Synthesis of Regioselectively Diiodinated Porphyrins; 5,20-Diaryl-12,13-diiodoporphyrins

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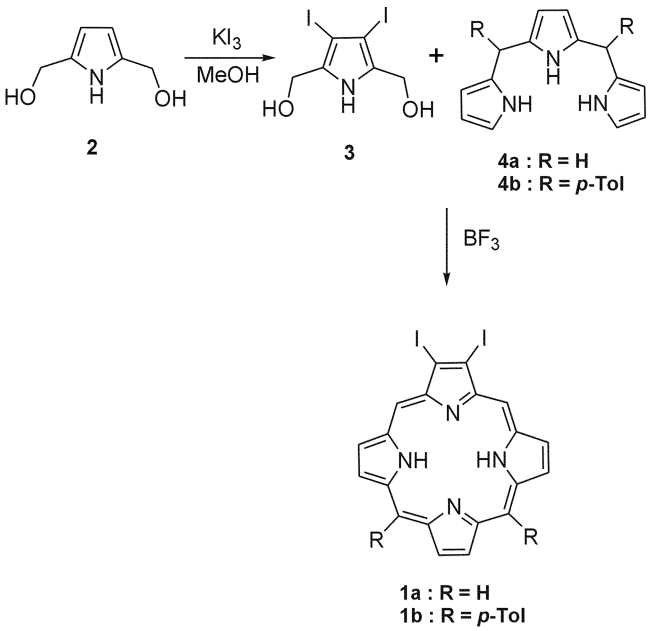
Over the past decade there has been a significant number of reports on the synthesis and physico-chemical properties of a wide variety of halogenated porphyrins. Their unique physico-chemical properties[1] are partly attributed to the nonplanarity of the macrocycle mainly induced by the repulsive interactions among the peripheral substituents. Especially the high-valent metalloporphyrins are of great use as catalysts in many organic transformations.[2] Their catalytic activities are sensitive to the peripheral substituents and introduction of halogens has been known to be crucial for enhanced selectivity and activities. The electron-deficient porphyrins are generally resistant to oxidation and accordingly affect redox potentials. Synthesis of perhalogenated porphyrins are well established and most of the reports so far mainly dealt with bromo-, chloro- and fluoro- substituted porphyrins.[3] Much less is known about their iodo counterparts on the other hand. Especially, availability of porphyrins bearing iodo-substitution in regioselective manner at β-pyrrolic positions has been limited. Introduction of two iodo groups at one of four pyrrolic β-positions would be more challenging when the porphyrin bears couple of different *meso*-substituents. The synthesis of β-iodo substituted porphyrins carrying multiple iodo groups has been reported in the case of duteroporphyrin IX dimethyl ester.[4] To the best of our knowledge on the other hand, there is no report on β-substitution of simple synthetic porphyrins with iodine. Herein, we report a simple '3 + 1' condensation route for the synthesis of diiodoporphyrin derivatives utilizing substituted 3,4-diiodopyrrole with tripyrromethanes. The condensation resulted in the formation of diiodoporphyrins **1a** and **1b** bearing idodo groups at regioselectively designated positions.



Scheme 1

The key component in the synthesis of target porphyrin is 3,4-diiodo-2,5-bis(hydroxymethyl)pyrrole **3**, which was synthesized by treating freshly prepared aqueous solution of KI_3 (1.0 M) with a methanolic solution of 2,5-bis(hydroxymethyl)pyrrole[5] **2**. Immediately the color changed to light pink and the desired product precipitated as light pink flaky solids upon addition of excess water in 60% yield. The compound is quite stable at room temperature and can be stored in freezer for long time but undergoes degradation on heating with liberation of iodine. The identity of diol **3** was easily confirmed by observing disapperance of β-pyrrolic protons in ^{1}H NMR spectra.

Condensation of **3** with simple unsubstituted tripyrromethanes[6] **4a** in the presence of catalytic amount of $BF_3{\cdot}O(Et)_2$ in acetonitrile followed by DDQ oxidation led to the formation of 2,3-diiodoporphyrin **1a**, albeit in very low yield (< 1%). However use of 5,10-ditolyltripyrromethane **4b** in same condensation process resulted in the formation of the corresponding porphyrin **1b** upto 5%.

The absorption data of **1a** (Table 1) showed *bathochromic* shift of the soret band compared to those of porphine[7] (**1c**), while similar trend is observed for the Q-IV and Q-III transitions of the visible part. The spectral pattern of the Q-bands changed from the phyllo-type (**1c**) to etio-type (**1a**)

Table 1. UV/VIS absorption data of porphine, 2,3-diiodoporphyrin (**1a**) and 2,3-diiodo-10,15-ditolylporphyrin (**1b**) in benzene

Comp	Soret	Q-IV	Q-III	Q-II	Q-I
1c	395 (261000)	490 (16000)	520 (3000)	569 (4400)	616 (890)
1a	404 (91400)	499 (6470)	534 (4600)	569 (3060)	
1b	419 (210800)	511 (14500)	545 (3200)	584 (4600)	639 (1520)

and the Q_1 band unusually disappeared (**1a** only showed three visible bands). In case of **1b** phyllo-type Q-band pattern is observed. Both the diiodoporphyrins **1a** and **1b** did not exhibit any fluorescence as expected due to the presence of heavy atom.

In summary, we have succeeded in the regioselective syntheses of two new di-iodoporphyrins by condensation of tripyrrins and diiodopyrrole derivatives. Currently we are expanding the methodology to the synthesis of other multiiodo-substituted porphyrins.

Experimental Section

Proton NMR spectra (400 MHz, Bruker DPX-400) were recorded using TMS as the internal standard. High and Low resolution FAB mass spectra were obtained on AUTO SPEC M-363 high-resolution mass spectrometer. Column chromatography was performed over silica gel (Merck, 230-400 mesh). Pyrrole was distilled at atmospheric pressure from CaH_2. Both CH_2Cl_2 and $CHCl_3$ (reagent grade) were distilled from K_2CO_3 to eliminate traces of acid. All other reagents were obtained from Aldrich and used as received unless noted otherwise.

3,4-Diiodo-2,5-bis(hydroxymethyl)pyrrole (3). K_2CO_3 (2.25 g, 16.3 mmol) dissolved in water (25 mL) added to **2** (1 g, 7.7 mmol) dissolved in methanol (25 mL). To the above solution freshly prepared aqueous 1 M KI_3 (16 mL) added and shaken. Immediately the solution became colored after which excess water was added to precipitate the desired product. The precipitate was filtered and dried in vacuo to obtain **3** as a light pink flaky solid. Yield: 60%. ^{1}H NMR (400 MHz, CD_3OD) δ = 4.56 (s, 4H); MS (EI): Calcd. for $C_6H_7I_2NO_2$ 379.82, found 380.20 (M^+), 382.2 (M^++2).

General procedure for the synthesis of the diiodoporphyrins. A solution of **3** (1 equiv. 0.01 M) and **4a or 4b** (1 equiv.) in acetonitrile was stirred for 15 min at 0°, and then $BF_3{\cdot}OEt_2$ (0.1 equiv.) was added. The mixture was stirred for 30 min, followed by the addition of DDQ (3 equiv.). Stirring was continued at room temperature for 60 min, followed by the addition of excess NEt_3 and stripped of the solvent *in vacuo*. The resulting residue was purified by column chromatography on silica gel using methylene chloride (methylene chloride/*n*-hexane 1 : 1 v/v for condensation of **3** and **4b**) as solvent to give the desired product **1a** in 0.4% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 10.30 (s, 2H, $C_{meso\text{-}H}$), 10.17 (s, 2H, $C_{meso\text{-}H}$), 9.54 (d, 2H, $C_{\beta\text{-}H}$, J = 4.55 Hz), 9.49 (d, 2H, $C_{\beta\text{-}H}$, J = 4.55 Hz), 9.33 (s, 2H, $C_{\beta\text{-}H}$), -4.46 (bs, 2H, -NH); MS (FAB): Calcd. For $C_{20}H_{12}I_2N_4$ 561.92, found 562.90 (M^++1). **1b**, yield: 5%. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 10.36 (s, 2H, $C_{meso\text{-}H}$), 9.49 (d, 2H, $C_{\beta\text{-}H}$, J = 4.8 Hz), 9.12 (d, 2H, $C_{\beta\text{-}H}$, J = 4.8 Hz), 8.83 (s, 2H, $C_{\beta\text{-}H}$), 8.10 (d, 2H, Ar-H, J = 7.8 Hz), 7.58 (d, 2H, Ar-H, J = 7.8 Hz), 2.77 (s, 6H, $-CH_3$), -3.32 (bs, 2H, -NH); MS (FAB): Calcd. for $C_{34}H_{24}I_2N_4$ 742.01, found 742.90 (M^++1).

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