([SbO_5E], [SbO_4FE], [SbO_3F_2E], [SbO_2F_3E], [SbO_4E], [SbO_3FE]) and secondary building units (Sb_2P,[14] Sb_2P_2,[9, 11–14] Sb_4P_2,[10, 14] Sb_3P_3,[14] and Sb_5P_3[14] rings), as well as the new Sb_6P_2 and Sb_8P_4 rings of the title compound. We have recently discovered additional molecular, chain, layered, and three-dimensional materials belonging to this large family. In addition to their novel architectures, Sb^{III}-based materials, unlike closed-shell zeolites and $AlPO_4$s, may have redox behavior or other interesting properties associated with their lone pairs of electrons.

Experimental Section

Hydrofluoric acid (49 wt%, Fisher) was added to antimony(III) oxide (Aldrich), and the mixture was stirred to give a clear solution. Phosphoric acid (85 wt%, Fisher), en (Aldrich), eg (Fisher), and water, were added with stirring to give a mixture with composition 1 Sb:0.6 P:3.1 F:1.0 en: 11 H_2O:37 eg. This was sealed in a PTFE-lined stainless steel autoclave and heated at 135 °C under autogeneous pressure for 5 d. The crystalline product was filtered, washed with ethanol, and dried at 90 °C in air. A single crystal (0.08 × 0.04 × 0.03 mm) was mounted on a glass fiber, and room temperature X-ray diffraction data were collected with a Siemens SMART CCD diffractometer equipped with a normal focus 2.4-kW sealed X-ray tube ($Mo_{K\alpha}$ radiation, $\lambda = 0.71073$ Å) operating at 45 kV and 35 mA. About 1.3 hemispheres of intensity data were collected in 1321 frames with ω scans (width 0.30°, exposure time 10 s per frame). A total of 8328 reflections were collected in the range $2.8 < 2\theta < 46.6°$ and merged to give 2648 unique reflections. Unit cell parameters were determined by a least-squares fit of 1724 reflections: monoclinic, space group $P2_1/c$ (no. 14), $a = 14.8222(14)$, $b = 13.7657(13)$, $c = 9.3022(9)$ Å, $\beta = 105.341(2)°$, $V = 1830.4(3)$ Å^3, $Z = 2$, $M = 935.09$, $\rho_{calcd} = 3.393$. Absorption correction was performed with the program SADABS.[20] Positions of Sb and P atoms were determined by direct methods with SHELXS-97.[21] Other non-hydrogen atoms were located in subsequent difference Fourier maps. Bond-valence parameters[22] unambiguously distinguished bridging atoms. The final structure model was established by full-matrix least-squares refinement against $|F|^2$ with SHELXTL-PLUS.[21] The hydrogen atoms were placed in calculated positions and held in the riding model. The final reliability factors obtained in the fitting of 265 parameters with 1809 independent reflections with $I > 2.0\sigma(I)$ were $R_1(F) = 0.0387$, $wR(F^2) = 0.0843$, $S = 0.985$. The final difference Fourier map had maximum and minimum peaks of 0.936 and -1.325 e Å^{-3}. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-133133. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

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A $p(O_2)$-Responsive MRI Contrast Agent Based on the Redox Switch of Manganese(II/III)–Porphyrin Complexes

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Contrast in magnetic resonance imaging (MRI) is largely determined by differences in the relaxation times of protons in tissues. Therefore, contrast agents (CAs) for this diagnostic methodology have mainly been sought among the coordination compounds of metal ions with several unpaired electrons,

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such as Mn^{II} (five unpaired electrons) and Gd^{III} (seven unpaired electrons).[1, 2] The potential ability of a paramagnetic complex to act as a CA for MRI is first tested in vitro by measuring its relaxivity (r_1), which represents the relaxation enhancement of solvent water protons in the presence of the paramagnetic complex at a concentration of 1 mM. The administration of CAs has entered into several diagnostic protocols and has proved particularly useful in the assessment of organ perfusion and abnormalities in the blood–brain barrier or in kidney clearance. The next generation of CAs will have high tissue specificity and the ability to act as reporters of the physico–chemical environment where they are distributed. Such systems may be claimed as "smart" CAs; examples include paramagnetic complexes whose relaxivity is dependent on pH, temperature, or even enzymatic activity.[3]

Among the various parameters that characterize a biological environment, the partial pressure of oxygen ($p(O_2)$) appears to be relevant in a number of pathological conditions including strokes and tumors. The availability of CAs whose relaxivity is dependent upon $p(O_2)$ would be useful to obtain a better separation of arterial and venous blood as well as to develop novel applications of functional MRI (f-MRI). The latter methodology is based on the contrast which is dependent on blood oxygenation levels; this contrast arises chiefly from the magnetic properties of deoxyhemoglobin, which influences the transverse relaxation time of water protons.[4] We have already tackled the problem of designing a CA which acts as a reporter of the blood oxygenation level by suggesting two Gd^{III} chelates which are able to recognize T and R forms of human hemoglobin.[5, 6] Unfortunately, the intracellular nature of these CAs sets severe limitations on the development of practical MRI applications. Thus, we resort to systems which may yield the same information while remaining confined in the extracellular space or in direct contact with the extracellular fluid when they bind to outer cell membranes.

The simplest design of $p(O_2)$-responsive CA is based on a complex whose metal ion can switch between two redox states characterized by different relaxation properties. A very efficient system could be provided by Eu^{II}/Eu^{III} complexes, for which relaxivities analogous to Gd^{III} would be expected for the lower oxidation state. However, it is not straightforward to control the stabilization of this oxidation state.

For this reason, we resort to manganese complexes for which modulation of the redox switch between the $+2/+3$ oxidation states appears more amenable. As a model for this application we have considered Mn^{II} and Mn^{III} complexes with 5,10,15,20-tetrakis-(*p*-sulfonatophenyl) porphinate (tpps), whose relaxometric properties have been widely investigated.[7, 8] Moreover, this system shows a high affinity to tumor cells and, because of this property, it has been considered as a potential candidate for photodynamic therapy of cancer.[9]

The complex $[(Mn^{II}\ tpps)^{4-}]$ is easily formed by treating $[(Mn^{III}\ tpps)^{3-}]$ with dithionite. A simple inspection of the $1/T_1$ nuclear magnetic resonance dispersion (NMRD) profiles of the two complexes from 0.01 to 90 MHz (Figure 1) suggests that their relaxivities are only very different at low frequencies. Whereas this observation may suggest further applications in the low-field MRI systems, it is evident that, at the magnetic field strengths currently employed in the commercial MRI tomographs (0.5–1.5 T), the relaxivities of the two complexes are too close to be exploited for the proposed application. However, it is important to recall that the similar relaxivity values shown by the two systems arise from quite different relaxation pathways.[7, 8] In fact, the relaxivity shown by $[(Mn^{III}\ tpps)^{3-}]$ is dominated by the electronic relaxation time, whereas the relaxivity of $[(Mn^{II}\ tpps)^{4-}]$ is controlled by the rotational motion of the complex (τ_R). On this basis, it was straightforward to pursue a better separation of r_1 values for the two complexes by forming an adduct with a macromolecular substrate; this would only cause a relaxation enhancement for the Mn^{II} system, whose relaxivity is determined by τ_R. This procedure has been widely explored for Gd^{III} chelates to pursue high relaxivities at the imaging fields. Usually the macromolecular adduct is formed through the noncovalent interaction between a suitable functionalized Gd^{III} chelate and serum albumin.[1, 2] In principle, one may exploit an analogous interaction for $[(Mn^{II/III}\ tpps)^{4/3-}]$ complexes, but we decided to work with a more defined system due to the involved chemistry of the porphyrin complexes.[10]

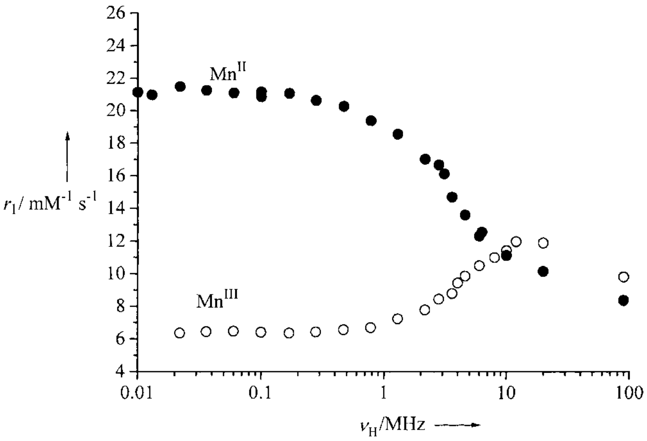
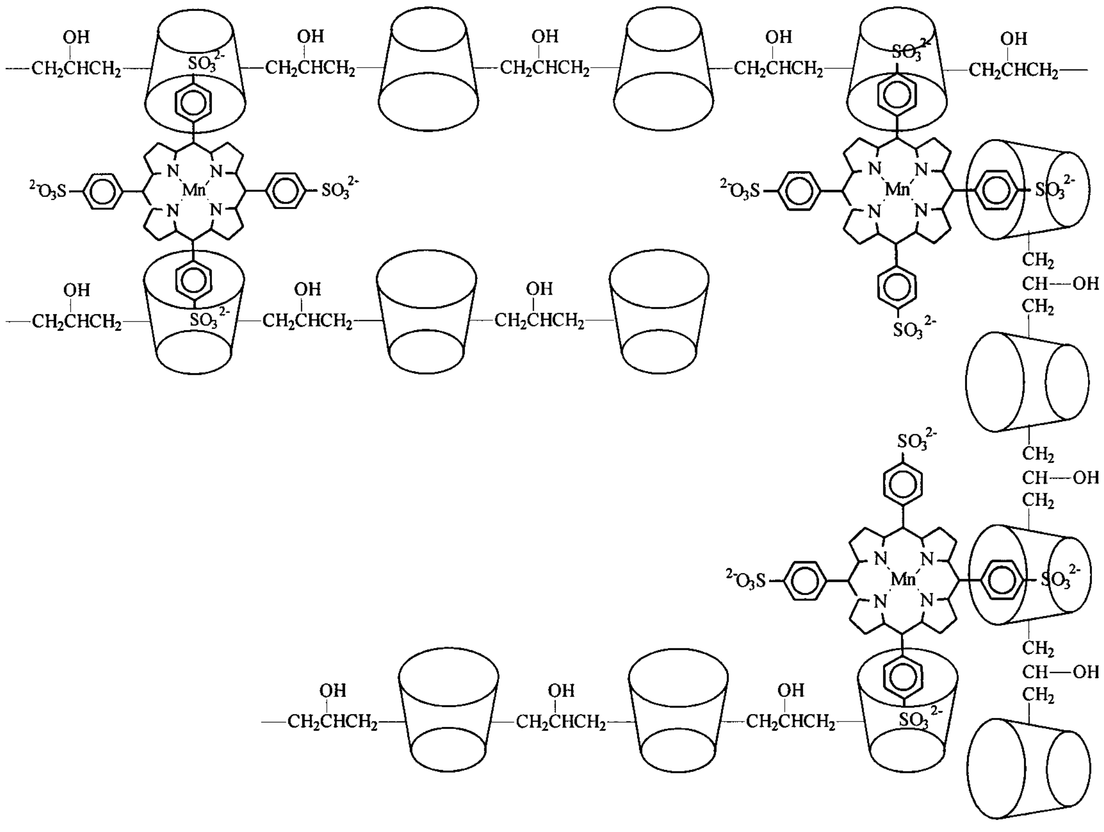


Figure 1. The $1/T_1$ NMRD profile of aqueous solutions (1 mM) of $[(Mn^{II}\ tpps)^{4-}]$ (●) and $[(Mn^{III}\ tpps)^{3-}]$ (○) at pH 7 and 25 °C.

It has been recently reported that, in order to inhibit dimerization reactions of porphyrins, each complex can be encapsulated into cyclodextrin (CD) hosts through the formation of strong interactions between the substituted phenyl rings of TPPS and the cavity of the CD molecule.[11] Although it has been claimed that β-CD can form 1:4 complexes with $[(Zn^{II}\ tpps)^{4-}]$ and $[(Fe^{III}\ tpps)^{3-}]$,[12] molecular modeling studies suggest that only two β-CDs can bind simultaneously to one porphyrin molecule.[13], [14]

To pursue a higher enhancement for $[(Mn^{II}\ tpps)^{4-}]$, a poly-β-CD was employed in place of the monomeric β-CD.[15] The commercially available, water-soluble poly-β-CD used in this work has an average molecular weight of 6000 Da and is a mixture of oligomers containing three to nine CD units. We expected that each poly-β-CD would bind with more than one paramagnetic complex, thus yielding τ_R values much higher than those attainable for the adducts containing only two β-CD units. Furthermore, the close proximity of several β-CD cavities should favor the interaction with the complex to result



Scheme 1. Schematic representation of the supramolecular adduct formed from [(Mn^{II} tpps)$^{4-}$] and the poly-β-CD.

in a high stability of the overall supramolecular adduct (Scheme 1).

In Figure 2, the titration of 0.3 mM solutions of [(Mn^{II} tpps)$^{4-}$] (●) and [(Mn^{III} tpps)$^{3-}$] (○) with poly-β-CD is reported. Analysis of the data gave an nK_A value (where n is the number of the interacting sites) of $9.7 \times 10^4\,M^{-1}$ and a relaxation enhancement factor of 4 for the [(Mn^{II} tpps)$^{4-}$] complex. The interaction strength of Mn^{III} complex was similar but, as expected, there was only a very small relaxation enhancement for the macromolecular adduct. It appears reasonable to assume that the latter enhancement arises from second- and/or outer-sphere water protons. It follows that the formation of macromolecular adducts with poly-β-CD allows us to deal with r_1 values of 40.8 mM^{-1}s^{-1} and 15.2 mM^{-1}s^{-1} for [(Mn^{II} tpps)$^{4-}$] and [(Mn^{III} tpps)$^{3-}$], respectively.

The ability of [(Mn^{II} tpps)$^{4-}$] to act as a $p(O_2)$-responsive agent has been tested in vitro by measuring the relaxation rates of solutions containing a fixed amount of the complex (0.125 mM) and variable amounts of added oxygen gas in a sealed NMR tube.

The results (Figure 3) clearly indicate that in the presence of 40 torr of O_2 (after 5 min and with vigorous shaking) there has been a complete oxidation of [(Mn^{II} tpps)$^{4-}$] into [(Mn^{III} tpps)$^{3-}$]. Below this value the observed relaxivities appear

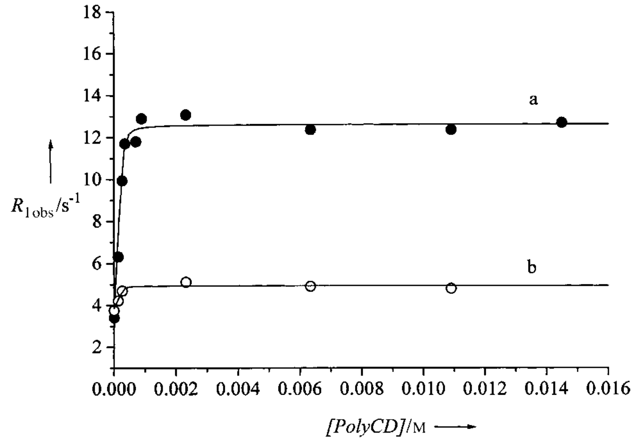


Figure 2. Plot of the water proton relaxation rate of solutions (0.2 mM) of [(Mn^{II} tpps)$^{4-}$] (●) and [(Mn^{III} tpps)$^{3-}$] (○) as a function of the poly-β-CD concentration (20 MHz, 25 °C, pH 7).

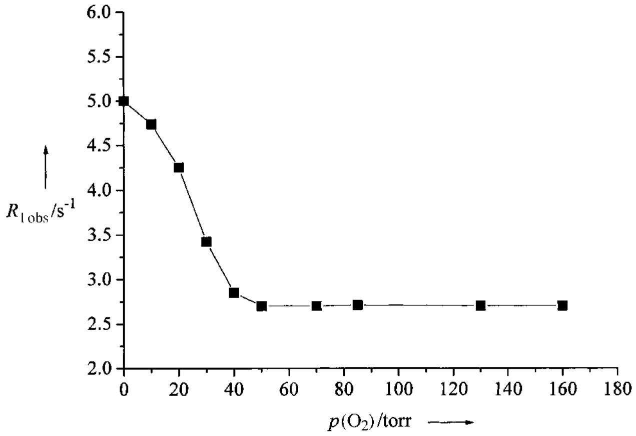


Figure 3. Plot of pO_2-dependence of the water proton relaxation rate of solutions (0.125 mM) of [(Mn^{II} tpps)$^{4-}$]/[(Mn^{III} tpps)$^{3-}$] (20 MHz, 25 °C, pH 7).

proportional to the applied $p(O_2)$, thus providing a very useful tool for reporting the relative amount of oxygen present in the region of interest in a magnetic resonance image.

The relaxometric response may be modulated, according to the requirements of a given functional protocol, by introducing suitable substituents on the aromatic moieties of the porphyrin ring to control the thermodynamics and kinetics of the Mn^{II}/Mn^{III} switch. Moreover one may envisage several ways to attain longer τ_R values—either by dealing with covalent macromolecular conjugates or by forming supramolecular adducts by interlocking of molecular components other than those used in this work.

Experimental Section

The formation of $[(Mn^{II}\ tpps)^{4-}]$ from $[(Mn^{III}\ tpps)^{3-}]$ (Porphyrin Products, UT, USA) and $Na_2S_2O_3$ was monitored by UV spectroscopy following the growth of the band at 428 nm and the disappearance of the band at 466 nm, typical for the +3 oxidation state. The binding affinity of the two complexes with poly-β-CD was determined by measuring the water proton relaxation rates of a solution of the complex (about 0.2 mM) with increasing amounts of the poly-β-CD substrate (0.2–14 mM). The data obtained were fitted with those calculated on the basis of the established theory of proton relaxation enhancement. The $1/T_1$ NMRD curves were obtained on a fully automatic Field-Cycling Relaxometer (Stelar, Mede, PV, Italy) in the frequency range of 0.01–12 MHz. Data at higher frequencies were obtained on a Stelar Spin-Master Relaxometer (20 MHz) and on a Jeol EX-90 (90 MHz). The titrations with poly-β-CD and the assessment of $[(Mn^{II}\ tpps)^{4-}]$ as a pO_2-responsive agent were carried out at 20 MHz and 298 K.

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Electrophilic Aromatic Substitution Reactions of a Metallabenzene: Nitration and Halogenation of the Osmabenzene [Os{C(SMe)CHCHCHCH}I(CO)(PPh$_3$)$_2$]**

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It was established at the outset, with the isolation of the first metallabenzenes,[1] that these compounds exhibit physical properties that are consistent with the presence of an aromatic ring system. The osmabenzene [Os(CSCHCHCHCH)(CO)(PPh$_3$)$_2$] displays ring planarity, equal Os–C distances intermediate between normal Os–C single and double bonds, C–C distances comparable to that found for benzene, and NMR chemical shifts appropriate for an aromatic system. The related iridabenzene [Ir(CHCMeCHCMeCH)(PEt$_3$)$_3$],[2] which has been extensively studied, shows similar physical properties.[3] A recently reported, but differently substituted iridabenzene, [Ir(CPhCPhCHCHCH)(CO)(PPh$_3$)$_2$], again shows physical properties consistent with aromaticity.[4]

Despite the considerable weight of physical evidence pointing towards aromaticity for metallabenzenes, the reaction chemistry so far reported does not entirely reflect this. For example the iridabenzene [Ir(CHCMeCHCMeCH)(PEt$_3$)$_3$] has a propensity to undergo cycloaddition reactions rather than electrophilic substitutions.[3a] Other metallabenzenes are unstable with respect to rearrangement to cyclopentadienyl–metal complexes.[5] One hint of more conventional aromatic behavior is given by the formation of η^6 complexes with other metal–ligand fragments, for example, [{η^6-CH=CMeCH=CMeCH=Ir(PEt$_3$)$_3$}Mo(CO)$_3$].[6] Several related metallabenzene η^6 complexes have also been described.[7]

Here we describe: 1) the first examples of electrophilic aromatic substitution of a metallabenzene, specifically both mononitration and monohalogenation of the osmabenzene [Os{C(SMe)CHCHCHCH}I(CO)(PPh$_3$)$_2$] (**1**) and 2) structure determinations of both the nitrated and brominated products, which reveal 3) the operation of a *para*-directing effect of the SMe ring substituent.

Treatment of the brown osmabenzene [Os(CSCHCHCHCH)(CO)(PPh$_3$)$_2$],[1, 8] with MeI produces the blue osmabenzene **1**, which bears an SMe substituent on the carbon atom adjacent to the osmium center (Scheme 1). The geometry of **1** has been confirmed by an X-ray crystal structure determination of its blue chloride analogue.[9] When **1** is subjected to the mild nitrating conditions offered by Cu(NO$_3$)$_2$/acetic anhydride and the crude reaction product

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