A Convenient Synthesis of β-Sulfonylenamines from α,β-Epoxysulfones

A. A. M. Houwen-Claassen, J. W. McFarland[1], B. H. M. Lammerink, L. Thijs, B. Zwanenburg*

Department of Organic Chemistry, University of Nijmegen, Toernooiveld, 6525 ED Nijmegen, The Netherlands

α,β-Epoxysulfones have been prepared by two principal routes, namely nucleophilic epoxidation of α,β-unsaturated sulfones[2,3] and by a modified Darzens condensation of carbonyl compounds with α-halosulfones[4–7]. Particularly, the latter route employing phase-transfer conditions[6] makes α,β-epoxysulfones readily accessible. In this communication, we describe an expeditious synthesis of β-sulfonylenamines from several new α,β-epoxysulfones.

β-Sulfonylenamines have previously been prepared by nucleophilic β-addition of a variety of amines to acetylenic sulfones[8–11], by an abnormal Knoevenagel-type condensation of bis[ethylsulfonyl]methane and benzaldehyde in the presence of an excess of piperidine[12], by reaction of some α-sulfonylacetaldehydes with aniline and N-methylaniline[13], and by treatment of enolates of α-alkoxy- and α-alkylthio-arylsulfonyl-acetaldehydes with aniline hydrochloride[14]. The preparation of morpholinoenamines of α-sulfonylketones was successful[15], however, the formation of pyrrolidino-enamines met with difficulties because of the interfering retro-condensation

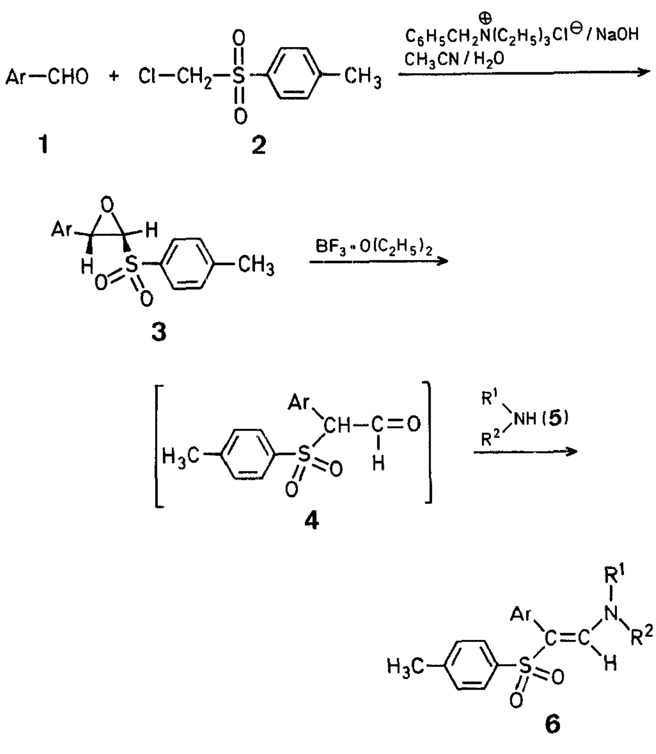
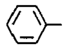
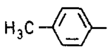
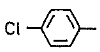
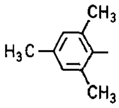
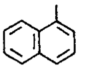
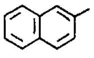


Table 1. α,β-Epoxysulfones 3 prepared

Product No.	Ar	Yield [%]	m.p. [°C] (solvent)	Molecular formula[a,b] or Lit. m.p. [°C]	^{1}H-N.M.R. (CDCl$_3$/TMS$_{int}$) δ [ppm]
3a		65	155-157°	155-158°[2]	2.43 (s, 3H); 4.12 (d, 1H, J=1.5 Hz); 4.52 (d, 1H, J=1.5 Hz); 7.1-7.9 (m, 9H_{arom})
3b		73	117-120° (C_2H_5OAc)	$C_{16}H_{16}O_3S$ (288.4)	2.29 (s, 3H); 2.46 (s, 3H); 4.11 (d, 1H, J=1.5 Hz); 4.48 (d, 1H, J=1.5 Hz); 7.1-7.9 (m, 8H_{arom})
3c		60	110-112° (C_2H_5OAc/ CH_3OH)	$C_{15}H_{13}ClO_3S$ (308.8)	2.45 (s, 3H); 4.09 (d, 1H, J=1.5 Hz); 4.50 (d, 1H, J=1.5 Hz); 7.1-7.9 (m, 8H_{arom})
3d		92	111-112° (C_2H_5OH)	$C_{18}H_{20}O_3S$ (316.4)	2.22 (s, 3H); 2.34 (s, 6H); 2.43 (s, 3H); 4.10 (d, 1H, J=1.5 Hz); 4.52 (d, 1H, J=1.5 Hz); 6.75 (s, 2H_{arom}); 7.35 (d, 1H_{arom}); 7.83 (d, 2H_{arom})
3e		76	115-116° (C_6H_6)	$C_{19}H_{16}O_3S$ (324.4)	2.40 (s, 3H); 4.08 (d, 1H, J=1.5 Hz); 5.07 (d, 1H, J=1.5 Hz); 7.15-8.0 (m, 11H_{arom})
3f		75	139-140° (C_2H_5OAc)	$C_{19}H_{16}O_3S$ (324.4)	2.50 (s, 3H); 4.27 (d, 1H, J=1.5 Hz); 4.72 (d, 1H, J=1.5 Hz); 7.15-7.62 (m, 4H_{arom}); 7.73-7.99 (m, 7H_{arom})

[a] I.R. (KBr): ν_{SO_2}= 1300-1325, 1145-1150 cm^{-1}.

[b] Satisfactory microanalyses obtained: C ±0.36, H ±0.10.

Table 2. β-Sulfonylenamines 6 prepared

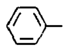
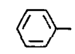
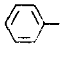
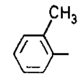
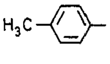
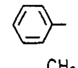
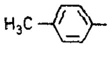
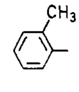
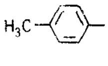
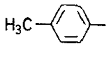
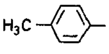
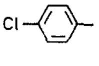
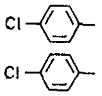
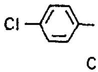
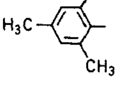
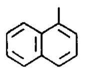
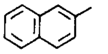
Product No.	Ar	R^1	R^2	Reaction time [h]	Yield [%]	m.p. [°C] (solvent)	Molecular formula[a,b]	^{1}H-N.M.R. (CDCl$_3$/TMS) δ [ppm]
6a		H_3C		19	31	139-140° (C_2H_5OH)	$C_{22}H_{21}NO_2S$ (363.5)	2.22 (s, 3H); 2.80 (s, 3H); 7.0-7.5 (m, 14H_{arom}); 8.03 (s, 1H)
6b		H_3C		25	64	149-150° (C_2H_5OH)	$C_{23}H_{23}NO_2S$ (377.5)	2.18 (s, 3H); 2.31 (s, 3H); 2.87 (s, 3H); 7.0-7.45 (m, 13H_{arom}); 7.68 (s, 1H)
6c		$-(CH_2)_2-O-(CH_2)_2-$		3	57	166-168° (C_2H_5OH)	$C_{19}H_{21}NO_3S$ (343.4)	2.30 (s, 3H); 2.96 (t, 4H, J=5 Hz); 3.47 (t, 4H, J=5 Hz); 6.9-7.4 (m, 9H_{arom} + =CH—)
6d		H_3C		26	84	135-137° (C_2H_5OH)	$C_{24}H_{25}NO_2S$ (391.5)	2.28 (s, 3H); 2.33 (s, 3H); 2.80 (s, 3H); 7.0-7.5 (m, 13H_{arom}); 8.03 (s, 1H)
6e		H_3C		22	83	196-199° (C_2H_5OH)	$C_{23}H_{23}NO_2S$ (357.5)	2.18 (s, 3H); 2.21 (s, 3H); 2.32 (s, 3H); 2.82 (s, 3H); 6.85-7.45 (m, 12H_{arom}); 7.62 (s, 1H)
6f		$-(CH_2)_2-O-(CH_2)_2-$		3	83	195-197° (C_2H_5OH)	$C_{20}H_{23}NO_3S$ (357.5)	2.27 (s, 3H); 2.33 (s, 3H); 2.98 (t, 4H, J=5 Hz); 3.50 (t, 4H, J=5 Hz); 6.85-7.5 (m, 8H_{arom} + =CH—)
6g		$-(CH_2)_4-$		2.5	70	162-165° (C_2H_5OH)	$C_{20}H_{23}NO_2S$ (341.5)	1.6-1.8 (m, 4H); 2.28 (s, 3H); 2.33 (s, 3H); 2.9-3.1 (m, 4H); 7.0-7.5 (m, 8H_{arom}); 7.68 (s, 1H)
6h		$-(CH_2)_5-$		1.5	46	132-133° (C_2H_5OH)	$C_{21}H_{25}NO_2S$ (355.5)	1.5 (m, 6H); 2.26 (s, 3H); 2.32 (s, 3H); 2.9 (m, 4H); 6.8-7.4 (m, 8H_{arom} + =CH—)
6i		$-(CH_2)_2-O-(CH_2)_2-$		3.5	64	229-231° (C_2H_5OH)	$C_{19}H_{20}ClNO_3S$ (377.9)	2.33 (s, 3H); 2.98 (t, 4H, J=5 Hz); 3.52 (t, 4H, J=5 Hz); 6.9-7.45 (m, 8H_{arom} + =CH—)
6j		$-(CH_2)_4-$		3	19	191.5-193° (C_2H_5OH)	$C_{19}H_{20}ClNO_2S$ (361.9)	1.7-1.9 (m, 4H); 2.35 (s, 3H); 2.8-3.2 (m, 4H)
6k		$-(CH_2)_5-$		4	34	164-166° (C_6H_6/ Hexane)	$C_{20}H_{22}ClNO_2S$ (375.9)	1.5 (m, 6H); 2.32 (s, 3H); 2.93 (m, 4H); 6.9-7.5 (m, 8H_{arom} + =CH—)
6l		$-(CH_2)_2-O-(CH_2)_2-$		2	64	194-195° (C_2H_5OH)	$C_{22}H_{27}NO_3S$ (385.5)	1.80 (s, 6H); 2.20 (s, 3H); 2.35 (s, 3H); 2.94 (t, 4H, J=5 Hz); 3.45 (t, 4H, J=5 Hz); 6.75 (s, 2H_{arom}); 7.10 (s, 1H); 7.15 (d, 2H_{arom}); 7.36 (d, 2H_{arom})

Table 2. (Continued)

Product No.	Ar	R^1	R^2	Reaction time [h]	Yield [%]	m.p. [°C] (solvent)	Molecular formula[a,b]	^{1}H-N.M.R. ($CDCl_3$/TMS) δ [ppm]
6m		$-(CH_2)_2-O-(CH_2)_2-$		2.5	74	157-158^c (C_2H_5OH)	$C_{23}H_{23}NO_3S$ (393.5)	2.18 (s, 3H); 2.80 (t, 4H, J=5 Hz); 3.25 (t, 4H, J=5 Hz); 6.85 (d, 2H); 7.14 (s, 1H); 7.25 (m, 6H_{arom}); 7.6 (m, 3H_{arom})
6n		$-(CH_2)_2-O-(CH_2)_2-$		2.5	87	113.5-115^c (C_2H_5OH)	$C_{23}H_{23}NO_3S$ (393.5)	2.30 (s, 3H); 2.97 (t, 4H, J=5 Hz); 3.40 (t, 4H, J=5 Hz); 7.05 (m, 3H_{arom}+=CH—); 7.5 (m, 9H_{arom})

[a] Characteristic I.R. (KBr): $\nu_{C=C}$: 1620-1610; ν_{SO_2}: 1290-1270, 1130-1120 cm^{-1}.

[b] Satisfactory microanalyses obtained: C ±0.57, H ±0.33, N ±0.19.

reaction[16]. The reaction of an enamine and an arylsulfonyl chloride leading to a β-sulfonylenamine has briefly been mentioned[17,18]. β,β'-Disulfonylenamines have also been reported[19].

The α,β-epoxysulfones **3** needed for our work are readily synthesized by reacting aldehydes **1** with chloromethyl 4-tolyl sulfone (**2**) under phase-transfer conditions[6] (Table 1). The first step in the synthesis of β-sulfonylenamines **5** is the facile boron trifluoride catalyzed rearrangement of **3** to α-sulfonylacetaldehydes **4**. Such an exclusive migration of the electronegative sulfonyl substituent has been demonstrated for epoxysulfones derived from benzaldehyde and some ketones[7,20,21]. Subsequent treatment of the thus-obtained α-aryl, α-sulfonyl-acetaldehydes **4**, without being isolated, with an appropriate secondary amine **5** then smoothly leads to β-sulfonylenamines **6** usually in good yields (Table 2). This method leads to β-aryl substituted β-sulfonylenamines which probably have the (*E*)-geometry. This type of sulfonylenamines has only been obtained by the abnormal Knoevenagel reaction cited above. Our method presented here has a much wider scope for the preparation of different types of β-sulfonylenamines **5** than the existing methods[8-19].

Combustion analyses were performed by Mr. J. Diersmann in the Micro-Analytical Department of our Laboratory. I.R. spectra were run on a Perkin Elmer 257 grating spectrometer. ^{1}H-N.M.R. spectra were recorded with a Varian Associates EM390 instrument using TMS as internal standard. Mass spectra were measured on a Varian SM 1B mass spectrometer or a Finnigan 3100 GC/MS instrument. Melting points were determined on a Kofler hot stage and are uncorrected. Dichloromethane was passed over an alumina column to remove ethanol and then distilled over calcium chloride.

α,β-Epoxysulfones 3; General Procedure[6] (Modified):

With vigorous stirring a 50% aqueous sodium hydroxide solution (40 ml) is added within 3 min to a solution of aldehyde **1** (60 mmol), chloromethyl 4-tolyl sulfone (**2**; 10.23 g, 50 mmol) and benzyltriethylammonium chloride (312 mg) in acetonitrile (15 ml) cooled in ice. After stirring for 1 h at room temperature the solid material is collected by filtration and washed with water until the filtrate is neutral. The resulting sticky solid is then crystallized from an appropriate solvent (Table 1).

β-Sulfonylenamines 6; General Procedure:

α,β-Epoxysulfone **3** (10 mmol) is dissolved in dichloromethane (75 ml) and cooled in ice. Then boron trifluoride-etherate (1.42 g, 10 mmol) in dichloromethane (10 ml) is added with stirring. The resulting solution is stirred for another 10 min at 0 °C and then a solution of secondary amine **5** (22 mmol) in dichloromethane (15 ml) is added. After stirring for the period indicated in Table 2 at room temperature, the amine-boron trifluoride complex is removed by filtration and the filtrate concentrated in vacuo. The products are crystallized from ethanol to give analytically pure materials.

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[1] On leave from the DePauw University, Dept. of Chemistry, Greencastle, Indiana 46135, U.S.A.

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