A novel enantiopure proline-derived triazacyclononane: synthesis, structure and application of its manganese complex

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The X-ray crystal structure and electrochemical data of a manganese complex $[L_2Mn_2^{III}(\mu\text{-}O)(\mu\text{-}AcO)_2][PF_6]_2$ with L being an enantiopure C_3-symmetric 1,4,7-triazacyclononane derived from L-proline are compared to those of $[Me_3\text{-}TACN_2Mn_2^{III}(\mu\text{-}O)(\mu\text{-}AcO)_2][PF_6]_2$; catalytic studies reveal the applicability of the complex in enantioselective epoxidations.

The tridentate macrocycle 1,4,7-triazacyclononane (TACN, **1**) and derivatives thereof, in particular 1,4,7-trimethyl-1,4,7-tri-azacyclononane (Me₃TACN, **2**), have extensively been used as ligands in the coordination chemistry of transition metals (Scheme 1).[1]

Triazacyclononanes imitate the coordination sphere of the three histidines which are often encountered in metalloproteins and therefore such (TACN) metal complexes are of interest as structural and functional enzyme models as well as catalysts. For example, dinuclear TACN–manganese complexes mimic enzymes like manganese superoxide dismutase and manganase catalase,[2] and in 1994 Unilever reported their use in low-temperature bleaching with hydrogen peroxide.[3] Bein and de Vos described stereospecific epoxidations of unfunctionalised olefins,[4] and with manganese complexes bearing chiral TACN derivatives we[5] and others[6] achieved enantioselective epoxidations. Other applications include oxidations of benzylic alcohols[7] and sulfides[8] to benzaldehydes and sulfones, respectively, and the use of perfluorinated TACN–Mn complexes.[9] Moreover, hydroxylation and hydroperoxidation of poorly reactive hydrocarbons was achieved by the activation with such complexes with acetic acid.[10] Here, we present the synthesis of the enantiopure C_3-symmetric trispyrrolidine-1,4,7-triazacyclononane (TP-TACN, **3**) and describe the preparation and characterisation of its dinuclear manganese complex **5** which is capable of catalysing enantioselective epoxidations.

TP-TACN **3** was obtained as an air-sensitive colourless oil by reduction of L-proline-derived cyclotripeptide **4**[11] with a large excess of borane–tetrahydrofuran (Scheme 2).[12] Isolation of the product was achieved by addition of MeOH to destroy the excess of borane followed by refluxing in 4 M HCl–dioxane. Treatment of this acidic mixture with solid NaOH followed by extraction with DCM liberated the triamine. Distillation of the crude product under reduced pressure (120–125 °C; 2.6×10^{-1} mbar) afforded **3** in 83% yield.† The dinuclear manganese(III) complex **6** (74% yield)‡ crystallised from a solvent mixture of MeOH and water containing triamine **3**, manganese(III) acetate, sodium acetate and ammonium hexafluorophosphate providing

single crystals suitable for X-ray diffraction analysis.§ The comparison of selected bond distances and angles of **6** with the corresponding values of Wieghardt's Me₃TACN manganese complex **5**[2a] reveals the structural similarity between both compounds. For example, the Mn–Mn distances in **6** [average value 3.155(2) Å] and the one in **5** [3.149(3) Å] overlap within their threefold standard deviation. Similarly, the Mn–O–Mn angle in **6** is 122.2(3)°, while the one reported for **5** is 120.9(1)°.

From temperature-dependent (4–300 K) magnetic susceptibility measurements (SQUID magnetometer) of solid **6** a ferromagnetic coupling ($J = +4.6$ cm⁻¹; $H = -2JS_1 \times S_2$; $S_1 = S_2 = 2$; $D1 = D2 = 2.3$ cm⁻¹; $g1 = g2 = 1.992$) yielding an $S = 4$ ground state was established in agreement with **5**.
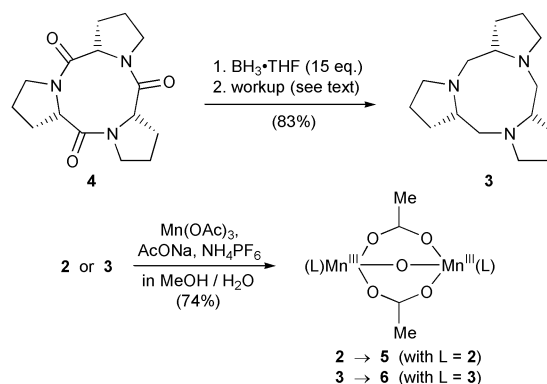
Fig. 1 shows the X-band EPR spectra of the electrochemically generated one electron reduced and oxidised states of the PF₆-salt of **6** in acetonitrile at 30 K. A detailed analysis of the multiline spectra is currently under investigation and will be published elsewhere.

The electrochemical properties of **5** and **6** have been studied by cyclic voltammetry (CV) under identical conditions in acetonitrile solution containing 0.1 M tetra-*n*-butylammonium hexafluorophosphate (TBAPF₆) as supporting electrolyte in the potential range +1.6 to −1.0 V. All redox potentials are referenced *vs.* the ferrocenium/ferrocene couple (Fc⁺/Fc). Scheme 3 summarises the data.

The CV of **6** exhibits one reversible one-electron reduction at $E_{1/2} = -0.62$ V corresponding to a $Mn^{III/III}/Mn^{III/II}$ transition and, in addition, two successive quasi reversible [$\Delta E^P = 109$ and 87 mV (scan rate: 50 mVs⁻¹)] one-electron oxidations at $E_{1/2} = 0.51$ and 1.12 V corresponding to $Mn^{III/III}/Mn^{III/IV}$ and $Mn^{III/IV}/Mn^{IV/IV}$ transitions, respectively. Thus, the redox behaviour of **6** is similar to that of **5**, however, all transitons are shifted towards more negative potentials (by 0.1, 0.08 and 0.09 V, respectively). These results show that TP–TACN and its manganese complex are chiral analogues of Me₃TACN and its corresponding metal complex. Furthermore, the CV data reveal that TP–TACN can better stabilise higher oxidation states than Me₃TACN, which could be particularly useful in oxidation
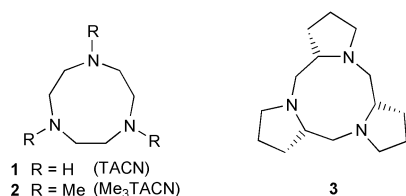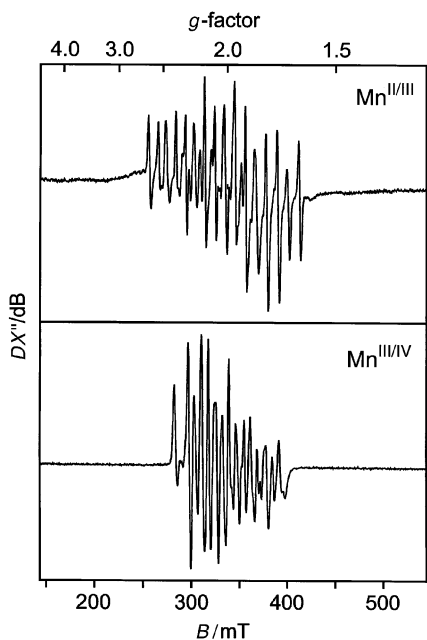

Scheme 1

Scheme 2

Fig. 1 X-band EPR spectra of the electrochemically generated one electron reduced and oxidised states of the PF$_6$-salt of **6** in acetonitrile at 30 K.

(for conditions see text)

Scheme 3

catalysis. In order to probe this hypothesis and to investigate the potential of **3** to serve as an asymmetric catalyst we briefly investigated enantioselective epoxidations of styrenes.

Catalytic activity of **5** was observed in the epoxidation of vinylarenes. With H$_2$O$_2$ as oxidant and 2 mol% of catalyst in acetone at −25 °C, approximately 28% conversion of styrene was observed after 2 h giving the corresponding epoxide with 24% ee (S-enantiomer; all ee-values were determined by GC using a chiral column). Extending the reaction time to 4 h increased the conversion (ca. 88%) of the olefin but reduced the enantioselectivity (15% ee). The significantly greater conversion coupled with the lower enantioselectivity after the longer reaction time suggests that the catalytic species is changing during the course of the reaction. Substituted arenes, such as 3-nitrostyrene and 4-chlorostyrene were epoxidised as well giving products with 26 and 21% ee, respectively.

Notes and references

† NMR data of **3**: ^{1}H NMR (CD$_3$OD) δ 3.12 (dt, J = 2.0, 6.0 Hz, 1H), 3.04 (m, 1H), 3.05 (t, J = 13.0 Hz, 1H), 2.76 (dd, J = 8.1, 2.7 Hz, 1H), 2.64 (q, J = 9.0 Hz, 1H), 1.95 (m, 1H), 1.70–1.85 (m, 2H), 1.54 (m, 1H); ^{13}C NMR (CD$_3$OD) δ 23.34, 31.40, 57.95, 59.50, 62.17.

‡ Selected analytical data of **6**: SIMS (NBA): m/z 742 (M$^+$), 363 (LMnOAc), 248 (ligand); C$_{34}$H$_{60}$N$_6$O$_5$Mn$_2$P$_2$F$_{12}$ required C, 39.5; H, 5.9; N, 8.1. Found: C, 39.4; H, 5.8; N, 8.1%. UV-Vis: λ_{max}/nm (ε, L mol^{-1} cm^{-1}) 250 (5500); 314 (8500); 485 (400); 521 (340); [α]$_D$ = +7.1° (c 0.05, CH$_3$CN). The ^{1}H-NMR spectrum of paramagnetic **6** in CD$_3$CN exhibits broad signals at δ = −157, −108, −76, −50, 34, 55, 62, 102, 108 and 116 ppm and an acetate signal at 80 ppm (assigned by exchange with deutero

acetate; see also in ref. 3c). Sharper signals were observed in the ranges 0 to 10 and 18 to 28 ppm.

§ *Crystal data* for C$_{34}$H$_{60}$N$_6$O$_5$F$_{12}$P$_2$Mn$_2$ (**6**): The compound crystallises in monoclinic space group $P2_1$ (No. 4) with two symmetrically independent molecules in the asymmetric unit. a = 11.1571(9), b = 16.8538(14), c = 23.1716(18) Å, γ = 98.367(3)°. M_r = 1032.70, Z = 2 × 2, D_c = 1.591 g cm^{-3}, μ = 7.32 cm^{-1}, absorption correction (*Gaussian*): min/max = 0.787/0.915. 47506 reflexions were collected at 100 K on a BRUKER SMART CCD using MoK$_\alpha$ radiation (λ = 0.71073Å). The structure was solved by direct methods (GENSIN/GENTAN) as implemented in the XTAL3.4 program package of crystallographic routines.[13] 7807 observed reflexions ($I > 4\sigma(I)$) in final least-squares full matrix refinement of 1099 parameters on F terminating at $R(R_w)$ = 0.084(0.050, w = σ^{-2}), a goodness of fit of 1.7924 and a residual electron density of −2.06/1.94 e Å^{-3}. CCDC 182/1847. See http://www.rsc.org/suppdata/cc/b0/b007059i/ for crystallographic files in .cif format.

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12 After concluding our investigations we were informed that **3** has also been synthesized by Reggelin and coworkers. We thank Professor Reggelin (Mainz) for sharing these unpublished results with us.

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