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Efficient Synthesis of ABAB Functionalized Phthalocyanines

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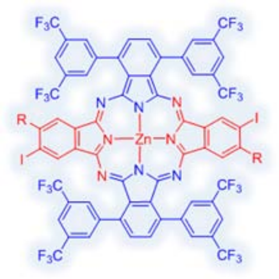
Supporting Information

ABSTRACT: ABAB-type Zn(II) phthalocyanines, crosswise-functionalized with two and four iodine atoms, respectively, have been efficiently prepared using statistical condensation procedures. Key to the selective preparation of the opposite ABAB isomers versus the adjacent AABB ones is the use of bulky 3,6-(3′,5′-bis(trifluoromethyl)phenyl)phthalonitrile with hampered self-condensation capabilities.



The extraordinary optoelectronic characteristics of phthalocyanines (Pcs)[1] have inspired researchers to implement these chromophores into multicomponent systems with other electroactive units,[2] and also to link them to nanomaterials[3] or semiconducting nanocrystalline materials to achieve systems for solar energy conversion schemes.[4] For that purpose, it is compulsory to prepare unsymmetrically substituted Pcs holding, at least, one reactive group for further chemical transformations. In this regard, most of the effort has been devoted to the preparation of the so-called A_3B Pcs,[5] provided that A and B refer to differently substituted isoindolic units forming the Pc core, the B unit containing the reactive group for further transformations. Statistical approaches are usually applied to prepare A_3B Pcs, even if they demand the use of chromatographic techniques for the isolation of the desired macrocycles from the mixture of compounds. Isolation of the desired Pc is facilitated if bulky, hydrophobic groups, affording solubility and hampering aggregation, are attached to the A unit.

On the other hand, A_2B_2 Pcs are elusive compounds, difficult to prepare by statistical condensation.[6] The reason is that the two possible isomers, namely ABAB and AABB, are formed and, as the two compounds show similar solubility features, they are frequently eluted in the same fractions. Examples of the preparation of ABAB and AABB Pcs by statistical methods are scarce.[7] Directed approaches have been applied for the selective preparation of each of the isomers.[6] Particularly appealing is the selective preparation of the D_{2h} ABAB isomer, since this geometry permits complex linear arrangements to be created, such as Pc-containing polymers,[7c] and also linking of different electroactive subunits to the chromophore. ABAB Pcs have been selectively prepared by cross-condensation of two different phthalyl derivatives, namely 1,3-diiminoisoindoline and 1,3,3-trichloroisoindolenine,[8] but this method is only feasible when the latter is either functionalized with NO_2 moieties or lacks any functional group. Therefore, ABAB Pcs programmed for their further implementation into more complex structures remain to be prepared.

Here, we report on the preparation of ABAB Pcs **1a,b** (see Scheme 1), containing two isoindoles functionalized with bulky bis(trifluoromethyl)phenyl groups at the nonperipheral positions and two faced isoindoles containing iodine atoms, by cross-condensation of the two corresponding precursors. The presence of rigid phenyl groups in the 3,6-positions of the phthalonitrile is a key factor in hampering their self-condensation. In fact, preparation of ABAB Pcs had been previously reported starting from 3,6-diphenylphthalonitrile[9] or 1,4-diphenyl-2,3-dicyanonaphthalene.[10] However, it should be noted that octakis[α-aryl]phthalocyanines have been prepared under certain conditions,[11] thus indicating that functionalization with bare phenyl rings at the α-positions of the dinitrile precursors is not enough to avoid the formation of Pcs with adjacent phenyl susbstituents. In this regard, the presence of bis(trifluoromethyl)phenyl groups in our target compound is not trivial; CF_3 is a rather bulky substituent,[12] with a van der Waals radius between those of *i*-Pr and *t*-Bu groups, thus favoring the process toward the formation of the crosswise Pc **1a,b** (see Scheme 1). Also, the intermolecular attractive force between fluorine-containing compounds is small,[13] which facilitates the separation of **1a,b** from the mixture of Pcs formed in the synthesis. On the other hand, the presence of iodine atoms in **1a,b** provides high relevance to the molecule, offering a tool for functional group interconversion, and also an anchoring point for linking the Pc to other units and/or nanomaterials through metal-catalyzed reactions.

A subset of our experiments toward the preparation of 3,6-(3′,5′-bis(trifluoromethyl)phenyl)phthalonitrile **3** are summarized in Table 1. The synthesis of 3,6-diarylphthalonitriles had been previously described in the literature, using phenylboronic

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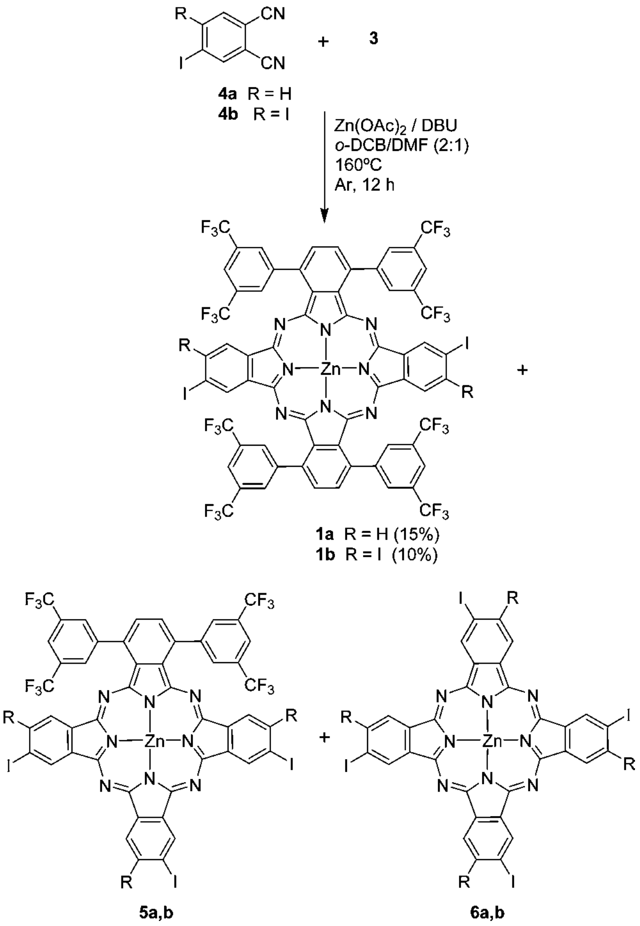
Scheme 1. Statistical Synthesis of Pcs 1a,b under Optimized Conditions

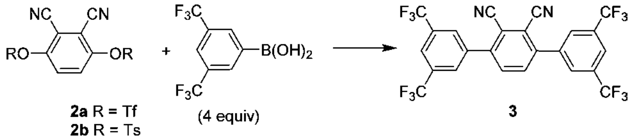


reagents and 3,6-bis(trifluoromethanesulfonyloxy)phthalonitrile **2a** with $Pd(PPh_3)_4$ as the catalyst and Na_2CO_3 as the base in toluene/water,[14] but in our case (i.e., use of 3,5-bis(trifluoromethyl)phenylboronic acid) the reaction proceeded with a very low yield (entry 1). In the past five years, nickel-catalyzed Suzuki–Miyaura conditions[15] have been successfully applied to many substrates. Using $NiCl_2(PCy_3)_2$ as the catalyst and $PCy_3 \cdot HBF_4$ as the ligand,[16] compound **3** was isolated in 25% yield (entry 2). Better conversions were achieved when using a Ni(II) catalyst and the bistosylate **2b**[17] as starting material (entry 3). However, a strong experimental drawback was that the reaction could not be scaled up above 150 mg. Considering that the yield was still low and that other species were formed during the process, we checked the thermal stability of the sulfonic esters **2a,b**. Evidence of degradation appeared when heating both compounds over 100 °C, driving us to reduce the temperature of the coupling reaction. Therefore, an improved 42% yield was obtained when using **2a**, $NiCl_2(PCy_3)_2$ as a catalyst, and K_3PO_4 as a base in 1,4-dioxane at 90 °C under MW irradiation (entry 4). Revisiting previously applied Pd(II)-catalyzed Suzuki–Miyaura conditions, but keeping the temperature below 100 °C (entries 6–7), did not afford appreciable conversions. Eventually, optimal yields were obtained by changing the base to K_2CO_3, in DMF as the solvent, and at 90 °C under MW irradiation (entry 8).

With the bulky phthalonitrile **3** in hand, we proceeded to carry out the mixed statistical condensation with 4-iodophthalonitrile **4a** to prepare Zn(II)Pc **1a** (Scheme 1). Usual conditions were first applied, namely, heating a 1:1 ratio of the precursors in the presence of $Zn(OAc)_2$ and DBU in penthanol for 12 h.

Under these conditions only three of the six possible Pcs were formed, which were satisfactorily separated by column chromatography. The first compound to elute was the target ABAB Pc **1a**, isolated in 4% yield, sequentially followed by the AB_3 Pc **5a** (18%) and the B_4 Pc **6a** (25%) (see Scheme 1).[18] It is important to mention that none of the possible compounds with adjacent bis(trifluoromethyl)phenyl-substituted isoindoles were formed. Therefore, the approach proved fruitful in terms of selectivity, but rather inefficient in terms of yield. Considering that phthalonitrile **3** is not consumed in self-condensation processes, relative yield in **1a** should be higher. Thus, 3,6-disubstituted phthalonitrile **3** seems much less reactive than 4-iodophthalonitrile **4a**, and the cross-condensation processes between them is not favored either. Aiming at increasing the yield in **1a** the proportion of sterically hindered phthalonitrile **3** was increased, but it did not afford a significant improvement and complicated the purification process. Further attempts to improve the yield in **1a** while maintaining the selectivity toward the formation of the less sterically hindered compounds were performed. First, microwave irradiation in

Table 1. Investigation of Conditions for the Suzuki–Miyaura Cross-Coupling Reaction of Sulfonic Esters 2a–b with 3,5-Bis(trifluoromethyl)phenylboronic Acid To Obtain 3



entry	catalyst	base	solvent	ester	yield
1	$Pd(PPh_3)_4$[a]	Na_2CO_3	toluene/H_2O[c]	**2a**	9%
2	$NiCl_2(PCy_3)_2/PCy_3 \cdot HBF_4$[a]	K_3PO_4	1,4-dioxane[c]	**2a**	25%
3	$NiCl_2(PCy_3)_2/PCy_3 \cdot HBF_4$[a]	K_3PO_4	1,4-dioxane[c]	**2b**	30%
4	$NiCl_2(PCy_3)_2/PCy_3 \cdot HBF_4$[a]	K_3PO_4	1,4-dioxane[d,e]	**2b**	42%
5	$NiCl_2(PCy_3)_2/PCy_3 \cdot HBF_4$[a]	K_3PO_4	1,4-dioxane[d,e]	**2a**	35%
6	$Pd(PPh_3)_4$[a]	Na_2CO_3	toluene/H_2O[d,e]	**2a**	–
7	$Pd(PPh_3)_4$[b]	Na_2CO_3	DME[c]	**2a**	8%
8	$Pd(PPh_3)_4$[b]	K_2CO_3	DMF[d,e]	**2a**	70%

[a] 10% mol. [b] 5% mol. [c] Reaction at reflux temperature. [d] Reaction at 90 °C. [e] Reaction under MW irradiation.

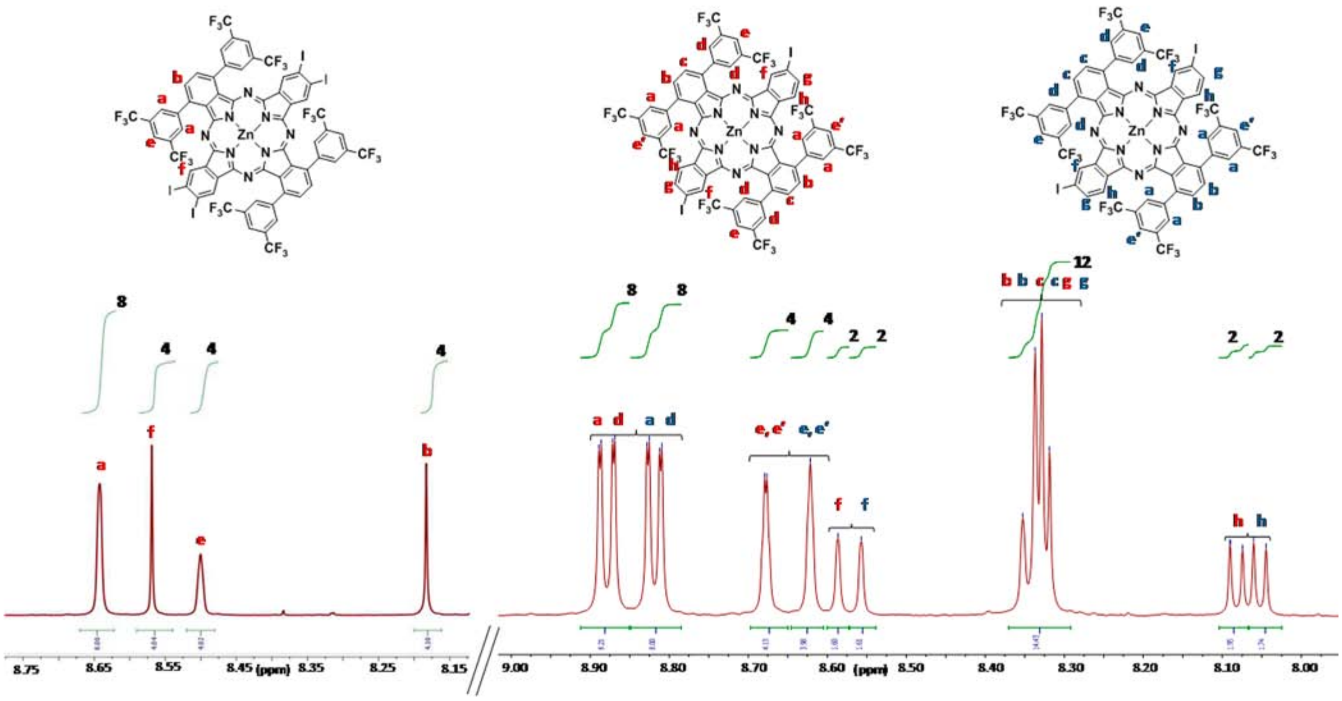


Figure 1. Magnification of the aromatic region of the ^{1}H NMR spectra in THF-d_8 of **1a** (right side) and **1b** (left side).

similar conditions brought about an increase in the yield from 4% to 10%. Major improvements were achieved by changing the solvent to DMF/*o*-DCB mixtures and increasing the reaction temperature to 160 °C, which led to a 15% yield of isolated product (i.e., **1a**) for a 1:1 ratio of the starting phthalonitriles (Scheme 1).[19] Changing to a 2:1 ratio of **3** and **4a**, respectively, did not afford a worthwhile increase of the yield in **1a**. Next, we undertook the preparation of **1b** under the optimized conditions found for **1a** (Scheme 1),[19] but only a 10% yield was achieved for this compound. The structure of Pcs **1a**,**b** was unequivocally confirmed by MALDI-TOF mass spectrometry, UV−vis, and NMR. Strong evidence of the successful preparation and isolation of the D_{2h} ABAB compounds arises from the highly symmetric ^{1}H NMR of **1b**. In Figure 1, magnification of the aromatic part shows two singlets for the protons of the bis(trifluoromethyl)phenyl rings, and two singlets for the two different types of aromatic, Pc-centered nuclei. For **1a**, however, splitting of the signals corresponding to the bis(trifluoromethyl)phenyl rings occurs, owing to the presence of different chemical environments imposed by the presence of only one substituent in the iodine-functionalized isoindoles. As a consequence of the latter, an increased number of signals corresponding to the Pc protons is also observed. Additionally, **1a** is comprised of a mixture of two regioisomers which differ in the relative position of the two iodine atoms (i.e., *syn* and *anti*). As shown in Figure 1, for each type of protons, two sets of signals of similar intensity are discernible, which are consistent with the different chemical environments for related protons of the two component regioisomers present in a nearly equimolar mixture. This assignment is supported by the COSY spectrum (see Supporting Information), which shows correlations between signals arising from the same isomer.[20] Also, the ^{19}F NMR spectrum of **1a** features four close singlets, owing to the presence of CF_3 groups with two different environments for each of the regioisomers. Worthy of mention is also the fact that all the signals for **1a** and **1b** are perfectly resolved, as expected for compounds with hampered aggregation capabilities.

The UV−vis spectrum of **1a** (Figure 2) showed symmetric, split Q bands (i.e., at 675 and 691 nm in THF), as it is generally observed in Pcs with D_{2h}-symmetry, and in face-to-face substituted derivatives in particular.[7d] However, D_{2h} Pc **1b** exhibits only one Q-band in its absorption spectrum (Figure 2). This observation can be rationalized considering not only the symmetry of the Pc derivative but also the effect that the substituents exert on the electronic levels of the aromatic core. Therefore, in the case of **1b**, the electronic effect imparted by this particular substitution counterbalances the splitting of the electronic levels produced by the symmetry.

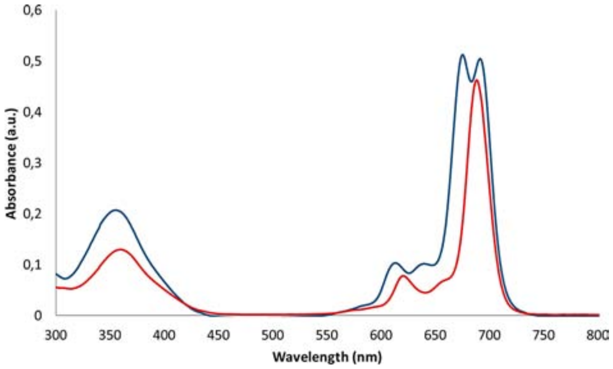


Figure 2. UV−vis of **1a** (blue line) (concn = 4.4 × 10^{-6} M) and **1b** (red line) (concn = 2.0 × 10^{-6} M) in THF.

In summary, ABAB Zn(II)Pcs **1a** and **1b** have been efficiently prepared using statistical condensation of iodophthalonitriles **4a**,**b** and bulky phthalonitrile **3**, which was synthesized following Suzuky−Miyaura protocols. Remarkably, Pcs containing adjacent bis(trifluoromethyl)phenyl moieties are not formed during the cyclization process; therefore, AABB isomers are not present in the mixture, thus facilitating the isolation of the target compounds **1a** and **1b**. The most relevant feature of this Pc is the crosswise functionalization of the Pc with iodine atoms, which can lead to unprecedented multicomponent systems based on Pcs.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Detailed experimental procedures, UV−vis, IR, NMR, and MALDI spectra. 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.

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(17) The use of tosylate **2b** is a very attractive alternative because it is an easily available starting material. The preparation of **2b** was previously reported: Kobayashi, N.; Ogata, H.; Nonaka, N.; Luk'yanets, E. A. *Chem.—Eur. J.* **2003**, *9*, 5123.

(18) Compounds **5a** and **6a** were identified by MALDI-TOF mass spectrometry.

(19) **3** (0.597 mmol, 330 mg), phthalonitrile **4a** or **4b** (0.597 mmol), and anhydrous Zn(OAc)$_2$ (0.597 mmol, 110 mg) were placed in a 25 mL flask equipped with a magnetic stirrer, and then 6 mL of *o*-diclorobenzene/DMF 2:1 were added. The mixture was heated to 160 °C for 12 h under an Ar atmosphere, and after cooling, the solvent was removed under vacuum. The crude was purified by silica-gel column chromatography (hexane/THF 4:1), the first fraction to elute containing the desired product, followed by compounds **5a,b** and **6a,b**.

(20) From the spectroscopic data available, it is not possible to assign each set of signals to a particular regioisomer.