Nucleophilic Substitution of Phthalimidomethyl Alkyl Sulfones. A New Convenient Synthesis of Sodium Alkanesulfinates

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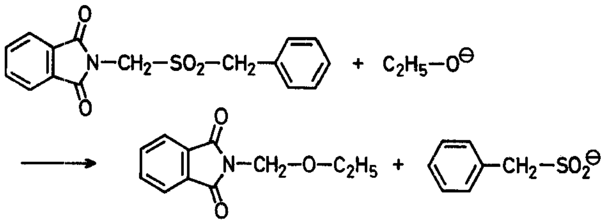
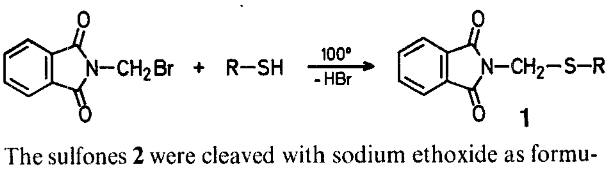
Because of the instability of the free alkanesulfinic acids, their salts may be used as a stable source of the free acids. However, no simple method is available for their synthesis in high yield and purity. In one of the usual methods, i.e., reaction of organometallic compounds with sulfur dioxide[1], side reactions may occur during work-up; the method of oxidation of thiols with *m*-chlorobenzoperoxoic acid[2] involves a troublesome operation at very low temperature. The method of alkaline cleavage of alkyl sulfones to alkali metal alkanesulfinates has been improved by using more reactive sulfones such as 1,2-dialkylsulfonylethanes[3], 3-alkylsulfonylpropanenitriles[4], and alkyl 3-alkylsulfonylacrylates[4]; however, in these methods yield and purity of the products are not sufficiently high. We have now found that benzyl phthalimidomethyl sulfones are readily cleaved by sodium ethoxide in ethanol to give sodium phenylmethanesulfinates in high yields.



The only moderate solubility in benzene of the *N*-(ethoxymethyl)-phthalimide formed in the reaction renders separation of the sodium sulfinate easy. In an experiment using a slight excess of ethoxide, clear separation to give the two products in both nearly quantitative amounts was achieved by benzene extraction. Sodium phenylmethanesulfinate thus obtained as a solid powder insoluble in benzene showed ~97% of sulfinate content by titration with potassium permanganate, and was identified as dibenzyl sulfone by reaction with benzyl chloride.

The only alkyl phthalimidomethyl sulfides and sulfones reported in the literature are the benzyl sulfide and sulfone[5], respectively. We prepared nine further alkyl phthalimidomethyl sulfides (**1**) and oxidized them to the sulfones (**2**) with potassium permanganate (Tables 1 and 2).



The sulfones **2** were cleaved with sodium ethoxide as formulated above for the benzyl sulfone to give almost quantitative yields of the corresponding sodium alkanesulfinates (**3**), and *N*-ethoxymethylphthalimide (Table 3). In the case of higher alkanesulfinates (**3**, R = n-$C_{12}H_{25}$, n-$C_{14}H_{29}$, n-$C_{16}H_{33}$), the crystalline product precipitated from the reaction solution and could thus be isolated in pure state by simple filtration.

Cleavage of the alkyl phthalimidomethyl sulfones **2** to give the sodium alkanesulfinates **3** can also be carried out with

Table 1. Alkyl Phthalimidomethyl Sulfides (**1**) prepared

R	Yield [%]	b.p./torr	m.p.	Molecular formula[a]
C_6H_5—CH_2—	84		113–114° (Ref.[5], m.p. 108°)	
n-C_5H_{11}	75	160–162°/ 0.15	40–41°	$C_{14}H_{17}NO_2S$ (263.4)
$(C_2H_5)_2CH$—	78	166–168°/ 0.09	34–37°	$C_{14}H_{17}NO_2S$ (263.4)
i-C_3H_7—$CH(CH_3)$—	80	149–152°/ 0.07	44–47°	$C_{14}H_{17}NO_2S$ (263.4)
n-C_6H_{13}—	81	168–169°/ 0.03	29–31°	$C_{15}H_{19}NO_2S$ (277.4)
n-C_7H_{15}—	72	171–173°/ 0.04	34–36°	$C_{16}H_{21}NO_2S$ (291.4)
n-C_8H_{17}—	75	177–178°/ 0.04	45–47°	$C_{17}H_{23}NO_2S$ (305.4)
n-$C_{12}H_{25}$—	73	188–191°/ 0.008	63–65°	$C_{21}H_{31}NO_2S$ (361.6)
n-$C_{14}H_{29}$—	85	—	66–67°	$C_{23}H_{35}NO_2S$ (389.6)
n-$C_{16}H_{33}$—	83	—	70–71°	$C_{25}H_{39}NO_2S$ (417.7)

[a] The microanalyses had the following maximum deviations from the calculated values: C, ±0.28%; H, ±0.13%; N, ±0.09%.

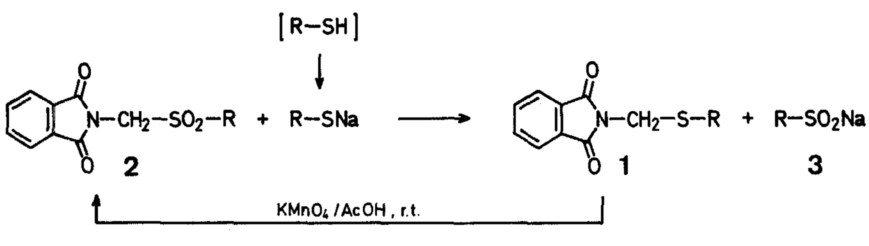
Table 2. Alkyl Phthalimidomethyl Sulfones (**2**) prepared

R	Yield [%]	m.p.	Molecular formula[a]
C_6H_5—CH_2—	89	188–189° (Ref.[5], m.p. 180°)[b]	
n-C_5H_{11}—	75	110–111°	$C_{14}H_{17}NO_4S$ (295.4)
$(C_2H_5)_2CH$—	81	111–112°	$C_{14}H_{17}NO_4S$ (295.4)
i-C_3H_7—$CH(CH_3)$—	83	104–106°	$C_{14}H_{17}NO_4S$ (295.4)
n-C_6H_{13}—	89	119–121°	$C_{15}H_{19}NO_4S$ (309.4)
n-C_7H_{15}—	81	104–106°	$C_{16}H_{21}NO_4S$ (323.4)
n-C_8H_{17}—	84	110–112°	$C_{17}H_{23}NO_4S$ (337.4)
n-$C_{12}H_{25}$—	95	114–115°	$C_{21}H_{31}NO_4S$ (393.6)
n-$C_{14}H_{29}$—	100	112–113°	$C_{23}H_{35}NO_4S$ (421.6)
n-$C_{16}H_{33}$—	96	110–111°	$C_{25}H_{39}NO_4S$ (449.7)

[a] The microanalyses had the following maximum deviations from the calculated values: C, ±0.31%; H, ±0.12%; N, ±0.12%.

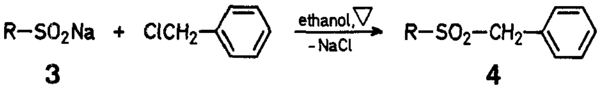
[b] Synthesized by oxidation of the corresponding sulfide with monoperphthalic acid in ether.

sodium alkanethiolates in ethanol. In this case, the resultant alkyl phthalimidomethyl sulfides (**1**) may be recycled upon oxidation with potassium permanganate.



Due to the high nucleophilicity of the thiolate ion, this latter cleavage reaction proceeds rapidly. Thus, sodium dodecanesulfinate (**3**, R = n-$C_{12}H_{25}$) is formed from the corresponding phthalimidomethyl sulfone and sodium dodecanethiolate in 100% yield within 3 h whereas the same reaction requires 10 h with sodium ethoxide (yield: 100%).

The sodium alkanesulfinates **3** were identified by conversion to alkyl benzyl sulfones (**4**).



3 **4**

Our method is also applicable to the synthesis of sodium arenesulfinates.

Alkyl Phthalimidomethyl Sulfides (**1**; Table 1):

These compounds are synthesized from N-bromomethylphthalimide and alkanethiols according to Ref.[5].

Preparation of Alkyl Phthalimidomethyl Sulfones (**2**; Table 2); **General Procedure:**

Powdered potassium permanganate (9.5 g, 0.06 mol) is added in portions to a stirred solution of the alkyl phthalimidomethyl sulfide (**1**; 0.05 mol) in acetic acid (100 to 1400 ml). Stirring is continued at room temperature overnight. The precipitated sulfone **2** is then collected by filtration, washed with cold water, and dried in vacuo. The filtrate still containing potassium permanganate is decolorized by the addition of aqueous sodium hydrogen sulfite; it is then evaporated under reduced pressure and the residue is washed with water. The crystalline products are combined and recrystallized from methanol or ethyl acetate.

Table 3. Sodium Alkanesulfinates (**3**) prepared

R	Method	Reaction time [h]	Yield [%]
C_6H_5—CH_2—	A	7	98
	B	3	93
n-C_5H_{11}—	A	5	92
	B	1	100
$(C_2H_5)_2CH$—	A	3.5	100
i-C_3H_7—$CH(CH_3)$—	A	5	100
n-C_6H_{13}	A	5	92
n-C_7H_{15}	A	6	100
n-C_8H_{17}	A	6	95
n-$C_{12}H_{25}$	A	10	100
	B	1	100
n-$C_{14}H_{29}$	A	15	100
	B	2	100
n-$C_{16}H_{33}$	A	20	100
	B	3	100

Cleavage of the Alkyl Phthalimidomethyl Sulfones (2) to Sodium Alkanesulfinates (3; Table 3); General Procedures:

Method A, with Sodium Ethoxide: A solution of sodium ethoxide is prepared from sodium (0.51 g, 0.022 g-atom) and ethanol (65 ml). To this solution, the alkyl phthalimidomethyl sulfone (**2**; 0.02 mol) is added and the mixture is stirred and refluxed under a stream of nitrogen for the time given in Table 3. In general, the mixture becomes homogeneous at the end of the reaction. The solution is then concentrated to dryness under reduced pressure. The residue is extracted with several portions of warm benzene and the alkanesulfinate is obtained as an insoluble powder; yield: 92–100%. The products are 94–98% pure as determined by titration with potassium permanganate. By evaporation of the benzene and recrystallization from ethanol, N-ethoxymethylphthalimide is obtained in nearly quantitative yield; m.p. 87–98°; Lit.[5], m.p. 83°. In the case of higher alkanesulfinates, most of the salts precipitate as pure crystals on cooling the reaction solution.

Method B, with Sodium Alkanethiolates: A solution of the sodium alkanethiolate corresponding to the alkyl phthalimidomethyl sulfone is prepared from the alkanethiol (0.02 mol) and clean cut sodium (0.46 g, 0.02 g-atom) in dry ethanol (65 ml). To this solution, the alkyl phthalimidomethyl sulfone (**2**; 0.02 mol) is added and the mixture is refluxed with stirring under a stream of nitrogen for the time given in Table 3. The alkyl phthalimidomethyl sulfide **1** is extracted from the mixture with benzene (5 × 30 ml) and recovered for recycling by evaporation and distillation in vacuo or recrystallization of the residue from diisopropyl ether or methanol; yield: 90–100%. The sodium alkanesulfinate is obtained as a benzene-insoluble powder. The products are 95–98% pure by titration with potassium permanganate.

For identification, the sodium alkanesulfinates thus obtained are converted into the corresponding *alkyl benzyl sulfones* (**4**) by reaction with benzyl chloride in boiling ethanol (Table 4).

Table 4. Alkyl Benzyl Sulfones (**4**) prepared from Sodium Alkanesulfinates (**3**) and Benzyl Chloride

R	Yield [%]	m.p. (Lit. m.p.)	Molecular formula[a]
$C_6H_5—CH_2—$	86	145–146° (151°)[6]	
n-$C_5H_{11}—$	80	97–98° (102–102.5°)[7]	
$(C_2H_5)_2CH—$	80	39–41°	$C_{12}H_{18}O_2S$ (226.3)
$(H_3)_2CH—CH(CH_3)—$	72	37–39°	$C_{12}H_{18}O_2S$ (226.3)
n-$C_6H_{13}—$	73	56–57°	$C_{13}H_{20}O_2S$ (240.4)
n-$C_7H_{15}—$	74	63–64°	$C_{14}H_{22}O_2S$ (254.4)
n-$C_8H_{17}—$	75	65–66°	$C_{15}H_{24}O_2S$ (268.4)
n-$C_{12}H_{25}—$	79	77–78°	$C_{19}H_{32}O_2S$ (324.5)
n-$C_{14}H_{29}—$	73	81–83°	$C_{21}H_{36}O_2S$ (352.6)
n-$C_{16}H_{33}—$	84	83–85°	$C_{23}H_{40}O_2S$ (380.6)

[a] The microanalyses had the following maximum deviations from the calculated values: C, ±0.32%; H, ±0.23%.

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