

Thiol Ester Aminolysis in Acetonitrile

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The kinetics of the reactions of *p*-nitrophenyl thiolacetate with several amines in acetonitrile was studied. Hydrazine exhibits considerably greater nucleophilicity than expected from its pK_a value. Common mechanism is suggested for the aminolysis of the thiol ester and its oxygen analogue.

Since the active sites of enzymes have solvent properties resembling dipolar aprotic solvents, reactions of esters and thiol esters with nucleophiles in such media are of considerable interest.

In this paper we present the first kinetic investigation of the aminolysis of a thiol ester in a dipolar aprotic solvent. Aminolysis rates of *p*-nitrophenyl thiolacetate were measured conductometrically at 25 ± 0.05 °C, under pseudo first order conditions. The initial concentration of the thiol ester was 5×10^{-5} M. Observed rate constants were reproducible to $\pm 4\%$.

The reactions follow the rate equation:

$$-\frac{d[\text{thiol ester}]}{dt} = (k[\text{amine}] + k'[\text{amine}]^2) [\text{thiol ester}].$$

Our results are listed in Table I.

Tab. I. Second order rate constants for the aminolysis of *p*-nitrophenyl thiolacetate in acetonitrile at 25 °C.

Amine	pK_a in acetonitrile ^a	k [$M^{-1}s^{-1}$]
1 Imidazole ^b	13.8	0.116
2 Hydrazine	16.61	38.3
3 Morpholine	16.61	2.68
4 Benzylamine	16.76	0.960
5 <i>n</i> -Propylamine	18.22	7.15
6 Piperidine	18.92	57.3

^a From ref. ²; ^b third order term only in the reaction with imidazole is detectable.

The Brønsted plot ($\log k$ vs pK_a , slope 0.49) shows considerable scatter ($r=0.951$). Examination of Table I, however, reveals that hydrazine undoubtedly exhibits an alpha effect *i.e.* a nucleophilicity significantly greater than expected from its pK_a value. Alpha effect has not previously been observed for thiol ester reactions in non-hydroxylic solvents.

Our kinetic results strongly suggest a common mechanism for the aminolysis of the thiol ester and its oxygen analogue in acetonitrile because

a) the Brønsted parameters are nearly identical (0.54 for the reaction of *p*-nitrophenyl acetate¹ at 30 °C showing similar scatter as for the thiol ester),

b) the logarithms of our second order rate constants ($\log k$) give an excellent linear correlation ($r=0.998$) with the same quantities for the reaction of the ester² ($\log k_0$) at 30 °C. The slope of the straight line is near unity (Fig. 1).

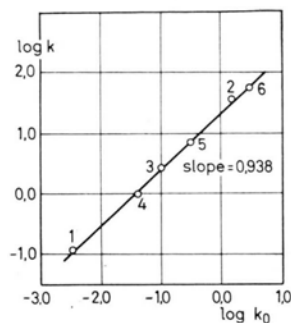


Fig. 1. $\log k$ vs $\log k_0$ plot. The numbering of the amines is the same as in Table I.

Thus, the aminolysis of *p*-nitrophenyl thiolacetate in acetonitrile involves the sulfur analogue of the tetrahedral intermediate demonstrated recently for ester aminolyses in dipolar aprotic solvents^{3,4}.

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