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A New Picket-Fence Porphyrin Precursor. Synthesis and Atropisomerism of Free Base and Zinc Complex of *meso*-Tetra(*o*-methoxycarbonylphenyl)porphyrin

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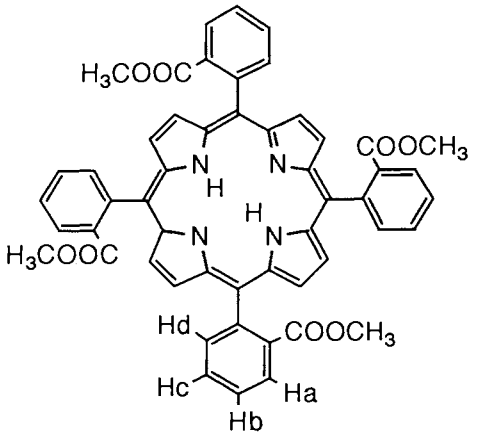
A new "picket-fence" porphyrin precursor with carboxy terminal groups has been prepared. Four atropisomers of *meso*-tetra(*o*-methoxycarbonylphenyl)porphyrin have been separated by chromatography. The conformational stability of the αααα-isomer was examined to the prolonged heating for both free base and zinc complex. The usefulness of *meso*-tetra(*o*-carbonylphenyl)porphyrin appeared to be not at all inferior to well-known *meso*-tetra(*o*-aminophenyl)porphyrin.

Collman's "picket-fence" porphyrin is based on one of the geometric isomers (atropisomers) of *meso*-tetra(*o*-aminophenyl)porphyrin.[1] The amino groups of αααα-isomer are used as anchors for fencing pivaloyl groups which also play as steric stabilizers. Before and after this, some *o*-substituted tetraphenylporphyrins have been studied for the thermal and photoatropisomerism.[2] However, due to the convenience in derivation, the αααα-isomer of *meso*-tetra(*o*-aminophenyl)porphyrin has been preferably employed to model the function of hemeproteins.[3] The delicate chemical equipment on the plain and rigid structure of a porphyrin ring is indispensable to construct new functional molecules. Accordingly, some of the atropisomers have been modified to embed the porphyrin ring in liposomes.[4] These fascinating investigations motivated us to attempt the incorporation of a different type of the anchoring group, *viz.* a carboxyl group in *o*-substituted tetraphenylporphyrin for convenience and variety in modification. The carboxyl group may accept amines and alcohols after activations to give the corresponding amides and esters. In addition, since the carboxyl group branches at very near the phenyl ring, also expected was the steric effect in increasing the stability of the desired atropisomer, that is, ROCO- and RNHCO- groups on the tetraphenylporphyrin may retain the advantage to RCONH- and RO- groups in the atropisomerism of the porphyrins.

The porphyrin **1** (Fig. 1) was prepared by condensation of pyrrole with methyl formylbenzoate in a similar manner as Collman *et al.*[1] The four atropisomers (**1a-d**) were separated and purified by silica gel chromatography with benzene/diethyl ether (5/1, v/v).[5] In order of elution they were assigned as αβαβ, ααββ, αααβ and αααα isomers according to the increasing polarity (Fig. 1). These assignments were confirmed by ^{1}H-NMR spectroscopy (Table 1). The enrichment of the αααα-isomer by treating with silica gel was also as successful as the literature.[6] As much as 3.8% of the αααα-isomer was isolated in the repeating conversion.

The thermal atropisomerism of αααα-isomer (**1a**) was observed by the aid of reverse-phase HPLC (Fig. 2). The free base **1a** turned to other atropisomers, **1b**, **1c**, and **1d** upon heating at 363 K in toluene, the time course being given in Fig. 3. From the kinetic treatment was obtained the free energy of



	Yield / %	Rf [a]
1a (αααα)	1.0	0.17
1b (αααβ)	2.3	0.39
1c (ααββ)	1.6	0.47
1d (αβαβ)	1.2	0.59

a) TLC; benzene/diethyl ether (5/1, v/v).

Fig. 1. Structure of *meso*-tetra(*o*-methoxycarbonylphenyl)porphyrin.
Yields and Rf values are shown in the annexed table.

Table 1. Proton NMR data of atropisomers of *meso*-tetra(*o*-methoxycarboxyphenyl)porphyrins[a]

Assignment	αβαβ	ααββ	αααβ	αααα
Internal NH	-2.44 (s, 2H)	-2.46 (s, 2H)	-2.45 (s, 2H)	-2.43 (s, 2H)
Methyl ester H	2.86 (s, 12H)	2.70 (s, 12H)	2.59 (s, 3H) 2.76 (s, 3H) 2.87 (s, 6H)	2.86 (s, 12H)
Phenyl Ha	8.18 (m, 4H)	8.15 (m, 4H)	8.13 (m, 4H)	8.07 (m, 4H)
Phenyl Hb	7.81 (m, 4H)	7.82 (m, 4H)	7.83 (m, 8H)	7.79 (m, 4H)
Phenyl Hc	7.85 (m, 4H)	7.86 (m, 4H)		7.85 (m, 4H)
Phenyl Hd	8.36 (m, 4H)	8.36 (m, 4H)	8.37 (m, 4H)	8.38 (m, 4H)
Pyrrole H	8.57 (s, 8H)	8.58 (s, 4H) 8.62 (s, 4H)	8.59 (m, 8H)	8.59 (s, 8H)

a) 400 MHz ^{1}H-NMR in $CDCl_3$ was carried out on a JEOL JNM GX-400 spectrometer.

activation,[2] with which **1a** is converted to **1b**, $\Delta G^{\neq}$ = 115 kJ·mol^{-1} at both 353 and 363 K (Table 2). This is greater than that of corresponding aminophenyl porphyrin (112 kJ·mol^{-1} at 338 K).[2b] The **2a** was prepared by reacting **1a** with zinc acetate in THF at 60 °C for 1.5 h.[7] During this reaction, a very little unfavorable isomer formation was detected. After purification, **2a** was also subjected to the thermal stability test. The free energy of activation was similarly determined to be $\Delta G^{\neq}$ = 122 kJ·mol^{-1}. As has been reported with *o*-aminophenyl derivative, the Zn complex (**2a**) appeared to be more stable.[2]

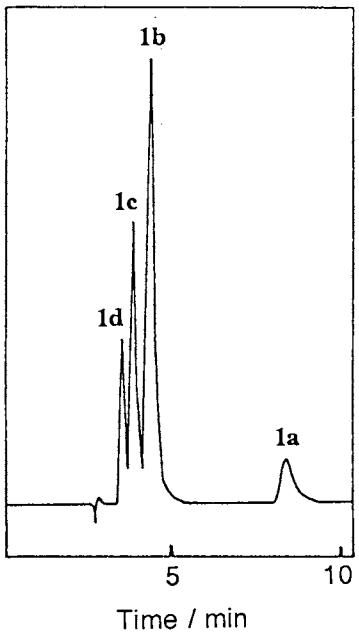


Fig. 2. Reverse-phase HPLC of atropisomers of *meso*-tetra(*o*-methoxycarbonylphenyl)porphyrin. Column, μBondasphere C18 (3.9 x 150 mm); eluent, CH_3CN/MeOH (9/1, v/v); flow rate, 2.0 ml/min; detected at 420 nm.

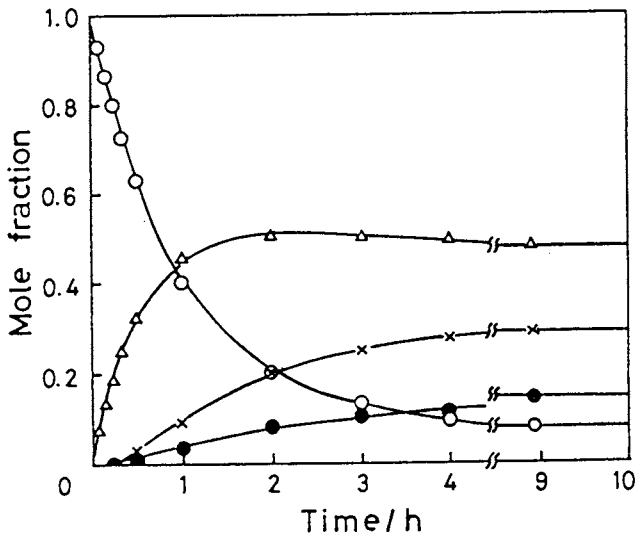


Fig. 3. Time course of the thermal atropisomerism from **1a** to other isomers. (○) **1a**, (△) **1b**, (X) **1c**, (●) **1d**. **1a** was heated at 363 K in toluene. Mole fraction was determined with the results of HPLC.

Table 2. The first-order rate constants and activation parameters for the atropisomerization[a)]

Porphyrin	Temp / K	k x 10^5 / s^{-1}	$\Delta G^{\neq}$ / kJ mol^{-1}
1a	363	24.3	115
1a	353	8.33	115
2a	373	6.67	122
2a	363	2.08	122

a) Atropisomerism from αααα- to ααβ-isomers.

Alkali hydrolysis of the methoxycarbonyl moiety afforded the carboxyphenyl derivatives.[8] Further reaction of the carboxyphenyl-porphyrin with amines after activation with oxarylchloride or by using DCC and 1-hydroxybenzotriazole gave the corresponding amides. Amino acid and peptide derivatives were also successfully coupled in good yields. Thus, a variety was added to other atropisomeric porphyrins valuable in design of peptide-porphyrin conjugates.

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5) **1a**: Absorption spectra in CH_2Cl_2 nm (logε), 422.0 (5.68), 519.2 (4.26), 554.4 (3.88), 598.8 (3.63), 653.2 (3.48); Anal. ($C_{52}H_{38}N_4O_8$) C, H, N; FD-MS, m/z 846 (M^+ 846.3 (calcd)).

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7) **2a**: Absorption spectra in CH_2Cl_2 nm (logε), 426.4 (5.68), 557.2 (4.27), 599.6 (3.71); Anal. ($C_{52}H_{36}N_4O_8$) C, H, N; FD-MS, m/z 910 (M^+ 909.6 (calcd))

8) The porphyrin **1a** (250 mg) in DMF (20 mL) was treated with 5 mol·dm^{-3} NaOH (2.4 mL) at room temperature overnight. To the reaction mixture was added 1mol·dm^{-3} HCl (18 mL) and H_2O (50 mL). The resulted solid was collected, washed with H_2O and dried *in vacuo*; 90%; Rf 0.38 ($CHCl_3$/MeOH/AcOH = 50/10/2, v/v); Anal. ($C_{48}H_{30}N_4O_4\cdot 2H_2O$) C, H, N; FD-MS, m/z 790 (M^+ 790.2 (calcd)). Other isomers with the free carboxyl groups were obtained in a similar manner as described.

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