Investigation of porphyrin-forming reactions. Part 4.[1] Examination of the reaction course in syntheses of porphyrins *via* dipyrromethanecarbinols[†]

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The dipyrromethanecarbinol motif is a key component in rational routes to a wide variety of porphyrinic macrocycles. We have investigated the dipyrromethane-monocarbinol self-condensation and the dipyrromethane-dicarbinol + dipyrromethane condensation under four different acid-catalysis conditions and have characterized the oligomer composition (by LD-MS), yield of porphyrin (by UV–Vis), and yield of N-confused porphyrin (by HPLC). Under conditions giving "no-scrambling", the condensations are rapid and afford an oligomer composition characterized by (1) absence of scrambling, (2) suppression of acidolysis, and (3) a disproportionate amount of long oligomers from which recovery does not occur. The irreversibility of the reaction and lack of recovery from the long oligomers may explain the lower yields of dipyrromethanecarbinol condensations (<30%) compared with reversible reactions of aldehyde + pyrrole (~50%). Modest levels of acidolysis and scrambling with the dipyrromethanecarbinols are obtained under reaction conditions that cause extensive scrambling in dipyrromethane + aldehyde condensations. Because both reactions give the same porphyrinogen, the scrambling processes must primarily involve the dipyrromethane or oligomer intermediates rather than the porphyrinogen. The dipyrromethane-monocarbinol self-condensation and dipyrromethane-dicarbinol + dipyrromethane condensation afford quite similar oligomer compositions, suggesting that both follow similar pathways to the porphyrinogen. Reaction conditions that suppress scrambling in the dipyrromethanecarbinol condensations were found to dramatically suppress formation of the N-confused porphyrin. Taken together, these experiments show how the greater reactivity of the dipyrromethanecarbinol unit (compared with the pyrrole + aldehyde reaction) facilitates synthesis of *meso*-substituted porphyrins without scrambling.

Introduction

Dipyrromethanecarbinols[‡] have recently emerged as critical intermediates in porphyrin chemistry, providing the basis for the rational synthesis of porphyrins bearing specific patterns of up to four different *meso*-substituents,[2–5] the synthesis of chlorins,[6] and the synthesis of more exotic porphyrinic species such as corroles[7] or heteroatom-substituted porphyrins.[8] The use of dipyrromethanecarbinols in such syntheses is dependent on the absence of scrambling[9] during condensation and oxidation. Early attempts to perform condensations of dipyrromethanecarbinols using conditions identical to those in room-temperature pyrrole + aldehyde (or dipyrromethane + aldehyde) condensations generally resulted in low yields or high levels of scrambling. We anticipated that the pyrrole-carbinol motif would be substantially more reactive than the intermediates involved in scrambling; accordingly, milder conditions than those required in dipyrromethane + aldehyde condensations could be employed that (1) inhibit scrambling and (2) provide a good yield of porphyrin. We identified conditions for the condensation of a sterically unhindered dipyrromethane + aldehyde that afforded a low level of scrambling but the yield of porphyrin also was quite low (<10%). Application of these "low-scrambling" conditions (termed BF_3/UH-DPM conditions) to the reactions with dipyrromethanecarbinols resulted in very rapid reaction, no detectable scrambling, and yields in the range of 15–35%. Those studies led to the identification of refined "no-scrambling" condensation conditions for reactions of dipyrromethanecarbinols that employ 30 mM TFA in acetonitrile at room temperature for a few minutes.[3] The refined "no-scrambling" conditions will be referred to as "TFA/DPM-carbinol" conditions.

In this paper we report our studies concerning the reaction course of dipyrromethanecarbinol condensations leading to porphyrin. The analysis of oligomer composition, acidolysis, and scrambling was performed using laser desorption mass spectrometry (LD-MS),[10,11] while the yield of N-confused porphyrin was assessed by HPLC.[12] Two general types of dipyrromethanecarbinol condensations were considered: (1) the self-condensation of a dipyrromethane-monocarbinol and (2) the condensation of a dipyrromethane-dicarbinol[§] + dipyrromethane (Scheme 1). In both cases, the selection of substituents provided a *trans*-A_2B_2-porphyrin identical to that considered in the previous paper,[1] enabling direct comparison with the dipyrromethane + aldehyde condensations. These experiments provide fundamental data for understanding the reaction course that is central to the rational synthesis of porphyrinic macrocycles bearing specific patterns of substituents.

[†] Electronic supplementary information (ESI) available: discussion of LD-MS peak assignments, and illustrative LD-MS spectra from condensations of dipyrromethane + aldehyde (both 5 mM) under standard-TFA catalysis and standard-BF_3 catalysis. See http://www.rsc.org/suppdata/p2/b0/b009101o/

[‡] The term carbinol has been abandoned by IUPAC; the IUPAC term for carbinol is a substituted methanol.

[§] We use the term dipyrromethane-dicarbinol in place of the previous term dipyrromethanediol,[2] dipyrromethane-monocarbinol in place of dipyrromethanecarbinol,[5] and dipyrromethanecarbinol as the generic all-encompassing term.

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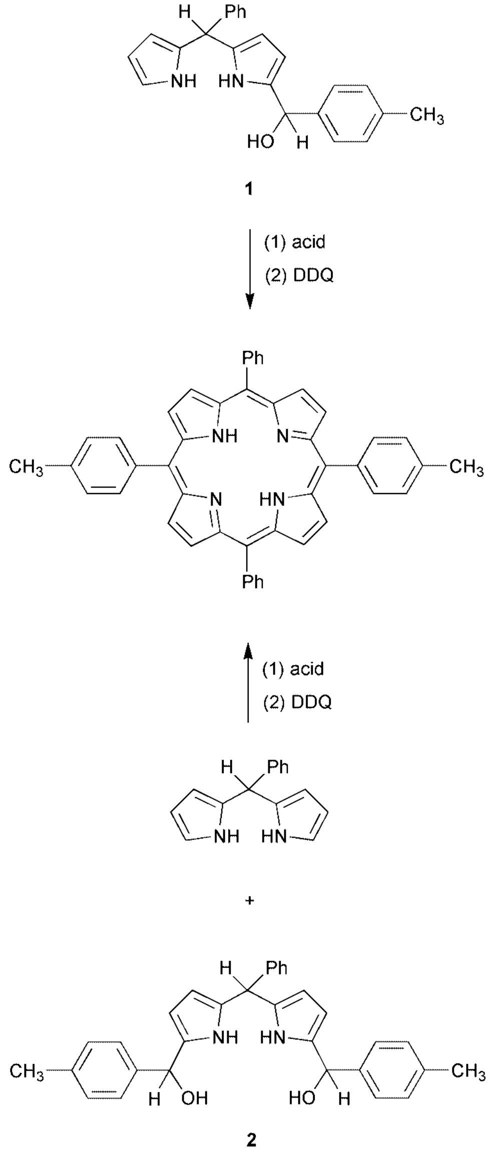
Table 1 Conditions examined in dipyrromethanecarbinol reactions yielding porphyrins[a]

Conditions	Solvent	Acid	T	Typical reaction
TFA/DPM-carbinol[b]	CH_3CN	TFA, 30 mM	rt	DPM-dicarbinol + DPM[e]
BF_3/UH-DPM[c]	CH_3CN	BF_3–Et_2O, 1.0 mM + NH_4Cl, 100 mmol L^{-1}	0 °C	Unhindered DPM + ArCHO[f]
Standard-TFA[d]	CH_2Cl_2	TFA, 20 mM	rt	Pyrrole + ArCHO[g]
Standard-BF_3[d]	CH_2Cl_2	BF_3–Et_2O, 1.0 mM	rt	Pyrrole + ArCHO[g]

[a] In each reaction DDQ is employed as the oxidant. [b] Ref. 3. [c] Ref. 9. [d] Ref. 13. [e] DPM = dipyrromethane. Previously used 10 mM of each; effective concentration of "pyrrole" = 40 mM. [f] Previously used 10 mM of each; effective concentration of "pyrrole" = 20 mM. [g] Pyrrole + aldehyde; previously used 10 mM of each.



Scheme 1 Synthesis of a *trans*-A_2B_2-porphyrin *via* self-condensation of a dipyrromethane-monocarbinol (**1**) or *via* condensation of a dipyrromethane-dicarbinol (**2**) + a dipyrromethane.

Results

Four types of reaction conditions were examined and are listed in Table 1. These include "TFA/DPM-carbinol" conditions empirically derived to prevent scrambling in dipyrromethane-dicarbinol condensations,[3] "BF_3/UH-DPM" conditions utilized in unhindered dipyrromethane + aldehyde condensations,[9] "standard-TFA" conditions employed in one-flask pyrrole + aldehyde condensations,[13] and "standard-BF_3" conditions used in one-flask pyrrole + aldehyde condensations.[13] Reaction samples were oxidized with DDQ prior to analysis. Crude oxidized reaction mixtures were analyzed for oligomer composition, extent of acidolysis, and level of scrambling by LD-MS as described previously (see supplementary information for discussion of peak assignments for these specific reactions). The oligomers could be grouped into one of three categories: expected, acidolysis, or scrambled.[1]

The self-condensation of a dipyrromethane-monocarbinol

(i) Oligomer composition, acidolysis, and scrambling. The dipyrromethane-monocarbinol **1** derived from 1-*p*-toluoyl-5-phenyldipyrromethane was employed in this self-condensation study (Scheme 1). A dipyrromethane-monocarbinol concentration of 5 mM was used in all cases to provide a 10 mM concentration of "pyrrole" and "aldehyde" units.

The self-condensation of dipyrromethane-monocarbinol **1** was performed under the four different acid catalysis conditions (Table 1). The oligomer composition and yield obtained at 8 min in each reaction is shown in Fig. 1. The reactions carried out under TFA/DPM-carbinol conditions and BF_3/UH-DPM conditions gave very simple LD-MS spectra. The dominant peaks were assigned to oligomers arising from dipyrromethane-monocarbinol self-condensation, and a small number of minor peaks were consistent with low levels of acidolysis. No peaks could be definitively assigned to scrambled oligomers.¶ In contrast, the reactions under standard-TFA conditions and standard-BF_3 conditions provided more complicated LD-MS spectra containing a significant number of peaks assigned to both acidolysis and scrambled oligomers. Nevertheless, the level of undesired oligomers was much lower than the nearly statistical distribution observed from condensations of 5-phenyldipyrromethane + *p*-tolualdehyde performed under standard-TFA or standard-BF_3 conditions (see supplementary information). At the reaction times corresponding to the optimal yield of porphyrin for each reaction, the level of undesired oligomers had increased, but was still far from statistical (Fig. 2). At 8 h, the TFA/DPM-carbinol conditions and BF_3/UH-DPM conditions again provided simple mass spectra, dominated by expected oligomers. Only low levels of scrambling were evident. The standard-TFA conditions and standard-BF_3 conditions at 1 h provided more complicated mass spectra than observed earlier in the reactions, though not a statistical distribution of oligomers.

Although the standard-TFA conditions and standard-BF_3 conditions provided undesired oligomers, the less than statistical nature of the acidolysis and scrambling prompted investigation of reaction conditions employing lower concentrations of acid. As the concentration of either TFA or BF_3–Et_2O in CH_2Cl_2 was decreased, the self-condensation of the dipyrromethane-carbinol gave decreased levels of undesired oligomers resulting in very simple LD-MS spectra (Fig. 3). At the lowest acid concentration examined, the crude reaction mixtures displayed no peaks consistent with scrambling and were nearly devoid of undesired oligomers formed through acidolysis. The predominant oligomers detected by LD-MS were due to extended oligomerization of the dipyrromethane-

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¶ The minor peaks at slightly higher *m*/*z* than the expected peaks also appeared in the self-condensation of the all-phenyl dipyrromethane-monocarbinol (**3**); thus, the minor peaks are probably not due to scrambling.

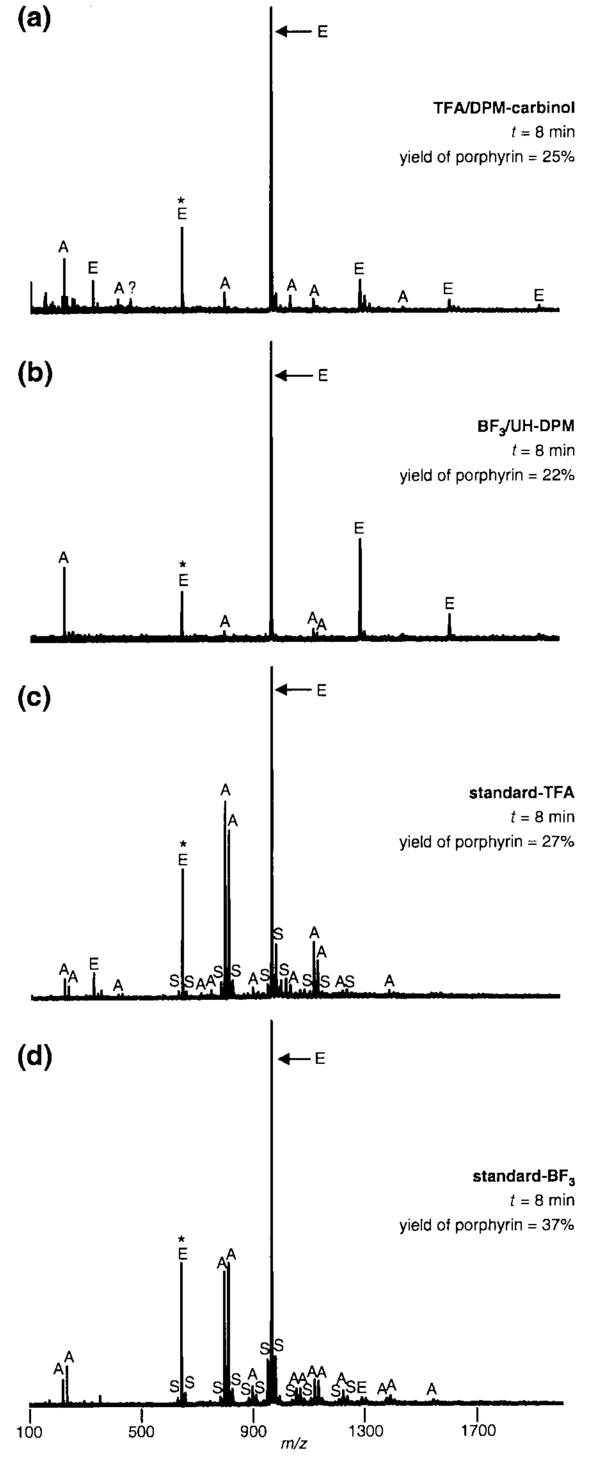

Fig. 1 Comparison of LD-MS spectra showing the oligomer compositions derived from self-condensation of dipyrromethane-monocarbinol **1** (5 mM) under four different reaction conditions at 8 min: (a) "TFA/DPM-carbinol" conditions; (b) "BF$_3$/UH-DPM" conditions; (c) "standard-TFA" conditions; (d) "standard-BF$_3$" conditions. The total porphyrin yield (UV–Vis) is noted. E = expected oligomers, A = acidolysis oligomers, S = scrambled oligomers. The peak with *m*/*z* corresponding to the desired *trans*-A_2B_2-porphyrin product is marked with an asterisk.

monocarbinol. The porphyrin yields obtained under those conditions were still respectable, with BF_3–Et_2O providing higher yields than TFA (30% and 21%, respectively).

(ii) Macrocycle yields. Under either the BF$_3$/UH-DPM or TFA/DPM-carbinol reaction conditions, the yield of porphyrin from self-condensation of dipyrromethane-monocarbinol **1** was ~25%. Application of these conditions gave very low

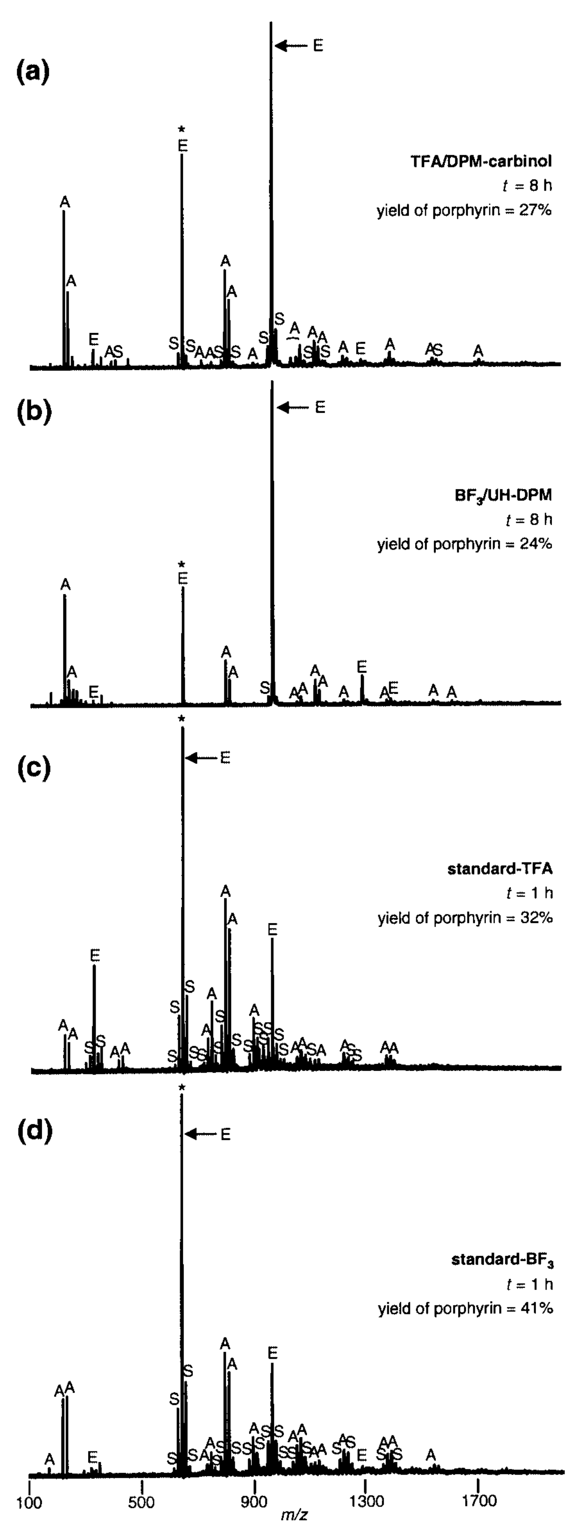

Fig. 2 Comparison of LD-MS spectra showing the oligomer compositions derived from the self-condensation of dipyrromethane-monocarbinol **1** (5 mM) under four different reaction conditions at the reaction time corresponding to the maximum yield of porphyrin: (a) "TFA/DPM-carbinol" conditions, 8 h; (b) "BF$_3$/UH-DPM" conditions, 8 h; (c) "standard-TFA" conditions, 1 h; and (d) "standard-BF$_3$" conditions, 1 h. The total porphyrin yield (UV–Vis) is noted. E = expected oligomers, A = acidolysis oligomers, S = scrambled oligomers. The peak with *m*/*z* corresponding to the desired *trans*-A_2B_2-porphyrin product is marked with an asterisk.

yields with pyrrole + benzaldehyde (<5%, 0% respectively) or 5-phenyldipyrromethane + *p*-tolualdehyde (<10%, 0% respectively). The yield of porphyrin upon self-condensation of **1** under the standard-TFA conditions or standard-BF$_3$ conditions was 32% or 41%, respectively. These yields can be

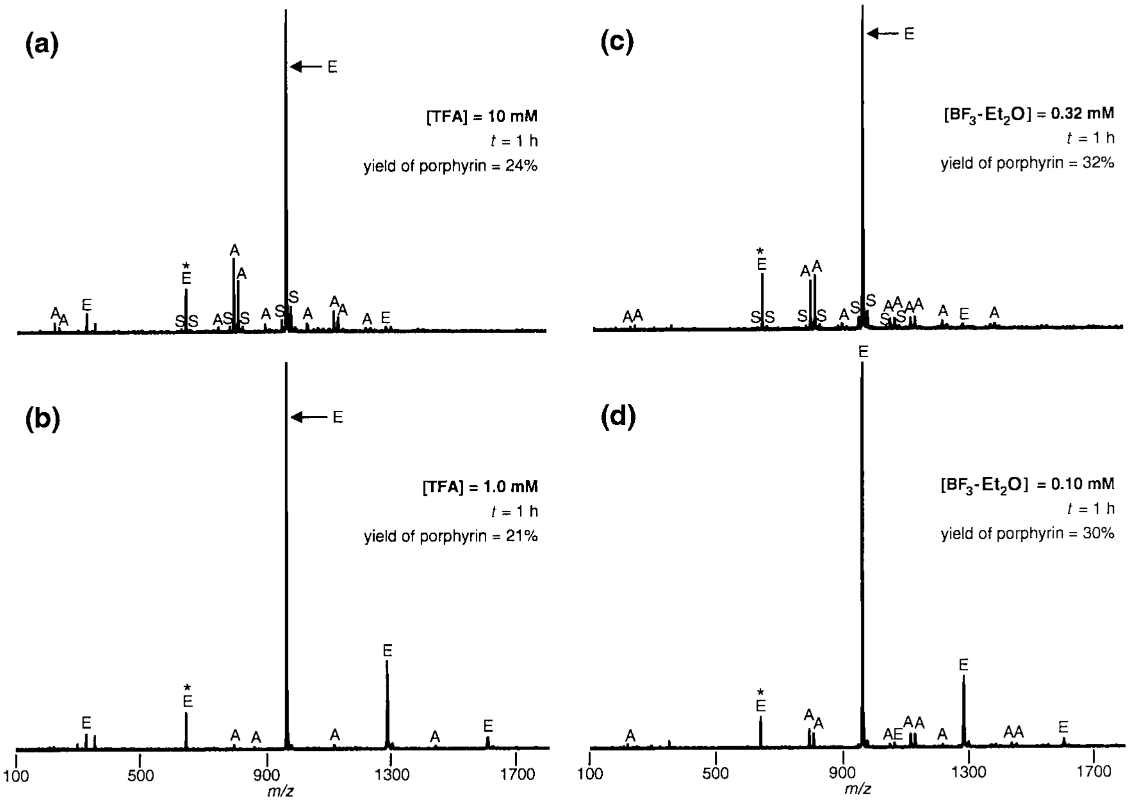

Fig. 3 LD-MS spectra showing the oligomer compositions derived from self-condensation of dipyrromethane-monocarbinol **1** (5 mM) under "standard" reaction conditions involving lower acid concentration. (a) 10 mM TFA, 1 h; (b) 1.0 mM TFA, 1 h; (c) 0.32 mM BF_3–Et_2O, 1 h; (d) 0.1 mM BF_3–Et_2O, 1 h. The total porphyrin yield (UV–Vis) is noted. E = expected oligomers, A = acidolysis oligomers, S = scrambled oligomers. The peak with *m*/*z* corresponding to the desired *trans*-A_2B_2-porphyrin product is marked with an asterisk.

Table 2 Effects of conditions on porphyrin yields from various reactions

	Yield of porphyrins (%)			
	Condensation conditions[a]			
Reaction	TFA/DPM-carbinol[b]	BF_3/UH-DPM[c]	Standard-TFA[d]	Standard-BF_3[e]
Self-condensation of DPM-monocarbinol **1**	25	25	32	41
DPM-dicarbinol **2** + 5-phenyldipyrromethane	31	—	36	47
5-Phenyldipyrromethane + *p*-tolualdehyde	0	<10	40	42
Pyrrole + benzaldehyde	0	<5	37	26

[a] The condensations were performed on a 10 mL scale for variable lengths of time, then a 0.5 μL aliquot was treated with 0.0075 mmol of DDQ (~2-fold excess) for at least 5 min followed by UV–Vis spectrophotometric analysis. [b] 30 mM TFA in acetonitrile at room temperature. [c] 1.0 mM BF_3–Et_2O and 100 mmol L^{-1} NH_4Cl in acetonitrile at 0 °C. [d] 20 mM TFA in CH_2Cl_2 at room temperature. [e] 1.0 mM BF_3–Et_2O in CH_2Cl_2 at room temperature.

compared with those from pyrrole + benzaldehyde (37%, TFA; 26%, BF_3–Et_2O) and from 5-phenyldipyrromethane + *p*-tolualdehyde (40%, TFA; 42%, BF_3–Et_2O). The total yields of porphyrin in these reactions are summarized in Table 2.

The yield of N-confused porphyrin was determined in self-condensation reactions of the dipyrromethane-monocarbinol (**3**) derived from 1-benzoyl-5-phenyldipyrromethane. The yields of tetraphenylporphyrin (TPP) and N-confused TPP (NC-TPP) in crude oxidized reaction mixtures were quantified by HPLC (Scheme 2).[12] || The standard one-flask reaction conditions were found to provide NC-TPP in yields of 9% (BF_3–Et_2O) and 4% (TFA). These yields are similar to those of pyrrole + benzaldehyde reactions. The reaction under TFA/DPM-carbinol or BF_3/UH-DPM produced a much lower level of NC-TPP. No NC-TPP was detected prior to 1 h under either set of reaction conditions, and maximum yields of 1% and <0.5% were obtained from the BF_3/UH-DPM and TFA/DPM-carbinol conditions, respectively.

Dipyrromethane-dicarbinol + dipyrromethane condensations

(i) Oligomer composition, acidolysis, and scrambling. The condensation of dipyrromethane-dicarbinol **2** + 5-phenyldipyrromethane served as the model reaction for this study (Scheme 1). The dipyrromethane-dicarbinol and dipyrromethane concentrations were 2.5 mM in all cases, in order to provide a 10 mM concentration of "pyrrole" and "aldehyde" units.

The condensation was performed under the TFA/DPM-carbinol, standard-TFA, and standard-BF_3 conditions. At a short reaction time of 8 min, the TFA/DPM-carbinol conditions provided a simple LD-MS spectrum dominated by expected peaks. This simple spectrum contrasts with the more complicated LD-MS spectrum obtained under the standard-

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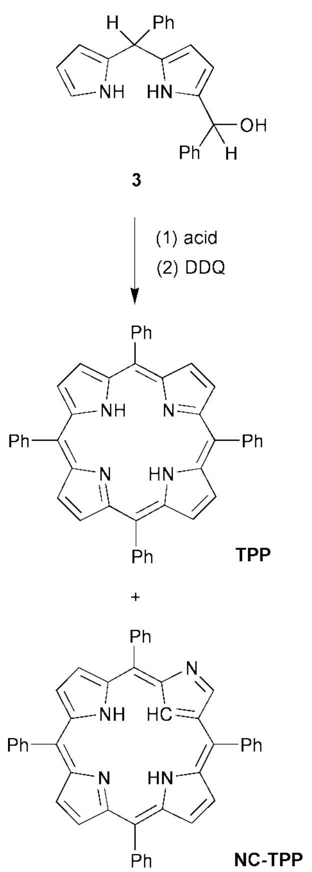
|| The HPLC assay for NC-TPP also enables quantitation of TPS. In each case where the yield of NC-TPP was examined, no TPS was detected (limit of detection = 0.5%).



Scheme 2 Self-condensation of dipyrromethane-monocarbinol (**3**).

TFA or standard-BF_3 conditions (Fig. 4); each such spectrum shows significant peaks assigned to oligomers derived from acidolysis and scrambling. In general, the oligomer compositions were similar to those obtained from the dipyrromethane-monocarbinol self-condensation experiments. The subtle differences displayed by the dipyrromethane-dicarbinol + dipyrromethane reactions include more intense peaks assigned to acidolysis and scrambling, and shorter oligomers tend to dominate the spectra. At reaction times corresponding to the maximum yield of porphyrin, the level of acidolysis and scrambling was increased under all three reaction conditions (Fig. 5). Again, the TFA/DPM-carbinol conditions provided a much simpler oligomer composition than did the standard-TFA or standard-BF_3 conditions. At these longer reaction times, the oligomer compositions were even more similar to those from the corresponding dipyrromethane-monocarbinol self-condensation reactions, though slightly higher levels of acidolysis and scrambling were observed.

(ii) Macrocycle yields. The reaction of dipyrromethane-dicarbinol **2** + 5-phenyldipyrromethane under the TFA/DPM-carbinol reaction conditions afforded porphyrin in 31% yield. This yield can be compared with that of the dipyrromethane-monocarbinol self-condensation (25%) or the reaction of pyrrole + benzaldehyde (0%) or 5-phenyldipyrromethane + *p*-tolualdehyde (0%). The same reaction under the standard-TFA or standard-BF_3 conditions gave porphyrin in 36% or 47% yield, respectively. These results are summarized in Table 2.

The yield of N-confused porphyrin was examined in condensations of dipyrromethane-dicarbinol **4** + 5-phenyldipyrromethane (Scheme 3).|| In general, the standard one-flask reaction conditions provided quantities of NC-TPP (10% from BF_3–Et_2O and 3% from TFA) similar to those of the dipyrromethane-monocarbinol self-condensation and pyrrole + benzaldehyde reactions. The TFA/DPM-carbinol reaction produced low levels of NC-TPP. At 1 h <1% NC-TPP was present and the maximum yield was <2%.

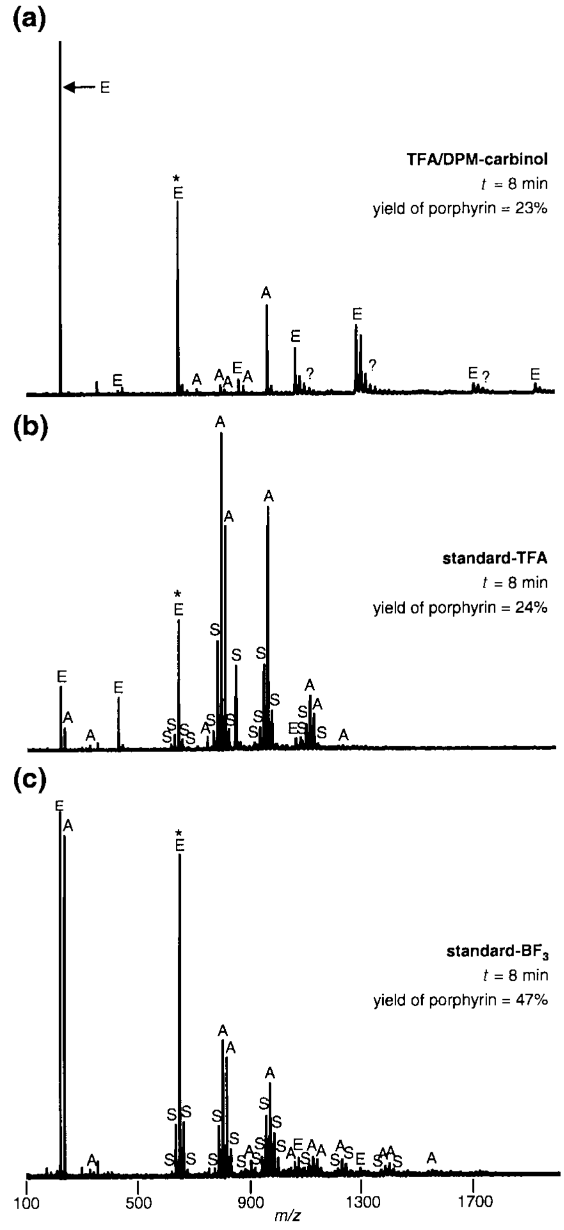


Fig. 4 Comparison of LD-MS spectra showing the oligomer compositions derived from condensation of dipyrromethane-dicarbinol **2** + 5-phenyldipyrromethane (2.5 mM each) under three different reaction conditions at 8 min: (a) "TFA/DPM-carbinol" conditions; (b) "standard-TFA" conditions; (c) "standard-BF_3" conditions. The total porphyrin yield (UV–Vis) is noted. E = expected oligomers, A = acidolysis oligomers, S = scrambled oligomers. The peak with *m*/*z* corresponding to the desired *trans*-A_2B_2-porphyrin product is marked with an asterisk.

Discussion

The dipyrromethanecarbinol motif is a highly valuable entity in porphyrin synthetic chemistry. Dipyrromethanecarbinols are highly reactive, enabling use of mild reaction conditions that lead to good yields of porphyrin with little or no scrambling. The reactions of the dipyrromethanecarbinols (self-condensation of a dipyrromethane-monocarbinol or condensation of a dipyrromethane-dicarbinol + dipyrromethane) under TFA/DPM-carbinol conditions or BF_3/UH-DPM conditions proceed in about 2- to 5-fold higher yield than the corresponding dipyrromethane + aldehyde condensations. Moreover, at reaction times corresponding to good yields of porphyrin, the oligomer composition is devoid of scrambled oligomers and even acidolysis appears to be suppressed. These findings support the notion that starting materials more reactive than the

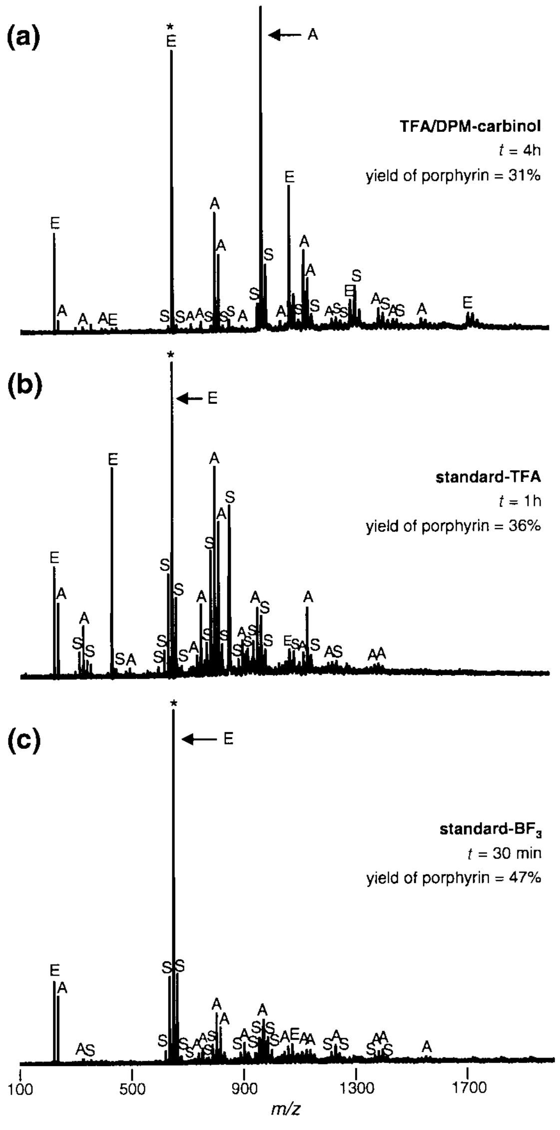
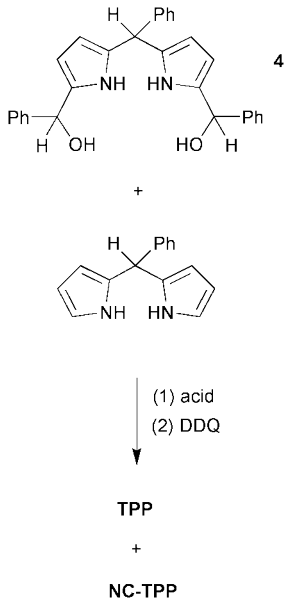


Fig. 5 Comparison of LD-MS spectra showing the oligomer compositions derived from condensation of dipyrromethane-dicarbinol **2** + 5-phenyldipyrromethane (2.5 mM each) under three different reaction conditions at the reaction time corresponding to the maximum yield of TPP: (a) "TFA/DPM-carbinol" conditions, 4 h; (b) "standard-TFA" conditions, 1 h; (c) "standard-BF$_3$" conditions, 30 min. The total porphyrin yield (UV–Vis) is noted. E = expected oligomers, A = acidolysis oligomers, S = scrambled oligomers. The peak with *m*/*z* corresponding to the desired *trans*-A_2B_2-porphyrin product is marked with an asterisk.

dipyrromethane + aldehyde enable use of mild conditions which inhibit scrambling processes, thereby affording increased yields of a single porphyrin product.

The examination of the oligomer composition and macrocycle yields from dipyrromethanecarbinol condensations have revealed the consequences of the reactivity of dipyrromethanecarbinols. The self-condensations of dipyrromethane-monocarbinols performed under the standard one-flask conditions (standard-TFA, standard-BF$_3$) provided much lower levels of oligomers derived from acidolysis and scrambling than were anticipated based on results from condensations of dipyrromethane + aldehyde. Furthermore, by simply decreasing the acid concentration, the level of undesired oligomers could be lowered almost below the limits of detection by LD-MS. These results indicate that the pathway to porphyrinogen formation *via* dipyrromethane-monocarbinols is inherently less prone to deleterious acidolysis and scrambling than the dipyrromethane + aldehyde reaction pathway. Thus, the preparation of porphyrins *via* carbinol chemistry is clearly superior to the dipyrromethane + aldehyde approach when the dipyrromethane is prone to scrambling (*i.e.*, dipyrromethanes with unhindered aryl substituents).



Scheme 3 Condensation of dipyrromethane-dicarbinol (**4**) + 5-phenyldipyrromethane.

The yields from pyrrole + aldehyde condensations can reach 50%, but yields of >30% are generally not obtained from the dipyrromethanecarbinol reactions under the reaction conditions which prevent scrambling. The LD-MS data indicate that at least a portion of the yield difference is due to formation of higher molecular weight oligomers in the dipyrromethanecarbinol reaction. We have observed a strong correlation between porphyrin yield and reaction reversibility, with conditions that provide reversible formation of oligomers affording higher yields of porphyrin. One interpretation is that longer oligomers formed in the dipyrromethanecarbinol reactions are kinetic products; the formation of the longer oligomers is favored due to the highly reactive pyrrole-carbinol motif. The reaction conditions that suppress scrambling prevent recovery from those longer oligomers.

The observations from this study have implications concerning the reaction course leading to porphyrin formation. Under standard-TFA conditions or standard-BF$_3$ conditions, reactions involving dipyrromethanecarbinols showed much less acidolysis and scrambling than was observed with dipyrromethane + aldehyde condensations. Because both reactions afford the same porphyrinogen, the primary cause of scrambling in the latter case cannot be reversible formation of the porphyrinogen, but must involve acidolysis of the dipyrromethane itself. We have found that the aldehyde is consumed slowly in the course of dipyrromethane + aldehyde condensations, indicating that the concentration of dipyrromethane decreases slowly. Furthermore, treating 5-phenyldipyrromethane alone (aldehyde omission experiment) under the acid-catalysis conditions (standard-TFA, standard-BF$_3$) results in extensive oligomer formation and good yields of porphyrin.[11] Thus, a major advantage of starting with a dipyrromethanecarbinol appears to be the avoidance of the slow addition of the aldehyde and the dipyrromethane. The overall similarities between the oligomer compositions and macrocycle distributions obtained from dipyrromethane-monocarbinol self-condensations and dipyrromethane-dicarbinol + dipyrromethane condensations suggest that the two syntheses provide similar pathways to the porphyrinogen. The slightly higher levels of scrambling observed with the dipyrromethane-dicarbinol + dipyrromethane condensations may be due to the presence of unreacted dipyrromethane early in the reaction. Finally, the TFA/DPM-carbinol conditions and the BF$_3$/

UH-DPM conditions are sufficiently mild to accentuate the differences in forming β-pyrrolic linkages *versus* α-pyrrolic linkages. These conditions decrease porphyrin formation by ~1.5 fold relative to the standard-TFA conditions or standard-BF_3 conditions, yet decrease formation of the N-confused porphyrin by 3- to 9-fold.

Conclusions

We have employed a battery of analytical methodologies, particularly LD-MS, to examine fundamental aspects of dipyrromethanecarbinol condensations. These experiments confirm our earlier preparative work that showed carbinol chemistry to be a very powerful approach to the synthesis of A_2B_2-, A_3B-, AB_2C-, and ABCD-porphyrins. The dipyrromethanecarbinol condensations were shown to be much more resistant to acidolysis and scrambling than the corresponding dipyrromethane + aldehyde condensations. In addition, 2- to 3-fold higher yields of porphyrin were obtained than in the corresponding dipyrromethane + aldehyde condensations. Further improvements in yield appeared to be limited by the production of long oligomers and by the necessary inhibition of reaction reversibility. The lower than statistical levels of acidolysis and scrambling in the dipyrromethanecarbinol reactions upon application of the standard reaction conditions for pyrrole + aldehyde condensations suggest that the key processes of scrambling involve the dipyrromethane rather than the porphyrinogen. The similarities between the dipyrromethane-monocarbinol self-condensation and the dipyrromethane-dicarbinol + dipyrromethane condensation suggest that both pathways leading to formation of the porphyrinogen are rather similar.

Experimental

Materials

The sources of catalysts, reagents, and solvents are listed in the preceding papers.[1,10,11] 5-Phenyldipyrromethane,[14] 1-*p*-toluoyl-5-phenyldipyrromethane,[5] 1-benzoyl-5-phenyldipyrromethane,[11] 1,9-di-*p*-toluoyl-5-phenyldipyrromethane,[3] and 1,9-dibenzoyl-5-phenyldipyrromethane[15] were synthesized according to published procedures. The reduction of the acyl compounds to the corresponding carbinols was performed using $NaBH_4$ in tetrahydrofuran–methanol.[3] In order to minimize variations in the condensation experiments due to day-to-day differences in the reduction step, a large quantity of a given acyl compound was reduced and the resulting carbinol was divided into separate reaction vessels for treatment with the various condensation conditions. Condensation reactions were performed within 15 min of carbinol preparation. Day-to-day repeatability was also examined and found to be excellent.

General reaction conditions for the dipyrromethane-monocarbinol self-condensation

All condensations were performed with 5 mM dipyrromethane-monocarbinol so that the concentration of "pyrrole" and "aldehyde" units was 10 mM. The four general reaction conditions listed in Table 1 were used. Reagents and catalysts were dispensed neat or as 1 M stock solutions in the reaction solvent, depending on the desired final concentration and reaction volume. The reactions were generally performed on a 10 mL scale (assuming additivity of volumes) in a 20 mL scintillation vial. The reaction mixtures were magnetically stirred in tightly capped vials shielded from light. The reactions of dipyrromethane-monocarbinols that required HPLC analysis were performed on a 30 mL scale in a stoppered 50 mL flask.

General reaction conditions for the dipyrromethane-dicarbinol + dipyrromethane condensation

All condensations were performed with 2.5 mM dipyrromethane-dicarbinol and 2.5 mM dipyrromethane so that the concentration of "pyrrole" and "aldehyde" units was 10 mM. Three general reaction conditions were used: "standard-TFA", "standard-BF_3", and "TFA/DPM-carbinol". Reagents and catalysts were dispensed neat or as 1 M stock solutions in the reaction solvent, depending on the desired final concentration and reaction volume. The reactions were generally performed on a 10 mL scale (assuming additivity of volumes) in a 20 mL scintillation vial. The reaction mixtures were magnetically stirred in tightly capped vials shielded from light. The reactions of dipyrromethane-dicarbinols that required HPLC analysis were performed on a 30 mL scale in a stoppered 100 mL flask.

Reaction work-up and analyses

The reactions were monitored from 1 min to 8 h. For the 10 mL reactions, at each time point 0.5 mL of the crude unoxidized reaction mixture was transferred to a 1 dram vial containing solid DDQ (1.7 mg, 0.0075 mmol). For the 30 mL reactions, at each time point 2.0 mL of the crude unoxidized reaction mixture was transferred to a 1 dram vial containing solid DDQ (6.8 mg, 0.030 mM). The oxidized mixtures were vortexed for 5 seconds. An aliquot (1 µL) of the oxidized reaction mixture was spotted onto a LD-MS target. Work-up for UV–Vis,[13] LD-MS,[10,11] TLC,[16] and HPLC[12] analyses was performed as described previously.

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