Octopus Manganese Porphyrin with Polyglycol Chains as a Catalyst for the -Selective Epoxidation of Cholesterol Derivatives

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Abstract: Synthesis of a novel octopus porphyrin with polyglycol chains **1a** was achieved. The catalytic activity of **1a**'s manganese complex for the epoxidation of cholesterol derivatives with PhIO give a satisfactory conversion and regioselectivity.

Keywords: Octopus porphyrin, synthesis, epoxidation, cholesterol derivatives.

Recently the biologic and catalytic activity of dendritic macromolecule metal complexes have been paid more and more attention^{1,2}. It inspired us to design the novel octopus porphyrin **1a** as shown in **Scheme 1**. **1a** reacts with $Mn(OAc)_2$ to form the complex of manganese porphyrin **1b**, which can catalyze the epoxidation of cholesterol derivatives using PhIO as oxidant. The reaction was highly -selective.



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Results and Discussion

From the convergent approach method for general dendrimer synthesis³, we synthesized the octopus porphyrin **1a**. The synthetic route of $\mathbf{1a}^4$ and its manganese complex $\mathbf{1b}^5$ is described as follows.



Reagents and conditions: a. CH_3SO_2Cl , NEt_3 , CH_2Cl_2 , -10; b. methyl 3,5-dihydroxy benzoate, K_2CO_3 , acetone, overnight reflux; c. LiAlH₄, THF, reflux 2 h; d. CH_3SO_2Cl , NEt_3 , CH_2Cl_2 , -10; e. propanic acid, 136, 20 min; f. K_2CO_3 , DMF, 80, 6 h.

Dendrimer **6** can be easily produced from polyethylene glycol monomethyl ether (PEG400, MW 428) **2** by four steps in turn⁶. Octopus porphyrin **1a** was obtained by a coupling reaction of four equivalents of dendrimer **6** to one equivalent of 5,10,15,20-tetrakis(4-hydroxyphenyl)porphyrin **8**⁷. **1a** was reacted with manganese(II) acetate in N,N-dimethylformamide to produce octopus manganese porphyrin complex **1b**.

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The 5,10,15,20-tetrakis(4-hydroxyphenyl) porphyrin **8** shows Soret band at 421 nm in the UV/Vis spectra. However the Soret band of manganese complex shifted to 481 nm. It demonstrated the formation of manganese complex.

It is well known that the epoxidation is one of the most important functionalization methods of carbon-carbon double bond, and the epoxides are valuable intermediates for laboratory synthesis as well as chemical manufacturing⁸. To evaluate catalytic properties of **1b**, we investigated its catalytic activities and selectivities in the epoxidation of cholesteryl acetate⁹ (**Scheme 3**). All the epoxidation reactions were carried out in a sealed flask under nitrogen. The substrate conversion, epoxide yield and the ratio of α - and β -isomers were determined¹⁰ by ¹H-NMR (400 MHz) measurements in the presence of *trans*-stilbene as internal standards.



1 R=AcO; 2 R=PhCOO; 3 R=MsO; 4 R=TsO; 5 R=Cl

Substrate	Conv.% ^b	Yield $\%(\alpha+\beta)^{b}$	β-selectivity% ^b
1	98	97	73
2	98	91	98
3	80	96	63
4	68	97	78
5	69	94	98

Table 1 Epoxidation of Δ^5 -steroids derivatives with PhIO catalyzed by $\mathbf{1b}^a$.

^aAll reactions were carried out in CH_2Cl_2 at 20 for 48 h with **1b** as the catalyst, the molar ratio of **1b**:PhIO:alkene was 1:1500:1250. ^bdetermined by ¹H-NMR.

It is confirmed from our research that catalyst **1b** exhibited high catalytic activity and selectivity toward the epoxidation of cholesterol derivatives with oxidant iodosylbenzene at proper temperature and time.

In conclusion, this is a convenient procedure for preparing **1b** without tedious chromatographic separation and this octopus catalyst has high catalytic reactivity and selectivity to unfunctionalized alkenes.

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- 4. Compound **1a:** ¹H-NMR (400 MHz, CDCl₃, TMS) δ (ppm): 7.74 (d, 8H, J=8Hz, Ph-H), 7.33 (d, 8H, J=8Hz, Ph-H), 6.86 (s, 8H, Ph-H), 6.78 (s, 4H, Ph-H), 6.59-6.40 (m, 8H, Pyrrol-H), 5.28 (s, 8H, OCH₂Ph), 3.67-3.50 (m, OCH₂-, N-H), 3.37 (s, 24H, CH₃O-); IR (KBr, cm⁻¹): 3484 (NH), 2872 (CH₂), 1596 (Ar-H), 1108 (C-O-C); UV/Vis (λ_{max} , CHCl₃, nm): 421(soret), 518, 555, 650.
- 5. Synthesis of **1b**:A mixture of **1a** (668 mg, 0.15 mmol), Mn(OAc)₂·4H₂O (98 mg, 0.4 mmol) and DMF (40 mL) was refluxed for 24 h, then distilled to dryness under reduced pressure. To the residue was added dichloromethane (30 mL). The solid was filtrated off. The filtrate was washed with water (3×10 mL), dried over Na₂SO₄ and evaporated to dryness. The residue was chromatographed on silica gel with methanol/dichloromethane (1:10) as the eluent to get green product (466 mg), yield 69%. The content of manganese 0.18 mmol/ 1 g **1b**. UV/Vis (λ_{max}, CHCl₃, nm): 481 (soret), 587, 624.
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- 9. Procedure for epoxidation of alkenes catalyzed by octopus manganese porphyrin **1b** using PhIO as oxidant. A mixture of alkene (20 mg, 0.046 mmol), PhIO (12.3 mg, 0.056 mmol), and **1b** (0.17 mg, 3.7×10⁻⁵ mmol) in CH₂Cl₂ (4 mL) were stirred at room temperature. When the reaction was completed (detected by TLC). The solid was filtrated off. The filtrate was evaporated *in vacuo* to remove the solvent and the residue was analyzed by ¹H-NMR(400 MHz) to determine the conversion, yield and selectivity.
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