tert-Butylsulfonyl (Bus), a New Protecting Group for Amines

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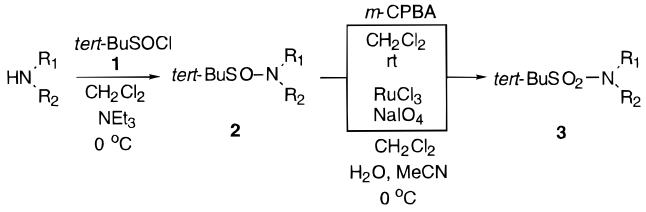
Sulfonyl groups have had a long history in protection of amines and other nitrogeneous functionality.[1] One of the most attractive features of sulfonamides, their stability to a wide array of reaction conditions, has commonly proven a liability, since removal is oftentimes problematic in highly functionalized, sensitive substrates. In recent years the arsenal of *N*-sulfonyl protecting groups has been improved by addition of new varieties amenable to mild removal.[2−4] In connection with some ongoing projects, we required a sulfonamide protecting group capable of withstanding strong metalation conditions and also one easily cleaved. Since virtually all known systems, including most arylsulfonyl groups, bear acidic protons, it became evident that development of a new type of sulfonamide was necessary. In this note we describe the utility of the *tert*-butylsulfonyl group (Bus) for protection of primary and secondary amines.

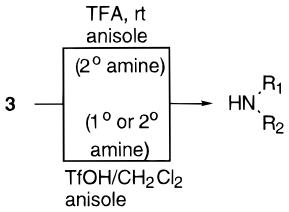
Undoubtedly *tert*-butylsulfonyl protection of amines has not previously been used since *tert*-butylsulfonyl chloride is quite unstable and furthermore does not normally undergo nucleophilic displacement at sulfur with amines.[5] Richey and Farkas have found, however, that readily prepared *tert*-butylsulfinyl chloride (**1**) reacts with diethylamine to give the corresponding sulfinamide (**2**, $R_1 = R_2 =$ Et), which could be oxidized with potassium permanganate to the *tert*-butylsulfonamide (**3**, $R_1 = R_2 =$ Et).[6] This sulfonamide was found to be stable to a variety of organolithium and Grignard reagents and clearly had the type of stability profile toward strong bases that we required.

We have found that sulfinyl chloride **1** reacts cleanly with a number of primary and secondary amines to give sulfinamides **2** (Scheme 1). Isolated yields of representative examples are given in Table 1.[7] Since $KMnO_4$ did not appear to be a generally attractive oxidant for sulfonamide formation, we have investigated two milder alternatives.[8] Thus, oxidation of sulfinamides **2** with either *m*-chloroperbenzoic acid or $RuCl_3$(cat)/$NaIO_4$[9] produced *N*-Bus derivatives **3** in high yields (Table 1).

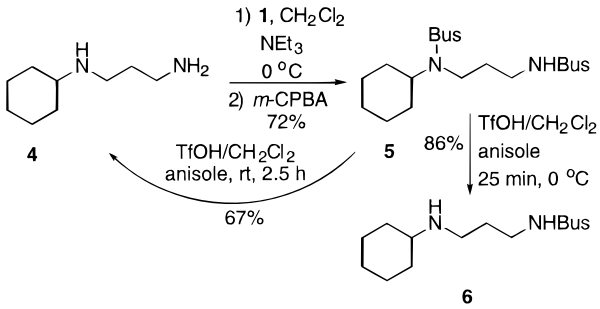
Scheme 1



Scheme 2



Scheme 3



The stability of these Bus-protected compounds toward a few sets of reaction conditions has been tested.[10] For example the *N*-Bus derivative of dibenzylamine is unaffected by (1) 0.1 N HCl/MeOH, rt, 1 h, (2) 0.1 N TFA/CH_2Cl_2, rt, 1 h, or (3) pyrolysis neat at 180 °C, 3 h. However, it was found that Bus-protected secondary amines can be cleaved with 0.1 N triflic acid in methylene chloride containing anisole as a cation scavenger at 0 °C for about 15 min (Scheme 2, Table 1). Interestingly, primary amine Bus derivatives are deprotected much more slowly than secondary, requiring 0.1 N TfOH at room temperature for approximately 2−3 h. It is also possible to remove the Bus group from secondary amines with neat TFA/anisole overnight at room temperature (Scheme 2). Some examples are shown in Table 1. We were surprised to find that Bus-protected primary amines are unchanged by neat TFA under the same conditions.

These experiments suggested that it might be feasible to selectively remove a Bus group from a secondary amine in the presence of a primary. Thus, diamine **4** was converted to bis-Bus-protected compound **5** (Scheme 3). Exposure to **5** to 0.1 N TfOH/CH_2Cl_2/anisole at 0 °C for 25 min led to monoamine **6** in good yield. Extending the reaction time to 2.5 h at room-temperature resulted in complete protecting group removal to give starting diamine **4**. In addition, the secondary Bus group of **5** can

† Author to be contacted about the X-ray crystal structure determination.

(1) For reviews, see: Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*; Wiley: New York; 2nd ed.; 1991; pp 379−86. Barton, J. W. Protection of N−H Bonds and NR_3. In *Protective Groups in Organic Chemistry*; McOmie, J. F. W., Ed.; Plenum: New York, 1973; pp 73−74.

(2) Vedejs, E.; Lin, S.; Klapars, A.; Wang, J. *J. Am. Chem. Soc.* **1996**, *118*, 9796 and references therein.

(3) Fukuyama, T.; Jow, C.-K.; Cheung, M. *Tetrahedron Lett.* **1995**, *36*, 6373. Fukuyama, T.; Cheung, M.; Jow, C.-K.; Hidai, Y.; Kan, T. *Tetrahedron Lett.* **1997**, *38*, 5831. See also: Maligres, P. E.; See, M. M.; Askin, D.; Reider, P. J. *Tetrahedron Lett.* **1997**, *38*, 5253.

(4) Weinreb, S. M.; Demko, D. M.; Lessen, T. A.; Demers, J. P. *Tetrahedron Lett.* **1986**, *27*, 2099.

(5) King, J. F.; Lam, J. Y. L.; Dave, V. *J. Org. Chem.* **1995**, *60*, 2831 and references therein.

(6) Richey, H. G., Jr.; Farkas, J., Jr. *J. Org. Chem.* **1987**, *52*, 479.

(7) Acidic workup of these sulfinamides should be avoided since partial hydrolysis occurs, lowering the yield of product. See: Wagner, B. J.; Doi, J. T.; Musker, W. K. *J. Org. Chem.* **1990**, *55*, 5940.

(8) Dimethyldioxirane also effects oxidation of sulfinamides **2** to sulfonamides **3**.

(9) Gao, Y.; Sharpless, K. B. *J. Am. Chem. Soc.* **1988**, *110*, 7538.

(10) Not surprisingly, considering the work of Richey and Farkas,[6] *N*-Bus-pyrrolidine is unreactive toward *sec*-BuLi/TMEDA. We thank A. Greenberg for conducting this experiment.

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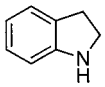
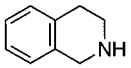
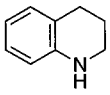
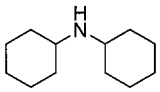
Table 1. Protection of Primary and Secondary Amines as Bus Derivatives and Subsequent Cleavage

Entry	Amine	Sulfinamide **2** (%)	Sulfonamide **3** (%)		Deprotected amine (%)	
			m-CPBA	$RuCl_3/NaIO_4$	TFA	TfOH
a	$(PhCH_2)_2NH$	100	97	96	90	92
b		100	84	87	85	88
c		78	92	77	88	100
d		88	94	85	84	100
e		100	92	99	69	92
f	$PhCH_2CH_2NH_2$	100	91	95	–	92
g	$n\text{-}C_9H_{20}NH_2$	83	98	94	–	58

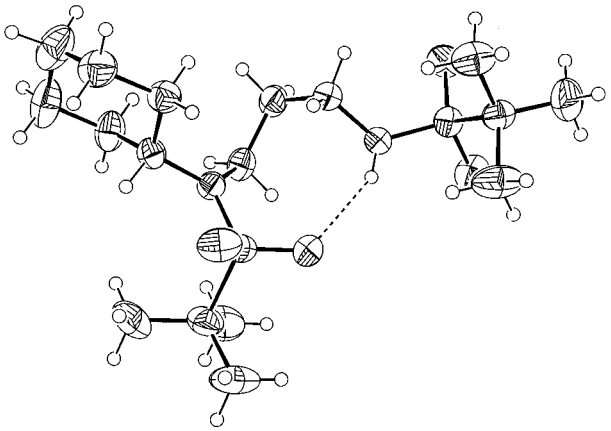


Figure 1. ORTEP plot of bis-sulfonamide **5**.

be selectively cleaved with TFA/anisole at room temperature overnight to give **6** in comparable yield (83%).

It is not clear a priori why the rate of solvolysis is so different for *tert*-butylsulfonamides of primary vs secondary amines. Studies by ^{15}N NMR have shown that protonation of sulfonamides occurs at nitrogen rather than oxygen.[11] However, it seems unlikely that there are significant enough differences in nitrogen basicity between the two types of sulfonamide systems to totally explain the large disparity in ease of cleavage. In an attempt to probe this selectivity issue, we determined the X-ray crystal structure of bis-sulfonamide **5**, and an ORTEP plot of this molecule is shown in Figure 1.[12] However, there do not appear to be any structural differences between the two types of sulfonamides which make the variation in cleavage rates immediately obvious. The N−S bond length in the secondary sulfonamide is slightly longer than that in the primary (0.03 Å), but not significantly so. Moreover, the S−C bond lengths are identical. There is a hydrogen bond evident in **5** between the primary sulfonamide N−H and an oxygen of the secondary sulfonamide, but this of course does not rationalize the similar rate differences seen among the simple monosulfonamides in Table 1. Thus, at this point we cannot provide a convincing explanation for these results.

In conclusion, we have developed an efficient two-step method for preparing *tert*-butylsulfonamides from primary and secondary amines. These Bus derivatives are stable to strong bases and metalation conditions and are cleaved to the parent amines by mild acidic solvolysis. An unexpected bonus with this protecting group is that secondary sulfonamides can be selectively cleaved in the presence of primary ones.

Experimental Section

***tert*-Butylsulfinyl Chloride (1).** A modification of the literature procedure was used.[6] Excess sulfur dioxide was bubbled through a solution of *tert*-butylmagnesium chloride (1.0 M in THF, 40 mL) at 0 °C in a fume hood allowing for adequate venting of excess SO_2. After 1 h,[13] the reaction mixture was cautiously diluted with ice-cold 5% aqueous HCl (40 mL). After effervescence subsided, the aqueous layer was extracted with 40 mL of CH_2Cl_2. The organic extracts were combined, dried over $MgSO_4$, and concentrated in vacuo to afford *tert*-butylsulfinic acid (4.35−4.59 g, 89−94%) as a white solid. The material was used without further purification.

To a solution of *tert*-butylsulfinic acid (6.53 g, 53.4 mmol) in THF (20 mL) was added dropwise thionyl chloride (4.68 mL, 64.1 mmol) in THF (15 mL) at rt. After 1 h, the solvent was removed under reduced pressure and excess thionyl chloride was evaporated in vacuo. The resulting *tert*-butylsulfinyl chloride (6.91 g, 92%) was used without further purification (brown liquid). A solution of the *tert*-butylsulfinyl chloride in dry CH_2Cl_2 (10 mL) can be stored in a freezer indefinitely. The neat compound decomposes much faster than a solution.

General Procedure for Formation of *tert*-Butylsulfinamides. *N,N*-Dibenzyltrimethylmethanesulfinamide (2a).

(11) Kricheldorf, H. R. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 442.

(12) The authors have deposited X-ray data with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, U.K.

(13) There is an induction period to the point where the solution becomes saturated with SO_2 and then there is a vigorous reaction. *Care must be taken to regulate the flow of the SO_2 to avoid an exotherm.* The reaction is complete when there is no longer any uptake of SO_2 by the solution.

To a solution of dibenzylamine (300 mg, 1.52 mmol) and triethylamine (2.21 mL, 15.2 mmol) in CH_2Cl_2 (20 mL) was added dropwise ice-cold *tert*-butylsulfinyl chloride (428 mg, 3.04 mmol) in CH_2Cl_2 (15 mL) at 0 °C. After 1 h (TLC monitoring, EtOAc:MeOH, 9:1 containing 3% NH_4OH), the mixture was diluted with saturated aqueous $NaHCO_3$.[7] The aqueous layer was extracted with CH_2Cl_2 (20 mL). The organic extracts were combined, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by flash column chromatography (EtOAc:hexanes, 1:4) to afford sulfinamide **2a** as a white solid (mp 54−56 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33−7.25 (m, 10 H), 4.30 (d, J = 15.0 Hz, 2 H), 4.05 (d, J = 15.0 Hz, 2 H), 1.22 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.7, 128.5, 128.3, 127.3, 58.4, 51.3, 23.1; CIMS *m*/*z* (relative intensity) 302 (MH^+, 7), 85 (75), 69 (100).

1-Indolinetrimethylmethanesulfinamide (2b). The general procedure was followed using 1-indoline (319 mg, 2.67 mmol), *tert*-butylsulfinyl chloride (753 mg, 5.35 mmol), triethylamine (2.98 mL, 21.4 mmol), and CH_2Cl_2 (15 mL). The crude product was purified by flash column chromatography (EtOAc:hexanes, 1:9) to afford sulfinamide **2b** (595 mg, 100%) as a colorless liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.15−6.88 (m, 4 H), 4.27 (dt, J = 6.6, 10.5 Hz, 1 H), 3.48 (dt, J = 6.9, 10.3 Hz, 1 H), 3.27−3.01 (m, 2 H), 1.31 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.9, 130.9, 127.2, 124.7, 122.2, 112.3, 57.8, 41.7, 29.3, 23.2; CIMS *m*/*z* (relative intensity) 224 (MH^+, 90), 167 (MH^+ − *t*-Bu, 75), 150 (100), 120 (MH^+ − *tert*-butylsulfinyl, 88).

1,2,3,4-Tetrahydroisoquinolinetrimethylmethanesulfinamide (2c). The general procedure was followed using 1,2,3,4-tetrahydroisoquinoline (319 mg, 2.40 mmol), *tert*-butylsulfinyl chloride (471 mg, 3.35 mmol), triethylamine (3.34 mL, 24.0 mmol), and CH_2Cl_2 (15 mL). The crude product was purified by flash column chromatography (EtOAc:hexanes, 1:4) to afford sulfinamide **2c** (430 mg, 78%) as a colorless liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.15−7.02 (m, 4 H), 4.28 (dd, J = 24.0, 15.7 Hz, 2 H), 3.47 (dt, J = 12.8, 6.0 Hz, 1 H), 3.32 (dt, J = 12.7, 6.2 Hz, 1 H), 2.90 (t, J = 5.7 Hz, 2 H), 1.21 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.1, 133.4, 128.8, 126.3, 126.1, 125.9, 58.2, 47.2, 45.3, 29.1, 22.9; CIMS *m*/*z* (relative intensity) 238 (MH^+, 100), 181 (MH^+ − *t*-Bu, 51), 132 (M^+ − *tert*-butylsulfinyl, 20).

1,2,3,4-Tetrahydroquinolinetrimethylmethanesulfinamide (2d). The general procedure was followed using 1,2,3,4-tetrahydroquinoline (318 mg, 2.39 mmol), *tert*-butylsulfinyl chloride (583 mg, 4.78 mmol), triethylamine (3.33 mL, 23.9 mmol), and CH_2Cl_2 (15 mL). The crude product was purified by flash column chromatography (EtOAc:hexanes, 1:9) to afford sulfinamide **2d** (501 mg, 88%) as a colorless liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.11−6.86 (m, 4 H), 4.11 (dt, J = 12.7, 4.0 Hz, 1 H), 3.09 (ddd, J = 13.2, 11.0, 2.7 Hz, 1 H), 2.80 (J = 8.3, 4.7 Hz, 2 H), 2.02−1.92 (m, 1 H), 1.85−1.73 (m, 1 H), 1.31 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.5, 129.6, 126.4, 125.8, 121.2, 117.9, 59.4, 39.1, 27.1, 23.7, 22.5; CIMS *m*/*z* (relative intensity) 238 (MH^+, 73), 181 (MH^+ − *t*-*t*-Bu, 83), 164 (100), 134 (MH^+ − *tert*-butylsulfinyl, 98).

***N,N*-Dicyclohexyltrimethylmethanesulfinamide (2e).** The general procedure was followed using dicyclohexylamine (273 mg, 1.51 mmol), *tert*-butylsulfinyl chloride (274 mg, 1.95 mmol), triethylamine (2.09 mL, 15.1 mmol), and CH_2Cl_2 (15 mL). The crude product was purified by flash column chromatography (EtOAc:hexanes, 1:1) to afford sulfinamide **2e** (431 mg, 100%) as a white solid (mp 110−112 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.16 (br s, 2 H), 1.91−1.54 (m, 14 H), 1.40−1.19 (m, 4 H), 1.16 (s, 9 H), 1.05 (tt, J = 12.6, 3.5 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 57.2, 33.6, 26.5, 26.2, 25.4, 24.4; CIMS *m*/*z* (relative intensity) 286 (MH^+, 58), 228 (M^+ − *t*-Bu, 46), 85 (88), 69 (100).

***N*-Phenethyltrimethylmethanesulfinamide (2f).** The general procedure was followed using phenethylamine (290 mg, 2.39 mmol), *tert*-butylsulfinyl chloride (506 mg, 3.59 mmol),[13] triethylamine (3.35 mL, 23.9 mmol), and CH_2Cl_2 (15 mL). The crude product was purified by flash column chromatography (EtOAc:hexanes, 1:1) to afford sulfinamide **2f** (538 mg, 100%) as a colorless liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31−7.17 (m, 5 H), 3.51−3.22 (m, 3 H), 2.92−2.81 (m, 1 H), 1.15 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.5, 128.8, 128.5, 126.4, 55.6, 46.9, 37.4, 22.5; CIMS *m*/*z* (relative intensity) 226 (MH^+, 100), 169 (MH^+ − *t*-Bu, 37).

***N*-Nonyltrimethylmethanesulfinamide (2g).** The general procedure was followed using nonylamine (300 mg, 2.09 mmol), *tert*-butylsulfinyl chloride (588 mg, 4.18 mmol), triethylamine (1.47 mL, 10.5 mmol), and CH_2Cl_2 (15 mL). The crude product was purified by flash column chromatography (EtOAc:hexanes, 1:4) to afford sulfinamide **2g** (422 mg, 83%) as a colorless liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.22−2.98 (m, 3 H), 1.53 (br tt, J = 6.9, 6.8 Hz, 2 H), 1.24 (br s, 12 H), 1.18 (s, 9 H), 0.85 (br t, J = 6.7 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.4, 45.7, 31.8, 31.0, 29.4, 29.2, 26.7, 22.6 (2C), 14.0; CIMS *m*/*z* (relative intensity) 248 (MH^+, 100), 191 (MH^+ − *t*-Bu, 41).

General Procedure for Formation of *tert*-Butylsulfonamides. *N,N*-Dibenzyltrimethylmethanesulfonamide (3a). A. To a solution of sulfinamide **2a** (100 mg, 0.33 mmol) in CH_2Cl_2 (5 mL) was added *m*-CPBA (55%, 135 mg, 0.43 mmol) at rt. After 45 min, the reaction mixture was diluted with a mixture of saturated aqueous $NaHSO_3$ (5 mL) and $NaHCO_3$ (5 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 5 mL). The organic extracts were combined, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by flash column chromatography (EtOAc:hexanes, 1:4) to afford sulfonamide **3a** (102 mg, 97%) as a white solid (mp 125−127 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30−7.20 (m, 10 H), 4.44 (s, 4 H), 1.52 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.8, 128.4, 128.4, 127.5, 61.8, 51.4, 24.8; CIMS *m*/*z* (relative intensity) 318 (MH^+, 7), 261 (MH^+ − *t*-Bu, 100), 196 (M^+ − *tert*-butylsulfonyl, 34); HRMS calcd for $C_{18}H_{23}NO_2S$ 317.1449, found 317.1454.

B. To a solution of sulfinamide **2a** (100 mg, 0.33 mmol) in a mixture of CH_2Cl_2 (3 mL), CH_3CN (3 mL), and H_2O (4.7 mL) were added $RuCl_3 \cdot H_2O$ (0.74 mg, 0.0033 mmol)[15] and $NaIO_4$ (85 mg, 0.40 mmol) at 0 °C. After 1 h, the mixture was diluted with CH_2Cl_2 (5 mL) and the aqueous layer was extracted with 12 mL of CH_2Cl_2. The organic extracts were combined, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by flash column chromatography as above giving the sulfonamide **3a** (101 mg, 97%) as a white solid.

1-Indolinetrimethylmethanesulfonamide (3b). A. The general procedure was followed using sulfinamide **2b** (200 mg, 0.90 mmol), *m*-CPBA (55%, 365 mg, 1.16 mmol), and CH_2Cl_2 (10 mL). The crude product was purified by flash column chromatography (EtOAc:hexanes, 1:4) to afford sulfonamide **3b** (180 mg, 84%) as a colorless liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40−6.92 (m, 4 H), 4.12 (t, J = 8.5 Hz, 2 H), 3.13 (t, J = 8.5 Hz, 2 H), 1.47 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.4, 130.5, 127.4, 124.9, 122.5, 114.1, 62.6, 51.9, 28.2, 24.6; CIMS *m*/*z* (relative intensity) 240 (MH^+, 63), 183 (MH^+ − *t*-Bu, 100), 118 (M^+ − *tert*-butylsulfonyl, 44).

B. The general procedure was followed using sulfinamide **2b** (84 mg, 0.38 mmol), $RuCl_3 \cdot H_2O$ (0.85 mg, 0.004 mmol), and $NaIO_4$ (105 mg, 0.49 mmol) in a mixture of CH_2Cl_2 (7 mL), CH_3CN (7 mL), and H_2O (11 mL). The crude product was purified by flash column chromatography as above to afford sulfonamide **3b** (78 mg, 87%).

1,2,3,4-Tetrahydroisoquinolinetrimethylmethanesulfonamide (3c). A. The general procedure was followed using sulfinamide **2c** (505 mg, 2.13 mmol), *m*-CPBA (55%, 868 mg, 2.77 mmol), and CH_2Cl_2 (20 mL). The crude product was purified by flash column chromatography (EtOAc:hexanes, 1:4) to afford sulfonamide **3c** (497 mg, 92%) as a white solid (mp 105−106 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20−7.04 (m, 4 H), 4.57 (s, 2 H), 3.66 (t, J = 5.9 Hz, 2 H), 2.96 (t, J = 5.8 Hz, 2 H), 1.41 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 133.4, 132.7, 129.1, 126.6, 126.2, 126.0, 61.3, 48.7, 44.9, 29.4, 24.4; CIMS *m*/*z* (relative intensity) 254 (MH^+, 49), 197 (MH^+ − *t*-Bu, 100), 132 (MH^+ − *tert*-butylsulfonyl, 75).

B. The general procedure was followed using sulfinamide **2c** (223 mg, 0.94 mmol), $RuCl_3 \cdot H_2O$ (2.12 mg, 0009 mmol), and $NaIO_4$ (241 mg, 1.13 mmol) in a mixture of CH_2Cl_2 (7 mL), CH_3CN (7 mL), and H_2O (11 mL). The crude product was purified by flash column chromatography as above to afford sulfonamide **3c** (183 mg, 77%).

1,2,3,4-Tetrahydroquinolinetrimethylmethanesulfonamide (3d). A. The general procedure was followed using sulfinamide **2d** (73 mg, 0.33 mmol), *m*-CPBA (55%, 136 mg, 0.43

(14) In this case, 1.5 equiv of *tert*-butylsulfinyl chloride was used to minimize formation of the *N,N*-bis(*tert*-butylsulfinyl)amine.

(15) The amount of ruthenium catalyst used is crucial. The color of the upper aqueous layer should be brown, not black. Low yields of sulfonamide were normally obtained if too much catalyst was used.

mmol), and CH_2Cl_2 (5 mL). The crude product was purified by flash column chromatography (EtOAc:hexanes, 1:9) to afford sulfonamide **3d** (73 mg, 94%) as a white solid (mp 77−78 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62−6.99 (m, 4 H), 3.75 (t, J = 5.6 Hz, 2 H), 2.85 (t, J = 6.8 Hz, 2 H), 2.07 (tt, J = 6.3, 5.9 Hz, 2 H), 1.49 (s, 9 H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 138.4, 129.5, 129.3, 126.1, 123.8, 123.2, 62.6, 48.4, 27.0, 25.2, 23.6; CIMS *m/z* (relative intensity) 254 (MH^+, 10), 197 ($MH^+ - t$-Bu, 100); HRMS calcd for $C_{13}H_{19}NO_2S$ 253.1136, found 253.1134.

B. The general procedure was followed using sulfinamide **2d** (170 mg, 0.72 mmol), $RuCl_3 \cdot H_2O$ (1.61 mg, 0.007 mmol), and $NaIO_4$ (184 mg, 0.86 mmol) in a mixture of CH_2Cl_2 (7 mL), CH_3CN (7 mL), and H_2O (11 mL). The crude product was purified by flash column chromatography as above to afford sulfonamide **3d** (154 mg, 85%).

***N,N*-Dicyclohexyltrimethylmethanesulfonamide (3e). A.** The general procedure was followed using sulfinamide **2e** (284 mg, 1.00 mmol), *m*-CPBA (55%, 407 mg, 1.30 mmol), and CH_2Cl_2 (10 mL). The crude product was purified by flash column chromatography (EtOAc:hexanes, 1:4) to afford sulfonamide **3e** (276 mg, 92%) as a white solid (mp 77−78 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.21 (br m, 2 H), 1.83−1.78 (m, 11 H), 1.63−1.58 (m, 3 H), 1.39 (s, 9 H), 1.32−1.08 (m, 6 H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 61.1, 59.3, 33.5, 26.7, 25.4, 25.3; CIMS *m/z* (relative intensity) 302 (MH^+, 22), 245 ($MH^+ - t$-Bu, 100), 181 (MH^+ − *tert*-butylsulfonyl, 19); HRMS calcd for $C_{16}H_{31}NO_2S$ 301.2075, found 301.2065.

B. The general procedure was followed using sulfinamide **2e** (163 mg, 0.57 mmol), $RuCl_3 \cdot H_2O$ (1.30 mg, 0.006 mmol), and $NaIO_4$ (147 mg, 0.69 mmol) in a mixture of CH_2Cl_2 (7 mL), CH_3CN (7 mL), and H_2O (11 mL). The crude product was purified by flash column chromatography as above to afford sulfonamide **3e** (171 mg, 99%).

***N*-Phenethyltrimethylmethanesulfonamide (3f). A.** The general procedure was followed using sulfinamide **2f** (489 mg, 2.17 mmol), *m*-CPBA (55%, 885 mg, 2.82 mmol), and CH_2Cl_2 (22 mL). The crude product was purified by flash column chromatography (EtOAc:hexanes, 1:4) to afford sulfonamide **3f** (477 mg, 91%) as a white solid (mp 97−98 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35−7.21 (m, 5 H), 4.31 (br t, J = 6.0 Hz, 1 H), 3.43 (td, J = 6.9, 6.6 Hz, 2 H), 2.88 (t, J = 7.1 Hz, 2 H), 1.35 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.0, 128.8, 126.6, 59.8, 46.0, 37.5, 24.1; CIMS *m/z* (relative intensity) 242 (MH^+, 27), 185 ($MH^+ - t$-Bu, 46), 122 (MH^+ − *tert*-butylsulfonyl, 100); HRMS calcd for $C_{12}H_{19}NO_2S$ 241.1136, found 241.1140.

B. The general procedure was followed using sulfinamide **2f** (241 mg, 1.07 mmol), $RuCl_3 \cdot H_2O$ (2.25 mg, 001 mmol), and $NaIO_4$ (275 mg, 1.28 mmol) in a mixture of CH_2Cl_2 (7 mL), CH_3CN (7 mL), and H_2O (11 mL). The crude product was purified by flash column chromatography as above to afford sulfonamide **3f** (244 mg, 95%).

***N*-Nonyltrimethylmethanesulfonamide (3g). A.** The general procedure was followed using sulfinamide **2g** (143 mg, 0.58 mmol), *m*-CPBA (55%, 236 mg, 0.75 mmol), and CH_2Cl_2 (10 mL). The crude product was purified by flash column chromatography (EtOAc:hexanes, 1:4) to afford sulfonamide **3g** (149 mg, 90%) as a white solid (mp 38−39 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.88 (br t, J = 5.6 Hz, 1 H), 3.16 (td, J = 7.0, 6.8 Hz, 2 H), 1.55 (tt, J = 17.3, 7.2 Hz, 2 H), 1.39 (s, 9 H), 1.26 (br s, 12 H), 0.87 (t, J = 6.7 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 59.8, 44.9, 31.8, 31.2, 29.4, 29.2, 26.5, 24.4, 22.6, 14.1; CIMS *m/z* (relative intensity) 264 (MH^+, 56), 207 ($MH^+ - t$-Bu, 100); HRMS calcd for $C_{13}H_{29}NO_2S$ 263.1919, found 263.1908.

B. The general procedure was followed using sulfinamide **2g** (194 mg, 0.78 mmol), $RuCl_3 \cdot H_2O$ (1.80 mg, 0.008 mmol), and $NaIO_4$ (201 mg, 0.94 mmol) in a mixture of CH_2Cl_2 (7 mL), CH_3CN (7 mL), and H_2O (11 mL). The crude product was purified by flash column chromatography as above to afford sulfonamide **3g** (170 mg, 82%).

General Procedure for Deprotection of *tert*-Butylsulfonamides. Cleavage of *N,N*-Dibenzyltrimethylmethanesulfonamide (3a). A. To a solution of sulfonamide **3a** (100 mg, 0.32 mmol) and anisole (0.68 mL, 6.3 mmol) in CH_2Cl_2 (9.5 mL) was slowly added trifluoromethanesulfonic acid (0.2 N in CH_2Cl_2, 9.5 mL) at 0 °C (the final concentration of the triflic acid solution is 0.1 N). After 1 h (TLC monitoring, EtOAc:hexanes, 1:4), 10% aqueous NaOH (20 mL) was added. The aqueous layer was extracted with CH_2Cl_2 (2 × 20 mL). The organic extracts were combined, dried over K_2CO_3, and concentrated under reduced pressure. The residue was purified by flash chromatography (EtOAc:MeOH, 9:1 containing 3% NH_4OH) to afford dibenzylamine (57 mg, 92%) as a colorless liquid.

B. A solution of sulfonamide **3a** (50 mg, 0.16 mmol) and anisole (0.34 mL, 3.15 mmol) in neat trifluoroacetic acid (5 mL) was stirred overnight at rt. The reaction mixture was then diluted with CH_2Cl_2 (10 mL) and quenched with 10% aqueous NaOH (50 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL). The organic extracts were combined, dried over K_2CO_3, and concentrated under reduced pressure. The residue was purified by flash chromatography as above to afford dibenzylamine (28 mg, 90%) as a colorless liquid.

Cleavage of 1-Indolinetrimethylmethanesulfonamide (3b). A. The general procedure was followed using sulfonamide **3b** (100 mg, 0.42 mmol), trifluoromethanesulfonic acid (0.2 N, 12.5 mL), anisole (0.55 mL, 5.02 mmol), and CH_2Cl_2 (12.5 mL). The crude product was purified by flash column chromatography (EtOAc:hexanes, 1:4) to afford 1-indoline (41 mg, 88%) as a colorless liquid.

B. The general procedure was followed using sulfonamide **3b** (194 mg, 0.78 mmol) and anisole (0.61 mL, 5.60 mmol) in neat trifluoroacetic acid (5 mL). The crude product was purified by flash column chromatography as above to afford 1-indoline (28 mg, 85%).

Cleavage of 1,2,3,4-Tetrahydroisoquinolinetrimethylmethanesulfonamide (3c). A. The general procedure was followed using sulfonamide **3c** (100 mg, 0.43 mmol), trifluoromethanesulfonic acid (0.2 N, 12.8 mL), anisole (0.93 mL, 8.52 mmol), and CH_2Cl_2 (12.8 mL). The crude product was purified by flash column chromatography (EtOAc:MeOH, 9:1 containing 3% NH_4OH) to afford 1,2,3,4-tetrahydroisoquinoline (57 mg, 100%) as a colorless liquid.

B. The general procedure was followed using sulfonamide **3c** (60 mg, 0.26 mmol) and anisole (0.56 mL, 5.11 mmol) in neat trifluoroacetic acid (5 mL). The crude product was purified by flash column chromatography as above to afford 1,2,3,4-tetrahydroisoquinoline (30 mg, 88%).

Cleavage of 1,2,3,4-Tetrahydroquinolinetrimethylmethanesulfonamide (3d). A. The general procedure was followed using sulfonamide **3d** (100 mg, 0.39 mmol), trifluoromethanesulfonic acid (0.2 N, 12.8 mL), anisole (0.93 mL, 8.52 mmol), and CH_2Cl_2 (12.8 mL). The crude product was purified by flash column chromatography (EtOAc:MeOH, 9:1 containing 3% NH_4OH) to afford 1,2,3,4-tetrahydroquinoline (53 mg, 93%) as a colorless liquid.

B. The general procedure was followed using sulfonamide **3d** (48 mg, 0.19 mmol) and anisole (0.41 mL, 3.79 mmol) in neat trifluoroacetic acid (5 mL). The crude product was purified by flash column chromatography as above to afford 1,2,3,4-tetrahydroquinoline (21 mg, 84%).

Cleavage of *N,N*-Dicyclohexyltrimethylmethanesulfonamide (3e). A. The general procedure was followed using sulfonamide **3e** (100 mg, 0.33 mmol), trifluoromethanesulfonic acid (0.2 N, 10.0 mL), anisole (0.72 mL, 6.63 mmol), and CH_2Cl_2 (10.0 mL). The crude product was purified by flash column chromatography (EtOAc:MeOH, 95:5 containing 3% NH_4OH) to afford dicyclohexylamine (55 mg, 92%) as a colorless liquid.

B. The general procedure was followed using sulfonamide **3e** (166 mg, 0.55 mmol) and anisole (1.20 mL, 11.0 mmol) in neat trifluoroacetic acid (5 mL). The crude product was purified by flash column chromatography as above to afford dicyclohexylamine (69 mg, 69%).

Cleavage of *N*-Phenethyltrimethylmethanesulfonamide (3f). A. The general procedure was followed using sulfonamide **3f** (100 mg, 0.41 mmol), trifluoromethanesulfonic acid (0.2 N, 12.4 mL), anisole (0.90 mL, 8.29 mmol), and CH_2Cl_2 (12.4 mL). After 2.5 h at rt (TLC monitoring, EtOAc:hexanes, 1:4), the crude product was purified by flash column chromatography (EtOAc:MeOH, 9:1 containing 3% NH_4OH) to afford phenethylamine (46 mg, 92%) as a colorless liquid.

Cleavage of *N*-Nonyltrimethylmethanesulfonamide (3g). A. The general procedure was followed using sulfonamide **3g** (73 mg, 0.28 mmol), trifluoromethanesulfonic acid (0.2 N, 8.2 mL), anisole (0.59 mL, 5.46 mmol), and CH_2Cl_2 (8.2 mL). After 2.5 h at rt (TLC monitoring, EtOAc:hexanes, 1:4), the crude product was purified by flash column chromatography (EtOAc:

MeOH, 9:1 containing 3% NH_4OH) to afford nonylamine (23 mg, 58%) as a colorless liquid.

Preparation of *N*-Cyclohexyl-1,3-propanediamino-*N,N′*-bis(trimethylmethanesulfonamide) (5). To a solution of *N*-cyclohexyl-1,3-propanediamine (**4**, 550 mg, 3.52 mmol) and triethylamine (7.36 mL, 52.8 mmol) in CH_2Cl_2 (20 mL) was added dropwise ice-cold *tert*-butylsulfinyl chloride (1.09 g, 7.74 mmol) in CH_2Cl_2 (15 mL) at 0 °C. After 1 h (TLC monitoring, EtOAc:MeOH, 1:1 with 3% NH_4OH), the mixture was diluted with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (20 mL). The organic extracts were combined, dried over $MgSO_4$, and concentrated under reduced pressure. The resulting mixture of diastereomeric sulfinamides was oxidized without further purification.

To a solution of the sulfinamides in CH_2Cl_2 (20 mL) was added *m*-CPBA (55%, 2.55 g, 8.14 mmol) at rt. After 45 min, the reaction mixture was diluted with a mixture of saturated aqueous $NaHSO_3$ (20 mL) and $NaHCO_3$ (20 mL). The aqueous layer was extracted with 20 mL of CH_2Cl_2. The organic extracts were combined, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by flash column chromatography (EtOAc:hexanes, 1:1) to afford the bis-sulfonamide **5** (1.01 g, 72% over two steps) as a white solid (mp 123−125 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.10 (br t, J = 6.3 Hz, 1 H), 3.52 (tt, J = 11.9 Hz, 1 H), 3.39 (br s, 2 H), 3.26 (q, J = 5.9 Hz, 2 H), 1.95−1.03 (m, 12 H), 1.37 (s, 9 H), 1.36 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 62.2, 59.8, 59.0, 41.8, 40.7, 33.1, 26.3, 25.3, 24.9, 24.3; CIMS *m/z* (relative intensity) 277 (MH^+ − *tert*-butylsulfonyl, 100), 157 (M^+ − 2 − *tert*-butylsulfonyl, 71).

Partial Cleavage of *N*-Cyclohexyl-1,3-propanediamino-*N,N′*-bis(trimethylmethanesulfonamide) (5). The general procedure was followed at 0 °C using sulfonamide **5** (109 mg, 0.26 mmol), trifluoromethanesulfonic acid (0.2 N, 8.2 mL), anisole (0.60 mL, 5.50 mmol), and CH_2Cl_2 (8.2 mL). After 25 min (TLC monitoring, EtOAc:hexanes, 3:2), the crude product was purified by flash chromatography (EtOAc:MeOH, 9:1 containing 3% NH_4OH) to afford the partially deprotected product **6** (65 mg, 86%) as a colorless liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.27 (t, J = 6.0 Hz, 3 H), 2.78 (t, J = 6.0 Hz, 3 H), 2.37 (tt, J = 10.3, 3.7 Hz, 2 H), 1.87−1.83 (m, 2 H), 1.70−1.53 (m, 5 H), 1.34 (s, 9 H), 1.29−0.94 (m, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 59.3, 56.6, 45.8, 44.9, 33.3, 29.8, 26.0, 24.8, 24.3; CIMS *m/z* (relative intensity) 277 (MH^+, 100).

Complete Cleavage of *N*-Cyclohexyl-1,3-propanediamino-*N,N′*-bis(trimethylmethanesulfonamide) (5). The general procedure was followed using sulfonamide **5** (99 mg, 0.25 mmol), trifluoromethanesulfonic acid (0.2 N, 12.5 mL), anisole (0.54 mL, 5.00 mmol), and CH_2Cl_2 (12.5 mL). After 2.5 h at rt (TLC monitoring, EtOAc:MeOH, 9:1 containing 3% NH_4OH). The crude product was purified by flash chromatography (EtOAc:MeOH, 1:1 containing 3% NH_4OH) to afford the diamine **4** (26 mg, 67%) as a colorless liquid.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra of new compounds and X-ray data for sulfonamide **5** (47 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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