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A Novel Synthesis of Aromatic Sulfinic Acids

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Aromatic sulfinic acids were synthesized conveniently by the direct oxidation of thiols with 30% aqueous hydrogen peroxide at room temperature in good yield.

Keywords——oxidation; thiol; sulfinic acid; benzenesulfinic acid; hydrogen peroxide

Sulfinic acids have been prepared either by the reduction of sulfonyl chlorides[1] or by the reaction of sulfur dioxide with hydrocarbons,[2] organometallics,[3] or diazonium salt.[4] These procedures, however, are accompanied with undesirable side reactions. Also, thiols are oxidized to the sulfonic acids by usual oxidizing agents since sulfinic acids, once produced, are easily oxidized to sulfonic acids successively.[5] Therefore, the oxidation of thiols to sulfinic acids is very difficult except for selected substrates.[6] Recently, Filby *et al.*[7] have reported the direct oxidation of thiols to sulfinic acids with *m*-chloroperoxybenzoic acid at $-30\,^{\circ}C$ in high yields.

TABLE I. Oxidation of Thiols to Sulfinic Acids with H_2O_2 at Room Temperature

$$ArSH \xrightarrow[NaOH\text{-}H_2O\text{-}C_2H_5OH]{30\%\ H_2O_2} ArSO_2H$$

Run	Substrate	NaOH (mol eq)	H_2O_2 (mol eq)	Yield (%)[a] ArSH	ArSSAr	$ArSO_2H$	$ArSO_3H$
1	PhSH	0	2.0	80	15	0	0
2		1.3	2.0	0	25	47	9
3		2.8	2.0	0	0	82	16
4		8.3	2.0	0	0	62	31
5		2.8	1.0	18	15	39	3[b]
6		2.8	2.9	0	0	47	40
7		2.8	3.9	0	0	28	64
8	$PhSO_2Na\cdot 2H_2O$[c]	0	1.0	—	—	82	18
9		4.7	1.0	—	—	97	Trace
10	$PhSO_2H$[c]	0	1.0	—	—	42	2
11	*p*-ClC_6H_4SH	2.8	2.0	0	0	79[d]	—
12	*p*-MeC_6H_4SH	2.8	2.0	0	0	85[d]	—
13	*o*-$HOOCC_6H_4SH$	2.8	2.0	0	0	52[d,e]	—
14	*p*-$NO_2C_6H_4SH$	2.8	2.0	0	0	65[d]	—
15	2-PySH	2.8	2.0	0	0	85[e,f]	—
16	4-PySH	2.8	2.0	2	0	74	—

A thiol (4.5 mmol), and H_2O–EtOH (1 : 1 v/v, 40 ml) were used. The reaction was carried out at room temperature for 10 min. *a*) The yield was determined by HPLC. *b*) $PhSO_2SPh$ in a yield of 7% was produced. *c*) $PhSO_2Na\cdot 2H_2O$ (2.3 mmol) or $PhSO_2H$ (2.3 mmol) was used. *d*) Isolated yield. *e*) The reaction time was 5 min. *f*) Isolated yield as sodium salt.

We found that oxidation of aromatic thiols to their sulfinic acids took place easily with 30% aqueous hydrogen peroxide at room temperature. Aqueous hydrogen peroxide is an attractive oxidation agent which is cheap and easy to handle, and, in addition, shows a moderate activity. The key point of our work is that the sodium salts of sulfinic acids are relatively stable to aqueous hydrogen peroxide.

As shown in Table I, aromatic thiols were oxidized with hydrogen peroxide in an alkaline EtOH–H_2O solution to give the corresponding sulfinic acids. In these reactions, sulfonic acids were obtained as by-products. In the absence of sodium hydroxide, thiophenol was converted to phenyl disulfide in a yield of 15%, and oxidation to the expected sulfinic acid did not occur (run 1). The yield of benzenesulfinic acid increased with increasing amount of sodium hydroxide. However, further increase of sodium hydroxide accelerated the over-oxidation to give benzenesulfonic acid (runs 2, 3, and 4). When thiophenol was treated with equimolar hydrogen peroxide, such by-products as phenyl disulfide and benzenethiolsulfonate were obtained in considerable amounts (run 5). Treatment with a 2-fold molar excess of hydrogen peroxide improved the yield of benzenesulfinic acid, and a maximum yield of 82% was obtained (run 3). When a large excess of hydrogen peroxide was used, over-oxidation to benzenesulfonic acid was predominant (run 7). Our work-up process was very simple and the present system could be used as a practical preparative method for sulfinic acids.

Experimental

Melting points were determined on a Yanagimoto micro-melting point apparatus, model MP-500, and are uncorrected. ^{1}H-Nuclear magnetic resonance (^{1}H-NMR) spectra were obtained on a Hitachi R-600 spectrometer at 60 MHz in $CDCl_3$ with tetramethylsilane as an internal standard. High-performance liquid chromatography (HPLC) was run on a Hitachi 633A instrument equipped with an ultraviolet (UV at 254 nm) detector and an M & S pack C-18 column, 4.6 mm × 150 mm, with a mobile phase of Tris-buffer (pH 7.4). The flow rate was maintained at 1.5 ml/min.

General Procedures——A thiol (4.5 mmol) was dissolved in a mixture of 20 ml of 2.5% aqueous NaOH and 20 ml of ethanol. Aqueous hydrogen peroxide (30%, 1 ml) was added to the solution with stirring at room temperature (exothermic). At intervals, a portion of the solution was pipetted out and the reaction was monitored by HPLC. After the reaction was complete, the solvent was evaporated off under reduced pressure. The residue was dissolved in water and acidified by the addition of diluted hydrochloric acid at 0 °C. The solution was extracted with ether, and the extract was dried over anhydrous magnesium sulfate, then the ether was removed to give the pure sulfinic acid. The sulfinic acids were recrystallized from water if necessary. The structures of the sulfinic acids were further confirmed by conversion to benzyl sulfones upon treatment with benzyl chloride in *N*,*N*-dimethylformamide (DMF) at 80 °C for 8 h.[8]

The following products were similarly obtained, and their yields are listed in Table I. Benzenesulfinic acid as phenyl benzyl sulfone: ^{1}H-NMR δ: 4.35 (s, 2H), 7.25 (m, 5H), 7.55 (m, 5H). mp 146—147 °C (lit.[9] mp 146—146.5 °C). *p*-Chlorobenzenesulfinic acid: mp 93—94 °C. *p*-Toluenesulfinic acid: mp 84.5—85.5 °C (lit.[1b] mp 84—85 °C). *o*-Carboxybenzenesulfinic acid: mp 124—125 °C (lit.[10] mp 125 °C). *p*-Nitrobenzenesulfinic acid: mp 124—126 °C.

Isolation of 2-Pyridinesulfinic Acid and 4-Pyridinesulfinic Acid——Pyridinesulfinic acids were isolated as the sodium salts; after the reaction was complete, evaporation of the solvent gave the crude sodium sufinate and the pure product was obtained by recrystallization from ethanol. Sodium 2-pyridinesulfinate: *Anal.* Calcd for $C_5H_4NNaO_2S$: C, 36.36; H, 2.44; N, 8.48. Found: C, 35.98; H, 2.70; N, 8.53. Sodium 4-pyridinesulfinate: *Anal.* Calcd for $C_5H_4NNaO_2S$: C, 36.36; H, 2.44; N, 8.48. Found: C, 36.13; H, 2.74; N, 8.53.

References and Notes

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