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A Tin-Complexation Strategy for Use with Diverse Acylation Methods in the Preparation of 1,9-Diacyldipyrromethanes

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The acylation of dipyrromethanes to form 1,9-diacyldipyrromethanes is an essential step in the rational synthesis of porphyrins. Although several methods for acylation are available, purification is difficult because 1,9-diacyldipyrromethanes typically streak extensively upon chromatography and give amorphous powders upon attempted crystallization. A solution to this problem has been achieved by reacting the 1,9-diacyldipyrromethane with Bu_2SnCl_2 to give the corresponding dibutyl-(5,10-dihydrodipyrrinato)tin(IV) complex. The reaction is selective for dipyrromethanes that bear acyl groups at both the 1- and 9-positions but otherwise is quite tolerant of diverse substituents. The diacyldipyrromethane−tin complexes are stable to air and water, are highly soluble in common organic solvents, crystallize readily, and chromatograph without streaking. Four methods (Friedel−Crafts, Grignard, Vilsmeier, benzoxathiolium salt) were examined for the direct 1,9-diacylation of a dipyrromethane or the 9-acylation of a 1-acyldipyrromethane. In each case, treatment of the crude reaction mixture with Bu_2SnCl_2 and TEA at room temperature enabled facile isolation of multigram quantities of the 1,9-diacyldipyrromethane−tin complex. The diacyldipyrromethane−tin complexes could be decomplexed with TFA in nearly quantitative yield. Alternatively, use of a diacyldipyrromethane−tin complex in a porphyrin-forming reaction (reduction with $NaBH_4$, acid-catalyzed condensation with a dipyrromethane, DDQ oxidation) afforded the desired free base porphyrin in yield comparable to that obtained from the uncomplexed diacyldipyrromethane. The acylation/tin-complexation strategy has been applied to a bis(dipyrromethane) and a porphyrin-dipyrromethane. In summary, the tin-complexation strategy has broad scope, is compatible with diverse acylation methods, and greatly facilitates access to 1,9-diacyldipyrromethanes.

Introduction

Diacyldipyrromethanes are critical intermediates in porphyrin synthesis.[1] The reduction of a 1,9-diacyldipyrromethane affords the corresponding diol, which can be reacted with a dipyrromethane to give the meso-substituted porphyrin. Diacyldipyrromethanes with identical substituents at the 1- and 9-positions can be used in the synthesis of A_3B-, *trans*-A_2B_2-, and *trans*-AB_2C-porphyrins, while diacyldipyrromethanes with different substituents at the 1- and 9-positions serve as precursors to *cis*-A_2B_2-, *cis*-AB_2C-, and ABCD-porphyrins. Thus, the preparation of porphyrins bearing distinct patterns of substituents requires effective procedures for the diacylation of dipyrromethanes. To carry out porphyrin syntheses at reasonable scale also requires acylation methods that can be implemented with limited reliance on chromatographic separation procedures.

Two distinct acylation strategies have been developed (Scheme 1). The direct diacylation approach introduces identical groups at the 1- and 9-positions in a one-flask reaction with a dipyrromethane (**1**). The sequential acylation process introduces different groups at the 1- and 9-positions. The first step entails reaction of the dipyrromethane with EtMgBr followed by a 2-*S*-pyridyl benzothioate, which gives the 1-acyldipyrromethane (**2**).[2] The subsequent acylation of **2** affords the 1,9-diacyldipyrromethane (**3**).[1] Both the direct diacylation process and the second acylation of the sequential acylation process typically afford mixtures of products that are separated with difficulty. Such limitations occur regardless of the acylation method that is employed.

The methods that have been employed for the acylation of meso-substituted, β-unsubstituted dipyrromethanes were originally developed for the acylation of pyrrole (Table 1). Friedel−Crafts acylation of pyrrole[3] with a Lewis acid and an acid chloride has been extended to core-modified dipyrromethanes[4−6] and *N*-confused dipyrromethanes.[7] Acylation of the "pyrrole Grignard reagent"[3]

(1) Rao, P. D.; Dhanalekshmi, S.; Littler, B. J.; Lindsey, J. S. *J. Org. Chem.* **2000**, *65*, 7323−7344.

(2) Rao, P. D.; Littler, B. J.; Geier, G. R., III; Lindsey, J. S. *J. Org. Chem.* **2000**, *65*, 1084−1092.

(3) Anderson, H. J.; Loader, C. E. In *Pyrroles. Part I*; Jones, R. A.; Ed., John Wiley & Sons: New York, 1990; pp 397−497.

(4) Cho, W.-S.; Lee, C.-H. *Bull. Korean Chem. Soc.* **1998**, *19*, 314−319.

(5) Lee, C.-H.; Cho, W.-S. *Tetrahedron Lett.* **1999**, *40*, 8879−8882.

(6) Cho, W.-S.; Kim, H.-J.; Littler, B. J.; Miller, M. A.; Lee, C.-H.; Lindsey, J. S. *J. Org. Chem.* **1999**, *64*, 7890−7901.

(7) Maeda, H.; Osuka, A.; Ishikawa, Y.; Aritome, I.; Hisaeda, Y.; Furuta, H. *Org. Lett.* **2003**, *5*, 1293−1296.

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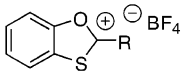
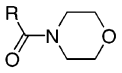
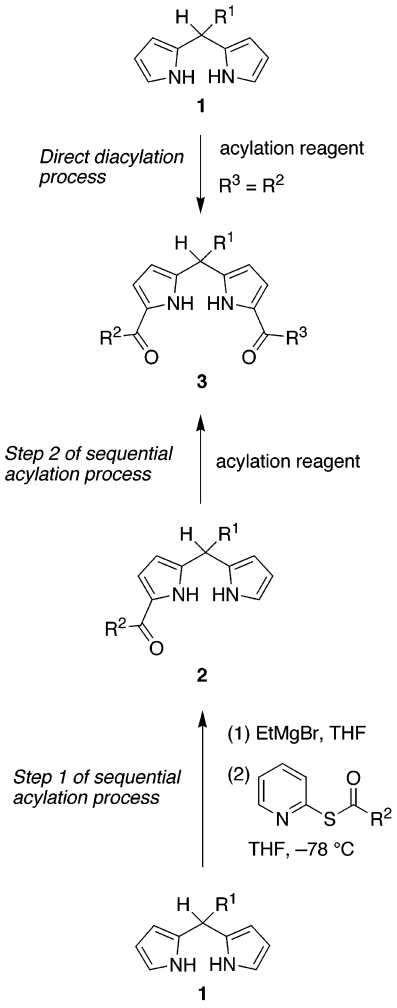
TABLE 1. Acylation Methods for Preparing 1,9-Diacyldipyrromethanes[a]

Method	Reaction	Reactant	Reagent	Known byproducts[f]
A	Friedel-Crafts	RCOCl	Lewis acid[d]	1-acyldipyrromethane 1,8-diacyldipyrromethane[d]
B	Grignard	RCOCl	EtMgBr	1-acyldipyrromethane
C	Benzoxathiolium[b]		HgO/HBF_4[e]	1,9-diacyldipyrrin[d,g]
D	Vilsmeier[c]		$POCl_3$	---

[a] Methods for the direct diacylation of a dipyrromethane or the acylation of a 1-acyldipyrromethane (step 2 in the sequential acylation process). [b] Acylation is achieved via a two-step process of alkylation followed by oxidative hydrolysis. [c] Vilsmeier formylation is achieved with DMF and $POCl_3$. [d] Results described herein. [e] Reagent for oxidative hydrolysis following alkylation. [f] Each method produces polar byproducts of unknown composition. The byproducts listed are those known to interfere with purification of the 1,9-diacyldipyrromethane. [g] A significant quantity of nonpolar byproducts also is formed.

SCHEME 1



(formed by reaction of pyrrole with EtMgBr) has been used extensively with dipyrromethanes.[1,8] The alkylation of pyrrole[9] with a benzoxathiolium tetrafluoroborate[10] followed by oxidative hydrolysis has been extended to dipyrromethanes.[8,11] Vilsmeier aroylation of pyrrole using *N*-acyl morpholides[12,13] has been extended to dipyrromethanes[13,14] (and also to bipyrroles[15]). Vilsmeier formylation of pyrrole using DMF/$POCl_3$ has been extended to dipyrromethanes.[16,17] Related substituents (nitrile,[18] amide[19]) have also been introduced at the 1- and 9-positions of dipyrromethanes.

Although the methods of acylation for dipyrromethanes are analogous to those for pyrrole, the acylation chemistry of dipyrromethanes is distinct from that of simple pyrroles in the following ways. (1) A dipyrromethane is more sensitive toward acid than pyrrole owing to the facile acidolysis of the pyrrole-meso-carbon bond. (2) A dipyrromethane is susceptible to dehydrogenation yielding the corresponding dipyrrin. (3) 1,9-Diacyldipyrromethanes are quite difficult to purify, generally giving amorphous powders upon attempted crystallization and extensive streaking upon chromatography. Indeed, the challenge of purifying a diacyldipyrromethane by column chromatography—typically a laborious process that consumes extensive amounts of solvent and chromatographic media—is one of the chief impediments to the implementation of rational syntheses of meso-substituted porphyrins.

Regardless of acylation strategy and acylation method, there remains a need for improvements in the synthesis

(8) Lee, C.-H.; Li, F.; Iwamoto, K.; Dadok, J.; Bothner-By, A. A.; Lindsey, J. S. *Tetrahedron* **1995**, *51*, 11645−11672.

(9) (a) Cadamuro, S.; Degani, I.; Fochi, R.; Gatti, A.; Regondi, V. *Synthesis* **1987**, 311−314. (b) Barbero, M.; Cadamuro, S.; Degani, I.; Fochi, R.; Gatti, A.; Regondi, V. *J. Org. Chem.* **1988**, *53*, 2245−2250.

(10) (a) Degani, I.; Fochi, R. *J. Chem. Soc., Perkin Trans. 1* **1976**, 323−325. (b) Barbero, M.; Cadamuro, S.; Degani, I.; Fochi, R.; Gatti, A.; Regondi, V. *Synthesis* **1986**, 1074−1076.

(11) Briñas, R. P.; Brückner, C. *Tetrahedron* **2002**, *58*, 4375−4381.

(12) White, J.; McGillivray, G. *J. Org. Chem.* **1977**, *42*, 4248−4251.

(13) Wallace, D. M.; Leung, S. H.; Senge, M. O.; Smith, K. M. *J. Org. Chem.* **1993**, *58*, 7245−7257.

(14) Gryko, D. T.; Tasior, M.; Koszarna, B. *J. Porphyrins Phthalocyanines* **2003**, *7*, 239−248.

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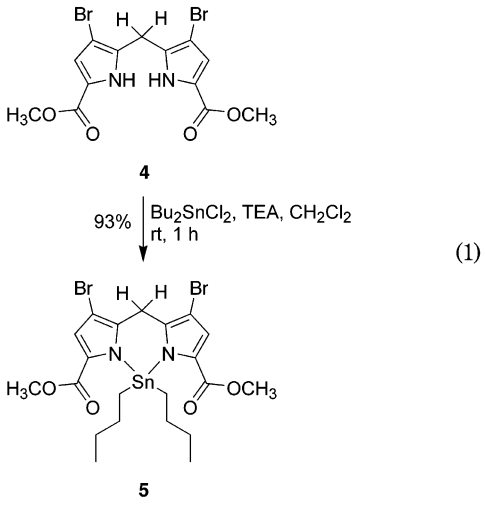
(16) Khoury, R. G.; Jaquinod, L.; Aoyagi, K.; Olmstead, M. M.; Fisher, A. J.; Smith, K. M. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2497−2500.

(17) Brückner, C.; Posakony, J. J.; Johnson, C. K.; Boyle, R. W.; James, B. R.; Dolphin, D. *J. Porphyrins Phthalocyanines* **1998**, *2*, 455−465.

(18) Boyle, R. W.; Karunaratne, V.; Jasat, A.; Mar, E. K.; Dolphin, D. *Synlett* **1994**, 939−940.

(19) Depraetere, S.; Dehaen, W. *Tetrahedron Lett.* **2003**, *44*, 345−347.

and purification of diacyldipyrromethanes. Kitamura and Yamashita recently reported the reaction of 1,9-dicarbomethoxy-3,7-dibromodipyrromethane (**4**) and dibutyltin dichloride (Bu_2SnCl_2) in the presence of TEA at room temperature to give the corresponding *N*,*N*-dibutyltin complex **5** in 93% yield (eq 1).[20] The complex was stable



(1)

to routine handling. Treatment of **5** with TFA regenerated the dipyrromethane **4** in high yield. We felt that this complexation/decomplexation chemistry might be exploited to facilitate isolation and purification of 1,9-diacyldipyrromethanes.

In this paper, we describe the use of tin complexation for the isolation and purification of 1,9-diacyldipyrromethanes. We characterize the selectivity of complexation of a variety of dipyrromethane species and the scope of complexation with a family of 1,9-diacyldipyrromethanes. Next, we investigate the use of tin complexation as a purification aid with four acylation methods (A−D, Table 1) applied to the 1,9-diacylation of a dipyrromethane and the 9-acylation of a 1-acyldipyrromethane. As part of this work, we have investigated refined methods for the Friedel−Crafts and for the benzoxathiolium procedures. An overarching objective has been to perform reactions at high concentration and with minimal solvent usage during purification. Taken together, this work dramatically simplifies the preparation and isolation of 1,9-diacyldipyrromethanes.

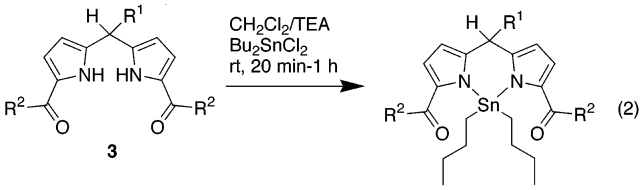
Results and Discussion

1. Tin Complexation Studies. Substrate Selectivity. We applied the tin-complexation reaction described by Kitamura and Yamashita with 1,9-bis(4-methylbenzoyl)-5-phenyldipyrromethane (**3a**). Thus, the reaction of **3a** and Bu_2SnCl_2 in CH_2Cl_2 containing TEA at room temperature afforded the corresponding tin complex **6a** in 90% yield (Scheme 2). The tin complex was readily isolated by filtration over a pad of silica, was easily crystallized from ethyl ether or precipitated from ethyl ether/methanol, and gave satisfactory purity upon elemental analysis.

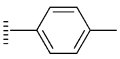
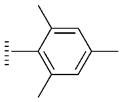
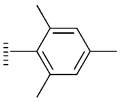
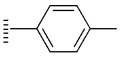
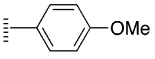
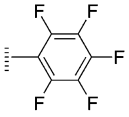
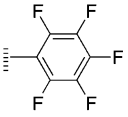
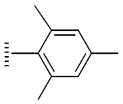
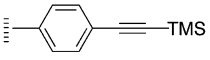
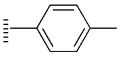
(20) Kitamura, C.; Yamashita, Y. *J. Chem. Soc., Perkin Trans. 1* **1997**, 1443−1447.

To explore the selectivity of tin complexation with various dipyrromethane species expected to be present in crude acylation mixtures, a set of control experiments was carried out (Scheme 2). A tin complex was not obtained upon treatment with Bu_2SnCl_2 and TEA in CH_2Cl_2 of a dipyrromethane (**1a**), 1-acyldipyrromethane (**2a**), 1,8-diacyldipyrromethane (**7**), or 1,9-diacyldipyrrin (**8**). Treatment of a mixture (1:1 molar ratio) of the dipyrromethane **1a** and the diacyldipyrromethane **3a** under the same conditions gave exclusively the diacyldipyrromethane−tin complex **6a**. The successful and highly selective complexation of a 1,9-diacyldipyrromethane indicated that tin complexation could form the basis for a purification procedure.

Scope with 1,9-Diacyldipyrromethanes. We examined the generality of the tin complexation with 1,9-diacyldipyrromethanes bearing different substituents (eq 2). In each case, the tin complex was relatively

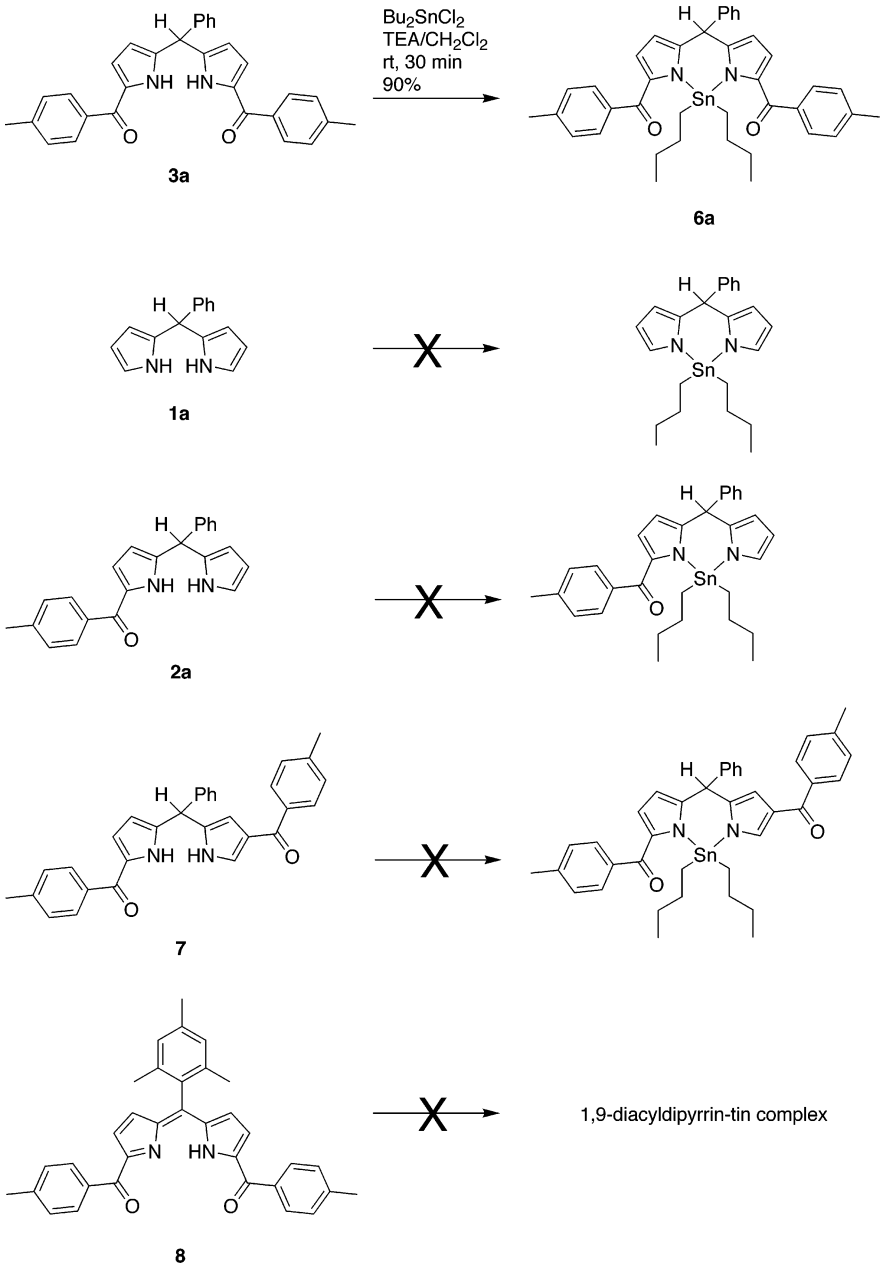


(2)

3	R^1	R^2	Product (Yield)
3a			**6a** (90%)
3b		—H	**6b** (86%)
3c			**6c** (90%)
3d	—H	—H	**6d** (74%)
3e	—H		**6e** (85%)
3f	—*n*-pentyl	—*n*-pentyl	**6f** (93%)
3g			**6g** (91%)
3h			**6h** (87%)
3i		—CF_3	**6i** (42%)[a]
3j			**6j** (89%)
3k			**6k** (95%)

[a]The product decomposed slowly upon storage at room temperature.

SCHEME 2

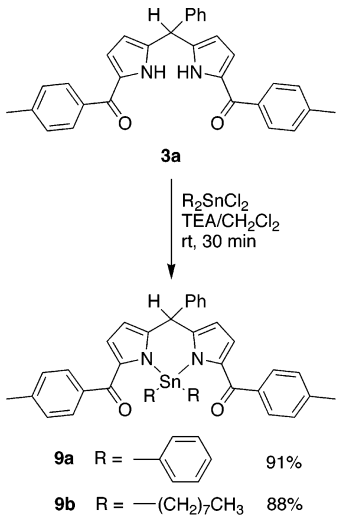


hydrophobic and was readily isolated by filtration over a pad of silica. The corresponding tin complex was typically obtained in good yield (74−93%). One exception was observed with diacyldipyrromethane **3i** (CF_3CO groups), which gave the tin complex in 42% yield but slowly decomposed upon storage at room temperature. Otherwise, the tin complexation works well regardless of the nature of the substituents at the 1,9-positions, including unhindered (formyl, **3b**), sterically hindered (mesitoyl, **3c**), alkanoyl (**3f**), electron-releasing (4-methoxybenzoyl, **3g**) and electron-withdrawing (pentafluorobenzoyl, **3h**) substituents. Substituents located at the meso (5-) position have little effect on the tin complexation, though a slightly lower yield (74%) was observed with the meso-unsubstituted diformyldipyrromethane (**3d**).

The reaction of diacyldipyrromethane **3a** with diphenyltin dichloride or dioctyltin dichloride afforded the complex **9a** or **9b** in 91% or 88% yield, respectively (eq 3). These results illustrate the generality of the tin-complexation process. From a practical standpoint, it is noteworthy that while most of the dibutyltin complexes were solids and gave large crystals, the diphenyltin complex gave a powder, and the dioctyltin complex was an oil.

Characterization. The diacyldipyrromethane−tin complexes are stable to water and routine handling. The stability to water distinguishes these complexes from trialkyltin-pyrroles such as *N*-(tributylstannyl)pyrrole, which decompose upon exposure to water or alcohols.[21] Unlike diacyldipyrromethanes, the diacyldipyrromethane−tin complexes can easily be precipitated/crystallized

(21) Pommier, J. C.; Lucas, D. *J. Organomet. Chem*. **1973**, *57*, 139−153.



(3)

from ethyl ether/methanol and afford satisfactory elemental analysis results.

The spectral changes upon tin complexation include disappearance of the IR stretch owing to the N−H bonds (3236 cm^{-1}) and the absence of the characteristic stretch in the region expected for typical C═O bonds (1614, 1599 cm^{-1}). The ^1H NMR spectra show the disappearance of the NH resonances and a ∼0.5 ppm downfield shift of the resonances of the H^2/H^8 protons (∼7.0 ppm). The butyl groups attached to the tin atom give two triplets for the terminal methyl groups as well as two sets of ^{13}C signals for diacyldipyrromethanes that bear two different meso substituents, owing to the different magnetic environment of the two butyl groups (*syn* or *anti* with respect to the meso substituent). The ^{119}Sn NMR spectra of selected 1,9-diacyldipyrromethane−tin complexes (**6a**, **6b**, **6e**, **6f**, **6p**, **6q**) showed only one singlet for each complex, ranging from −242 ppm for the diformyl species **6b** to −282 ppm for **6a**. In general, the diacyldipyrromethane−tin complexes afford very clean ^1H NMR spectra.

X-ray structural analyses were performed on **6a** and **6b** (Figure 1). Selected bond lengths and angles for the two structures are shown in Supporting Information. The tin atom in both structures adopts a highly distorted pseudo-octahedral geometry. The Sn−O bond lengths in both **6a** [2.461(2), 2.488(2) Å] and **6b** [2.515(2), 2.548(2) Å] are 0.1−0.2 Å shorter than the Sn−O bond lengths [2.519(5), 2.629(5) Å] of **5**.[20] The C−O bond length was longer in both **6a** [1.254, 1.259 Å] and **6b** [1.248, 1.249 Å] than for that in 2-benzoylpyrrole (1.234(4) Å).[22] In each structure, the two pyrrole units, two carbonyl groups, and the tin atom are nearly coplanar. Coordination of the two carbonyl groups and the two pyrrolic nitrogen atoms to the central tin atom effectively masks four groups that can engage in hydrogen bonding. The diminished conformational freedom and ensheathed α-acylpyrrole motifs are the source of the striking change in physical properties (polarity, crystallinity) upon conversion of a 1,9-diacyldipyrromethane to the corresponding tin complex.

The facile reaction of **4** with dibutyltin dichloride in the presence of a mild base to give tin complex **5** (eq 1)

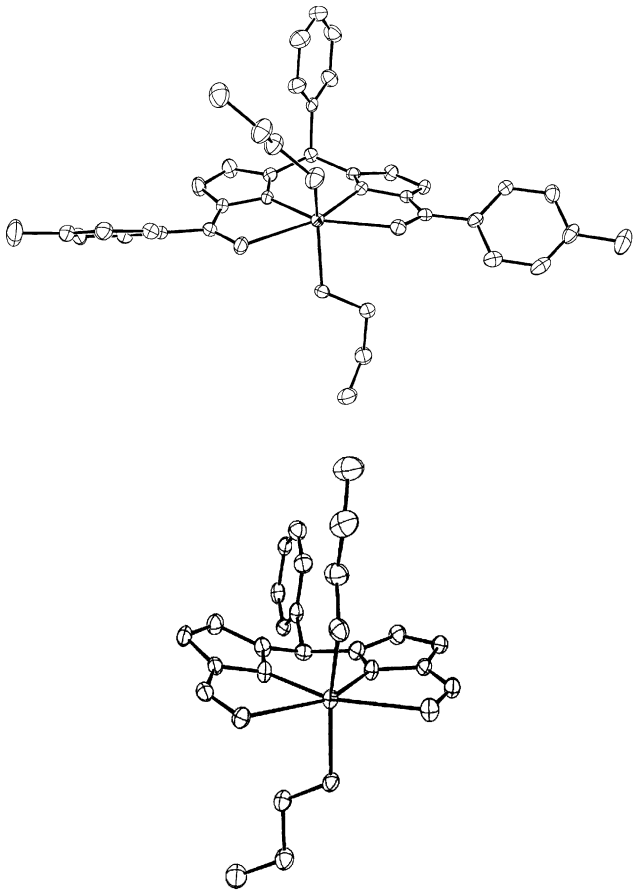


FIGURE 1. ORTEP drawings of a representative molecule in the crystal structure of **6a** (top) and **6b** (bottom). All hydrogens have been omitted for clarity.

was attributed to the increased acidity of the pyrrolic N−H groups caused by the presence of two electron-withdrawing groups per pyrrole unit.[20] Even a single acyl unit increases the N−H acidity significantly (pyrrole-2-carboxaldehyde has pK_a ∼15,[23] compared with a value of 17.5 for pyrrole[24]), thereby increasing the reactivity of the diacyldipyrromethane. On the other hand, the formation of stable tin complexes requires the appropriate coordination geometry for the central tin atom. Given that a stable tin complex was not obtained with the 1,8-diacyldipyrromethane **7** but was obtained with each 1,9-diacyldipyrromethane examined herein, including **3a** (an isomer of **7**), the structural requisites to give a stable complex appear to be the presence of one acyl unit at each α-position for coordination to the tin atom.

2. Tin Complexation as an Aid for Purification of 1,9-Diacyldipyrromethanes. Prior to examination of the various acylation methods, a process for using tin complexation as a means of purifying 1,9-diacyldipyrromethanes was established (Scheme 3). A crude reaction mixture obtained from the attempted diacylation of 5-phenyldipyrromethane (**1a**) using $SbCl_5$ and *p*-toluoyl chloride (method A, Table 1) was quenched with aqueous $NaHCO_3$, and the organic layer was separated, dried, and

(22) English, R. B.; McGillivray, G.; Smal, E. *Acta Crystallogr.* **1980**, *B36*, 1136−1141.

(23) Limage, M.-H.; Lautié, A.; Novak, A. *C. R. Acad. Sci., Ser. B* **1975**, *280*, 601−603.

(24) Yagil, G. *Tetrahedron* **1967**, *23*, 2855−2861.

SCHEME 3

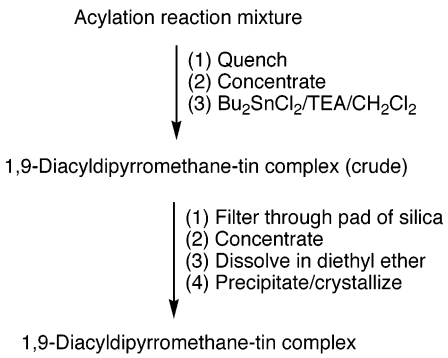
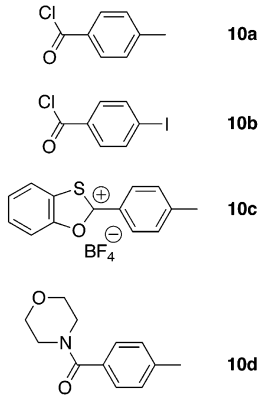


CHART 1



concentrated. The residue was dissolved in CH_2Cl_2 or $ClCH_2CH_2Cl$ and treated with TEA and Bu_2SnCl_2 at room temperature. Prior to tin complexation, the diacyldipyrromethane streaked [R_f = 0.5−0.3, CH_2Cl_2/ethyl acetate (7:1) on silica] and overlapped with some byproducts on TLC analysis. After complexation, the diacyldipyrromethane−tin complex was the least polar compound (R_f = 0.7, CH_2Cl_2 on silica) among the major products while the byproducts gave $R_f \leq 0.2$. Filtration over a silica pad (6 cm × 10 cm) gave the diacyldipyrromethane−tin complex (1.1 g) with a modest amount of solvent (300 mL) in a short period (30 min). (By contrast, isolation of a similar amount of 1,9-diacyldipyrromethane by chromatography typically consumes 1.2 L of solvent with a larger silica column (6 cm × 18 cm) over 3−4 h.) The product was dissolved in ethyl ether and precipitated upon addition of methanol, affording the diacyldipyrromethane−tin complex as a pale yellow solid in 58% yield. In a few instances, the diacyldipyrromethane−tin complex underwent decomplexation during filtration over silica, which appeared to be due to a given batch of silica gel rather than characteristic substituents on the diacyldipyrromethane. Regardless, the problem of decomplexation was easily avoided by using a basic eluant [e.g., CH_2Cl_2/hexanes (1:1) containing 1% of TEA] or by using alumina in place of silica.

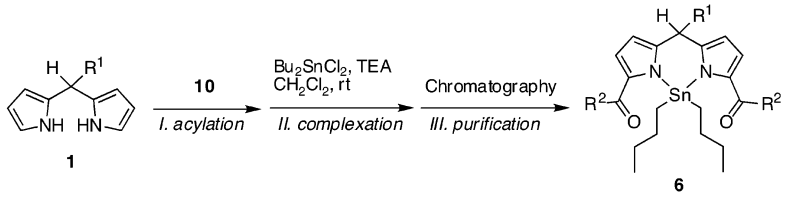
3. Acylation of Dipyrromethanes. Methods. The four acylation approaches listed in Table 1 were applied to the direct 1,9-diacylation of a dipyrromethane and the 9-acylation of a 1-acyldipyrromethane. The reactants (**10a**−**d**) for introducing acyl units are shown in Chart 1. Methods A (Friedel−Crafts) and C (benzoxathiolium) were studied extensively to develop suitable reaction conditions (see Supporting Information). Indeed, Friedel−Crafts acylation has not been used previously with dipyrromethanes. For method A, the best conditions entail use of $SnCl_4$ (equimolar with the acid chloride) in 1,2-dichloroethane or CH_2Cl_2 at room temperature with 500 mM dipyrromethane for 10 min or analogous conditions using $SbCl_5$ with 50 mM dipyrromethane for 5 min. For method C, the alkylation conditions entail 4 molar equiv of the benzoxathiolium tetrafluoroborate per dipyrromethane (a 2-fold excess) in THF and 4 molar equiv of DBU with 300 mM dipyrromethane at room temperature. The hydrolysis conditions entail HgO and aqueous HBF_4. Methods B (Grignard)[1] and D (Vilsmeier)[14] have been used as described previously.

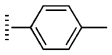
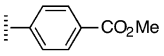
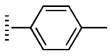
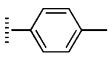
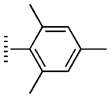
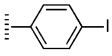
Direct 1,9-Diacylation. The results of the direct 1,9-diacylation of a dipyrromethane followed by tin complexation are shown in Table 2. Each method (A−D) was applied to the synthesis of diacyldipyrromethane−tin complex **6a** (entry 1). The tin complex was obtained with the simple purification process outlined in Scheme 3 (except for method C, which required a silica pad filtration prior to tin complexation), despite the different types of byproducts that are characteristic of the different acylation methods (Table 1). Friedel-Crafts acylation (method A) also was applied with the dipyrromethane (**1b**) bearing an ester substituent to give **6l**, a compound unavailable via the Grignard method. Application of method A to dipyrromethane (**1c**) and *p*-toluoyl chloride resulted in substantial decomposition, while the Grignard method (B) afforded **6e** in 54% yield. A similar reactivity profile was observed with *p*-iodobenzoyl chloride, where the Grignard method afforded the desired diacyldipyrromethane−tin complex **6m** in 32% yield. Regardless of the acylation method, application of the tin complexation method greatly facilitated the purification process. Indeed, the synthesis of **6a** was readily scaled (method B) with little change in yield to give 20 g of product.

Sequential 1,9-Acylation. 1-Acyldipyrromethanes **2a**−**d** were prepared following the general procedure described in the literature[2] with only slight modification of the workup method. The 9-acylation of a 1-acyldipyrromethane has been achieved by methods B (Grignard)[1] and C (benzoxathiolium),[9] but no prior examples of method A (Friedel−Crafts) have been reported. Appropriate conditions for the Friedel−Crafts acylation entail use of $SbCl_5$ (2 equiv) and the acid chloride (1.5 equiv) with a 1-acyldipyrromethane (50 mM) in 1,2-dichloroethane at room temperature for 5 min (see Supporting Information). The concentration of acid catalyst is greater than that for direct 1,9-diacylation; the higher level of acid is tolerable owing to the greater stability toward acid of the 1-acyldipyrromethane versus the dipyrromethane.

We investigated the various methods for 9-acylation in conjunction with tin complexation. In method A, the reaction of **2a** with *p*-toluoyl chloride gave the desired diacyldipyrromethane **3a** (∼70% yield) as well as an isomeric 1,8-diacyldipyrromethane **7** (∼10% yield; see Supporting Information for characterization). The 1,9-diacyldipyrromethane−tin complex **6a** was obtained selectively in 66% yield. Application of method B or C gave **6a** in 56 or 46% yield, respectively (Table 3, entry 1). Method A was applied to acylation of **2b**−**d**, affording the corresponding diacyldipyrromethane−tin complexes **6n**−**p** in 52−72% yield (entries 2−4). Note that the

TABLE 2. 1,9-Diacylation of Dipyrromethanes

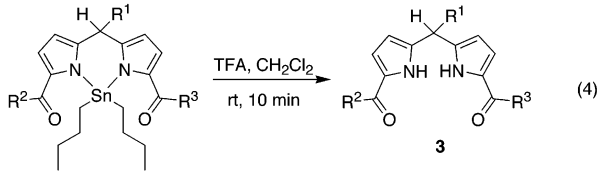


Entry	Starting material	R^1	R^2	Product	Method[a]	Yield
1	**1a**			**6a**	A	58%[b]
					B	46%
					C	37%
					D	63%
2	**1b**			**6l**	A	30%
3	**1c**			**6e**	A	5%
					B	54%
4	**1d**			**6m**	A	n.o.[c]
					B	32%

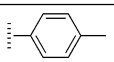
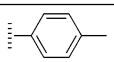
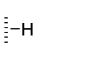
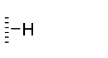
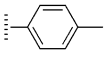
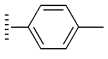
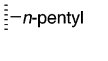
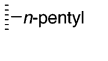
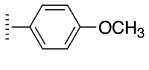
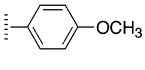
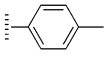
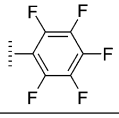
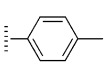
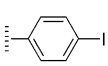
[a] The methods differ only in the conditions for acylation, and each method employed the same procedure for tin complexation (approximate concentrations given). Method A: 50 mM **1**, 100 mM acid chloride, 100 mM $SbCl_5$ in $ClCH_2CH_2Cl$. Method B: 100 mM **1**, 250 mM acid chloride, 500 mM EtMgBr in toluene/THF. Method C: (1) 300 mM **1**, 1.2 M benzoxathiolium tetrafluoroborate salt, 1.2 M DBU in THF; (2) 1.2 M HgO, 2.4 M HBF_4 (aq). Method D: 167 mM **1**, 667 mM *N*-acyl morpholide, 1.33 M $POCl_3$ in $ClCH_2CH_2Cl$. [b] The high concentration conditions (250 mM **1**, 750 mM acid chloride, 500 mM $SnCl_4$ in $ClCH_2CH_2Cl$) gave 39% yield. [c] The formation of a corresponding diacyldipyrromethane **3m** was not observed by TLC analysis.

acylation of **2d** with *p*-iodobenzoyl chloride followed by tin complexation afforded the desired **6p** in fair yield (Table 3, entry 4), whereas the direct 1,9-diacylation of a dipyrromethane with *p*-iodobenzoyl chloride was not successful (Table 2, entry 4). Treatment of **2a** with modified conditions for Vilsmeier formylation (DMF and *p*-toluoyl chloride)[11,25] afforded the corresponding 9-formyl product, which gave the tin complex **6q** in 58% yield (Table 3, entry 5). An alternative synthesis of an analogue proceeded via 9-alkylation of a 1-formyldipyrromethane with a benzoxathiolium tetrafluoroborate followed by oxidative hydrolysis.[11]

4. Decomplexation of 1,9-Diacyldipyrromethane−Tin Complexes. The diacyldipyrromethane−tin complexes were readily isolated and were stable on storage for months. Treatment of the diacyldipyrromethane−tin complexes with TFA afforded the corresponding uncomplexed diacyldipyrromethanes in high yields (eq 4).



(4)

Entry	R^1	R^2	R^3	Product (Yield)
1				**3a** (95%)
2				**3b** (98%)
3				**3e** (93%)
4				**3f** (92%)
5				**3n** (93%)
6				**3p** (82%)

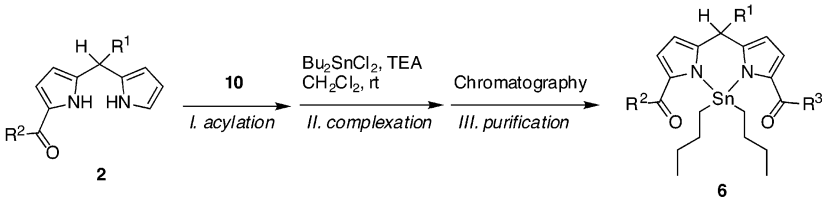
5. Applications. Tetraacylation of a Bis(dipyrromethane). 1,4-Bis(dipyrromethan-5-yl)benzene (**11**)[26] is readily available by reaction of terephthalaldehyde with excess pyrrole.[27] Such bis(dipyrromethanes) joined by a *p*-phenylene linker are potentially valuable intermediates in the synthesis of *p*-phenylene-linked multiporphyrin arrays.[28,29] However, the poor solubility of **11** and derivatives therefrom presents a major limitation to their use. Our prior attempts to prepare the tetraacyl derivative of **11** encountered intractable separations

(25) (a) Finkbeiner, H. *J. Org. Chem*. **1965**, *30*, 2861−2862. (b) Chong, R.; Clezy, P. S.; Liepa, A. J.; Nichol, A. W. *Aust. J. Chem*. **1969**, *22*, 229−238.

(26) Bennis, V.; Gallagher, J. F. *Acta Crystallogr*. **1998**, *C54*, 130−132.

(27) Lee, C.-H.; Lindsey, J. S. *Tetrahedron* **1994**, *50*, 11427−11440.

TABLE 3. 9-Acylation of 1-Acyldipyrromethanes

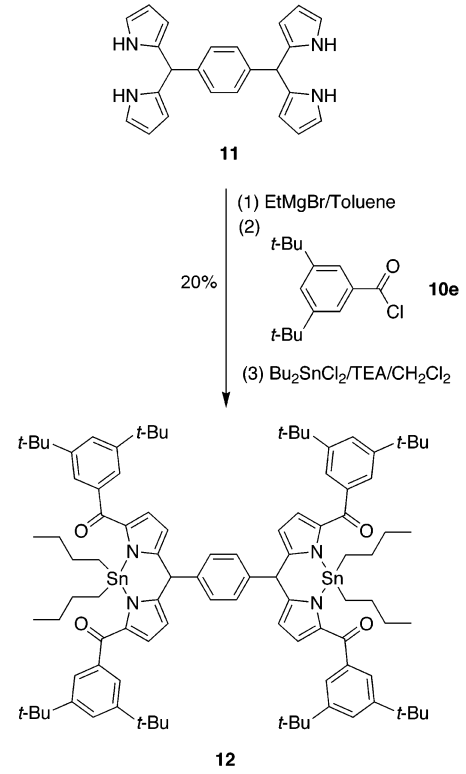


Entry	Starting material	R^1	R^2	R^3	Product	Method[a]	Yield
						A	66%[b]
1	**2a**				**6a**	B	56%
						C	46%
2	**2b**				**6n**	A	52%
3	**2c**				**6o**	A	72%
4	**2d**				**6p**	A	57%
5	**2a**				**6q**	D[c]	58%

[a] The methods differ only in the conditions for acylation; each method employed the same procedure for tin complexation (approximate concentrations given). Method A: 50 mM **2**, 75 mM acid chloride, 100 mM $SbCl_5$ in CH_2Cl_2. Method B: 250 mM **2**, 1.5 M EtMgBr (1.0 M solution in THF), 750 mM acid chloride in toluene. Method C: (1) 500 mM **2**, 1.0 M benzoxathiolium tetrafluoroborate salt, 1.0 M DBU; (2) 1.0 M HgO, 2.0 M HBF_4 (aq). [b] The high concentration conditions (500 mM **2**, 750 mM acid chloride, 1.0 mM $SnCl_4$ in CH_2Cl_2 or $ClCH_2CH_2Cl$) gave 60% yield. [c] A Vilsmeier formylation using 3.0 M **2**, 12 M *N*,*N*-dimethylformamide, and 4.5 M *p*-toluoyl chloride in $ClCH_2CH_2Cl$.

owing to the incomplete acylation and very poor solubility of the acylated products.

We addressed the separation and solubility problems through use of tin complexation (eq 5). Thus, a suspension of **11** in toluene was treated with EtMgBr followed by acid chloride **10e** (method B), affording several reaction products upon TLC analysis. Workup followed by tin complexation, filtration through a silica pad, and precipitation afforded the target compound **12** in 20% yield. This compound is quite soluble in organic solvents and can be used in the synthesis of *p*-phenylene-linked multiporphyrin arrays.



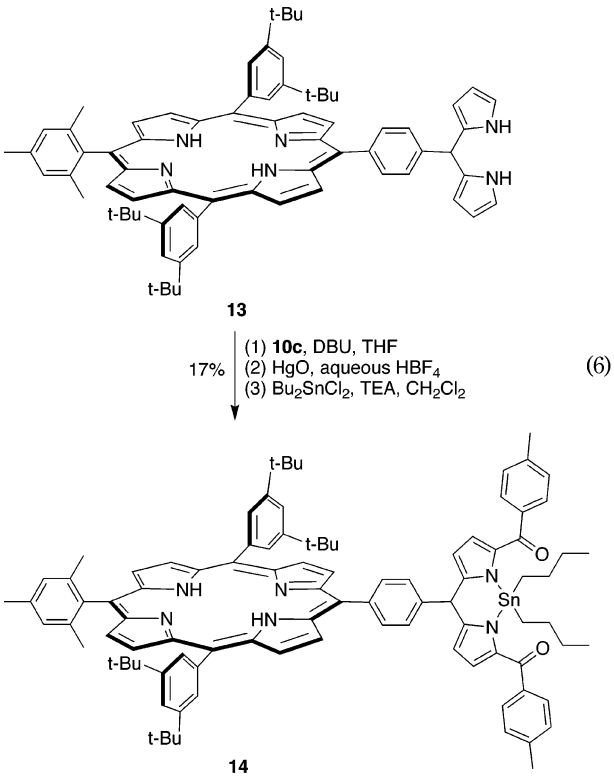
(5)

Diacylation of a Porphyrin-Dipyrromethane. We recently described the synthesis of *p*-phenylene-linked triads of porphyrins wherein the three porphyrins are present in distinct metalation states (Mg, Zn, free base).[29] The synthesis of the triads relied on the condensation of a porphyrin-dipyrromethane and a porphyrin-dipyr-

(28) (a) Khoury, R. G.; Jaquinod, L.; Paolesse, R.; Smith, K. M. *Tetrahedron* **1999**, *55*, 6713−6732. (b) Paolesse, R.; Pandey, R. K.; Forsyth, T. P.; Jaquinod, L.; Gerzevske, K. R.; Nurco, D. J.; Senge, M. O.; Licoccia, S.; Boschi, T.; Smith, K. M. *J. Am. Chem. Soc.* **1996**, *118*, 3869−3882. (c) Helms, A.; Heiler, D.; McLendon, G. *J. Am. Chem. Soc.* **1992**, *114*, 6227−6238. (d) Sessler, J. L.; Johnson, M. R.; Creager, S. E.; Fettinger, J. C.; Ibers, J. A. *J. Am. Chem. Soc.* **1990**, *112*, 9310−9329. (e) Sessler, J. L.; Johnson, M. R. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 678−680.

(29) Speckbacher, M.; Yu, L.; Lindsey, J. S. *Inorg. Chem.* **2003**, *42*, 4322−4337.

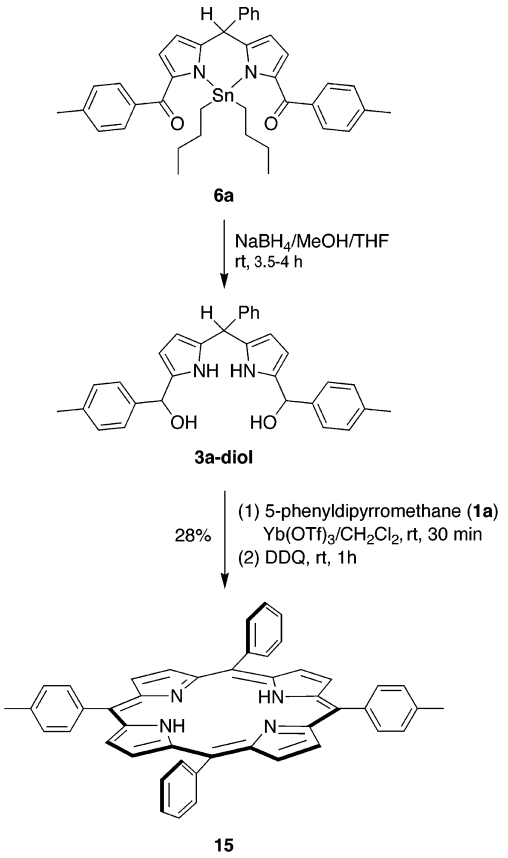
romethane-dicarbinol. Substantial difficulty was encountered in preparing the porphyrin-diacyldipyrromethane, which served as the precursor to the porphyrin-dipyrromethane-dicarbinol. We examined the applicability of the tin chemistry to the purification of the porphyrin-diacyldipyrromethane obtained upon direct 1,9-diacylation of the corresponding porphyrin-dipyrromethane (eq 6). Free base porphyrin **13** was reacted with benzoxathio-



lium salt **10c** (method C) followed by oxidative hydrolysis to give the porphyrin-diacyldipyrromethane. Multiple porphyrin products were obtained. Treatment to the tin complexation chemistry afforded a new, more mobile species that was readily isolated. The desired tin complex **14** was obtained in low yield (17%) but in exceptional purity. The high purity and facile isolation sets this synthesis apart from the previously reported preparation of the uncomplexed diacyldipyrromethane-porphyrin.[29]

Direct Synthesis of Porphyrins from a Diacyldipyrromethane−Tin Complex. It occurred to us that the diacyldipyrromethane−tin complexes might be used as precursors in the synthesis of porphyrins. Thus, diacyldipyrromethane−tin complex **6a** was reduced to the putative dicarbinol derivative (**3a-diol**) following a standard method[1] for the reduction of diacyldipyrromethanes using $NaBH_4$ (Scheme 4). Reduction of **6a** to the putative dipyrromethane-dicarbinol **3a-diol** took longer (3.5−4 h) than the corresponding reduction of **3a** to **3a-diol** (40 min to 1 h) as observed by TLC analysis. Condensation of **3a-diol** (obtained from the reduction of **6a**) with **1a** was carried out using a literature procedure:[30] $Yb(OTf)_3$ (3.2 mM) in CH_2Cl_2 (2.5 mM) at room temperature followed by oxidation with DDQ. The similar condensation of **3a-diol** (resulting from the direct reduction of **3a**) and **1a** was performed for comparison. The progress of the condensation was assessed by removing a reaction aliquot and oxidizing with DDQ, followed by UV−vis spectroscopic analysis to determine the yield of porphyrin (Figure 2). The key results are as follows. (1) In both cases, the yield of porphyrin peaked at ∼15 min (27−29%) and remained nearly constant up to 30 min. (2) No scrambled porphyrin products (derived from acidolysis of dipyrromethane species) were observed upon analysis of each crude reaction mixture by laser-desorption mass spectrometry (LD-MS). (3) No tin porphyrin was observed upon analysis of the crude reaction mixture (absence of m/z = 759.5, **Sn-15**: $C_{46}H_{32}N_4Sn$) by LD-MS or of the isolated porphyrin product by ^1H NMR, UV−vis, fluorescence and LD-MS analysis. (4) The isolated yield of porphyrin **15** (from **6a** and **1a**) was 28%, which was consistent with the yield observed spectroscopically.

SCHEME 4



6. Safety Considerations. We sought to determine the nature of the tin species formed during decomplexation or reduction of the diacyldipyrromethane−tin complexes. The crude reaction mixture obtained upon TFA decomplexation of **6a** (in CH_2Cl_2) was examined by ^{119}Sn NMR spectroscopy (standard; Me_4Sn = 0.00 ppm). Four peaks were obtained (−196.3, −174.5, −169.8, and −167.0 ppm). The peak at −196.3 ppm is attributed to $Bu_2Sn(O_2CCF_3)_2$ [−195 ppm is reported[31] for $Bu_2Sn(OAc)_2$], while the remaining three peaks likely stem from stannoxane oligomers of type $(Bu_2SnO)_n$ (−177 ppm[31]). The

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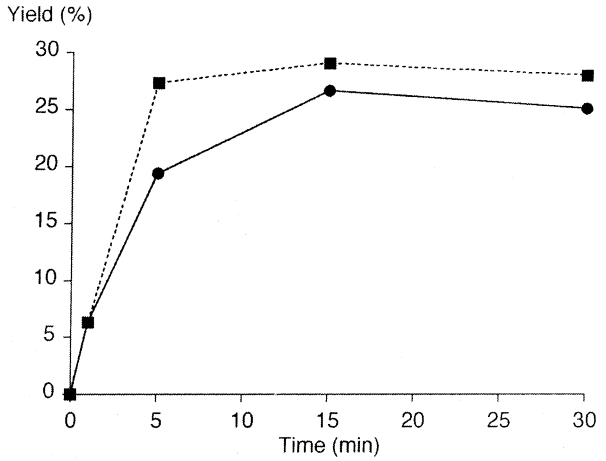

FIGURE 2. Comparison of the yield of porphyrin as a function of time upon reaction of dipyrromethane-dicarbinol **3a-diol** + dipyrromethane **1a**, where the **3a-diol** species was derived from the corresponding diacyldipyrromethane **3a** (●) or the diacyldipyrromethane−tin complex **6a** (■). The reaction was performed with catalysis by $Yb(OTf)_3$ in CH_2Cl_2 (the concentration of each reactant is 2.5 mM, the concentration of the catalyst is 3.2 mM) and oxidation by DDQ. Each data point is the average from duplicate reactions.

crude mixture obtained upon $NaBH_4$ reduction of **6a** (to give **3a-diol**) also was examined by ^{119}Sn NMR spectroscopy (in THF/MeOH (10/1)). A signal at −203.4 ppm was observed, which is consistent with dibutyltin dihydride (Bu_2SnH_2, −205 ppm[31]). Therefore, no species other than dibutyltin compounds were formed during decomplexation or reduction of the diacyldipyrromethane−tin complexes.

Organotin compounds are widely perceived to be quite toxic. In fact, the toxicity of organotin compounds varies substantially depending on the number and size of hydrocarbon substituents at the tin atom. Although trialkyltin and triaryltin compounds have been employed as biocides[32] and cause damage to the central nervous system of laboratory animals,[33] dialkyltin compounds are not useful as biocides and do not cause such damage in similar studies. Among dialkyltin compounds, dibutyltin compounds are less harmful than dimethyl- and diethyltin compounds as a result of their lower propensity for absorption into biological tissues.[32] Indeed, food-grade plastics incorporate dioctyltin compounds, which are considered practically nontoxic because of their low level of leaching into food materials and extremely poor biological uptake.[33,34] There is also no indication that dialkyltin compounds have any carcinogenic effect.[35] The acute toxicity of dibutyltin dichloride (LD_{50} = 100 mg/kg) is relatively low, and polymeric stannoxanes such as $(Bu_2SnO)_n$ are generally much less toxic (LD_{50} = 600−800 mg/kg).[36] Although little information is available regarding the toxicity of dialkyltin hydrides, dialkyltin hydrides react slowly in water to form gels, presumably of the corresponding stannoxane $(R_2SnO)_n$.[37] Taken together, the use of tin reagents in diacyldipyrromethane chemistry as described herein would not appear to warrant any extraordinary safety precautions.

Outlook

The previous difficulty in purifying 1,9-diacyldipyrromethanes has been overcome by conversion of the diacyldipyrromethane to the corresponding dialkyltin complex. Selective complexation of 1,9-diacyldipyrromethanes versus other dipyrromethane species originates in the requirement for acyl groups at both the 1- and 9-positions to give a stable coordination complex. The tin complexation process is tolerant of diverse substituents and can be used in conjunction with a variety of acylation methods. Formation of the tin complex alters the structure of the diacyldipyrromethane in two ways: (1) blocking of the pyrrolic nitrogen and carbonyl oxygen atoms, thereby ensheathing all sites that can engage in hydrogen bonding, and (2) enforcing a rigid structure with essentially coplanar pyrrole units. The resulting diacyldipyrromethane−tin complex is typically less polar than the corresponding diacyldipyrromethane, has high solubility in organic solvents, chromatographs as a sharp band, and crystallizes readily. The simplicity of the complexation/decomplexation process suggests the use of a catch-and-release strategy, where the tin-dichloride reagent is incorporated in an insoluble polymeric resin. Examples of resins are known where the tin-dichloride unit is located on a pendant group on a cross-linked polymer such as polystyrene.[38] In summary, although further improvements in acylation methods are still needed, the simplified isolation, purification, and handling of 1,9-diacyldipyrromethanes via the tin-complexation strategy described herein should help broaden the scope of porphyrin synthesis.

Experimental Section

Noncommercial Compounds. The dipyrromethanes **1a**−**c,e**−**g**[39] and **1d**[1] were prepared as described in the literature.[39] The known 1-acyldipyrromethanes **2a**,[2] **2c**[1], **2d**,[1] diacyldipyrromethanes **3a,c,f**−**h,k,q**,[1] **3b**,[30] **3j**[40] and **3d**;[41,17] acylating reagents **10c**,[10] **10d**,[14,42] **10e**,[43] **10f**,[10] and **10g**;[10] bis(dipyrromethane) **11**;[27] and porphyrin **13**[29] were prepared as described.

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Tin Complexation of a 1,9-Diacyldipyrromethane, Exemplified for Dibutyl[5,10-dihydro-1,9-bis(4-methylbenzoyl)-5-phenyldipyrrinato]tin(IV) (6a). A sample of **3a** (916 mg, 2.00 mmol) was treated with TEA (814 μL, 6.00 mmol) and Bu_2SnCl_2 (608 mg, 2.00 mmol) in CH_2Cl_2 (4 mL) at room temperature for 1 h. The mixture was filtered over a pad of silica (CH_2Cl_2). The eluant was concentrated to dryness. The resulting residue (often slightly brown) was dissolved in a minimum amount of diethyl ether. Then methanol was added, yielding a precipitate, which upon filtration afforded a colorless solid (1.25 g, 90%): mp 155−157 °C (dec); ^{1}H NMR δ 0.68 (t, J = 7.2 Hz, 3H), 0.73 (t, J = 7.2 Hz, 3H), 1.06−1.53 (m, 10H), 1.64−1.71 (m, 2H), 2.44 (s, 6H), 5.59 (s, 1H), 6.18 (d, J = 3.6 Hz, 2H), 7.08 (d, J = 3.6 Hz, 2H), 7.16−7.32 (m, 9H), 7.82 (d, J = 8.0 Hz, 4H); ^{13}C NMR δ 13.83, 13.84, 21.8, 24.2, 25.0, 26.21, 26.52, 27.44, 27.50, 45.9, 115.3, 123.9, 126.9, 128.38, 128.84, 129.30, 129.36, 135.2, 136.0, 142.4, 144.5, 151.7, 184.7; ^{119}Sn NMR δ −282.3; FAB-MS obsd 691.2374, calcd 691.2347 ($C_{39}H_{42}N_2O_2Sn$). Anal. Calcd for $C_{39}H_{42}N_2O_2Sn$: C, 67.94; H, 6.14; N, 4.06. Found: C, 68.00; H, 6.15; N, 4.07. Alternatively, the reaction could be carried out at the concentration of 100 or 50 mM (1,9-diacyldipyrromethane) with comparable results.

Direct 1,9-Diacylation of Dipyrromethanes with Subsequent Tin Complexation, Exemplified for 6a. Method A ($SbCl_5$ Catalysis). A solution of **1a** (1.11 g, 5.00 mmol) and *p*-toluoyl chloride (1.32 mL, 10.0 mmol) in $ClCH_2CH_2Cl$ (100 mL) was treated with $SbCl_5$ (1.34 mL, 10.0 mmol) at room temperature for 5 min. The reaction mixture was poured into saturated aqueous $NaHCO_3$ (50 mL) and stirred vigorously for 30 min. The organic layer was collected, washed (water and brine), dried (Na_2SO_4), and filtered. The filtrate was concentrated to dryness. The residue (typically blue or green) was treated with TEA (2.10 mL, 15.0 mmol) and Bu_2SnCl_2 (1.52 g, 5.00 mmol) in CH_2Cl_2 (10 mL) at room temperature for 30 min. The mixture was filtered over a silica pad (CH_2Cl_2). The eluant was concentrated to dryness. The residue was dissolved in a minimum amount of diethyl ether. Then methanol was added, yielding a precipitate, which upon filtration afforded a pale yellow solid (2.00 g, 58%) with satisfactory analytical data (mp, ^{1}H NMR spectrum, and elemental analysis).

Method A at High Concentration ($SnCl_4$ Catalysis). A solution of **1a** (2.22 g, 10.0 mmol) and *p*-toluoyl chloride (4.00 mL, 30.0 mmol) in $ClCH_2CH_2Cl$ (20 mL) was treated with $SnCl_4$ (2.30 mL, 20.0 mmol) at room temperature for 5 min. The reaction mixture was poured into saturated aqueous $NaHCO_3$ (50 mL) and stirred vigorously for 30 min. The organic layer was washed (water and brine), dried (Na_2SO_4), and filtered. The filtrate was concentrated to dryness. Treatment of the residue with TEA (4.18 mL, 30.0 mmol) and Bu_2SnCl_2 (3.04 g, 10.0 mmol) in $ClCH_2CH_2Cl$ (10 mL) at room temperature for 30 min followed by the standard purification technique as described in method A afforded pale yellow crystals (2.62 g, 39%) with satisfactory analytical data (mp, ^{1}H NMR spectrum, and elemental analysis).

Method B (Grignard). A solution of EtMgBr (50 mL, 50.0 mmol, 1.0 M solution in THF) was added slowly to a tap-water-cooled flask containing a solution of **1a** (2.22 g, 10.0 mmol) in toluene (200 mL) under argon. An exothermic reaction with gas evolution ensued. The resulting mixture was stirred at room temperature for 30 min. A solution of *p*-toluoyl chloride (3.31 mL, 25.0 mmol) in toluene (25 mL) was added over 10 min, and the resulting solution was stirred for 10 min. The reaction mixture was poured into saturated aqueous NH_4Cl (200 mL) and ethyl acetate (150 mL). The organic layer was washed (water and brine), dried (Na_2SO_4), and filtered. The filtrate was concentrated to dryness. Treatment of the residue with TEA (4.18 mL, 30.0 mmol) and Bu_2SnCl_2 (3.04 g, 10.0 mmol) in CH_2Cl_2 (40 mL) at room temperature for 30 min followed by the standard purification technique (described in method A) afforded a pale yellow solid (3.17 g, 46%) with satisfactory analytical data (mp, ^{1}H NMR spectrum, and elemental analysis).

Method B at Large Scale. A solution of EtMgBr (375 mL, 375 mmol, 1.0 M solution in THF) was added slowly to a tap-water-cooled flask containing a solution of **1a** (16.8 g, 75.0 mmol) in toluene (750 mL) under argon. An exothermic reaction with gas evolution ensued. The resulting mixture was stirred at room temperature for 30 min. A solution of *p*-toluoyl chloride (24.8 mL, 188 mmol) in toluene (188 mL) was added over 30 min, and the resulting solution was stirred for 30 min. The reaction mixture was poured into saturated aqueous NH_4Cl (1.50 L) and ethyl acetate (1.50 L). The organic layer was washed [water (2 × 1 L) and brine (2 × 1 L)], dried (Na_2SO_4), and filtered. The filtrate was concentrated to dryness. The residue was treated with TEA (31.4 mL, 225 mmol) and Bu_2SnCl_2 (22.8 g, 75.0 mmol) in CH_2Cl_2 (300 mL) at room temperature for 30 min followed by a slight modification of the silica-pad purification technique [silica, 6 × 27 cm; CH_2Cl_2/hexanes (1/1) with 1% TEA; total amount of eluant = 2.3 L, ∼1.5 h]. The eluant was concentrated to dryness. The residue was dissolved in diethyl ether, and then methanol was added, yielding a precipitate. Filtration afforded a pale yellow solid (20.3 g, 39%) that exhibited satisfactory analytical data (mp, ^{1}H NMR spectrum, and elemental analysis).

Method C (Benzoxathiolium Salt Dialkylation/Hydrolysis). A solution of benzoxathiolium salt **10c** (6.28 g, 20.0 mmol) in THF (13 mL) was treated with DBU (3.04 g, 20.0 mmol) at room temperature for 3 min in a sealed round-bottom flask. A solution of dipyrromethane **1a** (1.11 g, 5.00 mmol) in THF (4 mL) was injected into the reaction mixture, and the resulting mixture was stirred for 5 min. HgO (4.34 g, 20.0 mmol) and aqueous HBF_4 (5.23 mL of 48 wt % solution, 40.0 mmol) were added to the mixture. The mixture was stirred at room temperature for 3 h, and then 2 M aqueous NaOH (5 mL) was added. The mixture was poured into saturated aqueous NH_4Cl and CH_2Cl_2. The organic layer was washed (water and brine), dried (Na_2SO_4), and filtered. The filtrate was concentrated to dryness. The residue was filtered through a pad of silica with CH_2Cl_2, followed by CH_2Cl_2 with 10% ethyl acetate. The eluant was concentrated. Treatment of the residue with TEA (2.10 mL, 15.0 mmol) and Bu_2SnCl_2 (1.53 g, 5.00 mmol) in CH_2Cl_2 (10 mL) at room temperature for 1 h followed by the standard purification technique (described in method A) afforded a colorless solid (1.29 g, 37%) with satisfactory analytical data (mp, ^{1}H NMR spectrum, and elemental analysis).

Method D (Vilsmeier). A mixture of **10d** (8.21 g, 40.0 mmol) and $POCl_3$ (7.46 mL, 80 mmol) was stirred under argon at 65 °C for 3 h and then was cooled to room temperature. The reaction mixture was dissolved in $ClCH_2CH_2Cl$ (60 mL) and was treated with **1a** (2.22 g, 10.0 mmol) under reflux for 2 h. The reaction mixture was poured into saturated aqueous CH_3CO_2Na (60 mL) followed by heating at 65 °C for 1 h. The organic layer was collected, and the aqueous layer was extracted with CH_2Cl_2. The initial organic layer and the eluant were combined, washed (water and brine), dried (Na_2SO_4), and filtered. The filtrate was concentrated to dryness. Treatment of the residue with TEA (4.20 mL, 30.0 mmol) and Bu_2SnCl_2 (3.04 g, 10.0 mmol) in CH_2Cl_2 (20 mL) at room temperature for 15 min followed by the standard purification technique (described in method A) afforded a pale yellow solid (4.34 g, 63%) with satisfactory analytical data (mp, ^{1}H NMR spectrum, and elemental analysis).

Synthesis of 1-Acyldipyrromethanes, Exemplified for 1-(4-Methylbenzoyl)-5-phenyldipyrromethane (2a).[2] A solution of EtMgBr (50.0 mL, 50.0 mmol, 1.0 M in THF) was added slowly to a solution of **1a** (4.44 g, 20.0 mmol) in THF (20 mL) under argon. The resulting mixture was stirred at room temperature for 10 min and then cooled to −78 °C. A solution of *S*-2-pyridyl 4-methylbenzothioate (4.58 g, 20.0 mmol) in THF (20 mL) was added. The mixture was stirred at −78 °C for 10 min and then warmed to room temperature.

The reaction mixture was poured into saturated aqueous NH_4Cl (150 mL) and THF (10 mL). The organic layer was washed (water and brine), dried (Na_2SO_4), and filtered. The filtrate was chromatographed [silica (10 × 24 cm), CH_2Cl_2 (2.3 L)], affording a golden amorphous solid (5.82 g, 86%) with satisfactory analytical data (mp, ^{1}H NMR spectrum, and elemental analysis).

Acylation of 1-Acyldipyrromethanes with Subsequent Tin Complexation, Exemplified for 6a. Method A ($SbCl_5$ Catalysis). A solution of **2a** (1.70 g, 5.00 mmol) and *p*-toluoyl chloride (0.990 mL, 7.50 mmol) in CH_2Cl_2 (100 mL) was treated with $SbCl_5$ (1.28 mL, 10.0 mmol) at room temperature for 10 min. The reaction mixture was poured into saturated aqueous $NaHCO_3$ (100 mL) and stirred vigorously for 30 min. The organic layer was washed (water and brine), dried (Na_2SO_4), and filtered. The filtrate was concentrated to dryness. The residue was treated with TEA (2.10 mL, 15.0 mmol) and Bu_2SnCl_2 (1.52 g, 5.00 mmol) in CH_2Cl_2 (10 mL) at room temperature for 15 min. The mixture was filtered over a silica pad (CH_2Cl_2). The eluant was concentrated to dryness. The residue was dissolved in a minimum amount of diethyl ether. Then methanol was added, yielding a precipitate, which upon filtration afforded a pale yellow solid (2.26 g, 66%) with satisfactory analytical data (mp, ^{1}H NMR spectrum, and elemental analysis).

Method A at High Concentration ($SnCl_4$ Catalysis). A solution of **2a** (1.70 g, 5.00 mmol) and *p*-toluoyl chloride (0.990 mL, 7.50 mmol) in $ClCH_2CH_2Cl$ (10 mL) was treated with $SnCl_4$ (1.17 mL, 10.0 mmol) at room temperature for 10 min. The reaction mixture was poured into saturated aqueous $NaHCO_3$ (100 mL) and CH_2Cl_2 (50 mL) and stirred vigorously for 30 min. The organic layer was washed (water and brine), dried (Na_2SO_4), and filtered. The filtrate was concentrated to dryness. Treatment of the residue with TEA (2.10 mL, 15.0 mmol) and Bu_2SnCl_2 (1.52 g, 5.00 mmol) in CH_2Cl_2 (20 mL) at room temperature for 15 min followed by the standard purification technique (as described in method A) afforded a pale yellow solid (2.10 g, 60%) with satisfactory analytical data (mp, ^{1}H NMR spectrum, and elemental analysis).

Method B (Grignard). A solution of EtMgBr (30.0 mL, 30.0 mmol, 1.0 M solution in THF) was added slowly to a solution of **2a** (1.70 g, 5.00 mmol) in toluene (20 mL) under argon. The resulting mixture was stirred at room temperature for 10 min. A sample of *p*-toluoyl chloride (2.00 mL, 15.0 mmol) was added, and the mixture was stirred for 30 min. The reaction mixture was poured into saturated aqueous NH_4Cl (100 mL) and ethyl acetate (100 mL). The organic layer was washed (water and brine), dried (Na_2SO_4), and filtered. The filtrate was concentrated to dryness. Treatment of the residue with TEA (2.10 mL, 15.0 mmol) and Bu_2SnCl_2 (1.52 g, 5.00 mmol) in CH_2Cl_2 (10 mL) at room temperature for 15 min followed by the standard purification technique (as described in method A) afforded a pale yellow solid (1.93 g, 56%) with satisfactory analytical data (mp, ^{1}H NMR spectrum, and elemental analysis).

Method C (Benzoxathiolium Salt Alkylation/Hydrolysis). A solution of **10c** (3.14 g, 10.0 mmol) in THF (8 mL) was treated with DBU (1.52 g, 10.0 mmol) at room temperature for 3 min in a well-sealed round-bottom flask. A solution of **2a** (1.70 g, 5.00 mmol) in THF (4 mL) was injected into the reaction mixture, and the resulting mixture was stirred for 30 min. HgO (2.17 g, 10.0 mmol) and aqueous HBF_4 (2.61 mL of 48 wt% solution, 20.0 mmol) were added. The mixture was stirred at room temperature for 3 h, and then 2 M aqueous NaOH (5 mL) was added. The mixture was poured into saturated aqueous NH_4Cl, and CH_2Cl_2 was added. The organic layer was washed (water and brine), dried (Na_2SO_4), and filtered. The filtrate was concentrated to dryness. The residue was filtered through a pad of silica [CH_2Cl_2, then CH_2Cl_2/ethyl acetate (9:1)]. The eluant was concentrated. Treatment of the residue with TEA (2.10 mL, 15.0 mmol) and Bu_2SnCl_2 (1.53 g, 5.00 mmol) in CH_2Cl_2 (10 mL) at room temperature for 1 h followed by the standard purification technique (as described in method A) afforded a colorless solid (2.10 g, 37%) with satisfactory analytical data (mp, ^{1}H NMR spectrum, and elemental analysis).

Method D (Modified Vilsmeier Formylation), Affording Dibutyl[5,10-dihydro-1-formyl-9-(4-methylbenzoyl)-5-phenyldipyrrinato]tin(IV) (6q). A mixture of **2a** (1.02 g, 3.00 mmol) and DMF (929 μL, 12.0 mmol) in $ClCH_2CH_2Cl$ (1 mL) was treated with *p*-toluoyl chloride (595 μL, 4.50 mmol) at room temperature under argon. The mixture was heated at reflux for 45 min and then cooled to room temperature. The reaction mixture was poured into saturated aqueous Na_2CO_3. The organic layer was collected, and the aqueous layer was extracted with CH_2Cl_2. The initial organic layer and the eluant were combined, washed (water and brine), dried (Na_2SO_4), and filtered. The filtrate was concentrated to dryness. Treatment of the residue with TEA (1.25 mL, 9.00 mmol) and Bu_2SnCl_2 (912 mg, 3.00 mmol) in CH_2Cl_2 (12 mL) at room temperature for 25 min followed by chromatography (silica, CH_2Cl_2) afforded an orange oil (1.04 g, 58%): ^{1}H NMR δ 0.67−0.78 (m, 6H), 1.08−1.36 (m, 6H), 1.38−1.72 (m, 6H), 2.43 (s, 3H), 5.56 (s, 1H), 6.12 (d, J = 4.0 Hz, 1H), 6.21 (d, J = 4.0 Hz, 1H), 7.05 (d, J = 4.0 Hz, 1H), 7.12 (d, J = 4.0 Hz, 1H), 7.14−7.22 (m, 3H), 7.26−7.32 (m, 4H), 7.81 (d, J = 8.0 Hz, 2H), 9.19 (s, 1H); ^{13}C NMR δ 13.60, 13.64, 21.7, 23.9, 24.5, 26.04, 26.35, 27.2, 45.5, 114.7, 115.9, 123.88, 123.92, 126.8, 128.1, 128.7, 129.23, 129.26, 134.4, 135.5, 138.1, 142.6, 144.0, 151.5, 152.0, 178.7, 184.3; ^{119}Sn NMR δ −257.0; FAB-MS obsd 601.1906 [(M + H)$^+$], calcd 601.1879 ($C_{32}H_{36}N_2O_2Sn$). Anal. Calcd for $C_{32}H_{36}N_2O_2Sn$: C, 64.13; H, 6.05; N, 4.67. Found: C, 64.03; H, 6.04; N, 4.67.

Decomplexation of a 1,9-Diacyldipyrromethane−Tin Complex, Exemplified for 1,9-Bis(4-methylbenzoyl)-5-phenyldipyrromethane (3a). A solution of **6a** (345 mg, 0.500 mmol) in CH_2Cl_2 (5 mL) was treated with TFA (116 μL, 1.50 mmol) at room temperature for 10 min. The mixture was filtered through a pad of silica [hexanes/ethyl acetate (2:1)]. The eluant was concentrated to dryness. The residue was dissolved in diethyl ether, and then hexanes was added, causing formation of a precipitate. Filtration afforded a colorless solid (218 mg, 95%) with satisfactory analytical data (mp, ^{1}H NMR spectrum, and elemental analysis). In some cases (depending on substituents), the residue obtained from the silica-pad filtration could be washed with an organic solvent to obtain the product.

Synthesis of 1,4-Bis[dibutyl(5,10-dihydro-1,9-(3,5-di-*tert*-butylbenzoyl)-5-dipyrrinato)tin(IV)]benzene (12). A solution of EtMgBr (5.00 mL, 5.00 mmol, 1.0 M in THF) was added slowly to a tap-water-cooled flask containing a suspension of **11** (183 mg, 0.500 mmol) in toluene (30 mL) under argon. The resulting mixture was stirred at room temperature for 30 min. A solution of **10e** (632 mg, 2.50 mmol) in toluene (3.0 mL) was added over 5 min, and the mixture was stirred for 10 min. The reaction mixture was poured into saturated aqueous NH_4Cl (50 mL) and ethyl acetate (50 mL). The organic layer was washed (water and brine), dried (Na_2SO_4), and filtered. The filtrate was concentrated to dryness. Treatment of the residue with TEA (367 μL, 2.63 mmol) and Bu_2SnCl_2 (303 mg, 1.00 mmol) in CH_2Cl_2 (20 mL) at room temperature for 30 min followed by the standard purification (as described in method A) afforded a pale blue solid (165 mg, 20%): mp > 270 °C; ^{1}H NMR δ 0.66−0.76 (m, 12H), 1.04−1.76 (m, 96H), 5.55 (s, 2H), 6.19 (d, J = 3.9 Hz, 4H), 7.01 (d, J = 3.9 Hz, 4H), 7.14 (s, 4H), 7.59−7.62 (m, 4H), 7.69−7.72 (m, 8H); ^{13}C NMR δ 13.8, 13.9, 24.1, 25.4, 26.3, 26.5, 27.4, 27.5, 31.6, 35.2, 45.4, 115.3, 123.5, 124.0, 126.0, 128.5, 136.4, 137.3, 142.7, 151.1, 151.4, 185.9; FAB-MS obsd 1694.38, calcd 1694.84 ($C_{100}H_{134}N_4O_4Sn_2$). Anal. Calcd for $C_{100}H_{134}N_4O_4Sn_2$: C, 70.92; H, 7.98; N, 3.31. Found: C, 70.97; H, 7.98; N, 3.33.

Dibutyl[5,10-dihydro-1,9-bis(*p*-toluoyl)-5-(4-(10,20-bis-(3,5-di-*tert*-butylphenyl)-15-mesityl)porphin-5-yl)phenyldipyrrinato]tin(IV) (14). A sample of **10c** (66 mg, 0.21 mmol)

was added to a 5-mL round-bottomed flask containing a magnetic stirring bar. The flask was sealed with a septum and vented with a needle. Dry THF (1.0 mL) and DBU (32 mg, 0.21 mmol) were added, and then the venting needle was removed. The solution was stirred at room temperature for 3 min, during which time the benzoxathiolium salt dissolved and the solution turned pale yellow. A solution of **13** (54 mg, 53 μmol) in dry THF (1.0 mL) was injected into the reaction vessel. After 1 h, the reaction vessel was opened to the atmosphere, HgO (46 mg, 0.21 mmol) and aqueous HBF_4 (55 μL of 48 wt% solution 0.42 mmol) were added, and the vessel was sealed again. After 1 h, CH_2Cl_2 (3 mL) was added, the mixture was transferred into a 20-mL vial, saturated aqueous NH_4Cl (4 mL) was added. The organic layer was separated and washed with water, washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated to dryness. The residue was redissolved in CH_2Cl_2 (0.5 mL), and TEA (21 μL, 0.15 mmol) was added. A solution of Bu_2SnCl_2 (16 mg, 52 μmol) in 0.5 mL of CH_2Cl_2 was added, and the mixture was stirred for 2.5 h. The solution was diluted with hexanes (2 mL) and chromatographed (silica, hexanes/CH_2Cl_2 containing 1% TEA). The desired compound eluted as the second red band, yielding 10 mg of a purple solid. Fractions containing the impure product were rechromatographed under the same conditions, yielding an additional 3 mg of the pure title compound (total yield = 13 mg, 17%); mp 230−232 °C (dec); ^{1}H NMR δ −2.67 (s, 2H), 0.70−0.77 (m, 6H), 1.14−1.31 (m, 4H), 1.35−1.62 (m, 42H), 1.73−1.82 (m, 2H), 1.86 (s, 6H), 2.47 (s, 6H), 2.62 (s, 3H), 5.93 (s, 1H), 6.52 (d, J = 3.9 Hz, 2H), 7.24−7.27 (m, 4H), 7.34 (d, J = 8.0 Hz, 4H), 7.58 (d, J = 8.4 Hz, 2H), 7.77−7.79 (m, 2H), 7.90 (d, J = 8.0 Hz, 4H), 8.08−8.09 (m, 4H), 8.14 (d, J = 8.4 Hz, 2H), 8.69 (d, J = 4.8 Hz, 2H), 8.83−8.86 (m, 6H); ^{13}C NMR δ 13.9, 21.70, 21.89, 21.97, 24.23, 25.14, 26.29, 26.5, 27.6, 32.0, 35.3, 45.9, 115.6, 118.2, 119.7, 121.14, 121.29, 124.0, 126.7, 127.9, 129.36, 129.45, 130.28, 135.04, 135.28, 136.32, 137.83, 138.83, 139.62, 141.11, 141.27, 142.5, 143.9, 148.9, 151.7, 184.9; LD-MS obsd 1492.1; FAB-MS obsd 1493.7029 [(M + H)$^+$], calcd 1493.7321 ($C_{96}H_{104}N_6O_2Sn$); λ_{max} (toluene) 422, 486, 517, 550, 592, 649 nm.

Direct Porphyrin Formation from 6a, Yielding 5,15-Bis(4-methylphenyl)-10,20-diphenylporphyrin (15).[44] A solution of **6a** (276 mg, 0.400 mmol) in dry THF/MeOH (15 mL, 10:1) was treated with $NaBH_4$ (303 mg, 8.00 mmol, 20 equiv) in small portions with rapid stirring at room temperature. TLC analysis after 2 h [silica, hexanes/ethyl acetate (3/1)] indicated incomplete reduction. Therefore, an additional amount of $NaBH_4$ (303 mg, 8.00 mmol) was added in the same manner. After another 2 h, TLC analysis showed complete reduction of **6a**. The reaction was quenched by slow addition of saturated aqueous NH_4Cl. The reaction mixture was extracted with CH_2Cl_2, dried (K_2CO_3) and concentrated, affording **3a-diol** as a slightly yellow foamlike solid. The freshly prepared **3a-diol** was condensed with **1a** (89 mg, 0.40 mmol) in CH_2Cl_2 (160 mL) under catalysis with $Yb(OTf)_3$ (317 mg, 0.512 mmol, 3.2 mM) at room temperature for 30 min. DDQ (272 mg, 1.20 mmol) was added, and the reaction mixture was stirred for 1 h at room temperature. The reaction mixture was then neutralized with TEA and filtered through a pad of silica (eluted with CH_2Cl_2). The first fraction was collected and concentrated. The residue was suspended in methanol. The suspension was sonicated and then filtered, affording a purple solid (75 mg, 29%) with satisfactory analytical data (^{1}H NMR spectrum, UV−vis, LD-MS, fluorescence). The duplicate reaction afforded a similar result (71 mg, 28%).

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Supporting Information Available: A complete description of studies of improved methods for acylation of dipyrromethanes (Friedel−Crafts, benzoxathiolium); complete experimental section including characterization data for all new compounds; X-ray data for **6a** and **6b**; and ^{1}H NMR spectra for selected compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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