

Isotopic Exchange Reaction between an Aromatic Sulfonic Acid and its Anhydride

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p-Iodobenzene sulfonic acid labelled with ^{35}S or ^{131}I and unlabelled *p*-iodobenzene sulfonic anhydride in a homogeneous solution of nitromethane were observed to exchange radioactivity. The kinetics correspond to a typical first-order scheme. The rate constant of the first-order reaction is proportional to the ratio of the anhydride concentration to the acid concentration. The experimental data support the assumption that the exchange proceeds through a mechanism involving dissociation of a molecule of anhydride into a sulfonyl cation and a sulfonate anion.

In analogy with the acylium ion, RCO^+ , *cf.* Burton *et al.*¹ and Satchell², the occurrence of a sulfonyl cation, RSO_2^+ , has been stated on several occasions. In the AlCl_3 -synthesis of sulfones from sulfonylchlorides, the sulfonyl cation, free or as partner in an ion-pair, has been assumed to be the active component³⁻⁵, and arylsulfonyl perchlorates have been prepared⁶.

It was found of interest to investigate the possible formation of arylsulfonyl cation from aromatic sulfonic anhydride, $(\text{RSO}_2)_2\text{O}$. The exchange between a labelled sulfonic acid, RSO_3H , and the corresponding non-labelled sulfonic anhydride, $(\text{RSO}_2)_2\text{O}$, appeared to be experimentally feasible, and the kinetic data allow extraction of valuable information.

p-Iodobenzene sulfonic acid labelled with ^{35}S or ^{131}I and its corresponding anhydride were chosen as exchange-partners, since they are routinely produced in this laboratory. Nitromethane was chosen as solvent, partly because it is one of the few solvents in which both components can be dissolved at 50–80°C, partly because the solubility of the anhydride in nitromethane at 0° is so low that the recovery of the exchanged anhydride is a simple matter.

EXPERIMENTAL

Materials. The *p*-iodobenzene sulfonic anhydride was prepared as previously described⁷ with the following modifications: sulfur trioxide drawn from commercial oleum by a stream of dried air was trapped in an U-shaped glass-tube at –20°C. The sulfonic anhydride was recrystallised from nitromethane, m.p. 219–222°C.

The nitromethane was dried over CaCl_2 and distilled, only the middle 3/5 fraction was used.

The ether was dried over CaCl_2 and sodium wire and distilled immediately before use.

Labelled *p*-iodobenzene sulfonic acid was prepared by hydrolysis of the labelled anhydride as previously described⁷. The specific activity was 10–100 mC ^{35}S per mmole of sulfur (or in one experiment 0.5 mC ^{131}I per mmole of iodine).

The investigations by Taylor and Vincent⁸ on fluoro-, chloro- and bromobenzene sulfonic acid have shown that the monohydrates are obtained when concentrated solution of these acids are dried *in vacuo* over P_2O_5 at room temperature, while the anhydrous acids are prepared by heating the monohydrates slightly above their m.p. *in vacuo* for about an hour.

In these experiments both procedures have been used and the kinetics referred to later in this paper are consistent with the view that the product obtained by the former method, with m.p. 75–77° and neutralisation equivalent weight 301, is the monohydrate, (not the anhydrous acid as erroneously stated previously⁷) while that obtained by the latter method, m.p. 100–120°, neut. equiv. wt. 286, is the anhydrous acid. Both compounds are readily soluble in cold water and fairly soluble in cold nitromethane and ether.

Equipment and procedure. The experiments were carried out in bifurcated vessels with a capacity of 5 ml. Each experiment (a run) employed 3–5 vessels mounted on a shaking device and immersed in a water filled thermostat. The temperature in the vessel, 60° or 70°C, was kept within $\pm 0.2^\circ$ during the exchange experiments.

As the sulfonic anhydride is sparingly soluble in nitromethane at room temperature, it was impracticable to use a stock-solution. It was more convenient to weigh the dry material in the vessel itself.

A stock-solution of 50–150 mg labelled sulfonic acid in 10 ml anhydrous nitromethane was made up and various concentrations of sulfonic acid were obtained by dilution of this stock-solution with anhydrous nitromethane. One preparation of labelled sulfonic acid sufficed for 3–5 experiments.

After having placed the appropriate amount of anhydride in one leg of each vessel and recorded the weight, 3 ml of anhydrous nitromethane was added. To the other leg of each vessel was added 1 ml of sulfonic acid solution. Glass stoppers were loosely placed in the mouth of the vessels. The vessels were mounted on the shaker, and by gentle shaking, without mixing the contents, the anhydride was dissolved. Experiments showed that 3 min were required for the contents of the vessels to reach the temperature of the thermostat; the mixing of the contents was done after 10 min shaking. Protraction of this pre-heating periode to 30 min did not alter the apparent zero-time exchange significantly (*cf.* below).

Sampling was done by pouring the entire content of a vessel into an ice-cooled test-tube. The precipitated anhydride was washed with ether and pentane and dried. The weight of the recovered anhydride was recorded as a rough check that no hydrolysis had occurred during the experiment. In most experiments the isolated anhydride was recrystallised from nitromethane prior to sampling for measurement of radioactivity. Such recrystallised materials had m.p. 217°C. In other experiments sampling was done directly from the crude material, m.p. 212°–215°C. Experiments have shown that recrystallisation does not significantly change the specific activity of a sample.

Vessels and pipettes for handling the solution had been dried overnight at 120°C and kept for 2 h *in vacuo* over P_2O_5 before use.

^{35}S counting was performed with a calibrated end-window Geiger-Müller tube.

In one experiment with monohydrate the sulfonic acid was labelled with ^{131}I instead of ^{35}S . The product was prepared from ^{131}I labelled iodobenzene by sulfonation with sulfur trioxide in nitromethane. Counting was done with a calibrated scintillation-crystal equipment.

End-point of exchange. In most experiments the specific activity of the end-point, a_∞ , was not measured, but has been deduced from the equation expressing the conservation of radioactivity: $a_\infty = \beta \times T / (2Ah + T)$ where β is the initial specific activity in mC/millimole of the acid and T and Ah are the molar concentrations of the acid and anhydride, respectively.

That this method of calculation is correct has been confirmed by some experiments, where the end-points actually were measured on samples taken after about 10 half-lives.

Expt. No.	Calculated mC/mmole	Measured mC/mmole
11	1.26	1.28
17	0.42	0.40
19	9.2	9.1

The identity of the radioactivity. A sample of sulfonic anhydride made radioactive by exchange with ^{131}I labelled sulfonic acid was allowed to react with aniline in chloroform at 40° for 15 min. The insoluble anilinium sulfonate separated rapidly and from the chloroform filtrate the sulfonic anilide could be isolated (m.p. 148° after recrystallization from ethanol). The following specific activities (in arbitrary units) were measured with scintillation equipment (first column):

	c.p.s./ μg	c.p.s./ μg sulfur
Sulfonic anhydride	4.87	41.9
Anilinium sulfonate	3.17	37.4
Sulfonic anilide	3.69	40.3

The values of the second column have been computed taking the mole weights 550, 377, and 359, respectively. The low value of the sulfonate could be due to insufficient purification, but otherwise the experiment is good evidence that the radioactivity present in the sulfonic anhydride is due to labelled anhydride, not to other radioactive contaminants.

RESULTS

The apparent exchange fraction \bar{F} , being the ratio between the observed specific activity of the sulfonic anhydride, α , and the specific activity of the anhydride at the end-point, α_∞ , has been plotted on semilogarithmic paper *versus* time. Two typical graphs are shown in Fig. 1, and it will be seen that the first-order law, characteristic of simple exchange reactions, is obeyed with reasonable accuracy. However, an apparent zero-time exchange, indicating insufficient separation, contributes to the experimental errors. The pheno-

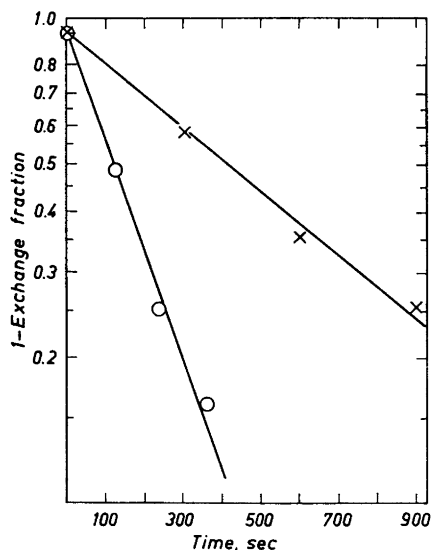


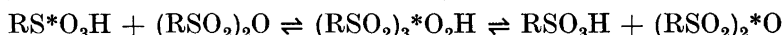
Fig. 1. Exchange between ^{35}S labelled sulfonic acid and unlabelled sulfonic anhydride in CH_3NO_2 at 70.0° . \times approx. 0.025 mmole anhydride per ml and 0.0064 mmole acid per ml. \circ approx. 0.025 mmole anhydride per ml and 0.0016 mmole acid per ml.

menon is not due to spontaneous dehydration of the acid, since when the preheating time was prolonged, no increase in zero-time exchange was observed.

The slope of a graph determines a rate constant, characteristic of each set of conditions. By comparing graphically obtained rate constants it may be shown that these constants are proportional to the ratio of the anhydride concentration to the acid concentration. (This first approximate treatment of data is not shown here, but as will be seen below the result corresponds with expression (14), when the anhydride is in excess, as in these experiments).

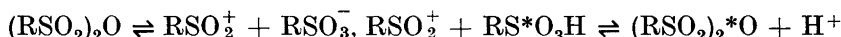
In order to interpret the kinetic data it is necessary to consider a number of mechanisms which could explain the occurrence of an isotopic exchange reaction between an acid and its anhydride.

Firstly, the exchange might occur through an intermediate:



This process is a bimolecular nucleophilic substitution and could be designated $\text{S}_{\text{N}}2$ according to Ingold⁹. Another possible $\text{S}_{\text{N}}2$ mechanism would be attack on the anhydride by the sulfonate ion.

Secondly, a fission of the anhydride might be involved:



this would be a $\text{S}_{\text{N}}1$ process, and here also the sulfonate ion could be the reacting component instead of the free acid. Thus, at least four simple mechanisms are possible.

For the development of the kinetic expressions the following abbreviations are introduced:

t	=	time in seconds
S	=	molar concentration of RSO_3H , free acid.
T	=	» » » RSO_3H , total acid.
H	=	» » » hydrogen ion, H^+
A	=	» » » RSO_3^-
C	=	» » » RSO_2^+
I	=	» » » $(\text{RSO}_2)_3\text{O}_2^-$ or $(\text{RSO}_2)_3\text{O}_2\text{H}$
Ah	=	» » » $(\text{RSO}_2)_2\text{O}$
X^*	=	» » » any of the above compounds X labelled with ^{35}S or ^{131}I .
X_n	=	» » » compound X at n sec.

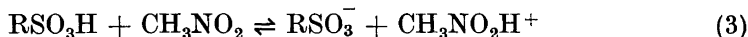
Rate equations. A simple isotopic exchange reaction in a homogeneous stable system follows a simple exponential law, regardless of the mechanism by which the exchange occurs¹⁰. It follows therefore that, *e.g.*, the rate of disappearance of the tagged species, in this case the acid, at any stage of the exchange reaction may be written

$$-\frac{dS^*}{dt} = K (S^* - S_\infty^*) \quad (1)$$

Two possibilities of acid dissociation need consideration. By the autoprotolysis:



the hydrogen ion concentration will become proportional to the acid concentration, while by the solvation:



it becomes proportional to the square root of the acid concentration.

In both cases it is assumed that the acid dissociation is rapid. From this follows:

$$\frac{A^*}{A} = \frac{S^*}{S} = \frac{T^*}{T} \quad (4)$$

and by inserting (4) in (1):

$$-\frac{dT^*}{dt} = K(T^* - T_\infty^*) \quad (5)$$

Since $T^* + \text{Ah}^* = T_\infty^*$, expression (5) may be written

$$-\frac{d\text{Ah}^*}{dt} = K(\text{Ah}^* - \text{Ah}_\infty^*)$$

or integrated

$$\log_{10}(1-F) \equiv \log_{10}(1-\text{Ah}^*/\text{Ah}_\infty^*) = -0.434 K \cdot t \quad (6)$$

The calculation of the coefficient K , which is a function of the concentrations, is the problem to be solved.

By restricting the considerations to the start of the exchange reactions, the value of K may be readily derived. At this point of time the concentration of the radioactive component is known, and eqn. (5) is fully applicable also at zero-time.

From $\frac{T_\infty^*}{T + 2\text{Ah}} = \frac{T_\infty^*}{T}$ it follows that

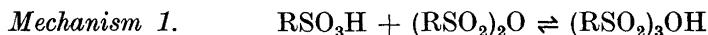
$$T_\infty^* = \frac{T + 2\text{Ah}}{2\text{Ah}} (T_\infty^* - T_\infty^*) \quad (7)$$

In addition use will be made of mass-laws for the macroscopic concentrations, since there is chemical equilibrium in the solution at any time during a run.

Finally it is assumed that the contribution of ions from the anhydride can always be neglected compared to the ions from the acid dissociation.

From this follows that the concentrations of sulfonate ion and hydrogen ion are equal.

In the following, K has been derived for the four simple mechanisms mentioned above.



According to this scheme the rate of disappearance of the labelled acid at zero-time is proportional to the concentration of the labelled undissociated acid and to the concentration of the anhydride:

$$-\left(\frac{dT^*}{dt}\right)_{t=0} = k_1 \cdot \text{Ah} \cdot S_\infty^*$$

By introducing (4) and (7) we get

$$-\left(\frac{dT^*}{dt}\right)_{t=0} = k'_1(T + 2Ah) \cdot S/T \cdot (T_o^* - T_\infty^*)$$

By comparison with (5) it is seen that

$$K = k'_1(T + 2Ah) \cdot S/T \quad (8)$$

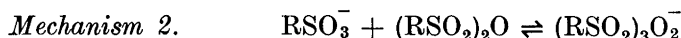
This expression contains the unknown concentration of undissociated acid.

If the acid is only slightly dissociated, $S \cong T$, and (8) becomes

$$K = k'_1(T + 2Ah) \quad (9)$$

If the acid is strongly dissociated, $S \ll T \cong A$. Bearing in mind that S is proportional to A^2 , and therefore also to T^2 , eqn. (8) may be changed into

$$K = k''_1(T + 2Ah)T \quad (10)$$



In this case the rate of disappearance of labelled acid at zero-time is proportional to the concentration of labelled sulfonate ion.

$$-\left(\frac{dT^*}{dt}\right)_{t=0} = k_2 \cdot Ah \cdot A_o^* = k'_2(T + 2Ah) \cdot A/T \cdot (T_o^* - T_\infty^*)$$

and the coefficient K is therefore

$$K = k'_2(T + 2Ah) \cdot A/T \quad (11)$$

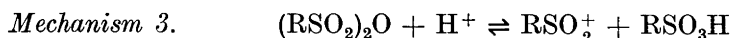
If the acid dissociation is almost complete, $A \cong T$, and if the acid is slightly dissociated according to eqn. (2), A is proportional to T ; in both instances the coefficient K becomes

$$K = k''_2(2Ah + T) \quad (12)$$

though with different values of k''_2 .

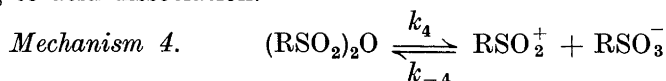
If the acid is slightly dissociated according to eqn. (3),

$$K = k'''_2(2Ah + T)/\sqrt{T} \quad (13)$$



$$-\left(\frac{dT^*}{dt}\right)_{t=0} = k_3 \cdot C \cdot S_o^* = k'_3 \cdot \frac{Ah \cdot H}{S} \cdot \frac{S}{T} \cdot T_o^* = k''_3(T + 2Ah) \cdot A/T \cdot (T_o^* - T_\infty^*)$$

The coefficient K is identical to (11) and may take the form (12) or (13) according to acid dissociation.



$$-\left(\frac{dT^*}{dt}\right)_{t=0} = k_{-4} \cdot C \cdot A_o^* = k_4 \cdot \frac{Ah}{A} \cdot A_o^* = k_4 \frac{(2Ah + T)}{2T} (T_o^* - T_\infty^*)$$

In this case

$$K = k_4(2Ah + T)/2T \quad (14)$$

independent of the acid dissociation, and k_4 is identical to the specific rate of fission of the sulfonic anhydride.

The values of K calculated above have been compiled in the following table.

K proportional to	Mechanism No.
$(2Ah + T)T$	1
$(2Ah + T)$	1,2,3
$(2Ah + T)/\sqrt{T}$	2,3
$(2Ah + T)/T$	4

In order to compare the experimental data with the theoretical expressions it is necessary that the expression $F = (\bar{F} - \bar{F}_0)/(1 - \bar{F}_0)$, where \bar{F}_0 is the apparent zero-time exchange¹⁰, be substituted for the apparent exchange fraction, $\bar{F} = \alpha/\alpha_\infty$.

The values of $\log(1-F)/t$ from experiments run at 70° are shown in a double logarithmic diagram, Fig. 2.

In most of the experiments there has been an excess of anhydride compared to acid, and while the acid concentration has been varied, the anhydride concentration has been rather constant. By introducing these conditions, four curves, corresponding to the four expressions for K listed above, have been drawn in the diagram.

It is seen that while mechanism 4 is acceptable, there is no support in the experimental data for any of the other suggested mechanisms.

The experimental values of the rate constant for the anhydride fission, k_4 , are shown in Table 1. Taking the following values as the most probable ones:

$$1.5 \times 10^{-4} \text{ sec}^{-1} \text{ at } 60^\circ$$

$$3.2 \times 10^{-4} \text{ sec}^{-1} \text{ at } 70^\circ$$

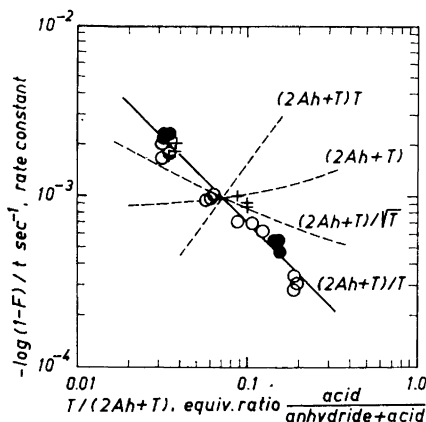


Fig. 2. Exchange between ^{35}S labelled sulfonic acid and unlabelled sulfonic anhydride in CH_3NO_2 at 70.0°. Points with identical signature relate to experiments made from the same preparation-batch of labelled sulfonic acid. Each point denotes one determination of exchange, each group of closely situated points refers to results from one run. The four curves correspond to the four rate expressions, the K -coefficients of which have been listed above.

Table 1. Values of k_4 for the exchange between labelled sulfonic acid and unlabelled sulfonic anhydride in CH_3NO_2 . Each experiment employs normally three determinations of exchange at various times. Range of molar concentrations, acid: 0.0015–0.02, anhydride: 0.02–0.06.

Modification of the sulfonic acid	Temp. °C	Number of experiments	k_4 , 10^{-5} sec^{-1} average and stand. dev.
Monohydrate	60	4	4.7 ± 1.0
Anhydrous	60	3	14.5 ± 2.0
Anhydrous	70	8	32.2 ± 4.7

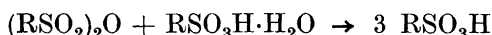
an activation energy of 17 kcal can be calculated for the dissociation of the sulfonic anhydride.

DISCUSSION

The reason for the apparent zero-time exchange could be insufficient separation or co-precipitation of the acid. That recrystallization does not effectively reduce this phenomenon is understandable, since this purification involves application of nitromethane at 80° – 90° to an acid/anhydride-ratio extremely favourable to exchange.

From the spreading of the experimental data shown in Fig. 2 and from the values of k_4 in Table 1, it will be seen that considerable errors are involved in the determination of the rate constant. Direct errors of measurement contribute significantly, since in a determination of k_4 three determinations of specific activities are involved, each of which with an experimental error of 2–3 %. A detailed calculation will show that these errors alone may cause an error in k_4 of 8 %.

However, still greater errors may be caused by uncontrolled amounts of water. Values of k_4 derived from experiments using the monohydrate are 3 times lower than values obtained from anhydrous acid at the same temperature. The reason is possibly a hydrolysis according to the scheme



which, if rapid compared to the exchange reaction, will immediately cause an increase of the concentration of the sulfonic acid to three times that calculated from the weighed amount and a decrease in the concentration of the anhydride.

An implication of this assumption is that even small unknown amounts of water, *e.g.* from insufficient drying of the acid, may cause serious errors in the determination of k_4 . Thus a content of 0.5 % water in the acid (w/w) decreases the value of k_4 by 15 %.

The exchange reaction between acetic acid and acetic anhydride was investigated among others by Evans *et al.*¹¹ Separation-induced exchange prevented accurate kinetic work, but it was concluded that the self-ionization of one of the compounds cannot be fast. Possibly, a mechanism similar to the above may also hold in the carboxyl acid/anhydride exchange.

Sulfonic anhydrides have not previously been investigated kinetically but it may be useful to compare the result of the present experiments with the

kinetics of alcoholysis and hydrolysis of aromatic sulfonyl chlorides. The alcoholysis has been shown to proceed by a S_N2 mechanism^{12,13}, and likewise the hydrolysis is a S_N2 mechanism in acetone-water medium with an activation energy of 13–14 kcal^{12,14,15}. However, in pure water the hydrolysis is changed to that of S_N1 with an activation energy of 18 kcal¹⁴.

Similar observations on the shift of mechanisms were also made on the hydrolysis of benzoyl chloride¹⁶.

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