Synthesis of 2,3-Dihydro- and 2,3,4,5-Tetrahydro-1,4-benzothia- and -benzoxazepines and their 14-Membered Macrocyclic Dimers with Chelating *Trans* N_2S_2 and N_2O_2 Donor Atom Arrangements: Crystal Structure of *cis*-$[NiCl_2(C_{18}H_{18}N_2S_2)]$

JOHN W. L. MARTIN, KEVIN P. WAINWRIGHT, K. D. V. WEERASURIA and STANLEY BRUCE WILD*

Research School of Chemistry, Australian National University, Canberra, A.C.T. 2601, Australia

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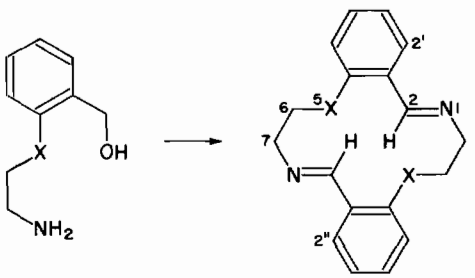
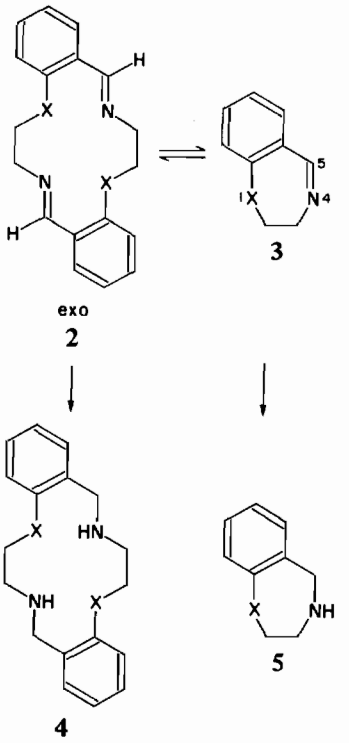
We have found a simple route to the new and highly desirable chelating macrocycles (**4**) that contain a *trans* arrangement of N_2S_2 and N_2O_2 donor atoms. They are obtained by reduction of the corresponding *trans–trans*-di-Schiff base precursor molecules (**2**) that result from the $BaMnO_4$ oxidation of appropriately substituted benzenemethanols (**1**). A satisfactory synthesis of *trans*-N_2X_2 macrocyclic quadridentates of this type has hitherto not been available [1]. The spontaneous double condensation of the presumed intermediate aldehydes takes place in high yield under ambient conditions, without regard to concentration or any of the other precautions usually taken to avoid polymerisation, such as use of a metal template. Diimines (**2**) (X = S or O) undergo facile acid-catalysed conversions into 2,3-dihydro-1,4-benzothiazepine (**3**) (X = S) and 2,3-dihydro-1,4-benzoxazepine (**3**) (X = O), respectively: the latter have been identified by isolation (X = O) and by reduction to the monomeric amines (**5**) (X = O and S). The monomer–dimer interconversion parallels closely the behaviour of 4,5-dihydro-3*H*-2-benzazepine and its dimer [2].



1 **2**



2 **3** **4** **5**

Thus, $BaMnO_4$ oxidation of 2-[2-aminoethylthio]-benzenemethanol (**1**) (X = S)** in dichloromethane produces in 55% yield, 3,4,10,11-dibenzo-1,8-*trans–trans*-1,8-diaza-5,12-dithiacyclotetradeca-1,3,8,10-tetraene (**2**) (X = S): mp. 206–209 °C; NMR ($CDCl_3$) δ 8.83 ($2,s,H_{2,9}$), 8.06 (2, dd, ^3J = 7.8 Hz, ^4J = 1.7 Hz, $H_{2',2''}$), 7.66–7.27 (6,m), 2.60 (4,t,^3J = 5.0 Hz, $H_{7,14}$), 3.38 (4,t,^3J = 5.0 Hz, $H_{6,13}$); IR (Nujol) 1640 cm^{-1} ($\nu_{C=N}$); mass spectrum, *m/e* 326 (M^+); mol wt (CH_2Cl_2) 324 (osmometry)†. The assignment of the non-chelating *trans–trans*–endo conformation to the free diimine is supported by molecular model considerations and by the strong deshielding of the azomethine (δ 8.83) and aromatic protons $H_{2'}$ and $H_{2''}$ (δ 8.06). In the 4,5-dihydro-3*H*-2-benzazepine dimer of similar structure the azomethine proton resonance occurs at 8.46 ppm [2]: the increased deshielding of these protons in the substituted compound further supports the assignment of the endo conformation to the free ligand. Diimine (**2**) (X = S) reacts with nickel(II) chloride to give the green complex *cis*-$[NiCl_2(C_{18}H_{18}S_2)]$, (**6**), with μ_{eff} = 3.23 B. M. at 20 °C. The complex contains both possible conformations of the molecule in each unit cell of

*Author to whom correspondence should be addressed.

**Prepared in 63% yield from sodium 2-hydroxymethylbenzenethiolate and 2-chloroethylamine in methanol as colorless plates with mp. 72–75 °C.

†All new compounds analyze satisfactorily.

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the triclinic crystals. In conformer (**6a**) the five-membered-ring-conformations are of opposite helicity (λδ) and in (**6b**) they have the same helicity (λλ or δδ) (Fig. 1). Compound (**6**) crystallizes in the triclinic space group $P\bar{1}$-C_i^1 (No. 2), with $a = 7.163(2)$ Å, $b = 14.399(4)$ Å, $c = 18.988(5)$ Å, $\alpha = 116.06(2)°$, $\beta = 93.10(2)°$, $\gamma = 90.42(2)°$, $V = 1824.2(9)$ Å^3, $Z = 4$. Diffraction data were collected on a computer-controlled Four-circle Nicolet Autodiffractometer at 20 ± 1 °C with use of molybdenum radiation. The structure was solved with use of Patterson and Fourier methods. Final least squares refinement with all non-hydrogen atoms anisotropic gave $R = 0.057$, $R_w = 0.079$ using 7061 unique reflections with $I > 3\sigma(I)$.

Lithium aluminium hydride reduction of (**2**) (X = S) produces the quadridentate amine (**4**) (X = S) as colorless needles: mp. 135–136 °C; NMR ($CDCl_3$) δ 7.26–6.99 (8,m), 3.85 (4,s,$H_{2,9}$), 3.24 (4,t,^3J = 5.3 Hz, $H_{7,14}$), 2.70 (4,t,^3J = 5.3 Hz; $H_{6,13}$); mass spectrum, *m/e* 330 (M^+); mol wt (CH_2Cl_2) 328 (osmometry). Similarly, oxidation of 2-[2-aminoethoxy]-benzenemethanol (**1**) (X = 0)†† provides a convenient route to the known macrocyclic diimine (**2**) (X = O) (65% yield): mp. 115–125 °C (Lit. [3] mp. 73–77 °C); NMR ($CDCl_3$) δ 8.88 (2,S,$H_{2,9}$), 7.69 (2,dd, ^3J = 7.6 Hz, ^4J = 1.6 Hz, $H_{2',2''}$), 7.38–6.81 (6,m), 4.21 (4,t,^3J = 4.3 Hz, $H_{7,14}$), 4.02 (4,t,^3J = 4.3 Hz, $H_{6,13}$); IR (Nujol) 1640 cm^{-1} ($\nu_{C=N}$); mass spectrum, *m/e* 294 (M^+); mol wt (CH_2Cl_2) 292 (osmometry). The structure of coordinated (**2**) (X = O) has been confirmed by the crystal structure determination of the paramagnetic red diiodonickel(II) complex: the metal atom and the four donor atoms of the 14-membered ring of exo conformation are accurately coplanar [4]. It is interesting to note that the corresponding *para*-methoxy compound is green and can be isolated as hexagonal or rhombic crystals: the rhombic form has a structure with cis iodine and nitrogen atoms and *trans* oxygen atoms, with a λδ arrangement of the five-membered ring conformations [5]. LAH reduction of (**2**) (X = O) affords the new macrocyclic diamine (**4**) (X = O): mp. 170–171 °C; NMR ($CDCl_3$) δ 7.28–6.82 (8,m), 4.16 (4,t,^3J = 4.6 Hz, $H_{6,13}$), 3.83 (4,s,$H_{2,9}$), 3.11 (4,t, ^3J = 4.6 Hz, $H_{7,14}$); mass spectrum, *m/e* 298 (M^+); mol wt (CH_2Cl_2) 299 (osmometry).

The conversion of the diimines (**2**) (X = S or O) into the monomeric imines (**3**) (X = S or O) occurs slowly in chloroform for both compounds, but is accelerated by trifluoroacetic acid. Within 16 h at 25 °C a chloroform solution of (**2**) (X = O) including 0.1 M TFA was shown by NMR spectroscopy to contain only (**3**) (X = O). Pure 2,3-dihydro-1,4-benzoxazepine was subsequently isolated in high yield by distillation: bp. 90 °C (0.2 mm Hg) (Kugelrohr) (Lit. [3] *ca.* 90 °C, 0.1 mm); NMR ($CDCl_3$) δ 8.21 (1,s,H_5), 6.99–7.46 (4,m), 4.30 (2,t,^3J = 5.0 Hz, H_3), 4.12 (2,t,^3J = 5.0 Hz, H_2); IR (Nujol) 1640 cm^{-1} ($\nu_{C=N}$); mass spectrum, *m/e* 147 (M^+); mol wt ($CHCl_3$) 161 (osmometry). LAH reduction of a tetrahydrofuran solution of (**3**) (X = O) gave 2,3,4,5-tetrahydro-1,4-benzoxazepine (**5**) (X = O): bp. 100 °C (0.05 mmHg) (Kugelrohr) (Lit. [6] bp. 103–105 °C, 4 mm); NMR ($CDCl_3$) δ 7.27–6.94 (4,m), 4.02 (2,t,^3J = 4.5 Hz, H_2), 3.95 (2,s,H_5), 3.20 (2,t,^3J = 4.5 Hz, H_3); mass spectrum, *m/e* 149 (M^+). The conversion of (**2**) (X = S) into monomer was much slower: after 4 days at 25 °C a chloroform solution of the dimer including 0.1 M TFA contained approximately equal proportions of monomer and dimer, as evidenced by the appearance of a new azomethine signal in the ^{1}H NMR spectrum at δ 8.53. Spontaneous dimerization occurred, however, upon removal of the solvent. Nevertheless, LAH reduction of a diethyl ether solution of (**3**) (X = S) obtained by stirring the dimer in this solvent for 5 days at 35 °C in the presence of *ca.* 0.1 M TFA produced a moderate yield of pure 2,3,4,5-tetrahydro-1,4-benzthiazepine

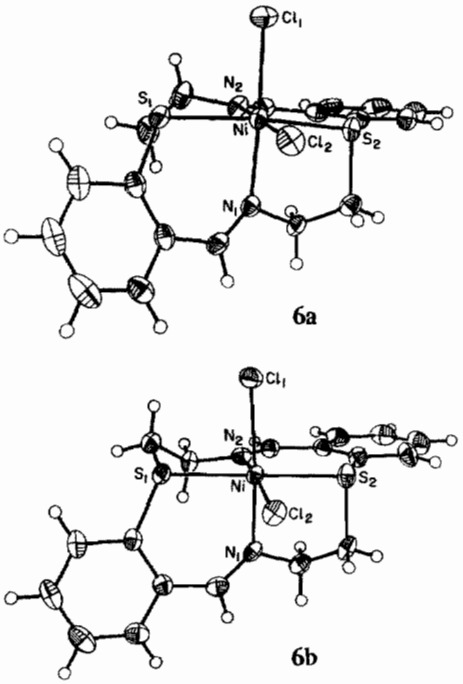

Fig. 1. Perspective ORTEP drawings of the two conformers of **6** present in *cis*-[$NiCl_2(C_{18}H_{18}N_2S_2)$]. Selected bond distances (Å) and angles (deg) are as follows (**6a**, **6b**): NiCl(1) = 2.418(1), 2.432(1), Ni–Cl(2) = 2.409(2), 2.408(1), Ni–N(1) = 2.114(4), 2.084(4), Ni–N(2) = 2.086(5), 2.077(4), Ni–S(1) = 2.370(2), 2.336(2), Ni–S(2) = 2.358(2), 2.357(2); Cl(1)–Ni–Cl(2) = 94.5(1), 96.1(1), N(1)–Ni–N(2) = 89.7(2), 83.9(2), S(1)–Ni–S(2) = 173.5(1), 178.9(1), Cl(1)–Ni–N(1) = 177.1(1), 174.1(1), Cl(2)–Ni–N(2) = 176.4(1), 173.0(1).

††Obtained from 2-hydroxybenzaldehyde following 2-bromoethylation of the phenoxo group, azide displacement of the bromide, and LAH reduction of the resulting azido-aldehyde: mp. 64–66 °C.

(5) (X = S): bp. 170 °C (0.05 mmHg) (Kugelrohr) NMR ($CDCl_3$) δ 7.58–7.10 (4,m), 4.13 (2,s,H_5), 3.38 (2,t,^3J = 5.1 Hz, H_3), 2.76 (2,t,^3J = 5.0 Hz, H_2); mass spectrum, *m/e* 165 (M^+). **5** (X = S)·HCl: mp. 239–240 °C (Lit. [7] mp. 237–238 °C).

The remarkable similarity in stability of the monomeric 2,3-dihydro compounds and their dimers is noteworthy. As well as affording a mild new method of synthesis of parent heterocyclic ring systems of this type, for which there appears to be a notable paucity of information in the literature [8], it may be anticipated that these new *trans*-N_2X_2 macrocyclic quadridentates will find important applications as metal ion selective reagents [9].

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