Influence of Structure on β-Diketo–Enol Equilibria: a Kinetic Study by the Relaxation Technique

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The effects of structural variation on the position of the tautomeric equilibrium of β-dicarbonyls of the type MeCO·CHR·COMe have been studied by the relaxation technique. The acidities of the enol and keto forms may be determined from the kinetic parameters of the equilibria in basic media without recourse to direct measurement of the enol content. This is not possible by classical techniques. The enol content may itself be calculated from the deprotonation constants of the ketones. Contrary to presently accepted views, it is shown that variation of the enol content as a function of the structure is due to variation in the energy of the ketones and not the enols. The reverse situation is found however in going from pentane-2,4-dione to ethyl acetoacetate. The decrease of the enol content in aqueous media relative to the gaseous state is identical for all members of the series except for R = H.

OUR understanding of the influence of substituents, R^1 and R^2, on the tautomeric equilibria of β-dicarbonyls of the type $R^1CO{\cdot}CHR^2{\cdot}COR^1$ arises essentially from measurements of the enol content of these systems.[1] Interpretation of these results is complicated by the problem of determining the effects of the substituents on the energy of each of the two tautomers, as was pointed out by Forsén and Nilsson who state [2] ' the interpretation of the substituent effects cannot always be made in a unique manner as the effects on the keto and/or enol forms are difficult to disentangle and solvent effects are often marked '. In particular, evidence has been presented that for compounds of the general formula MeCO·CHR·COMe, the variation of the alkyl group R induces a very strong diminution of the enol content [1a–c] relative to R = H, a situation which is also found in going from pentane-2,4-dione to ethyl acetoacetate.[3] Such results can be explained by postulating either a simultaneous variation of the energies of the keto and enol forms or by a variation of the energy of one of the forms with the energy of the other remaining essentially unaffected. The aim of this study is to demonstrate that for the β-dicarbonyl compounds investigated a complete kinetic analysis of the tautomeric equilibrium permits one to (*a*) choose one of the above hypotheses and to determine precisely the origin of the variations of the enol content as a function of structure, (*b*) measure the enol content from the rates of deprotonation of the ketones, and (*c*) measure directly the thermodynamic ionisation constants of the keto and enol forms (pK_{EH} and pK_{CH}) without a knowledge of the enol content.

The general reaction scheme for our system is shown in equation (1) where EH, CH, and E^- represent the

$$\mathrm{EH} + \mathrm{OH^-} \underset{k_{21}}{\overset{k_{12}}{\rightleftharpoons}} \mathrm{E^-} + \mathrm{H_2O} \underset{k_{32}}{\overset{k_{23}}{\rightleftharpoons}} \mathrm{CH} + \mathrm{OH^-} \quad (1)$$

enol, keto, and ionised forms respectively. For each compound, we have simultaneously determined k_{12}, k_{21}, k_{23}, and k_{32} by the temperature-jump method. This has the advantage over chemical methods in that it does not perturb the system by the introduction of reagents foreign to the system.

EXPERIMENTAL

Solvent and Reagents.—The solvent used was twice-distilled water, 0·1M in sodium perchlorate. The sodium perchlorate was recrystallised, dried, and stored in a desiccator. The β-dicarbonyl compounds (K and K or Aldrich) were purified by g.l.c. (Varian Autoprep column SE 30 on chromosorb B). The final purity was checked by g.l.c. (HyFi model 600, column as before). In all cases the purity was >99%. The n.m.r. (JEOL JNM-C-60 HL) and i.r. spectra (Perkin-Elmer 225) of the compounds in the liquid state were identical with published spectra.[1c]

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[1] (*a*) J. B. Conant and A. F. Thompson, *J. Amer. Chem. Soc.*, 1932, **54**, 4039; (*b*) K. V. Auwers and H. Jacobson, *Annalen*, 1922, **426**, 161; (*c*) Y. N. Molin, S. T. Ioffe, E. E. Zaev, E. K. Solov'eva, E. E. Kugucheva, V. V. Voevodskii, and M. I. Kabachnik, *Bull. Acad. Sci. U.S.S.R.*, 1965, 1523; (*d*) J. L. Burdett and M. T. Rogers, *J. Phys. Chem.*, 1966, **70**, 939; (*e*) G. Allen and R. A. Dwek, *J. Chem. Soc.* (*B*), 1966, 161.

[2] S. Forsén and M. Nilsson, ' The Chemistry of the Carbonyl Group,' Interscience, London, 1970, vol. 2, p. 198.

[3] A. S. N. Murthy, A. Balasubramanian, and C. N. R. Rao, *Canad. J. Chem.*, 1962, **40**, 2267; J. L. Burdett and M. T. Rogers, *J. Amer. Chem. Soc.*, 1964, **86**, 2105; *Canad. J. Chem.*, 1965, **43**, 1516.

Kinetic Measurements.—The relaxation times were determined with a commercial temperature-jump apparatus (Messanlagen Studiengesellschaft) coupled to a Hewlett-Packard model 141A oscilloscope. The principle of the temperature-jump method has already been adequately reviewed.[4] The initial temperature was such that the final temperature was 25 ± 1 °C, corresponding to an increase in temperature of *ca.* 3°. The ionic strength of the solution was maintained constant with sodium perchlorate. Relaxation times were obtained using aliquot portions of stock solutions of the β-dicarbonyl compounds, with the pH adjusted to the desired value with 1N-sodium hydroxide. Determinations of the pH were made with a Beckman 'Research pH Meter' before and after each relaxation experiment. The values used are those corresponding to averages of the initial and final values; the maximum divergence accepted was 0·2 pH units. The reactions were monitored by determining the change in optical density (and hence concentration) of the enolate ion as a function of time. Since the enolate ion is common to the two equilibria the complete relaxation spectra of the system is thus obtained directly.

In Figure 1, by way of example, the slow relaxation spectra of ethyl acetoacetate A and the rapid relaxation spectra of 3-acetylheptan-2-one B are given. The experimental conditions are: ethyl acetoacetate; pH 11·50, *t* 25 °C, initial concentration *ca.* 6 × 10^{-5}M, λ 273 nm, oscilloscope 0·020 V and 20 ms, and τ_2 40 ms; 3-acetylheptan-2-one; pH 10·45, *t* 25 °C, initial concentration *ca.* 8 × 10^{-4}M, λ 307 nm, oscilloscope 0·010 V and 100 μs, and τ_1 170 μs.

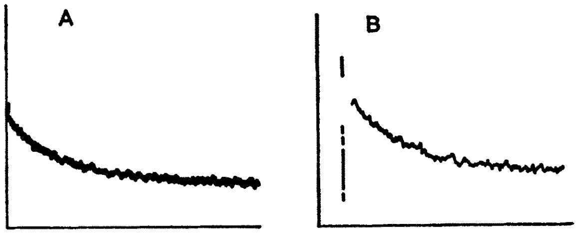


FIGURE 1 A, Slow relaxation spectrum of ethyl acetoacetate. B, Fast relaxation spectrum of 3-acetylheptan-2-one

RESULTS AND DISCUSSION

Rate Equations.—The Scheme illustrates all the possibilities of β-diketo–enol transformation. In basic media, the route through step 4 must be negligible. In addition, the equilibrium 2 $\rightleftharpoons$ 4 corresponds to the protolysis of water, $H_2O \underset{k_{42}}{\overset{k_{24}}{\rightleftharpoons}} H^+ + OH^-$ ($k_{42} = 1{\cdot}4 \times 10^{11}$ l mol^{-1} s^{-1}),[5] which is too rapid to be measured by our technique. It can also be shown that the autocatalytic route (1 $\rightleftharpoons$ 3) does not intervene here.† The reaction Scheme thus reduces to equation (1). The corresponding rate equations are given by equations (2)—(4). The

$$dC_{\mathrm{EH}}/dt = -k_{12}C_{\mathrm{EH}}C_{\mathrm{OH^-}} + k_{21}C_{\mathrm{E^-}} \qquad (2)$$

$$dC_{\mathrm{E^-}}/dt = k_{12}C_{\mathrm{EH}}C_{\mathrm{OH^-}} - (k_{21} + k_{23})C_{\mathrm{E^-}} + k_{32}C_{\mathrm{CH}}C_{\mathrm{OH^-}} \qquad (3)$$

$$dC_{\mathrm{CH}}/dt = -k_{32}C_{\mathrm{CH}}C_{\mathrm{OH^-}} + k_{23}C_{\mathrm{E^-}} \qquad (4)$$

relaxation times are given by equations (5) and (6),

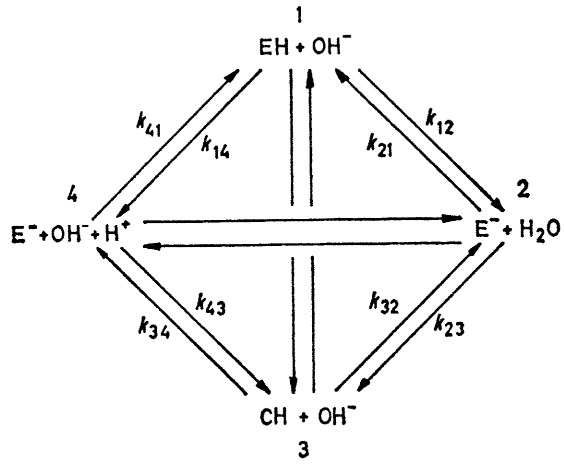
$$\tau_1^{-1} = k_{21} + k_{12}(\bar{C}_{\mathrm{OH^-}} + \bar{C}_{\mathrm{EH}}) \qquad (5)$$

$$\tau_2^{-1} = k_{23} + k_{32}(\bar{C}_{\mathrm{OH^-}} + \bar{C}_{\mathrm{CH}}) \qquad (6)$$

where $\bar{C}_{\mathrm{OH^-}}$, *etc.*, represent the equilibrium concentrations at 25 °C. Since under our conditions $\bar{C}_{\mathrm{OH^-}} \gg \bar{C}_{\mathrm{EH}}, \bar{C}_{\mathrm{CH}}$, the above expressions for the relaxation times simplify to equations (7) and (8).

$$\tau_1^{-1} = k_{21} + k_{12}\bar{C}_{\mathrm{OH^-}} \qquad (7)$$

$$\tau_2^{-1} = k_{23} + k_{32}\bar{C}_{\mathrm{OH^-}} \qquad (8)$$



SCHEME

Determination of Rate Constants.—Since for the same compound τ_2 is *ca.* 10^3 times greater than τ_1, their individual determinations do not pose any serious problem. The values of τ_1 and τ_2 were measured at variable base concentration with a minimum range of 1 pH unit. To obtain the four rate constants for each

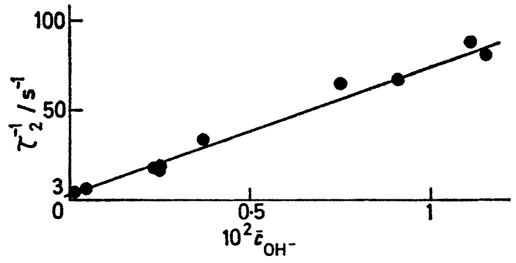


FIGURE 2 Plot of τ_2 versus *f* ($\bar{C}_{\mathrm{OH^-}}$) for ethyl acetoacetate. Each point corresponds to an average of three or four determinations of τ_2, for a particular pH value. The three closely grouped points were obtained from different initial concentrations of the keto-ester

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† At the same pH, important variations of the enolate ion concentration do not modify the values of τ_1 and τ_2 (see Figure 2). In addition, the reactivity of the diketo form of pentane-2,4-dione with the enolate ion of 5,5-dimethylcyclohexan-1,3-dione is *ca.* 10^3 times slower than with OH⁻ (M. Eigen, *Angew. Chem. Internat. Edn.*, 1964, **3**, 1). Consequently the keto and enol forms react essentially with OH⁻.

[4] M. Eigen and L. de Maeyer, in 'Techniques of Organic Chemistry,' ed. A. Weissberger, Interscience, New York, 1963, vol. 8.

[5] M. Eigen and L. de Maeyer, *Z. Elektrochem.*, 1955, **59**, 986.

compound we set $\tau_i = f_i(\bar{C}_{OH^-})$. The slopes represent k_{12} for τ_1 and k_{32} for τ_2; while the intercepts give k_{21} and k_{23} (an example is shown in Figure 2). The results of our determinations are shown in Table 1.

TABLE 1

Rate constants for the base-catalysed β-diketo–enol equilibrium of MeCO·CHR·COMe and $MeCO{\cdot}CH_2{\cdot}CO_2Et$ at 25 ± 1 °C

Compound	$10^{-7}k_{12}$ [a] / l mol^{-1} s^{-1}	$10^{-3}k_{21}$/ s^{-1}	k_{23}/s^{-1}	k_{32} / l mol^{-1} s^{-1}
Pentane-2,4-dione (1)	1·5 [b]	*c*	0·1	2·4 × 10^4 [b,e]
3-Methylpentane-2,4-dione (2)	0·64	0·44	0·1	130 [e]
3-Ethylpentane-2,4-dione (3)	0·93	1·7	0·4	38 [e]
3-Acetylhexan-2-one (4)	1·07	*c*	0·1	63 [e]
3-Isopropylpentane-2,4-dione (5)	*d*	*d*	1·5	8·0 [e]
3-Acetylheptan-2-one (6)	0·92	1·7	0·1	60
Ethyl acetoacetate (7)	25	0·75	3·0	0·67 × 10^4

[a] The uncertainty in k_{12} and k_{32} is of the order of 20%, of k_{23} of 50%. Although the uncertainty of k_{21} is greater, comparison with literature values of pK_{EH} is quite satisfactory (*cf.* Table 2). [b] $k_{12} = 1{\cdot}6 \times 10^7$ l mol^{-1} s^{-1} and $k_{32} = 4 \times 10^4$ l mol^{-1} s^{-1}, see M. Eigen, *Pure Appl. Chem.*, 1963, **6**, 97. [c] Least-squares treatment of the data for k_{21} yields a very small but negative intercept. [d] The rapid relaxation time is not observable, even though the enol content is sufficiently large (*ca.* 1%). [e] See ref. 10.

Determination of the Thermodynamic Ionisation Constants, K_{EH} *and* K_{CH}.—The constants K_{EH} and K_{CH} [equations (9) and (10)] were obtained from the individual rate constants for each equilibrium. Classically

$$K_{EH} = ([E^-][H_3O^+])/[EH] \qquad (9)$$

$$K_{CH} = ([E^-][H_3O^+])/[CH] \qquad (10)$$

K_{EH} and K_{CH} are calculated from the overall thermodynamic constant K_g and the enol content K_T,[6] so that a knowledge of the enol content is indispensible. Moreover in our series MeCO·CHR·COMe, the decomposition of the products in basic media is sufficient to hamper seriously the utility of these methods. This is certainly why, for the five compounds of this type reported in the literature, only one value of K_{EH} and two values of K_g are to be found. A comparison of our measurements with those of other authors (Table 2) yields a satisfactory agreement if one takes into consideration the diversity of definitions of acidity (overall p*K*, p*K* as a function of activities, of concentrations, *etc.*).

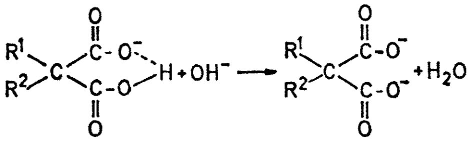
It is interesting to note that in our series of compounds MeCO·CHR·COMe only k_{32} varies strongly. If one compares the extreme values of the constants in each column, one obtains a variation of a factor of 2·4 for k_{12}, 3·8 for k_{21}, 15 for k_{23}, and 3000 for k_{32}. If one considers the constant k_{12}, one can assign to it a fundamental significance in that it provides an indication of the intensity of the intramolecular hydrogen bond of the enol form.[7] The order of magnitude (10^7—10^8 l mol^{-1} s^{-1}) is characteristic for systems of this type. In particular, Eyring *et al.*[8] obtained values varying from 28 × 10^7 to 4·5 × 10^7 l mol^{-1} s^{-1} for the rate of the second deprotonation of a series of malonic acids, thus showing the presence of an intramolecular hydrogen bond in these monoanions (values of *ca.* 10^{10} would have been expected if the reactions were diffusion controlled).

TABLE 2

Thermodynamic ionisation constants for the β-diketo–enol equilibrium of MeCO·CHR·COMe and $MeCO{\cdot}CH_2{\cdot}CO_2Et$ at 25 ± 1 °C

	pK_{EH} [a]		pK_{CH} [a]	
Compound	Meas. values	Lit. values	Meas. values	Lit. values [d]
(1)	*b*	8·13 [e]	8·6	9·3,[f] *8·94* [g] *8·77* [h]
(2)	9·8	9·50 [e]	10·9	*10·87*,[i] *11·06* [e]
(3)	10·3		12·0	*11·34* [i]
(4)	*b*		11·2	
(5)	*c*		13·3	
(6)	10·3		11·2	
(7)	8·5	8·09 [e]	10·6	*10·49*,[e] *10·81* [j] *10·68* [k]

[a] The uncertainty in pK_{EH} and pK_{CH} is *ca.* 0·2. [b] Absence of k_{21}. [c] Relaxation time not observed. [d] Values in italics correspond to the total acidity. They are very similar to the acidities of the keto forms. [e] Ref. 6*b*. [f] R. P. Bell, *Trans. Faraday Soc.*, 1943, **39**, 253. [g] G. Schwarzenbach and K. Lutz, *Helv. Chim. Acta*, 1940, **23**, 1147. [h] F. Hashimoto, J. Tanaka, and S. Nagakura, *J. Mol. Spectroscopy*, 1963, **10**, 401. [i] L. Laloi and P. Rumpf, *Bull. Soc. chim. France*, 1961, 1645. [j] W. Walisch and H. A. Ruppersberg, *Chem. Ber.*, 1959, **92**, 2622. [k] M. L. Eidinoff, *J. Amer. Chem. Soc.*, 1945, **67**, 2072.



If this view is accepted, the alkyl groups R must perturb the intensity of the intramolecular bond only very slightly. This is confirmed by an examination of the n.m.r. and i.r. spectra of the pure liquids. The results are shown in Table 3 on the assumption that the two spectroscopic parameters δ_{OH} and $\nu_{C=O}$ (enol) are

TABLE 3

Chemical shifts of the hydroxy-proton and frequencies of the symmetric vibration of the carbonyl group, of the enol forms of MeCO·CHR·COMe at 25 °C

Compound [a]	δ_{OH}/p.p.m.[b]	$\nu_{C=O}$/cm^{-1}
(1)	15·45	1615
(2)	17·65	1590
(3)	17·95	1580
(4)	18·0	1585
(5)	17·8 [c]	*d*
(6)	18·0	1595

[a] See Table 1. [b] From tetramethylsilane as internal standard. [c] See Figure 3. [d] No peak at *ca.* 1600 cm^{-1} due to the very small enol content.

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[6] (*a*) J. P. Calmon and P. Maroni, *Bull. Soc. chim. France*, 1965, 2525; (*b*) G. Schwarzenbach and E. Felder, *Helv. Chim. Acta*, 1944, **27**, 1701.

[7] M. Eigen and W. Kruse, *Z. Naturforsch.*, 1963, **18**b, 857.

[8] M. H. Miles, E. M. Eyring, W. W. Epstein, and R. E. Ostlund, *J. Phys. Chem.*, 1965, **69**, 467.

reflections of intramolecular hydrogen bonding.[9] Although the variations in these parameters in passing from R = H to alkyl are quite marked, subsequent internal variations in the alkyl group R yield differences of the order of magnitude of the experimental error.

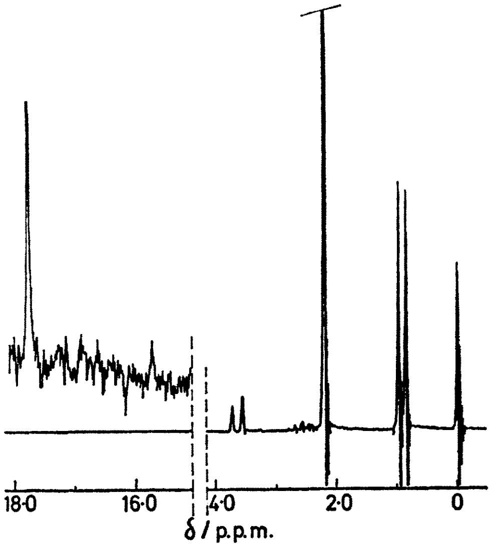

FIGURE 3 60 MHz N.m.r. spectrum of 3-isopropylpentane-2,4-dione as a pure liquid with tetramethylsilane as internal standard. The spectrum between δ 0 and 4 p.p.m. is due solely to the keto form. The signal at δ 17·8 p.p.m. is attributed to the OH proton of the enol, and is the first direct evidence for the existence of this enol

Our kinetic (k_{12}) and spectroscopic (δ_{OH}) results indicate that the intramolecular hydrogen bond is slightly stronger for the substituted products ($R \neq H$) than for pentane-2,4-dione (R = H). On the contrary, the enol content is much smaller for $R \neq H$ than for R = H. This shows definitely that the position of the β-diketo–enol tautomeric equilibrium is not governed by the strength of the hydrogen bond.

The thermodynamic ionisation constants K_{12} and K_{32}, corresponding to the equilibria $1 \rightleftharpoons 2$ and $3 \rightleftharpoons 2$ respectively, may be expressed by equations (11) and (12)

$$K_{12} = [E^-]/([EH][OH^-]) \qquad (11)$$

$$K_{32} = [E^-]/([CH][OH^-]) \qquad (12)$$

while the enol content K_T is expressed by equation (13).

$$K_T = \frac{K_{32}}{K_{12}} = \frac{k_{32} \times k_{21}}{k_{23} \times k_{12}} \qquad (13)$$

The enormous variations in enol content (K_T) cannot be explained by considering k_{12} (essentially constant) or k_{21} and k_{23} (very small variations); consequently, since K_T depends almost entirely on k_{32}, a specific relation should exist between k_{32} and K_T. If so, the enol content for any member of the series could be calculated simply from a knowledge of the rate constant for deprotonation of the keto form and *vice versa*. We examined the literature for values of enol content measured under conditions similar to ours. Since only two values were available (for R = H and Me),[6b] we then examined the vapour-phase data for which values of R = H, Me, and Et exist [1a] and derived the good linear relation (14).

$$\log k_{32} = 2{\cdot}1 \log K_T{}^{v} + 2{\cdot}2 \qquad (14)$$

In addition, if the available data [1a] for the enolisation of β-diketo-esters of general formula MeCO·CHR·CO$_2$Et (a series very similar to ours) is correlated in the same fashion, one obtains the linear relation (15).* Similar

$$\log k_{32} = 3{\cdot}0 \log K_T{}^{v} + 4{\cdot}5 \qquad (15)$$

relations will exist for the rate of deprotonation of the ketone and the enol content in aqueous systems. The two available data points (for R = H and Me) give equation (16).

$$\log k_{32} = 2{\cdot}7 \log K_T{}^{a} + 6{\cdot}4 \qquad (16)$$

The similarity in the slope of equation (16) to that of (14) and (15) indicates that there is indeed a relation between the two parameters (Figure 4). In this case line A includes four extrapolated points and line B, three such points. The fact that line C is experimental and that lines A—C have very similar slopes allows us to extrapolate the preceding values.†

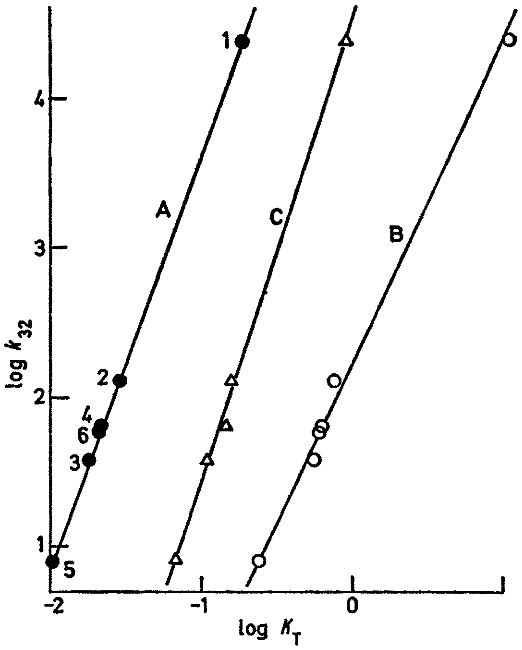

FIGURE 4 Equivalence of the effects of structure on the rate of deprotonation (k_{32}) and on the position of the β-diketo–enol equilibrium. A, Enol content in the aqueous phase for MeCO·CHR·COMe ($K_T{}^a$). B, Enol content in the vapour phase for MeCO·CHR·COMe ($K_T{}^v$). C, Enol content in the vapour phase for MeCO·CHR·CO$_2$Et ($K_T{}^v$). 1, R = H; 2, R = Me; 3, R = Et; 4, R = Pr^n; 5, R = Pr^i; 6, R = Bu^n.

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* We have used the series MeCO·CHR·COMe rather than MeCO·CHR·CO$_2$Et since in the latter case the enol content is too small (0·4% for R = H) to allow measurement of k_{12} (except for R = H), which is essential for our purpose.

† We are still measuring the enol content of the complete series in aqueous media.

[9] S. Forsén, F. Merényi, and M. Nilsson, *Acta Chem. Scand.*, 1964, **18**, 1208.

This type of relation between the rate constant for deprotonation of the keto form and the thermodynamic β-diketo–enol equilibrium constants [equations (14)—(16)] points to the unexpected conclusion that the variation of the enol content of compounds of the general formula MeCO·CHR·COMe (R = alkyl) depends uniquely on the energy of the diketo form. We have previously demonstrated[10] that the effect of structure on the rate of enolisation (k_{32}) was a phenomenon common to both acid and base catalysis, as well as for mono- and dicarbonyl compounds with one enolisation site. This effect was shown to operate mainly in the initial state of the reaction. We agree with Hughes[11] that the inductive, donating effect of the alkyl groups lowers the acidity of the proton α to the two carbonyl groups. However, considering the accepted order of electron release by alkyl groups, the above hypotheses do not explain the observed differences in reactivity nor the descending order of reactivities as a function of R. The considerable difference observed in passing from linear to branched substituents could indicate the operation of a steric effect[12] in conjunction with the electrical effect, a point which is currently under investigation.

A knowledge of K_T without considering other factors is not sufficient for the interpretation of the effects of structure on the position of the tautomeric equilibrium. In particular, the variation of K_T in passing from MeCO·CH$_2$·COMe to MeCO·CHMe·COMe, has been explained by a steric effect operating on the enol,[1c,13] between the two extreme and the central methyl groups, leading to a distortion of the molecule, although the original basis of this explanation is difficult to pin-point. This idea has been 'confirmed' by i.r. spectroscopic evidence, more precisely, by an examination of the position of the O–H vibration.[13a] However, from an examination of our spectra, we conclude that the assignment of the very weak vibration at 3400—3600 cm^{-1} to this mode is dubious. In addition it has been concluded that this vibrational band may be absent from β-dicarbonyl compounds in certain cases.[14]

We can apply our conclusions to the determination of the enol content for a series of 3-alkylpentane-2,4-diones (Table 4). The third column of Table 4 indicates that the enol content of all members of the series except the first is *ca.* 27 times higher in the vapour state than in aqueous solution. This represents the role that the solvent plays in the position of the tautomeric equilibrium.

Kabachnick *et al.*[1c] found 0·6% of enol by bromination of 3-isopropylpentane-2,4-dione. Their method, however, did not permit a distinction between the *cis*- and *trans*-enol. The remarkable agreement between this value and our own (0·6% enol in the neat liquid and 1% in water) is in line with the hypothesis favouring only the *cis*-enol. Thus we are in complete disagreement with the results of Tanaka *et al.*,[15] who quote in effect 0% of the *cis*-enol and 24% of the *trans*. We suggest that the 0% is invalid because the method of detection (n.m.r.) is subject to the sensitivity limitations of the spectrometer. In our opinion one should, instead of 0%, give an upper limit of the *cis*-enol concentration in terms of spectrometer sensitivity. The figure of 24% corresponds closely to the formation of an *O*-alkylated product (I) (27%[1c]) as in the alkylation of pentane-2,4-dione. In addition, the proton chemical shift used to identify the *trans*-enol is δ 5·4 p.p.m. Kabachnick *et al.*[1c] give a value of δ 5·59 p.p.m. for the vinylic proton of the enol ether. In our opinion the species identified by the Japanese authors as the *trans*-enol is really the *O*-alkylated product.

MeCO·CH⁚C(OPr^i)Me (I)

TABLE 4

Influence of solvent (H$_2$O) on the degree of enolisation of β-diketone MeCO·CHR·COMe

Compound *	K_T^a Aqueous solution	K_T^v Vapour state	K_T^v/K_T^a
(1)	0·19 [6b]	11 [1a]	58
(2)	0·029 [6b]	0·79 [1a]	27
(3)	*0·018*	0·55 [1a]	30
(4)	*0·023*	*0·63*	27
(5)	*0·010* [a]	*0·25*	25
(6)	*0·022*	*0·60*	27

* See Table 1.

Values in italics correspond to extrapolated values from equations (14) and (16). [a] It is interesting in this case to compare K_T^a and the enol content for the pure liquid (K_T^{pure}). To obtain K_T^{pure}, the following procedure was used. We compared the intensities of the n.m.r. signals for the hydroxy-protons of 3-ethyl- and 3-isopropyl-pentane-2,4-dione. The enol content of the first product is 28%,[1a] which gives 0·6% ($K_T^{pure} = 0{\cdot}006$) for 3-isopropylpentane-2,4-dione. For all the compounds MeCO·CHR·COMe, $K_T^{pure}/K_T^a \gg 1$, except for R = Pr^i, for which the ratio is 0·6. This last result is surprising in that it is probably the only case where the enol content does not decrease in passing from the pure liquid to the aqueous phase.

The interest in our method is that it may be extended to the resolution of three other problems. (*a*) K_T Can be obtained similarly for the 3-alkyl-β-diketo-esters. Our method is particularly interesting for this purpose in that due to the very small values (K_T = 0·4% for ethyl acetoacetate),[6b] spectroscopic and chemical methods are difficult to employ. (*b*) Similarly, K_T can be obtained for other protic solvents and the influence of the solvent can be evaluated quantitatively (Table 4). (*c*) Because of the relationship between the rate of deprotonation of the ketone (k_{32}) and the position of equilibrium, and since the enol content is smallest in

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aqueous media, one could expect an increase in the reactivity of the ketone (k_{32}) in all other protic solvents.

In going from pentane-2,4-dione to ethyl acetoacetate, the preceding interpretation is in all probability no longer valid, in that the order of magnitude of k_{32} remains practically constant, whereas significantly, there is a large increase of k_{12} from 1·5 to 25 × 10^7. This suggests a strong weakening of the intramolecular hydrogen bond of the enol. This hypothesis is confirmed by an examination of the n.m.r. spectra, the shift of the OH proton being only 13·1 p.p.m. Contrary to the preceding cases, the fall in enol content in this case is better explained by the destabilisation of the enol form.

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