# Computer Modelling of Metal Ion Recognition. Simulation of the Relative Thermodynamic Stabilities of the Nickel Complexes of Related $O_2N_3$-Donor Macrocyclic Ligands

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A previously observed stability pattern involving 'dislocation' discrimination has been modelled successfully using molecular mechanics procedures; as part of the study the *X*-ray structure of the nickel complex of an $O_2N_3$-donor macrocyclic ligand has been determined.

It had been well established that cavity size variation in macrocyclic ligands may be used to achieve metal ion recognition.[1] For a number of cyclic systems, maximum thermodynamic stability occurs when the ligand cavity provides an optimum fit for the metal ion of interest. Recently, we have described a second mechanism by which metal ion recognition may be achieved.[2,3] This mechanism involves the occurrence of a 'dislocation' in the complexation behaviour towards a metal ion along a series of closely related ligands. If the dislocation occurs at different points along the ligand series for different metal ions, then enhanced metal ion discrimination effects may be evident at the dislocation points.

It has been demonstrated that a dislocation of the above type occurs on passing from the nickel complex of (**1**) to the corresponding complex of the dimethylated derivative (**2**).[2] The log stability constants for the 1:1 nickel to ligand complexes of these two macrocycles are 10.0 and 6.9, respectively. In contrast, the respective log *K* values for the corresponding copper(II) complexes, at 14.4 and 14.3, indicate that the dislocation observed for nickel does not occur with this ion.

From physical measurements and consideration of molecular models, it was concluded that the different behaviour of the nickel complexes reflected steric crowding in the $N_3$-donor portion of the dimethyl derivative (**2**) resulting in destabilization of the co-ordination geometry assumed by (**1**) around nickel(II). Thus, in the absence of methyl substituents, it was postulated that the $N_3$-donor fragment assumes a facial co-ordination arrangement when co-ordinated to the above metal; the proposed co-ordination geometry is illustrated by (**3**). We now report the results of an *X*-ray study of $[NiL(H_2O)](ClO_4)_2$ where L = (**1**).† The results confirm that the solid state structure of this complex is of the type predicted. Structural details are given in Figure 1. In contrast, because of the steric crowding mentioned above, a meridional arrangement of the $N_3$-backbone was predicted to occur in the corresponding nickel complex of the dimethylated derivative (**2**).

We have developed a molecular mechanics program (based on the force field described by Allinger[4]) and have used it to investigate the different observed behaviour of (**1**) and (**2**) towards the nickel ion. Starting from the *X*-ray atomic co-ordinates for $[NiL(H_2O)]^{2+}$ [where L = (**1**)] the structure was minimized and its 'strain' energy recorded. The geometry

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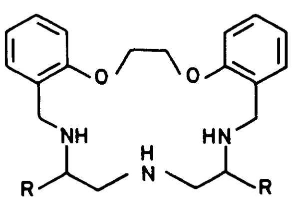
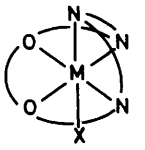
† *Crystal data:* $[NiL(H_2O)](ClO_4)_2$, L = (**1**), $C_{20}H_{27}Cl_2N_3NiO_{11}$, triclinic, space group $P\bar{1}$, $a = 9.697(3)$, $b = 13.027(4)$, $c = 10.988(4)$ Å, $\alpha = 100.49(10)$, $\beta = 106.36(11)$, $\gamma = 87.03(9)°$, $Z = 2$, $I/\sigma(I) \geqslant 3.0$, present *R*-value = 0.073 for 3952 reflections. The $ClO_4^-$ ions are seriously disordered; 12 oxygen sites were resolved for one ion and 8 for the other. The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.



**(1)** R = H

**(2)** R = Me



**(3)**

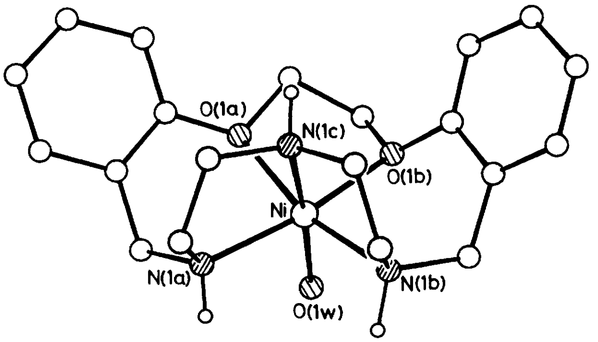


**Figure 1.** The $X$-ray structure of *fac*-$[NiL(H_2O)](ClO_4)_2$, L = (**1**). Selected bond lengths and angles are listed. Values obtained from the molecular mechanics calculation are given in parentheses after the $X$-ray values. Bond lengths (Å) to the Ni atom are: N(1a) 2.049 (2.056); N(1b) 2.060 (2.068); N(1c) 2.072 (2.075); O(1a) 2.231 (2.208); O(1b) 2.125 (2.140); and O(1w) 2.104 (2.101). Bond angles at the Ni atom (°) are: N(1a)–Ni–N(1b) 104.8 (104.1); O(1a)–Ni–O(1b) 77.6 (78.1); O(1a)–Ni–N(1b) 89.1 (87.5); N(1a)–Ni–O(1a) 88.8 (90.5); O(1a)–Ni–N(1c) 93.3 (92.1); O(1a)–Ni–O(1w) 88.6 (92.9); O(1b)–Ni–N(1c) 100.9 (98.3); O(1b)–Ni–O(1w) 84.5 (87.4); N(1b)–Ni–N(1c) 84.6 (87.6); N(1b)–Ni–O(1w) 94.9 (88.8); N(1a)–Ni–N(1c) 85.1 (87.9); and N(1a)–Ni–O(1w) 89.7 (87.3).

of the minimized structure differed in only minor detail from the $X$-ray structure. Such differences are to be expected since no account of crystal packing is incorporated in the molecular mechanics procedure. For comparison with the $X$-ray data, important bond distances and angles for the minimized structure are listed in the caption for Figure 1. Using molecular models as a guide, the atomic co-ordinates for the corresponding (hypothetical) meridional isomer were estimated and used as the initial co-ordinates for minimization by the molecular mechanics procedure. For this initial structure it was assumed that all donor atoms of the macrocycle remained bound to the nickel and that the sixth co-ordination site was again occupied by a water molecule. This minimized structure was found to be *ca.* 9.0 kJ/mol less stable than the corresponding minimized facial isomer. Thus, in agreement with the experimental evidence, the calculations clearly indicate that the facial form is preferred when (**1**) binds to nickel.

Similar calculations were performed for the corresponding meridional and facial complexes of (**2**). For the calculation involving the facial form, methyl substituents were 'added' to the $X$-ray structure given in Figure 1 and the atomic co-ordinates of this modified structure used as the starting co-ordinates. A similar procedure was adopted for the meridional isomer starting from the corresponding (estimated) co-ordinates for the (meridional) complex of (**1**). The calculations indicated a reversal of the stability order for this ligand system: the meriodional isomer is predicted to be *ca.* 7 kJ/mol more stable than its facial form. Once again this stability order corresponds to that observed experimentally. It should be noted that it is not the absolute values of the energy differences which are significant but rather their relative values: the differences will vary somewhat with the particular force field chosen. The calculated meridional form is illustrated in Figure 2. For this calculation it was assumed that (**2**) was present as its *meso* isomer‡ as was observed to occur by $X$-ray diffraction in the related complex $[NiL(NCS)_2]$ [where L = (**2**)];[5] in this complex the $N_3$-donor fragment also assumes a meridional arrangement.

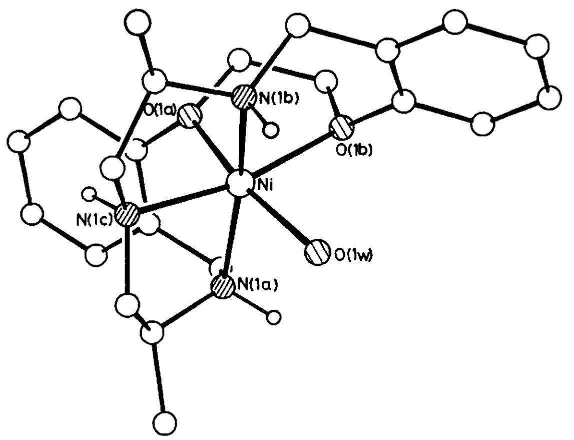


**Figure 2.** The structure of *mer*-$[NiL(H_2O)]^+$, L = (**2**), predicted by the molecular mechanics calculation.

The present work demonstrates that molecular mechanics calculations can be applied successfully to model 'dislocation' discrimination of the type described. Further, it appears feasible that such calculations may be used predictively for the design of new metal ion specific reagents.

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‡ Parallel calculations for the corresponding complexes of the racemic ligand isomer have been performed. For this system the meridional isomer is even more favoured over the facial isomer: the energy difference between the two isomers now being 23.1 kJ/mol.