Tetrahedron Letters No. 1, pp 61 - 62, 1978. Pergamon Press. Printed in Great Britain.

HYDROLYSIS OF ORTHOESTERS : APPLICATION TO COMPOUNDS WHICH HYDROLYSE WITH STEREOELECTRONIC CONTROL

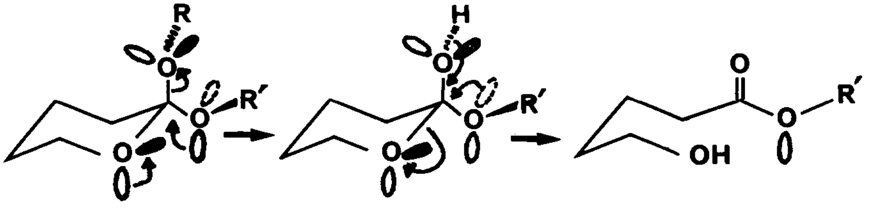
Otmane BOUAB, Claude MOREAU* and Mathias ZEH AKO

Laboratoire de Chimie Organique Physique, U.S.T.L., 34060 MONTPELLIER CEDEX, FRANCE

(Received in UK 18 October 1977; accepted for publication 11 November 1977)

We wish to report the results obtained for the hydrolysis of orthoesters which have been shown to hydrolyse with stereoelectronic control .

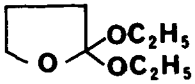
Stereoelectronic control implies that the specific cleavage of a carbon - oxygen bond is allowed only if the two other oxygens each have an orbital oriented antiperiplanar to the O-alkyl leaving group[1] . The important consequence of this control to the stereochemical course of hydrolysis of 2,2-dialkoxytetrahydropyrans has been unambiguously demonstrated[2] (scheme 1) but its influence on the kinetics of hydrolysis has not to date been established .



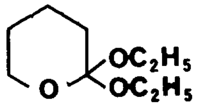
R	R′
CH_3	C_2H_5
CD_3	CH_3
C_2H_5	CH_3

Scheme 1

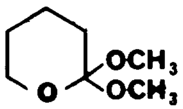
The results of such a study carried out on three orthoesters :2,2-diethoxytetrahydrofuran (I), 2,2-diethoxytetrahydropyran (II) and 2,2-dimethoxytetrahydropyran (III) are reported below in Table I :



I



II



III

Table I - Rate constants of orthoesters hydrolysis in buffered aqueous solutions (in $M^{-1}.s^{-1}$) . T = 25°C., μ = 0.1 M .

Catalyst	H_3O^+	AcOH	Me_2AsOOH	$H_2PO_4^-$	HBO_2	H_2O
I	$3.9\ 10^4$	3.03	$2.40\ 10^{-2}$	$4.75\ 10^{-2}$	$5.88\ 10^{-5}$	$9.0\ 10^{-8}$
II	$4.1\ 10^4$	4.07	$1.60\ 10^{-2}$	$3.69\ 10^{-2}$	$1.87\ 10^{-5}$	$8.8\ 10^{-8}$
III	$5.9.\ 10^3$	0.90	$2.22\ 10^{-2}$	$2.66\ 10^{-2}$	$3.76\ 10^{-5}$	$8.3\ 10^{-8}$

Reactions were monitored spectroscopically by following the appearance of hydroxy-ester at 215 nm.

From the results listed in table I two conclusions may be drawn namely :

1) The hydrolysis of these orthoesters is subject to general acid catalysis, the kind of catalysis currently observed with other orthoesters[3-5].

2) The measured Brönsted α coefficients obtained by plotting log $k_{catalyst}$ against the pK_a of the catalysts suggest that proton transfer is well advanced in the transition state : $\alpha = 0.67 \pm 0.04$ (r = 0.994) for I ; $\alpha = 0.68 \pm 0.05$ (r = 0.988) for II and $\alpha = 0.64 \pm 0.05$ (r = 0.989) for III .

The important question that arises then is whether general acid catalysis is consistent with the concept of stereoelectronic control .

It has been shown by theoretical calculations[6] and X-Ray diffraction[7] that if two lone pairs lie antiperiplanar to a polar bond, the polar bond is both weaker and longer than usual . The consequence of these two effects for our compounds is evident : already in the initial state the axial O-alkyl leaving group becomes the better one and the axial C-O-alkyl bond is easier to cleave (see scheme 1) . Such a situation would at the same time be expected to favour general acid catalysis .

As applied to the problem of acid-base catalysis stereoelectronic control is a new and we believe potentially useful concept .

References : 1 - P. DESLONGCHAMPS, Tetrahedron, 1975, 31, 2463 .
2 - P. DESLONGCHAMPS, R. CHENEVERT, R.J. TAILLEFER, C. MOREAU and J.K. SAUNDERS, Can. J. Chem., 1975, 53, 1601 .
3 - E.H. CORDES and H.G. BULL, Chem. Rev., 1974, 74, 581 .
4 - T.H. FIFE, Accounts Chem. Res., 1972, 5, 264 .
5 - W.P. JENCKS, Chem. Rev., 1972, 72, 705 .
6 - J.M. LEHN and G. WIPFF, J. Amer. Chem. Soc., 1974, 96, 4048 .
7 - H.B. BURGI, J.D. DUNITZ and E. SHEFTER, Acta Cryst., 1974, B30, 1517 .