

Angular Dependence of Substituent Effects in Rigid, Bicyclic Systems^{1,2}

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Summary The rates of alkaline hydrolysis of the isomeric ethyl 5,6-epoxybicyclo[2,2,2]octane-2-carboxylates and ethyl bicyclo[2,2,2]octane-2-carboxylate have been measured and the results analysed in terms of the two limiting models for the transmission of nonconjugative substituent effects—the σ -inductive and the field models.

IN order to evaluate the ability of the σ -inductive and field models in describing the transmission of nonconjugative substituent effects, the isomeric ethyl 5,6-epoxybicyclo[2,2,2]octane-2-carboxylates (I—IV) and ethyl bicyclo[2,2,2]octane-2-carboxylate (V) have been synthesized and their rates of alkaline hydrolysis measured in 50% (by

weight) aqueous ethanol at 25°. The second-order rate coefficients are summarized in Table 1.†

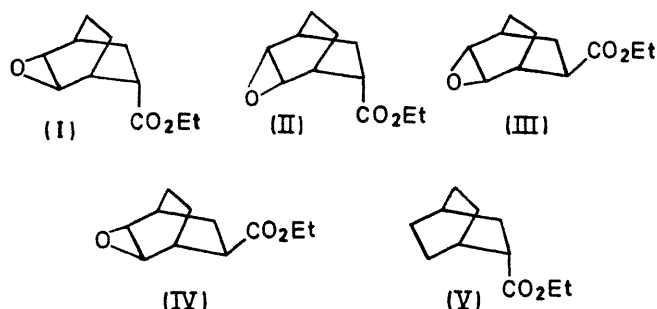


TABLE 1. Second-order rate constants for alkaline hydrolysis of bridge substituted bicyclo[2,2,2]octane esters

Compound	k (l/mole min $\times 10^3$)
(I)	31.2 \pm 0.4
(II)	0.442 \pm 0.014
(III)	5.59 \pm 0.06
(IV)	21.7 \pm 0.9
(V)	2.160 \pm 0.003

Using the σ -inductive model as defined by Ehrenson⁸ as the basis for comparison, the rates of alkaline hydrolysis of (I–IV) would be expected to be the same since the number of σ -bonds and the number of σ -bond pathways between the substituent and the reaction centre are identical. The field model, on the other hand, predicts substantially different rates since the distance and the angular disposition of the substituent with respect to the reaction centre is different in each case. Examination of the data in Table 1 reveals rates varying over a 70-fold range.

In order to evaluate quantitatively the field model, the

TABLE 2. Parameters and calculated values of $\log k_X/k_H$ for alkaline hydrolysis of isomeric epoxybicyclo[2,2,2]octane esters at 25°.

Ester	Parameters			Tanford sphere D_E	$\log k_X/k_H$ (Calc.)	$\log k_X/k_H$ (Exp.)
	R (Å)	μ (D)	θ			
(I)	3.76	2.01	19°52'	3.35	1.60	1.16
(II)	2.95	2.01	107°16'	2.88	-0.96	-0.69
(III)	4.21	2.01	73°10'	3.54	0.38	0.41
(IV)	4.53	2.01	39°54'	3.75	0.82	1.00

† Excellent second-order plots were obtained up to 80% reaction. Product analysis was carried out in all cases. Alkaline hydrolysis of (I) in 95% ethanol at 25° followed by acidification produced the corresponding acid in low yield (m.p. 121–125°; lit. 129–131°) which upon standing slowly converted into the 5-hydroxy- γ -lactone (m.p. 233–236°; lit. 235–237°). Alkaline hydrolysis of very small quantities of (II), (III), and (IV) followed by acidification produced oils which defied crystallization. Alkaline hydrolysis of (V) followed by acidification produced the acid corresponding to (V) in good yields (m.p. 83–84.5°; lit. 84–85°).

‡ Analysis of (II) by means of the Tanford modification of the Kirkwood–Westheimer cavity model was undertaken simply because the experimental data were available. Surprisingly, the model does an extraordinarily good job in predicting the correct relative order for the hydrolysis of this seemingly sterically hindered ester. The work reported in this communication is complementary to the observations made by several other workers⁶ in the field concerning the angular dependence of substituent effects.

¹ See: C. L. Liotta, W. F. Fisher, and G. H. Greene, *Chem. Comm.*, 1969, 1251.

² Abstracted in part from the Ph.D. Thesis of W. F. F., Georgia Institute of Technology (1970).

³ S. Ehrenson, *Progr. Phys. Org. Chem.*, 1964, 2, 175–251.

⁴ C. Tanford, *J. Amer. Chem. Soc.*, 1957, 79, 5348; J. G. Kirkwood and F. W. Westheimer, *J. Chem. Phys.*, 1938, 6, 506; F. H. Westheimer and J. G. Kirkwood, *ibid.*, p. 513; F. H. Westheimer and M. W. Shookhoff, *J. Amer. Chem. Soc.*, 1939, 61, 555; F. H. Westheimer, W. A. Jones, and R. A. Lad, *J. Chem. Phys.*, 1942, 10, 478.

⁵ M. L. Sage, *J. Chem. Phys.*, 1961, 35, 142.

⁶ M. J. S. Dewar and P. J. Grisdale, *J. Amer. Chem. Soc.*, 1962, 84, 3548; K. Bowden, *Canad. J. Chem.*, 1963, 41, 2781; K. Bowden and D. C. Parkin, *Chem. Comm.*, 1968, 75; W. Adcock and P. R. Wells, *Austral. J. Chem.* 1965, 18, 1351; W. Adcock and M. J. S. Dewar, *J. Amer. Chem. Soc.*, 1967, 89, 379; E. J. Grubbs and R. Fitzgerald, *Tetrahedron Letters*, 1968, 4901; D. S. Noyce and B. E. Johnston, *J. Org. Chem.*, 1969, 34, 1252; R. Golden and L. M. Stock, *J. Amer. Chem. Soc.*, 1966, 88, 5928.

data in Table 1 were analysed in terms of the following electrostatic equation:

$$\log \frac{k_X}{k_H} = \frac{e \mu \cos \theta}{2.3 k T R^2 D_E} \quad (1)$$

where e is the electronic charge, μ is the difference in bond moment between the carbon–substituent bond and the carbon–hydrogen bond, k is the Boltzmann constant, T is the absolute temperature, R is the distance between the centre of the dipole and the reaction centre, θ is the angle made by the carbon–substituent bond and the distance R , and D_E is the effective dielectric constant of the medium separating the substituent from the reaction centre as evaluated by means of the Tanford modification of the Kirkwood–Westheimer cavity model.⁴ The value of R was taken as the distance from the midpoint of the line joining the epoxide oxygen to the centre of the C-5–C-6 bond to the carbonyl carbon. The microwave spectrum of *cis*-2,3-epoxybutane has shown the dihedral angle between the epoxide ring and the C-1, C-2, C-3, C-4 plane to be 110°. Since the oxygen of the epoxides in question is buttressed against an ethylene bridge, the dihedral angle was chosen as 120°. The value of μ was found to be 2.01 D, also from the microwave spectrum.⁵ Table 2 summarizes the parameters used in the calculations as well as the calculated and experimental rate ratios. While agreement is only qualitatively good, the field model does predict the correct order of relative rates—something which the σ -inductive model does not do.^{†6}

It may be concluded that (i) the observed angular dependence of substituent effects on the rates of alkaline hydrolysis of (I–IV) demonstrates the operation of field effect and that (ii) the Tanford modification of the Kirkwood–Westheimer cavity model is a useful approach in qualitatively predicting relative rates.

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