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Synthesis of new metalloporphyrin derivatives from [5,10,15,20-tetrakis (pentafluorophenyl)porphyrin] and 4-mercaptobenzoic acid for homogeneous and heterogeneous catalysis

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ABSTRACT

Synthetic metalloporphyrins are catalysts that can efficiently insert oxygen and other atoms such as nitrogen and sulfur in hydrocarbons and in a wide variety of other organic compounds. This work reports on a synthetic strategy to prepare new metalloporphyrins via structural modification of [5,10,15,20-tetrakis (pentafluorophenyl)porphyrin], or [H_2(TPFPP)], with 4-mercaptobenzoic acid; it also describes their characterization and catalytic activity. The substituent groups present in the structure of the resulting porphyrins furnished structured solids, which could potentially serve as catalysts in heterogeneous medium. Investigation of the catalytic activity of the new derivatives in the oxidation of (Z)-cyclooctene, cyclohexane, and heptane, under homogeneous conditions, and in the oxidation of (Z)-cyclooctene, in heterogeneous medium, proved that the new metalloporphyrins constituted excellent catalysts for (Z)-cyclooctene epoxidation. As for alkane oxidation, they selectively gave the corresponding alcohol in good yields.

1. Introduction

The use of synthetic macrocycles as catalysts in oxidation reactions has generated great interest in bioinorganic chemistry [1,2], mainly when it comes to modeling the proven catalytic ability of biological systems like cytochrome P-450 and lignin peroxidases [3,4]. Researchers have successfully modulated the high selectivity and chemical efficiency of catalytic systems based on these two heme proteins they used synthetic metalloporphyrins bearing both simple and more sophisticated structures [5–12]. They have developed these synthetic catalytic systems [1,2,4,5,13] aiming to obtain complexes that can effectively generate compounds in much the same way as cytochrome P-450 enzymes do. Examples of such compounds are industrially important products like epoxides, alcohols, and acids; compounds of pharmaceutical interest, namely specific isomers with pharmacological activity, and high-purity precursors; and metabolites and drug analogs. To obtain the desired catalytic selectivity for certain products, high degree of sophistication may be necessary during the design of specific catalysts [1,13].

Work developed over the last 20 years has shown that catalysts based on Fe(III) and Mn(III) complexes of synthetic *meso*-tetraarylporphyrins are the most efficient and selective for oxidation reactions [14,15]. These systems constitute effective catalysts for the oxidative insertion of oxygen in organic compounds, namely hydrocarbons; they can also transfer an oxygen atom to sulfur- and nitrogen- containing substrates with great efficacy [16,17]. Additionally, the pharmaceutical industry has explored these systems to prepare oxidized metabolites from drugs [3]. In particular, the complexes of 5,10,15,20-tetrakis(pentafluorophenyl)porphyrin, [H_2(TPFPP)], an excellent template for further functionalization with nucleophiles [18,19], have found promising applications in catalysis [8,9,11,12,14,20] and in other areas [21,22]. It is easy to prepare catalytically active polymeric metalloporphyrins by reacting [H_2(TPFPP)] or the corresponding metal complexes with polyethylene glycol in the presence of sodium hydride using toluene as solvent [23]. The same template [H_2(TPFPP)] has been used to obtain derivatives with

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adequate amphiphilicity for application as photosensitizers that can photodynamically inactivate microorganisms [24].

Recently, we have reported that metalloporphyrins with appended ethylene glycol substituents efficiently catalyze (Z)-cyclooctene and cyclohexane oxidation under homogeneous and heterogeneous conditions [20].

Considering our research interest in the synthesis of efficient catalysts based on [H_2(TPFPP)] functionalization, here we report on the synthesis and catalytic activity of new metalloporphyrins obtained by structural modification of [H_2(TPFPP)] with 4-mercaptobenzoic acid. Depending on the number of *para*-fluorophenyl substituents that 4-mercaptobenzoic acid replaces during the synthesis, further metal insertion into the porphyrin complex will afford structured solids that are insoluble in most of the tested solvents. We investigated the catalytic activity of the synthesized metallocomplexes in (Z)-cyclooctene, cyclohexane, and heptane oxidation under homogeneous and heterogeneous catalytic conditions. We also assessed solid/heterogeneous catalysts recovery and reuse in the case that (Z)-cyclooctene was the substrate.

2. Experimental

All the chemicals used in this study were purchased from Aldrich, Sigma, or Merck and were of analytical grade. Iodosylbenzene (PhIO) was synthesized by hydrolysis of iodosylbenzenediacetate [25], and the obtained solid was carefully dried under reduced pressure and kept at 5 °C.

2.1. Synthesis of metalloporphyrins (see Fig. 1 for abbreviations)

The synthesis of the new metalloporphyrins involved three steps:

*(i) Synthesis of Porphyrin P**1***: the porphyrin ligand was prepared as described in the literature [26,27].

*(ii) Synthesis of the free-base porphyrins P**2**, P**3**, P**4**, P**5**, and P**6** from reaction of 4-mercaptobenzoic acid with porphyrin P**1*** (Fig. 1): In a round-bottom flask, 0.4 mmol of 4-mercaptobenzoic acid was dissolved in 15 mL of DMF containing 0.5 mL of pyridine. The reaction mixture was kept under magnetic stirring at room temperature for 30 min. Porphyrin P**1** (0.1 mmol) was added, and the reaction mixture was kept under magnetic stirring for 3 h and monitored by TLC. Then, the solvent was evaporated under reduced pressure, and the crude solid was purified by preparative TLC (thin-layer chromatography – silica was the stationary phase, and chloroform/methanol (9:1 v/v) was the mobile phase). In this process, several fractions were separated and numbered from 1 to 5.

The first fraction was identified as porphyrin P**2** (19% yield), m.p. > 300 °C. ^{1}H NMR: δ_H ppm (CD_3OD) 9.20 (broad, 8H, H-β), 8.07 (d, J = 9 Hz, 2H, S-C_6H_4-CO_2H), and 7.66 (d, J = 9 Hz, 2H, S-C_6H_4-CO_2H). ^{19}F NMR: δ_F ppm (CD_3OD) −188.35 to −188.17 (m, 6F, F-*meta*), −178.57 (t, J = 20.0 Hz, 3F, F-*para*), −163.67 (dd, J = 7.5 and 22.8 Hz, 6F, F-*ortho*), −162.80 (dd, J = 12.3 and 24.3 Hz, 2F, F-*meta*), and −158.51 (dd, J = 12.3 and 24.3 Hz, 2F, F-*ortho*). UV–vis ($CHCl_3$) λ_{max}, nm (log ε): 414 (5.20), 506 (4.08), 584 (3.90). HRMS (FAB^+) m/z: calcd for $C_{51}H_{16}F_{19}N_4O_2S$ $(M+H)^+$: 1109.0685; found: 1109.0667. The second and third fractions were identified as porphyrins P**3** and P**4**. Porphyrin P**3** (17% yield), m.p. > 300 °C. ^{1}H NMR: δ_H ppm (CD_3OD): 9.18 (broad, 8H, H-β), 8.08 (d, J = 8.4 Hz, 4H, S–C_6H_4–CO_2H), and 7.67 (d, J = 8.4 Hz, 4H, S–C_6H_4–CO_2H). ^{19}F NMR: δ_F ppm (CD_3OD) −188.67 to −188.49 (m, 4F, F-*meta*), −179.01 (t, J = 20.4 Hz, 2F, F-*para*), −163.73 (dd, J = 7.8 and 23.0 Hz, 4F, F-*ortho*), −162.89 (dd, J = 12.2 and 24.4 Hz, 4F, F-*meta*), and −158.68 (dd, J = 12.2 and 24.4 Hz, 4F, F-*ortho*). UV–vis ($CHCl_3$) λ_{max}, nm (log ε): 412 (5.24), 506 (4.06), 584 (3.90). HRMS (FAB^+) m/z: calcd for $C_{58}H_{21}F_{18}N_4O_4S_2$ $(M+H)^+$: 1243.0711; found: 1243.0696. Porphyrin P**4** (12% yield), m.p. > 300 °C. ^{1}H NMR: δ_H ppm (CD_3OD): 9.18 (broad, 8H, H-β), 8.08 (d, J = 8.2 Hz, 4H, S–C_6H_4–CO_2H), and 7.67 (d, J = 8.2 Hz, 4H, S–C_6H_4–CO_2H). ^{19}F NMR: δ_F ppm (CD_3OD) −190.20 to −190.03 (m, 4F, F-*meta*), −180.54 (t, J = 20.2 Hz, 2F, F-*para*), −165.27 (dd, J = 7.3 and 22.6 Hz, 4F, F-*ortho*), −164.41 (dd, J = 12.3 and 24.5 Hz, 4F, F-*meta*), and −158.68 (dd, J = 12.3 and 24.5 Hz, 4F, F-*ortho*). UV–vis ($CHCl_3$) λ_{max}, nm (log ε): 412 (5.22), 506 (4.08), 582 (3.66). HRMS (FAB^+) m/z: calcd for $C_{58}H_{21}F_{18}N_4O_4S_2$ $(M+H)^+$: 1243.0711; found: 1243.0675.

The fourth fraction was identified as porphyrin P**5** (37% yield), m.p. > 300 °C. ^{1}H NMR: δ_H ppm (CD_3OD): 9.24 (broad, 8H, H-β), 8.16 (d, J = 8.4 Hz, 6H, S–C_6H_4–CO_2H), and 7.75 (d, J = 8.4 Hz, 6H, S–C_6H_4–CO_2H). ^{19}F NMR: δ_F ppm (CD_3OD) −190.19 to −190.02 (m, 2F, F-*meta*), −180.53 (t, J = 20.4 Hz, 1F, F-*para*), −165.25 (dd, J = 7.6 and 22.6 Hz, 2F, F-*ortho*), −164.40 to 164.21 (m, 4F, F-*meta*), and −160.20 (dd, J = 12.3 and 24.7 Hz, 4F, F-*ortho*). UV–vis (CH_3OH) λ_{max}, nm (log ε): 410 (5.16), 504 (4.13), 582 (3.65). HRMS (FAB^+) m/z: calcd for $C_{65}H_{26}F_{17}N_4O_6S_3$ $(M+H)^+$: 1377.0738; found: 1377.0737. The protons signal relative to N–H was not observed, due to their replacement by deuterium from deuterated methanol in porphyrins P**2**–P**6**. Finally, the fifth fraction was identified as porphyrin P**6** (3.1% yield), m.p. > 300 °C, ^{1}H NMR: δ_H ppm (Acetone-d6) 9.46 (broad, 8H, H-β), 8.14 (d, J = 8.4 Hz, 8H, S–C_6H_4–CO_2H), 7.82 (d, J = 8.3 Hz, 8H, S–C_6H_4–CO_2H), and −2.87 (s, 2H, NH). ^{19}F NMR: δ_F ppm (Acetone-d6) −162.02 (dd, J = 11.9 and 24.7 Hz, 8F, F-*meta*), and −157.70 (dd, J = 11.9 and 24.7 Hz, 8F, F-*ortho*). UV–vis (Acetone) λ_{max}, nm (log ε): 412 (5.14), 504 (4.07), 582 (3.57). HRMS (FAB^+) m/z: calcd for $C_{72}H_{31}F_{16}N_4O_8S_4$ $(M+H)^+$: 1511.0764; found: 1511.0752.

The reaction yields described above were obtained after 3 h of reaction; when the reaction conducted under the same conditions was stopped after 1 h, the yield of porphyrin P**2** was higher 33.6%; porphyrins P**3** and P**4** were isolated in yields ranging from ca. 15% to 25%. To optimize the formation of porphyrin P**6**, the reaction was performed as described previously, but 0.72 mmol of 4-mercaptobenzoic acid, 15 mL of DMF, 4.0 mL of pyridine, and 0.102 mmol of porphyrin P**1** were used instead. After 48 h of reaction, porphyrin P**6** was isolated in 96% yield.

*(iii) Preparation of manganese, iron, and copper porphyrins (MP**x**)*: To insert a metal into the free-base porphyrins P**1**, P**2**, and P**6**, a modification of the conventional method described by Kobayashi [28] was employed. To obtain the iron complexes, the reactions were carried out using acetic acid (P**1**) or DMF (P**2** and P**6**) as solvent, iron(II) chloride, and sodium acetate (to aid deprotonation). The reactions were performed under reflux in argon atmosphere for 24 h, to yield FeP**1**, FeP**2**, and FeP**6** (confirmed by the observation of the characteristic bands by UV–vis analyses). The argon atmosphere was removed and solution reaction was kept under magnetic stirring at reflux system to ensure the total oxidation of Fe(II) to Fe(III).

To achieve the manganese complexes, manganese(II) acetate was used in the same solvents used for iron(III) metallation process. The reaction was conducted for 8 h, to afford MnP**1**, MnP**2**, and MnP**6**. The oxidation of Mn(II) to Mn(III) was also performed in air as described for FeP.

Copper was also inserted into porphyrins P**1** and P**6**, using copper(II) acetate, DMF as solvent, and reaction time of 3 h, to give CuP**1** and CuP**6**. After metal insertion, the solvents were removed under vacuum. The resulting solids were thoroughly washed with water, to remove excess metal salts. The complexes were purified by column chromatography using dichloromethane as eluent. The preparation of CuP**2** was not performed in this stage, since the material amount (free base porphyrin) was insufficient.

During metal insertion into porphyrin P**6**, the corresponding metalloporphyrins (MnP**6**, FeP**6**, and CuP**6**) precipitated, and the