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METHYL ORTHOBENZOATE HYDROLYSIS; THE RATE-DETERMINING STEP[1]

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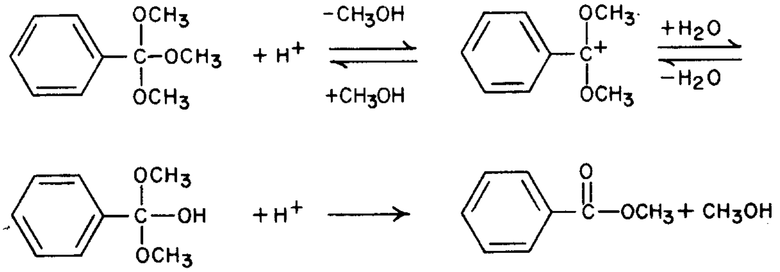
The first-order rate constants for the decomposition of methyl orthobenzoate in slightly acidic aqueous solution are independent of the concentration of several amines under conditions in which an appreciable fraction of the orthoester yields amine addition products[2]. This finding very strongly suggests that methyl orthobenzoate hydrolysis proceeds via a unimolecular, rather than bimolecular[3], reaction path, almost certainly that indicated below, and provides good evidence that the first step, carboxonium ion formation, is rate-determining. The magnitudes of the entropy of activation and the solvent deuterium isotope effect for the hydrolysis of several orthoesters[2,4], while consistent with and support for rate-determining carboxonium ion formation, are also consistent with rate-determining decomposition of dimethyl orthobenzoate. Consequently, it appears desirable to provide an experimental distinction



between these alternatives, if possible. To this end, the kinetics of the disappearance of the methyl protons of methyl orthobenzoate and the appearance of the methyl protons of methanol and methyl benzoate in mixtures of CD_3OD and D_2O have been studied with the aid of a Varian Associates A-60 nuclear magnetic resonance spectrometer. Since the singlets for the methyl protons of orthoester, methanol, and methyl benzoate are well separated, the simultaneous determination of the first-order rate constants for appearance or disappearance of each of these species is easily accomplished. The results of two such experiments are indicated in the Table.

If carboxonium ion formation were completely rate-determining for the hydrolysis of methyl orthobenzoate, the first-order rate constants for the appearance or disappearance of each of the species would be identical and the ratio of the integrated intensities, at infinite time, of the methyl protons of carboxylic ester and methanol to the aromatic protons would be 0.60 and 1.20, respectively. On the other hand, if the decomposition of dimethyl orthobenzoate were rate-determining, essentially all of the methyl groups of the orthoester would be exchanged for deuteromethyl groups in a pre-equilibrium reaction. Thus, the disappearance of the orthoester methyl protons and the appearance of the methyl protons of methanol would be considerably more rapid than the formation of methyl benzoate and little or no methyl benzoate, containing protons attached to the methyl carbon, would be formed. The ratio of integrated intensities, at infinite time, of the methyl protons of carboxylic ester and methanol to the aromatic protons would be approximately 0.0 and 1.8, respectively.

The data presented in the Table establish that the first-order rate constants for the appearance or disappearance of the three species under consideration are approximately equal and that a rather large fraction of the original orthoester yields methyl benzoate without exchanging with the

TABLE

First-order Rate Constants and Integrated Methyl Proton Intensities at Infinite Time Characterizing the Hydrolysis of Methyl Orthobenzoate in Deuteromethanol-Deuterium Oxide Solutions at 25°.

Run	$\frac{(CD_3OD)}{(D_2O)}$	k_{OE}[a] (min^{-1})	k_M[b] (min^{-1})	k_{MB}[c] (min^{-1})	R_M[d]	R_{MB}[e]
1.[f]	1.0	2.2×10^{-4}	2.9×10^{-4}	2.6×10^{-4}	1.46	0.45
2.[g]	2.0	1.1×10^{-3}	1.4×10^{-3}	1.3×10^{-3}	1.38	0.38

[a] First-order rate constant for the disappearance of the methyl protons of methyl orthobenzoate. [b] First-order rate constant for the appearance of the methyl protons of methanol. [c] First-order rate constant for the appearance of the methyl protons of methyl benzoate. [d] Ratio of the integrated intensities at infinite time of the methyl protons of methanol to the aromatic protons. [e] Ratio of the integrated intensities at infinite time of the methyl protons of methyl benzoate to the aromatic protons. [f] Carried out in the presence of 0.02 M acetate buffer, 50% base. [g] Carried out in the presence of 0.05 M formate buffer, 50% base.

deuteromethanol of the solvent. These results are clearly inconsistent with rate-determining decomposition of dimethyl orthobenzoate but are accounted for by a slow formation of a carboxonium ion which then partitions rapidly between deuterium oxide, yielding product, and deuteromethanol, yielding a partially deuterated orthoester which finally yields, in part, deuterated methyl benzoate. Thus, in the presence of the rather large amounts of deuteromethanol in these experiments, the second step in the reaction sequence is partially rate-determining and accounts for the significant exchange which has occurred, as judged from the ratio of integrated intensities at infinite time. A "back of an envelope" calculation, employing the ratio of integrated methyl benzoate methyl proton to aromatic proton intensities, suggests that deuteromethanol and deuterium oxide are about equally reactive toward the intermediate carboxonium ion. Consequently, in aqueous solution, in which the concentration of methanol is small compared to that of water throughout the course of the hydrolysis reaction, the formation of the carboxonium ion would be nearly completely rate-determining. It should be noted that the present results are consistent with rate-determining attack of water on the orthoester carbon atom, a reaction path which is, however, inconsistent with results of aminolysis studies[2], as indicated above.

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