Template synthesis of a macrobicyclic cryptand having mixed donors via [2 + 3] Schiff base condensation

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Abstract. *Tris*(2-aminoethyl)amine undergoes [2 + 3] Schiff base condensation with diisobutyraldehyde disulphide in presence of Cs^+ ion as the template. This Schiff base, on subsequent reduction by $NaBH_4$, affords the cryptand (3) in overall 52% yield.

Keywords. Macrobicyclic cryptand; template synthesis; transition metal cryptates.

Synthesis of cryptands for ligating metal ions is of considerable current interest (Ngwenya *et al* 1990; Mendoza *et al* 1991; Harding *et al* 1991; Beer *et al* 1992; Seel and Vogtle 1992). The topology of the donor atoms, as well as the rigidity of the binding sites are two most important features of any cryptand as a ligand for metal ions. By introducing rigid groups and suitable donor atoms into the ligand superstructure, unusual geometries can be imposed on to a metal ion like the protein matrix does in an intrinsic active site (Vallee and Williams 1968; Solomon *et al* 1992) of a metalloprotein. Also, if the macropolycyclic structure has more than one receptor site, polynuclear metal complexes can be formed and their magnetic and redox properties probed. The polynuclear metal cryptates are potentially useful as molecular magnets as well as multielectron redox catalysts (Lehn 1990), while dinuclear cryptates under suitable conditions, can recognize small molecules (Lehn 1980) to form cascade complexes. We have been involved in synthesizing cryptands with different donor atom topologies to achieve interesting properties towards transition metal ions (Ragunathan and Bharadwaj 1992). Herein, we report the synthesis of a ditopic cryptand having three disulphide groups. This is the first known cryptand having disulphide groups. Studies of molecular models suggest that the shape of the cavity is slipped ellipsoidal (figure 1). The present study was undertaken to probe metal-disulphide interactions which have important bioinorganic relevance (Branden 1967; Thich *et al* 1974; Deutsch *et al* 1982).

The first step towards the cryptand is to generate the dialdehyde (1) by homolytic cleavage of the S–Cl bond of sulphur monochloride with isobutyraldehyde (Corbin and Work 1976). The compound (3) was prepared via [2 + 3] Schiff base condensation of *tris*(2-aminoethyl)amine [tren] and the dialdehyde in the presence of Cs^+ ion as the template. In the absence of the Cs^+ ion or using other alkali/alkaline earth metal ions, no product of definite composition could be isolated. In a typical experiment,
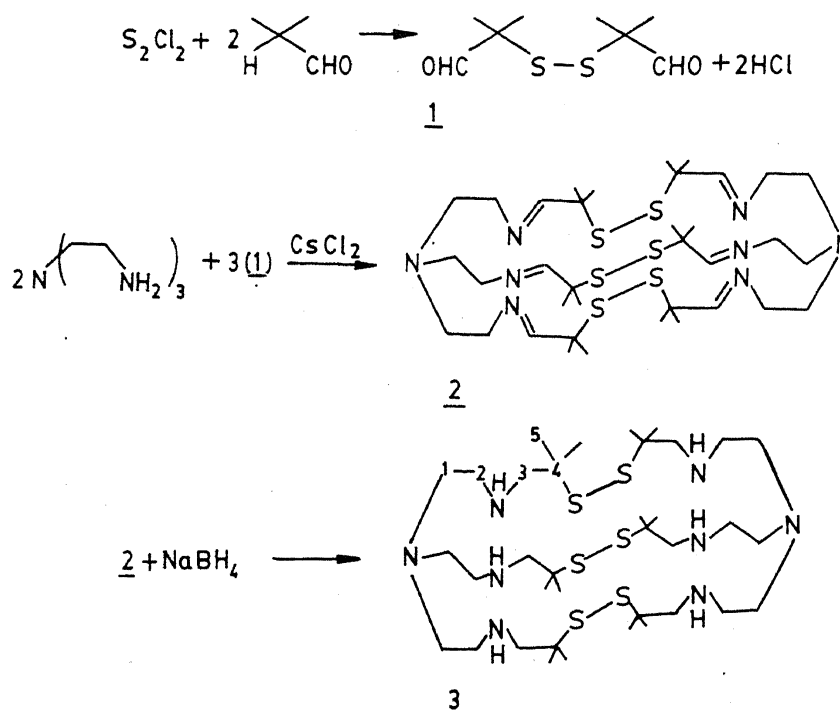
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$$S_2Cl_2 + 2 \; \underset{H}{\times}\!CHO \longrightarrow OHC\underset{}{\times}S-S\underset{}{\times}CHO + 2HCl$$

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$$2\,N\!\left(\!\diagup NH_2\right)_3 + 3\,(\underline{1}) \xrightarrow{\;CsCl_2\;} \quad \underline{2}$$

$$\underline{2} + NaBH_4 \longrightarrow \quad \underline{3}$$

Figure 1. Scheme for the synthesis of the macrobicyclic cryptand.

tren (0·7 g, 0·5 mmol) and CsCl (0·4 g, 0·25 mmol) were dissolved in 3% aqueous THF (400 ml) at 40°C. To this stirred solution, diisobutyraldehyde (1·6 g; 0·75 mmol) in THF (200 ml) was added slowly over a period of 6 h, maintaining the temperature at 40°C during addition. The resulting pale yellow solution was stirred for a further 6 h at 40°C. Then excess of solid NaBH$_4$ (1·5 mmol) was added in portions and the mixture allowed to reflux for 8 h. The residue obtained after removal of THF was dissolved in 25 ml of water and extracted with CHCl$_3$(2 × 50 ml). The CHCl$_3$ layer was dried over anhydrous Na$_2$SO$_4$ and all the CHCl$_3$ removed to obtain a light yellow oily liquid which was purified by passing through a neutral alumina column using chloroform:methanol (1:1) solvent system as the eluent. The pale yellow oily compound is stable at low temperature but decomposes very slowly at 25°C (yield 52%).

The 400 MHz ^{1}H NMR shows 3 peaks at 1·35, 2·6 and 2·75δ. The peak at 1·35δ is a singlet and accounts for the methyl protons on the C5-atom. The expanded spectrum in the region 2 to 3·3δ shows a triplet at 2·6δ corresponding to the protons on C1 and another triplet at 2·75δ which has an entirely different shape without any symmetry and is of double the intensity of the triplet at 2·6δ. This peak is attributable to the protons on C2 and C3 atoms. ^{13}C NMR (100 MHz) shows five peaks at 27·5, 47·8, 49·6, 53·0 and 59·1δ for the five kinds of carbon atoms present in the molecule. The FAB-mass spectrum shows a peak at m/z 816 which is the radical cation of the cryptand, [$\underline{3}$]$^+$.

The cryptand forms a hexapicrate derivative protonating all the six secondary amines. The bridgehead N-atoms are not protonated under the experimental conditions (Lehn *et al* 1977; Motekaitis *et al* 1988). The 400 MHz ^{1}H NMR spectrum shows a singlet at 1·4δ assignable to the C5 protons. It also shows a broad doublet peak at 2·9δ corresponding to the protons on C1 and a triplet without any symmetry at 3·9δ assignable to the protons on C2 and C3. Here, the protonation of the secondary

amino nitrogens shifts the resonance of the protons on C2 and C3 downfield by $1 \cdot 15\delta$. The shift for the C1 protons is only $0 \cdot 3\delta$. The picrate signal appears as a sharp singlet at $8 \cdot 7\delta$. The picrate salt gave satisfactory elemental analysis for C, H, and N.

Addition of two equivalents of $[Cu(H_2O)_6](ClO_4)_2$ gives a green solid in 75% yield. Electronic and ESR spectral, magnetic susceptibility and cyclic voltammetric studies indicate that two independent copper sites are present in the molecule similar to the ones reported earlier (Lehn *et al* 1977; Gisselbrecht *et al* 1980) with their binucleating cryptands. Likewise, with $[Ni(H_2O)_6](ClO_4)_2$, it forms a dinuclear cryptate. The coordination geometry around each metal ion in either cryptate is octahedral. Satisfactory elemental analyses were obtained for C, H, N and S for the two cryptates. Details of the transition metal cryptates will be published later.

Acknowledgement

References

Beer P D, Kochian O, Mortimer R J and Spencer P 1992 *J. Chem. Soc., Chem. Commun.* 602
Branden C 1967 *Acta Chem. Scand.* **21** 1000
Corbin J L and Work D E 1976 *J. Org. Chem.* 487
Deutsch E, Root M J and Nosco D L 1982 *Adv. Inorg. Bioinorg. Mech.* **1** 269
Gisselbrecht J P, Gross M, Alberts A H and Lehn J M 1980 *Inorg. Chem.* **19** 1386
Harding C, McKee V and Nelson J 1991 *J. Am. Chem. Soc.* **113** 9684
Lehn J M 1980 *Pure Appl. Chem.* **52** 2441
Lehn J M 1990 *Angew. Chem., Int. Ed. Engl.* **29** 1304
Lehn J M, Pine S H, Watanabe E and Williard A K 1977 *J. Am. Chem. Soc.* **99** 6766
Mendoza J D, Mesa E, Rodriguez-Ubis J C, Vazquez P, Vogtle F, Windscheif P M, Rissanen K, Lehn J M, Lilienbaum D and Ziessel R 1991 *Angew. Chem., Int. Ed. Engl.* **30** 1331
Motekaitis R J, Martell A E, Murase I, Lehn J M and Hosseini M W 1988 *Inorg. Chem.* **27** 3630
Ngwenya M P, Martell A E and Reibenspies J 1990 *J. Chem. Soc., Chem. Commun.* 1207
Ragunathan K and Bharadwaj P K 1992a *J. Chem. Soc., Dalton Trans.* 1351
Ragunathan K and Bharadwaj P K 1992b *Tetrahedron Lett.* 7581
Seel C and Vogtle F 1992 *Perspectives in coordination chemistry* (eds) A F Williams, C Floriani and A E Merbach (Weinheim: VCH) pp. 31–54
Solomon E I, Baldwin M J and Lowery M D 1992 *Chem. Rev.* 521
Thich J A, Mastropaolo D, Potenza J A and Schugar H J 1974 *J. Am. Chem. Soc.* **96** 726
Vallee B L and Williams R J P 1968 *Proc. Natl. Acad. Sci USA* **59** 398