The Kinetics of the Hydrolysis of 2-Naphthyl β-D-Glucuronide

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THE kinetics of the hydrolysis of glucuronides have recently been investigated by several groups of workers[1-8] and the results obtained used in discussions of the origin of the strong and weak linkages in polysaccharides containing uronic acid residues. In all these investigations the hydrolyses were studied in moderately concentrated acid solutions and it was found that usually the glucuronides reacted more slowly than the corresponding glucosides although not always as slowly as would be expected from the σ^* constant of the methoxycarbonyl group.[8] We have now investigated the kinetics of the hydrolysis of 2-naphthyl β-D-glucuronide (I) and 2-naphthyl β-D-glucoside (II) over a wide range of acidities (see Figure) and found that whereas the glucoside reacts 45 times faster than the glucuronide in 1M-hydrochloric acid, at pH 4·79 it reacts 35 times slower. This is a result of the rate law for the hydrolysis of the glucoside being (i) rate $= k$ [glucoside] h_0 with $k = 9{\cdot}4 \times 10^{-4}$ l. mole^{-1} sec.$^{-1}$ at 90·1° and that for the glucuronide being (ii) rate $= k_1$ [unionised glucuronide] $+ k_2$ [unionised glucuronide] h_0 with $k_1 = 7{\cdot}1 \times 10^{-6}$ sec.$^{-1}$ and $k_2 = 1{\cdot}2 \times 10^{-5}$ l. mole^{-1} sec.$^{-1}$ at 90·1°. In our view the first term on the right hand side of equation (ii) does not result from an intramolecularly catalysed

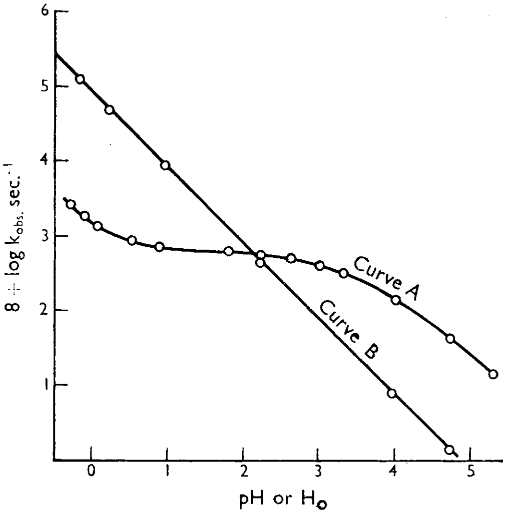

FIGURE: *Plot of log k_{obs} against pH or H_0 for the hydrolysis of* 2-*naphthyl β-D-glucuronide* (*curve A*) *and* 2-*naphthyl β-D-glucoside* (*curve B*) *at* 90·1°.

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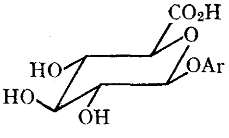
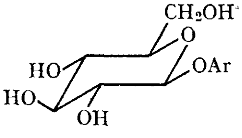
reaction of the unionised glucuronide[9] but from the kinetically equivalent specific hydrogen-ion-catalysed reaction of the ionised form of the glucuronide. The second order rate constant for this reaction, k^*, would be related to k_1 by the equation $k^* = k_1/K_a$ where K_a is the dissociation constant of the glucuronide. Using the value of the apparent K_a from the pH–rate profile at 90·1° of $3{\cdot}6 \times 10^{-4}$ mole l.$^{-1}$ (the measured K_a at 25° is $2{\cdot}9 \times 10^{-4}$ mole l.$^{-1}$) gives a value of k^* of $1{\cdot}9 \times 10^{-2}$ l. mole^{-1} sec.$^{-1}$ On this hypothesis then the relative rates of the specific hydrogen-ion-catalysed hydrolysis of the ionised glucuronide, glucoside, and unionised glucuronide are 1580 : 78 : 1 which correlate well with the inductive substituent constants[10] of the CO_2^-, CH_2OH, and CO_2H groups which have values $-0{\cdot}17$, $0{\cdot}05$, and $0{\cdot}33$ respectively.[10]



(I)



(II)

It therefore seems probable that the anomalies previously reported for the kinetics of the hydrolysis of glucuronides result from the measured rates being the sums of the rates for the ionised and unionised forms. The results now reported also suggest that it may be possible to hydrolyse polysaccharides containing uronic acid residues preferentially at the uronoside linkage by carrying out the reactions in solutions of low acidity.

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[9] For an example of intramolecular catalysis in the hydrolysis of a glycoside, see B. Capon, *Tetrahedron Letters*, 1963, 911.

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