Solution of t_{max}

$$\frac{k_{BC}}{k_{AB}} = \frac{e^{-k_{AB}t_{max}}}{e^{-k_{BC}t_{max}}}$$

$$\frac{k_{BC}}{k_{AB}} = e^{(k_{BC} - k_{AB})t_{max}}$$

$$\ln (k_{BC}/k_{AB}) = (k_{BC} - k_{AB})t_{max}$$

$$t_{max} = \frac{\ln (k_{BC}/k_{AB})}{k_{BC} - k_{AB}}$$

Solution of $[B]_{max}$. Substituting eq A in the first equation

$$[B]_{max} = \frac{[A]_0 k_{AB}}{k_{BC} - k_{AB}} \left(\frac{k_{BC}}{k_{AB}} e^{-k_{BC}t_{max}} - e^{-k_{BC}t_{max}}\right)$$

$$= \frac{[A]_0 k_{AB}}{k_{BC} - k_{AB}} \left(\frac{k_{BC} - k_{AB}}{k_{AB}} e^{-k_{BC}t_{max}}\right)$$

$$[B]_{max} = [A]_0 e^{-k_{BC}t_{max}}$$

Substituting the equivalent expression for t_{max}

$$[B]_{max} = [A]_0 e^{(-k_{BC}/k_{BC}-k_{AB})(\ln (k_{BC}/k_{AB}))}$$

Under the restriction that $k_{BC} >> k_{AB}$

$$[B]_{max} = \frac{[A]_0 k_{AB}}{k_{BC}}$$

and

$$t_{max} = \frac{\ln (k_{BC}/k_{AB})}{k_{BC}}$$

Registry No. $Cu(OH)_2$, 20427-59-2; OCl^-, 14380-61-1; OBr^-, 14380-62-2; Br^-, 24959-67-9; $Cu_2(OH)_6^{2-}$, 64332-60-1.

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Isokinetic Temperatures and Mechanisms of Metal Ion Promoted Hydrolyses of Amino Acid Esters

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The activation parameters of Cu^{2+}-, Ni^{2+}-, Zn^{2+}-, and Co^{2+}-promoted hydrolysis of ethyl *N,N*-diacetoxyglycinate (EGDA) as well as those of (methyl glycinato)iminodiacetatocopper(II) have been determined as well as the isokinetic temperature, 392 K. These data are compared to those for tetradentate Ni(II) chelate and metal–nitrilotriacetate (NTA) hydrolyses of methyl glycinate; $\beta = 274$ K. The different trends in metal ion promotion and thermodynamic behavior of the hydrolyses of M(EGDA) (enthalpy dependent) and $M(NTA)^-$ (entropy dependent) are discussed in terms of differing mechanisms. The possible significance of these data to biological systems is also discussed.

Introduction

Metal ion catalyzed hydrolysis of amino acid esters has been studied by a number of research groups[1-7] with hopes of elucidating the role of metal ions in corresponding biological systems. Three mechanisms have been proposed, two involving external attack of hydroxide ion on the carbonyl carbon which has been activated toward nucleophilic attack by the polarizing effect of the metal ion either via induction through a coordinated amine group or by direct interaction of the ester carbonyl oxygen with the metal. The third mechanism involves formation of a metal–hydroxo complex, followed by intramolecular attack by hydroxide ion. Previously, we established[7] an isokinetic relationship between Ni(II) chelate and metal–nitrilotriacetate promoted hydrolyses of methyl glycinate and that catalysis occurred via induction rather than direct metal interaction with carbonyl oxygen of the ester. A series

Table I. Rate Constants for Ethyl *N,N*-Diacetoxyglycinate Hydrolysis in the Presence of Cu(II), Zn(II), Ni(II), and Co(II) and Methyl Glycinate in the Presence of Iminodiacetatocopper(II) at 20, 25, 30, and 35 °C at $I = 0.10$ M (KNO_3)

pH	Temp, °C	$10^4 \times k_{obsd}$, s^{-1}	pH	Temp, °C	$10^4 \times k_{obsd}$, s^{-1}
	Cu(II)			Ni(II)	
7.00	20	10.2	8.60	20	5.60
7.25	20	14.4	8.75	20	8.26
7.50	20	29.1	9.00	20	9.72
6.75	25	12.7	8.50	25	9.10
7.00	25	22.9	8.75	25	14.6
7.25	25	37.8	9.00	25	24.7
6.50	30	10.1	8.00	30	5.98
6.75	30	22.0	8.25	30	10.4
7.00	30	37.4	8.50	30	17.1
6.25	35	5.22	7.75	35	6.17
6.50	35	8.82	8.00	35	10.9
6.75	35	15.9	8.25	35	23.2
	Zn(II)			Co(II)	
7.25	20	7.51	7.75	20	2.56
7.50	20	9.29	8.00	20	4.58
7.75	20	19.2	8.25	20	7.80
7.00	25	6.98	7.85	25	5.52
7.25	25	11.4	8.00	25	9.65
7.50	25	19.0	8.25	25	19.7
6.75	30	8.32	7.25	30	3.67
7.00	30	14.5	7.50	30	7.16
7.25	30	23.0	7.75	30	11.2
6.50	35	9.28	7.00	35	3.00
6.75	35	15.7	7.25	35	5.15
7.00	35	27.4	7.50	35	8.32
	Cu(IMDA)MeGly			Cu(IMDA)MeGly	
7.25	20	10.0	6.90	30	16.1
7.50	20	19.2	7.10	30	25.2
7.70	20	29.1	7.30	30	41.5
7.00	25	11.3	6.80	35	21.8
7.25	25	19.8	7.00	35	35.5
7.50	25	36.3	7.25	35	56.8

of metal complexes of ethyl *N,N*-diacetoxyglycinate known[8,10] to undergo hydrolysis via direct metal interaction have been studied to determine the activation parameters associated with hydrolysis and the existence of a possible isokinetic relationship. The activation parameters for iminodiacetatocopper(II)-promoted hydrolysis of methyl glycinate were also determined in hopes of determining its mechanism of catalysis.[11,12]

Experimental Section

Preparation of $C_2H_5O_2CCH_2N(CH_2COO)_2Ba$. Ethyl *N,N*-diacetoxyglycinate (EGDA) was prepared according to Schwarzenbach[13] as modified by Angelici.[8] NMR samples were obtained by adding Na_2SO_4 to a slurry of BaEGDA in D_2O and filtering off the $BaSO_4$. The NMR spectra obtained on a Varian A-60 spectrometer using 2,2-dimethyl-2-silapentane-5-sulfonate as an internal standard (0.00 ppm to TMS) indicated the presence of EGDA as well as glycine-*N,N*-diacetic acid, as reported by Angelici.[10] Solutions of BaEGDA were standardized by adding a known excess amount of acid followed by potentiometric titration (Corning Digital Research Model 112 pH meter).

Reagents. Reagent grade $Cu(NO_3)_2{\cdot}3H_2O$, $Zn(NO_3)_2{\cdot}6H_2O$, $Co(NO_3)_2{\cdot}6H_2O$, $Ni(NO_3)_2{\cdot}6H_2O$, $FeSO_4{\cdot}7H_2O$, $MnSO_4{\cdot}H_2O$, and 50% aqueous $Mn(NO_3)_2$ were used in the preparation of metal ion solutions which were standardized via standard ion-exchange techniques.[14] Aliquots were passed through a Dowex 50W-X8 strongly acidic cation-exchange resin and effluents were titrated with standardized NaOH to a phenolphthalein end point. IMDA (J. T. Baker) and MeGly·HCl (Sigma Chemical) solutions were standardized via potentiometric titration and ion-exchange techniques, respectively.

Kinetic Measurements. Rates of hydrolysis of EGDA in the presence of Cu(II), Ni(II), Zn(II), and Co(II) and of Cu(IMDA)MeGly were determined by pH stat techniques (Radiometer TTT2/ABU 11/SBR3) described elsewhere.[8] Ten-milliliter amounts of solutions containing 1:1 ratios of metal ion to EGDA plus NTA or 50:1 CuIMDA to MeGly and enough KNO_3 to give an ionic strength of 0.10 M were studied over a pH range of 0.50 log unit between 20 and 35 °C. The pH meter was calibrated in terms of H^+ concentration;[15] i.e., pH was defined as $-\log [H^+]$ instead of $-\log a_{H^+}$.

Table II. Rate Constants and Activation Parameters for H_2O Exchange and Ester Hydrolyses[a]

Metal[b]	log $k_{exchange}$ (H_2O)	ΔH^*	ΔS^*
Cu^{2+}	9.9	5	−4
Zn^{2+}	7.7		
Co^{2+}	6.0	8.0	−4
Ni^{2+}	4.5	11.6	0.6
Metal chelate	log k_{OH} (EGDA hydrolysis)	ΔH^*	ΔS^*
Pb^{2+} [c]	4.45	4.4	−23.5
Cu^{2+}	4.14	3.7 ± 0.6	−27 ± 1
Zn^{2+}	3.60	13.3 ± 1.9	+2 ± 2
Co^{2+}	2.78	12.9 ± 0.7	−2 ± 1
Ni^{2+}	2.21	13.8 ± 1.3	−2 ± 2
$M(NTA)^-$ [d]	log k_{OH} (MeGly hydrolysis)	ΔH^*	ΔS^*
Cu^{2+}	2.66	3.4	−38
Ni^{2+}	1.72	0.9	−47
Zn^{2+}	1.54	4.0	−38
Co^{2+}	1.27	1.5	−48
Cu(IMDA)	3.69	7.7 ± 1.4	−14 ± 2

[a] Hydrolyses at 25 °C and 0.10 M (KNO_3). ΔH^* in kcal/mol; ΔS^* in cal/(mol K). [b] Values from ref 18 and 19. [c] Values from ref 10. [d] Values from ref 7.

In all cases the solutions were equilibrated at the desired temperature under a constant nitrogen flow at pH 3–4, and then the pH was brought up to the desired value by addition of 0.018 M NaOH. The hydrolysis was then followed by automatic addition of base. The pseudo-first-order rate constants were obtained by plotting log (% end − % *t*) vs. time, where % end is the percent delivered at the end point and % *t* is that delivered at any time, *t*. The concentrations of M(EGDA) and Cu(IMDA) were 2.5×10^{-3} and 3.5×10^{-2} M, respectively. Since NTA^- was also present in the EGDA, solutions containing 10% and 25% excess mole percent of $MNTA^-$ were studied. Rates obtained using these solutions gave the same rates within experimental error as those without added $MNTA^-$, indicating that there was no rate dependence on $MNTA^-$ concentration.

Results

Pseudo-first-order rate constants, k_{obsd}, for the hydrolysis of EGDA in the presence of Cu^{2+}, Zn^{2+}, Co^{2+}, and Ni^{2+} at 20, 25, 30, and 35 °C at an ionic strength of 0.10 M (KNO_3) are listed in Table I along with those for MeGly hydrolysis in the presence of Cu(IMDA).

Under the conditions of these studies, the predominant reaction occurring may be written as

$$\text{MEGDA} + OH^- \rightarrow M(NTA)^- + C_2H_5OH \tag{1}$$

or

$$\text{M(IMDA)MeGly} + OH^- \rightarrow \text{M(IMDA)Gly}^- + CH_3OH \tag{2}$$

The total amount of NaOH consumed was always within 3% of the value expected from eq 1. The k_{obsd} values over a 0.5 pH range at each temperature agree with Leach and Angelici[11] that reaction 1 follows the rate law

$$\text{rate} = k_{OH}[\text{MEGDA}][OH^-] \tag{3}$$

and that reaction 2 follows the rate law

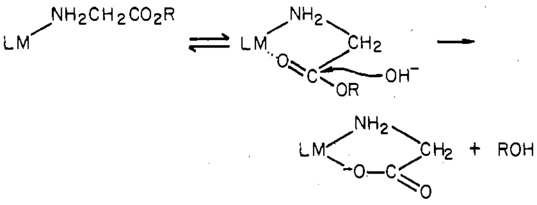
$$\text{rate} = k_{OH}[\text{M(IMDA)MeGly}][OH^-] \tag{4}$$

where $k_{OH} = k_{obsd}/[OH^-]$.[11,12] The activation parameters, ΔH^* and ΔS^*, for Cu(IMDA)MeGly and EGDA hydrolysis in the presence of Co^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+} are listed in Table II.

Unfortunately, we were not able to study the rates of EGDA hydrolyses in the presence of Fe^{2+} or Mn^{2+}. In both cases, precipitation, probably of metal hydroxides or oxides, occurred at neutral or basic pH values. The k_{obsd} values in Table I at 25 °C are all slightly lower than those previously reported by Leach and Angelici.[8] These differences may be due to ionic strength differences (0.10 M vs. 0.05 M) and/or to differing methods used to calibrate the glass electrode. Leach and Angelici[11] used buffer solutions and then converted a_{H^+} to $[H^+]$ using the Guggenheim equation; our glass electrodes were calibrated directly in terms of $[H^+]$ using HCl and NaOH solutions.[15]

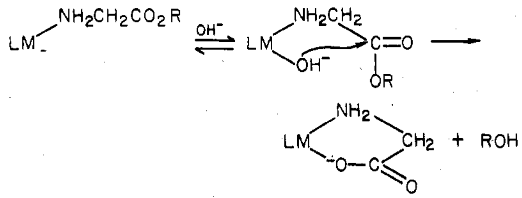
Discussion

Mechanisms of Metal Ion Promoted Hydrolysis of Amino Acid Esters. The overall metal chelate promoted hydrolysis of amino acid esters may be accounted for by three general mechanisms.[2-6] One involves an initial rapidly established equilibrium in which the carbonyl oxygen of the ester group coordinates to the metal, followed by rate-determining OH^- attack.



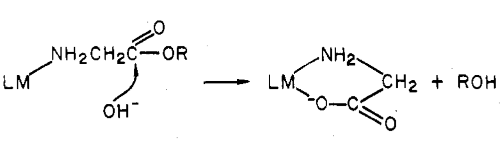
(5)

The second involves rapid, equilibrium formation of the M–OH complex, followed by intramolecular OH^- attack.



(6)

The third involves only OH^- attack at the ester carbonyl carbon of a noncoordinated ester group.



(7)

Buckingham, Foster, and Sargeson[16] via isotopic studies have shown that pathways 1 (eq 5) and 2 (eq 6) are important in the ester hydrolysis of the inert complex [*cis*-Co(en)$_2$Br(NH$_2$CH$_2$CO$_2$-*i*-Pr)$^{2+}$]. In labile metal complex catalyzed reactions of amino acid esters, it has been very difficult to establish whether one or a combination of the above mechanisms is involved in the observed hydrolysis. It is for this reason that we have chosen to initiate a series of studies into extrathermodynamic relationships associated with metal chelate promoted hydrolysis of amino acid esters. Recently, we have shown[7] that a series of tetradentate Ni(II) chelates and M–NTA complexes (Table I) promote ester hydrolysis via pathway 3 (eq 7) and we have determined the isokinetic temperature (β) as 274 K ($r^2 = 0.974$, the coefficient of determination from a linear regression analysis). Mechanism 3 was supported in that almost all of the metal chelates studied promoted ester hydrolysis to a lesser degree than a proton and in that the value of the isokinetic temperature indicates that solvent rather than electronic effects are probably more important.[17]

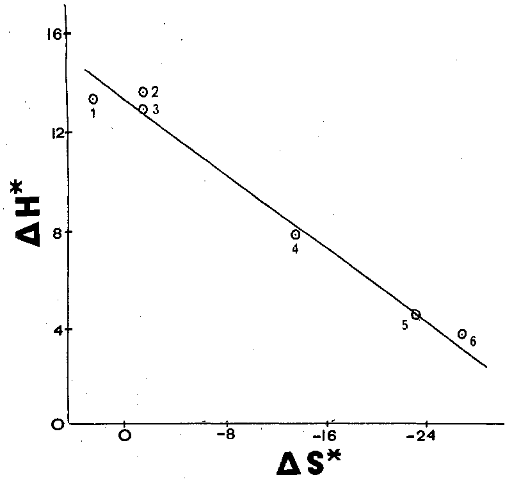


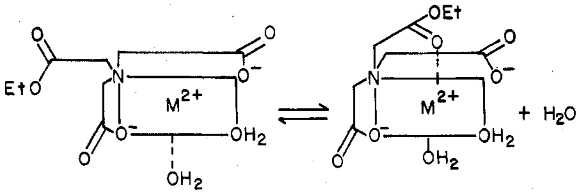
Figure 1. Plot of ΔH^* (kcal/mol) vs. ΔS^* (cal/(mol K)) for M^{n+}-promoted hydrolyses of ethyl *N*,*N*-diacetoxyglycinate and that of Cu(IMDA)MeGly: 1, Zn(EGDA); 2, Ni(EGDA); 3, Co(EGDA); 4, Cu(IMDA)MeGly; 5, Pb(EGDA); 6, Cu(EGDA).

Angelici and Leach[8-10] in a series of experiments have shown that the hydrolysis of monoesters of *N*,*N*-diacetates of amino acids in the presence of a series of metal ions proceeds via pathway 1 (eq 5). In Figure 1, a plot of ΔH^* vs. ΔS^* for the hydrolysis of EGDA in the presence of Cu^{2+}, Ni^{2+}, Co^{2+}, Zn^{2+}, and Pb^{2+} and of Cu(IMDA)MeGly yields a good straight line with a β value of 392 K ($r^2 = 0.983$). Parallel changes in ΔH^* and ΔS^* are often found to occur for a series of reactions involving common or common-type reactants and indicate a common mechanism.[17]

Metal Ion EGDA Hydrolysis. The trend for M(EGDA) hydrolysis is $Pb^{2+} > Cu^{2+} > Zn^{2+} > Co^{2+} > Ni^{2+}$ while that for M(NTA)$^-$-promoted hydrolysis is $Cu^{2+} > Ni^{2+} > Zn^{2+} > Co^{2+}$. The differing trends observed in the above two series are interesting and readily understood in terms of mechanism 3 (metal–nitrilotriacetate catalysis) and mechanism 1 (metal ion promoted hydrolysis of EGDA). It is expected that if mechanism 3 were operative, the predicted trend (based on inductive effects through a coordinated amine nitrogen) would be $Cu^{2+} > Ni^{2+} > Zn^{2+} > Co^{2+}$, i.e., the Irving–Williams series, as is observed for M(NTA)$^-$ hydrolysis of MeGly.[7] If mechanism 1 were operative, removal of a H_2O from the coordination sphere of a metal ion (eq 8) and subsequent

$$M(EGDA)(H_2O)_x \rightleftharpoons M(EGDA)(H_2O)_{x-1} + H_2O \qquad (8)$$

binding of the carbonyl oxygen of the ester should be important (eq 9). The trend for ligand-exchange reactions is $Cu^{2+} >$



(9)

$Zn^{2+} > Co^{2+} > Ni^{2+}$, the same as that observed for M(EGDA) hydrolysis. Figure 2 contains plots of ΔG^* and log $k_{exchange}$ for water exchange (eq 10) vs. log k_{OH} (Table II) for MEGDA

$$M(H_2O)_x{}^{2+} + H_2O^* \rightleftharpoons M(H_2O)_{x-1}(H_2O)^{*2+} + H_2O \qquad (10)$$

hydrolysis. Both plots yield good lines. The $k_{exchange}(H_2O)$ value for Zn^{2+} was determined in a different laboratory[18] than that of the other metal ions,[19] possibly explaining its position somewhat to right of the line (perhaps differing systematic

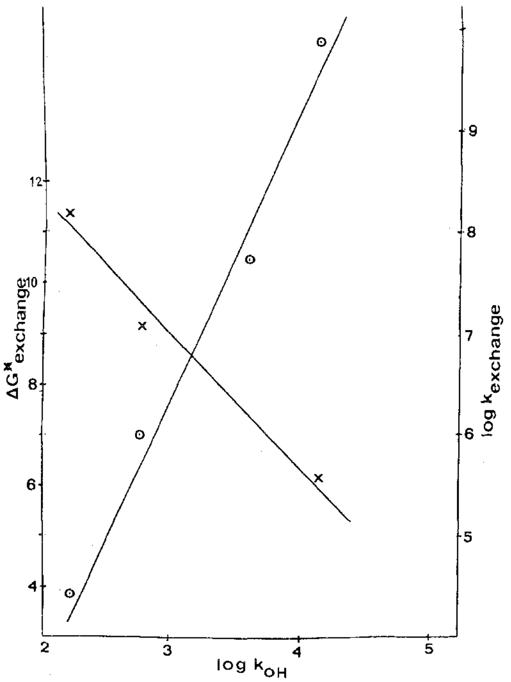


Figure 2. Plot of log $k_{exchange}(H_2O)$ (⊙) and $\Delta G^*_{exchange}(H_2O)$ (×) vs. log k_{OH}(M(EGDA) hydrolysis).

errors). Therefore, it appears that the preequilibrium step (eq 8) is primarily responsible for the major part of the activation energies needed for MEGDA hydrolysis. This seems reasonable considering the relatively large ΔH^* values for M(EGDA) hydrolysis, their similarities to ΔH^* values for H_2O exchange, the low ΔH^* values associated with M(NTA)$^-$ hydrolysis of MeGly, and the similarity of trends for both H_2O exchange and MEGDA hydrolysis. As expected, plots (not shown) of ΔG^* and log $k_{exchange}$ vs. log K_{OH} for M(NTA)$^-$-promoted hydrolysis of MeGly do not yield reasonable correlations.

One further point that should be mentioned is that the values used for log $k_{exchange}$ and ΔG^*[19] for H_2O exchange in Cu^{2+} are those determined for an axial position and not those for an equatorial one. If the values for an equatorial Cu^{2+} site are used, the points fall well off the line. This indicates either that catalysis takes place at the axial site or that at least initial ester coordination occurs at an axial site followed perhaps by possible inversion of the copper center to yield an equatorial coordinated ester group.[20]

Cu(NTA) and Cu(IMDA) Hydrolysis of MeGly. There has been some question as to the mechanism(s) of the hydrolysis of Cu(IMDA)MeGly[11,12] and Cu(NTA)MeGly$^-$.[7] It is quite clear that Cu(IMDA)MeGly falls nicely on the isokinetic line for pathway 1 (Figure 1) while Cu(NTA)MeGly$^-$ and Cu(NTA)EtGly$^-$ fall on that for mechanism 3.[7] Abrupt changes in mechanism can readily be ascertained by the position of compounds in isokinetic plots.[21] For example, in the acid-catalyzed hydrolysis of alkyl thioacetates in 62% acetone, a good isokinetic plot is obtained except for the gross deviation of the point for the trityl ester.[22] This compound was found to undergo cleavage of the alkyl–sulfur bond in contrast to the other compounds studied. Therefore, it appears that Cu(IMDA)MeGly and Cu(NTA)MeGly$^-$ undergo hydrolysis via different mechanisms, since they do not fall on the same isokinetic line. However, the relatively high rates of MeGly and EtGly hydrolyses in the presence of Cu(NTA)$^-$ (400 and 140 times faster than MeGly and EtGly, respectively) are in apparent disagreement with their positions on the isokinetic line for mechanism 3 in that Cu(NTA)$^-$ is more effective at promoting hydrolysis than a proton.

A reasonable explanation for the above could be that the Cu(NTA)$^-$-promoted hydrolyses do, indeed, involve direct interaction of the carbonyl oxygen with the metal but that in these cases, unlike those for M(EGDA) and Cu(IMDA)MeGly, the rate of H_2O exchange does not account for the major portion of ΔG^* (see Figure 2). Perhaps, in the Cu(NTA)$^-$ systems and the Ni^{2+} chelate and other M(NTA)$^-$ cases, hydroxide ion attack at the carbonyl carbon of the ester is responsible for most of ΔG^*. Such differences in contributions to ΔG^* should yield different isokinetic lines.[21] This explanation also appears to be in agreement with the observed isokinetic temperatures which indicate that M(EGDA) hydrolyses are enthalpy dependent (electronic effects are dominant) whereas those of Cu(NTA)$^-$ are entropy dependent (solvent effects are dominant). We have begun similar studies on other tetradentate Cu^{2+} chelates to hopefully better understand the thermodynamics associated with their catalytic activity.

Biological Significance. The apoenzyme of carboxypeptidase A is activated toward esterase activity by Zn^{2+}, Co^{2+}, and Ni^{2+}.[23] The relative order of activity, $Zn^{2+} > Co^{2+} > Ni^{2+}$,[23] is the same as that observed for the metal ion promoted hydrolysis of EGDA. However, Cu^{2+} which is active toward EGDA hydrolysis exhibits no esterase activity, perhaps due to its binding at a site in the apoenzyme different from that of Zn^{2+}, Co^{2+}, and Ni^{2+}. The binding of substrate to carboxypeptidase A involves among other interactions (1) the removal of H_2O from the coordination sphere of Zn^{2+} and (2) the metal ion binding of the carbonyl oxygen of the group to be hydrolyzed.[24,25] Although the M^{2+}–EGDA systems involve both of the above, the rates of hydrolysis are nonetheless much smaller than those for esters in the presence of the enzyme.

The above is disconcerting especially in view of the fact that in all the cases reported, free metal ions have shown higher catalytic activities than any of their corresponding metal chelates.[7,26] Apparently in the biological systems, something other than H_2O removal and metal ion binding of the carbonyl oxygen of the ester group is important. Perhaps the "nonaqueous" environment of the active enzyme site is important. The incorportion of M^{n+} into apoenzymes shows very large positive ΔS equilibrium values (eq 11),[27,28] which have

$$M^{n+} + \text{apoenzyme} \rightleftharpoons \text{M-enzyme complex} \qquad (11)$$

been attributed to the expulsion of a large number of water molecules upon metal ion complexation.[29] We have begun studies of hydrolyses in mixed-solvent systems and of phase-transfer catalysis in order to simulate "nonaqueous" environments.

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Registry No. Zn(EGDA), 64345-57-9; Ni(EGDA), 64345-56-8; Co(EGDA), 64345-55-7; Cu(EGDA), 64345-53-5; Cu(IMDA)MeGly, 64345-54-6.

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Conjugate Addition of Carbene Anions to α,β-Unsaturated Carbonyl Compounds

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The reaction of (2-oxacyclopentylidene)pentacarbonylchromium, **1**, with 1 equiv of base and methyl vinyl ketone followed by acidic workup gives a 41% yield of monoalkylated material **3**. The reaction of **1** with excess methyl vinyl ketone in the presence of a catalytic amount of base gives a 36% yield of **4**, the product of dialkylation followed by aldol condensation. The reactions of the anion of **1** with 2-cyclohexenone, *trans*-3-penten-2-one, *trans*-4-phenylbuten-2-one, and methyl *trans*-2-butenoate gave diastereomeric mixtures of monoalkylated adducts. The reactions of carbene anions with acetyl chloride, bromine, and ethylene sulfide are also reported.

Introduction

The evolution of metal–carbene complexes into useful reagents for organic synthesis[1,2] requires the development of general synthetic methods for the preparation of a wide variety of metal–carbene complexes. Recently, we demonstrated that anions generated α to the carbene carbon of metal–carbene complexes are synthetically useful intermediates for the elaboration of metal–carbene complexes.[3–7] These carbene anions are readily generated from metal–carbene complexes using convenient bases such as $NaOCH_3$ or *n*-BuLi.[7–9] Carbene complexes are remarkably acidic; in THF, $(CO)_5CrC(OCH_3)CH_3$ is as acidic as *p*-cyanophenol, which has a pK_a of 8 in water.[9] The high thermodynamic stability of carbene anions provides a driving force for the addition of a nucleophile to the carbon–carbon double bond of vinylcarbene complexes and thus makes vinylcarbene complexes excellent Michael acceptors.[10–13]

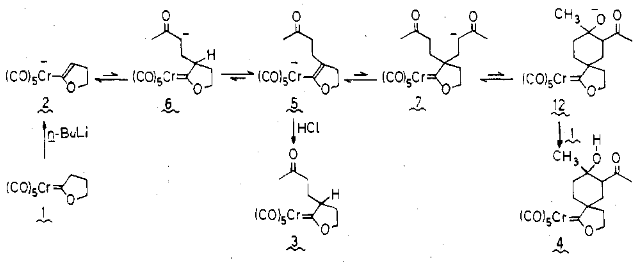
In spite of their high thermodynamic stability, carbene anions are moderately reactive toward electrophiles such as epoxides,[4] α-bromo esters,[4] aldehydes,[3] and chloromethyl methyl ether.[5] Here we report the reactions of carbene anions toward α,β-unsaturated carbonyl compounds.

Results and Discussion

Stoichiometric Reaction of Methyl Vinyl Ketone with the Anion of 1. The reaction of (2-oxacyclopentylidene)pentacarbonylchromium(0), **1**, with methyl vinyl ketone was studied extensively to define the course of the conjugate addition reaction. Reaction of the anion **2** (generated by addition of 1 equiv of *n*-BuLi to **1** at −78 °C) with methyl vinyl ketone in THF at 0 °C for 1 h gave 41% of the conjugate addition product **3** and 4% of recovered **1** after treatment with HCl. No dialkylated product **4** (vide infra) was observed.

When a similar reaction mixture was quenched with DCl, the monoaddition product **3** was found by NMR to be 43% deuterated at the position α to the carbene carbon atom; no deuterium incorporation α to the ketone was detected. The incomplete deuterium incorporation at the carbon α to the carbene carbon of **3** is probably due to partial washing out of the label on silica gel TLC during isolation; the rapid exchange of protons on the carbon α to the carbene carbon atom of **1** has been observed previously.[7–9,14] These results indicate that carbene anion **5** is the major species present before acidic workup (Scheme I). Carbene complex **1** and *p*-cyanophenol have comparable acidities in THF,[7,9] and it is therefore not surprising that carbene anion **5** greatly predominates over enolate anion **6** at equilibrium.

Scheme I



The conversion of carbene anion **2** to alkylated carbene anion **5** indicates that the Michael addition reaction is *favorable if an anion of comparable stability is the net product.* The absence of dialkylated materials such as **4** in the stoichiometric reaction could well be due to the reversible formation of the dialkylated anion **7** which is less stable than **5** since an enolate anion is substantially less stable than a carbene anion.

The above explanation implies that a tertiary carbene anion will not react with a Michael acceptor to give an addition product. Indeed, reaction of the anion of **8** with methyl vinyl