Sulfinic Acids and Related Compounds 23. Preparation of Sulfinic Acids by the Reaction of Sulfonyl Halides with Thiols[1,2]

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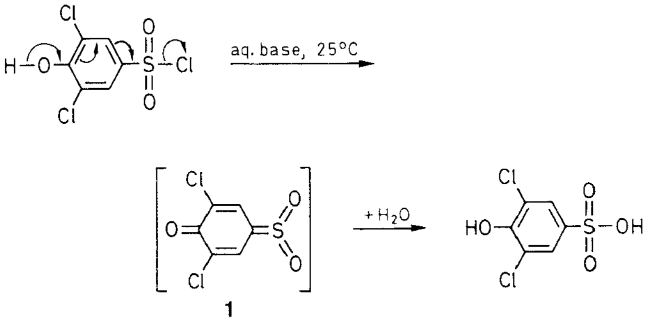
The reaction of arene- and alkanesulfonyl halides with *p*-thiocresol in the presence of triethylamine at − 76 °C gives triethylammonium sulfinates, which after acidification afford sulfinic acids of 95–100% purity in yields of 51–92% for 18 typical representatives. The synthesis succeeds in certain instances where conventional reduction with aqueous sodium sulfite fails and in other instances often is superior. The method is rapid, mild, selective, convenient, and general, although a few limitations are reported. Characterizations of the sulfinic acids are effected by titration with aqueous sodium nitrite, by IR and ^{1}H-NMR spectra, by preparation of either a *S*-benzylthiuronium salt or a *p*-nitrobenzyl ester, and either by elemental analyses or comparison with reported melting points of the acids and derivatives as appropriate.

In connection with other interests, synthesis became necessary of certain hydroxyarenesulfinic acids by reduction of the readily available hydroxyarenesulfonyl chlorides.[2,3] Of the various reducing agents that have been reviewed (cf. refs. 4–6, and references cited therein), several of the most attractive proved unpromising, as did others not reviewed.[2] A particular surprise was the failure with aqueous sodium sulfite, which is commonly used with good success. With the hydroxyarenesulfonyl chlorides, however, a major product (and sometimes the sole product) with the sulfite was the hydroxyarenesulfonate. Ultimately, evidence was developed that the sulfonate was not produced merely by simple hydrolysis but rather by formation, under the rather strongly basic conditions, of a thioquinone *S*,*S*-dioxide **1**, which was rapidly attacked by water[2,3] (Scheme **A**).



Scheme **A**

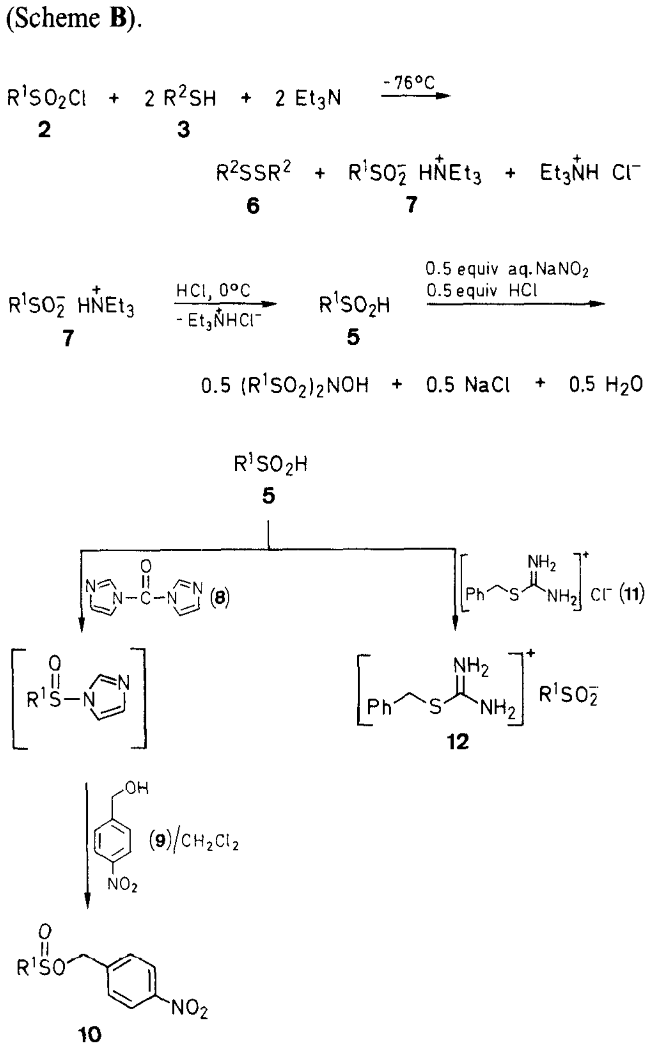
In our search for a mild means of reducing hydroxyarenesulfonyl chlorides to sulfinic acids, it then occurred to us that advantage might be taken of a side reaction that normally is merely a nuisance when thiosulfonates are prepared from sulfonyl chlorides and thiols. Many years ago,[7] Connor summarized this situation by stating that "... the reaction of sulfonyl chlorides with sulfhydryl compounds is not generally a satisfactory method for the preparation of thiosulfonic esters, although small yields (up to 25%) may be obtained in the presence of pyridine. The chief products of the reaction are usually sulfinic acid (RSO_2H) and disulfide (R'SSR'). It is likely that the ester is the precursor of these but that it reacts with the mercaptan to give the chief products." Connor's view can be formulated by the reaction of the sulfonyl chloride **2** and thiol **3** to give the thiosulfonate **4**, which then thioalkylates as yet unreacted **3** to give the sulfinic acid **5** (after acidification), along with the disulfide **6**.

$$\underset{\mathbf{2}}{R^1SO_2Cl} + \underset{\mathbf{3}}{R^2SH} + B \longrightarrow \underset{\mathbf{4}}{R^1SO_2SR^2} + BH^+Cl^-$$

$$\mathbf{3} + \mathbf{4} \xrightarrow[2.\ H^+]{1.\ Base} \underset{\mathbf{5}}{R^1SO_2H} + \underset{\mathbf{6}}{R^2SSR^2}$$

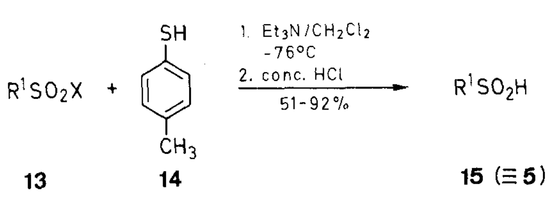
B = Base

Summation of these two equations implies that a one-pot synthesis of a sulfinic acid salt **7** from a sulfonyl chloride **2** might be feasible; acidification of the triethylammonium salt **7** then should produce the sulfinic acid **5** (Scheme **B**).



Scheme **B**

p-Toluenesulfonyl chloride (**13a**) therefore was used as a prototype to test the synthetic possibilities of the reaction of **2** and **3** to give **5** (≡**15**). With dichloromethane as a solvent, the yield of *p*-toluenesulfinic acid (**15a**) increases from 35% at room temperature to 88% at − 76 °C (Table 1). Toluene and ethyl acetate are almost as effective as solvents (67 and 77% yields, respectively. Water was avoided as a solvent because it led to formation of the sulfonic acid from hydroxysulfonyl chlorides. In a general procedure developed, which suffices with slight variations for the compounds **15a–r** (Table 1) two molar proportions each of *p*-thiocresol (**14**) and triethylamine are allowed to react for a few minutes with one molar proportion of the sulfonyl chloride at − 76 °C until the reaction is complete. Dichloromethane is the solvent, unless sparing solubility requires use of ethyl acetate. When reaction is complete, shaking with water then extracts the triethylammonium sulfinate (cf. see Scheme **B** for general equation), after which acidification at 0 °C and extraction gives the sulfinic acid **15** (Scheme **C**). By this means, the initially desired hydroxyarenesulfinic acids (4-hydroxy-, 3,5-dichloro-4-hydroxy-, and 3,5-dichloro-2-hydroxybenzenesulfinic acid) were obtained in yields of 67–78% and purities of 99–100%, although with sodium sulfite the second of these gave only the sulfonic acid salt and the third gave 44–60% of the sulfonic acid salt.[2,3]



10, 13 15	R¹	X (for 13)	10, 13 15	R¹	X (for 13)
a	$4\text{-}CH_3C_6H_4$	Cl	j	$3\text{-}FO_2SC_6H_4$	Cl
b	$4\text{-}ClC_6H_4$	Cl	k	$4\text{-}ClC_6H_4$	F
c	$3,5\text{-}Cl_2C_6H_3$	Cl	l	$3\text{-}HO_2C$, $4\text{-}ClC_6H_3$	F
d	$4\text{-}HO_2CC_6H_4$	Cl	m	2-naphthyl	Cl
e	$3\text{-}HO_2C, 4\text{-}ClC_6H_3$	Cl	n	2-thienyl	Cl
f	$2\text{-}MeO_2CC_6H_4$	Cl	o	*n*-C_3H_7	Cl
g	$2\text{-}O_2NC_6H_4$	Cl	p	*n*-C_4H_9	Cl
h	$3\text{-}O_2N$, $4\text{-}Cl\text{-}C_6H_3$	Cl	q	*n*-C_8H_{17}	Cl
i	$4\text{-}CH_3CONHC_6H_4$	Cl	r	*n*-$C_{16}H_{33}$	Cl

Scheme **C**

Since the method thus appears to be quite promising in terms of yield, purity, mildness, rapidity and convenience, the scope and limitations were explored with the compounds **15a–r** shown in Table 1. Special efforts were made to include sulfonyl halides that seemed likely to give poor results with sodium sulfite. All of the reactions of Table 1 proceed smoothly at − 76 °C and usually are complete in about 15 minutes. The purity of the products isolated is assayed,[8,9] by titration of the sulfinic acid **5** with acidified sodium nitrite (see the equation given in

Scheme **B**); as Table 1 shows, the purity ranges from 95% to 100%. Two sulfinic acids **15f, g** fail to react with nitrous acid, however, perhaps because the electron-withdrawing substituents reduce the nucleophilicity of the sulfinate anion too greatly. Each of the arenesulfinic acids synthesized is further characterized as a *S*-benzylthiuronium salt (cf. **12**) and each of the alkanesulfinic acids as a *p*-nitrobenzyl ester (cf. **10** and Table 2); we had used *p*-nitrobenzyl esters in earlier work, and it is worth adding that the present esterifications further illustrate the novel synthesis that we reported earlier, with carbonyldiimidazole (**8**) for a mild conversion of sulfinic acids to esters.[10] All products also were characterized by IR and ^{1}H-NMR spectra and either by elemental analyses or by reported melting points as appropriate.

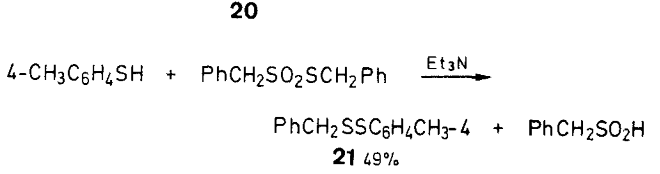
As already mentioned, the electron-donating methyl and hydroxyl groups are satisfactory as arene substituents. To ascertain the effect of electron withdrawal, reduction of sulfonyl chlorides **13b–h** to the acids **15b–h** was studied (Table 1). Mild electron withdrawal has no marked effect. Thus little significant difference is caused by the one or two chlorine atoms of **13b** and **13c**, by the carboxylic acid of **13d**, by the combination of carboxylic acid and chlorine of **13e**, or by the methoxycarbonyl of **13f**. Even one nitro group, **13g**, or a combination of nitro and chlorine, **13h**, has no particular effect. On the other hand, 2,4-dinitrobenzenesulfonyl chloride gives only unpromising mixtures, and no 2,4-dinitrobenzenesulfinic acid could be isolated.[2] The acetamido group, which is borderline in electronic effect, leads to somewhat lower yield than usual (with **13i**), but is satisfactory. With Hammett σ_{para} values as a measure of electronic effect, values for the groups discussed so far are: OH, -0.38; CH_3, -0.14; CH_3CONH, 0.0; Cl, 0.24; CO_2H, 0.44; CO_2Me, 0.44; and NO_2, 0.81.[11]

It would be of interest to learn the effect of the amino group (σ_{para}, -0.30),[11] but aminobenzenesulfonyl chlorides are not readily available. On the other hand, aminobenzenesulfonyl fluorides are available. For this reason, as well as for that of interest in the usually less reactive sulfonyl fluoride group *per se*, and because some sulfonyl chlorides either may be less stable or less available than the fluorides, the fluoro derivatives **13j, k, l** were studied. In the compound **13j**, which contains both sulfonyl fluoride and sulfonyl chloride groups, selective reduction of the sulfonyl chloride to give 3-fluorosulfonylbenzenesulfinic acid (**15j**) in 83% yield shows that the reduction of the sulfonyl fluoride function indeed is much slower than that of the sulfonyl chloride group (which presumably explains the availability of the aminobenzenesulfonyl fluorides). Both of the other sulfonyl fluorides **13k** and **13l** give good results and lead to the acids **15k** and **15l** in 75–87% yield. Nevertheless, neither *o*- nor *p*-aminobenzenesulfonyl fluoride give any sulfinic acid by the General Procedure, perhaps because electron donation is too extreme.

Use of representative nuclei other than phenyl leads to no difficulties; 2-naphthalenesulfinic acid (**15m**) and 2-thiophenesulfinic acid (**15n**) were obtained quite satisfactorily.

In the reduction of alkanesulfonyl chlorides **13o–r** to the alkanesulfinic acids **15o–r** yields were lower than with most of the arenesulfonyl halides, being in the range of 51–67% [1,4-bisbutanesulfonyl chloride may have given yields in the range of 35–54% (titration with sodium nitrite), but no effort was made to isolate the sulfinic acid; see the experimental section].

An interesting aberration occurs when the General Procedure is applied to α-toluenesulfonyl chloride (**16**). The result deserves attention since it may lend a clue to unexpected results that others may encounter with unusual sulfinic acids. Thus after the usual reaction and extraction with water, acidification of the aqueous extract gives only a trace of gum. The organic layer, however, contains two substances. One is di-*p*-tolyl disulfide (**19**, 49% yield), indicating that the usual thioalkylation occurrred (Scheme **D**). The other is benzyl *p*-tolyl disulfide (**21**, 49% yield); **21** was identified by elemental analysis, spectra and reduction to *p*-thiocresol and phenylmethanethiol. The most obvious explanation for the formation of **21** is that the usual reduction occurred first to give the sulfinate salt **18**, but that α-toluenesulfinic acid in equilibrium with the salt **18** disproportionates, so that **18** yields the products and stoichiometry expected of a sulfinic acid,[12] including the thiosulfonate **20**. The thiosulfonate **20** then thioalkylates as yet unchanged *p*-toluenethiol 17 to give benzyl *p*-tolyl disulfide **21** (Scheme **D**). If the thiol **17** is considered to be the limiting reagent, and if one assumes that the three preceding equations can be summarized by the Scheme **E**, then the combined yields of the disulfides **19** (49%) and **21** (49%) account for 98% of the thiol **17**.

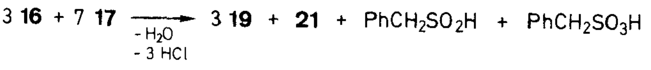


$$\underset{\mathbf{16}}{PhCH_2SO_2Cl} + 2\ \underset{\mathbf{17}}{4\text{-}CH_3C_6H_4SH} + 2\ Et_3N \xrightarrow{CH_2Cl_2,\ 76\ °C,\ 15\ min} \underset{\mathbf{18}}{PhCH_2SO_2^-H\overset{+}{N}Et_3} + \underset{\mathbf{19}\ 49\%}{(4\text{-}CH_3C_6H_4S)_2} + Et_3\overset{+}{N}HCl^-$$

$$3\ \mathbf{18} \xrightarrow[-H_2O]{} \underset{\mathbf{20}}{PhCH_2SO_2SCH_2Ph} + 2\ Et_3N + Et_3\overset{+}{N}HPhCH_2SO_3^-$$

$$4\text{-}CH_3C_6H_4SH + PhCH_2SO_2SCH_2Ph \xrightarrow{Et_3N} \underset{\mathbf{21}\ 49\%}{PhCH_2SSC_6H_4CH_3\text{-}4} + PhCH_2SO_2H$$

Scheme **D**



$$3\ \mathbf{16} + 7\ \mathbf{17} \xrightarrow[\substack{-H_2O\\ -3\ HCl}]{} 3\ \mathbf{19} + \mathbf{21} + PhCH_2SO_2H + PhCH_2SO_3H$$

Scheme **E**

In summary, reactions of sulfonyl chlorides or fluorides with *p*-thiocresol afford syntheses of sulfinic acids of a variety of types: arene, alkane, heterocyclic and multinuclear (ref. 13 cites a few earlier conversions involving much less advantageous techniques). The conditions are mild and nonaqueous, the procedure is rapid, and the

Table 1. Sulfinic Acids **15** Prepared

Sulfonyl Halide	Sulfinic Acid	Yield[a] (%)	Purity	mp (°C)	Molecular Formula[b] or Lit. mp (°C)	IR (KBr/neat) ν (cm^{-1})	^{1}H-NMR δ, J (Hz)	Thiuronium Salt[c] mp (°C)	
								found	reported
13a	**15a**	88 (88)^{13}	98	85–90	86–87^{14}	2900–2300 (br), 1595, 1495, 1400, 1320, 1280, 1180, 1090 (s), 1060 (s), 1025 (s), 1000 (s), 800 (s), 620	7.39–7.42 (d, 2H, J = 8.2), 7.57–7.60 (d, 2H, J = 8.1)	171–175	167–168^{15}
13b	**15b**	84–86 (81)^{16}	99	94–96	98–99^{16}	3000–2000 (br), 1570, 1460, 1380, 1320, 1070, 1030 (s), 980 (s), 860, 810, 730	7.55–7.58 (d, 2H, J = 8.6), 7.62–7.65 (d, 2H, J = 8.4)	175–176	170^{17}
13c	**15c**	78 (–)^{18}	99	90–92	–	3100–2300 (br), 1575, 1420, 1382, 1320, 1140, 1100, 1060 (s), 1038, 860, 820, 800, 606	7.57 (s)	160–162	–
13d	**15d**	79 (–)^{19}	100	230–250 (dec)	245^{19}	3150–2300 (br), 1700 (s), 1600, 1580, 1415, 1400, 1320, 1295 (s), 1080 (s), 1030 (s), 1010 (s), 850 (s), 760, 700	7.75–7.78 (d, 2H, J = 8.3), 8.13–8.16 (d, 2H, J = 8.3)	195–197	–
13e	**15e**	74	100	180–182 (dec)	$C_7H_5ClO_4S$ (220.6)	3100–2350 (br), 1720 (s), 1590, 1560, 1460, 1420, 1380, 1300, 1250, 1210, 1160, 1100, 1040, 910, 880, 840, 820, 730, 660	7.66–7.69 (d, 1H, J = 8.3), 7.76–7.79 (d, 1H, J = 10), 8.04 (s, 1H)	138–140	–
13f	**15f**	92 (88)^{20}	–[d]	96–99	89–92^{20}	3100–2100 (br), 1720 (s), 1680, 1585, 1460, 1430, 1275 (s), 1182, 1160, 1140, 1100, 1055, 1020 (br, s), 820, 750, 680	3.96 (s, 3H), 7.65 (t, 1H, J = 7.5), 7.82 (t, 1H, J = 9.0), 7.97–8.00 (d, 1H, J = 7.5), 8.02–8.05 (d, 1H, J = 9.0)	150–152	–
13g	**15g**	80	–[d]	123–125	124^{21}	2950–2000 (br), 1600, 1520 (s), 1340 (s), 1300 (s), 1105 (s), 1070 (s), 1040 (s), 990 (s), 830 (s), 780 (s), 730 (s), 700	7.71 (t, 1H, J = 8.7), 7.92 (t, 1H, J = 9.0), 8.06–8.09 (d, 1H, J = 8.0), 8.15–8.18 (d, 1H, J = 8.0)	145–147	–
13h	**15h**	72 (85)^{22}	98	94–96	100–103^{22}	3100–2300 (br), 1595, 1575, 1540 (s), 1460, 1340 (s), 1100, 1070 (s), 1040 (s), 880, 820 (s), 760, 740	7.77–7.80 (d, 1H, J = 8.3), 7.84–7.87 (d, 1H, J = 10), 8.20 (s, 1H)	140–142	–
13i	**15i**	64 (43–47)^{23}	98	150–152 (dec)	155 (dec)^{23}	3300, 3200, 3125, 3075–2300 (br), 1630, 1605, 1580, 1540, 1490, 1395, 1375, 1320, 1270, 1080 (s), 1070 (s), 810	2.15 (s, 3H), 7.63–7.66 (d, 2H, J = 8.7), 7.75–7.78 (d, 2H, J = 8.8)	203–205	–
13j	**15j**	83	100	85–87	$C_6H_5FO_4S_2$ (224.2)	3250–2150 (br), 1595, 1410 (s), 1300, 1210 (s), 1080 (s), 1060 (s), 1010 (s), 990 (s), 820 (br, s), 760 (s), 670	7.86 (t, 1H, J = 7.8), 8.10–8.13 (d, 1H, J = 7.8), 8.18–8.21 (d, 1H, J = 7.8), 8.31 (s, 1H)	120–122	–
13k	**15k** (≡**15b**)	75 (81)^{16}	99	96–99	98–99^{16}	–[e]	–[e]	–	–
13l	**15l** (≡**15e**)	87	97	179–180 (dec)	–[f]	–[f]	–[f]	–	–
13m	**15m**	83–84 (–)^{24}	100	95–100 (dec)	98 (dec)^{24}	3100–2000 (br), 1620, 1585, 1500, 1340, 1260 (br, s), 1060–990 (br, s), 850 (s), 830 (s), 800 (s), 740 (s)	7.59–7.63 (m, 2H), 7.74–7.77 (d, 1H, J = 8.4), 7.94–8.06 (m, 3H), 8.24 (s, 1H)	171–173	168–169^{15}
13n	**15n**	84 (–)^{25}	99	74–76	72–73^{25}	3125–2000 (br), 1500, 1400 (s), 1340, 1265, 1230 (s), 1090, 1040 (s), 1000 (s), 835 (s), 710 (s)	7.10–7.13 (dd, 1H), 7.46–7.47 (d, 1H, J = 3.7), 7.61–7.62 (d, 1H, J = 4.8), 8.01 (s, 1H)	144–146	–

Table 1. (continued)

Sulfonyl Halide	Sulfinic Acid	Yield[a] (%)	Purity	mp (°C)	Molecular Formula[b] or Lit. mp (°C)	IR (KBr/neat) ν(cm^{-1})	^{1}H-NMR δ, J(Hz)	Thiuronium Salt[c] mp (°C)	
								found	reported
3o	**15o**	62	95	oil	–[g]	3500–2000 (br, s), 1460, 1400, 1380, 1300 (br), 1080 (br, s), 1020 (br, s), 820 (br, s), 610	1.06 (t, 3H, J = 7.5), 1.70–1.82 (sext, 2H, J = 7.5), 2.81 (t, 2H)	–	–
3p	**15p**	51	98	oil	–[g]	3600–2100 (br), 1470, 1410, 1380, 1300, 1080 (s), 1040 (s), 915, 820, 600	0.95 (t, 3H, J = 9.0), 1.40–1.53 (sext, 2H, J = 7.2), 1.65–1.75 (quint, 2H, J = 7.8), 2.64 (t, 2H, J = 7.8)	–	–
3q	**15q**	52	99	oil	–[g]	3600–2100 (br, s), 1470, 1405, 1380, 1300 (br), 1060 (br, s), 1030 (br, s), 820 (br, s), 720, 600	0.88 (t, 3H, J = 7.0), 1.19–1.41 (m, 10H), 1.65–1.76 (quint, 2H, J = 7.8), 2.83 (t, 2H, J = 8.0)	–	–
3r	**15r**	67	100	55–57	54–55[26]	2950 (s), 2875 (s), 2600–2300 (br), 1475, 1410, 1380, 1330 (br), 1090, 1060 (s), 1040 (s), 1020, 820 (s), 720	0.88 (t, 3H, J = 7.0), 1.20–1.50 (m, 26H), 1.65–1.75 (quint, 2H, J = 7.5), 2.82 (t, 2H, J = 8.0)	–	–

Yield of isolated products. Literature yield prepared by the reduction of RSO_2Cl with Na_2SO_3 is given in parenthesis, wherever available; for compounds **15c**, **15d**, **15m** and **15n**, the preparation was reported in the literature, but no yield was given.

Satisfactory microanalyses obtained: C, H, F, S ±0.4.

All thiuronium salts were characterized by IR and NMR spectral data.[22] Satisfactory microanalyses obtained for new thiuronium salts, C, H, N ±0.4.

[d] No reaction occured.

[e] IR and ^{1}H-NMR spectral data identical with those of **15b**.

[f] IR, ^{1}H-NMR identical with those of **15e**.

[g] Analysed as the p-nitrobenzyl ester (see Table 2).

method is selective and convenient. Yields generally are good and purities are high. This reduction is the only one of many tried that is promising for hydroxyarenesulfonyl halides, and it often gives better results than other methods in other instances. The procedure fails with 2,4-dinitro- and aminoarenesulfonyl halides and gives anomalous results with α-toluenesulfonyl chloride.

Melting points were measured with a Thomas Hoover stirred-liquid apparatus by immersing at ca. 10 °C below the mp and then heating at 2–3 °C/min, and are corrected. IR spectra were recorded on a Perkin-Elmer Model 727 spectrophotometer. ^{1}H-NMR were recorded on an IBM NR 300 spectrometer at 300 MHz with D_2O/DSS, except for **13i** and **13m** (CD_3OD/TMS) and **13n–r** ($CDCl_3$/TMS). Where coupling constants are not reported, although the gross appearance of peaks was as reported (d, t, etc), second-order effects led to enough uncertainty that reporting coupling constants would be more misleading than helpful. TLC was performed on Whatman K6F preparative silica gel plates with visualization by UV. Flash chromatography was done with use of a 2.2 × 30 cm column prepared from Baker 7024 silica gel (40 μ). Elemental analyses were by Galbraith Laboratories, Knoxville, Tenn. All sulfonyl halides were commercial products used as received and were from Aldrich Chemical Co., except for 3,5-dichlorobenzenesulfonyl chloride (Lancaster Synthesis, Ltd.), 1-butane-, and 1-octanesulfonyl chloride (Fluka). All other materials were commercial products used as received.

Sulfinic Acids 15a–r; General Procedure:

p-Thiocresol **(14)** and Et_3N (each in a twofold molar ratio to the sulfonyl halide) are dissolved in CH_2Cl_2 (ca. 0.7–3.5 mL/mmol), and this solution is added in 0.5- to 1 mL portions during 1–5 min to a solution of the sulfonyl halide **13** (ca. 2–10 mmol) in CH_2Cl_2 (ca. 3–5 mL/mmol of sulfonyl halide, depending on solubility), which is cooled meanwhile at −76 °C. After the addition, the solution is stirred for 10–30 min more at −76 °C until the reaction is complete, as determined by disappearance of the thiol in TLC (CH_2Cl_2/hexane, 3 : 7). The mixture is shaken with H_2O (ca. 5 × 20 mL for the arene acids and ca. 1–2 × 20–30 mL for the alkane acids), the amount being kept at a minimum depending on the relative amount of CH_2Cl_2, in order to extract the triethylammonium salt of the sulfinic acid. The aqueous extract is washed once ot twice with Et_2O, CH_2Cl_2 or benzene (10–20 mL), cooled to 0 °C, and acidified with 2 (usually)-6 fold molar proportions of conc. HCl. If precipitate appears **(15a,k)**, it is extracted with Et_2O (ca. 4 × 25 mL) portions. Otherwise (or thereafter) the aqueous solution is saturated with NaCl and extracted with Et_2O (2–5 × 20–50 mL) until a sample of the extract contains no more sulfinic acid (as determined by immediate decolorization of 1% aqueous $KMnO_4$ when shaken with a sample of the extract). The ethereal extracts are combined and dried ($MgSO_4$). After removal of the Et_2O carefully at aspirator pressure, the sulfinic acid is obtained with the yield and properties reported in Table 1.

The following variations or addenda should be noted:

With **15a**: Yields with CH_2Cl_2 at various temperatures are 35% at 25 °C, 50–62% at 0 °C, and 88% (Table 1) at −76 °C; removal of the bath immediately after the addition and stirring for 15 min saves time compared with up to 30 min at −76 °C and gives comparable results with **15a** (and **15b** ≡ **15k**). Also at −76 °C, toluene as solvent leads to **15a** in 67% yield and EtOAc in 77% yield.

With **15d**, **15e**, **15h** and **15l**: Sparing solubilities lead to use of EtOAc as a solvent rather than CH_2Cl_2; ca. 2–5 mL/mmol is used to dissolve the thiol/Et_3N and for the sulfonyl halide ca. 5–7 mL/mmol of halide; with **15d**, EtOAc (50 mL) and Et_2O (50 mL) are used to extract the sulfinic acid from 4.53 mmol of halide.

With **15e** and **15l** ca. 3 mmol of Et_3N is used per mmol of sulfonyl

With **15f**: The mmol of thiol and Et_3N per mmol of sulfonyl chloride is 2.2. Only 1.25 mmol of HCl per mmol of sulfonyl chloride is used for acidification in order to minimize hydrolysis of the ester function (our experience has been that certain sulfinic esters are readily hydrolyzed);[27] the sulfonyl chloride used is 90% pure.

With **15i**: The amount of CH_2Cl_2 used per mmol of the sparingly soluble sulfonyl chloride is increased to 14 mL. After the acidification and saturation with NaCl, the precipitate of **15i** is removed by filtration, washed with iced H_2O (20 mL) and acetone (10 mL) and dried at 0.2 Torr to give the product reported in Table 1.

With **15j**: The liquid sulfinic acid crystallizes when rubbed with pentane.

With **15r**: After completion of the reaction with 3.08 mmol of halide at -76°C, CH_2Cl_2 is removed at aspirator pressure and 1 N aq NaOH (10 mL, 10 mmol) is added to the residual paste (because, in contrast to an aqueous solution of the Et_3N salt, one of the Na salt is not soapy). The resulting solution is washed with EtOAc (2 × 20 mL), cooled at 0°C, and acidified with conc HCl (2 mL, 24 mmol). The mixture is then saturated with NaCl, and the sulfinic acid is isolated as usual.

Determination of Purity of Sulfinic Acids by Titration with Aqueous $NaNO_2$ (cf. Table 1):

In a procedure based on one of Marvel and Johnson,[8,9] aqueous 0.24 N HCl (in the same molar amount as that of the sulfinic acid when assumed to be pure) is added to a solution of the sulfinic acid (ca. 0.1 g) in H_2O. The solution then is titrated with aq 0.05 M $NaNO_2$ solution. The end point is determined by using an outside indicator of starch-KI test paper, which shows an immediate purple color when the end point is reached. The purity of sulfinic acid shown in Table 1 is calculated as 2 (moles of $NaNO_2$ used) × 100/(moles of RSO_2H on the assumption that the sample is 100% pure).

S-Benzylthiuronium Salts 12 (cf. Scheme B) of Arenesulfinic Acids 15; General Procedure:

In a modification of a procedure of Kurzer and Powell,[15] a solution of *S*-benzylthiuronium chloride (**11**), in the same molar amount as that of the sulfinic acid (assumed to be 100% pure) is prepared in the least amount of H_2O at 40°C. This solution is added to a clear solution of the sulfinic acid **15** (0.1–0.3 g) dissolved in the least amount of H_2O at r.t. A precipitate usually forms immediately. The mixture is stirred for 10 min at 25°C and kept at 0°C until crystallization is complete (ca. 1 h). The precipitate is removed by filtration and is recrystallized once with a minimum of warm H_2O (40–50°C) or H_2O/MeOH. Removal of the crystals by filtration and drying at 0.2 Torr for 24 h gives the *S*-benzylthiuronium sulfinate **12** (Table 1). All of the *S*-benzylthiuoronium arenesulfinates in Table 1 had appropriate IR or NMR spectra (which are available).[2]

p-Nitrobenzyl Esters 10 of Alkanesulfinic Acids 15 (≡ 5) (cf. Scheme B):

A solution of carbonyldiimidazole (**8**; 1.1–1.5 mmol per mmol of **9**) in CH_2Cl_2 (5–10 mL) is added in one portion to a solution of the alkanesulfinic acid (ca. 1.1–1.2 mmol per mmol of **9**) in CH_2Cl_2 (ca. 10 mL) at r.t. and the resulting solution is stirred for 10–30 min. A solution of the alcohol **9** (0.6–1.7 mmol) in CH_2Cl_2 (5–10 mL) is added during 1 min, and the resulting solution is stirred for 1–2 h. The solution then is washed with 10% aq HCl (2–5 mL) and with H_2O (2 × 30–40 mL) and dried ($MgSO_4$). After evaporation of the CH_2Cl_2, preparative TLC (Table 2) gives the *p*-nitrobenzyl alkanesulfinates **10** (cf. Scheme B) (Table 29).

Limitations of the Method:

Among the arenesulfonyl halides, 2,4-dinitrobenzenesulfonyl chloride when submitted to the General Procedure leads to one TLC spot for di-*p*-tolyl disulfide (**19**) and another at R_f = 0 that perhaps corresponds to a triethylammonium sulfinate (**7**); however, several

Table 2. *p*-Nitrobenzyl Esters **10** of Alkanesulfinic Acids Prepared

Product	Yield (%)	Preparative TLC[a]	R_f	mp (°C)	Molecular Formula[a]	IR (neat) ν(cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS) δ, J(Hz)
10o	61	1 : 9	0.78	oil	$C_{10}H_{13}NO_4S$ (243.3)	3150, 3100, 2975, 2950, 2900, 1600 (s), 1520 (s), 1490, 1460, 1400, 1340 (s), 1310, 1300, 1205, 1180, 1120 (s), 1090, 1040, 990 (br, s), 850 (s), 805, 730, 670, 630	1.07 (t, 3H, J = 7.4), 1.72–1.85 (sext, 2H, J = 7.6), 2.74–2.92 (m, 2H), 5.09–5.20 (dd, 2H, J = 13, 20), 7.53–7.56 (d, 2H, J = 8.6), 8.23–8.26 (d, 2H, J = 8.7)
10p	44–52	1 : 9	0.76, 0.85	oil	$C_{11}H_{15}NO_4S$ (257.3)	2950, 1600, 1520, 1340 (s), 1130, 1000 (br), 850, 740	0.96 (t, 3H, J = 7.3), 1.41–1.53 (sext, 2H, J = 7.3), 1.67–1.77 (quint, 2H, J = 7.3), 2.76–2.94 (m, 2H), 5.09–5.19 (dd, 2H, J = 12, 20), 7.52–7.56 (d, 2H, J = 8), 8.23–8.26 (d, 2H, J = 8)
10q	34	1 : 19	0.72	oil	$C_{15}H_{23}NO_4S$ (313.4)	3150, 3125, 2975 (s), 2950 (s), 2875 (s), 1610 (s), 1530 (s), 1500, 1470, 1455, 1410, 1350 (s), 1320, 1300, 1210, 1180, 1130 (s), 990 (br, s), 850 (s), 810, 730, 680, 640	0.88 (t, 3H, J = 6.8), 1.25–1.50 (m, 10H), 1.68–1.78 (quint, 2H, J = 7.1), 2.75–2.93 (m, 2H), 5.08–5.19 (dd, 2H, J = 13, 20), 7.53–7.56 (d, 2H, J = 8.6), 8.23–8.26 (d, 2H, J = 8.7)
10r	60	1 : 19	0.38	59–61	$C_{23}H_{39}NO_4S$ (425.6)	2975, 2945, 2875, 1620, 1540 (s), 1500, 1470, 1350 (s), 1115 (s), 1060, 1035, 935, 850, 820, 760, 720[b]	0.93 (t, 3H, J = 6.9), 1.30–1.55 (m, 26H), 1.73–1.83 (quint, 2H, J = 7.8), 2.82–2.98 (m, 2H), 5.13–5.24 (dd, 2H, J = 13, 20), 7.58–7.61 (d, 2H, J = 8.5), 8.28–8.31 (d, 2H, J = 8.6)

[a] Ratio of solvent system EtOAc/CH_2Cl_2.

[b] Satisfactory microanalyses obtained: C, H, N ±0.4; **10o** S ±0.4.

[c] KBr Pellet.

additional spots are also seen, and even in several repetitions no 2,4-dinitrobenzenesulfinic acid can be isolated.

With *o*- or *p*-aminobenzenesulfonyl fluoride, when solutions of *p*-thiocresol **(14)** and Et_3N in EtOAc are added under otherwise usual conditions of the General Procedure, TLC (CH_2Cl_2/hexane 3:7) shows no formation whatsoever of di-*p*-tolyl disulfide **(19)** after 15 min at − 76 °C. When the solutions are stirred at r.t. for up to 24 h, occasional checks by TLC still reveals principally starting materials, with so small a trace of di-*p*-tolyl disulfide **(19)** that both reactions are abandoned.

Among the alkanesulfonyl chlorides, α-toluenesulfonyl chloride **(16)** gives anomalous results. Thus when the General Procedure is applied to a mixture of **16** (0.50 g, 2.62 mmol), thiol **14** (0.65 g, 5.23 mmol), and Et_3N (0.53 g, 5.24 mmol), after a typical period of 15 min at − 76 °C TLC (CH_2Cl_2/hexane, 1:6) shows major spots at R_f = 0, 0.46 and 0.62. Continuation of the General Procedure through the usual acidification of the aqueous layer, salting out, and extraction gave only 10 mg of unidentified gum. On the other hand, when the CH_2Cl_2 solution that had been extracted with H_2O to remove any triethylammonium α-toluenesulfinate is dried ($MgSO_4$) and evaporated, 0.60 g of yellow oil remains. Preparative TLC of 0.20 g (CH_2Cl_2/hexane, 1:6) gives Fraction I as a solid (90 mg, R_f = 0.62) and Fraction II as a pale yellow oil (30 mg, R_f = 0.46). Fraction I is di-*p*-tolyl disulfide **(19)**; 49% yield), as shown by the identity of the R_f value, mp and ^{1}H-NMR spectrum with those of authentic **19**. Fraction II is benzyl *p*-tolyl disulfide (**21**; 49% yield); this disulfide has been reported as a solid with mp 34–35 °C.[12]

$C_{14}H_{14}S_2$	calc.	C 68.25	H 5.73
(246.4)	found	67.99	5.92

21; IR (neat): ν = 3075, 3050, 2950, 2875, 1600, 1590, 1490 s, 1450 s, 1440, 1400, 1300, 1230, 1200, 1180, 1120, 1100, 1080, 1030, 1020, 800 s, 760 s, 690 s, 600 cm^{-1}.

^{1}H-NMR ($CDCl_3$): δ = 2.33 (s, 3 H), 3.93 (s, 2 H), 7.09–7.12 (d, 2 H, J = 8.4 Hz), 7.25–7.30 (m, 5 H), 7.34–7.36 (d, 2 H, J = 8.1 Hz).

The structure of **21** is confirmed by heating it with Zn dust and aq HCl for 10 min on a steam bath. After removal of Zn dust from the acidic solution, the thiols produced are extracted with CH_2Cl_2. After the CH_2Cl_2 has been dried ($MgSO_4$), TLC showed two spots that correspond with authentic *p*-thiocresol **(14)** and benzenemethanethiol.

An effort to convert 1,4-butanedisulfonyl chloride[10] to 1,4-butanedisulfinic acid by the General Procedure gives no sulfinic acid after the usual acidification and extraction, although TLC during the reaction shows disappearance of the *p*-thiocresol **(14)** and formation of di-*p*-tolyl disulfide **(19)**. The reason probably is the very sparing solubility of 1,4-butanedisulfinic acid in CH_2Cl_2, since titration with $NaNO_2$ is consistent with a yield in the aqueous solution of 35–54% (no effort is made to isolate and characterize the 1,4-butanedisulfinic acid, however).

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(1) Paper 22: Lee, C.; Stidham, D.B.; Field, L. *Phosphorus, Silicon, Sulfur, Relat. Elem.* **1990**, *47*, 53.

(2) The doctoral dissertation of C.L., from which this paper was abstracted, can be consulted for further details (Vanderbilt University, May, 1989); available by interlibrary loan or from University Microfilms International, 300 North Zeeb Road, Ann Arbor, MI 48106, USA.

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ERRATA AND ADDENDA

1989

- Freeman, F.; Keindl, M.C.; Po, H.N.; Brinkman, E.; Masse, J.A. *Synthesis* **1989**, 714. On page 714 the data for compounds **2d** and **2e** in the Table should be corrected as follows:

2d:

^{1}H-NMR (500 MHz, DMSO-d_6): δ = 7.213 (H-5), 7.225 (H-6), 7.547 (H-4), 7.558 (H-7); $J_{4,7}$ = 5.94 Hz, $J_{5,6}$ = 6.03 Hz, $J_{4,7}$ = 166.61 Hz, $J_{4,5}$ = 166.70 Hz.

^{13}C-NMR (500 MHz, DMSO-d_6): δ = 119.0 (br, C-7), 119.1 (br, C-4), 126.60 (C-5, C-6), 143.27 (C-3a, C-7a), 151.21 (C-2).

2e: mp 190–191 °C.

$C_{16}H_{14}N_4S_2.1.5H_2O$	calc.	C54.37	H4.85	N15.85	S18.14
(353.5)	found	54.71	4.63	15.66	17.94

^{1}H-NMR (500 MHz, DMSO-d_6): δ = 2.39 (s, 3H, CH_3), 7.04 (d, 1H, J = 8.11 Hz, H-5), 7.34 (s, 1H, H-7), 7.43 (d, 1H, J = 8.11 Hz, H-4).

^{13}C-NMR (500 MHz, DMSO-d_6): δ = 25.24 (CH_3), 118.05 (v. br, C-4, C-7), 128.13 (C-5), 136.14 (C-6), 142.42 (v. br, C-3a, C-7a), 150.37 (br, C-2).

EIMS (70 eV): m/z = 326 (m$^+$, 9.8%), 164 (100%).

CIMS: m/z = 327 (MH$^+$, 7.9%), 165 (100%).

1990

- Lin, Z.-Y.; Shi, W.; Zhang, L. *Synthesis* **1990**, 235. On page 236 compound **4b** should be named 7-acetoxy-4,8-dioxo-5-oxatetracyclo[8.2.1.0^{2,9}.0^{3,7}]tridec-11-ene; and compound **5** should be named 4,8-dioxo-5-oxatetracyclo-[8.2.1.0^{2,9}.0^{3,7}]tridec-11-ene.

- Lee, C.; Field, L. *Synthesis* **1990**, 391. On page 392 column 2, line 19, the statement in parenthesis should read: (cf. **7**; see Scheme **B** for general equation). While Scheme **C** should be: R^1 SO_2X + 4-MeC_6H_4SH (2 equiv) (conditions: 1. Et_3N (2 equiv)/CH_2CH_2, −76 °C; 2. conc HCl → R^1SO_2H

  On page 393 in Scheme **D** the temperature of the reaction of **16** with **17** should be −76 °C.

  On page 394–395 in Table 1, the yield of sulfinic acid **15g** should read: 80 (−)^{21}; the reference in footnote c should be Ref. 2 and not Ref. 22.

  On page 396 in Table 2 for compound **10p** the molecular formula should be referenced to Ref. 10; the 1130 cm^{-1} absorption in its IR spectral data should be designated (s).

  On page 397 the sentence should read: The structure of **21** (C, H anal ±0.3%) is confirmed by heating ...

- Lajoie, G.; Crivici, A.; Adamson, J.G. *Synthesis* **1990**, 571. On page 572 in the Table, compounds **1** and **2** should be **3** and **4**, respectively.

- Legraverend, M.; Boumchita, H.; Bisagni, E. *Synthesis* **1990** 587.

  On page 588, 2,5-diamino-4,6-dichloropyridine (**5**) should be replaced by 2,5-diamino-4,6-dichloropyrimidine (**5**).

- Tietze, L.F.; Wünsch, J.R. *Synthesis* **1990**, 985.

  On page 989, in the general procedure of the photoklysis sodium hydrogen carbonate (1.1 mmol) should be used instead of sodium hydrogen sulfate.