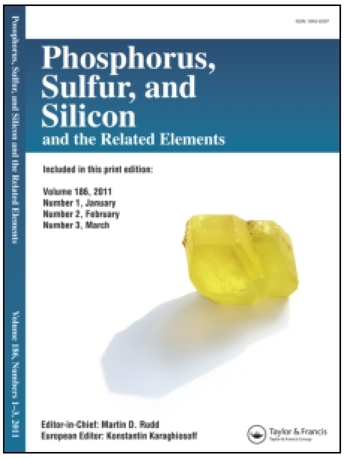

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Communication

INTRAMOLECULAR PARTICIPATION OF THE SULFINYL GROUP IN THE HYDROLYSIS OF THE ESTER FUNCTION OF AN α-PHOSPHORYL SULFOXIDE

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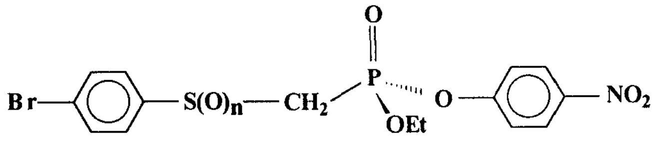
The alkaline hydrolysis of ethyl 4-nitrophenyl (4'-bromophenylsulfinyl)methylphosphonate is favored by the neighboring-group participation of sulfinyl oxygen.

Key words: Phosphoryl group transfer; hydrolysis; reaction mechanisms; neighboring group participation.

As part of our investigations on the role of carbanions as potential internal nucleophiles in dissociative elimination-addition (EA) mechanisms of alkaline hydrolysis of phosphoryl compounds,[1] we have undertaken a kinetic study on the hydrolysis of ethyl 4-nitrophenyl (4'-bromophenylthio)methylphosphonate **1**, ethyl 4-nitrophenyl (4'-bromophenylsulfinyl)methylphosphonate **2** and ethyl 4-nitrophenyl (4'-bromophenylsulfonyl)methylphosphonate **3** (alternatively named α-phosphoryl sulfide, sulfoxide and sulfone respectively).



1: n = 0; **2**: n = 1; **3**: n = 2.

RESULTS AND DISCUSSION

Reactions were carried out in water solution at 25°C and were followed spectrophotometrically by monitoring the release of 4-nitrophenoxide ion at 400 nm. The results are shown as pH-rate profiles in Figure 1. Only for the more acidic sulfone **3** the inflection due to the ionization of the substrate was observed in the exploitable pH range. The observed pseudo-first-order rate constants for the hydrolysis of

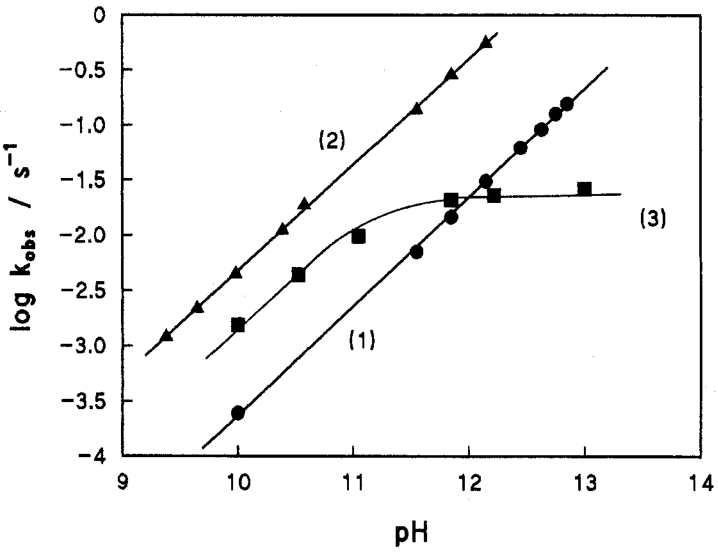


FIGURE 1 pH-rate profiles for the hydrolyses of the α-phosphoryl sulfide (**1**), sulfoxide (**2**) and sulfone (**3**) at 25°C in water; ionic strength 0.1 M (KCl).

esters **1** and **2** were proportional to hydroxide ion concentration according to the rate law (1):

$$k_{obs} = k_{OH}[OH^-] \tag{1}$$

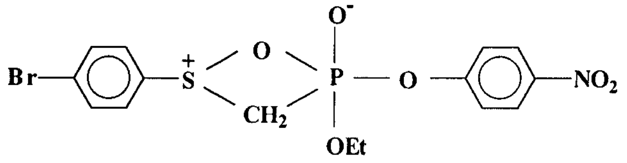
with $k_{OH} = 1.58 \pm 0.01$ dm^3 mol^{-1} s^{-1} for **1** and $k_{OH} = 48.67 \pm 1.62$ dm^3 mol^{-1} s^{-1} for **2**. The hydrolysis of ester **3** follows the rate law (2):

$$k_{obs} = k_a/1 + (a_H/K_a) \tag{2}$$

where $k_a = (2.63 \pm 0.04) \times 10^{-2}$ s^{-1} is the k_{obs} in the pH independent region and $pK_a = 11.27 \pm 0.03$ (kinetically determined) is the ionization constant of the substrate, from these data a value of 14.12 dm^3 mol^{-1} s^{-1} was calculated for the apparent second-order rate constant (k_aK_a/K_w).

Values of the activation entropy are quite negative (-25.0 ± 1.1, -34.4 ± 0.1 and -15.2 ± 1.5 cal mol^{-1} K^{-1}, for esters **1**, **2** and **3**, respectively), thus suggesting that associative mechanisms are operating for all the substrates; moreover, as it is often observed for this type of mechanism, weak catalysis by carbonate buffer was noticed in every case. Finally, also comparison between the second-order rate constants for the hydrolysis of esters **1–3** with that for the hydrolysis of ethyl 4-nitrophenyl phenylphosphonate ($k_{OH} = 1.09$ dm^3 mol^{-1} s^{-1}), which cannot react through EA mechanisms since it is devoid of acidic α-hydrogen, does not support the alternative pathway via a carbanion-promoted dissociative mechanism. This result is in agreement with our previous findings on the predominance of associative reactions at phosphorus in similar systems.[1]

However, it is surprising that the second-order rate constants do not follow the order expected on the basis of the well known electron-withdrawing effects of the thia, sulfinyl and sulfonyl groups.[2] This anomalous result could be due, in principle,



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either to an abnormally low reactivity of the sulfone **3** or to an abnormally high reactivity of the sulfoxide **2**. It has been reported, indeed, that the sulfonyl group may exert a retarding effect on S_N2 displacements at the α-carbon atom and it was suggested that this behavior is due to a combination of steric and field effects, vanishing in the β or more remote position.[3] However, taking into account that in compound **3** the sulfonyl group is in a β position with respect to the reaction centre, the phosphorus atom, and that most likely a smaller steric compression is exerted on addition of hydroxide ion to tetrahedral phosphorus than on addition of the nucleophiles employed in the previous works[3] on tetrahedral carbon atom, it is reasonable to discard a steric retarding effect in the present case. Examination of space-filling molecular models gives further support to this conclusion.

It is well known[2] that sulfoxides are stronger bases than sulfones; moreover the sulfoxide oxygen has high nucleophilic character, as shown by several examples reported in the literature.[4] In this connection we suggest that the increased reactivity of **2** may be due to the intervention of the adjacent sulfinyl group. It could be either direct nucleophilic assistance, in which the sulfoxide oxygen attacks the phosphorus atom (a similar assistance giving rise to cyclic intermediates or transition states has been proposed for the solvolysis of chloroalkylsulfoxides)[5] thus helping the attack of hydroxide ion onto phosphorus atom, or general base catalysis. The deuterium oxide solvent isotope effect observed in the hydrolysis of **2** (k_H/k_D = 0.87) provides a conventional argument[6] against general base catalysis thus suggesting that anchimeric assistance by sulfinyl oxygen occurs.

The hydrolysis of the α-phosphoryl sulfoxide **2** seems therefore to proceed through a two-stage process: the first step gives rise to a cyclic intermediate (**4**) which subsequently undergoes the attack of hydroxide ion in the second, rate-determining step. The intermediate **4**, resembling an oxathiaphosphetane, a four-membered cyclic derivative of the well known phosphetane,[7] may suffer the attack of hydroxide ion either on the sulfur atom, as previously reported for other systems,[4b] or on the phosphorus. In the latter case the involvement of an octahedral transition state, similar to those proposed in the putative hexacoordinate mechanism of phosphoryl transfer reactions,[7] would be required.

However, an alternative concerted mechanism, in which assistance of the sulfinyl oxygen and attack of hydroxide ion, on either sulfur or phosphorus, take place synchronously, cannot be discarded on the grounds of our preliminary results and further work is required to elucidate these mechanistic features.

The rate enhancement observed in the hydrolysis of **2** is moderate, but, if it is taken into account that the effectiveness of nucleophilic participation to reaction of the sulfinyl group could be considerably reduced owing to strong solvation by water,[4b] it is still noteworthy as it represents, to our knowledge, the first example of intramolecular assistance to nucleophilic displacement at the tetrahedral phosphorus.

EXPERIMENTAL

Ethyl (4-bromophenylthio)methylphosphonic acid, obtained by alkaline hydrolysis of the corresponding diethyl phosphonate,[9] was coupled with 4-nitrophenol in the presence of dicyclohexylcarbodiimide to afford **1**. This compound was readily oxidized by hydrogen peroxide/trifluoroacetic anhydride or 3-chloroperbenzoic acid to give **2** and **3**, respectively. Esters **1** and **2** are liquid compounds, and as it is known[10] that α-phosphoryl sulfoxides are thermally unstable and cannot be distilled they were purified by chromatography. The sulfone **3** was recrystallized from toluene (m.p. 108–9°C). All the esters gave excellent ^{1}H NMR spectra.

Kinetic experiments were carried out as previously described.[1]

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