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AN EFFICIENT METHOD FOR THE SYNTHESIS OF MANGANESE(III)*MESO*-TETRAARYLPORPHYRINS

Gholam A. Mirafzal*, Heather M. Bosse', and Jolene M. Summer

Department of Chemistry, Drake University, Des Moines, Iowa 50311
E-Mail: Gholam.Mirafzal@Drake.Edu.

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ABSTRACT: Manganese(III)*meso*-tetraarylporphyrins (e.g., MnTPPCl, MnT(PCl)PPCl, MnT(PMe)PPCl), MnT(ONO_2)PPCl, MnT(DCl)PPCl) were synthesized in a one-pot reaction from freshly distilled pyrrole and the corresponding pure aldehyde (benzaldehyde, *p*-chlorobenzaldehyde, *p*-methylbenzaldehyde, *o*-nitrobenzaldehyde, and 2,6-dichlorobenzaldehyde) by the action of manganese(II) chloride, $MnCl_2$, as a template in a phenol medium. Up to 71% yields of pure Manganese(III)*meso*-tetraarylporphyrins were obtained in a short period of time. © 1999 Elsevier Science Ltd. All rights reserved.

The modeling of cytochrome P-450 monooxygenase enzymes using simple chemical systems has been undertaken with the goal of understanding the essential components of oxygen activation and the nature of the active species responsible for the remarkable reactivity of the enzyme.

In 1979, Groves reported the first successful biomimetic catalytic system in which a synthetic metalloporphyrin catalyzes the hydroxylation and epoxidation of certain hydrocarbons in the presence of iodosylbenzene.[1] This important finding that cytochrome P-450 together with suitable oxygen atom donors will anaerobically oxygenate substrates has given birth to a new approach: direct formation of the high valent metal-oxo porphyrin species using synthetic metalloporphyrins and oxygen atom transfer reagents. The Groves' discovery sparked what is now a large and dynamic field dedicated to understanding better the chemistry of P-450 itself through the study of model reactions.[2]

Among the synthetic metalloporphyrins, manganese(III)*meso*-tetraarylporphyrins are widely used as catalysts for oxidation of hydrocarbons.[2] However, the published methods for its synthesis[3,5] lack one or more of the following criteria. (a) complete (100%) metal insertion into the porphyrin cavity, (b) short reaction time and/or high yield of porphyrin products, (c) ease of isolation and purification of the porphyrin products, (d) low cost of the overall experimental method and procedure.

In this paper, we wish to report the first one-pot synthesis of manganese(III)*meso*-tetraarylporphyrins, by reacting pyrrole and the corresponding aldehyde in the presence of $MnCl_2$ in phenolic media (Scheme I). This method not only is economical and convenient but also produces complete metallation in a shorter period of time with a higher yield of manganese tetraarylporphyrin products than any of the previously published methods.[3]

Since the new method gives products which are free of unmetallated tetraaryl porphyrins, purification becomes much easier.

All of the published literature methods for the synthesis of manganese(III)*meso*-tetraarylporphyrins begin with pure free-based porphyrins. For example, $TPPH_2$ is usually synthesized by Rothemund's condensation[3a], which gives a 20-25% yield of crystalline material, containing 1-2% of tetraphenylchlorin ($TPCH_2$). The $TPCH_2$ is removed either by column chromatography or more commonly by its oxidation with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ)[4] to the corresponding $TPPH_2$. The purified $TPPH_2$ is then subjected to the metallation process.[5] Our results show that these separated consecutive steps can be eliminated by preparing MnTPPCl, MnT(PCl)PPCl, MnT(PMe)PPCl, MnT(ONO_2)PPCl, and MnT(DCl)PPCl in a one-pot reaction by

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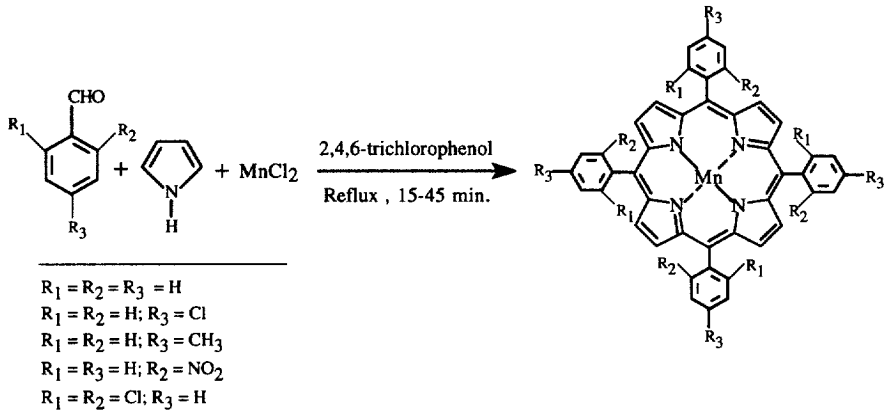
reacting pyrrole and the corresponding aldehyde in the presence of $MnCl_2$ in phenolic media (Scheme I).



Scheme I. One-Pot Synthesis of Manganese(III)*Meso*-Tetraarylporphyrins

This method produces MnTPPCl, MnT(PCl)PPCl, MnT(PMe)PPCl, MnT(ONO_2)PPCl, and MnT(DCl)PPCl catalysts in yields of 71%, 66%, 65%, 58%, 61% respectively. Under similar experimental conditions in the absence of $MnCl_2$, a much lower yield of corresponding free-based porphyrins were obtained suggesting that manganese chloride acts as a template in synthesizing these porphyrins (Table I). Our experimental procedures are not only very efficient, convenient, and cost effective, but also produces a higher yields of manganese porphyrin products in a shorter period of time.[6-8]

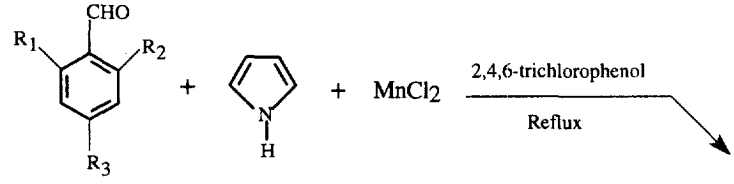
We found phenols, in particular, 2,4,6-trichlorophenol (pK_a = 6.1) as good choices of solvent for these acid-catalyzed reactions because the manganese tetraaryl porphyrins form rapidly in these media. This observation can be explained in terms of the solubility of the reactants in the phenol and particularly in terms of the high pK_a's associated with this class of compounds. Further, phenol can be easily converted to phenoxide ion and removed from the metalloporphyrin products by subsequent extraction with an aqueous solution of base (e.g., KOH, NaOH, etc.) and with the aid of dichloromethane solvent. Uv-vis spectra of porphyrin as solution in dichloromethane reveals absence of 2,4,6-trichlorophenol (λ max = 296 nm) in the mixture prior to purification by column chromatography.

This new method of synthesis for manganese(III)porphyrins works equally well for the sterically hindered porphyrins such as those of *meso*-tetrakis(2-nitrophenyl)porphyrinato manganese(III)chloride, *meso*-tetrakis(2,6-dichlorophenyl)porphyrinato manganese(III)chloride, and *meso*-tetrakis(2,4,6-trimethoxyphenyl) porphyrinato manganese(III)chloride.

The experimental results shown in Table I indicate that our methods and procedures are significantly better than the previously published methods for the synthesis of these manganese porphyrins. We believe that the formation of manganese porphyrins are improved greatly by using the one-pot reaction from the corresponding aldehyde and pyrrole, using a metal template than the separated consecutive steps reported in the literature.[3] Using the published methods and procedures, one is able to obtain a 20-25% yield of a mixture of products ($TPCH_2$ and $TPPH_2$) by Adler's method. Thus, even after oxidation of $TPCH_2$ to $TPPH_2$ by DDQ and conversion of pure $TPPH_2$ to MnTPPCl, one can not obtain more than 20-25% overall yields of the MnTPPCl

product. Our method and procedure not only is facile, efficient, and cost effective but also produce high yields of up to 71% for manganese porphyrins in a one-pot synthesis.

Table I. Summary of the Results for One-Pot Synthesis of Manganese(III) *Meso*-Tetraarylporphyrins in Phenolic Medium



Runs			Product(s)	Yield(%)	Reaction time(Min)
I. $R_1=R_2=R_3=H$	//	–	$TPPH_2$[a]	25	15
II. $R_1=R_2=R_3=H$	//	+	MnTPPCl[b]	71	15
III. $R_1=R_2=H;R_3=Cl$	//	–	$T(PCl)PPH_2$[a]	21	45
IV. $R_1=R_2=H;R_3=Cl$	//	+	MnT(PCl)PPCl[b]	66	45
V. $R_1=R_2=H;R_3=Me$	//	–	$T(PMe)PPH_2$[a]	22	30
VI. $R_1=R_2=H;R_3=Me$	//	+	MnT(PMe)PPCl[b]	65	30
VII. $R_1=R_3=H;R_2=NO_2$	//	–	$T(ONO_2)PPH_2$[a]	18	15
VIII. $R_1=R_3=H;R_2=NO_2$	//	+	$MnT(ONO_2)PPCl$[b]	58	15
IX. $R_1=R_2=Cl;R_3=H$	//	–	$T(DCl)PPH_2$[a]	19	45
X. $R_1=R_2=Cl;R_3=H$	//	+	MnT(DCl)PPCl[b]	62	45

[a] Contains tetraaryl chlorin.
[b] Yields are after final purification.

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6. Materials and Methods: Pyrrole, benzaldehyde, *p*-methylbenzaldehyde, *p*-chlorobenzaldehyde, *o*-nitrobenzaldehyde, 2,6-dichlorobenzaldehyde, manganese(II) chloride (anhydrous), and 2,4,6-trichlorophenol were all purchased from Aldrich Chemical Company and were used without further purification. Thin layer chromotography (TLC) was performed on Eastman Kodak TLC plates (coated film, #13179) with a fluorescence indicator. Ultraviolet and Visible spectra were measured on a Beckman DU 7500 spectrophotometer.
7. General Procedure: A mixture of 9.11×10^{-4} mole of aldehyde (benzaldehyde, *p*-chlorobenzaldehyde, *p* methylbenzaldehyde, *o*-nitrobenzaldehyde, 2,6-dichlorobenzaldehyde), 9.11×10^{-4} mole of pyrrole, 0.145 g (1.16×10^{-3} mol) of $MnCl_2$, 1.5 g of 2,4,6-trichlorophenol was brought to reflux, and the progress of reaction was monitored by TLC (CH_2Cl_2) and/or by UV-Visible spectroscopy in dichloromethane or methanol. After completion of reaction (100% metallation, 15-45 minutes), the heat was removed and the flask cooled to room temperature. The mixture was dissolved in a small amount of dichloromethane and passed through a column of activated neutral alumina eluting trichlorophenol with hexane, unmetallated porphyrin with dichloromethane, and metallated porphyrin with methanol.
   The following porphyrins were synthesized by this method:
   MnTPPCl: isolated yield, 71%; λ max(CH_2Cl_2)found: 376, 403, 478(Soret band), 532, 582, 619 nm.
   MnT(PCl)PPCl: isolated yield, 66%; λ max(CH_2Cl_2)found: 379, 405, 479(Soret band), 582, 621 nm.
   MnT(PMe)PPCl: isolated yield, 65%; λ max(CH_2Cl_2)found: 377, 400, 478(Soret band), 582, 619 nm.
   MnT(ONO_2)PPCl: isolated yield, 58%; λ max(CH_2Cl_2)found: 377, 401, 469(Soret band), 571, 611 nm.
   MnT(DCl)PPCl: isolated yield, 62%; λ max(CH_2Cl_2)found: 371, 398, 476(Soret band), 526, 580, 612 nm.
8. The large scale reaction involving 10 mmole of aldehyde (e.g., benzaldehyde), 10 mmole of pyrrole, 12.5 mmole (1.56 g) of $MnCl_2$, 15 g of 2,4,6-trichlorophenol produced manganese porphyrins with yields of about 10% lower than those listed in the table I. We suggest that in the large scale reactions, it is more practical to remove the 2,4,6-trichlorophenol by subsequent extraction with an aqueous solution of base (e.g., 2M potassium hydroxide) prior to purification of porphyrins by column chromatography.