Selective Monodesulfonylation of *N,N*-Disulfonylarylamines with Tetrabutylammonium Fluoride

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The monodesulfonylation reaction of *N,N*-bis(methylsulfonyl)-, *N,N*-bis(phenylsulfonyl)-, and *N,N*-bis(*p*-tolylsulfonyl)arylamines easily proceeded using tetrabutylammonium fluoride in tetrahydrofuran under mild conditions to give the corresponding *N*-monosulfonylarylamines in excellent yields.

Key words tetrabutylammonium fluoride; monodesulfonylation; disulfonylarylamine

Sulfonyl groups are useful protecting groups for amino groups, because of the electron-withdrawing effect, high stability, and ease of formation. 2-Unsubstituted and 2-substituted *N*-monosulfonylarylamines have been used for the synthesis of various indole derivatives. For example, the reaction of lithium *N*-(*p*-toluenesulfonyl)anilide with propynyliodonium triflate gave 2-methyl-1-(*p*-tolylsulfonyl)indole.¹⁾ The palladium(0)-catalyzed reaction of *N*-(2-iodophenyl)methanesulfonamide with terminal acetylenes yielded 2-substituted 1-(methylsulfonyl)indole directly instead of forming *N*-(2-ethynylphenyl)methanesulfonamides.²⁾ We have also reported that the palladium(II)-catalyzed cyclization reaction of *N*-(2-ethynylphenyl)methanesulfonamides in the presence of carbon monoxide or electron-deficient alkenes afforded 2-substituted 3-indolecarboxylates^{3a,b)} or 3-alkenylindoles.^{3c)}

However, the preparation of the *N*-sulfonylarylamines is sometimes troublesome in that the reaction of some arylamines with sulfonyl chlorides gives a mixture of *N*-monosulfonyl- and *N,N*-disulfonylarylamines. For example, in the course of our synthetic study concerning indole derivatives, when 2-iodo-4-bromoaniline was allowed to react with 1 eq of methanesulfonyl chloride in pyridine, the expected *N*-monosulfonylaniline was obtained in 63% yield along with the *N,N*-disulfonylaniline (5% yield) and the starting material (30% yield) as shown in Chart 1. When the reaction was carried out until the starting material disappeared with excess methanesulfonyl chloride, the product was a mixture of the *N,N*-disulfonylaniline and the *N*-monosulfonylaniline.

Few reports⁴⁾ for the monodesulfonylation of *N,N*-disulfonylarylamines are known. While *N,N*-bis(trifluoromethylsulfonyl)aniline was easily monodesulfonylated with various nucleophiles,^{4b)} relatively drastic conditions, hydrolysis with 20% aq. KOH in pyridine, for the monodesulfonylation of *N,N*-bis(methylsulfonyl)anilines was required.^{4a)} On the other hand, we reported⁵⁾ that tetrabutylammonium fluoride (TBAF) is a good desulfonylation reagent for *N*-sulfonyl heteroaromatic compounds. Based on this background, we now report the monodesulfonylation of *N,N*-disulfonylarylamines with TBAF in tetrahydrofuran (THF) at room temperature with a short reaction time.

Various arylamines were sulfonylated with an appropriate amount of sulfonyl chlorides in pyridine until the starting arylamines disappeared by silica gel TLC. From the results shown in Table 1, the tendency that anilines having electron-donating groups yielded monosulfonylated products (Table 1, runs 1—3) and anilines having electron-withdrawing groups

gave disulfonylated products (runs 4—10) was confirmed. *N,N*-Disulfonylated 2-methoxy- (**3a**) and 4-methylaniline (**3b**) were prepared by the sulfonylation of the corresponding *N*-monosulfonylanilines (**2a**, **b**) in the presence of sodium hydride in THF.

At first, the desulfonylation of *N,N*-bis(methylsulfonyl)-2-nitroaniline (**3fa**) with TBAF was examined. The reaction with 1.1 eq of TBAF at room temperature for 15 min gave *N*-methylsulfonyl-2-nitroaniline (**2fa**) in quantitative yield (Table 2, run 8). However, under the conditions using 0.5 eq of TBAF at room temperature, **3fa** was not completely monodesulfonylated (run 7). The monodesulfonylation reaction of *N,N*-bis(phenylsulfonyl)- (**3fb**) and *N,N*-bis(*p*-toluenesulfonyl)anilines (**3fc**) with 1.1 eq of TBAF at room temperature smoothly gave **2fb** and **2fc** in 93 and 97% yields, respectively (runs 9 and 10).

While the reaction of *N,N*-bis(phenylsulfonyl)-2-methoxyaniline (**3a**) with 1.1 eq of TBAF in THF for 0.5 h under reflux gave the corresponding *N*-monosulfonylaniline (**2a**) in 98% yield (Table 2, run 1), the reaction of **3a** at room temperature for 3 h did not proceed to completion and afforded **2a** in 30% yield (run 2). On the contrary, the monodesulfonylation reaction of *N,N*-disulfonylanilines with electron-withdrawing groups such as *N,N*-bis(*p*-tolylsulfonyl)-4-acetyl- (**3c**), *N,N*-bis(phenylsulfonyl)-4-ethoxycarbonyl- (**3d**), and *N,N*-bis(methylsulfonyl)-2-cyanoanilines (**3e**), easily proceeded in a short time to give the corresponding *N*-monosulfonylanilines (**2c**—**e**) in excellent yields (94—100%) without affecting the acetyl, ethoxycarbonyl, and cyano groups. As a result, the mono-desulfonylation reaction of *N,N*-disulfonylanilines having electron-withdrawing groups tended to proceed easily under these conditions.

The mono-desulfonylation reaction conditions were also applicable to *N,N*-disulfonyl heteroarylamines such as 2-[*N,N*-bis(methylsulfonyl)amino]pyridine (**3g**) and 2-[*N,N*-bis(phenylsulfonyl)amino]pyrimidine (**3h**) to give the desired *N*-monosulfonyl heteroarylamines (**2g**, **h**) in good yields.

From a practical view point, we next examined the synthesis of *N*-sulfonylarylamines. As shown in Chart 2, 2-aminobenzonitrile (**1e**) was allowed to react with 2 eq of methanesulfonyl chloride to give a mixture of the *N*-mono- (**2e**) and the *N,N*-bis(methylsulfonyl)anilines (**3e**) and the mixture was treated with 10 eq of TBAF at room temperature to give **2e** in quantitative yield. This result shows that even if a mixture of *N*-mono- and *N,N*-disulfonylarylamines is produced by the sulfonylation reaction of arylamines, *N*-mono-

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Chart 1

Table 1. Sulfonylation of Arylamines (1)

		$\text{ArNH}_2 \xrightarrow[\text{pyridine, time}]{\text{RSO}_2\text{Cl}} \text{ArNHSO}_2\text{R} + \text{ArN} \begin{smallmatrix} \text{SO}_2\text{R} \\ \text{SO}_2\text{R} \end{smallmatrix}$			
		1	2	3	

Run	ArNH ₂ (1)	RSO ₂ Cl		Temp. (°C)	Time (h)	Yield (%)	
		R	eq			2	3
1	2-Methoxyaniline (1a)	Ph	1	r.t.	24	97	0
2	2-Methoxyaniline (1a)	Ph	2	r.t.	12	100	0
3	4-Methylaniline (1b)	4-MeC ₆ H ₄	1	r.t.	24	90	0
4	4-Aminoacetophenone (1c)	4-MeC ₆ H ₄	5	r.t.	24	59	30
5	Ethyl 4-aminobenzoate (1d)	Ph	2	r.t.	24	86	12
6	2-Aminobenzonitrile (1e)	Me	1	r.t.	24	74	11
7	2-Aminobenzonitrile (1e)	Me	2	r.t.	48	17	83
8	2-Nitroaniline (1f)	Me	5	r.t.	24	8	67
9	2-Nitroaniline (1f)	Ph	7.5	r.t.	24	60	10
10	2-Nitroaniline (1f)	4-MeC ₆ H ₄	2	60	12	76	19
11	2-Aminopyridine (1g)	Me	3.6	r.t.	24	53	10
12	2-Aminopyrimidine (1h)	Ph	5	r.t.	24	82	3

Temp.=temperature. r.t.=room temperature.

Table 2. Monodesulfonylation of *N,N*-Disulfonylarylamines (3) with TBAF

<div> <div> $\text{ArN} \begin{matrix} \text{SO}_2\text{R} \\ \text{SO}_2\text{R} \end{matrix} \xrightarrow[\text{THF, temp., time}]{\text{TBAF}} \text{ArNHSO}_2\text{R}$ </div> <div> <div>3</div> <div>2</div> </div> </div>						
Run	3 Ar	R	TBAF (eq)	Temp. (°C)	Time (h)	Yield (%)
1	2-MeOC ₆ H ₄ (3a)	Ph	1.1	Reflux	0.5	98
2	2-MeOC ₆ H ₄ (3a)	Ph	1.1	r.t.	3	30 [69]
3	4-MeC ₆ H ₄ (3b)	4-MeC ₆ H ₄	1.1	Reflux	6	100
4	4-MeCOC ₆ H ₄ (3c)	4-MeC ₆ H ₄	1.1	r.t.	0.5	97
5	4-EtOOC ₆ H ₄ (3d)	Ph	1.1	r.t.	0.5	94
6	2-NCC ₆ H ₄ (3e)	Me	1.1	r.t.	0.25	100
7	2-O ₂ NC ₆ H ₄ (3fa)	Me	0.5	r.t.	3	49 [51]
8	2-O ₂ NC ₆ H ₄ (3fa)	Me	1.1	r.t.	0.25	100
9	2-O ₂ NC ₆ H ₄ (3fb)	Ph	1.1	r.t.	0.25	93
10	2-O ₂ NC ₆ H ₄ (3fc)	4-MeC ₆ H ₄	1.1	r.t.	0.25	97
11	2-Pyridinyl (3g)	Me	1.1	r.t.	0.5	88
12	2-Pyrimidinyl (3h)	Ph	1.1	r.t.	0.5	82

Values in bracket are recovery yields of *N,N*-disulfonylarylamines (3). Temp.=temperature. r.t.=room temperature.

Chart 2

sulfonylanilines can be prepared in high purity by monodesulfonylation reaction with TBAF without affecting other functional groups.

Experimental

General Comments All melting points are uncorrected. IR spectra were taken on a JASCO IR-810 spectrophotometer. ¹H-NMR spectra were recorded on Varian Gemini 2000 (300 MHz) and Hitachi R-300 (300 MHz) spectrometers. Chemical shifts are expressed in δ (ppm) values with tetramethylsilane (TMS) as an internal reference in CDCl₃, and coupling constants are expressed in hertz (Hz). The following abbreviations are used: s=singlet, d=doublet, t=triplet, m=multiplet, dd=doublet of doublet, br=broad, and brs=broad singlet. Mass spectra (MS) were recorded on JMS-DX303 and JMS-AX500 instruments.

General Procedure for the Sulfonylation Reaction of Arylamines (1) (Table 1) The sulfonyl chloride was added to a pyridine solution of an arylamine at 0°C. After stirring at the temperature and for the time shown in Table 1, the mixture was diluted with H₂O and extracted with AcOEt. The

AcOEt layer was dried over MgSO_4 , and the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography using an appropriate solvent as the eluent to give the product which was recrystallized from an appropriate solvent.

Methylsulfonylation Reaction of 4-Bromo-2-iodoaniline Methanesulfonyl chloride (46 mg, 0.4 mmol) was added to a pyridine (3 ml) solution of 4-bromo-2-iodoaniline (118 mg, 0.4 mmol) at 0 °C with stirring. After stirring at room temperature for 12 h, the mixture was diluted with H_2O (50 ml) and extracted with AcOEt (30 ml $\times$ 3). The AcOEt layer was dried over MgSO_4 , and the AcOEt was removed under reduced pressure. By analyzing the $^1\text{H-NMR}$ spectrum of the products, the yields of *N*-methylsulfonyl-4-bromo-2-iodoaniline and *N,N*-bis(methylsulfonyl)-4-bromo-2-iodoaniline, and the starting material were determined to be 63%, 5%, and 30%, respectively.

Phenylsulfonylation Reaction of 2-Methoxyaniline (1a) According to the general procedure, the crude product obtained from the reaction using benzenesulfonyl chloride (0.26 ml, 2.0 mmol), pyridine (10 ml), and 2-methoxyaniline (1a) (246 mg, 2.0 mmol) was purified by silica gel column chromatography using AcOEt–hexane (1 : 4) as the eluent to give *N*-(phenylsulfonyl)-2-methoxyaniline (2a) as colorless plates which were recrystallized from acetone–hexane. Yield 507.0 mg (97%), mp 87 °C. IR (KBr): 3250, 1355, 1170 cm^{-1} . $^1\text{H-NMR}$ (300 MHz) δ : 3.61 (3H, s), 6.72 (1H, dd, J = 1.4, 8.0 Hz), 6.92 (1H, dt, J = 1.4, 7.9 Hz), 7.00–7.05 (2H, m), 7.40 (2H, dt, J = 1.4, 8.5 Hz), 7.47–7.55 (2H, m), 7.75 (2H, d, J = 8.2 Hz). MS (EI) m/z : 263 (M^+ , 77), 122 (100). *Anal.* Calcd for $\text{C}_{13}\text{H}_{13}\text{NO}_3\text{S}$: C, 59.30; H, 4.98; N, 5.32; S, 12.18. Found: C, 59.41; H, 5.03; N, 5.32; S, 12.35.

***p*-Tolylsulfonylation Reaction of 4-Methylaniline (1b)** According to the general procedure, the crude product obtained from the reaction using *p*-toluenesulfonyl chloride (1.33 g, 7 mmol), pyridine (10 ml), and 4-methylaniline (1b) (750 mg, 7.0 mmol) was purified by silica gel column chromatography using AcOEt–hexane as the eluent to give *N*-(*p*-toluenesulfonyl)-4-methylaniline (2b) as colorless plates which were recrystallized from acetone–hexane. Yield 235.0 mg (90%), mp 116 °C (lit.⁶) mp 118 °C. IR (KBr): 3220, 1330, 1160 cm^{-1} . $^1\text{H-NMR}$ (300 MHz) δ : 2.39 (3H, s), 2.53 (3H, s), 7.02 (1H, br), 7.15 (2H, dt, J = 1.9, 8.8 Hz), 7.26 (2H, d, J = 8.3 Hz), 7.73 (2H, dt, J = 1.9, 8.3 Hz), 7.85 (2H, dt, J = 1.9, 8.8 Hz). MS (EI) m/z : 261 (M^+ , 40), 106 (100). High-resolution MS (EI) m/z : Calcd for $\text{C}_{14}\text{H}_{15}\text{NO}_2\text{S}$ (M^+): 261.0823. Found: 261.0819.

***p*-Tolylsulfonylation Reaction of 4-Aminoacetophenone (1c)** According to the general procedure, the crude products obtained from the reaction using *p*-toluenesulfonyl chloride (1.9 g, 10 mmol), pyridine (10 ml), and 4-aminoacetophenone (1c) (270 mg, 2.0 mmol) were purified by silica gel column chromatography using AcOEt–hexane (1 : 4) as the eluent to give 4-[*N,N*-bis(*p*-tolylsulfonyl)amino]acetophenone (3c) (270 mg, 30%) from the first fraction as colorless plates which were recrystallized from acetone–hexane and 4-[*N*-(*p*-tolylsulfonyl)amino]acetophenone (2c) (340 mg, 59%) from the second fraction as colorless crystals which were recrystallized from acetone–hexane. 3c: mp 182 °C. IR (KBr): 1685, 1380, 1165 cm^{-1} . $^1\text{H-NMR}$ (300 MHz) δ : 2.48 (6H, s), 2.62 (3H, s), 7.14 (2H, d, J = 8.8 Hz), 7.35 (4H, d, J = 8.2 Hz), 7.81 (4H, d, J = 8.2 Hz), 7.94 (2H, d, J = 8.8 Hz). MS (EI) m/z : 443 (M^+ , 45), 155 (100), 91 (72). *Anal.* Calcd for $\text{C}_{22}\text{H}_{21}\text{NO}_5\text{S}_2 \cdot 1/3\text{H}_2\text{O}$: C, 58.78; H, 4.86; N, 3.12; S, 14.26. Found: C, 58.67; H, 4.85; N, 3.11; S, 14.51. 2c: mp 203 °C (lit.⁷) mp 203 °C. IR (KBr): 3230, 1340, 1160 cm^{-1} . $^1\text{H-NMR}$ (300 MHz) δ : 2.39 (3H, s), 2.53 (3H, s), 7.02 (1H, br), 7.15 (2H, dt, J = 1.9, 8.8 Hz), 7.26 (2H, d, J = 8.3 Hz), 7.73 (2H, dt, J = 1.9, 8.3 Hz), 7.85 (2H, dt, J = 1.9, 8.8 Hz); MS (EI) m/z : 289 (M^+ , 100), 274 (98), 155 (44), 91 (98). High-resolution MS (EI) m/z : Calcd for $\text{C}_{15}\text{H}_{15}\text{NO}_3\text{S}$ (M^+): 289.0772. Found: 289.0810.

Phenylsulfonylation Reaction of Ethyl 4-Aminobenzoate (1d) According to the general procedure, the crude products obtained from the reaction using benzenesulfonyl chloride (0.51 ml, 4 mmol), pyridine (4 ml), and ethyl 4-aminobenzoate (1d) (330 mg, 2.0 mmol) were purified by silica gel column chromatography using AcOEt–hexane (1 : 4) as the eluent to give ethyl 4-[*N,N*-bis(phenylsulfonyl)amino]benzoate (3d) (103 mg, 12%) from the first fraction as colorless plates which were recrystallized from acetone–hexane and ethyl 4-[*N*-(phenylsulfonyl)amino]benzoate (2d) (540 mg, 86%) from the second fraction as colorless prisms which were recrystallized from acetone–hexane. 3d: mp 140 °C. IR (KBr): 1720, 1370, 1275, 1170 cm^{-1} . $^1\text{H-NMR}$ (300 MHz) δ : 1.39 (3H, t, J = 7.1 Hz), 4.39 (2H, q, J = 7.1 Hz), 7.11 (2H, d, J = 7.7 Hz), 7.56 (4H, t, J = 8.2 Hz), 7.69 (2H, t, J = 7.7 Hz), 7.93 (4H, d, J = 7.7 Hz), 8.04 (2H, d, J = 7.5 Hz). MS (EI) m/z : 445 (M^+ , 76), 305 (10), 141 (100), 77 (90). *Anal.* Calcd for $\text{C}_{21}\text{H}_{19}\text{NO}_6\text{S}_2$: C, 56.62; H, 4.30; N, 3.14; S, 14.39. Found: C, 56.70; H, 4.35; N, 3.15; S, 14.45. 2d: mp 183–184 °C. IR (KBr): 3220, 1690, 1365, 1235, 1160 cm^{-1} . $^1\text{H-NMR}$ (300

MHz) δ : 1.36 (3H, dq, J = 1.4, 7.1 Hz), 4.34 (2H, dt, J = 1.4, 7.1 Hz), 7.08 (1H, br), 7.14 (2H, d, J = 8.8 Hz), 7.47 (2H, dt, J = 1.4, 7.2 Hz), 7.55 (1H, tq, J = 1.4, 7.4 Hz), 7.84 (2H, dt, J = 1.4, 7.7 Hz), 7.93 (2H, d, J = 8.8 Hz). MS (EI) m/z : 305 (M^+ , 100), 260 (32), 164 (33), 77 (35). *Anal.* Calcd for $\text{C}_{15}\text{H}_{15}\text{NO}_4\text{S}$: C, 59.00; H, 4.95; N, 4.59; S, 10.50. Found: C, 59.22; H, 4.93; N, 4.53; S, 10.61.

Methylsulfonylation Reaction of 2-Aminobenzonitrile (1e) According to the general procedure, the crude products obtained from the reaction using methanesulfonyl chloride (0.16 ml, 2 mmol), pyridine (5 ml), and 2-aminobenzonitrile (1e) (118 mg, 1 mmol) were purified by silica gel column chromatography using AcOEt–hexane (1 : 3) as the eluent to give 2-[*N,N*-bis(methylsulfonyl)amino]benzonitrile (3e) (227 mg, 83%) from the first fraction as pale yellow plates which were recrystallized from acetone–hexane and 2-[*N*-(methylsulfonyl)amino]benzonitrile (2e) (33 mg, 17%) from the second fraction as colorless plates which were recrystallized from acetone–hexane. 3e: mp 169 °C. IR (KBr): 2230, 1355, 1160 cm^{-1} . $^1\text{H-NMR}$ (300 MHz) δ : 3.54 (6H, s), 7.51 (1H, dd, J = 0.5, 7.7 Hz), 7.63 (1H, t, J = 7.7 Hz), 7.74 (1H, dt, J = 1.6, 7.7 Hz), 7.83 (1H, dd, J = 1.6, 7.4 Hz). MS (EI) m/z : 274 (M^+ , 38), 196 (79), 118 (100). *Anal.* Calcd for $\text{C}_9\text{H}_{10}\text{N}_2\text{O}_4\text{S}_2$: C, 39.41; H, 3.67; N, 10.21; S, 23.38. Found: C, 39.21; H, 3.66; N, 10.16; S, 23.33. 2e: mp 103 °C (lit.⁸) mp 103 °C. IR (KBr): 3250, 2230, 1330, 1150 cm^{-1} . $^1\text{H-NMR}$ (300 MHz) δ : 3.14 (3H, s), 7.12 (1H, br), 7.30 (1H, dt, J = 1.1, 7.7 Hz), 7.73 (1H, dd, J = 1.1, 8.0 Hz), 7.61–7.67 (2H, m). MS (EI) m/z : 196 (M^+ , 41), 118 (100), 90 (32). High-resolution MS (EI) m/z : Calcd for $\text{C}_8\text{H}_8\text{N}_2\text{O}_2\text{S}$ (M^+): 196.0306. Found: 196.0305.

Methylsulfonylation Reaction of 2-Nitroaniline (1f) According to the General Procedure, the crude products obtained from the reaction using methanesulfonyl chloride (1.93 ml, 25 mmol), pyridine (20 ml), and 2-nitroaniline (1f) (690 mg, 5 mmol) were purified by silica gel column chromatography using AcOEt–hexane (1 : 3) as the eluent to give *N,N*-bis(methylsulfonyl)-2-nitroaniline (3fa) (985 mg, 67%) from the first fraction as pale yellow plates which were recrystallized from MeOH and *N*-(methylsulfonyl)-2-nitroaniline (2fa) (87 mg, 8%) from the second fraction as pale yellow plates which were recrystallized from acetone–hexane. 3fa: mp 148–149 °C (lit.^{4a}) mp 185–186 °C. IR (KBr): 1530, 1360, 1160 cm^{-1} . $^1\text{H-NMR}$ (300 MHz) δ : 3.50 (6H, s), 7.53 (1H, dt, J = 1.6, 7.7 Hz), 7.65–7.76 (2H, m), 8.09 (1H, dt, J = 1.6, 7.7 Hz). MS (EI) m/z : 294 (M^+ , 34), 216 (100). *Anal.* Calcd for $\text{C}_8\text{H}_{10}\text{N}_2\text{O}_6\text{S}_2$: C, 32.65; H, 3.42; N, 9.52; S, 21.79. Found: C, 32.56; H, 3.44; N, 9.48; S, 21.68. 2fa: mp 102 °C (lit.^{4a}) mp 102–104 °C. IR (KBr): 3270, 1345, 1170 cm^{-1} . $^1\text{H-NMR}$ (300 MHz) δ : 3.16 (3H, s), 7.25 (1H, dt, J = 1.4, 8.5 Hz), 7.70 (1H, dt, J = 1.6, 8.5 Hz), 7.90 (1H, dd, J = 1.1, 8.5 Hz), 8.28 (1H, dd, J = 1.4, 8.5 Hz), 9.77 (1H, br). MS (EI) m/z : 216 (M^+ , 64), 138 (100). High-resolution MS (EI) m/z : Calcd for $\text{C}_7\text{H}_8\text{N}_2\text{O}_4\text{S}$ (M^+): 216.0204. Found: 216.0194.

Phenylsulfonylation Reaction of 2-Nitroaniline (1f) According to the general procedure, the crude products obtained from the reaction using benzenesulfonyl chloride (2.0 ml, 15 mmol), pyridine (10 ml), and 2-nitroaniline (1f) (277 mg, 2 mmol) were purified by silica gel column chromatography using AcOEt–hexane (1 : 3) as the eluent to give *N,N*-bis(phenylsulfonyl)-2-nitroaniline (3fb) (81 mg, 10%) from the first fraction as colorless prisms which were recrystallized from MeOH and *N*-phenylsulfonyl-2-nitroaniline (2fb) (333 mg, 60%) from the second fraction as pale yellow plates which were recrystallized from acetone–hexane. 3fb: mp 190 °C (lit.⁹) mp 189.8–190.5 °C. IR (KBr): 1540, 1360, 1170 cm^{-1} . $^1\text{H-NMR}$ (300 MHz) δ : 7.15 (1H, dd, J = 1.4, 7.4 Hz), 7.53–7.73 (8H, m), 7.96 (4H, dd, J = 1.4, 7.4 Hz), 8.03 (1H, dd, J = 1.9, 8.0 Hz). MS (EI) m/z : 418 (M^+ , 20), 144 (78), 77 (100). High-resolution MS (EI) m/z : Calcd for $\text{C}_{18}\text{H}_{14}\text{N}_2\text{O}_6\text{S}_2$ (M^+): 418.0292. Found: 418.0272. 2fb: mp 101 °C (lit.⁹) mp 102.2–102.5 °C. IR (KBr): 3250, 1580, 1350, 1180 cm^{-1} . $^1\text{H-NMR}$ (300 MHz) δ : 7.17 (1H, t, J = 1.4, 7.4 Hz), 7.48 (2H, tt, J = 1.4, 7.4 Hz), 7.55–7.62 (2H, m), 7.83–7.88 (3H, m), 8.11 (1H, dd, J = 1.4, 8.5 Hz), 9.82 (1H, br). MS (EI) m/z : 278 (M^+ , 84), 141 (77), 77 (100). High-resolution MS (EI) m/z : Calcd for $\text{C}_{12}\text{H}_{10}\text{N}_2\text{O}_4\text{S}$ (M^+): 278.0361. Found: 278.0342.

***p*-Tolylsulfonylation Reaction of 2-Nitroaniline (1f)** According to the general procedure, the crude products obtained from the reaction using *p*-toluenesulfonyl chloride (1.24 g, 6.5 mmol), pyridine (25 ml), and 2-nitroaniline (1f) (420 mg, 3.0 mmol) were purified by silica gel column chromatography using AcOEt–hexane (1 : 3) as the eluent to give *N,N*-bis(*p*-tolylsulfonyl)-2-nitroaniline (3fc) (256 mg, 19%) from the first fraction as colorless prisms which were recrystallized from acetone–hexane and *N*-(*p*-tolylsulfonyl)-2-nitroaniline (2fc) (665 mg, 76%) from the second fraction as pale yellow plates which were recrystallized from acetone–hexane. 3fc: mp 193 °C. IR (KBr): 1530, 1360, 1170 cm^{-1} . $^1\text{H-NMR}$ (300 MHz) δ : 2.47 (6H, s), 7.15 (1H, dd, J = 1.9, 7.4 Hz), 7.34 (4H, d, J = 8.8 Hz), 7.54–7.65 (2H,

m), 7.84 (4H, d, $J=8.5$ Hz), 8.02 (1H, dd, $J=1.9$, 8.0 Hz). MS (EI) m/z : 446 (M^+ , 20), 155 (96), 91 (100). *Anal.* Calcd for $C_{20}H_{18}N_2O_6S_2$: C, 53.80; H, 4.06; N, 6.27; S, 14.36. Found: C, 53.75; H, 4.14; N, 6.30; S, 14.20. **2f**: mp 103 °C (lit.¹⁰) mp 115 °C). IR (KBr): 3250, 1525, 1330, 1150 cm^{-1} . 1H -NMR (300 MHz) δ : 2.39 (3H, s), 7.15 (1H, t, $J=8.5$ Hz), 7.26 (2H, d, $J=8.5$ Hz), 7.58 (1H, dt, $J=1.4$, 8.5 Hz), 7.74 (2H, d, $J=8.2$ Hz), 7.85 (1H, dd, $J=1.1$, 8.5 Hz), 8.12 (1H, dd, $J=1.4$, 8.2 Hz), 9.86 (1H, br). MS (EI) m/z : 292 (M^+ , 35), 155 (64), 91 (100). High-resolution MS (EI) m/z : Calcd for $C_{13}H_{12}N_2O_4S$ (M^+): 292.0517. Found: 292.0533.

Methylsulfonylation Reaction of 2-Aminopyridine (1g) According to the general procedure, the crude products obtained from the reaction using methanesulfonyl chloride (1.93 ml, 25 mmol), pyridine (20 ml), and 2-aminopyridine (**1g**) (651 mg, 6.93 mmol) were purified by silica gel column chromatography using AcOEt–hexane (1 : 2) as the eluent to give 2-[*N,N*-bis(methylsulfonyl)amino]pyridines (**3g**) (173.1 mg, 10%) from the first fraction as colorless plates which were recrystallized from acetone–hexane and 2-[*N*-(methylsulfonyl)amino]pyridine (**2g**) (631 mg, 53%) from the second fraction as colorless prisms which were recrystallized from $CHCl_3$. **3g**: mp 171 °C. IR (KBr): 1360, 1160 cm^{-1} . 1H -NMR (300 MHz) δ : 3.58 (6H, s), 7.36 (1H, dt, $J=0.8$, 8.5 Hz), 7.42 (1H, ddd, $J=0.8$, 4.7, 5.8 Hz), 7.87 (1H, dt, $J=1.9$, 7.4 Hz), 8.59 (1H, ddd, $J=0.8$, 1.1, 4.7 Hz). MS (EI) m/z : 250 (M^+ , 26), 172 (100), 157 (70). *Anal.* Calcd for $C_7H_{10}N_2O_4S_2$: C, 33.59; H, 4.03; N, 11.19; S, 25.62. Found: C, 33.44; H, 4.12; N, 11.17; S, 25.45. **2g**: mp 194 °C (lit.¹¹) mp 194 °C). IR (KBr): 2950, 1390, 1120 cm^{-1} . 1H -NMR (300 MHz) δ : 3.13 (3H, s), 6.90 (1H, t, $J=6.0$ Hz), 7.35 (1H, d, $J=8.8$ Hz), 7.73 (1H, t, $J=8.8$ Hz), 8.21 (1H, d, $J=5.2$ Hz). MS (EI) m/z : 172 (M^+ , 47), 157 (45), 94 (100). High-resolution MS (EI) m/z : Calcd for $C_6H_8N_2O_2S$ (M^+): 172.0306. Found: 172.0322.

Phenylsulfonylation Reaction of 2-Aminopyrimidine (1h) According to the general procedure, the crude products obtained from the reaction using benzenesulfonyl chloride (5.35 ml, 41.65 mmol) pyridine (40 ml), and 2-aminopyrimidine (**1h**) (792.5 mg, 8.33 mmol) were purified by silica gel column chromatography using AcOEt–hexane (1 : 2) as the eluent to give 2-[*N,N*-bis(phenylsulfonyl)amino]pyrimidine (**3h**) (89.3 mg, 3%) from the first fraction as colorless plates which were recrystallized from acetone–hexane and 2-[*N*-(phenylsulfonyl)amino]pyrimidine (**2h**) (1.6 g, 82%) from the second fraction as colorless prisms which were recrystallized from $CHCl_3$. **3h**: mp 210 °C. IR (KBr): 1350, 1170 cm^{-1} . 1H -NMR (300 MHz) δ : 7.38 (1H, t, $J=4.7$ Hz), 7.60 (4H, tt, $J=1.6$, 8.2 Hz), 7.69 (4H, tt, $J=1.6$, 7.1 Hz), 8.29 (4H, dt, $J=1.4$, 7.1 Hz), 8.83 (2H, d, $J=4.7$ Hz). MS (FAB) m/z : 376 ($M+1$). *Anal.* Calcd for $C_{16}H_{13}N_3O_4S_2$: C, 51.19; H, 3.49; N, 11.19; S, 17.08. Found: C, 51.05; H, 3.51; N, 11.17; S, 17.14. **2h**: mp 230 °C (lit.¹²) mp 229–230 °C). IR (KBr): 3200–2400, 1340, 1160 cm^{-1} . 1H -NMR (300 MHz) δ : 6.98 (1H, t, $J=4.9$ Hz), 7.51 (2H, dt, $J=1.6$, 6.9 Hz), 7.60 (1H, dt, $J=1.6$, 7.4 Hz), 8.14 (2H, dd, $J=1.6$, 6.9 Hz), 8.61 (2H, d, $J=4.9$ Hz), 10.66 (1H, br). MS (FAB) m/z : 236 ($M+1$). *Anal.* Calcd for $C_{10}H_9N_3O_2S$: C, 51.05; H, 3.86; N, 17.86; S, 13.63. Found: C, 50.92; H, 3.87; N, 17.95; S, 13.52.

Preparation of *N,N*-Bis(phenylsulfonyl)-2-methoxyaniline (3a) Under Ar atmosphere, a THF solution (5 ml) of *N*-(phenylsulfonyl)-2-methoxyaniline (**2a**) (507.0 mg, 1.92 mmol) was added to a suspension of sodium hydride (120 mg, 3 mmol) in dry THF (20 ml), and the whole was stirred for 0.5 h at room temperature. The mixture was cooled to 0 °C and benzenesulfonyl chloride (0.38 ml, 3 mmol) was added at that temperature. After stirring for 15 h at room temperature, the mixture was diluted with H_2O (100 ml) and extracted with AcOEt (60 ml $\times$ 3). The AcOEt layer was dried over $MgSO_4$, and the AcOEt was removed under reduced pressure. The residue was purified by silica gel column chromatography using AcOEt–hexane (1 : 3) as the eluent to give *N,N*-bis(phenylsulfonyl)-2-methoxyaniline (**3a**) (465.0 mg, 60%) as colorless plates which were recrystallized from

acetone–hexane, mp 164 °C. IR (KBr): 1380, 1170 cm^{-1} . 1H -NMR (300 MHz) δ : 3.37 (3H, s), 6.83 (1H, d, $J=8.2$ Hz), 6.95 (1H, dt, $J=1.4$, 7.7 Hz), 7.13 (1H, dd, $J=1.6$, 8.0 Hz), 7.40 (1H, dt, $J=1.6$, 8.8 Hz), 7.52 (4H, t, $J=8.0$ Hz), 7.65 (2H, t, $J=7.4$ Hz), 7.96 (4H, d, $J=8.4$ Hz). MS (EI) m/z : 403 (M^+ , 65), 262 (100), 121 (48). *Anal.* Calcd for $C_{19}H_{17}NO_5S_2 \cdot 1/3H_2O$: C, 55.73; H, 4.35; N, 3.42; S, 15.66. Found: C, 55.72; H, 4.47; N, 3.41; S, 15.95.

Preparation of *N,N*-Bis(*p*-tolylsulfonyl)-4-methylaniline (3b) Under Ar atmosphere, a THF solution (10 ml) of *N*-(*p*-tolylsulfonyl)-4-methylaniline (**2b**) (235 mg, 1.8 mmol) was added to a suspension of sodium hydride (400 mg, 10 mmol) in dry THF (50 ml), and the whole was stirred for 0.5 h at room temperature. The mixture was cooled to 0 °C and a THF solution (10 ml) of *p*-toluenesulfonyl chloride (1.33 g, 7 mmol) was added at that temperature. After stirring for 24 h at room temperature, the mixture was diluted with H_2O (100 ml) and extracted with AcOEt (60 ml $\times$ 3). The AcOEt layer was dried over $MgSO_4$, and the AcOEt was removed under reduced pressure. The residue was purified by silica gel column chromatography using AcOEt–hexane (1 : 3) as the eluent to give *N,N*-bis(*p*-tolylsulfonyl)-4-methylaniline (**3b**) (1.04 g, 40%) as colorless plates which were recrystallized from acetone–hexane, mp 161 °C. IR (KBr): 1370, 1160 cm^{-1} . 1H -NMR (300 MHz) δ : 2.48 (6H, s), 2.62 (6H, s), 7.14 (2H, dt, $J=1.9$, 8.8 Hz), 7.35 (4H, d, $J=8.2$ Hz), 7.81 (4H, d, $J=8.2$ Hz), 7.94 (2H, dt, $J=1.9$, 8.8 Hz). MS (EI) m/z : 415 (M^+ , 76), 260 (60), 196 (71), 155 (53), 139 (73), 91 (100). *Anal.* Calcd for $C_{21}H_{21}NO_5S_2$: C, 60.70; H, 5.09; N, 3.37; S, 15.43. Found: C, 60.56; H, 5.05; N, 3.31; S, 15.47.

General Procedure for the Monodesulfonylation of Disulfonylarylamines by TBAF (Table 2) A THF solution of TBAF was added dropwise to a THF solution of the an *N,N*-disulfonylarylamines (**3**) at room temperature. After stirring at the temperature and for the time shown in Table 2, the mixture was diluted with H_2O and extracted with AcOEt. The AcOEt layer was dried over $MgSO_4$, and the AcOEt was removed under reduced pressure. The residue was purified by silica gel column chromatography using AcOEt–hexane (1 : 3) as the eluent to give an *N*-monosulfonylarylamines (**2**).

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