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Synthesis of water-soluble subphthalocyanines

Łukasz Łapok[a], Christian G. Claessens[b], D. Wöhrle[a,*], T. Torres[b,*]

[a] Institute of Organic and Macromolecular Chemistry, NW 2, University of Bremen, Bremen, Germany
[b] Universidad Autónoma de Madrid, Departamento de Química Orgánica, Campus de Cantoblanco, Madrid, Spain

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ABSTRACT

The syntheses of positively and zwitterionically charged subphthalocyanines (SubPcs) are described for the first time. The SubPcs contain alkylated pyridinium substituents located either at the peripheral or at the axial positions of the macrocycle. The compounds were shown to be fairly water soluble.

The development of new water-soluble dyes is a research area of constant interest on account of their multiple applications in catalytic photooxidation,[1] photodynamic therapy,[2] and for other biologically relevant purposes. In this context, phthalocyanines[3] (Pcs) are among the most popular dyes that were shown to be particularly relevant photosensitizers in many different photoinduced processes.[4] In contrast, little is known about their lower homologues, the subphthalocyanines[5] (SubPcs) comprising a 14 π-electron non-planar aromatic macrocycle made of three diiminoisoindole units *N*-fused around a central boron atom. SubPcs show very attractive photophysical and electrochemical properties, and are interesting for applications as chromophores in nonlinear optics,[6] in OLEDs,[7] in photovoltaic devices,[8] and in multicomponent donor-acceptor systems.[9] Synthesis of water-soluble subphthalocyanines still remains a particularly difficult task,[10] since many phthalonitriles successfully employed in phthalocyanine synthesis are incompatible with boron trihalides employed in their formation reaction.[11] The present Letter summarizes efforts toward making these compounds water-soluble through their functionalization with pyridinium salts.

Triiodosubphthalocyanine **1** was prepared in 24% overall yield in a one-pot procedure by cyclotrimerization of 4-iodophthalonitrile with BCl_3 followed by chlorine exchange with phenol.[12] The presence of phenol improves solubility and stability of the resulting subphthalocyanine. SubPc **1** was obtained as a 3 to 1 mixture of C_1 and C_3 regioisomers, respectively. Apart from the expected signals, ^{1}H NMR spectrum of **1** shows a somewhat shielded doublet at 5.36 corresponding to the protons close to the SubPc ring, which feel the strong ring current produced by the aromatic core.

The 3-pyridylethynyl groups were grafted at the periphery of the macrocycle, as illustrated in Scheme 1, by Sonogashira catalytic cross-coupling reaction between SubPc **1** and an excess of 3-ethynylpyridine in triethylamine in the presence of catalytic amounts of $Pd(PPh_3)_2Cl_2$ and CuI. The reaction gave a mixture of mono- (**2c**, 1.3%), di- (**2b**, 14%), and tri-substituted (**2a**, 56%) subphthalocyanines that were characterized individually.

Treatment of **2a** with an excess of methyl iodide in DMF afforded tricationic SubPc **3** in 78% yield (Scheme 2). Quaternization of **2a** with an excess of 1,3-propanesultone led to the zwitterionic subphthalocyanine **4** in 83% yield. Compounds **3** and **4** were characterized by ESI mass spectrometry and IR spectroscopy. The presence of SO_3 group in **4** gave rise to strong absorptions at 1191 cm^{-1} (ν_{as}, SO_2) and 1043 cm^{-1} (ν_{sym}, SO_2).

The next target compound was the more flexible tris-2-pyridylethylsubphthalocyanine **7**. The strategy described above to prepare compound **2a** was adapted to the synthesis of precursor **5a** with its subsequent conversion into **7** (Scheme 3).[13] Thus, 2-ethynylpyridine was coupled to triiodosubphthalocyanine **1** in triethylamine at room temperature using catalytic amounts of $Pd(PPh_3)_2Cl_2$ and CuI. The main product was identified as tri-substituted derivative **5a**, and was isolated in 42% yield. The two other fractions were characterized as di-substituted **5b** and mono-substituted **5c** derivatives, and were isolated in 20% and 5% yields, respectively (Scheme 3). Treatment of **5a** with a stream of gaseous hydrogen in the presence of Pd/C catalyst gave SubPc **6** in 61% yield after column chromatography on silica gel. The Q-band of **6** experiences a bathochromic shift with respect to that

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* Corresponding authors. Tel.: +34 91 497 4151; fax: +34 91 497 3966 (T.T.).
E-mail address: tomas.torres@uam.es (T. Torres).

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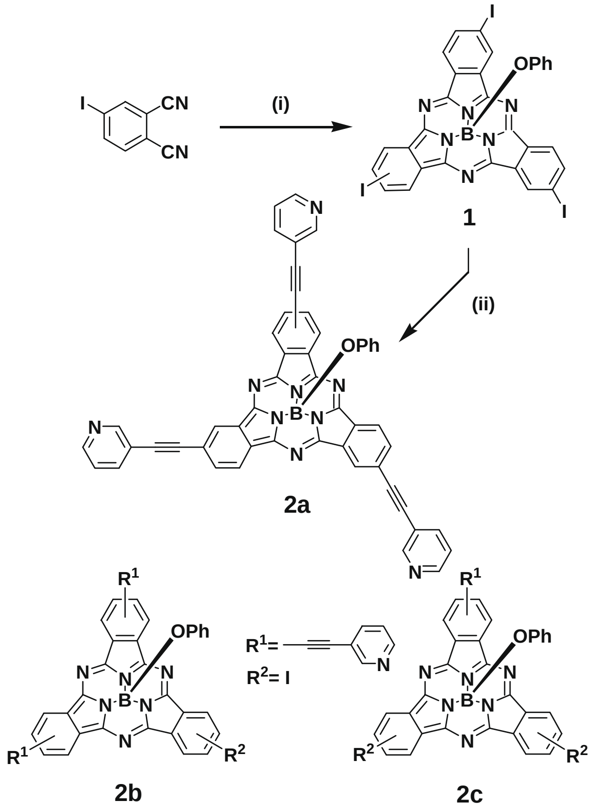
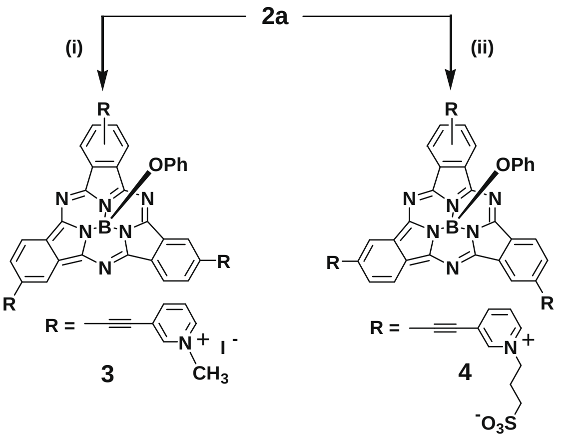
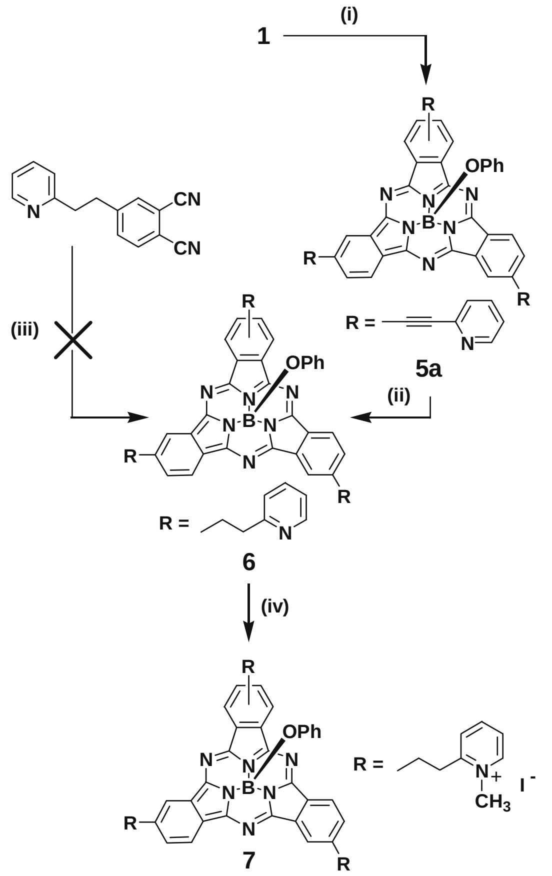


Scheme 1. Synthesis of SubPcs **1** and **2a-c**. Reagents and conditions: (i) BCl_3, *p*-xylene, reflux, N_2, 1 h, then phenol, toluene, 120 °C, 12 h (24%); (ii) $PdCl_2(PPh_3)_2$, CuI, TEA, rt, N_2, 20 h.



Scheme 2. Synthesis of cationic SubPc **3** and zwitterionic SubPc **4**. Reagents and conditions: (i) DMF, CH_3I, 50 °C, N_2, 4 h (78%); (ii) DMF, 1,3-propanesultone, 50 °C, N_2, 4 h (83%).



Scheme 3. Synthesis of SubPcs **5a**, **6** and **7**. Reagents and conditions: (i) $PdCl_2(PPh_3)_2$, CuI, TEA, rt, N_2, 20 h (42%); (ii) $MeCN/CH_2Cl_2$, Pd/C, H_2, 7 h (61%); (iii) BCl_3, *p*-xylene, reflux, 15 min; (iv) DMF, CH_3I, rt, N_2, 4 h (87%).

of **5a**, indicating a decrease of the conjugation associated with the reduction of the unsaturated carbon–carbon bonds of **5a**. The strong absorption in the IR spectrum of **5a** at 2213 cm^{-1} characteristic of a triple bond is no longer present in that of SubPc **6**. Instead, new bands appear at ca. 2900 cm^{-1} in accordance with the presence of alkyl functionality in **6**. The reaction of SubPc **6** with an excess of methyl iodide in DMF at room temperature afforded tricationic SubPc **7** in 87% yield (Scheme 3). SubPc **7** was characterized by ESI–MS (*m/z* 282.8 $[M]^{3+}$).

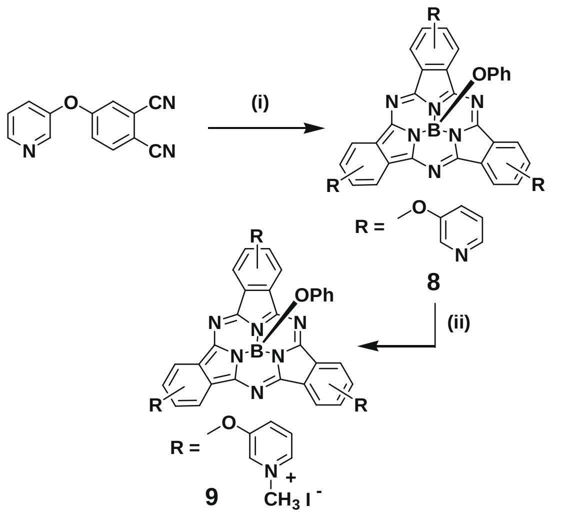
The formation of SubPcs from arylether phthalonitriles is usually fairly low yielding as a consequence of their poor compatibility with boron trihalides.[14] Nonetheless, we decided to employ 4-(3-pyridyloxy)phthalonitrile since this moiety, when quaternized, provides very good water solubility in the case of Pcs.[15]

Thus, 4-(3-pyridyloxy)phthalonitrile was condensed in the presence of BCl_3 in *p*-xylene at reflux for 15 minutes to afford SubPc **8** in 12% yield (Scheme 4). The resulting SubPc was reacted in situ with phenol in toluene, so as to incorporate an axial phenoxy group. This functionalization was found necessary since column chromatography of the chloro-substituted intermediate over silica gel yielded considerable amounts of axially hydroxy-substituted SubPc.

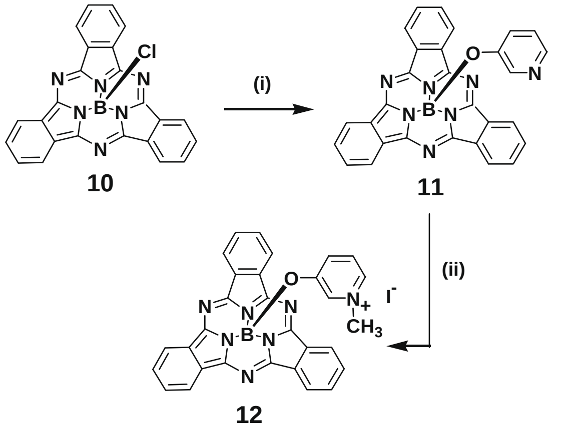
SubPc **8** was N-methylated with methyl iodide in DMF. The reaction gave SubPc **9** in 98% yield. Both SubPc **8** and **9** show absorption bands at around 1272 cm^{-1} in their IR spectra in accordance with the presence of arylether groups (Ar–O–Ar).

In order to attach the water-solubilizing pyridinium group at the apical position of the macrocycle, chlorosubphthalocyanine **10** and 3-hydroxypyridine were reacted in toluene at 120 °C to give subphthalocyanine **11** in 63% yield (Scheme 5). The structure of **11** was confirmed by ESI–MS and ^{1}H NMR. N-Methylation of **11** with an excess of methyl iodide in DMF afforded after 2 h the final 3-(***N***-methyl)pyridyloxy[subphthalocyaninato] boron(III) iodide **12** in 93% yield.

Positively charged SubPcs **3**, **7**, and **9**, with the exception of axially substituted SubPc **12**, exhibit good solubility in water (see Table 1). SubPc **12** is only sparingly soluble in water, as it incorporates only one pyridinium group. Zwitterionic compound **4** exhibits lower solubility in water in comparison to the positively charged derivatives (Table 1). The solubility of **4** is greatly in-



Scheme 4. Synthesis of pyridyloxy-substituted SubPc **8**. Reagents and conditions: (i) BCl_3, *p*-xylene, N_2, reflux, 15 min, then phenol, DMF, N_2, 120 °C, 2 h (12%); (ii) DMF, CH_3I, 50 °C, N_2, 2 h (98%).



Scheme 5. Synthesis of axially substituted water-soluble subphthalocyanine **12**. Reagents and conditions: (i) toluene, 120 °C, N_2, 12 h (63%); (ii) DMF, CH_3I, N_2, 2 h (93%).

Table 1
Solubility of positively charged photosensitizers[a]

Compound	Solubility					
	H_2O	DMF	DMSO	MeOH	Acetone	CH_2Cl_2
3	+++	+++	+++	+++	–	–
4	++	+	++	+	–	–
7	+++	+++	+++	++	–	–
9	+++	+++	+++	++	–	–
12	+	+++	+++	++	++	++

[a] +++ very good solubility, ++ moderate solubility, + only sparingly soluble, – not soluble.

creased at higher pH value or in the presence of inorganic salts (e.g., 6 M KCl solution), as increasing ionic strength tends to disaggregate putative zwitterionic networks.

Table 2
UV–vis data of water-soluble SubPcs: band positions, extinction coefficients, and fluorescence emission (recorded in DMF)

Compound	Solvent	Absorption (nm) ($\varepsilon \times 10^5\ M^{-1}\ cm^{-1}$)
3	H_2O	585(0.75), 285(0.74), 216(0.81)
4	H_2O 0.6 M KCl	579(0.2), 547(0.21), 286(0.46), 205(0.6)
7	H_2O	567(0.31), 309(0.17)
9	H_2O	562(0.21)
12	DMF	565(0.64)

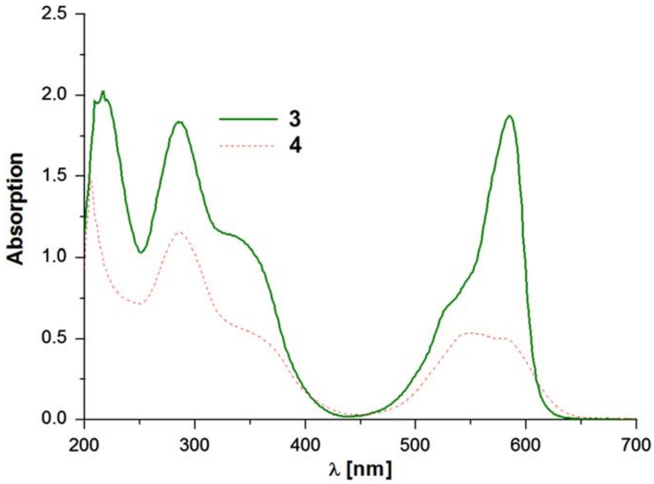


Figure 1. UV–vis spectra of positively charged SubPc **3** in water solution and zwitterionic SubPc **4** in 0.6 M water solution of KCl. Concentration 2.49 × 10^{-5} M.

UV–vis spectra of subphthalocyanines are comparable to those obtained for phthalocyanines in that they both show a Q band and a Soret B band as in other aza aromatic macrocycles. The position of Q and Soret bands of water-soluble SubPcs **3**, **4**, **7**, **9**, and **12** as well as their corresponding absorption coefficients is collected in Table 2. It can be inferred from these results that extension of the conjugation of the SubPc macrocycle with triple bonds produces a bathochromic shift of the Q band in SubPcs **3** and **4** with respect to SubPc **7** containing a saturated ethylene bridge, whereas the presence of oxygen atoms covalently linked to the periphery does not bring any change. UV–vis spectra of the positively charged SubPcs **3**, **7**, **9**, and **12** showed that they remain disaggregated in water through a wide range of concentrations, and that the addition of an anionic detergent such as SDS has insignificant influence on this respect. This is undoubtedly a consequence of the conical structure of SubPcs associated with their axial substituents that preclude any type of aggregative behavior. Not surprisingly, SubPc **4** exhibits strong intermolecular interaction, a fact usually observed with zwitterionic compounds of this type. Hence, SubPc **4** could be solubilized in water only upon addition of an electrolyte (0.6 M KCl), and this still showed broad features characteristic of aggregated chromophoric species (Fig. 1).

In conclusion, we have described for the first time the syntheses of five novel water-soluble positively and zwitterionically charged SubPcs in moderate to good yields as far as subphthalocyanine chemistry is concerned. To the best of our knowledge, the introduction of pyridinium functionality through palladium-catalyzed cross-coupling methodology followed by quaternization with methyl iodide is the most straightforward way to reach cleanly and efficiently water-soluble subphthalocyanines. Recently, we described a remarkable improvement of the photocatalytic activity in the case of co-sensitization by employing triazatetrabenzcorolles, phthalocyanines and tetrapyridylporphyrins as sensitizers that absorb at different wavelengths.[16] In this context, the present water-soluble SubPcs could be used as complementary sensitizers since their Q bands lie in a region different from that of the other sensitizers. Work is in progress in this direction.

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Supplementary data

Supplementary data (compounds and reagents) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2009.02.066.

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