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Bis-Pyridine-Tetramide 18 - Membered Macrocycles. Role of Increased Preorganisation on Ag^+ / Pb^{2+} Selectivity

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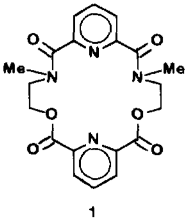
Abstract : Enhanced preorganisation induced by four substituted amide groups in macrocycles **4a** and **4b** increases the Ag^+ extraction efficiency by >30% to 74 - 81% and Ag^+ / Pb^{2+} selectivity by >300% to 245 - 283 times than in **1**.

The in-built configurational rigidity induced by N-substituted amides present in the periphery of macrocycles invokes preorganisation conducive to ionophoric selectivity[1,2]. Amide substitution in pyridine based diamide - diester (**1**) -18-membered macrocycle is responsible for its preorganisation and consequently Ag^+ selectivity[2a,2b]. We now report that N-substituted tetramide analogs **4** depict rigid preorganised cup shaped topology which exihibts a high order of Ag^+ selectivity even against similar sized Pb^{2+} cation.



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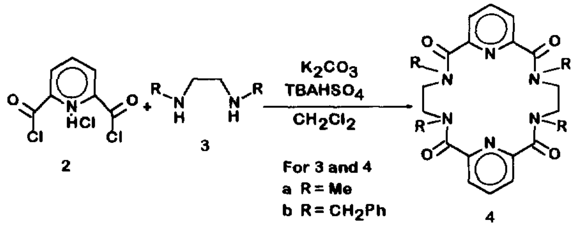

The phase transfer catalysed (K_2CO_3 - CH_2Cl_2 - tetrabutylammonium hydrogensulphate) nucleophilic displacement in **2** with respective diamines **3** gave macrocycles **4a** (26%), m.p. 272°C, M^+ m/z 438(35%); **4b** (2%), m.p. 210°C, M^+ m/z 742 (76%). The macrocycle **4a** in its ^1H nmr spectrum shows a singlet due to N-Me (δ 3.23) but NCH_2 protons appear as AB quartet at 3.65, 4.28 (J = 9.0 Hz). The ^1H nmr of **4b** shows AB quartets both due to $NCH_{2\,(ring)}$ [3.78, 4.05(J = 9.0 Hz)] and $NCH_{2(benzyl)}$ [4.39, 5.94(J = 16Hz)]. However, their ^{13}C nmr spectra show normal signals due to each chemically non-equivalent carbon. Therefore, macrocycles **4a** and **4b** have rigid structures, where two methylene protons absorb at different frequencies. The X-ray crystal structure of **4b** (fig 1) shows the placement of alternate substituents of the four amide groups in opposite direction with respect to mean plane of pyridine rings. The macrocyclic ring thus possesses a crystallographic two fold axis of rotation at its centre and the cavity is protected by benzyl groups, two on each side. From the 8H of four CH_2 units 4H are directed into the cavity and the other 4H are placed outside the cavity (not shown in fig. 1), resulting in their non-equivalence and appearance as AB quartets, in the ^{1}H nmr spectra. Therefore, both solution (^{1}H nmr) and solid (X-ray) state structure studies show puckered and rigid structures for macrocycles **4a** and **4b**.

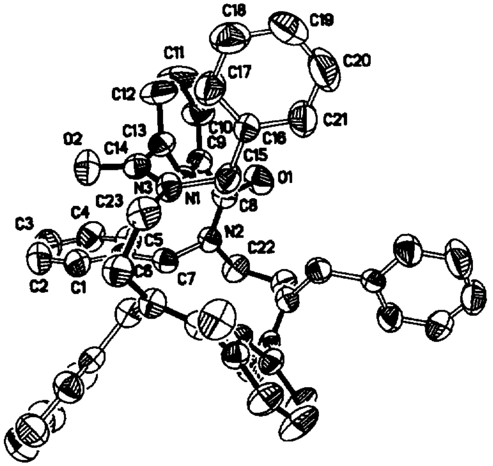

Fig 1. X-ray cryctal structure[3] of macrocycle 4b showing its perspective drawing.

The macrocycle **4a** extracts Ag^{+} picrate (74%) (fig. 2) nearly 283 times than Pb^{2+} (0.26%) and **4b** shows further enhancement of extraction of Ag^{+} (81%) but Ag^{+} vs. Pb^{2+} selectivity is marginally lowered to 245. The alkali and alkaline earth cations are extracted only marginally. However, pyridine- diamide -diester **1** has been reported to show 56% Ag^{+} extraction and Ag^{+} vs. Pb^{2+} selectivity is 63. The considerable difference in configuration of ligand **1** and **1** in **1.AgNO$_3$** complex (X-ray)[4] and similarity in that of **4b** with the latter point to the status of preorganisation in **4b** which situation **1** attained only after complexation. However, the collapse of ^{1}H nmr AB quartet (δ 3.97) of **4a** to singlet (δ 3.12) on addition of Ag^{+} picrate shows that during complexation some conformational changes still occur.

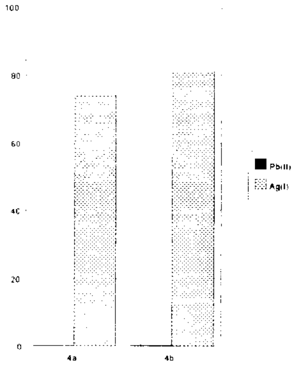

Fig 2. Extraction (%) profile[2c] of macrocycles 4a-4b.

Evidently, the replacement of two ester units of **1** with two amide units in **4a** and **4b** remarkably enhances the rigidity and preorganisation of the macrocycles and as a result the extraction efficiency and selectivity towards Ag^{+} over Pb^{2+}, Tl^{+}, alkali and alkaline earth cations is increased.

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3. The crystal was measured on Phillips PW1100 four circle diffractometer using θ-2θ scan mode. The structure was solved by using direct methods (SHELXS-93) and refined using SIEMENS SHELXTL-PC computer programs. Crystal data: **4b**, $C_{46}H_{42}N_6O_4$, monoclinic, space group I2/c, a = 19.425(5), b = 9.904(2), c = 20.300(5) Å, β = 93.03(2)°, V = 3876.06(12) Å^{-3}, z = 4, Dc = 1.237 g cm^{-1}, μ = .66 mm^{-1}, CuKα = 1.5418 Å, Structure solution based on 1473 reflections converged to R = 0.040. Extinction correction was applied, however no absorption correction was made.
4. Hundal, G.; Kumar, S.; Hundal, M.S.; Kaur, N.; Singh, H., Unpublished results

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