Tetrahedron Letters No. 31, pp. 2905-2906, 1971. Pergamon Press. Printed in Great Britain.

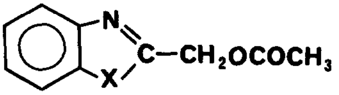
RATE OF ALKALINE HYDROLYSIS OF SOME UNUSUAL ACETATE ESTERS

Robert D. Cook[1] and Syrus Razmara[2]

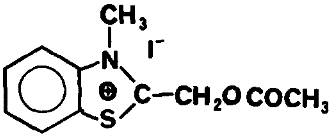
Department of Chemistry, American University of Beirut, Beirut, Lebanon

(Received in UK 21 June 1971; accepted in UK for publication 2 July 1971)

The alkaline hydrolysis of the acetates of 2-hydroxymethylbenzimidazole (I), 2-hydroxymethylbenzthiazole (II), N-methyl-2-hydroxymethylbenzimidazole (III), and N-methyl-2-hydroxymethylbenzthiazolium iodide (IV) was studied.

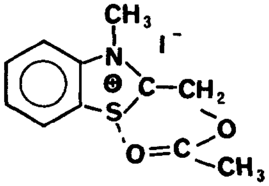


I X = N-H
II X = S
III X = N-CH_3

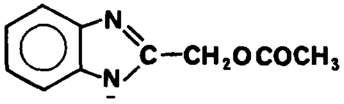


IV

These unusual benzylic-type acetates are interesting because of the possibility of intramolecular catalysis during hydrolysis. Imidazole has been shown to be a catalyst in ester hydrolysis, acting both as a nucleophile[3] and as a general base[4]. The azolium compound (IV) presents the possibility of electrophilic catalysis, which could be visualized as an electrostatic interaction that would increase the electropositivity of the carbonyl carbon (IVa)[5].



IVa



Ia

The rates of hydrolysis of I, II, and III were followed titrimetrically and were shown to be second order; first order in base and first order in ester (Table I). Compound IV was completely hydrolyzed into the expected alcohol and acid in five minutes.

The fact that the rates of hydrolysis of I, II, and III are dependent on base concentration seems to rule out intramolecular catalysis, where it has been shown that overall first order kinetics should prevail[3]. The data suggests that the mechanism is a nucleophilic acyl substitution. The relative rates qualitatively follow the order of expected basicity (on the basis of electronegativity) of the leaving alkoxide. Robinson and Matheson[6] have recently gathered a large amount of data on different esters, including acetates, which indicates that there is a

Table I

Second Order Rate Constants for the Alkaline Hydrolysis[a] at 0°C in 90% Dimethoxyethane-Water

Compound	$k_2 \times 10^3 M^{-1} sec^{-1}$	Relative Rate
I	28	2.3
II	126	10.5
III	167	14
IV	$>10^3$	$>10^2$
Benzyl Acetate	12	1

[a] (Ester) = (Base) = 0.005M.

linear relationship between the rate of alkaline hydrolysis of the ester and the pKa of the corresponding alcohol. The rate for compound I is, however, lower than one would expect on this basis. This low rate can be attributed to a small degree of ionization of the N-H bond of the imidazole. The ionized ester Ia would be expected to hydrolyze slowly with respect to I.

The pKa of the corresponding alcohol of ester IV would be expected to be low[7], and therefore the rate of hydrolysis should be quite fast. More work, especially in buffered solutions, is therefore needed to determine what part electrophilic catalysis is playing, if any.

Acknowledgement: The authors thank the Arts and Sciences Research Committee of the American University of Beirut for financial support.

References:

1. To whom correspondence should be addressed.
2. Syrus Razmara, M.S. Thesis, American University of Beirut, 1970.
3. G.L. Schmir and T.C. Bruice, J. Am. Chem. Soc., 80, 1173 (1958); T.C. Bruice, ibid., 81, 5444 (1959); U.K. Pandit and T.C. Bruice, ibid., 82, 3386 (1960).
4. T.C. Bruice and G.L. Schmir, ibid., 79, 1663 (1957).
5. J. Casanova, Jr., N.D. Werner, and H.R. Kiefer, ibid., 89, 2411 (1967).
6. J.R. Robinson and L.E. Matheson, J. Org. Chem., 34, 3630 (1969).
7. J. Crosby, R. Stone, and D.E. Lienhard, J. Am. Chem. Soc., 92, 2891 (1970). In a footnote of the above paper the pKa of the thiazolium alcohol (2-(1-hydroxyethyl)-3,4-dimethylthiazolium ion is reported to be 11.4.