Effect of Stacking Interactions in Co-ordination Kinetics

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Summary Large rate enhancements in complex formation reactions are attributed to the stacking interactions of incoming ligands with co-ordinated ligands.

Formation rate constants for the reactions of aromatic and heterocyclic ligands with nickel(II) can be increased a thousand-fold over that for aquonickel ion by using a co-ordinated ligand which can participate in forming a stacked

outer-sphere complex with the incoming ligand. The rate constants (k_f/l mol^{-1} s^{-1}; 25°) for the reactions of [Ni-(H$_2$O)$_6$]$^{2+}$ with pada,[1]† terpy,[2] and tptz[3] are 1·35 × 10^3, 1·5 × 10^3, and 2·0 × 10,[3] respectively. Using stopped-flow techniques we have measured the corresponding rate constants for the reaction of these ligands with [Ni(3,4,7,8-Me$_4$-phen)(H$_2$O)$_4$]$^{2+}$. The values are 1·38 × 10^6, 1·12 × 10^6, and 5·8 × 10^6, respectively. Smaller but significant rate enhancements have been observed in the formation of bis-terpyridyl complexes of iron(II), cobalt(II), and nickel-(II).[4] The water exchange rate constant for [Ni(terpy)-(H$_2$O)$_3$]$^{2+}$ cannot account for the effect.[5] A systematic variation of the incoming and bound ligands in the present work suggests that the rate enhancements are due to ligand association prior to the water substitution process.

TABLE

Formation rate constants[a] and rate enhancements due to stacking interactions.

Complex	Ligand	k_f/l mol^{-1} s^{-1}	Rate enhancement
[Ni(phen)]$^{2+}$	NH$_3$	1·5 × 10^{3b}	1·0
	Benzylamine	1·53 × 10^3	1·7
	phen	3 × 10^3 c	0·8
	bipy	3·70 × 10^4	23
	Me$_2$bipy	1·58 × 10^5	52
	pada	9·64 × 10^4	70
	terpy	1·00 × 10^5	65
	tptz	1·29 × 10^5	63
[Ni(terpy)]$^{2+}$	pada	4·45 × 10^5	190
	bipy	2 × 10^4 d	7
	terpy	2·76 × 10^5	106
[Ni(bipy)]$^{2+}$ ..	terpy	5·60 × 10^4	23
	pada	5·25 × 10^4	24
[Ni(5-Mephen)]$^{2+}$ ..	terpy	1·75 × 10^5	108
[Ni(3,4,7,8-Me$_4$phen)]$^{2+}$	terpy	1·12 × 10^6	543
	pada	1·38 × 10^6	744
	tptz	5·8 × 10^6	2110
[Ni(phen)]$^{2+}$	NH$_3$e	1·01 × 10^3	—
	terpye	4·83 × 10^3	ca. 4·8
[Ni(3,4,7,8-Me$_4$phen)]$^{2+}$	terpye	2·53 × 10^4	ca. 19

[a] 25·0 °C, in 0·1M NaClO$_4$ solution. [b] Data from D. W. Margerum and H. Rosen, *J. Amer. Chem. Soc.*, 1967, **89**, 1067. [c] Data from M. J. G. Williams and R. G. Wilkins, *J. Chem. Soc.*, 1957, 4514. [d] Data from R. G. Wilkins, *Accounts Chem. Res.*, 1970, **3**, 408. [e] In MeOH–H$_2$O (65 : 35 w/w).

The proposed stacking interaction will assist the substitution rate only if the incoming ligand is sufficiently flexible to permit one donor group to be orientated in a position suitable to replace a co-ordinated water molecule while the rest of the molecule is in a stacked arrangement. Thus, bipy addition to [Ni(phen)(H$_2$O)$_4$]$^{2+}$ (*cf.* Table) is 25 times faster than ammonia addition, while phen addition is only twice as fast. The more flexible bipy can interact as shown in Figure 1 while phen cannot. The experimental data indicate that the larger the area of interaction between the stacking molecules the greater is the formation rate constants. There is a general increase in the formation rate constants for ligands reacting with [Ni(phen)(H$_2$O)$_4$]$^{2+}$ as the number of aromatic rings in the ligand increases. Even benzylamine reacts faster with [Ni(phen)(H$_2$O)$_4$]$^{2+}$ than it does with [Ni(H$_2$O)$_6$]$^{2+}$ as shown by the rate enhancement

values in the Table. The rate enhancement is defined as the ratio of formation rate constants [k_L(NiX)/k_L(Ni$_{aq}$)] divided by the ratio of water exchange rate constants k(NiX–H$_2$O)/k(Ni$_{aq}$–H$_2$O), and is as large as 70 for the reaction of pada with [Ni(phen)(H$_2$O)$_4$]$^{2+}$.
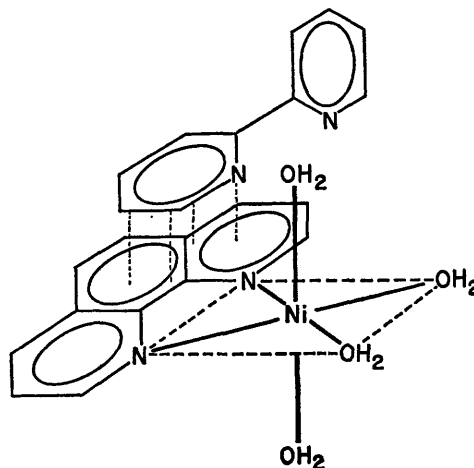

FIGURE 1. A possible orientation of the stacking interaction between bipy and [Ni(phen)(H$_2$O)$_4$]$^{2+}$ immediately prior to first-bond co-ordination of bipy.

An increase in the number of aromatic groups in the bound ligand also increases the formation rate constants as seen for the reactions of [Ni(bipy)(H$_2$O)$_4$]$^{2+}$, [Ni(phen)-(H$_2$O)$_4$]$^{2+}$ and [Ni(terpy)(H$_2$O)$_3$]$^{2+}$ with terpy. The enhancement factor is only 7 for [Ni(terpy)(H$_2$O)$_3$]$^{2+}$ + bipy because only one pair of rings can stack while the enhancement factor is 23 for [Ni(bipy)(H$_2$O)$_4$]$^{2+}$ + terpy where two pairs of rings can stack.
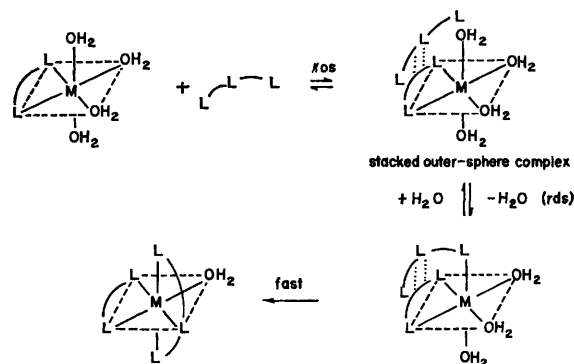

FIGURE 2. Proposed mechanism for ternary complex formation with stacking interaction.

The magnitude of the formation rate constants also depends on the number of methyl substituent groups on the phenanthroline rings. As seen in the Table, the rate enhancements are large even after correcting for the increased lability of the co-ordinated water molecules.[6] Methyl groups on the incoming ligands also increase the rate constants (*cf.* Me$_2$bipy with bipy). The effectiveness of pada may be due in part to its methyl groups.

† Abbreviations used are phen: 1,10-phenanthroline; 5-Mephen: 5-methyl-1,10-phenanthroline; 3,4,7,8-Me$_4$phen: 3,4,7,8-tetra-methyl-1,10-phenanthroline; bipy: 2,2′-bipyridyl; Me$_2$bipy: 4,4′-dimethyl-2,2′-bipyridyl; terpy: 2,2′,2″-terpyridyl; pada: pyridine-2-azo-p-dimethylaniline; tptz: 2,4,6-tripyridyl-s-triazine.

Figure 2 shows the general mechanism proposed for these reactions. The water molecules co-ordinated axially are favourably positioned to be replaced by a dentate group of the stacked ligand. The rate-determining step must be early in the formation reaction in order to maintain any advantage from stacking interactions. A consequence of this mechanism is that the dissociation rate constants, k_d, must also be accelerated by stacking interactions and we find this to be the case (e.g., k_d/s^{-1} at 25°) for pada is ca. 0·1,[1] 3·6, and 26·4 for the mixed complexes with Ni^{2+}, [Ni(phen)]$^{2+}$ and [Ni(3,4,7,8-Me$_4$(phen)]$^{2+}$, respectively.

Stacking interaction is a noncommital term which includes hydrophobic bonding and polarization effects.[7] It is possible using the present reactions to divide the hydrophobic and polarization effects in an approximate manner by observing the formation rate constants in mixed MeOH–H$_2$O solvents. In 65% MeOH–H$_2$O nickel ion is still predominantly solvated by H$_2$O,[8] but the water structure is

greatly altered[9] and the hydrophobic bonding effects are reduced. In this solvent mixture the rate enhancements are greatly decreased. The decrease is a factor of 14 for the reaction of terpy with [Ni(phen)]$^{2+}$. Thus, hydrophobic bonding accounts for a major fraction of this stacking interaction. The relative rate dependence on the number of methyl groups is much less affected by the solvent composition. It would seem that the methyl groups are contributing more to the polarization effect.

The importance of stacking interactions in biological systems is recognized[10] and this effect may be important in attracting and positioning substrates in enzymatic reactions. Co-ordination kinetics provide a convenient method of measuring stacking interactions.

[1] M. A. Cobb and D. N. Hague, J.C.S. Faraday I, 1972, 68, 932.
[2] W. S. Melvin, D. P. Rablen, and G. Gordon, Inorg. Chem., 1972, 11, 488.
[3] T. S. Roche and R. G. Wilkins, J. Amer. Chem. Soc., 1974, 96, 5082.
[4] R. H. Holyer, C. D. Hubbard, S. F. A. Kettle, and R. G. Wilkins, Inorg. Chem., 1966, 5, 622.
[5] D. Rablen and G. Gordon, Inorg. Chem., 1969, 8, 395.
[6] R. K. Steinhaus and D. W. Margerum, J. Amer. Chem. Soc., 1966, 88, 441.
[7] W. P. Jencks, 'Catalysis in Chemistry and Enzymology,' McGraw-Hill, New York, 1969, ch. 8.
[8] M. J. MacKellar and D. B. Rorabacher, J. Amer. Chem. Soc., 1971, 93, 4379.
[9] H. P. Bennetto and E. F. Caldin, J. Chem. Soc. (A), 1971, 2207.
[10] 'Molecular Association in Biology,' ed. B. Pullman, Academic Press, New York, N.Y., 1968.