Reactions of metal ions with β-ketoamides

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The kinetics and mechanisms of the reactions of copper(II), iron (III) and dioxouranium(VI) with acetoacetamide have been investigated in aqueous solution at 25 °C and ionic strength 0.5 mol dm^{-3} NaClO$_4$ using stopped-flow spectrophotometry. Mechanisms have been proposed which account satisfactorily for the kinetic data. Unlike β-diketones where in many instances the metal ion reacts exclusively with the enol tautomer, co-ordination of the amide tautomer of acetoacetamide is favoured by increased basicity of the carbonyl oxygen as a consequence of amide resonance.

Cu^{2+} and Fe^{3+} and $Fe(OH)^{2+}$ react with the keto tautomer of acetoacetamide with rate constants of 10.0, 14.1 and 50 dm^3 mol^{-1} s^{-1} respectively.

Introduction

The metal complexes of β-diketones have been extensively investigated during the past 50 years[1] while catalytic effects observed during the metal complex formation reactions of these ligands have been recently reported.[2] Although β-ketoamides are closely related to β-diketones, neither the ligands themselves nor their complexes have been investigated to the same extent as the latter.

A number of studies have reported details of preparative methods for transition metal complexes of β-ketoamides, copper(II),[3–10] iron(III),[11–13] beryllium(II), aluminium(III) and chromium(III).[13] Others have reported some stability constant data[14–16] while another study[17] reports details of the keto : enol ratios of these ligands in a variety of organic solvents.

To date, there have been no reports of studies of the kinetics and mechanisms of the reactions of metal ions with β-ketoamides. In general, β-carbonyl compounds such as ketoamides exist in solution as both enol and keto tautomers. The equilibrium may be represented as shown in reaction (1)

$$\mathrm{HK} \underset{k_\mathrm{f}}{\overset{k_\mathrm{e}}{\rightleftharpoons}} \mathrm{HE} \qquad (1)$$

where k_e and k_f are the rates of enolisation and ketonisation respectively.

In the case of certain β-diketones such as pentane-2,4-dione (Hpd) it has been shown that some metal ions react with both the keto and enol tautomers while others react exclusively with the enol tautomer.[1] On the other hand although the predominant form of ligands such as 4,4,4-trifluoro-1-(2-thienyl)-butane-1,3-dione (Htftbd) in aqueous solution is the keto form, the reactions of such ligands with metal ions occur exclusively *via* the enol tautomer.

In this paper, we report on the kinetics and mechanisms of the reactions of copper(II) and iron(III) with acetoacetamide in aqueous solution.

Experimental

Materials

Acetoacetamide (Aldrich) was used as supplied. $Fe(NO_3)_3 \cdot 9H_2O$ (BDH AnalaR), $Cu(NO_3)_2 \cdot 3H_2O$ (Riedel-de Haën) and $UO_2(NO_3)_2 \cdot 6H_2O$ (BDH AnalaR) were used as sources of iron(III), copper(II) and dioxouranium(VI) respectively. Stock solutions of both copper(II) and iron(III) were standardised by titration of the iodine liberated on addition of an excess of potassium iodide with sodium thiosulfate in the presence of starch indicator. The sodium thiosulfate had been previously standardised against potassium iodate. Perchloric acid (Riedel-de Haën) was used as the source of hydrogen ions and all solutions were adjusted to an ionic strength of 0.5 mol dm^{-3} with sodium perchlorate (Aldrich).

Methods

UV–VIS spectra were recorded at 25 °C on either Cary 1 or Shimadzu UV260 spectrophotometers. pH Measurements were made with an AGB 3000 pH meter equipped with a Russell combination electrode. The filling solution in the reference compartment was 3 mol dm^{-3} NaCl. The electrode was calibrated to read hydrogen ion concentration by titrating solutions of perchloric acid (0.001–0.002 mol dm^{-3}) with standard sodium hydroxide solutions. Titrations were carried out in jacketed titration vessels through which water at 25 °C was circulating. End points were determined using the method of Johansson.[18]

Rate constants for both the complex formation and dissociation reactions were measured using a HiTech SF20 stopped-flow apparatus which was interfaced to a PC *via* a DataLab DL901 transient recorder. Pseudo-first-order rate constants were calculated from the experimental absorbance data (*ca.* 500 data points) using the OLIS KINFIT routines.[19] The reported rate constants are the average of at least three determinations.

The stability constant of the copper(II) complex together with the proton stability constant of the ligand were determined by a potentiometric technique. Titrations were carried out using a Metrohm 716 Titrino at 25 °C. Refinement of the potentiometric data was carried out using SUPERQUAD.[20]

The stability constant for the mono-complex of iron(III) with acetoacetamide (β_1) was determined spectrophotometrically. A series of 15 solutions containing known concentrations of hydrogen ion, acetoacetamide and iron(III) were allowed to react at 25 °C until no further absorbance change occurred. The spectra were then recorded in the wavelength range 450–550 nm. The absorbance data were digitised at 10 nm intervals and these together with the reactant concentrations were used as input for SQUAD.[21]

Results

Table 1 shows the values obtained for the stability constants of the 1 : 1 complexes of copper(II), dioxouranium(VI) and iron(III) with acetoacetamide in aqueous solution. The kinetics of the reactions of both copper(II) and iron(III) with acetoacetamide in aqueous solution were investigated using stopped-flow spectrophotometry. The reactions were studied in the forward direction (complex formation) and in the reverse direction (hydrolysis).

Table 1 Stability constants for formation of the 1 : 1 complexes of acetoacetamide in aqueous solution at 25 °C and ionic strength 0.5 mol dm^{-3}

Metal ion	log β_1
H^+	11.24
Cu^{2+}	7.22 (0.03)
$[UO_2]^{2+}$	9.48 (0.06)
Fe^{3+}	12.03 (0.05)

For both metal ions a single reaction step was observed for the forward reaction. However, in the case of copper, two reaction steps were observed for the reverse reaction. A very rapid initial absorbance decrease was followed by a slower absorbance decrease. Fig. 1 shows a typical stopped flow trace for this reaction.

Fig. 2 shows plots of the kinetic data obtained for the forward reaction (*i.e.* complex formation) of copper(II) with acetoacetamide at three different hydrogen ion concentrations. While the pseudo-first-order rate constants are pH dependent, the reaction could only be investigated over a relatively narrow pH range. At the lower end, studies were limited by the requirement to have a sufficient degree of complex formation in order to afford measurable absorbance changes while at the upper end they were limited by the onset of precipitation of hydrated copper(II) oxide.

The general mechanism for reaction of metal ions with β-diketones which exist predominantly in the keto form in solution is shown in reaction (2) below.[1,22] Complex formation

$$\mathrm{HK} \underset{k_f}{\overset{k_e}{\rightleftharpoons}} \mathrm{HE} \underset{k_{-\mathrm{HE}}[\mathrm{H}^+]}{\overset{k_{\mathrm{HE}}[\mathrm{M}^{n+}]}{\rightleftharpoons}} [\mathrm{ME}]^{(n-1)+} + \mathrm{H}^+ \qquad (2)$$

usually takes place by a mechanism in which the metal species reacts exclusively with the enol tautomer, the keto tautomer is totally unreactive towards the metal ion on the timescale of the kinetic measurements.

For ligands where loss of a proton involves cleavage of an O–H or N–H bond, the proton transfer reactions are generally more rapid than the reactions of labile metal ions with the ionised form of the ligand such that the latter may be assumed to be in a steady state. However, because loss of a proton from a β-diketone involves the breaking of a C–H bond, the proton transfer reactions of β-diketones are generally much slower than those of most protonated ligands and previous investigations have shown that arising from this, the steady state approximation is not applicable to the reactions of metal ions with these ligands.[1] Such systems must be treated as a series of coupled first-order reactions. General methods for solving such systems are well described.[23–25] Applying these methods to the mechanism shown in reaction (1) shows that two possible rate constants, λ_1 and λ_2, given by eqns. (3) and (4), may be observed.

$$\lambda_1 = k_e + k_f + k_{\mathrm{HE}}[\mathrm{M}] + k_{-\mathrm{HE}}[\mathrm{H}^+] - \frac{k_e k_{\mathrm{HE}}[\mathrm{M}] + (k_e + k_f)k_{-\mathrm{HE}}[\mathrm{H}^+]}{k_e + k_f + k_{\mathrm{HE}}[\mathrm{M}] + k_{-\mathrm{HE}}[\mathrm{H}^+]} \qquad (3)$$

$$\lambda_2 = \frac{k_e k_{\mathrm{HE}}[\mathrm{M}] + (k_e + k_f)k_{-\mathrm{HE}}[\mathrm{H}^+]}{k_e + k_f + k_{\mathrm{HE}}[\mathrm{M}] + k_{-\mathrm{HE}}[\mathrm{H}^+]} \qquad (4)$$

Depending on the metal ion and the ligand, one or two reactions may be observed experimentally. In the event that only a single reaction is observed, it may correspond to the faster (λ_1) of the two possible reactions, eqn. (3) or the slower (λ_2), described by eqn. (4).[1] A detailed analysis of the kinetic data for the forward reaction of copper(II) with acetoacetamide clearly demonstrates that they are not consistent with eqn. (3).

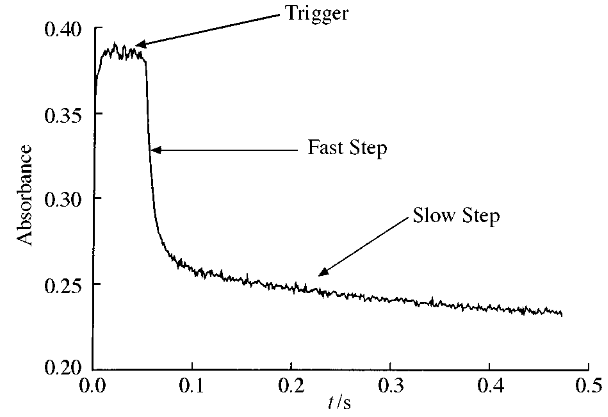


Fig. 1 Stopped-flow trace for hydrolysis of copper(II) 1 : 1 complex with acetoacetamide in aqueous solution at 25 °C and ionic strength 0.5 mol dm^{-3}

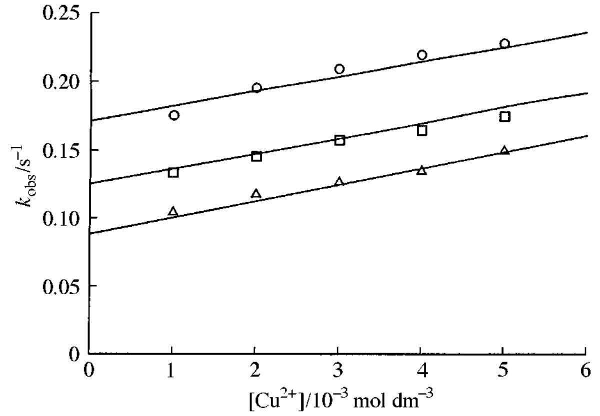


Fig. 2 Kinetic data for reaction of copper(II) with acetoacetamide in aqueous solution at 25 °C and ionic strength 0.5 mol dm^{-3}; ○, pH 5.52; □, pH 5.72, △, pH 6.00

In eqn. (3), the terms to the left of the minus sign usually predominate and the term to the right only makes a minor contribution. In all cases, the pseudo-first-order rate constant (k_{obs}) values obtained in the complex formation reaction of copper(II) with acetoacetamide are smaller than ($k_e + k_f$), the values of which were reported during studies of the keto–enol ratio.[26] Thus the data are not consistent with eqn. (3). A non-linear least squares analysis of the kinetic data also show them to be inconsistent with eqn. (4). Similar arguments apply to the reactions with iron(III).

We propose that reaction of both copper(II) and iron(III) with acetoacetamide occurs by direct reaction of the metal ion with the keto tautomer (Scheme 1). Both the metal and acid dependence of the rate constants (see Figs. 2 and 3) can be accounted for by assuming a reaction involving the hydrated metal ion with the keto tautomer (k_1 path) and the enolate ion (k_2 path) or alternatively, a reaction between the hydrolysed form of the metal species and the keto tautomer (k_3 path).

$$\mathrm{M}^{n+} \overset{K_h}{\rightleftharpoons} \mathrm{M(OH)}^{(n-1)+} + \mathrm{H}^+ \qquad (5)$$

$$\mathrm{M}^{n+} + \mathrm{HK} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} [\mathrm{ME}]^{(n-1)+} + \mathrm{H}^+ \qquad (6)$$

$$\mathrm{M}^{n+} + \mathrm{E}^- \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} [\mathrm{ME}]^{(n-1)+} \qquad (7)$$

$$(\mathrm{MOH})^{(n-1)+} + \mathrm{HK} \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} [\mathrm{ME}]^{(n-1)+} + \mathrm{H_2O} \qquad (8)$$

Scheme 1

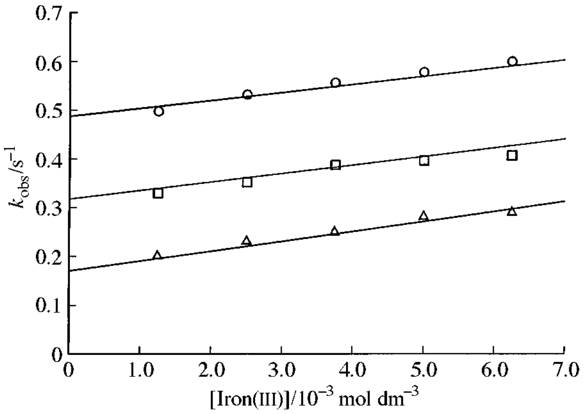


Fig. 3 Kinetic data for reaction of iron(III) with acetoacetamide in aqueous solution at 25 °C and ionic strength 0.5 mol dm^{-3}; ○, pH 1.50; □, pH 1.70; △, pH 2.0

The copper(II) data were analysed in terms of the k_1 and k_2 pathways. In this instance, k_{obs} has the form of eqn. (9) where K_a

$$k_{\text{obs}} = \left(\frac{k_1}{1+\dfrac{K_a}{[\text{H}^+]}} + \frac{k_2}{1+\dfrac{[\text{H}^+]}{K_a}}\right)[\text{M}]_o + k_{-1}[\text{H}^+] + k_{-2} \qquad (9)$$

is the dissociation constant of the ligand ($10^{-11.24}$) and $[\text{M}]_o$ is the total concentration of metal ion. When the kinetic data were fitted to eqn. (9) values of 10.0 (±1.8), 3.39 (±3.0) × 10^5 and 4.12 (±0.3) × 10^4 dm^3 mol^{-1} s^{-1} were obtained for k_1, k_2 and k_{-1} respectively with $k_{-2} = 4.68\ (\pm 0.66) \times 10^{-2}$ s^{-1}. The relative constancy of the slopes of the plots in Fig. 2 irrespective of pH suggests that the contribution made by the k_2 pathway under the experimental conditions is insignificant. This is confirmed by further analysis of the data and omitting this path or setting k_2 to zero results in little change in the values given above for the other parameters. This is not surprising in view of the extremely low concentrations of the enolate ion present under the experimental conditions. As can be seen from Table 2 and Fig. 2, eqn. (9) gives a good representation of the kinetic data.

Support for the mechanism outlined in Scheme 1 comes from the following observation. When solutions of acetoacetamide and $[\text{UO}_2]^{2+}$ were mixed in the stopped-flow apparatus, a very rapid absorbance change was observed with $t_{\frac{1}{2}} < 10^{-3}$ s. This is in marked contrast to the situation that occurs when metal ions react with β-diketones.[1] For example, when solutions of $[\text{UO}_2]^{2+}$ and pentane-2,4-dione (Hpd) were mixed in the stopped-flow apparatus, two separate reactions were observed, both of which were considerably slower than that observed in the present investigation.[27] The faster of these was ascribed to reaction of $[\text{UO}_2]^{2+}$ with the enol tautomer of Hpd while the slower corresponded to a reaction between the metal species and the keto tautomer. The rate of enolisation (k_e) of Hpd is 1.5 × 10^{-2} s^{-1} while that of acetoacetamide is considerably less, *ca.* 2.3 × 10^{-3} s^{-1}. Consequently, if the normal mechanism for reaction of metal ions with β-diketones were operative [reaction (2)], the measured rate constants should be smaller for acetoacetamide than for pentane-2,4-dione. The results obtained with $[\text{UO}_2]^{2+}$ strongly support a direct reaction between the metal species and the keto tautomer of the ligand, the major species present under the experimental conditions. While the mechanisms for formation of metal complexes of β-diketones have been interpreted in terms of the formation of a so-called precursor complex,[1,28–30] it would appear that the adduct/assembly formed on direct reaction of a metal ion with acetoacetamide is considerably more labile from the point of view of proton loss than that formed by β-diketones.

Table 2 Rate constants[a] for reaction of Cu^{2+} with acetoacetamide[b] in water at 25 °C and ionic strength 0.5 mol dm^{-3} NaClO$_4$

[Cu^{2+}]/10^{-3} mol dm^{-3}	[H$^+$]/10^{-6} mol dm^{-3}	k_{obs}/s^{-1}	k^c_{calc}/s^{-1}
1.00	3.02	0.175	0.182
2.00	3.02	0.195	0.193
3.00	3.02	0.209	0.203
4.00	3.02	0.219	0.214
5.00	3.02	0.227	0.225
1.00	1.91	0.133	0.136
2.00	1.91	0.145	0.147
3.00	1.91	0.157	0.158
4.00	1.91	0.164	0.169
5.00	1.91	0.174	0.180
1.00	1.00	0.104	0.100
2.00	1.00	0.117	0.112
3.00	1.00	0.126	0.124
4.00	1.00	0.134	0.136
5.00	1.00	0.149	0.148

[a] $\lambda = 290$ nm. [b] Concentration = 5.0 × 10^{-4} mol dm^{-3}. [c] Values calculated using eqn. (9).

When solutions containing appreciable quantities of $[\text{CuE}]^+$ were reacted with solutions containing hydrogen ions in the stopped-flow apparatus, two separate reactions were observed (Fig. 1). This is similar to the observation of Elias and coworkers[31] in their investigations of the kinetics of acid dissociation of cobalt(II), nickel(II) and copper(II) complexes with 3-(*N*-acetylamido)pentane-2,4-dione in aqueous solution. In both this and the current work, the faster of the two steps is ascribed to a rapid equilibrium in which the free amine group on the ligand is protonated. This is followed by a slower step in which the protonated complex dissociates to yield the equilibrium mixture of metal ion and ligand. During or subsequent to this step, the proton is transferred to an oxygen atom of the ketoamide to yield the enol tautomer which then equilibrates to yield the equilibrium mixture of keto and enol tautomers. The kinetic data for the slow step are described by eqn. (10). In view of the complex nature of the hydrolysis

$$k_{\text{obs}} = 0.773 + 1390[\text{H}^+] \qquad (10)$$

reaction, it is not possible to assign the rate constants obtained in eqn. (10) to individual steps.

The kinetics of formation of the 1 : 1 complex of iron(III) with acetoacetamide were studied with the metal in pseudo-first-order excess. Reactions were studied in the hydrogen ion concentration range 1.0 × 10^{-2}–3.16 × 10^{-2} mol dm^{-3} by monitoring the absorbance changes at 500 nm. A single exponential was observed. Fig. 3 shows plots of the kinetic data at different hydrogen ion concentrations. When the kinetic data were fitted to eqn. (9), they suggested values of *ca.* 10^9 dm^3 mol^{-1} s^{-1} for k_2. This is clearly inconsistent with the known reactivity of Fe^{3+} which has a water exchange rate of 160 s^{-1} (ref. 32) and consequently, the data were fitted in terms of the k_1 and k_3 pathways for which k_{obs} has the form of eqn. (11) where K_h is the hydrolysis constant for Fe^{3+} forming Fe(OH)$^{2+}$ ($10^{-2.70}$).

$$k_{\text{obs}} = \left(\frac{k_1}{1+\dfrac{K_a}{[\text{H}^+]}} + \frac{k_3}{1+\dfrac{K_h}{[\text{H}^+]}}\right)[\text{M}]_o + k_{-1}[\text{H}^+] + k_{-3} \qquad (11)$$

The fitting procedure resulted in values of 14.0 (±3.6), 50 (±27) and 14.6 (±0.6) dm^3 mol^{-1} s^{-1} for k_1, k_3 and k_{-1} respectively with k_{-3} equal to 2.37 (±1.4) × 10^{-2} s^{-1}s^{-1}. Table 3 and Fig. 3 show that eqn. (11) gives an excellent representation of the kinetic data.

Only a single reaction was observed for hydrolysis of the iron complex. The kinetics are described by eqn. (12). The simplest

$$k_{\text{obs}} = 0.183 + 13.5[\text{H}^+] \qquad (12)$$

Table 3 Rate constants[a] for reaction for Fe^{3+} with acetoacetamide[b] in water at 25 °C and ionic strength 0.5 mol dm^{-3} $NaClO_4$

$[Fe^{3+}]/10^{-3}$ mol dm^{-3}	$[H^+]/10^{-2}$ mol dm^{-3}	k_{obs}/s^{-1}	$k_{calc}{}^{c}/s^{-1}$
1.25	1.00	0.201	0.196
2.50	1.00	0.231	0.221
3.75	1.00	0.250	0.246
5.00	1.00	0.281	0.271
6.25	1.00	0.289	0.296
1.25	2.00	0.329	0.339
2.50	2.00	0.351	0.360
3.75	2.00	0.387	0.382
5.00	2.00	0.396	0.404
6.25	2.00	0.406	0.426
1.25	3.16	0.497	0.508
2.50	3.16	0.532	0.528
3.75	3.16	0.556	0.548
5.00	3.16	0.577	0.568
6.25	3.16	0.598	0.589

[a] $\lambda = 500$ nm. [b] Concentration = 5.0×10^{-4} mol dm^{-3}. [c] Values calculated using eqn. (11).

mechanism for hydrolysis would yield the rate law, given in eqn. (13). This results in a value of 13.5 for k_{-1} in good

$$k_{obs} = k_{-3} + k_{-1}[H^+] \qquad (13)$$

agreement with that obtained from the formation studies (14.6). However, the agreement between the values obtained for k_{-3} in the formation and hydrolysis reactions is less satisfactory and may be a consequence of k_{-3} in eqn. (13) being a composite quantity arising from a multi-step dissociation mechanism. Further evidence for this is obtained by comparing the stability constant obtained from kinetic data with the directly obtained values. The following relationships hold [eqns. (14) and (15)],

$$\frac{k_1}{k_{-1}} = \beta K_a \qquad (14)$$

$$\frac{k_3}{k_{-3}} = \frac{\beta K_a}{K_{MOH}} \qquad (15)$$

where β is the stability constant for formation of the 1:1 complex, K_a is the acid dissociation constant of the ligand and K_{MOH} is the hydrolysis constant of Fe^{3+} ($10^{-2.7}$).

While the value of k_3/k_{-3} obtained from kinetic data, 2.1×10^3, is in good agreement with the value of 3.1×10^3 obtained from equilibrium data, the agreement between the value of k_1/k_{-1} obtained from kinetic data, 1, is significantly different to the value of 6 obtained from equilibrium data. The reason for the discrepancy is not immediately obvious, but is probably due to the fact that the intimate mechanism is actually more complicated than that shown in Scheme 1.

Discussion

Table 4 summarises the results obtained for complex formation of copper(II) and iron(III) with acetoacetamide. It is apparent that the mechanism for complex formation reactions of acetoacetamide is considerably different to that observed for reaction of metal ions with conventional β-diketones such as pentane-2,4-dione for which the mechanism shown in reaction (1) is valid. Such a mechanism requires that the kinetic data are described by eqns. (3) and (4), irrespective of whether the reaction is monitored in the forward (complex formation) or reverse (acid dissociation, hydrolysis) direction. Such is not the case for the complex formation reactions of acetoacetamide reported here.

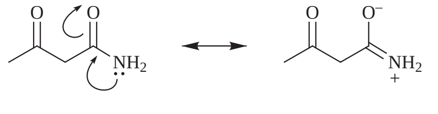
Table 4 Summary of kinetic data for reaction of metal ions with acetoacetamide

Metal	Ligand	k/dm^3 mol^{-1} s^{-1}
Cu^{2+}	HK	10.0 (±1.9)
Fe^{3+}	HK	14.0 (±3.6)
$Fe(OH)^{2+}$	HK	50 (±27)
$UO_2{}^{2+}$	HK	$t_{\frac{1}{2}} <$ m s^{-1}

The Eigen–Wilkins–Tamm mechanism[33] predicts a rate constant of approximately 36 dm^3 mol^{-1} s^{-1} for the reaction of Fe^{3+} with an uncharged ligand, a value which is only 2.5 times the value reported in the present investigation. The rate constant obtained for the reaction of Cu^{2+} with the keto form of acetoacetamide is many orders of magnitude less than that predicted by an interchange–dissociative (I_d) mechanism[34] in which solvent exchange is the rate-determining step. However, it compares favourably with the value of 12 dm^3 mol^{-1} s^{-1} obtained for reaction of Cu^{2+} with the keto tautomer of pentane-2,4-dione.[28] These workers ascribed the slow rate of reaction of Cu^{2+} with the enol tautomer of pentane-2,4-dione (Hpd) to a sterically controlled substitution mechanism in which closure of a six-membered chelate ring was sterically hindered. However, this is contradicted by the relatively normal reactivity of Cu^{2+} and indeed other metal ions towards the enolate ion generated on loss of a proton from Hpd. The slow rate of reaction of Cu^{2+} with acetoacetamide is in all probability due to a combination of the fact that the ketoamide is a poor entering group coupled with the requirement to cleave a C–H bond in order to complete formation of the complex.

In the case of the iron(III) metal species, Fe^{3+} and $Fe(OH)^{2+}$ have water exchange rates of 160 and 1.2×10^5 s^{-1} respectively.[32] While both are considerably less labile than Cu^{2+}, it is apparent that the retardation is considerably greater in the case of the more labile $Fe(OH)^{2+}$ ion. This is consistent with previous observations for reactions of Fe^{3+} with β-diketones where on the basis of the Eigen–Williams–Tamm mechanism, only minimal retardation was observed.[1]

The question must be posed as to why the mechanism for complex formation reactions of metal complexes of acetoacetamide are so different to those of β-diketones. One plausible explanation lies in the fact that in aqueous solution, the predominant keto tautomer of acetoacetamide may exist in two resonance forms.[35] This charge distribution is favourable due to the relative stability of the ions RO^- and $RNH_3{}^+$. The right-hand canonical form contributes significantly to the properties of the amide bond and when the amide group acts as a nucleophile, it is usually the oxygen atom which carries a partial negative charge which is the nucleophilic atom. Due to the increased basicity of the oxygen carrying the negative charge, the precursor complex formed when the metal ion reacts with this species would be appreciably more stable than that formed by a 1,3-diketone and this in turn would lead to an increased rate of proton loss. Thus unlike the keto tautomers of many 1,3-diketones which must first undergo enolisation before they can react with a metal ion, the presence of resonance forms of the types shown above ensures that β-ketoamides do not have to undergo such a transformation in order to react. This we believe is the origin of the difference observed in the kinetic behaviour of the two apparently similar types of ligands. Similar arguments have been used by Cassatt and Wilkins[36] to rationalise the enhanced reactivity of H_2EDTA^{2-} towards metal ions compared to $IDAH^-$. Both of these species might be expected to have similar reactivity in view of the fact that



H_2EDTA^{2-} approximates two joined halves of the relatively unreactive $IDAH^-$. The enhanced reactivity in explained by the presence of a small amount of H_2EDTA in which one of the protons is located on the oxygen atom leaving the nitrogen free to co-ordinate to a metal ion.

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