

Cobalt(II) and Zinc(II) Complexes of Thiourea as Catalysts for the Reactions between Carbonyl Compounds and Anilines

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The kinetics of the reactions between p-nitrobenzaldehyde and p-toluidine and between acetone and p-anisidine have been examined in non-aqueous solutions and in the presence of Zinc(II) and Cobalt(II) complexes of thiourea which act as catalysts. The reaction between 2,4-Dinitrophenyl acetate and p-toluidine is not catalysed by these metal complexes. The kinetics of the p-Nitrobenzaldehyde reaction are straight-forward with first order dependence on each of the reactants and on the catalyst and a second order rate determining step. For the reaction in acetonitrile d₃ catalysed by tetrakis Zn(II) thiourea perchlorate a third order rate constant of $25.0 \pm 1.5 \text{ M}^{-2} \text{ s}^{-1}$ has been measured. The kinetics of the acetone/p-anisidine reaction are quite different and closely parallel similar reactions studied previously. The results for the two reactions cannot be fitted to a common mechanism. All three reactions involve nucleophilic attack of an aniline on a carbonyl group but two are catalysed by different mechanisms and the third is not catalysed at all. It is suggested that catalysis can occur either by coordination of the carbonyl compound or by coordination of the adduct formed by the carbonyl compound and the aniline. If neither of these reactants is capable of forming a sufficiently long lived metal complex there will be no catalysis.

Introduction

Anils are commonly formed by the reaction of carbonyl compounds with primary amines, *i.e.*:
 $\text{RR}'\text{CO} + \text{R}''\text{NH}_2 \rightarrow \text{RR}'\text{C}=\text{NR}'' + \text{H}_2\text{O}$

The mechanisms of these reactions in aqueous solution have been extensively discussed [1]. In general an intermediate carbinolamine, $\text{RR}'\text{C}(\text{OH})\text{NHR}''$, is first formed and a molecule of water is then eliminated to give the product imine [2, 3]. Depending on the conditions (notably pH) either the formation of carbinolamine or the elimination of water may be

the rate determining step. A recent review [4] has discussed in some detail the mechanisms available for reactions of this type which proceed by nucleophilic attack of one molecule (the amine) on a second molecule (the carbonyl). This review emphasized particularly the role played by the lifetime of the primary addition product (in this case $\text{RR}'\text{C}(\text{OH})\text{NHR}''$) in determining the subsequent mechanistic pathway.

We have been interested for some time in the catalysis of this type of reaction by metal complexes in non-aqueous solution. Specifically reactions between acetone and substituted anilines show very large rate accelerations in the presence of catalytic concentrations of Zn(II) and Co(II) complexes of thiourea and a mechanism has been suggested for these reactions [5–7]. In the present paper we report studies of the catalysis of the reaction between p-nitrobenzaldehyde and p-toluidine by the same metal complexes and also some studies on the acetone/p-anisidine reaction, which supplement the earlier results. The two reactions clearly proceed by different mechanisms. A third reaction between 2,4-Dinitrophenyl acetate and p-toluidine has also been examined but this is not catalysed. A clear understanding of these catalytic mechanisms would be of considerable predictive value in choosing catalysts for nucleophilic substitution and elimination reactions.

Experimental

The preparation and purification of the catalysts used in this study has been described previously [5]. p-Toluidine and p-nitrobenzaldehyde (Eastman) were sublimed before use. Acetonitrile (J. T. Baker Chemical Co.) and d₃-acetonitrile (Norrel Chemical Co.) were dried over activated molecular sieves 4A and then distilled three times under vacuum to remove water. The anil was prepared by refluxing equimolar quantities of p-toluidine and p-nitrobenzaldehyde in benzene for 2 or 3 hours. Water and benzene were then removed by distillation. Yellow crystals thus obtained were dried under vacuum. The yield was $95 \pm 3\%$. Initial rates were measured using a Varian

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EM-390 nmr spectrometer (probe temperature 29.6 °C). The reaction was followed by monitoring the singlet proton signals of the reactants and products. The sample containing the aniline and the catalyst was thermally equilibrated in the probe. It was then rapidly removed, and p-nitrobenzaldehyde solution was injected with a syringe; and timing was started simultaneously. After mixing the reactants, the sample was replaced in the probe. The whole operation could be carried out in about 40 seconds. The first spectrum may be obtained about 50 seconds after the reaction had commenced.

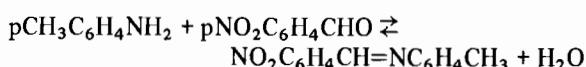
Equilibrium constants were obtained by measuring the thiourea proton NMR chemical shift on the addition of potential ligands. The procedure has been described previously [5].

The reactions between p-toluidine and acetone and between 2,4-Dinitrophenyl acetate and p-toluidine were also monitored by measuring the change of UV absorbance using a Pye Unicam SP8-100 spectrometer.

Reactions

The Reaction between p-Nitrobenzaldehyde and p-Toluidine

The equilibrium constant for the reaction



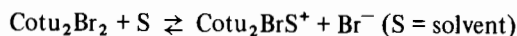
was obtained using proton NMR. To a solution in acetonitrile d_3 containing known quantities of aniline and aldehyde a small quantity of catalyst ($\text{Zntu}_4(\text{ClO}_4)_2$ tu = thiourea) was added and the mixture maintained at 35 °C in a thermostated bath for 24 hours to ensure equilibration. From the relative intensities of the NMR peaks an equilibrium constant $K = 180 \pm 5$ was obtained. In a second experiment equilibrium was attained by hydrolysis of the anil. This gave a value of $K = 185 \pm 6$. This large value of the equilibrium constant indicates that the forward reaction can be followed more conveniently than the anil hydrolysis.

The kinetics of the uncatalyzed reaction in acetonitrile d_3 are straightforward. The reaction was followed by repetitively scanning the aldehydic region of the PMR spectrum and observing both the decrease in intensity of the aldehyde signal and the increase in intensity of the corresponding anil peak. Initial rates were obtained in a manner described in more detail previously [7]. The reaction is first order in both aldehyde and amine and a second order rate constant of $4.0 \pm 0.5 \times 10^{-5} \text{ M}^{-1} \text{ s}^{-1}$ was obtained. This may be compared with the reported value of $2.5 \times 10^{-5} \text{ M}^{-1} \text{ s}^{-1}$ for the formation of the aniline-benzaldehyde anil in benzene [8].

The reaction is catalyzed by Zn(II) and Co(II) complexes of thiourea. Thus in the presence of 10^{-3} M Zinc(II) tetrathiourea perchlorate the rate is increased by a factor of 600. This acceleration may be compared with a factor of 7300 observed with the same concentration of catalyst for the acetone-p-toluidine reaction [5]. These factors are of course not of direct significance since the mechanisms of the catalysed and uncatalysed reactions are probably different.

The dependence of the initial rate of anil formation on aniline and aldehyde concentrations has been determined using PMR to monitor the reaction. At constant catalyst concentration the rate was found to be first order with respect to each of the reactants. Fig. 1 shows a plot of rate versus p-toluidine concentration. Plots of $\log(\text{initial rate})$ versus $\log([\text{p-toluidine}])$ or $\log[\text{p-nitrobenzaldehyde}]$ both have slopes of 0.99 ± 0.1 . Clearly simple second order kinetics are preserved in the catalytic reaction. This result is in sharp contrast to the catalysed p-toluidine/acetone reaction which followed more complex kinetics giving an approximately linear plot of $1/\text{Rate}$ versus $1/[\text{An}]$.

Table I presents data illustrating the dependence of the rate on catalyst concentration for five thiourea complexes. For three of these complexes the dependence is linear, *i.e.* Zntu_2Cl_2 , $\text{Zntu}_4(\text{ClO}_4)_2$ and $\text{Cotu}_4(\text{ClO}_4)_2$. There is a small intercept which corresponds well with the rate of the uncatalysed reaction. For $\text{Zntu}_4(\text{ClO}_4)_2$ a plot of $\log(\text{initial rate})$ versus $\log([\text{Zntu}_4(\text{ClO}_4)_2])$ has a slope of 0.98 ± 0.04 confirming first order dependence. For the other two catalysts Cotu_2Cl_2 and Cotu_2Br_2 there is pronounced curvature of the rate versus catalyst concentration plots with the latter compound showing the largest deviation from linearity. We attribute this to ionic dissociation, *e.g.*,



The ionized complex is the more efficient catalyst, as found previously, and dissociation is more pronoun-

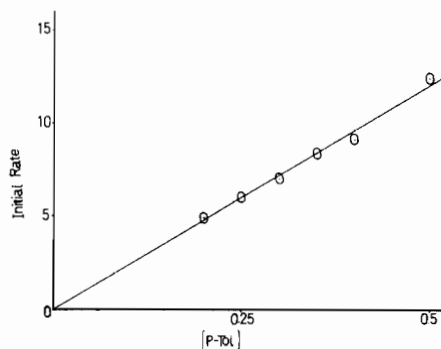


Fig. 1. Dependence of initial rate of p-nitrobenzaldehyde anil formation ($\text{M s}^{-1} \times 10^5$) on concentration of p-toluidine (M). Catalyst $\text{Zntu}_4(\text{ClO}_4)_2$ at a concentration of $5 \times 10^{-5} \text{ M}$.

TABLE I. Dependence of the Second Order Rate Constant for p-Nitrobenzaldehyde Anil Formation on Catalyst Concentration in d₃-Acetonitrile^a (29.6 °C).

$C_M \times 10^4 M$	$k \times 10^3 M^{-1} \text{sec}^{-1}$				
	CoTu ₂ Cl ₂	CoTu ₂ Br ₂	CoTu ₄ (ClO ₄) ₂	ZnTu ₂ Cl ₂	ZnTu ₄ (ClO ₄) ₂
0.0	0.04	0.04	0.04	0.04	0.04
0.5	1.04	2.21	0.41	0.11	1.02
1.0	1.91	3.16	0.80	0.22	2.55
2.0	2.89	4.36	1.63	0.32	5.31
3.0	3.44	5.11	2.45	0.60	8.43
4.0	—	5.32	3.21	0.70	11.9
5.0	—	5.83	4.06	0.91	13.2

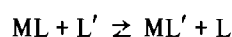
^ap-toluidine, 0.1 M. p-nitrobenzaldehyde, 0.1 M.

ced at lower concentrations. Addition of AgNO₃ gives a precipitate with these compounds in acetonitrile but not in acetone. Conductivities have been measured and we find for example that 10⁻² M CoTu₂Cl₂ has a specific conductance of 9.23 ohm⁻¹ cm⁻¹ in acetonitrile. It seems likely that correct allowance for this dissociation would lead to a linear dependence on catalyst concentration for the cobalt halide catalysts.

For catalysts other than the Co(II) halide complexes a third order rate constant may be calculated. Thus for the case of Zn(tu)₄(ClO₄)₂ from the slopes of the plots of the rate dependence on catalyst, aldehyde and p-toluidine third order rate constants of 24.0, 24.9 and 26.2 M⁻² s⁻¹ were obtained, leading to an average value of 25.0 ± 1.5 M⁻² s⁻¹.

It is to be anticipated that catalysis of this type of reaction will proceed by coordination of one or more of the reacting species or intermediates to the metal ion. If this is the case addition of competing ligands should lead to inhibition of the catalytic reaction. This has been observed. Thus in one experiment the initial rate of anil formation in the presence of 5 × 10⁻⁵ M Zntu₄(ClO₄)₂ was found to be 4.9 × 10⁻⁵ M s⁻¹. On addition of 0.01 M 1,10-phenanthroline (a chelating ligand) the rate was reduced to 4.1 × 10⁻⁶ M s⁻¹. Further addition of 1,10-phenanthroline to 0.2 M had no additional effect. In a second experiment the rate of anil formation in the presence of 5 × 10⁻⁵ M, Cotu₂Cl₂ was 3.76 × 10⁻⁶ M s⁻¹. On addition of 2.5 × 10⁻³ M thiourea this was reduced to 2.24 × 10⁻⁶ M s⁻¹. Increasing the thiourea concentration to 7.5 × 10⁻² M lead to a further reduction to 8.6 × 10⁻⁷ M s⁻¹.

We have previously used experiments involving dilution of the reaction mixture with an inert solvent to infer the molecularity of the rate determining step [7]. The argument is as follows. In a given solution there will be a complex mixture of free and metal ion-coordinated reactants the relative concentrations of which will be determined by a set of equilibria of the type:



If the metal ion has the same coordination number for all the complexes involved, and if the diluting solvent does not participate as either a first sphere or a second sphere ligand it may be readily shown that dilution will not affect the relative concentrations of any of the species in solution but will reduce each concentration by an equal factor. If therefore the rate determining step depends on the concentration of a single intermediate the initial rate will be reduced in direct proportion to the fraction of inert solvent added, e.g., dilution by a factor of two will half the rate. If on the other hand the rate determining step involves the product of the concentration of two reacting species the initial rate will be reduced by a factor proportional to the square of the fraction of inert solvent added, e.g., dilution by a factor of two will diminish the initial rate by a factor of four. We note that Asperger and his collaborators have used essentially similar experiments to distinguish between D and I_d mechanisms for the substitution reactions of pentacyano ferrate(II) complexes [9, 10]. It is recognized that solvent effects on reaction rates are inherently complex and that specific stabilizing or destabilizing interactions with a given intermediate could invalidate the above simple argument.

If this were the case we could not expect any simple dependence of rate on solvent composition as indeed has been demonstrated by Langford *et al.* for a number of metal complex reaction [11]. The observation of a simple dependence argues against the occurrence of such complications.

In the present case carbon tetrachloride has been used as the diluting solvent. This is a very poor first or second sphere ligand [12]. There is also good evidence that both Co(II) and Zn(II) remain tetrahedral and four coordinate with all the ligands involved. In a typical experiment a stock solution of p-toluidine in acetonitrile with a quantity of Zntu₄(ClO₄)₂ added was prepared and diluted with aliquots of carbon tetrachloride to make up five samples.

Standard aldehyde solution was added to each sample sufficient to keep the relative concentrations of p-toluidine, catalyst and aldehyde constant. The initial rates of the reaction were measured and relative rates obtained by dividing by the measured rate for the undiluted sample. The results of such an experiment are shown in Table II and a plot against the square of the dilution factor in Fig. 2. Within the limitations set out above a bimolecular rate determining step is clearly indicated. For the sake of comparison similar data relating to the anil of p-toluidine and acetone, taken from an earlier paper, are included in Table II. The latter data was interpreted to indicate a unimolecular rate determining step. The results of the two experiments clearly indicate different mechanisms.

The Reaction between Acetone and p-Anisidine

In view of the differences in kinetics between the catalysed reactions of p-nitrobenzaldehyde and acetone with p-toluidine noted above, it seemed desirable to confirm the acetone results with some additional data. We have therefore examined the reaction of p-anisidine with acetone using $Zn(tu_4(ClO_4)_2)$ as a catalyst. The results prove to be very similar to those previously reported [5-7] with p-toluidine and we therefore report them only briefly.

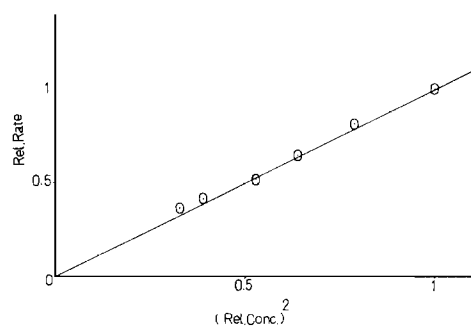


Fig. 2. Dependence of relative rate of p-Nitrobenzaldehyde anil formation on relative concentration in carbon tetrachloride/acetone mixtures.

TABLE II.

p-Nitrobenzaldehyde/p-toluidine				p-toluidine acetone anil hydrolysis ^a		
Fraction CCl ₄	Rel. Conc.	(Rel. conc.) ²	Relative Initial Rate	Fraction CCl ₄	Rel. Conc.	Rel. Rate
0	1.0	1.0	1.0	0	1.0	1.0
0.11	0.89	0.79	0.82	0.20	0.80	0.72
0.20	0.80	0.64	0.65	0.40	0.60	0.57
0.27	0.73	0.53	0.52	0.60	0.40	0.41
0.385	0.62	0.38	0.42	0.80	0.20	0.18
0.43	0.57	0.33	0.37			

^aData from ref. 7.

At high concentrations of p-anisidine ($\sim 0.1 M$) the reaction was followed by monitoring the methoxy PMR. At low concentrations ($\sim 10^{-4} M$) the UV bands of the anisidine and its anil were monitored at 280 nm. The equilibrium constant for the anil formation reaction in acetonitrile was determined to be 2.45×10^{-2} at 29.6 °C by NMR. Given this small formation constant the formation of the anil can conveniently be studied in acetone and the hydrolysis in acetonitrile.

Both the rate of formation and the rate of hydrolysis are directly proportional to catalyst concentration as illustrated in Fig. 3. The rate is not directly

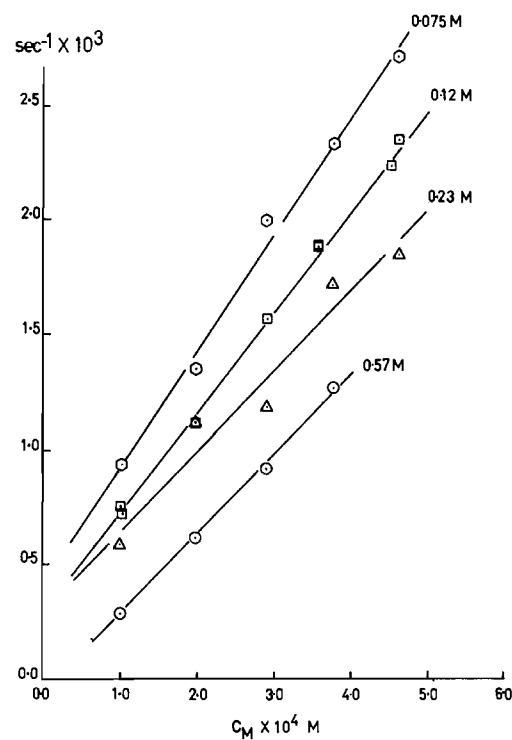


Fig. 3. Dependence of the rate of anil formation (F_f) on catalyst ($Zn(tu_4(ClO_4)_2)$) for the reaction between p-anisidine and acetone. The different lines represent different p-anisidine concentrations.

proportional to anisidine concentration. This is illustrated by a plot of F_f versus anisidine concentration shown in Fig. 4 where:

$$F_f = \frac{\text{Initial rate of aniline consumption}}{\text{Initial concentration of aniline}}$$

F_f would be constant if the reaction were first order in aniline. Data for the previously studied p-toluidine reaction is also included on this plot showing that the two reactions are qualitatively very similar. Similar plots for the anil dependence of the hydrolysis reaction show the same behaviour but in a more marked fashion (Fig. 5). Fig. 6 shows the dependence of the hydrolysis rate on water concentrations. The anomalous behaviour at low concentrations may well reflect the non-ideal behaviour of acetonitrile/water mixtures. All of these results parallel closely those obtained with p-toluidine. It is not meaningful to present rate constants for these reactions since there is no simple concentration dependence.

The Reaction between 2,4-Dinitrophenyl Acetate and Aniline

The reactions between substituted phenyl acetates and amines have been extensively studied in aqueous solution. More limited results have been reported in non-aqueous solvents [14]. In acetonitrile we have obtained a rate of $4.0 \pm 0.5 \times 10^{-4} \text{ s}^{-1}$ for a solution containing 0.101 M p-toluidine and $9.4 \times 10^{-3} \text{ M}$ Dinitrophenyl acetate. This rate is consistent with literature values. On addition of 10^{-3} M $\text{Zn}(\text{tu}_4(\text{ClO}_4)_2)$ a rate of $4.5 \pm 0.5 \times 10^{-4} \text{ s}^{-1}$ was found. Increasing the catalyst concentration to 10^{-2} M produced no appreciable increase in the rate. This reaction is clearly not catalysed by these metal complexes.

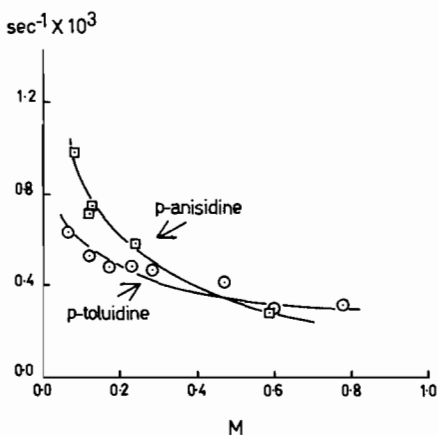


Fig. 4. Dependence of the rate of anil formation (F_f) on aniline concentration for the reactions of p-anisidine and p-toluidine with acetone. Catalyst $\text{Zn}(\text{tu}_4(\text{ClO}_4)_2)$ concentration $1.0 \times 10^{-4} \text{ M}$ for p-anisidine and $1.2 \times 10^{-4} \text{ M}$ for p-toluidine.

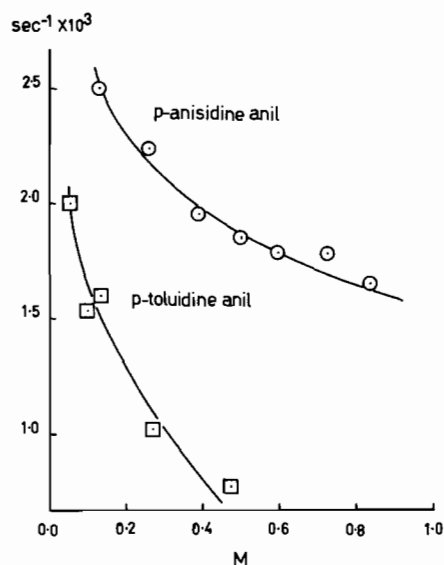


Fig. 5. Dependence of the rate of anil hydrolysis (F_f) on anil concentration. Catalyst $\text{Zn}(\text{tu}_4(\text{ClO}_4)_2)$ solvent acetonitrile. p-anisidine anil 1.0 M , H_2O $2 \times 10^{-3} \text{ M}$ catalyst. p-toluidine anil 0.25 M , H_2O $6.4 \times 10^{-4} \text{ M}$ catalyst.

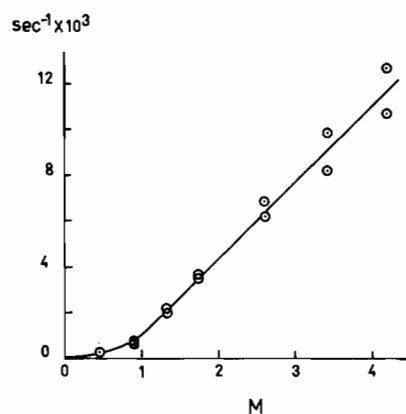
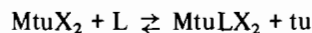


Fig. 6. Effect of water concentration on the rate of hydrolysis (F_f) of p-anisidine/acetone anil. Catalyst $\text{Zn}(\text{tu}_4(\text{ClO}_4)_2)$ $4.0 \times 10^{-5} \text{ M}$, p-anisidine anil $6.2 \times 10^{-4} \text{ M}$.

Equilibrium Measurements

Mechanistic analysis of the above rate data requires a knowledge of equilibrium constants for ligand exchange reactions of the type:



Given such a set of equilibrium constants we may in principle calculate the concentration of any of the metal complex species in solution as a function of the concentration of a reactant and seek to correlate the observed rates with the concentrations of hypothetical intermediates. NMR provides a convenient method for determining these equilibrium constants if all the ligand exchange reactions are rapid leading

to averaged resonances (as they are in the present case) and if the chemical shifts are large (as they are for the paramagnetic cobalt catalysts). A set of equilibrium constants relating to the displacement of thiourea from CoTu_2Cl_2 by p-toluidine, p-anisidine, the acetone and p-nitrobenzaldehyde anils of these anilines, water, acetonitrile, acetone and p-nitrobenzaldehyde, is given in Table III. It should be noted that the equilibrium constant for the last ligand is very small and only an upper limit was obtained. In using these values it is further assumed (i) the equilibrium constant is independent of the nature of the other ligands complexed and (ii) the values are the same for Co(II) and Zn(II). Neither of these assumptions will be more than approximately valid. More than qualitative prediction of the dependence of rates on concentrations of reactants is not therefore to be anticipated.

Discussion

The three reactions discussed above all involve attack of an aniline on a carbonyl group. Two are catalysed by the metal complexes used and the third is not. The two which are catalysed show different kinetic behaviour indicating different mechanisms. We seek a way to rationalize this behaviour.

It seems reasonable to suppose that catalysis requires coordination of one of the reacting species to the metal ion. Coordination of the aniline is counter productive since it removes its ability to act as a nucleophile and is inconsistent with the observed kinetics [7]. Coordination of the carbonyl complex is expected to give rise to catalysis since it activates the carbon for nucleophilic attack by polarizing the group in the sense $\text{C}=\text{O} \rightarrow \text{M}$. The data of Table III show that acetone is a poor ligand relative to p-anisidine or p-toluidine and that p-nitrobenzaldehyde is an even worse ligand. There is no evidence for complexing of Dinitrophenylacetate. This latter observation could rationalize the lack of catalysis for the reaction of Dinitrophenyl acetate and aniline.

If the mechanism for the catalysis involves initial coordination of the carbonyl, inhibition by excess aniline is expected since the aniline will compete favourably for a coordination position on the metal. Calculations have shown that the kinetic data for acetone/aniline reactions can be successfully fitted to this model with the additional postulate that the attacking aniline is held in the second coordination sphere of the complex so that the rate determining step is unimolecular. The surprising feature of the present results is that the catalysed reaction between p-nitrobenzaldehyde and p-toluidine is clearly first order in the aniline with no inhibition at higher concentrations of p-toluidine. Since the p-nitrobenzaldehyde is an even poorer ligand than acetone

TABLE III. Equilibrium Constants for the Replacement of Thiourea by Various Ligands. CoTu_2Cl_2 complex in acetonitrile (29.6 °C).

Ligand	K
Thiourea	1
p-Toluidine	2.7×10^{-2}
p-Toluidine-(p-nitrobenzaldehyde) anil	3.7×10^{-4}
Water	4.3×10^{-4}
Acetonitrile	1.4×10^{-4}
Acetone	1.1×10^{-5}
p-Nitrobenzaldehyde	less than 10^{-5}
p-Anisidine	5.3×10^{-2}
p-Toluidine acetone anil	0.21

even more pronounced inhibition would be anticipated.

We suggest that the initial step in the catalysed p-nitrobenzaldehyde reaction is identical with that of the uncatalysed reaction, namely formation of the intermediate



by nucleophilic attack of the aniline on the carbonyl. This intermediate can then be stabilized by coordination to the metal ion. It is reasonable to suppose that such a polar molecule is a much better ligand than the original aldehyde and therefore competes favourably with the aniline for a position in the metal ion coordination sphere. Such a mechanism leads immediately to the simple third order kinetics observed. The catalysis in this case does not arise from activation of the carbonyl group but from the increased life-time of the intermediate and the facilitation of the subsequent proton transfer steps.

There still remains the question as to why the reaction of 2,4 Dinitrophenylacetate is not catalysed by this mechanism. It could certainly be argued that the intermediate I in this case will be a poorer ligand than the corresponding p-nitrobenzaldehyde derivative due to the greater electron withdrawing properties of the substituents and possibly steric limitations imposed by the bulk of the molecule. Another way of looking at the problem is in terms of the lifetimes of the intermediates. If the residence time of the reactant on the metal ion is short the probability of completing the catalysed reaction is low. Similarly if the lifetime of an intermediate such as I is short the probability of forming a metal complex is small. The lifetimes of complexed ligands may be inferred from ligand exchange rates. The rates for CoTu_2X_2 complexes have been investigated by NMR [15]. The reactions proceed by an associative mechanism (A or Ia) and depend upon both the entering and leaving ligands. Typically for the replacement of thiourea

by acetone the second order rate constant* is $\sim 10^2 M^{-1} s^{-1}$ for the replacement of thiourea by thiourea $\sim 10^5 M^{-1} s^{-1}$ and for the replacement of acetone by thiourea $\sim 10^7 M^{-1} s^{-1}$. From Table II thiourea is a better ligand than acetone by a factor of 10^5 . Clearly the trend is the expected one—a good ligand will replace a poor ligand rapidly but a poor ligand will replace a good ligand only slowly. Benzaldehyde is a poor ligand and its complexed form will therefore have a very short lifetime in the presence of competing ligands—even solvent acetonitrile. Pathway I is therefore not available. Aldehydes are reactive carbonyl compounds so the intermediate *I* will be relatively stable. Further, this intermediate has a negative charge on the oxygen and will therefore be a better ligand than the parent benzaldehyde. It may therefore be reasonable to anticipate reaction with catalyst within the lifetime of the intermediate *I*. The second pathway is therefore possible. Acetone, on the other hand, is a relatively unreactive carbonyl compound so *I* will be unstable. It does however form complexes of significant stability. In the course of this process the carbonyl bond is polarized in the sense $\overset{\ominus}{C}-\overset{\oplus}{O}$ activating it for nucleophilic attack. For the reverse reaction of hydrolysis of the anil the importance of polarizing the C=N bond can be demonstrated directly by studies of catalysed isomerization by rotation about this bond [16]. The first pathway therefore provides a reasonable mechanism. Both of these pathways are cooperative in the sense that the first step facilitates the second. 2,4-Dinitrophenyl acetate, like all esters, is a poor ligand thus ruling out pathway I. The intermediate *I* is still non-competitive as a ligand. Hence the lack of catalysis may be rationalized. The ancillary ligand on the catalyst and the solvent both play important roles in determining the effectiveness of the catalyst. In aqueous solution water will displace poorer ligands and limit the lifetimes of potential intermediates. The ancillary ligand

(in this case thiourea) provides solubility in non-aqueous solvents and sites for second sphere complexation.

Acknowledgements

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*For the case of replacement of a ligand by solvent the second order rate constant is not physically meaningful (see ref. 11) but provides a convenient measure for comparison.