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NOVEL CHIRAL PORPHYRINS WITH C_2 SYMMETRY[1]

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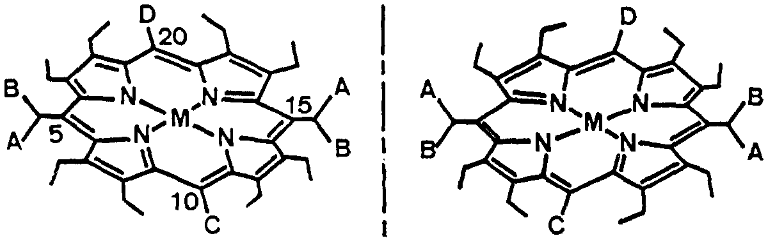
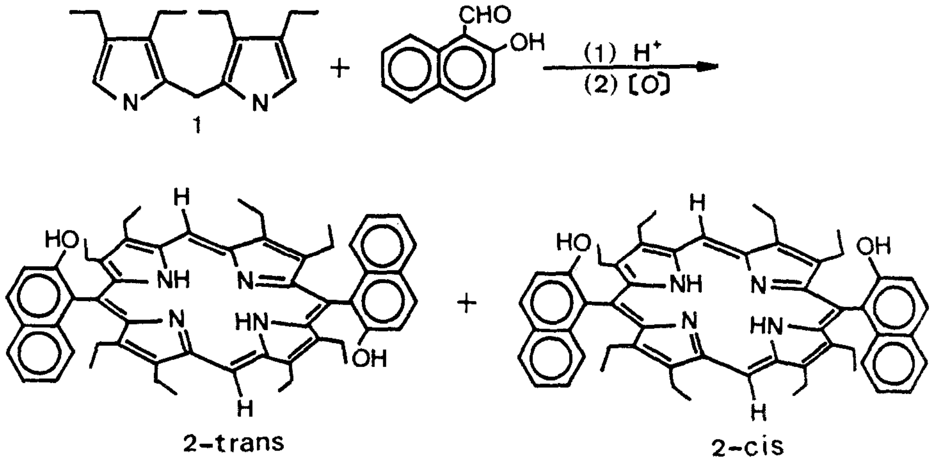
Summary: Described is the preparation of chiral octaethylporphyrin derivatives having two 2-substituted naphthyl groups in a trans orientation at the 5- and 15-meso positions and formyl or hydroxymethyl or alkoxymethyl group derived therefrom at the 10-meso position. One of the derivatives has been successfully resolved into enantiomers by means of HPLC.

Metalloporphyrins are able to catalyze various types of organic reactions. Chiral modification of metalloporphyrins, therefore, is an interesting approach to the catalytic asymmetric organic synthesis.[3] In order to achieve a high degree of chiral recognition, the conformational flexibility of chiral porphyrin catalyst should be minimized and porphyrin-substrate interaction should be maximized via multi-site interaction. We wish to report the preparation and chromatographic optical resolution of novel mesosubstituted chiral octaethylporphyrins, of the general structure shown below, with C_2 symmetry. The asymmetric spatial arrangement of meso-substituents (A, B, C, and D) is identical at both sides of the porphyrin plane, and is expected to provide a steady chiral space or reaction field surrounding the central metal, at which or in the vicinity of which reactions of substrates occur.



The reaction of 3,3',4,4'-tetraethyl-2,2'-dipyrromethane (1)[4] with 2-hydroxynaphthaldehyde by the procedure of either Ogoshi, et. al.,[5] (condensation in benzene with CF_3CO_2H followed by oxidation with O_2/2,6-lutidine/alumina) or Chang, et. al.,[6] (condensation in methanol with TsOH to give the porphyrinogen followed by its oxidation with chloranil in THF) for the preparation of 5,15-diaryloctaethylporphyrin afforded 5,15-bis(2-hydroxynaphthyl)-

octaethylporphyrin (2-trans and 2-cis, eq 1). The atropisomers were separated by means of chromatography on silica gel with chloroform as an eluent into 2-trans (37%, TLC R_f 0.67 (silica/CH_2Cl_2)) and 2-cis (27%, TLC R_f 0.07), which showed almost identical spectroscopic properties.[7] The structures of atropisomers were elucidated by intramolecular bridging of two cis hydroxyl groups; 2-cis reacted with 1,8-dibromooctane under basic conditions to give cyclophane porphyrin (3, 50%).[8] The rotation of naphthyl ring was found to be completely inhibited; there was no evidence for the interconversion of 2-trans $\rightleftharpoons$ 2-cis when a toluene solution of 2-trans or 2-cis was heated at 100 °C for 6 h.



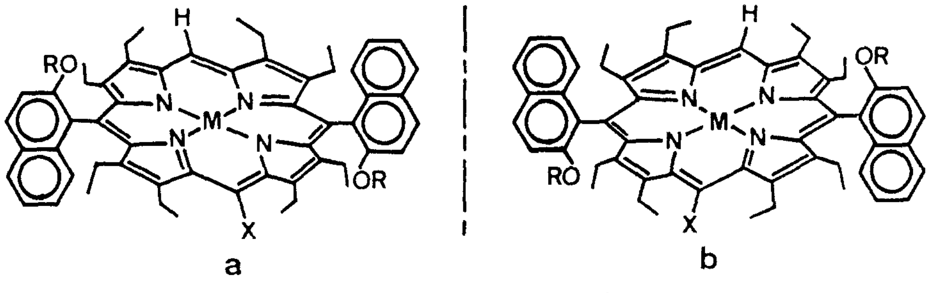
1

2-trans

2-cis

(1)

In order to convert 2-trans into a chiral porphyrin, various attempts were made to introduce one formyl group at the free meso-positions. The best results were obtained when 2-trans was first converted to its nickel complex (nickel acetate, ~100%) and then formylated under Vilsmeyer conditions ($POCl_3$/DMF)[9] to give racemic Ni(II) complex of 10-formyl-5,15-trans-bis(2-hydroxynaphthyl)octaethylporphyrin (4a and 4b, 65%): δ 11.28 (s, 1H, CHO), 9.00 (s, 1H, meso); ν_{CO} 1620 cm^{-1}; λ_{max} (log ε) 442 (4.99), 554 (3.69), 671 nm (4.09)



a

b

4 : R=H, X=CHO, M=Ni(II)
5 : R=H, X=CHO, M=2H
6 : R=H, X=CH_2OH, M=Ni(II)
7 : R=$CH_2C_6H_5$, X=$CH_2OCH_2C_6H_5$, M=Ni(II)

for a CH_2Cl_2 solution unless otherwise stated. Demetalation of 4 under acidic conditions (HCl/CF_3CO_2H) afforded racemic free bases (5a and 5b, ∿100%): δ 12.04 (s, 1H, CHO), 9.62 (s, 1H, meso); ν_{CO} 1620 cm^{-1}; m/e 818 (M^+-CO). This compound in CH_2Cl_2 solutions underwent ready decarbonylation in a day at 30°C and in a week even at -20°C. Reduction of the formyl group in 4 with $NaBH_4$ suspension in ether gave the 10-hydroxymethyl derivative (6, ∿100%): δ 6.03 (double d, 2H, CH_2OH); m/e 905 (M^+); λ_{max} (log ε) 429 (5.25), 554 (4.10), 592 nm (4.21). Alkylation of the three OH groups in 6 with benzyl bromide (NaH/dioxane) afforded the tri(benzyl ether) derivative (7, 23%): δ 5.64 (s, 2H, $10\text{-C}\underline{H}_2OCH_2C_6H_5$), 5.07 (s, 4H, $OC\underline{H}_2C_6H_5$), ca. 3.45 (2H, $10\text{-CH}_2OC\underline{H}_2C_6H_5$ overlapping with $C\underline{H}_2CH_3$); λ_{max} (log ε) 235 (5.02), 283 (4.33), 324 (4.11), 428 (4.97), 552 (3.87), 592 nm (4.04) for a n-hexane-2-propanol (99:1) solution.

By means of HPLC using an optically active column prepared from cellulose tris(3,5-dimethylphenylcarbamate),[10] the racemic mixture of 7 was successfully resolved into two components (1:1) having retention times of 25 and 32 min.[11] These were unambiguously identified as enantiomers since they showed the CD spactra with opposite signs (Figure 1).

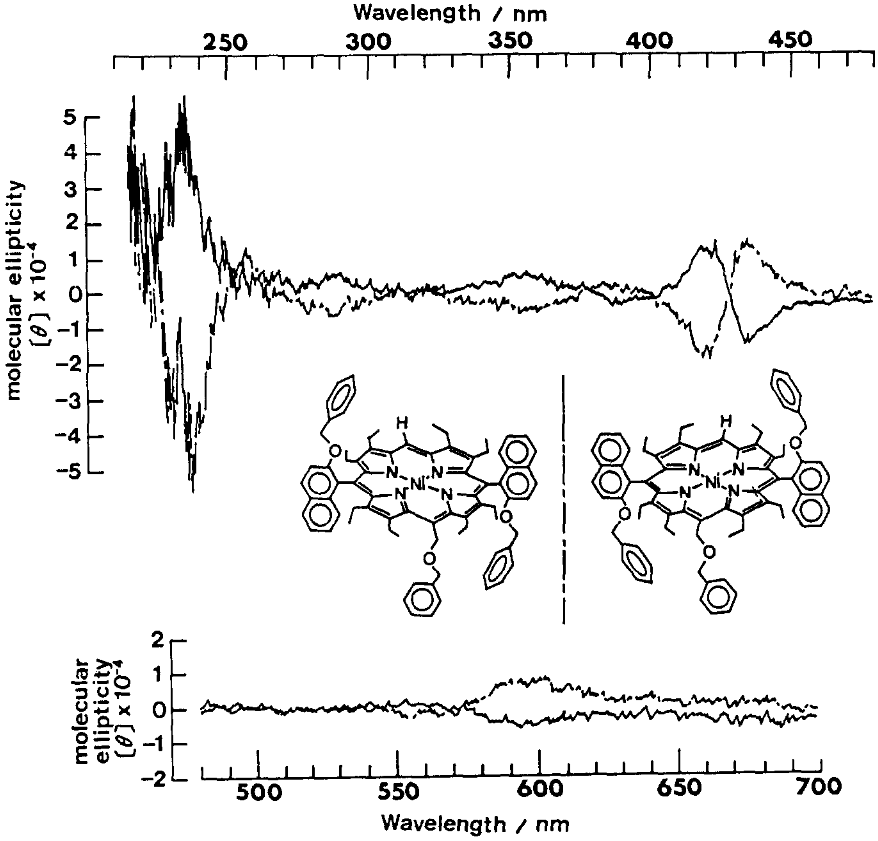


Figure 1. Circular dichroism (CD) spectra of optically pure enantiomers of 7 in n-hexane-2-propanol (99:1): enantiomer having retention time of 25 min (——) and that of 32 min (– – –). The spectra were obtained with a JASCO-J40 spectrometer using a cell of 1-cm path length,

Further work is now under way to obtain various derivatives, to establish the relationships between steric and electronic properties of substituents R and X and extents of chiral recognition, and to determine the absolute configuration of enantiomer by X-ray crystallography.

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REFERENCES AND NOTES

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3. For asymmetric reactions with iron porphyrins with chiral substituents, see: (a) J. T. Groves and R. S. Myers, J. Am. Chem. Soc., 105, 5791 (1983). (b) D. Mansuy, P. Battioni, J. -P. Renaud, and P. Guerin, J. Chem. Soc., Chem. Commun., 155 (1985).
4. Prepared in 80% yield from 2-methyl-3,4-diethyl-5-benzyloxycarbonylpyrrole by successive reactions of oxidative dimerization [$Pb(OAc)_4$], hydrolysis (OH^-), and decarboxylation (100°C) (cf.reference 6).
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7. 2-Trans: ^{1}H NMR ($CDCl_3$) δ 10.33 (s, 2H, meso), 5.23 (s, 2H, OH), 4.00 (m, 8H, CH_2), 2.84 (m, 4H, CH_2), 2.62 (m 4H, CH_2), 1.87 (t, 12H, CH_3), 0.96 (t, 12H, CH_3) and naphthalene ring protons at 8.29 (d, 2H), 8.06 (d, 2H), 7.61 (d, 2H), 7.37 (t, 2H), 7.01 (t, 2H), and 6.84 (d, 2H); IR (KBr) 3530 cm^{-1} (ν_{OH}); mass spectrum m/e 818 (M^+), 801 (M^+-OH), 789 (M^+-C_2H_5), 675 (M^+-$C_{10}H_7O$), 662 (M^+-$C_{10}H_7O$-CH_2), 647 (M^+-$C_{10}H_7O$-C_2H_5). The ^{1}H NMR, IR, and mass spectra of 2-cis were almost the same as those of 2-trans. Electronic spectra for CH_2Cl_2 solutions: 2-trans, λ_{max} (log ε) 413 (5.32), 510 (4.25), 545 (3.90), 576 (3.90), 628 nm (3.53); 2-cis, 413 (5.33), 510 (4.26), 545 (3.89), 576 (3.89), 628 nm (3.55).
8. 3: ^{1}H NMR for octamethylene moiety δ 3.20 (t, 4H, OCH_2-), 0.43 (m, 4H, $OCH_2\underline{CH_2}$-), -0.43 (m, 4H, $OCH_2CH_2\underline{CH_2}$-), -1.51 (m, 4H, $OCH_2CH_2CH_2\underline{CH_2}$-); m/e 928 ($M^+$).
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11. Eluent: n-hexane-2-propanol (99:1) (0.5 mL/min). Column dimension: 25 x 0.46 cm.

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