*Journal of Inclusion Phenomena and Molecular Recognition in Chemistry* **12**: 175–186, 1992.

© 1992 *Kluwer Academic Publishers. Printed in the Netherlands.*

# Macrobicyclic Aminals #

ANNALISE ATKINSON, NEIL A. BAILEY, DAVID E. FENTON*,
PAUL D. HEMPSTEAD and GARY P. WESTWOOD
*Department of Chemistry, The University, Sheffield, S3 7 HF, U.K.*

(Received 31 July 1990; in final form: 26 December 1990)

**Abstract.** The synthesis of Schiff base macrocycles in the absence of templating cations and in non-protic and non-coordinating solvent media is reported. The reaction of pyridine-2,6-dicarboxaldehyde with the diamines 1,2-bis(2-aminophenoxy)ethane and 1,4-bis(2-aminophenoxy)butane has been found to give the corresponding macrobicyclic aminals. The chemical properties of the aminals are reported together with a preliminary study of their metal complexation reactions. The X-ray crystal structure of the aminal derived from pyridine-2,6-dicarboxaldehyde and 1,2-bis(2-aminophenoxy)ethane has been determined and verifies the macrobicyclic nature of the product.

**Key words.** Macrobicyclic, aminals, X-ray crystal structure, tetraimine macrocycles, Schiff base.

**Supplementary Data** relating to this article are deposited with the British Library as Supplementary Publication No. sup 82116 (16 pages).

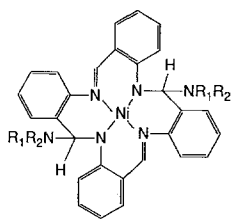
## 1. Retrospect

In 1969 I* was appointed as a Senior Scientific Officer at the Agricultural Research Council's Unit of Structural Chemistry in London. This unit was led by the late Professor Sir Ronald Nyholm (as Honorary Director) and Professor Mary R. Truter and was studying the coordination chemistry of the alkali and alkaline earth metals. A few months later we were joined by a quiet and unassuming American chemist who had recently retired from a long career with du Pont and who had published, in 1967, a seminal paper on the coordination of alkali metals by cyclic polyethers. The unit was involved in solving the X-ray crystal structures of these complexes and part of my task, as a resident chemist, was to prepare complexes and grow crystals suitable for examination. Charlie Pedersen's visit to London was, of course, very influential. Not only was it possible to learn the techniques of polyether synthesis directly from their discoverer but it was possible to benefit from Charlie's wide-ranging chemical experience. It was quite exciting, some time later, to share in the discovery of the dinucleating ability of the cyclic polyethers, perhaps the one combination that had eluded Charlie in his investigations. Aside from the chemistry Charlie had a love for England and one abiding memory is of a day spent exploring the Essex and Cambridgeshire countryside and watching the morris dancing on the green at Finchingfield, reputed to be one of the prettiest villages in England. A visit to du Pont and to New Salem in 1971 served to reinforce impressions gained in London that Charlie was a chemist extraordinary and it is an honor to present this paper in tribute to Charlie and his achievements.

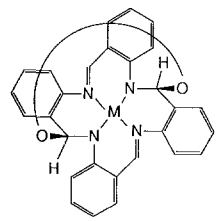
# This paper is dedicated to the memory of the late Dr C. J. Pedersen.
* Author for correspondence

## 2. Introduction

The susceptibility of the imine bond to nucleophilic attack is well known [1]. Addition of water will regenerate the precursor carbonyl and primary amine via the generally unstable carbinolamine intermediate. The addition of alcohols, alkoxides, thiols and thiolates to the imine bond to give isolable products is also known and often occurs when the imine nitrogen is coordinated to a metal [2]. When the nucleophile is a primary amine the intermediate *gem*-diamine (aminal) addition product is generally not stable, although it is known to be stabilised by coordination to a metal centre. The addition of a range of nucleophiles across the imine bonds present in cyclic tetrameric complexes derived from *o*-aminobenzaldehyde serves as a representative example [3]. The nucleophiles either add singly to *trans*-imine linkages (**1**) or, if difunctional as are the bis(2-hydroxyethyl)sulphide and bis(2-hydroxyethyl)methylamine anions, they can add across the molecule to produce 'basket-like' structures (**2**).



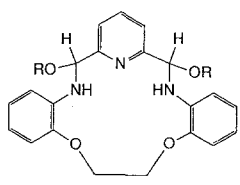

1




2

The link is $CH_2CH_2XCH_2CH_2$
( X = S or NMe ; M = Cu, Ni)

In a study of the formation of Schiff base macrocycles via the cyclocondensation of pyridine-2,6-dicarboxaldehyde with $\alpha,\omega$-diamines in alcoholic media in the presence of alkaline earth templating devices we noted that it was possible to recover the metal-free macrocycles (**3**) when magnesium salts were used as potential templates [4]. The facile formation of the macrocycles was interpreted as suggesting that the macrocyclic di-imine precursors could be formed in a non-template process and that subsequent addition of an alcohol across an imine occurs in order to relieve angular strain in the Schiff base macrocycle. It was then established that (**3**) could be prepared in the absence of the metal template.




3

R = Me, Et, *n*-Bu

In this paper we present results concerning the synthesis of Schiff base macrocycles in the absence of templating cations and in non-protic and non-coordinating solvent media. The X-ray crystal structure of the novel macrobicyclic aminal derived from pyridine-2,6-dicarboxaldehyde and 1,2-bis(2-amino-phenoxy)ethane is also presented.

## 3. Experimental

Pyridine-2,6-dicarboxaldehyde [5], and the diamines 1,2-bis(2-aminophenoxy) ethane, 1,3-bis(2-aminophenoxy)propane and 1,4-bis(2-aminophenoxy)butane [6] were prepared according to literature procedures.

### 3.1. PREPARATION OF THE '2 + 2' TETRAIMINE MACROCYCLE (4)

A solution of pyridine-2,6-dicarboxaldehyde (0.27 g, 2 mmol) in dry (sodium) benzene (30 mL) was added to a stirred solution of 1,2-bis(2-aminophenoxy)ethane (0.48 g, 2 mmol), in dry benzene (30 mL). The mixture was refluxed for 4 h and the product filtered off. Yield 68%; m.p. 136–138°C.; IR (KBr disc): $\nu_{C=N}$ 1640 $cm^{-1}$, $\nu_{CH-Benzene}$ 690 $cm^{-1}$; m.s. (e.i.): 686 amu.; Microanalysis (%) *found* (required) for $C_{42}H_{34}N_6O_4 \cdot C_6H_6$: C 74.99 (75.38), H 5.08 (5.27), N 10.84 (10.99).

### 3.2. DIGESTION OF (4) IN ALCOHOLS

A suspension of the macrocycle (0.69 g, 1 mmol) in absolute ethanol (70 mL) was brought to reflux. After 1 h all the solid had dissolved, and after heating for a further hour the hot solution was filtered and left to cool. The product crystallised out as long white filaments and was confirmed as the bis-ethoxy addition product of the di-imine macrocycle (**3**,R = Et) by comparison with an authentic sample [4] Yield 65%; m.p. 174–176°C.; IR (KBr disc): $\nu_{NH}$ 3400 $cm^{-1}$, $\nu_{C-O}$ 1050 $cm^{-1}$; m.s. (e.i.): 435 amu.; Microanalysis (%) *found* (required) for $C_{25}H_{29}N_3O_4$: C 68.95 (68.95), H 6.57 (6.71), N 9.63 (9.65).

The corresponding bis-methoxy addition product was also prepared by the same method, in methanol solvent, and isolated as fine white needles. Yield 59%; m.p. 130–132°C.; IR (KBr disc): $\nu_{NH}$ 3380 $cm^{-1}$, $\nu_{C-O}$ 1045 $cm^{-1}$; m.s. (e.i.): 407 amu.; Microanalysis (%) *found* (required) for $C_{23}H_{25}N_3O_4$: C 68.02 (67.80), H 6.06 (6.18), N 10.31 (10.31).

### 3.3. AMINAL (5a)

A solution of pyridine-2,6-dicarboxaldehyde (0.68 g, 5 mmol) in acetonitrile (250 mL) was added dropwise to a stirred solution of 1,2-bis(2-aminophenoxy)ethane (1.22 g, 5 mmol) in acetonitrile (250 mL) over a period of 2 h. A white precipitate formed over a period of 12 h. The crude product was recrystallised from a chloroform/acetonitrile mixture as colourless crystals. The same product can be obtained by using bench benzene or toluene as the solvent and the

yield of the reaction can be increased using a diamine : dicarbonyl ratio of 2 : 1. Yield 77%; m.p. 156–158°C.; IR (KBr disc): $\nu_{NH}$3370 cm$^{-1}$; m.s. (e.i.): 587 amu.; Microanalysis (%) *found* (required) for $C_{35}H_{33}N_5O_4$: C 71.39 (71.53), H 5.60 (5.66), N 11.86 (11.92); $^1$H NMR ($CD_2Cl_2$) $\delta$: 7.55–6.60 (19H, *m*, ArH), 5.98 (*t*, CH), 5.53 (*d*, NH), 4.30 (8H, *s*, $CH_2$).

### 3.4. AMINAL (**5b**)

The compound was synthesised by the above method using 1,4-bis(2-aminophenoxy)butane (1.36 g, 5 mmol). Yield 74%; m.p. 106–108°C.; IR (KBr disc): $\nu_{NH}$3415 cm$^{-1}$; m.s. (pos. f.a.b.): 643 amu.; Microanalysis (%) *found* (required) for $C_{39}H_{41}N_5O_4$: C 72.25 (72.76), H 6.25 (6.42), N 10.66 (10.88); $^1$H NMR ($CDCl_3$) $\delta$: 7.60–6.60 (19H, *m*, ArH), 6.00 (*t*, CH), 5.45 (*d*, NH), 4.15–3.80 (8H, *m*, $CH_2$), 2.10–1.80 (8H, *m*, $CH_2$).

### 3.5. PRODUCT (**5d**)

The preparation was exactly as described previously but using 1,3-bis(2-aminophenoxy) propane (1.29 g, 5 mmol). The brown product was insoluble in common organic solvents preventing recrystallisation and further analysis. Yield 68%; m.p. 300+°C.; IR (KBr disc): $\nu_{NH}$3380 cm$^{-1}$.

### 3.6. PREPARATION OF Cu(**4**)$(ClO_4)_2$ AND Cu(**4**)$(NO_3)_2$

A solution of the appropriate copper(II) salt (perchlorate or nitrate) (1 mmol) in absolute ethanol (10 mL) was added to a suspension of the macrocycle (0.69 g, 1 mmol) in ethanol (15 mL). The mixture was refluxed for 30 min and the resultant green solution was filtered. On cooling the product precipitated out as a golden brown solid and was washed with a little ethanol and dried.

Cu(**4**)$(NO_3)_2 \cdot 2\,H_2O$: Yield 57%; m.p. 230°C. (dec.); IR (KBr disc): $\nu_{C=N}$1595 cm$^{-1}$, $\nu_{N-O}$1380 cm$^{-1}$; m.s. (pos. f.a.b.): 812 [Cu(**4**)$(NO_3)$]$^+$, 750 amu. [Cu(**4**)]$^+$; Microanalysis (%) *found* (required) for $CuC_{42}H_{38}N_8O_{12}$: C 54.89 (55.41), H 3.84 (4.21), N 12.32 (12.31).

Cu(**4**)$(ClO_4)_2 \cdot 2\,H_2O$: Yield 59%; IR (KBr disc): $\nu_{C=N}$1595 cm$^{-1}$, $\nu_{ClO}$1095, 625 cm$^{-1}$; m.s. (pos. f.a.b.): 848 [Cu(**4**)$(ClO_4)$]$^+$, 750 amu. [Cu(**4**)]$^+$; Microanalysis (%) *found* (required) for $CuC_{45}H_{38}N_6O_{14}Cl_2$: C 51.20 (51.20), H 3.67 (3.89), N 8.43 (8.53), Cl 7.22 (7.20).

### 3.7. REACTION OF IRON(III) CHLORIDE WITH LIGAND (**4**)

The method was exactly as described for the previous complexation, but using iron (III) chloride hexahydrate (0.27 g, 1 mmol). The product, Fe(**6a**)$Cl_3$ was isolated as a dark green solid. Yield 61%; m.p. 300+°C.; IR (KBr disc): $\nu_{C=N}$1595 cm$^{-1}$; m.s. (pos. f.a.b.): 469 [Fe(**6a**)$Cl_2$]$^+$, 434 [Fe(**6a**)Cl]$^+$, 399 amu. [Fe(**6a**)]$^+$; Microanaylsis (%) *found* (required) for $FeC_{21}H_{17}N_3O_2Cl_3 \cdot 1.5\,H_2O$: C 50.85 (50.74), H 3.98 (4.05), N 8.37 (8.45), Cl 14.19 (14.26).

### 3.8. REACTION OF MANGANESE(II) PERCHLORATE WITH LIGAND (4)

The preparation was exactly as before, using manganese(II) perchlorate hexahydrate. The product was obtained as a yellow solid and all analyses correspond to those of an authentic sample of Mn(**6a**)$(ClO_4)_2$ [10]. Yield 27%; IR (KBr disc): $\nu_{C=N}$ 1590 $cm^{-1}$, $\nu_{Cl-O}$ 1120, 620 $cm^{-1}$; m.s. (pos. f.a.b.): 497 $[Mn(\mathbf{6a})(ClO_4)]^+$, 398 amu. $[Mn(\mathbf{6a})]^+$; Microanalysis (%) *found* (required) for $MnC_{21}H_{17}N_3O_{10}Cl_2$: C 42.29 (42.23), H 3.26 (2.87), N 6.91 (7.04), Cl 11.48 (11.87).

### 3.9. REACTION OF α,ω-DIAMINES WITH LIGAND (4)

A solution of the appropriate α,ω-diamine (1 mmol) in acetonitrile (25 mL) was added to a suspension of the tetraimine macrocycle (**4**) (0.34 g, 0.5 mmol) in acetonitrile (25 mL). The mixture was refluxed for 1 h. The solution was filtered and left to cool. Crystals of the product deposited and were filtered off, washed with a little acetonitrile and dried.

### 3.9. *a. Preparation of* (**5a**) *from Ligand* (**4**)

Using 1,2-bis(2-aminophenoxy)ethane as the diamine in the above procedure leads to isolation of ligand (**5a**) (yield 67%). The product was characterised as the macrobicyclic aminal after comparison with an authentic sample of (**5a**) which had been prepared and characterised as described above.

### 3.9. *b. Preparation of* (**5c**) *from Ligand* (**4**)

The reaction was carried out, using the above method, with 1,4-bis(2-aminophenoxy)butane (0.27 g, 1 mmol). The product (**5c**) was isolated as white needles. Yield 69%; m.p. 114–116°C.; IR (KBr disc): $\nu_{NH}$ 3400 $cm^{-1}$; m.s. (pos. f.a.b.): 615 amu.; Microanalysis (%) *found* (required) for $C_{37}H_{37}N_5O_4$: C 75.15 (72.18), H 6.16 (6.06), N 11.12 (11.37); $^1H$ NMR ($CDCl_3$) $\delta$: 7.55–6.60 (19 H, *m*, ArH), 5.98 (*t*, CH), 5.65 (*d*, NH), 5.40 (*d*, NH), 4.35–3.90 (8 H, *m*, $CH_2$—O), 2.05 (4 H, *m*, $CH_2$).

### 3.10. REACTION OF MANGANESE(II) PERCHLORATE WITH LIGAND (5a)

A solution of manganese(II) perchlorate hexahydrate (0.36 g, 1 mmol) in acetonitrile (15 mL) was added to a suspension of (**5a**) (0.59 g, 1 mmol) in acetonitrile (30 mL). The mixture was stirred at room temperature for 5 min. The starting materials quickly dissolved and the resultant orange solution was filtered. The product was precipitated out as a yellow powder by addition of ether to the filtrate. The solid was washed with a little ether and dried (yield 24%). Comparison with an authentic sample [10] showed it to be Mn(**6a**)$(ClO_4)_2$.

### 3.11. REACTION OF MANGANESE(II) PERCHLORATE WITH LIGAND (5b)

Carrying out the same complexation with ligand (**5b**) leads to the isolation of an orange solid, characterised as the complex Mn(**6b**)$(ClO_4)_2$ [6]. (Yield 27%). IR

(KBr disc): $\nu_{C=N}$ 1595 $cm^{-1}$, $\nu_{Cl-O}$ 1110, 630 $cm^{-1}$; m.s. (pos. f.a.b.): 525 $[Mn(\mathbf{6b})(ClO_4)]^+$, 426 $[Mn(\mathbf{6b})]^+$, 371 amu. $[(\mathbf{6b})]^+$; Microanalysis (%) *found* (required) for $MnC_{23}H_{21}N_3O_{10}Cl_2 \cdot H_2O$: C 42.71 (42.94), H 3.85 (3.60), N 6.41 (6.53), Cl 11.16 (11.02).

### 3.12. DIGESTION OF LIGAND (**5a**) IN ALCOHOL

A suspension of ligand (**5a**) (0.59 g, 1 mmol) in ethanol (50 mL) was refluxed for 4 h. During this time the solid dissolved and the resultant solution was filtered and left to cool. The product precipitated out as white needles (yield 57%) and was characterised as the bis-ethoxy addition product of the di-imine macrocycle (**3**), R = Et [4].

The bis-methoxy product was prepared in the same way by digestion in methanol (yield 51%).

## 4. Crystal Structure Data and Determination

Crystal data for the macrobicyclic aminal (**5a**); $C_{35}H_{33}N_5O_4$; $M = 587.68$; crystallises from chloroform/acetonitrile as colourless rhombic prisms; crystal dimensions 0.95 × 0.50 × 0.30 mm. Triclinic, $a = 11.334(12)$, $b = 12.155(18)$, $c = 12.155(13)$ Å, $\alpha = 85.58(10)$, $\beta = 71.15(8)$, $\gamma = 70.12(10)°$, $U = 1496.8(32)$ Å$^3$; $D_c = 1.304$ g $cm^{-3}$, $Z = 2$. Space group $P\bar{1}$. Mo$K_\alpha$ radiation ($\lambda = 0.71069$ Å), $\mu$(Mo$K\alpha$) = 0.81 $cm^{-1}$.

Three-dimensional, room temperature X-ray data were collected in the range $3.5 < 2\theta < 40°$ on a Nicolet R3 four-circle diffractometer by the omega scan method. The 1965 independent reflections (of 2813 measured) for which $|F|/\sigma(|F|) > 3.0$ were corrected for Lorentz and polarisation effects. The structure was solved by direct methods and Fourier techniques and refined by blocked cascade least squares methods. Hydrogen atoms bound to carbon atoms were included in calculated positions, with isotropic thermal parameters related to those of the supporting atom, and refined in riding mode. Hydrogen atoms bound to nitrogen atoms were refined with isotropic thermal parameters related to those of the supporting atom. Refinement converged at a final $R$ 0.060, $R_w = 0.055$ (409 parameters, maximum shift/e.s.d. 0.006), with allowance for the thermal anisotropy of all non-hydrogen atoms. A final difference electron density synthesis showed peaks of −0.25 and +0.20 $e$ Å$^{-3}$. Complex scattering factors were taken from Ref. [7] and from the program package SHELXTL [8] as implemented on the Data General Nova 3 computer, which was used for structure solution and refinement. A weighting scheme $w^{-1} = [\sigma^2(F) + 0.00066(F)^2]$ was used in the latter stages of the refinement. Table I lists atomic positional parameters with estimated standard deviations. Tables II and III list the bond lengths and angles.

## 5. Results and Discussion

The reaction of pyridine-2,6-dicarboxaldehyde and 1,2-bis(2-aminophenoxy)-ethane in 1 : 1 ratio in dry benzene gave an off-white powdery material. This product gave a band at 1641 $cm^{-1}$ in the IR spectrum, which could be attributed to an imine

Table I. Atom coordinates ( $\times 10^4$) and temperature factors (Å $\times 10^3$)

| atom | $x/a$ | $y/b$ | $z/c$ | $U$ |
|---|---|---|---|---|
| N(1) | 4420(4) | 3063(3) | −1843(3) | 49(2)* |
| Hn(1) | 4341(46) | 2817(40) | −2471(38) | 60 |
| Hn(2) | 1540(39) | 2417(34) | −3673(34) | 66 |
| Hn(4) | 4390(39) | 734(35) | −1471(34) | 66 |
| Hn(5a) | 2616(38) | 407(34) | −2514(33) | 66 |
| N(2) | 837(4) | 2261(3) | −3424(3) | 55(2)* |
| N(3) | 2233(4) | 1973(3) | −1484(3) | 48(2)* |
| N(4) | 4642(4) | 1136(3) | −1121(4) | 57(2)* |
| N(5) | 1955(4) | 412(4) | −2713(4) | 58(2)* |
| O(1) | 3843(3) | 4316(3) | −3627(3) | 51(2)* |
| O(2) | 1402(3) | 4267(3) | −3926(3) | 56(2)* |
| O(3) | 6130(3) | −962(3) | −2342(3) | 66(2)* |
| O(4) | 4458(3) | −763(3) | −3703(3) | 61(2)* |
| C(1) | 3974(4) | 4295(4) | −1733(4) | 41(2)* |
| C(2) | 3861(4) | 4901(4) | −763(4) | 46(3)* |
| C(3) | 3568(5) | 6115(5) | −722(4) | 57(3)* |
| C(4) | 3359(5) | 6746(4) | −1678(4) | 61(3)* |
| C(5) | 3421(5) | 6183(4) | −2651(4) | 52(3)* |
| C(6) | 3716(5) | 4976(4) | −2679(4) | 45(3)* |
| C(7) | 3284(5) | 4901(4) | −4513(4) | 54(3)* |
| C(8) | 1786(5) | 5303(4) | −4126(4) | 55(3)* |
| C(9) | 65(5) | 4404(4) | −3483(4) | 52(3)* |
| C(10) | −955(6) | 5471(5) | −3307(4) | 63(3)* |
| C(11) | −2277(6) | 5504(6) | −2837(5) | 68(3)* |
| C(12) | −2583(5) | 4488(6) | −2588(6) | 68(3)* |
| C(13) | −1555(5) | 3399(5) | −2797(4) | 63(3)* |
| C(14) | −219(5) | 3340(4) | −3238(4) | 48(3)* |
| C(15) | 849(5) | 1492(4) | −2406(4) | 51(2)* |
| C(16) | 983(5) | 2126(4) | −1431(4) | 50(3)* |
| C(17) | −108(5) | 2842(4) | −590(4) | 56(3)* |
| C(18) | 116(6) | 3453(4) | 192(5) | 61(3)* |
| C(19) | 1404(6) | 3308(4) | 166(4) | 58(3)* |
| C(20) | 2436(5) | 2552(4) | −690(4) | 48(3)* |
| C(21) | 3889(5) | 2357(4) | −865(4) | 47(3)* |
| C(22) | 5975(5) | 632(4) | −1168(4) | 49(3)* |
| C(23) | 6556(5) | 1117(4) | −550(5) | 64(3)* |
| C(24) | 7877(5) | 556(5) | −598(5) | 65(3)* |
| C(25) | 8632(6) | −464(5) | −1252(5) | 65(3)* |
| C(26) | 8055(6) | −951(5) | −1859(5) | 66(3)* |
| C(27) | 6741(6) | −409(4) | −1803(4) | 54(3)* |
| C(28) | 6578(5) | −960(5) | −3551(4) | 70(3)* |
| C(29) | 5810(5) | −1484(4) | −4067(4) | 62(3)* |
| C(30) | 3593(5) | −1037(4) | −4148(4) | 47(2)* |
| C(31) | 3947(6) | −1842(4) | −5023(5) | 60(3)* |
| C(32) | 2986(6) | −2009(4) | −5422(5) | 61(3)* |
| C(33) | 1645(6) | −1355(5) | −4920(5) | 62(3)* |
| C(34) | 1287(5) | −538(4) | −4035(4) | 60(3)* |
| C(35) | 2249(5) | −362(4) | −3624(4) | 44(2)* |

* Equivalent isotropic $U$ defined as one third of the trace of the orthogonalised $U_{ij}$ tensor.

Table II. Bond lengths (Å).

| | | | |
|---|---|---|---|
| N(1)—Hn(1) | 0.885(56) | N(1)—C(1) | 1.411(6) |
| N(1)—C(21) | 1.501(6) | Hn(2)—N(2) | 0.837(46) |
| Hn(4)—N(4) | 0.842(53) | Hn(5a)—N(5) | 0.857(49) |
| N(2)—C(14) | 1.417(6) | N(2)—C(15) | 1.498(6) |
| N(3)—C(16) | 1.344(7) | N(3)—C(20) | 1.360(8) |
| N(4)—C(21) | 1.437(6) | N(4)—C(22) | 1.408(7) |
| N(5)—C(15) | 1.445(6) | N(5)—C(35) | 1.393(7) |
| O(1)—C(6) | 1.401(7) | O(1)—C(7) | 1.448(7) |
| O(2)—C(8) | 1.447(7) | O(2)—C(9) | 1.389(7) |
| O(3)—C(27) | 1.430(9) | O(3)—C(28) | 1.399(6) |
| O(4)—C(29) | 1.421(6) | O(4)—C(30) | 1.402(8) |
| C(1)—C(2) | 1.390(8) | C(1)—C(6) | 1.418(7) |
| C(2)—C(3) | 1.399(8) | C(3)—C(4) | 1.388(8) |
| C(4)—C(5) | 1.387(9) | C(5)—C(6) | 1.391(8) |
| C(7)—C(8) | 1.515(7) | C(9)—C(10) | 1.388(7) |
| C(9)—C(14) | 1.425(8) | C(10)—C(11) | 1.408(10) |
| C(11)—C(12) | 1.380(10) | C(12)—C(13) | 1.409(7) |
| C(13)—C(14) | 1.412(8) | C(15)—C(16) | 1.540(9) |
| C(16)—C(17) | 1.389(6) | C(17)—C(18) | 1.387(10) |
| C(18)—C(19) | 1.399(10) | C(19)—C(20) | 1.390(6) |
| C(20)—C(21) | 1.526(8) | C(22)—C(23) | 1.416(10) |
| C(22)—C(27) | 1.387(6) | C(23)—C(24) | 1.401(8) |
| C(24)—C(25) | 1.377(8) | C(25)—C(26) | 1.405(11) |
| C(26)—C(27) | 1.389(9) | C(28)—C(29) | 1.534(10) |
| C(30)—C(31) | 1.370(8) | C(30)—C(35) | 1.416(6) |
| C(31)—C(32) | 1.406(11) | C(32)—C(33) | 1.403(8) |
| C(33)—C(34) | 1.388(8) | C(34)—C(35) | 1.420(9) |

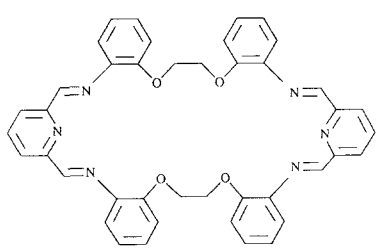
stretch; no amine or carbonyl bands were observed and so a macrocyclisation was likely to have occurred. The $^1$H NMR spectrum, in $CDCl_3$, showed a signal at 8.70 ppm corresponding to an imine proton and no signal assignable to an aldehydic proton, thus reinforcing this suggestion. The spectrum, however, is rapidly complicated by the ingrowth of signals due to (**5a**) during the data collection. The m.s. (E.I. mode) gave a very intense peak at 686 a.m.u. which corresponds to a '2 + 2' cyclocondensation leading to the tetraimine Schiff base (**4**) – a weak intensity peak was noted at 343 a.m.u. The IR spectrum showed a band at 690 $cm^{-1}$ and $^1$H NMR spectrum gave a singlet at 7.37 ppm and these, together with the microanalytical data, indicate the presence of one molecule of benzene for every molecule of '2 + 2' macrocycle. This suggests that an inclusion compound is likely, probably as a sandwich species with the benzene providing the filling. The benzene could be interacting with the lateral oxygen or nitrogen donor atoms of the macrocycle or with the aromatic $\pi$-cloud of a pyridinyl head-unit.

The macrocycle (**4**) can be converted into (**3**, R = Et) by recrystallisation from ethanol. Also the f.a.b. m.s. of (**4**) run in a 3-nitrobenzyl alcohol (NOBA) matrix shows peaks corresponding to $[(\mathbf{4}) + H]^+$, $[(\mathbf{4}) + NOBA + H]^+$ and $[(\mathbf{4}) + 2\,NOBA + H]^+$, indicating the facile addition of an alcohol across the imine bond. It appears that in the absence of a group capable of adding to the imine and so relieving molecular strain in the '1 + 1' macrocycle, formation of the '2 + 2'

Table III. Bond angles (deg.).

| | | | |
|---|---|---|---|
| Hn(1)—N(1)—C(1) | 112.1(28) | Hn(1)—N(1)—C(21) | 106.7(32) |
| C(1)—N(1)—C(21) | 120.4(3) | Hn(2)—N(2)—C(14) | 107.0(26) |
| Hn(2)—N(2)—C(15) | 110.4(30) | C(14)—N(2)—C(15) | 116.4(3) |
| C(16)—N(3)—C(20) | 118.7(4) | Hn(4)—N(4)—C(21) | 119.2(25) |
| Hn(4)—N(4)—C(22) | 113.8(23) | C(21)—N(4)—C(22) | 123.9(5) |
| Hn(5a)—N(5)—C(15) | 113.8(25) | Hn(5a)—N(5)—C(35) | 115.6(24) |
| C(15)—N(5)—C(35) | 125.5(5) | C(6)—O(1)—C(7) | 119.2(3) |
| C(8)—O(2)—C(9) | 118.6(3) | C(27)—O(3)—C(28) | 113.7(4) |
| C(29)—O(4)—C(30) | 117.8(4) | N(1)—C(1)—C(2) | 123.4(4) |
| N(1)—C(1)—C(6) | 119.7(5) | C(2)—C(1)—C(6) | 116.7(4) |
| C(1)—C(2)—C(3) | 122.6(5) | C(2)—C(3)—C(4) | 118.9(5) |
| C(3)—C(4)—C(5) | 120.5(5) | C(4)—C(5)—C(6) | 119.9(5) |
| O(1)—C(6)—C(1) | 114.0(4) | O(1)—C(6)—C(5) | 124.6(5) |
| C(1)—C(6)—C(5) | 121.3(5) | O(1)—C(7)—C(8) | 113.6(4) |
| O(2)—C(8)—C(7) | 107.4(4) | O(2)—C(9)—C(10) | 124.8(5) |
| O(2)—C(9)—C(14) | 114.8(4) | C(10)—C(9)—C(14) | 120.4(5) |
| C(9)—C(10)—C(11) | 119.7(6) | C(10)—C(11)—C(12) | 121.2(5) |
| C(11)—C(12)—C(13) | 119.5(6) | C(12)—C(13)—C(14) | 120.7(6) |
| N(2)—C(14)—C(9) | 119.5(5) | N(2)—C(14)—C(13) | 122.0(5) |
| C(9)—C(14)—C(13) | 118.5(4) | N(2)—C(15)—N(5) | 111.0(3) |
| N(2)—C(15)—C(16) | 109.6(4) | N(5)—C(15)—C(16) | 108.0(4) |
| N(3)—C(16)—C(15) | 115.1(4) | N(3)—C(16)—C(17) | 122.6(6) |
| C(15)—C(16)—C(17) | 122.3(5) | C(16)—C(17)—C(18) | 117.9(6) |
| C(17)—C(18)—C(19) | 120.9(4) | C(18)—C(19)—C(20) | 117.1(6) |
| N(3)—C(20)—C(19) | 122.7(5) | N(3)—C(20)—C(21) | 114.2(4) |
| C(19)—C(20)—C(21) | 123.0(6) | N(1)—C(21)—N(4) | 109.3(3) |
| N(1)—C(21)—C(20) | 110.6(4) | N(4)—C(21)—C(20) | 109.4(5) |
| N(4)—C(22)—C(23) | 122.6(4) | N(4)—C(22)—C(27) | 119.1(6) |
| C(23)—C(22)—C(27) | 118.3(5) | C(22)—C(23)—C(24) | 120.2(5) |
| C(23)—C(24)—C(25) | 120.8(7) | C(24)—C(25)—C(26) | 119.1(6) |
| C(25)—C(26)—C(27) | 120.4(5) | O(3)—C(27)—C(22) | 118.7(5) |
| O(3)—C(27)—C(26) | 120.0(4) | C(22)—C(27)—C(26) | 121.2(6) |
| O(3)—C(28)—C(29) | 110.8(5) | O(4)—C(29)—C(28) | 108.4(4) |
| O(4)—C(30)—C(31) | 126.1(4) | O(4)—C(30)—C(35) | 113.3(4) |
| C(31)—C(30)—C(35) | 120.6(6) | C(30)—C(31)—C(32) | 120.7(5) |
| C(31)—C(32)—C(33) | 120.1(5) | C(32)—C(33)—C(34) | 119.2(7) |
| C(33)—C(34)—C(35) | 121.3(5) | N(5)—C(35)—C(30) | 117.6(5) |
| N(5)—C(35)—C(34) | 124.3(4) | C(30)—C(35)—C(34) | 118.1(5) |

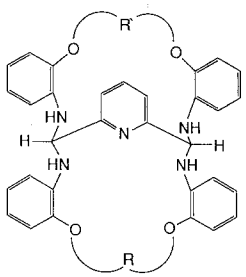
macrocycle is preferred. The latter is presumably less strained than the '1 + 1' macrocycle and in any given situation the least strained system is the one produced.



4

The macrocycle (**4**) is also obtainable from dry toluene, but if bench toluene, benzene, or acetonitrile are used as solvents then a different product is obtained. The white powder has no imine or carbonyl stretches in the IR spectrum but shows a band at 3370 $cm^{-1}$ indicative of a secondary amine; the $^1H$ NMR spectrum is more complex and without a signal due to a aldehydic proton. The f.a.b. m.s. in NOBA gave a strong peak at 334 a.m.u., corresponding to the '1 + 1' Schiff base macrocycle, and that run in sulfolane gave a highest mass peak at 587 a.m.u. Crystals suitable for X-ray structural analysis were grown from acetonitrile–chloroform and the structure was solved revealing that addition of 1,2-bis(2-aminophenoxy)ethane across the imines of a '1 + 1' Schiff base macrocycle had occurred to give a macrobicyclic aminal (**5a**).

The molecular structure of (**5a**) is shown in Figure 1. Bond lengths and angles are listed in Tables II and III and are unexceptional. The conformation of the molecule is best described in terms of the relative orientations of the four planar 2-aminophenoxy units (i.e. C(1) to C(6), N(1) and O(1); C(9) to C(14), O(2) and N(2); C(22) to C(27), N(4) and O(3); C(30) to C(35), N(5) and O(4) to the pyridyl fragment (C(15) to C(21) and N(3)). The first two aminophenoxy units lie in two mutually perpendicular planes, which are inclined at 78° to the pyridyl unit. The third aminophenoxy unit is inclined at 20° to the pyridyl unit. The fourth aminophenoxy



**5**

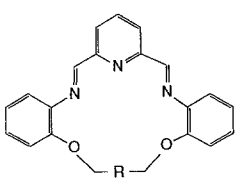
**5a** R = $CH_2CH_2$ R' = $CH_2CH_2$

**5b** R = $(CH_2CH_2)_2$ R' = $(CH_2CH_2)_2$

**5c** R = $CH_2CH_2$ R' = $(CH_2CH_2)_2$

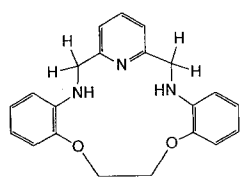
**5d** R = $(CH_2)_3$ R' = $(CH_2)_3$

unit is inclined at 6° to the pyridyl unit and 13° to the third aminophenoxy unit. The overall result is a macrobicycle in which the first two aminophenoxy units and the pyridyl unit define three approximately perpendicular planes (c.f. $Mo(CO_3$ [(**7**)] · $CH_2Cl_2$ [9] whereas the pyridyl unit and the other two aminophenoxy units, lie in an approximately planar conformation (c.f. Mn[(**6a**)] $(ClO_4)_2$) [10].



**6a**, R= $CH_2CH_2$

**6b**, R= $(CH_2)_4$



**7**

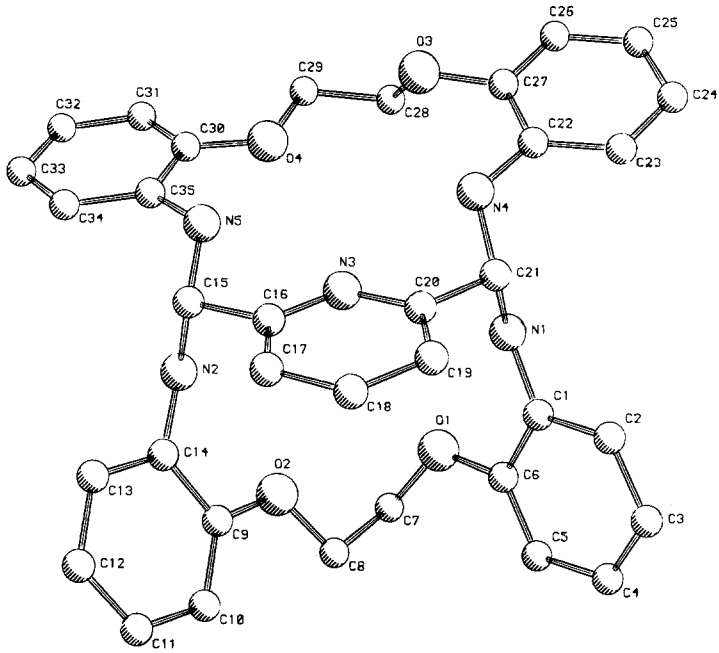



Fig. 1. The molecular structure of the macrobicyclic aminal (**5a**).

The macrobicyclic aminal (**5b**) is readily prepared by reaction of pyridine-2,6-dicarboxaldehyde and 1,4-bis(2-aminophenoxy)butane in 1 : 1 ratio in dry benzene, toluene or acetonitrile. Compound (**5b**) has been characterised by IR, NMR, and m.s. and crystals were grown from a chloroform–acetonitrile solution. The X-ray structure of (**5b**) is similar to that of (**5a**) confirming aminal formation; owing to the presence of disordered solvent molecules it has not, to date, been possible to refine the structure beyond an *R*-factor of 0.175. The reaction of pyridine-2,6-dicarboxaldehyde and 1,3-bis(2-aminophenoxy)propane under the conditions described above gave a product (**5d**) having an IR spectrum similar to those of (**5a**) and (**5b**).The high melting point ( $> 300°C$) and insolubility in common organic solvents suggest that this product may be polymeric in nature.

By increasing the 1,2-bis(2-aminophenoxy)ethane content in the original sythesis to give a 2 : 1 reactant ratio the yield of (**5a**) is greatly enhanced. This suggested that mixed aminals could be made available and addition of the corresponding diamine having a tetramethylene bridge to an acetonitrile solution of (**4**) led to the isolation of the mixed aminal (**5c**) which has been characterised by IR, NMR and m.s. The reaction of (**4**) with the more flexible aliphatic diamine 1,8-diaza-3,6-dioxaoctane did not give a mixed aminal. The macrobicyclic aminal (**5a**) can also be recovered when either (**3**), R = Et, or (**4**) is recrystallised from an acetonitrile–chloroform mixture. Recrystallisation of (**5a**) from ethanol or methanol gave [(**3**), R-Et or Me], further illustrating the fragility of (**5a**) in solution.

Preliminary metal complexation studies show that (**5a**) and (**5b**) react with Mn(II) to give the complexes [Mn(**6a**)$X_2$] and [Mn(**6b**)$X_2$] and that (**4**) reacts with

Fe(II) and Mn(II) to give the complexes [Fe(**6a**)$X_2$] and [Mn(**6a**)$X_2$]. In each case only products from the '1 + 1' macrocycle are recovered. In contrast the reaction of (**4**) with Cu(II) gives the mononuclear complex [Cu(**4**)$X_2$]. It has not yet been possible to isolate a dinuclear complex of (**4**).

## Acknowledgements

We thank the S.E.R.C for awards (to P.D.H. and G.P.W.) and the S.E.R.C. and the Royal Society for assistance in the purchase of the diffractometer and computing facilities.

## References

1. R. W. Layer: *Chem. Rev.* **63**, 489 (1963).
2. S. M. Nelson, C. V. Knox, M. McCann and M. G. B. Drew: *J. Chem. Soc., Dalton Trans.* 1669 (1981).
3. V. Katovic, L. T. Taylor and D. H. Busch: *Inorg. Chem.* **10**, 458 (1971).
4. D. H. Cook and D. E. Fenton: *Inorg. Chim. Acta* **25**, L95 (1977).
5. P. Moore, N. W. Alcock, R. G. Kingston and C. Pierpoint: *J. Chem. Soc., Dalton Trans.* 1941 (1989).
6. A. Bashall, D. E. Fenton, A. J. Leong, L. F. Lindoy, M. McPartlin, B. P. Murphy and P. A. Tasker: *J. Chem. Soc., Dalton Trans.* 2543 (1987).
7. *International Tables for X-ray Crystallography*, Vol. 4, Kynoch Press, Birmingham (1974), distr. Kluwer Academic Publishers, Dordrecht, the Netherlands.
8. G. M. Sheldrick: *SHELXTL*, An integrated system for solving, refining and displaying crystal structures from diffraction data (Revision 4), University of Göttingen, F.R. Germany 1983).
9. H. Adams, N. A. Bailey, D. E. Fenton, P. D. Hempstead, B. A. Hewes, S. J. Kitchen, and M. J. Winter: *Polyhedron* **8**, 1857 (1989).
10. P. Tasker, N. W. Alcock, D. C. Liles and M. McPartlin: *J. Chem. Soc., Chem Commun.* 727 (1974).