The Reactions of Zinc(II) with 1,3-Diketones in Aqueous Solution. Catalysis by Cacodylic Acid during Complex Formation

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The reactions of zinc(II) with three 1,3-diketones have been investigated in aqueous solution at 25 °C and an ionic strength of 0.5 mol dm^{-3} $NaClO_4$. The catalytic effect of cacodylic acid on the reactions of zinc(II) with pentane-2,4-dione has been demonstrated. In addition, the effect of cacodylic acid on the hydrolysis of the nickel(II) and copper(II) triglycine complexes has been investigated.

The kinetics and mechanisms of the reactions of metal ions with 1,3- or β-diketones have been the subject of a number of previous investigations and the results have recently been reviewed.[1] In general, the rates of formation of the 1:1 complexes of metal ions with β-diketones are lower than those predicted by the Eigen–Wilkins–Tamm[2,3] mechanism on the basis of the outer-sphere association constants and the rates of solvent exchange. It has been noted that the reduction in the 'expected' rates of metal complex formation is metal dependent. The reduction is least for 'hard' metal ions such as iron(III), oxovanadium(IV) and dioxouranium(VI) which form complexes of high stability with ligands having oxygen-donor atoms. These metal ions also react directly with both the keto and enol tautomers while other metal ions such as nickel(II) and zinc(II) only react with the enol tautomer. However, in most of the reactions investigated to date, the rate of reaction of metal ions with the enolate ion, obtained by loss of a proton from either the enol or keto tautomers, is close to that predicted by the Eigen–Wilkins mechanism.

Only one previous kinetic study of the reactions of Zn^{2+} with β-diketones has been reported.[4] Subsequent work has shown that the mechanism proposed was deficient and that the steady-state approach used is not valid for reactions where the rates of proton transfer are either comparable to or less than the rates of reaction of the metal ion with the ligand.[1] We have recently shown in a preliminary communication that the reactions of Zn^{2+} with pentane-2,4-dione are catalysed by cacodylic acid (dimethylarsinic acid), a buffer frequently used to control the hydrogen-ion concentration during studies of complex formation reactions.[5] We now report the complete results of our investigations of the reactions of zinc(II) with pentane-2,4-dione (Hpd), 1,1,1-trifluoropentane-2,4-dione (Htfpd) and 4,4,4-trifluoro-1-(2-thienyl)butane-1,3-dione (Htftbd). We have also investigated the catalytic effects of cacodylic acid on the hydrolysis of the nickel(II) triglycine complex. Despite the widespread use of cacodylic acid as a buffer, there have been few reports of its catalytic effect on the reactions of metal ions with ligands.

Experimental

Zinc(II) nitrate trihydrate (May and Baker) was used as the source of zinc(II). Stock solutions were standardized by titration with ethylenediaminetetraacetate using Eriochrome Black-T indicator. The titration was carried out at pH 10 in the presence of a NH_4OH–NH_4Cl buffer.

Reagent grade pentane-2,4-dione (BDH) was freshly distilled under reduced pressure prior to use. 1,1,1-Trifluoropentane-2,4-dione (Koch Light) and 4,4,4-trifluoro-1-(2-thienyl)butane-1,3-dione (Koch Light) were used as supplied. Stock solutions of the sodium salt of cacodylic acid (Fluka) were standardized by titration against standard sulfamic acid.

AnalaR grade perchloric acid (BDH) was used as the source of hydrogen ions. Reagent grade sodium perchlorate (Riedel de Haën) was used to adjust the ionic strength. In order to remove any traces of iron(III) present, stock solutions of sodium perchlorate adjusted to *ca.* pH 3 with $HClO_4$ were passed through a column of cation-exchange resin (BDH Amberlite IR-120) in the sodium form.

The UV/VIS spectra were recorded on a Shimadzu UV260 spectrophotometer. The pH measurements were made using an AGB 3000 pH & ion meter equipped with a Russell combination electrode. The filling solution of the reference section was a 3 mol dm^{-3} aqueous solution of sodium chloride. The pH meter was calibrated to read hydrogen-ion concentration directly by titrating solutions of perchloric acid (0.001–0.005 mol dm^{-3}) with standard sodium hydroxide solution. The endpoints of these titrations were determined using the method of Johansson.[6]

Metal-ion stability constants were determined by the potentiometric technique. Titrations were carried out in jacketed titration vessels through which water at 25 °C was

Table 1 Ratio of enol (HE) to keto (HK) tautomers, [HE]/[HK], apparent dissociation constants of ligands K_{HA}, and of their enol and keto tautomers, K_{HE} and K_{HK} respectively, and rate constants for enolization (k_e) and ketonization (k_f) for pentane-2,4-dione (Hpd), 1,1,1-trifluoropentane-2,4-dione (Htfpd) and 4,4,4-trifluoro-1-(2-thienyl)butane-1,3-dione (Htftbd)

Ligand	[HE]/[HK]	K_{HA}/mol dm^{-3}	K_{HE}/mol dm^{-3}	K_{HK}/mol dm^{-3}	k_e/s^{-1}	k_f/s^{-1}
Hpd	0.13	7.08×10^{-10}	6.09×10^{-9}	8.01×10^{-11}	1.5×10^{-2}	0.114
Htftbd	4.4×10^{-3}	4.4×10^{-7}	1.31×10^{-4}	4.48×10^{-7}	8.4×10^{-3}	2.46
Htfpd	4.1×10^{-3}	8.13×10^{-7}	1.37×10^{-4}	8.18×10^{-7}	1.49×10^{-3}	2.49

circulated. All titrations were carried out in an atmosphere of oxygen-free nitrogen. The data were refined using the program SUPERQUAD.[7]

Kinetic measurements were made on a Hitech SF-20 stopped-flow apparatus which was interfaced to a BBC microcomputer. Pseudo-first-order rate constants were calculated by fitting the absorbance data (70–100 data points) to equation (1) using a three-parameter curve-fitting routine in

$$A = A_\infty(1 - e^{-kt}) + A_0e^{-kt} \qquad (1)$$

which the absorbance at time zero, A_0, the absorbance at infinity time, A_∞, and the rate constant, k, were treated as variables. Data for three to four half-lives were utilized in these calculations. The reported rate constants are the average of at least three determinations. The standard deviation in individual runs was usually less than 1%.

All solutions were freshly prepared for the kinetic runs.

Table 2 Equilibrium data for reaction of Zn^{2+} with pentane-2,4-dione (Hpd), 1,1,1-trifluoropentane-2,4-dione (Htfpd) and 4,4,4-trifluoro-1-(2-thienyl)butane-1,3-dione (Htftbd) in aqueous solution at 25 °C and ionic strength 0.5 mol dm^{-3}

Ligand	log β_1	K*	K_E	K_K
Hpd	4.68 (±0.03)	3.39×10^{-5}	2.92×10^{-4}	3.84×10^{-5}
Htftbd	3.45 (±0.02)	1.26×10^{-3}	0.370	1.26×10^{-3}
Htfpd	2.72 (±0.03)	4.27×10^{-4}	7.18×10^{-2}	4.3×10^{-4}

* $1/K = 1/K_E + 1/K_K$.

Results

Tables 1 and 2 contain the relevant equilibrium constants for the ligands and the 1:1 complexes formed with Zn^{2+}. The rate constants for enolization (k_e) and ketonization (k_f) of the ligands are also included.

Tables 3, 4 and 5 list the kinetic data for reaction of zinc(II) with all three ligands studied. Only a single relaxation was observed in all cases. The mechanism proposed to account for the kinetic data is shown in Scheme 1 where HK and HE

$$\mathrm{HK} + Zn^{2+} \underset{k_f}{\overset{k_e}{\rightleftharpoons}} \mathrm{HE} + Zn^{2+} \underset{k'_{-HE}}{\overset{k'_{HE}}{\rightleftharpoons}} [\mathrm{ZnE}]^+ + H^+$$

Scheme 1

represent the keto and enol tautomers respectively, $k'_{HE} = k_{HE}[Zn^{2+}]$ and $k'_{-HE} = k_{-HE}[H^+]$. The general solution of the secular equations obtained from Scheme 1 yields equations (2)–(4) with parameters p, q and b defined by expressions (5)–(7).[8,9] The λ_1 solution is trivial and need not be considered further.

$$\lambda_1 = 0 \qquad (2)$$

$$\lambda_2 = 0.5(p + q) \qquad (3)$$

$$\lambda_3 = 0.5(p - q) \qquad (4)$$

$$p = k_e + k_f + k_{HE}[Zn^{2+}] + k_{-HE}[H^+] \qquad (5)$$

$$q = (p^2 - 4b)^{\frac{1}{2}} \qquad (6)$$

$$b = k_ek_{HE}[Zn^{2+}] + (k_{-e} + k_{-f})k_{-HE}[H^+] \qquad (7)$$

Table 3 Kinetic data for reaction of zinc(II) with pentane-2,4-dione (Hpd) in aqueous solution at 25 °C and I = 0.5 mol dm^{-3} NaClO$_4$ (λ = 310 nm)

$10^3[Zn^{2+}]$/ mol dm^{-3}	$[H^+]$/ mol dm^{-3}	$10^3[Me_2As(O)OH]$/ mol dm^{-3}	k_{obs}/s^{-1}
5.0	1.0×10^{-3}		0.104
5.0	2.0×10^{-3}		0.103
5.0	3.0×10^{-3}		0.102
5.0	4.0×10^{-3}		0.103
5.0	5.0×10^{-3}		0.103
1.0	3.0×10^{-3}		0.094
2.0	3.0×10^{-3}		0.096
3.0	3.0×10^{-3}		0.097
4.0	3.0×10^{-3}		0.1031
5.0	3.0×10^{-3}		0.106
3.0	0.05		0.100
3.0	0.10		0.099
3.0	0.15		0.102
3.0	0.20		0.104
3.0	0.25		0.105
2.0	0.01	1.0	0.0988
2.0	0.01	2.0	0.0959
2.0	0.01	3.0	0.0953
4.0	0.01	1.0	0.0966
4.0	0.01	2.0	0.102
4.0	0.01	3.0	0.107
1.0	5.50×10^{-8}	1.27	0.289
2.0	7.08×10^{-8}	1.27	0.254
3.0	7.94×10^{-8}	1.27	0.250
4.0	8.32×10^{-8}	1.27	0.257
5.0	7.59×10^{-8}	1.27	0.270
1.0	1.95×10^{-7}	1.27	0.439
2.0	2.09×10^{-7}	1.27	0.389
3.0	2.19×10^{-7}	1.27	0.356
4.0	2.24×10^{-7}	1.27	0.344
5.0	2.34×10^{-7}	1.27	0.362
1.0	8.90×10^{-7}	1.27	0.439
2.0	1.02×10^{-6}	1.27	0.399
3.0	1.15×10^{-6}	1.27	0.394
4.0	1.09×10^{-6}	1.27	0.383
5.0	1.09×10^{-6}	1.27	0.379
1.0	1.20×10^{-6}	1.27	0.484
2.0	1.32×10^{-6}	1.27	0.405
3.0	1.38×10^{-6}	1.27	0.382
4.0	1.26×10^{-6}	1.27	0.378
5.0	1.66×10^{-6}	1.27	0.390
1.0	3.39×10^{-7}	2.54	0.978
2.0	3.16×10^{-7}	2.54	0.859
3.0	3.55×10^{-7}	2.54	0.789
4.0	3.39×10^{-7}	2.54	0.743
5.0	3.47×10^{-7}	2.54	0.746
1.0	3.09×10^{-7}	1.27	0.514
3.0	3.47×10^{-7}	1.27	0.416
5.0	3.39×10^{-7}	1.27	0.397
2.0	1.18×10^{-7}	1.27	0.382
4.0	1.38×10^{-7}	1.27	0.373
3.0	3.09×10^{-7}	1.27	0.385
3.0	3.09×10^{-7}	2.54	0.665
3.0	3.24×10^{-7}	3.81	0.994
3.0	1.22×10^{-7}	1.27	0.338
3.0	1.15×10^{-7}	3.18	0.751
3.0	1.05×10^{-7}	6.36	1.42
3.0	4.90×10^{-7}	7.62	1.72
3.0	5.62×10^{-7}	1.27	0.363
3.0	4.62×10^{-7}	3.18	0.811
3.0	4.68×10^{-7}	6.36	1.62
3.0	4.79×10^{-7}	7.62	1.97
1.0	3.39×10^{-7}	1.27	0.459
1.0	3.54×10^{-7}	2.54	0.835
1.0	3.24×10^{-7}	3.81	1.25
1.0	3.16×10^{-7}	5.08	1.65
1.0	3.39×10^{-7}	6.36	2.00
3.0	3.63×10^{-7}	1.27	0.364
3.0	3.54×10^{-7}	2.54	0.668
3.0	3.24×10^{-7}	3.81	0.972
3.0	3.39×10^{-7}	5.08	1.28
3.0	3.39×10^{-7}	6.36	1.58
5.0	3.89×10^{-7}	1.27	0.342
5.0	3.63×10^{-7}	2.54	0.629
5.0	3.39×10^{-7}	3.81	0.937
5.0	3.54×10^{-7}	5.08	1.22
5.0	3.47×10^{-7}	6.36	1.50

Table 4 Kinetic data for reaction of zinc(II) with 4,4,4-trifluoro-1-(2-thienyl)butane-1,3-dione (Htftbd), in aqueous solution at 25 °C and I = 0.5 mol dm^{-3} NaClO$_4$ (λ = 300 nm)

$10^3[Zn^{2+}]$/mol dm^{-3}	$[H^+]$/mol dm^{-3}	k_{obs}/s^{-1}	k_{calc}/s^{-1}
1.0	0.005	2.57	2.46
1.0	0.025	2.54	2.46
1.0	0.050	2.52	2.46
1.0	0.100	2.54	2.46
1.0	0.200	2.42	2.46
1.0	0.250	2.35	2.46
2.0	3.24×10^{-5}	0.165	0.156
4.0	3.24×10^{-5}	0.094	0.097
6.0	3.02×10^{-5}	0.066	0.075
2.0	6.64×10^{-5}	0.346	0.285
4.0	6.76×10^{-5}	0.184	0.161
6.0	6.76×10^{-5}	0.127	0.120
8.0	6.76×10^{-5}	0.099	0.099
10.0	6.76×10^{-5}	0.084	0.086
2.0	1.05×10^{-4}	0.376	0.421
4.0	1.07×10^{-4}	0.235	0.233
6.0	1.10×10^{-4}	0.172	0.172
8.0	1.12×10^{-4}	0.134	0.140
10.0	1.10×10^{-4}	0.110	0.118

Table 5 Kinetic data for reaction of zinc(II) with 1,1,1-trifluoropentane-2,4-dione (Htfpd) in aqueous solution at 25 °C and I = 0.5 mol dm^{-3} NaClO$_4$ (λ = 300 nm)*

$10^3[Zn^{2+}]$/mol dm^{-3}	$[H^+]$/mol dm^{-3}	k_{obs}/s^{-1}
5.0	5.0×10^{-3}	2.20
5.0	6.0×10^{-3}	2.23
5.0	7.0×10^{-3}	2.28
5.0	0.01	2.30
5.0	0.025	2.45
5.0	0.05	2.46
5.0	0.10	2.48
5.0	0.20	2.45

* k_{calc} = 2.49 s^{-1}.

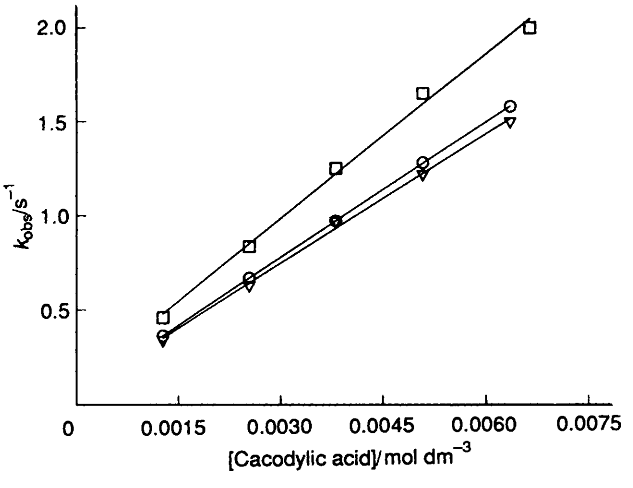

Fig. 1 Plot of k_{obs} against total cacodylic acid concentration for reaction of Zn^{2+} with pentane-2,4-dione in aqueous solution at 25 °C and I = 0.5 mol dm^{-3} NaClO$_4$, pH = 6.5, $[Hpd]_{total}$ = 0.0001, $[Zn]_{total}$ = 0.001 (□), 0.002 (○) or 0.003 (▽) mol dm^{-3}

Factoring the q term, expanding the factor $[1 - (4b/p^2)]^{\frac{1}{2}}$ using the binomial expansion and retaining only the first two terms gives equation (8).

$$q = p - 2(b/p) \tag{8}$$

It is apparent that the mechanism in Scheme 1 may give a maximum of two relaxations irrespective of whether the reaction is monitored in the forward direction (complex formation) or the reverse direction (hydrolysis). The faster of these two relaxations is described by equation (9) while the slower is described by equation (10).

$$\lambda_2 = p - (b/p) \tag{9}$$

$$\lambda_3 = b/p \tag{10}$$

Substituting for p and b in equations (9) and (10) from equations (5) and (7) respectively while noting that $K_E = k_{HE}/k_{-HE}$ and rearranging the terms gives equations (11) and (12) for the fast and slow relaxations respectively. Since k_e, k_f and K_E are all known (Tables 1 and 2) equations (11) and (12) now contain only one unknown parameter, k_{HE}.

$$\lambda_2 = k_e + k_f + k_{HE}[Zn^{2+}] + (k_{HE}[H^+]/K_E) - \left\{\frac{k_e k_{HE}[Zn^{2+}] + [(k_e + k_f)k_{HE}[H^+]/k_E]}{k_e + k_f + k_{HE}[Zn^{2+}] + (k_{HE}[H^+]/k_E)}\right\} \tag{11}$$

$$\lambda_3 = \frac{k_e k_{HE}[Zn^{2+}] + [(k_e + k_f)k_{HE}[H^+]/K_E]}{k_e + k_f + k_{HE}[Zn^{2+}] + (k_{HE}[H^+]/K_E)} \tag{12}$$

An examination of the kinetic data in Table 3 shows that at concentrations of hydrogen ion $\geqslant$0.001 mol dm^{-3}, the rate constant for reaction of Zn^{2+} with Hpd is independent of both the metal- and hydrogen-ion concentrations and is approximately equal to $(k_e + k_f)$. Consideration of previously published data[1] suggests that in equations (11) and (12) the dominant terms are those containing k_{HE}/K_E and that the contribution of the terms to the right of the minus sign in equation (11) to λ_2 is usually quite small. Consequently, it becomes obvious that the kinetic data are not consistent with equation (11). An examination of the magnitude of the various terms in equation (12) shows that at large hydrogen-ion concentrations (> 0.001 mol dm^{-3}), the numerator is dominated by the $(k_e + k_f)k_{HE}[H^+]/K_E$ term while the denominator is dominated by the $k_{HE}[H^+]/K_E$ term. Under these conditions, equation (12) reduces to equation (13). This explains why the

$$\lambda_3 = (k_e + k_f) \tag{13}$$

pseudo-first-order rate constants obtained for reaction of Zn^{2+} with Hpd at relatively large hydrogen-ion concentrations are independent of both variation in metal- and hydrogen-ion concentration as observed in Table 3.

In order to obtain further insight into the mechanisms of the reactions of Zn^{2+} with Hpd, further studies were carried out at lower concentrations of hydrogen ion. A study of species distribution showed that the optimum pH range for studying the complex formation reactions in the forward direction was 6.5–7.5. In this pH range, the widely-used buffer cacodylic acid was used to maintain a constant pH during the kinetic runs. During a test to ascertain if the buffer exerted any influence on the rate constants, it was found that changing the buffer concentration exerted a significant effect on the pseudo-first-order rate constants. This is clearly evident from the data in Table 3. Fig. 1 also demonstrates the effect.

Recent studies have shown that buffers such as cacodylic acid can catalyse the enolization of 2- and 3-acetylthiophenes.[10] In order to ascertain if cacodylic acid exerted such an effect on the rates of enolization and ketonization of Hpd, a study of these reactions in the presence of various concentrations of the buffer was undertaken. However, an attempt to measure the rate of enolization (k_e) of Hpd in the presence of an excess of cacodylic acid using the usual bromination technique did not meet with success. Separate experiments showed that the bromine also reacted with the cacodylic acid at a rate comparable to that of its reaction with the diketone. Since it is known that k_e/k_f =

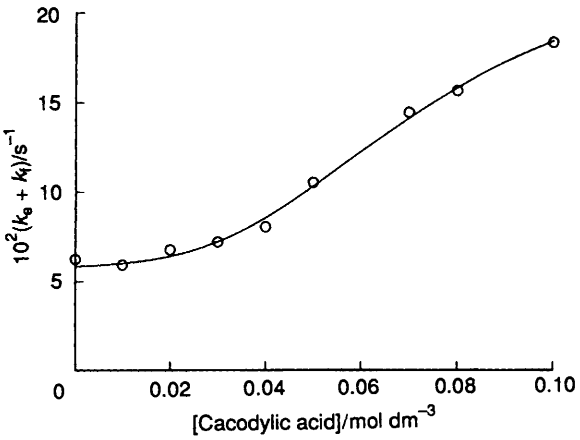

Fig. 2 Plot of $(k_e + k_f)$ against cacodylic acid for pentane-2,4-dione

[HE]/[HK], it is apparent that if k_f or $(k_e + k_f)$ together with the enol:keto ratio could be measured, then the magnitude of the effect of cacodylic acid on k_e could be ascertained. Consequently, ketonization reactions were carried out in the presence of large excesses of cacodylic acid. Solutions of Hpd to which various concentrations of cacodylic acid had been added were raised to a pH at which appreciable concentrations of the enolate anion were present. These solutions were then treated with an excess of acid in the stopped-flow device. The measured pseudo-first-order rate constant is equal to $(k_e + k_f)$. The results are shown in Fig. 2. It is apparent that the concentrations of cacodylic acid used to control the pH during the complex formation reactions of Zn^{2+} with Hpd ($\leqslant 7.5 \times 10^{-3}$ mol dm^{-3}) have minimal effect on the magnitude of $(k_e + k_f)$. NMR studies of solutions of Hpd containing cacodylic acid showed that the buffer did not affect the enol:keto ratio which remained constant at 0.13.

In order to evaluate the degree of interaction between Zn^{2+} and cacodylic acid, two titrations were carried out. In the first, a solution containing 0.01 mol dm^{-3} cacodylic acid was titrated against standard sodium hydroxide while in the second titration a solution containing 0.01 mol dm^{-3} cacodylic acid and 0.01 mol dm^{-3} Zn^{2+} was titrated against the same base. Between pH 2.5 and 6.5 the two titration curves overlapped indicating that no significant complex formation occurred.

Fig. 1 clearly shows that the cacodylic acid path predominates in the reaction of Zn^{2+} with Hpd. The rate data are broadly described by equation (14) where $[HB]_T$ is the total cacodylic acid concentration, K_a is the dissociation constant of cacodylic acid (5.37×10^{-7} mol dm^{-3}), A represents the

$$k_{obs} = A + \frac{B[HB]_T}{1 + (K_a/[H^+])} + \frac{C[HB]_T}{1 + ([H^+]/K_a)} \qquad (14)$$

cacodylic acid independent pathway while B and C represent pathways catalysed by the protonated and deprotonated forms of cacodylic acid respectively. The values of A, B and C are 0.067 (± 0.024), 326 (± 26) and 203 (± 15) respectively. The goodness of fit as evidenced by the uncertainties in A, B and C is relatively good over the wide range of Zn^{2+}, cacodylic acid and H^+ concentrations. This equation does not take into account the effect of $[Zn^{2+}]$ on k_{obs}. An examination of the data in Table 3 shows that typically, increasing the zinc(II) concentration by a factor of five reduces k_{obs} by approximately 25%. Thus the effect of changing zinc(II) concentration is relatively minor and the magnitude of the effect demonstrated here is less than that reported by De Maria *et al.*[10] during metal-catalysed iodination of 2- and 3-acetylthiophenes in the presence and absence of Ni^{2+}. Arising from this, they claimed that their k_e values were independent of $[Ni^{2+}]$.

In his investigations of the metal-catalysed iodination of 2-acetylpyridine, Cox[11] observed that the rate constants increased linearly with increasing metal-ion concentration at low metal-ion concentrations but levelled off and approached a limiting value at higher concentrations. This was ascribed to complex formation between the metal-ion catalyst and 2-acetylpyridine. The results presented here could be interpreted in terms of complex formation between the protonated diketone and the metal ion. Fig. 1 shows that under the conditions of the present experiment, the system is too close to saturation to allow an accurate determination of the equilibrium constant from the kinetic data.

If the reaction of Zn^{2+} with Hpd is similar to that of other metal ions, then it is unlikely that its rate of reaction with the enol tautomer would be greater than *ca.* 20 dm^3 mol^{-1} s^{-1}. On the other hand, the reactions of metal ions with the enolate tautomers of 1,3-diketones are normal on the basis of the Eigen–Wilkins–Tamm mechanism so that one can reasonably assume a rate constant of the order of 10^7 dm^3 mol^{-1} s^{-1} for reaction of Zn^{2+} with the enolate form of Hpd (pd^-). Using these values together with the dissociation constant of the ligand, it can be readily shown that at the pH values at which the complex formation reactions were carried out, the reaction of Zn^{2+} with pd^- will predominate over the direct reaction between Zn^{2+} and Hpd. Based on these assumptions, it is calculated that if the faster of the two reactions was being monitored [equation (11)], k_{obs} should have values greater than *ca.* 500 s^{-1} while if the slower of the two relaxations is being monitored [equation (12)] k_{obs} should have values of the order of 0.05 s^{-1}. Significantly, the uncatalysed pathway as represented by A in equation (14) is of similar magnitude to the k_{obs} predicted on this basis.

The kinetic data for reaction of Zn^{2+} with Htftbd are given in Table 4. The mechanism shown in Scheme 1 is also operative in this instance. It is apparent that at the higher hydrogen ion concentrations, the k_{obs} values approximate to $(k_e + k_f)$ while at lower hydrogen-ion concentrations, an inverse acid path is evident. As shown above, this can only occur in a situation where the slower of the two possible relaxations is being observed [equation (12)]. A close examination of equation (12) shows that at the lower hydrogen-ion concentrations, every term in the numerator is significant while the dominant term in the denominator is $k_{HE}[M]$. Allowing for this, equation (12) reduced to equation (15). A plot of k_{obs} against $[H^+]/[M]$

$$k_{obs} = k_e + \frac{(k_e + k_f)}{K_E}\frac{[H^+]}{[M]} \qquad (15)$$

should give a straight line of slope $(k_e + k_f)/K_E$ and intercept k_e. The plot gives a value for K_E of 0.34 compared to the directly determined value of 0.37.

Table 5 gives the kinetic data for reaction of Zn^{2+} with Htfpd. This reaction could not be studied in the forward direction at pH values where appreciable concentrations of the 1:1 complex existed due to the fact that under these conditions, some of the ligand would have ionized and the absorption due to the enolate ion would mask any absorption changes due to complex formation. The k_{obs} values are approximately equal to $(k_e + k_f)$ and the interpretation of the rate data is similar to that obtained for the reaction with Htftbd.

The well-characterized acid dissociation of the nickel(II) triglycine complex has previously been used as a model to investigate the catalytic activity of both buffers and their conjugate bases.[12–17] An investigation of the effect of cacodylic acid on this reaction has now been carried out. In order that the results might be directly compared with previous results, the investigations were carried out at an ionic strength of 0.3 mol dm^{-3} $NaClO_4$. The kinetic data are shown in Table 6. Previous studies have shown that k_{obs} has the general form of equation (16). In equation (16), k_{H_2O} is the acid-independent pathway, k_H

Table 6 Kinetic data for cacodylic acid catalysed dissociation of nickel(II) triglycine in aqueous solution at 25 °C and $I = 0.3$ mol dm^{-3} $NaClO_4$

$10^7[H^+]$/mol dm^{-3}	[Cacodylic acid]/mol dm^{-3}	k_{obs}/s^{-1}
0.550	0.025	1.50
1.35	0.05	3.70
1.86	0.075	5.99
2.14	0.100	8.16
2.34	0.125	10.5
0.355	0.025	0.308
0.229	0.050	1.03
0.398	0.0750	2.22
0.501	0.100	3.33
0.589	0.125	4.51
2.13	0.025	2.65
4.37	0.050	6.66
5.50	0.075	10.2
6.31	0.100	13.4
6.76	0.125	16.9

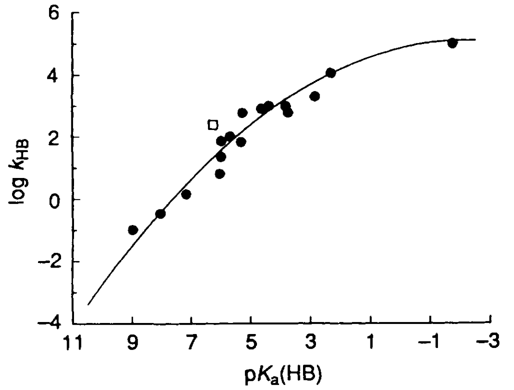

Fig. 3 Brønsted plot for the acid-dissociation reactions of nickel(II) triglycine in aqueous solutions at 25 °C and $I = 0.3$ mol dm^{-3} $NaClO_4$. From left to right the filled circles refer to the general acids HB: H_3BO_3, $H_3\overset{+}{N}C(CH_2OH)_3$, H_2im^+ (Him = imidazole), H_2edta^{2-} (H_4edta = ethylenediaminetetraacetic acid), 2-methylpyridinium ion, 3-methylpyridinium ion, $Hmal^-$ (H_2mal = malonic acid), pyridinium ion, $Hsucc^-$ (H_2succ = succinic acid), acetic acid, $Hfum^-$ (H_2fum = fumaric acid), glycolic acid, formic acid, chloroacetic acid, $Hgly^+$ (gly = glycine), H_3O^+. The open square refers to cacodylic acid. The solid line was calculated using equation (16) with $W_R = 44$ kJ mol^{-1}, $\lambda = 26.8$ kJ mol^{-1} and $C = 14.7$ kJ mol^{-1}

$$k_{obs} = k_{H_2O} + k_H[H^+] + k_{HB}[HB] + k_B[B] \quad (16)$$

$$k_{obs} = k_{H_2O} + k_H[H^+] + \frac{k_{HB}[HB]_T}{1 + (K_a/[H^+])} + \frac{k_B[HB]_T}{1 + ([H^+]/K_a)} \quad (17)$$

is the H^+-catalysed pathway, k_{HB} is the general acid catalysis pathway and k_B is the general base catalysis pathway. In terms of the dissociation constant of cacodylic acid (K_a), equation (16) may be written as equation (17) where $[HB]_T$ is the total cacodylic acid concentration present. For the nickel(II) triglycine complex, the values of k_{H_2O} and k_H in the medium used in these investigations have been previously reported to be 0.088 s^{-1} and 9.5 × 10^4 dm^3 mol^{-1} s^{-1} respectively[16] and are of course independent of the buffer used. In the present investigation which was carried out in the region of pH 6.2, the contributions of both of these terms to the k_{obs} values are quite small. Fitting the kinetic data to equation (17) gives values of 286 (±10) and 30 (±3) dm^3 mol^{-1} s^{-1} for k_{HB} and k_B respectively. While the value of k_B is relatively small, it is evident from the k_{HB} term that cacodylic acid is quite an effective general-acid catalyst comparable to $Hmal^-$ (pK_a 5.7) and considerably better than either H_2edta^{2-} (pK_a = 6.0) or 2-methylpyridinium (pK_a = 6.06).[16]

Fig. 3 shows a Brønsted plot for the acid dissociation of nickel(II) triglycine. The solid curve has been calculated using the modified Marcus theory approach as used by Bannister and Margerum,[16] equation (18). In equation (18), W_R is the work

$$\Delta G^{\ddagger} = W_R + \frac{\lambda}{4}\left(1 + \frac{\Delta G^{\circ}_{HB} - C}{\lambda}\right)^2 \quad (18)$$

required to bring the reactants together to form the reaction complex. In view of the fact that the reaction medium was the same as that previously used, the previously determined values of W_R (44 kJ mol^{-1}), λ (26.8 kJ mol^{-1}) and C (14.7 kJ mol^{-1}) were used. Fig. 3 clearly shows that cacodylic acid is more efficient at peptide protonation than calculated using equation (18). The calculated value of k_{HB} is 21.5 dm^3 mol^{-1} s^{-1} compared to the experimental value of 242 dm^3 mol^{-1} s^{-1}.

A similar investigation of the effect of cacodylic acid on the hydrolysis of the copper(II) triglycine complex gave a value of 3 × 10^3 dm^3 mol^{-1} s^{-1} for k_{HB}.

Discussion

The kinetic data for the reactions of Zn^{2+} with Htfpd, Htftbd and Hpd at the higher acid concentrations are consistent with the mechanism outlined in Scheme 1. The kinetic data do not allow k_{HE}, the rate constant for reaction of the metal ions with the enol tautomers of the ligands, to be determined. Only a lower limit can be calculated and the data for Hpd suggest that k_{HE} is greater than 0.1 dm^3 mol^{-1} s^{-1}.

In the case of Hpd, the reactions at the lower hydrogen-ion concentrations are dominated by the cacodylic acid catalysed pathway. It has been recently suggested that complex formation reactions of 1,3-diketones can be viewed as metal-ion catalysed proton transfer reactions.[18,19] There are a number of reports in the literature of both catalysis and inhibition of proton transfer reactions by metal ions.[10,11,20] The effect has been termed the 'metal activating factor' (m.a.f.).[10] The results are however, quite varied and there appears to be no definite pattern, in that a particular metal ion may catalyse one proton transfer reaction but may not catalyse another quite similar reaction. It has been proposed that the m.a.f. in the catalysis of certain β-ketoesters is due to a small amount of complexing between the metal ion and the keto form of the ester.[10,11,21,22] However, in some instances where there was no apparent complex formation, there were significant m.a.f.s and in such cases, the observed rate acceleration was ascribed to the participation of the metal cations in stabilizing the corresponding reaction transition states.[10] Rather surprising also is the fact that although the stabilities of nickel(II) complexes with a given ligand are usually greater than those of their Zn^{2+} or Cd^{2+} counterparts, Ni^{2+} does not catalyse the enolization of 2- and 3-acetylthiophenes while Zn^{2+} and Cd^{2+} do.[10] Furthermore, experiments carried out in this laboratory have shown that the catalytic effect of cacodylic acid on the reaction of Ni^{2+} with Hpd is relatively small compared to its effect on the reaction of Zn^{2+} with this ligand.

In the present instance, potentiometric data indicate that no significant complex formation occurs between Zn^{2+} and cacodylic acid in the pH range in which the kinetic investigations were carried out. Nevertheless, the rate of reaction of Zn^{2+} with Hpd is significantly accelerated by the presence of cacodylic acid. Previous studies have interpreted the reactions of metal ions with β-diketones in terms of a 'precursor complex' in which the metal ion is loosely bonded to either the keto or enol tautomer of the ligand.[1,18,19,23] Assuming that a similar mechanism obtains for the reactions of

Zn^{2+}, the observed rate acceleration due to cacodylic acid must result from the participation of cacodylic acid in the transition state, where it assists in the removal of the proton, to complete the complex formation reaction. The active participation of cacodylic acid in the transition state is supported by the apparent absence of complex formation between it and Zn^{2+} and by the fact that it does not appear to catalyse the enolization of unco-ordinated Hpd. Both cacodylic acid and its conjugate base catalyse the reaction.

This work clearly demonstrates the potential hazards in using cacodylic acid as a buffer in ligand substitution reactions where proton transfer reactions are involved. In certain circumstances, the acid can cause significant catalysis of this type of reaction and experiments in which the concentration of buffer is varied should always be carried out in order to highlight any catalytic effects.

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