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Dimethyl and Diethyl 2-Oxo-1,3-propanedisulfonates as Practical Alkylating Reagents

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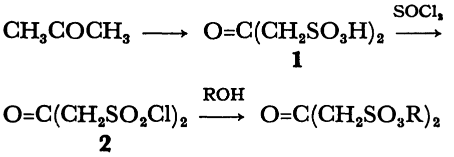
Synopsis. The title sulfonates, easily accessible from acetone, were found to be effective and practical alkylating agents.

2-Oxo-1,3-propanedisulfonic acid (**1**), *sym*-disulfonic acid of acetone, was readily prepared by sulfonation with fuming sulfuric acid as a highly hygroscopic crystalline solid.[1,2] The sulfonic acid (**1**) was converted to the dichloride (**2**) with $SOCl_2$ containing a small amount of nitromethane, and **2** was reacted with methanol and ethanol to yield methyl and ethyl esters (**3** and **4**) respectively.

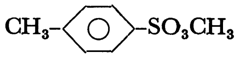
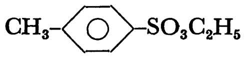


$$CH_3COCH_3 \longrightarrow \underset{\mathbf{1}}{O{=}C(CH_2SO_3H)_2} \xrightarrow{SOCl_2} \underset{\mathbf{2}}{O{=}C(CH_2SO_2Cl)_2} \xrightarrow{ROH} O{=}C(CH_2SO_3R)_2$$

3: $R=CH_3$, **4**: $R=C_2H_5$

With the purpose of utilizing these disulfonates as practical alkylating reagents, we studied the alkylation of phenol with them. Thus, phenol was alkylated with **3** or **4** in aq NaOH, and the reaction products were submitted to quantitative gas-chromatographic analysis. For comparison, the alkylation of phenol with conventional reagents was carried out under the same reaction conditions, and the products were analyzed similarly. The combined results are shown in Table 1. From the results obtained, it can be concluded that **3** and **4** react as effectively as dialkyl sulfates in the alkylation.[3] Furthermore, they have several advantages over the sulfates worthy of comment: 1. In **3** and **4** both alkyl groups could be used for the alkylation quite smoothly. 2. No severe toxicity such as that of the dialkyl sulfates was observed. 3. The sulfonates were stable compounds and had a good crystallinity in spite of their low melting points. Therefore, they were easy to handle and showed good reactivities, even in the aq-phase reactions. At present we have not yet tried these sulfonates on many kinds of substrates. However, considering the above results, they seem to be highly promising reagents. For example, sodium *S*-methyl thiosulfate (Bunte salt) was prepared in a good yield by the reaction of sodium thiosulfate on **3**.

Table 1. Comparison of alkylating reagents in the alkylation of phenol

Alkylating agent[a)]	Reaction conditions[b)]		Yield/%
	Temp/°C	Time/h	
3	40	1	76.0
		2	89.8
		3	89.8
		4	95.4
		6	97.2
$(CH_3O)_2SO_2$[c)]	40	1	81.5
		2	82.7
		3	84.0
		4	83.8
		6	83.1
$CH_3SO_3CH_3$	40	6	92.6
	40	4	68.4
CH_3I	40	4	16.9
4	30	2	70.8
		3	79.9
		6	82.5
$(C_2H_5O)_2SO_2$[c)]	30	2	65.1
		3	71.2
		5.5	84.5
	30	6	33.5
$H_2C(CH_2SO_3C_2H_5)_2$	30	2	80.6
C_2H_5Br	30	6	7.5
C_2H_5I	30	6	2.5

a) The molar ratios of alkylating agents to phenol were 1 : 2 for the three disulfonates and 1 : 1 for all the other cases. b) As a base, 12 M aq NaOH was used in 1.5 times and twice the molar quantity of phenol for methylation and ethylaiton respectively. c) Only one alkyl group could be used for the alkylation under these conditions.

Experimental

The melting points were not corrected. The solvents were of a reagent grade. All the known compounds were confirmed by a comparison of the melting points, spectroscopic data, and retention times with those of the authentic samples or the reported data. The ^1H-NMR spectra were recorded on a JEOL PMX-60 spectrometer, and the shifts were given in δ units from internal TMS. The gas-chromatographic analysis was performed on a Yanagimoto GCG-550T gas chromatograph equipped with a TCD, using helium as a carrier gas.

2-Oxo-1,3-propanedisulfonyl Dichloride (2): 2-Oxo-1,3-propanedisulfonic acid (**1**, 221.7 g, 1.02 mol)[1)] was mixed with $SOCl_2$ (850 g, 7.14 mol) containing nitromethane (31 g, 0.51 mol),[4)] and the mixture was refluxed for 6 h to obtain a clear solution. Crystals deposited on cooling were collected by means of suction filtration and washed with cold abs benzene. The chloride (169.3 g, 65%) could be used directly for a further reaction. Recrystallized crystals (from abs benzene) showed a mp of 106—107 °C. ^1H-NMR(CD_3COCD_3): 5.17 (s, CH_2). Found: S, 25.30%. Calcd for $C_3H_4O_5Cl_2S_2$: S, 25.10%.

Dimethyl 2-Oxo-1,3-propanedisulfonate (3): To a chilled and stirred methanol (13 g, 0.41 mol), **2** (5.0 g, 0.02 mol) was added, portion by portion, to keep the temperature of the reaction mixture below −10 °C. The mixture was concen-

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trated under reduced pressure immediately after the addition was complete, and ice-cold water was added to the residue. The crystals thus precipitated were collected by means of suction filtration was washed with cold water. Colorless crystals (4.21 g, mp 69—69.5 °C, 87.8%) were thus obtained. ^{1}H-NMR ($CDCl_3$): 2.98 (s, CH_3, 6H), 4.47 (s, CH_2, 4H). Found: C, 24.63; H, 4.15%. Calcd for $C_5H_{10}O_7S_2$: C, 24.39; H, 4.09%.

Diethyl 2-Oxo-1,3-propanedisulfonate (**4**): By the same procedure, **4** was prepared from **2** and EtOH as colorless crystals (mp 45.5—46.5 °C) in an 80.1% yield. ^{1}H-NMR ($CDCl_3$): 1.43 (t, CH_3, 3H), 4.38 (q, CH_2, 2H), 4.43 (s, CH_2, 2H). Found: C, 30.50; H, 5.10%. Calcd for $C_7H_{10}O_7S_2$: c, 30.65; H, 5.14%.

Alkylation of Phenol and the Quantitative Product Analysis by Gas Chromatography: As an example, the methylation with **3** will be described below. Phenol (0.423 g, 4.49 mmol) was dissolved in 12 M aq NaOH (0.56 ml, 6.72 mmol). To the stirred solution, **3** (0.556 g, 2.25 mmol) and octane (an internal standard, 0.336 g, 2.94 mmol) were added, and the mixture was reacted at 40 °C for a definite time (Table 1). The reaction mixture was then diluted with ice-cold water and extracted with ether. The extract was washed with 1 M aq NaOH, dried, and subjected to gas-chromatographic analysis with the following column: $3\phi \times 200$ mm packed with Apiezon grease L. (15%) on Uniport B (80—100 mesh).[5]

Sodium S-*Methyl Thiosulfate*: To an aq solution of $Na_2S_2O_3$ (30.50 g, 192.9 mmol in 52 ml H_2O), **3** (15.19 g, 61.75 mmol) was added, and the mixture was stirred at room temp for 17 h. The mixture was then concentrated to dryness under reduced pressure, and the residual solid was extracted with EtOH. Ether was added to the extracts to precipitate the Bunte salt as colorless crystals of monohydrate (15.07 g, 72.63%); mp 156—157 °C (decomp). ^{1}H-NMR (DMSO-d_6): 2.33 (s, CH_3, 3H), 3.33 (s, 2H, H_2O): In D_2O, a singlet methyl peak was observed at a filed 2.57 δ lower from internal DSS. Found: C, 7.14; H, 2.80%. Calcd for $CH_3O_3S_2Na \cdot H_2O$: C, 7.14; H, 3.00%.

Diethyl 1,3-Propanedisulfonate: To a stirred ethanol solution of sodium ethoxide, prepared from sodium (1.91 g, 83 mmol) and ethanol (40 g), 1,3-propanedisulfonyl dichloride[6] (10 g, 41 mmol) was added at −5 °C. After stirring for 1 h at 26 °C, the mixture was concentrated under reduced pressure, poured into cold water, and extracted with ether. Before extraction, the pH of the mixture was adjusted to 4 with HCl. The combined extracts were dried (Na_2SO_4) and concentrated under reduced pressure to yield the sulfonate as a light yellow oil (8.0 g, 74.1%), which solidified in a freezer. ^{1}H-NMR ($CDCl_3$): 1.40 (t, CH_3, 6H), 2.32 (quin, CH_2, 2H), 3.33 (t, CH_2, 4H), 4.30 (q, CH_2, 4H).

References

1) W. G. Grot, *J. Org. Chem.*, **30**, 515 (1965); H. Yamaguchi and K. Monden, *Bulletin of the Faculty of Engineering, Hiroshima University*, **24**, 13 (1975).

2) The diammonium salt of **1** is obtained as a by-product of the industrial process of manufacturing methyl methacrylate. G. Schroeder, H. Fink, and G. Goth, Japan Patent 45-29170 (1970).

3) Diethyl 1,3-propanedisulfonate was also a good ethylating reagent, and both ethyl groups could be used easily. However, this reagent was not so easily accessible as **4** and was rather unstable. Methyl methanesulfonate was also a good methylating agent, but it was rather unstable and expensive.

4) Nitromethane was essential for the smooth reaction, and without it a poor reproducibility was often observed.

5) The thermal-response factors necessary for the analysis were determined in separate experiments. Nonane was used as an internal standard for the ethylation.

6) W. Autenrieth and E. Bölli, *Ber.*, **58**, 2144 (1925); P. W. Clutterbuck and J. B. Cohen, *J. Chem. Soc.*, **121**, 125 (1922).