

RING-CHAIN TAUTOMERISM. PART 10⁺. THE REACTION OF OXOCARBOXYLIC ACIDS WITH DIAZODIPHENYLMETHANE

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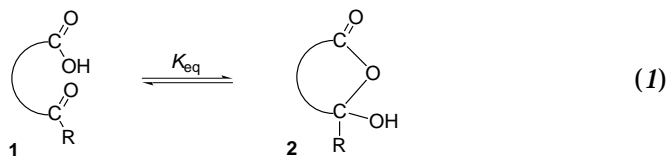
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Dedicated to Professor Otto Exner on the occasion of his 75th birthday in recognition of his outstanding contributions to physical organic chemistry.

The rate coefficients for the esterification of a series of oxocarboxylic acids with diazodiphenylmethane have been determined in ethanol or 2-methoxyethanol at 30.0 °C. These and the rates of reaction with model compounds have been used to estimate the equilibrium constants for ring-chain tautomerism for the oxocarboxylic acids.

Key words: Ring-chain tautomerism; Diazodiphenylmethane; Esterification; Reaction kinetics; Equilibrium constants.

Ring-chain tautomerism has been shown to occur in a number of oxocarboxylic acids². Thus, this has been shown to give rise to both ring **2** and chain **1** forms (Eq. (1)) of these systems, with an equilibrium constant, K_{eq} , given by Eq. (2).



$$K_{eq} = a_{\text{ring}} / a_{\text{chain}} \quad (2)$$

+ For Part 9 see ref.¹

Quantitative measurements of this behaviour can be made directly, *e.g.* by IR, UV-VIS and ^1H NMR spectroscopic methods, or indirectly, *e.g.* by $\text{p}K_{\text{a}}$ measurements. For the former, the measurements are limited to those systems having K_{eq} in the range of *ca* 0.02 to 50, together with having observable spectroscopic difference between **1** and **2**. For the latter, the observed $\text{p}K_{\text{a}}$ can be related to the true $\text{p}K_{\text{a}}^{\text{T}}$ by Eq. (3) (ref.³). If a reliable estimate of $\text{p}K_{\text{a}}^{\text{T}}$ can be made, K_{eq} can be found by measuring $\text{p}K_{\text{a}}$.

$$\text{p}K_{\text{a}}^{\text{T}} = \text{p}K_{\text{a}} - \log(K_{\text{eq}} + 1) \quad (3)$$

In principle, $K_{\text{eq}} > \text{ca } 2$ could be estimated with reasonable certainty using this method. This method depends on the significantly greater acidity of the carboxylic acid than that of the hydroxylactone.

The principal problems in measuring K_{eq} values for ring-chain tautomerism of oxocarboxylic acids are those where K_{eq} is very large or small, where the spectral difference between tautomers is small or where solvent effect makes direct spectral measurement impractical. A possible method, which could overcome some of these problems, is based on the measurement of the reactivity of the ring-chain tautomeric system in which only one tautomer, normally the chain, is significantly more reactive and where the reactivity of that tautomer alone can be reliably estimated. The observed rate coefficient k_2 is related to the true rate coefficient k_2^{T} as shown in Eq. (4).

$$k_2 = k_2^{\text{T}} a_{\text{chain}} / (a_{\text{chain}} + a_{\text{ring}}) \quad (4)$$

This enables the calculation of K_{eq} if both k_2 and k_2^{T} are known, as shown in Eq. (5).

$$K_{\text{eq}} = (k_2^{\text{T}} / k_2) - 1 \quad (5)$$

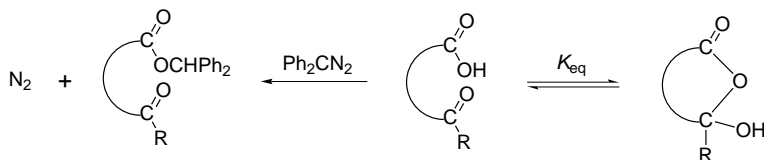
Carboxylic acids react at convenient rates with diazodiphenylmethane (DDM) and the reaction can be followed spectroscopically⁴. The mechanism of this reaction and rate-reactivity relations have been studied in detail⁵. Bell *et al.*⁶ have developed a reactivity-based method in which the catalytic effect of the anions of the carboxylic acids in water on the decomposition of nitramide and on the mutarotation of glucose was measured.

Using the relation between the catalytic constants of carboxylic acid anions and their pK_a values to determine the true pK_a^T , the equilibrium constant K_{eq} can be evaluated from the observed pK_a using Eq. (3).

In the present study, the rates of reaction of a series of oxocarboxylic acids with DDM have been measured. Using model compounds to estimate the true rate coefficients, K_{eq} values for these acids have been determined.

RESULTS AND DISCUSSION

In Table I the rate coefficients for the esterification of the oxocarboxylic acids with DDM at 30.0 °C are shown. A reaction pathway is shown in Scheme 1. The oxocarboxylic acids selected are those with K_{eq} values which are either known or expected⁷ to be >2 . For these acids, k_2 and k_2^T will be sufficiently different to enable determination of K_{eq} with reasonable



SCHEME 1

certainty. The solvent employed in this study was ethanol, except for those acids too insoluble in the latter for which 2-methoxyethanol was used. The rate coefficients were reproducible to $\pm 3\%$ and are the observed rate coefficients, k_2 , for these oxocarboxylic acids. The true rate coefficients, k_2^T , are also shown in Table I. These have been estimated from model systems. The rate coefficients for the esterification of 2-substituted benzoic acids with DDM have been measured by Chapman and co-workers⁸. The k_2^T values for the 2-acylbenzoic acids are estimated from the “*ortho*”- ρ value for the DDM esterification of 2-substituted benzoic acids⁹ in ethanol at 30 °C and the σ_p values for the acyl substituents¹⁰. Furthermore, 2-benzoylbenzoic and 9-oxofluorene-1-carboxylic acids have K_{eq} values that can be confidently estimated to be <0.1 in ethanol, *cf.* refs^{2,7}. The former acid has been used as a point of reference for the estimation of k_2^T for the 2-acylbenzoic acids. The value for the (*Z*)-3-benzoyl-2,3-diphenylacrylic acid has been based on the values for (*E*)-2-phenylcinnamic and (*Z*)-3-substituted acrylic acids^{9,11} in ethanol at 30 °C and for the 8-acyl-1-naphthoic acids, as well as 5-formylphenanthrene-4-carboxylic acid, on the values for the 8-substituted 1-naphthoic acids studied previously¹² in 2-methoxyethanol at 30 °C. The former estimate was based on the corresponding “ ρ ” value⁹ and σ_p of the

TABLE I
Rate coefficients, k^2 , for the esterification of the oxocarboxylic acids with diazodiphenylmethane and ring-chain equilibrium constants, K_{eq} , at 30.0 °C^a

Acid	$k_2/\text{dm}^3 \text{ mol}^{-1} \text{ min}^{-1}$	$k_2^T/\text{dm}^3 \text{ mol}^{-1} \text{ min}^{-1}$	K_{eq}
2-Substituted benzoic acids			
In ethanol			
H	1.00 (0.990) ^b	–	–
CHO	1.17	7.9	5.8(4.6, 14.8, 5.6) ^{c,d,e}
COCH ₃	1.54	7.7	4.0(2.4, 3.2, 3.0) ^{c,d,e}
COCH ₂ CH ₃	1.50	7.7	4.1(3.5, 2.6) ^{c,d}
COCH(CH ₃) ₂	1.49	7.7	4.2(2.2, 1.9, 5.6) ^{c,d,e}
COC(CH ₃) ₃	1.21	7.7	5.4(4.6, 3.2) ^{c,d}
COCH ₂ Ph	1.96	7.8	3.0(2.6, 2.5) ^d
COCOPh	16.5	60	2.6
COCCl ₃	0.370	36	96(78) ^f
COBr ₃	0.360	36	99(100) ^f
COPh	7.70	–	^g
9-Oxofluorene-1-carboxylic	7.18	–	^g
(Z)-3-Benzoyl-2,3-diphenylacrylic	0.0263	28	1 100(1 600) ⁱ
In 2-methoxyethanol			
H	0.650 (0.640) ^b	–	–
8-Substituted 1-naphthoic acids			
H	0.810(0.802) ^b	–	–
CHO	0.00470	6.0	1 300(1 200) ^h
COCH ₃	0.0764	6.0	78(100, 130) ^{e,h}
5-Substituted phenanthrene-4-carboxylic acid			
CHO	0.00482	13	2 700(3 000) ^h

^a Rate coefficients are reproducible to $\pm 3\%$ or better and are the mean of at least two determinations. ^b Refs^{4,5,12}. ^c In 80% aqueous 2-methoxyethanol (¹H NMR spectroscopic method)⁷. ^d In methanol (¹H NMR spectroscopic method)⁷. ^e In water (catalytic/pK_a method)⁶. ^f In water (pK_a method)⁷. ^g K_e estimated to be <0.1, cf. refs^{3,7}. ^h In 80% aqueous 2-methoxyethanol (pK_a method)⁷.

benzoyl group¹⁰, while the latter was based on the corresponding “ ρ ” value¹² and σ_p for the formyl and acetyl groups¹⁰. The uncertainties in k_2^T values can be estimated to be $\pm 5\%$ for the 2-acylbenzoic acids and to be $\pm 10\%$ for the remainder. The calculated K_{eq} values for ethanol shown in Table I can be estimated to have uncertainties of $\pm 8\%$ for the first group and $\pm 13\%$ for the second group. The literature K_{eq} values are also shown in Table I for either methanol and 80% aqueous 2-methoxyethanol, using a direct ¹H NMR spectroscopic method, or for water and 80% aqueous 2-methoxyethanol, using indirect pK_a methods^{6,7}. However, ring-chain tautomeric equilibrium constants for oxocarboxylic acids are known to be solvent-dependent^{2,13}. The literature K_{eq} values shown in Table I are those for solvent systems of comparable solvating power to that of ethanol¹⁴. There is good agreement, in general, between the K_{eq} values obtained by the present novel method using the DDM reaction and those obtained using both direct and indirect methods studied previously^{2,13}. An advantage of the DDM reaction method is that this reaction can be studied in an extremely wide range of solvents⁴.

EXPERIMENTAL

Materials

All the oxocarboxylic acids had been prepared for use in previous studies⁷. The purity of the compounds were monitored by m.p., ¹H and ¹³C NMR and IR spectroscopy. Solvents were purified by standard methods¹⁴. DDM was prepared by the oxidation of the corresponding hydrazone⁵.

Rate Measurements

These were determined, using a Perkin-Elmer lambda 16 UV-VIS spectrophotometer, at 30.0 (± 0.05) °C in a similar manner to that described previously^{5a,9,11,12} using, normally, a 10-fold excess of acid (0.06 mol dm⁻³). An alternative procedure was employed for acids available in very limited quantity. The acid solution (3 ml, 0.06 mol dm⁻³) was placed in the cuvette, thermostatted at 30.0 °C, and a DDM solution (3 \times 10⁻³ ml, 6 mol dm⁻³) added to initiate the reaction. When required, the second-order rate coefficients were checked by the method devised by Corbett¹⁵, which can be applied if the excess used is less than 10-fold.

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REFERENCES

1. Bowden K., Hiscocks S. P., Perjéssy A.: *J. Chem. Soc., Perkin Trans. 2* **1988**, 291.

2. Valters R. E., Flitsch W.: *Ring-Chain Tautomerism*. Plenum Press, New York 1985.
3. Pascual C., Wegmann D., Graf U., Scheffold R., Sommer P. F., Simon W.: *Helv. Chim. Acta* **1964**, *47*, 213.
4. Dack M. R. J.: *J. Chem. Educ.* **1972**, *49*, 600.
5. a) Bowden K., Buckley A., Chapman N. B., Shorter J.: *J. Chem. Soc.* **1964**, 3380; b) More O'Ferrall R. A., Kwok W. K., Miller S. I.: *J. Am. Chem. Soc.* **1964**, *86*, 5553.
6. a) Bell R. P., Cox B. G., Timini B. A.: *J. Chem. Soc. B* **1971**, 2247; b) Bell R. P., Covington A. D.: *J. Chem. Soc., Perkin Trans. 2* **1975**, 1343; c) Bell R. P., Earls D. W., Henshall J. B.: *J. Chem. Soc., Perkin Trans. 2* **1976**, 39.
7. a) Bowden K., Taylor G. R.: *J. Chem. Soc. B* **1971**, 1390; b) Bowden K., Last A. M.: *J. Chem. Soc., Perkin Trans. 2* **1973**, 1144; c) Bowden K., Malik F. P.: *J. Chem. Soc., Perkin Trans. 2* **1993**, 635; d) Bowden K., Byrne J. M.: *J. Chem. Soc., Perkin Trans. 2* **1997**, 123; e) Bowden K., Raja S.: *J. Chem. Soc., Perkin Trans. 2* **1999**, 39.
8. a) Chapman N. B., Shorter J., Utley J. H. P.: *J. Chem. Soc.* **1962**, 1824; b) Buckley A., Chapman N. B., Shorter J.: *J. Chem. Soc. B* **1969**, 195.
9. Bowden K.: *Can. J. Chem.* **1965**, *43*, 3354.
10. Hansch C., Leo A., Hockman D.: *Exploring QSAR Hydrophobic, Electronic and Steric Constants*. American Chemical Society, Washington 1995.
11. Bowden K., Parkin D. C.: *Can. J. Chem.* **1968**, *46*, 3909.
12. Bowden K., Parkin D. C.: *Can. J. Chem.* **1969**, *47*, 185.
13. Bhatt M. V., Kamath K. M.: *J. Chem. Soc. B* **1968**, 1036.
14. Reichardt C.: *Solvent and Solvent Effects in Organic Chemistry*, 2nd ed. VCH, Weinheim 1988.
15. Corbett J. F.: *J. Chem. Educ.* **1972**, *49*, 663.