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Sulfonation of Unsaturated Compounds. I. Sulfonation of Branched-Chain Ketones with Sulfur Trioxide. A One-Step Synthesis of Tetramethylene Sulfate through a Retro Pinacol-Type Rearrangement

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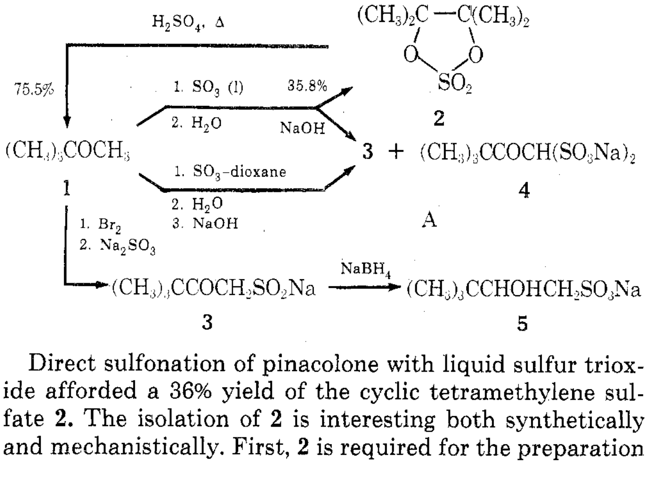
The sulfonation of aldehydes,[1] ketones,[1,2] and carboxylic acids[3] with sulfur trioxide and its adducts[4] is a facile process[4] leading to the corresponding sulfonic acids in which the sulfo group is attached α to the carboxylic function.[1-4] The products are isolated ordinarily as the corresponding salts after neutralization of the acidic sulfonation mixture. Consequently, the nature of possible intermediates has not been established and the presence of some by-products may have been overlooked. Moreover, the purity of the isolated products is questionable in many cases, since disulfonates may accompany the desired monosulfonates, and the separation between the two might prove to be very difficult.

It has been established[1,3] that carbonyl compounds which contain no α-hydrogen atoms are inert toward sulfur trioxide. It has also been shown that sulfonation of γ-branched olefins[5] is accompanied by the migration of either methyl or hydrogen to the incipient adjacent positive center.

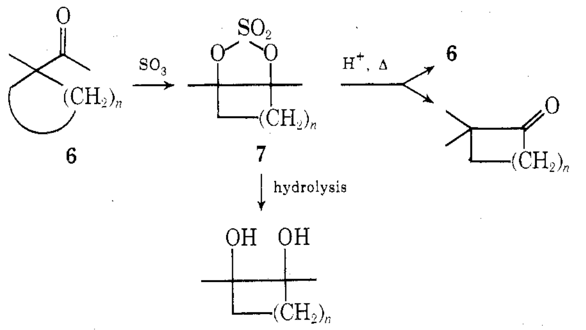
This note presents results of a study of sulfur trioxide sulfonation of pinacolone as a model compound (Scheme I).

Scheme I

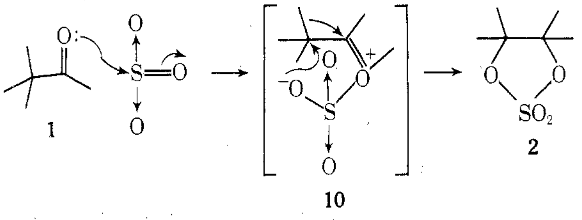


Direct sulfonation of pinacolone with liquid sulfur trioxide afforded a 36% yield of the cyclic tetramethylene sulfate **2**. The isolation of **2** is interesting both synthetically and mechanistically. First, **2** is required for the preparation of highly C-methylated compounds.[6] Alternative methods of preparation are laborious and result in overall low yields.[6] Secondly, other cyclic sulfates may be prepared using the same method. An extension of our findings would be the development of useful methods for initial ring expansion followed by formation of either ketones or glycols according to Scheme II.

Scheme II



In accord with the suggested mechanisms for the sulfonations of ketones,[1] and for the anhydrous acid-catalyzed epoxide–ketone[7] rearrangement the following mechanism for the formation of **2** is proposed.



The yield of sulfate **2** shows that migration of a methyl group from the adjacent quarternary carbon, to form a stable tertiary carbonium ion, successfully competes with the abstraction of available hydrogen from the α position. Rearranged products obtained in the sulfonation of γ-branched olefins[5] presumably arise from an analogous zwitterionic species.

We have found that heating of **2** under aqueous acidic conditions resulted in a rapid pinacol-type rearrangement to give back the starting pinacolone in good yield. This appears to be the first example of a direct transformation from a cyclic sulfate to a ketone.

The monoketosulfonate[8] **3** was not the only sulfonate obtained by direct sulfonation of pinacolone. The nmr spectrum of the initial product (after extractions and crystallizations) always revealed two types of *t*-butyl groups[9] and both methylene and methine protons. This and the finally separated disulfonate **4** after numerous crystallizations clearly showed the main product **3** to contain an appreciable amount of the disulfonate **4**. Disulfonate **4** was formed regardless of whether sulfur trioxide itself or the dioxane complex[4] was used. The alternative route *via* bromination followed by the Strecker reaction[10] proved to be the way of choice for obtaining pure **3** (Scheme I). Selective reduction of **3** with sodium borohydride afforded **5** in high yield. This suggests a convenient method of obtaining hydroxysulfonic acids from ketosulfonates.

Experimental Section

Tetramethylethylene sulfate (2). Sulfur trioxide (20.5 g, 0.256 mol) was distilled out of Sulfan (stabilized liquid sulfur trioxide, Allied Chemicals) into a cooled (0–5°) stirred solution of 1,2-dichloroethane (100 ml). Pinacolone **1** (25.65 g, 0.256 mol) in 45 ml of 1,2-dichloroethane was added over a period of 25 min. The exothermic reaction caused the temperature of the reaction mixture to reach 11°. Stirring was continued for 20 min, allowing the temperature to reach 15°. Water (200 ml) was added with stirring for an additional 30 min at room temperature. The two layers were separated; the organic layer was washed with water, 5% sodium bicarbonate, and again with water and dried (Na_2SO_4). The solvent was removed under reduced pressure to give 16.5 g (35.8%) of the cyclic sulfate **2**. Recrystallization from ethanol–water or ether–petroleum ether yielded colorless crystals: mp 129–131° (dec), lit.[10] mp 131° (dec); ir [(KBr) 2993, 1469, 1405, 1352, 1214, 1201, 961 883 cm^{-1}] and nmr [δ 1.7 (s)] are consistent with this structure.

Anal. Calcd for $C_6H_{12}O_4S$: C, 40.00; H, 6.67; S, 17.78. Found: C, 40.12; H, 6.56; S, 18.03.

The aqueous layer was neutralized with 20% aqueous sodium hydroxide and evaporated under reduced pressure to yield 25.5 g of a crude mixture of sulfonic acids A (Scheme I). Crystallization of A from 60% aqueous alcohol afforded a mixture of **3** and **4** containing very little inorganic sulfate. Nmr of the mixture (D_2O) reveals peaks at δ 5.75 and 1.16 (**4**) and at δ 4.13 and 1.08 (**3**).

Several recrystallizations from 60% alcohol afforded relatively pure **4**, the assigned structure of which is based on its nmr and ir spectra [(KBr) 3550, 3410, 2980, 1690, 1275, 1240, 1043, 690 cm^{-1}].

Anal. Calcd for $C_6H_{10}Na_2O_7S_2$: C, 23.69; H, 3.32; Na, 15.11; S, 21.07. Found: C, 23.55; H, 4.07; Na, 15.36; S, 21.55.

Sulfonation of Pinacolone with Dioxane–Sulfur Trioxide Complex. To the dioxane–sulfur trioxide complex prepared in the usual manner[11] from sulfur trioxide (23.45 g, 0.293 mol), dioxane (25.8 g, 0.293 mol), and dry 1,2-dichloroethane (125 ml) was added dropwise with stirring 29.3 g (0.293 mol) of pinacolone over a period of 40 min, followed by additional stirring for 60 min at room temperature. Water (200 ml) was added and the organic layer separated. The aqueous layer was neutralized with 15% aqueous sodium hydroxide, and the neutralized solution was evaporated to dryness to yield about 60 g of a crude mixture of sulfonic acids A (Scheme I), containing inorganic sulfate.

Nmr integration of mixture A showed the molar ratio of monosulfonate **3** to disulfonate **4** to be within the range of 1.8–2.5:1. The ratio of **3**:**4** in the mixture is changed with every recrystallization from aqueous alcohol.

Rearrangement of 2. A dispersion of **2** (0.518 g, 2.875 mmol) in 3 ml of 20% sulfuric acid was refluxed for 15 min, followed by addition of 5 ml of water. Extraction with methylene chloride, drying (Na_2SO_4), filtration, and removal of the solvent under reduced pressure gave 0.217 g (75.5%) of pinacolone (**1**) identical with an authentic sample.

Sodium 2-Keto-3,3-dimethylbutanesulfonate (3). Bromination of pinacolone according to the procedure of Boyer and Siraw[12] gave the α-bromination product in 82.3% yield, which was converted to **3** according to the method of Parkes and Tinsley.[13] Recrystallization from 60% aqueous ethanol yielded **3** as colorless plates: mp 216.5–218°; ir (KBr) 3580, 3520, 2970, 2935, 1710, 1645, 1392, 1245, 1215, 1203, 1161, 1056, 745 cm^{-1}; nmr (DMSO-d_6) δ 3.75 (s, 2, CH_2), 1.1 (s, 9, CH_3).

Anal. Calcd for $C_6H_{11}NaO_4S$: C, 35.64; H, 5.48; Na, 11.37; S, 15.84. Found: C, 35.55; H, 5.61; Na, 11.47; S, 15.98.

Sodium 2-Hydroxy-3,3-dimethylbutanesulfonate (5). To a solution of **3** (3.5 g, 17.3 mmol) in 20 ml of distilled water was added sodium borohydride (0.4 g, 10.57 mmol) in 3.5 ml of water dropwise over a period of 20 min, followed by stirring of the reaction mixture for an additional 3.5 hr. Acidification with 2% aqueous sulfuric acid (about 28 ml) was followed by the addition of methanol to make the solution 60% methanolic (v/v). The hydroxysulfonic salt **5** crystallized on cooling. The total amount of two crops was 3.45 g (97.5%): mp 272–276°; ir (KBr) 3385, 2958, 2870, 1630, 1364, 1238, 1168, 1050, 810 cm^{-1}; nmr (D_2O) δ 3.78 (m, 1, CH), 3.03 (m, 2, CH_2), 0.92 (s, 9, CH_3).

Anal. Calcd for $C_6H_{13}NaO_4S$: C, 35.32; H, 6.42; Na, 11.27; S, 15.69. Found: C, 35.73; H, 6.37; Na, 11.49; S, 15.25.

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Registry No.—**1**, 75-97-8; **2**, 52393-63-2; **3**, 52393-64-3; **4**, 52393-65-4; **5**, 52393-66-5; SO_3, 7446-11-9

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Chemistry of "Naked" Anions. III. Reactions of the 18-Crown-6 Complex of Potassium Cyanide with Organic Substrates in Aprotic Organic Solvents[1,2]

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Following Pedersen's discovery that macrocyclic polyethers ("crown" ethers) possess the ability to form crystalline complexes with a variety of inorganic salts and also the ability to solubilize these salts in aprotic organic solvents,[3] attention has been gradually focused toward utilizing the anion of the complex for synthetic purposes.[4] It has recently been reported that poor nucleophiles such as fluoride and acetate ions, solubilized as the potassium salt in CH_3CN or C_6H_6 containing 18-crown-6 (1,4,7,10,13,16-hexaoxacylooctadecane, **1**),[3] become sufficiently nucleophilic to react smoothly and quantitatively with a variety of organic substrates.[1,2] These reactive species have been termed "naked" anions.[1] We now wish to report the preparation of the "naked" cyanide reagent and its utilization in a variety of synthetically useful reactions. Substitution, elimination, and addition processes have been explored.

The results are summarized in Table I. The reactions were carried out by simply pouring a substrate–crown solution directly over excess, dry KCN, and stirring the two-phase system vigorously at ambient or reflux temperature until reaction was complete. Little or no reaction was found to take place in the absence of **1** under the same conditions covering the same periods of time (runs 20 and 21, Table I). In all cases, **1** was present in catalytic quantities, indicating that it behaves as a phase-transfer catalyst.[5] In general, the reactions are more rapid in CH_3CN than in C_6H_6.

The reaction of "naked" cyanide with benzyl chloride proceeded quickly and quantitatively to product under mild conditions (run 20, Table I). With primary-substituted alkyl halides, the conversions to nitrile compounds were quantitative, with no elimination products detected (runs 1–12, Table I).[6] Displacement at secondary carbon produced primarily substitution products with only a small percentage of elimination products. These results compare favorably to those obtained with "naked" acetate,[2] but are in direct contrast to those of "naked" fluoride,[1] where large quantities of alkenes were obtained. It appears therefore, that "naked" fluoride may be a stronger base than either "naked" cyanide or "naked" acetate. Cyclohexyl halides gives exclusively elimination product with "naked" cyanide (runs 17 and 18, Table I). No reaction was observed with *o*-dichlorobenzene (run 22, Table I).