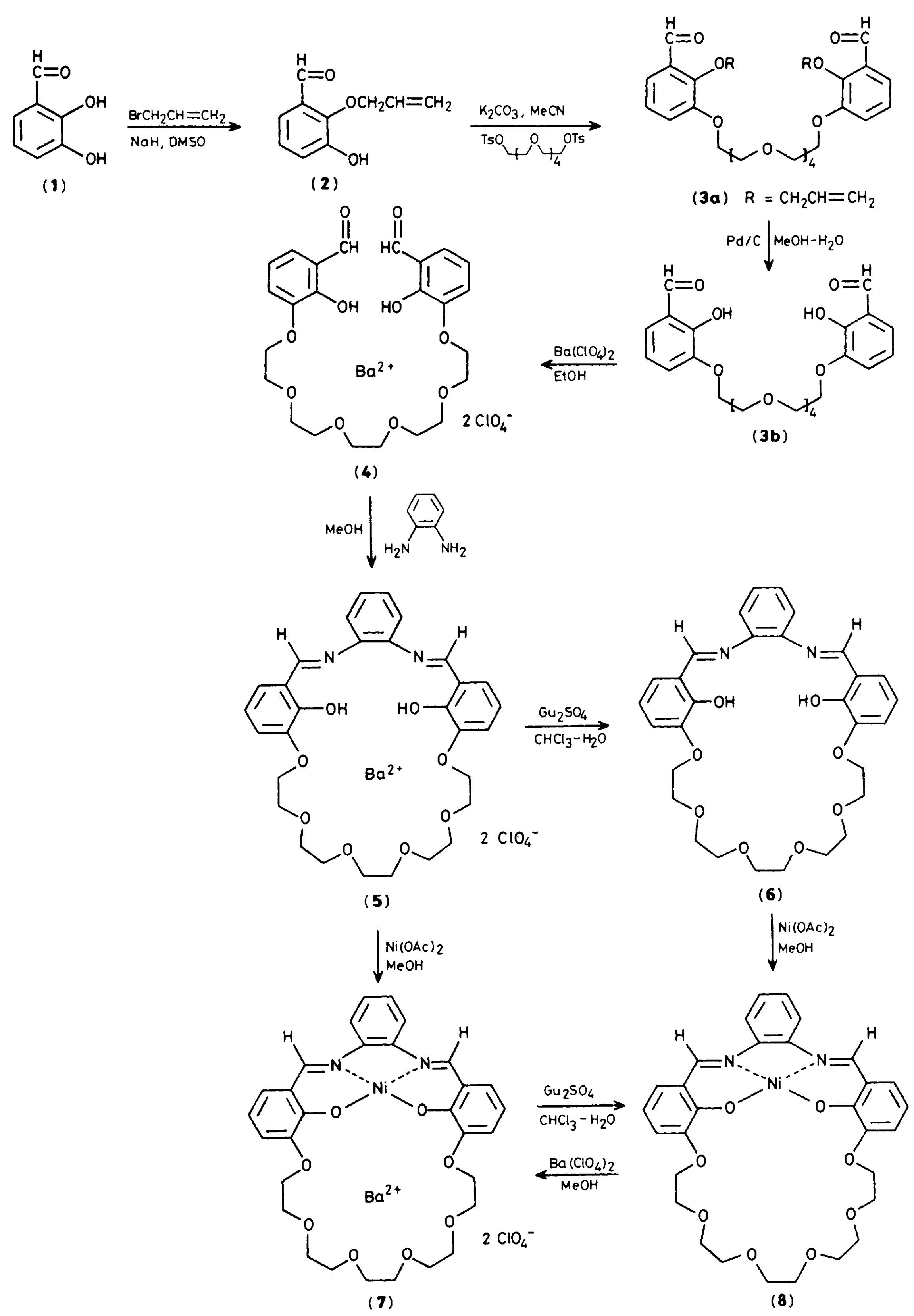
Synthesis, Complexation, and *X*-Ray Structure of a New Type of Binucleating Macrocycle Incorporating Both Soft and Hard Ligating Sites

Catherina J. van Staveren,[a] David N. Reinhoudt,*[a] Johan van Eerden,[b] and Sybolt Harkema[b]

Laboratories of [a]Organic Chemistry and [b]Chemical Physics, University of Twente, P.O. Box 217, 7500 AE Enschede, The Netherlands

A macrocyclic ligand with both a Schiff base moiety and a polyether cavity forms mono- and bi-nuclear complexes; *X*-ray analysis of the mononuclear $Ba(ClO_4)_2$ complex shows that Ba^{2+} is co-ordinated in the polyether cavity.

During the last two decades, many (macrocyclic) ligands that are capable of forming binuclear complexes have been reported, because these may serve as models for metalloproteins, such as superoxide dismutase, oxidases, and peptidases. The majority of these papers deal with *homo*binucleating macrocyclic ligands usually with two identical binding sites that are composed of the 'soft'[1] donor atoms nitrogen and sulphur.[2] Only a few, mostly symmetrical, *hetero*binucleating cyclic ligands have been reported.[3] Fenton and co-workers have reported a series of non-cyclic heterobinucleating ligands, with both a hard O_2O_2 and a softer O_2N_2 cavity, derived from the condensation of 1,3,5-triketones with



Scheme 1. Ts = tosyl; Gu = guanidinium.

diamines.[4] Very recently Lehn and co-workers have described polytopic receptor molecules, with both porphyrin and polyether subunits, capable of forming mixed complexes with organic substrates and metal ions within one complex.[5]

Here, we report the synthesis, complexation, and *X*-ray crystal structure of a new type of macrocyclic ligand with two very different cavities combined within one molecule. The macrocycle contains both a polyether cavity that can bind hard cations, and a salen [salen = *N,N'*-ethylenebis(salicylideneaminato)] moiety[6] capable of binding softer cations like Ni^{2+}, Cu^{2+}, Co^{2+}, *etc.*

The syntheses are outlined in Scheme 1. Selective protection[7] of 2,3-dihydroxybenzaldehyde was achieved by reaction of (**1**) with 1 equiv. of NaH in dimethyl sulphoxide (DMSO) at room temperature, followed by the addition of 3-bromoprop-1-ene. Aqueous workup and recrystallisation from light petroleum (b.p. 40—60 °C) afforded 2-allyloxy-3-hydroxybenzaldehyde (**2**) in 60% yield, m.p. 80—81 °C.† This compound was treated with penta(ethylene glycol) bis(*p*-toluenesulphonate) in acetonitrile with K_2CO_3 as a base, to give the linear dialdehyde (**3a**) (70%) as an oil. Upon deprotection (5% Pd/C, $HClO_4$, H_2O–MeOH, reflux) the compound (**3b**) was obtained in 88% yield. In the ^1H n.m.r. spectrum the phenolic OH groups are present as a sharp singlet at δ 10.78.

We found that the macrocyclisation of (**3b**) with 1,2-diaminobenzene required *a template ion* and therefore the complex of (**3b**) with $Ba(ClO_4)_2$, complex (**4**), was prepared. In this case the complex of the linear compound (**3b**) and the template ion for cyclisation could be isolated as a crystalline solid.[8] This white solid complex (m.p. 234—235 °C) was used in the cyclisation step.

The subsequent ring closure was carried out by slow addition of separate solutions of the $Ba(ClO_4)_2$ complex (**4**) and 1,2-diaminobenzene to refluxing methanol over 2 hours. The bright orange $Ba(ClO_4)_2$ complex (**5**) crystallised upon cooling and addition of a small amount of light petroleum (b.p. 40—60 °C) (m.p. 288—290 °C, yield 59%). In the ^1H n.m.r. spectrum a singlet at δ 8.91 showed that the imine linkage was present and the presence of a singlet at δ 13.13 proved that in this complex the phenolic OH groups are not deprotonated. In the mass spectrum the signal with the highest *m/z* corresponded to the mass of the salt-free ligand (**6**).

The structure of the $Ba(ClO_4)_2$ complex (**5**) was determined by *X*-ray crystallography and is shown in Figure 1. The barium cation is tenfold co-ordinated in the polyether cavity, by six ether oxygens ($Ba^{2+} \cdots O$ 2.84—2.99 Å), the two phenolic oxygens ($Ba^{2+} \cdots O$ 2.72—2.75 Å), one perchlorate oxygen ($Ba^{2+} \cdots O$ 2.74 Å), and by the oxygen of MeOH ($Ba^{2+} \cdots O$ 2.81 Å). Similar values were reported for other polyether · Ba^{2+} complexes.[14] The second perchlorate anion is probably hydrogen bonded to MeOH ($O \cdots O$ 2.81 Å), although the hydrogen involved could not be located (see Figure 1). The Schiff base compartment deviates strongly from planarity; the angles between the mean planes of adjacent aromatic rings are 25° and 27°. This deformation allows the phenolic oxygens to complete the Ba^{2+} co-ordination.

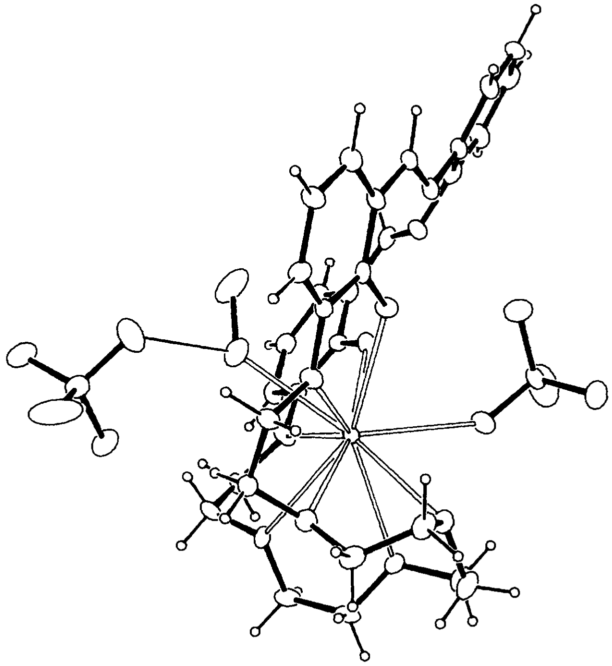


Figure 1. ORTEP[9] view of the $Ba(ClO_4)_2$ complex (**5**) · MeOH, showing the co-ordination of the Ba^{2+} by the macrocycle, one perchlorate anion, and the molecule of methanol. *Crystal data:* $C_{31}H_{38}O_{17}N_2Cl_2Ba$, monoclinic, space group $P2_1/n$, a = 10.869(10), b = 10.791(10), c = 30.076(15) Å, β = 93.46(6)°, U = 3521(11) Å^3, Z = 4, D_c = 1.73 g cm^{-3}, μ = 13.6 cm^{-1}. 6162 Reflections were measured (at 100 K) in the ω–2θ scan mode (3° < θ < 25°) on an Enraf–Nonius CAD4 diffractometer (Mo-K_α radiation, graphite monochromator). A direct methods[10] solution gave the position of the heavy barium atom and the rest of the structure was revealed by successive Fourier syntheses. 5197 Reflections [$F_o^2 > 3\sigma(F_o^2)$] were used in the refinement. All hydrogens on the carbon atoms of the macrocycle were put in calculated positions and were treated as riding on their parent C atoms [C–H distance 0.96 Å, $B_{iso}(H) = 1.2\,B_{eqv}(C)$]. The phenolic hydrogens and the hydrogens of methanol could not be located on a difference Fourier map. Empirical[11] as well as semi-empirical[12] absorption corrections failed to improve agreement between observed and calculated structure factors, and were therefore rejected. Refinement converged at R = 6.8%, R_w = 9.6% (unit weights), with 479 parameters refined: scale factor, isotropic extinction parameter, positional, and anisotropic thermal parameters for non-H atoms. All calculations were done using SDP.[13] Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

When this mononuclear $Ba(ClO_4)_2$ complex (**5**) was treated with $Ni(OAc)_2$ in MeOH the heterobinuclear Ni · $Ba(ClO_4)_2$ complex (**7**) was obtained which precipitated as dark red crystals (56%, m.p. 310 °C). Satisfactory elemental analysis was obtained. In the ^1H n.m.r. spectrum of complex (**7**) the phenolic hydrogen absorptions as in (**5**) are absent. The CH=N proton showed a very broad signal at δ 9.6, which sharpened at higher temperatures. The protons of the aromatic ring derived from *o*-phenylene diamine, which exhibit a singlet in the mononuclear $Ba(ClO_4)_2$ complex (**5**), showed a characteristic splitting in the binuclear complex. These signals appear as multiplets at δ 8.0—8.2 and 7.2—7.4. The signals of the other aromatic protons are shifted to slightly higher field relative to the corresponding signals in the mononuclear $Ba(ClO_4)_2$ complex. High resolution mass spectrometry showed a parent peak at *m/z* 606.141, which corresponds to $M^+ - Ba(ClO_4)_2$ and demonstrates that the nickel ion is tightly bound in the complex. These observations indicate that the nickel ion is complexed in the N_2O_2 cavity.

The mononuclear complex (**5**) could be decomplexed by reaction with guanidinium sulphate in $CHCl_3$–H_2O. Isolation of the product was straightforward because the free macrocycle (**6**) is soluble in $CHCl_3$ and $BaSO_4$ precipitated from the

---

† Satisfactory elemental analyses, ^1H and ^{13}C n.m.r., and mass spectra were obtained for all new compounds.

mixture. After evaporation of the solvent, the uncomplexed macrocycle was obtained as an orange oil. Spectral data were in agreement with the uncomplexed macrocycle.

When the free macrocycle (**6**) was treated with $Ni(OAc)_2$ in methanol, the nickel complex (**8**) was obtained as deep red crystals, m.p. 130—132 °C. In the ^1H n.m.r. spectrum, the CH=N signal is present as a sharp singlet at δ 8.57.

The mononuclear nickel complex forms a complex with $Ba(ClO_4)_2$ to yield the same heterobinuclear $Ni \cdot Ba(ClO_4)_2$ complex that was obtained *via* the mononuclear complex (**5**). From this complex $Ba(ClO_4)_2$ could be removed by reaction with guanidinium sulphate to yield the mononuclear nickel complex (**8**).

Complexes of similar macrocycles with different ring-sizes and with other metal cations are presently being investigated together with the co-complexation of neutral organic guest molecules in the macrocyclic cavity of the heterobinuclear and mononuclear complexes.

These investigations were supported by the Netherlands Technology Foundation (STW), Future Technical Science Branch of the Netherlands Organisation for the Advancement of Pure Research.

Received, 2nd December 1986;‡ Com. 1714

References

1 R. G. Pearson, *J. Am. Chem. Soc.*, 1963, **85**, 3533.

2 F. Acholla, F. Tukasagawa, and K. Bowman Mertes, *J. Am. Chem. Soc.*, 1985, **107**, 6902; F. Acholla and K. Bowman Mertes, *Tetrahedron Lett.*, 1984, **25**, 3269; R. O. Gould, A. J. Lavery, and M. Schröder, *J. Chem. Soc., Chem. Commun.*, 1985, 1492; M. G. B. Drew, M. McCann, and S. M. Nelson, *ibid.*, 1979, 481; S. M. Nelson, *Inorg. Chim. Acta*, 1982, **62**, 39; P. K. Coughlin, S. J. Lippard, A. E. Martin, and J. E. Bulkowski, *J. Am. Chem. Soc.*, 1980, **102**, 7616; P. K. Coughlin, A. E. Martin, J. C. Dewan, E.-I. Watanabe, J. E. Bulkowski, J.-M. Lehn, and S. J. Lippard, *Inorg. Chem.*, 1984, **23**, 1004; A. E. Martin and S. J. Lippard, *J. Am. Chem. Soc.*, 1984, **106**, 2579; P. K. Coughlin and S. J. Lippard, *ibid.*, 1984, **106**, 2328; Y. Agnus, R. Louis, J.-P. Gisselbrecht, and R. Weiss, *ibid.*, 1984, **106**, 93; R. J. Motekaitis, A. E. Martell, J.-M. Lehn, and E.-I. Watanabe, *Inorg. Chem.*, 1982, **21**, 4253; M. G. B. Drew, J. Nelson, F. Esho, V. McKee, and S. M. Nelson, *J. Chem. Soc., Dalton Trans.*, 1982, 1837; N. A. Bailey, M. M. Eddy, D. E. Fenton, G. Jones, S. Moss, and A. Kukhopadhyay, *J. Chem. Soc., Chem. Commun.*, 1981, 628; S. M. Nelson, F. S. Esho, and M. G. B. Drew, *ibid.*, 1981, 388; M. G. B. Drew, S. G. McFall, S. M. Nelson, and C. P. Waters, *J. Chem. Res. (S)*, 1979, 16.

3 M. G. B. Drew, M. McCann, and S. M. Nelson, *J. Chem. Soc., Dalton Trans.*, 1981, 1868; R. Gagné, L. M. Henling, and J. T. Kistenmacher, *Inorg. Chem.*, 1980, 1227; L. Banci, A. Bencini, and D. Gatteschi, *Inorg. Chim. Acta*, 1979, **36**, L419; R. R. Gagné, C. A. Koval, T. J. Smith, M. C. Cimolino, *J. Am. Chem. Soc.*, 1979, **101**, 4571; S. L. Lambert, C. L. Spiro, R. R. Gagné, and D. N. Hendrickson, *Inorg. Chem.*, 1982, **21**, 68.

4 N. A. Bailey, D. E. Fenton, S. E. Gayda, and C. A. Phillips, *J. Chem. Soc., Dalton Trans.*, 1984, 2289; N. A. Bailey, K. C. Cox, C. P. Falshaw, D. E. Fenton, S. E. Grundy, P. Haigh, and C. A. Phillips, *ibid.*, 1983, 2241; N. A. Bailey, S. F. Davidson, J. R. Elliot, D. E. Fenton, E. Godbehere, S. K. Holdroyd, and C. Rodrigue de Barbarin, *ibid.*, 1984, 1073; D. E. Fenton and S. E. Gayda, *ibid.*, 1977, 2109; D. E. Fenton, S. E. Gupta, U. Casellato, P. A. Vigato, and M. Vidali, *Inorg. Chim. Acta*, 1978, **27**, 9.

5 A. Hamilton, J.-M. Lehn, and J. L. Sessler, *J. Am. Chem. Soc.*, 1986, **108**, 5158.

6 H. Diehl and C. C. Hach, 'Inorganic Synthesis,' ed. L. F. Audrieth, McGraw-Hill, 1950, New York, Toronto, London, Vol. III, pp. 196—201; R. H. Holm, G. W. Everett, Jr., and A. Chakravorty, 'Progress in Inorganic Chemistry,' vol. 7, ed. F. A. Cotton, Interscience Publ., 1966.

7 S. V. Kessar, Y. P. Gupta, T. Mohammed, M. Goyal, and K. K. Sawal, *J. Chem. Soc., Chem. Commun.*, 1983, 400.

8 S. M. Nelson, C. V. Knox, M. McCann, and M. G. B. Drew, *J. Chem. Soc., Dalton Trans.*, 1981, 1669.

9 C. K. Johnson, ORTEP, Report ORNL-3794, Oak Ridge National Laboratory, Tennessee, 1965.

10 G. Germain, P. Main, and M. M. Woolfson, *Acta Crystallogr., Sect. A*, 1971, **27**, 368.

11 N. Walker and D. Stuart, *Acta Crystallogr., Sect. A*, 1983, **39**, 158.

12 A. C. T. North, D. C. Phillips, and F. Scott Mathews, *Acta Crystallogr., Sect. A*, 1968, **24**, 351.

13 B. A. Frenz, Structure Determination Package, 1983, B. A. Frenz and Associates Inc., College Station, Texas, and Enraf-Nonius, Delft.

14 D. L. Hughes, C. L. Mortimer, and M. R. Truter, *Acta Crystallogr., Sect. B*, 1978, **34**, 800; G. Weber, F. Hirayama, W. Saenger, and G. M. Sheldrick, *ibid.*, *Sect. C*, 1984, **40**, 1570; N. K. Dalley, D. Sypherd, and R. D. George, *J. Heterocycl. Chem.*, 1984, **21**, 497.

---

‡ Received in revised form, 16th March 1987.