

Synthesis of a New Type of Binucleating Macrocyclic Incorporating both the Dithiolato and Diimino Functionality and a Polyether Compartment

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A series of novel macrocyclic systems have been prepared using 5-chloro-4-formyl pyrazoles (*via* selective N-1 alkylation) as heterocyclic building blocks; a binuclear Ni^{II}-Ti^{IV} complex derived from such a ligand has also been characterised.

The design and synthesis of macrocyclic molecules containing more than one recognition site for binding of metal ions is currently of considerable interest.¹⁻⁴ These systems are potential models of metalloproteins, such as hemocyanin, tyrosinase, and cytochrome c oxidase. The selective incorpor-

ation into macrocyclic ligands of certain cations depends upon a number of parameters such as the ring size and the type of binding atoms. There are several examples of systems combining imine nitrogens and polyether functions,⁴⁻⁸ whereas macrocyclic ligands containing thiolato functions are still

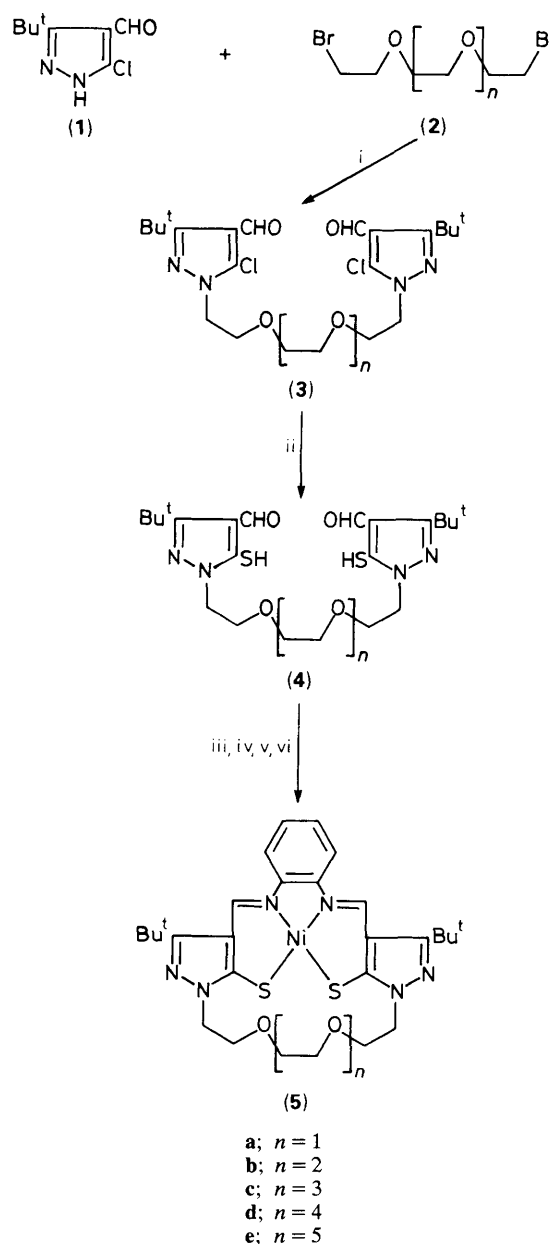
very rare.⁹ As the thiolato functions can be expected to be effective mediators of steric and electronic effects these systems may have promising applications such as chemical sensors. Binucleating ligands constructed around central thiolato centres have shown promising catalytic activities.^{10,11}

In this Communication we have used the strategy based on heterocyclic *o*-chloroaldehydes already developed for the synthesis of sterically constrained quadridentate N₂S₂ ligands¹² and report an efficient synthetic route to a series of ligand systems in which a soft donor site is combined with a hard polyether site *via* two hinging central thiolato functions. Using this method we have obtained the necessary synthons for construction of macrocyclic ligands combining imine nitrogen donors, thiolato sulphur functions, and a polyether cavity.

Barium ions have been used as a templating device for the preparation of otherwise unobtainable macrocyclic Schiff's bases.⁵ Once prepared, these ligands readily form mononuclear complexes with nickel(II) and heterobinuclear complexes with nickel(II) and thallium(I) ($n = 2$).

The syntheses are outlined in Scheme 1. Selective N-1 alkylation of 5-chloro-4-formyl pyrazole was achieved by substituting a *t*-butyl group at the 3-position of the pyrazole ring (1) and thus favourably directing the N-1 alkylation, probably by steric hindrance at the N-2 position. Hence 5-chloro-4-formyl-3-*t*-butyl-1*H*-pyrazole (1) was treated with dibromo ethers (2) ($n = 1, 2, 3, 4, 5$) in dimethylformamide (DMF) with K₂CO₃ as a base, to give dichlorodialdehydes (3) (70–80%) as oils.† When a dichlorodialdehyde such as (3b) was treated with potassium hydrogen sulphide (30%) in absolute ethanol (reflux under N₂) the corresponding dithiodialdehyde (4b) was obtained as an oil. The mass spectrum of (4b) showed the molecular ion peak at m/z 527 and according to the ¹H n.m.r. spectrum the yield of (4b) was >90%, however the crude product could not be purified as work-up on silica gel resulted in partial decomposition. Therefore the crude product was used directly in the subsequent macrocyclisation. Thus reaction of (4b) with 1,2-diaminobenzene in the presence of Ni-acetate in methanol resulted in the formation of an almost black precipitate. The final cyclisation was carried out using barium ion as a template. Thus the macrocyclisation of (4b) with 1,2-diaminobenzene in the presence of Ba(ClO₄)₂, in high dilution, was carried out by slow addition of separate solutions of (4b) in methylene chloride and 1,2-diaminobenzene in methanol to a refluxing

solution of Ba(ClO₄)₂ in methanol over a period of 4 h whereupon a methanolic solution of Ni-acetate was added. The resulting dark brown residue was then treated with an aqueous solution of guanidinium sulphate in chloroform whereupon isolation of the final product was straightforward as the free macrocycle (5b) is soluble in chloroform and BaSO₄ precipitated from the mixture. Concentration of the organic phase followed by preparative layer chromatography gave the mononuclear Ni-complex (5b) (R_f 0.71; CHCl₃:MeOH, 9.50:0.50) as dark brown crystals (m.p. 340–42 °C, yield 68%). The ¹H n.m.r. spectrum of (5b) showed the expected peaks and among these a singlet at δ 8.66, corresponding to



† All new compounds gave spectroscopic and analytical data in accordance with the assigned structures. Data are quoted for compounds (3b), (5b), and the Ni-Tl complex (6b). For (3b): 78% yield; oil; ¹H n.m.r. (CDCl₃), δ 9.81 (s, 2H, CHO), 4.21 (t, 4H, -NCH₂), 3.80 (t, 4H, CH₂O-), 3.62 (m, 8H, -OCH₂CH₂O-), 1.26 (s, 18H, Bu^t); electron impact (e.i.) m.s., m/z 531 (M^+ , 20% for ³⁵Cl); i.r., ν_{max} (KBr) 1687 (-CH=O) cm⁻¹.

For (5b): 68% yield; m.p. 340–42 °C; ¹H n.m.r. (CDCl₃), δ 8.66 (s, 2H, -CH=N), 7.74 (m, 2H, ArH), 7.33 (m, 2H, ArH), 4.25 (t, 4H, -NCH₂), 3.74 (t, 4H, CH₂O-), 3.58 (m, 8H, -OCH₂CH₂O-), 1.39 (s, 18H, Bu^t); high resolution (peak matching) m.s., m/z 654.19594 (M^+ , 100%) (calc. for C₃₀H₄₀N₆O₃S₂Ni 654.19561); i.r., ν_{max} (KBr) 1595 (C=N) cm⁻¹; u.v., λ_{max} (CHCl₃) (ϵ) 669(230), 448 sh (3.95×10^3), 373 (1.73×10^4), 298 sh (2.34×10^4), 271 nm (3.52×10^4 mol⁻¹ dm³ cm⁻¹).

For (6b): 100% yield; m.p. >350 °C; ¹H n.m.r. (trifluoroacetic acid, TFA), δ 8.65 (s, 2H, CH=N), 7.28 (m, 2H, ArH), 7.22 (m, 2H, ArH), 4.60 (d, 1H), 4.45 (bs, 4H, NCH₂), 3.82 (bs, 8H, -OCH₂CH₂O-), 3.67 (bs, 4H, CH₂O-), 3.17 (dq), 3.04 (dq), 1.9 (s, 3H, CH₃CO₂), 1.33 (s, 18H, Bu^t); f.a.b.m.s., m/z 859 (M^+); i.r., ν_{max} (KBr) 1597 (C=N) cm⁻¹; u.v., λ_{max} (CHCl₃) (ϵ) 670(343), 446 sh (2.82×10^3), 371 (1.55×10^4), 296 sh (1.81×10^4), 271 nm (2.76×10^4 mol⁻¹ dm³ cm⁻¹).

Scheme 1. Reagents and conditions: i, K₂CO₃ (1 equiv.), dry DMF; ii, KSH (2 equiv.), absolute ethanol; iii, Ba(ClO₄)₂ (1 equiv.), methanol; iv, *o*-phenylenediamine (1 equiv.), methanol; v, Ni(OAc)₂·4 H₂O (1 equiv.), methanol; vi, guanidinium sulphate (4 equiv.), water.

the presence of an imine linkage. In the ^1H n.m.r. spectra of macrocyclic complexes (**5b**–**e**) the shifts of the $-\text{CH}=\text{N}-$ methine protons were all in the range δ 8.66–8.84, however in compound (**5a**; $n = 1$) this proton was found at δ 7.95, while the rest of the spectra did not show any significant difference. In the mass spectrum of (**5b**) the base peak occurred at m/z 654 (M^+) (accurate mass 654.19594; calc. for $\text{C}_{30}\text{H}_{40}\text{N}_6\text{O}_3\text{S}_2$ Ni 654.19561). The isotopic pattern expected for nickel was seen in the base peak. The ability of the new macrocyclic systems to form binuclear complexes was demonstrated through the reaction of the Ni-complex (**5b**) and thallium acetate in absolute ethanol resulting in the binuclear $\text{Ni}^{\text{II}}-\text{Tl}^{\text{I}}$ complex (**6b**). The fast atom bombardment (f.a.b.) mass spectrum, obtained from a solution of (**6b**) in *m*-nitrobenzyl alcohol, showed a molecular ion peak at m/z 859 (M^+). Moment analysis¹³ of the isotopic pattern confirmed the molecular formula ($\text{C}_{30}\text{H}_{40}\text{N}_6\text{O}_3\text{S}_2\text{NiTl}$) (expected relative second moment: 2.41135, measured: 2.47934). The u.v.–visible spectra of compounds (**5a**–**e**) and (**6b**) are very similar, the bands seen at 670 and 450 nm are suggested to arise from the thiolate to nickel(II) charge transfer transitions, in analogy with similar non-cyclic complexes.¹⁴

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References

- 1 H. Ogino, *J. Coord. Chem.*, 1987, **15**, 187.
- 2 T. N. Sorrel, *Tetrahedron*, 1989, **45**, 3.
- 3 O. Kahn, *Struct. Bonding*, 1988, **68**, 89.
- 4 J.-M. Lehn, *Chem. Scri.*, 1988, **28**, 237.
- 5 C. Van Staveren, D. N. Reinhoudt, J. Van Eerden, and S. Harkema, *J. Chem. Soc., Chem. Commun.*, 1987, 974.
- 6 P. D. Beer and C. G. Crane, *Polyhedron*, 1988, **7**, 2649.
- 7 J. C. Chambron and J. P. Sauvage, *Tetrahedron Lett.*, 1986, **27**, 865.
- 8 R. C. Coombes, J. P. Costes, and D. E. Fenton, *Inorg. Chim. Acta.*, 1983, **77**, L173.
- 9 Y. Okuno, K. Uoto, Y. Sasaki, O. Yonemitsu, and T. Tomohiro, *J. Chem. Soc., Chem. Commun.*, 1987, 874.
- 10 M. Louey, P. D. Nichols, and R. Robson, *Inorg. Chim. Acta*, 1980, **47**, 87.
- 11 C. J. McKenzie and R. Robson, *Inorg. Chem.*, 1987, **26**, 3615.
- 12 J. Becher, H. Toftlund, and P. H. Olesen, *J. Chem. Soc., Chem. Commun.*, 1983, 740.
- 13 K. F. Bloom, *Org. Mass Spectrom.*, 1988, **23**, 194.
- 14 O. E. Anderson, J. Becher, H. Frydendahl, K. S. Murray, and H. Toftlund, *Inorg. Chem.*, submitted for publication.