

METAL-FREE MACROCYCLES VIA TEMPLATE METHOD: A STARTING POINT FOR
SELECTIVE COMPLEXATION STUDIES.

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ABSTRACT. A new range of structurally-related macrocyclic ligands have been prepared and their potential as metal-ion discriminating agents examined.

INTRODUCTION. The recognition and binding of metal ions by organic ligands has obvious implications for many aspects of chemistry and biochemistry. Valinomycin and the actin series of cyclic ionophores [1] are examples of how Nature has made use of the special properties of macrocycles to achieve discriminatory behaviour. The chemist, on the other hand, has through the years developed many 'classical' analytical reagents [2] which show reasonable specificity for particular ions, but their introduction has often resulted from chance observation rather than a systematically designed program.

While much elegant work has been produced on the selective behaviour of the polyether macrocycles towards alkali and alkaline earth metal ions [3], studies involving the transition and base metal ions have been relatively scant. We report here a versatile route to a new range of structurally similar macrocycles as the first part of a longer term project aimed at the elucidation of the principles governing metal ion selectivity.

DISCUSSION. There are basically two routes to the synthesis of macrocyclic ligands. These are:

(1) The in situ or template method, where the intervention of a metal ion directs the course of reaction towards cyclic rather than polymeric products. The product is usually a macrocyclic complex of the template metal used, and the macrocyclic cavity is normally of a size commensurate with the metal's ionic radius. While this technique has resulted in the isolation of many macrocycles which are not available by other means its main drawback is that demetallation to produce free ligand is not always possible; often the macrocycles prove unstable in the unco-ordinated state.

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Scheme 1

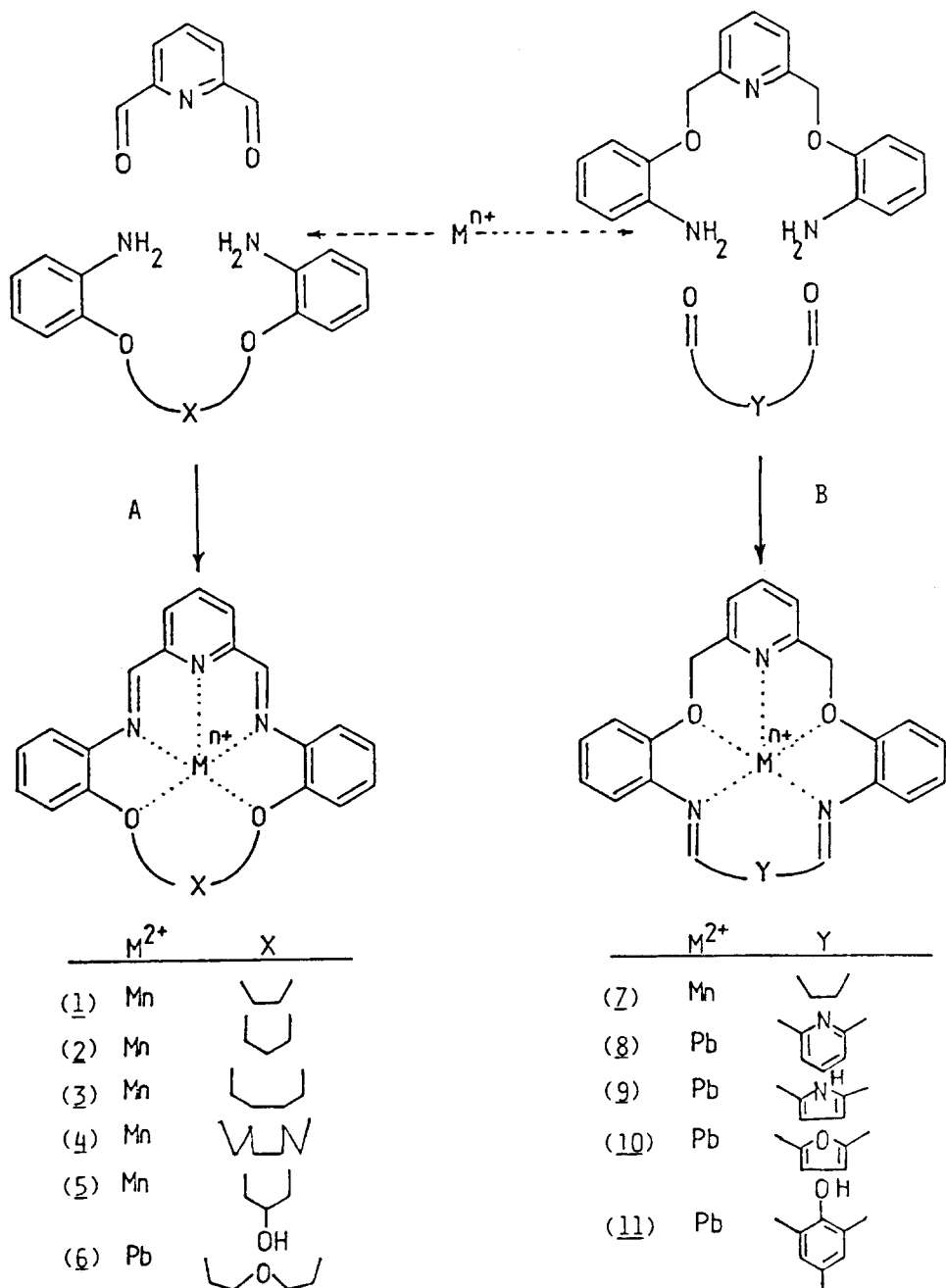
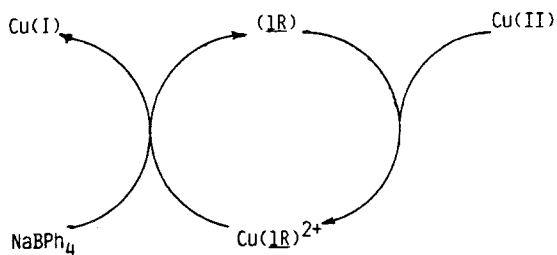


TABLE 1

F.A.B. Mass Spectroscopy

F.A.B. m.s. of The Template Products		M/M'	$M(1R)^+$	$\%$
		Cu^{63}/Ni^{58}	409/404	100/67
		Cu^{63}/Co^{59}	409/405	100/9
		Cu^{63}/Mn^{55}	409/401	100/-
		$Cu^{63}/Ag^{107}/Pb^{208}$	$409/^{453}/^{554}$	100/-/-
m/e	Assignment			
496	$[Mn(1)(C_{10}_4)]^+$			
511	$[Mn(2)(C_{10}_4)]^+$			
525	$[Mn(3)(C_{10}_4)]^+$		(1R) = 347	
-	$[Mn(4)(C_{10}_4)]^+$			
527	$[Mn(5)(C_{10}_4)]^+$			
-	$[Pb(6)(C_{10}_4)]^+$		Table 2	
497	$[Mn(7)(C_{10}_4)]^+$			
727	$[Pb(8)(C_{10}_4)]^+$			
614	$[Pb(9)]^+$			
716	$[Pb(10)(C_{10}_4)]^+$			
655	$[Pb(11)]^+$			
1104	$[Pb(11)_2]^+$			
1205	$[Pb(11)_2(C_{10}_4)]^+$			
684	$[Pb(12)(C_{10}_4)]^+$			



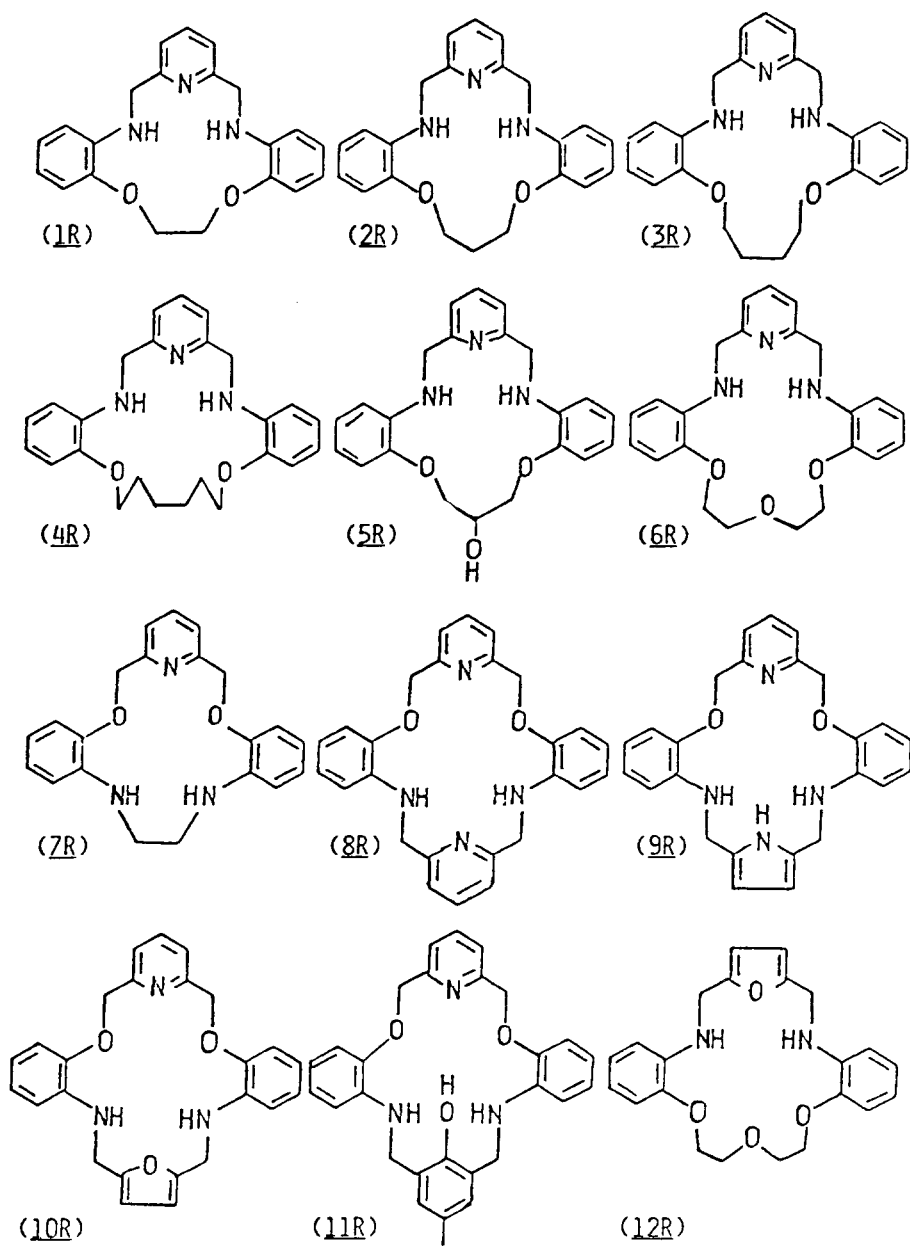
Scheme 2

(2) Direct synthesis, usually employing high dilution conditions, can be used. This approach produces the macrocycle in a form which not only makes spectroscopic characterisation easier, but which is also more amenable to organic modification.

The methods reported herein make use of the more favourable aspects of both routes.

Two approaches have been adopted (Scheme (1)) A - condensation of 2,6-diformylpyridine with various diamines and B - condensation of various dicarbonyls with a pyridyl diamine. Mn(II) or Pb(II) were used to template the reactions to produce the di-imine macrocyclic complexes.

The F.A.B. mass spectra results (Table 1) demonstrate the mono-nuclear di-imine nature of all but one of the products. The exception

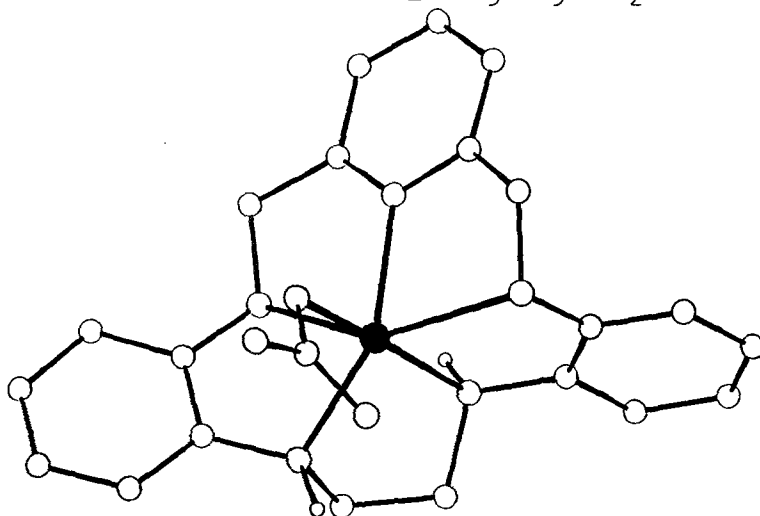


Matrix of Structural Types

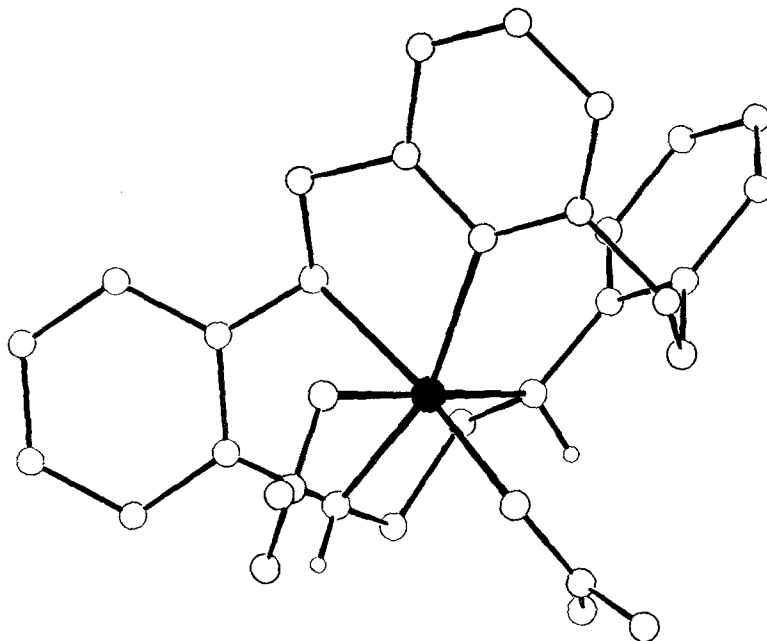
Figure 1

Fig. 2

The structure of $[\text{Cu}(\underline{7R})(\text{NO}_3)]\text{NO}_3 \cdot 0.5\text{H}_2\text{O}$ (Log K 6.84)



The structure of $[\text{Ni}(\underline{7R})(\text{NO}_3)_2] \cdot 0.5\text{H}_2\text{O}$ (Log K < 3.0)



is thought to exist as a 'triple decker' - macrocyclic sandwich. The 2:1 and 1:1 [(11):Pb] fragments of $[Pb_2(11)_3][ClO_4]_2 \cdot 3H_2O$ can be seen.

The complexes of (1) to (12)* can be demetallated and reduced (using sodium borohydride) to give, in economic yields, the free macrocycles (1R) to (12R) which constitute a matrix of ligand structural types (Fig. 1) systematic variation in ring size, the number type and disposition of donors has been achieved.

Empirical discrimination for Cu(II) has already been observed with (1R) (Scheme 2). Intense green colouration occurs on mixing MeCN solutions. Treatment with $NaBPh_4$ liberates the metal as soluble Cu(I); the macrocycle being recovered from solution. No colour changes are observed with the other first row transition metals.

Preliminary results from F.A.B. mass spectroscopy experiments have demonstrated the potential that this technique may have as a screening method for selectivity (Table 2).

Equimolar quantities of (1R) and pairs or mixtures of metal ion chlorides were dissolved in 3-NOBA (3-Nitrobenzyl alcohol), the matrix for the F.A.B. experiment. The results confirm the above empirical observation in that Cu(II) consistently returns with 100% abundance for the species $[Cu(1R)]^+$ over all competitors.

Complementary X-ray diffraction and stability constant data (Fig.2) for the macrocycle (7R) indicate an enhanced ligand propensity for Cu(II) relative to Ni(II). The origins of this discriminatory behaviour can be seen from the crystal structures to lie in the ability of Cu(II) and the inability of Ni(II) to accommodate the complete array of macrocyclic donor atoms. A complete study of this matrix of ligands is currently underway.

CONCLUSION. Facile and economic routes to a new series of macrocyclic ligands have been achieved. Within this series the deliberate and systematic variation of many of the features of the macrocycles lends them particularly well to a designed program aimed at rationalizing the factors which govern discriminatory behaviour towards metal ions.

* (12R) obtained via route A (Scheme 1) using 2,5-diformylfuran as dicarbonyl.

REFERENCES.

- (1) D.E.Fenton: Chem. Soc. Rev., 6, 325 (1977).
- (2) See for example Organic Reagents for Metals, W.C.Johnson, Ed., Hopkin and Willimas Ltd., Chadwell Heath, 1964 and Solvent Extraction of Metals, R.A.Chalmers, Ed., Van Nostrand Reinhold, London, 1970.
- (3) See for example B.Dietrich, J. Chem. Ed., 62, 954 (1985).

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