Synthesis of water soluble axially disubstituted silicon (IV) phthalocyanines with alkyne & azide functionality

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Abstract

Phthalocyanines (Pcs) are a class of photosensitizers (PSs) with a strong tendency to aggregate in aqueous solutions, which has a negative influence on their photosensitizing ability for photodynamic therapy. Four new axially disubstituted, non-aggregated silicon phthalocyanines (SiPcs), containing azide or alkyne functional groups have been synthesized and characterized. The method of synthesis is based on the reaction of silicon phthalocyanine dichloride with variable length poly(ethylene glycol) (PEG) chains in the presence of NaH. All synthesized dyes are highly soluble in alcohols, THF, CH₂Cl₂, acetone, DMF and other common polar organic solvents, with the PEGylated silicon phthalocyanines (SiPcs) also being soluble in water. Photophysical and electrochemical properties of the dyes have been investigated. The presence of alkyne or azide groups in the phthalocyanine dyes, coupled with their high aqueous solubility, make these compounds useful as building blocks in copper catalyzed Huisgen azide-alkyne cycloaddition reactions (i.e. click chemistry).

2 Introduction

Phthalocyanines (Pcs) and their metal complexes have intense absorption in the far red region, low dark toxicity, good chemical stability, and a propensity to generate reactive oxygen species when excited[1, 2]. These properties make Pcs interesting for the development of new photosensitizers (PS) for photodynamic therapy (PDT)[3]. Currently, PDT is broadly used in medicine for the treatment of various conditions, including a variety of cancers[4-6]. Pcs used for PDT include zinc phthalocyanines (ZnPcs)[7, 8], aluminum phthalocyanines (AlPcs)[6, 9, 10], and silicon phthalocyanines (SiPcs)[11-14]. However, most of these compounds exhibit high levels of aggregation in common organic solvents and aqueous media. Silicon Pcs have a relatively reduced tendency to aggregate in solution, which accounts for their high solubility and more pronounced fluorescence lifetimes[15, 16]. Despite the large amount of non-aggregated, axially substituted SiPc derivatives presented in the past few years[12-14, 17-21], these systems tend to exhibit broad emission characteristics and are not amenable for use in more complex heterostructures due to their limited chemical attachment sites. The main goal of this research was the synthesis of new, versatile, non-aggregated axially disubstituted silicon phthalocyanine (SiPc) complexes, which can be used in future investigations either as small molecules or as a part of a larger heterostructure. These systems were modified with substituents containing azide or alkyne functional groups making them amenable for use in reactions which exploit the copper catalyzed Huisgen azide-alkyne cycloaddition (i.e. “click chemistry”)[22]. Current efforts have been presented of Pcs modified for use in click chemistry with azide groups[23-25] or alkyne groups[26-31], but all of these compounds have the substituents in peripheral positions, with only one SiPc complex having axially attached substituents containing an alkyne[32]. The main challenge of peripherally substituted Pcs is their high propensity to aggregate and their limited synthetic approach[33, 34, 11]. Axially substituted Pcs are much less likely to aggregate due to the interruption of the π -system by the non-planar substituents issuing from the center metal atom[35].

For the purpose of increasing the solubility of SiPc complexes in water and other common organic solvents, we have synthesized a new series of axially disubstituted, non-aggregated SiPcs, containing either alkyne or azide functionality. These new symmetrical SiPc complexes can be easily modified by click reactions with

other appropriate small molecules, nano- or micro-particles, polymers, and proteins. This feature makes them valuable for future investigations because the nature of the substituents has a strong influence on the optical and physical parameters of phthalocyanines. Photophysical and electrochemical properties of the synthesized compounds have been studied.

3 Experimental

3.1 Materials and equipment

Silicon phthalocyanine dichloride (SiPcCl_2), triethylene glycol, and polyethylene glycol 600 (PEG 600) were purchased from Sigma-Aldrich. Other reagents were purchased from Alfa Aesar. All commercial reagents were used without further purification. All solvents were dried according to standard methods. Triethylene glycol and PEG 600 were dried in THF solutions over A4 molecular sieves. ^1H and ^{13}C NMR spectra were recorded on a JEOL ECX300 spectrometer (300MHz for proton and 76MHz for carbon). Chemical shifts for protons are reported in parts per million downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent (CDCl_3 : δ 7.26 ppm, DMSO-d_6 : δ 2.50 ppm). Electrospray (ESI) mass spectra were obtained using Finnigan LCQ spectrometer and HP 1100 (HPLC). Absorption spectra were taken using a Perkin-Elmer Lambda 950 UV/VIS/NIR spectrophotometer. Photoluminescence (PL) spectra were collected using a Photon Technology International QuantaMaster 60 NIR with a PMT spectrofluorometer and a Thermo Oriel xenon arc lamp (Thermo Oriel 66902) mated with a Thermo Oriel Cornerstone 7400 1/8 m monochromator (Thermo Oriel 7400). Fourier transform infrared (FTIR) spectra were obtained with a Nicolet 6700 by Thermo Scientific FT-IR spectrometer and all spectra were measured with FTIR-ATR with a diamond head.

Cyclic voltammetry was utilized to determine the electrochemical characteristics of the SiPc compounds. A three electrode system was utilized with a platinum disk working electrode, a platinum coiled wire counter electrode, and a Ag/AgCl reference electrode with an outer junction to prevent water contamination of the solutions. The Pt disk was polished with 5 μm alumina between runs. 0.1M TEABF_4 in ACN was used as the electrolyte. For each test, 2 mL of electrolyte was added to a vial and bubbled with N_2 . A background

scan was collected. After the background had been collected, 200 μL of 11mM SiPc complexes in ACN were added to the solution (concentration in solution was 1 mM), and purged with N_2 . Three sweeps were performed from 0 V to 1.6 V and then to -1.4 V at 100 mV/s. After the CV of the SiPc derivatives were completed, 10 μL of 25 mM FC in 0.1M TBABF₄ was added to the solution, and the scans were repeated in the same manner after purging with N_2 . The addition of ferrocene resulted in no shifting or interaction with the SiPcs. FC had a $E_{(1/2)}$ of 0.412 V, and ΔE_p of 78 mV.

3.2 Synthesis and characterization data

3.2.1 Synthesis of compound 1a

Compound **1a** was synthesized according to literature[36]. Sodium hydride (0.32 g, 13.32 mmol) was added to the solution of triethylene glycol (2 g, 13.32 mmol) in tetrahydrofuran (30 ml). The obtained mixture was stirred at room temperature for 30 min then propargyl bromide solution (80%) in toluene (2 g, 13.45 mmol) was added. The mixture was stirred for 6 h at room temperature and filtered. The filtrate was evaporated; the residue was extracted with dichloromethane and washed with water. The organic solution was dried with Na_2SO_4 , filtered, and evaporated under reduced pressure to yield a brown oil. The crude product was purified by flash column chromatography on silica. The first eluent was dichloromethane, which serves to remove a majority of the impurities. A second eluent, acetone, was used to collect the product. Yield: 1.63 g (65%), pale yellow oil. ^1H NMR (CDCl_3) δ 2.43 (t, 1H, $J=2.4$ Hz, CCH), 3.61 (m, 2H, OCH_2), 3.67-3.74 (m, 10H, OCH_2), 4.21 (d, 2H, $J=2.4$ Hz, CH_2CC).

3.2.2 Synthesis of compound 1b

Compound **1b** was synthesized according to the above procedure. The crude product was washed with hexanes twice, decanted, dried, and used in the next step without further purification. Yield: 83%, clear oil. ^1H NMR (CDCl_3) δ 1.83 (s, 1H, OH), 2.43 (t, 1H, $J=2.4$ Hz, CCH), 3.60-3.71 (m, 56H, OCH_2), 4.20 (d, 2H, $J=2.4$ Hz, CH_2CC).

3.2.3 Synthesis of compound 2a

Methanesulfonyl chloride (3.2 g, 27.94 mmol) was added to the solution of triethylene glycol (4 g, 26.64 mmol) in dichloromethane (50 ml). The reaction was cooled with ice. Triethylamine (2.97 g, 29.3 mmol) was added dropwise to the stirred solution. The ice bath was removed, and the obtained mixture was stirred at room temperature for 6h. The reaction mixture was then washed with water twice. The organic solution was dried with Na₂SO₄, filtered, and evaporated under reduced pressure. The obtained product contains approximately 10% of bis-methylsulfonylated triethylene glycol and was used in the next step without additional purification. Yield: 3.6 g (59%), clear oil. ¹H NMR (CDCl₃) δ 3.07 (s, 3H), 3.61 (m, 2H, CH₂OH), 3.67 (m, 4H), 3.76 (m, 4H), 4.37 (m, 2H, CH₂OSO₂).

3.2.4 Synthesis of compound 2b

Compound **2b** was synthesized according to the above procedure and was used in the next step without additional purification. Yield: 87%, clear oil. ¹H NMR (CDCl₃) δ 3.07 (s, 3H), 3.58-3.72 (m, 40H), 3.75 (m, 2H), 4.37 (m, 2H, CH₂OSO₂).

3.2.5 Synthesis of compound 3a

Compound **2a** (3.6 g, 15.77 mmol) was dissolved in acetonitrile (20ml), and sodium azide (2.56 g, 39.38 mmol) was added to the solution. The obtained mixture was stirred and refluxed for 16h. After cooling, the mixture was extracted with dichloromethane and was washed with water. The organic solution was dried with Na₂SO₄, filtered, and evaporated under reduced pressure. The obtained product contains about 10% of bis-azido-derivative, but it was used in the next step without additional purification. Yield: 2.47 g (89%), clear oil. ¹H NMR (CDCl₃) δ 3.38 (t, 2H, *J*=4.8 Hz, CH₂N₃), 3.59-3.79 (m, 10H).

3.2.6 Synthesis of compound 4a

Silicon phthalocyanine dichloride (0.2 g, 0.33 mmol) was mixed with dry toluene (4ml), and the solution of compound **3a** (0.17 g, 0.97 mmol) in toluene (2 ml) was added to the reaction mixture. The mixture was stirred under a nitrogen atmosphere for 5 minutes and sodium hydride (0.023 g, 0.96 mmol) was added. The

mixture was refluxed for 20 h. After cooling, the solution was extracted with ethyl acetate and was washed with water. The organic solution was dried with Na₂SO₄, filtered, and evaporated under reduced pressure. The residue was washed with hexanes. The organic solution was decanted away from the insoluble product, and the product was purified by flash column chromatography on silica with an eluent of a solution of dichloromethane:acetone (10:1), R_f=0.3. The dry product was dissolved in a minimum of dichloromethane and was added dropwise to hexane solution. The precipitates from this solution were filtered, collected, and dried. Yield: 0.13 g (45%), blue crystals, mp 169-170 °C with destruction. ¹H NMR (CDCl₃) δ -1.91 (t, 4H, *J*=5.5 Hz, CH₂OSi), 0.42 (t, 4H, *J*=5.5 Hz, CH₂), 1.66 (t, 4H, *J*=4.8 Hz, CH₂), 2.45 (t, 4H, *J*=4.8 Hz, CH₂), 2.92 (m, 8H, CH₂CH₂N₃), 8.34 (dd, 8H, *J*=3.1 Hz, ArH), 9.63 (dd, 8H, *J*=3.1 Hz, ArH). ¹³C NMR (CDCl₃) δ 50.36, 54.92, 68.83, 69.24, 69.54, 69.58, 123.78, 131.03, 136.13, 149.38 (CN). ESI⁺ Mass (m/z): calculated for C₄₄H₄₀N₁₄O₆Si [M+Na]⁺ 911.29, found 911.0

3.2.7 Synthesis of compound 4b

Compound **4b** was synthesized according to the procedure of **4a** with the substitution of compound **3b** for compound **3a**. Compound **4b** was purified by flash column chromatography on silica with an eluent of a solution of dichloromethane:methanol (10:1). R_f=0.4. Yield: 66%, dark blue oil. ¹H NMR (CDCl₃) δ -1.92 (t, 4H, *J*=5.5 Hz, CH₂OSi), 0.37 (t, 4H, *J*=5.5 Hz, CH₂), 1.66 (t, 4H, *J*=4.8 Hz, CH₂), 2.44 (t, 4H, *J*=5.2 Hz, CH₂), 2.96 (t, 4H, *J*=4.8 Hz, CH₂), 3.21 (t, 4H, *J*=5.2 Hz, CH₂), 3.37 (m, 8H, CH₂), 3.44 (m, 4H, CH₂), 3.51-3.69 (m, 70H, CH₂), 8.33 (dd, 8H, *J*=3.1 Hz, ArH), 9.62 (dd, 8H, *J*=3.1 Hz, ArH). ¹³C NMR (CDCl₃) δ 50.79, 54.80, 68.68, 69.46, 69.90, 70.16, 70.20, 70.39, 70.48, 70.54, 70.69-70.81 (m), 123.77, 130.98, 136.10, 149.34 (CN). ESI⁺ Mass (m/z): calculated for compound **4b** avg. C₈₆H₁₂₄N₁₄O₂₆Si [M+H]⁺ 1797.87, found multiple peaks starting from 1963 (See Supplementary Information).

3.2.8 Synthesis of compound 5a

Silicon phthalocyanine dichloride (0.2 g, 0.33 mmol) was mixed with dry toluene (4ml) and the solution of compound **1a** (0.19 g, 1.0 mmol) in toluene (2 ml) was added to the reaction vessel. The obtained mixture was stirred under a nitrogen atmosphere for 5 minutes and sodium hydride (0.023 g, 0.96 mmol) was added.

The mixture was stirred and refluxed for 20h. After cooling, the mixture was extracted with ethyl acetate and was washed with water. The organic solution was collected, dried with Na₂SO₄, filtered, and evaporated under reduced pressure. Compound **5a** was purified by flash column chromatography on silica with an eluent of a 3:1 dichloromethane:acetone solution, R_f =0.2. The dry product was dissolved in a minimum of dichloromethane and added dropwise to hexanes solution. The precipitates from this solution were filtered, collected, and dried. Yield: 53%, blue crystals, mp 172-173 °C. ¹H NMR (CDCl₃) δ -1.90 (t, 4H, J =5.5 Hz, CH₂OSi), 0.40 (t, 4H, J =5.5 Hz, CH₂), 1.67 (t, 4H, J =4.8 Hz, CH₂), 2.34 (t, 2H, J =2.4 Hz, CCH), 2.46 (t, 4H, J =4.8 Hz, CH₂), 2.98 (t, 4H, J =4.8 Hz, CH₂), 3.29 (t, 4H, J =4.8 Hz, CH₂), 3.95 (d, 4H, J =2.4 Hz, CH₂CC), 8.34 (dd, 8H, J =3.1 Hz, ArH), 9.63 (dd, 8H, J =3.1 Hz, ArH). ¹³C NMR (CDCl₃) δ 54.85, 58.29, 68.72, 68.84, 69.48, 69.53, 69.75, 74.47, 79.76, 123.79, 131.0, 136.13, 149.37 (CN). ESI⁺ Mass (m/z): calculated for C₅₀H₄₆N₈O₈Si [M+Na]⁺ 937.31, found 937.13.

3.2.9 Synthesis of compound **5b**

Compound **5b** was synthesized according to the procedure of **5a** with the substitution of compound **1b** for compound **1a**. Compound **5b** was purified by flash column chromatography on silica. Two eluents were employed. The first eluent was ethyl acetate and was used to remove the majority of impurities. The second eluent was a 3:1 solution of dichloromethane:methanol and was used to remove the remaining impurities and to wash the product from the silica. R_f =0.2. Yield: 64%, dark blue oil. ¹H NMR (CDCl₃) δ -1.92 (t, 4H, J =5.5 Hz, CH₂OSi), 0.37 (t, 4H, J =5.5 Hz, CH₂), 1.64 (t, 4H, J =4.8 Hz, CH₂), 2.44 (m, 6H, J =4.8 Hz, CH₂ and CCH), 2.96 (m, 4H, CH₂), 3.20 (m, 4H, CH₂), 3.36 (m, 4H, CH₂), 3.44 (m, 4H, CH₂), 3.49-3.71 (m, 80H, CH₂), 4.21 (d, 4H, J =2.4 Hz, CH₂CC), 8.34 (dd, 8H, J =2.8 Hz, ArH), 9.62 (dd, 8H, J =2.8 Hz, ArH). ¹³C NMR (CDCl₃) δ 54.80, 58.53, 68.68, 69.21, 69.43, 69.46, 69.89, 70.20, 70.38, 70.47, 70.52, 70.68 (m), 74.69, 79.77, 123.77, 130.99, 136.10, 149.35(CN). ESI⁺ Mass (m/z): calculated for compound **5b** avg. (n=10-11) C₉₀H₁₂₆N₈O₂₈Si [M+K]⁺ 1817.83, found 1818.40.

3.3 Results & Discussion

3.3.1 Synthesis and characterization

The new axially disubstituted SiPc complexes **4a, b** and **5a, b** were synthesized starting from commercially available silicon phthalocyanine dichloride (SiCl_2Pc), as presented in Figure 2. SiCl_2Pc reacts with modified triethylene glycols of variable molecular weights in the presence of NaH in a toluene solution. The reaction requires high temperatures and leads to the nucleophilic substitution of two chlorine atoms with good yields of the final products after purification. For this method, the nucleophilic substituent ligands can vary.[21] As key intermediates, we used either triethylene glycol derivatives (**1a** or **3a**) with azide or alkyne terminal groups and the corresponding PEG 600 derivatives (**1b** or **3b**). The synthetic pathway to compounds **1a, b** and **3a, b** is described in Figure 1.

Compounds **1a, b** were synthesized in one step from triethylene glycol or PEG600 by the nucleophilic substitution of one hydrogen in the hydroxyl group to the propargyl group. The reaction was performed in THF in the presence of NaH and propargyl bromide. Compounds **3a, b** were synthesized in two steps from the same starting material used for the synthesis of **1a, b**. The first intermediate is mesylates (**2a, b**). The reaction of triethylene glycol with a small excess of methanesulfonyl chloride in dichloromethane yields **2a**. The obtained compound **2a** contains a small amount of bismesylated derivative, but it can be used in the next step without additional purification because disubstituted impurities will not react with SiPcCl_2 in the final stage of the synthesis of compound **5a**. Compound **2b** was synthesized similarly to **2a**. Treatment of **2a, b** with sodium azide in refluxed acetonitrile yields mono-azide derivatives of triethylene glycol and PEG 600 (**3a, b**) with high yields.

All synthesized axially disubstituted SiPcs were verified by ^1H , ^{13}C NMR, and ESI Mass analyses. The presence of azide groups in PEGylated SiPc (**4b**) was also confirmed by FTIR analysis. The azide groups on **4b** have a strong absorption at 2098 cm^{-1} (see Supplementary Information). The ^1H NMR spectra of the final products **4a, b** and **5a, b** shows the shielding of the axial substituent protons by the electron cloud of the SiPc ring. Well-separated, upfield shifted triplets, starting from -1.92 ppm , show methylene protons (cf. Figure 4).

The closer the atoms of the axial substituents are to the point of attachment to the SiPc ring, the larger the upfield shift of the methylene groups in the proton spectrum. The obtained NMR spectrum corresponds to previous reports for similar compounds[11, 13, 21]. Alkyne protons in modified triethylene glycols **1a, b** and PEGylated SiPcs **5b** show a triplet at 2.43 ppm, while, for the shorter analog **5a**, the signal is shifted to 2.34 ppm. The same behavior is observed for CH₂ protons attached to the azide group; the triplet from 3.37 ppm (**3a, b** and **4b**) is shifted to 2.93 ppm in compound **4a**. Aromatic protons in the final SiPcs show two, well-separated downfield shifted multiplets.

Figure 3 shows the ESI mass analysis of SiPc **5b**. Multiple peaks are separated by 44 mass units [OCH₂CH₂]⁺ starting from molecular ion M⁺. Compound **4b** shows similar results (see Supplementary Information).

SiPcs **4a, b** and **5a, b** are soluble in alcohols, acetone, dichloromethane and other common, polar, organic solvents excluding diethyl ether. PEGylated SiPcs **4b** and **5b** have good solubility in water. Crude products were easily purified by flash column chromatography on silica.

3.3.2 Photophysical properties

The UV-Vis absorption spectra of **4a, b** and **5a, b**, in methanol, are displayed in Figure 5. The relevant spectroscopic parameters are summarized in Table 1. All synthesized SiPcs showed a sharp, intense, well-defined absorption peak (Q-band) at 671-676 nm along with two vibrational bands at 604 and 645 nm, and a B-band at 330-360 nm, depending on the particular SiPc. These absorption bands are indicative of a non-aggregated SiPc for all newly synthesized SiPcs. The same results were obtained in THF and DMSO; all compounds did not show any aggregation. The maximum fluorescence emission for compounds **4a, b** and **5a, b**, in methanol, occurred at 680 nm when excited at 630 nm.

The absorption spectra for SiPcs **4b** and **5b**, in water, is provided in Figure 6. PEGylated SiPc **4b**, was dissolved in water at a concentration of 5 µg/mL, and it showed a strong absorption peak at 676 nm, which is characteristic of non-aggregated SiPc. The water solubility of **4b** is 3 mg/mL. Compound **5b** shows a strong Q band in water at 720 nm, which suggests that the dye molecules are self-associating. The water solubility of **5b** is 0.2 mg/mL. The aggregation behavior of **5b** can be explained by the presence of lipophilic

alkyne groups at the end of the PEG chains; it decreases solubility in water and makes aggregation easier. Increasing the length of the PEG chains in SiPcs could allow for new dyes with even greater solubility in water. The emission spectra of both **4b** and **5b** show J-aggregates at 761 nm and 757 nm, respectively. This red-shifted peak does suggest that there are aggregates of **4b** and **5b** forming, but these peaks are much less pronounced than in the spectra of similar SiPcs, which indicates that there is minimal aggregation in this system. It should also be noted that **4b** has just a slight J-aggregate peak, with **5b** having quite a large J-aggregate peak, which agrees with the absorption spectra obtained for both of these molecules. J-aggregates occur when the dye has self associated with itself and are characterized by a longer emission wavelength than the “isolated” dye molecule. J-aggregates are undesirable in this case because they represent a path of non-radiative energy transfer, which will decrease singlet oxygen generation when the dye is utilized in PDT[37].

The molar extinction coefficient (ϵ) and fluorescence quantum yield (ϕ_F) for all synthesized phthalocyanines were calculated. The data is summarized in Table 2. ZnPc ($\phi_F = 0.3$) and 1% pyridine in toluene solution as a standard was used for fluorescence quantum yield calculations.[38] All silicon phthalocyanine derivatives had a much greater fluorescence quantum yield than the standard ZnPc, which indicates that the SiPc derivatives have more electrons that fluoresce upon excitation and relaxation. This is beneficial because less electrons, upon relaxation, go toward non-radiative energy transfers. Therefore, it can be concluded that silicon phthalocyanines are good candidates for use as photosensitizers in PDT as they have a higher propensity to fluoresce and generate singlet oxygen. To further support this claim, the molar extinction coefficient was calculated for all derivatives. It was found that all derivatives had molar extinction coefficients between 200,000 and 260,000 $\text{M}^{-1}\text{cm}^{-1}$ with methanol as the solvent. These values are in good agreement with the value found for zinc phthalocyanine ($\epsilon=281,800$) when dissolved in pyridine.[39] Unfortunately, zinc phthalocyanine is only soluble in pyridine so an exact comparison between the standard and the silicon phthalocyanine derivatives could not be made.

Being non-aggregated compounds, new SiPc derivatives can be modified by “click” reactions with appropriate small molecules, polymers, nano or microparticles, or proteins (cf. Figure 7). An example of such a system is presented in Figure 8, where the photoluminescence spectra of 67 nm poly(propargyl acrylate)

(PA) particles, which have been surface modified with **4a,b** (PA/SiPcs) through copper(I)-catalyzed azide alkyne cycloaddition (CuAAC), is presented. Clearly, the attachment of the fluorophores to the particles have not significantly altered their spectral profile since both exhibit an emission peak at ca. 680 nm.

Previously studied, similar, axially disubstituted PEGylated SiPcs have been shown to be potent photosensitizers and have consistent photocytotoxicity[11, 13, 21]. The properties of these new phthalocyanines (**4a, b** and **5a, b**) are good candidates for photodynamic therapy (PDT) and the PA/SiPcs assemblies are currently being investigated as phototsentizers with an enhanced permeability and retention (EPR) effect.

3.3.3 Electrochemical Measurements

Voltammograms were analyzed in order to derive onset potential (E_{onset}), half-wave potentials ($E_{(1/2)}$), peak to peak potential separation for reversible processes (ΔE_p (mV)) and peak separation between the first oxidation and first reduction (E_{gap}). The results are presented in Table 3. The voltammograms exhibit one irreversible one electron transfer oxidation process that has an E_{onset} of 0.95 V for the short chain alkyne derivatized SiPc(**5a**). Two reversible reductions are visible with the first $E_{(1/2)}$ occurring at 0.61 V and the second at 1.06 V. Similarly, the azide derivatized SiPcs (**4a** and **4b**) and the PEG 600 alkyne SiPc derivative (**5b**) exhibit an irreversible one electron oxidative process with similar onset potentials (cf. Table 3 and two reversible reductions. All the redox activity occurring in **4a**, **4b**, **5a**, and **5b** is attributed to the phthalocyanine ring due to the central silicon atom being redox inactive.

The prediction of LUMO energies through a CV route can often be quite poor due to the difficulty in assigning the voltage for the oxidation process due to its irreversibility; therefore, Table 3 also presents LUMO ($LUMO_{op}$) energies based on the difference of CV-derived HOMO values and the energy at the experimentally observed electronic absorption band edge. Clearly, there is a good agreement between the CV and optically derived bandgaps, where the difference between these values is no greater than 0.11 eV for all the compounds.

4 Conclusion

New axially disubstituted, non-aggregated silicon phthalocyanines (SiPcs), containing azide or alkyne groups have been synthesized and characterized. All obtained SiPcs are highly soluble in common polar, organic solvents with the PEGylated derivatives (**4b** and **5b**) being soluble in water and other physiologically relevant buffers. The presence of azide and alkyne functional groups in dye molecules, and their high fluorescence and solubility in various solvents make these new compounds useful as a versatile building block in “click” reactions, allowing for the synthesis of a broad spectrum of new compounds for use in biomedical imaging and cancer therapies. The synthetic pathway presented in this paper can be applicable for the synthesis of a variety new axially disubstituted SiPc derivatives with alkyne or azide groups.

5 Acknowledgments

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Figure 1: Synthetic route to compounds **1a, b**, **2a, b**, and **3a, b**; (i) Propargyl bromide, NaH, THF, r.t.; (ii) MeSO₂Cl, Et₃N, CH₂Cl₂, r.t.; (iii) NaN₃, m acetonitrile, reflux.

Figure 2: Synthetic route to compounds **4a,b** and **5a,b**; (i) Reaction conditions: NaH, toluene, reflux.

Figure 3: ESI Mass analysis of **5b**, positive ionization.

compound	λ_{abs} (nm)	λ_{em} (nm)
4a	352, 606, 671	683
4b	358, 607, 676	680
5a	354, 604, 672	681
5b	355, 604, 672	680

Table 1: Absorption and emission of **4a, b** and **5a, b** in methanol at a concentration of 5 $\mu\text{g/mL}$. Excitation at 630 nm.

compound	$\varepsilon^a (\text{M}^{-1}\text{cm}^{-1})$	ϕ_F^b
4a	259900	0.50
4b	209200	0.51
5a	208600	0.52
5b	218500	0.51

Table 2: Molar extinction coefficient and fluorescence quantum yield of all four silicon phthalocyanine derivatives. ^aSolvent is methanol. ^bSolvent is toluene with 1% pyridine. Excitation at 665 nm.

Figure 4: ^1H NMR spectrum of **5b** in CDCl_3 . Methylene groups closest to the SiPc ring have the highest upfield shift.

Figure 5: Absorption of **4a**, **b** and **5a**, **b** in methanol at a concentration of $5\ \mu\text{g/mL}$.

Figure 6: Absorption (pink) and emission (green) of (a) **4b** and (b) **5b** in water at a concentration of 5 $\mu\text{g/mL}$. Excitation at 630 nm.

compound	ΔE_{op}^a	$E(V)^b$	HOMO ^c	LUMO ^d	ΔE^e	LUMO ^f _{op}
4a	1.653	0.948	5.348	3.808	1.544	3.695
		-0.592				
4b	1.653	0.948	5.348	3.804	1.540	3.695
		-0.596				
5a	1.653	0.948	5.368	3.794	1.570	3.695
		-0.606				
5b	1.653	0.948	5.348	3.794	1.554	3.695
		-0.606				

Table 3: Electronic characteristics of SiPc compounds measured through cyclic voltammetry and UV-vis spectroscopy; all energies are relative to the vacuum level. ^aoptical bandgap taken from electronic absorption band edge ^b $E_1/2$ for reduction ($E_{pa} + E_{pc}$)/2 vs. Ag/AgCl at 100 mV s⁻¹. Oxidation was irreversible, onset potential utilized ^c $E_{HOMO} = -E_{R1(1/2)} - 4.4$ ^d $E_{LUMO} = -E_{O1(onset)} - 4.4$ ^e $\Delta E = E_{LUMO} - E_{HOMO}$ ^fvalue based on difference of CV-derived HOMO energy and energy at experimentally observed electronic absorption band edge

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