

## Thermal Mutarotation in Polycrystalline $\alpha$ -D-Glucose

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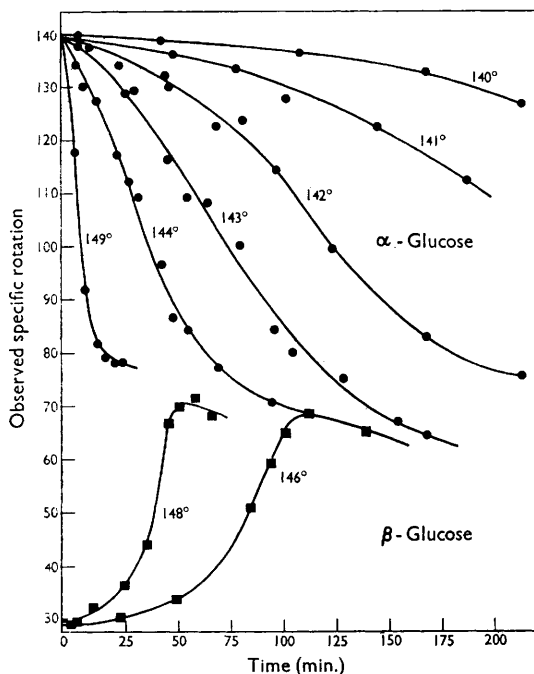
THE kinetic treatment of reactions in frozen solutions at low temperatures should, in principle, be applicable to some thermal reactions in crystalline samples at higher temperatures. When the thermal decomposition of a solid is accompanied by the development of a liquid phase, considerable reaction may occur in the growing liquid regions before they make a normally visible appearance. As with reactions in frozen solutions,<sup>1</sup> the observed rate of reaction below the melting point of a pure solid would be a function of *both* the concentration of reactant in the liquid phase and the total volume of the liquid phase.<sup>2</sup> Therefore, in contrast to the difficult kinetics of true solid-state reactions,<sup>3</sup> the rate of reaction above the eutectic point of the reactant-product system may be readily defined, e.g., for the simple first-order reaction  $A_{\text{solid}} \rightarrow A_{\text{liquid}} \rightarrow B_{\text{liquid}}$ ,  $dm_B/dt = k[A]_l V_l$ , where  $m_B$  is the moles of B present in the total system,  $[A]_l$  is the molar concentration of A in the liquid part of the system and  $V_l$  is the total volume of liquid regions.

To investigate the kinetic features of such thermal reactions in solids, we have studied the mutarotation of polycrystalline samples of  $\alpha$ -D-glucose below its melting point. A study of the mutarotation of *molten* glucose has recently been presented and a solid-state mutarotation at lower temperatures was suggested.<sup>4</sup>

Weighed samples of dry crystalline  $\alpha$ -D-glucose in individual volumetric flasks were heated in a constant temperature bath. The flasks were cooled to quench the reaction, and the contents dissolved in dimethyl sulphoxide in which no mutarotation occurs at room temperature. Optical rotations were measured and specific rotations then calculated from the weight of glucose in the samples. The observed specific rotations at various times (see Fig. 1) were independent of sample size (0.2 to 1.2 g.) and largely independent of crystal size and the origin of the glucose.\*

As illustrated in the Figure, the heating of either  $\alpha$ - or  $\beta$ -glucose results initially in attainment of mutarotational equilibrium, but the many reactions

\* British Drug Houses Analytical Reagent grade  $\alpha$ -D-glucose and U.S. National Bureau of Standards dextrose (standard sample no. 41) gave the same rotations at identical times. Samples used were first dried in vacuum at 110°; the presence of water accelerated the reaction.



FIGURE

which give rise to complex mixtures are not far behind.<sup>4,5</sup> More surprising is the great variation of rate with a temperature change of only a few degrees. Plots of  $\log(\theta_A - \theta_t)$  against time\* for the first few points of each run gave observed initial rate constants ( $k_{\text{obs}}$ ) of 1.7, 2.2, 4.4, 8.2, and  $11 \times 10^{-4} \text{ sec.}^{-1}$  at 140°, 141°, 142°, 143°, and 144°, respectively. This seven-fold increase over only a four degree temperature range seems unreasonable for any true rate constant for glucose mutarotation, and a composite, apparent rate constant (of the type observed for reactions in frozen solutions<sup>1</sup>) is indicated.

Application of "frozen solution kinetics" to the reversible pseudo-first order mutarotation of

glucose ( $A_{\text{solid}} \rightarrow A_{\text{liquid}} \xrightleftharpoons[k_{\beta}]{k_{\alpha}} B_{\text{liquid}}$ ) accounts

for this temperature effect. Impurities or  $\beta$ -glucose in the crystalline  $\alpha$ -glucose create liquid regions at temperatures near the ideal melting point. As  $\beta$ -isomer (and other products) are formed, the liquid regions grow in volume by melting more of the  $\alpha$ -glucose. Before the sample has completely

melted phase equilibrium keeps the concentrations ( $[A]_h$  and  $[B]_h$ ) of  $\alpha$ - and  $\beta$ -glucose in the liquid regions constant, while the total volume of the liquid phase increases in proportion to the moles of product, *i.e.*,  $V_h = m_B/[B]_h$ . The initial part of the reaction then takes the form of a first order auto-accelerating reaction in which the rate of product formation is proportional to the moles of product,

$$dm_B/dt = (k_{\alpha}[A]_h - k_{\beta}[B]_h)V_h = \{ (k_{\alpha}[A]_h - k_{\beta}[B]_h) / [B]_h \} m_B.$$

According to this relationship the observed rate constant is  $k_{\text{obs}} = (k_{\alpha}[A]_h - k_{\beta}[B]_h) / [B]_h$  where the concentrations  $[A]_h$  and  $[B]_h$  as well as  $k_{\alpha}$  and  $k_{\beta}$  are functions of temperature only.<sup>1</sup> The reaction is much faster at higher temperatures not only because the true rate constant  $k_{\alpha}$  increases with temperature, but, for a given number of moles of product, the volume of melted glucose is also greater (*i.e.*,  $[B]_h$  decreases and therefore  $k_{\text{obs}}$  greatly increases with an increase in temperature). The rate constant  $k_{\alpha}$  may vary normally with temperature, while the observed rate constant  $k_{\text{obs}}$  is unusually sensitive to temperature.

The mutarotation continues to accelerate until the solid phase is nearly consumed. When the glucose has completely liquified the situations regarding changes in volume and in concentration are reversed; the volume of melt ( $V_h$ ) remains constant and the concentrations ( $[A]_h$  and  $[B]_h$ ) now vary. The kinetic form becomes that of a normal reversible reaction,  $dm_B/dt = (k_{\alpha}[A]_h - k_{\beta}[B]_h)V_h = k_{\alpha}m_A - k_{\beta}m_B$ . As samples were observed to be completely melted after the specific rotation of *ca.* 100 was passed, such a relationship occurs in the lower part of the rotation-time curves shown in the Figure for  $\alpha$ -glucose.† The effects of accelerative melting and then the further approach to mutarotational equilibrium account for the S-shaped curves.

The quantitative comparison of the observed rate constants with values calculated according to the treatment given above requires experimental determinations of the simple rate constants ( $k_{\alpha}$  and  $k_{\beta}$ ) together with the phase relationship of  $\alpha$ -glucose to products. However, the high rate of mutarotation in completely molten glucose precludes such measurements. In more favourable cases the rates of reactions in crystalline solids by this mechanism might be predicted and more directly compared with observations.

\* The function  $(\theta_A - \theta_t)$ , where  $\theta_A$  is the specific rotation of the purest  $\alpha$ -D-glucose and  $\theta_t$  the specific rotation at time  $t$ , is proportional to the mole fraction of  $\beta$ -glucose. Rotations were measured at 5461 Å.

† This neglects the ensuing complexity of products, (see ref. 5) some of which may be autocatalytic.

The thermal decomposition of crystalline solids during the process of melting is a common phenomenon. Some cases of reactions in melting solids<sup>6</sup> have been treated by equations suggested originally for the growth of crystalline defects in true solid-state reactions.<sup>7</sup> The "sigmoid" shaped reaction against time curves of many solid-state reactions<sup>7</sup> are similar to those observed in melting solids (see Figure and ref. 6), but if a reaction occurs only in liquid regions in equilibrium with solid, application of a solid-state kinetic treatment may be only superficially useful (*e.g.*, in obtaining straight kinetic plots). For mutarotation in crystalline

$\alpha$ -glucose, the kinetic scheme based on the growth of a liquid phase accounts at least qualitatively for the available observations. In any case, in crystalline materials above the eutectic temperature of the reacting system, a liquid phase is present. Even at temperatures considerably below the formal melting point of a pure solid, the occurrence of a true solid state reaction can only be definitely established by separating out any reaction which may readily proceed in an existing liquid phase.

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<sup>1</sup> R. E. Pincock and T. E. Kiovsky, *J. Chem. Educ.*, 1966, **43**, 358.

<sup>2</sup> T. E. Kiovsky and R. E. Pincock, *J. Amer. Chem. Soc.*, 1966, **88**, 4455, 4704.

<sup>3</sup> *cf.*, F. C. Tompkins, in "The Reactivity of Solids", Butterworths, London, 1965.

<sup>4</sup> A. Broido, Y. Houminer, and S. Patai, *J. Chem. Soc. (B)*, 1966, 411.

<sup>5</sup> Twenty-two of the many products of glucose decomposition (after 2.5 hr. at 150°) have recently been identified. H. Sugisawa, *J. Food Sci.*, 1966, **31**, 381; H. Sugisawa and H. Edo, *ibid.*, 1966, **31**, 561.

<sup>6</sup> A. D. Yoffe, *Proc. Roy. Soc.*, 1951, **A**, 208, 188; I. E. Puddington, *Canad. J. Res.*, 1948, **26**, *B*, 415; J. Vaughan and L. Phillips, *J. Chem. Soc.*, 1949, 1560; D. F. Debenham and A. J. Owen, *J. Chem. Soc. (B)*, 1966, 675; S. Patai and Y. Gotshal, *ibid.*, 1966, 489.

<sup>7</sup> E. G. Prout and F. C. Tompkins, *Trans. Faraday Soc.*, 1944, **40**, 488.