Synthesis of Phthalocyanines with a Pentafluorosulfanyl Substituent at Peripheral Positions

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The pentafluorosulfanyl (SF₅) group is more electronegative, lipophilic and sterically bulky relative to the well-explored trifluoromethyl (CF₃) group. As such, the SF₅ group could offer access to pharmaceuticals, agrochemicals and optoelectronic materials with novel properties. Here, the first synthesis of phthalocyanines (Pcs), a class of compounds used as dyes and with potential as photodynamic therapeutics, with a SF₅ group directly attached on their peripheral positions is disclosed. The key for this work is the preparation of a series of SF₅-containing phthalonitriles, which was beautifully regio-controlled by a stepwise cyation via ortho-lithiation/iodination from commercially available pentafluorosulfanyl arenes. The macrocyclization of the SF₅-containing phthalonitriles to SF₅-substituted Pcs required harsh conditions with the exception of the synthesis of β-SF₅-substituted Pc. The regiospecificity of the newly developed SF₅-substituted Pcs observed by UV/Vis spectra and fluorescence quantum yields depend on the peripheral position of the SF₅ group.

The pentafluorosulfanyl (SF₅) group likely has the greatest potential to alter the properties of original compounds when it is introduced into suitable positions on parent molecules, due to its specific physical and chemical properties.[1] Despite the first appearance of this unique motif in the 1950s, the chemistry of the SF₅ group is one of the least explored in fluorine chemistry, causing it to be dubbed as the "forgotten functional group".[2] The SF₅ group has an octahedral geometry, and the sulfur atom is in a hypervalent state with five fluorine atoms surrounding it, imparting SF₅ group with greater electronegativity, lipophilicity and steric size relative to the well-explored trifluoromethyl (CF₃) group. Indeed, the electronegativity of SF₅ is closer to that of a nitro (NO₂) group, and the size of SF₅ is equivalent to a tert-butyl group.

The SF₅ group has been nicknamed “super CF₃” for good reason.[3] The field of CF₃ chemistry has blossomed over the past decades to become an extremely rich area of a variety of research fields, including pharmaceuticals, agrochemicals and optoelectronic materials,[4] and SF₅-containing compounds could represent the next epoch in these areas.[5] Examples of SF₅-containing analogues of CF₃-substituted drugs and functional materials have seen success to varying degrees.[6] Although the synthetic methods to access SF₅-containing compounds were previously limited and tedious,[7] the discovery by Umemoto in 2008 of an efficient construction of an SF₅ unit on a benzene ring from a aryl disulfide[8] allowed simple SF₅-substituted arenes (1) to become commercially available with the collaboration of Ube Industries Ltd.[9] Even the synthesis of SF₅-substituted pyridines 2 was recently achieved by Dolbier[10] under modified Umemoto conditions. By virtue of these facts, it is hoped that direct functionalization of readily available simple SF₅-substituted arenes at all positions of the aromatic ring would allow for the synthesis of more complex SF₅-containing molecules,[11] including SF₅-containing macrocycles.

Phthalocyanines (Pcs) are heterocyclic macrocycles and are used as artificial blue or green organic dyes with high robustness.[10] Pcs are very popular pigments (e.g., Pigment Blue 16, Pigment Green 7) with big sales worldwide, but they have also been extensively researched in industry and academia for the development of organic solar cells, semiconductors, optical recording materials and medicinal agents for photodynamic therapy of cancer due to their strong optical absorption at wavelengths longer than 650 nm. Since these optical properties of Pcs vary significantly with substitutions on peripheral positions, the design and synthesis of Pcs with various substituitions has attracted much attention.[11] In particular, strong electron-withdrawing substituents, such as NO₂ remarkably decrease the basicity of the parent macrocycle, resulting in an increase in the stability of the Pc towards oxidation.[12] However, Pcs suffer from poor solubility in organic solvents. Fluoro-functionalized Pcs have thus emerged as lipophilic and stabilized Pcs to overcome these shortcomings.[13] These fluorinated Pcs are also expected to exhibit novel and unique properties, and triﬂuoroethoxy-Pcs[14] and perfluoroisopropyl Pc[13ab] are two representative examples of this compound class. Many reports have documented the synthesis of Pcs having fluorinated functional groups on peripheral positions[13] but there is no example of the synthesis of Pcs having an SF₅ moiety directly in their peripheral positions.[14] As part of our research program on fluorinated Pcs,[15] we report herein the synthesis of directly functionalized SF₅-substituted Pcs 3a–c, and disclose the regio-
The synthesis of 3,5-bis(pentafluorosulfanyl)phthalonitrile (4c) from commercially available 3,5-bis(pentafluorosulfanyl)-1-bromobenzene (11) was attempted (Scheme 3). Cyanation of bromide 11 proceeded smoothly with potassium ferrocyanide and 1-butyl imidazole in the presence of copper(I) iodide to furnish 12 in 74% yield. The ortho-lithiation/iodination of 12 required three equivalents of lithium tetramethylpiperide (LiTMP), was followed by iodination with I₂ to furnish 6 in 38% yield. The iodo-function of 6 was next converted into a cyano group using copper(I) cyanide in dimethylformamide (DMF) at 110 °C to give 4a in 43% yield (Scheme 1).
ride in N,N-dimethyl-2-aminoethanol (DMAE) at 140 °C, 4-(pentafluorosulfonyl)phthalonitrile (4a) was converted into β-SF₂-substituted Pc 3a in 10% yield as a mixture of regioisomers. However, SF₂-phthalonitrides 4b and 4c failed to be cyclized under these conditions. This is presumably due to the steric hindrance and strong electronegativity of the SF₂ group on the neighboring cyano moiety. Finally, desired α-SF₅-substituted Pc 3b and α,β-SF₅-substituted 3c were obtained under harsh conditions, that is, without solvent at higher reaction temperatures (180–200 °C), in 28% and 7.8% yield, respectively, as a mixture of regioisomers.

The UV/Vis and fluorescence spectroscopy were used to investigate their optical properties of SF₂-substituted Pcs 3a–c in dichloromethane, α,α,α-trifluorotoluene (CF₃Ph) and 1,4-dioxane (dioxane) (see Table 1 and Figure 2a; detailed data is provided in the Supporting Information). In dichloromethane, the UV/Vis spectra of α-SF₅-substituted Pc 3b and α,β-SF₅-substituted 3c are sharp, while the region of the 630 nm to 640 nm band of β-SF₂-substituted 3a is broad (Figure 2a). Next, the UV/Vis spectra in CF₃Ph and dioxane were investigated (spectra for 3a are shown in Figure 2b; spectra for 3b,c, see Supporting Information). Interestingly, the absorption of β-SF₂ 3a is remarkably weaker than that of α-SF₅ 3b and α,β-SF₅ 3c. The 630 nm region of β-SF₂ 3a is weak and broad, indicating H-aggregation in CF₃Ph, while both α-SF₅ 3b and α,β-SF₅ 3c show sharp spectra of non-aggregation in CF₃Ph. The Q-band of α,β-SF₅ 3c lies almost in the same blue-shift position as α-SF₅ 3b, independent of the existence of an additional β-SF₂ group in 3c, while a red-shift was observed for β-SF₂ 3a. These results suggest that the effect of an SF₂-substitution at a peripheral α-position is much larger than that at a β-position. The blue-shift caused by α-substitution arises due to the presence of an electron-withdrawing NO₂ group, which is the opposite observation to that seen when an electron-donating n-butoxy (nBuO) group is present; in that case, α-substitution induces a red-shift of the Q-band.

To consider the origin of the differences in Q-bands, HOMO–LUMO energy levels of 3a–c were next calculated by computation, and they were compared with those of conventional zinc phthalocyanine (ZnPc) (DFT/B3LYP/6-31G*) (Figure 3). In all cases, the HOMO levels were stabilized as the number of SF₂ substitution arises due to the presence of an additional NO₂ group. The opposite observation to that seen when an electron-donating n-butoxy (nBuO) group is present; in that case, α-substitution induces a red-shift of the Q-band. The blue-shift caused by α-substitution arises due to the presence of an electron-withdrawing NO₂ group.interestingly, the absorption of β-SF₂ 3a is remarkably weaker than that of α-SF₅ 3b and α,β-SF₅ 3c. The 630 nm region of β-SF₂ 3a is weak and broad, indicating H-aggregation in CF₃Ph, while both α-SF₅ 3b and α,β-SF₅ 3c show sharp spectra of non-aggregation in CF₃Ph. The Q-band of α,β-SF₅ 3c lies almost in the same blue-shift position as α-SF₅ 3b, independent of the existence of an additional β-SF₂ group in 3c, while a red-shift was observed for β-SF₂ 3a. These results suggest that the effect of an SF₂-substitution at a peripheral α-position is much larger than that at a β-position. The blue-shift caused by α-substitution arises due to the presence of an electron-withdrawing NO₂ group, which is the opposite observation to that seen when an electron-donating n-butoxy (nBuO) group is present; in that case, α-substitution induces a red-shift of the Q-band.

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substitutions increased, which is in good agreement with the stabilization of Pcs by electron-withdrawing functional groups. The stabilization effect on the HOMO level by β-SF₅ substitution is slightly stronger than that of α-SF₅ substitution, and approximate additivity was observed for α,β-SF₅ substitution. Energy gaps of HOMO and LUMO correlate well with the Q-band positions of 3a–c in Table 1. The Q-band of β-SF₅ 3a is shifted to a long wavelength, which is very consistent with calculations in which the energy gap of HOMO and LUMO of β-SF₅ 3a is smallest (2.19 eV), while that of α-SF₅ 3b and α,β-SF₅ 3c are almost the same (2.25 and 2.26 eV, respectively). These results clearly indicate that a SF₅ group at an α-position increases the energy gap (3b: 2.25 eV; 3c: 2.26 eV), while β-substitution with a SF₅ group does not affect it (energy gap: ZnPc = 2.19 eV; 3a = 2.19 eV).

Fluorescence of β-SF₅ 3a is considerably stronger than that of 3b–c, having a α-SF₅ moiety, especially in dioxane; fluorescence quantum yield of 3a is very high (Φₐ = 0.95), and fluorescence decreases in the order β-SF₅ 3a > α,β-SF₅ 3c > α-SF₅ 3b (Table 1). It is interesting to note that the electron-donating nBuO group on Pcs shows a similar tendency, namely that the Φₐ value becomes smaller with the α-substitution of nBuO groups, as reported by Kobayashi and co-workers. They explained this phenomenon as a decrease in the energy gap between HOMO and LUMO, suggesting that the excited states become unstable in systems showing a Q-band at lower energy, due to the ease of electron transfer. However, in our case, electron-withdrawing SF₅ groups were not related to HOMO–LUMO energy gaps. Fundamentally, the effects on optical properties by electron-withdrawing substituents are much smaller than those by an electron-donating group. This indicates that an α-SF₅-substitution induces a non-radiative transition process presumably due to the distortion of the phthalocyanine plane by a bulky SF₅ group on the α-position, while a β-SF₅-substitution inhibits it, although further investigation is required.

In conclusion, a series of directly-substituted SF₅-containing phthalocyanines (Pcs) were regioselectively synthesized from commercial available simple SF₅-substituted arenes by stepwise cyanation via ortho-lithiation/iodination. Regiospecific spectroscopic properties were observed. The aggregation of Pcs is controlled regioselectively with the SF₅ substitution at a peripheral α-or a β-position. The effect of SF₅ substitution at a peripheral α-position is much larger than that at a β-position, observed both in the UV/Vis spectra and fluorescence quantum yields, and an approximate but non-linear additivity exists. The electron-withdrawing property of the SF₅ group mainly contributes to the UV/Vis spectra of SF₅-substituted Pcs, while fluorescence quantum yields seem to be affected by the bulkiness of the SF₅ group due to the distortion of the Pc plane. More systematic analysis on the effect of SF₅ substituents is under investigation.

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