Cytotoxicity: HL-60 (human promyelocytic leukemia) cells were cultured in a 24-well culture plate (5×10^4 mL^{-1}). The cells were exposed to various amounts of LDH (1–1000 μg mL^{-1}). A control experiment was performed without LDH under the same conditions. Cell viability was determined daily over four days by an MTT assay.[9]

HL-60 cell growth: HL-60 cells were cultured in a 24-well culture plate (5×10^4 mL^{-1}). The cells were exposed to As-*myc*-LDH (20 μM). The sequence of As-*myc* is 5′-d-(AACGTTGAGGGGCAT)-3′ and complementary to the initiation codon and the next four codons of c-*myc* mRNA. Control experiments were performed with only As-*myc* (20 μM) and without As-*myc* or As-*myc*-LDH complex under the same conditions. Cell viability was determined daily over four days by MTT assay.[9]

Received: March 24, 2000
Revised: May 30, 2000 [Z14893]

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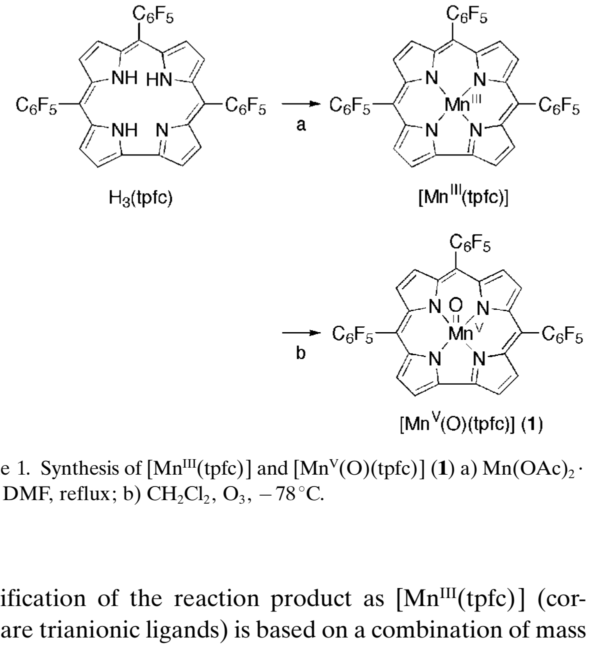
Epoxidation Catalysis by a Manganese Corrole and Isolation of an Oxomanganese(V) Corrole**

Zeev Gross,* Galina Golubkov, and Liliya Simkhovich

The milestones in metalloporphyrin-catalyzed oxygenation of hydrocarbons are the 1979 and 1980 publications of Groves, Hill, and their coworkers about the utilization of iron(III) and manganese(III) porphyrins as catalysts for the epoxidation of olefins by iodosylbenzene.[1] Similar mechanisms were proposed in both cases, oxygen atom transfer from iodosylbenzene to the catalyst to form a *formally* oxometal(V) porphyrin intermediate, which subsequently transfers its oxygen atom to the substrate.[2] But, while trapping and extensive spectroscopic characterization of the intermediate in the iron porphyrin catalysis started as soon as 1981,[3] oxomanganese(V) porphyrins remained elusive for a very long time.[4] Only in 1999 did Jin and Groves succeed in obtaining the ^{1}H NMR spectrum of such a complex, the diamagnetism of which provides the strongest proof of the structure.[5]

Recently we got involved in the chemistry of corroles; long known tetrapyrroles, whose skeleton may be viewed as either the one carbon atom short analogues of porphyrins or as the aromatic version of corrin, the ligand bound to cobalt in the coenzyme of Vitamin B_{12}.[6, 7] We first introduced an extremely facile synthesis of 5,10,15-tris(pentafluorophenyl)corrole (H_3(tpfc)),[8, 9] from which a novel class of chiral macrocycles can easily be obtained.[10] In addition, we have demonstrated that the metal complexes of H_3(tpfc) are potent catalysts.[11] Specifically, the iron(IV) complex [Fe(tpfc)Cl]-catalyzed the oxygen-atom transfer from iodosylbenzene to both styrene and ethylbenzene. Assuming an analogy to metalloporphyrin catalysis, in which manganese complexes are equally or even more active than iron porphyrins,[2a] we decided to investigate manganese corroles.[12] Motivation for the present research was that the ability of corroles to stabilize high oxidation states is superior to that of porphyrins,[13] the thermal stability of iron(IV) corroles being the most relevant example.[14] Herein we report that the manganese(III) complex [Mn(tpfc)] is an interesting epoxidation catalyst and the successful isolation of an oxomanganese(V) corrole.

The metallation of H_3(tpfc) was achieved in high yields by reaction with excess $Mn(OAc)_2\cdot 4H_2O$ in DMF (Scheme 1).[15]



Scheme 1. Synthesis of [Mn^{III}(tpfc)] and [Mn^{V}(O)(tpfc)] (**1**) a) $Mn(OAc)_2\cdot 4H_2O$, DMF, reflux; b) CH_2Cl_2, O_3, −78 °C.

Identification of the reaction product as [Mn^{III}(tpfc)] (corroles are trianionic ligands) is based on a combination of mass spectroscopy, NMR, and UV/Vis spectroscopy, and comparison to reported manganese corroles. Interestingly, both the green color and the UV/Vis spectrum of [Mn(tpfc)] (Figure 1a) are remarkably similar to that of manganese(III) porphyrins.[16] Most relevant are the split Soret band and the

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[**] We acknowledge the partial support of this research by “The Fund for the Promotion of Research at the Technion”.

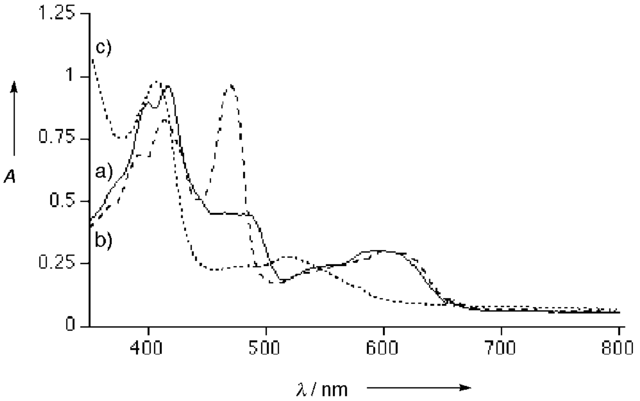
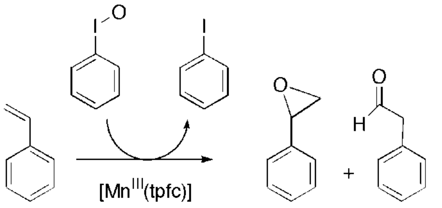


Figure 1. The electronic spectrum of a) [Mn^{III}(tpfc)] in CH_2Cl_2 (full line) and the changes upon addition of b) triphenylphosphane oxide (broken line), and c) iodosylbenzene (dotted line). *A* = absorbance.

changes in the relative intensities of the bands at 398 and 414 nm, and the band at 478 nm upon coordination of triphenylphosphane oxide (Figure 1a and b). But, the [Mn^{III}(tpfc)]-catalyzed epoxidation of styrene by iodosylbenzene (Scheme 2) proceeded very differently to the same reaction with manganese(III), iron(III) porphyrins, or even [Fe^{IV}(tpfc)Cl] as catalysts. First, although the expected products—styrene oxide and phenyl acetaldehyde—were formed in high yields (Scheme 2), it took 4–10 h for completion of the reaction. More importantly, we noted an immediate color change from bright green to light red upon addition of iodosylbenzene, which persists until all the oxidant is consumed. Furthermore, the red color and the single Soret band at 412 nm (Figure 1c) are very similar to those of oxomanganese(IV) and oxomanganese(V) porphyrins.[17]



Scheme 2. The [Mn^{III}(tpfc)]-catalyzed epoxidation of styrene by iodosylbenzene. Reaction conditions: styrene (1.2 mmol), iodosylbenzene (0.12 mmol), catalyst (1.2 μmol), solvent (1 mL benzene or CH_2Cl_2), room temperature, 4–10 h, under Ar or aerobic. Results, in benzene, under Ar, 10 h: 77 % epoxide, 12 % aldehyde. In benzene, aerobic, 4 h, 74 % epoxide, 16 % aldehyde. In CH_2Cl_2, under Ar, 6 h: 76 % epoxide, 22 % aldehyde. In CH_2Cl_2, aerobic, 6 h, 80 % epoxide, 20 % aldehyde.

Since we suspected that the observed species is an oxomanganese(V) corrole, we examined the low-temperature oxidation of [Mn(tpfc)] by spectroscopy. Instead of iodosylbenzene, which is very insoluble and also produces iodobenzene, ozone was chosen as the oxidant. The only byproduct from the reaction with ozone is the easily removable O_2, and has been successfully utilized for the clean oxidation of iron(III) porphyrins to oxoiron(IV) porphyrin cation radicals.[18] The large spectroscopic changes that occur upon the ozonolysis of [Mn^{III}(tpfc)] to [Mn^{V}(O)(tpfc)] (**1**; Scheme 1) are shown in Figures 2 and 3.[19] The ^{19}F NMR spectrum of [Mn^{III}(tpfc)] displays paramagnetically broadened resonances (Figure 2a), which in the spectrum of **1** are fully converted into sharp signals containing the expected F,F coupling pattern (Figure 2b, and also Figure 2c which shows the ^{1}H NMR spectrum of the same solution). In addition, the color of the mixture changes from green to red, this is accompanied by large changes in the electronic spectrum (Figure 3a). Finally, the addition of excess triphenylphosphane to the ozonolysis product **1** resulted in its conversion into the triphenylphosphane oxide coordinated manganese(III) corrole [Mn($OPPh_3$)(tpfc)], as may be appreciated by comparing Figure 3b and Figure 1b. All these results—the mass spectroscopy, the diamagnetism demonstrated in the NMR spectra, the red color, the single Soret band, and the oxidation of triphenylphosphane—lead to the safe conclusion that **1** is indeed an authentic oxomanganese(V) corrole, [Mn^{V}(O)(tpfc)].[20]

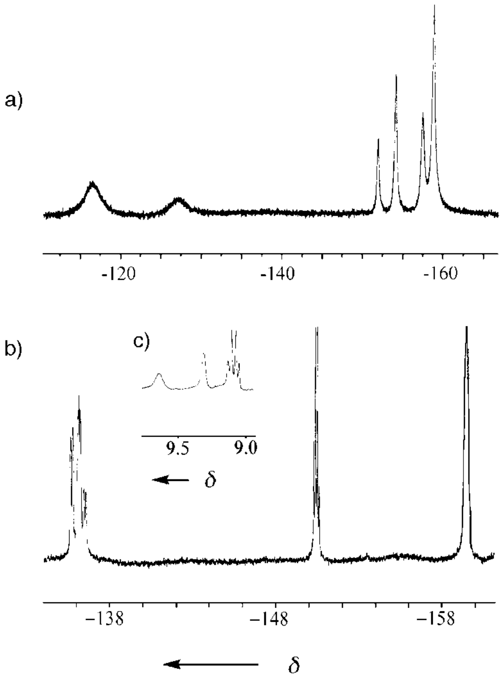


Figure 2. The −80 °C ^{19}F NMR spectra of a) [Mn^{III}(tpfc)] and b) **1**, c) the ^{1}H NMR spectrum of the same solution of **1**.

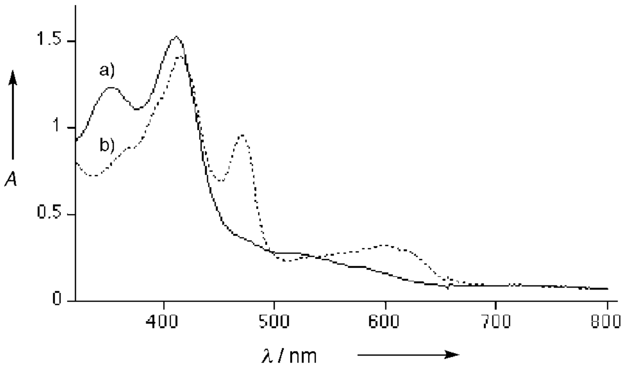


Figure 3. a) the room temperature UV/Vis spectrum of [Mn^{V}(O)(tpfc)] (**1**) (full line) and b) after the addition of triphenylphosphane (dotted line). *A* = absorbance.

Importantly, the color and UV/Vis spectrum of **1** produced by ozonolysis (Figure 3a) are identical to those observed during the room-temperature catalytic reaction (Figure 1c). This observation suggests that the catalytic epoxidation of styrene proceeds by fast oxygen-atom transfer from iodosylbenzene to [Mn(tpfc)], followed by slow oxidation of the olefin by **1**. To check this postulate, we took aliquots of a concentrated solution of **1** in CH_2Cl_2 at low temperature and transferred them into a spectrophotometric cell with solvent (either benzene or CH_2Cl_2) at room temperature. Much to our surprise, the complex is stable under these conditions for many hours. Furthermore, even the addition of a large excess of styrene did not affect the spectrum (whereas **1** reacted with triphenylphosphane, see above). Accordingly, **1** can not be *the* reactive intermediate in the epoxidation of styrene by iodosylbenzene. A plausible explanation to account for all the observations—styrene being oxidized in the catalytic reaction, clear evidence for the formation of **1** during catalysis, and the inertness of isolated **1** toward styrene—is that a higher valent complex, formed by disproportionation of **1**, is *the* reactive intermediate. Supporting evidence for this proposal comes from the observation that the life time of **1** at *room temperature* depends very much on its concentration. In the dilute solutions used for the UV/Vis experiments (in the range of 10^{-5} M) it is stable for many hours, but it bleaches within less than one minute at higher concentrations (in the range of 10^{-3} M).

In conclusion, we have demonstrated that [Mn^{III}(tpfc)] is a mild epoxidation catalyst and an excellent precursor for preparation of an authentic oxomanganese(V) corrole, that is much more stable than corresponding porphyrin complexes. Further investigation of this and other high-valent metal corrole complexes will certainly lead to additional unique complexes, which will serve to address the puzzle of the peculiar stabilization of high oxidation states by corroles.

Received: February 15, 2000 [Z14707]

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[15] A solution of H_3(tpfc) (50 mg, 63 μmol) and manganese(II) acetate tetrahydrate (154 mg, 630 μmol) in DMF (10 mL) was heated to reflux for 10 min. Evaporation of the solvent, followed by column chromatography on silica gel (32–63 Å, 10:1 hexane:ethyl acetate), resulted in the isolation of [Mn(tpfc)] (48.8 mg, 91%). MS (CI^+, isobutane): *m/z* (%): 849 (95) [MH^+], 848 (100) [M^+]; UV/Vis (CH_2Cl_2): λ_{max}[nm]($\lg \varepsilon$) = 400 (4.62), 416 (4.64), 482 (4.29); ^1H NMR ($CDCl_3$): $\delta = 21.4$ (br s, 2H), −17.0 (br s, 2H), −42.0 (br s, 2H), −116.5 (v br s, 2H); ^{19}F NMR ($CDCl_3$): $\delta = -116.5$ (br s, 2F), −127.1 (br s, 4F), −151.9 (br s, 1F), −154.0 (br s, 2F), −157.4 (br s, 2F), −158.7 (br s, 4F).

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[19] A solution of [Mn(tpfc)] (3–10 mg) in CD_2Cl_2 or CH_2Cl_2 (1–5 mL) cooled in a dry ice/acetone bath was purged with a stream of O_3/O_2 until the color change from green to red was complete, the mixture was then purged with N_2. The solutions were stable for weeks at −80 °C. Evaporation of the solvent at −78 °C gave a red solid. Dilute solutions ($< 10^{-5}$ M) of the solid material were stable for many hours at room temperature, but more concentrated solutions decomposed quite fast (in less than one minute for a 10^{-3} M solution), as indicated by the color change to brown and by UV/Vis spectroscopy (absence fo λ_{max} at >350 nm). [Mn(O)(tpfc)] (**1**): MS (CI^+, isobutane): *m/z* (%): 865 (3) [MH^+], 864 (3) [M^+], 849 (100) [$MH^+ - O$], 848 (85) [$M^+ - O$]; UV/Vis (CH_2Cl_2): λ_{max}[nm] = 412 (Soret), 515 (sh). ^1H NMR (CD_2Cl_2, 193 K): $\delta = 9.6$ (br s, 2H), 9.3 (br s, 2H), 9.12 (d, $J = 5.0$ Hz, 2H), 9.06 (d, $J = 5.0$ Hz, 2H); ^{19}F NMR (CD_2Cl_2, 193 K): $\delta = -135.7$ (d, $J = 20.5$ Hz, 2F), −136.2 (two overlapping d, 3F), −136.5 (d, $J = 19.4$ Hz, 1F), −150.4 (t, $J = 21.4$ Hz, 2F), −150.5 (t, $J = 21.1$ Hz, 1F), −159.5 (m, 6F).

[20] The alternative formulation of **1** as an oxomanganese(IV) corrole radical, in which the d^3 metal is low spin and antiferromagnetically coupled to the radical, is much more restrictive. Also, such a complex is expected to absorb in the >700 nm region and to be green.