Synthesis of acetylglycosylated metalloporphyrins and their catalysis for cyclohexane oxidation with PhIO under mild conditions

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Abstract

Tetrakis[2-(2,3,4,6-tetraacetyl-β-D-glucopyranosyl)-1-*O*-phenyl]porphyrin (T(*o*-glu)PPH$_2$) and tetra[3-(2,3,4,6-tetra-acetyl-β-D-glucopyranosyl)-1-*O*-phenyl]porphyrin (T(*m*-glu)PPH$_2$) were synthesized from the reaction of pyrrole with *ortho*-acetylglycosylated benzaldehyde and *meta*-acetylglycosylated benzaldehyde, respectively, by Lindsay's method. These free acetylglycosylated porphyrins were metallized into acetylglycosylated metalloporphyrins, chloro[tetra(*o*-2,3,4,6-tetraacetyl-β-D-glucopyranosyl-1-*O*-phenyl)porphinato]iron (T(*o*-glu)PPFeCl), chloro[tetra(*o*-2,3,4,6-tetraacetyl-β-D-gluco-pyranosyl-1-*O*-phenyl)porphinato]manganese, (T(*o*-glu)PPMnCl), chloro[tetra(*m*-2,3,4,6-tetraacetyl-β-D-glucopyranosyl-1-*O*-phenyl)porphinato]iron (T(*m*-glu)PPFeCl) [tetra(*m*-2,3,4,6-tetraacetyl-β-D-glucopyranosyl-1-*O*-phenyl)porphinato]-manganese T(*m*-glu)PPMnCl. The newly synthesized compounds were characterized by UV–VIS spectroscopy, ^{1}HNMR and elemental analysis. The catalysis of these acetylglycosylated metalloporphyrins for cyclohexane oxidation with PhIO as an oxidant at room temperature and under atmospheric pressure was studied. The changes of the catalytic power of metalloporphyrins were observed when acetylglycosyl groups were introduced into porphyrin rings. In contrast with metalloporphyrins without sugar groups, cyclohexane oxidation catalyzed by acetylglycosylated metalloporphyrins have higher ratio of cyclohexanol to cyclohexanone as well as reaction rates and yields. The catalytic turnover numbers of acetylglycosylated metalloporphyrins were doubled compared to metalloporphyrins without sugar groups. The results indicated that acetylglycosylated metalloporphyrins had better antioxidative stability than metalloporphyrins without sugar groups. © 2000 Elsevier Science B.V. All rights reserved.

Keywords: Acetylglycosylated metalloporphyrins; Cyclohexane; PhIO

Since the late 1970s, a great number of porphyrin compounds have been synthesized [1]. They found applications as catalysts for hydrocarbon oxidation [2,3] as well as models of important biological systems, for instance that of the photosynthetic reaction centers of plants and bacteria [4]. In recent years, there has been increasing interest in carbohydrate–porphyrins [5,6] as carbohydrates and porphyrins are all existing in organisms. Carbohydrate–porphyrins are worthwhile investigating in asymmetric synthesis owing to their chiral nature. Driaf et al. [7] synthesized a number of carbohydrate–

porphyrin compounds which found application in the photochemistry therapy (PDT) of tumors. Maillard et al. described the synthesis of the acetylglycosylated porphyrins derived from meso-tetraphenylporphyrins in which mono- or disaccharide moieties were linked at the *ortho-* [8] or *para-* [5] positions of the phenyl groups. With the introduction of the chiral sugar substituents, acetylglycosylated porphyrins become chiral and easier soluble in both aqueous and anhydrous reagents. Comparing to metalloporphyrins without sugar groups, they are more similar to the chemical environment in an organism and can better model on cytochrome

P-450 monooxygenase in catalytic oxidation of alkane and alkene. It was reported that metallic complexes of these acetylglycosylated porphines were active catalysts for alkene epoxidation with asymmetric induction [9–12]. In contrast with metalloporphyrins without sugar groups, the epoxidation catalyzed by metalloporphyrin with sugar groups had higher yield and better stereoselectivity. It has not been reported up to now whether glycoconjugated metalloporphyrins has the catalytic selectivity for alkane oxidation.

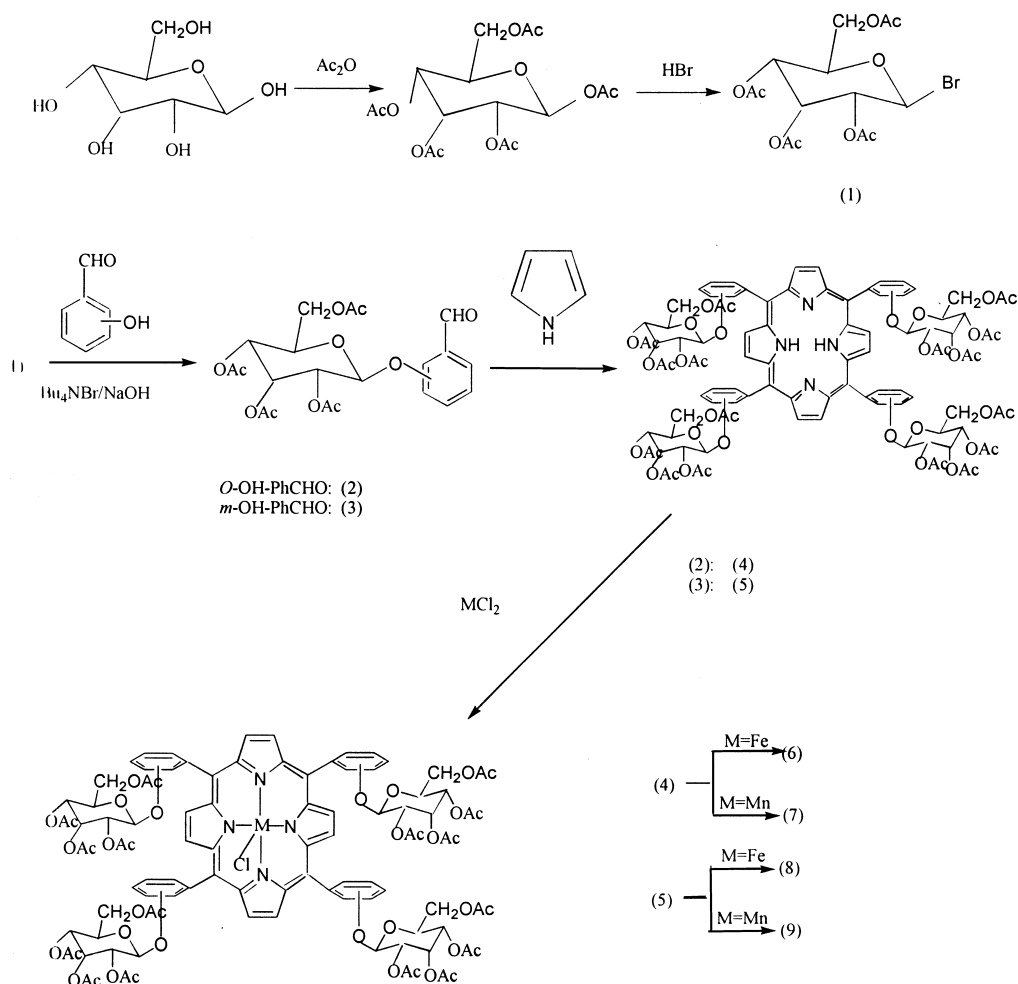We synthesized four acetylglycosylated metalloporphyrins (AcGM) according to the route

Fig. 1. Synthetic scheme of acetylglycosylated metalloporphyrins.

shown in Fig. 1, i.e., chloro[tetra[*o*-(2,3,4,6-te-traacetyl-β-D-glucopyranosyl)-1-*O*-phenyl)phinato]iron (**1**, T(*o*-glu)PPFeCl), chloro[tetra[*o*-(2,3,4,6-tetraacetyl-β-D-glucopyranosyl)-1-*O*-phenyl)phinato]manganese (**2**, T(*o*-glu)PPMnCl), chloro[tetra[*m*-(2,3,4,6-tetraacetyl-β-D-glucopyranosyl-1-*O*-phenyl)phinato]iron (**3**, T(*m*-glu)PPFeCl) and chloro[tetra[*m*-(2,3,4,6-tetraacetyl-β-D-glucopyranosyl-1-*O*-phenyl)phinato]manganese (**4**, T(*m*-glu)PPMnCl). The oxygenation of cyclohexane with PhIO as an oxidant catalyzed by the synthesized metalloporphyrins at room temperature and pressure has been studied. So far, the carbon–hydrogen bond oxidation catalyzed by metalloporphyrins with sugar groups have not yet been reported. Comparing to the metalloporphyrins without sugar groups, the acetylglycosylated metalloporphyrins show an increased ratio of cyclohexanol to cyclohexanone and enhanced the reaction rates and yields for cyclohexane oxidation. The study results indicated that the mechanism of cyclohexane oxidation catalyzed by AcGM was consistent with that of the reactions involving cytochrome *P*-450 monooxygenase.

1. Experimental

1.1. Instruments and reagents

^{1}H NMR spectra were recorded on a Bruker AG80 spectrometer in CDCl$_3$ as solvent. UV–VIS spectra were obtained with a Lambda 17 Perkin-Elmer spectrophotometer. IR spectra were recorded on a Perkin-Elmer model 783 IR spectrophotometer; GC analysis was performed on a Shimadzu GC-16A gas chromatograph with flame ionization detection (30×0.125 in. OV-101-5% CHP 100–125 mesh column). Perkin-Elmer 2400 elementary analyser and model 5012 constant temperature water bath were used.

Before used, benzene, dichloromethane and benzaldehyde were subjected to simple distillation from K$_2$CO$_3$; pyrrole and 2-methylbutane

were redistilled at atmospheric pressure from CaH$_2$. Other reagents were analytically pure or chemically pure as received.

PhIO was synthetized according to documented procedures [13], the purity measured by iodimetry was 99%. Chloro[tetraphenyl-porphinatoiron] (TPPFe^{III}Cl) and Chloro[tetraphenylporphinatomanganese] (TPPMn^{III}Cl) were synthetized according to documented procedures [14,15] and confirmed by elementary analysis, IR spectra and UV–VIS spectroscopy.

1.2. Synthesis of 1-bromo-2,3,4,6-tetra-O-acetylglucose (1)

Following a known procedure [16]: 66 g of glucose was reacted with 280 ml of acetic anhydride affording the straw yellow pulpiness penta-*O*-acetylglucose. The latter was reacted with dry hydrogen bromide affording a bright yellow solution. The solution was evaporated to dryness under reduced pressure and 60°C with a water bath, affording 115 g of 1-bromo-2,3,4,6-tetra-*O*-acetylglucose (**1**) (85%), with mp 87–88°C after crystallization from 250 ml of absolute isopropyl ether.

1.3. Synthesis of ortho-2,3,4,6-tetraacetyl-β-D-glucopyranosyl-1-O-benzaldehyde (2)

Following a known procedure [17], 10.24 g of 2-hydroxybenzaldehyde was reacted with 11.5 g of (**1**) affording the crude yellow oil. Twice chromatographic procedures obtained 11.86 g of pure product (51%). Anal: calc. for C$_{21}$H$_{24}$O$_{11}$: C, 55.75; H, 5.35. Found: C: 55.91; H: 5.32.

1.4. Synthesis of meta-2,3,4,6-tetraacetyl-β-D-glucopyranosyl-1-O-benzaldehyde (3)

Following the general procedure described for compound (**2**), 11.5 g of (**1**) was reacted with 10.24 g of 3-hydroxybenzaldehyde. Column chromatography (silica-gel. hexane/ethyl acetate 1:4) afforded 10.2 g (44%) of *meta* 2,

3,4,6-tetraacetyl-β-D-glucopyranosyl-1-*O*-benz-aldehyde (**3**). Anal. calc. for $C_{21}H_{24}O_{11}$: C, 55.75; H, 5.35. Found: C: 55.88; H: 5.33.

1.5. Synthesis of T(o-glu)PPH₂ (4)

Following a known procedure [18], 4.5 g of (**2**) was reacted with 0.668 g of freshly distilled pyrrole and 0.4 ml of $BF_3 \cdot Et_2O$ at room temperature for 20 h. After addition of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), the reaction mixture was refluxed for a further 2 h. Then 20 g of silica was added and the solvent evaporated. The residue was purified by column chromatography (silica, CH_2Cl_2/acetone 7:1). After removing of the solvent, 1.3 g (25.8%) of tetra(*o*-2,3,4,6-tetraacetyl-β-D-glucopyranosyl-1-*O*-phenyl)porphyrin (T(*o*-glu)PPH₂, (**4**) was obtained. Anal. calc. for $C_{100}H_{102}N_4O_{40}$: C, 60.1; H, 5.1; N 2.8. Found: C: 59.7; H: 5.2; N: 3.0. UV–VIS (CH_2Cl_2): λ_{max}: 418(ε,370 000), 516(17 000), 544.5(6000), 587.5(7000), 654(5500) nm. ^{1}HNMR(CDCl₃) δ(ppm): 8.84 (s, 4H, pyrrole), 8.67 (s, 4H, pyrrole) 7.86 (d, 4H, benzene), 7.78 (t, 4H, benzene), 7.70 (d, 4H, benzene) 7.51 (d, 4H, benzene) 4.79 (d, 4H, glucose) 4.68 (t, 4H, glucose) 4.62 (t, 4H, glucose) 4.14 (s, 12H, glucose) 3.68 (m, 4H, glucose) 2.18 (s, 12H, CH₃CO-) 1.92 (s, 12H, CH₃CO-) 1.28 (s, 12H, CH₃CO-) −1.18 (s, 12H, CH₃CO-), −2.81 (s, 2H, NH).

1.6. Synthesis of T(m-glu)PPH₂ (5)

Following the general procedure described for compound 4, 4.5 g of (**3**) reacted with 0.668 g of pyrrole. Column chromatography (silica-gel. CH_2Cl_2/acetone 7:1) afforded 1.1 g (22%) of T(*m*-glu)PPH₂ (**5**). Anal. calc. for $C_{100}H_{102}N_4O_{40}$: C, 60.1; H, 5.1; N, 2.8. Found: C: 59.85; H: 5.3; N: 3.2. UV–VIS (CH_2Cl_2): λ_{max}, 415.5, 513.5, 546 588, 650nm. ^{1}HNMR(CDCl₃) δ(ppm) 8.72 (d, 8H, pyrrole), 8.10 (d, 8H, benzene), 7.62 (d, 8H, benzene), 5.33 (m, 12H, glucose) 4.41 (d, 4H, glucose) 4.32 (t, 4H, glucose) 4.17 (m, 8H, glucose) 2.20

(s, 12H, CH₃CO-) 2.12 (s, 12H, CH₃CO-) 1.62 (s, 12H, CH₃CO-) 1.06 (s, 12H, CH₃CO-) −2.97 (s, 2H, NH).

1.7. Synthesis of T(o-glu)PPFeCl (6)

A solution of 200 mg of (**4**) in 50 ml DMF was stirred under refluxing with $FeCl_2$ for 1 h. TLC (silica-gel, CH_2Cl_2) showed the complete disappearance of the starting material and UV–VIS spectroscopy showed the absence of non-metallized porphyrin. After the mixture was cooled to room temperature and cautiously acidified with 50 ml 10% HCl, the product became crystalline. Recrystallization from hexane–benzene afforded 150 mg (75%) of T(*o*-glu)PPFeCl (**6**). Anal. calc. for $C_{100}H_{100}N_4O_{40}$FeCl: C, 57.49; H, 4.79; N, 2.68. Found: C: 57.11; H: 4.81; N: 2.65. UV–VIS (CH_2Cl_2): λ_{max}: 394, 424, 558, 594 nm.

1.8. Synthesis of T(o-glu)PPMnCl (7)

A solution of 200 mg of (**4**) in 50 ml of DMF was stirred under refluxing with $MnCl_2$ for 6 h. TLC (silica-gel, CH_2Cl_2) showed the complete disappearance of the starting material and UV–VIS spectroscopy showed the absence of non-metallized porphyrin ring. After evaporation of the solvent in vacuo, the residue was dissolved in CH_2Cl_2 and washed with water. Column chromatography (silica-gel, CH_2Cl_2) afforded 170 mg (85%) of T(*o*-glu)PPMnCl (**7**). Anal. calc. for $C_{100}H_{100}N_4O_{40}$MnCl: C, 57.51; H, 47.9; N, 2.68. Found: C: 57.31; H: 47.6; N: 2.69. UV–VIS (CH_2Cl_2): λ_{max}: 399, 426, 510, 575, 654 nm.

1.9. Synthesis of T(m-glu)PPFeCl (8)

Following the general procedure described for compound (**7**), 200 mg of (**5**) was metallized with $FeCl_2$. Column chromatography (silica-gel. hexane/ether acetate 1:4) afforded 170 mg (85%) of T(*m*-glu)PPFeCl (**8**). Anal. calc. for $C_{10}H_{100}N_4O_{40}$FeCl: C, 57.49; H, 4.79; N, 2.68.

Found: C: 57.69; H: 4.81; N: 2.64. UV–VIS (CH_2Cl_2): λ_{max}: 398, 422, 557, 595 nm.

1.10. Synthesis of T(m-glu)PPMnCl (9)

Following the general procedure described for compound (8), 200 mg of (5) was metallized with $MnCl_2$. Column chromatography (silica hexane/ether acetate 1:4) afforded 160 mg (80%) of T(*m*-glu)PPMnCl (9). Anal. calc. for $C_{100}H_{100}N_4O_{40}MnCl$: C, 57.51; H, 4.79; N, 2.68 Found: C: 57.55; H: 4.73; N: 2.66. UV–VIS (CH_2Cl_2): λ_{max}: 403, 425, 514, 575, 651 nm.

1.11. Cyclohexane hydroxylation with PhIO

Cyclohexane hydroxylation was carried out under a nitrogen atmosphere in the following procedures unless otherwise specified. A solution of PhIO (100 mg, 4.5×10^{-4} mol), metalloporphyrin 1.55×10^{-6} mol), 5 ml of chlorobenzene and 2 ml of cyclohexane was warmed to $30 \pm 0.5°C$ using thermo-stated circulating water and stirred 2 h with an eletromagnetic stirrer. Products were analysed by gas chromatography. Yields were calculated based on the input mole of PhIO. Samples were collected from reactant system with a micro-injector regularly to do kinetics analysis. Quantitation calculations used an internal standard method. The standard material was *para*-dichlorobenzene.

2. Results and discussion

2.1. Synthesis and spectral characteristic of acetylglycosylated metalloporphyrins

Maillard et al [17] synthesized (2) by the reaction of 1-bromo-2,3,4,6-tetraacetylglucose with 2-hydroxybenzaldehyde, then synthesized (4) by Lindsey's method [18]. Our studies showed that Maillard's synthetic method of (4) could be used to the synthesis of (5).

We tried to synthesize 5-(2,3,4,6-tetraacetyl-β-D-glucopyranosyl-1-*O*-phenyl)-10,15,20-triphenyl)-porphyrin from the reaction of 5-*para*hydroxylphenyl-10,15,20-triphenylporphyrin with 1-bromo-2,3,4,6-tetraacetylglucose, but, unfortunately, failed.

The reaction of (4) and (5) with $FeCl_2$ and $MnCl_2$ provided (6), (7), (8) and (9), respectively. In order to avoid forming μ-oxo-dimer of AcGM during the course of the reaction, we used the modified Adler's method [14] by slowly adding 6 mol/l hydrochloric acid into the hot reactants until AcGM precipitated. The reaction completed within 1 h.

The solubility of acetylglycosylated porphyrins is better than porphyrins without sugar group. Literature [17] reported that the solubility of tetra[*o*-β-glucosylphenyl]porphyrin in neutral water is larger than 10^{-5} mol/l, while tetraphenylporphyrin and the other porphyrins without sugar group are nearly insoluble in water. Our experiments showed that the solubility of acetylglycosylated porphyrins in water is smaller than that of tetra[*o*-β-glucosylphenyl]porphyrin, while the solubility of acetylglycosylated porphyrins in non-aqueous solvents is larger than that of tetra[*o*-β-glucosylphenyl]porphyrin and porphyrins without sugar group. This might be related to their different solvation.

The electronic spectra of (4) and (5) were the same as those of tetraphenylporphyrin TPPH$_2$. The electronic spectra of their metal complexes (6), (7), (8) and (9) were essentially same as those of the metal complexes of tetraphenylporphyrin, TPPFeCl and TPPMnCl. This showed that there was no evidence of the effect of acetylglucose group linking onto porphyrin benzene ring on electronic absorption of porphyrin. In contrast with ^{1}HNMR of TPPH$_2$, (4) and (5) had ^{1}HNMR peaks of acetyl group at 1.06–2.23 ppm and glucose group at 4.07–5.33 ppm, and ^{1}HNMR of tetraphenylporphyrin ring split into complicated multiple peaks after acetylglucose group being introduced on porphyrin benzene ring. Above phenomenon showed that it was

possible that there existed some interaction among the protons of acetylglucose group and porphyrin ring. Moreover, ^{1}HNMR of (**4**) showed an absorption peak at −1.2 ppm, which is not the case with (**5**). This was due to an acetyl group that was affected by the ring current of the macrocycle [17]. This proposed rather different stereochemistry of acetylglycosylated porphyrin when an acetylglucose group was introduced on *ortho*- and *meta*-position of the porphyrin benzene ring.

2.2. Product selectivity in cyclohexane oxidation catalyzed by acetylglycosylated metalloporphyrin under mild conditions

In order to study acetylglycosylated metalloporphyrin's capacity for catalytic oxidation of alkane, we built the model system of PhIO-acetylglycosylated metalloporphyrin-cyclohexane and chose six metalloporphyrins in Table 1 for comparing experiments. The research showed that AcGM were capable of catalytic oxidation of alkane under mild conditions, and the sugar substituents of the macrocycles would influence the catalytic capablity. The results are shown in Table 1.

One could see from Table 1 that the product yields catalyzed by AcGM and turnover numbers of catalysts were obviously higher than the metalloporphyrins without sugar groups. For example, with catalysts changing from TPPFeCl

to (**6**), the total yields of cyclohexanol and cyclohexone changed from 16.8% to 33.5%, and the total turnover numbers of catalysts changed from 4.9 to 9.8. The above fact means that AcGM have better antioxidative stability than tetraphenylporphyrin, and the sugar residues protected by acetyl group are able to bear the oxidative damage.

It was reported [18] that (**6**) and (**7**) existed different atropoisomers which showed different enantioselectivity in the asymmetric epoxidation of *para*-chlorostyrene. In this work we had even used the αβαβ- and αααβ-atropoisomers of (**6**) as catalysts, but no obvious differences in the yields and selectivity of the reaction were observed.

The selectivity of the oxidation of cyclohexane catalyzed by AcGM was obviously higher than metalloporphyrins without sugar groups, which show that the catalytic behavior of the acetylglycosylated metalloporphyrin was closer to the cytochrome *P*-450.

2.3. Tentative exploring of the mechanism of oxidation of cyclohexane catalyzed by acetylglycosylated metalloporphyrins

In order to explore the possible reaction mechanism of the model of PhIO-acetylglycosylated metalloporphyrin-clyclohexane, we tried to measure the kinetics of cyclohexane oxidation catalyzed by AcGM. The results

Table 1
Product selectivity in cyclohexane oxidation catalyzed by metalloporphyrins

Metalloporphyrin		Yield[a] (%)*			ol:one	Turnover[b]
Compound	Mol no. (10^{-5})	Cyclohexanol	Cyclohexanone	Total yield		
T(*o*-glu)PPFeCl	1.55	31.3	2.2	33.5	14.4	9.8
T(*m*-glu)PPFeCl	1.55	28.3	2.0	30.3	14.2	8.9
TPPFeCl	1.55	15.1	1.7	16.8	9.0	4.9
T(*o*-glu)PPMnCl	1.55	34.4	3.1	37.5	11.1	11.0
T(*m*-glu)PPMnCl	1.55	34.0	3.0	37.0	11.4	10.9
TPPMnCl	1.55	14.3	1.8	16.1	8.1	4.7

[a]Yield is based on the input PhIO.
[b]Number of molecules of cyclohexanol and cyclohexanone oxided by one molecule of catalyst for a duration of 2 h.
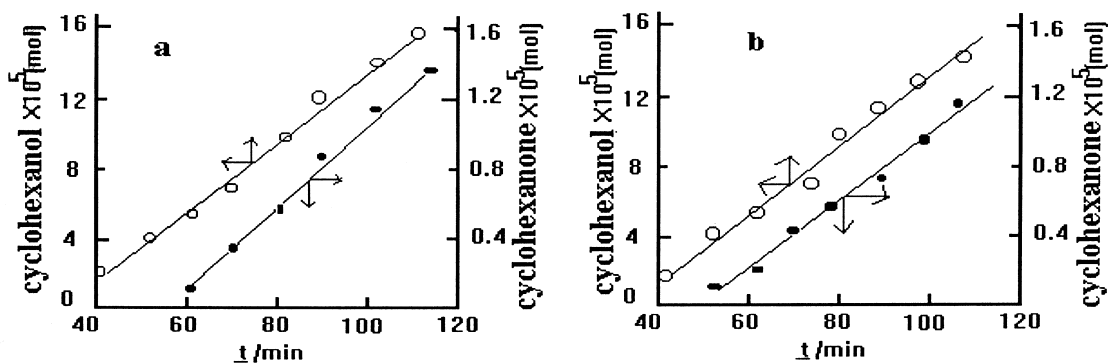
Fig. 2. Comparison of the yields plotted versus time in cyclohexane oxidation by (a) T(*o*-glu)PPMnCl and, (b) T(*m*-glu)PPMnCl.

showed that the reaction rates by AcGM were quicker than that by metalloporphyrins without sugar groups. TPPFeCl needed 2 h to complete reaction, while (**6**) and (**8**) needed only 20 min. As the reactions catalyzed by (**6**) and (**8**) were too fast to obtain enough data with GC for the kinetic curves, we could only obtain the kinetic curves of the clyclohexane oxidation catalyzed by two Mn complexes ((**7**) and T(*m*-glu)-PPMnFeCl) (Fig. 2).
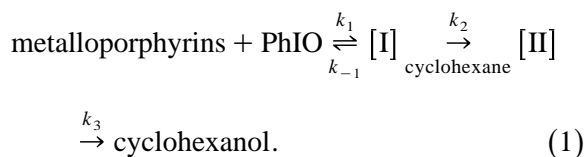
Fig. 2 showed that for the reaction catalyzed by acetylglycosylated Mn-porphyrins, the yield of cyclohexane oxidation had the linear relationship with the reaction time. The reaction was a zero-order kinetic reaction:

$$\frac{\mathrm{d}p}{\mathrm{d}t} = k$$

k is the estimated constant. Table 2 listed the estimated constant k of the cyclohexane oxidation catalyzed by (**7**) and (**9**).

Above research results show that AcGM has the similar behavior to cytochrome *P*-450 monooxygenase in catalyzing oxidation of hydrocarbon. If their catalytic mechanism was the same, according to the general cytochrome *P*-450 monooxygenase-catalyzed procedures, one could express simply the cyclohexane oxidation catalyzed by AcGM with PhIO as follows:

$$\text{metalloporphyrins} + \text{PhIO} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} [\text{I}] \underset{\text{cyclohexane}}{\overset{k_2}{\rightarrow}} [\text{II}]$$

$$\overset{k_3}{\rightarrow} \text{cyclohexanol}. \qquad (1)$$

Here [I] is the radical cation of a high-valent metal–oxygen, and [II] is a radical abstract.

For the above procedures, the rate of formation of the clyclohexanol could be shown as follows:

$$\frac{\mathrm{d}[\text{cyclohexanol}]}{\mathrm{d}t} = K_3[\text{II}]. \qquad (2)$$

Table 2
Estimated constant k of reaction

Metalloporphyrin	T(*o*-glu)PPMnCl		T(*m*-glu)PPMnCl	
Product	Cyclohexanol	Cyclohexanone	Cyclohexanol	Cyclohexanone
$k \times 10^6$ (mol/min)	1.90	0.23	1.86	0.26

The steady-state approximation was made:

$$\frac{d[I]}{dt} = K_1[\text{metalloporphyrins}][\text{PhIO}]$$
$$- (K_{-1} + K_2[\text{cyclohexanol}])[I] = 0 \tag{3}$$

$$\frac{d[II]}{dt} = K_2[I][\text{cyclohexane}] - K_3[II] = 0. \tag{4}$$

Eqs. (3) and (4) might be solved for [II] to give:

$$[II] = \frac{K_1 K_2}{K_3}$$
$$\cdot \frac{[\text{PhIO}][\text{cyclohexane}][\text{metalloporphyrins}]}{K_1 + K_2[\text{cyclohexane}]} \tag{5}$$

The rate of formation of cyclohexanol was then obtained from Eq. (2):

$$\frac{d[\text{cyclohexanol}]}{dt} = \frac{K_1 K_2}{K_1 + K_2[\text{cyclohexane}]}$$
$$\cdot [\text{PhIO}] \cdot [\text{cyclohexane}]$$
$$\cdot [\text{metalloporphyrins}] \tag{6}$$

Under our conditions, the cyclohexane was in 1000 times excess. The concentration of PhIO was maintained constant by the continuous stirring and metalloporphyins' concentration was generally unchanged. So, Eq. (6) could be simplified as:

$$\frac{d[\text{cyclohexanol}]}{dt} = K$$

or

$$[\text{cyclohexanol}] = kt + b. \tag{7}$$

One could see from Eq. (7) that the amount of cyclohexanol is linearly related with the reaction time. The results of kinetic experiments consisted with the Eq. (7), which showed that the reaction mechanism of cyclohexane oxidation catalyzed by AcGM was the same as that of cytochrome *P*-450 monooxygenase.

Acknowledgements

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