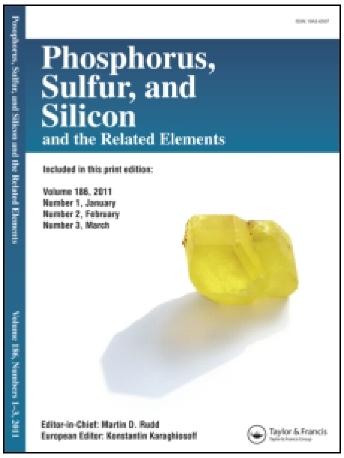

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Direct Sulfonylation of Aromatic Rings with Aryl or Alkyl Sulfonic Acid Using Supported P_2O_5/Al_2O_3

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Direct sulfonylation of aromatic rings with aryl or alkyl sulfonic acid supported P_2O_5/Al_2O_3 (w/w 50%) under heterogeneous conditions in short reaction time and high yields.

Keywords Diphosphorus pentoxide; sulfonylation; sulfones

INTRODUCTION

Aryl sulfones are useful compounds in organic synthesis and industry.[1,2] Diaryl sulfones are important biological molecules against leishmaniasis, malaria, infections in patients with AIDS, and discoid lupus erythematosus.[3,4] Diaryl or aryl/alkyl sulfones can be synthesized by

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Friedel-Crafts sulfonylation of aromatic compounds[5–10] or by direct sulfonylation of arenes by sulfonic acids by using Nafion-H,[11] polyphoshphoric acids,[12] or phospours pentoxide/methansulfonic acid.[13,14] Unfortunately most of these methods suffer at least from one of the following disadvantages: (1) high cost of preparations, (2) long reaction time, (3) hygroscopisity, (4) high acidity, (5) instability, and (6) tedious work-up procedures. Using P2O5:MeSO3H has certain unfortunate such as time consuming, didtllation of methansufonic acid before using thermal decomposition of a reagent and using 10 fold of methansulfonic acid.

RESULTS AND DISCUSSION

Over the last two decades, the use of solid supports has become popular due to their characteristic properties such as enhanced selectivity and reactivity, a straightforward work-up procedure, milder reaction conditions, and associated ease of manipulation.[15,16] Because of our interest in the development of using solid support in organic chemistry,[17] we wish to report an efficient procedure for the preparation of aromatic sulfones from aryl or alkyl sulfonic acid with P_2O_5/Al_2O_3 under heterogeneous conditions. Based on the ability of P_2O_5, and in order to decrease air sensitivity of it, we supported P_2O_5 on Al_2O_3[16] and used for synthesis of sulfones *via* direct sulfonylation of aromatic rings. Preparation of symmetric and unsymmetric aromatic sulfones was achieved in moderate to good yields (55–90%) *via* a Friedel-Crafts type of sulfonylation of arenes with various sulfonic acids (Scheme 1).

$$R_1 - SO_3H + Ar - H \xrightarrow[\text{reflux}]{P_2O_5/Al_2O_3\,(\text{w/w } 50\%)} R_1SO_2Ar$$

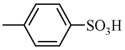
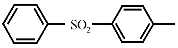
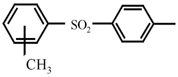
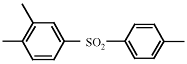
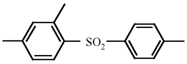
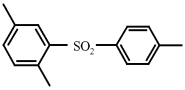
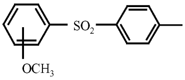
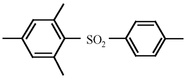
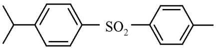
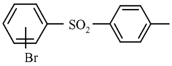
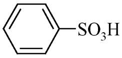
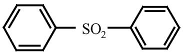
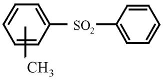
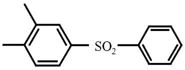
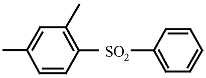
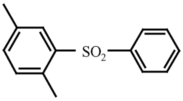
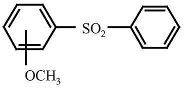
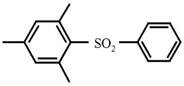
$$R_1 = \text{alkyl or aryl}$$

SCHEME 1

The sulfonylation reactions were carried out by refluxing a stirring mixture of the corresponding aryl or alkyl sulfonic acid in excess of the aromatic compounds in the presence of supported P_2O_5/Al_2O_3 (w/w 50%) (Table I). The starting aromating compounds act either as a substrate or a solvent. The present method provides an efficient, clean, and fast approach for the preparation of sulfones without any by-product. We found that the optimized reaction time for all of the reaction was 1 h under refluxing conditions.

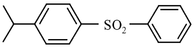
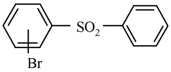
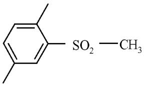
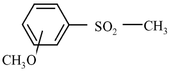
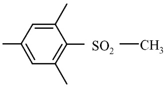
In order to evaluate the synergy between P_2O_5 and Al_2O_3, we performed several experiments. When we examined the reaction of 5 mL of

TABLE I Sulfonylation of Aromatic Rings by Aryl or Alkyl Sulfonic Acid in the Presence of Supported P_2O_5/Al_2O_3 (w/w 50%).

Entry	Sulfonic acid	Aromatic compound	Product[a]	Yield (%)[b] (O:P)	Yield (%)[c]	Melting point (°C)
1		Benzene		55	25	125–127
2		Toluene		75 (10:90)	32	147–150[d]
3		O-xylene		80	35	118–120
4		M-xylene		82	38	58–60
5		P-xylene		85	35	105–107
6		Anisole		90 (15:85)	44	79–81[d]
7		Mesitylene		80	30	115–117
8		Cumene		70	32	100–104
9		Bromobenzene		60 (10:90)	0	125–128[d]
10		Benzene		56	25	117–118
11		Toluene		82 (20:80)	35	83–85[d]
12		O-xylene		70	34	111–114
13		M-xylene		72	37	88–90
14		P-xylene		75	35	104–106
15		Anisole		87 (40:60)	47	80–82[d]
16		Mesitylene		85	32	79–81

(Continued on next page)

TABLE I Sulfonylation of Aromatic Rings by Aryl or Alkyl Sulfonic Acid in Presence of Supported P_2O_5/Al_2O_3 (w/w 50%) *(Continued)*

Entry	Sulfonic acid	Aromatic compound	Product[a]	Yield (%)[b] (O:P)	Yield (%)[c]	Melting point (°C)
17		Cumene		80	30	96–97
18		Bromobenzene		65 (15:85)	0	85–87[d]
19	CH_3—SO_3H	P-xylene		60	—	136–138
20		Anisole		65 (18:82)	—	110–112[d]
21		Mesitylene		55	—	126–128

[a] All the products were characterized by ^{1}H-NMR, FT-IR, TLC and physical data with authentic samples.[9]

[b] In excess of substrate in 1 h.

[c] In 1,2-dicholoroethane in 2 h.

[d] Melting point of mixture product.[9]

anisole and one molar ratio of *p*-toluenesulfonic acid with P_2O_5 without using any Al_2O_3, the yield was only 60% after 10 h of refluxing. We also treated 1 mmol of anisole with 1 mmol of *p*-toluenesulfonic acid with the supported P_2O_5 on Al_2O_3 (0.34 g) in $ClCH_2CH_2Cl$ under refluxing conditions. The yield was 50% after 10 h of refluxing, as is shown in Table I. The yield of the reaction 1,2-dicholoroethane is lower and the reaction time is longer. Therefore, we decided to perform the reaction of sulfonic acid derivatives in excess aromatic compounds with supported P_2O_5 on Al_2O_3.

In summary, the advantage of this methodology over the reported methods is the availability of the starting materials, simplicity of sulfonylation procedure, a clean work-up, a short reaction time, high yields, and an easily handled and inexpensive reagent.

EXPERIMENTAL SECTION

All yields refer to isolated products. The products were characterized by comparison with authentic samples (IR, ^{1}H-NMR spectra, melting and boiling points, and TLC). All ^{1}H-NMR spectra were recorded at 300 MHz in $CDCl_3$ and CCl_4 relative to TMS (0.00 ppm).

Preparation of P_2O_5/Al_2O_3 (w/w 50%)

We placed Al_2O_3 (active acidic-0.063–0.200 mm) in an oven at 120°C for 24 h and then P_2O_5 (5 g, weighed out in a drybox) was added on Al_2O_3 (5 g), mixed, and then placed in a stoppered flask for use.

Preparation of Mesityl Tolyl Sulfone

Typical Procedure

To a mixture of *p*-toluene-sulfonic acid monohydrate (0.38 g, 2 mmol) and dry mesitylene (5 mL) was added to P_2O_5/Al_2O_3 (w/w 50%, 0.67 g). The solution was refluxed continuously with stirring for 1 h. The reaction mixture was filtered and washed with 10% $NaHCO_3$ solution to remove the unreacted sulfonic acid. After washing with water and drying with anhydrous Na_2SO_4, excess mesitylene was distilled off by a vacuum and the residue was recrystalized from cyclohexane to afford mesityl tolyl sulfone as a white crystalline solid (0.44 g, 80%), mp.: 115–117°C (reported: 115–117°C),[6] ^{1}H NMR δ (90 MHz, $CDCl_3$) 7.66 (d, 2H), 7.33 (d, 2H), 6.96 (S, 2H), 2.62 (S, 6 H), 2.42 (S, 3H), 2.32 (S, 3H), IR (KBr) cm^{-1}: 1140 (S, SO_2), 1310 (S, SO_2).

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