

Mutarotation of α -D-Glucose Catalysed by Pyridine-Phenols and Pyridine-Water Catalyst Pairs in Dimethylformamide

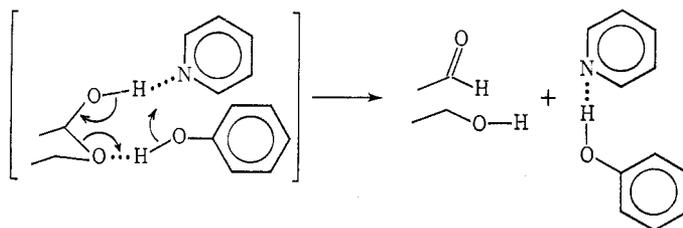
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Abstract

The rate of mutarotation of α -D-glucose is at a maximum for close to 1 : 1 molar composition of acid and base catalysts when pyridine-phenol, pyridine-*p*-cresol and pyridine-*p*-chlorophenol catalyst pairs are used in dimethylformamide solutions at 34.6°C. The evidence favours a termolecular bifunctional catalytic mechanism. No rate maximum is detectable for the pyridine-water catalyst pair under the same conditions. Two water molecules appear to be operative at the rate-determining step in dilute dimethylformamide solution.

It is generally agreed that the mutarotation of glucose proceeds through the rate-determining step of ring-opening to form the aldehyde sugar, followed by a quick ring formation.¹ Lowry and Faulkner found that the rate of mutarotation of tetra-*O*-methyl-D-glucopyranose in the mixed solvent of pyridine and cresol was 20 times faster than in water alone and suggested a cooperative catalysis by the acid and the base.² Swain and Brown, in their experiment with tetra-*O*-methyl-D-glucopyranose in benzene, proposed a concerted bifunctional mechanism catalysed by both acid and base, in which the proton in the 1-hydroxyl group of the sugar is pulled by the base at the same time as a proton is donated to the ring oxygen of the pyranose by the acid as the ring-opening proceeds.³



In the present work, the effect of the catalyst composition on the rate of mutarotation of α -D-glucopyranose in dilute solutions in dimethylformamide is studied polarimetrically; the catalysts used are pyridine and phenols. The effect of water is

¹ Bell, R. P., 'The Proton in Chemistry' p. 153 (Cornell University Press: Ithaca, N.Y., 1959); Benson, S. W., 'The Foundation of Chemical Kinetics' p. 559 (McGraw-Hill: New York 1960); Rony, P. R., *J. Am. Chem. Soc.*, 1968, **90**, 2824; Kergomard, A., and Renard, M., *Tetrahedron Lett.*, 1968, 769.

² Lowry, T. M., and Faulkner, I. J., *J. Chem. Soc.*, 1925, **127**, 2883.

³ Swain, C. G., and Brown, J. F., Jr, *J. Am. Chem. Soc.*, 1952, **74**, 2534, 2538.

also examined. The overall rate constant, k_{obs} , is plotted in Fig. 1 against the mole fraction of pyridine with respect to the phenols. The enhanced rate at close to 1 : 1 catalyst composition may be considered due to the bifunctional catalysis involving both acid and base catalysts. The contribution of such a ring-opening step requires a third-order term, $k[\text{glucose}][\text{phenol}][\text{pyridine}]$, in the rate expression. *p*-Chlorophenol, which most readily donates a proton, has the largest k value. The more acidic phenols also produce their maximum effect at a higher molar ratio of pyridine to phenol; the pK_a values of *p*-cresol, phenol and *p*-chlorophenol are 10.17, 10.0 and 9.39, respectively at 25°C.⁴ No rate maximum is observed for the pyridine–water system in dimethylformamide under these experimental conditions contrary to the result in pyridine–water mixed solvent observed by Lowry and Faulkner. When there was no

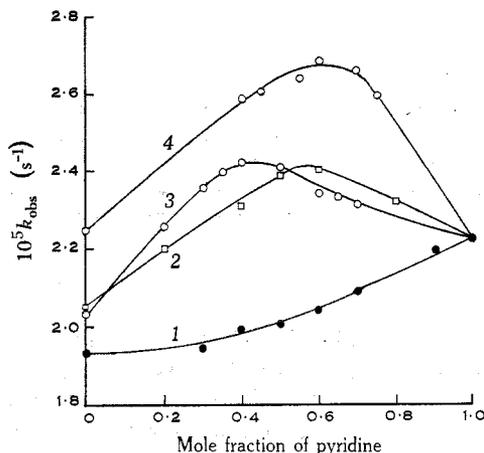
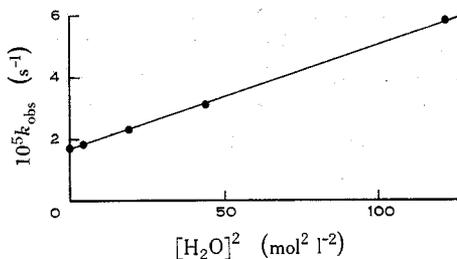


Fig. 1. Overall rate constant as a function of catalyst composition in dimethylformamide at 34.6°C: $[\alpha\text{-D-glucose}]$ 0.1554 M; $[\text{pyridine} + \text{acid}]$ 0.4444 M; 1, pyridine + water; 2, pyridine + phenol; 3, pyridine + *p*-cresol; 4, pyridine + *p*-chlorophenol.

Fig. 2. Plot of overall rate constant against square of water concentration in dimethylformamide: $[\alpha\text{-D-glucose}]$ 0.2205 M; $[\text{pyridine}]$ 0.0988 M; at 34.6°C.



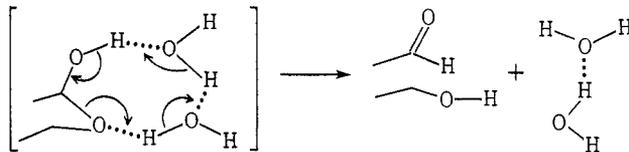
diluent, they observed a rate maximum at a pyridine mole fraction of 0.054, the rate being 19 times as fast as in water alone.² Although a cooperative mechanism involving a base and water molecules has been suggested,⁵ the proton-donating ability of water in dimethylformamide may be too weak compared with that of phenols to exhibit an apparent rate maximum. Under these experimental conditions, water and pyridine appear to act nearly independently. The concave shape of the pyridine–water curve in Fig. 1 suggests non-first-order contribution of water. Gram, Hveding and Reine reported that in water-rich water–dimethylformamide mixed solvent, two water molecules participated in the rate-determining step when the mole fraction of water in the solvent mixture was more than 0.75.⁶ The molecularity of water is examined in the

⁴ Fieser, L. F., and Fieser, M., 'Advanced Organic Chemistry' p. 744 (Reinhold: New York 1961).

⁵ Eigen, M., *Discuss. Faraday Soc.*, 1965, **39**, 7; Lowry, T. M., *J. Chem. Soc.*, 1927, 2554.

⁶ Gram, F., Hveding, J. A., and Reine, A., *Acta Chem. Scand.*, 1973, **27**, 3616.

presence of a small amount of pyridine in dimethylformamide when the mole fraction of water is below 0.516. The result in Fig. 2 agrees with a second-order participation of water molecules at the rate-determining step. Probably the amphiprotic water acts through a cyclic transition state involving two water molecules:



Experimental

The AR grade dimethylformamide (British Drug Houses) and pyridine (BDH) were fractionally distilled. Phenol (BDH), *p*-cresol (BDH) and *p*-chlorophenol (BDH) were recrystallized from petroleum spirit (60–70°C) and carbon tetrachloride before use. A polarimeter manufactured by Bellingham and Stanley Ltd, London, equipped with a water-jacketed 20-cm cell, was used to follow the mutarotation. The temperature was controlled to $\pm 0.1^\circ\text{C}$ by circulating water from a thermostat. AR grade α -D-glucose (BDH) was dissolved in dimethylformamide at the temperature of measurement and dimethylformamide solutions of pyridine and phenols or water were added to make up 25 cm³ of solution at that temperature. The solution was quickly transferred to the preheated cell in the polarimeter. The overall rate constant, k_{obs} , was obtained by the following equation

$$tk_{\text{obs}} = -\ln[(\alpha_t - \alpha_\infty)/(\alpha_0 - \alpha_\infty)]$$

where, α_0 , α_∞ and α_t were the specific rotations of pure α -D-glucopyranose, at equilibrium and at time t , respectively. The plot of $\ln(\alpha_t - \alpha_\infty)$ against time was strictly a straight line over a long period of time as had always been observed.

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