STERICALLY HINDERED DODECAARYLPORPHYRINS: HIGH-YIELD SYNTHESIS VIA ADLER-LONGO AND LINDSEY REACTIONS[1)]

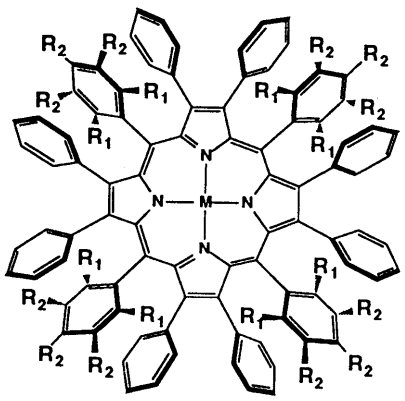
Jun TAKEDA* and Mitsuo SATO

Biophysics Division, Faculty of Pharmaceutical Sciences, Teikyo University, Sagamiko, Kanagawa 199-01, Japan

Dodecaarylporphyrins bearing *ortho* disubstituted phenyl groups at the *meso* positions are synthesized in satisfactory yield. These sterically hindered porphyrins are characterized by UV-visible and ^{1}H NMR spectra.

KEYWORDS porphyrin; dodecaphenylporphyrin; steric hinderance; synthesis; nonplanar conformation; distortion

Highly substituted dodecaarylporphyrins,[1-4)] with their macrocycles distorted significantly by the steric overcrowding of the peripheral substituents, are of great interest in connection with the ruffled conformation of tetrapyrrole macrocycles in ferrochelatase,[2b)] chlorophylls and cofactor F430.[3)] Dodecaphenylporphyrin (H_2DPP)[2,3)] has a permanently and highly distorted macrocycle and, as such, is an important model for the ruffled macrocycles in such biological systems. We have recently developed a surprisingly simple method for preparing H_2DPP in high yield (55%). The method consists only of condensation of 3,4-diphenylpyrrole with benzaldehyde and subsequent oxidation.[2b)] On the other hand, sterically hindered porphyrins of another type such as *meso*-tetrakis(2,6-dichlorophenyl)porphyrin (H_2TCl$_8$PP)[5)] have become the principal species in recent porphyrin chemistry. The steric hindrance in these porphyrins is produced by the bulky phenyl groups with substituents at the ortho (2 and 6) positions. The bulky groups serve to create an open well cavity and to avoid undesirable dimerization and decomposition of the porphyrin macrocycles. We herein report an application of the method to the synthesis of "sterically more hindered dodecaarylporphyrins" bearing *ortho* disubstituted phenyl groups at the *meso* positions. Recent X-ray studies[3b,6)] have revealed that H_2DPP is distorted to saddle-like conformation with the four pyrrole rings tilted alternately above and below the mean porphyrin plane.



M = 2H and Zn

	R_1	R_2	Yield, %	
			Method a	Method b
H_2DPP	H	H	55	22
H_2DF$_{20}$PP	F	F	17	44
H_2DF$_8$PP	F	H	30	43
H_2DCl$_8$PP	Cl	H	1	34
H_2DMx$_8$PP	OCH_3	H	16	45

Chart 1

Two different methods were used to prepare sterically hindered dodecaarylporphyrins. One method involves classical Adler-Longo reaction[7)] with some modifications[2b)] (method a), and the other involves recently developed Lindsey reaction[8)] (method b). In method a, the condensation reaction of 3,4-diphenylpyrrole with an equivalent of aldehyde in refluxing acetic acid for 20 h followed by oxidation with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) for 2 h gave crude dodecaarylporphyrins.[2b)] After the solvent was evaporated to dryness, the crude free-base porphyrins were metalated with zinc acetylacetonate in refluxing CH_2Cl_2 for 1h, or with zinc acetate in refluxing DMF for 30 min. We note that these procedures can be carried out in one flask and that the chromatographic purification is performed more efficiently with the zinc complexes than with the free bases. Thus, the resulting reaction mixture of

zinc complexes was subjected to silica gel chromatography (CH_2Cl_2-hexane as an eluent); the desired zinc porphyrins came off as the first reddish-green band and were recrystallized from CH_2Cl_2-heptane to give purple crystals. The free base porphyrins were easily obtained in 90-100% yield by demetalation of the zinc complexes; stirring of the CH_2Cl_2 solution with 1N HCl, neutralization, and recrystallization from CH_2Cl_2-heptane gave purple crystals of the free bases.

In method b, the condensation between 3,4-diphenylpyrrole and aldehyde was performed in CH_2Cl_2 in the presence of $BF_3{\cdot}Et_2O$ for 20 h at room temperature. After the reaction was quenched by addition of triethylamine, the solvent was evaporated to dryness. The crude porphyrinogens were dissolved in hot toluene and oxidized with DDQ under reflux for 20 h. In this method, all the porphyrins can be directly purified by column chromatography without conversion to zinc complexes.

The yields isolated (not optimized) by the two methods are listed in Chart 1. Surprisingly, the yields obtained by the present methods for the dodecaarylporphyrins are high enough to be compared to those obtained by the Lindsey method for the corresponding *meso*-tetraarylporphyrins (46% for H_2TF_8PP, 25% for $H_2TF_{20}PP$, 11% for $H_2TMx_{12}PP$, and 24% for H_2TCl_8PP).[8b] In addition, our contention is that method a is favorable for the preparation using unhindered aldehydes, while method b is suitable for the preparation even with hindered aldehydes. The exceptionally low yield for H_2TCl_8PP (method a) may be caused by steric repulsion between the ortho Cl groups and the neighboring β-phenyl groups.

UV-visible spectral data of the free-base and zinc dodecaarylporphyrins are summarized in Table I. Noteworthy is the Soret and Q bands that are remarkably red-shifted relative to those of the corresponding *meso*-tetraarylporphyrins. The large red-shifts indicate that all the dodecaarylporphyrins studied have nonplanar saddle-like macrocycles similar to H_2DPP.[1,3a] However, additive red-shift effects such as increased π-electron conjugation between the porphyrin and the *meso*-phenyl rings, electron-donating properties of peripheral substituents, and solute-solvent interactions[3c] cannot be neglected. Thus, introduction of electron withdrawing substituents at the ortho positions of the *meso*-phenyl groups results in the blue-shifted Soret and Q bands in comparison with the unsubstituted H_2DPP and ZnDPP. These blue-shifts are probably due to reduction and/or cancellation of the additive effects described above. The order of the Soret absorption maximum, $DF_{20}PP < DF_8PP < DMx_8PP < DCl_8PP < DPP$ for the free bases and zinc complexes, seems to be correlated with Sternhell's steric parameters Σr* for ortho-substituted tetraarylporphyrins (F < Mx < Cl).[9] On the other hand, electron-withdrawing *meso*-substituents stabilize the HOMOs more than LUMOs and hence result in blue-shifted bands. In fact, the Soret absorption maxima of $H_2DF_{20}PP$ and $ZnDF_{20}PP$ are blue-shifted by 7-8 nm in comparison with those of H_2DF_8PP and $ZnDF_8PP$. The conjugation effect in $DF_{20}PP$ does not differ greatly from that in DF_8PP. Another effect of the ortho substitution is to decrease substantially the intensity ratio of the Q(0,0) to Q(1,0) bands. The free-base dodecaarylporphyrins show the phyllo type visible spectrum. Similar intensity relations are observed for the zinc complexes. The Q(0,0) band cannot be detected for $ZnDCl_8PP$ and $ZnDMx_8PP$ due to its decreased intensity ratio.

Table I UV-Visible and ^1H NMR Spectral Data for Dodecaarylporphyrins

	UV-Visible,[a] λ_{max}/nm					^1H NMR,[b] δ/ppm		
Porphyrin	Soret	$Q_y(1,0)$	$Q_y(0,0)$	$Q_x(1,0)$	$Q_x(0,0)$	NH	meta[c]	para[c]
H_2DPP	464	559	609		715	-1.0	6.75	6.80
$H_2DF_{20}PP$	444	536	575	616	674	-1.49		
H_2DF_8PP	452	546	587	623	692	-1.09	6.18	6.69
H_2DCl_8PP	463	557	599	636	702	-0.92	6.68	6.55
H_2DMx_8PP	453	544	583	630	695	-0.58	5.69	6.54
ZnDPP	461	587	637				6.63	6.73
$ZnDF_{20}PP$	441	565	596					
$ZnDF_8PP$	448	572	608				6.08	6.60
$ZnDCl_8PP$	458	585					6.64	6.49
$ZnDMx_8PP$	451	575					5.52	6.44

[a] UV-visible spectra were recorded in toluene. [b] ^1H NMR spectra were recorded in $CDCl_3$ at 27 °C. [c] Chemical shifts of *meso*-phenyl protons.

The ^1H NMR spectra of the free-base and zinc dodecaarylporphyrins[10] show high field shifts (~1 ppm) for the *meso*-phenyl protons in comparison with the corresponding *meso*-tetraarylporphyrins. The shifts are attributed in part to the ring current effect of the neighboring β-phenyl rings. On the other hand, the NH resonances are shifted to lower fields by 1.5~2.5 ppm. This is due to the overall reduction of porphyrin ring current caused by nonplanar distortion of the macrocycles. The chemical shift differences between the meta and the para protons of the *meso*-phenyl groups are similar for both the free-base and the zinc dodecaarylporphyrins. It seems that the nonplanar saddle-like conformation similar to H_2DPP is retained even with the zinc incorporation and with the introduction of the ortho substituents. Most important, the ortho substituents may affect the tilting angle of the *meso*-phenyl rings with respect to the mean porphyrin plane. UV-visible and NMR data are consistent with the view that the macrocycle nonplanarity and the meso-phenyl tilting are greater in DCl_8PP than in DPP macrocycle.

ACKNOWLEDGEMENT We are grateful to Ms J. Shimode for the technical assistance. This work was partially supported by a Grand-in-Aid for Scientific Resech from the Ministry of Education, Science and Culture, Japan.

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10) **H_2DF_8PP:** δ -1.09 (2H, br s, internal pyrr NH), 6.18 (8H, dd, J_{HH} = 8.51, J_{HF} = 7.06, *meso*-PhH_m), 6.69 (4H, tt, J_{HH} = 8.51, J_{HF} = 6.44 Hz, *meso*-PhH_p), 6.75-6.80 (24H, m, β-$PhH_{m,p}$), 6.90 (16H, m, β-PhH_o); **$ZnDF_8PP$:** δ 6.08 (8H, dd, J_{HH} = 8.54, J_{HF} = 7.32, *meso*-PhH_m), 6.60 (4H, tt, J_{HH} = 8.54, J_{HF} = 6.41 Hz, *meso*-PhH_p), 6.74-6.79 (24H, m, β-$PhH_{m,p}$), 6.89-6.91 (16H, m, β-PhH_o); **$H_2DF_{20}PP$:** δ -1.49 (2H, br s, internal pyrr NH), 7.00 (40H, br m, β-$PhH_{o,m,p}$); **$ZnDF_{20}PP$:** δ 6.98-7.00 (24H, m, β-$PhH_{m,p}$), 7.02-7.04 (16H, m, β-PhH_o); **H_2DCl_8PP:** δ -0.92 (2H, br s, internal pyrr NH), 6.55 (4H, t, J = 8.10 Hz, *meso*-PhH_p), 6.68 (8H, d, J = 8.10 Hz, *meso*-PhH_m), 6.74-6.77 (24H, m, β-$PhH_{m,p}$), 6.97-7.00 (16H, br m, β-PhH_o); **$ZnDCl_8PP$:** δ 6.49 (4H, t, J = 8.55 Hz, *meso*-PhH_p), 6.64 (8H, d, J = 8.55 Hz, *meso*-PhH_m), 6.71-6.75 (24H, m, β-$PhH_{m,p}$), 6.97-7.00 (16H, m, β-PhH_o); **H_2DMx_8PP:** δ -0.58 (2H, br s, internal pyrr NH), 3.39 (24H, s, OCH_3), 5.69 (8H, d J = 8.59 Hz, *meso*-PhH_m), 6.54 (4H, t, J = 8.59 Hz, *meso*-PhH_p), 6.63-6.72 (40H, m, β-$PhH_{o,m,p}$); **$ZnDMx_8PP$:** δ 3.21 (24H, s, Me), 5.52 (8H, d, J = 8.55 Hz, *meso*-PhH_m), 6.44 (4H, t, J = 8.55 Hz, *meso*-PhH_p), 6.50-6.70 (40H, m, β-$PhH_{o,m,p}$).

(Received March 2, 1994; accepted March 10, 1994)