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Oxygen Exchange of Benzenesulfinic Acids in Water[1]

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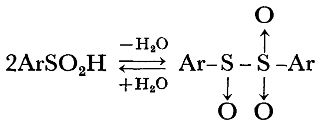
When arenesulfinic acids were heated in water ($H_2{}^{18}O$, 1.52 atom%) at 90—100°C for several hours, the ^{18}O contents of the disproportionation products (thiolsulfonate and sulfonic acid) and the sulfinic acid recovered were approximately the same. The rate of oxygen exchange of *p*-toluenesulfinic acid was much faster than that of methyl phenyl sulfoxide, whereas the rate of oxygen exchange of benzoic acid was much slower than that of benzaldehyde. A mechanism consistent with the kinetic results is proposed for the oxygen-exchange reaction, involving the formation of the sulfinic anhydride (sulfinylsulfone) as an intermediate.

It has long been known that a benzenesulfinic acid yields a thiolsulfonate and a benzenesulfonic acid by disproportionation.[2]

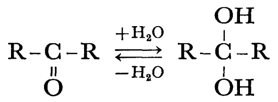
$$3ArSO_2H \longrightarrow ArSO_2SAr + ArSO_3H$$

Kice and his co-workers investigated the mechanism of this reaction in detail; they proposed that the initial step of this multi-step reaction is reversible formation of a sulfinylsulfone.[3]



$$2ArSO_2H \underset{+H_2O}{\overset{-H_2O}{\rightleftarrows}} Ar-\underset{\underset{O}{\downarrow}}{S}-\underset{\underset{O}{\downarrow}}{\overset{\overset{O}{\uparrow}}{S}}-Ar$$

Carbonyl compounds such as aldehydes or carboxylic acids undergo oxygen exchange in water *via* a tetrahedral intermediate, and the rate is first order in the carbonyl compound.[4]



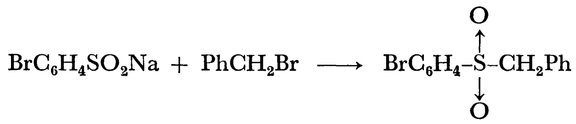
$$R-\underset{\underset{O}{\parallel}}{C}-R \underset{-H_2O}{\overset{+H_2O}{\rightleftarrows}} R-\underset{\underset{OH}{|}}{\overset{\overset{OH}{|}}{C}}-R$$

Since the nature of the oxygen exchange of sulfinic acids appears to be so different from that of the well-known oxygen exchange of carbonyl compounds, a detailed study of this interesting reaction has been carried out, and the results will be described in this paper.

Experimental

Disproportionation of Arenesulfinic Acid in Water-^{18}O. *p*-Bromobenzenesulfinic acid was precipitated by mixing its sodium salt and dilute sulfuric acid in water, the crystals thus formed were washed well with water and dried. An ampoule containing 1.2 g of *p*-bromobenzenesulfinic acid and 3 m*l* of water (^{18}O content, 1.52%) (not all sulfinic acid dissolved in the water at room temperature) was heated at 90±5°C for 12 hr. Crystals of the thiolsulfonate appeared after 2 hr of heating. After 12 hr the crystals of thiolsulfonate were filtered off while the solution was still hot, recrystallized twice from benzene, identified by infrared spectroscopy, and then subjected to the ^{18}O analysis which will be described below.

When the mother liquor was cooled, unchanged sulfinic acid precipitated as white crystals; these crystals were filtered and then converted to the acid's sodium salt by addition of a sodium hydrogen carbonate solution. The well-dried sodium sulfinate was converted, by heating it in an ampoule with 2 g of benzyl bromide, into *p*-bromophenyl benzyl sulfone, which was recrystallized from hexane and then subjected to the ^{18}O analysis.



$$BrC_6H_4SO_2Na + PhCH_2Br \longrightarrow BrC_6H_4-\underset{\underset{O}{\downarrow}}{\overset{\overset{O}{\uparrow}}{S}}-CH_2Ph$$

When an aqueous solution of *S*-benzylisothiuronium chloride was added to the filtrate from the mother liquor, crystals of *S*-benzylisothiuronium *p*-bromobenzenesulfonate appeared; these crystals were filtered, recrystallized from hexane, and then subjected to the ^{18}O analysis. The products of disproportionation of *p*-toluenesulfinic acid and *p*-nitrobenzenesulfinic acid under similar conditions were separated and analyzed by the same procedure.

Rates of Oxygen Exchange of p*-Bromobenzenesulfinic Acid and* p*-Toluenesulfinic Acid.* Sodium salts of the sulfinic acids were converted to the corresponding sulfinic acids by the method described above. By the use of purified dioxane and water (^{18}O content, 1.52 mol %), 1.131 M solution of *p*-bromobenzenesulfinic acid and 1.324 M solution of *p*-toluenesulfinic acid in 30% (v/v) aqueous dioxane were prepared. Aliquots (4 m*l* each) of these solutions were sealed in ampoules, which were then placed in a constant-temperature bath.

After suitable intervals, ampoules were removed from the bath and the reaction was stopped by cooling the ampoules in ice-water and by then converting the acids to sodium sulfinates. By separate experiments it was established that no oxygen exchange of sulfinic acids took place in alkaline media. Evaporation of the solvent *in vacuo* yielded white crystals of sodium sulfinate and excess sodium carbonate. These crystals were dried well *in vacuo* at 90—100°C, and were then allowed to react with benzyl bromide at 105—110°C for 7—10 hr. Then, 50 m*l* of water and 50 m*l* of ether were added to the mixture, and the ethereal solution containing an aryl benzyl sulfone was dried over magnesium sulfate. Evaporation of the ether yielded crude crystals of the sulfone, which were then recrystallized from hexane. From each ampoule, 200—400 mg of a sulfone was obtained.

Synthesis of p*-Bromobenzenesulfinic Acid-^{18}O.* *p*-Bromobenzenesulfinic acid (5 g) was heated in 15 m*l* of water (^{18}O, 1.52 mol %) at 90°C for 2 hr. The solution was cooled with ice, and the crystals thus obtained were filtered. In order to remove completely any *p*-bromobenzenesulfonic acid which might be present in these crystals, the crystals were quickly recrystallized from ordinary water and then

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[1] Organic Sulfur Compounds, Part XXIX.

[2] R. Otto, *Ann.*, **145**, 13,317 (1868).

[3] a) J. L. Kice and K. W. Bowers, *J. Amer. Chem. Soc.*, **84**, 605 (1961). b) J. L. Kice, G. Guaraldi, and C. G. Venier, *J. Org. Chem.*, **84**, 605 (1961). c) J. L. Kice and G. Guaraldi, *J. Amer. Chem. Soc.*, **88**, 5242 (1966).

[4] E. S. Gould, "Mechanism and Structure in Organic Chemistry," Henry Holt and Co., New York (1959), p. 539.

thoroughly dried. The excess oxygen-18 content was 1.232 atom %.

Comparison of the Rates of Oxygen Exchange between p-*Toluenesulfinic Acid and Methyl Phenyl Sulfoxide.* In 19 m*l* of 30% (v/v) aqueous ($H_2{}^{18}O$, 1.52 atom %) dioxane, 3 g of methyl phenyl sulfoxide and 1.7 g of *p*-toluenesulfinic acid were mixed; the solution was then divided into two ampoules, which were placed in a bath at 60°C. One ampoule was removed after 5 hr of heating, while the other was removed after 23.3 hr.

The reaction was stopped by addition of a 5% sodium carbonate solution, after which the sulfoxide was extracted by chloroform. The chloroform solution was dried over magnesium sulfate; the subsequent evaporation of the solvent yielded crude sulfoxide, which was then purified by distillation under reduced pressure (102°C/2 mmHg). The sodium sulfinate present in the aqueous layer was analyzed in a manner similar to that described above.

Comparison of the Rates of Oxygen Exchange between Benzoic Acid and Benzaldehyde. Into 10 m*l* of 30% (v/v) aqueous ($H_2{}^{18}O$, 1.52 atom %) dioxane, 2.5 g of benzoic acid and 1 g of benzaldehyde were mixed; an ampoule containing the solution was then heated at 60°C for 5 hr. Then a 5% sodium carbonate solution was added, and the benzaldehyde was extracted with 50 m*l* of benzene. The benzene solution was dried over anhydrous magnesium sulfate; the subsequent evaporation of the solvent yielded benzaldehyde, which was then purified by distillation under reduced pressure. The aqueous layer was acidified with a dilute hydrochloric acid solution, and the benzoic acid was extracted with ether. The ethereal solution was dried over anhydrous magnesium sulfate; the subsequent evaporation of the solvent yielded crude benzoic acid, which was then recrystallized from hexane.

Analysis of Samples Containing Oxygen-18. By the method reported by Rittenberg,[5] a sample was pyrolyzed in the presence of mercuric chloride and mercuric cyanide at 400°C for 4 hr; the carbon dioxide thus obtained was analyzed by mass spectrometry.

Results and Discussion

At 90°C a 1.25M aqueous solution ($H_2{}^{18}O$, 1.52 atom %) of *p*-bromobenzenesulfinic acid was heated in an ampoule for 12 hr. Similar reactions were carried out with a 4.0M aqueous solution of *p*-toluenesulfinic acid at 100°C for 2 hr and with a 1.5M aqueous solution of *p*-nitrobenzenesulfinic acid at 100°C for 5 hr. The results of the mass-spectrometric analyses of the sulfinic acid recovered are summarized in Table 1.

TABLE 1. INCORPORATION OF ^{18}O IN THE SULFINIC ACIDS RECOVERED AND THE PRODUCTS FORMED ON HEATING IN $H_2{}^{18}O$

	Excess oxygen-18 atom %		
	p-BrC_6H_4-SO_2H	*p*-$CH_3C_6H_4$-SO_2H	*p*-$O_2NC_6H_4$-SO_2H[a]
Recovered			
RSO_2H	1.38	1.02	1.04
Products			
RSO_3H	1.29	0.95	1.15
RSO_2SR	1.31	1.04	1.14

a) No incorporation of ^{18}O in NO_2 group.

The fact that both the sulfinic acid and the reaction products contain approximately the same amount of oxygen-18 indicates that the rate of oxygen exchange is considerably faster than that of disproportionation.

Carbonyl compounds such as carboxylic acids or aldehydes undergo oxygen exchange in water in the presence of an acid, and the rate is first order in the substrate. The rates of oxygen exchange of benzoic acid and benzaldehyde and those of *p*-toluenesulfinic acid and methyl phenyl sulfoxide were determined, the results are summarized in Table 2.

TABLE 2. COMPARISON OF THE RATES OF OXYGEN EXCHANGE[a]

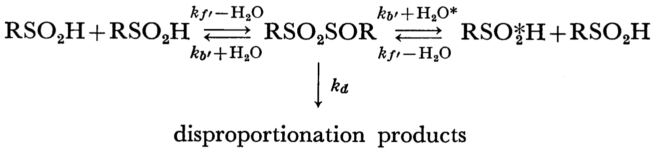
	Excess oxygen-18 atom %	
	5 hr	23.3 hr
p-$CH_3C_6H_4SO_2H$	0.06	0.28
$CH_3\text{-}\underset{\substack{\downarrow\\ O}}{S}\text{-}Ph$	0.03	0.03
Ph-CO_2H	0.01	—
Ph-CHO	0.80	—

a) In 30% (v/v) aqueous ($H_2{}^{18}O$) dioxane, at 60°C.

In the pair of the carbonyl compounds, the rate of oxygen exchange of the aldehyde was much faster than that of the acid, whereas in the pair of the sulfinyl compounds the rate of oxygen exchange of the acid was much faster than that of the sulfoxide, which underwent almost no exchange of oxygen even when it was heated at 60°C for 23.3 hr.

These findings suggest that the mechanism of oxygen exchange of a sulfinic acid is quite different from that of a carbonyl compound.

Kice and his co-workers proposed that the initial step of the disproportionation of a benzenesulfinic acid is reversible formation of a sulfinylsulfone,[2] the following reaction scheme seems plausible as the mechanism for incorporation of oxygen-18 in the sulfinic acid recovered:



$$\begin{tikzcd} RSO_2H+RSO_2H \arrow[r, shift left, "k_{f'}-H_2O"] & RSO_2SOR \arrow[l, shift left, "k_{b'}+H_2O"] \arrow[r, shift left, "k_{b'}+H_2O^*"] \arrow[d, "k_d"] & RSO_2^*H+RSO_2H \arrow[l, shift left, "k_{f'}-H_2O"] \\ & \text{disproportionation products} & \end{tikzcd}$$

The rate of increase of the labelled sulfinic acid, RSO_2^*H, is expressed by the following:

$$\frac{d[RSO_2^*H]}{dt} = k_b[RSO_2SOR][H_2O^*] - k_f[RSO_2^*H][RSO_2H]_T \quad (T = \text{total})$$

By a steady-state assumption for the sulfinylsulfone, the following equations are obtained:

$$\frac{d[RSO_2SOR]}{dt} = k_f[RSO_2H]_T{}^2 - k_b[RSO_2SOR][H_2O]_T - k_d[RSO_2SOR] = 0$$

$$\frac{d[RSO_2^*H]}{dt} = \frac{k_f k_b[H_2O^*]}{k_d+k_b[H_2O]_T}[RSO_2H]_T{}^2 - k_f[RSO_2^*H][RSO_2H]_T$$

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[5] D. Rittenberg and L. Ponticorvo, *Int. J. Appl. Radiat. Isotopes.*, **1**, 208 (1956).

When $k_b[H_2O]_T \gg k_d$,

$$\frac{d[RSO_2^*H]}{dt} = k_f[RSO_2H]_T{}^2\left(\frac{[H_2O^*]}{[H_2O]_T} - \frac{[RSO_2^*H]}{[RSO_2H]_T}\right)$$

$$\frac{d([RSO_2^*H]/[RSO_2H]_T)}{dt} = k_f[RSO_2H]_T\{([H_2O^*]/[H_2O]_T) - ([RSO_2^*H]/[RSO_2H]_T)\}$$

Since both $[RSO_2H]_T$ and $([H_2O^*]/[H_2O]_T)$ are approximately constant under mild conditions,

$$k_f = (1/[RSO_2H]_T \cdot t) \ln [([H_2O^*]/[H_2O]_T)/\{([H_2O^*]/[H_2O]_T) - ([RSO_2^*H]/[RSO_2H]_T)\}]$$

The rates of increase of oxygen-18 in the sulfinic acids recovered were measured, and found to follow the first-order equation described above. The results are shown in Table 3.

Table 3. Rates of ^{18}O-increase in benzenesulfinic acids in 30% (v/v) aqueous dioxane

Sulfinic Acid		p-MeC_6H_4-SO_2H	p-BrC_6H_4-SO_2H	$PhSO_2H$
$[RSO_2H]_0$ (mol/l)		1.32	1.13	1.30
$H_2{}^{18}O$ (atom %)		1.52	1.52	1.52
$10^7 \times k_f$ (M^{-1} sec^{-1})	20.0°C	1.37	2.49	1.42
	40.0°C	12.9	17.4	8.28
	60.0°C	110	—	35.5
	65.0°C	—	133	—
E_a (kcal/mol)		21.5	17.4	15.6
ΔS^* (e. u.)		−21.9	−31.3	−29.4

It is often desirable to prepare ^{18}O-labelled benzenesulfinic acids, which can easily be converted to ^{18}O-labelled sulfoxides and other derivatives; for this purpose the rate constants in Table 3 are valuable for predicting the rates of ^{18}O-incorporation. Under mild conditions, k_d is much smaller than $k_b[H_2O]_T$, and $k_f[RSO_2H]^2$ is approximately equal to the rate of production of the ^{18}O-labelled sufinic acids.

Kice and his co-workers observed that the exchange of oxygen was first-order in a sulfinic acid when a sulfinic acid-^{18}O was subjected to oxygen exchange in acetic aicd containing sulfuric acid as the catalyst or in 60% aqueous dioxane containing perchloric acid and sodium bromide.[6] However, their experimental conditions are quite different from those of the present investigation; the concentration of the mineral acid added as the catalyst was greater than, or equal to, the concentration of a sulfinic acid, and the concentration of a sulfinic acid was very low. Under such highly acidic conditions, it seems likely that the oxygen exchange takes place through a reaction between a protonated sulfinic acid and water, thus it is understandable why the rate was first-order in the sulfinic acid under their conditions.

If the oxygen exchange under our reaction conditions is due to the direct reaction between a sulfinic acid and $H_2{}^{18}O$, the rate of increase in the ^{18}O-content in the sulfinic acid must be independent of the initial concentration of the sulfinic acid. If the oxygen exchange takes place *via* the sulfinylsulfone formed by bimolecular dehydration of the sulfinic acid, the rate of increase in the ^{18}O-content must be greater when the initial concentration of the sulfinic acid is greater.

Table 4. Increase of ^{18}O-content in benzenesulfinic acid in 30% (v/v) aqueous dioxane[a]

$[PhSO_2H]_0$ (mol/l)	Excess oxygen-18 atom % in $PhSO_2H$				
	40°C		60°C		
	24 hr	72 hr	5 hr	7 hr	10 hr
0.649	0.297	0.423	—	0.335	0.371
1.298	0.419	0.551	0.302	—	0.402

a) $H_2{}^{18}O$ atom %, 1.52.

The rates of oxygen exchange were determined in solutions of different sulfinic acid concentrations; the results are summarized in Table 4. The rates of exchange are faster in the solutions with greater sulfinic acid concentrations, this finding made unlikely any direct reaction between the sulfinic acid and water under our experimental conditions.

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[6] J.L. Kice, private communication.