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Synthesis of sulfonamide-substituted phthalocyanines

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ABSTRACT

The synthesis and characterization of new phthalocyanines bearing eight *N*-alkyl or *N*-aryl sulfonamide groups is described. The synthetic route involves the chorosulfonation of 4,5-diphenoxyphthalonitrile with chlorosulfonic acid and reaction of the resulting 4,5-bis(*p*-chlorosulfonylphenoxy)phthalonitrile with amines. The sulfonamide-substituted phthalonitriles are then cyclotetramerized to yield the title compounds in good yields (50–83%).

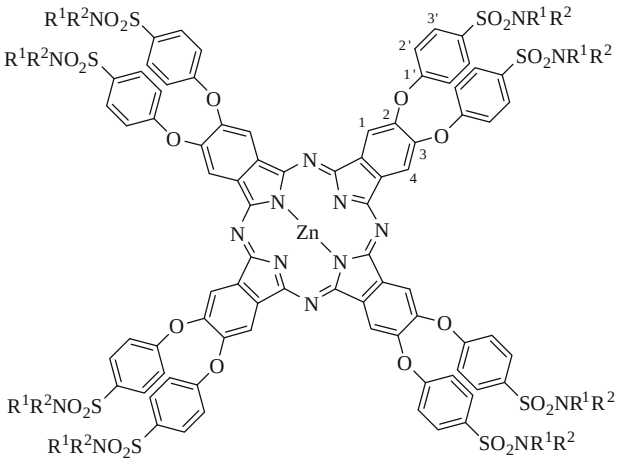
1. Introduction

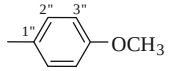
The pursuit of new materials for novel applications is a continuous purpose for organic and material chemists. Peripheral modulation of known aromatic core compounds is still an attractive and challenging pathway for materials with new, or improved, properties. In this context, phthalocyanines, the long known bluish pigments, appear to still have some niches of novelty that should continue to be explored.

Due to their properties, phthalocyanines have a vast area of applications,[1] namely as dyes,[2] catalysts,[3,4] chemical sensors,[5,6] as sensitizers in photodynamic therapy,[7–10] and in nonlinear optics (NLO),[11–13] optical data storage or light-harvesting.[14–16]

Considering applications that require soluble compounds, such as the pharmacological ones, for instance, the extreme insolubility of phthalocyanines in water and in most organic solvents is a clear disadvantage. Functionalization of the periphery of a phthalocyanine with appropriate polar groups can afford phthalocyanine derivatives with increased solubility in polar organic solvents or in aqueous media. Typical examples are the phthalocyanines bearing cationic groups,[17] sugar moieties,[18] or cyclodextrin units.[19] Sulfonated phthalocyanines, both in the sulfonato and sulfonamide forms, are another group of such compounds.[20,21] Some sulfonated phthalocyanines show potential application as catalysts,[4,22] sensors,[20,23] while others are being studied as photosensitizers for photodynamic therapy.[24,25]

In this Letter we describe a new method to synthesize symmetrically substituted phthalocyanines bearing eight sulfonamide groups. It involves the chlorosulfonation of a diphenoxyphthalonitrile, followed by the reaction of the chlorosulfonyl groups with alkyl or aryl amines and then the macrocyclization of the resulting sulfonamide-substituted phthalonitriles.



9: $R^1 = H$, $R^2 =$ 

10: $R^1 = R^2 = -(CH_2)_{11}CH_3$

2. Results and discussion

Sulfonation of phthalocyanines usually produces a mixture of positional isomers or compounds with a varying number of sulfonic acid groups. In order to circumvent these two problems, we decided to use a symmetrical phthalonitrile and to introduce

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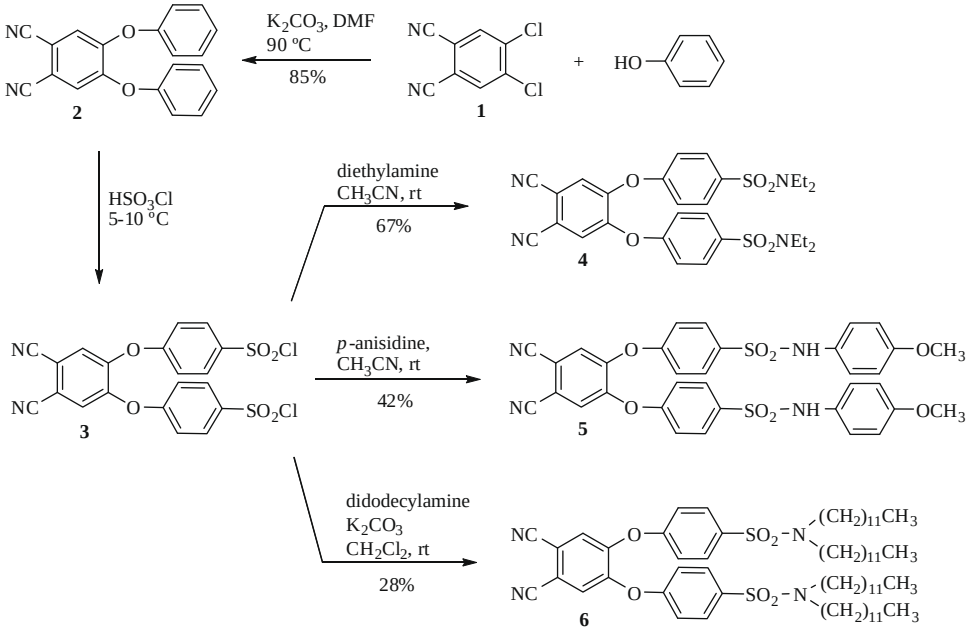
the sulfonamide groups in the phthalocyanine precursors. Nucleophilic substitution of the two chlorine atoms by phenoxy groups at the commercially available 4,5-dichlorophthalonitrile (**1**) afforded 4,5-diphenoxyphthalonitrile (**2**) in 85% yield (Scheme 1).[26] Treatment of 4,5-diphenoxyphthalonitrile with chlorosulfonic acid produced 4,5-bis(*p*-chlorosulfonylphenoxy)phthalonitrile (**3**).[27] Reaction of **3** with various amines, namely diethylamine, *p*-anisidine, and didodecylamine, gave the desired sulfonamide-substituted phthalonitriles **4**–**6**, respectively, in moderate to good yields.[28] The 4,5-bis(*p*-chlorosulfonylphenoxy)phthalonitrile (**3**) was isolated simply by filtration after precipitation from cold water, without any further purification.

Cyclotetramerization of phthalonitrile **4**, in a solution of magnesium bis(pentan-1-olate) in octan-1-ol,[12] afforded the expected phthalocyanine **7** in 50% yield (Scheme 2).[29] Treatment of phthalocyanine **7** with CF_3COOH in THF gave phthalocyanine free-base **8** in 72% yield.[30]

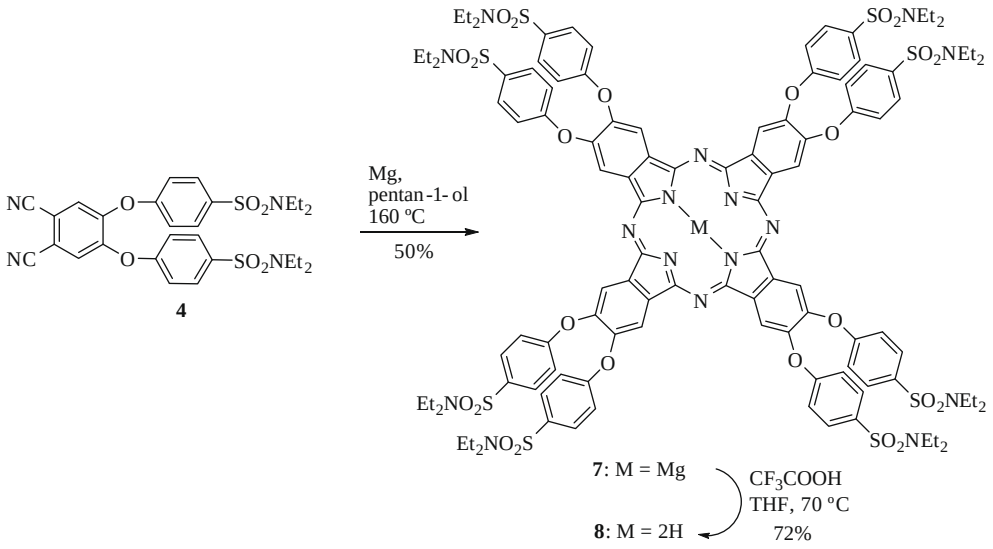
Phthalocyanines **9** and **10** were synthesized in high yields (69% and 83%, respectively) by a slightly different method ($Zn(OAc)_2$ in *N*,*N*-dimethylaminoethanol at reflux).[31,32]

The electronic absorption spectra of the sulfonamide-substituted phthalocyanines **7–10** are exemplified in Figure 1 and summarized in Table 1. Figure 1 shows the UV–vis spectra of the magnesium complex **7** and the metal-free phthalocyanine **8**. Both compounds display UV–vis spectra typical for metallo- and free-base phthalocyanines: a Soret band (B band) at 359 nm and a Q band at 677 nm for **7**, while compound **8** shows a Soret band at 348 nm and typical split Q bands at 662 and 697 nm.

As expected, the ^{1}H NMR spectra of compounds **7**–**10** display common features corresponding to the signals of the phthalocyanine α protons and phenoxy groups. For instance, the ^{1}H NMR spectrum of compound **7** shows a singlet at $\delta = 9.21$ ppm corresponding to the eight phthalocyanine H-1 protons and two doublets at $\delta = 7.20$ ppm ($J = 8.8$ Hz) and at $\delta = 7.82$ ppm ($J = 8.8$ Hz)



Scheme 1.



Scheme 2.

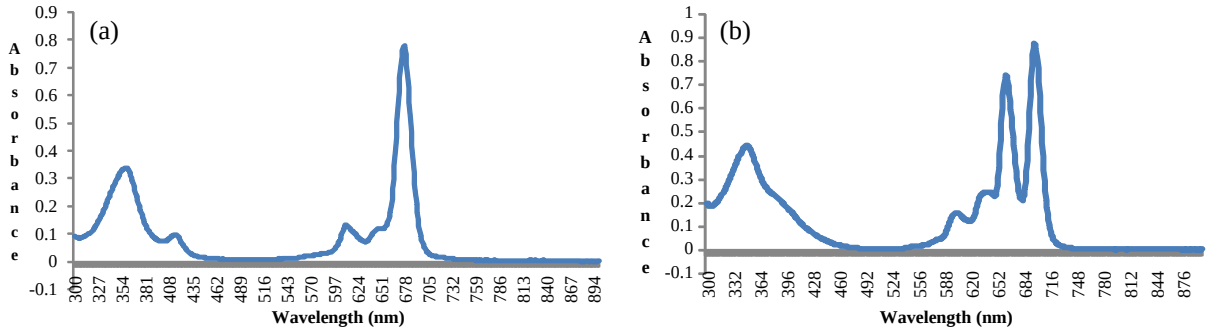


Figure 1. UV–vis spectra of phthalocyanines **7** (a) and **8** (b) recorded in CH_2Cl_2.

Table 1
UV–vis data for compounds **7**–**10** (recorded in CH_2Cl_2)

Phthalocyanine	B band (nm)	Q band(s) (nm)
7	359	677
8	348	662 and 697
9	355	674
10	356	677

due to the resonances of the protons H-2′ and H-3′, respectively. The signals corresponding to the protons of the ethyl groups appear as a triplet at $\delta = 1.16$ ppm and a quartet at $\delta = 3.26$ ppm. The ^{1}H NMR spectrum of phthalocyanine **9** shows, in the aliphatic region, a diagnostic singlet at $\delta = 3.64$ ppm corresponding to the OCH_3 group. The ^{1}H NMR spectrum of phthalocyanine **10** shows, in the aliphatic region, signals at $\delta = 0.86$, 1.24, and 3.10 ppm corresponding to the resonances of the CH_3, CH_2, and NCH_2 protons, respectively.

In conclusion, the method reported here allows the synthesis, in high yields, of phthalocyanines bearing eight sulfonamide groups as single compounds. Since many types of amines can be used (primary or secondary amines, alkyl amines with short or long alkyl groups, aryl or hetaryl amines), this method is useful for the preparation of a range of new sulfonamide-substituted phthalocyanines specifically designed for a given application.

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27. 4,5-Bis(4-chlorosulfonylphenoxy)phthalonitrile, **3**. 4,5-Diphenoxyphthalonitrile (1.65 g, 5.29 mmol) was slowly added to ice cooled chlorosulfonic acid (3.5 mL, 52 mmol). The reaction mixture was stirred for 45 min at 0 °C and then it was poured onto ice (200 g). The resulting solid was filtered, washed with cold water, and dried under vacuum. Compound **3** was used in the subsequent reactions without any further purification.
28. *Typical procedure:* Synthesis of 4,5-bis[4-(diethylaminosulfonyl)phenoxy]phthalonitrile, **4**. Phthalonitrile **3** (1.00 g, 1.96 mmol) was dissolved in acetonitrile (5 mL) and the solution was cooled to 0 °C. Diethylamine (1.24 mL, 12 mmol) was added slowly. The reaction mixture was then stirred at room temperature for 3 h. The reaction mixture was poured into water (100 mL) with ice (200 g) and the resulting solid was filtered off. The product was crystallized from methanol. Yield: 0.77 g (67%), mp 164–165 °C. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.15$ (t, 12H, $J = 7.1$ Hz, CH_3), 3.25 (q, 8H, $J = 7.1$ Hz, CH_2), 7.05 (dd, $J = 6.8$ and 2.1 Hz, 4H, H-2′, H-6′), 7.42 (s, 2H, H-3, H-6), 7.85 (dd, $J = 6.8$ and 2.1 Hz, 4H, H-3′, H-5′); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 14.2$, 42.1, 112.5, 114.3, 118.7, 124.9, 129.7, 137.6, 150.5, 157.4; HRMS (MALDI-TOF): *m/z* calcd for $C_{28}H_{31}N_4O_6S_2$ $[M+H]^+$ 583.1685, found 583.1697.
29. {2,3,9,10,16,17,23,24-Octakis[4-(diethylaminosulfonyl)phenoxy]phthalocyaninato}magnesium(II), **7**. Magnesium turnings (9.27 mg) were added to

pentan-1-ol (0.5 mL) and the suspension was heated to 150 °C (reflux) and maintained at that temperature until the complete formation of the alkoxide (~1 h). Octan-1-ol (1 mL) was added to the suspension, followed by phthalonitrile **4** (100 mg, 0.172 mmol). The reaction mixture was stirred at 160 °C for 3 h and, after cooling to rt, it was poured onto a 5/1 methanol/water mixture (20 mL). The resulting precipitate was isolated by filtration and washed several times with methanol. Yield: 50.5 mg (50%). Mp >300 °C, ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.16 (t, 48H, J = 7.1 Hz, CH_3), 3.26 (q, 32H, J = 7.1 Hz, CH_2), 7.20 (d, 16H, J = 8.8 Hz, H-2′), 7.82 (d, 16H, J = 8.8 Hz, H-3′), 9.21 (s, 8H, Pc-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.6, 41.5, 116.1, 116.6, 128.6, 134.2, 135.9, 147.7, 152.8, 160.1; UV–vis (CH_2Cl_2): λ_{max} (log ε) = 359 (5.39), 610 (4.87), 677 (5.76) nm; MS (MALDI-TOF): m/z 2353.6 $[M+H]^+$.

30. *Spectroscopic data for* **8**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = −2.1 (s, 2H, NH), 1.16 (t, 48H, J = 7.1 Hz, CH_3), 3.26 (q, 32H, J = 7.1 Hz, CH_2), 7.20 (d, 16H, J = 8.8 Hz, H-2′), 7.82 (d, 16H, J = 8.8 Hz, H-3′), 9.21 (s, 8H, Pc-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.6, 41.5, 116.1, 116.6, 128.6, 134.2–135.9, 147.7, 152.8, 160.1; UV–vis (CH_2Cl_2): λ_{max} (log ε) = 348 (5.15), 607 (5.54), 662 (5.38), 697 (5.55) nm; MS (MALDI-TOF): m/z 2331.7 $[M+H]^+$.
31. *Spectroscopic data for* **9**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.64 (s, 24H, OCH_3), 6.79–7.09 (m, 48H, H-2′, H-2″, H-3″); 7.54–7.71 (m, 16H, H-3′); 9.28 (s, 8H, Pc-H); 9.87 (s, 8H, NH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.7, 115.1, 117.3, 117.6, 124.9, 130.3, 131.1, 134.6, 148.6–149.2, 151.6, 158.2, 161.1; UV–vis (THF): λ_{max} (log ε) = 355 (5.03), 608 (4.65), 673 (5.53) nm; MS (MALDI-TOF): m/z 2792.4 $[M]^{+\cdot}$.
32. *Spectroscopic data for* **10**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.86 (t, 48H, J = 7.1 Hz, CH_3), 1.22–1.25 (m, 320H, CH_2), 3.10 (q, 32H, J = 8.1 Hz, NCH_2), 7.19 (d, 16H, J = 8.8 Hz, H-2′, H-6′), 7.82 (d, 16H, J = 8.8 Hz, H-3′, H-5′), 9.22 (s, 8H, Pc-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.5, 22.1–31.3, 47.9, 115.3, 116.6, 128.9, 134.0, 135.7, 147.9, 152.9, 160.2; UV–vis (CH_2Cl_2): λ_{max} (log ε) = 356 (5.16), 610 (4.69), 677 (5.63) nm; MS (MALDI-TOF): m/z 4636.3 $[M+H]^+$.