Cathodic Cleavage of Alkyl α-Benzenesulfonylcarboxylates

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The cathodic reduction of benzenesulfonylacetic acid ethyl ester and four alkyl- and aryl-substituted derivatives thereof has been studied at mercury in N,N-dimethylformamide solution. Polarographic half-wave potentials and cyclic voltammetry peak potentials are given, as well as preparative electrolysis products. The compounds undergo cleavage to yield benzenesulfinate ion and esters.

The cathodic reduction of sulfones containing a second functional group has been studied for various classes of compounds. Thus, cathodic reduction of β-ketosulfones,[1] α-benzenesulfonylnitriles,[2] and α,β-unsaturated sulfones [3] gives high yields of ketones, nitriles, and unsaturated hydrocarbons, respectively. These cleavage reactions can be utilized in synthesis in the following way. A sulfonyl group makes an adjacent methylene group acidic, and if the latter is also activated by a keto or a cyano group, the acidity becomes sufficient to allow alkylation by ion-pair extraction techniques.[4] After serving as an acidifying substituent, the sulfonyl group can be easily removed. One is thus provided with a route to substituted ketones and nitriles. The reaction sequence is given in Scheme 1.
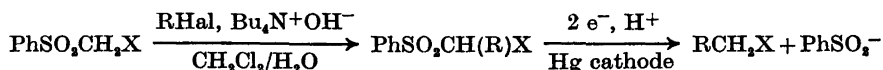
As an alternative to electrochemical cleavage of the substituted sulfones, dissolving metals have been used, e.g., zinc in acetic acid for β-ketosulfones.[5] Recently, the cleavage of α-benzenesulfonyl esters with sodium amalgam was described.[6] High yields were obtained under mild reaction conditions. However, the practical problem of scaling up an amalgam reduction is obvious, and it appeared to us that an electrochemical method would be more convenient. Ethyl benzenesulfonylacetate and some representative derivatives of it were therefore synthesized and electrochemically investigated. The methods used were DC polarography, cyclic voltammetry at a hanging mercury drop electrode, and gram-scale electrolysis followed by product identification.

RESULTS AND DISCUSSION

Polarography. Half-wave potentials for the compounds studied in this work are given in Table 1. For comparison, methyl phenyl sulfone was also included. The supporting electrolyte was tetraethylammonium perchlorate (TEAP), 0.1 M in DMF. The reference electrode was a saturated calomel electrode, galvanically connected *via* an aqueous 0.1 M tetraethylammonium bromide (TEAB) solution and a gel bridge made from methyl cellulose and 0.1 M TEAB in DMF.[7]

The compounds are all easier to reduce than methyl phenyl sulfone. The diffusion-limited currents (Table 1) indicate apparent one-electron processes, except the one obtained for the dimethylated substance *3*. The reason for this is that the acidity of the α hydrogen(s) in the substrates *1, 2, 4,* and *5* is sufficient for the compounds to act as proton donors in the

$$\text{PhSO}_2\text{CH}_2\text{X} \xrightarrow[\text{CH}_2\text{Cl}_2/\text{H}_2\text{O}]{\text{RHal, Bu}_4\text{N}^+\text{OH}^-} \text{PhSO}_2\text{CH(R)X} \xrightarrow[\text{Hg cathode}]{\text{2 e}^-,\ \text{H}^+} \text{RCH}_2\text{X} + \text{PhSO}_2^-$$

Scheme 1. Alkylation and cathodic cleavage of substituted sulfones. X = COR, CN, or COOEt.

Table 1. Polarographic half-wave potentials, limiting currents, and cyclic voltammetry peak potentials in DMF. Substrate conc. 5×10^{-4} M, supporting electrolyte 0.1 M TEAP.

Compound		$E_{1/2}{}^a$/V	$i_d{}^b$/μA	$i_d{}^c$/μA	$E_{pc}{}^d$/V
$PhSO_2CH_2COOEt$	(1)	−1.86	1.80	2.65	−1.93
$PhSO_2CHMeCOOEt$	(2)	−1.91	1.85	2.41	−1.97
$PhSO_2CMe_2COOEt$	(3)	−1.93	3.75	4.01	−1.98
$PhSO_2CHBzlCOOEt$	(4)	−1.86	1.90	2.57	−1.91
$PhSO_2CHPhCOOEt$	(5)	−1.80	2.00	2.80	−1.87
$PhSO_2Me$		−2.28	3.90		

[a] Polarographic half-wave potentials *vs.* SCE. [b] Plateau current in aprotic medium. [c] Plateau current with phenol concentration 2×10^{-3} M. [d] Cathodic peak potential at a sweep rate of 75 mV s^{-1}.

system. The resulting anions are not electroactive, giving the impression that the substrate concentration is only half of its actual value. Addition of phenol causes the wave heights to increase (Table 1), but less than by the expected factor of 2. This may mean that the sulfonyl esters are at least as strong acids as phenol. The addition of a stronger proton donor, *e.g.*, acetic acid, doubles the wave heights. No change in half-wave potential occurs when either acid is added.

The esters seem to be stronger acids than the corresponding α-benzenesulfonylnitriles, since the latter compounds, with one exception, give two-electron waves even in the absence of phenol.[2]

The change in half-wave potential is small upon substitution of the α carbon with one or two alkyl groups or a benzyl group. Introduction of a phenyl group causes an anodic shift of about 100 mV. This can be explained by the relative stability of the benzylic anion formed in the cleavage reaction. For the corresponding α-benzenesulfonylnitriles, a phenyl or a benzyl group in the α position causes an anodic shift of about 300 mV. The difference between nitriles and esters is hard to explain. Perhaps the more bulky ester group prevents the phenyl and benzyl groups to conjugate with and thus stabilize the negative charge on the α carbon in the transition state.

Cyclic voltammetry at a hanging mercury drop under the same conditions as used in polarography and a sweep rate of 75 mV s^{-1} gave the peak potentials shown in Table 1. The peak potentials follow the same order as the polarographic half-wave potentials. No anodic peak could be detected on the reverse sweep. The peak currents increased in the same way as in polarography when phenol was added.

Table 2. Preparative electrolysis data. For identity of substrates, see Table 1.

Compound	E^a/V	n^b/F mol^{-1}	$PhSO_2Me{}^c$	Ester^d	Phenol^e
1	−1.50	2.22	—	q	+
1	−1.50	1.78	71	q	—
2	−1.50	1.92	—	q	+
2	−1.50	1.84	73	q	—
3	−1.60	2.00	—	99	+
4	−1.55	2.06	—	89	+
5	−1.65	2.03	—	96	+
5	−1.55	1.18	32	42	—

[a] Cathode potential *vs.* Ag,AgI in 0.1 M tetrabutylammonium iodide in DMF. These values are 0.32 V more positive than those *vs.* SCE. See Ref. 15. [b] Coulometric amount of electricity. [c] Percent yield after work-up. −, no alkylation was made in the work-up. [d] Percent yield after work-up. q, qualitative identification. [e] +, excess phenol present; −, no phenol present.

Electrolyses. The compounds were reduced at a mercury cathode in DMF solution, containing tetraethylammonium perchlorate (TEAP). A divided cell with a glass frit was employed. In most of the experiments, phenol was added as a proton donor. The runs were made at constant cathode potential, and the current decreased exponentially with time, the half-life being about 30 min. The electrolyses were allowed to proceed until the background current was reached. The reaction products were identified with GLC and [superscript]H NMR. The results are summarized in Table 2.

All the substrates were cleaved between the sulfonyl group and the α carbon atom, giving an ester and benzenesulfinate ion. The latter was, in some runs, identified *via* conversion to methyl phenyl sulfone.[8]

Compound *1* gave ethyl acetate and benzenesulfinate ion. The ethyl acetate was qualitatively identified by GLC. In a run without phenol, alkylation of the sulfinate ion was made. Compound *2* gave, both with and without phenol, ethyl propionate as the exclusive product. Electrolysis of *3* gave a good yield of ethyl isobutyrate. In this run, no identification of the benzenesulfinate ion was made. Compound *4* gave ethyl dihydrocinnamate, determined by GLC and [superscript]H NMR. For comparison, this substance was independently synthesized through hydrogenation of ethyl cinnamate.

The reduction of *5* in the presence of phenol gave a good yield of ethyl phenylacetate. When the electrolysis was run without a proton donor, the electricity consumption was 1.18 F mol[superscript]-1, which is half the expected amount. The catholyte was allowed to react with methyl iodide. A thin-layer chromatogram showed several spots, and a separation was made on a silica gel column using toluene as the eluent, which was gradually changed to methylene chloride. One fraction contained ethyl phenylacetate, representing 42 % yield. The theoretical yield is 50 % due to conversion of half the amount of substrate to its conjugate base. Another fraction contained methyl phenyl sulfone, 32 %, together with ethyl α-benzenesulfonyl-α-phenyl-propionate, 10 %. The latter compound was independently synthesized by alkylation of *5* with methyl iodide. As in polarography, when *5* is reduced without phenol, half of it forms an

electroinactive anion, which is alkylated upon the treatment with methyl iodide. No diethyl 2,3-diphenylsuccinate, a possible dimer, was formed, contrasting with the behaviour of the corresponding nitrile.[2]

Synthetic utility. The alkylation of *1* gave high yields of the monoalkylated products, using the ion-pair extraction technique by Brändström.[4] In the corresponding study of α-benzenesulfonyl nitriles,[2] alkylation gave mixtures of non-, mono-, and dialkylated products, which were hard to separate. Alkylation with conventional bases like alkoxides also works.[9] In the present study, no *O*-alkylation was observed. Alkylation followed by cathodic cleavage thus makes this sequence a good alternative to the malonic ester route in the preparation of carboxylic acids. The malonic ester route requires strong bases or acids in the hydrolysis step, and the decarboxylation often needs a high temperature. Both of these conditions are avoided when the electrochemical method is used. The selectivity of the cathodic cleavage of the C−S bond seems to be better than that of chemical methods. For example, the use of lithium in amines can lead to reduction of aromatic rings, eliminations and isomerisations.

EXPERIMENTAL

General. [superscript]H NMR spectra were recorded on a Bruker WH 270 instrument. For GLC, a Perkin-Elmer 3920 B instrument was used, combined with a Hewlett-Packard integrator Model 3380 A. Melting points were determined on a Kofler Hot Stage microscope. "Usual work-up" means dilution with cold water, repeated extraction with ether, washing, drying and vacuum evaporation.

Syntheses. Ethyl benzenesulfonylacetate (1) was prepared in 0.5 molar scale from sodium benzenesulfinate and ethyl bromo-acetate [superscript]10 using dimethyl sulfoxide at 40−50 °C as the solvent. After usual work-up, the crude product was distilled *in vacuo*, b.p. 170 °C at 5.0 Torr. The distilled product crystallized, m.p. 42 °C, lit.[10] 41−42 °C, yield 77 %. [superscript]H NMR (270 MHz, CDCl$_3$): δ 0.98 (3 H, t), 3.85 (2 H, s), 3.95 (2 H, q), 7.3−7.9 (5 H, m).

Ethyl α-benzenesulfonylpropionate (2) was prepared from sodium sulfinate and ethyl 2-bromopropionate using the same method [superscript]11 as for *1*, b.p. 132 °C at 0.2 Torr, yield 61 %. [superscript]H NMR (270 MHz, CDCl$_3$): δ 1.15 (3 H, t), 1.6 (3 H, d), 4.1 (3 H, m), 7.6−7.9 (5 H, m).

Compounds *2−4* were made by alkylation of *1* using ion-pair extraction technique.[4] The

alkylation agents were methyl iodide and benzyl chloride. The yields were almost quantitative both for mono- and dialkylated products. Physical data for *3*: m.p. 35 °C, lit.[12] 38 − 39 °C, [1] H NMR (270 MHz, CDCl$_3$): δ 1.17 (3 H, t), 1.62 (6 H, s), 4.12 (2 H, q), 7.45 − 7.9 (5 H, m). For *4*: m.p. 96 °C, lit.[13] 95 − 96 °C, ^{1}H NMR (270 MHz, CDCl$_3$): δ 0.97 (3 H, t), 3.16 − 3.48 (2 H, m), 3.95 (2 H, q), 4.18 (1 H, dd, *J* 11.5 and 3.5 Hz), 7.03 − 8.23 (10 H, m).

Ethyl α-bromophenylacetate. This compound was prepared starting with 20 g (0.15 mol) of phenylacetic acid using the literature procedure.[14]

Ethyl α-thiophenoxyphenylacetate. To a solution of 15 g (0.14 mol) of thiophenol and 5.5 g (0.14 mol) of sodium hydroxide in 100 ml of ethanol was added 30 g (0.12 mol) of the crude ethyl α-bromophenylacetate during 30 min at 30 °C. The mixture was then heated to reflux during 4 h. The ethanol was vacuum evaporated. The usual work-up gave 38 g of the crude product as an oil.

Ethyl α-benzenesulfonylphenylacetate (5). The above oil was dissolved in 100 ml of glacial acetic acid, and 40 ml of 35 % hydrogen peroxide was slowly added. Heating at 60 °C for 4 h completed the oxidation. After cooling, the solution was poured into 1.5 l of ice water and the precipitate was filtered off. Recrystallization from ethanol gave 23 g of colourless crystals (50 %), m.p. 100 − 101 °C. ^{1}H NMR (270 MHz, CDCl$_3$): δ 1.23 (3 H, t), 4.21 (2 H, m) 5.1 (1 H, s), 7.2 − 7.6 (10 H, m).

Ethyl α-benzenesulfonyl-α-phenylpropionate. A solution of 1 g (3 mmol) of *5* in 20 ml of DMF was mixed with 1 g of potassium carbonate. Methyl iodide, 3 ml, was added and the solution was stirred for 24 h at 40 °C. The usual work-up gave an oil which could not be induced to crystallize but which was pure according to TLC and ^{1}H NMR. Yield 1 g (96 %). ^{1}H NMR (270 MHz, CDCl$_3$): δ 1.26 (3 H, t), 2.16 (3 H, s), 4.25 (2 H, m), 7.18 − 7.6 (10 H, m).

Polarography and cyclic voltammetry. The solvent (DMF) and supporting electrolyte (TEAP) were purified as described before.[2,15] A three-electrode polarograph similar to the Heath Model EUW 401 was used. The substrate concentration was 5×10^{-4} M, and that of TEAP, 0.1 M.

Preparative electrolyses. A cell divided by a glass frit and with a cathode surface of 12 cm^2 was used. The solvent was DMF with TEAP, 0.1 M in the catholyte, 0.2 M in the anolyte. Some dimethyl sulfoxide was added to the anolyte as depolarizer.[2] The catholyte was agitated with a magnetic stirring bar, floating on the mercury. The catholyte was purged with nitrogen. A platinum wire served as anode. The catholyte volume was 50 ml. A silver iodide coated silver wire in 0.1 M tetrabutylammonium iodide DMF solution served as reference electrode. Current was provided by a 200 V/1 A potentiostat built in this laboratory.

The instrument was equipped with an electronic integrator to determine the charge, and an oscilloscope to check the system stability. The initial substrate amount was about 1 g, giving an initial current of approximately 150 mA.

For the work-up, two different methods were used. The first one involved treatment of the catholyte with 10 ml of methyl iodide and heating at 40 − 50 °C for 2 h. After the usual work-up, the residue was analyzed by GLC (2 m SE-30 columns) and ^{1}H NMR. The second method of work-up differed from the above only insofar that the methyl iodide treatment was omitted.

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