Convenient Syntheses of Sulfinic Ester Derivatives

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Sulfinic esters of varied types have been previously prepared by a variety of methods. A useful, one-step synthesis consists in the oxidation of thiols or disulfides with lead(IV) acetate in an appropriate alcohol[1,2]. In the case of alkyl thiols or disulfides, however, the procedure gives lower yields and a little persistent impurity[3]. The most commonly used method is the reaction of sulfinyl chlorides with alcohols[4] and sodium sulfinates with chlorocarbonates in alcohols[5]. This is the method of choice, especially in view of the ease with which sulfinyl chlorides can be prepared. Other methods including alkylation of sulfinic acids are also known[6-9], but these are of limited applicability. Recently, a useful one-step synthesis of alkyl *t*-alkanesulfinates was reported[10].

We now wish to report three convenient methods for the preparation of sulfinic esters, starting from sulfinic acids, which would be widely applicable as general syntheses of alkyl sulfinates.

The first method consists of a one-step synthesis including the reaction of sulfinic acids **1** with 1-methyl-2-chloropyridinium iodide (**2**) and appropriate alcohols (Method A). Recently, Mukaiyama[11] reported a convenient method for the preparation of carboxylic esters. In the present study, the synthetic application of this procedure was extended to alkyl sulfinates **4**. The reaction was successfully carried out by heating the mixture of **1**, **2**, an appropriate alcohol, and triethylamine in dichloromethane for 3 h under reflux to afford **4** in 21–76 % yields. This reaction seems to involve the initial formation of the intermediates **3**, followed by the reaction with the alcohols to give **4** and *N*-methyl-2-pyridone.

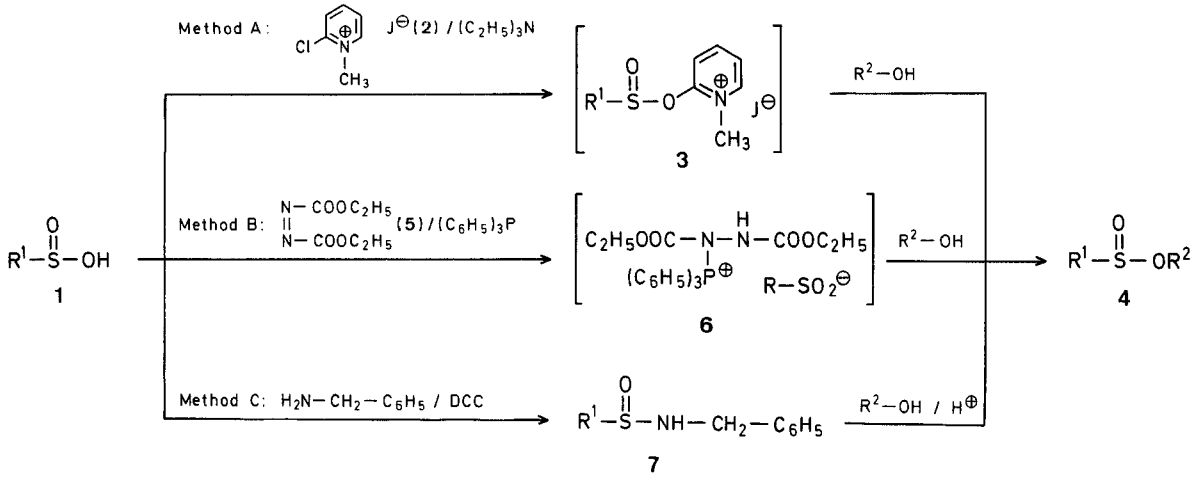
The second method is the condensation of sulfinic acids **1** with alcohols in the presence of diethyl azodicarboxylate (**5**) and triphenylphosphine (Method B). Mitsunobu[12] reported that carboxylic esters were obtained from carboxylic acids and alcohols in the presence of the same reagents. The application of this method for the preparation of **4** was also achieved by the reaction of **1** with **5** and triphenylphosphine to give the intermediates **6** followed by the treatment with alcohols to afford **4** in yields of 27–39 %.

Next, the reaction of *N*-benzylsulfinamide **7**, readily prepared from **1**, benzylamine, and dicyclohexylcarbodiimide (DCC)[13], with alcohols was examined in benzene with stirring in the presence of a few drops of concentrated sulfuric acid for 3 h under reflux (Method C). The yields of the resulting **4** were in the range of 21-58 % after purification by distillation or recrystallization.

All of the compounds **4** obtained are listed in the Table, along with yields, physical data, and spectra data. The structures of **4** were established by I.R., U.V. spectral data and by microanalyses.

It is of interest that, although *t*-butyl sulfinate was comparatively easily prepared by Method C, Methods A and B produced mainly aryl arenethiolsulfonate with no formation of the expected *t*-butyl sulfinate. The nucleophilic attack of the *t*-butyl group to the sulfinyl sulfur atom in the intermediates **3** and **6** does not occur effectively because of its bulkiness and instead the aryl arenethiolsulfonate might be formed by the simple disproportionation of **1**.

As can be seen from the Table, the specific rotations of *l*-menthyl *p*-toluenesulfinate (**4f**) obtained by these three methods were $[\alpha]_D^{15}$: −196.8°, −198.7°, and −190.4°, respectively, after recrystallization once from acetone and water. The authentic compound **4f** prepared by the reaction of *p*-toluenesulfinyl chloride with *l*-menthol is known to show $[\alpha]_D^{15}$: −199.2°[15] and possess the (*S*)-configuration at the sulfinyl sulfur atom, which results from asymmetric induction due to the *l*-menthyl group. The agreement of the observed specific rotation indicates that the configuration of the sulfinyl sulfur atom of **4f** obtained by the three methods is also *S*.



General Procedures for Preparation of Sulfinic Ester Derivatives 4:

Method A: Powdered **2** (2 mmol) is added with stirring to a solution of **1** (5 mmol) and triethylamine (6 mmol) in dichloromethane (10 ml). The reaction mixture is refluxed with stirring for 3 h under a nitrogen atmosphere and then poured into diethyl

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Table. Preparation of Sulfinic Ester Derivatives **4**

Product	R^1	R^2	Yield [%] Method A	Yield [%] Method B	Method C	b.p./torr or m.p. (Lit. b.p./torr or m.p.)	Molecular formula[a]	I.R. (KBr) ν_{max} [cm^{-1}]	U.V. (*n*-hexane) λ_{max} [nm] (ε)
4a	4-H_3C—C_6H_4	C_2H_5	76	36	43	96°/2.0 (100°/1.0)[7]	$C_9H_{12}SO_2$ (184.3)	1133	254 (3194), 223 (9040), 203 (9030)
4b	4-H_3C—C_6H_4	H_2C=CH—CH_2	52	32	51	114°/2.0	$C_{10}H_{12}SO_2$ (196.3)	1138	257 (3240), 225 (8895), 203 (10147)
4c	4-H_3C—C_6H_4	*n*-C_4H_9	75	31	47	104°/1.5 (90–95°/0.1)[4]	$C_{11}H_{16}SO_2$ (212.3)	1137	255 (1720), 224 (4890), 202 (5720)
4d	4-H_3C—C_6H_4	*n*-C_8H_{17}	60	39	49	152°/2.0	$C_{15}H_{24}SO_2$ (268.4)	1139	254 (3317), 224 (9205), 201 (12400)
4e	4-H_3C—C_6H_4	C_6H_5—CH_2	65	35	43	161°/2.5	$C_{14}H_{14}SO_2$ (246.3)	1137	254 (1131), 225 (4880), 199 (12720)
4f	4-H_3C—C_6H_4	*l*-menthyl	35[b]	27[c]	23[d]	105–106° (106–107°)[15]	$C_{17}H_{26}SO_2$ (294.5)	1139	256 (4300), 224 (11400), 201 (16850)
4g	4-H_3C—C_6H_4	*t*-C_4H_9	—[e]	—[f]	42	98°/2.0	$C_{11}H_{16}SO_2$ (212.3)	1131	252 (5600), 224 (12800), 203 (14100)
4h[g]	*n*-$C_{12}H_{25}$	C_2H_5	62	33	58	134–135°/2.5	$C_{14}H_{30}SO_2$ (262.5)	1131	223 (1691), 196 (1815)

[a] All products gave satisfactory microanalyses (C ±0.3 %, H ±0.3 %) except **4g, h** (C ±0.48 %).
[b] $[\alpha]_D^{15}$: −198.7° (*c* 1.9, acetone).
[c] $[\alpha]_D^{15}$: −190.4° (*c* 2.5, acetone).
[d] $[\alpha]_D^{15}$: −196.8° (*c* 1.9, acetone).
[e] 82 % yield of *p*-tolyl *p*-toluenethiolsulfonate.
[f] 31 % yield of *p*-tolyl *p*-toluenethiolsulfonate.
[g] Laurylsulfinic acid was prepared by introducing sulfur dioxide gas into a ethereal solution of laurylmagnesium chloride[14].

ether (20 ml). The solution is washed with water (10 ml), 1 % sodium hydrogen carbonate (10 ml), then twice with water (10 ml), and dried with anhydrous sodium sulfate. After removal of the solvent, the residue is purified by distillation under reduced pressure or recrystallization from acetone and water (18:2).

Method B: A solution of **1** (5 mmol) in dry benzene (5 ml) is added to a solution of **5** (5 mmol) and triphenylphosphine (5 mmol) in dry benzene (10 ml) at room temperature. The benzene solution is stirred for 30 min and alcohol (5 mmol) is added. The reaction mixture is then stirred for an additional 5 h at room temperature and allowed to stand overnight. The benzene solution is washed with 1 normal hydrochloric acid (15 ml), 1 % sodium hydrogen carbonate (15 ml), and twice with water (15 ml), dried over anhydrous sodium sulfate, and evaporated to dryness under reduced pressure. The residue is extracted twice with *n*-hexane (10 ml). After removal of the solvent, the residue is passed through a silica gel column with chloroform as eluent.

Method C: Compounds **7** are synthesized by the reaction of **1** with benzylamine in anhydrous dioxane using DCC as dehydrating agent[13]. A solution of **7** (3 mmol), anhydrous alcohol (3 mmol), and a few drops of concentrated sulfuric acid in dry benzene (20 ml) is heated for 3 h under reflux. The benzene solution is washed with 1 normal hydrochloric acid (15 ml), 1 % sodium hydrogen carbonate (10 ml), and finally with water (10 ml), and then dried with anhydrous sodium sulfate. After removal of benzene, the residue is purified by distillation under reduced pressure or recrystallization from acetone and water (18:2).

Reaction of Sulfinic Acid 1 (R^1 = 4-H_3C—C_6H_4) with *t*-Butyl Alcohol

Following the procedures given above for Methods A and B *p*-tolyl *p*-toluenethiolsulfonate is obtained: yield: 82 and 31 %, respectively; m.p. 76–77°.

$C_{14}H_{14}O_2S_2$	calc.	C 60.40	H 5.07
(278.3)	found	60.49	5.19

I.R. (KBr): ν_{max} = 1318, 1126 cm^{-1} (—S—SO_2).

^{1}H-N.M.R. ($CDCl_3$): δ = 7.23 (q, 4H_{arom}); 7.10 (s, 4H_{arom}); 2.38 (s, 3H, CH_3), 2.33 ppm (s, 3H, CH_3).

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