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# Synthesis of 5,15-Diaryltetrabenzoporphyrins

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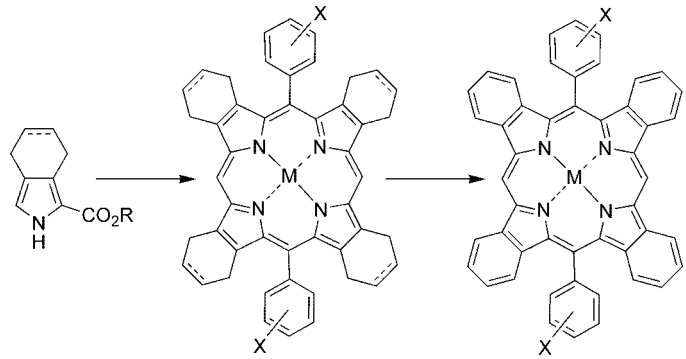


5,15-$Ar_2$TBP

A general method of synthesis of 5,15-diaryltetrabenzoporphyrins ($Ar_2$TBPs) has been developed, based on 2 + 2 condensation of dipyrromethanes followed by oxidative aromatization. Two pathways to $Ar_2$TBPs were investigated: the tetrahydroisoindole pathway and the dihydroisoindole pathway. In the tetrahydroisoindole pathway, precursor 5,15-diaryltetracyclohexenoporphyrins (5,15-$Ar_2$TCHPs) were assembled from cyclohexeno-fused *meso*-unsubstituted dipyrromethanes and aromatic aldehydes or, alternatively, by way of the classical MacDonald synthesis. In the first case, scrambling was observed. Aromatization by tetracyclone was more effective than aromatization by DDQ but failed in the cases of porphyrins with electron-withdrawing substituents in the *meso*-aryl rings. The dihydroisoindole pathway was found to be much superior to the tetrahydroisoindole pathway, and it was developed into a general preparative method, consisting of (1) the synthesis of 4,7-dihydroisoindole and its transformation into *meso*-unsubstituted dipyrromethanes, (2) the synthesis of 5,15-diaryloctahydrotetrabenzoporphyrins (5,15-$Ar_2$OHTBPs), and (3) their subsequent aromatization by DDQ. $Ar_2$TBP free bases exhibit optical absorption spectra similar to those of *meso*-unsubstituted tetrabenzoporphyrins and fluoresce with high quantum yields. Pd complex of $Ph_2$TBP was found to be highly phosphorescent at room temperature.

## Introduction

$\pi$-Extended porphyrins form a class of porphyrinoids in which pyrrole rings are fused with external aromatic fragments via the $\beta$-carbon atoms. The best known representatives of this class are symmetrically $\pi$-extended porphyrins, such as tetrabenzoporphyrins and tetranaphthoporphyrins, whose optical and other properties attract interest in materials research,[1] biomedical imaging and sensing,[2] up-conversion of noncoherent NIR light,[3] and photodynamic and boron neutron-capture therapy.[4]

Until recently, synthetic approaches to tetrabenzo- and tetranaphthoporphyrins were limited by the so-called "template condensation" method and variants thereof, [5] which require severe reaction conditions and prohibit introduction of many useful functionalities into the macrocycle. In the search for more

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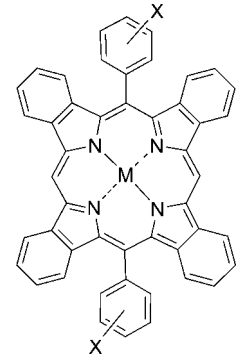
practical approaches, efforts were mainly directed toward tetraarylated tetrabenzo- and tetranaphthoporphyrins ($Ar_4$TBPs and $Ar_4$TNPs), whose modification can be conveniently accomplished via the *meso*-aryl rings. The method employing oxidative aromatization[6]has emerged as a straightforward and $Ar_4$TNPs.[8] and practical approach to $Ar_4$TBPs[7] The synthesis in this route proceeds via the well-established Lindsey chemistry,[9]allowing for a variety of functional groups to be placed at the macrocycle periphery. This strategy was later extended on the synthesis of *meso*-unsubstituted tetrabenzo- and tetranaphthoporphyrins (TBPs and TNPs).[10]

Recently, a useful extension of the oxidative aromatization method was developed, which is based on a convenient precursor, 4,7-dihydroisoindole.[11] Using this method, we synthesized and for the first time unambiguously characterized *meso*-5,15-diphenyltetrabenzoporphyrin,[12] the simplest representative of the class of 5,15-diaryltetrabenzoporphyrins

**CHART 1. 5,15-Diaryltetrabenzoporphyrin ($Ar_2$TBP)**




($Ar_2$TBP, Chart 1).[13] It appeared that the optical absorption spectrum of free base 5,15-$Ph_2$TBP ($H_2Ph_2$TBP) strongly resembled the spectra of *meso*-unsubstituted $H_2$TBPs,[10,14] suggesting that $H_2Ar_2$TBPs also possess undistorted planar geometries[15] and highly emissive excited states.[2a,14,16] The combination of the red absorption, strong emissivity, and ease of functionalization suggests that $Ar_2$TBPs can be utilized in a wide variety of applications, including biomedical imaging, optical sensing, and PDT.

In addition to forming a distinct group among $\pi$-extended porphyrins, $Ar_2$TBPs belong to a much wider family of *meso*-5,15-diarylporphyrins ($Ar_2$Ps). $Ar_2$Ps have been known since 1968,[17] and over the years, they have become one of the most widely used building blocks for construction of porphyrin-based macrostructures. The latter include, but are not limited to, porphyrin dimers,[18] linear[19] and branched[20] arrays, models of the photosynthetic antenna and reaction center,[21] supramolecular assemblies,[22] strapped porphyrins, including biomimetic models,[23] porphyrin-based catenanes and rotaxanes,[24] dyads and

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triads in combination with other electro- and/or optically active fragments, [25] and scaffolds for chiral organopalladium complexes.[26] $Ar_2$Ps have also been studied as agents for PDT,[27] recognition motifs for aminoacids and other small molecules,[28] cores for dendrimers,[29] and ligands for DNA intercalation.[30]

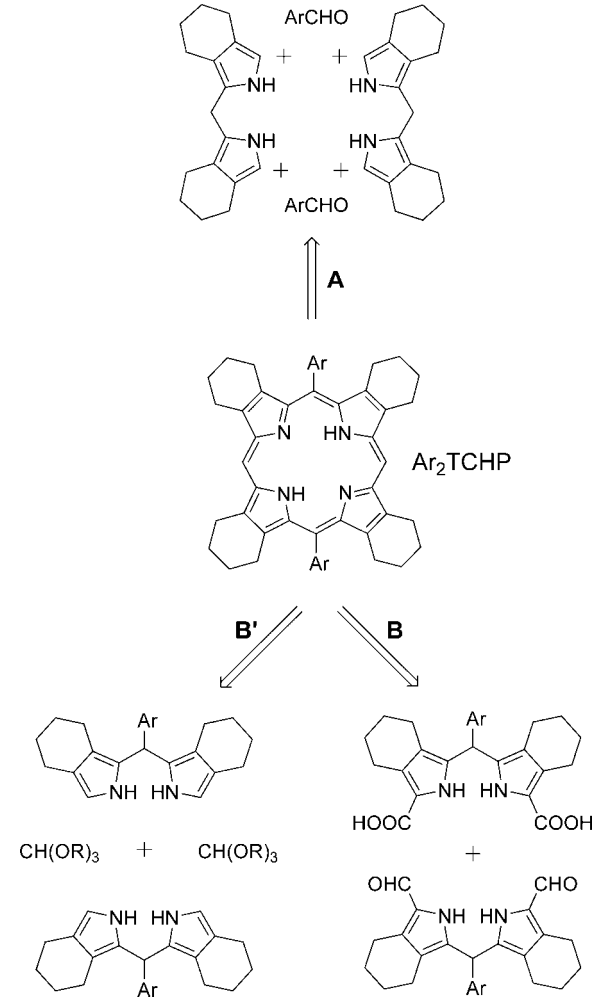
Given such an overwhelming array of applications, it appeared interesting and relevant to complement the $Ar_2$P family by their $\pi$-extended relatives, which on one hand bear the key structural features of $Ar_2$P but on the other hand possess distinctly different optical properties. In this paper, we report a detailed account on the synthesis of $Ar_2$TBPs with variously substituted *meso*-aryl groups, suitable for further functionalization.

## Results and Discussion

**I. Synthesis of $Ar_2$TBPs via Tetrahydroisoindole Route. Assembly of Precursor Porphyrins ($Ar_2$TCHPs).** Initially, we examined the approach to $Ar_2$TBPs via aromatization of 5,15-diarylhexadecahydrotetrabenzoporphyrins or, simpler, 5,15-diaryltetracyclohexenoporphyrins ($Ar_2$TCHPs), using the methodology developed earlier for $Ar_4$TBPs and TBPs.[7,8] $Ar_2$TCHPs can be assembled using either of the two orthogonal pathways, **A** and **B**/**B′**, depicted in Scheme 1.

Route **A** is based on the acid-catalyzed condensation of *meso*-unsubstituted dipyrromethanes with aromatic aldehydes.[17,31] This route has been used in the past for preparation of various types of 5,15-diaryloctaalkylporphyrins.[21,31b,32] The alternative route has two major variants: **B**, the classical MacDonald's method,[33] in which the substituent-free methine groups in the target porphyrin originate from the formyl groups in 1,9-diformyldipyrromethanes, and **B′**, the method of Baldwin et al.,[34] which makes use of the condensation of 1,9-unsubstituted 5-aryldipyrromethanes with orthoformate. A variant of the latter reaction, employing *N*,*O*-acetal of formaldehyde ($EtOCH_2NBn_2$), has been used to synthesize $Ar_2$TCHPs,[35] but the practical value of this method was undermined by a significant degree of scrambling.

**SCHEME 1. Approaches to $Ar_2$TCHPs**

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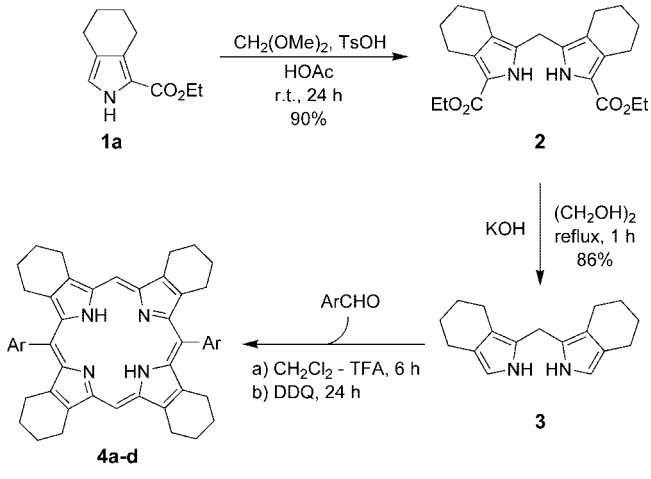
(32) Other examples: (a) Liddell, P. A.; Kodis, G.; Kuciauskas, D.; Andreasson, J.; Moore, A. L.; Moore, T. A.; Gust, D. *Phys. Chem. Chem. Phys.* **2004**, *6*, 5509–5515. (b) Inokuma, Y.; Osuka, A. *Org. Lett.* **2004**, *6*, 3663–3666. (c) Gunter, M. J.; Jeynes, T. P.; Turner, P. *Eur. J. Org. Chem.* **2004**, 193–208. (d) Shinmori, H.; Kajiwara, T.; Osuka, A. *Tetrahedron Lett.* **2001**, *42*, 3617–3620. (e) Shiratori, H.; Ohno, T.; Nozaki, K.; Yamazaki, I.; Nishimura, Y.; Osuka, A. *J. Org. Chem.* **2000**, *65*, 8747–8757. (f) Rhee, S. W.; Na, Y. H.; Do, Y.; Kim, J. *Inorg. Chim. Acta* **2000**, *309*, 49–56. (g) Plieger, P. G.; Burrell, A. K.; Jameson, G. B.; Officer, D. L. *Dalton Trans.* **2004**, 319–326. (h) Zhang, X. X.; Fuhrmann, P.; Lippard, S. J. *J. Am. Chem. Soc.* **1998**, *120*, 10260–10261. (i) Noss, L.; Liddell, P. A.; Moore, A. L.; Moore, T. A.; Gust, D. *J. Phys. Chem. B* **1997**, *101*, 458–465. (j) Lecas, A.; Boitrel, B.; Rose, E. *Tetrahedron Lett.* **1992**, *33*, 481–484. (k) Nagata, T. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 3005–3016.

(33) (a) Arsenault, G. P.; Bullock, E.; MacDonald, S. F. *J. Am. Chem. Soc.* **1960**, *82*, 4384. (b) Markovac, A.; MacDonald, S. F. *Can. J. Chem.* **1965**, *43*, 3364.

**SCHEME 2. Synthesis of $Ar_2TCHPs$ 4a−e Following Route A (Scheme 1)**




| | Ar | Yield (%) |
|---|---|---|
| **4a** | $C_6H_5$ | 48 |
| **4b** | 4-$NO_2C_6H_4$ | 13 |
| **4c** | 4-$BrC_6H_4$ | 27 |
| **4d** | 4-$MeO_2C$-$C_6H_4$ | 60 |
| **4e** | $C_6F_5$ | 10[a] |

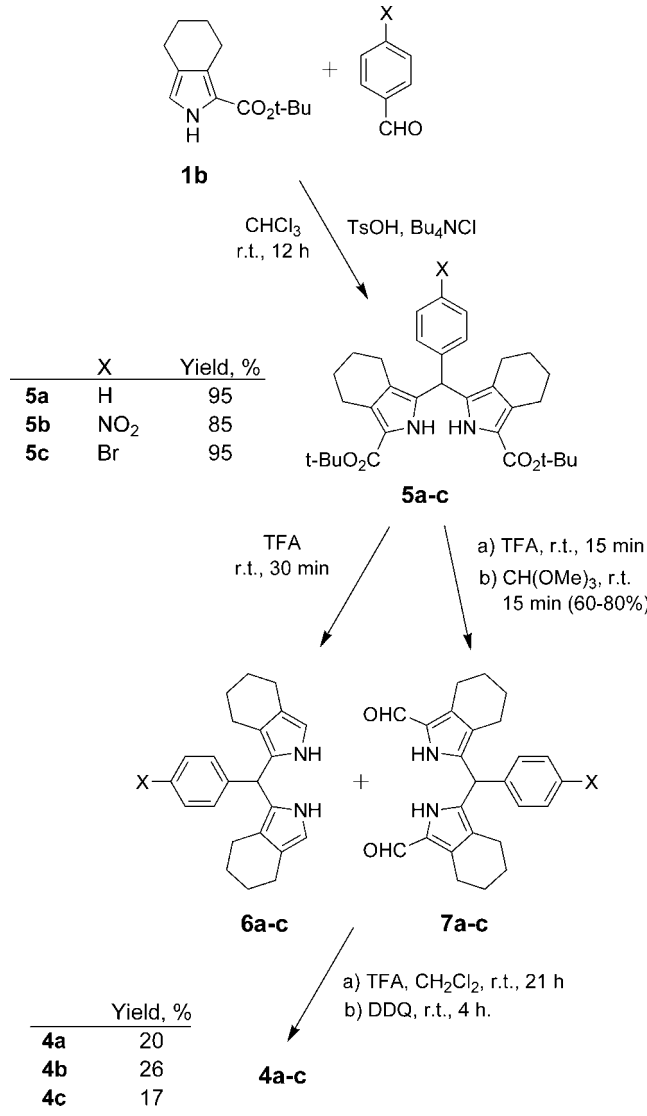
[a] Inseparable mixture of scrambling products.

Our goal was to establish the simplest, most versatile approach to $Ar_2TCHPs$ and, at the same time, allow alternative protection−deprotection schemes in the syntheses of intermediate pyrrole derivatives, permitting different types of sensitive peripheral functionalities.[36] Potentially, approach **A** could lead to scrambling since formation of the methylene bridges between pyrrole residues is reversible under acidic conditions.[37] Nevertheless, this route appeared more simple and straightforward, as it required only one dipyrromethane derivative.

In route **A**, *meso*-unsubstituted dipyrromethane **3** was synthesized in high yield using a published procedure[38] from readily available tetrahydroisoindole ester **1a**[39] and introduced into the condensation with aromatic aldehydes to afford $Ar_2TCHPs$ **4a−e** in good overall yields (Scheme 2).

MALDI-TOF MS analysis revealed that in the majority of cases scrambling was insignificant, and only small amounts of "defective" porphyrins (i.e., monoaryl- or *meso*-unsubstituted) could be detected in reaction mixtures. However, in the case of strongly electrophilic pentafluorobenzaldehyde, extensive scrambling occurred, yielding a mixture of porphyrins with one, two, or no *meso*-aryl groups. As a result, porphyrin **4e** could not be isolated in the pure form.

**SCHEME 3. Synthesis of $Ar_2TCHPs$ 4a−c from 5-Aryldipyrromethanes Following Route B from Scheme 1**




| | X | Yield, % |
|---|---|---|
| **5a** | H | 95 |
| **5b** | $NO_2$ | 85 |
| **5c** | Br | 95 |

| | Yield, % |
|---|---|
| **4a** | 20 |
| **4b** | 26 |
| **4c** | 17 |

The classical MacDonald's synthesis (pathway **B** in Scheme 1) requires two dipyrromethane derivatives: dialdehyde and diacid. The common precursors of both components are *tert*-butyl esters of 5-aryldipyrromethane-1,9-dicarboxylic acids **5a−c**, which were synthesized as shown in Scheme 3.

The yields of esters **5a−c** could be improved significantly in the presence of anhydrous tetrabutylammonium chloride. Condensation of pyrrole-2-carboxylates with aldehydes usually results in yields not exceeding 60−70%, which is likely to be caused by side reactions, promoted by strong acids in the presence of the liberated water. Addition of anhydrous $Bu_4NCl$, a highly hygroscopic compound, raised the yields of dipyrromethanes **5a−c** nearly up to quantitative, suggesting the salt effected water scavenging.[40] Notably, in the original MacDonald synthesis, water was sometimes removed by azeotropic distillation.[41]

Diesters **5a−c** were further converted into 1,9-unsubstituted dipyrromethanes **6a−c** or, alternatively, *ipso*-formylated to give 1,9-diformyldipyrromethanes **7a−c** for the following porphyrin

(34) (a) Baldwin, J. E.; Crossley, M. J.; Klose, T.; Orear, E. A.; Peters, M. K. *Tetrahedron* **1982**, *38*, 27–39. (b) Boyle, R. W.; Bruckner, C.; Posakony, J.; James, B. R.; Dolphin, D. *Org. Synth.* **1999**, *76*, 287–293. (c) Boitrel, B.; Lecas, A.; Renko, Z.; Rose, E. *New J. Chem.* **1989**, *13*, 73–99. (d) Boitrel, B.; Lecas, A.; Renko, Z.; Rose, E. *Chem. Commun.* **1985**, 1820–1821. (e) Lecas-Nawrocka, A.; Levisalles, J.; Mariacher, C.; Renko, Z.; Rose, E. *Can. J. Chem.* **1984**, *62*, 2054–2058. (f) Lecas-Nawrocka, A.; Levisalles, J.; Renko, Z.; Rose, E. *Tetrahedron Lett.* **1984**, *25*, 1563–1566.

(35) Hombrecher, H. K.; Horter, G.; Arp, C. *Tetrahedron* **1992**, *48*, 9451–9460.

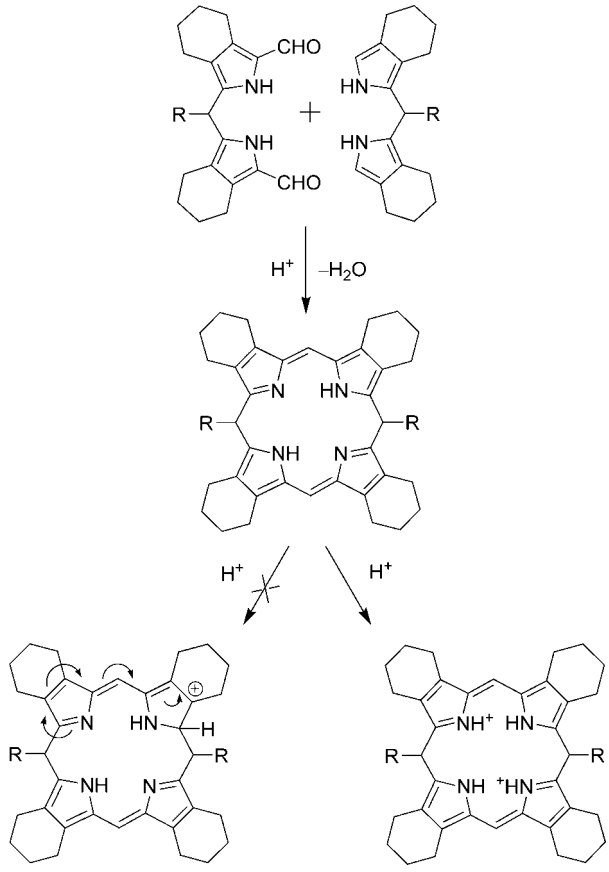
(36) Jolicoeur, B.; Chapman, E. E.; Thompson, A.; Lubell, W. D. *Tetrahedron* **2006**, *62*, 11531–11563.

(37) Scrambling has been extensively investigated for regular $A_2B_2$ porphyrins: (a) Wilson, G. S.; Anderson, H. L. *Synlett* **1996**, 1039–1040. (b) Littler, B. J.; Ciringh, Y.; Lindsey, J. S. *J. Org. Chem.* **1999**, *64*, 2864–2872.

(38) Novak, B. H.; Lash, T. D. *J. Org. Chem.* **1998**, *63*, 3998–4010.

(39) Tetrahydroisoindole derivatives could also be obtained via the modified Knorr chemistry, avoiding expensive malodorous isocyanides required in the Barton−Zard reaction: (a) Zavyalov, S. I.; Skoblik, T. I. *Bull. Acad. Sci. USSR Div. Chem. Sci.* **1977**, *26*, 2559–2562. (b) Hombrecher, H. K.; Horter, G. *Synthesis* **1990**, 389–391. The standard Knorr reaction also can be used: (c) May, D. A. *J. Org. Chem.* **1992**, *57*, 4820–4828.

**SCHEME 4. Protonation of Porphodimethenes Occurs Predominantly at Their Pyrrolenine Nitrogens (*ipso*-Protonation, Required for Scrambling, is Improbable)**




synthesis. Since the synthesis of **6a**−**c** and the Lindsey reaction[9] required practically the same conditions, **6a**−**c** could be used without isolation and purification. The acid-catalyzed ester cleavage/decarboxylation of **5a**−**c** was followed by the immediate addition of diformyldipyrromethanes **7a**−**c** and oxidation by DDQ to afford target porphyrins **4a**−**c** in good yields.

MALDI MS analysis of the crude reaction mixtures containing **4a**−**c** did not reveal any traces of scrambling. Notably, condensation of diformyldipyrromethane with dipyrromethane gives porphodimethene,[42] but not porphyrinogen—the key intermediate in the type **A** condensations (Scheme 1). Porphodimethenes are expected to be much more stable toward the acid-catalyzed cleavage. Unlike porphyrinogens, whose fission is initiated by protonation of their α-carbons, porphodimethenes contain more basic nitrogen atoms in the azafulvene rings (Scheme 4).[43] Besides, even if the *ipso*-protonation was to occur, it would result in an unfavorable σ-complex, destabilized by the pyrrolenine nitrogen on the conjugation path.

For comparison, we have implemented the standard MacDonald's protocol, for which dipyrromethanes **6** and **7** had to be isolated and purified. Overall, this method appeared to be less efficient, as it was more labor intensive and fraught with losses due to the poor stability of 1,9-unsubstituted dipyrromethanes.

**Aromatization of $Ar_2$TCHPs Using DDQ.** Conversion of tetracyclohexenoporphyrins into tetrabenzoporphyrins requires removal of 16 hydrogens by way of oxidative aromatization.[6] For this reaction, $Ar_4$TCHPs need to be first transformed into their metal complexes,[7a] whereas *meso*-unsubstituted TCHPs can be converted into TBPs with or without metalation.[10]

Our attempts to synthesize $Ar_2$TBPs by oxidizing metalated $Ar_2$TCHPs surprisingly turned out unsuccessful. First of all, the metalation itself appeared to be difficult because of the very poor solubility of **4a**−**c** free bases ($H_2Ar_2$TCHP). For example, prolonged refluxing of $H_2Ar_2$TCHPs with Zn or Cu salts in common solvents ($CHCl_3$, $CHCl_3$/MeOH, MeCN, or DMF) gave only traces of the corresponding metal complexes, while the attempts to insert Pd in either DMF or PhCN simply led to decomposition of the starting porphyrins. Using porphyrin dications ($H_4Ar_2TCHP^{2+}$), which are much more soluble than free bases, improved the metalation yields. In a typical procedure, a mixture containing the dication chloride (or trifluoroacetate) and, for example, Cu or Zn acetate was brought to reflux in $CHCl_3$/MeOH and treated with triethylamine ($Et_3N$). The free base, formed instantaneously upon the addition of $Et_3N$, was metalated prior to aggregation and precipitation. To insert Pd, a similar procedure in benzonitrile was adopted. Metalated $Ar_2$TCHPs ($MAr_2$TCHP: M-4, M = Zn, Ni, Cu, Pd) appeared to be much more soluble than the corresponding free bases, especially in $CHCl_3$ and $CH_2Cl_2$.

The second, more serious, problem was encountered during the aromatization step. The protocol developed for the synthesis of $MAr_4$TBPs,[7] that is, treatment of $MAr_2$TCHPs with DDQ in boiling solvents, failed to give $MAr_2$TBPs. Analysis of the reaction mixtures revealed that aromatization of $MAr_2$TCHPs occurred very slowly and never came to completion. $MAr_2$TCHPs remained largely unaffected even when DDQ was activated by Lewis acids (e.g., $Sc(OTf)_3$). Initially, we speculated that *meso*-unsubstituted porphyrins undergo oxidative oligomerization,[44] which could account for the disappearance of both DDQ and the starting metalloporphyrins. However, MALDI MS spectra showed no presence of dimers or trimers. Lower reactivity of $MAr_2$TCHPs compared to that of either $MAr_4$TCHPs or MTCHPs remains to be understood.

We further attempted to carry out aromatization of $Ar_2$TCHPs without premetalation[6a]—a strategy employed successfully in the synthesis of *meso*-unsubstituted TBPs.[10] Refluxing free bases **4** in toluene with DDQ indeed effected some oxidation, although complete conversions could not be achieved. Therefore, in terms of reactivity, $H_2Ar_2$TCHPs occupy an intermediate position between $H_2Ar_4$TCHPs, which are altogether inactive in aromatization,[7a] and *meso*-unsubstituted $H_2$TCHPs, which can be fully aromatized by DDQ.[10] Such trend in the reactivity could be a consequence of different basicities of the respective free bases;[45] that is, more basic $H_2Ar_4$TCHPs form dications easier

(40) $Bu_4NCl$ has been occasionally used in the porphyrin syntheses as a water scavenging agent: Zaidi, S. H. H.; Fico, R. M., Jr.; Lindsey, J. S. *Org. Process Res. Dev.* **2006**, *10*, 118–134.

(41) (a) Archibald, J. L.; Walker, D. M.; Shaw, K. B.; Markovac, A.; F., M. S. *Can. J. Chem.* **1966**, *44*, 345. (b) Senge, M. O.; Medforth, C. J.; Forsyth, T. P.; Lee, D. A.; Olmstead, M. M.; Jentzen, W.; Pandey, R. K.; Shelnutt, J. A.; Smith, K. M. *Inorg. Chem.* **1997**, *36*, 1149–1163.

(42) (a) Dolphin, D. *J. Heterocycl. Chem.* **1970**, *7*, 275. (b) Harmjanz, M.; Gill, H. S.; Scott, M. J. *J. Org. Chem.* **2001**, *66*, 5374–5383. (c) Bonomo, L.; Solari, E.; Scopelliti, R.; Latronico, M.; Floriani, C. *Chem. Commun.* **1999**, 2227–2228. (d) Botulinski, A.; Buchler, J. W.; Abbes, N. E.; Scheidt, W. R. *Justus Liebigs Ann. Chem.* **1987**, 305–309. (e) Senge, M. O.; Runge, S.; Speck, M.; Ruhlandt-Senge, K. *Tetrahedron* **2000**, *56*, 8927–8932.

(43) Wood, T. E.; Thompson, A. *Chem. Rev.* **2007**, *107*, 1831–1861, and references therein.

(44) Osuka, A.; Shimidzu, H. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 135–137.

(45) Finikova, O. S.; Cheprakov, A. V.; Carroll, P. J.; Dalosto, S.; Vinogradov, S. A. *Inorg. Chem.* **2002**, *41*, 6944–6946.

than $H_2TCHPs$, and dications are inactive in aromatization. Another possible reason for lower reactivity of $H_2Ar_2TCHPs$ is their poor solubility.

The yields of aromatization were greatly improved by using molten naphthalene as a solvent. We have found that molten naphthalene provides an excellent solubilizing medium for poorly soluble porphyrins. However, in this particular reaction, the role of naphthalene could not be fully explained by its solubilizing capacity. No other high-boiling solvent, such as di- or trichlorobenzenes, benzonitrile, nitrobenzole, or durene, was as effective as naphthalene, but at the same time, aromatization in mixtures containing small amounts of naphthalene was in some cases as effective as that in neat naphthalene.

The reaction of $H_2Ar_2TCHPs$ **4a**−**d** with DDQ in molten naphthalene at 180−190 °C resulted in the full conversion after about 10 h. Unfortunately, MALDI MS analysis revealed the presence of chlorinated $Ar_2TBPs$ as satellite products, and similar results were obtained when PhCN was used as a solvent for aromatization of Pd complexes (**Pd-4**). Preparative separation of $Ar_2TBPs$ from chlorinated $Ar_2TBPs$ is not feasible since introduction of the chlorine atom(s) into a large porphyrin molecule produces only negligible effect on its chromatographic mobility.

In summary, all attempts to use DDQ for aromatization of $Ar_2TCHPs$ failed to produce pure $Ar_2TBPs$. The reactions were either incomplete or suffered from inseparable byproduct.

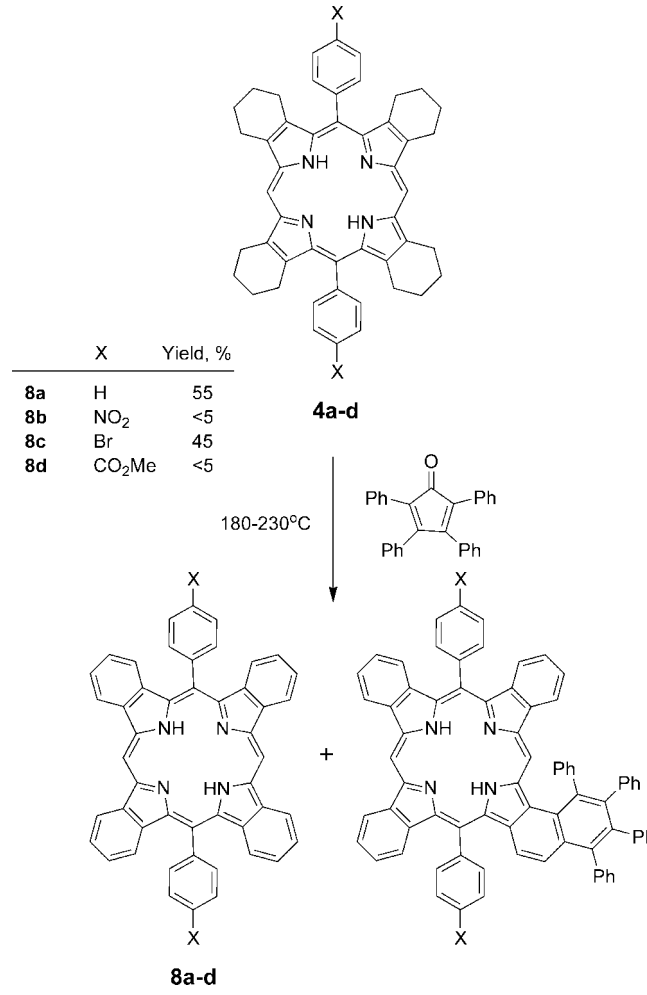
**Aromatization of $Ar_2TCHPs$ Using Tetracyclone.** Recently, we have found that 2,3,4,5-tetraphenylcyclopentadienone (tetracyclone) provides an effective alternative to DDQ in aromatization of porphyrins.[46] Tetracyclone is not a single electron-transfer agent, and therefore, it is incapable of inducing oxidative oligomerization. On the other hand, it does not contain chlorine atoms. Heating of porphyrins **4a**−**d** with tetracyclone in the absence of solvent at 180−230° (Scheme 5) led to their complete aromatization into $Ar_2TBPs$. MALDI MS analysis revealed only two products in the reaction mixtures (i.e., $Ar_2TBPs$ **8a**−**d**) and the Diels−Alder adducts of the intermediate porphyrins and tetracyclone, which were aromatized by way of CO extrusion.[47] The byproduct did not form in large quantities, and $Ar_2TBPs$ could be purified by chromatography.

Porphyrins **8a** (Ar = Ph) and **8c** (Ar = 4-$BrC_6H_4$) were obtained in moderate yields; however, yields of **8b** and **8d** were quite low. Even prolonged heating of the corresponding precursors with tetracyclone resulted in very low conversions. The reason for such dramatic difference in reactivity of $Ar_2TCHPs$ with different substituents in the *meso*-aryl rings remains unclear.

In conclusion, because of the problems arising at the stage of aromatization, tetrahydroisondole approach as a whole was not regarded as general, although in certain cases, it was a relatively straightforward and cost-effective way to $Ar_2TBPs$.

**II. Synthesis of $Ar_2TBPs$ via Dihydroisoindole Route.** Recently, we have demonstrated that problems associated with oxidative aromatization in the synthesis of tetrabenzoporphyrins can be effectively overcome by employing 4,7-dihydroisoindoles.[11] The latter compounds lead to precursor porphyrins with fewer hydrogen atoms in the pendant rings, facilitating aromatization. Earlier, we have shown that reduction in the number of hydrogens greatly improved the efficiency of aromatization in a similar synthesis of $Ar_4TNPs$.[8]

**SCHEME 5. Aromatization of $Ar_2TCHPs$ 4a−d by Tetracyclone**




| | X | Yield, % |
|---|---|---|
| **8a** | H | 55 |
| **8b** | $NO_2$ | <5 |
| **8c** | Br | 45 |
| **8d** | $CO_2Me$ | <5 |

4,7-Dihydroisoindoles are studied very scarcely, although the first representative of this class was synthesized over 60 years ago.[48] An early attempt to approach $\pi$-extended porphyrins via dihydroisoindole—the closest relative of thermodynamically unstable 2*H*-isoindole—was performed by Fuhrhop et al. in 1985[49] but was unsuccessful. 4,7-Dihydroisoindole was prepared using the classical Paal−Knorr chemistry (Scheme 6A) under conditions which probably harmed the electron-rich pyrrole ring. The apparent instability of 4,7-dihydroisoindole led researchers to conclude that it was not a useful intermediate in the porphyrin chemistry. It turned out that changing the conditions made it possible to isolate 4,7-dihydroisoindole, which proved to be an extremely practical synthon on the way to tetrabenzoporphyrins.

4,7-Dihydroisoindole is accessible in three major steps from readily available tosylacetylene (Scheme 6B).[11] A modified variant of the Barton−Zard reaction[50] (Scheme 6B) allows synthesis of 2-alkoxycarbonyl derivatives of 4,7-dihydroisoindole, which are perfectly stable and, in fact, do not differ much

(46) Presented in part at ICPP-4 (2006), Rome, Italy: Filatov, M. A.; Cheprakov, A. V. *J. Porphyrins Phthalocyanines* **2006**, *10*, 629.

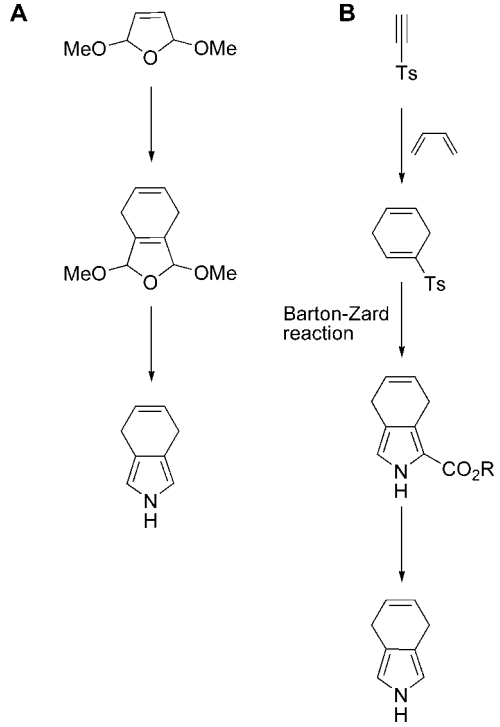
(47) Ogliaruso, M. A.; Romanell, M. G.; Becker, E. I. *Chem. Rev.* **1965**, *65*, 261–367.

(48) Schenck, G. O. *Chem. Ber.* **1947**, *80*, 226–231.

(49) Fuhrhop, J. H.; Hosseinpour, D. *Justus Liebigs Ann. Chem.* **1985**, 689–695.

(50) (a) Barton, D.; Zard, S. *Chem. Commun.* **1985**, 1098–1100. (b) Barton, D.; Kervagoret, J.; Zard, S. *Tetrahedron* **1990**, *46*, 7587–7598. (c) Abel, Y.; Haake, E.; Haake, G.; Schmidt, W.; Struve, D.; Walter, A.; Montforts, F. P. *Helv. Chim. Acta* **1998**, *81*, 1978–1996.

**SCHEME 6. Approaches to 4,7-Dihydroisoindole**




in their chemical behavior from well-known and much studied $\beta$-disubstituted 2-alkoxycarbonylpyrroles. Removal of the alkoxycarbonyl group can be accomplished either under acidic (trifluoroacetic acid in $CH_2Cl_2$) or basic (reflux with KOH in ethylene glycol) conditions. In either case, the double bond remains intact.

Similarity in the behavior of 4,7-dihydroisoindole and tetrahydroisoindole enabled us to directly apply methods developed for the tetrahydroisondole pathway to the syntheses originating in 4,7-dihydroisoindole. Both routes shown in Scheme 1 (**A** and **B**) were realized in this pathway, leading to precursor 5,15-diaryloctahydrotetrabenzoporphyrins ($Ar_2$OHTBPs).

Route **B** (Scheme 7) almost entirely matched its tetrahydroisoindole analogue (see Scheme 3).

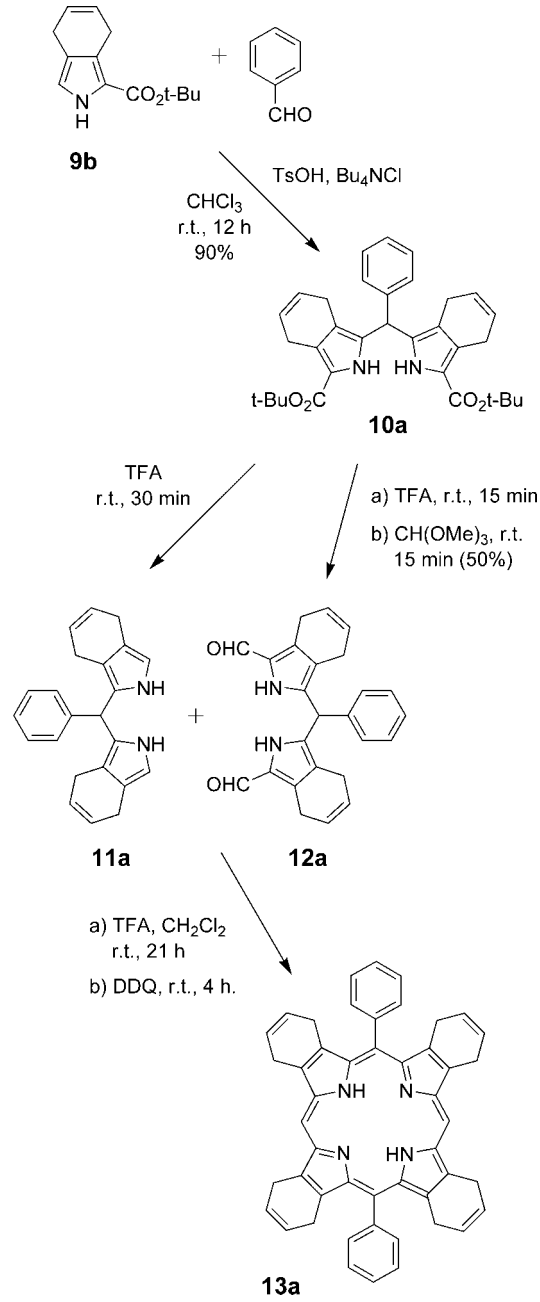
Similar to the synthesis depicted in Scheme 3, addition of $Bu_4NCl$ improved the yield of dipyrromethane **10a**. In this case, water scavenging was especially beneficial, as in the absence of $Bu_4NCl$, tarring occurred, and **10a** could be isolated only in a modest yield. Apparently, in the presence of water, the double bond of the cyclohexadiene ring interferes with acid-catalyzed condensations.

The formylation reaction, leading to dipyrromethane **12a**, gave a somewhat lower yield than the similar reaction in the synthesis of $Ar_2$TCHPs (Scheme 3). This also could be caused by side reactions, affecting the isolated double bonds in the presence of the strong electrophilic reagent.

In general, route **A** (Scheme 1) when applied to the dihydroisoindole pathway appeared to be more reliable than route **B**, and therefore, it was developed into a general preparative protocol (Scheme 8).

*meso*-Unsubstituted dipyrromethane **15** was obtained in a good yield from 2-ethoxycarbonyl-4,7-dihydroisoindole **9a**. Remarkably, the double bond tolerated harsh conditions of the ester cleavage and decarboxylation. Dipyrromethane **15** was introduced into the condensation with aromatic aldehydes under Lindsey conditions to yield the respective $Ar_2$OHTBPs **13a**−**e**.

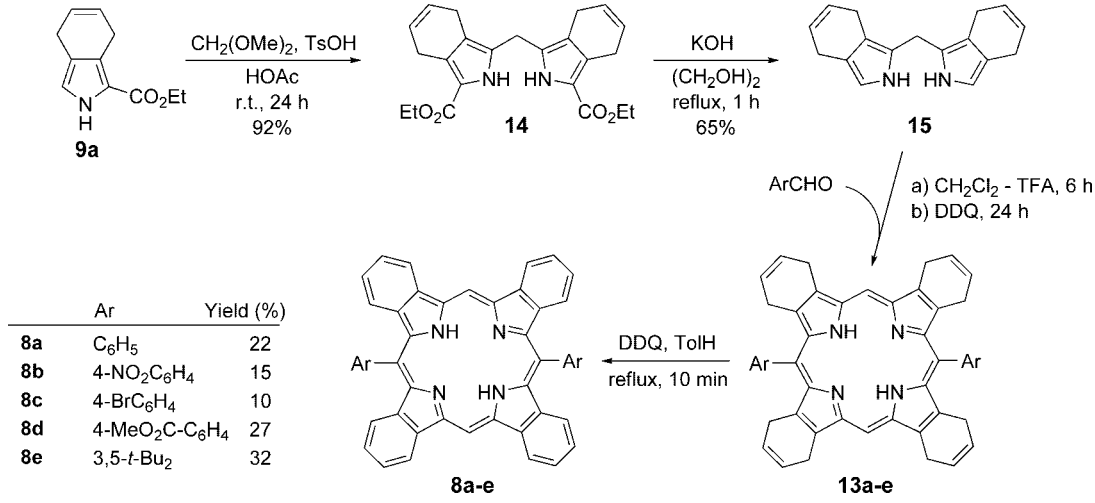
**SCHEME 7. Synthesis of 5,15-Diphenyloctahydrotetrabenzoporphyrin**




These porphyrins were identified in the reaction mixtures by MALDI MS analysis, although they were not isolated and/or characterized. The MALDI spectra revealed only an insignificant degree of scrambling, that is, porphyrins with different numbers of aryl groups. The aromatization was effected directly by changing the solvent to higher-boiling toluene, followed by a short heating with an extra portion of DDQ. Like in the synthesis of $Ar_4$TNPs,[8] no metalation was required for aromatization.

Interestingly, in spite of the overall facile reaction, electron-withdrawing groups in *meso*-aryls, especially the nitro group, decreased the rate of aromatization. Porphyrins **13a** and **13d** were oxidized almost instantaneously upon bringing their solutions with DDQ to reflux, porphyrin **13c** had to be refluxed for 30 min, but 4-nitrophenyl-substituted porphyrin **13b** could not be completely aromatized even after prolonged heating. For quantitative aromatization, **13b** had to be treated with DDQ in

**SCHEME 8. Synthesis of Ar2TBPs via Dihydroisoindole Pathway (Route A from Scheme 1)**




| | Ar | Yield (%) |
|---|---|---|
| **8a** | $C_6H_5$ | 22 |
| **8b** | 4-$NO_2C_6H_4$ | 15 |
| **8c** | 4-$BrC_6H_4$ | 10 |
| **8d** | 4-$MeO_2C$-$C_6H_4$ | 27 |
| **8e** | 3,5-*t*-$Bu_2$ | 32 |

benzonitrile. It is possible that this effect is associated with solubility rather than with electronic factors. In general, contrary to the tetrahydroisoindole pathway, aromatization of the precursors was smooth and no traces of chlorination byproduct were observed.

Overall, the dihydroisoindole pathway is by far the method of choice for the synthesis of $Ar_2$TBPs, permitting introduction of various functionalities and giving pure target compounds in good yields.

**III. Optical Properties of $Ar_2$TBPs.** In this section, we only briefly outline the optical properties of $Ar_2$TBPs, leaving the detailed discussion for a separate account.

The optical absorption and fluorescence spectra of porphyrin **8a** are shown in Figure 1A. The optical absorption spectra of free base **8a** (A) are strikingly similar to those of *meso*-unsubstituted $H_2$TBPs,[14] showing a well-resolved vibronic structure in the Q-band region and a significant (750 $cm^{-1}$) splitting of the B (Soret) band. This feature is typically attributed to a strong mixing of the Q and B states and to an increase in the oscillator strengths of the Q-bands in TBPs compared to regular nonextended porphyrins.[14a,51] The fluorescence of **8a** exhibits a sharp band ($\lambda_{max}$ = 670 nm), characterized by a very small Stokes shift (only 2 nm) and a very high for porphyrins quantum yield ($\varphi_{fl}$ = 0.38), pointing toward rigid planar structure, similar to that of *meso*-unsubstituted $H_2$TBP.[15]

The Pd complex of **8a**, prepared by refluxing the free base with $PdCl_2$ in benzonitrile, exhibits spectral properties (Figure 1B) close to those of *meso*-unsubstituted PdTBPs.[2a,10,16b,52] An unusual feature of **Pd-8a** is the slight splitting of the Q-band ($\lambda_{max}$ = 615 nm) and a shoulder of the main band in the phosphorescence spectrum ($\lambda_{max}$ = 796 nm). The latter property is unique for **Pd-8a** and probably for other $PdAr_2$TBPs since *meso*-unsubstituted PdTBPs and Pd *meso*-tetraaryl-TBPs exhibit quite symmetrical phosphorescent bands, accompanied by small vibrational satellites. The phosphorescence lifetime of **Pd-8a**, measured in Ar-purged dimethylacetamide solution, was found to be 490 $\mu$s, and on air, the phosphorescence was completely quenched. The phosphorescence quantum yield in the absence of oxygen was 0.19, which is quite high compared to the other Pd tetrabenzoporphyrins.[7,10] These characteristics suggest suitability of $PdAr_2$TBPs for oxygen sensing and imaging[2] as well as for PDT.[4]

Conjugated porphyrin-based molecules are currently under intensive scrutiny as nonlinear optical materials.[19a,53] Tetrabenzoporphyrins in particular have been investigated as potential two-photon probes for biomedical imaging.[2g] We have determined that, upon irradiation with 110 fs pulses from a Ti:sapphire laser (76 MHz rep. rate), solutions of **8a** exhibit strong fluorescence, whose intensity was proportional to the square of the excitation flux, confirming that the two-photon absorption was the main process underlying the emission from the singlet excited state (Figure 2).

The two-photon absorption cross-section ($\sigma_2$) of **8a**, determined by the relative fluorescence method versus Rhodamine B in methanol ($\sigma_2$ = 210 GM,[54] $\lambda_{ex}$ = 840 nm, $\varphi_{fl}$ = 0.5[55]), was found to be 28 GM (1 GM = $10^{-50}$ $cm^4$ s $photon^{-1}$), which is several times higher than the values reported for regular nonextended porphyrins.[56] This value is consistent with other measurements performed on tetrabenzoporphyrins,[57] confirming that $\pi$-extension has a profound effect on nonlinear absorption of tetrapyrroles.

In conclusion, $Ar_2$TBPs possess an array of useful optical properties. They combine strong emissivity of the planar TBP system and enhanced two-photon absorption cross-sections with the possibility of derivatization via functional substituents in the *meso*-aryl rings. These characteristics suggest a wide array of utilities, including biomedical imaging, sensing, and nonlinear optical applications. The developed method of synthesis provides a general route to $Ar_2$TBPs with various substituents, facilitating engagement of these molecules into applied research.

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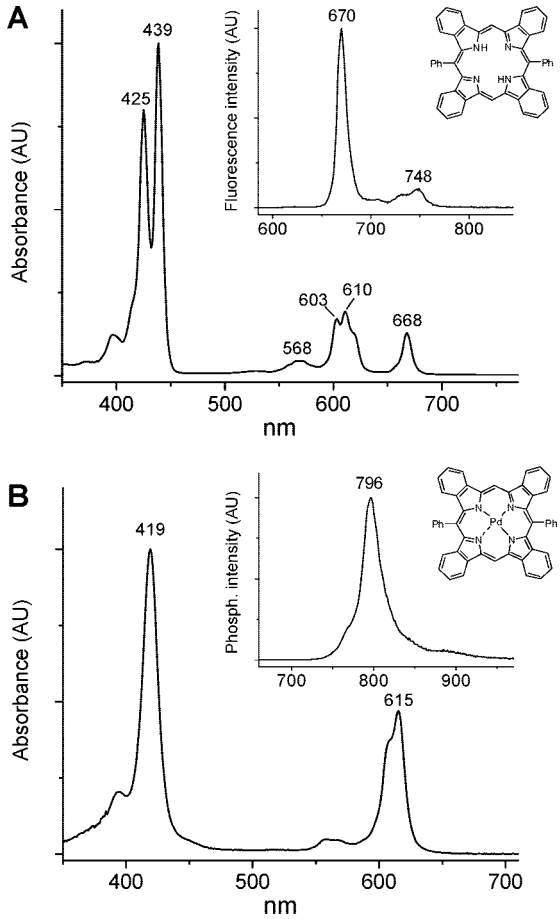


**FIGURE 1.** Absorption and emission (insets) spectra of **8a** (A) in toluene and of **Pd-8a** (B) in Ar-purged dimethylacetamide at 23 °C. A (inset): fluorescence, $\lambda_{ex} = 571$ nm, $\varphi_{fluo} = 0.38$. B (inset): phosphorescence, $\lambda_{ex} = 610$ nm, $\varphi_{phos} = 0.19$.

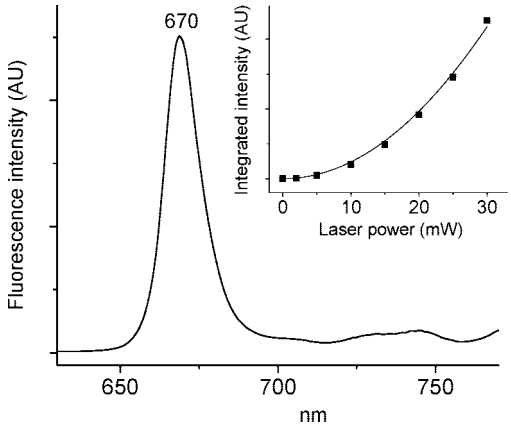


**FIGURE 2.** Fluorescence of **8a** induced by two-photon absorption at 840 nm (110 fs, 76 MHz rep. rate) and its dependence on the incident laser power (inset). The data points (integrated fluorescence intensity ($I$) versus excitation power ($P$)) were fitted to a quadratic function $I(P) = aP^2$ (solid line).

## Experimental Part

For general description of methods, see Supporting Information. Tetrahydroisoindole esters **1a** and **1b**[39] and dihydroisoindole **9b**[11] were synthesized as described previously.

**Bis(3-ethoxycarbonyl-4,5,6,7-tetrahydro-2*H*-isoindolyl)methane (2).** A mixture of 2-ethoxycarbonyl-4,5,6,7-tetrahydro-2*H*-isoindole **1a** (1.93 g, 10 mmol), dimethoxymethane (0.38 g, 5 mmol), and *p*-toluenesulfonic acid (0.095 g, 0.5 mmol) was dissolved in acetic acid (50 mL). The mixture was stirred at room temperature for 24 h and poured into cold water (200 mL). The precipitate formed, and it was collected by filtration, dried in vacuum over $P_2O_5$, and recrystallized from ethanol: yield 1.79 g (90%), white powder, mp 210−211 °C; $^1$H NMR ($CDCl_3$-$d_6$-DMSO) $\delta$ 10.86 (br s, 2H), 4.15 (q, $J = 7.11$ Hz, 4H), 3.60 (s, 2H), 2.62 (m, 4H), 2.38 (m, 4H), 1.60 (m, 8H), 1.23 (t, $J = 7.11$ Hz, 6H); $^{13}$C NMR ($CDCl_3$-$d_6$-DMSO) $\delta$ 161.2, 129.7, 127.5, 117.3, 115.7, 58.7, 22.9, 22.8, 22.8, 21.2, 20.9, 14.2. Anal. Calcd for $C_{23}H_{30}N_2O_4$ (398.49): C, 69.32; H, 7.59; N, 7.03. Found: C, 69.40; H, 7.50; N, 7.31.

**Bis(4,5,6,7-tetrahydro-2*H*-isoindolyl)methane (3) and Bis(4,7-dihydro-2*H*-isoindolyl)methane (15).** A mixture of the corresponding dipyrromethane **2** or **14** (3 mmol), KOH (18 mmol, 1.00 g) and ethylene glycol (30 mL) was refluxed under argon for 1 h. The mixture was cooled to room temperature, diluted with $CH_2Cl_2$ (50 mL), and washed with water (5 × 100 mL) and saturated brine (20 mL). The mixture was concentrated by evaporation in vacuum, passed through a short silica gel column (5 cm, eluent: $CH_2Cl_2$), and evaporated in vacuum to dryness. The obtained dipyrromethane was either immediately used in the porphyrin synthesis without further purification or stored at −18 °C.

**Ar$_2$TCHPs (4a−d) via Route A (Scheme 2).** Dipyrromethane **3** (1 mmol, 0.25 g) and aromatic aldehyde (1 mmol) were dissolved in $CH_2Cl_2$ (60 mL) and freshly distilled over $CaH_2$. The mixture was stirred for 10 min under Ar, and trifluoroacetic acid (TFA) (0.135 mmol, 0.015 g) was added and the mixture stirred for 6 h. A solution of DDQ (1.5 mmol, 0.34 g) in toluene (20 mL) was added, and the mixture was stirred for an additional 2 h, evaporated in vacuum, and chromatographed on silica gel (eluent: $CH_2Cl_2$/$Et_3N$, 100:1 v/v). Fractions containing the desired porphyrins (selected by UV−vis spectroscopy) were combined, evaporated in vacuum to dryness, treated with TFA (0.02 mL), dried in vacuum, and precipitated from $CH_2Cl_2$ solution as free bases upon addition of diethyl ether.

**4a**: Yield 0.16 g (48%), dark red crystalline powder, mp >300 °C; UV/vis ($CH_2Cl_2$/TFA) $\lambda_{max}$ (log $\epsilon$) 426 (5.62), 566 (4.28), 610 (3.93); $^1$H NMR ($CDCl_3$/TFA) $\delta$ 10.12 (s, 2H), 8.22 (m, 4H), 7.88 (m, 6H), 3.78 (m, 8H), 2.66 (m, 8H), 2.31 (m, 8H), 1.73 (m, 8H), −2.14 (br s, 4H); $^{13}$C NMR ($CDCl_3$/TFA) $\delta$ 142.6, 140.6, 139.1, 138.5, 138.2, 134.9, 130.0, 128.7, 119.3, 96.7, 25.2, 23.6, 22.9, 22.1; ESI HRMS $m/z$ 679.3823; calcd for $C_{48}H_{47}N_4$ ($MH^+$) 679.3801.

**4b**: Yield 0.049 g (13%), dark red crystalline powder, mp >300 °C; UV/vis ($CH_2Cl_2$/TFA) $\lambda_{max}$ (log $\epsilon$) 432 (5.47), 568 (4.28), 614 (3.91); $^1$H NMR ($CDCl_3$/TFA) $\delta$ 10.18 (s, 2H), 8.77 (m, 4H), 8.49 (m, 4H), 3.79 (m, 8H), 2.63 (m, 8H), 2.33 (m, 8H), 1.76 (m, 8H), −1.94 (br s, 4H); $^{13}$C NMR ($CDCl_3$/TFA) $\delta$ 148.9, 143.6, 141.4, 139.8, 137.7, 135.8, 123.7, 116.5, 97.7, 25.7, 23.6, 22.8, 21.9; MALDI-TOF MS $m/z$ 768.96; calcd for $C_{48}H_{45}N_6O_4$ ($MH^+$) 769.35.

**4c**: Yield 0.11 g (27%), dark red crystalline powder, mp >300 °C; UV/vis ($CH_2Cl_2$/TFA) $\lambda_{max}$ (log $\epsilon$) 428 (5.61), 562 (4.26), 612 (3.83); $^1$H NMR ($CDCl_3$/TFA) $\delta$ 10.14 (s, 2H), 8.12 (m, 4H), 8.05 (m, 4H), 3.78 (m, 8H), 2.70 (m, 8H), 2.33 (m, 8H), 1.77 (m, 8H), −2.24 (br s, 4H); $^{13}$C NMR ($CDCl_3$/TFA) $\delta$ 142.3, 140.9, 139.3, 138.1, 137.0, 136.3, 132.1, 125.3, 117.7, 97.0, 25.5, 23.6, 22.9, 22.0; MALDI-TOF MS $m/z$ 836.77; calcd for $C_{48}H_{45}Br_2N_4$ ($MH^+$) 837.20.

**4d**: Yield 0.24 g (60%), dark red crystalline powder, mp >300 °C; UV/vis ($CH_2Cl_2$/TFA) $\lambda_{max}$ (log $\epsilon$) 428 (5.59), 568 (4.23), 612 (3.82); $^1$H NMR ($CDCl_3$/TFA) $\delta$ 10.18 (s, 2H), 8.58 (m, 2H), 8.35 (m, 2H), 4.15 (s, 3H), 3.79 (m, 8H), 2.65 (m, 8H), 2.32 (m, 8H), 1.74 (m, 8H), −2.37 (br s, 4H); $^{13}$C NMR ($CDCl_3$-TFA) $\delta$ 167.1, 142.0, 141.7, 140.9, 139.6, 138.3, 135.0, 131.3, 129.8, 118.0, 97.2, 52.8, 25.4, 23.5, 22.8, 21.9; ESI HRMS $m/z$ 795.3878; calcd for $C_{52}H_{51}N_4O_4$ ($MH^+$) 795.3905; MALDI-TOF MS $m/z$ 795.33; calcd for $C_{52}H_{51}N_4O_4$ ($MH^+$) 795.39.

**Arylbis(3-*tert*-butoxycarbonyl-4,5,6,7-tetrahydro-2*H*-isoindolyl)-methanes (5a−c).** *p*-Toluenesulfonic acid (0.25 mmol, 0.048 g) and *n*-tetrabutylammonium chloride (0.1 mmol, 0.028 g) were added to a solution of 2-*tert*-butoxycarbonyl-4,5,6,7-tetrahydro-2*H*-isoindole **1b** (5 mmol, 1.105 g) and the corresponding aldehyde (2.5 mmol) in $CHCl_3$ (50 mL). The reaction mixture was stirred at room temperature under argon for 12 h, washed by $NaHCO_3$ (10% aqueous solution, 20 mL) and saturated brine (20 mL), and dried over $Na_2SO_4$. The solution was evaporated to dryness, and the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate, 5:1). The fractions containing the target dipyrromethane were identified by TLC (silica gel plates, eluent: petroleum ether/ethyl acetate, 5:1). Upon heating to 150 °C the spots with $R_f$ 0.85−0.9 turned red. These fractions were combined and evaporated to dryness.

**5a**: Yield 1.26 g (95%), orange amorphous solid; $^1$H NMR ($CDCl_3$) $\delta$ 8.27 (br s, 2H), 7.36−7.26 (m, 3H), 7.12 (m, 2H), 5.39 (s, 1H), 2.78 (m, 4H), 2.17 (m, 4H), 1.69 (m, 8H), 1.54 (s, 18H); $^{13}$C NMR ($CDCl_3$) $\delta$ 161.2, 138.8, 129.9, 129.0, 128.2, 127.4, 119.4, 117.8, 80.1, 41. 4, 28.5, 23.3, 23.2, 23.1, 21.2. Anal. Calcd for $C_{33}H_{42}N_2O_4$ (530.70): C, 74.69; H, 7.98; N, 5.28. Found: C, 74.93; H, 8.16; N, 4.94.

**5b**: Yield 1.22 g (85%), yellow amorphous solid; $^1$H NMR ($CDCl_3$) $\delta$ 8.52 (br s, 2H), 8.09 (m, 2H), 7.22 (m, 2H), 5.47 (s, 1H), 2.74 (m, 4H), 2.13 (m, 4H), 1.65 (m, 8H), 1.50 (s, 18H); $^{13}$C NMR ($CDCl_3$) $\delta$ 161.2, 147.1, 146.7, 129.2, 128.3, 128.1, 124.1, 119.9, 118.7, 80.6, 40.9, 28.5, 23.3, 23.1, 21.4. Anal. Calcd for $C_{33}H_{41}N_3O_6$ (575.70): C, 68.85; H, 7.18; N, 7.30. Found: C, 68.41; H, 7.47; N, 7.02.

**5c**: Yield 1.44 g (95%), orange amorphous solid; $^1$H NMR ($CDCl_3$) $\delta$ 8.30 (s, 2H), 7.41 (m, 2H), 6.95 (m, 2H), 5.32 (s, 1H), 2.74 (m, 4H), 2.13 (m, 4H), 1.66 (m, 8H), 1.51 (s, 18H); $^{13}$C NMR ($CDCl_3$) $\delta$ 161.2, 138.0, 132.1, 130.0, 129.2, 128.2, 121.3, 119.5, 118.1, 80.2, 40.5, 28.5, 23.3, 23.1, 23.1, 21.3. Anal. Calcd for $C_{33}H_{41}BrN_2O_4$ (609.59): C, 65.02; H, 6.78; Br, 13.11; N, 4.60. Found: C, 65.42; H, 6.77; N, 4.21.

**Arylbis(3-formyl-4,5,6,7-tetrahydro-2*H*-isoindolyl)methanes (7a−c).** Dipyrromethanes **5a−c** (2 mmol) were dissolved in TFA (20 mL) under argon. The solution was stirred for 5 min and cooled to 0 °C on an ice bath. Trimethoxymethane (20 mmol, 2.1 g) was added dropwise to the mixture. The mixture was stirred for 15 min at room temperature, diluted with $CH_2Cl_2$ (50 mL), washed with saturated aqueous $NaHCO_3$ (2 × 20 mL) and saturated brine (20 mL), and dried over $Na_2SO_4$. The resulting solution was evaporated to dryness, and the remaining solid was chromatographed on silica gel (eluent: $CH_2Cl_2$/MeOH). Compounds **7a−c** could not be recrystallized due to their rather poor solubility, and therefore, they did not give satisfactory elemental analyses.

**7a**: Yield 0.46 g (60%), gray powder, mp >300 °C; $^1$H NMR ($CDCl_3$) $\delta$ 9.85 (br s, 2H), 9.35 (s, 2H), 7.30 (m, 3H), 7.11 (m, 2H), 5.50 (s, 1H), 2.83 (m, 4H), 2.30 (m, 4H), 1.77 (m, 8H); $^{13}$C NMR ($CDCl_3$) $\delta$ 176.2, 138.1, 129.0, 128.6, 128.2, 127.5, 127.5, 120.9, 40.4, 23.1, 22.7, 21.0, 20.9.

**7b**: Yield 0.69 g (80%), gray powder, mp >300 °C; $^1$H NMR ($CDCl_3$-$d_6$-DMSO) $\delta$ 11.31 (s, 2H), 9.38 (s, 2H), 8.02 (m, 2H), 7.16 (m, 2H), 5.50 (s, 1H), 2.74 (m, 4H), 2.41 (m, 4H), 1.70 (m, 8H); $^{13}$C NMR ($d_6$-DMSO) $\delta$ 176.8, 147.3, 146.4, 133.7, 129.4, 127.7, 123.6, 120.3, 30.3, 22.8, 22.3, 20.5.

**7c**: Yield 0.56 g (60%), gray powder, mp >300 °C; $^1$H NMR ($d_6$-DMSO) $\delta$ 11.39 (br s, 2H), 9.43 (s, 2H), 7.51 (m, 2H), 6.99 (m, 2H), 5.56 (s, 1H), 2.75 (m, 4H), 2.40−2.18 (m, 4H), 1.64 (m, 8H); satisfactory $^{13}$C NMR spectrum could not be obtained because of the very low solubility.

**Ar$_2$TCHPs (4a−d) via Route B (Scheme 3).** Aryldipyrromethanes **5a−c** (1 mmol) were dissolved in TFA (20 mL) under argon. The solution was stirred for 5 min, diluted with $CH_2Cl_2$ (50 mL), and added to a solution of the respective diformyldipyrromethane **7a−c** in $CH_2Cl_2$ (45 mL). The resulting mixture was stirred at room temperature for 4 h, treated with DDQ (1.5 mmol, 0.34 g), and stirred for an additional 2 h. The workup and the isolation of the target compounds were performed as in route **A**. Yields: **4a** 0.07 g (20%), **4b** 0.10 g (26%), **4c** 0.07 g (17%).

**Metal Complexes of Porphyrins 4a−c.** Porphyrins **4a−c** (0.1 mmol) were dissolved in TFA (0.2 mL), and the solution was evaporated to dryness. The remaining solid was dissolved in $CH_2Cl_2$ (50 mL), and a solution of Cu or Zn acetate in MeOH (5 mL) was added. The mixture was stirred for 5 min, and $Et_3N$ (0.05 mL) was added in one portion by a pipet. The mixture was stirred for an additional 5 min, transferred to a separatory funnel, washed with water (20 mL) and brine (20 mL), and dried over $Na_2SO_4$. The solution was concentrated in vacuum to about 10 mL, and the resulting metal complex was precipitated by ether. The crystalline solid was filtered off, washed with ether, and dried. The purity of the metal complex was assessed by MALDI MS analysis and UV−vis spectroscopy.

**Aromatization of Porphyrins 4a and 4c by 2,3,4,5-Tetraphenylcyclopentadienone (Tetracyclone) (Scheme 5).** A mixture of the porphyrin (**4a** or **4c**) (0.1 mmol) and tetracyclone (2.6 mmol, 1 g) was placed into a high-pressure glass tube, which was purged with Ar and closed with a PTFE screw cap. The mixture was heated to at 230 °C and kept under stirring for 3 h. After cooling to the room temperature, the mixture was dissolved in $CH_2Cl_2$ and chromatographed on silica gel (eluent: $CH_2Cl_2$). Further purification of porphyrins **8a** and **8c** was achieved by recrystallization from $CH_2Cl_2$/ether. Yields: **8a** 0.036 g (55%), **8c** 0.037 g (45%). See the analytical data for porphyrins **8a** and **8c** below.

**2-Ethoxycarbonyl-4,7-dihydro-2*H*-isoindole (9a). 9a** was obtained by the method used previously for the synthesis of *tert*-butyl ester **9b**:[11] yield 73%, white powder, mp 87−88 °C; $^1$H NMR ($CDCl_3$) $\delta$ 8.97 (br s, 1H), 6.70 (m, 1H), 5.87 (m, 2H), 4.30 (q, $J$ = 7.12 Hz, 2H), 3.43 (m, 2H), 3.22 (m, 2H), 1.35 (t, $J$ = 7.12 Hz, 3H); $^{13}$C NMR ($CDCl_3$) $\delta$ 161.6, 124.9, 124.4, 123.8, 118.9, 117.5, 59.8, 24.0, 22.3, 14.5. Anal. Calcd for $C_{11}H_{13}NO_2$ (191.23): C, 69.09; H, 6.85; N, 7.32. Found: C, 68.77; H, 7.00; N, 7.03.

**Bis(3-ethoxycarbonyl-4,7-dihydro-2*H*-isoindolyl)methane (14).** Compound **14** was obtained from **9a** by the same procedure as used in the synthesis of dipyrromethane **2**: yield 1.81 g (92%), white powder, mp 269−270 °C; $^1$H NMR ($CDCl_3$-$d_6$-DMSO) $\delta$ 11.21 (br s, 2H), 5.76 (m, 4H), 4.18 (q, $J$ = 7.08 Hz, 4H), 3.71 (s, 2H), 3.25 (m, 4H, overlapped with solvent), 3.00 (m, 4H), 1.26 (t, $J$ = 7.08 Hz, 4H); $^{13}$C NMR ($CDCl_3$-$d_6$-DMSO) $\delta$ 160.7, 129.3, 124.0, 123.9, 123.1, 115.3, 114.2, 58.6, 23.8, 21.6, 21.4, 14.2. Anal. Calcd for $C_{23}H_{26}N_2O_4$ (394.46): C, 70.03; H, 6.64; N, 7.10. Found: C, 69.88; H, 6.34; N, 6.85.

**Ar$_2$TBPs 8a−d via Dihydroisoindole Pathway (Scheme 8).** Freshly prepared dipyrromethane **15** (1 mmol, 0.25 g) was dissolved in $CH_2Cl_2$ (60 mL), distilled over $CaH_2$, and the aromatic aldehyde (1 mmol) was added to this solution. The mixture was stirred under Ar at room temperature for 10 min and treated with TFA (0.135 mmol, 0.015 g). The reaction mixture was stirred at room temperature for 4 h, treated with DDQ (1.5 mmol, 0.34 g) in toluene (20 mL), and stirred for an additional 2 h. The solution was evaporated to dryness, and the residue was dissolved in either toluene (30 mL, **8a**,**c**,**d**) or in benzonitrile (30 mL, **8b**). DDQ (2 mmol, 0.45 g) was added, and the mixture was refluxed for 5−30 min under Ar. The reaction was monitored by UV−vis spectroscopy. The solvent was removed in vacuum, and the residue was purified by chromatography on silica gel (eluent: $CH_2Cl_2$). Emerald green fractions were collected, combined, and evaporated to dryness. The residue was treated with TFA (0.01 mL) and dried in vacuum. The porphyrins were additionally purified by reprecipitation from $CH_2Cl_2$ solutions by ether. Porphyrins **8a−e** were isolated as free bases.

**8a**: Yield 0.073 g (22%), the material was characterized in ref 11.

**8b**: Yield 0.056 g (15%), green powder, mp >300 °C; UV/vis ($CH_2Cl_2$/TFA) $\lambda_{max}$ (log $\epsilon$) ($CH_2Cl_2$) as free base 394 (4.92), 420 (5.70), 436 (5.62), 570 (4.64), 612 (4.99), 666 (4.75); $^1$H NMR

($CDCl_3$/TFA) $\delta$ 11.01 (s, 2H), 9.36 (d, $J$ = 7.96 Hz, 4H), 8.32 (m, 4H), 8.24 (m, 4H), 8.20 (m, 4H), 7.94 (m, 4H), 7.69 (d, $J$ = 8.34 Hz, 4H), −0.35 (br s, 4H); $^{13}$C NMR ($CDCl_3$/TFA) $\delta$ 139.9, 139.0, 137.3, 136.0, 133.4, 132.9, 131.9, 130.8, 130.6, 125.9, 125.2, 123.6, 114.9, 92.4; LDI-TOF MS *m*/*z* 752.17; calcd for $C_{48}H_{28}N_6O_4$ ($M^+$) 752.22. Anal. Calcd for $C_{48}H_{28}N_6O_4 \cdot 0.33Et_2O$: C, 76.21; H, 4.06; N, 10.81. Found: C, 76.07; H, 4.20; N, 10.73.

**8c**: Yield 0.041 g (10%), green powder, mp >300 °C; UV/vis ($CH_2Cl_2$/TFA) $\lambda_{max}$ (log $\epsilon$) as dication 454 (5.67), 616 (4.30), 672 (4.84), as free base 394 (4.78), 422 (5.64), 436 (5.71), 570 (4.35), 610 (4.88), 666 (4.59); $^1$H NMR ($CH_2Cl_2$/TFA) $\delta$ 11.00 (s, 2H), 9.36 (d, $J$ = 7.96 Hz, 4H), 8.36 (m, 4H), 8.22 (m, 8H), 7.93 (m, 4H), 7.70 (d, $J$ = 8.21 Hz, 4H), 0.02 (br s, 4H); $^{13}$C NMR ($CDCl_3$/TFA) $\delta$ 139.9, 139.0, 137.4, 136.0, 133.3, 132.9, 131.9, 130.6, 130.4, 125.8, 125.2, 123.5, 114.9, 92.4; ESI HRMS *m*/*z* 819.0765; calcd for $C_{48}H_{29}N_4Br_2$ ($MH^+$) 819.0759.

**8d**: Yield 0.105 g (27%), green powder, mp >300 °C; UV/vis ($CH_2Cl_2$/TFA) $\lambda_{max}$ (log $\epsilon$) as dication salt 454 (5.64), 618 (4.40), 672 (4.92), ($CH_2Cl_2$) as free base 394 (4.90), 422 (5.59), 436 (5.62), 570 (4.52), 610 (4.93), 666 (4.72); $^1$H NMR ($CH_2Cl_2$/TFA) $\delta$ 11.04 (s, 2H), 9.37 (d, $J$ = 7.96 Hz, 4H), 8.73 (m, 4H), 8.60 (m, 4H), 8.22 (m, 4H), 7.88 (m, 4H), 7.60 (d, $J$ = 8.21 Hz, 4H), 4.25 (s, 6H), −0.24 (br s, 4H); $^{13}$C NMR ($CH_2Cl_2$/TFA) $\delta$ 168.1, 142.7, 139.4, 139.2, 134.8, 133.0, 131.9, 131.8, 131.2, 130.8, 130.7, 125.2, 123.7, 115.0, 92.7, 53.4; LDI-TOF MS *m*/*z* 778.11; calcd for $C_{52}H_{34}N_4O_4$ ($M^+$) 778.26. Anal. Calcd for $C_{52}H_{34}N_4O_4 \cdot 0.5Et_2O$: C, 79.49; H, 4.82; N, 6.87. Found: C, 79.30; H, 4.72; N, 6.74.

**8e**: Yield 0.14 g (32%), green crystals, mp > 300 °C; UV/vis ($CH_2Cl_2$/TFA) $\lambda_{max}$ (log $\epsilon$) ($CH_2Cl_2$) as free base 394 (4.85), 420 (5.51), 438 (5.55), 570 (4.44), 612 (4.86), 666 (4.70); $^1$H NMR as dication ($CH_2Cl_2$/TFA) $\delta$ 10.97 (s, 2H), 9.32 (d, $J$ = 7.83 Hz, 4H), 8.33 (d, $J$ = 1.01 Hz, 4H), 8.15 (dd, $J_{app}$ = 7.33 Hz, 4H), 8.13 (d, 2H, overlapped), 7.80 (dd, $J_{app}$ =7.83 Hz, 4H), 7.60 (d, $J$ = 8.08 Hz, 4H), 1.55 (s, 36H), 0.49 (br s, 4H); $^1$H NMR as free base ($CH_2Cl_2$) $\delta$ 11.13 (s, 2H), 9.70 (d, $J$ = 6.94 Hz, 4H), 8.19 (m, 4H), 8.12 (m + d overlapped, 6H), 7.77 (m, 4H), 7.51 (m, 4H), 1.57 (s, 36H), −1.33 (br s, 2H); $^{13}$C NMR ($CH_2Cl_2$) $\delta$ 151.7, 141.8, 139.0, 138.9, 137.2, 127.2, 127.0, 126.7, 125.3, 122.0, 120.8, 117.8, 92.8, 35.4, 31.7; ESI HRMS *m*/*z* 887.5054; calcd for $C_{64}H_{63}N_4$ ($MH^+$) 887.5053.

**Pd-8a**. Porphyrin **8a** (11 mg, 0.017 mmol) was dissolved in PhCN (5 mL) and heated to about 100 °C. $PdCl_2$ (10 mg, 0.056 mmol) was added, and the mixture was refluxed under Ar. The reaction was stopped when the absorption bands of the free base porphyrin disappeared. Complete conversion required refluxing for about 2 h. The solvent was evaporated in vacuum. The remaining emerald green solid was dissolved in a small volume of $CH_2Cl_2$ (~3 mL) and chromatographed a silica gel column (∅2 × 20 cm, eluent: $CH_2Cl_2$). The emerald green band was collected, and evaporation of the solvent gave **Pd-8a** as a dark green powder: yield 11 mg (86%); $^1$H NMR (DMF-$d_7$, 100 °C) $\delta$ 11.11 (s, 2H), 9.75 (s, 4H), 8.64 (aa′bb′, $J_1$ = 6.83 Hz, $J_2$ = 1.46 Hz, 4H), 8.30 (t, $J$ = 6.8 Hz, 4H), 8.06 (overlapped with solvent), 7.60 (m, 4H), 7.23 (d, $J$ = 7.71 Hz, 4H); MALDI-TOF (*m*/*z*) calcd for $C_{48}H_{28}N_4O_{12}Pd$ 767.2, found 770.9 [M + $H^+$].

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**Supporting Information Available:** Additional procedures, details of photophysical experiments, and characterization data for the new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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