 149.1, 137.7, 137.5, 134.1, 129.4 (4°), 137.1, 136.9 (CHCH₂OH), 134.9, 134.8, 129.6, 129.5, 129.3, 129.2, 123.4 (3°), 124.1, 124.0 (CFCHCH), 117.1 (CCF), 111.7, 111.6, 111.5, 111.3 (CFCHCH), 70.4, 70.1 (SCH), 58.6, 58.5 (CH₂OH), 53.2, 53.1 (OCH₃), 34.1 (*p*-ArCH), 29.3 (*o*-ArCH), 29.0, 27.8 (SCHCH₂), 24.6, 24.6 (*o*-ArCH(CH₃)₂), 23.6 (*p*-ArCH(CH₃)₂); *m/z* (CI) 679 [M+NH₄]⁺, 586, 425, 301, 272 (Found [M+H]⁺, 662.2416. C₃₄H₄₁F₂NO₆S₂ requires [M+H]⁺, 662.2422) (Found: C, 61.77; H, 6.18; N, 2.11. C₃₄H₄₁F₂NO₆S₂ requires C, 61.70; H, 6.24; N, 2.12).

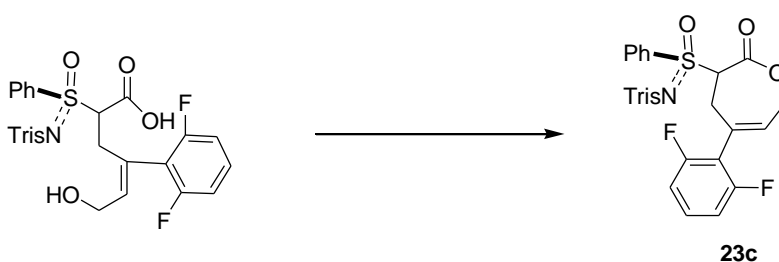
(±)-(*E*)-4-(2,6-Difluorophenyl)-6-hydroxy-2-(*N*-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)hex-4-enoic acid



According to general procedure **F**, a solution of (±)-methyl (*E*)-4-(2,6-difluorophenyl)-6-hydroxy-2-(*N*-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)hex-4-enoate (491 mg, 0.74 mmol, 1.0 equiv.) in THF (1.85 mL) was treated with 2 M aq. LiOH (1.85 mL) to give (±)-(*E*)-4-(2,6-difluorophenyl)-6-hydroxy-2-(*N*-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)hex-4-enoic (402 mg, 84%) as a colourless foam, which was used without further purification; ν_{max} (film) 3427, 2961, 2929, 2870, 1707, 1622, 1599, 1463, 1398, 1265, 1232, 1146, 1095, 1064, 1021, 998, 738 cm⁻¹; δ_H (400 MHz; CD₃OD) 7.80 (2H, d, *J* 7.5 Hz, *o*-Ph), 7.71 (1H, 2 × t, *J* 7.5 Hz, *p*-Ph), 7.53 (2H, 2 × t, *J* 7.5 Hz, *m*-Ph), 7.31 (1H, m, *o*-ArF), [7.14, 7.13] (2H, 2 × s, *m*-SO₂Ar), 6.92 (2H, 2 × t, *J* 8.0 Hz, *m*-ArF), [5.80, 5.74] (1H, 2 × t, *J* 6.5 Hz, CHCH₂OH), [4.39, 4.29] (2H, 2 × dd, *J* 13.5, 7.0 Hz, CH₂OH), 4.17 (2H, 2 × sept, *J* 6.5 Hz, *o*-ArCH), 3.96 (1H, d, *J* 11.5 Hz, SCH), [3.44, 3.22, 2.85] (2H, 3 × m, SCHCH₂), 2.91 (1H, 2 × sept, *J* 7.0 Hz, *p*-ArCH), 1.18–1.10 (18H, m, CH(CH₃)₂); δ_C (100 MHz; CD₃OD) 169.0, 168.7 (C=O), 162.9, 160.5 (CF), 153.7, 153.5, 150.5,

150.4, 138.7, 138.1, 135.8, 129.4 (4°), 137.9, 137.4, 136.9, 135.4, 135.3, 130.8, 130.6, 130.4, 130.2, 130.1, 126.8, 126.6 (3°), 124.4 (CFCHCH), 119.2, 119.0, 118.8 (CCF), 112.8, 112.7, 112.7, 112.5, 112.5 (CFCHCH), 74.6 (SCH), 59.2, 59.1 (CH₂OH), 35.4 (*p*-ArCH), 30.3 (*o*-ArCH), 25.1, 25.0, 24.9 (*o*-ArCH(CH₃)₂), 24.1 (*p*-ArCH(CH₃)₂); *m/z* (CI) 621 [M-CO₂+NH₄]⁺, 370, 301 (Found [M-CO₂+NH₄]⁺, 621.2609. C₃₃H₃₉F₂NO₆S₂ requires [M+NH₄]⁺, 621.2632) (Found: C, 61.18; H, 6.14; N, 2.16. C₃₃H₃₉F₂NO₆S₂ requires C, 61.19; H, 6.07; N, 2.16).

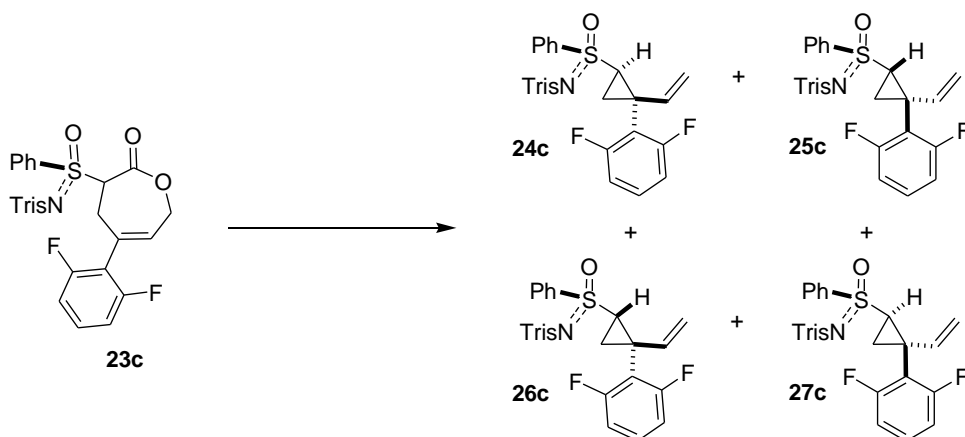
(±)-5-(2,6-Difluorophenyl)-3-(N-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)-4,7-dihydrooxepin-2(3H)-one **23c**



According to general procedure **G**, (±)-(*E*)-4-(2,6-difluorophenyl)-6-hydroxy-2-(N-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)hex-4-enoic (360 mg, 0.56 mmol, 1.0 equiv.) in CH₂Cl₂ (2.8 mL) at 0 °C was treated with EDCI (118 mg, 0.62 mmol, 1.1 equiv.). Purification by chromatography (30% EtOAc–petrol) (±)-5-(2,6-difluorophenyl)-3-(N-(2,4,6-triisopropylphenylsulfonyl)phenylsulfonimidoyl)-4,7-dihydrooxepin-2(3H)-one **23c** (289 mg, 82%) as a colourless solid; mp 86–87 °C; *R_f* 0.69 (50% EtOAc–petrol); *v*_{max} (film) 2959, 1756, 1623, 1599, 1464, 1401, 1267, 1234, 1148, 1092, 1064, 1023, 998, 738 cm⁻¹; *δ*_H (400 MHz) 8.12 (2H, 2 × d, *J* 8.5 Hz, *o*-Ph), 7.69 (1H, 2 × t, *J* 8.5 Hz, *p*-Ph), 7.56 (2H, 2 × t, *J* 8.0 Hz, *m*-Ph), 7.27 (1H, m, *o*-ArF), [7.12, 7.10] (2H, 2 × s, *m*-SO₂Ar), 6.91 (2H, m, *m*-ArF), 5.98 (1H, m, CHCH₂O), [5.96, 5.90] (1H, 2 × dd, *J* 13.0, 3.5 Hz, SCH), [5.27, 5.21] (1H, 2 × ddd, 16.0, 13.0, 3.5 Hz, OCH₂), 4.68 (1H, ddd, *J* 16.0, 7.5, 4.5 Hz, OCH₂), 4.3 (2H, sept, *J* 6.5 Hz, *o*-ArCH), [3.54, 3.36] (1H, 2 × d, *J* 17.5 Hz, SCHCH₂), 2.88 (1H, sept, *J* 6.5 Hz, *p*-ArCH), 2.78 (1H, m, SCHCH₂) 1.27–1.12 (18H, m, CH(CH₃)₂); *δ*_C (100 MHz) 166.0, 165.9 (C=O), 161.0, 161.0, 160.9, 158.6, 158.5, 158.4 (CF), 152.3, 152.2, 149.3, 149.0, 137.1, 136.6, 134.9, 133.7, 133.6, (4°), 131.0, 130.9, 130.1, 130.0, 129.9 (CFCHCH), 128.9, 128.8, 127.9, 127.7, 123.5 (3°), 117.7, 117.6, 117.5, 117.4, 117.3, 117.2 (CCF), 112.0, 111.9, 111.7, 111.7 (CFCHCH), 66.0, 65.4 (SCH), 63.8, 63.7

(OCH₂), 34.1 (*p*-ArCH), 31.7, 30.5 (SCHCH₂), 29.3 (*o*-ArCH), 24.7, 24.5 (*o*-ArCH(CH₃)₂), 23.6 (*p*-ArCH(CH₃)₂); *m/z* (CI) 647 [M+NH₄]⁺, 603, 586, 425, 370, 352, 335, 301, 240 (Found [M+NH₄]⁺, 647.2405. C₃₃H₃₇F₂NO₅S₂ requires [M+NH₄]⁺, 647.2425) (Found: C, 62.83; H, 5.85; N, 2.15. C₃₃H₃₇F₂NO₅S₂ requires C, 62.94; H, 5.92; N, 2.22).

(S*_S,1R,2R)-S-(2-(2,6-Difluorophenyl)-2-vinylcyclopropyl)-S-phenyl-N-(2,4,6-triisopropylphenylsulfonyl)sulfoximine **24c**, (S*_S,1S,2S)-S-(2-(2,6-difluorophenyl)-2-vinylcyclopropyl)-S-phenyl-N-(2,4,6-triisopropylphenylsulfonyl)sulfoximine **25c**, (S*_S,1S,2R)-S-(2-(2,6-difluorophenyl)-2-vinylcyclopropyl)-S-phenyl-N-(2,4,6-triisopropylphenylsulfonyl)sulfoximine **26c**, and (S*_S,1R,2S)-S-(2-(2,6-difluorophenyl)-2-vinylcyclopropyl)-S-phenyl-N-(2,4,6-triisopropylphenylsulfonyl)sulfoximine **27c**



According to general procedure **H**, lactone **23c** (74 mg, 0.12 mmol, 1.0 equiv.) in DMF (0.6 mL) was treated with KOAc (1.2 mg, 0.012 mmol, 0.1 equiv.) and BSA (29 μ L, 0.12 mmol, 1.0 equiv.). Purification by chromatography (10–20% Et₂O–petrol) gave the sulfoximines **24c–27c** as a colourless gum (56 mg, 78%) as an inseparable mixture of diastereoisomers (ratio **24c:25c:26c:27c** = 49:11:36:4); *R_f* 0.75 (50% EtOAc–petrol); ν_{\max} (film) 2960, 2869, 1625, 1599, 1585, 1467, 1448, 1312, 1296, 1236, 1148, 1100, 1052, 1006, 910, 788, 772, 735, 684 cm⁻¹; δ_{H} (500 MHz) [8.09, 8.02] (2H, 2 \times d, *J* 7.5 Hz, *o*-Ph), 7.71–7.47 (m, Ph), 7.24 (m, Ph), [7.14, 7.08] (2H, 2 \times s, SO₂Ar), 6.84 (2H, t, *J* 8.0 Hz, *m*-ArF), 6.56 (1H, t, *J* 8.0 Hz, *p*-ArF), 6.42 (1H, dd, *J* 17.0, 10.5 Hz, CH=CH₂ **24c**), 6.11 (1H, dd, *J* 17.0, 10.5 Hz, CH=CH₂ **25c**), 5.62 (1H, dd, *J* 17.0, 10.5 Hz, CH=CH₂ **27c**), 5.59 (1H, dd, *J* 17.0, 10.5 Hz, CH=CH₂ **26c**), 5.18 (1H, d, *J* 10.5 Hz, CH=CH₂ *cis* **24c**), 5.10 (1H, d, *J* 10.5 Hz, CH=CH₂ *cis* **27c**),

5.09 (1H, d, *J* 10.5 Hz, CH=CH₂ *cis* **25c**), 5.06 (1H, d, *J* 10.5 Hz, CH=CH₂ *cis* **26c**), 4.87 (1H, d, *J* 17.0 Hz, CH=CH₂ *trans* **27c**), 4.80 (1H, d, *J* 17.0 Hz, CH=CH₂ *trans* **26c**), 4.70 (1H, d, *J* 17.0 Hz, CH=CH₂ *trans* **24c**), 4.55 (1H, d, *J* 17.0 Hz, CH=CH₂ *trans* **25c**), [4.44, 4.39, 4.30] (2H, 3 × sept, *J* 6.5 Hz, *o*-ArCH), [3.40, 2.94, 2.82] (1H, 3 × m, SCH), 2.91 (1H, sept, *J* 6.5 Hz, *p*-ArCH), [2.51, 2.38] (1H, 4 × dd, *J* 6.5, 6.5 Hz, SCHCH₂), [2.11, 1.82] (1H, 2 × dd, *J* 9.0, 7.0 Hz, SCHCH₂), 1.30–1.19 (18H, m, CH(CH₃)₂); δ_C (125 MHz) 162.4, 162.4, 160.4, 160.4 (CF), 151.8, 149.3, 149.0, 139.8, 137.8, 137.7, 137.6, 137.1 (4°), 133.8, 133.3 (CH=CH₂), 129.2, 128.9, 128.4, 127.7, 123.3, 123.2, 123.2 (3°), 130.2, 130.1, 130.0, 129.9, 129.8, 129.7 (CFCHCH), 118.3, 115.5 (CH=CH₂), 112.2, 112.0, 111.8, 111.6, 111.2, 111.0 (CFCHCH), 49.2, 46.0 (SCH), 34.1 (*p*-ArCH), 29.8, 29.7, 29.5, 29.3, 29.2, 29.1 (*o*-ArCH), 24.9, 24.7, 24.7, 24.6, 24.6, 23.8, 23.8, 23.7, 23.6 (CH(CH₃)₂), 20.2, 18.5, 18.4 (SCHCH₂); *m/z* (CI) 603 [M+NH₄]⁺, 586, 425 (Found [M+H]⁺, 586.2255. requires [M+H]⁺, 586.2261).

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