

Supporting Information

Zinc-Catalyzed Aminosulfonation of Hydrocarbons

Biswajit Kalita and Kenneth M. Nicholas*
Department of Chemistry and Biochemistry
University of Oklahoma, Norman OK 73019

Includes:

Summary of screening/optimization experiments

Representative experimental procedure for preparation of compounds in Table 1

Spectroscopic and characterizational data for all products

PhI=NTs/ZnBr₂/benzene trapping experiment

General information.

All starting materials were obtained from commercial sources and were used as such (or purified wherever necessary). ZnBr₂, ZnI₂, CdCl₂, and HgCl₂ were purchased from Aldrich and were used as obtained. Benzene was freshly distilled over Na/benzophenone; CH₃CN and CH₂Cl₂ were freshly distilled over CaH₂; and anhydrous 1,1,1-trifluorotoluene was purchased from Aldrich and used as such under an Ar balloon. TsN=IPh was synthesized according to a known method.¹ Temperatures mentioned refer to the external oil bath temperature. All additions and manipulations were done under a dry N₂ atmosphere. Flash column chromatography was done using 230-400 mesh silica gel. Preparative TLC was done using commercial silica plates with UV absorbance.

All ¹H (300 MHz) and ¹³C (75 MHz) NMR spectra were recorded at a Varian Mercury spectrometer and chemical shifts (δ ppm) were reported relative to the residual solvent peaks. Mass spectra were recorded using Finnigan TSQ 700 spectrometer with an electrospray source. Melting points were recorded with a Mel-Temp apparatus using open capillaries and are uncorrected.

Summary of optimization studies.

The effectiveness of the screening reactions was judged by TLC and H-NMR analysis of the crude reaction mixtures (amine product: unreacted substrate:TsNH₂).

Ratios of substrate (ethyl benzene or ethyl anisole) to TsN=IPh or TsNH₂/PhI(Oac)₂, reaction temperature, and time: Rxns. were conducted at rt and 50 °C; over 5-30 h; 1:1 to 1:5 substrate: N-reagent.

Catalysts: ZnBr₂, ZnI₂, CdCl₂, HgCl₂ all produced the amine derived from ethylanisole with the Zn salts being superior at rt in benzene.

Catalyst loading (mol % ZnBr₂) was assessed from 5-50 mol%; increased rate/conversion was found with higher catalyst loading.

Solvent screening: Solvents screened were dry CH_2Cl_2 (CaH_2), dry Benzene (Na - benzophenone) and dry 1,1,1-trifluorotoluene (Aldrich). Of these solvents, dry benzene was found to be the most suitable solvent (from ^1H NMR of the crude reaction residue).

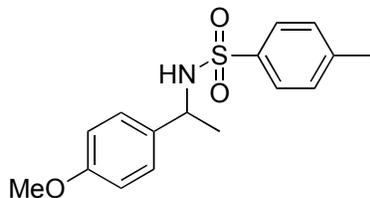
Representative procedure.

Caution: The dry solids TsN=IPh and ZnBr_2 should not be mixed together since we have observed a strongly exothermic process upon mixing the two solid compounds in mmol quantities.

To an oven-dried Schlenk tube (or a test tube) under N_2 was transferred anhydrous ZnBr_2 (15-20 mol% of the substrate) and 2 mL of dry benzene. To this was added TsN=IPh (1.0 mmol), 4 Å molecular sieves, 4-ethyl anisole (0.50 mmol), and another 3 mL of dry benzene by syringe. The suspension was stirred at room temperature (or at 50°C , Table 1) under N_2 . Another 0.5 mmol of TsN=IPh was added to the reaction mixture under N_2 atmosphere after 5-6 h and stirring was continued for the specified time period (Table 1) during which the reaction mixture became almost homogenous and the color changed into dark brown. When TLC analysis indicated no further conversion, the reaction mixture was filtered through filter paper, washed with CHCl_3 (~15-20 ml) and the solvent removed by rotary evaporation. The crude residue thus obtained was purified by flash column chromatography or preparative thin layer chromatography eluting with ethyl acetate/petroleum ether mixtures.

Characterizational data:

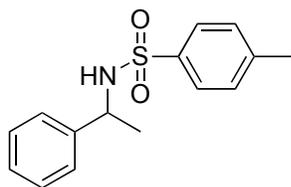
***N*-[1-(4-Methoxy-phenyl)-ethyl]-4-methyl benzenesulfonamide (1).**



Yield: 71%. white solid, m.p. 88-89 °C (lit² 87-88 °C).

¹H NMR (CDCl₃, 300 MHz) δ 7.64 (d, 2H, J=8.1 Hz), 7.20 (d, 2H, J=8.7 Hz), 7.03 (d, 2H, J=8.7 Hz), 6.73 (d, 2H, J=9 Hz), 5.09 (d, 1H, J=6.9 Hz), 4.43-4.38 (m, 1H), 3.75 (s, 3H), 2.39 (s, 3H), 1.40 (d, 3H, J=6.9 Hz). ESI-MS m/z 328 [M+Na⁺, 100], 632.73 [(Mx2)+Na⁺, 39].

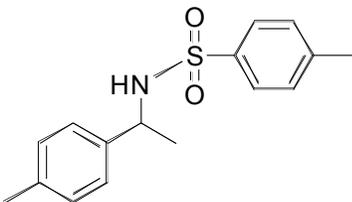
4-Methyl-*N*-(1-phenyl-ethyl)-benzenesulfonamide (2).



Yield: 48%, white solid, m.p. 77-78 °C (lit³ 78-80 °C).

¹H NMR (CDCl₃, 300 MHz) δ 7.64 (d, 2H, J=8.1 Hz), 7.20-7.09 (m, 7H), 5.20 (d, 1H, J=6.9 Hz), 4.48-4.43 (m, 1H), 2.39 (s, 3H), 1.42 (d, 3H, J=6.9 Hz). ESI-MS m/z 298 [M+Na⁺, 40], 572.80 [(Mx2)+Na⁺, 27].

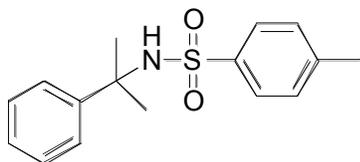
4-Methyl-*N*-(1-*p*-tolyl-ethyl)-benzenesulfonamide (3)⁴.



Yield: 52%, white solid, m.p. 108-111°C .

^1H NMR (CDCl_3 , 300 MHz) δ 7.81 (d, 2H, $J=8.1$ Hz), 7.36 (d, 2H, $J=8.1$ Hz), 7.16 (br, s, 4H), 5.29 (d, 1H, $J=7.2$ Hz), 4.62-4.52 (m, 1H), 2.56 (s, 3H), 2.45 (s, 3H), 1.57 (d, 3H, $J=6.9$ Hz). ESI-MS m/z 311.93 [$\text{M}+\text{Na}^+$, 91], 600.73 [$(\text{Mx}2)+\text{Na}^+$, 83].

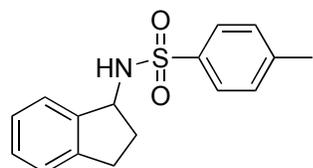
4-Methyl-*N*-(1-methyl-1-phenyl-ethyl)-benzenesulfonamide (4)⁵.



Yield: 38%, white solid, m.p. 138-141°C.

^1H NMR (CDCl_3 , 300 MHz) δ 7.59 (d, 2H, $J=8.4$ Hz), 7.33-7.31 (m, 2H), 7.20-7.15 (m, 5H), 5.23 (br, s, 1H), 3.39 (s, 3H), 1.63 (s, 6H). ESI-MS m/z 312 [$\text{M}+\text{Na}^+$, 100], 600.73 [$(\text{Mx}2)+\text{Na}^+$, 31].

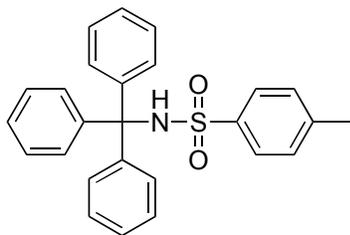
***N*-Indan-1-yl-4-methyl-benzenesulfonamide (5).**



Yield: 41%, white solid, m.p. 140-143 °C (lit⁶ 141-142 °C).

^1H NMR (CDCl_3 , 300 MHz) δ 7.85 (d, 2H, $J=8.1$ Hz), 7.35 (d, 2H, $J=8.1$ Hz), 7.22-7.08 (m, 4H), 4.87-4.80 (m, 1H), 4.74-4.71 (m, br, 1H), 2.96-2.86 (m, 1H), 2.80-2.69 (m, 1H), 2.46 (s, 3H), 2.39-2.29 (m, 1H), 1.82-1.69 (m, 1H). ESI-MS m/z 310 ($\text{M}+\text{Na}^+$, 100), 596.80 [$(\text{Mx}2)+\text{Na}^+$, 60.8].

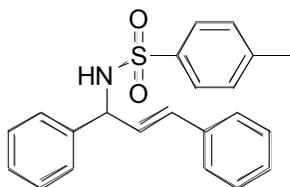
4-Methyl-*N*-trityl-benzenesulfonamide (6).



Yield: 38%, white solid, m.p. 240-242° C (lit⁷ 242-243° C).

¹H NMR (CDCl₃, 300 MHz) δ 7.35–7.32 (m, 6H), 7.19-7.17 (m, 9H), 7.10 (d, 2H, J=8.4 Hz), 6.97 (d, 2H, J=8.4 Hz), 5.91 (s, 1H), 2.34 (s, 3H). ESI-MS m/z 243.07 [M-Ts, 87], 435.93 [M+Na⁺, 49], 848.80 [(Mx2)+Na⁺, 100].

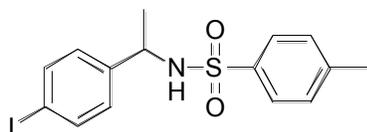
N-(1,3-Diphenyl-allyl)-4-methyl-benzenesulfonamide (7).



Yield: 28%, white solid, m.p. 152-154°C (lit⁸ 153-154°C).

¹H NMR (CDCl₃, 300 MHz) δ 7.67 (d, 2H, J=8.4 Hz), 7.31-7.16 (m, 12H), 6.39-6.34 (d, 1H, 16.2 Hz), 6.12-6.05 (dd, 1H, J=6.6 Hz & J=6.6 Hz), 5.12 (t, 1H, J=6.9 Hz), 4.81 (d, 1H, J=7.2 Hz), 2.34 (s, 3H). ¹³C NMR (CDCl₃, 75 MHz) δ 143.5, 139.8, 137.8, 136.2, 132.4, 129.6, 128.9, 128.6, 128.3, 128.1, 127.5, 127.2, 126.7, 59.9, 21.6. ESI-MS m/z 386.07 [M+Na⁺, 74], 748.87 [(Mx2)+Na⁺, 100].

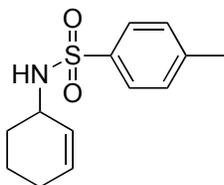
N-[1-(4-Iodo-phenyl)-ethyl]-4-methyl-benzenesulfonamide (8).



Yield: 42%, white solid, m.p. 138-141°C.

^1H NMR (CDCl_3 , 300 MHz) δ 7.58 (d, 2H, $J=8.4$ Hz), 7.48 (d, 2H, $J=8.1$ Hz), 7.18 (d, 2H, $J=8.4$ Hz), 6.85 (d, 2H, $J=8.7$ Hz), 5.31 (d, 1H, $J=6.9$ Hz), 4.43-4.38 (m, 1H), 2.42 (s, 3H), 1.37 (d, 3H, $J=7.2$ Hz). ^{13}C NMR (CDCl_3 , 75 MHz) δ 143.5, 141.8, 137.6, 137.5, 129.6, 128.4, 127.2, 92.9, 53.4, 23.4, 21.7. ESI-MS m/z 230.93 [M-TsNH], $\text{M}+\text{Na}^+$, 85], 824.53 [$(\text{Mx}_2)+\text{Na}^+$, 100]. Anal. calcd. for $\text{C}_{15}\text{H}_{16}\text{INO}_2\text{S}$ (%) C 44.9, H 4.0, N 3.5; found C 45.2, H 4.0, N 3.5.

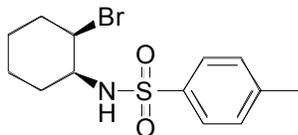
***N*-Cyclohex-2-enyl-4-methyl-benzenesulfonamide (10a).**



Yield: 40%, white solid, m.p. 102-104 °C (lit⁹ 101-102 °C).

^1H NMR (CDCl_3 , 300 MHz) δ 7.79 (d, 2H, $J=9.0$ Hz), 7.32 (d, 2H, $J=8.4$ Hz), 5.80-5.74 (m, 1H), 5.36-5.30 (m, 1H), 4.49 (br, d, 1H, $J=8.7$ Hz), 3.82-3.80 (br, m, 1H), 2.43 (s, 3H), 1.94-1.91 (m, 2H), 1.77-1.73 (m, 1H), 1.61-1.51 (m, 3H). ESI-MS m/z 274 [$\text{M}+\text{Na}^+$, 89], 524.93 [$(\text{Mx}_2)+\text{Na}^+$, 80.7].

***N*-(*cis*-2-Bromo-cyclohexyl)-4-methyl-benzenesulfonamide (10b).**

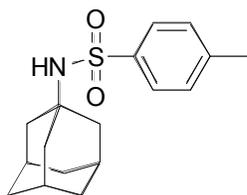


Yield: 10%, white solid, m.p. 109-112°C.

^1H NMR (CDCl_3 , 300 MHz) δ 7.79 (d, 2H, $J=8.4$ Hz), 7.33 (d, 2H, $J=8.1$ Hz), 4.81 (d, 1H, $J=9.3$ Hz), 4.32-4.31 (m, 1H), 3.23-3.21 (m, 1H), 2.44 (s, 3H), 1.82-1.23 (m, 8H). ESI-MS m/z 353.93 [$\text{M}+\text{Na}^+$, 100], 355.93 [$\text{M}+2+\text{Na}^+$, 77], 252.13 [M-Br , 59].

The *cis*-stereochemistry assigned to **10b** is supported by its close ¹H-NMR spectral similarity to the corresponding *cis*-2-chloro analog whose structure has been established by X-ray diffraction (ref. 5). Moreover, the ¹H NMR spectrum of **10b** is distinctly different from that of the known *trans*-isomer (ref. 10).

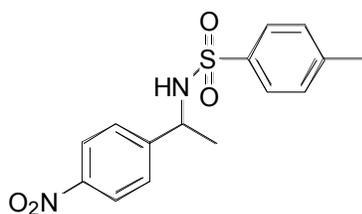
***N*-Adamantan-1-yl-4-methyl-benzenesulfonamide (11)¹¹.**



Yield: 22%, white solid, 158-161°C.

¹H NMR (CDCl₃, 300 MHz) δ 7.80 (d, 2H, J=8.4 Hz), 7.29 (d, 2H, J=7.8 Hz), 4.57 (s, 1H), 2.43 (s, 3H), 2.01 (br, s, 3H), 1.79 (d, 6H, J=3 Hz), 1.61-1.57 (m, 6H). ESI-MS m/z 305.87 [M+1, 29], 322.93 [(M-Ts)_{x2}+Na⁺, 55], 632.93 [(M_{x2})+Na⁺, 100].

4-Methyl-*N*-[1-(4-nitro-phenyl)-ethyl]-benzenesulfonamide (12).



Yield: 10%, m.p. 156-159 °C (lit¹¹ 157-159 °C).

¹H NMR (CDCl₃, 300 MHz) δ 8.05 (d, 2H, J=8.7 Hz), 7.59 (d, 2H, J=8.1 Hz), 7.32 (d, 2H, J=9 Hz), 7.19 (d, 2H, J=7.8 Hz), 5.02 (d, 1H, J=6.3 Hz), 4.62-4.53 (m, 1H), 2.39 (s, 3H), 1.42 (d, 3H, J=6.9 Hz).

Reaction of PhI=NTs with ZnBr₂ in benzene (no substrate)

To ZnBr₂ suspended in 4 mL of dry benzene was added 4Å molecular sieves and then PhI=NTs (200 mg). The mixture was stirred at rt for 30 h and then heated at 50 °C for another 15 h. After solvent evaporation an NMR spectrum of the residue (d₄-methanol) indicated the formation of TsNH₂ primarily. TLC analysis (1:7 ether/pet. ether) showed only two additional spots. The major non-polar spot was identified as PhI (by comparison of R_f, appearance and H-NMR spectrum). A second, minor non-polar component could be isolated by preparative TLC on silica gel (1:7 ether/pet. ether). The ¹H NMR spectrum of this material [CDCl₃, 7.90 (d, J= 8 Hz, 4H), 7.40 (d, J= 8 Hz, 4H), 2.50 (s, 3H)] and its EI-MS (338 = M⁺ for C₁₄H₁₄N₂S₂O₄) showed it to be TsN=NTs.

S.I. References:

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