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Synthesis of D_2-Symmetric 5,10,15,20-Tetraarylporphyrins from C_2-Symmetric Benzaldehydes and Achiral Aryldipyrromethanes

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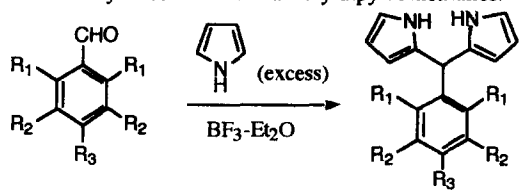
Abstract: A series of new enantiomerically pure D_2- symmetric 5,10,15,20-tetraarylporphyrins has been synthesized by condensation of C_2-symmetric substiuted benzaldehydes with achiral aryldipyrromethanes in 22-40% yield. The mild conditions used enable selective incorporation of the chiral arenes at the 5,15-positions and the achiral arenes at the 10,20-positions. Due to the incorporation of the C_2-symmetric chiral arenes, no atropisomers are possible in these D_2-symmetric ligands. Manganse complexes of these ligands are catalysts for the enantioselective epoxidation of cis-β-methylstyrene.

Chiral tetraarylporphyrins have been successfully applied as catalysis in a number of asymmetric transformations such as epoxidation of unfunctionalized alkenes,[1] cyclopropanations of alkenes,[2] asymmetric oxidation of sulfide,[3] and hydroxylation of activated methylenes.[3a] Approaches for the preparation of chiral tetraarylporphyrins (TPP's) have included the derivatization of functionalized achiral tetraarylporphyrins,[4] and the direct condensation of chiral aromatic aldehydes with pyrrole.[5] We have applied the second method for the condensation of four equivalents of C_2-symmetric benzaldehydes with pyrrole to form D_4-symmetric metalloporphyrins.[6] The atropisomers commonly found when C_1-symmetric arenes are incorporated into TPP are inherently avoided through the use of the C_2-symmetric benzaldehydes and the desired D_4-symmetric tetraarylporphyrins can be prepared in good yields and quantities. However, since the chiral auxiliaries are introduced to all four *meso* positions at same time, the steric range of possible chiral auxiliaries and the systematic study of electronic and steric effects are limited. A more flexible series of related C_2-symmetric tetrarylporphyrins of the substitution type ABAB–but still devoid of atropisomers–could be obtained by incorporating C_2-symmetric arenes at the 5,15-positions and achiral, easily variable arenes at the 10,20-positions. Herein we report the mild condensation of resolved C_2-symmetric benzaldehydes with aryldipyrromethanes to produce selectively such D_2-symmetric tetraarylporphyrins.

It has been reported that the acid-promoted condensation of aryldipyrromethanes with benzaldehydes containing a different phenyl group leads to a mixture of tetraarylporphyrins.[7] Under the forcing reaction conditions, the dipyrromethanes revert to monopyrromethanes which can react to form undesired AAAB and AABB side products in addition to the desired symmetrical ABAB tetraarylporphyrin. The known alternate, stepwise syntheses of ABAB-substituted tetraarylporphyrins[7a] were judged too lengthy for use with synthetic chiral benzaldehydes. Since the most direct route for the preparation of the desired D_2-symmetric porphyrins would be the selective condensation of C_2-symmetric benzaldehdyes with achiral phenyldipyrromethanes,[8] we concentrated on optimizing these conditions.

Scheme 1. Synthesis of Achiral Aryldipyrromethanes.



1a: $R_1 = R_3 = H$; R_2 = t-Bu
1b: R_1, R_2 = $-(CH_2)_3-$; R_2=H
1c: $R_1 = R_3 = CH_3$; R_2=H

2a: (74%)
2b: (41%)
2c: (44%)

The desired achiral aryldipyrromethanes were available in moderate to good yield by a modification of Lindsey's method for the condensation of aromatic aldehydes in the presence of a large excess of pyrrole.[8] Thus, condensation of 2,4-di-*tert*-butylbenzaldehyde (**1a**),[9] *s*-indacene-8-carboxyaldehyde (**1b**)[10] and mesitylaldehyde (**1c**) with pyrrole in presence of BF_3-Et_2O gave aryldipyrromethanes **2a** (74%), **2b** (41%) and **2c** (44%) (Scheme 1). The yields of aryldipyrromethanes were generally higher and there were fewer side products when BF_3-Et_2O was used in place of CF_3COOH.[8] For example, **2b** was obtained in 41% yield using BF_3-Et_2O, but the yield drops to 20% when CF_3COOH was used.. These alkyl-substituted aryldipyrromethanes could be efficiently purified by plugging through a short pad of silica gel covered with decolorizing charcoal using alkane eluents.

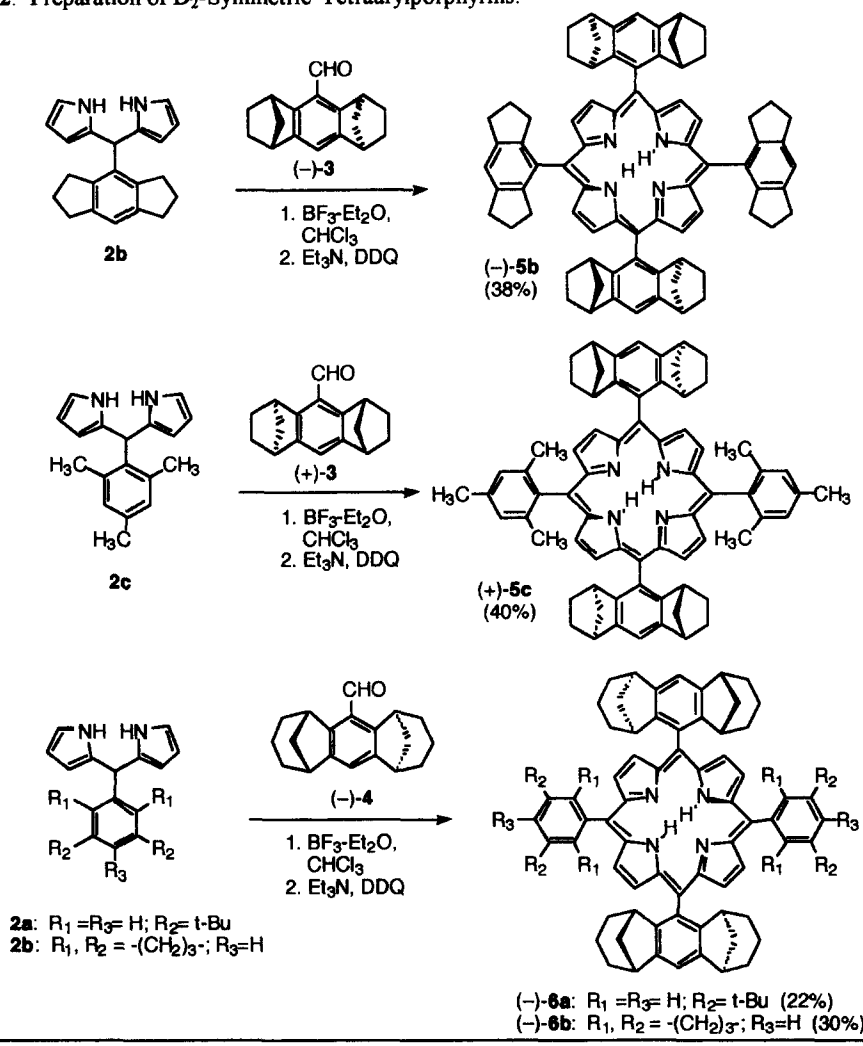
In order to minimize the reverse condensation reactions which could lead to a lack of seletivity and lower yields of tetraarylporphyrins,[7a] mild reaction conditions were employed for the condensation of these achiral dipyrromethanes with enantiomerically pure C_2-symmetric benzaldehydes **3**[6] or **4**.[11] The condensation reactions themselves were performed at room temperature. The oxidative aromatization of the intermediate porphyrinogens was performed under neutral or slightly basic conditions through the addition of triethylamine along with the DDQ oxidant. Under these conditions good yields of readily purified D_2-symmetric tetraaryl porphyrins (–)-**5b** (38%), (+)-**5c** (40%), (–)-**6a** (22%) and (–)-**6b** (30%)[12] were obtained through the condensation of aryldipyrromethanes (**1a-c**) with chiral C_2-symmetric aromatic aldehydes (–)-**3** or (+)-**3** or (–)-**4** (Scheme 2). Both the ^1H and ^{13}C NMR spectra were consistent only with the D_2-symmetric structures of the tetraarylporphyrins shown in Scheme 2; the appropriate number of signals for this symmetry was observed. In each case a single highfield (ca. -2.6 ppm) broad singlet for the pyrrolic-NH protons was observed and although these protons are shown on one set of pyrroles, they are presumably rapidly exchanging between all four pyrrolic nitrogens. Careful examination of the ^1H NMR spectra of the crude tetraarylporphyrin products indicated the presence of what could be 5 to 10% of isomeric tetraarylporphyrins arising from reversion of the starting aryldipyrromethanes, but the traces of these impurities were efficiently removed in the column chromatography and these side products were not conclusively identified. The desired pure D_2-symmetric products were obtained free of side products in the good yields reported above.

An illustrative experimental procedure is as follows: To a solution of aryldipyrromethane **1b** (143 mg, 0.47 mmol) and chiral benzaldehyde (–)-**3**[6] (112 mg, 0.47 mmol) in chloroform (40 mL) was added BF_3-Et_2O (13 mL, 0.10 mmol) at room temperature.[13] The solution was stirred at room temperature for 2 h, triethylamine (38 mL, 1.0 mmol) was added to neutralize the BF_3-Et_2O, and then excess DDQ (80 mg, 0.35 mmol) was added. After stirring at room temperature for 2 h, the solvent was evaporated to give crude product as a greenish powder, which was chromatographed on silica gel with 30% CH_2Cl_2 in petroleum ether to afford (–)-**5b** (93 mg, 38%) as a purple solid, mp>300 °C, $[\alpha]_D^{23}$= -175° ($CHCl_3$, c= 4 x 10^{-3} g/100 mL).[12]

Manganese chloride complexes of (–)-**6a** and (–)-**6b** were prepared in the standard manner[4,6] and the preliminary activity of these complexes as catalysts for the enantioselective epoxidation of alkenes has been studied. The epoxidation of one equivalent of cis-β-methylstryrene in the presence of 0.005 equiv. of the manganese chloride complexes of (–)-**6a** or (–)-**6b**, 0.15 equiv. 4-*tert*-butylpyridine and excess aqueous bleach in

methylene chloride[6] gave after 3 h the (−)-1*S*,2*R*-isomer of the epoxide in 80% or 75% yield and 23% e.e. or 18% e.e. respectively.

Scheme 2. Preparation of D_2-Symmetric Tetraarylporphyrins.



In summary, a new synthesis of D_2-symmetric tetraarylporphyrins enables the introduction of chiral auxiliaries at the 5,15-positions selectively and in good yield. Through the facile variation of the achiral aryl units, this method provides an efficient tool for tuning the reactivity of chiral metallotetraarylporphyrins. While the initial enantioselecitivities in the epoxidations are low, the flexibility of the synthesis should lend itself to facile improvements.

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9. **1a** was prepared from known 3,5- di-t-butyl-1-methylbenzene (prepared according to: Risch, N.; Meyer-Roscher, B.; Langhals, M. *Z. Naturforsch* **1994**, *49b*, 141) in 50% yield by oxidation using ceric ammonium nitrate (according to: Trahanovsky, W.S.; Young, L.B. *J. Org. Chem.* **1966**, *36*, 2033-2035).
10. **1b** was synthesized from known *s* -indacene (prepared from indane according to: Arnold, R. T.; Rondestcedt, E. *J. Am. Chem. Soc.* **1945**, *67*, 1265.) by formylation with CH_3OCHCl_2 in the presence of $TiCl_4$ (see: Rieche, A.; Gross, H.; Höft, E. *Org. Synth.* Col. Vol V, p 49, 1973.)
11. Halterman, R. L.; Mei, X. unpublished results.
12. Spectroscopic data: **5b:** ^{1}H NMR (300 Mhz, $CDCl_3$): 8.70 (br s, 8H), 7.49 (br s, 2H), 7.38 (br s, 2H), 3.57 (br s, 4H), 3.14 (dd, J = 7.0, 7.0 Hz, 8H), 2.75 (br s, 4H), 2.45 (dd, J = 7.0, 7.0 Hz, 8H), 2.06 (m, 12 H), 1.84 (m, 4H), 1.53 (br s, 4H), 1.42-1.22 (m, 12H), 1.00 (br s, 4H), -2.66 (br s, 2H); ^{13}C NMR ($CDCl_3$): 148.01, 144.49, 143.99, 141.63, 132.00-129.05 (br band, weak), 128.50, 120.21, 117.26, 113.61, 49,36, 44.35, 42.38, 33.22, 32.33, 27.56, 26.78, 25.78; **5c:** ^{1}H NMR (300 Mhz, $CDCl_3$): 8.69 (d, J = 4.5 Hz, 4 H), 8.62 (d, J = 4.5 Hz, 4 H), 7.37 (br s, 2 H), 7.26 (br s, 4 H), 3.56 (br s, 4 H), 2.73 (br s, 4 H), 2.60 (br s, 6H), 2.00 (d, J = 8.0 Hz, 4 H), 1.87 (br s, 12 H), 1.81 (b, 4 H), 1.55 (br s, 4 H), 1.40-1.15 (m, 8 H), 0.97 (m, 4H), -2.56 (br s, 2 H); ^{13}C NMR ($CDCl_3$): 148.02, 143.99, 139.46, 138.50, 137.58, 130.86 (m, weak), 128.38, 127.70, 117.63, 116.20, 113.65, 49.31, 44.34, 42.36, 27.52, 26.74, 21.86, 21.46; **6a:** ^{1}H NMR (300 Mhz, $CDCl_3$): 8.86 (d, J = 5.0 Hz, 4 H), 8.82 (d, J = 5.0 Hz, 4 H), 8.09 (d, J = 2.0 Hz, 4H), 7.77 (t, J = 2.0 Hz, 2H), 7.37 (br s, 2H), 3.39 (br s, 4 H) 2.60 (br s, 4 H), 2.53 (m, 4H), 1.80-1.66 (br s, 8 H), 1.55 (br s, 4H), 1.54 (s, 18 H), 1.43-1.29 (m, 4H), 0.96-0.82 (m, 4 H), 0.78-0.5 (m, 4 H), -2.71 (br s, 2 H); ^{13}C NMR ($CDCl_3$): 124.88, 123.50, 121.35, 119.75, 114.00, 112.40, 112.33 (m, weak), 106.37, 106.19, 103.58, 103.23; **6b:** ^{1}H NMR (300 Mhz, $CDCl_3$): 8.74 (d, J = 5.0 Hz, 4 H), 8.69 (d, J = 5.0 Hz, 4 H), 7.48 (s, 2 H), 7.35 (s, 2 H), 3.37 (br s, 4 H), 3.15 (m, 8 H), 2.55 (br s, 4 H), 2.44 (m, 4 H), 2.36 (m, 4 H), 1.98 (m, 8 H), 1.70 (br s, 8 H), 1.52 (m, 8 H), 1.34 (m, 8 H), 1.23 (m, 8 H), 0.87 (m, 4 H), 0.69 (m, 4 H), -2.75 (br s, 2 H); ^{13}C NMR ($CDCl_3$): 146.47, 144.45, 143.43, 141.62, 134.89, 131.94, 129.89 (m, weak), 120.19, 117.06, 116.75, 115.86, 45.20, 41.77, 39.70, 33.20, 32.24, 29.78, 28.34, 25.78, 19.30. UV (1.23 x 10^{-5} $\underline{M}$, CH_2Cl_2) 420 nm (ε = 1.47 x 10^5 cm^{-1} $\underline{M}^{-1}$), 514 nm (ε = 6.84 x 10^3 cm^{-1} $\underline{M}^{-1}$), 548 nm (ε = 2.60 x 10^3 cm^{-1} $\underline{M}^{-1}$), 588 nm (ε = 2.24 x 10^3 cm^{-1} $\underline{M}^{-1}$).
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