Synthesis and Characterization of β-Cyclodextrin Bonded Metal Porphyrins

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Reactions of 5-(*p*-aminophenyl)-10,15,20-triphenyl porphyrin (1) with $Ru_3(CO)_{12}$ or $M(OCOCH_3)_2$ (M = Ni, Mn) afforded metalloporphyrins (4—6), respectively. 6-Deoxy-6-iodo-β-cyclodextrin (2) and mono(6-*O*-trifluoromethanesulfonyl) permethylated β-cyclodextrin (3) reacted with complexes 4—6 to give β-cyclodextrin bonded metal porphyrins (7—9) and permethylated β-cyclodextrin bonded me-tal porphyrins (10—12) respectively. These new complexes were identified by MS, IR, UV-visible and ^1H NMR spectra, and elemental analysis.

Keywords β-cyclodextrin bonded metal porphyrins, synthesis, characterization

Introduction

The metalloporphyrin as enzymatic model is a very active research field,[1,2] which shows the ability to eliminate different harmful radicals at the same time, such as $ONOO^-$ decomposition and superoxide anion radical ($O_2^{\cdot -}$) (or $HO^{\cdot}$) dismutation. The [Mn^{III}TMPyP] and [Fe^{III}TMPyP] have showed very efficient behavior as peroxynitrite reductase and can deplete $O_2^{\cdot -}$ during the catalytical process, and the relevant mechanisms were also been put forward. Our research group also found that different carbonyl ruthenium porphyrins and their derivatives have the ability to eliminate the $O_2^{\cdot -}$, $\cdot OH$ and anti lipid peroxidation.[3,4] Unfortunately, most porphyrins, natural or synthetic, are not sufficiently soluble in aqueous surroundings particularly at or near pH = 7, while most of the harmful radicals such as $O_2^{\cdot -}$, $ONOO^-$ exist in the aqueous phase in the human body. The cyclodextrin (CD) and its derivatives are hydrophilic, cheap, available in high purity, nontoxic, *etc*. The metal complexes of functionalized cyclodextrins have attracted considerable attention because they can be used as chiral receptors and enzymatic models, and changing the functional groups in the cyclodextrin primary face and the second face can get the better aqueous-phase solubility and different biological activity.[5] Here, the synthesis and structure characterization of bonded metalloporphyrins of β-cyclodextrin and its derivatives were reported.

Experimental

Instruments and materials

Microanalyses were performed by Perkin-Elmer 204B. Infrared spectra were measured with a Perkin-Elmer 1600 spectrometer (as KBr disc, values in cm^{-1}). Mass spectra were obtained on a Finnigan TSQ7000 spectrometer. ^1H NMR spectra were collected on a JEOL EX-300 (300 MHz) or a Bruker DPX-400 (400 MHz) spectrometer. The proton chemical shifts were reported in δ relative to tetramethylsilane (TMS). UV-visible spectra were measured with a Milton Roy 3000 Array spectrophotometer. The element analyses were measured with a Perkin-Elmer 204B apparatus.

Literature methods were used to make the 5-(*p*-aminophenyl)-10,15,20-triphenyl porphyrin (**1**),[6] 6-de-

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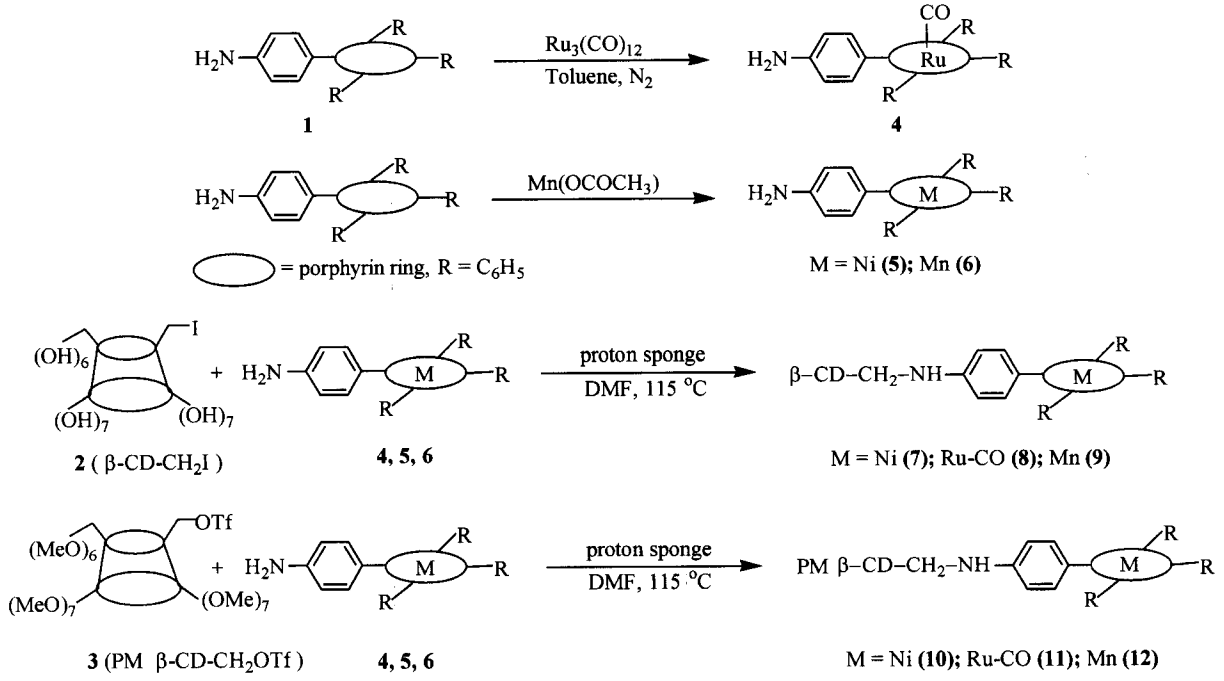
oxy-6-iodo-β-cyclodextrin (β-CD-CH_2I) (**2**),[7,8] mono(6-*O*-trifluoromethanesulfonyl) permethylated β-cyclodextrin (PM β-CD-CH_2OTf) (**3**).[9,10] 1,8-Bis(dimethylamino)-naphthalene (proton sponge) and trifluoromethanesulfonyl anhydride were purchased from Aldrich Company.

Synthesis of β-cyclodextrin bonded metalloporphyrins

The synthetic routes to novel metal porphyrins are summarized in Scheme 1.

Scheme 1



Preparation of complex **4**

The solution of 5-(*p*-aminophenyl)-10,15,20-triphenyl porphyrin (**1**) (100 mg, 0.16 mmol) in 30 mL of toluene was heated to reflux under N_2, and then $Ru_3(CO)_{12}$ (120 mg, 0.19 mmol) was added. The solution was refluxed with stirring under N_2 for 24 h. The solvent was removed under vacuum at 40 ℃. The crude product was purified with column chromatography on silica gel using $CHCl_3$ as the eluent to afford complex **4** (85 mg, yield 69%). ^1H NMR ($CDCl_3$, 300 MHz) δ: 8.83 (s, 8H, H_β), 8.14—8.02 (m, 8H, H_o $H_{o'}$),[11] 7.78—7.64 (m, 11H, H_m, H_p $H_{m'}$),[11] 3.86 (s, 2H, NH_2); IR (KBr) ν: 3128 (N—H), 1946 (Ru→C≡O), 1598, 1400 (-Ar-), 1008 (OSMB).[12] UV-vis ($CHCl_3$) λ: 416 (Soret band) and 534 nm; Anal. calcd for $C_{45}H_{29}N_5RuO$: C 71.42, H 3.86, N 9.25; found C 70.81, H 3.58, N 8.87; FAB MS: *m/z* 756.5.

Preparation of complexes **5** *and* **6**

The metalloporphyrins **5** and **6** were prepared by the method of reference 13. A solution of compound **1** and M($OAc)_2$ (M = Ni and Mn) in chloroform with 5% methanol was refluxed 2 h. The crude product was purified with column chromatography on silica gel using $CHCl_3$ as the eluent. Removal of solvent afforded red solid **5** (yield 65%), and deep green solid for **6** (yield 58%).

5 ^1H NMR ($CDCl_3$, 300 MHz) δ: 8.67 (s, 8H, H_β), 8.20—7.97 (m, 8H, H_o, $H_{o'}$), 7.74—7.71 (m, 11H, H_m, H_p, $H_{m'}$), 4.11 (br, 2H, amino-NH); IR (KBr) ν: 3129 (N—H), 1597, 1616 (-Ar-), 1003 (OSMB); UV-vis ($CHCl_3$) λ: 418 (Soret band) and 530 nm; Anal. calcd for $C_{44}H_{29}N_5Ni$: C 76.97, H 4.23, N 10.20; found C 77.21, H 4.12, N 9.97.

6 The ^{1}H NMR and IR spectra of complex **6** are similar to complex **5**. IR (KBr) ν: 3137 (N—H), 1606, 1496, 1110 (- Ar -), 1006 (OSMB); UV-vis ($CHCl_3$) λ: 472 (Soret band) and 620 nm; Anal. calcd for $C_{44}H_{29}N_5Mn$: C 77.42, H 4.25, N 10.26; found C 77.21, H 4.58, N 10.77.

Preparation of complexes **7—12**

Complexes **7—12** were prepared by the modified method of reference 14 with some modification.

7 A solution of **2** (200 mg, 0.16 mmol), proton sponge (30 mg) and complex **5** (50 mg, 0.07 mmol) in dry DMF was stirred under N_2 at 115 ℃ for 3 h. The mixture was cooled to r.t. and added dropwise to a large amount of acetone to generate the precipitate. After filteration, filtrate was dissolved in warm water (about 15 mL) and washed 3 times with chloroform. The water solution was added to acetone (about 150 mL) to give precipitate. Filteration and drying orer at 60 ℃ afforded red solid (84 mg, yield 64 %). ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 8.67 (s, 8H, H_β), 8.20—7.97 (m, 8H, H_o $H_{o'}$), 7.74—7.71 (m, 11H, H_m, H_p, $H_{m'}$), 4.84 (s, 7H, C_1-H), 3.66—3.57 (m, 28H, $C_{3,5,6}$-H), 3.38—3.30 (m, 14H, $C_{2,4}$-H); IR (KBr) ν: 3375 (OH), 2927 (C—H), 1595, 1508, 1467 (- Ar -), 1417, 1369, 1334 (C—H), 1115, 1080, 1031 (C—C), 1003 (OSMB). UV-vis ($CHCl_3$) λ: 417 (Soret band) and 530 nm; Anal. calcd for $C_{86}H_{97}N_5O_{34}Ni \cdot 3H_2O$: C 55.61, H 5.59, N 3.78; found C 55.23, H 5.78, N 3.44.

8 Complex **8** was prepared by the same method used for **7**, red solid, yield 51%. ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 8.77 (s, 8H, H_β), 8.20—8.16 (m, 8H, H_o $H_{o'}$), 7.83—7.78 (m, 11H, H_m, H_p, $H_{m'}$), 4.84 (s, 7H, C_1-H), 3.65—3.52 (m, 28H, $C_{3,5,6}$-H), 3.35—3.31 (m, 14H, $C_{2,4}$-H); UV-vis ($CHCl_3$) λ: 412 (Soret band) and 534 nm; IR (KBr) ν: 3370 (OH), 2925 (C—H); Anal. calcd for $C_{87}H_{97}$-$N_5O_{35}Ru \cdot 3H_2O$: C 54.20, H 5.39, N 3.63; found C 54.38, H 5.62, N 3.31.

9 In a similar way to complex **7**, complex **9** was obtained in 65% yield (deep green solid); IR (KBr) ν: 3135 (N—H), 2989, 2927 (C—H); 1606, 1496, 1110 (- Ar -), 1005 (OSMB); UV-vis ($CHCl_3$) λ: 471 (Soret band) and 622 nm. Anal. calcd for $C_{86}H_{97}$-$N_5O_{34}Mn$: C 57.40, H 5.43, N 3.89; found C 57.01, H 5.58, N 3.47.

10 To a solution of complex **5** (50 mg, 0.073 mmol) and proton sponge (30 mg) in dry DMF (5 mL) was added droppwise a solution of mono(6-*O*-trifluoromethanesulfonyl) permethylated β-cyclodextrin (**3**) (250 mg, 0.16 mmol) in dry DMF (4 mL). The reaction mixture was stirred at r.t. under N_2 for 6 h. The solvent was removed under vacuum at 40 ℃ and residue was diluted with chloroform (15 mL), and then washed with water (2 × 5 mL), dried with magnesium sulfate. The crude product was chromatographed on a silica gel column using $CHCl_3$/MeOH (100/5, *V*/*V*) as the eluent to give red solid (97 mg, 64%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.73 (s, 8H, H_β), 8.04—7.92 (m, 8H, H_o $H_{o'}$), 7.72—7.60 (m, 11H, H_m, H_p $H_{m'}$), 5.25—5.15 (m, 7H), 3.76—3.31 (m, 102H); IR (KBr) ν: 2923, 2851 (C—H), 1618, 1598, 1458 (- Ph -), 1186, 1162, 1142, 1107, 1037 (C—C), 1003 (OSMB); UV-vis ($CHCl_3$) λ: 416 (Soret band) and 530 nm; Anal. calcd for $C_{106}H_{137}O_{34}N_5Ni$: C 61.09, H 6.63, N 3.36; found C 60.82, H 6.84, N 3.25.

11 In a similar way to complex **7**, comlpex **11** was obtained red solid, yield 59%. Selected characterization data: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.56 (s, 8H, H_β), 8.09—8.02 (m, 8H, H_o $H_{o'}$), 7.69—7.65 (m, 11H, H_m, H_p $H_{m'}$), 5.06—5.01 (m, 7H), 3.57—3.29 (m, 102H); IR (KBr) ν: 2979, 2929, 2833 (C—H), 1928 (Ru→C≡O), 1605, 1458 (- Ar -), 1161, 1141, 1109, 1070, 1037 (C—C), 1001 (OSMB); UV-vis ($CHCl_3$) λ: 417 (Soret band), 534 nm; Anal. calcd for $C_{107}H_{137}O_{35}N_5Ru$: C 59.65, H 6.41, N 3.26; found C 59.23, H 6.87, N 3.67.

12 The preparation and spectra data of complex **12** were similar to those of complexes **6** and **9** (deep green solid). Anal. calcd for $C_{106}H_{137}O_{34}N_5Mn$: C 61.15, H 6.64, N 3.37; found C 60.85, H 6.88, N 3.21.

Results and discussion

Synthesis

The starting materials **1—3** were prepared according to literature procedures, and their characterization data are in good agreement with these results reported.[6-10]

During the preparation of the complexes **7—12**, choosing DMF as the solvent and 1,8-bis(dimethylamino) naphthalene (proton sponge) as the base can get the products in higher yields. It is easier to separate complex-

es **7**—**9** by dropping the crude reaction mixture to a large amount of acetone . For complexes **10**—**12**, using the method of preparative TLC chromatography with suitable eluent ($CHCl_3$/MeOH) can offer the best isolation effect.

Spectral properties

The spectral data of new complexes are listed in experiment sections. The spectra properties for several complexes are described as follows, respectively.

^{1}H NMR *spectra of new porphyrins* The proton signals of H_β, H_o H_m H_p of phenyl ring on porphyrin ring are appeared at δ 7.0—10.0. Compared with the compounds **4**—**6**, there are special protonpeaks of β-cyclodextrn at about δ 5.25—3.31 in the complexes **7**—**9**, and the additional proton signals of permethylated β-cyclodextrin at about δ 4.84—3.30 for complexes **10**—**12**.

IR *spectra of complexes* **7**—**12** They all have the intense bands at 2830—2980 cm^{-1} which can be easily assigned to the ν(C-H). The wide bands at 1162—1037 cm^{-1} belong to the ν(C-C) of β-cyclodextrin and derivatives.

UV-vis spectra of complexes **7**—**12** Soret bonds and Q bonds of complexes **7**—**12** are all blue-shifted (about 5—7 nm) compared with compounds **4**—**6**. When the metalloporphyrins are connected with rich-electron group cyclodextrin and derivatives lead to the increasing of electron density and the energy level elevating of the π-orbit on the porphyrin rings. Since the UV absorption of porphyrin compounds is determined by their π-orbits, their UV absorption bands blue-shifted, which is consistent with the experimental results.

Water solubility

Compounds **7**—**12** have better water solubility than parent compounds **4**—**6**. Since the complexes **7**—**9** expose hydroxies on the cyclodextrin, their water-solubility is better than that of the permethylated counterparts **10**—**12**.

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