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Studies on the Base-catalyzed Solvolysis of Propane-2-sulphonic Acid p-Cresylester

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Dedicated to Prof. Dr. h. c. H.G.O. Becker on the Occasion of his 70th Birthday

Abstract. Products of the reaction of propane-2-sulphonic acid p-cresylester with sodium butoxide in butanol are the sodium salt of propan-2-sulphonic acid, di-n-butyl ether, p-cresyl-n-butyl ether and p-cresol. The reaction proceeds via propane-2-sulphonic acid n-butylester which is formed from the starting compound by an elimination-addition (sulphene) mechanism. The elimination step is an E1-cB reaction.

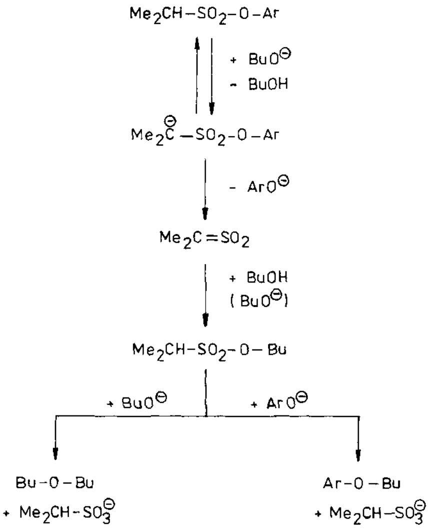
Some years ago we found that in the saponification of sec-alkane sulphonic acid phenylesters with potassium hydroxide in ethylene glycol phenyl glycol ether is formed as the main product. To elucidate this unexpected reaction we studied the solvolysis of propane-2-sulphonic acid p-cresylester in n-butanol/sodium butoxide. The final products besides the sodium salt of propan-2-sulphonic acid were di-n-butyl-ether, p-cresyl-n-butyl ether and p-cresol (Table 1). No m-cresyl-n-butyl ether was found; this proves that the p-cresyl-n-butyl ether is not formed by a nucleophilic aromatic substitution via the corresponding aryne. The amount of di-n-butyl ether increases and the amount of p-cresyl-n-butyl ether decreases with increasing ratio of sodium butoxide to propane-2-sulphonic acid p-cresylester. This result shows that the p-cresyl-n-butyl ether cannot be formed by a normal S_NAr substitution. If the formation of p-cresyl-n-butyl ether proceeded according to a S_NAr mechanism the amount of this ether would increase with an increasing ratio of sodium butoxide to propane-2-sulphonic acid p-cresylester.

Following the course of the reaction between propane-2-sulphonic acid phenylester with sodium butoxide/n-butanol we found that propane-2-sulphonic acid n-butylester is an intermediate in the formation of both ethers, finally found (di-n-butyl ether and phenyl-n-butyl ether) (Fig. 1). Obviously the ethers are formed by alkylation of sodium butoxide or sodium phenolate by propane-2-sulphonic acid n-butylester. This explains why the amount of di-n-butyl ether increases with increasing ratio of sodium butoxide to propane-2-sulphonic acid p-cresylester. If this ratio is low then after the butanolysis of the starting

Table 1 Final products of the solvolysis of propane-2-sulphonic acid p-cresylester in sodium butoxide/n-butanol

$[\text{ester}]_0$ mol l^{-1}	$[\text{n-BuONa}]_0$ mol l^{-1}	$\frac{[\text{n-BuONa}]_0}{[\text{ester}]_0}$	temperature °C	reaction time h	products[a) A Mol-%	B Mol-%	C Mol-%
0.187	0.468	2.5	25	72	70.8	17.4	70.1
0.187	0.935	5.0	25	72	91.1	9.1	92.1
1.080	1.188	1.1	200	3	20.5	72.7	19.9
0.187	0.468	2.5	200	3	68.9	25.2	57.7
0.187	0.935	5.0	200	3	88.3	11.3	86.7

[a)] after an ester conversion of 100%; all yields with respect to the starting ester. A: di-n-butyl ether; B: p-cresyl-n-butyl ether; C: p-cresol



Formula Scheme 1 Individual steps of the reaction between propane-2-sulphonic acid arylesters and sodium butoxide in n-butanol

ester the concentration of sodium p-cresolate becomes higher than that of sodium butoxylate and accordingly more p-cresyl-n-butyl ether is formed than di-n-butyl ether. The higher the ratio of sodium butoxide to propane-2-sulphonic acid p-cresylester the more di-n-butyl ether is to be expected.

Now the question arises, what mechanism is valid in the solvolysis of propane-2-sulphonic acid aryl esters by sodium butoxide/n-butanol. This reaction can proceed both according to an addition-elimination ($B_{Ac}2$) and an elimination-addition (sulphene) mechanism. One possibility to confirm elimination-addition mechanisms is the proof of kinetic isotope effects in the reaction of deuterated starting compounds [1, 2]. So we determined the rate constants of 2-deuteropropane-2-sulphonic acid p-cresylester and the non-deuterated compound in the saponification with $NaOH/H_2O$ in dioxane as the solvent. The results are shown in Table 2; no primary kinetic isotope effect can be recognized ($k_H : k_D = 1.02$). This is an argument against the sulphene mechanism, but this argument is valid only if no H/D exchange takes place prior to the solvolysis. Therefore we tested the H/D exchange of the starting ester with the solvent used (Table 3).

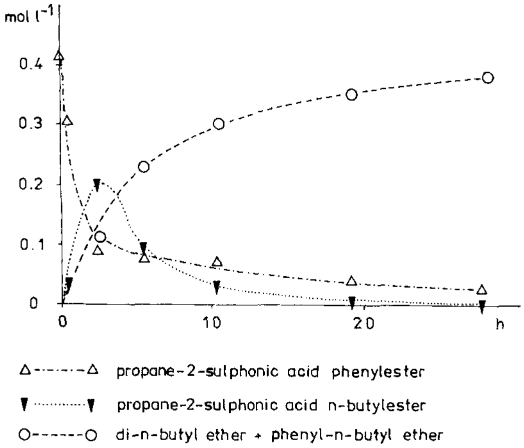


Fig. 1 Reaction of propane-2-sulphonic acid phenylester with sodium butoxide/n-butanol at 40 °C
$[n\text{-}BuO^{\ominus}]_o = 0.9\,mol\,l^{-1}$
$[\text{propane-2-sulphonic acid phenylester}]_o = 0.4\,mol\,l^{-1}$

We found that 2-deuterated propane-2-sulphonic acid p-cresyl ester lost most of its deuterium after only 14 % conversion in the saponification with $NaOH/H_2O$ in dioxane; on the other hand undeuterated propane-2-sulphonic acid p-cresylester proved to be 2-deuterated after 21 % conversion in the saponification with $NaOD/D_2O$ in dioxane. Also during the solvolysis of 2-deuteropropane-2-sulphonic acid p-cresylester in sodium butoxide/n-butanol a rapid H/D exchange takes place in the starting ester. So the question of the mechanism of the solvolysis of propane-2-sulphonic acid arylesters cannot be elucidated on the basis of the kinetic isotope effect.

The proof of an elimination-addition mechanism is possible if one demonstrates the non-identity of the rate determining (elimination) and the product-determining (addition) step [1, 2]. In seperate experiments we established that propane-2-sulphonic acid p-cresyl-ester reacts far more rapidly with sodium butoxide/n-butanol than with piperidine (Table 4). When the same ester reacted with a mixture of sodium butoxide and piperidine far more propane-2-sulphonic acid piperidide than propane-2-sulphonic acid n-butylester was formed (Table 4). These experiments prove the non-identity of the rate determining and the product determining steps in the formation of both products. The rate-determining step is the elimination; it proceeds more rapidly with sodium butoxide than with piperidine. The product-determining step is the addition to the intermediate sulphene; this step is faster with piperidine than with sodium butoxide/n-butanol.

Evidently, the solvolysis of the starting propane-2-sulphonic acid p-cresylester in sodium butoxide/n-butanol proceeds according to an elimination-addition

Table 2 Saponification of 2-deutero-propane-2-sulphonic acid p-cresyl ester and of the undeuterated ester with sodium hydroxide in dioxane/water (60 : 40) at 70 °C

starting ester	$k \cdot 10^4$ $l\,mol^{-1}\,s^{-1}$
deuterated	7.25
undeuterated	7.36
$k_H : k_D = 1.02$	

Table 3 H/D-exchange in base-catalyzed reactions of propane-2-sulphonic acid p-cresylester

starting compound	reaction	conversion %	2-deuterium in the recovered propane-2-sulphonic acid p-cresylester %
deuterated ester (89.2 % 2-D)	saponification with NaOH in dioxane/H_2O (60 : 40) at 80 °C	14	1.1[a]
undeuterated ester	saponification with NaOD in dioxane/D_2O (60 : 40) at 80 °C	21	83.4[a), b)]
deuterated ester (89.2 % 2-D)	solvolysis in n-BuONa/n-BuOH at 45 °C	30	10.0[a]

[a] ^{1}H-n.m.r. analysis
[b] mass-spectrometric analysis

Table 4 Evidence for the non-identity of the rate-determining and the product-determining steps in the base-catalyzed solvolysis of propane-2-sulphonic acid p-cresylester. Reactions of the ester with sodium butoxide and with piperidine at 90 °C

reaction	reaction time h	conversion[a] %	yield of piperidide[b] %
2 mmol ester + 5.8 mmol n-BuONa in 10 ml n-BuOH	0.5	84.4	–
2 mmol ester + 100 mmol piperidine	3.0	5.2	[c]
2 mmol ester + 5.8 mmol n-BuONa + 46 mmol piperidine + 5.5 ml n-BuOH	3.0	100	66
10 mmol ester + 25.5 mmol n-BuONa + 152 mmol piperidine	3.0	100	94

[a] of the starting ester; [b] propane-2-sulphonic acid piperidide; [c] not determined

reaction via the corresponding sulphene. The rapid H/D exchange of the starting compound proves that the sulphene-forming elimination has E1-cB character. Formula Scheme 1 shows the total mechanism of the reaction of propane-2-sulphonic acid p-cresyl ester with sodium butoxide/n-butanol.

Our results correspond with those of the working groups of J.F. King [3] and of R.V. Vizgert [4].

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Experimental

Propane-2-sulphochloride

30.5 (0.4 mol) isopropyl mercaptane were dissolved in a mixture of 140 ml glacial acetic acid and 120 g ice. The mixture was given into a 500 ml flask equipped with a stirrer, a thermometer, a gas inlet tube and a gas outlet tube. A vigorous stream of chlorine was introduced under stirring of the mixture. The temperature was kept between 5 and 10 °C. The reaction was finished when the mixture became green-yellow and when this colour did not disappear for five minutes. The reaction mixture was poured onto 350 g ice. The resulting emulsion was extracted three times with 100 ml ether each time. The combined ether extracts were washed with 100 ml water and with 50 ml of a 5 % aqueous solution of $NaHCO_3$ and then dried over Na_2SO_4. The ether was removed in vacuo. The remaining propane-2-sulphochloride was distilled in vacuo from a water bath (bp: 63 °C/1.1 kPa; yield: 42.8 g)

Propane-2-sulphonic acid p-cresylester

14.3 g (0.1 mol) propane-2-sulphochloride and 11.9 g (0.11 mol) p-cresol were dissolved in 100 ml dioxane, the solution was given into a 300 ml Erlenmeyer flask equipped with a magnetic stirrer. The flask was cooled with an ice bath and 45 ml of a 5 % aqueous solution of NaOH was poured into the vigorously stirred mixture. After 20 min stirring the emulsion was extracted three times with 50 ml ether each time. The combined ether extracts were washed five times with 50 ml water each time and then dried over Na_2SO_4. The ether was removed in vacuo and the residue distilled in vacuo from an oil bath.

Propane-2-sulphonic acid p-cresylester; bp: 125 °C/ 0.4 kPa; yield: 17.5 g. Propane-2-sulphonic acid phenylester was prepared analogously; 10.3 g (0.11 mol) phenol were used instead of the p-cresol. Propane-2-sulphonic acid phenylester; bp: 133 – 135 °C/0.8 kPa; yield: 15.1 g.

2-Deutero-propane-2-sulphonic acid p-cresylester

1.425 g (0.01 mol) propane-2-sulphochloride and 1.296 g (0.012 mol) p-cresol were dissolved in 20 ml dioxane. The mixture was given into a 50 ml Erlenmeyer flask equipped with a magnetic stirrer. The flask was cooled with an ice bath and a solution of 0.5 g (0.0125 mol) NaOH in 10 g of D_2O was poured into the vigorously stirred mixture. After 20 min stirring at 0 – 10 °C the emulsion was extracted three times with 10 ml ether each time. The combined ether extracts were washed twice with 15 ml D_2O each time and once with 15 ml H_2O. The ether solution was dried over Na_2SO_4, then the ether was removed in vacuo. The residue was distilled in vacuo from an oil bath. 2-Deutero-propane-2-sulphonic acid p-cresylester; bp: 126 – 127 °C/0.6 kPa; yield: 1.81 g.

Propane-2-sulphonic acid n-butylester

45 ml of a 1.5 n sodium butoxide/n-butanol solution were added to 8.55 g (0.06 mol) of propane-2-sulphochloride. After vigorous shaking for 3 min 65 ml of an 1 n aqueous solution of hydrogen chloride were added. The organic phase was separated and the aqueous phase extracted three times with 20 ml ether each time. The organic phases were combined, washed with 50 ml of a 5 % aqueous solution of $NaHCO_3$ and three times with 30 ml water each time. After drying over Na_2SO_4 the mixture was distilled in vacuo. Propane-2-sulphonic acid n-butylester was obtained as the second fraction: bp: 96 – 98 °C/0.7 kPa; yield: 6.7 g.

Propane-2-sulphonic acid piperidide

10.2 g (0.12 mol) piperidine in 10 ml ether were dropped during 10 min into a stirred solution of 7.13 g (0.05 mol) propane-2-sulphochloride in 50 ml ether. After 10 min stirring at room temperature 50 ml of an 1 n aqueous solution of hydrogen chloride were added. The organic phase was separated, washed with 10 ml of a 5 % aqueous solution of $NaHCO_3$ and three times with 15 ml water each time. After drying with Na_2SO_4 the ether was removed in vacuo. The remaining propane-2-sulphonic acid piperidide was distilled in vacuo from an oil bath; bp: 135 – 140 °C/0.5 kPa; yield: 7.4 g.

p-Cresyl-n-butyl ether

A mixture of 100 ml 1.5 n sodium butoxide/n-butanol, 16.2 g (0.15 mol) p-cresol and 14.7 g (0.1 mol) n-butyl bromide was refluxed for 5 h. The n-butanol was distilled off under vacuum and the residue was treated with 50 ml water and 50 ml ether.

The organic phase was separated and washed three times with 15 ml of 5 % aqueous NaOH each time. After additional washing with 20 ml water and drying over $CaCl_2$ the ether was removed in vacuo and the remaining p-cresyl-n-butyl ether distilled; bp: 85 °C/0.4 kPa; yield: 13.1 g. m-Cresyl-n-butyl ether (bp: 85 °C/0.4 kPa; yield: 12.1 g) and phenyl-n-butyl ether (bp: 68 °C/0.4 kPa; yield: 11.7 g) were prepared analogously.

Reaction of propane-2-sulphonic acid p-cresylester with sodium butoxide/n-butanol

Exactly weighed amounts of propane-2-sulphonic acid p-cresylester and of the internal standard n-undecane were given into a 25 ml graduated flask. An exactly measured volume of 1.5 n sodium butoxide/n-butanol was added, and the flask was filled up with n-butanol. 5 ml each time of the mixture were filled into 4 glass ampoules, sealed and thermostated for a definite time to 25 or 200 °C (Table 1). The ampoules were opened, and to the reaction mixtures 10 ml of 1 n aqueous hydrogen chloride (saturated with KCl) and 10 ml ether were added. The organic phase was separated, the aqueous phase was extracted twice with 10 ml ether each time. The combined organic phases were dried over Na_2SO_4 and the ether was cautiously distilled off using a 15 cm Vigreux column. The residue was analyzed gaschromatographically (3 m column with 15 % beeswax on porolith; 155 °C; 21 h^{-1} H_2; heat conductivity detector) to determine di-n-butyl ether (R_t: 5.6 min), n-undecane (R_t: 16.5 min), p-cresol (R_t: 26.6 min) and p-cresyl-n-butyl ether (R_t: 48.8 min). The results are collated in Table 1. In two separate experiments at 15 and 200 °C mixtures of 4.2 g (19.8 mmol) propane-2-sulphonic acid p-cresylester and 35 ml 1.5 n sodium butoxide/n-butanol were sealed into ampoules and thermostated for 72 h (at 25 °C) or 3 h (at 200 °C). After finishing the reaction and opening the ampoules 30 ml ether were added, the solutions were washed three times with 10 ml of 5 % aqueous NaOH each time and three times with 10 ml water each time. After drying over Na_2SO_4 and distilling off the ether and the n-butanol the p-cresyl-n-butyl ether (which could not be separated gaschromatographically from m-cresyl-n-butyl ether) was isolated by preparative gaschromatography (2 m column with 10 % dexsil on porolith; 130 °C; 21 h^{-1} H_2; heat conductivity detector), and the ^{13}C-n.m.r. spectrum was taken. Comparison with the spectra of authentic samples of both p-cresyl- and m-cresyl-n-butyl ethers showed that only p-cresyl-n-butyl ether was present (Table 5).

Reaction of propane-2-sulphonic acid phenylester with sodium butoxide/n-butanol

2.00 g (10 mmol) propane-2-sulphonic acid phenylester, 0.276 g n-tridecane (internal standard) and 15 ml of 1.5 n sodium butoxide/n-butanol were given into a 25 ml graduated flask. The flask was filled up with n-butanol and then thermostated at 40 °C; 1 ml samples were taken after definite times. The base content was determined by titration with 0.5 n aqueous hydrochloric acid (bromophenol blue as the indicator). Another 1 ml sample was extracted with 3 ml 1 n aqueous HCl (saturated with KCl) and then analyzed gaschromatographically (2 m column with 10 % dexsil on porolith; 120 °C; 2 l h^{-1} H_2; heat conductivity detector) to determine the propane-2-sulphonic acid n-butylester (R_t: 42.9 min) and the n-tridecane (R_t: 34.3 min). The concentrations of the starting ester and of the two ethers were calculated according to the stoichiometry of the reactions taking place. The results are shown in Fig. 1.

Kinetics of the saponification of propane-2-sulphonic acid arylesters

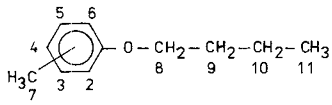
A definite amount of the starting ester was exactly weighed and given into a 25 ml graduated flask. A definite volume of

Table 5 ^{13}C-n.m.r. spectra of authentic samples of p-cresyl-n-butyl and of m-cresyl-n-butyl ethers and of the ether formed in the reaction of propane-2-sulphonic acid p-cresylester with sodium butoxide/n-butanol

ether	chemical shift (δ in ppm)[a] of C atom[b]										
	1	2	3	4	5	6	7	8	9	10	11
p-cresyl-n-butyl	157.2	114.5	129.8	129.6	129.8	114.5	19.3	67.7	31.5	20.4	13.8
m-cresyl-n-butyl	159.3	115.5	139.4	121.3	129.2	111.5	19.3	67.5	31.5	21.5	13.8
ether separated from the reaction mixture											
reaction at 25 °C	157.0	114.7	130.0	130.4	130.4	114.7	19.4	68.0	31.6	20.4	13.8
reaction at 200 °C	157.1	114.7	130.2	130.0	130.2	114.7	19.3	67.8	31.6	20.4	13.7

[a] solvent: $CDCl_3$; internal standard: hexamethyl disiloxane (δ = 1.91 ppm)

[b] numbering see formula



10% aqueous NaOH was added and the flask filled up with a dioxane/water mixture (60:40). The mixture was thermostated at 70 °C; 1 ml samples were taken at definite times and titrated with 0.05 n aqueous $HClO_4$ (bromophenol blue as the indicator). The concentration of the starting ester was calculated according to the stoichiometry. The constants k of the rate law

$r = k\,[\text{ester}]\,[OH^{\ominus}]$

were determined with a special computer program [5].

The results are shown in Table 2.

H/D exchange of 2-deutero-propane-2-sulphonic acid p-cresylester during the reaction with sodium butoxide/n-butanol

4.3 g (20 mmol) of the deuterated ester and 33 ml of a 1.5 n solution of n-BuONa in n-BuOH were given into a 50 ml graduated flask. The flask was filled up with n-butanol. The mixture was thermostated at 45 °C for 30 min. Then an 1 ml sample was taken. A weighed amount (51 mg) of n-octadecane, 3 ml of 1 n aqueous hydrogen chloride (saturated with KCl) and 1 ml ether were added, the mixture was vigorously shaken. The organic phase was separated and analyzed by gaschromatography (2 m column with 10% dexsil 400 on porolith; 190 °C; 21 h^{-1} H_2; heat conductivity detector) in order to determine propane-2-sulphonic acid p-cresylester (R_t: 19.8 min) and the internal standard n-octadecane (R_t: 23.8 min). The main part of the reaction mixture was poured into 75 ml of an 1 n aqueous solution of HCl (saturated with KCl). The organic phase was separated, the aqueous phase was extracted three times with 15 ml ether each time. The combined organic phases were washed twice with 10 ml water each time and dried over Na_2SO_4. The ether and the main part of the n-butanol were removed in vacuo. The starting ester was separated from the residue by preparative gas chromatography (2 n column with 10% dexsil 400 on porolith; 180 °C; 21 h^{-1} H_2; heat conductivity detector), and the D-content was determined by ^{1}H-n.m.r. The results are given in Table 3.

H/D exchange of propane-2-sulphonic acid p-cresylester during the saponification with NaOH in dioxane/water

1.71 g (8 mmol) propane-2-sulphonic acid p-cresylester and 0.6 g (15 mmol) NaOH were given into a 100 ml graduated flask. The flask was filled up with dioxane/D_2O (60:40). The mixture was thermostated at 80 °C for 60 min. The conversion was determined by titration of an 1 ml sample with 0.05 n aqueous $HClO_4$ (bromophenol blue as the indicator).

The main part of the reaction mixture was poured into 20 ml of 1 n aqueous HCl (saturated with KCl) and extracted three times with 30 ml ether each time. The combined ether phases were washed three times with 10 ml water each time and dried over Na_2SO_4. The ether and dioxane were removed in vacuo. From the residue the starting ester was separated by preparative gas chromatography (2 m column with 10% dexsil 400 on porolith; 180 °C; 21 h^{-1} H_2; heat conductivity detector), and the D-content was determined by ^{1}H-n.m.r. The H/D exchange of 2-deuteropropane-2-sulphonic acid p-cresyl ester was studied analogously; in this case dioxane/H_2O (60:40) was used as the solvent.

The results of all H/D exchange experiments are shown in Table 3.

Determination of the D-content in propane-2-sulphonic acid p-cresylester

The ^{1}H-n.m.r. spectra were taken in $CDCl_3$ with the aid of a 100 MHz spectrometer. The signal of the 2-H in the propane-2-sulphonyl residue appeared as a multiplet with δ = 3.36 – 3.44. The intensity of this signal was compared with the intensities of the signals of either the methyl groups of the isopropyl group (δ = 1.49 – 1.56) or the methyl group of the p-cresyl residue (δ = 2.33); thus the deuterium content could be calculated.

The mass-spectrometric determination of the D-content was possible by comparison of the intensities of the peaks 215 and 214 (molecule peaks) or of the peaks 44 and 43 (isopropyl fragment peaks).

Competitive reactions of propane-2-sulphonic acid p-cresyl-ester with sodium butoxide and piperidine

The reaction conditions are given in Table 4. In all cases n-hexadecane was used as the internal standard for the gaschromatographic determination of the conversion and of the yield of propane-2-sulphonic acid piperidide.

After the times given in Table 4 the reaction mixtures were poured into 75 ml 1 n aqueous HCl (saturated with KCl) and vigorously shaken. The resulting mixture was extracted three times with 15 ml ether each time. The combined organic phases were washed twice with 10 ml water each time and dried over Na_2SO_4. The ether was removed in vacuo and the residue analyzed gaschromatographically (2 m column with 10% dexsile 400 on porolith; 170 °C; 21 h^{-1} H_2; heat conductivity detector). Retention times: n-hexadecane 19.8 min; propane-2-sulphonic acid piperidide 24.5 min; starting ester 35.8 min.

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