# Effect of Hydrophobic Interaction on the Rate of Aminolysis of *p*-Nitrophenyl Acetate by Decylamine

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*Summary* The self-catalysed reaction of decylamine with *p*-nitrophenyl acetate is at least 200 times faster than the corresponding reaction of ethylamine.

HYDROPHOBIC forces provide much of the driving force for interactions between non-polar molecules or side chains in aqueous solution.[1] They are important in enzyme–substrate binding[2] and in maintaining the tertiary structure of proteins.[3]

There are a few reports of quite striking rate increases of simple reactions through hydrophobic interaction.[4–6] One of the more convincing examples is the demonstration by Knowles and Parsons[5] that the reaction between *p*-nitrophenyl decanoate and decylamine proceeds at least 100 times faster than would be predicted from the corresponding reaction between *p*-nitrophenyl acetate and ethylamine.[1,5]

I have investigated the reaction between *p*-nitrophenyl acetate and decylamine in ethanol–water. Under these conditions, I could use higher amine concentrations than Knowles and Parsons without exceeding the critical micelle concentration.[7] In concentrations of ethanol < 8M the reaction clearly shows a greater than first-order dependence on amine concentration, indicating catalysis of the aminolysis by a second amine molecule.

In general, aminolysis of an ester can proceed by both amine-catalysed or uncatalysed (water-catalysed) pathways[8] but amine catalysis of the reaction between an ester as labile as *p*-nitrophenyl acetate and amine as strongly basic as decylamine ($pK = 10{\cdot}64$)[9] has not previously been reported.[10] I have confirmed that the reaction with ethylamine ($pK = 10{\cdot}60$)[11] remains strictly first order with respect to amine concentration in the presence of up to at least 10M-ethanol. Rate constants and experimental conditions are summarised in the Table. The rate constants for decylamine in the absence of ethanol are the least reliable because the concentration range is restricted by the low critical micelle concentration (0·005M). Curvature is just detectable (see Figure) and by carrying out a large number of runs, I was able to measure $k_2$ with an accuracy of better than 20%.

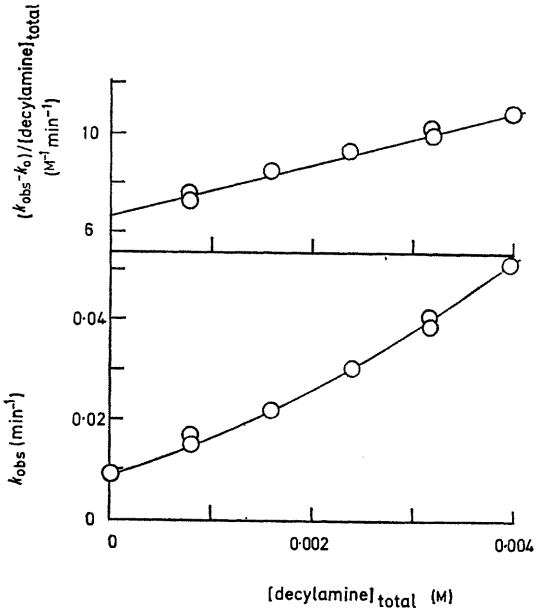


FIGURE. *The effect of increasing amine concentration on observed first-order rate constants,* $k_{obs}$, *and apparent second-order rate constants,* $(k_{obs}-k_0)/[amine]$, *for the reaction of* p-*nitrophenyl acetate with decylamine in the absence of ethanol.*

The different behaviour of ethylamine and decylamine

cannot be rationalised without invoking hydrophobic forces. Their basicities are not sufficiently different ($\Delta pK = 0.04$) to account for it. Steric effects, also, can be discounted because amine catalysis of aminolysis of phenyl acetate is *more* difficult to detect for n-butylamine than for methylamine.[12] All experiments were carried out below the critical micelle concentration.

To determine the magnitude of the effect, the decylamine reaction should be compared with the corresponding self-catalysed reaction of ethylamine.

This rate constant cannot be measured directly because the catalysed reaction accounts for such a small fraction of the observed rate of disappearance of *p*-nitrophenyl acetate. However, I estimated upper limits for it by assuming that a 10% increase in the observed rate due to the catalysed reaction could have gone undetected. This treatment shows (see Table) that with decylamine the catalysed reaction proceeds at least 200 times faster than with ethylamine. Jencks and Salvesen[13] have shown that the intramolecular general base-catalysed aminolysis of acetylimidazole by ethylenediamine is 1000 times faster than aminolysis by glycine which has almost the same basicity. Approximation of the long-chain amine molecules by hydrophobic interaction has much the same effect as the combination of two amine groups on a single molecule in ethylenediamine.

*Rate constants*[a] *for the aminolysis of* p-*nitrophenyl acetate at* 25°

| | Ethylamine[b] | | | | Decylamine[c] | | | |
|---|---|---|---|---|---|---|---|---|
| [EtOH] (M) | Number of runs | $k_0$[d] ($min^{-1}$) | $k_1$[e] ($M^{-1}min^{-1}$) | $k_2$[f] ($M^{-2}min^{-1}$) | Number of runs | $k_0$[d] ($min^{-1}$) | $k_1$[d] ($M^{-1}min^{-1}$) | $k_2$[f] ($M^{-2}min^{-1}$) |
| 0 | 6 | 0·0111 | 7·22 | < 5[g] | 10 | 0·0087 | 6·7[h] | *ca.* 1000[h] |
| 2·53 | 6 | 0·0130 | 15·6 | < 5[g] | 6 | 0·0135 | <10[i] | 6820 |
| 4·63 | 6 | 0·0246 | 28·8 | < 5[g] | 6 | 0·0238 | <10[i] | 8300 |
| 6·43 | 6 | 0·0282 | 37·2 | <10[g] | 6 | 0·0290 | 64 | 3100 |
| 7·93 | 6 | 0·0298 | 47·2 | — | 6 | 0·0383 | 72 | — |
| 9·21 | 6 | 0·0340 | 41·0 | — | 6 | 0·0428 | 76 | — |

[a] Obtained by following the formation of *p*-nitrophenolate ion at 400 nm. All rate constants have been calculated in terms of total amine concentration ([B] + [$BH^+$]). The initial ester concentration was $3 \times 10^{-5}$M.
[b] 2·2% free base, in 0·05M-borate buffer. (There was no detectable buffer catalysis.) Concentration range: 0—0·018M-total amine.
[c] 1·2% free base, in 0·05M-borate buffer. Concentration range: 0—0·010M-total amine, unless otherwise stated. (There was no detectable buffer catalysis.)
[d] Rate constant at zero amine concentration.
[e] Slope of $k_{obs}$ *vs.* amine concentration or, for curved plots, the intercept at zero amine concentration of $(k_{obs} - k_0)$/[amine] *vs.* [amine].
[f] Slope of $(k_{obs} - k_0)$/[amine] *vs.* [amine].
[g] See text.
[h] Concentration range: 0—0·004M-total amine.
[i] Maximum intercept of $(k_{obs} - k_0)$/[amine] *vs.* [amine] at zero amine concentration, which the data allow.

As would be expected,[3] large concentrations of ethanol (> 7·93M) greatly reduce or destroy the hydrophobic interaction and in these solutions $k_2$ is too small to be measurable. Interestingly, $k_2$, for decylamine, has its *maximum* observed value in 4·63M-ethanol, following the change in the structure of the mixed solvent with increasing ethanol concentration.[14] Increased solvent structure appears to increase the driving force for hydrophobic interaction.

(*Received, August 28th,* 1970; *Com.* 1447.)

[1] W. P. Jencks, "Catalysis in Chemistry and Enzymology," McGraw-Hill, New York, 1969.
[2] W. P. Jencks, *Ann. Rev. Biochem.*, 1963, **32**, 639.
[3] C. Tanford, *J. Amer. Chem. Soc.*, 1962, **84**, 4240.
[4] R. P. Bell, E. Gelles, and E. Moller, *Proc. Roy. Soc.*, 1949, **198A**, 308.
[5] J. R. Knowles and C. A. Parsons, *Chem. Comm.*, 1967, 755.
[6] T. W. Wagner, C. J. Hsu, and C. S. Pratt, *J. Amer. Chem. Soc.*, 1967, **89**, 6366.
[7] A. Vies and C. W. Hoerr, *J. Colloid Sci.*, 1960, **15**, 427.
[8] T. C. Bruice and S. J. Benkovic, "Bioorganic Mechanisms," Benjamin, New York, 1966, vol. 1.
[9] C. W. Hoerr, M. R. McCorkle, and A. W. Ralston, *J. Amer. Chem. Soc.*, 1943, **65**, 238.
[10] T. C. Bruice and M. F. Mayahi, *J. Amer. Chem. Soc.*, 1960, **82**, 3067.
[11] H. T. S. Britton and W. G. Williams, *J. Chem. Soc.*, 1935, 796.
[12] W. P. Jencks and M. Gilchrist, *J. Amer. Chem. Soc.*, 1966, **88**, 104.
[13] W. P. Jencks and K. Salvesen, *Chem. Comm.*, 1970, 548.
[14] F. Franks and D. J. G. Ives, *Quart. Rev.*, 1966, **20**, 1.