Friedel–Crafts reactions of a sulfonyl-substituted vinylic epoxide with various aromatics

Svante Brandänge,* Jan-Erling Bäckvall and Hans Leijonmarck

Department of Organic Chemistry, Arrhenius Laboratory, Stockholm University, SE-l06 91 Stockholm, Sweden

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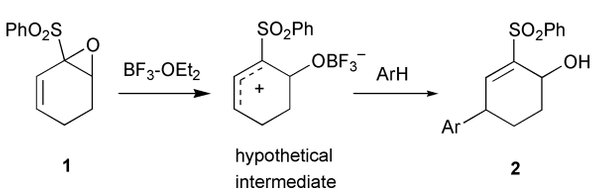
The phenylsulfonyl-substituted vinylic epoxide **1** was allowed to react with $BF_3{\cdot}OEt_2$ and various aromatics. A highly regioselective but moderately stereoselective mono-Friedel–Crafts reaction occurred which led to products **2** (Table 1). The fluorine-containing compounds **3a**–**b** and **4** were obtained as side products.

Introduction

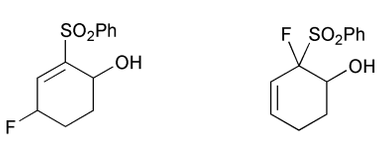
On treatment with a Brønsted acid, or preferably a Lewis acid, an epoxide can be transformed into a carbonyl compound with a concomitant 1,2-shift of one of the groups bonded to the epoxide ring carbons.[1] With α,β-epoxysulfones a migration of the sulfonyl group can occur.[2] On the other hand, in vinylic epoxides (*i.e.* monoepoxides of 1,3-dienes) the double bond could be expected to stabilize an incipient carbocation and thus govern the regioselectivity of the rearrangement.

Results and discussion

In compound **1**, available in two steps from cyclohexa-1,3-diene,[3] the two rearrangement modes are in conflict. To find out which reaction mode predominates we treated epoxide **1** with boron trifluoride–diethyl ether ($BF_3{\cdot}OEt_2$, 1 equiv., 20 °C) in benzene. ^{1}H NMR analysis of the reaction product mixture showed that the major reaction of **1** was not a rearrangement but instead a reaction with benzene (Scheme 1). A mixture of *cis* and *trans* isomers of compound **2a** (Ar = Ph, *cis* : *trans*, 20 : 80) was obtained in an isolated yield of 47%. The main side products were diphenyl sulfone (14%) and the fluoro alcohol **3** (9%; 80 : 20 mixture of stereoisomers; see *e.g.* ref. 1*b* for the formation of fluorohydrins from epoxides). A plausible mechanism involves BF_3-induced epoxide ring opening to form a sulfonyl-substituted allylic cation, or a related polarised complex, which then reacts in a Friedel–Crafts[4] manner with benzene. All three product types are possibly formed *via* the same intermediate; a plausible route to diphenyl sulfone involves deprotonation of the intermediate to form a sulfonyl-substituted cyclohexadienol followed by acid-catalysed elimination of water.

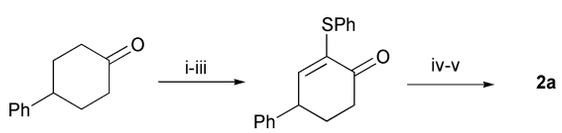


Scheme 1



3a-b **4**

A reaction between **1**, benzene and $BF_3{\cdot}OEt_2$ which was started at −78 °C (DCM–benzene 5 : 1; w : w) and finally kept at −16 °C for 20 h did not give a higher yield of **2a** but more **3**. The stereoselectivity was slightly increased and now the *cis* : *trans* ratio of **2a** was 15 : 85 according to HPLC and ^{1}H NMR. The use of less than 1 equiv. of $BF_3{\cdot}OEt_2$ also worked well but led to the formation of more of the side products (TLC). The structure of **2a** was confirmed by an independent synthesis (Scheme 2) which gave a mixture of isomers similar to that obtained in the Friedel–Crafts reaction. Compound **2a** and its aryl analogues are air-sensitive compounds.



Scheme 2 *Reagents*: i, Me_3SiCl, DBU; ii, PhSOCl, $SnCl_4$; iii, Ac_2O, $MeSO_3H$; iv, $LiAlH_4$; v, MCPBA. The *cis* : *trans* ratio of **2a** was 30 : 70.

Analysis of the ^{1}H NMR spectra of the two isomers **2a** indicates that the major isomer has the *trans* and the minor isomer the *cis* configuration. The latter shows (after shaking with D_2O) a triplet at δ 4.39 (C*H*OH, *J* 2.8 Hz) and a triplet at δ 3.47 (C*H*Ph, *J* 8.0 Hz). These values are indicative of a dominant half-chair conformation in which the OH group occupies a pseudo-axial position and the phenyl group a pseudo-equatorial position (thus *cis*). Electron-attracting allylic substituents in the cyclohexene ring are known to prefer the pseudo-axial position.[5] In the major isomer the C*H*OH signal is at δ 4.46 (t, *J* 4.4 Hz) and the C*H*Ph signal at δ 3.75 (q, *J* 4.8 Hz). The values of *J* for this isomer (*trans*) indicate that the two half-chair conformations are more equally represented. Support for these stereochemical assignments was obtained from a reaction between **1** and lithium diphenylcuprate (1.1 equiv., from 0 to 22 °C, 1 h, Et_2O). The reaction afforded **2a** as an essentially pure stereoisomer (*ca.* 20% yield) together with other, unidentified products (full conversion of **1**). This stereoisomer is identical to the one which had been ascribed the *trans* configuration in the ^{1}H NMR analysis. It is the expected stereoisomer in the diphenylcuprate reaction since the S_N2' reaction of cyclohexa-1,3-diene monoepoxide with lithium diphenylcuprate is known to give *trans*-4-phenylcyclohex-2-en-1-ol.[6] A palladium-catalysed reaction with a phenylstannane also leads to this isomer.[7]

The results from reactions between **1** and various aromatic compounds are given in Table 1. The aromatics used here are cheap compounds that were used in large excess in order to favour the 1 : 1 reaction product. Electron-rich aromatics such

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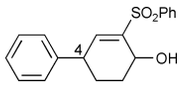
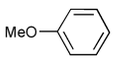
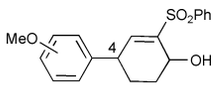
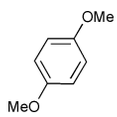
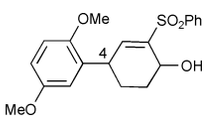
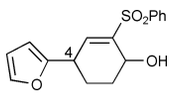
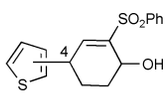
Table 1 Products obtained in the Friedel–Crafts reactions of sulfonyl epoxide **1** with $BF_3{\cdot}OEt_2$ and various aromatic compounds

Aromatic compound used	Product **2**	Yield of **2** (%)	^{1}H NMR data for C(4)H	Isomer ratios[a]	Structure assignments
		47	δ 3.75; q; J 4.8 δ 3.47; t; J 8.1	80 20	*trans*-**2a** *cis*-**2a**
		69	δ 4.11; q; J 4.6 δ 3.89; t; J 8.1 δ 3.70; q; J 4.6 δ 3.42; t; J 8.1	35 25 25 15	*ortho*-*trans*-**2b** *ortho*-*cis*-**2b** *para*-*trans*-**2b** *para*-*cis*-**2b**
		65	δ 4.09; q; J 4.9 δ 3.86; t; J 7.1	60 40	*trans*-**2c** *cis*-**2c**
		55	δ 3.84; m; $W_{1/2}$ ~9.5 Hz δ 3.61; t; J 7.5	70 30	2-furyl-*trans*-**2d** 2-furyl-*cis*-**2d**
		42	δ 4.05; q; J 3.9 δ 3.85; q; J 4.5 δ 3.79; t; J 7.7 δ 3.62; t; J 7.7	55 20 20 5	2-thienyl-*trans*-**2e** 3-thienyl-*trans*-**2e** 2-thienyl-*cis*-**2e** 3-thienyl-*cis*-**2e**

[a] ^{1}H-NMR ratios, except for **2b** (HPLC); numbers are given as multiples of 5.

as anisole and 1,4-dimethoxybenzene reacted well with **1** (Table 1); small amounts of diphenyl sulfone (5–6%) were also obtained. Anisole gave four isomeric products, **2b**. Two of these showed a ^{1}H NMR signal from the benzylic hydrogen, C(4)H, which was similar to the corresponding signals from the two isomers of **2a** (Table 1). The signals from C(4)H in the other two isomers are similar to the corresponding signals from compound **2c** (which has an *ortho*-methoxylated aryl substituent). From these similarities (Table 1) it was concluded that the former two are the *para* and the latter two the *ortho* isomers. There was a preponderance of *ortho* substitution products (o : p, 60 : 40), which is typical for kinetically controlled Friedel–Crafts alkylations of anisole.[8]

Furan is an acid-sensitive aromatic which cannot be alkylated using classical Friedel–Crafts conditions.[9] Accordingly, a reaction with furan, performed as above, led to large amounts of side products. It appeared necessary to neutralise strongly acidic components. A mixture of **1**, *N*-ethyldiisopropylamine and $BF_3{\cdot}OEt_2$ in the molar ratios 1 : 2.1 : 1.1 proved useful for the conversion of furan into **2d**. Two strongly dominating isomers were obtained; these were assumed to be 2-substituted furans in analogy with other reactions of furan.

Thiophene reacted well without added amine and gave four product isomers. The ^{1}H NMR signals from C(4)H in these isomers were well separated (Table 1) and indicated, as for **2b**, the presence of two *trans* isomers and two *cis* isomers. Evidence regarding the position of substitution in the thiophene rings was gained from literature ^{1}H NMR data of various 2- or 3-monoalkylated thiophenes.[10] These data show a) that the C(5) hydrogen appears at higher chemical shift than the other hydrogens in the thiophene ring irrespective of the substitution pattern and b) that C(5)H in a 3-monoalkylated thiophene shows splittings of *ca.* 5 and 3–3.5 Hz whereas C(5)H in a 2-monoalkylated thiophene shows splittings of *ca.* 5 and 1–1.5 Hz. From these generalisations it was concluded that the substitution had occurred mainly at the 2-position (*ca.* 75%). Friedel–Crafts alkylation of thiophene with 2-chloropropane and $AlCl_3$ yields a *ca.* 60 : 40 mixture of 2- and 3-isopropylthiophene.[11]

If no aromatic compound was present one equiv. of $BF_3{\cdot}OEt_2$ (DCM; 22 °C) converted **1** into a roughly 2 : 1 mixture of **3** and diphenyl sulfone. When *N*-ethyldiisopropylamine was included the formation of diphenyl sulfone (8%) was suppressed and **3** was isolated in a 51% yield. A third type of product was formed as a single stereoisomer (*ca.* 10%, ^{1}H NMR). This compound was also detected as a minor product in some of the Friedel–Crafts reactions. It was never prepared in a pure form; yet NMR analysis clearly indicated the structure **4**. The two stereoisomers **3a**,**b** were formed in a ratio which varied strongly between different experiments. In one case an almost inverted ratio was found: 25 : 75 instead of 80 : 20.

To the best of our knowledge there is only one reported example of a Friedel–Crafts reaction with a vinylic epoxide.[12] After the initial Friedel–Crafts reaction between ethenyloxirane and toluene, induced by $BF_3{\cdot}OEt_2$, there was a fairly easy reaction with a second molecule of toluene forming products of the 1 : 2 composition type. Such 1 : 2 reaction products were negligible in our reactions with **1** despite the use of a large excess of aromatic compound.

The hypothetical intermediate in our Friedel–Crafts reactions belongs to a class of compounds which has been called destabilised or electronegatively substituted carbocations.[13] A similar 1-sulfonylated allylic carbocation has shown unusual features as an intermediate in substitution reactions.[14]

Experimental

Reactions with **1**[3] were performed in flame-dried glassware under an atmosphere of nitrogen or argon. DCM was distilled over CaH_2 and THF over sodium benzophenone ketyl. Commercial $BF_3{\cdot}OEt_2$ (99%, Lancaster) and MCPBA (Aldrich) were used. Flash chromatography purifications were carried out using Merck silica gel 60 A (35–70 μ) and TLC using Merck silica gel 60 F_{254} plates. Equipment used for analytical HPLC: Waters 501, Porasil 100–5 column; for preparative HPLC: Bischoff, Kromasil column (100 SIL, 5 μm, 250 × 20 mm); refractive index detector in both cases. ^{1}H NMR (400 MHz), ^{13}C NMR (100 MHz) and ^{19}F NMR spectra (375 MHz) were recorded on a Varian Mercury spectrometer using $CDCl_3$ as solvent. TMS was used as internal reference for ^{1}H and ^{13}C NMR. ^{19}F NMR shifts are relative to external $PhCF_3$ (in C_6D_6) set at −64 ppm. Chemical shifts (δ) are reported in ppm; coupling constants (J) are given in Hz. Multiplicities given as s, d, t, or q should not be taken literally. For many ^{1}H NMR signals there are small extra splittings, *e.g.* for those of C(4)H (Table 1). These often unsymmetrical signals were poorly resolved at 400 MHz; an adequate characterisation in the text was not possible.

High-resolution MS were run using a JEOL JMS SX/SX102A instrument (direct inlet, electron impact, 70 eV).

4-Phenyl-2-phenylsulfonylcyclohex-2-enol (2a)

To a stirred solution of epoxide **1**[3] (400 mg, 1.7 mmol) in benzene (3.0 cm^3, 20 °C, 20 equiv.) was added $BF_3{\cdot}OEt_2$ (1.7 mmol) in small portions. After 3.5 h the reaction mixture was poured under stirring into half-saturated aqueous $NaHCO_3$ (15 cm^3) and Et_2O (20 cm^3). The ether phase was separated and the aqueous phase extracted with another portion of Et_2O. The organic phases were combined, the solvent was evaporated and DCM (10 cm^3) was added. After drying (Na_2SO_4) and evaporation of the solvent a residue (490 mg) was obtained. The components were separated on a silica gel column (2 × 30 cm) using light petroleum (bp 40–60)–ethyl acetate (5 : 2) as eluant. Diphenyl sulfone (48 mg) was first eluted, then **2a** as a *ca.* 20 : 80 mixture of isomers (252 mg, 47%) and finally the fluoro compound **3** (9%). The isomers of **2a** were separated by preparative HPLC; δ_H for major (*trans*) isomer of **2a** (sample shaken with D_2O): 7.97 (2 H, dd, *J* 8.1, 1.1, ArH), 7.68 (1 H, tt, *J* 7.3, 1.6, ArH), 7.60 (2 H, t, *J* 7.5, ArH), 7.34–7.22 (3 H, m, ArH), 7.21 (1 H, d, *J* 4.0, C(3)H), 6.99 (2 H, d, *J* 7.0, ArH), 4.46 (1 H, t, *J* 4.4, C(1)H), 3.75 (1 H, q, *J* 4.8, C(4)H), 3.21 (1 H, d, *J* 1.8, OH, seen only when D_2O was omitted), 2.26 (1 H, m, 1 × C*H*$_2$), 1.82–1.70 (2 H, m, 2 × C*H*$_2$), 1.68–1.58 (1 H, m, 1 × C*H*$_2$); δ_C for major isomer: 143.8, 142.9, 141.6, 139.9, 133.6, 129.3, 128.7, 127.9, 127.7, 127.0, 62.3 (C(1)), 41.2 (C(4)), 27.5 (*C*H$_2$), 25.9 (*C*H$_2$); *m*/*z* 314 (M^+, 10%), 296 (91), 173 (67), 155 (100), 77 (59); *m*/*z* 314.0942; $C_{18}H_{18}O_3S$ requires 314.0977.

δ_H for minor (*cis*) isomer of **2a** (sample shaken with D_2O): 7.93 (2 H, d, *J* 8.4, ArH), 7.66 (1 H, t, *J* 7.3, ArH), 7.57 (2 H, t, *J* 7.9, ArH), 7.38–7.16 (6 H, m, 5 × ArH + C(3)H), 4.39 (1 H, t, *J* 2.8, C(1)H), 3.47 (1 H, t, *J* 8.0, C(4)H), 3.16 (1 H, br s, OH, seen only when D_2O was omitted), 2.07 (1 H, dq, *J* 13.8, 3.2, 1 × C*H*$_2$), 1.93 (2 H, m, 2 × C*H*$_2$), 1.67–1.57 (1 H, m, 1 × C*H*$_2$); δ_C for minor isomer: 145.2, 142.4, 141.8, 139.3, 128.8, 128.0, 127.6, 127.1, 60.9 (C(1)), 43.8 (C(4)), 30.2 (*C*H$_2$), 25.7 (*C*H$_2$); two signals were not detected with certainty (the ^{13}C NMR sample was a mixture of *cis* and *trans* isomers).

Synthesis of 4-phenyl-2-phenylsulfonylcyclohex-2-enol (2a) from 4-phenylcyclohexanone

4-Phenylcyclohexanone was transformed into the corresponding TMS enol ether as described for cyclohexanone;[15] the crude enol ether was converted into 4-phenyl-2-(phenylsulfinyl)cyclohexanone (*cis* + *trans*) as described for 2-(phenylsulfinyl)-cyclohexanone.[16] The sulfoxide was subjected to a Pummerer reaction using the technique applied to 2-(phenylsulfinyl)cyclohexanone.[17] The crude product was purified (silica gel, toluene) to give 4-phenyl-2-phenylthiocyclohex-2-enone in an 85% yield; mp (uncorr.) 110–111 °C (from Et_2O); δ_H: 7.48 (2 H, d, *J* 7.0, ArH), 7.38–7.22 (6 H, m, ArH), 7.10 (2 H, d, *J* 7.0, ArH), 6.39 (1 H, dd, *J* 3.3, 1.1, C(3)H), 3.72 (1 H, m, C(4)H), 2.69 (1 H, ddd, *J* 16.5, 5.5, 4.7, 1 × C(6)H), 2.58 (1 H, ddd, *J* 16.5, 11.7, 4.7, 1 × C(6)H), 2.35 (1 H, m, 1 × C(5)H), 2.02 (1 H, m, 1 × C(5)H); δ_C(relative to $CDCl_3$ at 77.2): 195.2 (CO), 146.1 C(3), 143.1 (quat. C), 138.9 (quat. C), 134.6, 131.6 (quat. C), 129.8, 129.1, 128.9, 127.7, 127.3, 44.1, 37.4, 32.8. This ketone (140 mg, 0.50 mmol), dissolved in THF (3 cm^3), was reduced (0 °C then 22 °C for 2 h) with $LiAlH_4$ (19 mg, 0.50 mmol). Work-up gave 4-phenyl-2-phenylthiocyclohex-2-enol as an oil (81%); ^1H NMR showed a 3 : 7 mixture of stereoisomers which were not separated; δ_H of major isomer (salient signals only): 6.20 (1 H, d, *J* 3.7, C(3)H), 4.21 (1 H, t, *J* 5.1, C(1)H), 3.57 (1 H, m, C(4)H), 2.42 (1 H, br s, OH); δ_H of minor isomer (salient signals only): 6.21 (1 H, d, *J* 3.7, C(3)H), 4.11 (1 H, s with shoulders, C(1)H), 3.48 (1 H, m, C(4)H), 2.28 (1 H, br s, OH). The mixture (57 mg, 0.20 mmol) in DCM (2 cm^3) was *S*-oxidised selectively[18] (0 °C, 90 min) with MCPBA (138 mg of a 50–60% suspension in water; 0.40–0.48 mmol). Work-up with aq. $Na_2S_2O_3$ and $NaHCO_3$ gave a mixture of sulfones (*cis* : *trans* = 3 : 7) in more than 90% yield. These sulfones were indistinguishable (^1H NMR) from those (**2a**) which had been prepared from **1**.

4-(2-Methoxyphenyl)-2-phenylsulfonylcyclohex-2-enol (2b) and 4-(4-methoxyphenyl)-2-phenylsulfonylcyclohex-2-enol (2b)

To a well-stirred mixture (−78 °C) of **1** (236 mg, 1.00 mmol) and anisole (1.08 g, 10.0 mmol) in DCM (4 cm^3) was slowly added $BF_3{\cdot}OEt_2$ (0.13 cm^3, 1.0 mmol). The temperature was allowed to rise to −15 °C during 2.5 h and the mixture was then kept at −17 °C for 2 days. Work-up was initiated by pouring the reaction mixture into a cold (−17 °C) mixture of triethylamine (1.2 mmol) and MeOH (10 cm^3). Conventional extractions gave a crude product which was purified on a short column of silica gel (pentane–EtOAc 5 : 2) to obtain a mixture of **2b** (69%; four isomers) and **3** (10%). ^1H and ^{13}C NMR spectra were in full accord with the structures. ^1H NMR data for C(4)H in the four isomers are given in Table 1.

4-(2,5-Dimethoxyphenyl)-2-phenylsulfonylcyclohex-2-enol (2c)

The reaction was performed as for **2a** (22 °C; 10 equiv. of 1,4-dimethoxybenzene); the ^1H NMR spectrum was in full accord with the structure; data for C(4)H are given in Table 1.

4-(2-Furyl)-2-phenylsulfonylcyclohex-2-enol (2d)

$BF_3{\cdot}OEt_2$ (4.2 mmol) was added to a mixture of **1** (473 mg, 2.00 mmol), furan (5.8 cm^3, 40 equiv.) and *N*-ethyldiisopropylamine (284 mg, 2.2 mmol). The mixture was stirred in a sealed vessel at 20 °C (1 h). Diethyl ether was added and the mixture was washed with aq. $NaHCO_3$ and then with aq. acid to remove the amine. After drying (Na_2SO_4) and evaporation of the solvent, a residue (534 mg) was obtained. Purification on silica gel gave the title compound (337 mg, 55%) as a 70 : 30 mixture of stereoisomers. NMR spectra were run using this mixture. The ^1H NMR multiplet at 4.34 is most likely due to overlapping signals from the two isomers. δ_H for major isomer of **2d**: 8.0–7.9 (2 H, m, ArH), 7.7–7.4 (3 H, m, ArH), 7.33 (1 H, dd, *J* 1.8, 0.7, furyl-C(5)H), 7.23 (1 H, d, *J* 4.4, C(3)H), 6.28 (1 H, dd, *J* 3.3, 1.8, furyl-C(4)H), 5.85 (1 H, dd, *J* 3.3, 0.7, furyl-C(3)H), 4.34 (1 H, C(1)H), 3.84 (1 H, m, $W_{1/2}$ ~ 9.5, C(4)H), 3.10 (1 H, br s, OH), 2.3–1.5 (4 H, m, 4 × C*H*$_2$); δ_C for major isomer: 153.1 (furyl-C(2)), 142.4 (quat. C), 141.7 (CH), 140.4 (CH), 139.0 (quat. C), 133.4 (CH), 129.1 (CH), 127.7 (CH), 109.9 (furyl-CH), 106.0 (furyl-CH), 61.6 (C(1)), 34.9 (C(4)), 27.1 (CH_2), 21.8 (CH_2).

δ_H for minor isomer of **2d**: 8.0–7.9 (2 H, m, ArH), 7.7–7.4 (3 H, m, ArH), 7.37 (1 H, dd, *J* 1.8, 0.7, furyl-C(5)H), 7.26 (1 H, d, *J* 0.7, C(3)H), 6.33 (1 H, dd, *J* 3.3, 1.8, furyl-C(4)H), 6.12 (1 H, dd, *J* 3.3, 0.7, furyl-C(3)H), 4.34 (1 H, C(1)H), 3.61 (1 H, t, *J* 7.5, C(4)H), 3.10 (1 H, br s, OH), 2.3–1.5 (4 H, m, 4 × C*H*$_2$); δ_C for minor isomer: 153.8 (furyl-C(2)), 141.8 (CH), 141.5 (CH), 141.4 (quat. C), 138.8 (quat. C), 133.4 (CH), 129.1 (CH), 127.7 (CH), 110.1 (furyl-CH), 105.3 (furyl-CH), 61.0 (C(1)), 36.9 (C(4)), 29.6 (CH_2), 21.5 (CH_2).

4-(2-Thienyl)-2-phenylsulfonylcyclohex-2-enol (2e) and 4-(3-thienyl)-2-phenylsulfonylcyclohex-2-enol (2e)

Compound **2e** was prepared (0 °C, 1 h) analogously to **2a** from **1** (118 mg, 0.50 mmol), thiophene (420 mg, 5.00 mmol) and $BF_3{\cdot}OEt_2$ (71 mg, 0.50 mmol) in DCM (2.5 cm^3). The ^1H NMR spectrum of the concentrated reaction product mixture (147 mg) indicated a yield of *ca.* 60% for **2e** and *ca.* 15% for **3**. Purification on a silica gel column (30 × 2 cm; pentane–EtOAc 5 : 2) gave a fraction (84 mg) consisting of **2e** (42% yield) and **3**. Preparative HPLC showed three peaks from **2e** and two peaks from **3**. First eluted (peak 1) was a 7 : 3 mixture of 2-thienyl-*trans*-**2e** (major isomer of **2e**) and 2-thienyl-*cis*-**2e**; δ_H: 7.97–7.90

(2 H, m, ArH), 7.70–7.54 (3 H, m, ArH), 7.27–7.24 (0.7 H, m, C(3)H, partly obscured by solvent peak), 7.21 (0.3 H, dd, *J* 5.1, 1.5, C(3)H), 7.18 (1 H, dd, *J* 5.1, 1.1, thienyl-C(5)H), 6.98 (0.3 H, dd, *J* 5.1, 3.7, thienyl-C(4)H), 6.94 (0.7 H, dd, *J* 5.1, 3.7, thienyl-C(4)H), 6.90 (0.3 H, dt, *J* 3.7, 1.1, thienyl-C(3)H), 6.68 (0.7 H, dt, *J* 3.3, 1.1, thienyl-C(3)H), 4.40 (0.3 H, m, C(1)H), 4.34 (0.7 H, m, C(1)H), 4.05 (0.7 H, q, *J* 3.9, C(4)H), 3.79 (0.3 H, t, *J* 7.7, C(4)H), 3.23 (0.7 H, s, OH), 3.09 (0.3 H, s, OH), 2.36–2.25 (0.7 H, m, CH_2), 2.10–2.00 (1 H, m, CH_2), 1.86–1.69 (2.3 H, m, CH_2); peak 2 (3-thienyl-*cis*-**2e**, contaminated with a small amount of **4**): δ_H 7.94–7.90 (2 H, m, ArH), 7.68–7.54 (3 H, m, ArH), 7.33 (1 H, dd, *J* 4.8, 2.9, thienyl-C(5)H), 7.20 (1 H, d, *J* 1.8, C(3)H), 7.06 (1 H, ddd, *J* 2.9, 1.5, 0.7, thienyl-C(2)H), 6.98 (1 H, dd, *J* 5.1, 1.5, thienyl-C(4)H), 4.37 (1 H, ddd, *J* 4.0, 2.6, 1.1, C(1)H), 3.62 (1 H, t, *J* 7.7, C(4)H), 2.28 (br s, OH), 2.05 (1 H, dq, *J* 13.9, 3.3, CH_2), 2.00–1.91 (3 H, m, CH_2), 1.60 (1 H, m, CH_2); peak 3 (3-thienyl-*trans*-**2e**): δ_H 7.98–7.92 (2 H, m, ArH), 7.70–7.56 (3 H, m, ArH), 7.30 (1 H, dd, *J* 4.8, 2.9, thienyl-C(5)H), 7.25 (1 H, d, *J* 4.4, C(3)H), 6.86 (1 H, dd, *J* 4.9, 1.3, thienyl-C(4)H), 6.73 (1 H, m, thienyl-C(2)H), 4.39 (1 H, t, *J* 4.0, C(1)H), 3.85 (1 H, q, *J* 4.5, C(4)H), 2.50 (1 H, br s, OH), 2.23 (1 H, m, CH_2), 1.84–1.75 (1 H, m, CH_2), 1.72–1.61 (2 H, m, CH_2); peaks 4 and 5: **3a** and **3b** respectively.

4-Fluoro-2-phenylsulfonylcyclohex-2-enol (3a and 3b)

Compounds **3a** and **3b** were obtained (9% yield) as a 4 : 1 mixture of stereoisomers in the synthesis of **2a** from **1**; this mixture was used to obtain ^{13}C NMR data. The isomers were separated by preparative HPLC; δ_H for **3a** (major isomer): 7.92 (2 H, d, *J* 7.5, ArH), 7.68 (1 H, tt, *J* 7.5, 1.8, ArH), 7.58 (2 H, t, *J* 7.7, ArH), 7.03 (1 H, ddd, *J* 10.6, 2.2, 1.1, C(3)H), 5.12 (1 H, dddd, *J* 46.9, 9.9, 5.5, 2.2, C(4)H), 4.36 (1 H, m, C(1)H), 3.10 (1 H, t, *J* 2.0, OH), 2.18–1.98 (3 H, m, CH_2), 1.67–1.55 (1 H, m, CH_2); δ_C for **3a** (J_{C-F}): 144.1 (*J* 8.4, C(2)), 138.1 (*J* 23.7, C(3)), 138.1 (ArC), 133.8 (ArC), 129.2 (ArC), 128.0 (ArC), 86.9 (*J* 171.7, C(4)), 61.1 (*J* 1.5, C(1)), 27.9 (*J* 9.9, C(6)), 23.2 (*J* 18.3, C(5)); δ_F for **3a**: −47.5 (dm, *J* 45.8); retention time in analytical HPLC (pentane–EtOAc 5 : 1), 34.0 min; *m*/*z* 256 (M^+, 7%), 210 (24), 125 (33), 115 (100), 77 (43); *m*/*z* 256.0532; $C_{12}H_{13}O_3FS$ requires 256.0569.

δ_H for **3b** (minor isomer): 7.92 (2 H, d, *J* 8.2, ArH), 7.68 (1 H, tt, *J* 7.7, 1.6, ArH), 7.59 (2 H, t, *J* 7.7, ArH), 7.05 (1 H, t, *J* 4.6, C(3)H), 5.17 (1 H, dq, *J* 46.3, 4.1, C(4)H), 4.37 (1 H, quintet, *J* 3.4, C(1)H), 3.11 (1 H, dd, *J* 2.2, 1.5, OH), 2.16 (1 H, dm, *J* 33.0, C(5)H), 1.98–1.77 (3 H, m, CH_2); δ_C for **3b** (J_{C-F}): 146.0 (*J* 9.9, C(2)), 137.9 (ArC), 134.7 (*J* 19.1, C(3)), 133.8 (ArC), 129.2 (ArC), 128.0 (ArC), 83.3 (*J* 168.6, C(4)), 61.6 (*J* 2.3, C(1)), 25.8 (*J* 1.5, C(6)), 23.8 (*J* 20.3, C(5)); δ_F for **3b**: −44.3 (dddt, *J* 45.8, 33.6, 16.8, 3.8); retention time in analytical HPLC (pentane–EtOAc 5 : 1), 36.8 min.

4-Fluoro-2-phenylsulfonylcyclohex-2-enol (3)

Compound **3** was more efficiently prepared when **1** (118 mg, 0.50 mmol) in DCM (1 cm^3) was added to a mixture of $BF_3 \cdot OEt_2$ (0.09 cm^3, 0.75 mmol) and *N*-ethyldiisopropylamine (32 mg, 0.25 mmol) in DCM (1 cm^3, 22 °C). Work-up after 18 h gave a crude product mixture (100 mg). Separation on a silica gel column (pentane–EtOAc 1 : 1) first gave diphenyl sulfone (8%), then a pool (78 mg) of **3** and **4** (82 : 18, ^1H NMR). This corresponds to a 51% yield of **3** and an 11% yield of **4**. The retention times in analytical HPLC (pentane–EtOAc 5 : 1) were 24.0 (**4**), 34.0 (**3a**) and 36.8 min (**3b**); the ratio **3a** : **3b** was 44 : 56.

2-Fluoro-2-phenylsulfonylcyclohex-3-enol (4)

δ_H (salient signals only): 7.97 (2 H, d, *J* 8.1, ArH), 6.41 (1 H, ddt, *J* 10.2, 4.2, 2.9, olefinic H), 5.50 (1 H, ddt, *J* 9.8, 4.6, 2.2, olefinic H), 4.56 (1 H, ddd, *J* 12.6, 9.5, 3.3, C(1)H), 2.75 (1 H, br s, OH); δ_C (J_{C-F}): 142.1 (*J* 8.4), 134.8, 134.5 ?, 130.6 (*J* 1.5), 129.1, 117.7 (*J* 19.8, C(3)), 103.7 (*J* 219.7, C(2)), 66.1 (*J* 17.5, C(1)), 26.4, 23.4 (*J* 3.0); δ_F: −152.3 (m)

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