A New Cyclam providing the First Example unequivocally proven by *X*-Ray Crystallography of a Pendent Co-ordinated Pyridyl Group

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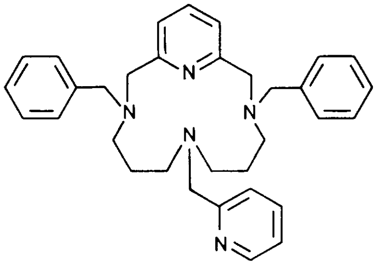
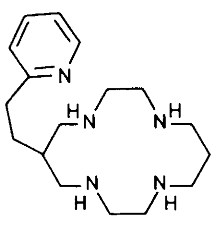
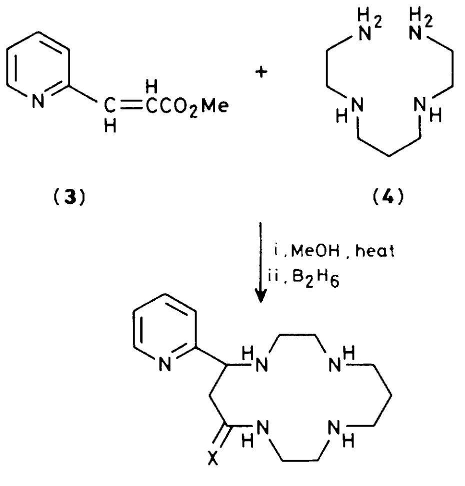
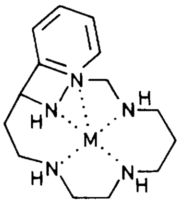
A new class of 14-membered tetra-azamacrocycle (cyclam) functionalised with a pendent pyridine ligand is reported; the *X*-ray crystal structure of its Ni^{II} complex (**7a**) provides the first unequivocal example of co-ordination of the pyridyl side-arm to the centrally placed metal ion.

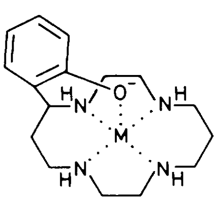
Recently, Moore synthesized the tetra-azamacrocycle (**1**) with a pyridyl side arm.[1] Earlier, we had reported a pyridyl-pendent cyclam (**2**) that axially binds with Ni^{III} placed in the macrocyclic hole.[2] However, this pyridyl co-ordination did not occur to the high-spin Ni^{II}, probably owing to a dominant entropy disadvantage.


(**1**)


(**2**)




(**7**)
a; M = Ni^{II}
b; M = Fe^{II}


(**8**)
a; M = Ni^{II}
b; M = Fe^{II}

We now report the new pyridyl-pendent cyclam (**6**) that is much simpler to synthesise and more versatile than (**1**) and moreover gives for the first time metal complexes (**7**) unequivocally proven to have an axially co-ordinated pyridyl ligand. The acrylate (**3**) (60 mmol) and 1,9-diamino-3,7-diazanonane (**4**) (60 mmol) were refluxed in MeOH (2 l) for 16 days. After evaporation *in vacuo*, the residue was crystallized from MeCN to give the amide (**5**) in 40% yield: m.p. 181—182 °C; M^+, m/z 291; i.r. (KBr) $\nu_{C=O}$ 1660 cm^{-1}. Reduction of the amide with B_2H_6 in tetrahydrofuran (THF) yielded compound (**6**) as colourless crystals in 24% yield: m.p. 145—146 °C; M^+, m/z 277; ^{1}H n.m.r. (90 MHz, $CDCl_3$) δ 1.5—2.1 (4H), 2.3—3.2 (18H), 3.7—3.9 (1H), 6.9—7.2 (2H), 7.4—7.6 (1H), and 8.4—8.5 (1H). The pK_a values for (**6**) are 11.47 ± 0.03, 10.00 ± 0.02, <3, <2, and <2 at $I = 0.1$ M ($NaClO_4$) and 25 °C. The proximity of the pyridyl N to the macrocycle in (**6**) is well illustrated by its extremely low pK_a value of <3 under the strong influence of the diprotonated N_4 ring; the pK_a value for the pyridyl N in (**2**) is 5.32.[2]

Purple crystals of (**7a**)·$2ClO_4$·H_2O were isolated from an aqueous solution (pH 7) of $NiSO_4$ and (**6**) in the presence of excess of $NaClO_4$, and its crystal structure has been determined (Figure 1).†

The five-co-ordinate, square-pyramidal co-ordination of the ligand (**6**) around nickel is evident. The pyridine ring is vertically above the cyclam N_4 plane so that N(16) is axially co-ordinated. However the pyridyl nitrogen N(16) is considerably displaced from the apex of a regular pyramidal arrangement; *e.g.* the N(16)–Ni–N(4) angle is 79.2(1)°, implying some strain in its axial co-ordination. The Ni–N(16) bond distance of 2.124(3) Å is longer than the equatorial Ni–N bond lengths. The axial Ni–O_w(H_2O) distance is much longer [2.237(3) Å] indicating a weak co-ordinate bond. The atoms N(1), N(4), N(8), and N(11) in the cyclam skeleton are coplanar, and the nickel atom is in this plane, with Ni–N bond distances of 2.068(3), 2.056(3), 2.093(3), and 2.058(3) Å. The average Ni–N bond distance of ~2.07 Å is compatible with Ni^{II} in a high-spin state.[3] The cyclam moiety takes the normal *trans*-III conformation (*i.e.* the 1,3-diaminopropane rings have a chair conformation) as in Ni^{II}–cyclam[3,4] or the axial phenolate-pendent cyclam–Ni^{II} complex (**8a**).[5]

In pink aqueous solutions of (**7a**) the pyridyl-co-ordinating, high-spin Ni^{II} state is retained [$\lambda_{max.}$ 523 nm, ε 8; $\mu_{eff.}$ = 2.88 μ_B by the Evans method[6] at 35 °C and $I = 0.1$ M ($NaClO_4$)],

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† *Crystal data:* $C_{15}H_{27}N_5Ni{\cdot}2ClO_4{\cdot}H_2O$, $M = 553.05$, orthorhombic, space group *Pbca*, $a = 15.123(8)$, $b = 26.738(14)$, $c = 11.045(7)$ Å, $U = 4466$ Å^3, $Z = 8$, $D_c = 1.645$ g cm^{-3}. The structure was solved by the heavy-atom method and refined using 3534 unique data [$I > 2\sigma(I)$] measured on a Philips PW1100 diffractometer with Cu-K_α radiation, $\mu = 5.0$ cm^{-1}. The final R value is 0.056. 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, 1986.

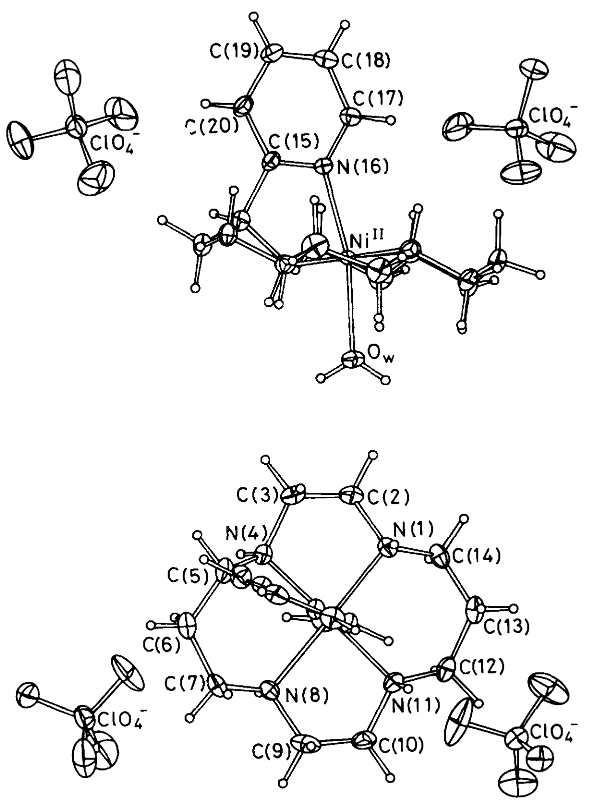

Figure 1. ORTEP[8] drawings of complex (**7a**)–2ClO_4·H_2O: (a) side-on view; (b) view from above. Atoms are drawn with 30% probability ellipsoids. Important bond lengths (Å) and bond angles (°): Ni–N(1) 2.068(3), Ni–N(4) 2.056(3), Ni–N(8) 2.093(3), Ni–N(11) 2.058(3), Ni–N(16) 2.124(3), Ni–O$_w$ 2.237(3); N(1)–Ni–N(4) 85.1(1), N(1)–Ni–N(16) 94.0(1), N(1)–Ni–O$_w$ 89.8(1), N(4)–Ni–N(8) 94.7(1), N(4)–Ni–N(16) 79.2(1), N(8)–Ni–N(16) 89.0(1), N(11)–Ni–N(16) 99.9(1), N(4)–Ni–O$_w$ 88.0(1), Ni–N(16)–C(15) 111.2(3).

which shows an Ni$^{\text{III/II}}$ redox potential of +0.61 V *vs.* saturated calomel electrode (S.C.E.), which is significantly *higher* than the +0.50 V for Ni$^{\text{III/II}}$–cyclam and Ni$^{\text{III/II}}$–(**2**) complexes[2] (0.5 M Na_2SO_4, pH 7, 25 °C). Addition of further pyridine (up to 10 equiv.) does not affect the redox behaviour of Ni$^{\text{III/II}}$–cyclam. The higher Ni$^{\text{III/II}}$ potential illustrates the effect of pyridine (as π-acceptor) when it is axially co-ordinated in (**7a**). Earlier, we found that the Ni$^{\text{III/II}}$ potential was lower (+0.35 V) when phenolate (as σ-donor) was axially co-ordinated in (**8a**).[5]

The e.s.r. spectrum at 77 K of the electrochemically oxidized product obtained from (**7a**) (at a constant potential of +0.8 V *vs.* S.C.E.) shows an axially N co-ordinated, low-spin, d^7 Ni$^{\text{III}}$ complex having $g_\perp = 2.17$, $g_\| = 2.026$ [analogous to Ni$^{\text{III}}$–(**2**)[2] having $g_\perp = 2.20$ and $g_\| = 2.01$], and $A_\| = 21.2$ G (1 G = 10^{-4} T).

The axial co-ordination of the pendent pyridyl groups also occurs in the Fe$^{\text{II}}$ complex (**7b**). As for the Ni complex, the Fe$^{\text{III/II}}$ redox potential of +0.12 V in (**7b**) is more positive with respect to that of (**8b**) (−0.16 V).[7]

Received, 12th May 1986; Com. 633

References

1 N. W. Alcock, K. P. Balakrishnan, and P. Moore, *J. Chem. Soc., Chem. Commun.*, 1985, 1731.
2 E. Kimura, T. Koike, R. Machida, R. Nagai, and M. Kodama, *Inorg. Chem.*, 1984, **23**, 4181.
3 V. J. Thöm, C. C. Fox, J. C. A. Boeyens, and R. D. Hancock, *J. Am. Chem. Soc.*, 1984, **106**, 5947.
4 B. Bosnich, R. Mason, P. J. Pauling, G. B. Robertson, and M. L. Tobe, *Chem. Commun.*, 1965, 97.
5 Y. Iitaka, T. Koike, and E. Kimura, *Inorg. Chem.*, 1986, **25**, 402.
6 D. F. Evans, *J. Chem. Soc.*, 1959, 2003.
7 E. Kimura, T. Koike, and M. Takahashi, *J. Chem. Soc., Chem. Commun.*, 1985, 385.
8 C. K. Johnson, ORTEP, Report ORNL-3794, Oak Ridge National Laboratory, Oak Ridge, TN, 1965.