JOC The Journal of Organic Chemistry

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Role of Steric Hindrance in the Newman-Kwart Rearrangement and in the Synthesis and Photophysical Properties of Arylsulfanyl Tetrapyrazinoporphyrazines

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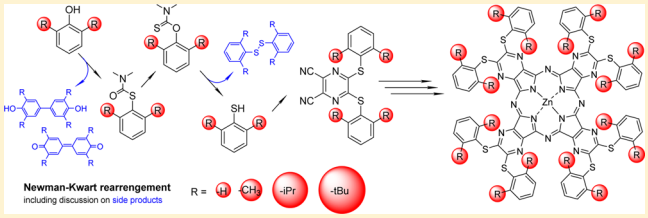
Supporting Information

ABSTRACT: Conditions for the Newman-Kwart rearrangement of phenols into thiophenols were investigated in relation to the bulkiness of substituents at the 2 and 6 positions of the starting phenol derivative with an emphasis on eliminating side reactions. Thiophenols with different 2,6-disubstitution patterns (including hydrogen, methyl, isopropyl or *tert*-butyl groups) were used for the synthesis of 5,6-bis(arylsulfanyl)-pyrazine-2,3-dicarbonitriles that underwent cyclotetramerization leading to the corresponding zinc tetrapyrazinoporphyrazines (TPyzPz), aza-analogues of phthalocyanines. Several methods for the cyclotetramerization were attempted to eliminate problematic side reactions. Magnesium butoxide was found as the most suitable cyclotetramerization agent and afforded TPyzPzs in reasonable yields of approximately 30% under mild conditions. The varying arrangements of the peripheral substitutions resulting from the different bulkiness of the substituents were demonstrated by the X-ray structures of the pyrazine-2,3-dicarbonitriles. The prepared zinc arylsulfanyl TPyzPzs showed an absorption maximum at a Q-band over 650 nm, fluorescence quantum yields between 0.078 and 0.20, and singlet oxygen quantum yields ranging 0.58−0.69. TPyzPzs with isopropyl groups were found to be the best derivatives in this series as they combined facile cyclotetramerization, no aggregation, and good photophysical properties, which makes them potentially suitable for photodynamic therapy.



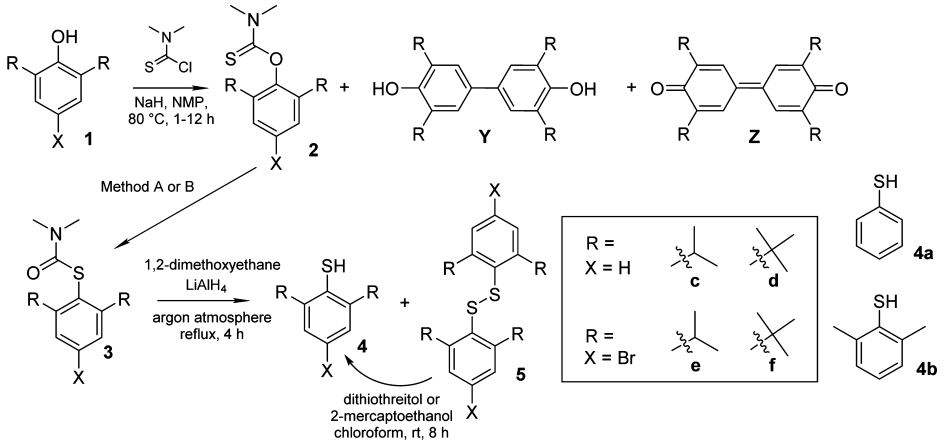
INTRODUCTION

Phthalocyanines (Pcs) have attracted steady attention since their synthesis was first described in a publication in 1907.[1] In the next hundred years, synthesis of Pcs became an interesting subject of research[2,3] that has also resulted in their wide application potential.[4] Their aza-analogs, azaphthalocyanines, in particular, tetrapyrazinoporphyrazines (TPyzPz), are characterized by similar properties. However, the presence of additional nitrogen atoms in the macrocyclic core renders the azaphthalocyanines significantly electron-deficient,[5] which enables the use of TPyzPzs in new applications that are not available for Pcs.[6,7] Thus, the syntheses of a number of alkyl-,[8] alkenyl-,[9] alkinyl-,[10] aryl-,[11] heteroaryl-,[11,12] alkylsulfanyl-,[13] alkyl/arylamino-,[13−15] and alkyl/aryloxy-[8,13,16] substituted TPyzPzs have been published. Notably, TPyzPz molecules bearing bulky phenoxy substituents[16,17] were found to maintain a monomeric form, improving their solubilities and photophysical properties. TPyzPzs bearing arylsulfanyl groups on their periphery are absent from the TPyzPz family despite the fact that (hetero)arylsulfanyl Pcs are routinely synthesized[18,19] and widely studied because of their electrochemical properties,[20,21] their efficient binding to various nanoparticles,[22,23] and their potential as photosensitizers in photodynamic therapy (PDT)[24] or models in catalysis.[25,26] The reason for the lack of these derivatives in TPyzPzs may be the instability of the thioether linkage during the harsh conditions of the cyclotetramerization reaction to form the TPyzPz macrocycles. Thus, the synthesis of arylsulfanyl TPyzPzs has represented a challenge for chemists since the first unsuccessful synthetic attempt of Mørkved in 1996.[27]

Peripheral substitution in TPyzPzs significantly influences their aggregation, solubility, and photophysical properties, including fluorescence emission, singlet oxygen production, and to some extent the position and shape of the absorption maximum. The nonaggregating character of TPyzPzs is

Received: December 17, 2013
Published: February 18, 2014

Scheme 1. Synthesis of Thiophenols 4c–f (4a and 4b Are Commercially Available Compounds) By the Newman-Kwart Rearrangement[a]



[a]Method A: melting the reactant in a preheated metal block at 260 °C; Method B: microwave irradiation in a closed vessel (300 W, 280 °C) in *N,N*-dimethylacetamide.

believed to be the key factor responsible for their high solubility and desirable photophysical parameters. The bulkiness of the peripheral substituents maintains TPyzPzs in their monomeric form.[28] Considering the central metal in this study, zinc TPyzPz complexes were chosen to investigate the potential of prepared compounds in the field of PDT. Coordination of a closed-shell metal with a high atomic number into the center of a macrocycle prolongs the lifetimes of the triplet states and enhances relaxation of the excited state through the intersystem crossing followed by production of singlet oxygen. This is known as the heavy atom effect[16,29] and is used favorably in PDT.

The aim of this work is to synthesize the previously unreported arylsulfanyl TPyzPzs and describe the detailed investigation of their synthesis and photophysical behavior with respect to the bulkiness of their peripheral substituents. A reliable synthetic pathway based on a Newman-Kwart rearrangement[30] leading to suitable thiophenols will be discussed in the first part of this paper along with a discussion of the role of the bulkiness of the *ortho* substituent.

RESULTS AND DISCUSSION

Synthesis. A brief retrosynthetic analysis revealed that arylsulfanyl TPyzPzs can be prepared by the cyclotetramerization of 5,6-bis(arylsulfanyl)pyrazine-2,3-dicarbonitriles. These precursors result from the nucleophilic substitution of 5,6-dichloropyrazine-2,3-dicarbonitrile with the appropriate thiophenols. Both thiophenol (**4a**) and 2,6-dimethylthiophenol (**4b**) are commercially available. Thus, the synthesis of thiophenols starting from phenols with bulky substituents in the 2 and 6 positions remained a key goal of the project. The exchange of an oxygen atom for a sulfur atom in a molecule can be achieved through the use of thionation agents such as P_2S_5,[31] thiourea,[32] or Lawesson's reagent.[33] However, such approaches, which have often been reported for aliphatic alcohols, amides, carbonyls, or esters, failed with 2,6-diisopropylphenol or 2,6-di(*tert*-butyl)phenol. The Newman-Kwart rearrangement[30] was found to be the only suitable approach (Scheme 1 and Table 1). Concisely, the phenolic OH group of **1** was deprotonated with NaH and reacted with thiocarbamoyl chloride to form *O*-aryl thiocarbamates **2**. Heating **2** to temperatures exceeding 250 °C initiated its rearrangement and provided the more stable *S*-aryl thiocarbamates **3**. Subsequent cleavage of the *S*-aryl thiocarbamates with $LiAlH_4$ afforded the required thiophenols **4**.

Table 1. Synthesis of Thiophenols 4c–f[a]

starting material	reaction conditions	yield
1c	NaH, NMP, DMTCC, 1 h, 80 °C	**2c** (45%), **Y-c** (traces), **Z-c** (traces)
1d	NaH, NMP, DMTCC, 12 h, 80 °C	**2d** (22%), **Y-d** (38%); **Z-d** (2%)
1e	NaH, NMP, DMTCC, 2 h, 80 °C	**2e** (81%), **Y-c** (traces), **Z-c** (traces)
1f	NaH, NMP, DMTCC, 4 h, 80 °C	**2f** (19%), **Y-d** (41%); **Z-d** (6%)
2c	Method A (260 °C, 1 h)	**3c** (89%)
2d	Method A (260 °C, 1 h)	n.w.[b]
2d	Method B (mw, DMA, 280 °C, 4 h)	**3d** (70%)
2e	Method A (260 °C, 1 h)	**3e** (85%)
2f	Method A (260 °C, 1 h)	n.w.[b]
2f	Method B (mw, DMA, 280 °C, 3 h)	**3f** (57%)
3c	DME, $LiAlH_4$, argon, rt, 4 h	**4c** (79%), **5c** (9%), or only **4c** (88%)[c]
3d	DME, $LiAlH_4$, argon, rt, 4 h	**4d** (~82%), **5d** (traces) or only **4d** (82%)[c]
3e	DME, $LiAlH_4$, argon, rt, 4 h	**4e** (75%), **5e** (10%), or only **4e** (84%)[c]
3f	DME, $LiAlH_4$, argon, rt, 4 h	**4f** (~52%), **5d** (traces), or only **4f** (52%)[c]

[a]DMTCC = dimethylthiocarbamoyl chloride, NMP = *N*-methyl-2-pyrrolidinone, mw = microwave irradiation, DME = 1,2-dimethoxyethane, DMA = *N,N*-dimethylacetamide. [b]n.w. = not working, starting compound was recovered. [c]After treatment of reaction mixture with dithiothreitol.

The role of the bulkiness of the substituents at the *ortho* positions of the phenol/thiophenol groups was obvious in all steps of the synthetic pathway. The reaction with thiocarbamoyl chloride proceeded well with 2,6-diisopropylphenol (**1c**) and 3-bromo-2,6-diisopropylphenol (**1e**) with yields of 45% and 81% for **2c** and **2e**, respectively. However, both 2,6-di(*tert*-butyl)phenol (**1d**) and its 3-bromo derivative (**1f**) underwent a side reaction under basic conditions that lowered the yields of

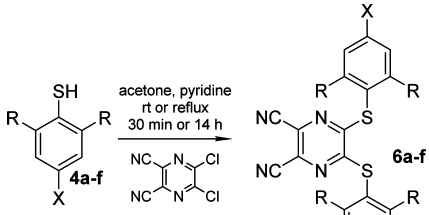
dx.doi.org/10.1021/jo402791c | J. Org. Chem. 2014, 79, 2082–2093

2d and **2f** to 22% and 19%, respectively. Side products **Y-d** and **Z-d** were also isolated in yields of 38% and 2%, respectively, starting from compound **1d** and in yields of 41% and 6%, respectively, starting from compound **1f**. A possible explanation for this side reaction is that the steric hindrance of bulky *tert*-butyl groups protected the phenol OH from attacking the thiocarbamoyl chloride. As a consequence, the competitive and well-known formation of a C−C bond between two molecules of **1d** or **1f** predominated.[34] Notably, this side reaction was negligible for **2c** and **2e**, and only traces of corresponding **Y-c** and **Z-c** were observed on the TLC (not isolated). In the next step, the rearrangement was accomplished using two different methods based on the principle of heating the reactant to a high temperature. Method A involved melting the reactant in a preheated metal block at 260 °C, and method B utilized microwave irradiation in a closed vessel (300 W, 280 °C) with *N,N*-dimethylacetamide as the solvent. The rearrangement of **2c−f** to form **3c−f** was easily detected by the change in the R_f value from approximately 0.5 to 0.2 (the mobile phase was chloroform/toluene 1:1) or in the shifts of the carbon C═O (187−190 ppm) and C═S (166−168 ppm) signals in the ^{13}C NMR spectrum. Method A showed several advantages with compounds bearing isopropyl moieties (**3c**, **3e**), including solvent-free conditions, an easier purification procedure, and lack of a microwave reactor. However, this method was not effective for **3d** and **3f**, which possessed bulkier *tert*-butyl groups. No products were formed at all, and the starting compounds **2d** and **2f** were completely recovered from the reaction mixture, even at temperatures over 260 °C. On the other hand, **3d** and **3f** were obtained via method B in reasonable yields of 70% and 57%, respectively. Differing reactivities were also observed in the last step involving the cleavage of the *S*-aryl thiocarbamates to thiophenols. Disulfides **5c** and **5e** were always obtained in noticeable yields (9% and 10%, respectively) as side products in addition to the desired products, thiophenols **4c** and **4e**. This side reaction was significantly suppressed for **4d** and **4f**, with bulky *tert*-butyl groups attached at positions 2 and 6, due to the steric constraint (the side products appeared as traces on TLC only and were not isolated). The treatment of the reaction mixtures with a reducing agent at the end of the synthesis (dithiothreitol or a large excess of 2-mercaptoethanol) in a one-pot reaction ensured the cleavage of the disulfides and gave thiophenols **4c−f** in yields over 52%.

Thiophenols **4a−f** were further used in reactions with 5,6-dichloropyrazine-2,3-dicarbonitrile (see Scheme 2). The electron deficient carbons at positions 5 and 6 of the latter are highly activated for nucleophilic aromatic substitution. Different solvents (DMF and THF) and bases (NaOH, K_2CO_3, and NaH) and direct reaction with sodium thiophenolate were tested, but only traces of products **6a−f** were detected by TLC. The best results were only achieved using acetone as the solvent and pyridine as the base to afford the desired products **6a−f** in reasonable yields of 67−94%. Thiophenols **4a−c** and **4e** reacted immediately at room temperature, irrespective of the bulkiness of the substituent at the *ortho* position (i.e., hydrogen, methyl, or isopropyl). On the other hand, thiophenols **4d** and **4f**, bearing bulky *tert*-butyl substituent groups, required heating at reflux and prolonged reaction times of up to 14 h to react.

Precursors **6e** and **6f** substituted with bromine were added to the series because they can serve as building blocks for further modification of the TPyzPz peripheral groups. Arylbromides are known to undergo coupling reactions.[35] Thus, several

Scheme 2. General Synthesis of 5,6-Disubstituted Pyrazine-2,3-Dicarbonitriles

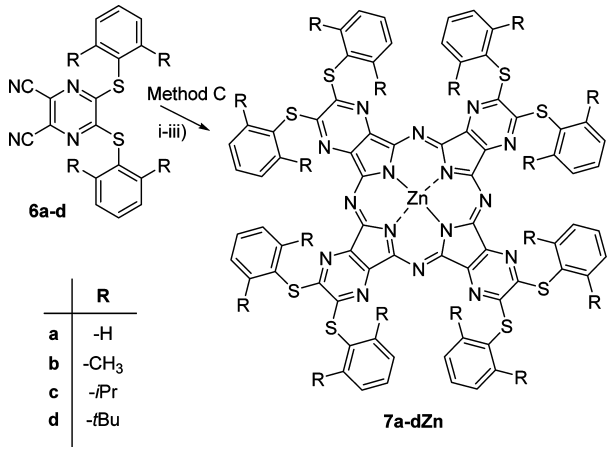


	R	X	reaction cond.	yield of 6
a	-H	-H	30 min, rt	71 %
b	$-CH_3$	-H	30 min, rt	94 %
c	-iPr	-H	30 min, rt	85 %
d	-tBu	-H	14 h, reflux	82 %
e	-iPr	-Br	30 min, rt	90 %
f	-tBu	-Br	14 h, reflux	67 %

moieties influencing the solubility, photophysical properties, or targeting ability can be introduced onto the TPyzPz periphery via these precursors. Modification of precursor **6a** via coupling reactions will be included in a follow-up project studying application potential of arysulfanyl TPyzPz in detail.

In general, TPyzPzs are prepared through two different approaches: the template method or the successive construction of the macrocycle using alkoxide to initiate the reaction. The latter method usually gives higher yields but may suffer from the nucleophilic substitution of labile peripheral groups with the alkoxy groups of the initiator. This side reaction was described in detail in several published papers concerning alkyloxy- and aryloxy-TPyzPzs.[36,37] This is also the reason that the first and only attempt to synthesize arylsulfanyl TPyzPz by Mørkved failed.[27] The cyclotetramerization of precursors **6a−d** with magnesium butoxide (method C, Scheme 3) was tested first. It gave, in all cases, magnesium TPyzPzs as green products that were demetalated under acidic conditions and transformed to zinc complexes. Interesting relationships were observed in the **6a−d** series using mass spectrometry (MS) when considering the extent of the undesirable exchange reaction[38] (see Table 2 or the mass

Scheme 3. Synthesis of TPyzPzs 7a−d by Method C[a]



	R
a	-H
b	$-CH_3$
c	-*i*Pr
d	-*t*Bu

[a](i) $Mg(OBu)_2$, BuOH, reflux, 5 h; (ii) *p*-TSA, THF, rt, 1 h; and (iii) $Zn(CH_3COO)_2$, pyridine, reflux, 1 h; (other possible synthetic pathways discussed in text are described in the Experimental Section).

dx.doi.org/10.1021/jo402791c | J. Org. Chem. 2014, 79, 2082−2093

Table 2. Summary of the Different Cyclotetramerization Methods

				relative intensities of the signal in the mass spectra, %[a]								
cpd.	method	cyclotetramerization agent	yield of isolated zn complex	8 × SAr 0 × OBu	7 × SAr 1 × OBu	6 × SAr 2 × OBu	5 × SAr 3 × OBu	4 × SAr 4 × OBu	3 × SAr 5 × OBu	2 × SAr 6 × OBu	1 × SAr 7 × OBu	0 × SAr 8 × OBu
7aZn	C	$Mg(OBu)_2$[b]	29%[c]	100	66	37	16	3	-	-	-	-
7aZn	D	$Zn(CH_3COO)_2$, DMF[d]	2%	100	-	-	-	-	-	-	-	-
7aZn	E	$Zn(quinoline)_2Cl_2$[e]	15%	100	-	-	-	-	-	-	-	-
7bZn	C	$Mg(OBu)_2$[b]	27%[f]	100	2	-	-	-	-	-	-	-
7cZn	C	$Mg(OBu)_2$[b]	35%[f]	100	-	-	-	-	-	-	-	-
7cZn	D	$Zn(CH_3COO)_2$, DMF[d]	23%	100	-	-	-	-	-	-	-	-
7cZn	E	$Zn(quinoline)_2Cl_2$[e]	23%	100	-	-	-	-	-	-	-	-
7cZn	F	LiOBu[g]	60%[c]	-	-	-	-	-	10	38	30	100
7cZn	G(1)	DBU (1)[h]	54%[c]	45	89	100	63	25	10	-	-	-
7cZn	G(10)	DBU (10)[i]	17%[c]	52	86	100	51	9	-	-	-	-
7dZn	C	$Mg(OBu)_2$[b]	23%[f]	100	-	-	-	-	-	-	-	-

[a]Analyzed directly from the crude reaction mixture before purification (for the appropriate MS spectra see Figures S1−S10 in the Supporting Information). [b]$Mg(OBu)_2$, BuOH, reflux, 5 h; *p*-TSA, THF, rt, 1 h; $Zn(OAc)_2$, pyridine, reflux, 1 h. [c]Yield of the TPyzPzs mixture (after a column chromatography). [d]$Zn(CH_3COO)_2$, DMF, reflux, 3−10 h, argon atmosphere. [e]$Zn(quinoline)_2Cl_2$, 250 °C, 5 min. [f]Yield of pure TPyzPzs (with 8 × SAr) from three step reaction. [g]LiOBu, BuOH, reflux, 2.5 h. [h]$Zn(CH_3COO)_2$, DBU (1 equiv), BuOH, reflux, 6 h. [i]$Zn(CH_3COO)_2$, DBU (10 equiv), BuOH, reflux, 6 h.

spectra in the Supporting Information). The *tert*-butyl and isopropyl substituents on the phenyl were bulky enough to protect the reactive electron-deficient carbons in the pyrazine ring from attack by magnesium butoxide. No side products due to the exchange of peripheral substituents were detected by MS in the **7c** and **7d** series. Traces of TPyzPzs with some arylsulfanyl groups exchanged for butoxy groups were observed in the crude reaction mixture of **7bZn**, but the pure octaarylsulfanyl complexes **7b** were easily obtained by column chromatography. The susceptibility to this side reaction was most pronounced in the **7a** series, in which the butoxide anion can easily reach the reactive center, and a mixture of inseparable TPyzPzs with butoxy and phenylsulfanyl substituents was obtained. The results for the **7a** series were in good agreement with those published by Mørkved, who noticed the exchange of peripheral substituents during the cyclotetramerization of 5,6-bis(*p*-tolylsulfanyl)pyrazine-2,3-dicarbonitrile with magnesium propoxide.[27] Thus, method C is not suitable for the synthesis of **7a** complexes and unhindered arylsulfanyls in general. The mass spectrum of compound **7dZn** showed not only the correct mass ($[M]^+$ = 2345.8) and the sodium and potassium adducts, but also a mass of 2287.7 and the corresponding potassium adduct. However, **7dZn** appeared as the only spot on the TLC (see Figure S11 in the Supporting Information) and also provided satisfactory elemental analysis results. The NMR spectra did not provide any answers regarding this second observed mass peak, and only signals corresponding to the expected hydrogen or carbon atoms were observed (see Figure S12 in the Supporting Information). Unfortunately, the origin of the unexplained mass peak has not yet been explained.

The cyclotetramerization conditions were then studied further. Precursor **6c**, bearing isopropyl groups, was chosen as a model precursor for this purpose. First, several reactions for the alkoxide approaches, which differed in the manner in which the alkoxide was formed (i.e., methods C, F, and G), were performed. Surprisingly, the reactivity of **6c** differed significantly when magnesium, lithium, or 1,8-diazabicyclo[5.4.0]-undec-7-ene (DBU) was used to form the butoxide. No exchange of the peripheral substituents was detected with the use of magnesium butoxide; however, the side reaction partially proceeded in the case of DBU (with 1 or 10 equiv of DBU to **6c**). Only a mixture of products containing mostly butoxy substituents was obtained when lithium butoxide was used (see Table 2 or Figures S1−S10 in the Supporting Information). This approach showed that the strength of the butoxide attack increases in the following order: magnesium ≪ DBU < lithium. From this perspective, magnesium butoxide can be considered a mild cyclotetramerization agent. The reaction conditions for the cyclotetramerization using template methods were also studied. Template cyclotetramerization is usually performed in high boiling solvents with a metal salt. Cyclotetramerization proceeds in different manner than the previous method. The metal serves as a template that allows four precursor molecules to approach each other and form a TPyzPz macrocycle after heating. Thus, heating **6c** with anhydrous zinc acetate in DMF (method D) or performing the cyclotetramerization in a melt with $Zn(quinoline)_2Cl_2$ (method E) gave pure **7cZn** in 23% yield in both cases. These yields, however, were lower than those for the magnesium butoxide method (35% for the three step reaction, calc. from **6c**). As mentioned above, the alkoxide approach cannot be used for the cyclotetramerization of **6a**, and the template methods with zinc acetate in DMF (method D) or melting with $Zn(quinoline)_2Cl_2$ (method E) must be used. In this case they provided pure **7aZn** in yields of 2% and 15%, respectively. In addition to the lower efficiencies of the template methods, the very low yields can partially be explained by the difficult purification that results from the low solubility of **7aZn**, caused by aggregation.

UV−vis Spectra. Prepared TPyzPzs had absorption spectra profiles typical for this group of compounds with a high energy B-band at 380 nm and a low energy Q-band at 660 nm and extinction coefficients up to 133 000 and 237 000 M^{-1} cm^{-1}, respectively (see Figure 1a and Figure S13 in the Supporting Information). The shapes of the Q-bands of most of the complexes suggested that they were in the monomeric form in THF even at high concentrations (up to 10^{-5} M). However, **7aMg** and **7aH** tended to aggregate, which was indicated by a broadening of the absorption spectra, a decrease in the

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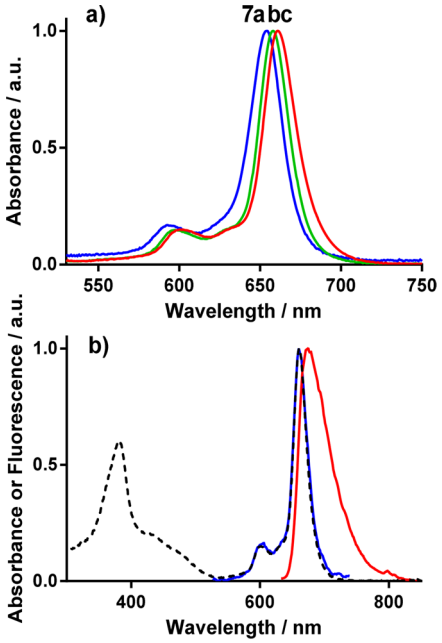

Figure 1. Spectral properties of TPyzPzs in THF: (a) Q-band area of the normalized absorption spectra of **7a–cZn** (**7aZn** blue, **7bZn** green, and **7cZn** red); (b) normalized absorption (black), emission (red), and excitation (blue) spectra of **7cZn**.

extinction coefficient, and their lower solubility. It must be noted that samples **7aMg** and **7aH** were mixtures containing some exchanged butoxy substituents, which may also contribute to the aggregation. **7aZn** was a pure compound prepared by the template method and did not show aggregation. Similarly, the metal-free derivative **7bH** from the **7b** series exhibited aggregation in THF, while the corresponding zinc and magnesium complexes were highly soluble and monomeric at all of the tested concentrations (up to 10^{-5} M). Compounds from the **7c** series remained in their monomeric forms throughout all of the measurements and were highly soluble in common organic solvents (chloroform, dichloromethane, THF, DMF, and pyridine), indicating that the bulkiness of the isopropyl substituents completely prevented aggregation. The aggregation phenomenon also correlates well with the rotation of the phenyl out of the plane of the pyrazine ring, as discussed in the paragraph dedicated to the X-ray analysis of precursors **6a–d** in Supporting Information. From this perspective, derivatives from the **7d** series bearing *tert*-butyl groups should behave similarly to those from the **7c** series. However, the Q-band of **7dZn** and **7dMg** contained a shoulder at approximately 720 nm (see Figure S13d in the Supporting Information). The presence of residual metal free impurity in **7dZn** and **7dMg** stocks comes as one of the plausible explanations. This assumption can be, however, excluded due to only one clear spot of **7dMg** and **7dZn** on TLC with quite different retention factors from **7dH** (see TLC in Figure S11b in the Supporting Information; $R_{f(7dH)}$ = 0.86, $R_{f(7dMg)}$ = 0.16, $R_{f(7dZn)}$ = 0.32 in toluene/THF 40:1 as a mobile phase). No presence of **7dH** mass (*m*/*z* 2225.83) in mass spectra of **7dMg** and **7dZn** supports this interpretation. The band at 720 nm cannot be attributed even to aggregation, due to the extreme bulkiness of the substituents, but indicates that the composition of this sample is more complex, as already suggested by the mass spectra. The absorption spectrum of metal-free **7dH** was fully distorted in the Q-band, thus supporting these suggestions.

The position of the Q-band is primarily influenced by the conjugated bond system of the TPyzPz core, while the peripheral groups usually play a minor role. Nevertheless, Q-bands of the prepared arylsulfanyl TPyzPzs were shifted by 10 nm compared to the alkylsulfanyl TPyzPzs[13] (as an example, see TPyzPz **8Zn** in Table 3) most likely due to the enlargement

Table 3. Absorption and Photophysical Data of the TPyzPzs Involved in the Study Determined in THF at Room Temperature

compound	peripheral substituent	λ_{abs}/nm	λ_{em}/nm	Φ_F	Φ_Δ
7aZn	PhS	656	662	0.18	0.61
7bZn	2,6-diMe-PhS	658	668	0.18	0.64
7cZn	2,6-bis(*i*Pr)PhS	661	677	0.12	0.69
7dZn	2,6-bis(*t*Bu)PhS	659	665	0.078[a]	0.58[a]
8Zn[b]	*t*BuS	649	656	0.35	0.55
9Zn[b]	2,6-bis(*i*Pr)PhO	624	630	0.41	0.50

[a]Ambiguous composition (see discussion). [b]Data from literature.[13]

of the conjugated system with the attached arylsulfanyl moieties. This indicates that some level of electronic communication between the peripheral phenyl groups and the TPyzPz core persists despite the almost perpendicular orientation of these two moieties (see the X-ray analysis data and discussion of **6a–d** in Supporting Information). Considering the role of the connecting heteroatom, sulfur is advantageous compared to isosteric oxygen due to the significant bathochromic shift of almost 40 nm (Table 3, compare **7cZn** with the isosteric TPyzPz **9Zn**). These observations are in accord with the literature[13] where Q-bands of alkyloxy TPyzPzs are hypsochromically shifted from the alkylsulfanyl TPyzPzs by 30 nm. Absorption at a longer wavelength is advantageous for any biological application (e.g., for PDT) because red light is less scattered and is not absorbed by endogenous chromophores, thus resulting in the ability of the light to penetrate deeper into biological material.

An interesting relationship of the Q-band position was observed in the prepared TPyzPz series, as the Q-band maxima in THF were located at 656, 658, and 661 nm for **7aZn**, **7bZn**, and **7cZn**, respectively (see Figure 1a). This can most likely be explained by the slight distortion of the macrocyclic core as a result of the increased bulkiness of the peripheral substituents. A similar distortion effect was described by Chambrier for nonperipherally substituted Pc.[39] The absorption maxima of **7dMg**, **7dH**, and **7dZn** were an exception because the Q-band position was shifted to slightly shorter wavelengths and an additional broad band in the absorption spectrum was observed at 720 nm. This fact could be connected with the complex composition of the sample described above.

Photophysical Properties. Fluorescence emission and singlet oxygen production, the two main excited state relaxation pathways of the prepared TPyzPzs **7a–dZn**, were investigated in THF. Singlet oxygen is the main cytotoxic species in PDT, and strong red fluorescence can be used for visualization in PDT or for detection purposes. The fluorescence emission spectra showed the typical shapes for Pcs and related compounds and mirrored the absorption spectra (Figure 1b). Only the small Stokes shifts documented in Table 3 were observed, and they did not exceed 10 nm, which is also typical for this group of compounds. The fluorescence excitation spectra for the compounds in the monomeric forms matched the absorption spectra (Figure 1b). This fact further confirmed

dx.doi.org/10.1021/jo402791c | J. Org. Chem. 2014, 79, 2082–2093

that aggregation of the studied compounds **7a−dZn** did not occur. The fluorescence quantum yields (Φ_F) as well as the singlet oxygen quantum yields (Φ_Δ) were determined by comparative methods using zinc phthalocyanine as a reference. The data are summarized in Table 3. The Φ_F and Φ_Δ values of **7a−cZn** did not differ much within the series and reached values of 0.12−0.18 and 0.61−0.69, respectively. The photophysical data of the alkylsulfanyl TPyzPz **8Zn** and the aryloxy TPyzPz **9Zn** are provided in Table 3 for comparison. It is obvious that the photophysical properties of the arylsulfanyl TPyzPzs differed from the related alkylsulfanyl derivative **8Zn**. Arylsulfanyl TPyzPzs **7a−cZn** preferred relaxation of their excited states through singlet oxygen production, and fluorescence emission was significantly suppressed. Comparison of **7cZn** with the isosteric **9Zn** confirmed that the oxygen linkage in the peripheral substitution led to higher Φ_F and lower Φ_Δ values compared with the sulfur linkage. Similar relationships have been described for alkyloxy and alkylsulfanyl TPyzPzs.[13] The photophysical data of **7dZn** were also studied. Excitation spectrum corresponded well with the absorption spectrum (see Figure S16 in Supporting Information), but the Φ_F and Φ_Δ did not fully correlate with the others of the series reaching only 0.078 and 0.58, respectively. We believe that the decrease cannot be attributed to the cofacial aggregation (typically H-dimers) due to extreme bulkiness of peripheral substitution, but probably to the ambiguous composition of the sample (see above).

CONCLUSIONS

The Newman-Kwart rearrangement was demonstrated to be useful for the synthesis of thiophenols bearing bulky aliphatic substituents in positions *ortho* to SH groups; however, suitable reaction conditions must be selected to avoid side products in the reactions. Furthermore, 5,6-bis(arylsulfanyl)pyrazine-2,3-dicarbonitriles were synthesized and used for the preparation of TPyzPzs. Different cyclotetramerization methods were tested, leading to the conclusion that magnesium butoxide is the best reagent to ensure the initiation of cyclotetramerization under mild conditions with reasonable product yields. Bulkiness of the peripheral substituents played an important role not only during the synthesis but also in the properties of the TPyzPzs. The isopropyl group was found to be bulky enough to completely prevent undesirable side reactions during cyclotetramerization and maintain the TPyzPzs in their monomeric form in solution. *Tert*-butylsulfanyl TPyzPz showed unexpected and unclarified behavior. All of these data indicate that arylsulfanyl TPyzPzs bearing isopropyl substituents in the *ortho* positions seem to be most appropriate compounds for further development in this group of compounds. Fluorescence quantum yields up to 0.20 and in particular high singlet oxygen quantum yields (up to 0.69) significantly exceeding both aryloxy isosters and alkylsulfanyl analogues in addition to absorption maximum over 650 nm show the potential of arylsulfanyl TPyzPzs in the field of photodynamic therapy.

EXPERIMENTAL SECTION

Syntheses. *General.* Unsubstituted zinc phthalocyanine as a reference compound was purchased from Sigma-Aldrich. A CEM Discover and Explorer 24 Automated Microwave Synthesis Workstation with a 24-position reaction deck (CEM Corporation, Matthews, North Carolina, USA) was used for the reactions under microwave irradiation. Reaction temperatures during microwave heating were controlled by external infrared sensor.

*4-Bromo-2,6-diisopropylphenol (**1e**).* Compound **1e** was prepared using a previously published method.[40] Bromine was added dropwise to a solution of 2,6-diisopropylphenol (3 g, 16.8 mmol) in acetic acid (50 mL) until discoloration of the solution stopped. After stirring at rt for the next 1 h, the solution was poured into water (100 mL) and extracted three times with ethyl acetate. The organic layers were collected, dried over anhydrous Na_2SO_4, and purified by column chromatography on silica with hexane/toluene 2:1 as the eluent. Yield: 4.06 g of yellowish oil (94%); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.25 (d, J = 6.9 Hz, 12H), 3.12 (hept, J = 6.8 Hz, 2H), 4.75 (s, 1H), and 7.15 ppm (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.5, 27.2, 113.3, 126.4, 136.0, 149.0 ppm; IR (ATR): ν = 2961, 1910, 2869, 1457, 1442, 1385, 1362, 1338, 1294, 1241, 1196, 1148, 1108, 1072, and 935 cm^{-1}.

General Procedure for the Synthesis of *O*-Substituted Dimethylcarbamothioates (2). The appropriate phenol (1 equiv) was dissolved in *N*-methyl-2-pyrrolidone under an argon atmosphere and cooled in an ice/water bath. NaH (60% dispersion in mineral oil; 1.1 equiv.) was slowly added in several portions. The cooling bath was removed and the reaction mixture was stirred at rt for 30 min. Dimethylcarbamoyl chloride (1.3 equiv) dissolved in *N*-methyl-2-pyrrolidone was added dropwise, and the reaction was heated to 80 °C for 1−12 h (specified for each compound below). The reaction mixture was diluted with water and extracted with ethyl acetate (3×). The organic layer was collected, dried over anhydrous Na_2SO_4, and concentrated under high vacuum. The crude product was purified two times by column chromatography on silica. The exact amounts of the reactants as well as the mobile phases are specified for each compound below.

*O-(2,6-Diisopropylphenyl)dimethylcarbamothioate (**2c**).* 2,6-Diisopropylphenol (1.78 g, 10 mmol), NaH (440 mg 60% dispersion in mineral oil, 11 mmol), dimethylthiocarbamoyl chloride (1.66 g, 13 mmol); reaction time of 1 h; purification by recrystallization from EtOH; Yield: 1.19 g of yellow needles (45%); melting point 144.7−146.5 °C (EtOH; lit. 152.5−154.0 °C[13]); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.18 (d, J = 6.9 Hz, 6H), 1.27 (d, J = 6.9 Hz, 6H), 2.93 (hept, J = 6.9 Hz, 2H), 3.40 (s, 3H), 3.50 (s, 3H), and 7.15−7.23 ppm (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.2, 24.4, 27.4, 38.4, 43.3, 123.8, 126.5, 140.9, 148.5, and 187.8 ppm; IR (ATR): ν = 2964, 2875, 1531, 1462, 1440, 1393, 1360, 1333, 1287, 1254, 1178, 1139, 1095, 1060, 937, 833, 799, and 768 cm^{-1}; Elemental analysis calcd. (%) for $C_{15}H_{23}NOS$: C 67.88, H 8.73, N 5.28; found 67.98, H 8.09, N 5.49.

*O-[2,6-Di(tert-butyl)phenyl]dimethylcarbamothioate (**2d**).* 2,6-Di(*tert*-butyl)phenol (3.6 g, 17.5 mmol), NaH (772 mg 60% dispersion in mineral oil, 19.3 mmol), dimethylthiocarbamoyl chloride (2.81 g, 22.8 mmol); reaction time of 12 h; toluene as the eluent (R_f = 0.4); recrystallization from MeOH; Yield: 1.13 g of white needles (22%); melting point 115.0−115.8 °C (MeOH); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.37 (s, 18H), 3.45 (s, 3H), 3.47 (s, 3H), 7.21−7.14 (m, 1H), and 7.30−7.34 ppm (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 32.0, 35.9, 38.7, 43.2, 125.4, 126.6, 142.6, 150.8, and 189.7 ppm; IR (ATR): ν = 3004, 2967, 2875, 1521, 1479, 1419, 1396, 1386, 1362, 1283, 1223, 1187, 1161, 1140, 1116, 1049, 887, 843, 800, and 766 cm^{-1}; Elemental analysis calcd. (%) for $C_{17}H_{27}NOS$: C 69.58; H 9.27; N 4.77; found C 69.38, H 9.54, N 4.74.

*O-(4-Bromo-2,6-diisopropylphenyl)dimethylcarbamothioate (**2e**).* 4-Bromo-2,6-diisopropylphenol (3.5 g, 13.6 mmol), NaH (599 mg 60% dispersion in mineral oil, 15.0 mmol), dimethylthiocarbamoyl chloride (2.19 g, 17.7 mmol); reaction time of 2 h; hexane/toluene 2:1 as the eluent (R_f = 0.22); Yield: 3.8 g of white needles (81%); melting point 114.0−115.1 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.15 (d, J = 6.9 Hz, 6H), 1.25 (d, J = 6.9 Hz, 6H), 2.88 (hept, J = 6.9 Hz, 2H), 3.38 (s, 3H), 3.48 (s, 3H), and 7.26 ppm (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.0, 24.2, 27.5, 38.5, 43.4, 120.0, 127.1, 143.4, 147.6, and 187.2 ppm; IR (ATR): ν = 2967, 2925, 2863, 1572, 1537, 1464, 1449, 1410, 1392, 1363, 1330, 1287, 1236, 1179, 1126, 1097, 1071, 1059, 945, 878, 861, 843, 779, and 758 cm^{-1}; Elemental analysis calcd. (%) for $C_{15}H_{22}BrNOS$: C 52.33, H 6.44, N 4.07; found C 52.53, H 6.50, N 4.16.

*O-[4-Bromo-2,6-di(tert-butyl)phenyl]dimethylcarbamothioate (**2f**).* 4-Bromo-2,6-di(*tert*-butyl)phenol (5 g, 17.5 mmol), NaH (772

dx.doi.org/10.1021/jo402791c | J. Org. Chem. 2014, 79, 2082−2093

mg 60% dispersion in mineral oil, 19.3 mmol), dimethylthiocarbamoyl chloride (2.82 g, 22.8 mmol); reaction time of 4 h; hexane/toluene 1:1 as the eluent; Yield: 1.21 g of yellowish solid (19%); melting point 133.9−134.7 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.34 (s, 18H), 3.43 (s, 3H), 3.46 (s, 3H), and 7.40 ppm (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 32.1, 36.5, 39.1, 43.6, 119.5, 130.0, 145.2, 150.3, and 189.5 ppm; IR (ATR): ν = 2959, 1563, 1529, 1482, 1418, 1387, 1365, 1285, 1253, 1198, 1141, 1113, 1053, 948, 887, 869, 776, and 735 cm^{-1}; Elemental analysis calcd. (%) for $C_{17}H_{26}BrNOS$: C 54.83, H 7.04, N 3.76; found C 55.09, H 7.17, N 3.82; MS (ESI): m/z: 371.87 $[M+H]^+$.

Side Product ***Y-d****: 3,3′,5,5′-Tetra(tert-butyl)-(1,1′-biphenyl)-4,4′-diol.* Isolated from column chromatography of **2f**. Yield: 2.95 g of yellow solid (41%); melting point 181.2−182.8 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.51 (s, 36H), 5.20 (s, 2H), and 7.32 ppm (s, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 30.3, 34.4, 124.1, 133.9, 135.9, and 152.8 ppm; IR (ATR): ν = 3630, 2915, 2957, 2846, 1466, 1424, 1389, 1359, 1318, 1303, 1247, 1227, 1202, 1139, 1105, 1022, 933, 885, and 871 cm^{-1}.

Side Product ***Z-d****: 3,3′,5,5′-Tetra(tert-butyl)-[1,1′-bi-(cyclohexylidene)]-2,2′,5,5′-tetraene-4,4′-dione.* Isolated from column chromatography of **2f**. Yield: 430 mg of yellow solid (6%); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.36 (s, 36H) and 7.70 ppm (s, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 29.6, 36.0, 126.0, 136.1, 150.4, and 186.5 ppm; IR (ATR): ν = 2959, 2921, 2866, 1640, 1603, 1567, 1541, 1482, 1458, 1389, 1363, 1339, 1290, 1262, 1092, 1043, 997, 934, and 899 cm^{-1}.

General Procedures for the Synthesis of the *S*-Substituted Dimethylcarbamothioates (3). *Method A. O*-substituted dimethylcarbamothioate (**2**) was placed into a metal block preheated to 260 °C which was maintained at this temperature for 1 h. The crude product was purified by column chromatography on silica (the mobile phases are specified for each compound below).

Method B. O-substituted dimethylcarbamothioate (**2**) was dissolved in *N,N*-dimethylacetamide and heated under microwave irradiation (300 W, 280 °C) for 3−4 h. The crude product was purified by column chromatography on silica (the mobile phases are specified for each compound below).

*S-(2,6-Diisopropylphenyl)dimethylcarbamothioate (**3c**). Method A.* **2c** (330 mg, mmol); chloroform/toluene 1:1 as the eluent; Yield: 294 mg of colorless oil that solidifies to yellow solid (89%); melting point 105.4−105.8 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.22 (d, J = 7.1 Hz, 12H), 2.94−3.25 (m, 6H), 3.61 (hept, J = 6.9 Hz, 2H), 7.18−7.25 (m, 2H), and 7.35−7.42 ppm (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.1, 27.9, 33.1, 119.6, 121.9, 126.3, 149.6, and 162.7 ppm; IR (ATR): ν = 2960, 2927, 2869, 1726, 1664, 1575, 1459, 1407, 1381, 1326, 1312, 1264, 1180, 1100, 1053, 934, and 824 cm^{-1}. HRMS (ESI-Q-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{24}NOS$ 266.1579; Found 266.1606.

*S-[2,6-Di(tert-butyl)phenyl]dimethylcarbamothioate (**3d**). Method A.* Did not work.

Method B. **2d** (100 mg, 0.34 mmol); 4 h; chloroform/toluene 1:2. Yield: 70 mg of colorless needles (70%); melting point 110.2−111.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.49 (s, 18H), 3.06 (s, 6H), 7.28 (t, J = 7.6 Hz, 1H), and 7.44 ppm (d, J = 7.6 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 32.0, 36.9, 37.7, 125.6, 128.0, 129.4, 156.1, and 168.2 ppm; IR (ATR): ν = 3000, 2954, 2920, 1664, 1507, 1458, 1406, 1387, 1363, 1253, 1216, 1099, 1042, 909, 873, 799, and 746 cm^{-1}; Elemental analysis calcd. (%) for $C_{17}H_{27}NOS$: C 69.58; H 9.27; N 4.77; found C 69.78, H 9.46, N 4.72.

*S-(4-Bromo-2,6-diisopropylphenyl)dimethylcarbamothioate (**3e**). Method A.* **2e** (6.3 g, 18.3 mmol); toluene as an eluent (R_f = 0.15) changed to chloroform/toluene 1:1 during column chromatography; Yield: 5.13 g of colorless oil that solidifies to white solid (85%); melting point 104.2−106.4 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.19 (d, J = 6.8 Hz, 12H), 3.02 (s, 3H), 3.16 (s, 3H), 3.56 (hept, J = 6.8 Hz, 2H), and 7.32 ppm (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.8, 31.9, 37.1, 125.0, 125.5, 127.0, 155.7, and 165.9 ppm; IR (ATR): ν = 2961, 2928, 2873, 1716, 1655, 1561, 1458, 1419, 1368, 1315, 1260, 1235, 1098, 1060, 1045, 910, 891, 867, and 805 cm^{-1}. Elemental analysis calcd. (%) for $C_{15}H_{22}BrNOS$: C 52.33, H 6.44, N 4.07; found C 52.50, H 6.62, N 3.83.

*S-[4-Bromo-2,6-di(tert-butyl)phenyl]dimethylcarbamothioate (**3f**). Method A.* Did not work.

Method B. **2f** (225 mg, 0.60 mmol); 3 h; chloroform/toluene 1:1. Yield: 129 mg of yellow oil (57%); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.47 (s, 18H), 2.99 (s, 3H), 3.13 (s, 3H), and 7.54 ppm (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 29.5, 31.8, 37.0, 37.9, 126.9, 127.3, 129.0, 158.0, and 167.6 ppm; IR (ATR): ν = 2959, 2874, 1562, 1529, 1396, 1285, 1255, 1198, 1141, 1113, 1052, and 869 cm^{-1}; HRMS (ESI-Q-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{27}BrNOS$ 372.0997; Found 372.1015.

General Procedure for the Synthesis of the Thiols (4). Compound **3c−f** (1 equiv) in 1,2-dimethoxyethane was added dropwise to a suspension of $LiAlH_4$ (1.5 equiv) in 1,2-dimethoxyethane under an argon atmosphere while being cooled in an ice/water bath. Then, the cooling bath was removed, and the reaction was heated at reflux for 4 h under argon. Excess $LiAlH_4$ was quenched with several drops of MeOH until gas evolution stopped. Then, the reaction mixture was diluted with water, acidified with diluted sulfuric acid (5% v/v), and extracted three times with diethylether. The organic layer was dried over anhydrous Na_2SO_4. The crude product was dissolved in chloroform and an excess of 2-mercaptoethanol (20−50 equiv) was added and stirred at rt for 8 h to cleave the disulfide bond of side product **5** (observed on TLC with a slightly higher R_f than the product). The excess 2-mercaptoethanol was removed under reduced pressure, and the crude product was purified by column chromatography on silica (the mobile phases are specified for each compound below).

*2,6-Diisopropylbenzenethiol (**4c**).* **3c** (420 mg, 1.58 mmol); $LiAlH_4$ (90 mg, 2.37 mmol); hexane/toluene 3:1 as an eluent. Yield: 271 mg of yellowish oil (88%); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.28 (d, J = 6.8 Hz, 12H), 3.23 (s, 1H), 3.48 (hept, J = 6.7 Hz, 2H), 7.11−7.24 ppm (m, 3H). ^{13}C NMR (75 MHz,$CDCl_3$): δ = 23.1, 31.7, 123.1, 126.4, 127.7, and 147.8 ppm.

*2,6-Di(tert-butyl)benzenethiol (**4d**).* **3d** (480 mg, 1.64 mmol); $LiAlH_4$ (186 mg, 4.91 mmol); hexane as an eluent (R_f = 0.42); Yield: 297 mg of colorless oil (82%); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.60 (s, 18H), 3.72 (s, 1H), 7.15−7.06 (m, 1H), and 7.37 ppm (d, J = 8.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 31.3, 37.2, 125.3, 125.7, 129.6, and 150.8 ppm; IR (ATR): ν = 2959, 2917, 2872, 2360, 2343, 1572, 1482, 1460, 1393, 1384, 1363, 1252, 1243, 1215, 1188, 1151, 1105, 1044, 925, 792, and 728 cm^{-1}.

*4-Bromo-2,6-diisopropylbenzenethiol (**4e**).* **3e** (5.0 g, 14.5 mmol); $LiAlH_4$ (789 mg, 20.8 mmol); hexane/toluene 1:1 as an eluent. Yield: 3.35 g of yellowish oil (84%); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.25 (d, J = 6.8 Hz, 12H), 3.16 (s, 1H), 3.43 (hept, J = 6.8 Hz, 2H), and 7.24 ppm (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.9, 31.8, 121.03, 126.4, 150.0, and 155.7 ppm; IR (ATR): ν = 2963, 2928, 2871, 1716, 1675, 1563, 1460, 1412, 1384, 1363, 1323, 1234, 1153, 1106, 1060, 1046, 889, 864, and 805 cm^{-1}.

*4-Bromo-2,6-di-tert-butylbenzenethiol (**4f**).* **3f** (300 mg, 0.81 mmol); $LiAlH_4$ (48 mg, 1.26 mmol); hexane as an eluent; Yield: 126 mg of yellowish oil that solidifies to yellowish solid (52%); melting point 60.0−61.8 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.56 (s, 18H), 3.66 (s, 1H), and 7.46 ppm (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 31.0, 32.2, 37.3, 120.8, 128.4, 128.7, and 152.9 ppm; IR (ATR): ν = 3105, 2955, 2919, 2872, 1730, 1558, 1485, 1398, 1382, 1363, 1243, 1198, 1161, 1101, 1043, 918, 871, 843, and 769 cm^{-1}; Elemental analysis calcd. (%) for $C_{14}H_{21}BrS$: C 55.81, H 7.03; found C 56.66, H 7.05; HRMS (ESI-Q-TOF) m/z: $[M - H]^-$ Calcd for $C_{14}H_{20}BrS$ 299.0469; Found 299.0476.

*1,2-Bis(2,6-diisopropylphenyl)disulfane (**5c**).* In one instance, the disulfide side product **5c** was isolated from the reaction mixture before cleavage with 2-mercaptoethanol to confirm its identity. Reaction mixture was dissolved in 20% NaOH; undissolved precipitate was collected and purified by column chromatography on silica with hexane/toluene 3:1 as an eluent. Melting point 127.0−127.9 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.03 (d, J = 6.9 Hz, 24H), 3.56 (hept, J = 6.9 Hz, 4H), 7.06−7.11 (m, 4H), and 7.22−7.29 ppm (m, 2H); ^{13}C

dx.doi.org/10.1021/jo402791c | J. Org. Chem. 2014, 79, 2082−2093

NMR (75 MHz,$CDCl_3$): δ = 23.8, 31.4, 123.6, 130.0, 132.3, and 153.5 ppm; IR (ATR): ν = 3057, 2961, 2866, 1573, 1463, 1421, 1381, 1360, 1337, 1309, 1248, 1179, 1104, 1056, 928, and 797 cm^{-1}; Elemental analysis calcd. (%) for $C_{24}H_{34}S_2$: C 74.55, H 8.86; found C 74.88, H 9.01; Pure **5c** was subsequently reduced affording **4c** as follows: **5c** (50 mg, 0.13 mmol) and dithiothreitol (60 mg, 0.40 mmol) were dissolved in chloroform. Triethylamine (0.054 mL, 0.04 mmol) was then added and mixture was stirred at rt for 5 h. Product was extracted three times with water; organic layer was dried over anhydrous Na_2SO_4, and purified by column chromatography on silica with hexane/toluene 3:1 as an eluent. Yield: 42 mg (76%) of yellow oil. The analytical data corresponded well with those for **4c**.

General Procedure for the Synthesis of 5,6-Disubstituted Pyrazine-2,3-Dicarbonitriles (6). Compound **4a−f** (2.2 equiv) was added to 5,6-dichloropyrazine-2,3-dicarbonitrile (1 equiv) in acetone. Then, pyridine (5 equiv) was added at rt. The reactions proceeded immediately with **4a−c** and **4e**. Heating at reflux and a reaction time of 14 h was necessary for thiophenols **4d** and **4f** which had bulky *tert*-butyl substituents. The crude product was purified by column chromatography on silica and recrystallized from EtOH or MeOH. The exact amounts of reactants and the mobile phases are specified for each compound below.

*5,6-Bis(phenylsulfanyl)pyrazine-2,3-dicarbonitrile (**6a**).* 5,6-Dichloropyrazine-2,3-dicarbonitrile (1.0 g, 5.0 mmol), **4a** (1.22 g, 11.1 mmol), pyridine (2.01 mL, 25.0 mmol), 30 min rt, chloroform/toluene 1:1 as an eluent; Yield: 1.23 g of yellow solid (71%); melting point 202.0−203.4 °C (MeOH); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.46−7.61 ppm (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 113.3, 124.8, 127.5, 129.9, 130.9, 135.4, and 159.2 ppm; IR (ATR): ν = 2238 (CN), 1574, 1481, 1439, 1365, 1284, 1136, 1069, 1023, 976, 846, 750, and 703 cm^{-1}; Elemental analysis calcd. (%) for $C_{18}H_{10}N_4S_2$: C 62.41, H 2.91, N 16.17; found 62.54, 3.27, N 16.17.

*5,6-Bis(2,6-dimethylphenylsulfanyl)pyrazine-2,3-dicarbonitrile (**6b**).* 5,6-Dichloropyrazine-2,3-dicarbonitrile (320 mg, 1.64 mmol), **4b**(510 mg, 3.62 mmol), pyridine (0.66 mL, 8.22 mmol), 30 min rt, chloroform/acetone 1:1 as an eluent; Yield: 600 mg of yellowish solid (94%); melting point 261.8−263.9 °C (MeOH); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.42 (s, 12H), 7.22−7.28 (m, 4H), and 7.32−7.39 ppm (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.6, 113.4, 124.7, 127.2, 128.9, 130.9, 143.5, and 159.0 ppm; IR (ATR): ν = 2969, 2234 (CN), 1584, 1478, 1463, 1376, 1360, 1301, 1280, 1146, 1134, 1113, 1048, 973, 780, and 732 cm^{-1}; Elemental analysis calcd. (%) for $C_{22}H_{18}N_4S_2$: C 65.64, H 4.51, N 13.92; found 65.14, H 4.57, N 13.91.

*5,6-Bis(2,6-diisopropylphenylsulfanyl)pyrazine-2,3-dicarbonitrile (**6c**).* 5,6-Dichloropyrazine-2,3-dicarbonitrile (470 mg, 2.34 mmol), **4c** (1.0 g, 5.16 mmol), pyridine (1.0 mL, 11.7 mmol), 30 min rt, chloroform/toluene 1:1 as an eluent; Yield: 1.02 g of yellow solid (85%); melting point 217.6−218.4 °C (MeOH); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.21 (br, 24H), 3.42 (hept, J = 6.7 Hz, 4H), 7.30−7.35 (m, 4H), and 7.49−7.56 ppm (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.0, 32.5, 113.2, 122.8, 124.6, 127.2, 131.8, 153.4, and 160.0 ppm; IR (ATR): ν = 2966, 2925, 2869, 2239 (CN), 1581, 1482, 1382, 1360, 1343, 1283, 1181, 1152, 1137, 1054, 977, 930, 802, 794, and 746 cm^{-1}; Elemental analysis calcd. (%) for $C_{30}H_{34}N_4S_2$: C 70.00, H 6.66, N 10.88; found 69.91, H 6.44, N 11.01.

*5,6-Bis[(2,6-di(tert-butyl)phenylsulfanyl]pyrazine-2,3-dicarbonitrile (**6d**).* 5,6-Dichloropyrazine-2,3-dicarbonitrile (134 mg, 0.67 mmol), **4d** (330 mg, 1.48 mmol), pyridine (277 μL, 3.44 mmol), 14 h reflux, toluene as an eluent; Yield: 315 mg of yellowish solid (82%); melting point 283.4−284.6 °C (EtOH); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.42 (s, 36H), 7.40 (m, 2H) and 7.56−7.48 ppm (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 32.0, 37.7, 113.5, 123.1, 126.4, 126.7, 130.9, 156.3, and 161.3 ppm; IR (ATR): ν = 2963, 2872, 2235, 1575, 1474, 1396, 1387, 1365, 1358, 1300, 1280, 1252, 1215, 1151, 1107, 1032, and 973 cm^{-1}; Elemental analysis calcd. (%) for $C_{34}H_{42}N_4S_2$: C 71.54, H 7.42, N 9.81; found C 71.30, H 7.44, N 9.98.

*5,6-Bis(4-bromo-2,6-diisopropylphenylsulfanyl)pyrazine-2,3-dicarbonitrile (**6e**).* 5,6-Dichloropyrazine-2,3-dicarbonitrile (439 mg, 2.21 mmol), **4e** (3.0 g, 4.85 mmol), pyridine (888 μL, 11.0 mmol), 30 min rt, hexane/toluene 1:1 as an eluent (R_f = 0.38), mobile phase changed to chloroform/toluene 1:2 after impurities eluted from column; Yield: 1.33 g of white solid (90%); melting point 261.9−263.3 °C (EtOH); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.18 (br, 24H), 3.35 (hept, J = 6.8 Hz, 4H), and 7.43 ppm (s, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.3, 32.6, 113.0, 121.7, 127.3, 127.5, 128.1, 155.5, and 159.2 ppm; IR (ATR): ν = 2967, 2925, 2856, 2243, 1481, 1362, 1284, 1181, 1152, 1055, and 977 cm^{-1}; Elemental analysis calcd. (%) for $C_{30}H_{32}Br_2N_4S_2$: C 53.58, H 4.80, N 8.33; found C 53.35, H 4.70, N 8.38.

*5,6-Bis{[4-bromo-2,6-di(tert-butyl)phenyl]sulfanyl}pyrazine-2,3-dicarbonitrile (**6f**).* 5,6-Dichloropyrazine-2,3-dicarbonitrile (45 mg, 0.27 mmol), **4d** (150 mg, 0.50 mmol), pyridine (91 μL, 1.13 mmol), 14 h reflux, toluene/hexane 1:1 as an eluent; Yield: 110 mg of yellowish solid (67%); melting point 287.4−288.1 °C (EtOH); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.40 (s, 36H) and 7.64 ppm (s, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 31.8, 37.9, 113.3, 122.2, 126.7, 126.8, 130.2, 158.2, and 160.6 ppm; IR (ATR): ν = 3000, 2970, 2870, 2234, 1556, 1481, 1397, 1386, 1365, 1301, 1279, 1246, 1198, 1148, 1134, 1035, and 974 cm^{-1}; Elemental analysis calcd. (%) for $C_{30}H_{32}Br_2N_4S_2$: C 53.58, H 4.80, N 8.33; found C 53.30, H 4.84, N 7.96.

General Procedures for the Cyclotetramerization to Zinc TPyzPz (7a-dZn). The reaction mixtures that were used to assess the level of transetherification by MS were analyzed as crude mixtures without purification by column chromatography (the MS data are summarized in Table 2). The yields and analytical data mentioned below are for the purified compounds after column chromatography (including the MS data for purified compounds).

Method C − with Mg(OBu)$_2$ in BuOH. This method included the synthesis of magnesium complexes, and their demetalation and subsequent complexation with zinc. The magnesium and metal-free derivatives were also isolated and fully characterized.

7a−dMg. Magnesium turnings (7 equiv) and a small crystal of iodine were refluxed in anhydrous butanol for 3 h. Then, the appropriate precursor **6a−d** (1 equiv) was added and heating at reflux continued for the next 5 h. The mixture was left to cool, concentrated under reduced pressure, and diluted with water/MeOH/acetic acid 10:5:1. The precipitate was collected and thoroughly washed with water and MeOH. The crude product was purified by column chromatography on silica (the eluents are specified for each compound below) and washed with MeOH to obtain the magnesium complexes of **7a−d** as green solids.

7a−dH. The magnesium complex **7a−dMg** (1 equiv) was dissolved in THF and stirred at rt for 1 h with *p*-toluenesulfonic acid (*p*-TSA, 10 equiv). Then, the reaction mixture was concentrated under reduced pressure and diluted with water. The crude product was purified by column chromatography on silica (the eluents are specified for each compound below) to obtain a green solid.

7a−dZn. Anhydrous zinc acetate (7 equiv) was added to a solution of appropriate metal-free **7a−dH** (1 equiv) in pyridine. The reaction mixture was heated at reflux for 1 h. Then, the solvent was partially removed under reduced pressure, and water was added. The precipitate was collected and thoroughly washed with water and MeOH. The crude product was purified by column chromatography on silica (the eluents are specified for each compound below) to obtain a green solid.

Method D − with Zn(CH$_3$COO)$_2$ in DMF. The appropriate precursor **6** (1 equiv) and anhydrous zinc acetate (2 equiv) were dissolved in anhydrous DMF under an argon atmosphere. The reaction mixture was heated at reflux for 3−10 h. Water was added; a dark precipitate was collected and washed with water and MeOH. The crude product was purified by column chromatography on silica (the eluents are specified for each compound below).

Method E − with Zn(quinoline)$_2$Cl$_2$ in a Melt. The appropriate precursor **6** (1 equiv) and Zn(quinoline)$_2$Cl$_2$ (1 equiv; prepared according to the literature[41]) were thoroughly mixed and heated at 250 °C for 5 min. The green mixture was left to cool. MeOH was added, the mixture was sonicated for 10 min, and the solid was collected and thoroughly washed with MeOH. The crude product was purified by

dx.doi.org/10.1021/jo402791c | J. Org. Chem. 2014, 79, 2082−2093

column chromatography on silica (the eluents are mentioned for each compound below).

Method F – with LiOBu in BuOH. The compound **6c** (1 equiv) was dissolved in anhydrous BuOH (5 mL) and heated to reflux. Lithium (7 equiv) was added, and refluxing was continued for next 2.5 h. The reaction mixture was left to cool and water/MeOH/acetic acid 10:5:1 (15 mL) was added. A dark precipitate was collected and washed with water and MeOH. The crude product (approximately 40 mg) was dissolved in pyridine (5 mL), anhydrous zinc acetate (approximately 7–10 equiv) was added, and the reaction mixture was refluxed for 1 h. Then, the reaction mixture was diluted with water; the precipitate was collected, and washed with water and MeOH. The product was purified by column chromatography on silica with chloroform as the eluent.

Method G – with DBU in BuOH. The compound **6c** (1 equiv) and anhydrous zinc acetate (either 0.25 equiv or 0.5 equiv) were dissolved in anhydrous BuOH (5 mL). 1,8-Diazabicycloundec-7-ene (DBU; either 1 equiv or 10 equiv) was added and reaction was heated at reflux for 6 h under an argon atmosphere. Then, water was added; a green precipitate was collected, and washed thoroughly with water and MeOH. The crude product was purified by column chromatography on silica with chloroform as the eluent.

Reaction Details and Analytical Data of the Prepared TPyzPzs. *2,3,9,10,16,17,23,24-Octakis(phenylsulfanyl)-1,4,8,11,15,18,22,25-(octaaza)phthalocyaninato Magnesium(II) (**7aMg**). Method C.* Magnesium (200 mg, 8.08 mmol); **6a** (400 mg, 1.15 mmol); the low solubility of the product did not allow chromatographic purification. The compound was dissolved in the mixture of chloroform/pyridine 10:1 and dropped into MeOH. The precipitate was collected and thoroughly washed with MeOH and hexane. This purification procedure was repeated three times. The purity of the product was monitored by TLC with chloroform/THF 3:1 as the eluent. Yield: 238 mg of a green solid (58%). This compound was obtained as a mixture of TPyzPz with some peripheral substituents replaced with butoxy groups. ^{1}H NMR ($CDCl_3$/pyridin-d_5, 300 MHz) δ = 7.75–7.50 (br, 16H), 7.19–7.03 ppm (br, 24H); Signals of butoxy substituents were also detected at δ 3.43, 1.75, 1.44, and 0.60 ppm as small and broad signals; ^{13}C NMR ($CDCl_3$/pyridin-d_5, 75 MHz) no signal was detected in carbon NMR except one small broad signal at δ 129.5 ppm that corresponds to aromatic carbons of phenyl; IR (ATR): ν = 3050, 1641, 1582, 1518, 1477, 1440, 1390, 1328, 1244, 1156, 1085, 1024, 1001, 965, 853, 780, and 738 cm^{-1}; MS (MALDI-TOF) *m/z*: 1446.90 $[M+K]^+$, 1407.94 $[M]^+$, 1372.01 $[M-SC_6H_5+OC_4H_9]^+$, 1336.07 $[M-2\times SC_6H_5+2\times OC_4H_9]^+$; UV/vis (THF): λ_{max} (ε): 658 (217 100), 628sh, 598 (31 700), 458sh, 388 nm (123 500 mol^{-1}cm^{-1} L).

*2,3,9,10,16,17,23,24-Octakis(phenylsulfanyl)-1,4,8,11,15,18,22,25-(octaaza)phthalocyanine (**7aH**). Method C.* Compound **7aMg** (140 mg, 0.11 mmol), *p*-TSA (200 mg, 1.1 mmol); chloroform/THF 3:1 as a mobile phase; Yield: 90 mg of green solid (67%). This compound was obtained as a mixture of TPyzPz with some peripheral substituents exchanged for butoxy. ^{1}H NMR ($CDCl_3$/pyridin-d_5, 300 MHz) δ = 8.31–7.97 (m, 16H), 7.81–7.06 (m, 24H; overlaps with the residual signal of solvent); signals of butoxy substituents were also detected at δ 0.40–5.19 ppm as broad signals; ^{13}C NMR ($CDCl_3$/pyridin-d_5, 75 MHz) only some aromatic signals (phenyl) were detected at δ = 134.2, 129.8, 129.6, 129.3 ppm together with 14.3, 19.9, 24.2, 25.9, 26.4, 26.8, 30.0, 31.5, 46.5, 46.8, 47.3, 48.1, 49.4 ppm (butoxy groups); IR (ATR): ν = 3048, 1641, 1581, 1514, 1476, 1440, 1401, 1311, 1261, 1170, 1085, 1067, 1026, and 960 cm^{-1}; MS (MALDI-TOF) *m/z*: 1446.90 $[M+K]^+$, 1430.93$[M+Na]^+$, 1407.95 $[M]^+$, 1372.00 $[M-SC_6H_5+OC_4H_9]^+$, 1336.07 $[M-2\times SC_6H_5+2\times OC_4H_9]^+$.

*2,3,9,10,16,17,23,24-Octakis(phenylsulfanyl)-1,4,8,11,15,18,22,25-(octaaza)phthalocyaninato Zinc(II) (**7aZn**). Method C.* Compound **7aH** (50 mg, 0.036 mmol), $Zn(CH_3COO)_2$ (65 mg, 0.36 mmol); chloroform/toluene/THF 3:3:1 as a mobile phase; Yield: 40 mg of green solid (74%). This compound was obtained as a mixture of TPyzPz with some peripheral substituents exchanged for butoxy. ^{1}H NMR ($CDCl_3$/pyridin-d_5, 300 MHz) δ = 7.97–760 (br, 16H), 7.52–6.99 ppm (br, 24H; overlaps with residual signal of solvent). Signals of butoxy substituents were also detected at δ = 3.56, 1.49, 1.32, and 0.60 ppm as small and broad signals; ^{13}C NMR ($CDCl_3$/pyridin-d_5, 75 MHz) no signal was detected in carbon NMR except one small broad signal at δ 129.5 ppm that corresponds to aromatic carbons of phenyl; IR (ATR): ν = 3056, 2945, 1736, 1581, 1518, 1476, 1440, 1395, 1304, 1246, 1155, 1087, 1068, 1024, 1001, 967, and 912 cm^{-1}; MS (MALDI-TOF) *m/z*: no signals were detected due to weak ionization of sample.

Method D. **6a** (50 mg, 0.14 mmol); anhydrous zinc acetate (50 mg, 0,29 mmol); 3 h; chloroform/THF 3:1 as an eluent; Yield: 0.8 mg of green solid (2%); ^{1}H NMR ($CDCl_3$/pyridin-d_5, 300 MHz) δ = 7.23–7.72 ppm (m, 40 H); IR (ATR): ν = 2924, 2838, 1476, 1440, 1395, 1246, 1155, 1088, 1024, 967, and 778 cm^{-1}; ^{13}C NMR ($CDCl_3$/pyridin-d_5, 75 MHz) δ = 29.8, 129.7, the other signals were not detected due to low solubility of the sample; MS (MALDI-TOF) *m/z*: 2934.73 $[2M+K]^+$, 2918.77 $[2M+Na]^+$, 2895.75 $[2M]^+$, 1486.83 $[M+K]^+$, 1470.87 $[M+Na]^+$, 1447.89 $[M]^+$; UV/vis (THF): λ_{max}:657, 628sh, 599 and 383 nm.

Method E. **6a** (150 mg, 0.14 mmol); $Zn(quinoline)_2Cl_2$ (165 mg, 0.14 mmol); chloroform/THF 3:1 as an eluent; Yield: 23 mg of green solid (15%); MS (MALDI-TOF) *m/z*: 1447.89 $[M]^+$, 1470.89 $[M+Na]^+$, 1486.85 $[M+K]^+$, 2895.74 $[2M]^+$; The other analytical data correspond well with those mentioned in Method D.

*2,3,9,10,16,17,23,24-Octakis(2,6-dimethylphenylsulfanyl)-1,4,8,11,15,18,22,25-(octaaza)phthalocyaninato magnesium(II) (**7bMg**). Method C.* Magnesium (170 mg, 7.03 mmol); **6b** (400 mg, 1.00 mmol); eluent chloroform/THF 10:1 (R_f = 0.2); Yield: 300 mg of green solid (72%); ^{1}H NMR ($CDCl_3$/pyridin-d_5, 300 MHz) δ = 7.22–7.15 (m, 8H), 7.09 (d, *J* = 7.4 Hz; 16H), 2.40 ppm (s, 48H); ^{13}C NMR ($CDCl_3$/pyridin-d_5, 75 MHz) δ = 22.6, 129.0, 129.2, 130.0, 143.9, 147.2, and 157.0 ppm; IR (ATR): ν = 3058, 2955, 1514, 1462, 1377, 1239, 1164, 1104, 1050, 966, 849, 775, and 750 cm^{-1}; Elemental analysis calcd. (%) for $C_{88}H_{72}MgN_{16}S_8\times 4H_2O$: C 61.94, H 4.73, N 13.13; found C 61.77, H 4.74, N 12.98; MS (MALDI-TOF) *m/z*: 3264.35 $[2M]^+$, 1671.12 $[M+K]^+$, 1655.16 $[M+Na]^+$, 1632.16 $[M]^+$; UV/vis (THF): λ_{max} (ε): 660 (186 300), 631sh (25 700), 600 (26 400), 465sh (17 700), 388 nm (107 200 mol^{-1} cm^{-1} L).

*2,3,9,10,16,17,23,24-Octakis(2,6-dimethylphenylsulfanyl)-1,4,8,11,15,18,22,25-(octaaza)phthalocyanine (**7bH**). Method C.* Compound **7bMg** (190 mg, 0.12 mmol), *p*-TSA (230 mg, 1.22 mmol); chloroform/toluene/THF 70:30:3 as a mobile phase; Yield: 90 mg of green solid (46%). ^{1}H NMR ($CDCl_3$/pyridin-d_5, 300 MHz) δ = 2.38 (s, 48H), aromatic signals were too weak and overlapped with residual signal of solvent; ^{13}C NMR ($CDCl_3$/pyridin-d_5, 75 MHz) no signal was detected in carbon NMR; IR (ATR): ν = 3288, 3063, 2963, 1517, 1462, 1438, 1376, 1310, 1226, 1159, 1114, 1080, 1050, 1025, 962, 767, 746, and 718 cm^{-1}; Elemental analysis calcd. (%) for $C_{88}H_{74}N_{16}S_8\times 2H_2O$: C 64.13, H 4.77, N 13.60; found C 63.83, H 4.69, N 13.54; MS (MALDI-TOF) *m/z*: 1649.18 $[M+K]^+$, 1633.21 $[M+Na]^+$, 1610.22 $[M]^+$, 1546.25 $[M-SC_8H_8+OC_4H_9]^+$, 1506.19 $[M-C_8H_8]^+$; UV/vis (THF): λ_{max} (ε): 678 (93 900), 653 (75 700), 623 (25 800), 599 (19 800), 472 (38 400), 373 nm (86 100 mol^{-1} cm^{-1} L).

*2,3,9,10,16,17,23,24-Octakis(2,6-dimethylphenylsulfanyl)-1,4,8,11,15,18,22,25-(octaaza)phthalocyaninato Zinc(II) (**7bZn**). Method C.* Compound **7bH** (40 mg, 0.025 mmol), $Zn(CH_3COO)_2$ (45 mg, 0.25 mmol); chloroform/THF 10:1 as a mobile phase; Yield: 30 mg of green solid (81%). ^{1}H NMR ($CDCl_3$/pyridin-d_5, 500 MHz) δ signal were too weak and broad. The quality of the spectrum did not allow proper assignation of the signals; ^{13}C NMR ($CDCl_3$/pyridin-d_5, 125 MHz) 156.2, 145.7, 143.0, 130.8, 130.4, 129.2, 128.1, 21.6 ppm; IR (ATR): ν = 3295, 2912, 1623, 1517, 1462, 1376, 1321, 1240, 1163, 1114, 1050, 966, 847, 776, and 745 cm^{-1}; Elemental analysis calcd. (%) for $C_{88}H_{72}N_{16}S_8Zn\times 4H_2O$: C 60.48, H 4.61, N 12.82; found C 60.14, H 4.71, N 12.44; MS (MALDI-TOF) *m/z*: 1711.10 $[M+K]^+$, 1695.12 $[M+Na]^+$, 1672.13 $[M]^+$, 1568.10 $[M-C_8H_8]^+$; UV/vis (THF): λ_{max} (ε): 658 (236 500), 630sh, 598 (35 100), 473sh, 431sh and 381 nm (133 200 mol^{-1} cm^{-1} L).

2,3,9,10,16,17,23,24-Octakis(2,6-diisopropylphenylsulfanyl)-1,4,8,11,15,18,22,25-(octaaza)phthalocyaninato magnesium(II)

dx.doi.org/10.1021/jo402791c | J. Org. Chem. 2014, 79, 2082–2093

*(**7cMg**). Method C.* Magnesium (165 mg, 6.80 mmol); **6c** (500 mg, 0.971 mmol); eluent chloroform/THF 100:1 (R_f = 0.2); Yield: 399 mg of green solid (79%); ^{1}H NMR (300 MHz, $CDCl_3$/pyridine-d_5 3:1): δ = 1.32 (s, 48H), 1.34 (s, 48H), 4.00 (hept, J = 6.8 Hz, 16H), 7.44−7.51 (m, 16H), and 7.61−7.70 ppm (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$/pyridine-d_5 3:1): δ = 24.3, 32.8, 124.5, 126.6, 130.9, 145.8, 154.0, and 156.8 ppm; IR (ATR): ν = 2962, 2857, 1577, 1506, 1463, 1383, 1362, 1314, 1235, 1159, 1101, 1086, 1054, 1032, 964, 929, 846, 798, 773, 751, and 741 cm^{-1}; Elemental analysis calcd. (%) for $C_{120}H_{136}MgN_{16}S_8 \times 3H_2O$: C 67.43, H 6.70, N 10.49; found C 67.70, H 6.71, N 10.56; MS (MALDI-TOF) m/z: 2119.65 [M+K]$^+$, 2103.67 [M+Na]$^+$, 2080.68 [M]$^+$, 2037.75 [M-*i*Pr]$^+$; UV/vis (THF): λ_{max} (ε): 663 (230 800), 633sh, 605 (38 060), 467sh, 388 nm (154 000 mol^{-1} cm^{-1} L).

*2,3,9,10,16,17,23,24-Octakis(2,6-diisopropylphenylsulfanyl)-1,4,8,11,15,18,22,25-(octaaza)phthalocyanine (**7cH**). Method C.* Compound **7cMg** (250 mg, 0.12 mmol), *p*-TSA (230 mg, 1.1 mmol); chloroform/THF 50:1 as a mobile phase; Yield: 110 mg of green solid (45%). ^{1}H NMR (300 MHz, $CDCl_3$/pyridine-d_5 3:1): δ = −1.39 (s, 2H), 1.39 (s, 48H), 1.41 (s, 48H), 4.00 (hept, J = 6.8 Hz, 16H), 7.52−7.58 (m, 16H), and 7.72−7.79 ppm (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$/pyridine-d_5 3:1): δ = 24.4, 33.0, 124.7, 126.0, 131.3, 144.5, 146.9, 154.1, and 158.8 ppm; IR (ATR): ν = 3268, 3049, 2960, 2878, 1576, 1540, 1507, 1463, 1418, 1384, 1361, 1304, 1221, 1190, 1149, 1078, 1054, 1030, 1008, 956, 940, 799, 743, and 712 cm^{-1}; Elemental analysis calcd. (%) for $C_{120}H_{138}N_{16}S_8$: C 69.93, H 6.75, N 10.87; found C 69.70, H 6.72, N 10.86; MS (MALDI-TOF) m/z: 2097.67 [M+K]$^+$, 2081.70 [M+Na]$^+$, 2058.72 [M]$^+$, 2015.83 [M-*i*Pr]$^+$; UV/vis (THF): λ_{max} (ε): 680 (135 000), 658 (105 300), 627sh, 603sh, 479 (56 070), 377 nm (128 800 mol^{-1} cm^{-1} L).

*2,3,9,10,16,17,23,24-Octakis(2,6-diisopropylphenylsulfanyl)-1,4,8,11,15,18,22,25-(octaaza)phthalocyaninato Zinc(II) (**7aZn**). Method C.* Compound **7cH** (40 mg, 0.019 mmol), $Zn(CH_3COO)_2$ (35 mg, 0.19 mmol); chloroform as a mobile phase; Yield: 40 mg of green solid (99%). ^{1}H NMR (300 MHz, $CDCl_3$/pyridine-d_5 3:1): δ = 1.32 (s, 48H), 1.34 (s, 48H), 3.98 (hept, J = 6.8 Hz, 16H), 7.44−7.50 (m, 16H), and 7.61−7.69 ppm (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$/pyridine-d_5 3:1): δ = 24.3, 32.8, 124.6, 126.4, 131.0, 146.5, 150.3, 154.0, and 157.4 ppm; IR (ATR): ν = 3050, 2963, 2838, 1578, 1507, 1461, 1383, 1362, 1314, 1227, 1158, 1103, 1054, 1032, 965, 929, 843, 798, 775, and 741 cm^{-1}; Elemental analysis calcd. (%) for $C_{120}H_{136}N_{16}S_8Zn \times 4H_2O$: C 65.62, H 6.61, N 10.20; found 65.65, H 6.35, N 10.16; MS (MALDI-TOF) m/z: 2159.54 [M+K]$^+$, 2143.58 [M+Na]$^+$, 2120.57 [M]$^+$, 2077.69 [M-*i*Pr]$^+$; UV/vis (THF): λ_{max} (ε): 661 (190 900), 633sh, 601 (28 500), 477sh, 434sh, and 382 nm (115 200 mol^{-1} cm^{-1} L).

Method D. **6c** (50 mg, 0.097 mmol); anhydrous zinc acetate (77 mg, 0,097 mmol); chloroform as an eluent; Yield: 12 mg of green solid (23%); MS (MALDI-TOF) m/z: 2159.55 [M+K]$^+$, 2120.58 [M]$^+$, 2077.65 [M-iPr]$^+$.

Method E. **6c** (50 mg, 0.097 mmol); $Zn(quinoline)_2Cl_2$ (38 mg, 0.14 mmol); chloroform/THF 3:1 as an eluent; Yield: 12 mg of green solid (23%); MS (MALDI-TOF) m/z: 2159.56 [M+K]$^+$, 2143.57 [M+Na]$^+$, 2120.58 [M]$^+$, 2077.37 [M-*i*Pr]$^+$, 1928.51 [M-2,6-di*i*PrPhS]$^+$.

Method F. **6c** (50 mg, 0.097 mmol); lithium (123 mg, 0.68 mmol); crude product (approximately 40 mg); and anhydrous zinc acetate (35.5 mg, 0.19 mmol). Yield: 31 mg of green solid (60%); MS (MALDI-TOF) m/z: 2320.71 [2(M-8 × SC_6H_5+8 × OC_4H_9)]$^+$, 1520.45 [M-5 × SC_6H_5+5 × OC_4H_9]$^+$, 1400.43 [M-6 × SC_6H_5+6 × OC_4H_9]$^+$, 1280.40 [M-7 × SC_6H_5+7 × OC_4H_9]$^+$, 1160.38 [M-8 × SC_6H_5+8 × OC_4H_9]$^+$.

Method G(1). **6c** (50 mg, 0.097 mmol); anhydrous zinc acetate (9.6 mg, 0.02 mmol); DBU (0.014 mL, 0.095 mmol). Yield 28 mg of a green solid (54%); MS (MALDI-TOF) m/z: 2159.53 [M+K]$^+$, 2120.63 [M]$^+$, 2077.55 [M-*i*Pr]$^+$, 2039.53 [M-SC_6H_5+OC_4H_9+K]$^+$, 2000.56 [M-SC_6H_5+OC_4H_9]$^+$, 1957.57 [M-SC_6H_5+OC_4H_9-*i*Pr]$^+$, 1919.51 [M-2 × SC_6H_5+2 × OC_4H_9+K]$^+$, 1880.52 [M-2 × SC_6H_5+2 × OC_4H_9]$^+$, 1837.48 [M-2 × SC_6H_5+2 × OC_4H_9-*i*Pr]$^+$, 1760.49 [M-3 × SC_6H_5+3 × OC_4H_9]$^+$, 1640.48 [M-4 × SC_6H_5+4 × OC_4H_9]$^+$.

Method G(10). **6c** (50 mg, 0.097 mmol); anhydrous zinc acetate (19 mg, 0.04 mmol); DBU (0.14 mL, 0.95 mmol); Yield: 6 mg of green solid (17%); MS (MALDI-TOF) m/z: 2159.52 [M+K]$^+$, 2143.55 [M+Na]$^+$, 2121.57 [M+H]$^+$, 2077.52 [M-*i*Pr]$^+$, 2039.50 [M-SC_6H_5+OC_4H_9+K]$^+$, 2023.53 [M-SC_6H_5+OC_4H_9+Na]$^+$, 2000.55 [M-SC_6H_5+OC_4H_9]$^+$, 1957.50 [M-SC_6H_5+OC_4H_9-*i*Pr]$^+$, 1919.48 [M-2 × SC_6H_5+2 × OC_4H_9+K]$^+$, 1880.52 [M-2 × SC_6H_5+2 × OC_4H_9]$^+$, 1837.47 [M-2 × SC_6H_5+2 × OC_4H_9-*i*Pr]$^+$, 1761.50 [M-3 × SC_6H_5+3 × OC_4H_9]$^+$.

*2,3,9,10,16,17,23,24-Octakis(2,6-di-tert-butylpropylphenylsulfanyl)-1,4,8,11,15,18,22,25-(octaaza)phthalocyaninato Magnesium(II) (**7dMg**). Method C.* Magnesium (107 mg, 4.42 mmol); **6d** (360 mg, 0.63 mmol); eluent chloroform/THF 20:1 (R_f = 0.41); Yield: 143 mg of green solid (39%); ^{1}H NMR (300 MHz, $CDCl_3$/pyridine-d_5 3:1): δ = 1.64 (s, 144H), 7.45 (t, J = 8 Hz, 8H), and 7.62 ppm (d, J = 8 Hz, 16H); ^{13}C NMR (75 MHz, $CDCl_3$/pyridine-d_5 3:1): δ = 32.8, 38.3, 126.0, 126.8, 130.8, 145.6, 157.5, and 158.4 ppm; IR (ATR): ν = 2963, 2931, 2868, 1573, 1481, 1458, 1393, 1362, 1314, 1248, 1225, 1151, 1103, 1036, and 962 cm^{-1}; Elemental analysis calcd. (%) for $C_{136}H_{168}MgN_{16}S_8 \times 6H_2O$: C 67.62, H 7.51, N 9.28; found C 67.75, H 7.58, N 9.17; MS (MALDI-TOF) m/z: 2305.88 [M]$^+$, 2247.80; UV/vis (THF): λ_{max} (ε): 720sh, 661 (238 610), 633 (35 090), 600 (31 780), 466sh, and 382 nm (146 730 mol^{-1} cm^{-1} L).

*2,3,9,10,16,17,23,24-Octakis(2,6-di-tert-butylpropylphenylsulfanyl)-1,4,8,11,15,18,22,25-(octaaza)phthalocyanine (**7dH**). Method C.* Compound **7dMg** (35 mg, 0.015 mmol), *p*-TSA (20 mg, 0.11 mmol); toluene/THF 30:1 as a mobile phase; Yield: 29 mg of green solid (84%). ^{1}H NMR (300 MHz, $CDCl_3$/pyridine-d_5 3:1): δ = 1.66 (s, 144H), 7.55 (t, J = 8 Hz, 8H), and 7.70 ppm (d, J = 8 Hz, 16H); ^{13}C NMR (75 MHz, $CDCl_3$/pyridine-d_5 3:1): δ = 32.7, 38.2, 125.6, 126.7, 130.8, and 157.3 ppm; IR (ATR): ν = 3325, 2964, 2917, 2867, 1573, 1508, 1481, 1456, 1393, 1361, 1306, 1240, 1221, 1193, 1139, 1105, 1076, 1034, and 955 cm^{-1}; Elemental analysis calcd. (%) for $C_{136}H_{170}N_{16}S_8 \times 2H_2O$: C 70.36, H 7.55, N 9.65; found C 70.55, H 7.70, N 9.57; MS (MALDI-TOF) m/z: 2321.85 [M+K]$^+$, 2305.90 [M+Na]$^+$, 2282.90 [M]$^+$, 2225.83; UV/vis (THF): λ_{max} (ε): 715 (71 450), 683 (64 650), 654 (41 650), 472sh, and 379 nm (100 180 mol^{-1} cm^{-1} L).

*2,3,9,10,16,17,23,24-Octakis(2,6-di-tert-butylpropylphenylsulfanyl)-1,4,8,11,15,18,22,25-(octaaza)phthalocyaninato Zinc(II) (**7dZn**). Method C.* Compound **7dH** (30 mg, 0.013 mmol), $Zn(CH_3COO)_2$ (24 mg, 0.13 mmol); toluene/THF 3:3:1 as a mobile phase; Yield: 22 mg of green solid (71%). ^{1}H NMR (300 MHz, $CDCl_3$/pyridine-d_5 3:1): δ = 1.71 (s, 144H), 7.49 (t, J = 8 Hz, 8H), and 7.66 ppm (d, J = 8 Hz, 16H); ^{13}C NMR (75 MHz, $CDCl_3$/pyridine-d_5 3:1): δ = 32.8, 38.3, 125.9, 126.8, 130.9, 145.5, 157.5, and 158.7 ppm; IR (ATR): ν = 2964, 2903, 2861, 1575, 1507, 1507, 1481, 1457, 1394, 1362, 1315, 1249, 1227, 1151, 1105, 1037, and 963 cm^{-1}; Elemental analysis calcd. (%) for $C_{136}H_{168}N_{16}S_8Zn \times 4H_2O$: C 67.47, H 7.33, N 9.26; found C 67.21, H 7.42, N 9.07; MS (MALDI-TOF) m/z: 2384.76 [M+K]$^+$, 2368.77 [M+Na]$^+$, 2345.80 [M]$^+$, 2325.72, 2287.73; UV/vis (THF): λ_{max} (ε): 659 (237 870), 631sh, 599 (31 650), 472sh, 434sh, and 382 nm (143 490 mol^{-1} cm^{-1} L).

Singlet Oxygen Production and Fluorescence Emission. Samples for photophysical measurements were taken from Method A (**7bZn**, **7cZn**, and **7dZn**) or from Method C (**7aZn**) and purified further by scrapping from TLC plate (mobile phases mentioned for each compound in synthetic part), extracting to THF, and evaporation to dryness under the reduced pressure.

Singlet oxygen quantum yields (Φ_Δ) were determined in THF according to a previously described method[42] using the decomposition of 1,3-diphenylisobenzofuran (DPBF) with unsubstituted zinc phthalocyanine (ZnPc) as the reference ($\Phi_{\Delta(THF)}$ = 0.53). In detail, the procedure was as follows: 2.5 mL of a stock solution of DPBF in THF (5 × 10^{-5} M) was transferred into a 10 × 10 mm quartz optical cell and bubbled with oxygen for 1 min. Defined amount of concentrated stock solution of the tested TPyzPz in THF (usually 20 μL) was added. Absorbance of the final solution in Q-band maximum was always about 0.1. The solution was stirred and irradiated for defined times using a xenon lamp (100 W, ozone free XE

dx.doi.org/10.1021/jo402791c | J. Org. Chem. 2014, 79, 2082−2093

DC short arc lamp, Newport). Incident light was filtered through a water filter (6 cm) and cutoff filter OG530 to remove heat and light under 523 nm, respectively. Decrease of DPBF in solution with irradiation time was monitored at 415 nm. The Φ_Δ of the TPyzPz was calculated using eq 1:

$$\Phi_\Delta^S = \Phi_\Delta^R \frac{k^S I_{aT}^R}{k^R I_{aT}^S} \quad (1)$$

where k is a slope of the plot of the dependence of $\ln(A_0/A_t)$ on irradiation time t, with A_0 and A_t being the absorbances of the DPBF at 415 nm before irradiation and after irradiation time t, respectively. I_{aT} is a total amount of light absorbed by the TPyzPz. Superscripts R and S indicate reference and sample, respectively. I_{aT} is calculated as a sum of intensities of the absorbed light I_a at wavelengths from 523 to 850 nm (step 0.5 nm). Light under 523 nm is completely filtered off by OG530 filter and light above 850 nm is not absorbed by the studied TPyzPzs. I_a at given wavelength is calculated using Beer's law (eq 2):

$$I_a = I_0(1 - e^{-2.3A}) \quad (2)$$

where I_0 is a transmittance of the filter at the given wavelength and A absorbance of the TPyzPz at this wavelength. All experiments were performed three times and data presented in the paper represent a mean of these three experiments. Estimated error ±10%.

Fluorescence quantum yields (Φ_F) were determined in THF by a comparative method with ZnPc as the reference ($\Phi_{F(THF)} = 0.32$[13]). The Φ_F was calculated using eq 3:

$$\Phi_F^S = \Phi_F^R \left(\frac{F^S}{F^R}\right)\left(\frac{1 - 10^{-A^R}}{1 - 10^{-A^S}}\right) \quad (3)$$

where F is the integrated area under the emission spectrum, and A is the absorbance at the excitation wavelength. Superscripts R and S correspond to the reference and sample, respectively. Absorption in Q-band was kept below 0.05 in order to eliminate an inner filter effect. Excitation wavelength was set at 600 nm, emission wavelength monitored during collecting the excitation spectra was 730 (**7aZn**, **7bZn**, and **7dZn**) or 750 nm (**7cZn**). All experiments were performed three times and presented data represent the mean of these three experiments. Estimated error ±15%.

■ ASSOCIATED CONTENT

Supporting Information

MS spectra of **7a-dZn**, TLC of **7dZn**, TLC of **7dMg**, **7dH** and **7dZn**, Absorption spectra of **7a−d** (magnesium, metal free and zinc complexes), Emission spectra **7a−dZn**, Comprehensive discussion on X-ray structures of **6a−d**, and ^{1}H NMR and ^{13}C NMR spectra of all new prepared compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Financial support from Czech Science Foundation (Project No. 13-27761S) is gratefully acknowledged. Authors would like thank Lucie Novakova for the measurement of HR-MS.

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