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Naphthalene-Catalysed Reductive Desulfonylation with Lithium: Alkyllithiums from Alkyl Phenyl Sulfones

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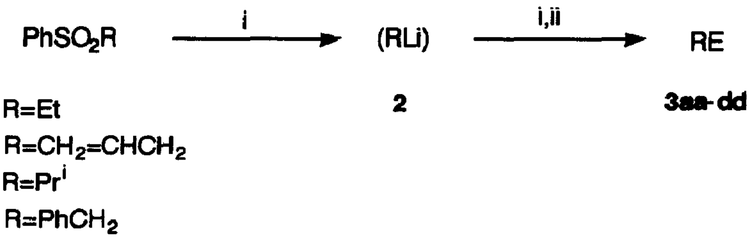
Abstract: The reaction of alkyl aryl sulfones **1** with an excess of lithium powder and a catalytic amount of naphthalene (8 mol %) in the presence of a carbonyl compound [Pr^iCHO, PhCHO, Et_2CO, $\overline{(CH_2)_5CO}$] or trimethylchlorosilane (Barbier-type conditions) in THF at temperatures ranging between -78 and 20°C leads, after hydrolysis with water, to the expected coupling products, arising from the corresponding alkyllithium *in situ* generated, in 30-61% yields.

Sulfones are important intermediates in organic synthesis[1] above all in carbon-carbon formation reactions through the corresponding α-carbanions[2a]. However, molecules bearing the sulfone functionality are rarely target structures in synthetic chemistry and, in general, the sulfone group should be removed at the end of the process. Two reactions are mostly employed for this purpose: (a) β-elimination of sulfinate, which leads to olefins[2b] and (b) reductive desulfonylation, which achieves a sulfone/hydrogen exchange[2c]. Among the reductive desulfonylation procedures (which have found the major aplication in the case of unsymmetric alkyl aryl sulfones), the use of group I-III metals or amalgams in the presence of a proton source has been widely used[3]. Thus, mixtures such as sodium/liquid ammonia[4], lithium/ethylamine[5], sodium amalgam/ethanol[6] or ultrasonically dispersed potassium/toluene[7] have proven to be effective for the replacement of the sulfone moiety by hydrogen. However, to the best of our knowledge, the carbanionic intermediates in all these reductions have been never used for a coupling reaction with an electrophile different than the proton. Only very recently[8] the sulfone group/lithium exchange in *gem*-bissulfones with lithium naphthalenide was described: in this case the carbanionic centre formed is located at the α-position with respect to the remaining sulfone functionality[9]. We report here the naphthalene-catalysed lithiation[10] of alkyl phenyl sulfones and the *in situ* reaction of the organolithium formed with carbonyl compounds or trimethylchlorosilane in a Barbier-type process[11].

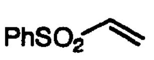
The reaction of different alkyl phenyl sulfones[12] **1** with an excess of lithium powder (1:14 molar ratio) and a catalytic amount of naphthalene (1:0.16 molar ratio; 8 mol %) in the presence of a carbonyl compound (isobutyraldehyde, benzaldehyde, 2-pentanone or cyclohexanone) or trimethylchlorosilane (1:1.2 molar ratio) (Barbier-type conditions) in tetrahydrofuran at temperatures ranging between -78 and 20°C gave, after hydrolysis with water, the expected coupling products **3aa-dd** in moderate yields (Scheme 1 and Table 1). Although the reaction can be applied to primary, secondary, allylic or benzylic intermediates, the secondary sulfone **1c** gave the best result working at -30 to 20°C (Table 1, entry 3 and footnote f). On the other hand, for sulfones **1a** and **1b** the best yields were obtained performing the reaction in the presence of boron trifluoride etherate (1:2.2 molar ratio) (Table 1, entries 1 and 2)[13]. In addition, in all the reactions a small amount (<10%) of pinacol-type compounds was obtained as by-products.



1a : R=Et
1b : R=CH$_2$=CHCH$_2$
1c : R=Pr^i
1d : R=PhCH$_2$

Scheme 1. *Reagents and conditions*: i, Li powder, $C_{10}H_8$ cat. (8 mol %), E^+=Pr^{i}CHO, PhCHO, Et_2CO, $\overline{(CH_2)_5CO}$, Me_3SiCl, THF, -78 to 20°C; ii, H_2O.

The reaction shown in Scheme 1 is not applicable to vinylic sulfone. Thus, when sulfones **1e,f**[14] were treated under the same reaction conditions as for compound **1a**, using benzaldehyde as the electrophile, diphenylcarbinol (**4**) was the only coupling product isolated (25 and 49%[15] yield, respectively). This result indicates clearly that in the case of vinylic sulfones the sulfone-phenyl bond reductive cleavage is preferred instead of the corresponding sulfone-vinyl one.



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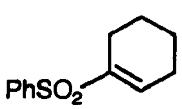

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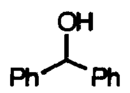

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It is noteworthy that the organolithium intermediate **2** (Scheme 1) survives under the reaction conditions and prefers to react with the electrophile present in the reaction media instead of abstracting a proton from the α-position of the starting sulfone **1**. This is a consequence of working under Barbier-type reaction conditions at low temperature: when the reaction was performed in two steps, first lithiation and then (after desapearing of the sulfone) the reaction with the electrophile, no reaction products of the type **3** were isolated, although the starting sulfone was completely consumed.

In conclusion, we have described here a new reaction, which permits the transformation of alkyl phenyl sulfones into alkyllithium reagents and the *in situ* reaction of these carbanionic intermediates with electrophilic reagents. Work is in progress in order to stablish the scope and limitations of this procedure.

Table 1. Preparation of Compounds **3**

Entry	Starting sulfone **1**	Electrophile E^+	Product **3**[a]				
			no.	R	E	Yield (%)[b]	*R*$_f$[c]
1[d]	**1a**	PhCHO	**3aa**	Et	PhCHOH	61	0.35
2[d]	**1b**	PhCHO	**3ba**	$CH_2{=}CHCH_2$	PhCHOH	47	0.54[e]
3[f]	**1c**	PhCHO	**3ca**	Pr^i	PhCHOH	30	0.76
4	**1d**	Pr^iCHO	**3da**	$PhCH_2$	Pr^iCHOH	46	0.54
5	**1d**	Et_2CO	**3db**	$PhCH_2$	Et_2COH	54	0.44
6	**1d**	$\overline{(CH_2)_5C}O$	**3dc**	$PhCH_2$	$\overline{(CH_2)_5C}OH$	57	0.30
7	**1d**	Me_3SiCl	**3dd**	$PhCH_2$	Me_3Si	44	0.43[g]

[a] All products **3** were >95% pure (GLC and 300 MHz ^1H NMR) and were fully characterised by their spectroscopic data (IR, ^1H and ^{13}C NMR, and mass spectra). [b] Isolated yield after column chromatography (silica gel, hexane/ethyl acetate) based on the starting sulfone **1**. [c] Silica gel, hexane/ethyl acetate: 6/1. [d] The reaction was carried out in the presence of $BF_3{\cdot}Et_2O$ (see text). [e] silica gel, hexane/ethyl acetate: 4/1. [f] The reaction was performed at -30 to 20°C. [g] Silica gel, hexane.

In a *typical reaction* to a green suspensión of lithium powder (100 mg, 14 mmol) and naphthalene (20 mg, 0.16 mmol) in THF (5 ml) was added a solution of the corresponding sulfone **1** (1 mmol) and the electrophile (1.2 mmol) [and $BF_3{\cdot}Et_2O$ (2.2 mmol) for starting sulfones **1a,b**] in THF (4 ml) at -78°C (-30°C for compound **1c**) under argon for 15 min. Stirring was continued for 5 additional h allowing the temperature to rise till 20°C. The resulting mixture was hydrolysed with water (5 ml), extracted with diethyl ether (2x20 ml) and the organic layer dried over anhydrous Na_2SO_4. Solvents were evaporated (15 Torr) and the resulting residue was chromatographied (silica gel, hexane/ethyl acetate) to afford pure products **3**. In the case of using $BF_3{\cdot}Et_2O$ as co-reagent the final hydrolysis was carried out with 2 N HCl and extracted with diethyl ether. The organic layer was successively washed with 2 N NaOH (2x 10 ml) and water (2x10 ml) and dried and purified as above.

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REFERENCES AND NOTES

1. For recent reviews, see: (a) Patai, S.; Rappoport, Z.; Stirling, C. J. M. Eds. *The Chemistry of Sulfones and Sulfoxides* ; J. Wiley & Sons: Chichester, 1988. (b) Simpkins, N. S. *Sulfones in Organic Synthesis* ; Pergamon Press: Oxford, 1993.
2. (a) Ref. 1b, chapter 3. (b) Ref. 1b, chapter 7. (c) Ref. 1b, chapter 9.
3. Other methodologies for the reductive desulfonylation of alkyl aryl sulfones involving different reagents than metals in solution, are, for instance: (a) SmI$_2$: Kende, A. S.; Mendoza, J. S. *Tetrahedron Lett.* **1990**, *31*, 7105-7108. Künzer, H.; Stahnke, M.; Sauer, G.; Wiechert, R. *Tetrahedron Lett.* **1991**, *32*, 1949-1952. (b) LiAlH$_4$: Dufort, N.; Jodoin, B. *Can. J. Chem.* **1978**, *56*, 1779-1781. (c) LiAlH$_4$/Ni-reagent: Becker, S.; Fort, Y.; Caubère, P. *J. Org. Chem.* **1990**, *55*, 6194-6198. Chan, M.-C.; Cheng, K.-M.; Ho, K. M.; Ng, C. T.; Yam, T. M.; Kang, B. S. L.; Luh, T.-Y. *J. Org. Chem.* **1988**, *53*, 4466-4471. Ho, K. M.; Lam, C. H.; Luh, T.-Y. *J. Org. Chem.* **1989**, *54*, 4474-4476. (d) Photolysis: Cheng, C.; Stock, L. M. *J. Org. Chem.* **1991**, *56*, 2436-2443. (e) Electrolysis: Lamm, B. *Tetrahedron Lett.* **1972**, 1469-1470. Lamm, B.; Nilsson, A. *Acta Chem. Scand., B* **1983**, *37*, 77-78.
4. Marshall, J. A.; Cleary, D. G. *J. Org. Chem.* **1986**, *51*, 858-863.
5. (a) Truce, W. E.; Frank, F. J. *J. Org. Chem.* **1967**, *32*, 1918-1920. (b) Paquette, L. A.; Fischer, J. W.; Browne, A. R.; Doecke, C. W. *J. Am. Chem. Soc.* **1985**, *107*, 686-691. (c) Hutchinson, D. K.; Fuchs, P. L. *J. Am. Chem. Soc.* **1987**, *109*, 4755-4756.
6. (a) Trost, B. M.; Arndt, H. C.; Strege, P. E.; Verhoeven, T. R. *Tetrahedron Lett.* **1976**, 3477-3478. (b) Anderson, M. B.; Ranasinghe, M. G.; Palmer, J. T.; Fuchs, P. L. *J. Org. Chem.* **1988**, *53*, 3125-3127.
7. (a) Chou, T.; You, M.-L. *Tetrahedron Lett.* **1985**, *26*, 4495-4498. (b) Chou, T.; You, M.-L. *J. Org. Chem.* **1987**, *52*, 2224-2226. (c) Chou, T.; Hung, S.-H.; Peng, M.-L.; Lee, S.-J. *Tetrahedron Lett.* **1991**, *32*, 3551-3554.
8. Yu, J.; Cho, H.-J.; Falck, J. R. *J. Org. Chem.* **1993**, *58*, 5892-5894.
9. For a similar reaction using an α-sulfonyl carbonyl compound and lithium naphthalenide to give the corresponding lithium enolate, see: Beau, J.-M.; Sinaÿ, P. *Tetrahedron Lett.* **1985**, *26*, 6193-6195.
10. Yus, M.; Ramón, D. J. *J. Chem. Soc., Chem. Commun.* **1991**, 398-400.
11. For other arene-catalysed lithiation from our laboratory, see: (a) Yus, M.; Ramón, D. J. *J. Org. Chem.* **1992**, *57*, 750-751. (b) Yus, M.; Ramón, D. J. *Tetrahedron Lett.* **1992**, *33*, 2217-2220. (c) Ramón, D. J.; Yus, M. *Tetrahedron* **1992**, *48*, 3585-3588. (d) Guijarro, D.; Mancheño, B.; Yus, M. *Tetrahedron* **1992**, *48*, 4593-4600. (e) Guijarro, D.; Mancheño, B; Yus, M. *Tetrahedron Lett.* **1992**, *33*, 5597-5600. (f) Guijarro, A.; Ramón, D. J.; Yus, M. *Tetrahedron* **1993**, *49*, 469-482. (g) Guijarro, D.; Mancheño, B.; Yus, M. *Tetrahedron* **1993**, *49*, 1327-1334. (h) Almena, J.; Foubelo, F.; Yus, M. *Tetrahedron Lett.* **1993**, *34*, 1649-1652. (i) Guijarro, A.; Yus, M. *Tetrahedron Lett.* **1993**, *34*, 2011-2014. (j) Gómez, C.; Ramón, D. J.; Yus, M. *Tetrahedron* **1993**, *49*, 4117-4126. (k) Gil, J. F.; Ramón, D. J.; Yus, M. *Tetrahedron* **1993**, *49*, 4923-4938. (l) Guijarro, A.; Yus, M. *Tetrahedron Lett.* **1993**, *34*, 3487-3490. (m) Guijarro, D.; Yus, M. *Tetrahedron* **1993**, *49*, 7761-7768. (n) Gil, J. F.; Ramón, D. J.; Yus, M. *Tetrahedron* **1993**, *49*, 9535-9546. (o) Ramón, D. J.; Yus, M. *Tetrahedron* **1993**, *49*, 10103-10110. (p) Ramón, D. J.; Yus, M. *Tetrahedron Lett.* **1993**, *34*, 7115-7118.
12. Starting sulfones **1** were easily prepared according to the literature method: Trost, B. M.; Schmuff, N. R. *J. Am. Chem. Soc.* **1985**, *107*, 396-405.
13. In absence of BF$_3$·Et$_2$O, and under the same reaction conditions, 46 and 23% isolated yield for compounds **3aa** and **3ba** were, respectively, obtained (compare to Table 1, entries 1 and 2).
14. (a) Inomata, K.; Kobayashi, T.; Sasaoka, S.; Kinoshita, H.; Kotake, H. *Chem. Lett.* **1986**, 289-292. (b) Brace, N. O. *J. Org. Chem.* **1993**, *58*, 4506-4508.
15. In the reaction with the starting material **1f** a 20% of diphenylmethane was also isolated; this compound results from the reductive dehydroxylation of the main product **4**. See, for instance: (a) Birch, A. J. *J. Chem. Soc.* **1945**, 809-813. (b) Birch, A. J.; Mukherji, S. M. *J. Chem. Soc.* ***1949**, 2531-2536.*

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