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# Nucleophilic Catalysis in the Hydrolysis of Methoxymethyl Benzenesulfenate, a Formaldehyde Acetal

Tadashi OKUYAMA* and Takayuki FUENO
Faculty of Engineering Science, Osaka University,
Toyonaka, Osaka 560

Acid-catalyzed hydrolysis of methoxymethyl benzenesulfenate is accelerated by nucleophiles ($Cl^-$, $Br^-$, $I^-$, $R_2S$, $AcO^-$, tertiary amines, and the substrate itself) through the attack at the proformyl carbon while water attacks at the sulfenyl sulfur.

Methoxymethyl benzenesulfenate (**1**) has dual structural characteristics as an ester of sulfenic acid and as an acetal of formaldehyde. Typical sulfenate esters undergo nucleophilic attack at the sulfur to result in the S-O bond cleavage.[1)] Cleavage of a formaldehyde acetal occurs by nucleophilic assistance to avoid the formation of unstable methoxymethyl cation as an intermediate,[2)] in contrast to the acid-catalyzed hydrolysis of usual acetals, which proceeds through unimolecular formation of a carbocation intermediate (A-1 mechanism).[3)] The present paper describes hydrolysis of **1** which is strongly catalyzed by various nucleophiles including the substrate itself and occurs mostly by the carbon attack. Only water attacks the sulfur.

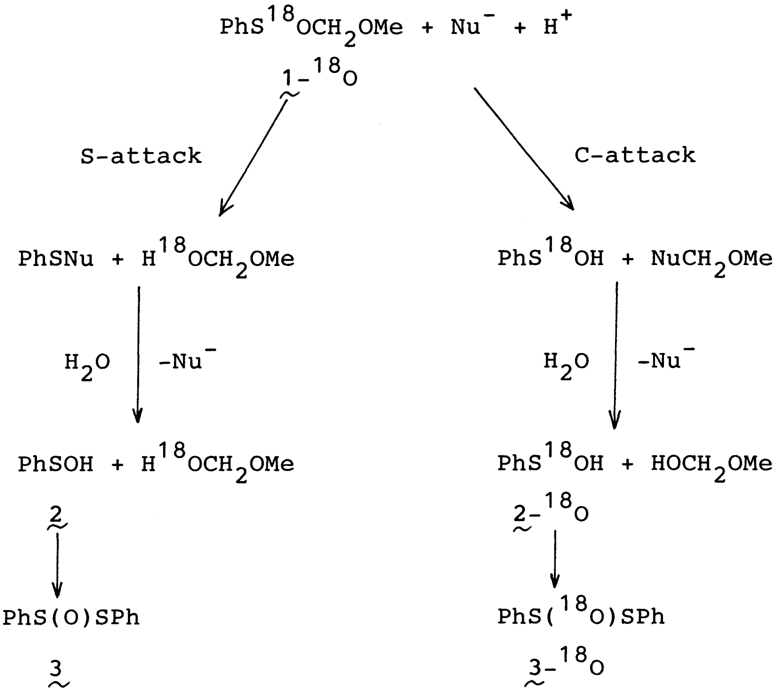
Compound **1**[4)] reacted in water to give S-phenyl benzenethiosulfinate (**3**) which was rapidly formed from the initial hydrolysis product, benzenesulfenic acid (**2**) (Eqs. 1 and 2). Scans of the UV revealed that the spectrum of **1**

$$\underset{\mathbf{1}}{\mathrm{PhSOCH_2OMe}} + \mathrm{H_2O} \longrightarrow \underset{\mathbf{2}}{\mathrm{PhSOH}} + \mathrm{HOCH_2OMe} \qquad (1)$$

$$\mathbf{2} + \underset{\mathbf{1}\ \mathrm{or}\ \mathbf{2}}{\mathrm{PhSOR}} \longrightarrow \underset{\mathbf{3}}{\mathrm{PhS(O)SPh}} + \mathrm{ROH} \qquad (2)$$

smoothly transforms into that of 3 with an isosbestic point at 251 nm. HPLC analysis showed that 3 is formed in > 90% yield. Rates for the formation of 3 were monitored spectrophotometrically at 275 nm. Although pseudo-first-order plots were usually linear to > 90% conversion in buffer solutions and in the presence of nucleophilic catalysts (see below), first-order kinetics broke down in perchloric acid solutions in the absence of added nucleophile. The apparent initial rates increase with increasing concentration of 1 in $HClO_4$. The observed pseudo-first-order rate constant $k_{obsd}$ measured at 25 °C and an ionic strength of 0.5 ($NaClO_4$) in the presence of nucleophile followed the equation, $k_{obsd} = k_0 + k_H[H^+] + k_{Nu}[Nu] + k_{Nu}^H[H^+][Nu]$, relative $k_{Nu}^H$ being $Cl^-$: $Br^-$: $I^-$: $(HOCH_2CH_2)_2S$ : 1 = 1 : 5.8 : 110 : 640 : ca. 50.

To determine which of the S-O and O-C bonds breaks during the reaction (Scheme 1),$^{6)}$ the $^{18}O$-labelled 1$^{7)}$ was subjected to the reaction under essentially the same conditions as those employed for kinetic measurements (10 vol % of acetonitrile was used as a cosolvent). The reaction was quenched at about 50% conversion. The product 3 was extracted with dichloromethane, separated from unreacted 1 by HPLC, and analyzed by mass spectrometry. From the relative intensities of peaks at m/e 234 and 236, the fraction of $^{18}O$ content and



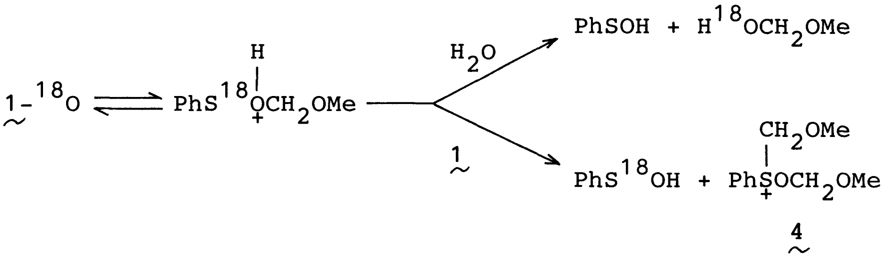
Scheme 1.

Table 1. Bond Cleavage of **1**-$^{18}O$ in 10 vol % Aqueous Acetonitrile[a)]

| $[H^+]$/ mol $dm^{-3}$ | Nucleophile (conc/mol $dm^{-3}$) | $10^3[\mathbf{1}]_0$/ mol $dm^{-3}$ | % $^{18}O$ retention[b)] |
|---|---|---|---|
| $2 \times 10^{-3}$ | none | 0.21 | 32.3 |
| | | 0.62 | 53.0 |
| | | 1.5 | 70.8 |
| | | 3.0 | 79.4 |
| $5 \times 10^{-4}$ | $Cl^-$ (0.10) | 2.0 | 88.6 |
| $2 \times 10^{-4}$ | $R_2S$[c)] ($5 \times 10^{-4}$) | 1.0 | 90.8 |
| | | 2.0 | 87.3 |
| [AcOH]=[$AcO^-$]=0.10 mol $dm^{-3}$ [d)] | | 2.0 | 96.7 |
| [$MESH^+$]=[MES]=0.025 mol $dm^{-3}$ [e)] | | 2.0 | 89.4 |

a) Reaction was carried out at 25 °C and quenched after about one halftime of reaction. b) % $^{18}O$ retained in the product **3**. c) $(HOCH_2CH_2)_2S$. d) Acetate buffer. e) A buffer solution of 2-morpholinoethanesulfonate.

% retention of $^{18}O$ in **3** were calculated (Table 1). The latter values correspond to % reaction occurring at the carbon if the $^{18}O$ exchange in **2** and **3** can be neglected. Data in Table 1 show that the nucleophile-catalyzed reactions occur mostly at the carbon (> 90%), while the reaction in the absence of added nucleophile (in $HClO_4$) greatly depends on $[\mathbf{1}]_0$. This and the kinetic observation that the rate increases with $[\mathbf{1}]_0$ indicate that **1** is acting as a nucleophilic catalyst, attacking at the carbon while water attacks at the sulfenyl sulfur (Eqs. 3 and 4).



(3)

$$\mathbf{4} + H_2O \longrightarrow HOCH_2OMe + \mathbf{1} \qquad (4)$$

In accord with these results, reaction of 1 in ethanol catalyzed by *p*-toluenesulfonic acid was found to be mostly alcohol exchange in the absence of added nucleophile, while it was the formation of 3 in the presence of $Br^-$.

In conclusion, acid-promoted nucleophilic reaction of 1 occurs mostly at the proformyl carbon except for water. This exception may be related to the low nucleophilicity of water which makes the reaction proceed through the early transition state. Although the reaction can be viewed as a hydrolysis of a formaldehyde acetal with sulfenic acid as a leaving group, the apparent kinetic features are much different from those observed for the acetals of phenols.[8] The unique structural feature of the leaving sulfenic acid, an "α-effect" nucleofuge, may have some bearing on the observed reactivities.

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References

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3) E. H. Cordes and H. G. Bull, Chem. Rev., 74, 581 (1974).

4) Compound 1 was obtained through rearrangement by vacuum distillation of methoxymethyl phenyl sulfoxide.[5]

5) T. J. Maricich and C. K. Harrington, J. Am. Chem. Soc., 94, 5115 (1972).

6) Cleavage at the methoxy oxygen might be possible, but is less likely from leaving ability and electrophilicity considerations.

7) The labelled compound $1\text{-}^{18}O$ was prepared by the reaction sequence:

$$\mathrm{PhSCH_3} \xrightarrow{\mathrm{Br_2,\ H_2{}^{18}O}} \mathrm{PhS(^{18}O)CH_3} \xrightarrow{\mathrm{Br_2}} \mathrm{PhS(^{18}O)CH_2Br} \xrightarrow{\mathrm{MeONa}}$$

$$\mathrm{PhS(^{18}O)CH_2OMe} \xrightarrow{\Delta} 1\text{-}^{18}\mathrm{O}.$$ The $^{18}O$ content was about 91%.

8) The formaldehyde acetal of 2,4-dinitrophenol was subject only to very weak nucleophilic catalysis without any assistance of acid[2] while the acetal of *p*-chlorophenol did not undergo any nucleophilic catalysis.[9]

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