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A CONVENIENT AND GENERAL SYNTHESIS OF ALKANE SULFINIC ACIDS

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2-(Alkylsulfonyl)benzothiazoles are reduced with sodium tetrahydroborate to give alkane sulfinic acids in good yield.

A sulfinic acid, one of the fundamental organosulfur compounds, is useful synthetic intermediate and a substrate in a palladium chemistry.1) The direct oxidation of thiols, however, offers no practical preparative method for sulfinic acids, since it is generally difficult to stop the oxidation at the sulfinic acid stage. Sulfinic acids are generally prepared either by the reduction of sulfonyl chlorides, or the reaction of sulfur dioxide with organometals.2) These methods, however, involve a troublesome operation, and yields and purity of the products are not sufficiently high.

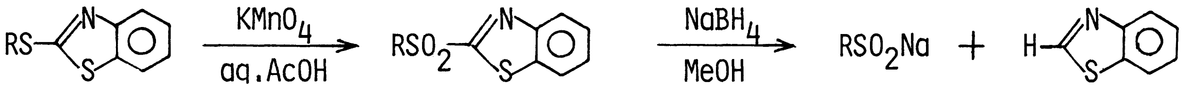
$$RSH \longrightarrow (RSO_2H) \longrightarrow RSO_3H \longrightarrow RSO_2Cl \longrightarrow RSO_2H$$

We wish to report here a new type of synthetic method based upon the oxidation of the protected thiols and subsequent deprotection. The key point of our approach is a choice of the protecting group, which prevents the substrates from the over-oxidation to sulfonic acids, and which should be easily removed at the final stage to produce the desired sulfinic acids.

$$RS-\boxed{\text{Protecting group}} \xrightarrow[\text{2) Deprotection}]{\text{1) Oxidation}} RSO_2H$$

We found that 2-benzothiazolyl group (BT group) works well as a protecting group. Thus, 2-(alkylthio)benzothiazoles ($\underline{1}$)3) are oxidized to sulfones ($\underline{2}$)

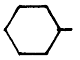
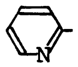
with potassium permanganate in aq. acetic acid. The resulting sulfones (2) are cleanly cleaved to sodium alkanesulfinates (3) and benzothiazole (4) upon treatment with sodium tetrahydroborate. Both oxidation and reductive deprotection proceed smoothly (≈ 0.5 h) at room temperature.



1 2 3 4

Sodium alkanesulfinates (3) are very hygroscopic white solids, which show characteristic IR bands at 1000-1050 cm^{-1} and 980-990 cm^{-1} due to the sulfinate (SO-O) group. Although the yields of 3 should be the same to those of benzothiazole (4), the exact yields of 3 are difficult to estimate because of their hygroscopic nature. The structure of 3 is further confirmed by conversion to the known benzyl sulfone (RSO_2CH_2Ph) (5) upon treatment with benzylchloride in refluxing acetonitrile. The results are summarized in the Table 1.

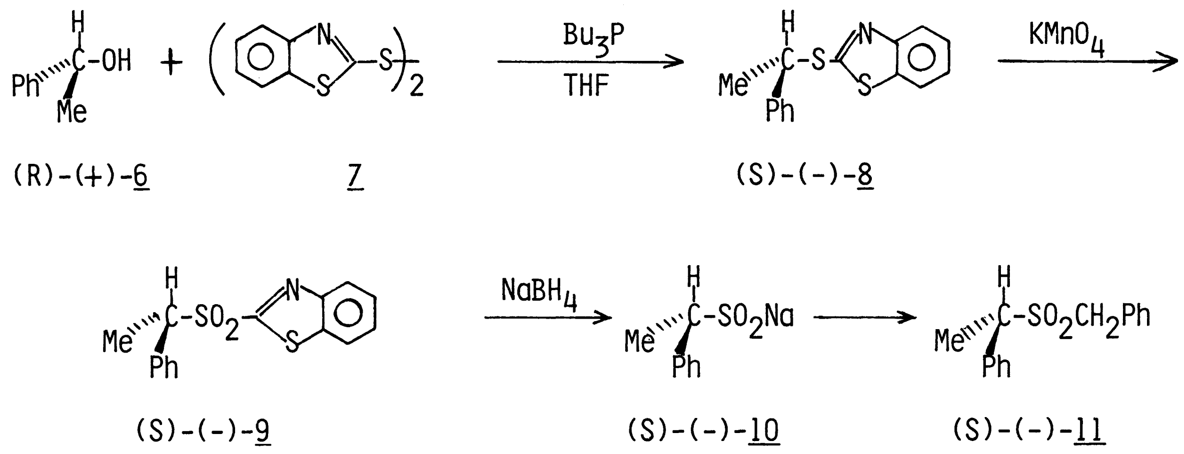
Table 1. Preparation of sodium alkanesulfinates (3)

	Sulfones (2)		Na sulfinates (3) (RSO_2Na)	Yield of 5[b)]	Yield of 4
	R	Yield/%	^{1}H-NMR (D_2O)[a)]	% (RSO_2CH_2Ph)	%
a	Me	81	2.27 (3H,s)	87	96
b	$PhCH_2$	83	3.67 (2H,s), 7.38 (5H,s)	77	96
c	$PhCH_2CH_2$	97	2.46-3.11 (4H,m), 7.37 (5H,s)	84	82
d	$CH_3(CH_2)_5$	90	0.46-2.01 (11H,m), 2.13-2.63 (2H,m)	82	100
e		84	0.91-2.21 (11H,m)	81	88
f		82	7.37-8.24 (3H,m), 8.45-8.67 (1H,m)	82	92

a) A strong peak due to H_2O appears at ca. 4.50 ppm.

b) Yield of 5 is based on the amount of sulfone (2) employed.

The method is applied to the preparation of optically pure chiral sulfinic acid and sulfone. Thus, (R)-(+)-α-methylbenzylalcohol (6) reacted with disulfide (7) in the presence of tributylphosphine to give chiral sulfide (8) in 86% yield. The oxidation of 8 and subsequent reduction gave optically pure sodium sulfinate (10) via sulfone (9). The optical purity of 10 was confirmed by the conversion to the chiral sulfone (11).[4)] Similarly, (R)-(+)-sulfide (8') was prepared starting from (S)-(-)-α-methylbenzylalcohol.[5)] The results are summarized in the Table 2.



(R)-(+)-6 7 (S)-(-)-8

(S)-(-)-9 (S)-(-)-10 (S)-(-)-11

Table 2. Chiral sodium sulfinate and sulfone

Compound	Yield/%	Mp/°C	$[\alpha]_D/°$	
8	86	67.5-68.5	(S)-(-)	-355.4 (EtOH, c 2.86, 22.9 °C)
8'	90	65-66	(R)-(+)	+352.4 (EtOH, c 2.87, 28.0 °C)[5)]
9	77	86-87	(S)-(-)	-164.7 ($CHCl_3$, c 2.08, 21.8 °C)
10[a)]	(98)[b)]			
11	57[c)]	106-107	(S)-(-)	-58.9 (acetone, c 0.86, 25.2 °C)[d)]

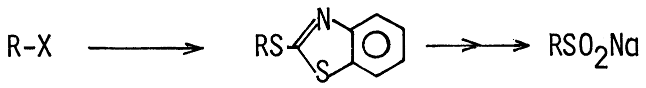
a) ^{1}H-NMR (D_2O) 1.45 (3H,d,J=7.4 Hz), 3.34 (1H,q,J=7.4 Hz), 7.39 (5H,s).

b) The yield of benzothiazole (4). c) The yield is based on the sulfone 9.

d) The $[\alpha]_D$ of authentic sample is -57° (acetone).[4)]

In summary, the present reaction offers a new synthetic route to alkanesulfinic acids. The advantage of the method is a vast choice of the starting materials.

Thus, alkyl halides, thiols, alcohols, and amines[5)] can be easily converted to alkanesulfinic acids.[6)]



(X=Cl, Br, SH, OH, NH_2)

A typical experimental procedure is as follows. To a solution of disulfide (7) (1.07 g, 3.21 mmol) and (R)-(+)-α-methylbenzylalcohol (0.4 ml, 3.21 mmol) in dry tetrahydrofuran (THF) (15 ml), was added a solution of tributylphosphine (0.79 ml, 3.21 mmol) in THF (5 ml) at room temperature. The mixture was stirred for 1 h. Usual work up and purification by column chromatography on silica gel (hexane: ether=9:1) gave sulfide (8) in 86% yield. To a solution of (8) (0.27 g, 0.995 mmol) in acetic acid (30 ml) was added a solution of potassium permanganate (0.19 g, 1.19 mmol) in water (20 ml). The mixture was stirred for 2 h at room temperature, then treated with aqueous solution of sodium sulfite to decolorize. Extraction with ether and usual work up gave sulfone (9) in 77% yield.

The mixture of sulfone (9) (0.239 g, 0.788 mmol) and sodium tetrahydroborate (0.06 g, 1.58 mmol) in ethanol (8 ml) was stirred for 2 h at room temperature. Evaporation of the solvent followed by addition of hexane caused white precipitates of sodium sulfinate (10) (0.227 g). Evaporation of hexane layer afforded benzothiazole (0.105 g, 98%).

References

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2) W. E. Truce and A. M. Murphy, Chem. Rev., 48, 69 (1950).

3) The compound (2) was easily prepared by alkylation of 2-mercaptobenzothiazole with alkyl halides, or substitution of 2-chlorobenzothiazole with sodium alkyl thiolates.

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6) Sekiya et al., reported the preparation of sulfinic acid from thiol (RSH ⟶ RSO_2Na) via alkyl phthalimidomethyl sulfone.
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