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One-Flask Synthesis of *Meso*-Substituted Dipyrromethanes and Their Application in the Synthesis of *Trans*-Substituted Porphyrin Building Blocks

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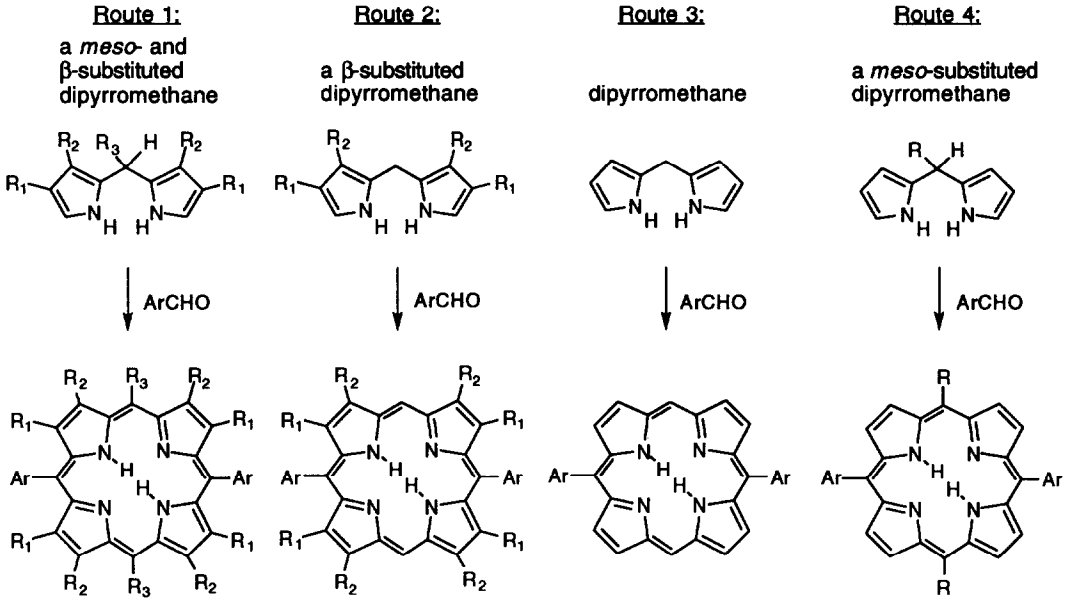
Abstract: The reaction at room temperature of an aldehyde with excess pyrrole in the absence of solvent affords the *meso*-substituted dipyrromethane. The reaction is catalyzed with trifluoroacetic acid or with $BF_3{\cdot}O(Et)_2$. The dipyrromethane is purified by crystallization or by flash chromatography on silica with eluants containing 1% triethylamine. The reaction is compatible with aliphatic or aromatic aldehydes, including 2,6-disubstituted benzaldehydes. Nine dipyrromethanes have been prepared in this manner in yields of 47-86%, indicating the broad scope of the reaction. The dipyrromethanes are stable in the purified form in the absence of light and air. Similar reaction with terephthalaldehyde and pyrrole affords the corresponding bis-dipyrromethane. The reaction of a *meso*-substituted dipyrromethane with an aldehyde under the conditions of the two-step one-flask porphyrin synthesis affords a direct route to *trans*-substituted *meso*-porphyrins. Acidolysis of the dipyrromethane is negligible under the conditions of the porphyrin-forming reaction. Four porphyrins bearing peripheral functional groups and facially-encumbering groups have been prepared which serve as key building blocks in the synthesis of linear porphyrin arrays.

As part of a building block approach toward porphyrin model systems,[2-4] we had need of a direct synthesis of *trans*-substituted porphyrins. *Trans*-substituted porphyrins can be prepared by mixed aldehyde condensations, but the *cis* and *trans*-substituted porphyrins usually are difficult to separate. Direct approaches to *trans*-substituted porphyrins are provided by condensation of dipyrromethanes with aldehydes. Four such routes, each distinguished by the type of dipyrromethane employed, are shown in Scheme 1.

In Route 1, reaction of a β-substituted, *meso*-substituted dipyrromethane with an aldehyde affords a porphyrin bearing substituents at the eight β and four *meso*-positions.[5,6] In Route 2, reaction of a β-substituted dipyrromethane (lacking a *meso*-substituent) with an aldehyde affords a porphyrin bearing substituents at the eight β and two *meso*-positions.[7] Steric interactions of the β and *meso*-substituents cause such porphyrins to be ruffled, and syntheses of β-substituted dipyrromethanes have often required laborious syntheses, yet these routes have been widely utilized due to lack of better alternatives. In Route 3, reaction of dipyrromethane (lacking β and *meso*-substituents) with an aldehyde affords the *trans*-substituted porphyrin bearing only two *meso*-substituents.[8] However, the synthesis of dipyrromethane involves a three-step procedure starting from pyrrole and thiophosgene. For our purposes *trans*-substituted *meso*-porphyrins without β-pyrrole substituents were the most desirable for model systems applications. As shown in Route 4, these porphyrins require access to *meso*-substituted dipyrromethanes.

The chemistry of *meso*-substituted dipyrromethanes has been rather undeveloped. With the exception of the work by Nagarkatti and Ashley,[9] who showed that condensation of 4-pyridine carboxaldehyde with pyrrole in acidified methanol afforded crystals of the hydrochloride salt of *meso*-(4-pyridyl)dipyrromethane, direct syntheses of *meso*-substituted dipyrromethanes have emerged only recently. Casiraghi *et al.* prepared dipyrromethanes by reaction of aliphatic aldehydes with the bromomagnesium reagent of pyrrole in the presence of $TiCl_4$.[10] Recently Vigmond *et al.* published a direct synthesis of *meso*-substituted dipyrromethanes involving reaction of pyrrole and an aryl aldehyde in tetrahydrofuran/acetic acid.[11] A similar synthesis employing reaction in acidified methanol was described by Mizutani *et al.*[12] In addition to these direct syntheses, two stepwise syntheses of *meso*-substituted, β-unsubstituted dipyrromethanes have been developed.[13,14] We also have developed a one-flask synthesis of *meso*-substituted dipyrromethanes. We now present our approach, which appears to offer advantages for application in porphyrin chemistry.

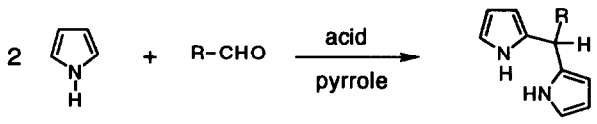


Scheme 1. Use of dipyrromethanes in routes to four types of *trans*-substituted porphyrins.

RESULTS AND DISCUSSION

Dipyrromethane formation:

Aldehydes and pyrrole readily undergo acid-catalyzed condensation at room temperature.[15-17] In solution at equimolar concentrations, the condensation yields oligomers and the cyclic porphyrinogen. In order to achieve a direct synthesis of dipyrromethanes without continued oligomerization, we have performed the pyrrole-aldehyde condensation in the presence of a large excess of pyrrole. Pyrrole serves as the reactant in excess and as the solvent for the reaction, giving direct formation of the dipyrromethane (Scheme 2).



Scheme 2. One-flask synthesis of *meso*-substituted dipyrromethanes.

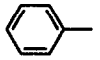
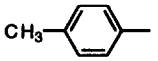
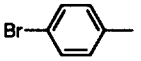
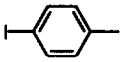
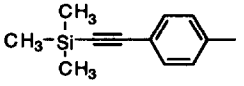
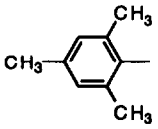
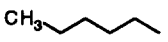
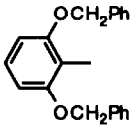
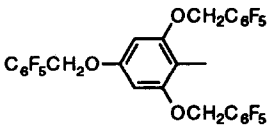
Thus treatment of a solution of benzaldehyde (1 mmol) in 3 mL pyrrole (43 mmol) with a catalytic amount of trifluoroacetic acid (0.1 mmol) for 15 min at room temperature results in complete disappearance of the aldehyde. The crude product is obtained by dilution with CH_2Cl_2, washing with dilute NaOH, and concentration of the organic layer. The excess pyrrole is recovered by vacuum distillation at room temperature. Column chromatography on silica of the resulting brownish solid affords the white *meso*-phenyldipyrromethane (**1**) in 49% yield. With a 70:1 molar ratio of pyrrole:aldehyde the yield increased to 67%. With pyrrole:aldehyde ratios less than ~20:1 the dipyrromethane yield was significantly diminished and increased amounts of materials were observed streaking behind the dipyrromethane on TLC analysis.

This method has been applied to the synthesis of a variety of *meso*-substituted dipyrromethanes (Table 1). Pyrrole easily dissolves each aldehyde examined at the molar ratios employed (pyrrole:aldehyde:acid = 40:1:0.1). The high yields are contingent on using purified aldehydes. The reactions were catalyzed with trifluoroacetic acid and gave dark brown solutions which usually turned pale yellow upon washing with dilute NaOH. However, the reaction with mesitaldehyde afforded a dark red solution, which did not clarify upon washing with base. The mesityldipyrromethane (**6**) was isolated in 60% yield following chromatography. The same condensation with $BF_3{\cdot}O(Et)_2$ catalysis gave a light-brown solution and the product was obtained in 55% yield by direct crystallization from the reaction mixture, thereby avoiding chromatography. Following removal of the excess pyrrole by vacuum distillation at room temperature, TLC analysis of each reaction mixture shows the dipyrromethane, a tiny amount (< 5%) of a tailing component, and some material at the origin of the TLC plate. Upon exposure to Br_2 vapor the dipyrromethane appears red or pink and the tailing material appears violet-brown. In the synthesis of **4** we isolated the tailing component and provisionally assign it by ^1H NMR spectroscopy as the corresponding tripyrromethane. This compound is less stable than the dipyrromethanes and turned from a white solid to a black material over one day at room temperature.

The dipyrromethanes are readily isolated, either by direct crystallization from the reaction mixture after removal of pyrrole (e.g., **3** and **6**), or by chromatography. The direct crystallization requires removal of all traces of pyrrole, leaving an amorphous solid which upon washing with cyclohexane or hexanes yields white crystals. For the dipyrromethanes that do not crystallize directly, flash chromatography on silica in a mildly basic medium (cyclohexane/ethyl acetate/triethylamine = 80/20/1) provides straightforward isolation of the purified dipyrromethane. We find that ~1% triethylamine is essential to prevent decomposition of the dipyrromethane on silica columns, which are slightly acidic. Cyclohexane/ethyl acetate also seems essential as an eluant since hexanes/ethyl acetate or CH_2Cl_2/hexanes (1:1) did not give ready separation of the tailing material from the dipyrromethane. Hexanes could be used in place of cyclohexane in those cases where significant tailing components were not present, as with dipyrromethanes **8** and **9**.

Most of the dipyrromethanes are stable indefinitely in the purified form upon storage at 0 °C in the absence of light. The pentyldipyrromethane (**7**) is a pale yellow liquid and is not as stable as the solids. Dipyrromethane (**5**) is a lower melting solid and slowly discolors upon storing in the freezer. Achieving high purity dipyrromethanes is essential for their application in the synthesis of *trans*-substituted porphyrins.

Table 1. *meso*-(R)dipyrromethanes.

R-	compound	Yield
	1	49%
	2	76%
	3	55%
	4	57%
	5	47%
	6	55%
	7	60%
	8	56%
	9	86%

The ^{1}H and ^{13}C NMR spectra of **4** are shown in Figures 1 and 2. The singlet arising from the benzylic *meso*-proton is rather distinctive for the *meso*-dipyrromethanes, appearing at δ 5.40-5.50 ppm for dipyrromethanes **1-5**, at ~5.9 ppm for **6** and **9**, at 3.96 ppm for the pentyldipyrromethane **7**, and at 6.32 ppm for the dibenzyloxyphenyldipyrromethane **8**.

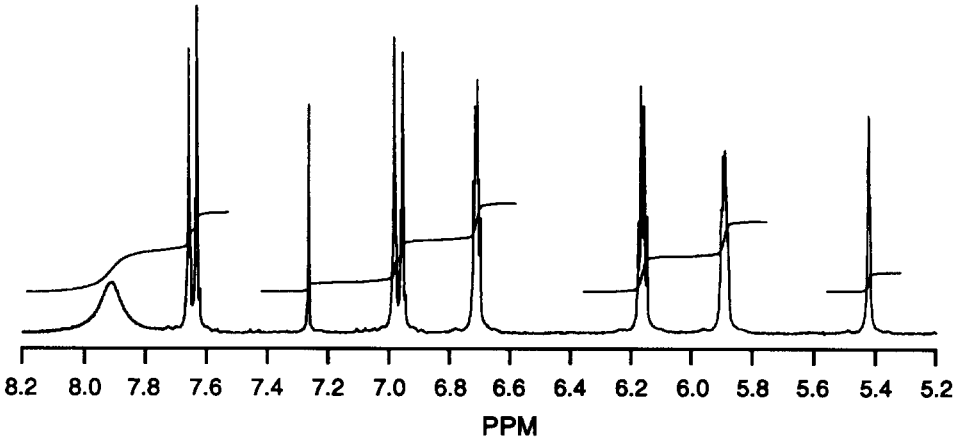


Figure 1. ^{1}H NMR spectrum of *meso*-(4-iodophenyl)dipyrromethane (**4**) in $CDCl_3$.

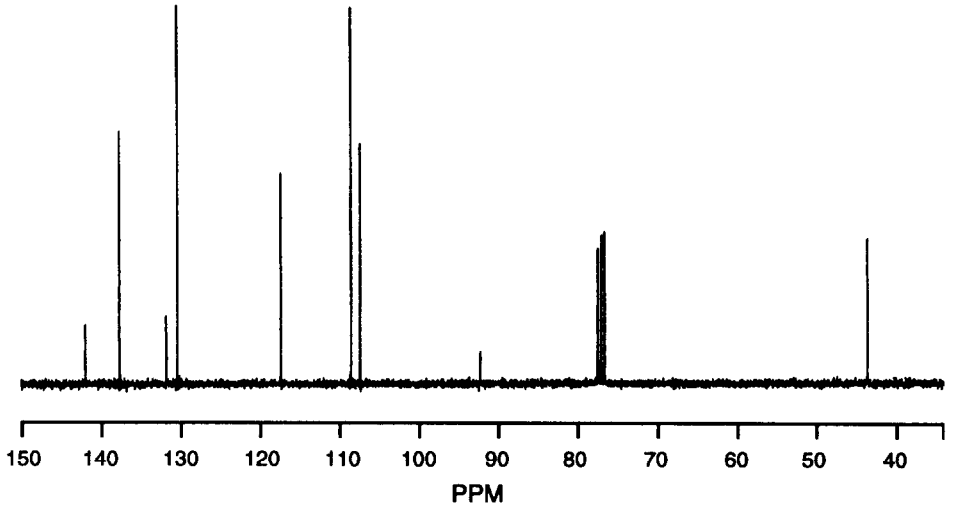
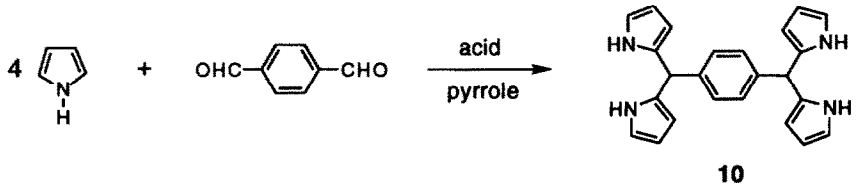


Figure 2. ^{13}C NMR spectrum of *meso*-(4-iodophenyl)dipyrromethane (**4**) in $CDCl_3$.

This one-flask reaction also can be employed with dialdehydes (Scheme 3). Reaction of terephthalaldehyde with pyrrole afforded the bis-dipyrromethane (**10**) in 41% yield. Similar syntheses have been performed with β-substituted pyrroles, yielding β-substituted, *meso*-substituted dipyrromethanes.[6]



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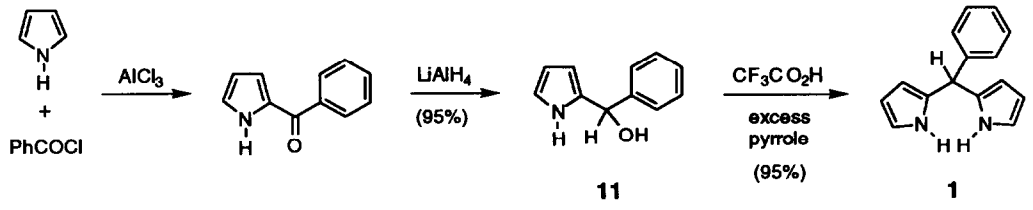
Scheme 3. One-flask synthesis of a bis-dipyrromethane.

The chemistry of dipyrromethanes is such that slightly different synthetic methods and conditions can yield significantly different results. For example, the procedure of Vigmond *et al.* begins with a solution of pyrrole (~3 M) in acetic acid to which is added a stoichiometric amount of the aldehyde in THF/acetic acid (9:1).[11] Our procedure employs pyrrole (~10 M) in excess relative to the aldehyde, no solvent, and a catalytic amount of an acid. The results of these procedures differ in the following manner. First, the yields by the solventless method are 1.5-3 times higher and the products are cleaner. Dipyrromethanes **1** and **2** provide a direct comparison of the two methods. We obtain *meso*-phenyldipyrromethane (**1**) as a white solid with mp 100-101 °C rather than a liquid,[11] and *meso*-(p-tolyl)dipyrromethane (**2**) has mp 110-111 °C rather than 75 °C[11] (or an oil[13]). Second, we find that the chromatography of the *meso*-dipyrromethanes on silica is best performed using mildly basic eluants. The use of neutral organic solvents leads to decomposition of the dipyrromethane on silica. The differing chromatography conditions may partially explain the higher yields and cleaner products we obtain. Third, Vigmond *et al.* report that using 4 equiv of pyrrole causes a decline in yield of the dipyrromethane. We find that in the absence of a solvent, the amount of excess pyrrole can be varied from 40-70 fold with only slight effect on the dipyrromethane yield. We believe the simplicity, cleanliness, and versatility of this method afford advantages for the preparation of *meso*-substituted dipyrromethanes to be used in porphyrin-forming reactions.

We performed several reactions in CH_2Cl_2 with benzaldehyde (6.7×10^{-2} M) and a 10-20 fold excess of pyrrole, but in each case a mixture of products was obtained that streaked from the origin of the TLC plate. The dipyrromethane can be isolated from these reactions but the yields are <10%. Thus the reaction in CH_2Cl_2, even with a large excess of pyrrole, gives a mixture in which the dipyrromethane is not the major product.

An alternative method for preparing *meso*-substituted dipyrromethanes is shown in Scheme 4. It is known that 2-[(α-hydroxy-α-phenyl)methyl]pyrrole (**11**) undergoes self-condensation in acidic solution.[18,19] Indeed, the condensation of benzaldehyde and pyrrole is believed to proceed through such a pyrrylmethanol intermediate (**11**) in the formation of dipyrromethanes and in condensations leading to the porphyrinogen. We treated **11** with excess pyrrole and a catalytic amount of acid using the same conditions employed for the one-flask synthesis of dipyrromethanes **1**-**9**. Condensation proceeded cleanly in 5 min, giving the *meso*-phenyldipyrromethane (**1**) in 95% yield. The tailing impurity found in the condensation of aldehyde and excess pyrrole (Scheme 2) was not observed. The high yield of the dipyrromethane via this approach is offset by the steps required for preparing the precursor alcohol. One advantage of this route may lie in synthesizing asymmetric dipyrromethanes.

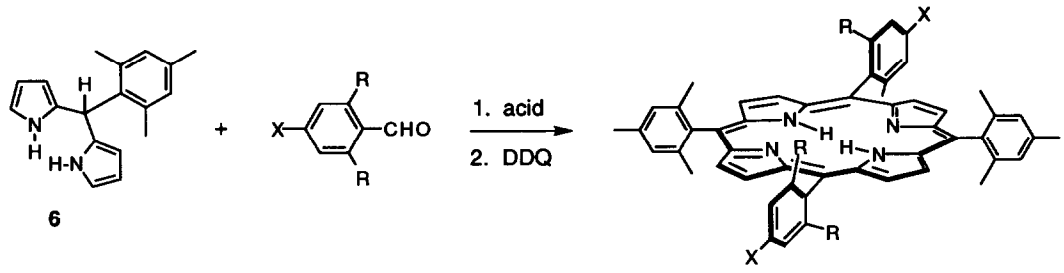


Scheme 4. Directed synthesis of a dipyrromethane.

Porphyrin formation:

One of our objectives has been to develop a set of porphyrin building blocks that can be combined in a rational manner to form multi-porphyrin arrays and related porphyrin model systems.[2-4] A molecular design goal is to prepare porphyrins that bear peripheral functional groups and facially-encumbering groups. The former provide sites for joining porphyrins into arrays and the latter engender enhanced solubility of the porphyrins in organic media. Porphyrins bearing peripheral functional groups and facially-encumbering groups in a *trans*-relationship are readily prepared using *meso*-substituted dipyrromethanes.

A dipyrromethane can be condensed with an aldehyde to afford the *trans*-substituted porphyrin. The conditions of reaction are nearly identical to those for forming a symmetric *meso*-porphyrin from an aldehyde and pyrrole.[15-17] Thus condensation of *meso*-(mesityl)dipyrromethane (**6**) with 4-iodobenzaldehyde afforded porphyrin **12** bearing two facially-encumbering mesityl groups and two *p*-iodophenyl groups (Scheme 5). Similar reaction with 2,6-dimethyl-4-(trimethylsilylethynyl)benzaldehyde[3] afforded the bis-ethynyl porphyrin **13**, which has all *ortho*-positions substituted with methyl groups.



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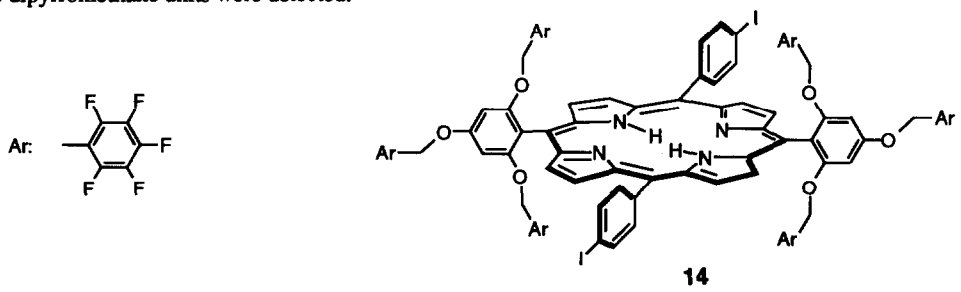
X	R	porphyrin
I—	H—	**12**
$CH_3-Si(CH_3)_2-C\equiv C-$	CH_3—	**13**

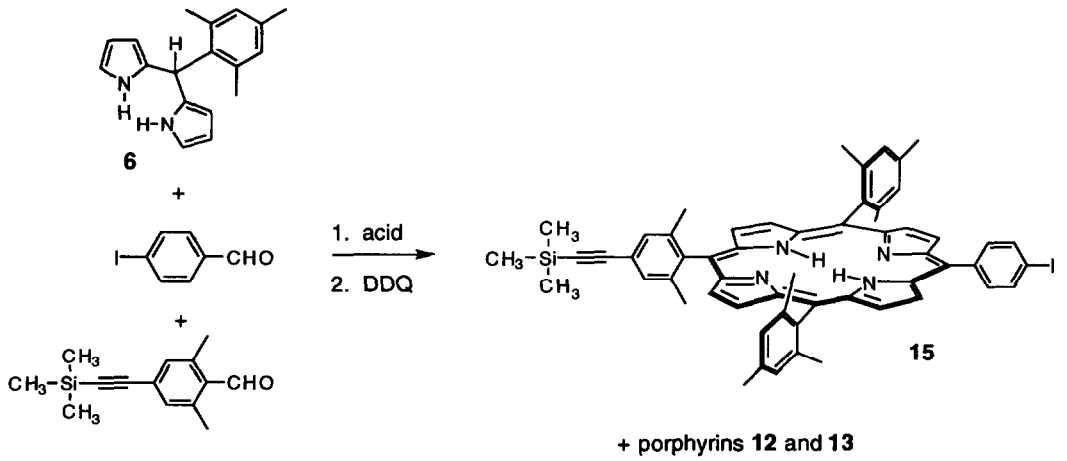
Scheme 5. Synthesis of *trans*-substituted *meso*-porphyrins.

Reaction with dipyrromethane **9** afforded the even more encumbered porphyrin **14** (Scheme 6). In each of these syntheses, only one porphyrin was formed. No porphyrins resulting from acid-catalyzed redistribution of the dipyrromethane units were detected.



Scheme 6. A *trans*-substituted porphyrin bearing large facially-encumbering groups.

Mixed condensations also can be performed. Thus condensation of mesityldipyrromethane (**6**) with 4-iodobenzaldehyde and 2,6-dimethyl-4-(trimethylsilylethynyl)benzaldehyde afforded three porphyrins (Scheme 7). The desired porphyrin **15** bears facially-encumbering groups at three *meso*-sites, one iodo group, and one protected ethynyl group, and was obtained in 13% yield. The three porphyrins were easily separated by chromatography. The related condensation of 4-iodobenzaldehyde and 4-(trimethylsilylethynyl)benzaldehyde[20] affords a mixture of three porphyrins that is extremely difficult to separate. We have previously summarized our findings concerning the roles of substituent polarity and facial encumbrance in the chromatographic separability of porphyrin mixtures formed by mixed-aldehyde condensations.[3] Porphyrin **15** serves as an ideal building block for the preparation of linear covalent arrays of porphyrins.



Scheme 7. Mixed-aldehyde condensation forming *trans*-substituted porphyrins.

It is noteworthy that porphyrin **15** also could be obtained by condensation of mesitaldehyde with iodo-substituted dipyrromethane **4** and an appropriate trimethylsilylethynyl-substituted dipyrromethane. However, the synthesis employing two aldehydes and one dipyrromethane (Scheme 7) provides **15** with one less synthetic step than is incurred in the synthesis employing one aldehyde and two dipyrromethanes.

Acidolysis experiment:

In order to assess the acidolysis of dipyrromethanes under porphyrin-forming conditions, a 0.01 M solution of dipyrromethane **1** in CH_2Cl_2 (or $CHCl_3$) was acidified with 1 (or 3.3) mM $BF_3{\cdot}O(Et)_2$. After 1 h, TLC analysis showed the major component to be the dipyrromethane, with a small amount of material streaking behind the dipyrromethane, purple material at the origin, and no detectable aldehyde. Removal of a sample and oxidation with DDQ in toluene showed the yield of porphyrin to be 2.0 - 2.5% after 1 h under both conditions. The same experiment with dipyrromethane **4** showed no porphyrin yield after 1 h. These observations indicate that acidolysis of the dipyrromethane can occur to a limited extent during the timescale for porphyrin formation, and the extent varies with the nature of the *meso*-substituent. However, this slow dipyrromethane acidolysis has negligible impact during the aldehyde-dipyrromethane condensation leading to *trans*-substituted porphyrins. We find that the aldehyde-dipyrromethane condensations are rapid and generally are complete within 15-20 min. We usually add DDQ after 45-60 min, thereby stopping the condensation. We have observed no detectable porphyrins resulting from acidolysis of dipyrromethanes during the syntheses of porphyrins **12-15**.

CONCLUSION

The one-flask reaction of an aldehyde with excess pyrrole at room temperature makes available a wide variety of *meso*-substituted, β-unsubstituted dipyrromethanes. Though 5,5'-unsubstituted dipyrromethanes have traditionally been regarded as unstable, we find they can be handled in a stable manner under neutral or basic conditions. The dipyrromethanes can conceivably be subjected to many of the same reactions that have traditionally been employed for functionalizing pyrrole. The dipyrromethanes react with an aldehyde under the conditions of the two-step one-flask porphyrin synthesis, affording direct access to *meso*-substituted porphyrins bearing groups in a *trans*-substitution pattern. *Trans*-substituted porphyrins that are facially-encumbered and that bear peripheral functional groups are well-suited for applications in the preparation of linear porphyrin arrays, and these building blocks are now readily available.

EXPERIMENTAL

^1H NMR spectra (300 MHz, General Electric GN 300NB and IBM FT-300), IR spectra (Nicolet 5DXB), and absorption spectra (HP 8451A, Cary 3) were collected routinely. Preparative centrifugal TLC was performed with a Harrison Research Chromatotron Model 7924T. Column chromatography was performed on silica (Merck, 230 - 400 mesh) or alumina (Fisher A540, 80-200 mesh). Pyrrole was distilled at atmospheric pressure from CaH_2. CH_2Cl_2 (Fisher, reagent grade) was distilled from K_2CO_3. $CHCl_3$ (Fisher certified A.C.S.) containing 0.75% ethanol was distilled from K_2CO_3. Trifluoroacetic acid was used as obtained from Aldrich. All other reagents were obtained from Aldrich unless noted otherwise. The dipyrromethanes are easily visualized upon exposure of thin layer chromatography plates to Br_2 vapor.[21] The dipyrromethanes were analyzed by high resolution electron impact mass spectrometry (EI MS). The porphyrins were analyzed by ^{252}Cf plasma desorption mass spectrometry (PDMS).[22]

***Meso*-phenyldipyrromethane (1).** A solution of benzaldehyde (0.1 mL, 1 mmol) and pyrrole (2.8 mL, 40 mmol) was degassed by bubbling with argon for 10 min, then trifluoroacetic acid (0.008 mL, 0.1 mmol) was added. The solution was stirred for 15 min at room temperature, at which point no starting aldehyde was shown by TLC analysis. The mixture was diluted with CH_2Cl_2 (50 mL) then washed with 0.1 N aq NaOH, washed with water and dried (Na_2SO_4). The solvent was removed under reduced pressure and then the unreacted pyrrole was removed by vacuum distillation at room temperature. The resulting yellow amorphous solid was dissolved in a minimal quantity of the eluant and was purified by flash chromatography (silica, 4 cm dia x 20 cm long, 230-400 mesh, cyclohexane/ethyl acetate/triethylamine = 80/20/1). Any remaining pyrrole elutes first, followed slowly by the dipyrromethane, and followed later by tailing materials. Elution of the dipyrromethane required about 500-700 mL solvent. Yield 0.11 g (49%); mp 100-101 °C; ^{1}H NMR ($CDCl_3$) δ 7.89 (bs, 2 H, NH), 7.35-17.19 (m, 5 H, ArH), 6.69 (q, 2 H), 6.15 (q, 2 H), 5.91 (m, 2 H), 5.47 (s, 1 H, *meso*-H); elemental analysis ($C_{15}H_{14}N_2$) calcd C 81.05, H 6.35, N 12.6; obsd C 81.13, H 6.36, N 12.44; EI MS calcd 222.1157, obsd 222.1165.

***Meso*-(*p*-tolyl)dipyrromethane (2).** A sample of *p*-tolualdehyde (0.5 g, 4.15 mmol) was treated identically as for **1**, affording 0.75 g (76%) of a tan solid. mp 110-111 °C; ^{1}H NMR ($CDCl_3$) δ 7.91 (bs, 2 H, NH), 7.12 (dd, ArH), 6.69 (q, 2 H), 6.16 (q, 2 H), 5.92 (1, 2 H), 5.45 (s, 1 H, *meso*-H), 2.33 (s, 3 H, $ArCH_3$); EI MS ($C_{16}H_{16}N_2$) calcd 236.1313, obsd 236.1305.

***Meso*-(4-bromophenyl)dipyrromethane (3).** A sample of 4-bromobenzaldehyde (5.0 g, 27 mmol) was treated identically as for **1**. Upon removal of unreacted pyrrole, the resulting tan viscous oil was treated with cyclohexane and refrigerated overnight, yielding 4.5 g (55%) of a white solid. mp 125-125.5 °C; ^{1}H NMR ($CDCl_3$) δ 7.91 (bs, 2 H, NH), 7.25 (m, 4 H, ArH), 6.71-6.67 (m, 2 H), 6.16-6.14 (m, 2 H), 5.89 (d, 2 H), 5.43 (s, 1 H, *meso*-H); EI MS ($C_{15}H_{13}N_2Br$) calcd 300.0262, obsd 300.0268.

***Meso*-(4-iodophenyl)dipyrromethane (4).** A sample of 4-iodobenzaldehyde (247 mg, 1.06 mmol) was treated identically as for **1**. Upon removal of unreacted pyrrole, the resulting brown solid was purified by column chromatography (silica, 230-400 mesh, cyclohexane/ethyl acetate/triethylamine 80:20:1). Evaporation of the solvent followed by trituration with hexane afforded 200 mg of a light tan solid (57%). mp 145-146 °C; ^{1}H NMR ($CDCl_3$) δ 7.90 (bs, 2 H, NH), 7.79 (dd, 4 H, ArH), 6.70 (q, 2 H), 6.16 (q, 2 H), 5.88 (m, 2 H), 5.41 (s, 2 H, *meso*-H); ^{13}C NMR ($CDCl_3$) δ 141.9, 137.6, 131.7, 130.4, 117.4, 107.4, 103.5, 92.2, 43.6; EI MS ($C_{15}H_{13}N_2I$) calcd 348.0123, obsd 348.0125.

***Meso*-[4-(trimethylsilylethynyl)phenyl]dipyrromethane (5).** A sample of 4-(trimethylsilylethynyl)benzaldehyde[20] (0.4 g, 2 mmol) was treated identically as for **1**. Upon removal of excess pyrrole, chromatography of the viscous oil (silica 4 x 25 cm, 230-400 mesh, cyclohexane/ethyl acetate/triethylamine = 70/30/1) afforded 0.3 g (47%) of a yellow solid. mp 44-46 °C; ^{1}H NMR ($CDCl_3$) δ 7.90 (bs, 2 H, NH), 7.28 (q, 2 H), 6.18-6.14 (q, 2 H), 5.88 (s, 2 H), 5.46 (s, 1 H, *meso*-H), 0.24 (s, 9 H, $SiCH_3$); EI MS ($C_{20}H_{22}N_2Si$) calcd 318.1552, obsd 318.1558.

***Meso*-(mesityl)dipyrromethane (6).** A solution of mesitaldehyde (1.47 mL, 10 mmol) and pyrrole (27.8 mL, 40 mmol) was degassed for 20 min then BF_3-$O(Et)_2$ (0.369 mL, 3.0 mmol) was injected. The light brown mixture was stirred for 30 min at room temperature, then diluted with 50 mL CH_2Cl_2 and immediately

washed with 0.1 N aq NaOH (~50 mL). The organic layer was washed with water and dried (Na_2SO_4). Evaporation of the solvent under reduced pressure resulted in a brown oil. Unreacted pyrrole was removed by vacuum distillation at room temperature, yielding a tacky white solid with light brown splotches. This solid was washed with cyclohexane and then with hexanes, giving a white solid which was collected by filtration. Yield 1.4 g (55%); mp 166-167 °C; ^{1}H NMR ($CDCl_3$) δ 7.93 (bs, 2 H, NH), 6.87 (s, 4 H, ArH), 6.67 (t, 2 H), 6.18 (q, 2 H), 6.01 (t, 2 H), 5.92 (s, 1 H, *meso*-H); EI MS ($C_{18}H_{20}N_2$) calcd 264.1626, obsd 264.1625.

***Meso*-(n-pentyl)dipyrromethane (7).** A sample of hexanal (0.5 mL, 5.0 mmol) was treated identically as for **1**, affording 0.6 g (60%) of a yellowish oil. ^{1}H NMR δ 7.72 (bs, 2 H, NH), 6.62-6.59 (m, 2 H), 6.15-6.12 (q, 2 H), 6.06 (m, 2 H), 3.96 (t, 1 H, *meso*-H), 1.96-1.88 (m, 2 H), 1.32-1.26 (m, 6 H), 0.96 (t, 3 H); EI MS ($C_{14}H_{20}N_2$) calcd 216.1616, obsd 216.1620.

***Meso*-[(2,6-dibenzyloxy)phenyl]dipyrromethane (8).** A sample of 2,6-dibenzyloxybenzaldehyde[4] (318 mg, 1 mmol) was treated identically as for **1**, affording 0.24 g (56%) of a viscous pale yellow oil that remained an oil at room temperature but solidified at 0 °C. ^{1}H NMR δ 8.33 (bs, 2 H, NH), 7.33 (bs, 10 H, PhH), 7.15 (t, 1 H, ArH), 6.70 (d, 2 H, ArH), 6.52 (m, 2 H), 6.08 (q, 2 H), 5.90 (bs, 2 H), 6.32 (s, 1 H, *meso*-H), 5.00 (bs, 4 H, benzylic H); EI MS ($C_{29}H_{26}N_2O_2$) calcd 434.1994, obsd 434.1986.

***Meso*-[2,4,6-tris(pentafluorobenzyloxy)phenyl]dipyrromethane (9).** A sample of 2,4,6-tris(pentafluorobenzyloxy)benzaldehyde[4] (0.35 g, 0.5 mmol) was treated identically as for **1**, affording 0.35 g (86%) of a pale yellow oil that slowly solidified. mp 51 °C; ^{1}H NMR δ 8.21 (bs, 2 H, NH), 6.50-6.48 (m, 2 H), 6.42 (s, 2 H, ArH), 5.95 (q, 2 H), 5.89 (s, 1 H, *meso*-H), 5.70 (bs, 2 H), 5.10 (s, 2 H), 5.02 (s, 4 H); EI MS ($C_{36}H_{17}F_{15}N_2O_3$) calcd 810.1000, obsd 810.2.

1,4-Bis(2,2'-dipyrromethyl)benzene (10). A sample of 1.5 g of terephthalaldehyde (11.2 mmol) was dissolved in 20 mL pyrrole (288 mmol) and the solution was purged with argon for 10 min. Then trifluoroacetic acid (0.086 mL, 0.1 mmol) was injected and the solution was stirred for 30 min at room temperature. The solution was combined with 100 mL CH_2Cl_2, then immediately washed with 0.1 N NaOH, washed with water twice, and dried (Na_2SO_4). The organic layer was concentrated and the remaining pyrrole was vacuum distilled at room temperature. The resulting dark yellow solid was chromatographed (silica, cyclohexane/ethyl acetate/triethylamine, 80/20/1). The first fraction, a fast-moving bright yellow component, was the desired product and yielded 1.69 g (41%). mp 188 °C; ^{1}H NMR ($CDCl_3$) δ 7.93 (bs, 4 H, NH), 7.17 (s, 4 H, ArH), 6.70 (t, 4 H), 6.15 (q, 4 H), 5.91 (s, 4 H), 5.46 (s, 2 H, *meso*-H). EI MS ($C_{20}H_{22}N_2Si$) calcd 318.1552, obsd 318.1558.

Directed synthesis of *meso*-phenyldipyrromethane (1).

A solution of 2-(α-hydroxy-α-phenyl)methyl pyrrole (**11**)[19,23] (0.15 g, 0.85 mmol) and pyrrole (10 mL, 144 mmol) was degassed for 10 min, then trifluoroacetic acid (0.013 mL, 0.17 mmol) was injected. The reaction mixture was stirred for 5 min, then diluted with 50 mL CH_2Cl_2, and then washed with 0.1 N NaOH, water, and dried (Na_2SO_4). Evaporation of the solvent and vacuum distillation of the remaining pyrrole left a colorless liquid, which solidified during vacuum drying. Yield 0.18 g (95%). The analytical properties of this product were identical with that obtained by reaction of benzaldehyde with excess pyrrole.

5,15-Bis(mesityl)-10,20-bis(4-iodophenyl)porphyrin (12). A solution of 4-iodobenzaldehyde (58 mg, 0.25 mmol) and *meso*-(mesityl)dipyrromethane (66 mg, 0.25 mmol) in 25 mL $CHCl_3$ was purged with argon for 10 min, then $BF_3{\cdot}O(Et)_2$ (33 μL of 2.5 M stock solution in $CHCl_3$, 3.3 mM) was added. The solution was stirred for 1 h at room temperature then DDQ (43 mg, 0.19 mmol) was added. The mixture was stirred at room temperature for an additional 1 h and then the solvent was removed. Column chromatography (silica, 4 x 20 cm, CH_2Cl_2) afforded the porphyrin as the first moving band (38 mg, 32% yield). Comparable yields were obtained upon reaction with trifluoroacetic acid catalysis (0.01 - 0.05 M) in CH_2Cl_2. ^1H NMR ($CDCl_3$) δ 8.76 (dd, 8 H, β-pyrrole), 7.99 (AA'BB', 8 H, 4-iodophenyl-H), 7.28 (s, 4 H, mesityl-H), 2.62 (s, 6 H, p-CH_3), 1.82 (s, 12 H, o-CH_3); λ_{abs} (CH_2Cl_2/ethanol, 3:1) 419, 514, 551, 591, 646 nm; PDMS ($C_{50}H_{40}N_4I_2$) calcd 950.1, obsd 949.9.

5,15-Bis(mesityl)-10,20-bis[2,6-dimethyl-4-(trimethylsilylethynyl)phenyl]porphyrin (13). Samples of 2,6-dimethyl-4-(trimethylsilylethynyl)benzaldehyde[3] (58 mg, 0.25 mmol) and *meso*-(mesityl)dipyrromethane (66 mg, 0.25 mmol) were condensed in 25 mL $CHCl_3$ at room temperature with $BF_3{\cdot}O(Et)_2$ (33 μL of 2.5 M stock solution in $CHCl_3$, 3.3 mM). After 1 h DDQ (43 mg, 0.188 mmol) was added and the mixture was stirred for 1 h at room temperature. The reaction mixture was evaporated to dryness and flash chromatography (silica, CH_2Cl_2/hexanes 1:1) gave the porphyrin (30 mg, 25 % yield). ^1H NMR ($CDCl_3$) δ 8.64 (d, 4 H, J = 4.8 Hz, β-pyrrole), 8.56 (d, 4 H, J = 4.8 Hz, β-pyrrole), 7.61 (s, 4 H, ArH), 7.24 (s, 4 H, ArH), 2.61 (s, 6 H, p-$ArCH_3$), 1.92 (s, 6 H, o-$ArCH_3$), 1.90 (s, 12 H, o-$ArCH_3$), 0.42 (s, 9 H, $SiCH_3$), -2.54 (bs, 2 H, NH); λ_{abs} (CH_2Cl_2/ethanol, 3:1) 418, 514, 546, 590, 646 nm; PDMS ($C_{64}H_{66}N_4Si_2$) calcd mass 946.5, obsd 946.4.

5,15-Bis[2,4,6-tris(pentafluorobenzyloxy)phenyl]-10,20-bis(4-iodophenyl)porphyrin (14). A solution of 4-iodobenzaldehyde (46 mg, 0.2 mmol) and *meso*-[2,4,6-tris(pentafluorobenzyloxy) phenyl]dipyrromethane **9** (139 mg, 0.2 mmol) in 50 mL CH_2Cl_2 was purged with argon for 10 min, then trifluoroacetic acid (15 μL, 0.2 mM) was added. The mixture was stirred for 50 min at room temperature then DDQ (91 mg, 0.4 mmol) was added. The mixture was stirred at room temperature for an additional 1 h and then the solvent was removed. Column chromatography (silica, 4 x 25 cm, CH_2Cl_2/hexane 2/1 followed by $CHCl_3$) afforded the desired porphyrin (53 mg, 13% yield). ^1H NMR ($CDCl_3$) δ 8.65 (dd, 8 H, β-pyrrole), 6.86 (s, 4 H, ArH), 5.45 (s, 4 H, p-benzylic H), 4.88 (s, 8 H, o-benzylic H), -3.00 (s, 2 H, NH); λ_{abs} ($CHCl_3$) 422, 515, 549, 590, 646 nm; PDMS ($C_{86}H_{34}N_4F_{30}I_2O_6$) calcd avg mass 2043.0, obsd 2043.8.

5,15-Bis(mesityl)-10-(4-iodophenyl)-20-[2,6-dimethyl-4-(trimethylsilylethynyl)phenyl] porphyrin (15). Samples of 2,6-dimethyl-4-(trimethylsilylethynyl)benzaldehyde[3] (29 mg, 0.125 mmol), 4-iodobenzaldehyde (29 mg, 0.125 mmol), and *meso*-(mesityl)dipyrromethane **6** (66 mg, 0.25 mmol) were condensed in 25 mL $CHCl_3$ at room temperature with $BF_3{\cdot}O(Et)_2$ (33 μL of 2.5 M stock solution in $CHCl_3$, 3.3 mM). After 80 min a sample was removed and oxidized, giving a 47% yield of porphyrins upon spectroscopic examination. Then DDQ (43 mg, 0.188 mmol) was added and the mixture was stirred for 1 h at room temperature. Flash chromatography (silica, from CH_2Cl_2/hexanes 1:1 to 10:1) gave the mixture of three porphyrins. Column chromatography (Fisher A-540 alumina, from hexanes/toluene 2:1 to 100% toluene) gave the bis-ethynyl porphyrin **12** (10 mg, 8.4% yield), the desired iodo-ethynyl porphyrin **15** (16 mg, 13% yield), and the bis-iodo porphyrin **13** (33 mg, 28% yield). The same reaction scaled up linearly to 450 mL $CHCl_3$ gave 170 mg (8%) **12** and 340 mg (16%) **15**. The silica column was eluted with CH_2Cl_2/hexanes 1:1 and

porphyrin **13** remained on the column and was not isolated. Analytical properties for **15**: ^{1}H NMR ($CDCl_3$) δ 8.77 (d, 2 H, J = 4.8 Hz, β-pyrrole), 8.70 (d, 2 H, J = 4.8 Hz, β-pyrrole), 8.65 (d, 2 H, J = 4.8 Hz, β-pyrrole), 8.58 (d, 2 H, J = 4.8 Hz, β-pyrrole), 8.08 (AA'BB', 2 H, ArH), 7.94 (AA'BB', 2 H, ArH), 7.62 (s, 2 H, ArH), 7.29 (s, 4 H, ArH), 2.63 (s, 6 H, p-$ArCH_3$), 1.86 (s, 6 H, o-$ArCH_3$), 1.84 (s, 12 H, o-$ArCH_3$), 0.37 (s, 9 H, $SiCH_3$), -2.60 (bs, 2 H, NH); λ_{abs} (CH_2Cl_2/ethanol, 3:1) 418, 514, 546, 590, 646 nm; PDMS ($C_{57}H_{53}N_4SiI$) calcd mass 948.3, obsd 949.2.

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