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INTRAMOLECULAR CATALYSIS IN GLYCOSIDE HYDROLYSIS

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Interest in intramolecular catalysis in reactions of carboxylic acid derivatives has been stimulated by analogies to enzymic catalysis.(1) Intramolecular catalysis of other classes of reactions has received much less attention, and the first quantitative investigation of intramolecular catalysis in glycoside hydrolysis is now reported. *o*-Carboxyphenyl β-*D*-glucoside has been noted previously(2) to undergo facile hydrolysis but the reaction was not investigated in details.

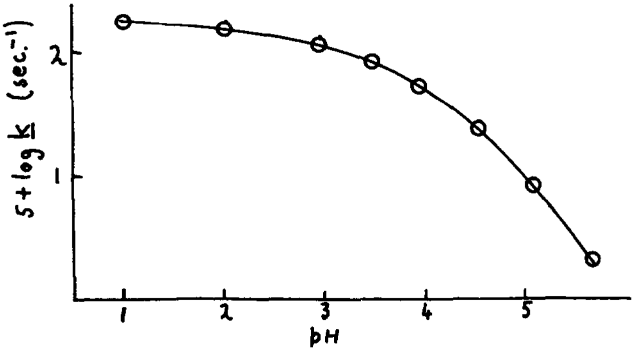
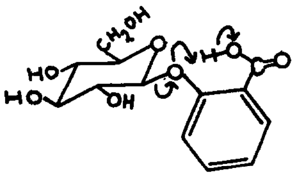


Fig. 1
pH-rate profile for the hydrolysis of *o*-carboxyphenyl β-*D*-glucoside at 91.35°

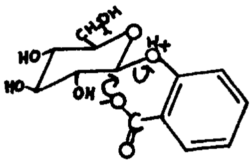
The pH-rate profile (Fig.1), now determined, indicates a rate law of the form :

$$\begin{aligned}\frac{d[\text{Salicylic acid}]}{dt} &= \underline{k}[\text{Gl-O-C}_6\text{H}_4\cdot\text{CO}_2\text{H}]\\ &= \frac{\underline{k}[\text{Gl-O-C}_6\text{H}_4\cdot\text{CO}_2^-]\,[\text{H}_3\text{O}^+]}{\underline{K}_a}\end{aligned}$$

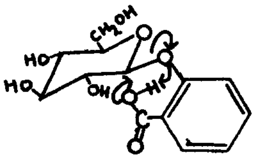
if the not unreasonable value of 3.5 is assumed for $p\underline{K}_a$ at 91.35°. (At 25° $p\underline{K}_a = 3.7$). At a pH of 3.5 the rate of hydrolysis is about 10^4 times greater than that estimated for p-carboxyphenyl-β-D-glucoside by extrapolation from results at higher acidities. Mechanisms involving (i) intramolecular general-acid catalysis (as I), (ii) an intramolecular displacement by the carboxylate ion on the O-1 protonated glucoside (as II) or (iii) intramolecular nucleophilic-electrophilic catalysis (as III) are consistent with these results. Mechanisms (ii) and (iii) would involve



(I)



(II)



(III)

α-D-glucosyl salicylate as an intermediate but the observed equality of the spectrophotometric and polarimetric rate constants indicates that if formed its rate of hydrolysis must be much faster than its rate of formation. Mechanism (i) which is similar to that considered by Rånby and Marchessault (3) for the hydrolysis of polysaccharides containing glucuronic acid residues, involves an increase in the leaving-group ability of the aryloxonium ion through intramolecular general-acid catalysis. The possibility that similar catalysis operates in other classes of reactions is at present being investigated. Although the rate increase resulting from this intramolecular catalysis is large it is still 10^2-10^3 times less than that observed with catalysis by emulsin.(4)

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