and the PHI-560 by the Brisbane Surface Analysis Centre, and we are grateful to these centers for instrumental time. We thank Jeffrey Dyason for assistance in the preparation of some of the samples used in the study and Barry Wood for valuable help in obtaining the XPS results. Chemical analyses were completed by the University of Queensland Microanalytical Service.

Registry No. **1**, 25753-82-6; **2**, 25753-81-5; **3a**, 25753-80-4.

Supplementary Material Available: Tables SUP-I–SUP-X, listing non-hydrogen thermal parameters, the derived hydrogen atom positions, and ligand non-hydrogen geometries (12 pages); tables of calculated and observed structure factors (35 pages). Ordering information is given on any current masthead page.

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Kinetics of Interaction of Copper Ion with Four Diaza–Crown–Alkanoic Acid Complexes

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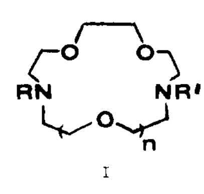
Received November 12, 1987

Thermodynamic considerations have dominated the subject of metal ion complexing of macrocyclic ligands, as an examination of a recent comprehensive review of cation–macrocycle interaction clearly shows.[2] Increasing attention is however being given to the kinetic aspects of complex formation with porphyrins,[3] crown ethers,[4] cryptands,[5] and aza macrocycles.[6] We are however still far from understanding the general details of ligand conformational changes necessary to present the macrocycle in a correct orientation before and during metal binding. An interesting and as yet little explored aspect is the complexing of macrocycles with pendent arms capable of coordinating.[7,8]

We have recently studied the kinetics of formation of complexes of metal ions with the macrocyclic ligands 1,4,7,10-tetraazacyclododecane-*N,N′,N″,N‴*-tetraacetate (DOTA) and 1,4,8,11-tetraazacyclotetradecane-*N,N′,N″,N‴*-tetraacetate (TETA).[8] For a number of metal ions, including Cu^{2+}, the kinetic data conformed to the rapid formation of an adduct, which either converted to the final complex or acted as a "dead-end" complex, in which case the reactants interacted separately by a second-order process to give the final complex.

In this note we report the kinetics of the complexing of copper ion by the four macrocycles 1,4,10,13-tetraoxa-7,16-diazacyclooctadecane-7,16-diacetic acid (Ia), -7,16-di-α-propionic acid (Ib), and -7-acetic acid (Ic) and 1,4,10-trioxa-7,13-diazacyclopentadecane-7,13-diacetic acid (Id). One and two pendent carboxylate residues as well as 15- and 18-membered macrocycles are presented to the metal ion by this selection of ligands. The structures of the solid Cu^{2+} complexes of Ia and Ib have been solved.[9,10] The copper is coordinated by the two amino acid residues in a transplanar configuration. The copper is also contained in the macrocycle ring with axial binding to two ether oxygens. It is reasonable to suppose that these structures persist in solution. Models show that the smaller 15-membered macrocycle ring present in Id brings the ether oxygens closer to the copper than does the 18-membered counterpart in Ia, and this may account[11,12] for the enhanced Cu(II) formation constant for Id ($10^{16.0}$)[11] over that for Ia ($10^{14.5}$).[13] With Ic in the solid state, coordination with Cu^{2+} is via the two N's and the one carboxylate sidearm of the macrocycle, as well as via O(4) and O(13) ether oxygens.[14] The effect of pendent arms, pH, and ring size on the kinetic characteristics can therefore be assessed.



I

Ia, $R = R^1 = CH_2COOH$, $n = 2$

Ib, $R = R^1 = CH(CH_3)COOH$, $n = 2$

Ic, $R = CH_2COOH$, $R^1 = H$, $n = 2$

Id, $R = R^1 = CH_2COOH$, $n = 1$

Experimental Section

Ligands Ia, Ib, and Id were prepared by literature methods.[12,15] Ligand Ic was prepared as follows: A 10-mmol quantity of chloroacetic acid in 25 mL of water was adjusted to pH 9.5 with 4 M NaOH. The solution was added dropwise over a period of 4 h to a boiling solution of 15 mmol of Kryptofix 22 (50% excess) in 20 mL of water. The mixture was refluxed for 10 h, and then it was adjusted to pH 12 with 4 M NaOH. The solution was extracted with chloroform (3 × 50 mL) to remove any unreacted Kryptofix 22. The aqueous layer was concentrated in vacuo and purified by passing through an ion-exchange column (Amberlite IR-120). The product was recrystallized from ethanol and dried in vacuo over P_4O_{10} (yield 70%). Anal. Calcd for $C_{14}H_{28}N_2O_6{\cdot}H_2O$: C, 49.70; H, 8.88; N, 8.28. Found: C, 49.45; H, 8.86; N, 8.28. These analyses were carried out at the Institute of Organic Chemistry.[1]

The compound appears not to have been described previously, although it was used, unpurified, as an intermediate in the preparation of an unsymmetrical N,N′-disubstituted Kryptofix 22 derivative.[16]

All studies were carried out at 25 °C and at an ionic strength of 0.1 M maintained with a lightly buffered sodium acetate/acetic acid and NaCl mixture. Most of the reactions were carried out at pH 3.75–4.75, with copper ion in excess (1–10 mM) over ligand (0.1–0.2 mM) and with monitoring at 330 nm. The kinetic data were independent of the concentration of the species in deficiency and of a change of wavelength from 300–350 to 600 nm (small absorbance change). A change of concentration of acetate ion from 0.01 to 0.05 M had no effect on the rate, indicating that the reactivity of the copper acetate species was similar to that of the aqua ion. The experiments were carried out in a Gibson-Dionex stopped-flow apparatus interfaced with an OLIS data collection system. Each rate constant quoted in Table I is the mean of several determinations and can be considered to have ±5% accuracy.

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Table I. Kinetic Data for Reaction of Cu^{2+} with Macrocycles Ia–Id at I = 0.1 M and 25 °C

	k_{obsd}, s^{-1}				
$[Cu^{2+}]$, mM	pH 3.75	pH 4.0	pH 4.25	pH 4.5	pH 4.75
			Macrocycle Ia		
1.00	9.4	20 (22)[a]		62	85
2.50		44 (48)[a]			
3.00	22			156	201
3.75		56 (65)[a]			
5.00	31	67 (71)[a]		209	317
7.50	38	84		255	366
10.0	47	99 (97)[a]		267	
12.5	52	109			
16.6		116			
			Macrocycle Ib		
0.50		1.3	3.0 (3.1)[b]		9.5
1.00		2.6	5.0 (6.0)[b]	8.6	19
1.50		3.9	7.5	13	24
2.50		6.1	10 (11)[b]	19	32
5.00		9.3	15 (17)[b]	26	48
7.50		12	18 (20)[b]	33	57
10.0		14	21	38	
			Macrocycle Ic		
1.00		13 (12, 1.0)[c]	17 (16, 1.3)[c]		
1.25	(11, 1.0)[c]				
2.00		19 (16, 0.8)[c]	29 (27, 1.2)[c]		
2.50	17 (16, 0.9)[c]			63 (61, 0.9)[c]	107
3.00		27 (22, 0.8)[c]	39 (33, 1.2)[c]		
3.75	23 (21, 0.9)[c]	(30, 1.0)[c]		100 (95, 1.2)[c]	156
4.00		33	51		
5.00	29 (23, 0.9)[c]	39 (35, 0.9)[c]	59 (54, 1.6)[c]	128 (119, 1.2)[c]	192
7.50	38 (31, 1.0)[c]	54 (46, 1.0)[c]	77 (70, 1.1)[c]	172	243
10.0	45	57 (48, 1.0)[c]	92 (107, 1.1)[c]	215 (210, 1.4)[c]	
12.5	50				
15.0		75	113		
			Macrocycle Id		
1.00	13, 0.7	18, 1.0	22, 2.5 (25, 2.2)[d]	29, 2.3	39, 2.4
1.50	16, 1.0	25, 1.2	30, 2.6 (33, 2.4)[d]	41, 2.6	57, 2.6
2.00		30, 2.6	38, 2.7		
3.00	28, 1.9	43, 3.0			
3.50			54, 3.0		
5.00	42, 2.2	55, 3.2	70, 3.2 (78, 3.0)[d]	102, 3.0	144, 2.7
7.50	53, 2.6	72, 3.7	92, 3.4 (105, 3.3)[d]	135, 3.0	192, 2.7
10.0	62, 3.7	82, 3.9	111, 3.5 (130, 3.3)[d]	170, 3.1	236, 2.8

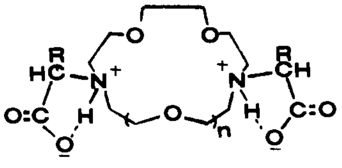
[a] Concentrations of Ia in excess; $[Cu^{2+}]$ = 0.2 mM. [b] Concentrations of Ib in excess: $[Cu^{2+}]$ = 0.1 mM; pH 4.3. [c] Concentrations of Ic in excess; two reactions. [d] Concentrations of Id in excess; two reactions for both Cu^{2+} and ligand in excess.

Table II. Data for Cu^{2+} Complex Formation with Ia–Id at I = 0.1 M and 25 °C

ligand	pH	$10^{-2}K$, M^{-1}	$10^{-1}k_1$, s^{-1}	$10^{-4}k_2$, $M^{-1}\ s^{-1}$
Ia	3.75	1.2	8	0.93
	4.0	1.4	17	2.3
	4.5	1.4	49	7.1
	4.75	1.2	78	9.5
Ib	4.0	1.2	2.5	0.30
	4.25	2.0	3.1	0.61
	4.5	1.8	6.6	1.2
	4.75	2.5	8.6	2.1
Ic	3.75	0.9	10	0.83
	4.0	0.9	13	1.1
	4.25	0.85	19	1.6
	4.5	0.47	66	3.1
	4.75	0.74	67	4.9
Id	3.75	0.86	14	1.2
	4.0	1.3	14	1.8
	4.25	1.3	19	2.5
	4.5	1.0	31	3.2
	4.75	0.9	48	4.3

Results and Discussion

Ia and Ib. For both ligands, single first-order reactions were observed, very similar in character regardless of whether the excess reagent was provided by the copper ion or by the ligand. There was no sign of a slower reaction over several seconds. Identical absorbance changes at a particular wavelength for different excess reagent concentrations and acidities confirm that the formation of the complex is complete with all conditions used, consistent with the known pK values of Ia[11,17] and the Cu(II) formation constant.[11] In all studies at pH 3.75–4.75, the ligand is in one predominant diprotonated (dizwitterionic) form II.[17] The reaction studied is



II

LH_2

therefore (1). The values of k_{obsd} were nonlinear with $[LH_2]$ or

$$Cu^{2+} + LH_2 \rightarrow CuL + 2H^+ \qquad (1)$$

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(17) Titration of the ligands shows two buffer regions. One at pH 5–9 corresponds to the addition of protons to the nitrogen atoms of the free ligand L to give the zwitterion LH_2. The two pK values are 8.45 and 7.8 for the appropriate forms of Ia and 9.02 and 8.79 for those of Id. The other buffer region is from pH 2.9–5, and this corresponds to the addition of one proton to give one $^+NHCHRCOOH$ residue. The pK values are 2.9 for IaH^+ ($\equiv LH_3^+$) and 2.95 for IdH^+ ($\equiv LH_3^+$). These results are at 25 °C and I = 0.1 M ($(CH_3)_4NCl$)).[11,13]

[Cu^{2+}] in excess at all pHs (Table I), conforming to the relationship (2), where X = [Cu^{2+}] or [LH_2]. Usually Cu^{2+} was used

$$k_{obsd} = \frac{A[X]}{1 + B[X]} \tag{2}$$

in excess. This behavior resembles closely that shown by the Cu^{2+}–DOTA system,[8] where "saturation kinetics" were observed. A similar treatment and explanation of the results were adopted. The reaction of Cu^{2+} with Ia or Ib was therefore interpreted in terms of eq 3–6. The overall reaction can proceed by a com-

$$LH_2 \rightleftarrows LH^- + H^+ \quad K_3 \tag{3}$$

$$Cu^{2+} + LH_2 \rightleftarrows Cu^{2+}{\cdot}LH_2 \quad K \tag{4}$$

$$Cu^{2+}{\cdot}LH_2 \rightarrow CuL + 2H^+ \quad k_1 \tag{5}$$

$$Cu^{2+} + LH_2 \rightarrow CuL + 2H^+ \quad k_2 \tag{6}$$

bination of (4) and (5), in which a rapidly formed adduct (formation constant K) is more slowly transformed into the final complex (k_1). With this mechanism, $A = k_1K$ and $B = K$.[8] Alternatively, the adduct is rapidly formed in (4) but is not on the reaction pathway to the final product, which results only from step 6, where $A = k_2$.[8] The values of K_1, k_1, and k_2 are collected in Table II. We formulate the adduct and its breakdown as in (4) and (5) because of the invariance of K with pH and the dependence of k_1 on $[H^+]^{-1}$ (Table II). This latter point means that the breakdown of the adducts $Cu^{2+}{\cdot}LH_2$ in (5) must involve several steps, including a preequilibrium in which one proton features in the product. The variation of k_2 with pH (Table II) indicates that, for Ia and Ib, LH_2 is much less reactive than LH^-. It is easily shown[8] then that $k_2 = k_{LH^-}[1 + K_3^{-1}[H^+]]^{-1}$. From the appropriate plot and a knowledge of K_3,[17] the value of k_{LH^-} for Ia can be calculated as 1.6×10^8 M^{-1} s^{-1}. A similar behavior for the fast step of Id (see below) allows an estimate for the reactivity of LH^-.

Ic. Again, a single first-order reaction using excess metal ion was observed, with characteristics similar to those of Ia and Ib and explainable in terms of (3)–(6). An adduct with formation constant $K \sim 10^2$ M^{-1}, approximately independent of pH (Table II), was deduced. Either the breakdown of this adduct (k_1) or the second-order formation rate constant (k_2) was inversely dependent on [H^+] (Table II). The constancy of absorbance changes with changing Cu^{2+} and H^+ concentrations indicated that formation of a complex was complete, despite the presence of only one pendent $-CH_2CO_2^-$ group in the ligand. It was assumed that this group was present as the diprotonated $^+HNCH_2COOH$ moiety in the pH region examined. When ligand was used in excess, two reactions were observed, both of which showed increasing and comparable absorbance changes at 330 nm. The two stages were sufficiently different in rates to be easily resolvable. The fast reaction appeared very similar to that observed when excess copper ion was used, both in absorbance changes and in rate constant/Cu^{2+}/pH characteristics. The slower reaction rate was independent of Cu^{2+} concentrations and pH and was 1.1 ± 0.1 s^{-1}. Unlike those for the other three ligands examined therefore, the absorbance changes were different when ligand instead of copper ion was used in excess. The slower step probably arises from the formation of higher species (ligand:Cu^{2+} = 2), since such complexes have been isolated.[18] It is apparent that the formation of this higher species is controlled by a first-order process, probably involving some necessary rearrangement of the macrocycle after the mono complex has formed and before the bis species can arise.

Id. The behavior of this ligand was the most interesting of the four examined. Two reactions were observed that were identical in characteristics regardless of whether copper ion or ligand (examined only at pH 4.25) was used in excess (Table I). The constancy of the total absorbance changes with differing Cu^{2+} and H^+ concentrations, as well as considerations of stability constants,[11,13,17] showed that complex formation was complete and that the same species resulted from use of either reactant in excess. The predominant ligand species at pH 3.75–4.75 is the dizwitterion LH_2 (II, R = H, n = 1).

The fast step had the characteristics of the first step in binding by Ia–Ic. The associated formation and rate constants are shown in Table II. The slow step had a constant rate (3.0 ± 0.2 s^{-1}) independent of Cu^{2+} concentration above 2.0 mM in the pH range 4.0–4.75. There was some indication from absorbance changes of an equilibrium for the first step at lower Cu^{2+} concentration and pH (3.75) but not for the overall reaction, and these data were not used in calculating the results in Table II.

Conclusions

Even one carboxylate arm in Ic is sufficient to promote copper complexing. No interaction is observed spectrally when 10 mM Kryptofix 22 (I, R = R′ = H, n = 2) is mixed with copper ion (2 mM) at pH 4.75. The reported stability constants for Cu^{2+} complexing with Kryptofix 22 are quite low, $10^{6.2}$ or $10^{7.6}$ at 25 °C in 0.1 M Et_4NClO_4.[19,20] The kinetic data indicate that in the reaction of excess Cu^{2+} with Ia–Id, there is a common first step in which there is a rapidly formed adduct between the metal ion and the zwitterionic forms of the ligand. If the formation of the final complex circumvents this adduct, then the process involves a second-order reaction of Cu^{2+} with LH^- (Ia, Ib, Id), which contains one $>NCHRCO_2^-$ and one $>N^+HCHRCO_2^-$ residue, or with LH (Ic), which has one $>N^+H_2$ and one $>NCH_2CO_2^-$ entity. From the known ionization constants for ligands Ia and Id and the approach outlined previously,[8] the rate constant for the reaction of Cu^{2+} with LH^- can be calculated as 1.6×10^8 and 3.0×10^8 M^{-1} s^{-1} for Ia and Id, respectively.[21] These values are close to those measured for Cu^{2+} with $NH_2CH_2CO_2^-$ and with the monoprotonated forms of DOTA and TETA.[8] The diprotonated forms LH_2 (II) and LH_2^+ (Ic) are unreactive.[22] The binding of the $>NCH_2CO_2^-$ residue in LH^- (Ia, Ib) or LH (Ic) to Cu^{2+} is followed by a rapid, intramolecular completion of complexing, with the remaining $>N^+HCH_2CO_2^-$ (Ia, Ib) or $>N^+H_2$ (Ic) groups aided perhaps by the ether oxygens. With the less flexible 15-membered ligand (Id) it appears that, after the initial binding to the $>NCH_2CO_2^-$ residue, the completion of complexing is controlled by a first-order process, k = 3.0 s^{-1}, which may be a conformational change in the macrocycle so as to orient the $>N^+HCH_2CO_2^-$ group in the correct position.

Acknowledgment. This work was supported by a National Science Foundation grant, which is gratefully acknowledged.

Registry No. Ia, 82353-42-2; Ib, 72912-01-7; Ic, 86952-04-7; Id, 81963-61-3; Cu^{2+}, 15158-11-9.

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(21) The ionization constants for Ib and Ic can be assumed to be similar to those for Ia and Id; therefore, it is assumed that $k_{LH} \sim 10^8$ M^{-1} s^{-1} for these also.

(22) The data in Table II indicate that there is a small contribution to the rate from the LH_2 species for Id with $k \sim 10^4$ M^{-1} s^{-1}.

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Formation of Diboron Complex Cations

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Received October 16, 1987

Earlier, we reported briefly that the reaction of bis(trimethylamine)hexahydrotriboron(1+) octahydrotriborate(1−), $B_3H_6{\cdot}2N(CH_3)_3^+$ $B_3H_8^-$, with trimethylamine resulted in the cleavage of the triboron cation framework to produce a new

0020-1669/88/1327-1836$01.50/0