Tetrahedron Letters No.43, pp. 3839-3841, 1965. Pergamon Press Ltd.
Printed in Great Britain.

SUPERIMPOSED GENERAL BASE CATALYSIS IN ANILIDE HYDROLYSIS[1]

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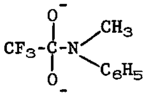
(Received 14 August 1965)

Biechler and Taft[2] showed that 2,2,2-trifluoro-N-methylacetanilide (I) hydrolyzes at a rate given by eq. 1, and attributed the term second-order in hydroxide to the intermediacy of the dinegative ion II.

$$-d[I]/_{dt} = [I]\ (k_1[HO^-] + k_2[HO^-]^2) \qquad (1)$$



II

We have confirmed eq. 1 and have in addition shown by studies in buffered solutions (Table I) that general base catalysis is superimposed on hydroxide-ion catalysis in the hydrolysis of I. The complete rate expression in basic solution is then given by eq. 2, where the summation is over all bases, B_i, present. The values of k_i for various bases are shown in Table II.

$$-d[I]/_{dt} = [I]\ [HO^-]\quad (k_1 + \sum_i k_i[B_i]) \qquad (2)$$

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[1] This research was supported by the National Institutes of Health under Research Grant No. GM-12477-01.

[2] S. S. Biechler and R. W. Taft, Jr., J. Amer. Chem. Soc., 79, 4927 (1957).

TABLE I.

Hydrolysis of 2,2,2-Trifluoro-N-methylacetanilide in Glycine/Glycinate Buffers at 25.5°

Sodium Glycinate,[a] M.	$k_{obs}/[HO^-]$, M.$^{-1}$sec.$^{-1}$
0.00238	4.4
0.00476	6.2
0.00594	6.8
0.00952	9.1

a. [glycine]/[glycinate] = 1.05; μ = 0.010 (added potassium chloride).

TABLE II.

Catalytic Constants[a] for Superimposed General Base Catalysis of the Hydrolysis of 2,2,2-Trifluoro-N-methylacetanilide at 25.5°

B_i	k_i (M.$^{-2}$sec.$^{-1}$)
H_2O	2.0/55.5
D_2O	2.5/55.4
$NH_3^+CH_2CO_2^-$	(1.9×10^2)[b]
$NH_2CH_2CO_2^-$	(3.3×10^2)
HO^-	5.6×10^2
DO^-	9.3×10^2

a. Constants for H_2O and D_2O are determined as second-order rate constants, those for all other bases as third-order rate constants.

b. See footnote 4.

The Brönsted catalysis law[3] is obeyed by the catalysts water, glycinate ion and hydroxide ion with $\beta \sim 0.25$, but glycine exceeds its predicted efficiency, probably because of general-acid or bifunctional catalytic activity.[4]

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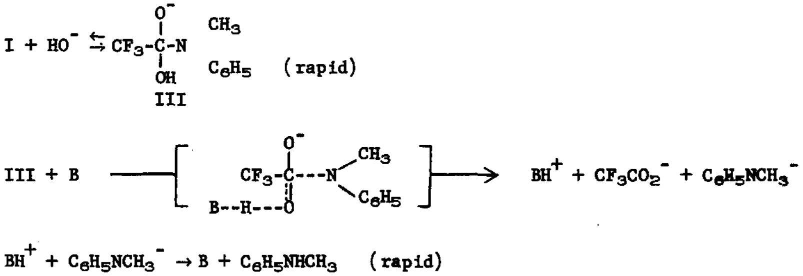
[3] A. A. Frost and R. G. Pearson, Kinetics and Mechanism, 2nd ed., pp. 218ff. John Wiley and Sons, Inc., New York (1961).

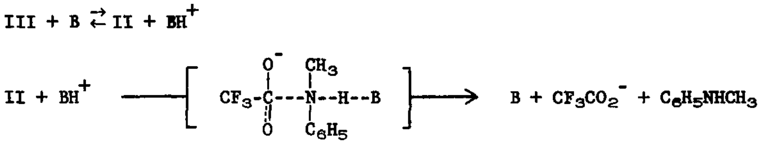
[4] The rate constant for glycine may be spuriously large due to simple nucleophilic catalysis by glycinate ion, a possibility we are investigating.

Mechanisms A ("classical general base catalysis") and B ("inverse classical general base catalysis"), the latter involving the Biechler-Taft intermediate, appear the most reasonable explanations of the observations. Our continuing studies of this and related reactions are directed toward the distinction of these mechanisms.

Mechanism A.



Mechanism B.



Kirsch and Jencks[5] have observed a similar type of catalysis of the hydrolysis of esters, in which general-base catalysis (by hydroxide ion and imidazole) is superimposed on nucleophilic catalysis by imidazole. General catalysis, difficult to characterize more exactly at present, has been observed by Mader in the hydrolysis of trifluoroacetanilide.[6]

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5. J. F. Kirsch and W. P. Jencks, J. Amer. Chem. Soc., **86**, 833 (1964).
6. P. M. Mader, J. Amer. Chem. Soc., **87**, 3191 (1965).