The conformational bias of aryl, arylsulfonyl geminally substituted tertiary carbon centers: applications in substrate-based stereocontrol†

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Intramolecular nitrile oxide–olefin cycloaddition to form hexahydrobenzisoxazole **14**, which engenders a phenylsulfonyl, 2,5-difluorophenyl geminally substituted carbon substructure, proceeds with up to 99% ds. A rationalization of the high level of substrate-based stereo-induction observed in this and related ketone and acrylonitrile metallohydride reductions, supported by single crystal X-ray crystallography, is presented.

Introduction

As part of a programme at Merck Research Laboratories directed toward the identification of γ-secretase inhibitors,[1] we have prepared a number of cyclohexane derivatives **1** bearing a common structural motif, in which one of the six membered ring carbons is geminally substituted with an aryl and arylsulfonyl moiety (Fig. 1). During the course of our synthesis of these derivatives, we encountered a number of substrate-controlled diastereoselective transformations in which unanticipated high levels of stereo-induction were observed. Herein we document our observations and propose a rationalization for the observed stereochemical outcomes.

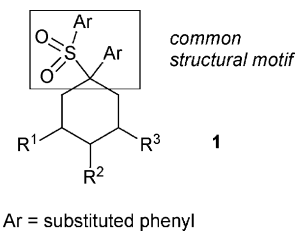
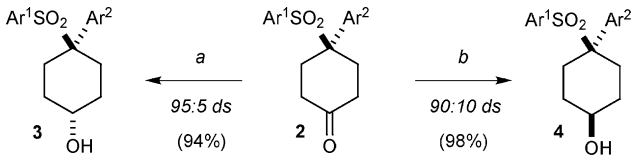


Fig. 1

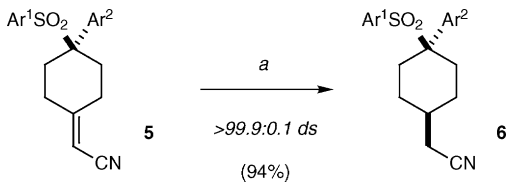
Results and discussion

The 4-[4-(chlorophenyl)sulfonyl]-4-(2,5-difluorophenyl)cyclohexanone **2** served as a key intermediate through which structure–activity relationships were explored (Scheme 1). Early in our synthetic studies, we examined metallohydride reductions of **2** and found that using $NaBH_4$ in EtOH at −10 °C, the



Scheme 1 *Reagents and conditions*: (a) $NaBH_4$, EtOH, −10 °C; (b) L-Selectride®, THF, −70 °C; H_2O_2, NaOH, NaCl, H_2O, 5 °C. Ar^1 = 4-chlorophenyl; Ar^2 = 2,5-difluorophenyl.

trans-cyclohexanol product **3** was obtained preferentially with 95% ds (94% yield).[2] Switching to the sterically encumbered L-Selectride® reagent[3] the sense of induction was reversed, affording the *cis*-cyclohexanol **4** preferentially with 90% ds (98% yield). By way of comparison, sodium borohydride reduction of 4-(*tert*-butyl)cyclohexanone has been reported to afford 87% ds (0 °C, MeOH) favoring the *trans* 4-(*tert*-butyl)cyclohexanol (axial hydride addition)[4] whilst L-Selectride® (−78 °C, THF) favored the *cis* diastereomer to the extent of 97% ds (equatorial hydride addition).[3] Reduction of exocyclic acrylonitrile derivative **5** provides a further example of the influence of the geminal aryl, arylsulfonyl substructure on hydride reduction stereochemistry (Scheme 2). Under the optimized conditions which use a reaction temperature of −60 °C, L-Selectride® reduction proceeds in a conjugate manner to afford the desired *cis* diastereomer **6** with >99.9 ds (94% yield). Moreover, even at $T \leq -10$ °C the diastereoselection remains >99 : 1.[5]



Scheme 2 *Reagents and conditions*: (a) L-Selectride®, THF, $-60 < T < -55$ °C; H_2O_2, NaOH, NaCl, H_2O, 5 °C. Ar^1 = 4-chlorophenyl; Ar^2 = 2,5-difluorophenyl.

The stereochemical course of the hydride reductions of **2** and **5** is consistent with the rationale that the most reactive conformers populated in solution have the 4-chlorophenylsulfonyl

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† Electronic supplementary information (ESI) available: stereochemical assignments of **9**, **10** and **14** and the single crystal X-ray structures of **2** and **4** (CIF files). Copies of ^1H and ^{13}C spectra for **3**, **10** and **12**. See DOI: 10.1039/b601647b

group preferentially adopting an equatorial orientation on the substituted cyclohexane ring, whilst the 2,5-difluorophenyl group is axial. The sense of diastereocontrol is then dictated by the steric bulk of the hydride source employed.[6] The single crystal X-ray structure[7] of cyclohexanone **2** supports this rationale (Fig. 2), with the cyclohexanone ring having a slightly distorted chair conformation in which the 4-chlorophenyl ring of the equatorial sulfone moiety effectively stacks with the axial 2,5-difluorophenyl ring. The latter ring exposes the π-surface toward the cyclohexanone ring, thereby minimizing steric interactions of the *ortho*-hydrogen and fluorine with the *syn* axial hydrogens. The X-ray structure of *cis*-cyclohexanol **4**, which confirms the relative stereochemical outcome of the hydride reductions of **2**, demonstrates a similar axial/equatorial conformational preference for the 2,5-difluorophenyl and 4-chlorophenylsulfonyl substituents in the solid state.[7]

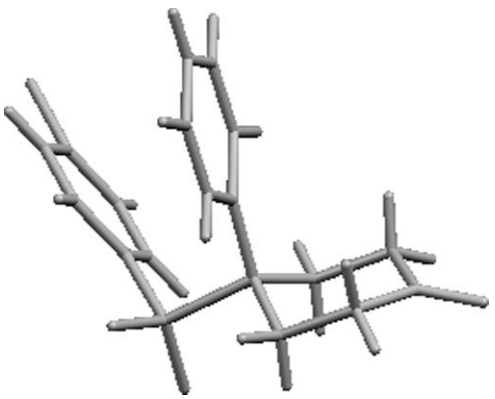
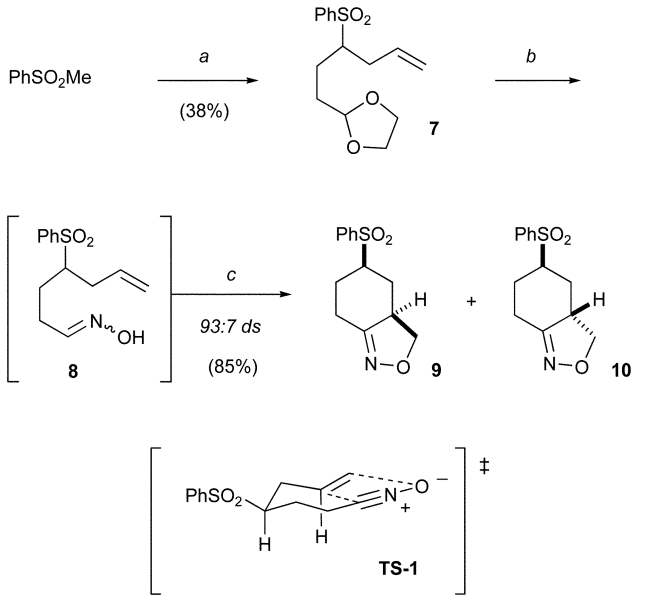


Fig. 2 X-Ray structure of cyclohexanone **2** (CCDC 236716).

We were intrigued as to whether the conformational bias apparently operative in the hydride reductions of **2** and **3** could be extended to control the diastereoselection of a 5-hexenyl intramolecular nitrile oxide–olefin cycloaddition.[8,9] Initially we examined the cycloaddition sequence to prepare isoxazoline **9** (Scheme 3) in which the stereo-induction afforded by an isolated phenylsulfonyl group was evaluated. The required cycloaddition precursor **7** was prepared by one-pot dialkylation of phenylmethylsulfone using LHMDS in successive deprotonations with 2-(2-bromoethyl)-1,3-dioxolane and allyl bromide as the required alkylating agents. Although overalkylation was a significant competitive pathway,[10] the required sulfone **7** could be isolated in 38% yield following chromatography. Exposure of **7** to hydroxylamine hydrochloride in a 1 : 1 CH_3CN–H_2O mixture at 60 °C then allowed dioxolane deprotection and formation of the oximes **8** (1 : 1 *E* : *Z*), avoiding the necessity for isolation of the intermediate primary aldehyde. These oximes were also not isolated but directly oxidised with chloramine-T[11] to effect nitrile oxide formation and [3 + 2] dipolar cycloaddition. Temperature was found to impact the observed diastereoselection in the formation of isoxazolines **9** and **10** (Table 1) and a preparative run at 5 °C afforded 93 : 7 ds (85% yield). The relative stereochemistries of these isoxazolines were secured by NOE studies (see Supporting Information†) and are consistent with the phenylsulfonyl group occupying a pseudo-equatorial orientation in preferred transition state **TS-1**, thereby leading to **9** as the major diastereomeric product (Scheme 3).



Scheme 3 *Reagents and conditions*: (a) LHMDS, 2-(2-bromoethyl)-1,3-dioxolane, THF, DMPU, 0 → 25 °C; LHMDS, allyl bromide, 0 → 25 °C. (b) $NH_2OH.HCl$, CH_3CN, H_2O, 60 °C. (c) Chloramine-T, 5 °C.

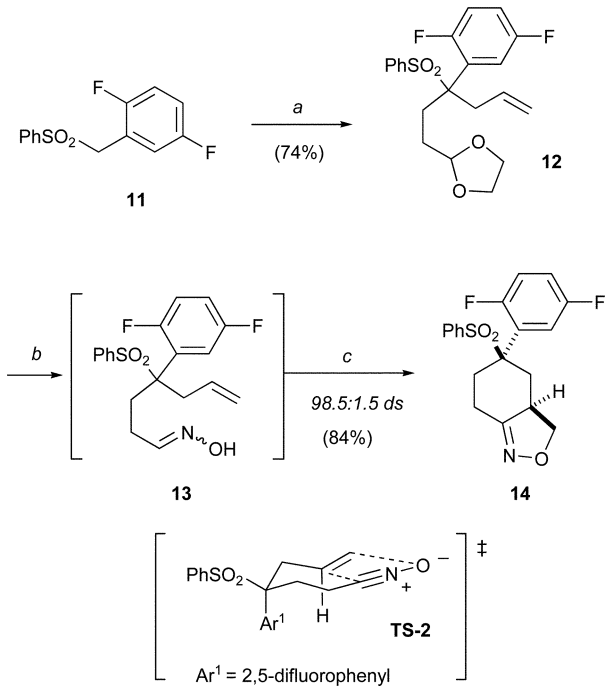
Next we examined the impact of the introduction of a geminal 2,5-difluorophenyl group onto sulfone **7** which would lead eventually to isoxazoline **14** (Scheme 4). The required dioxolane **12** for the cycloaddition sequence was prepared by sequential alkylations of 2,5-difluorobenzyl phenyl sulfone **11**[12] using LHMDS as base, in an analogous manner to **7**. In this instance, the addition of DMPU was found to be beneficial to obtaining high conversion in the second alkylation with allyl bromide and the sterically congested tertiary sulfone **12** could be isolated in 74% yield. Exposure of **12** to hydroxylamine hydrochloride in a 1 : 1 CH_3CN–H_2O mixture at 60 °C then allowed deprotection and formation of the oximes **13** (1 : 1 *E* : *Z*) within 4 h. These underwent oxidation and [3 + 2] ring closure on addition of chloramine-T, with a preparative run at 25 °C affording isoxazoline **14** in 84% yield. Strikingly, the cycloaddition diastereoselection increased with the introduction of the additional geminal 2,5-difluorophenyl moiety, with isoxazoline **14** formed with up to 99% ds (Table 1). The relative stereochemistry of **14** was secured by NOE studies (see Supporting Information†) and is consistent with a cycloaddition proceeding by way of **TS-2** (Scheme 4).[13]

The additivity of conformational energies or *A* values ($-\Delta G^\circ$) in geminally substituted cyclohexanes is generally unreliable due to

Table 1 Temperature dependence of diastereoselection in cycloadditions to form **9** and **14**

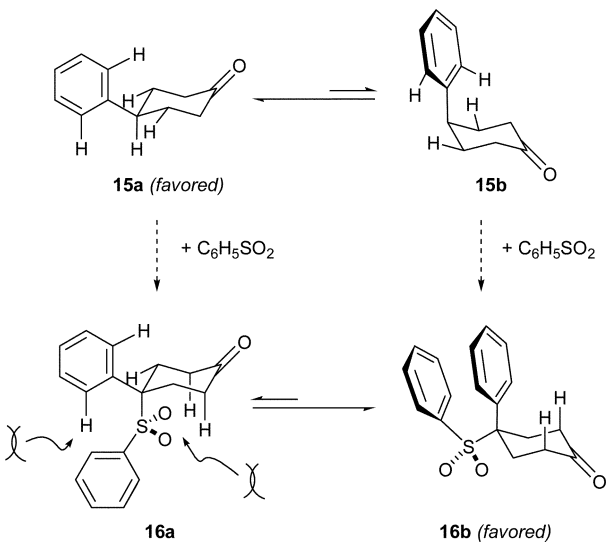
Cycloadduct	Temp/°C[a]	Diastereoselectivity[b]
9	5	93 : 7
9	25	90 : 10
9	50	90 : 10
14	5	99 : 1
14	25	98.5 : 1.5
14	50	96 : 4

[a] Temperature at which chloramine-T was added. [b] Determined by reverse phase HPLC analysis of unpurified reaction mixtures.



Scheme 4 *Reagents and conditions*: (a) LHMDS, 2-(2-bromoethyl)-1,3-dioxolane, THF, −10 → 25 °C; LHMDS, allyl bromide, THF, DMPU, −10 → 25 °C. (b) $NH_2OH.HCl$, CH_3CN, H_2O, 60 °C. (c) Chloramine-T, 25 °C.

steric interactions of the two substituents not otherwise present in the monosubstituted parents. A well-documented example is provided by 1-methyl-1-phenylcyclohexane,[14] where the axial phenyl-equatorial methyl is preferred by 0.32 kcal mol^{-1}, in spite of the individual conformational values for methyl (1.74 kcal mol^{-1} at 300 K)[14a] and phenyl (2.87 kcal mol^{-1} at 173 K).[15] The *A* value for phenylsulfonyl is reported to be 2.94 kcal mol^{-1} at 298 K,[16] comparable to that of phenyl. Considering the effect of the introduction of a phenylsulfonyl group onto the parent 4-phenylcyclohexanone conformers **15a** and **15b** (Scheme 5), in which conformer **15a** is favored,[14,17] the origins of the underlying



Scheme 5

bias toward conformer **16b** becomes evident. The alternative cyclohexane chair conformation **16a** engenders a number of energetically unfavorable interactions, notably the oxygen-inside interaction with the *syn* axial hydrogens required for the sulfone to occupy the axial orientation. This interaction has been attributed a value of *ca.* 1.6 kcal mol^{-1}.[16] Eclipsing interactions of the two aryl rings are also inevitable if the equatorial phenyl ring in **16a** is to maintain the otherwise preferred parallel alignment with the symmetry plane of the cyclohexanone ring.[18] A similar argument can be applied to rationalize the cycloaddition diastereoselection to form **14**.

In summary, we have found that cyclohexanone **2** and acrylonitrile **5** undergo stereocontrolled metallohydride reductions consistent with the population of conformers in solution having a strong bias for the 4-chlorophenylsulfonyl moiety to sit equatorial, with the 2,5-difluorophenyl substituent axial. This conformational bias is supported by the observed single crystal X-ray crystallographic structures[7] of cyclohexanone **2** and *cis*-cyclohexanol **4** and was found to extend to controlling the relative stereochemical outcome of an intramolecular nitrile–oxide olefin cycloaddition, affording isoxazoline **14** with up to 99% ds. The geminal aryl, arylsulfonyl moiety can thus be considered to behave analogously to the well-documented conformational biasing ability of a *tert*-butyl group. Further examples and applications of this stereochemical control element encountered in our studies will be reported in due course.

Experimental

Commercially available materials were used without further purification. Full preparative and characterisation data for **2**, **5** and **6** will be reported elsewhere.

trans-4-[4-(Chlorophenyl)sulfonyl]-4-(2,5-difluorophenyl)cyclohexanol 3

To a stirred solution of sodium borohydride (3.9 g, 104 mmol) in EtOH (200 mL) at −10 °C was added 4-[4-chlorophenyl)sulfonyl]-4-(2,5-difluorophenyl)cyclohexanone **2** (20.0 g, 52.0 mmol) portion wise such that $T \leq 0$ °C. The reaction mixture was aged for 2 h and then quenched by addition of 2 M HCl (50 mL). Water (250 mL) and IPAc (200 mL) were added and the layers cut. Filtration of the organic layer through a silica gel plug (using IPAc as eluant) afforded the title compound (18.8 g, 94%) as a white solid as a 95 : 5 mixture with **4**. A diastereomerically pure sample of **3** could be obtained by further crystallisation from IPAc; mp 156–158 °C (from IPAc); ^{1}H NMR (400 MHz, d_6-DMSO, 328 K) δ 7.65–7.55 (2 H, m), 7.43–7.38 (2 H, m), 7.35–7.28 (1 H, m), 7.20–7.12 (2 H, m), 4.41 (1 H, d, *J* 5.0), 3.59–3.45 (1 H, m), 2.79–2.65 (2 H, m), 2.05–1.85 (4 H, m), 1.05–0.95 (2 H, m); ^{13}C NMR (100 MHz, d_6-DMSO, 328 K) δ 159.2 (d, *J* 245), 158.6 (d, *J* 248), 140.0, 134.3, 132.1, 129.5, 121.7 (dd, *J* 7.0 and 11.4), 119.4 (dd, *J* 4.0 and 25.0), 119.2 (dd, *J* 9.0 and 17.0), 118.9–118.4 (m, 2C), 70.7 (d, *J* 4.0), 68.2, 31.6, 28.7 (d, *J* 6.0); HRMS (ES) Calcd. for $C_{18}H_{21}ClF_2NO_3S$ (M + NH_4) 404.0899. Found 404.0891.

cis-4-[4-(Chlorophenyl)sulfonyl]-4-(2,5-difluorophenyl)cyclohexanol 4

To a stirred solution of 4-[4-chlorophenyl)sulfonyl]-4-(2,5-difluorophenyl)cyclohexanone **2** (2.0 g, 5.2 mmol) in THF (14 mL)

at −70 °C was added L-Selectride® (1 M in THF, 8.3 mL, 8.3 mmol) dropwise over 30 min. The mixture was aged for 2 h and then NaCl (1.5 g) in H_2O (8.4 mL) added dropwise followed by 48% NaOH (8 drops). 27% Aq. H_2O_2 (3.4 mL) was then added at $T < 5$ °C and the mixture warmed to ambient and aged 30 min. A solution of sodium metabisulfite (1.2 g) in H_2O (10.4 mL) was then added dropwise ($T < 25$ °C) and aged for 1 h. IPAc (24 mL) was added and the layers cut. Brine (10% aq., 14 mL) was added and the layers were separated. The organics were concentrated *in vacuo* and then passed through a plug of silica gel using CH_2Cl_2 and IPAc as eluants. Evaporation *in vacuo* afforded the title compound as a 90 : 10 diastereomeric mixture of **4** and **3** respectively (1.97 g, 98%). Crystallisation from IPAc–heptane afforded diastereomerically pure **4** for analytical purposes (Found: C, 55.83; H, 4.36. $C_{18}H_{17}ClF_2O_3S$ requires C, 55.89; H, 4.43%); mp 183–184 °C (from IPAc–heptane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.38 (4 H, s), 7.14–7.02 (2 H, m), 6.92–6.83 (1 H, m), 3.94 (1 H, t, *J* 2.7), 2.90–2.20 (4 H, m), 1.92–1.78 (3 H, m), 1.52–1.35 (2 H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1 (d, *J* 245), 158.6 (d, *J* 242), 140.8, 133.6, 131.7, 128.8, 121.0, 119.1 (dd, *J* 4.2 and 25.3), 118.2 (dd, *J* 9.9 and 24.0), 70.9 (d, *J* 4.1), 63.9, 29.3, 23.7 (d, *J* 6.8).

2-[3-(Phenylsulfonyl)hex-5-en-1-yl]-1,3-dioxolane 7

A stirred solution of phenyl methyl sulfone (3.0 g, 19.2 mmol) in THF (9 mL) and DMPU (3.6 mL) was cooled to 0 °C. LHMDS (1 M in THF, 21.1 mL, 21.1 mmol) was added dropwise over 15 min at $T < 2$ °C. The resulting solution was stirred for 10 min and then 2-(2-bromoethyl)-1,3-dioxolane (2.42 mL, 20.1 mmol) added dropwise over 10 min at $T < 5$ °C. The mixture was then warmed to ambient and aged 1 h before recooling to −20 °C. LHMDS (1 M in THF, 21.1 mL, 21.1 mmol) was added dropwise over 5 min and the mixture aged for 10 min. Allyl bromide (2.50 mL, 28.8 mmol) was added in one portion and the mixture warmed to ambient and aged 1 h. H_2O (45 mL) and IPAc (135 mL) were added and the layers partitioned. The organics were washed with H_2O (3 × 20 mL) and then evaporated *in vacuo.* Purification by silica gel chromatography (34 : 66 heptane–ethyl acetate) afforded the title compound (2.14 g, 38%) as a pale yellow oil (Found C, 60.75; H, 6.80. $C_{15}H_{20}O_4S$ requires C, 60.79; H, 6.80%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79–7.76 (2 H, m), 7.56–7.53 (1H, m), 7.47–7.43 (2 H, m), 5.63 (1 H, ddt, *J* 7.1 and 9.8 and 18.9), 4.99–4.92 (2 H, m), 4.66 (1 H, t, *J* 4.0), 3.80–3.62 (4 H, m), 3.09–3.02 (1H, m), 2.55–2.46 (1H, m), 2.27–2.17 (1H, m), 1.89–1.79 (1 H, m), 1.79–1.69 (1H, m), 1.69–1.58 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.7, 133.7, 133.3, 129.1, 128.8, 118.3, 103.6, 64.8, 63.2, 32.2, 30.1, 21.4.

cis-5-(Phenylsulfonyl)-3,3a,4,5,6,7-hexahydro-2,1-benzisoxazole 9

To a stirred solution of sulfone **7** (1.0 g, 3.4 mmol) in CH_3CN (12.5 mL) and H_2O (12.5 mL) was added $NH_2OH{\cdot}HCl$ (0.47 g, 6.8 mmol) and the mixture aged at 60 °C for 2 h. The mixture was then cooled to 5 °C and chloramine-T trihydrate (1.81 g, 6.4 mmol) added in one portion. After aging at this temperature for 2.5 h, H_2O (25 mL) was added and the CH_3CN evaporated *in vacuo.* IPAc (60 mL) was added and the layers partitioned. The organics were washed with NaOH (0.66 M, 12 mL), H_2O (60 mL) and evaporated *in vacuo.* Purification by silica gel chromatography (50 : 50 heptane–IPAc) afforded the title compound as a 90 : 10 mixture of **9** and **10**, respectively (0.76 g, 85% combined yield). Data for **9**: Found 58.60; H, 5.67; N 5.21. $C_{13}H_{15}NO_3S$ requires C, 58.85; H, 5.70; N 5.28%; mp 128–129 °C (from IPAc–heptane); ^{1}H NMR (400 MHz, C_6D_6) δ 7.72–7.68 (2 H, m), 7.03–6.93 (3 H, m), 3.89 (1 H, dd, *J* 8.3 and 10.4), 3.22 (1 H, dd, *J* 8.3 and 10.3), 2.51 (1 H, m), 2.43–2.36 (1 H, m), 2.22–2.11 (1 H, m), 2.05–1.98 (1 H, m), 1.91–1.84 (1 H, m), 1.35 (1 H, ddt, *J* 1.2 and 5.2 and 13.4 Hz), 1.32–1.17 (1 H, m), 1.16–1.06 (1 H, m); ^{13}C NMR (100 MHz, C_6D_6) δ 156.1, 137.8, 133.5, 129.2, 129.1, 73.0, 61.2, 46.7, 30.9, 25.8, 22.9.

2-[3-Phenyl-3-(2,5-difluorophenylsulfonyl)hex-5-en-1-yl]-1,3-dioxolane 12

A slurry of 2,5-difluorobenzyl phenyl sulfone **11**[12] (4.0 g, 14.9 mmol) in THF (10 mL) was cooled to −10 °C and LHMDS (1 M in THF, 19.4 mL, 19.4 mmol) added over 5 min. The resultant solution was aged 10 min. and then 2-(2-bromoethyl)-1,3-dioxolane (2.98 g, 16.4 mmol) added dropwise over 2 min. The solution was aged at ambient for 12 h and then quenched with H_2O (100 mL). IPAc (100 mL) was added and the layers partitioned. The organic layer was evaporated *in vacuo* and the residue dissolved in THF (12 mL) and DMPU (4 mL). This solution was cooled to −10 °C and LHMDS (1 M in THF, 19.4 mmol, 19.4 mL) added over 5 min. After aging 5 min, allyl bromide (1.81 mL, 20.9 mmol) was added and the mixture warmed to ambient and aged 0.5 h prior to quenching with H_2O (150 mL). IPAc (150 mL) was added and the layers partitioned. The organic layer was washed with H_2O (2 × 150 mL), concentrated *in vacuo* and the residue purified by silica gel chromatography (70 : 30 heptane–IPAc) to afford the title compound (4.51 g, 74%) as a colourless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61–7.55 (1 H, m), 7.42–7.35 (4 H, m), 7.05–6.95 (2 H, m), 6.85–6.75 (1 H, m), 5.97–5.86 (1 H, m), 5.28–5.13 (2 H, m), 4.88 (1 H, t, *J* 4.4), 3.98–3.91 (2 H, m), 3.90–3.82 (2 H, m), 3.30–3.23 (1H, m), 3.15–3.05 (1 H, m), 2.55–2.45 (2 H, m), 2.05–1.95 (1 H, m), 1.60–1.50 (1 H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.3 (2C, d, *J* 246 Hz), 135.2, 133.9, 132.3, 130.3, 128.4, 123.5 (dd, *J* 8.0 and 13), 119.4, 118.7 (dd, *J* 4.3 and 26), 117.9 (dd, *J* 8.5 and 29), 117.5 (dd, *J* 9.9 and 24), 103.8, 71.6, 65.0 (d, *J* 6.3), 36.3 (d, *J* 6.9), 28.3, 25.7 (d, *J* 5.4); HRMS (ES) Calcd. for $C_{21}H_{22}F_2O_4NaS$ (M + Na) 431.1105. Found 431.1100.

cis-5-Phenyl-5-(2,5-difluorophenylsulfonyl)-3,3a,4,5,6,7-hexahydro-2,1-benzisoxazole 14

To a stirred solution of sulfone **12** (2.74 g, 6.7 mmol) in CH_3CN (5 mL) and H_2O (5 mL) was added $NH_2OH{\cdot}HCl$ (0.93 g, 13.4 mmol) and the mixture aged at 60 °C for 4.5 h. After cooling to 25 °C, chloramine T monohydrate (2.9 g, 12.8 mmol) was added and the mixture aged for 1 h at this temperature. The CH_3CN was removed *in vacuo* and then IPAc (150 mL) and aq. NaOH (2 M, 50 mL) added. The layers were partitioned and the organic washed with aq. NaOH (2 M, 50 mL) and H_2O (50 mL). The organics were concentrated *in vacuo* and the residue crystallised from IPAc and heptane to afford the title compound (2.13 g, 84%) as a white solid (Found: C, 60.30; H, 4.52, N 3.58. $C_{19}H_{17}F_2NO_3S$ requires C, 60.47; H, 4.54, N 3.71); mp 188–190 °C (from IPAc–heptane);

^{1}H NMR (600.1 MHz, d_7-DMF, 350 K) δ 7.77 (1 H, m), 7.58 (2 H, m), 7.52 (2 H, m), 7.35–7.30 (2 H, m), 7.16 (1 H, ddd, *J* 13.6 and 9.1 and 4.9), 4.50 (1 H, dd, *J* 9.8 and 7.9), 3.87 (1 H, dd, *J* 10.2 and 7.9), 3.32–3.22 (2 H, m), 3.17 (1 H, m), 2.84 (1 H, m), 2.23–2.15 (2 H, m), 2.09 (1 H, td, *J* 12.5 and 1.9); ^{13}C NMR (150.9 MHz, d_7-DMF, 350 K) δ 159.38 (dd, *J* 247.8 and 2.4), 158.96 (dd, *J* 241.1 and 2.4), 157.36, 135.35, 134.61, 130.44, 129.17, 120.74 (dd, *J* 11.6 and 7.3), 119.37 (dd, *J* 26.2 and 4.3), 118.90 (dd, *J* 29.3 and 8.5), 118.59 (dd, *J* 23.8 and 10.4),73.03, 70.62 (d, *J* 4.3), 45.33, 35.54 (d, *J* 6.1), 30.72 (d, *J* 7.3), 21.33.

Crystal structure determination of compounds 2 and 4

Single crystals of cyclohexanone **2** suitable for X-ray diffraction were obtained from IPAc–heptane and for cyclohexanol **4** from acetonitrile.

Crystal data for 2. $C_{18}H_{15}ClF_2O_3S$, $M = 384.81$, orthorhombic, $a = 15.450(10)$, $b = 10.490(7)$, $c = 10.828(7)$ Å, $U = 1755(2)$ Å^3, $T = 298(2)$ K, space group $Pca2(1)$, $Z = 4$, $\mu = 0.371$ mm^{-1}, 13 312 reflections measured, 3373 unique ($R_{int} = 0.1182$) which were used in the calculations. The final w$R(F^2)$ was 0.1225 (all data). CCDC 236717. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b601647b.

Crystal data for 4. $C_{18}H_{17}ClF_2O_3S$, $M = 386.83$, monoclinic, $a = 6.9274(5)$, $b = 8.4158(6)$, $c = 29.301(2)$ Å, $U = 1706.3(2)$ Å^3, $T = 223(2)$ K, space group $P2_1/c$, $Z = 4$, $\mu = 0.382$ mm^{-1}, 17 593 reflections measured, 3513 unique ($R_{int} = 0.0271$) which were used in the calculations. The final w$R(F^2)$ was 0.1054 (all data). CCDC 600829. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b601647b

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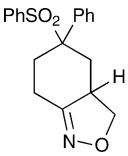

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