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Kinetics of the Sulfonation of Some *o*-Alkylphenols

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The sulfonation of *o*-alkylphenols with chlorosulfonic acid in dichloromethane was studied. The reaction mixture was analyzed by HPLC. The rate process was found to be first order in the intermediate phenyl hydrogen sulfate. An *o*/*p* ratio of 5:1 was found when the reaction was run in a 0.1 M solution. The influence of HCl on the reaction was studied and a mechanism is discussed on the basis of kinetic data.

The kinetics and mechanism for the sulfonation of phenols has mainly been studied by Karavaev [1] and Spryskov *et al.*[2] Chlorosulfonic acid has been used as the sulfonating agent in these investigations. Their analysis procedure was rather complicated, however, with UV-measurements for the sulfonic acid mixture and partial work-up procedures for studying other products. Since the reaction products precipitate from the solution, the kinetics had to be run batch-wise, which placed very high demands on the reproducibility. In order to investigate this sulfonation reaction properly and to avoid the solubility problems, we studied the corresponding reaction with *o*-isopropylphenol and *o*-cyclohexylphenol using HPLC technique to analyze the reaction mixture.

RESULTS AND DISCUSSION

In the mechanism proposed by Spryskov *et al.*[3,4] it is suggested that the formation of the phenolsulfonic acids is a result of an attack by chlorosulfonic acid on the initially formed phenyl hydrogen sulfate, followed by an elimination of the ester group. The kinetics of the reaction is claimed to be second order in phenyl hydrogen sulfate.[3]

For the understanding of the reaction it is important to realize that chlorosulfonic acid is reported to be in equilibrium with HCl[5] according to:

$$ClSO_3H \rightleftharpoons SO_3 + HCl \qquad (1)$$

If $ClSO_3H$ is the sulfonating agent and A is the compound which is sulfonated, a rate equation of the form $k[A][ClSO_3H]$ may be expected. If the sulfonating agent is SO_3, a rate expression of the form $k[A][ClSO_3H]/[HCl]$ is more probable since $[SO_3] = K[ClSO_3H]/[HCl]$.

In principle it should thus be possible to reveal the dominating electrofile by a careful study of the reaction at several different concentrations of HCl. In practice, however, this is rather difficult, since the reaction has to be performed at low temperature and is very sensitive to traces of water.

Since our own interest is mainly in the preparative field, we performed a few experiments to reveal the best conditions for *ortho*-sulfonation. At the same time, we obtained some useful data which enabled us to suggest a mechanism for this type of sulfonation.

Our observations disagree in some important aspects with Spryskov's work [4] and we wish to report the following observations.

I. It seems as if the reaction consists of two different phases. The first one is a fast attack of the chlorosulfonic acid on the phenol hydroxy group, forming the alkylphenyl hydrogen sulfate (*E*). In the same initial phase there seems to be some direct sulfonation of the aromatic ring. The second phase of the reaction is the conversion of *E* to the corresponding *ortho* and *para* hydroxybenzenesulfonic acids

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Table 1a. HPLC measurements from the kinetic experiment in the sulfonation of *o*-isopropylphenol.

Time h	*1*		*2*		*3*		*o*-Isopropyl-phenol mmol/l
	Found mmol/l	Calc. [a] mmol/l	Found mmol/l	Calc. [a] mmol/l	Found mmol/l	Calc. [a] mmol/l	
0	65.6	65.8	27.2	30.0	5.2	5.1	3.8
0.25	62.1	60.4	33.4	34.6	6.3	6.0	3.1
0.5	56.7	55.4	38.3	38.9	6.6	6.9	2.1
1.0	47.3	46.6	47.0	46.4	8.0	8.3	1.2
1.5	37.2	39.4	56.4	52.5	9.9	9.5	2.4
2.0	31.4	33.6	59.1	57.4	10.4	10.5	2.6
3.0	23.0	24.4	67.8	65.2	12.1	12.0	1.1
5.0	12.4	12.7	75.5	75.2	13.9	14.0	1.5
7.0	6.6	6.5	80.2	80.5	15.0	15.0	1.1
9.0	3.9	3.0	81.6	83.4	15.6	15.6	1.4
13.25	1.2	0.3	84.0	86.2	16.2	16.1	0.8

[a] Calculated from $C_n = k_n \, {}_0\int^t C_1 \, dt + C_n^0$; $n = 1-3$.

Table 1b. Rate constants in the transformation of *1* to *2* and *3*.

Reaction	Rate const. h^{-1}	Standard deviation
Disappearance of *1*	0.340	0.007
Formation of *2*	0.289	0.010
Formation of *3*	0.057	0.001

(*O*) and (*P*). The velocity of the last reactions can be followed at −20 to −30 °C. The rate process was studied over up to 6 periods of half life and was found to be first order in the ester (*E*) and not second order as claimed by Spryskov for phenol (Table 1 and Fig. 1).

II. If *o*-isopropylphenol is treated with slightly less than the theoretical amount of chlorosulfonic acid to give the ester, and then another phenol, *o*-methylphenol, is added to the solution, which is afterwards allowed to stand for a period sufficient to convert most of the esters to sulfonic acids, about 1/3 of the sulfonic acids formed originates from *o*-methylphenol. Transesterification having a transition state with the sulfur atom binding 5 oxygen atoms seems improbable. This is demonstrated by the very high stability of compounds of the type $ArOSO_2OAr$ with respect to hydrolysis. To convince us that no unexpected reactions occurred, we treated this diarylester with another phenol and HCl in dichloromethane and found no aryl exchange. Since a transesterification without a separation of the phenol from the SO_3 group seems improbable, the aryl exchange observed seems to be due to a reversible reaction between the phenol and chlorosulfonic acid.

III. When a reaction mixture of *o*-cyclohexylphenol and chlorosulfonic acid in dichloromethane is divided into two equal parts, and one of them is diluted with the same volume of dichloromethane, the rate constant observed for the formation of the *ortho* hydroxy sulfonic acid increases from 0.147 in the undiluted to 0.180 in the diluted solution. For the formation of the *para* hydroxy sulfonic acid, the constants are 0.091 in the undiluted and 0.075 in the diluted case (Table 2 and Fig. 1).

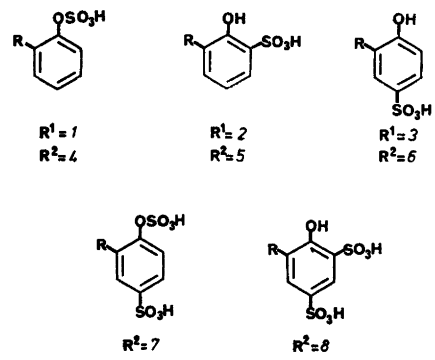

Fig. 1. R^1 = isopropyl and R^2 = cyclohexyl.

Table 2a. HPLC measurements from the kinetic experiment in the sulfonation of *o*-cyclohexylphenol.

Time	*4*		*5*		*6*		*7*	*8*	
h	Found mmol/l	Calc. [a] mmol/l	Found mmol/l	Calc. [a] mmol/l	Found mmol/l	Calc. [a] mmol/l	Found mmol/l	Found mmol/l	Calc. [b] mmol/l
Concentrated solution									
0	317.5	317.5	88.5	92.4	53.0	49.8	21.0	2.0	2.9
0.5	290.0	283.6	111.5	114.7	60.5	63.6	—	4.0	—
1.5	224.0	226.6	158.0	152.3	86.5	87.0	26.0	6.0	5.7
3.0	155.5	163.8	201.0	193.8	112.5	112.7	25.0	9.5	8.8
5.0	104.5	106.5	231.5	231.5	136.0	136.2	24.0	13.5	12.8
8.0	59.5	53.0	261.0	266.8	159.0	158.1	20.5	17.5	18.8
Diluted solution									
0	157.8	161.4	50.0	52.5	24.5	24.4	9.8	1.5	1.7
0.5	146.0	141.0	64.0	66.1	29.8	30.1	10.5	2.3	2.3
1.5	109.5	106.8	94.3	88.9	40.5	39.7	10.3	3.8	3.5
3.0	66.8	71.9	114.0	112.3	48.5	49.4	9.4	5.3	5.2
5.0	41.0	43.5	133.3	131.3	57.8	57.4	7.8	7.3	7.2
8.0	22.3	18.7	143.3	147.8	—	64.3	5.5	9.3	9.5

[a] Calculated from $C_n = k_n \, {}_0\int^t C_4 \, dt + C_n^0$; $n = 4-6$. [b] Calculated from $C_8 = k_8 \, {}_0\int^t C_7 \, dt + C_8^0$.

Table 2b. Rate constants in the transformation of *4* to *5* and *6* and *7* to *8*, respectively.

Reaction		Concentrated solution		Diluted solution	
		Rate constant h^{-1}	Standard deviation	Rate constant h^{-1}	Standard deviation
Disappearance of	*4*	0.223	0.006	0.269	0.010
Formation of	*5*	0.147	0.006	0.180	0.009
Formation of	*6*	0.091	0.002	0.075	0.002
Formation of	*8*	0.081	0.006	0.115	0.004

Table 3. HPLC measurements from the sulfonation of *o*-isopropylphenol in a 0.5 M solution of HCl in dichloromethane compared with the sulfonation in 0.1 M solution.[a]

Time	*1*		*2*		*3*	
h	In 0.5 M HCl mmol/l	In 0.1 M HCl mmol/l	In 0.5 M HCl mmol/l	In 0.1 M HCl mmol/l	In 0.5 M HCl mmol/l	In 0.1 M HCl mmol/l
0.25	50.8	62.1	20.6	33.4	15.6	6.3
2.0	15.2	31.4	49.5	59.1	24.6	10.4
20	0.3	0.07 [b]	59.6	83.0 [c]	26.6	16.2 [c]

[a] Rate constants in the transformation of *1* to *2* and *3* in 0.5 M HCl/dichloromethane solution. $k_1 = 0.69$ h^{-1}, $k_2 = 0.56$ h^{-1}, $k_3 = 0.18$ h^{-1}. [b] Calculated from $C = C^\circ e \exp(-kt)$. [c] Calculated from $C = C^\circ + \frac{k_i}{k_1} C_1^\circ$ (1-exp(-$k_1 t$)); $i = 2$ or *3*.

Fig. 2. A general description of the sulfonation.

IV. When a solution of *o*-isopropylphenol in dichloromethane is saturated with HCl before the chlorosulfonic acid is added, the *ortho:para* ratio in the initial step is about 1 instead of about 5 in the reaction where no HCl is added. The rate constants for the formation of the *ortho* and *para* hydroxy sulfonic acids from the ester increase about two times for the *ortho* compounds and about three times for the *para* compound. The concentration of HCl in this experiment is increased from 0.1 mol l^{-1} to about 0.5 mol l^{-1}. The data are given in Table 3.

These results may be summarized by Fig. 2 which gives a general description of the sulfonation of a phenol and we must find rate equations for each of the six steps. The fact that the *o/p* ratio obtained in the first rapid phase of the reaction is reduced from 5 to 1 when HCl is added to the solution, eliminates several otherwise plausible combinations.

At least three possibilities have to be discussed in order to explain these results.

1. Suppose that the decrease in the *o/p* ratio, when HCl is added, depends on differences in mechanisms for the $A \rightarrow O$ and $A \rightarrow P$ reactions in such a way that the $A \rightarrow P$ reaction is catalyzed by HCl to a higher degree than the $A \rightarrow O$ reaction, or that the $A \rightarrow O$ reaction is retarded by HCl to a higher degree than the $A \rightarrow P$ reaction. The most plausible examples of rate expressions of this kind are $k_{AP}[A][ClSO_3H]$ for the $A \rightarrow P$ reaction and $k_{AO}[A][ClSO_3H]/[HCl]$ for the $A \rightarrow O$ reaction. These are the rate equations expected if the $A \rightarrow P$ sulfonation occurs with $ClSO_3H$, whereas the $A \rightarrow O$ sulfonation occurs with SO_3 since $[ClSO_3H]/[HCl]$ in the rate expression can be replaced by $[SO_3]$. This possibility cannot be correct because a sulfonation of a phenol with SO_3 in dichloromethane does not give a higher *o/p* ratio than one with $ClSO_3H$.

2. If the $E \rightarrow O$ and $E \rightarrow P$ reactions have a lower *o/p* ratio than the $A \rightarrow O$ and $A \rightarrow P$ reactions and the increase in HCl results in a higher contribution of $E \rightarrow O$ and $E \rightarrow P$ reactions, a decrease in the total *o/p* ratio is expected when HCl is added. If this had been the case, the highest contribution of $E \rightarrow P$ and $E \rightarrow O$ reactions should have been expected at the start of the slow phase of the biphasic reaction since both E and HCl have their highest values at this point. From the experiments, however, we know that the rate of formation of O and P at this point is low compared with the rates in the rapid phase of the reaction and therefore there must be another explanation to the observations.

3. If we assume, in contrast to the latter case, that the $E \rightarrow O$ and $E \rightarrow P$ reactions have a higher *o/p* ratio than the $A \rightarrow O$ and $A \rightarrow P$ reactions and the increase in HCl results in a lower contribution of $E \rightarrow O$ and $E \rightarrow P$ reactions, a decrease in the total *o/p* ratio is expected when HCl is added even in this case. The simplest set of rate equations which fulfil this is given in Scheme 1.

Process	Rate
$A \rightarrow E$	$k_{AE}[A][ClSO_3H]$
$E \rightarrow A$	$k_{EA}[E][HCl]$
$A \rightarrow O$	$k_{AO}[A][ClSO_3H]$
$A \rightarrow P$	$k_{AP}[A][ClSO_3H]$
$E \rightarrow O$	$k_{EO}[E]$
$E \rightarrow P$	$k_{EP}[E]$

Scheme 1.

It will be shown that this can explain the experimental facts available. For the slow second phase the "steady state" approximation applied to A gives

$$[A][ClSO_3H] = \frac{k_{EA}}{k_{AE} + k_{AO} + k_{AP}} \times [E][HCl] \qquad (2)$$

It is reasonable to expect that the phenols A, O and P and the ester E are protonated to at least some extent during the reaction. The total quantity of strong acids present is constant during the slow second phase of the reaction. We can thus assume that the fraction X_E of E present in the unprotonated form is constant and thus

$$[E] = X_E C_E \qquad (3)$$

where C_E is the total concentration of E. X_E can be expected to be constant or decreased

Reaction	Rate	
$E \rightarrow A \rightarrow O$	$\frac{k_{EA}\, k_{AO}}{k_{AE}+k_{AO}+k_{AP}} X_E C_E[\mathrm{HCl}] = k'_{AO} X_E C_E[\mathrm{HCl}]$	(4)
$E \rightarrow A \rightarrow P$	$\frac{k_{EA}\, k_{AP}}{k_{AE}+k_{AO}+k_{AP}} X_E C_E[\mathrm{HCl}] = k'_{AP} X_E C_E[\mathrm{HCl}]$	(5)
$E \rightarrow O$	$k_{EO} X_E C_E$	(6)
$E \rightarrow P$	$k_{EP} X_E C_E$	(7)
Disappearance of E	$k_{\mathrm{obs}}(\mathrm{E}) C_E$	(8)
Total formation of O	$k_{\mathrm{obs}}(O) C_E$	(9)
Total formation of P	$k_{\mathrm{obs}}(P) C_E$	(10)

Scheme 2.

if HCl is added but increased if the solution is diluted.

If eqns. (2) and (3) are introduced we obtain the rate expressions for the steps in the second phase of the reaction given in Scheme 2.

The rate of formation of O has been found to be first order in C_E. Thus it must be equal to $k_{\mathrm{obs}}(O)C_E$ and is the sum of the rate of the steps $E \rightarrow A \rightarrow O$ and $E \rightarrow O$. We thus obtain

$$k_{\mathrm{obs}}(O) = (k'_{AO}[\mathrm{HCl}] + k_{EO}) X_E \quad (11)$$

$$k_{\mathrm{obs}}(P) = (k'_{AP}[\mathrm{HCl}] + k_{EP}) X_E \quad (12)$$

Since we can expect that [HCl] is almost constant during the slow step which is followed by kinetic measurements, k_{obs} should be constant in each run. This is in good agreement with the experimental findings.

The formation of O is the sum of two reactions. The first is $E \rightarrow A \rightarrow O$, with a rate which is increased with an increase in HCl, and the second is $E \rightarrow O$, with a rate which is decreased with an increase in HCl. The same is valid for the formation of P. The experiment when HCl was added can be interpreted in such a way that the effect on $E \rightarrow A \rightarrow O$ became dominant and $k_{\mathrm{obs}}(O)$ increased. The same was valid for $k_{\mathrm{obs}}(P)$. We can also conclude that when we increase the importance of the reactions $E \rightarrow A \rightarrow O$ and $E \rightarrow A \rightarrow P$, the ratio o/p decreases. The direct rearrangement of $E \rightarrow O$ and $E \rightarrow P$ is therefore more *ortho* selective than the sulfonation of A by the steps $A \rightarrow O$ and $A \rightarrow P$.

The dilution experiment can be interpreted in such a way that the effect on $E \rightarrow O$ becomes dominant over that on $E \rightarrow A \rightarrow O$ with the result that $k_{\mathrm{obs}}(O)$ increases slightly on dilution. Since the o/p ratio in the concentrated solution is rather low we might expect that the step $E \rightarrow P$ does not dominate over $E \rightarrow A \rightarrow P$ and might therefore expect that $k_{\mathrm{obs}}(P)$ will decrease when the solution is diluted, in good agreement with the experimental results.

During the first rapid phase of the reaction, an addition of HCl might have a slight rate depressing effect on the reaction $E \rightarrow O$ and $E \rightarrow P$ but a rate increasing effect on the reaction $E \rightarrow A$ (Fig. 2). The addition of HCl will thus decrease the quantities of O and P coming from the reactions $E \rightarrow O$ and $E \rightarrow P$. This effect is still more accentuated by the increase in the rate of the reaction $E \rightarrow A$ which makes less E available for the reactions $E \rightarrow O$ and $E \rightarrow P$. The result of the addition of HCl is thus that we strongly increase the importance of the reactions $A \rightarrow O$ and $A \rightarrow P$ at the expense of $E \rightarrow O$ and $E \rightarrow P$ with a strong decrease in *ortho* selectivity in the first rapid phase of the reaction.

The biphasic nature of the reactions is readily understood by the mechanism proposed. Strong acids are formed in a quantity at least equivalent to $E+O+P$. They can add to the weak base A and the concentration of A is therefore strongly reduced. The velocity of the reaction thus drops dramatically as soon as the quantity of strong acids which are formed exceeds the quantity of weak bases (A, O and P) present. Another very important factor is that $ClSO_3H$ is consumed in the first rapid

phase and is present is very small amounts when the bulk of A has been converted to E, O and P.

CALCULATIONS

The constants k_{obs} are obtained from eqns. (8) – (10). The equation containing k_{obs} (E) is first order in E and is therefore readily integrated. In the present fairly uncomplicated case the expression $C_E = C_E^{\circ}\exp(-tk_{obs}(E))$ which is obtained by direct integration, may be substituted into the other equations which can then be integrated.

A more general method is to use the integral ${}_0\int^t C_E \, dt$ as a variable instead of t as suggested by Wideqvist.[6] This method has the following characteristics:

1. It formally reduces the order of the reaction by one step. A first order reaction is reduced to zero order reaction *etc.*

2. In an ordinary least squares treatment of data we minimize errors in concentrations and not in their logarithms.

3. In the calculation of k_{obs} for O and P we do not need any knowledge or assumption of the formation or reaction of E. We only state that the rates of formation of O and P are directly proportional to C_E. The values obtained for $k_{obs}(O)$ and $k_{obs}(P)$ are thus not directly affected by the error in the estimation of $k_{obs}(E)$.

An integral ${}_0\int^t X \, dt$ is readily obtained by numerical integration. The simplest method is by the trapezoid formula where the curve between the points $(t_i, X_i$ and $t_{i+1}, X_{i+1})$ is approximated by straight lines. A very good improvement is obtained, however, if the curve between the two points is approximated by exponentials of the type $X_{i+1} = X_i \exp[-k(t_{i+1}-t_i)]$ going through the two points. From this we can deduce

$$\int_0^t X \, dt = \sum_{i=0}^{n-1} \frac{(X_i - X_{i+1})(t_{i+1} - t_i)}{\ln X_i - \ln X_{i+1}}$$

With this formula ${}_0\int^t C_E \, dt$ is readily calculated with the aid of a small desk calculator. The formula has the obvious advantage that if the points (t_i, X_i) fit an exponential curve, the integral is exact. This method is used in all our calculations.

EXPERIMENTAL

The phenols used in the kinetic experiments were purified by distillation. The purity was found to be better than 99 % by GLC analysis on a 3 % OV 17 column. Dichloromethane was dried over molecular sieves. Chlorosulfonic acid was purified by distillation under reduced pressure. The methods for the HPLC measurements are briefly described in Ref. 7 and will be published in detail.[8] The reference compounds *1* – *8* for these measurements were tested for water content by the Karl Fischer method and the absence of sulfate and chloride ions was established by precipitation tests with $BaCl_2$ and $AgNO_3$.

NMR measurements. The structure of the reference compounds was established by ^1H and ^{13}C NMR analysis using a Varian CFT 20 instrument at 79.54 MHz for ^1H and at 20 MHz for the ^{13}C measurements. D_2O was used as solvent and sodium 3-trimethylsilyltetradeuteriopropionate and dioxane, respectively, as internal standards.

The assignments in the ^{13}C spectra were based on comparison with calculated shift values,[9] together with the fact that carbon atoms carrying a substituent give peaks with strongly reduced intensities. The chemical shift factors for the $-OSO_3^-$ group are given in Ref. 7.

1. ^1H δ 7.33, 7.30, 7.29 (4 H, m), 3.37 (1 H, m, J 6.7 Hz), 1.21 (6 H, d, J 6.9 Hz). ^{13}C δ 149.3 (C1), 142.4 (C2), 122.0 (C6), 27.3 (Cα), 23.1 (Cβ), 127.9, 127.6, 127.3 (not assigned peaks).

2. ^1H δ 7.56, 7.54, 7.47, 7.45, 7.39, 7.37 (2 H, 3d, J 1.8 Hz), 6.98 (1 H, dd, J 7.7 Hz), 3.38 (1 H, m, J 6.8 Hz), 1.20 (6 H, d, J 6.9 Hz). ^{13}C δ 150.4 (C2), 138.2 (C3), 130.8 (C4), 127.6 (C1), 125.2 (C6), 121.0 (C5), 27.0 (Cα), 22.6 (Cβ).

3. ^1H δ 7.66 (1 H, d, J 2.2 Hz), 7.50 (1 H, dd, J 8.2 and 2.4 Hz), 6.92 (1 H, d, J 8.4 Hz) 3.23 (1 H, m, J 7.0 Hz), 1.22 (6 H, d, J 6.9 Hz). ^{13}C δ 156.2 (C4), 136.6 and 135.3 (C1,C3), 125.2 and 124.8 (C2,C6), 116.0 (C5), 27.1 (Cα), 22.5 (Cβ).

4. ^1H δ 7.32 (4 H, m), 3.0 (1 H, m), 1.75, 1.37 (10 H, m). ^{13}C δ 148.8 (C1), 140.7 (C2), 37.4 (Cα), 127.7, 126.9, 126,5, 121.6, 34.2, 27.6, 26.9 (not assigned peaks.

5. ^1H δ 7.46 (1 H, dd, J 7.2 and 1.7 Hz), 7.15 (1 H, dd, J 7.2 and 1.8 Hz), 6.82 (1 H, dd, J 7.6 Hz), 2.85 (1 H, m), 1.69, 1.24 (10 H, m). ^{13}C δ 150.7 (C2), 136.8 (C3), 37.4 (Cα), 130.6, 127.7, 125.3, 120.5, 33.6, 27.4, 26.8, 26.2 (not assigned peaks).

6. ^1H δ 7.55 (1 H, d, J 2.0 Hz), 7.32 (1 H, dd, J 8.4 and 2.2 Hz), 6.94 (1 H, d, J 8.3 Hz), 2.46 (1 H, m), 1.75, 1.30 (10 H, m). ^{13}C δ 156.5 (C4), 135.3 and 135.0 (C1,C3), 37.4 (Cα), 125.0, 115.6, 33.2, 27.3, 26.5 (not assigned peaks).

7. ^1H δ 7.82, 7.80, 7.74, 7.64, 7.61, 7.54, 7.44 (3 H, m) 3.08 (1 H, m), 1.78, 1.40 (10 H, m). ^{13}C δ 151.4 (C4), 142.0 and 140.9 (C1,C3),

37.7 (Cα), 125.7, 124.7, 122.1, 33.5, 27.0, 26.3 (not assigned peaks).

8. ^{1}H δ 7.91 (1 H, d, *J* 2.3 Hz), 7.79 (1 H, d, *J* 2.2 Hz), 2.98 (1 H, m), 1.80, 1.10 (10 H, m). ^{13}C δ 153.2 (C4), 128.1 and 122.9 (C2,C6), 37.4 (Cα), 138.4, 135.0, 122.6, 33.2, 27.5, 26.4 (not assigned peaks).

The reference compounds 1–8 used in the HPLC-analysis were synthesized in the same way as in Ref. 7 using ion pair technique in the separation and purification procedure.

The sulfuric acid esters. The general procedure given in Ref. 10 was used for the synthesis.

The kinetic experiment with o-*isopropylphenol*. A 500 ml three-necked round-bottomed flask was dried at 120 °C overnight and filled with argon during the cooling. Then 5.4 g, 40 mmol, of *o*-isopropylphenol was added and dissolved in 400 ml of dried dichloromethane and the solution was cooled to −40 °C under magnetic stirring. With the aid of a dried 25 ml dropping funnel 4.7 g, 40 mmol, of chlorosulfonic acid dissolved in 14 ml of dried dichloromethane was then added dropwise during about 20 min so that the temperature never exceeded −30 °C. When the addition was completed the reaction flask was placed in a cryostat at −20 °C. (The total volume of the reaction mixture was found to be 400 ml at this temperature). As soon as the mixture had reached this temperature (after about 5 min) a zero-time sample of 20 ml of the mixture was taken out with a cooled pipette and immediately poured into an ice-cooled solution of 3.4 ml of 1 M KOH and 25 ml of water. As rapidly as possible the pH was adjusted to 6.5–7. The organic layer was then separated and the aqueous layer extracted with 2 × 25 ml of dichlormethane. The combined organic phases were washed with a 5 ml portion of water to compensate for incomplete separation. The combined aqueous layers were adjusted to pH 7, diluted to 100 ml in a volumetric flask, and kept in a refrigerator overnight until HPLC analysis was performed. Ten other 20 ml samples were taken out at different times and treated in the same way (Table 1). (Attempts to run this experiment with higher phenol concentrations failed since the products precipitated from the solution).

Competitive sulfonation of o-*isopropyl- and* o-*methylphenol*. A solution of 5.71 g, 42 mmol of *o*-isopropylphenol in 200 ml of dichlormethane was cooled to −35 °C. Under magnetic stirring 4.7 g, 40 mmol, of chlorosulfonic acid dissolved in 15 ml of dichloromethane was added. The reaction mixture was left at −30 °C for 1 h in order to complete the sulfatation. A solution of 4.5 g, 42 mmol, of *o*-methylphenol in 25 ml of dichloromethane, cooled to −30 °C, was then added. The mixture was allowed to stand for another 30 min, whereupon 40 ml was removed. The temperature in this sample was raised slowly to 10 °C over 1.5 h and the mixture was then poured into water and neutralized to pH 7 with 1 M KOH. The same procedure was repeated with another sample after 4 h. Each of the aqueous phases from these samples was extracted twice with dichloromethane, evaporated and analyzed by means of NMR. They were found to contain sulfonic acids from *o*-methylphenol and *o*-isopropylphenol in the proportions 1:2.

Phenol exchange in di(4-methylphenyl)sulfate. 0.55 g, 2 mmol, of di(4-methylphenyl)sulfate prepared according to Ref. 11, and 0.19 g, 2 mmol, of phenol were dissolved in 20 ml of dried dichloromethane. The solution was cooled to −30 °C and 0.5 g, 13 mmol, of HCl gas was inlet. The reaction mixture was put into a cryostat at −20 °C for 23 h. At 3, 6 and 23 h 5 ml of the mixture was taken out and poured into 5 ml of water. The phases were separated and extraction with 2 × 5 ml of dichloromethane was performed. The combined organic phases were dried over Na_2SO_4 and analyzed by means of GLC. No traces of *p*-methylphenol could be found.

Sulfonation of o-*cyclohexylphenol*. Chlorosulfonic acid, 14.2 g, 120 mmol, was added dropwise under magnetic stirring to a solution of 17.6 g, 100 mmol, of *o*-cyclohexylphenol in 170 ml of dichloromethane, cooled to −40 °C. The addition time was about 50 min and the total volume of the mixture was 200 ml at −40 °C. At this point the mixture was divided into two equal volumes which means that 100 ml was taken out with a cooled pipette and poured into 100 ml of dichloromethane at −45 °C in another flask. The two reaction flasks were put in a cryostat and, as soon as they had reached −20 °C, samples were taken out at different times and treated in the same way as in the kinetic experiment with *o*-isopropylphenol. The results from the HPLC analysis are given in Table 2.

Sulfonation of o-*isopropylphenol in 0.5 M HCl solution*. To a solution of 5.4 g, 40 mmol, of *o*-isopropylphenol in 400 ml of dried dichloroethane cooled at −15 °C, 6.1 g, 165 mmol, of HCl gas was added. The solution was cooled to −40 °C and a solution of 4.7 g, 40 mmol, of chlorosulfonic acid, dissolved in 15 ml of dichloromethane, was added dropwise. At the end of the addition the mixture became inhomogeneous due to the precipitation of sulfonic acids. The temperature was raised to −20 °C and under vigorous stirring 20 ml samples were taken out at different times and treated in the same way as in the kinetic experiment with *o*-isopropylphenol. The results from the HPLC-analysis are given in Table 3.

Sulfonation of o-*methylphenol with* SO_3. A solution of 9 g, 55 mmol, of SO_3 in 25 ml of dichloromethane [12] was added dropwise at −30 °C to a solution of 10.8 g, 50 mmol, of *o*-methylphenol in 100 ml of dichloromethane. After 1 h at −30 °C and 1.5 h at room temperature the solution was poured into water, neutralized with 1 M KOH and the water layer

was evaporated. NMR analysis of the reaction mixture showed that there were approximately equal amounts of products sulfonated *ortho* and *para* to the hydroxy-group.

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