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Synthesis of β-Aryl Substituted Porphyrins by Palladium-catalysed Cross-coupling Reactions

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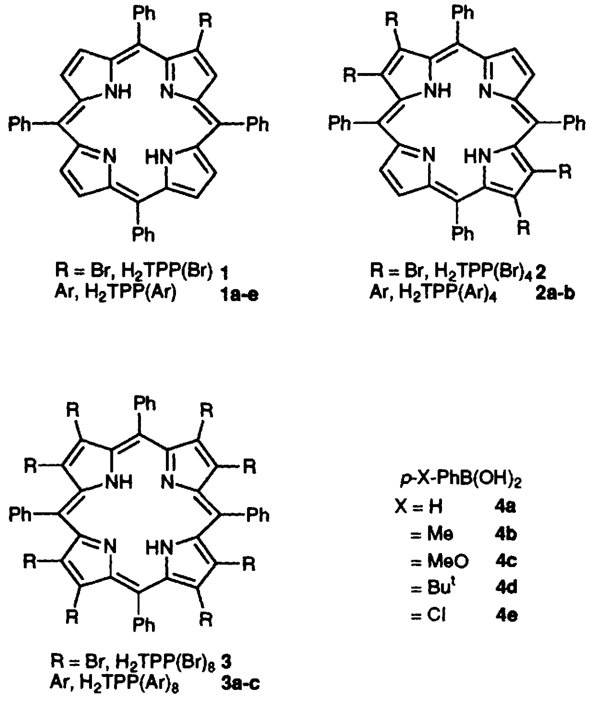
β-Bromoporphyrins undergo Suzuki cross-coupling reactions with aryl boronic acids to give β-arylporpyrins in high yields and X-ray analysis shows that $H_2TPP(Ph)_4$ **2a** (TPP = tetraphenylporphyrin) is centrosymmetric and possesses a hydrogen-bonded inner core.

Substituents at the β-positions of porphyrins exert much larger steric and electronic effects on the porphyrin ring than substituents at the *meso* aryl positions.[1] The β-substituents also induce the porphyrin ring into a non-planar conformation which may control the biological properties in tetrapyrrole systems like the P-450 and photosynthetic centres.[1] The synthesis of these β-substituted porphyrins often requires the relatively inaccessible 3-substituted or 3,4-disubstituted pyrroles for acid-catalysed condensation with aldehydes.[1-3] Furthermore, regioisomeric mixtures, which require chromatographic purification, often result in the preparation of unsymmetrical porphyrins. Since β-brominated porphyrins are obtained easily from the controlled bromination of the porphyrins or metalloporphyrins, the transformation of the bromine substituents into other functional groups would provide a facile entry into β-substituted prophyrins. We now report the synthesis of β-aryl substituted porphyrins by Suzuki cross coupling[4] with β-bromoporphyrins.



Scheme 1

β-Monobromo $[H_2TPP(Br)]$ **1**,[5a] β-tetrabromo $[H_2TPP(Br)_4]$ **2**,[5b] and β-octabromophenyl $[H_2TPP(Br)_8]$ **3**[6] porphyrins all underwent smooth Suzuki cross-coupling reactions with *p*-substituted aryl boronic acids **4** to give high yields (50–88%) of β-aryl tetraphenyl porphyrins [Scheme 1].[7]§ Both electron-donating and -withdrawing groups were introduced with little difference in the rate and yields (**1a–e**). The reactions were carried out in anhydrous toluene with solid K_2CO_3 at 90–100 °C under nitrogen for 1–7 days. Anhydrous conditions were essential as little reaction was observed in a mixed solvent of toluene and aq. K_2CO_3. No protection of the acidic N–H of the porphyrin ring was necessary which is advantageous to the cross-coupling of bromo-substituted zinc porphyrins with organozinc reagents.[7] The use of **4** instead of **2**

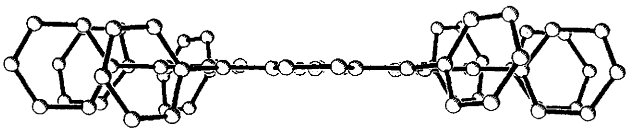


Fig. 2 Perspective view of $H_2TPP(Ph)_4$ **2a** looking from one side in the plane of the porphyin ring

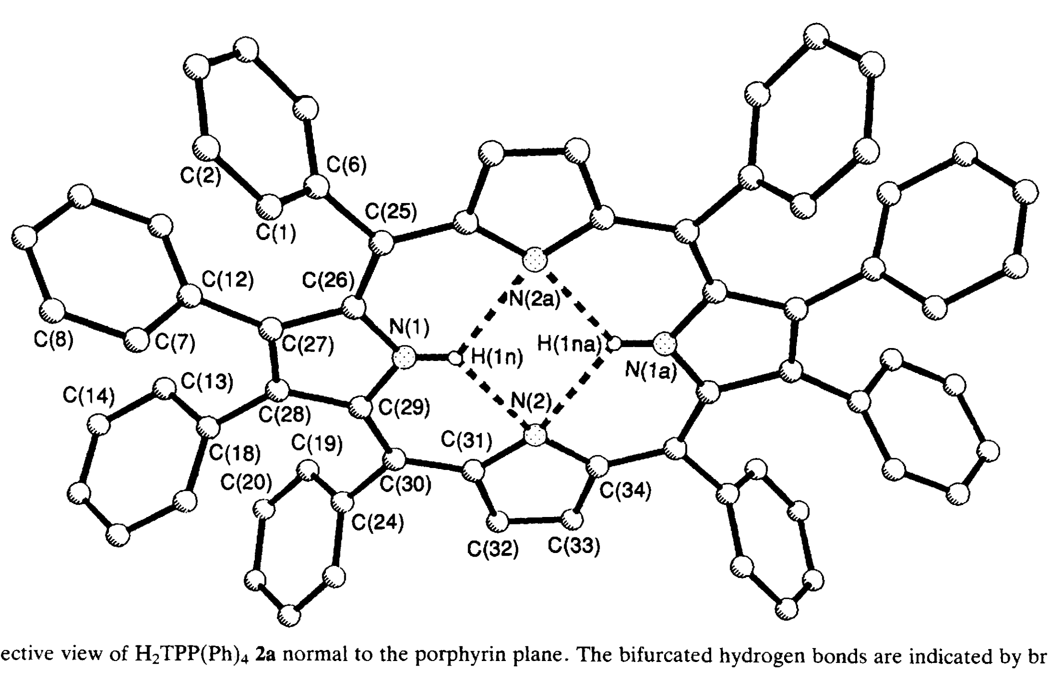


Fig. 1 Perspective view of $H_2TPP(Ph)_4$ **2a** normal to the porphyrin plane. The bifurcated hydrogen bonds are indicated by broken lines.

equiv. of phenyl boronic acid reduced the reaction time of **2** with **4a** to give **2a** from 36 to 24 h but had little effect on the yield.

The centrosymmetric structure of the β-tetraphenylated porphyrin **2a** was determined by single X-ray analysis (Fig. 1).† The regiochemistry of the bromination is thus confirmed as the one proposed by Crossley who rightly corrected an earlier misassignment of $H_2TPP(Br)_4$.[8] Furthermore, it is interesting to note that the porphyrin ring in $H_2TPP(Ph)_4$ is planar (Fig. 2) in direct contrast with the non-planar structures of octa-substituted porphyrins.[1,9]

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Footnotes

† *Crystal data*: dark-blue flat prism, $C_{68}H_{46}N_4$, **2a**, M_r = 919.1, monoclinic, space group $P2_1/c$ with a = 7.474(2), b = 13.301(3), c = 24.814(8) Å, and β = 92.00(2)°, 293 K, Z = 2, $F(000)$ = 964, Mo-Kα radiation (λ = 0.71073 Å). μ = 0.072 mm^{-1}, transmission factors 0.943 to 1.00. Refinement of 1460 reflections with $F > 4.0\sigma(F)$ and 250 parameters yield a final R = 0.065, R_w = 0.075 with $w^{-1} = \sigma^2(F) + 0.002\,|F|^2$. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Information for Authors, Issue No. 1.

§ All new compounds have satisfactory spectral data and elemental analyses.

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