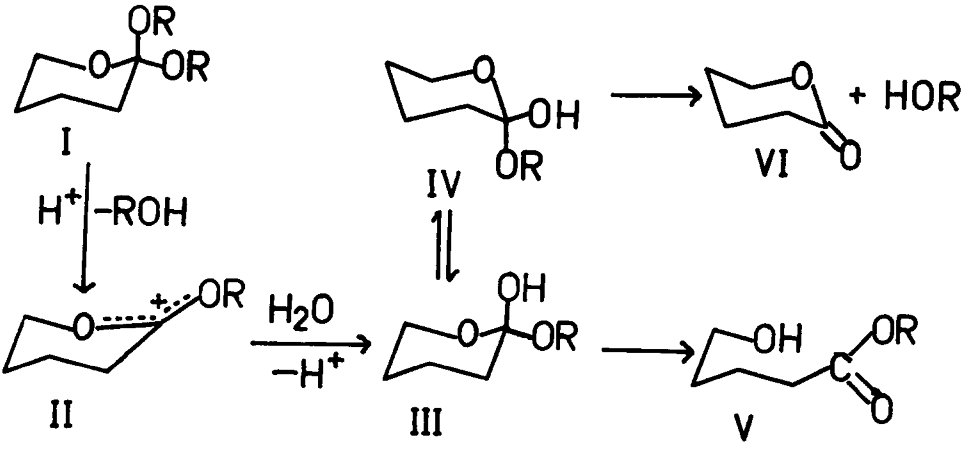
Tetrahedron Letters,Vol.23,No.46,pp 4823-4826,1982 0040-4039/82/464823-04$03.00/0
Printed in Great Britain

THE PRODUCTS OF HYDROLYSIS OF 2,2-DIMETHOXY- AND 2,2-DIETHOXY-TETRAHYDROPYRAN

Brian Capon* and Duncan McL.A. Grieve
Chemistry Department, University of Glasgow, Glasgow G12 8QQ, Scotland, U.K.

Abstract. The hydrolyses of 2,2-dimethoxy and 2,2-diethoxy-tetrahydropyran under a variety of conditions yield 20 - 40% δ-valerolactone and 80 - 60% of methyl or ethyl 5-hydroxyvalerate.

Deslongchamps has proposed a theory[1,2] for the decomposition of tetrahedral intermediates in which it was postulated that "the precise conformation of the tetrahedral intermediate is transmitted into the products of the reaction and that the specific decomposition of such an intermediate is controlled by the orientation of the lone-pair orbitals of the heteroatoms".[1] That is, the rate of cleavage of a carbon-oxygen or carbon-nitrogen bond in any conformer is determined by the orientation of the lone pairs on the other heteroatoms in that conformer. This theory has also been applied to the decomposition of orthoesters. One of the most important pieces of evidence brought forward to support the theory was that on hydrolysis 2,2-diethoxytetrahydropyran (I, R = Et) yielded only ethyl 5-hydroxyvalerate and no valerolactone.[3] This was explained by assuming that, in accord with the above theory, 2,2-diethoxy-



tetrahydropyran (I, R = Et) underwent initial cleavage of the axial ethoxy bond to yield cation (II, R = Et). It was then assumed that this ion reacted with water by the microscopic reverse of this process to yield the tetrahedral intermediate (III, R = Et) which decomposed faster to V (R = Et) than it underwent conformational inversion to yield conformation (IV, R = Et). Since in conformation (III) only the ring C-O has, according to the above theory, the lone-pairs on the other heteroatoms correctly oriented for bond fission, formation of ethyl 5-hydroxyvalerate (V, R = Et) rather than of δ-valerolactone (VI) was explained.[3]

We have investigated the products of hydrolysis of 2,2-dimethoxytetrahydropyran (I, R = Me) under a variety of conditions and found that 30 - 40% of δ-valerolactone is always formed. This is shown qualitatively very clearly in the ^{1}H n.m.r. spectrum by the appearance of a signal at $\delta = 4.3$ downfield from the other signals and characteristic of the $-CH_2-O-CO-$ of the lactone. The amount of lactone formed was best estimated from the relative intensities of CH_3 signals of the methanol ($\delta = 3.28$) and methyl ester ($\delta = 3.62$). If no lactone had been formed these should, of course, have been equal but this was never found to be so, and the percentage lactone was estimated from the equation %-lactone = $100 \times (I_{MeOH} - I_{MeOCO-})/(I_{MeOH} + I_{MeOCO-})$ (Table).

Table. Percentage of δ-Valerolactone (±5%) Formed on Hydrolysis of 2,2-Dimethoxy- and 2,2-Diethoxy-Tetrahydropyran as Determined by ^{1}H n.m.r. Spectroscopy at 35°.[a]

Volume Ratio D_2O^b:Solvent	Solvent and Compound CD_3COCD_3 I, R = Me	CD_3CN I, R = Me	CD_3SOCD_3 I, R = Me	CD_3COCD_3 I, R = Et
10:90	33	40	43	22
20:80	33	39	38	25
30:70	33	39	39	28
40:60	30	38	40	29
50:50	29	40	41	26
60:40	32	40	41	31
70:30	32	42	41	30
80:20	34	44	40	31
90:10	33	44	44	30
100:0	33	-	41	31

Table (continued)

[a] Determined by integration of the CH_3 peaks of the methanol and methyl 5-hydroxyvalerate or of the CH_2 peaks of ethanol and ethyl 5-hydroxyvalerate.

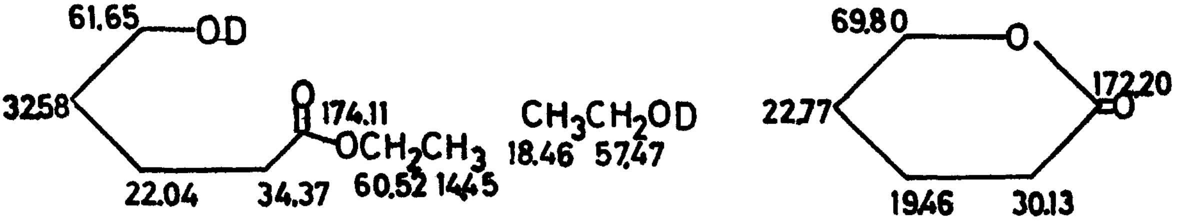
[b] The D_2O was 10^{-3} $\underline{\underline{M}}$ in toluene-p-sulphonic acid before dilution.

In order to check that the δ-valerolactone was being formed directly from I (R = Me) and not by subsequent hydrolysis of methyl 5-hydroxyvalerate the reactions were followed over a period of time in order to find out if the proportions of lactone to ester changed. Only with an acid concentration as high as 0.2 $\underline{\underline{M}}$ HCl was there any evidence for an increase in the proportion of lactone over a period of 20 minutes. Since most of the experiments were carried out at much lower acid concentrations it was concluded that under these conditions all the lactone was formed directly from I (R = Me).

The products of the reaction of I (R = Me) were also investigated under conditions as close as possible to those used previously[3] to study I (R = Et). 2,2-Dimethoxytetrahydropyran (I, R = Me) (0.5 mmoles) was dissolved in CD_2Cl_2 (0.05 ml), cooled to 0° and poured onto D_2O (0.5 ml) which contained toluene-p-sulphonic acid (10^{-3} $\underline{\underline{M}}$) at 0°C. After agitating the mixture vigorously for 20 minutes it was quenched in CD_3COCD_3 (3 ml) at 0° to give a single phase. The ^1H n.m.r. spectrum was then measured at 0° and the percentage lactone calculated as before. The average of 8 experiments was 35% lactone.

In order to check whether or not the formation of δ-valerolactone was just a property of 2,2-dimethoxytetrahydropyran experiments were also carried out with 2,2-diethoxytetrahydropyran, the compound originally studied.[3] It was now found that 20 - 30% of lactone was formed by ^1H n.m.r. spectroscopy (Table). This reaction was also studied by ^{13}C n.m.r. spectroscopy since it had previously been reported[3] that the lactone could not be detected in the reaction product by this technique. The reaction was carried out in D_2O(10^{-3} $\underline{\underline{M}}$ $CH_3C_6H_4SO_3H$) : CD_3COCD_3(10:90, v/v) and signals which were attributed to both ethyl 5-hydroxyvalerate and δ-valerolactone were observed and confirmed by using authentic samples (see Scheme). The intensity of the signal of the carbonyl group of δ-valerolactone (δ = 172.20) was about 25% that of the carbonyl group of ethyl 5-hydroxyvalerate, consistent with the ^1H n.m.r. results.

These results imply that either bond cleavage in the reactions of I, II and/or III are not controlled by orientations of the lone-pair orbitals in the initial states or/and that conformational inversion of III is rapid compared with its lifetime. That the latter is almost certainly correct is seen from the direct detection of a number of similar tetrahedral intermediates by n.m.r.[4] and u.v.[5] spectroscopy. Clearly in applying any stereoelectronic



Scheme. δ-Values of Signals in the ^{13}C n.m.r. Spectrum of the Products of Hydrolysis of 2,2-Diethoxytetrahydropyran.

theory it is not sufficient to consider just the "precise conformation" of the initial state. The possibility of reaction through another conformation must be allowed for. This point is also clearly illustrated by some recent work on a gas-phase reaction by Caserio and her co-workers[6] and by the work of Perrin and Arrhenius.[7] These latter workers had to assume however the "absence of lactone products" which they attributed to "product development control". Our work now shows that for the hydrolysis of 2,2-dimethoxy- and 2,2-diethoxy-tetrahydropyran this is unnecessary.

Acknowledgment. We thank the SERC for support and Professor P. Deslongchamps for a valuable correspondence.

References

1. P. Deslongchamps, Tetrahedron, 1975, 31, 2463.
2. P. Deslongchamps, Heterocycles, 1977, 7, 1271.
3. P. Deslongchamps, R. Chenevert, R.J. Taillefer, C. Moreau, and J.K. Saunders, Canad. J. Chem., 1975, 53, 1601.
4. B. Capon, J.H. Gall, and D. McL.A. Grieve, J. Chem. Soc., Chem. Commun., 1976, 1034; B. Capon and D.McL.A. Grieve, J. Chem. Soc., Perkin Trans. 2, 1980, 300; B. Capon and A.K. Ghosh, J. Am. Chem. Soc., 1981, 103, 1765; B. Capon, A.K. Ghosh and D.McL.A. Grieve, Accounts Chem. Res., 1981, 14, 306.
5. M. Ahmad, R.G. Bergstrom, M.J. Cashen, A.J. Kresge, R.A. McClelland, and M.F. Powell, J. Am. Chem, Soc., 1977, 99, 4827; M. Ahmad, R.G. Bergstrom, M.J. Cashen, Y. Chiang, A.J. Kresge, R.A. McClelland, and M.F. Powell, ibid, 1979, 101, 2669; R.A. McClelland and M. Ahmad, J. Org. Chem., 1979, 44, 1855; R.A. McClelland, M. Ahmad, J. Bohonek, and S. Gedge, Canad. J. Chem., 1979, 57, 1531; R.A. McClelland and M. Alibahi, ibid, 1981, 59, 1169; R.A. McClelland and G. Patel, J. Am. Chem. Soc., 1981, 103, 6809, 6912.
6. M.C. Caserio, Y. Suma, and J.K. Kim, J. Am. Chem. Soc., 1981, 103, 6712.
7. C.L. Perrin and G.M.L. Arrhenius, J. Am. Chem. Soc., 1982, 104, 2839.

(Received in UK 14 September 1982)