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Synthesis of asymmetric derivatives of 1,4,7-triazacyclononane and trigonal prismatic Mn(II) complexes

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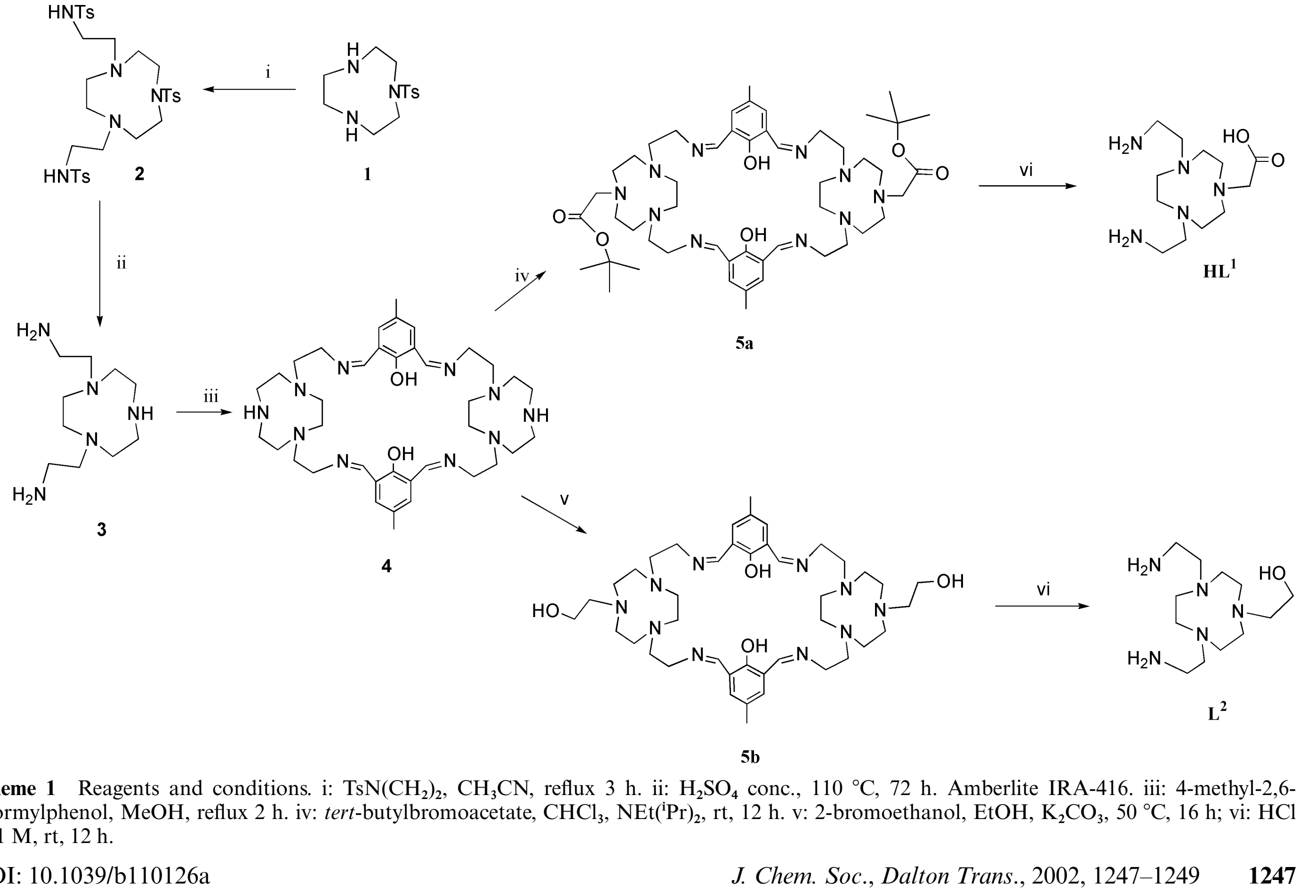
A new route to the asymmetric functionalisation of [9]aneN_3 has been achieved *via* the use of macropolycyclic Schiff-base intermediates; novel trigonal prismatic Mn(II) complexes of these asymmetric ligands have been synthesised and structurally characterised.

Symmetric N-functionalisation of 1,4,7-triazacyclononane ([9]aneN_3) *via* incorporation of three pendant arms bearing N-, O-, S- and P-donor groups has afforded a wide range of hexadentate ligands which have been studied extensively.[1] Due to synthetic difficulties, however, fewer derivatives of [9]aneN_3 bearing only one[2] or two[3] pendant arms having co-ordinating donor groups have been reported. Even less work has been reported on the synthesis of derivatives of [9]aneN_3 having different pendant donor groups, reflecting the increased and significant synthetic difficulty encountered in the preparation of these types of ligands. Generally, the synthetic routes to asymmetric derivatives of [9]aneN_3 involve either reaction of excess [9]aneN_3 with the appropriate electrophile to give mono- or di-functionalised derivatives which are subsequently functionalised on the remaining free N-donor atom(s) of the ring, or *via* the use of different protecting groups for one or two N-centres of the macrocycle and followed by functionalisation of the remaining free nitrogen centre(s) and subsequent deprotection(s).[2–5] However, synthetic difficulties can arise if a variety of donor pendant arms are incorporated into the target ligand. These types of ligands are of major interest because they can be used for the construction of multifunctional materials such as dendrimers,[6] and their complexes exhibit specific chemical properties[7] and have practical applications including radio-labelling[8] and selective cation binding.[9] We were specifically interested in developing a route which would allow high-yield syntheses of derivatives of [9]aneN_3 with different types of donor groups in the presence of amine pendant arms. We report herein the synthesis of two new asymmetric derivatives of [9]aneN_3 and their co-ordination chemistry towards Mn(II), such species being of interest for the development of new catalysts[10] and as model compounds for Mn-containing enzymes.[11]

The reaction of 1-(*p*-tolylsulfonyl)-1,4,7-triazacyclononane, **1**,[4] with two equivalents of *N*-tosylaziridine gave **2** (Scheme 1) in 96% yield, detosylation of which with concentrated H_2SO_4 afforded **3** in 92% yield. Functionalisation of the secondary macrocyclic N-centre of **3** in the presence of two tertiary and two primary amines was achieved *via* protection by Schiff-base condensation with 4-methyl-2,6-diformylphenol to give **4**, which is a rare example of a cage containing two connected triazacyclononane units.[12] Having 14 potential co-ordination sites, **4** can also be effectively used for the formation of binuclear



Scheme 1 Reagents and conditions. i: $TsN(CH_2)_2$, CH_3CN, reflux 3 h. ii: H_2SO_4 conc., 110 °C, 72 h. Amberlite IRA-416. iii: 4-methyl-2,6-diformylphenol, MeOH, reflux 2 h. iv: *tert*-butylbromoacetate, $CHCl_3$, $NEt(^iPr)_2$, rt, 12 h. v: 2-bromoethanol, EtOH, K_2CO_3, 50 °C, 16 h; vi: HCl 0.01 M, rt, 12 h.

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complexes with various metal ions. Imines are not normally used as protective groups for amines because of their low stability in water and potential high reactivity, especially under acidic conditions. However, **4** can be transformed to **5a** and **5b** *via* reaction with *tert*-butylbromoacetate and 2-bromoethanol, respectively (Scheme 1). **5a** and **5b** can be isolated as thick orange oils, but can also be used *in situ* for subsequent reactions. Thus, hydrolysis of the imino bonds in **5a** and **5b** with dilute aqueous HCl afforded the hydrochloric salts of the two desired products HL^1 and L^2,† respectively, in good yields. In the case of **5a**, the reaction with dilute aqueous HCl also hydrolyses the *tert*-butyl ester group to the free carboxylic acid function in HL^1.

Reaction of **3** with one molar equivalent of $Mn(NO_3)_2$ in MeOH at room temperature gave colourless columnar crystals following partial removal of the solvent and diffusion of Et_2O vapour into the remaining solution.† A single crystal X-ray determination‡ confirms the product to be a mononuclear complex [Mn(**3**)(NO_3)](NO_3) with the Mn(II) ion co-ordinated to the five N-donors of the ligand and one oxygen from a nitrate anion. Interestingly, the co-ordination geometry around the Mn(II) centre is trigonal prismatic, with one face taken up by the three N-donors of the triaza ring [Mn–N 2.247(2)–2.388(2) Å] and the other occupied by the two primary amines [Mn–N(3A) 2.228(2) and Mn–N(3B) 2.250(2) Å] and by the oxygen atom [Mn–O(4) 2.268(2) Å]. The two triangular faces of the prism are almost parallel, being inclined to each other by only 6.1°, and only slightly twisted (average of 4.3°). Interestingly, intermolecular and intramolecular H-bonds are observed between nitrate oxygens and both the primary amines and the N–H group on the ring; we believe that it is these interactions that facilitate the observed trigonal prismatic stereochemistry with a very low twist angle. Fig. 1 shows two complex cations linked by a bridging nitrate and also the six-membered ring formed by the nitrate [N(2N), O(4) and O(5)], the metal and N(3B). These hydrogen bonds (N–H ··· O) have H ··· O distances between 2.14 and 2.47 Å and N–H ··· O angles of 142–154°. The Mn–N bond distances are comparable to those reported for a Mn(II) complex of 4,7-bis(2-methylpyridyl)-1,4,7-triazacyclononane[13] in which no internal H-bonding is observed and, therefore, a more distorted trigonal prismatic geometry with a twist angle of 23.4° results. To our knowledge, this is only the second example of a metal complex of a pendant-arm ligand based on [9]aneN_3 which has trigonal prismatic geometry. Peacock and co-workers[14] have reported a mixed valence Mn(II)/Mn(IV) hydrogen-bridged dimer with the ligand 1,4,7-tris(2*S*)-2-hydroxypropyl-1,4,7-triazacyclononane in which the Mn(II) is present in a trigonal prismatic geometry. Other reports suggest that high spin d^5 Mn(II) complexes can accommodate this geometry more readily than ions with other electronic configurations.[15]

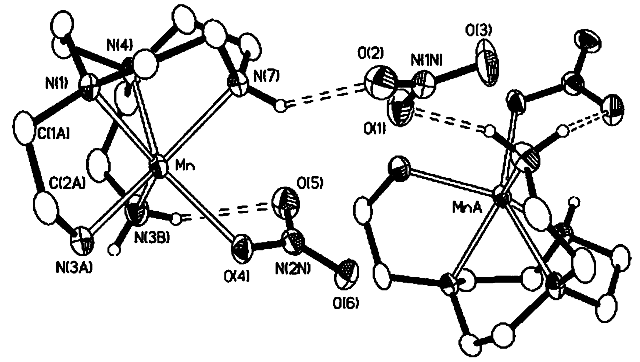

Fig. 1 View of two complex cations connected by bridging nitrates in [Mn(**3**)(NO_3)](NO_3) with numbering scheme adopted showing inter- and intra-molecular H-bonding. Hydrogen atoms on carbon atoms have been omitted for clarity and hydrogen bonds are drawn as double dotted lines. Displacement ellipsoids are drawn at 50% probability. Symmetry operation: A = $-x + 1, y + 1/2, -z + 1/2$.

Colourless crystals were obtained from the reaction of Li(L^1) and of L^2 with one molar equivalent of $Mn(ClO_4)_2$ in MeOH. Analytical and mass spectrometric data for the two products were consistent with the formulations [Mn(L^1)](ClO_4)·MeOH and [Mn(L^2)]$(ClO_4)_2$, respectively. The single crystal X-ray structure of [Mn(L^1)](ClO_4)·MeOH shows a mononuclear complex with the Mn(II) ion co-ordinated by five N-donors and one O-donor from the ligand. The co-ordination geometry around the Mn(II) centre is again a slightly distorted trigonal prism with one face taken up by the three N-donors of the triaza ring [Mn–N 2.300(2)–2.326(2) Å] and the other face defined by the two primary amines [Mn–N(3A) 2.227(2) and Mn–N(3B) 2.204(2) Å] and by the carboxylate oxygen [Mn–O(4C) 2.129(1) Å] (Fig. 2). In [Mn(L^1)](ClO_4)·MeOH the two triangular planes of the prism are inclined by 4.1° with the two triangular faces twisted by only 12.9°. Again, hydrogen-bonding interactions between NH_2 and anion O-centres connect more units together (H ··· O distances of 2.28 and 2.43 Å and N–H ··· O angles of 153 and 149°). A quite short H-bond between the OH of MeOH and the carboxylate oxygen not involved in the co-ordination of the metal can also be observed with H ··· O distance of 2.01 Å and N–H ··· O angle of 156°.

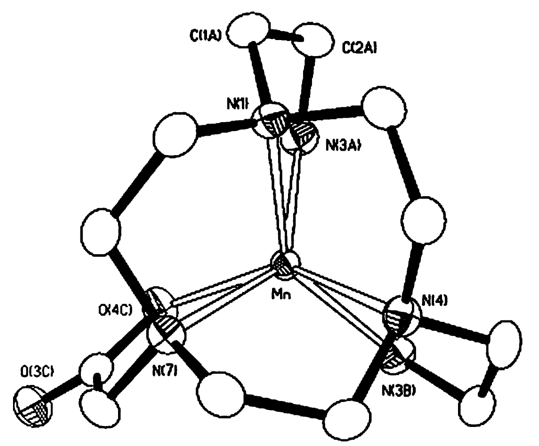

Fig. 2 Crystal structure of the complex cation [Mn(L^1)]$^+$ with numbering scheme adopted. The ClO_4^- anion, the MeOH molecule and hydrogen atoms have been omitted for clarity. Displacement ellipsoids are drawn at 50% probability.

In summary, we have shown that the co-facial macropolycycle **4** can be used as a useful synthon for asymmetric derivatisation of [9]aneN_3 with the Schiff-base used as a selective protection for primary amino functions. This new synthetic methodology is likely to be generally applicable to related functionalised macrocyclic systems. Furthermore, new trigonal prismatic Mn(II) complexes showing, and controlled by, inter- and intra-molecular H-bonding have been prepared and characterised.

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Notes and references

† Selected data for HL^1·3HCl·2H_2O. ^1H NMR: δ (D_2O, 298 K, 300 MHz) 2.77 (CH_2 ring, 4H, s) 2.92 (NCH_2 ring, 4H, t, $J = 5.76$ Hz), 3.03 (NCH_2 arms, 4H, t, $J = 6.42$ Hz), 3.15 (CH_2NH_2, 4H, t, $J = 6.42$ Hz), 3.25 (NCH_2 ring, 4H, br) and 3.89 (CH_2COOH, 2H, s). ^{13}C NMR: δ (D_2O, 298 K, 75 MHz) 37.17 ($NCH_2CH_2NH_2$), 46.78 (NCH_2 ring), 51.07 (NCH_2 ring), 53.45 (NCH_2 ring), 53.81 ($NCH_2CH_2NH_2$) and 58.10 (CH_2COOH). FAB mass spectrum (Glycerol/H_2O/MeOH matrix) m/z = 274 [M + H^+]. Elemental analysis: found (calc. for $C_{12}H_{30}Cl_3N_5O_2$·2H_2O): C, 34.48 (34.42); H, 8.03 (8.18); N, 16.81% (16.72%).

For L^2·3HCl·H_2O. ^1H NMR: δ (D_2O, 298 K, 300 MHz) 2.78 (CH_2 ring, 4H, s) 2.95–3.08 (NCH_2 arms and ring, 8H, m), 3.17 ($CH_2NH_3^+$, 4H, t, $J = 6.98$ Hz), 3.34 (NCH_2 ring, 4H, t, $J = 5.84$ Hz), 3.40 (NCH_2-CH$_2$OH, 2H, t, $J = 5.10$ Hz) and 3.87 (CH_2OH, 2H, t, $J = 5.10$ Hz). ^{13}C NMR: δ (D$_2$O, 298 K, 75 MHz) 36.19 (NCH$_2$CH$_2$NH$_2$), 46.26 (NCH$_2$ ring), 49.57 (NCH$_2$ ring), 51.18 (NCH$_2$ ring), 52.45 (NCH$_2$CH$_2$NH$_2$) 54.94 (CH$_2$CH$_2$OH) and 57.06 (CH$_2$OH). FAB mass spectrum (Glycerol/H$_2$O/MeOH matrix) $m/z = 260$ [M + H$^+$]. Elemental analysis: found (calc. for $C_{12}H_{32}Cl_3N_5O\cdot H_2O$): C, 37.10 (37.26); H, 8,76 (8.86); N, 18.02% (18.11%).

For [Mn(**3**)](NO$_3$)$_2$. FAB mass spectrum (3-NOBA matrix): m/z = 332 (M$^+$ [Mn(**3**)(NO$_3$)]$^+$). Elemental analysis: found (calc. for $C_{10}H_{25}MnN_7O_6$): C, 30.57 (30.46); H, 6.55 (6.39); N, 25.04% (24.87%). IR spectrum (KBr disc): ν 3318m, 3264m, 2920m, 2851m, 1472m, 1384s, 1006w, 802w cm^{-1}.

For [Mn(L^1)](ClO$_4$)·MeOH: FAB mass spectrum (3-NOBA matrix) m/z = 327 (M$^+$ [Mn(L^1)]$^+$). Elemental analysis: found (calc. for $C_{12}H_{27}ClMnN_5O_6\cdot$MeOH): C, 34.22 (34.03); H, 6.63 (6.59); N, 15.58% (15.26%). IR spectrum (KBr disc): ν 2921m, 2850m, 1617m, 1472m, 1396s, 1121s, 1094m, 634w cm^{-1}.

For [Mn(L^2)](ClO$_4$)$_2$: FAB mass spectrum (3-NOBA matrix) m/z = 413 (M$^+$ [Mn(L^2)(ClO$_4$)]$^+$) and 313 (M^{2+} [Mn(L^2)]$^{2+}$). Elemental analysis: found (calc. for $C_{12}H_{29}Cl_2MnN_5O_9$): C, 28.29 (28.08); H, 5.82 (5.70); N, 13.51% (13.65%). IR spectrum (KBr disc): ν 3300m, 3262m, 2922m, 2855m, 1473m, 1109s, 1089s, 627m cm^{-1}.

‡ Crystal data for [Mn(**3**)(NO$_3$)](NO$_3$): $C_{10}H_{25}MnN_7O_6$, M = 394.31, $a = 7.8382(7)$, $b = 14.3920(10)$, $c = 14.6130(10)$ Å, $U = 1648.5(2)$ Å^3, T = 150(2) K, space group $P2_12_12_1$, $Z = 4$, μ(Mo-Kα) = 0.845 mm^{-1}. 10415 reflections measured, 3918 unique [$R_{\mathrm{int}} = 0.045$] which were used in all calculations. The final R_1 was 0.0329, wR_2 [all data] = 0.0803.

Crystal data for [Mn(L^1)](ClO$_4$)·MeOH: $C_{13}H_{30}ClMnN_5O_7$, M = 458.81, $a = 8.7577(9)$, $b = 14.199(2)$, $c = 15.771(2)$ Å, $\beta = 92.543(2)°$, $U = 1959.2(4)$ Å^3, T = 150(2) K, space group $P2_1/n$, $Z = 4$, μ(Mo-Kα) = 0.856 mm^{-1}. 18071 reflections measured, 4742 unique [$R_{\mathrm{int}} = 0.039$] which were used in all calculations. The final R_1 was 0.0367, wR_2 [all data] = 0.0967.

Data were collected on a Bruker SMART1000 CCD area detector diffractometer, using graphite-monochromated Mo-Kα radiation. Both structures were solved using direct methods[16] and all non-H atoms were located using subsequent difference Fourier methods.[17] Hydrogen atoms were placed in calculated positions (ΔF synthesis for MeOH H in [Mn(L^1)](ClO$_4$)·MeOH) and thereafter allowed to ride on their parent atoms (MeOH H in [Mn(L^1)](ClO$_4$)·MeOH were refined as a rotating rigid body). CCDC reference numbers 173798 and 173799. See http://www.rsc.org/suppdata/dt/b1/b110126a/ for crystallographic data in CIF or other electronic format.

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