SHORT PAPER

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Synthesis, separation and characterisation of diastereomeric mixtures of 3-*p*-toluenesulfonyl-1,3-diaryl-propan-1-ols[†]

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Four diastereomeric mixtures of 3-*p*-toluenesulfonyl-1, 3-diarylpropan-1-ols were prepared by the reduction of the corresponding β–sulfonyl ketones and the stereochemistry of the individual separated (HPLC) diastereomers was established on the basis of PMR data.

Keywords: 3-*p*-toluenesulfonyl-1, 3-diaryl-propan-1-ols

3-*p*-toluenesulfonyl-1,3 diaryl-propan-1-ols are intermediates in the synthesis of 1-*p*-toluenesulfonyl-1,2 diaryl-cyclopropanes.[1] However these alcohols were obtained as diasteromeric mixtures and their separation by fractional crystallisation and column chromatography was not successful.

A literature survey revealed that these sulfonyl alcohols can be obtained by the photooxidation of the corresponding sulfides to sulfones.[2] However the present scheme involves Michael addition of *p*-toluenesulfonic acid to α,β-unsaturated ketones,[3] *i.e.* propenones **1a–d**, to form β-sulfonyl ketones **2a–d** (76–90% yield) followed by sodium borohydride reduction. This resulted in the formation of the diastereomeric mixtures of 3-*p*-toluenesulfonyl-1,3-diaryl-propan-1-ols **3a–d** (86–96% yield), which were characterised by their elemental analysis, IR and PMR data.

The most preferred conformation for the sulfonyl ketones **2a–d** would be the one in which the two largest substituents *viz.* –COAr′ and –Ar are anti to each other and the *p*-toluenesulfonyl group is gauche with respect to –COAr′.The contribution of the –Ar to the steric interaction was assumed to be larger than that due to the $–SO_2Ar$ group. Support for this assumption came from the observed confomational free energy in cyclohexane derivatives which was 2.53 kcal/mol for $–SO_2Ph$ and is reported to be 2.64 or 3.15 kcal/Mol for –Ph group.[4] Another important feature would be the electrostatic attraction between the oxygen of the carbonyl and the sulfur of the sulfone group.

Reduction of **2a–d** was carried out using sodium borohydride in THF. The products which were obtained were the corresponding diasteromeric mixtures of the sulfonyl alcohols **3a–d**, which were characterised by elemental analysis, IR and PMR data. These mixtures (200 mg each) were subjected to HPLC separation using column chromatographic grade silica gel (50 g) as adsorbent and benzene–4%ethyl acetate mixture as eluant. The Miniprep column of Jobin Vyon HPLC instrument was used, in which the column and solvent pressures were maintained at 14.5 and 10 bars respectively. In each case two characteristic peaks were seen on the chromatograph. Fractions corresponding to these peaks were collected and evaporated when solid compounds were obtained which were by m.p., elemental analysis, IR and PMR data shown to be the separated diasteromers **4a–d** and **5a–d** respectively.

The structures which can be allotted to the separated diastereomers involve a five membered ring with donor–acceptor interaction between oxygen and sulfur atoms.[2,5,6] The geometry of the diastereomers was established on the basis of chemical shift considerations and coupling data. In case of the *cis* 1,3-diaryl series **4a–d**, the C_1H appears as a broad doublet (bd, $J = 9Hz$), in the range δ 4.35–4.39, whereas the same proton appears as a triplet (t, $J = 7$ Hz) in the range δ 4.65–4.76 in the *trans* 1,3-diaryl compounds **5a–d**. This clearly indicates that the C_1 H in the *trans* isomer is quite deshielded as it is *cis* to the C_3 aromatic ring and lies in its

Table 1

Compound	M.p/°C [Lit.]	Yield /%	IR/cm^{-1}	PMR(δ) $CDCl_3$
1a	56° [56–57][7]	72	1670, 1610, 990, 755, 690	8.0 (2H, dd, $J = 2,8$, ArH *ortho* to CO at C_1) 7.20–7.85 (10H, m, *i.e.* ArH at C_3, 3 ArH at C_1 and Ha at C_3 Hb at C_2)
1b	91° [90–92][8]	90	1660, 1600, 990, 820, 780, 700	8.01 (2H, dd, $J = 2$, 8 Hz, ArH *ortho* to CO at C_1) 7.80 (1H, d, $J = 15$ Hz Ha at C_3) 7.50 (6H, m. *i.e.* Hb at C_2-, 3 ArH at C_1 and 2 ArH *meta* to $ArCH_3$ at C_3) 7.18 (2H, d. $J = 2$, 8 Hz, ArH *ortho* to $ArCH_3$ at C_3) 2.38 (3H, s $ArCH_3$ at C_3)
1c	73.4° [74][9]	80	1680, 1620, 1600, 990, 840, 790, 700	8.0 (2H, dd $J = 2$, 7 Hz, ArH *ortho* to CO at C_1) 7.80 (1H, d, $J = 15$ Hz Ha at C_3) 7.20–7.68 (6H, m, *i.e.* Hb at C_2 3 ArH at C_1 and 2ArH *meta* to Ar OCH_3 at C_3) 6.90 (2H, d, $J = 8$ Hz, ArH *ortho* to Ar–OCH_3 at C_3) 3.80 (3H, s, Ar–OCH_3 at C_3)
1d	103.4° [107][10]	89.5	1660, 1600, 970, 820, 760, 690	7.98 (2H, d, $J = 8$ Hz, ArH *ortho* to CO at C_1) 7.15–7.70 (7H, m, *i.e.* 5ArH at C_3 Hb at C_2 and Ha at C_3) 6.90 (2H, d, $J = 8$ Hz, ArH *ortho* to Ar–OCH_3 at C_1) 3.80 (3H, s, Ar –OCH_3 at C_1)

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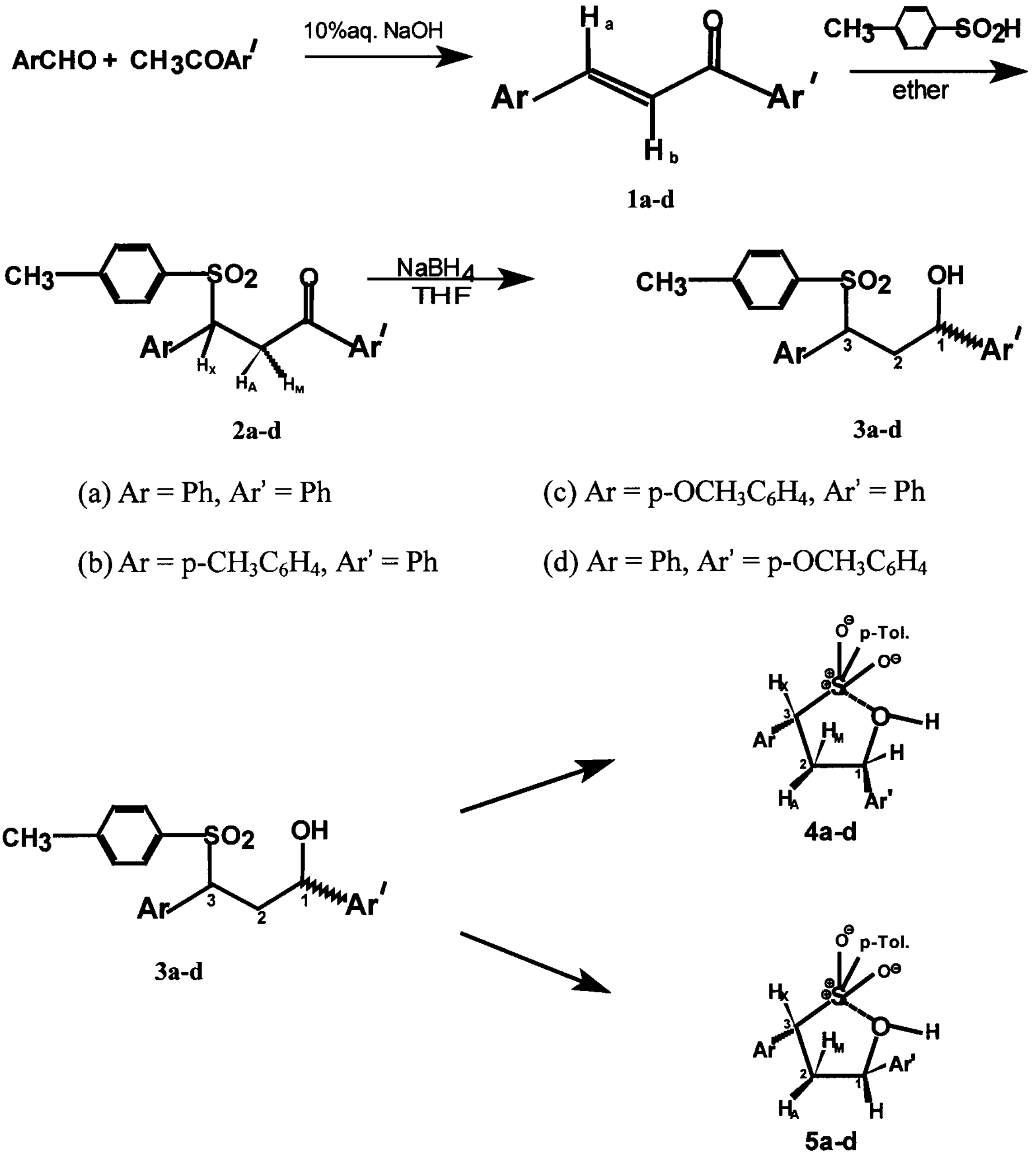
[†] This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*



(a) Ar = Ph, Ar' = Ph

(b) Ar = p-$CH_3C_6H_4$, Ar' = Ph

(c) Ar = p-$OCH_3C_6H_4$, Ar' = Ph

(d) Ar = Ph, Ar' = p-$OCH_3C_6H_4$

Scheme 1

deshielding zone. Another interesting feature is that the C_3–H in the *cis* isomers **4a–d** appears as a doublet of doublet (dd, $J = 4.11$ Hz) in the range δ 4.49–4.52, whereas the same proton in the *trans* isomers **5a–d** appears as a doublet of doublet (dd, $J = 6.9$ Hz) in the range δ 3.95–4.05. This shows that it is considerably shielded due to syn–axial like interaction between the C_3 H and C_1 aromatic ring which results in its shielding. The C_2 protons in both sets of isomers appear as a multiplet in the range δ 2.20–3.00.

Experimental

Preparation of chalcones[7] (**1a–d**): To a well stirred and ice cooled solution of aqueous sodium hydroxide (4.4 g in 40 ml water) in ethanol (25 ml), ketone (0.01 mol) was added and further stirred for 10 min in ice bath. Freshly distilled aldehyde (0.01 mol) was then added dropwise maintaining the temperature at 25°C and stirring vigorously for 2–3 hours. Reaction mixture was kept in refrigerator overnight. The solid was filtered, washed with ice cold water till the washings were neutral to litmus and dried under reduced pressure. The product was recrystallised from hexane–ether system. The yields, m.p., IR and PMR(90 MH_Z) data for these compounds are listed in Table 1.

Preparation of β-sulfonyl ketones (**2a–d**): An aqueous solution (15 ml) of sodium *p*-toluenesulfonate dihydrate (10 g, 0.0467 mol) was neutralised with concentrated hydrochloric acid and shaken with ether. The ether layer was filtered (through cotton plug), dried over anhydrous sodium sulfate and decanted into a flask containing the unsaturated ketone (0.02 mol). The reaction was kept at room temperature for 24 hours. The white solid obtained was filtered, washed with ether and dried under vacuum. The yield, m.p., elemental analysis IR and PMR(90MH_Z) data are shown in Table 2.

Preparation of sulfonyl alcohol (**3a–d**): A suspension of the sulfonyl ketone **2a–d** (1.66 mol) and sodium borohydride (150 mg., 3.95 mol) in distilled THF (10 ml) was stirred for 1–2 hours at room temperature. TLC indicated the completion of reaction. After complete solvent removal (by flushing air), crushed ice and solid ammonium chloride was added and the product was extracted with ether (20 ml). The extract was dried over anhydrous sodium sulfate and decanted. The solvent was evaporated to give a compound which was recrystallised from hexane–methylene chloride. The yield, m.p., elemental analysis, IR and PMR(90 MH_Z) data are listed in Table 3.

Table 2

Compound	M.p./°C [Lit.]	Yield /%	Elemental analysis Calc. %C %H	 Found %C %H	IR/cm^{-1}	PMR(δ) $CDCl_3$
2a	180°°° [177]^{11}	76	72.51 5.53	72.84 5.75	1680,1590, 1300, 1135, 810,745, 690	7.92(2H, dd, *J* = 2,8,*ortho* H of-COPh); 7.50(3H, m, *meta* and *para* H of-COPh); 7.45 (2H, d, *J* = 8, *ortho* to –SO_2); 7.20(5H, s, PhH); 7.15 (2H, d, *J* = 8, *meta* to -SO_2); 4.90 (1H, dd, *J* = 4, 9, H_X); 4.15(1H, dd, *J* = 4, 18, H_M); 3.85(1H, dd, *J* = 9,18,H_A); 2.38(3H, s, $ArCH_3$)
2b	173° [173]^1	80	73.00 5.86	72.84 5.75	1690, 1600, 1300, 1150, 820, 775, 680	7.92(2H, dd, *J* = 2,7 *ortho* H of-COPh); 7.60–6.90(11H, m, ArH); 4.90(1H, dd, *J* = 4, 9, H_X); 4.10(1H, dd, *J* = 4, 19, H_M); 3.82(1H, dd, *J* = 9,19 ,H_A); 2.39(3H, s, $ArCH_3$ of Ts group); 2.28(3H, s, $ArCH_3$ of *p*-$C_6H_4CH_3$ group)
2c	163–164° [161]^{12}	76	70.04 5.62	70.32 5.70	1670, 1600, 1285, 1145, 810, 805 730	7.92(2H, dd, *J* = 2.7, *ortho* H of–COPh); 7.70–7.00(9H, m, ArH); 6.73(2H, d, *J* = 9, *ortho* to –OCH_3); 4.85(1H, dd, *J* = 4,9, H_X); 4.08(1H, dd, *J* = 4.18, H_M) 3.90(1H, dd, *J* = 9.18 H_A) 3.72(3H, s, Ar–OCH_3) 2.38(3H, s, Ar–CH_3)
2d	182–184° [182]^{12}	78	70.04 5.62	65.95 5.75	1660, 1250, 1140	7.80(2H, d, *J* = 9, *ortho* H of –of COPh); 7.32(2H,d, *J* = 9, *ortho* to –SO_2); 7.15(5H, m, ArH); 7.11(2H, d, *J* = 9 meta to -SO_2); 6.82(2H, d, *J* = 9, *ortho* to –OCH_3); 4.84(1H, dd, *J* = 4,9, H_X); 4.06(1H, dd, *J* = 4,16 H_M); 3.84(1H, dd, *J* = 9,16, H_A); 3.77 (3H, s, Ar–OCH_3); 2.40(3H, s, Ar–CH_3).

Table 3 Data of separated diastereomers

4a	m.p.: 171°C, IR(cm^{-1}): 3500, 1600, 1290, 1145, 810, 805, 705, ^{1}HNMR (δ): 4.39 1H,m bd, *J* = 9 Hz, C_1H); 2.25–3.00 (2H, m, C_2H), 4.53 (1H, dd. *J* = 4, 11 Hz, C_3H), 2.38 (3H, s, $ArCH_3$), 1.70 (1H, bs, OH), 6.90–7.5 (14H, m, Arh) Found: C 72.37%; H, 6.10%, $C_{22}H_{22}O_3S$ required C, 72.11%; H, 6.05%
4b	m.p.: 153°C, IR(cm^{-1}): 3450, 1600, 1290, 1140, 820, 805, 710, ^{1}HNMR (δ): 4.35 (1H, bd, *J* = 9 Hz, C_1H), 2.25–3.00 (2H, m, C_2H), 4.51 (1H, dd. *J* = 4,12 Hz, C_3H), 2.32 (3H, s, $ArCH_3$), 2.38 (3H, s, ArH), 2.05 (1H, bs, –OH), 6.80–7.5 (13H, m, ArH) Found: C, 72.78%; H, 6.40%, $C_{23}H_{24}O_3S$ requires C, 72.61%; H, 6.36%
4c	m.p. 156°C, IR(cm^{-1}): 3450, 1600, 1290, 1140, 820, 710, ^{1}HNMR (δ): 4.35 (1H, bd, *J* = 4, 10 Hz, C_1H), 2.25–3.00 (2H,m, C_2H), 4.49 (1H, dd. *J* = 4, 11 Hz, C_3H), 2.38 (3H, s, $ArCH_3$), 3.79 (3H, s, OCH_3), 1.95 (1H, bs, –OH), 6.60–7.5 (13H, m, ArH) Found: C, 69.42%; H, 6.16%, $C_{23}H_{24}O_4S$ requires C, 69.68%; H, 6.10%
4d	m.p.: 159°C, IR(cm^{-1}): 3450, 1600, 1290, 1140, 820, 810, 710, ^{1}HNMR (δ): 4.35 (1H, dd, *J* = 3, 10 Hz, C_1H), 2.25–3.00 (2H, m, C_2H), 4.50 (1H, dd, *J* = 4,11 Hz, C_3H), 2.35 (3H, s, $ArCH_3$), 3.78 (3H, s, OCH_3), 1.85 (1H, bs, –OH), 6.70–7.5 (13H, m, ArH) Found: C, 69.65%; H, 6.23%, $C_{23}H_{24}O_4S$ requires C, 69.68%; H, 6.10%
5a	m.p.: 121°C, IR(cm^{-1}): 3500, 1600, 1285, 1140, 815, 810, 710, ^{1}HNMR (δ): 4.76 (1H, t, *J* = 7 Hz, C_1H), 240–3.00 (2H, m, C_2H), 43.05 (1H, dd. *J* = 6,8Hz, C_3H), 2.38 (3H, s, $ArCH_3$), 2.05 (1H, bs, OH), 6.90–7.5 (14H, m, ArH) Found: C 72.35%; H, 6.20%, $C_{22}H_{22}O_3S$ requires C, 72.11%; H, 6.05%
5b	m.p.: 146°C IR(cm^{-1}): 3500, 1600, 1290, 1140, 820, 810, 715, ^{1}HNMR (δ): 4.75 (1H, t, *J* = 7Hz, C_1H), 2.25–3.00 92H, m, C_2H), 3.98 (1H, dd. *J* = 6, 9 Hz, C_3H), 2.32 (3H, s, $ArCH_3$), 2.38 (3H, s, ArH_3), 1.70 (1H, bs, -OH), 6.80–7.5 (13H, m, ArH) Found: C, 72.72%; H, 6.37%, $C_{23}H_{24}O_3S$ requires C, 72.61%; H, 6.36%
5d	m.p.: 130°C, IR(cm^{-1}): 3450, 1600, 1280, 1140, 830, 820, 710, ^{1}HNMR (d): 4.65 (1H, t, *J* = 7 Hz, C_1H), 2.30–3.00 (2H, m, C_2H), 3.95 (1H, dd. *J* = 4, 9 Hz, C_3H), 2.35 (3H, s, $ArCH_3$), 3.76 (3H, s, OCH_3), 2.30s (1H, bs, –OH), 6.70–7.5 (13H, m, ArH) Found: C, 69.60%; H, 6.11s %, $C_{23}H_{24}O_4S$ requires C, 69.68 %; H, 6.10%

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