

# Nafion-H catalysed sulfonylation of aromatics with arene/alkenesulfonic acids for the preparation of sulfones<sup>1a†</sup>

George A. Olah,\* Thomas Mathew and G. K. Surya Prakash\*

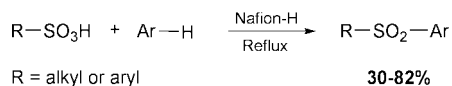
Loker Hydrocarbon Research Institute and Department of Chemistry, University of Southern California, Los Angeles, CA 90089-1661, USA

Received (in Corvallis, OR, USA) 21st May 2001, Accepted 17th July 2001

First published as an Advance Article on the web 16th August 2001

Synthesis of both symmetric and unsymmetric diaryl/aryl alkyl sulfones is easily achieved by Friedel–Crafts type sulfonylation of aromatics with suitable arene- or alkane-sulfonic acids in the presence of Nafion-H, a perfluorinated resinsulfonic acid catalyst.

The wide use of organosulfones as very versatile synthons in organic synthesis is well known for the past few decades.<sup>1b–d</sup>

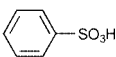
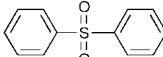
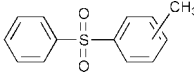
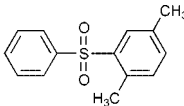
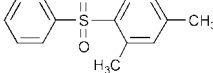
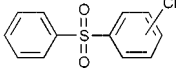
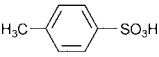
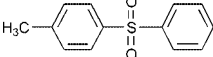
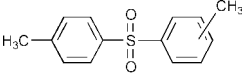
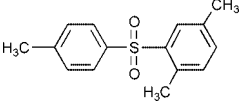
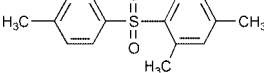
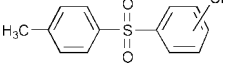
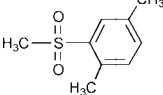


Scheme 1

Diaryl sulfones are important drugs active against malaria, leishmaniasis, infections in patients with AIDS and discoid lupus erythematosus.<sup>2–4</sup> Various methods for the synthesis of sulfones involve the conventional Friedel–Crafts type sulfonylation of aromatics using sulfonyl halides,<sup>5</sup> oxidation of the corresponding sulfides,<sup>6</sup> reactions of sulfonyl fluorides with organolithium compounds or Grignard reagents,<sup>7</sup> etc. Recently, effective synthesis of sulfones from aryl trifluoromethyl sulfone using Grignard reagents and sulfonyl halides and anhydrides using metal triflates and zeolites as catalysts<sup>8</sup> have been reported. Thus far no convenient synthetic method is available for the synthesis of sulfones using sulfonic acids directly.

In this communication, we would like to report an efficient preparation of aromatic sulfones directly from arene- or

Table 1 Nafion-H catalysed sulfonylation of aromatics using sulfonic acids

Sulfonic acid	Substrate	Time/h	Yield (%)	Sulfone
	Benzene	20	48	
	Toluene	20	52	
	<i>p</i> -Xylene	16	82	
	<i>m</i> -Xylene	16	80	
	Chlorobenzene	20	52	
	Benzene	20	50	
	Toluene	20	57	
	<i>p</i> -Xylene	8	78	
	<i>m</i> -Xylene	8	70	
	Chlorobenzene	20	55	
CH <sub>3</sub> SO <sub>3</sub> H	<i>p</i> -Xylene	8	30	

alkenesulfonic acids with the use of Nafion-H, a solid perfluorinated resin sulfonic acid polymer as a catalyst. We have previously found that Friedel–Crafts type intramolecular acylation with suitably *ortho* substituted benzoic acids in the presence of Nafion-H affords ketones in good yields.<sup>9</sup> Nafion membranes have also been found to allow permeation of sulfonating reagents such as SO<sub>3</sub> and 20% oleum during sulfonation reactions.<sup>10</sup> Preparation of aromatic symmetric and unsymmetric sulfones could be achieved in good yields (30–80%) by intermolecular Friedel–Crafts type sulfonylation of arenes with suitable sulfonic acids (Scheme 1).

Nafion-H has been found to be a suitable solid acid catalyst with high selectivity and catalytic activity giving good yields of sulfones. The reaction with the use of Nafion-H conveniently eliminates the use of volatile or noxious reagents. After the reactions with Nafion-H, the catalyst is easily regenerated.<sup>11</sup> This solid resin catalyst is more convenient and environmentally friendly in comparison with corrosive acid catalysts (liquid acids) generally used in reactions involving strong acids.

The sulfonylation reactions were carried out by refluxing a stirred mixture of the corresponding arene- or alkanesulfonic acid and excess arene in the presence of the solid Nafion-H catalyst. The arenes act as both the substrate and the solvent. The products were isolated after filtering the reaction mixture and distilling off the excess arene.<sup>12</sup>

The sulfonylation reactions are general for sulfonic acids such as benzenesulfonic acid, toluenesulfonic acid and methanesulfonic acid. Activated aromatics such as *p*-xylene and *m*-xylene afforded the corresponding sulfones in good yields (~80%). The yield of the corresponding sulfones from benzene and toluene were, however, low (5–15%) due to the insufficient activation of Nafion-H under the used relatively mild refluxing conditions. On the other hand, when the reactions with benzene and toluene were conducted under pressure at 160–165 °C, the product yields increased considerably (48–57%). Along with the product and the unreacted starting material, minor amounts of side products due to alkylation and dealkylation were also observed.

Azeotropic removal of water using a Dean–Stark trap increases the yields. As shown in Table 1, the present method provides an easy approach to sulfones with no undesired side products. Sulfonylation of toluene and chlorobenzene, afforded *para* substituted sulfones as the major product indicating a typical electrophilic aromatic sulfonylation. The method developed is simple, uses readily available arene- or alkanesulfonic acids instead of sulfonyl halides, anhydrides, *etc.*, used in Friedel–Crafts reactions. The substitution of the typical Friedel–Crafts type catalyst with this resin and its convenient regeneration bodes well for the protocol and its overall applicability.

Support of our work by Loker Hydrocarbon Research Institute is gratefully acknowledged.

## Notes and references

† Dedicated to our colleague, Professor William P. Weber on the occasion of his sixtieth birthday.

- (a) Considered as catalysis by solid super acids, Part 34. For Part 33, see ref. 9; (b) K. Tanaka and A. Kaji, *Synthetic Uses of Sulfones in The Chemistry of Sulphones and Sulphoxides*, Eds. S. Patai, Z. Rappoport and C. J. M. Stirling, Wiley-Interscience, New York, 1988, ch. 15, pp. 759; (c) B. M. Trost, *Bull. Chem. Soc. Jpn.*, 1988, **61**, 107; (d) L. Field, *Synthesis*, 1978, 713.
- R. C. Hastings and S. G. Franzblau, *Ann. Rev. Pharmacol. Toxicol.*, 1966, **28**, 231.
- G. Wozel, *Int. J. Dermatol.*, 1989, **28**, 17.
- J. S. Lo, R. E. Berg and K. J. Tomecki, *Int. J. Dermatol.*, 1989, **28**, 497.
- J. B. Hendrickson and K. W. Bair, *J. Org. Chem.*, 1977, **42**, 3875; G. A. Olah and H. C. Lin, *Synthesis*, 1974, 342.
- G. A. Olah and B. G. B. Gupta, *J. Org. Chem.*, 1983, **48**, 3585; D. J. Procter, *J. Chem. Soc., Perkin Trans. 1*, 2000, **1**, 835.
- Y. Shiota, T. Nagai and N. Tokura, *Tetrahedron*, 1969, **25**, 3193; L. L. Frye, E. L. Sullivan, K. P. Cusack and J. M. Funaro, *J. Org. Chem.*, 1992, **57**, 697.
- R. W. Steensma, S. Galabi, J. R. Tagat and S. W. McCombie, *Tetrahedron Lett.*, 2001, **42**, 2281; R. P. Singh, R. M. Kamble, K. L. Chandra, P. Sravanan and V. K. Singh, *Tetrahedron*, 2001, **57**, 241; S. Repichet, C. Le Roux, P. Hernandez, J. Dubac and J. R. Desmurs, *J. Org. Chem.*, 1999, **64**, 6479; B. M. Chaudhary, N. S. Chaudhari and M. L. Kantam, *J. Chem. Soc., Perkin Trans. 1*, 2000, **16**, 2689.
- G. A. Olah, T. Mathew, M. Farnia and G. K. S. Prakash, *Synlett*, 1999, 1067.
- R. J. Vaughan, *US Patent*, 4308215, 1981; *Chem. Abstr.*, 1982, **96**, 87450a.
- G. A. Olah, P. S. Iyer and G. K. S. Prakash, *Synthesis*, 1986, 513 and references therein; T. Yamato, C. Hideshima, G. K. S. Prakash and G. A. Olah, *J. Org. Chem.*, 1991, **56**, 3192; M. Hachoumy, T. Mathew, E. C. Tongo, Y. D. Vankar, G. K. S. Prakash and G. A. Olah, *Synlett*, 1999, 363; G. K. S. Prakash, T. Mathew, S. Krishnaraj, E. R. Marinez and G. A. Olah, *Appl. Catal., A*, 1999, **181**, 283.
- Typical sulfonylation procedure is as follows: to a solution of dry benzenesulfonic acid (790 mg, 5.0 mmol) in dry *p*-xylene (40 mL), Nafion-H (400 mg, 50 wt%) was added and stirred. The flask was fitted with a Dean–Stark trap and the solution was refluxed continuously with stirring for 16 hours (water formed during the reaction was removed completely by introducing dry molecular sieves, ≈2.0 g, in the trap). The reaction mixture was filtered and washed with 10% NaHCO<sub>3</sub> solution to remove any amount of unreacted sulfonic acid. After washing with water and drying with anhydrous Na<sub>2</sub>SO<sub>4</sub>, excess *p*-xylene was distilled off and the residue was recrystallized from a mixture of dichloromethane and *n*-hexane (1:2) to afford 2,5-dimethylphenyl phenyl sulfone as a white crystalline solid, (1.0 g, 82%) mp 101–103 °C.