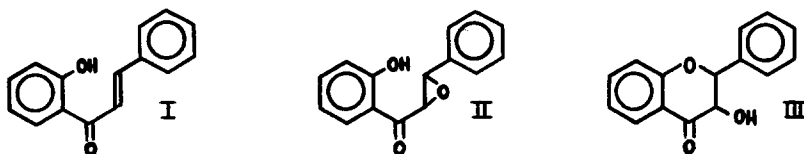


THE KINETICS AND MECHANISM OF THE CYCLISATION OF 2'-HYDROXYCHALCONE EPOXIDE  
TO 3-HYDROXYFLAVANONE IN WATER

Lyndsay Main\* and K. Barry Old  
School of Science, University of Waikato, Hamilton, New Zealand

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Even though 2'-hydroxychalcone epoxides (II) have been postulated<sup>1</sup> as intermediates in the biosynthesis of 3-hydroxyflavanones (III) and other flavonoids from 2'-hydroxychalcones (I), they are to our knowledge unknown compounds, having never been isolated from or detected in natural sources, nor synthesised except in cases where the hydroxy group is protected as an ether or ester. Consequently, we are developing our own synthesis of unprotected 2'-hydroxychalcone epoxides and in pilot experiments have succeeded in preparing the parent epoxide (II).<sup>2</sup> We present here kinetic data which show that in water the epoxide is very unstable, particularly at and above neutral pH.



The epoxide (II) undergoes cyclisation to *trans*-3-hydroxyflavanone (III). By following the decrease in absorbance at 262 nm as (II) reacts, pseudo first order rate constants have been determined. They are plotted as points in the Figure in which the line is theoretical, being based on the following kinetic form:

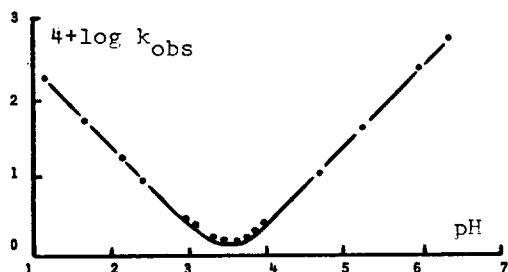
$$-d[\text{II}]/dt = 0.235[\text{II}]\{\text{H}^+\} + 1.85 \times 10^6 [\text{II}]\{\text{OH}^-\} \text{ mol l}^{-1} \text{ s}^{-1}$$

The correlation between the line and the experimental points supports this kinetic form.

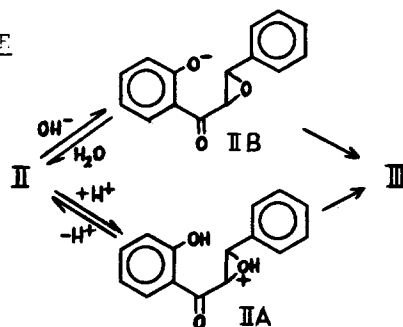
Buffer (formate, acetate, phosphate) dilution studies establish that there is no significant general acid or general base catalysis: e.g. at pH 4.57 with total acetate concentrations of 0.100, 0.020 and 0.0050 mol l<sup>-1</sup>,  $k_{\text{obs}}$  values of 0.061, 0.062 and 0.063 s<sup>-1</sup> were determined respectively.

The kinetic data are consistent, therefore, with the Scheme.

FIGURE: pH-rate profile for  
 II→III; 30°;  $\mu=0.5(\text{KCl})$ ;  
 $k_{\text{obs}}$  in  $\text{s}^{-1}$



SCHEME



The important conclusions to be drawn are as follows. 2'-Hydroxychalcone epoxides are likely to be highly unstable near and above neutrality (by extrapolation of the Figure,  $t_{1/2}$  for (II) at pH 7 can be estimated as about 2.5s). As a consequence, it seems that if these compounds are intermediates in flavonoid biosynthesis, they may well be present in natural sources in insufficient concentration to be isolated or even detected.

2'-Hydroxychalcone epoxides have also been postulated as intermediates in the AFO reaction in which 3-hydroxyflavanones (III) and flavonols are formed from 2'-hydroxychalcones by the action of alkaline hydrogen peroxide<sup>3</sup>. There would be little possibility, however, of detecting them in this reaction if indeed they are formed: the rate constant for the conversion of the anion (IIB) to (III) can be estimated, by assuming that the  $\text{pK}_a$  of (II) is<sup>4</sup> about 10, to be approximately  $185 \text{ s}^{-1}$ . At pH 11, for instance, where (II) would be nearly completely ionised to (IIB), the half-life of the epoxide would therefore be of the order of 4 milliseconds.

#### REFERENCES AND NOTES

1. H.Grisebach, "Biosynthetic Patterns in Microorganisms and Higher Plants" (Wiley, New York: 1967) p.10.
2. The epoxide (II) was prepared by the reaction of 2'-hydroxychalcone with 3-chloroperbenzoic acid in dichloroethane. It has  $m/e$  240 ( $\text{M}^+$ );  $\text{ir } \nu_{\text{C=O}}$   $1650 \text{ cm}^{-1}$  (H-bonded);  $\text{nmr}$  ( $\text{CDCl}_3$ )  $\delta$  4.13 (d,  $J=2$ , 1H), 4.33 (d,  $J=2$ , 1H), 6.8-8.0 (m, 9H), 11.90 (s, 1H, H-bonded OH).
3. H.Wagner and L.Farkas in "The Flavonoids", ed. J.B. Harborne, T.J. Mabry and H.Mabry (Chapman and Hall, London: 1975) p.144.
4. By comparison with the  $\text{pK}_a$  of 2-hydroxyacetophenone (10.06); D.D. Perrin, *Nature*, 1958, 182, 741.