

## Rate-limiting Hemiacetal Breakdown in the Aqueous Bromination of $\alpha$ -Methoxystyrene

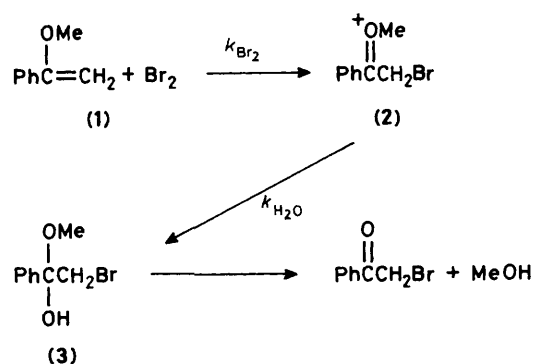
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The slow step in product formation in the aqueous bromination of  $\alpha$ -methoxystyrene is the breakdown of the methyl hemiacetal of  $\alpha$ -bromoacetophenone.

The bromination of  $\alpha$ -methoxystyrene (1) proceeds by way of the 'open' oxocarbenium ion intermediate (2).<sup>1</sup> In aqueous solutions this should be trapped preferentially by the solvent to give the hemiacetal (3) and ultimately  $\alpha$ -bromoacetophenone and methanol (Scheme 1). The disappearance of bromine in this system is extremely rapid with the rate constant  $k_{\text{Br}_2}$  approaching the diffusion limit.<sup>1</sup> Hydration of the cation is also expected to be extremely fast.<sup>2,3</sup> With these two stages so rapid the possibility arises that the slow stage in the overall reaction is the breakdown of the hemiacetal. We demonstrate here that this is the case, and that under appropriate kinetic conditions rate constants for the hemiacetal decomposition can be precisely measured.

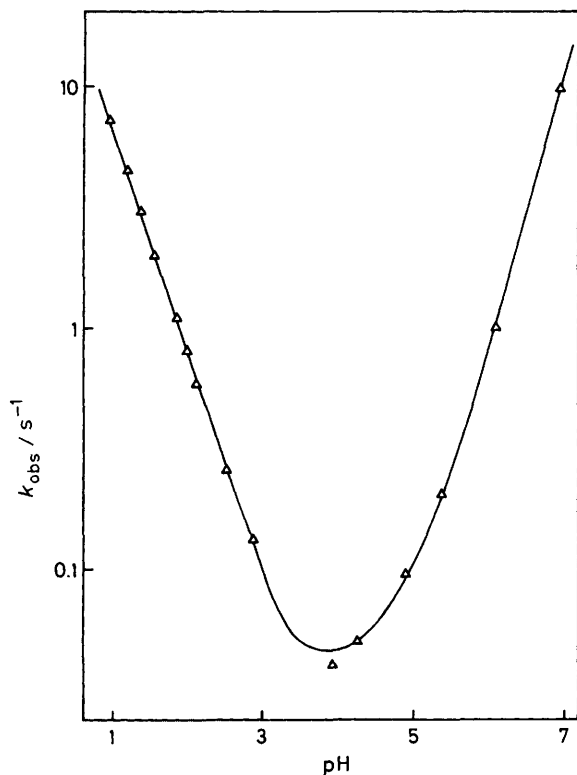
Kinetic experiments were conducted using a stopped-flow spectrophotometer, with  $5 \times 10^{-5} \text{ M}$   $\alpha$ -methoxystyrene in dilute base placed in one syringe, and  $2\text{--}5 \times 10^{-4} \text{ M}$  bromine in HCl solutions, acetate buffers, or phosphate buffers in the second syringe. Wavelengths were monitored in the region 230–260 nm, where bromine contributes little absorbance. The product of mixing is  $\alpha$ -bromoacetophenone,  $\lambda_{\text{max}}$  248 nm, as verified by comparison with the spectrum of authentic material. The vinyl ether has a significant spectrum with  $\lambda_{\text{max}}$  241 nm, but on mixing with the bromine solution this spectrum disappeared. This is not surprising since with  $k_{\text{Br}_2}$  expected to be of the order  $10^9\text{--}10^{10} \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$ , under the conditions of these experiments the half-life of the vinyl ether should be of the order of microseconds. What is



Scheme 1

observed initially on mixing however is not the spectrum of the ketone product but rather a spectrum characterized by having very little absorbance above 230 nm. The spectrum of the ketone grows in with time, in a process exhibiting excellent first-order kinetics with rate constants independent of the initial bromine concentration. The observed rate constants do vary with pH, as shown in Figure 1.

The explanation is that under the kinetic conditions of excess of bromine the bromination stage (and hydration stage) are complete within the 2 ms mixing time (dead-time) of the



**Figure 1.** First-order rate constants (25.0°C, ionic strength 0.1 M) for the breakdown of the methyl hemiacetal of  $\alpha$ -bromoacetophenone, as measured in the aqueous bromination of  $\alpha$ -methoxystyrene. (Values above pH 3 are based upon extrapolation to zero buffer concentration.)

stopped-flow apparatus. The breakdown of the hemiacetal however is significantly slower. Upon mixing the hemiacetal is therefore quantitatively generated, and the observed spectral change represents its conversion into products. The observed rate constants measure directly this process. The rate-pH profile (Figure 1) does have the expected form, showing regions of hydronium ion catalysis ( $k_{\text{H}} 75 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$ ), hydroxide ion catalysis ( $k_{\text{OH}} 3.9 \times 10^7 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$ ) and 'water' catalysis ( $k_{\text{O}} 0.03 \text{ s}^{-1}$ ). Catalysis by acetate ion ( $k_{\text{OAc}} 1.0 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$ ) and hydrogen phosphate ( $k_{\text{HPO}_4} 80 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$ ) is also observed.

In summary the slow step in product formation for the aqueous bromination of the vinyl ether  $\alpha$ -methoxystyrene is the breakdown of the methyl hemiacetal of  $\alpha$ -bromoacetophenone, and rate constants for this process can be directly monitored. This represents a further example of a system where under appropriate kinetic conditions a system of high energy provides a direct entry into an unstable tetrahedral adduct.<sup>4,5</sup>

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