Aromatic Macrocycles

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Triflate-Subphthalocyanines: Versatile, Reactive Intermediates for Axial Functionalization at the Boron Atom**

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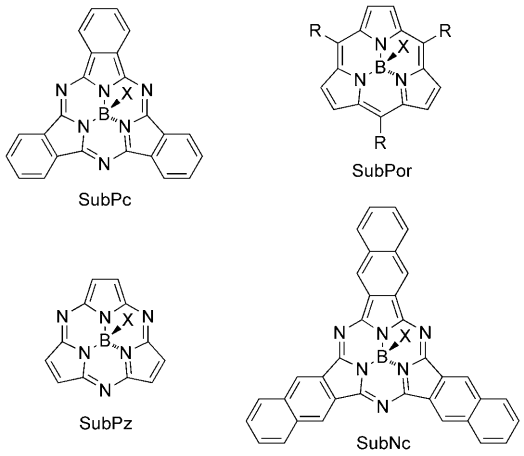
Dedicated to Professor Luis Echegoyen on the occasion of his 60th birthday

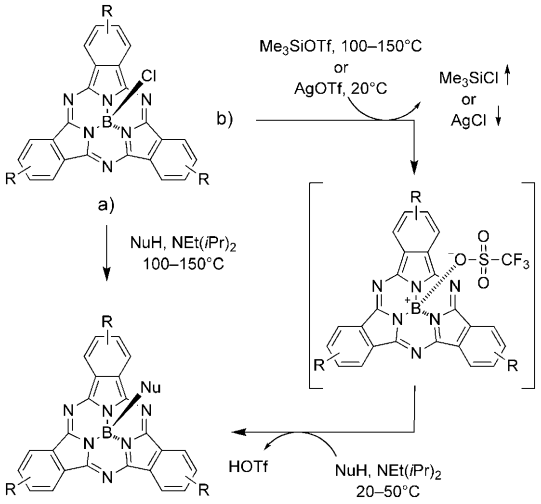
The development of simple, high-yielding, and reliable synthetic methodologies to attach different molecular fragments to a core molecule is of paramount importance in view of the increasing complexity of the molecular systems studied in modern chemistry.[1] Such methods allow, for instance, the efficient incorporation of photoactive units into polymers, biomolecules, surfaces, or multicomponent organic materials for fluorescence sensing, light-harvesting, or photovoltaics.[2] Among these units, the submacrocycles (Scheme 1)[3] that comprise the subphthalocyanines (SubPcs), subporphyrazines (SubPzs), subnaphthalocyanines (SubNcs), and the subporphyrins (SubPors), are becoming an important family of chromophores that exhibit outstanding photophysical properties.[4] They show strong electronic absorption, high fluorescence quantum yields, low Stokes shifts and reorganization energies,[5] and have only a small tendency to aggregate in solution. These singular 14π-electron aromatic molecules share a cone-shaped rigid structure constituted by three nitrogen heterocycles fused around a boron atom, which is also linked to an axial ligand (X in Scheme 1).



Scheme 1. Structure of some relevant submacrocycles.

The functionalization of submacrocycles may be performed by different routes that involve the peripheral[6] or axial positions.[7] The axial approach bears the double advantage that the macrocycle preserves its electronic characteristics, since the substitution pattern on the benzene rings remains unaltered, and that the tedious preparation of unsymmetrically substituted SubPcs is not required. For the subazamacrocycles the most recurrent method is to replace the original axial Cl (and sometimes Br) atom by alcohols, to give the corresponding boronic esters.[3b,7] However, the tetracoordinated boron atom of submacrocycles, in which the vacant *p* orbital is occupied by formation of a dative bond with one of the nitrogens in the macrocycle, is rather unreactive. Most often, the standard axial reaction with nucleophiles (path a in Scheme 2) is not selective enough and requires high temperatures, which may ultimately lead to SubPc ring opening and decomposition.

Based on these premises, we set out to investigate general, simple, and selective strategies for the axial ligand exchange reaction through the intermediacy of activated electrophilic boron SubPc species. Herein we report our results: a one-pot,



Scheme 2. Synthesis of axially substituted SubPcs by direct substitution reaction with a nucleophile (NuH) (path a) or, as we propose herein, via an activated triflate-SubPc intermediate (path b).

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two-step methodology to efficiently substitute the original axial halide atom of SubPc macrocycles with diverse nucleophiles (path b in Scheme 2). In a first step we make use of well-known halophiles, such as Ag^+ ions or the Me_3Si group, to irreversibly remove the axial chlorine atom and to obtain a "SubPcB$^+$" species[8] with a weakly coordinating triflate (OTf^-) anion. This activated triflate-SubPc intermediate shows considerable reactivity towards nucleophilic attack at the boron atom, hence being a universal substrate for the synthesis of a wide variety of axially substituted SubPcs.

The generation of triflate-SubPcs was performed by axial chlorine exchange in the presence of commercially available, cheap, and easy to handle AgOTf or Me_3SiOTf reagents. The precipitation of the AgCl or the evaporation of the Me_3SiCl (b.p. = 57 °C) products, respectively, shifts this metathesis equilibrium towards the activated SubPc$^+$OTf$^-$ species. In general, the reactions with AgOTf are faster and milder than the reactions with Me_3SiOTf. The benefit of using this reagent resides, however, in the possibility to fully eliminate the volatile Me_3SiCl by-product from the reaction medium. The formation of the SubPcBOTf intermediate can be easily monitored by TLC or NMR spectroscopy.[9] Figure 1 shows the ^{1}H and ^{11}B NMR spectra of this species in comparison to that of the starting SubPcBCl. Aside from a small downfield shift in the ^{1}H and ^{11}B signals, the SubPcBOTf product exhibits a much higher solubility.

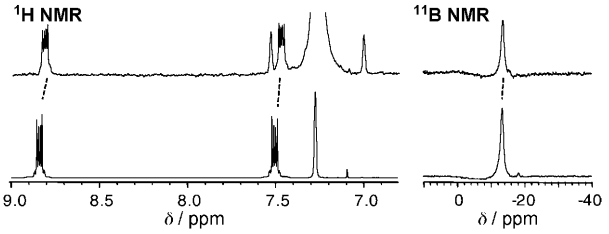
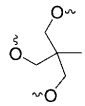
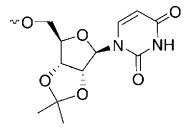
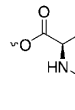
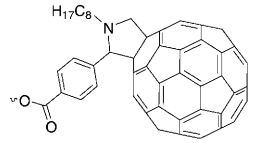
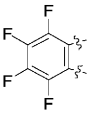
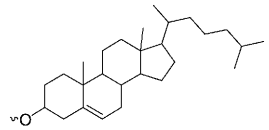
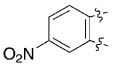
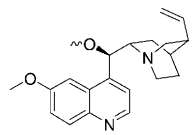
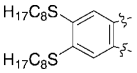


Figure 1. ^{1}H and ^{11}B NMR spectra of SubPcBCl (top) and the presumed SubPcBOTf intermediate (bottom) in [D_6]benzene. The latter was obtained by reaction with 2 equiv. of AgOTf in [D_6]benzene.

The nucleophile (NuH; see Table 1 and Table 2) was added to the reaction mixture in a second step without isolation of the activated SubPcBOTf species (Scheme 2). A hindered tertiary amine ($NEt(iPr)_2$) was also added in order to neutralize the triflic acid generated in this step, which can promote unwanted secondary reactions. The reaction has to be performed under strictly anhydrous conditions. Otherwise, the presence of traces of water immediately leads to a mixture of hydroxy-SubPc (**1**) and the μ-oxo dimer.[9,10] We found that the formation of these by-products is the main source that hampers quantitative conversion.[11]

In contrast to chloro- or even bromo-SubPcs, these novel triflate-SubPcs exhibit an extraordinary reactivity toward nucleophiles and the reactions could be completed within just a few hours at room temperature. For comparison, some of the reactions were also carried out directly from chloro-SubPcs (path a in Scheme 2). As shown in Table 1, the yields obtained by this new method with both alcohols and carboxylic acids are excellent, especially for aliphatic or

Table 1: Axial substitution reactions with O-nucleophiles via an activated SubPcBOTf intermediate (see Scheme 2).

SubPcBCl R	Nu	Yield[a]	SubPcBNu Product
		86%[b]	**1**
		71% (5%)[c]	**2**
		79%[c]	**3**
		92%[b]	**4**
		85% (8%)[c]	**5**
		36% (0%)[b]	**6**
		88% (81%)[c]	**7**
		71%[b]	**8**
		61%[b]	**9**
		86%[d]	**10**
		35% (0%)[b]	**11**
		79%[c]	**12**
		66%[b]	**13**
		78% (11%)[c]	**14**
		65% (0%)[c]	**15**
		87% (62%)[b]	**16**
		90% (58%)[b]	**17**
		41%[b]	**18**
		75%[b]	**19**

[a] Yields calculated with respect to the starting chloro-SubPc. For comparison, the yield obtained by path a in Scheme 2 is given in parentheses. [b] SubPcBOTf was generated with AgOTf. [c] SubPcBOTf was generated with Me_3SiOTf. [d] Obtained from the reaction between SubPcBCl and CF_3CO_2Ag.[9]

Table 2: Axial substitution reactions with S, N, and C nucleophiles via an activated SubPcBOTf intermediate (see Scheme 2).

SubPcBCl	Nu	Yield (%)[a]	SubPcBNu Product
R	~S	45%[b]	**20**
	~S	67% (0%)[b]	**21**
	N	33%[b]	**22**
	N	89% (0%)[c]	**23**
	N	51% (0%)[b]	**24**
	N N	27%[b]	**25**
	~CH_2CH_3	55% (0%)[c]	**26**
	~	68%[b]	**27**[13]
F F F F	S N	83% (0%)[b]	**28**
(Cl)	S N	53%[b]	**29**[9]

[a] Yields calculated with respect to the starting chloro-SubPc. For comparison, the yield obtained by path a in Scheme 2 is given in parentheses. [b] SubPcBOTf was generated with AgOTf. [c] SubPcBOTf was generated with Me_3SiOTf.

sterically hindered nucleophiles (see products **5**, **6**, **15**, and **18**) that tend to be quite unreactive when using the direct approach and usually lead to decomposed by-products. The high reactivity of triflate-SubPcs towards axial ligand exchange is explicitly manifested in the reaction with nucleophiles that have multiple reactive groups, such as 1,1,1-tris(hydroxymethyl)-ethane, to give the corresponding SubPc trimer product **6**. Moreover, the reaction is generally applicable for peripherally substituted SubPcs, equipped either with donor (entry **19**) or acceptor groups (entries **14**–**17**; see also Table 2).

This novel synthetic approach opens the door to the functionalization of submacrocyclic chromophores with biologically relevant molecules. As shown in Table 1, the reaction with protected peptides (*Z*-L-isoleucine; **11**), nucleosides (uracil; **9**), steroids (cholesterol; **15**), or quinine (**18**), produced the corresponding axially substituted SubPcs in moderate to high yields.

Interestingly, this axial functionalization methodology is not only limited to oxygen nucleophiles. We observed that the activated SubPcBOTf species can also react with sulfur, nitrogen, or even carbon nucleophiles (Table 2), which provides an entry to a whole new family of submacrocyclic chromophores. The reaction is general for different thiols or amines, although we observed that both the yield and the stability of the pure products are lower for the aliphatic ligands. Thiophenols or anilines, in contrast, are excellent reagents that yield stable products (entries **21**, **23**, **28**, and **29**). Aromatic nitrogen heterocycles like imidazole are quite reactive but very sensitive to acidic media. Interestingly, pyrrole is also reactive under our experimental conditions, giving SubPc **24**. Aliphatic and aromatic carbon nucleophiles in the form of magnesium bromides (RMgBr) are also readily incorporated into the SubPc axial position in moderate yields (entries **26** and **27**).[12]

All new products were characterized by ^{1}H NMR, ^{13}C NMR, UV/Vis, FT-IR spectroscopy, MS, and HRMS.[9] Suitable crystals for X-ray diffraction analysis were obtained in some cases, and their resolved structure is shown in Figure 2.[9,14] The present work thus provides an ideal opportunity for the identification of some characteristic features of diverse B–X bonds in submacrocycles, like bond distances, ^{11}B NMR signals and B–X vibrational bands. Some selected information is shown in Table S1, together with the values predicted by DFT calculations.

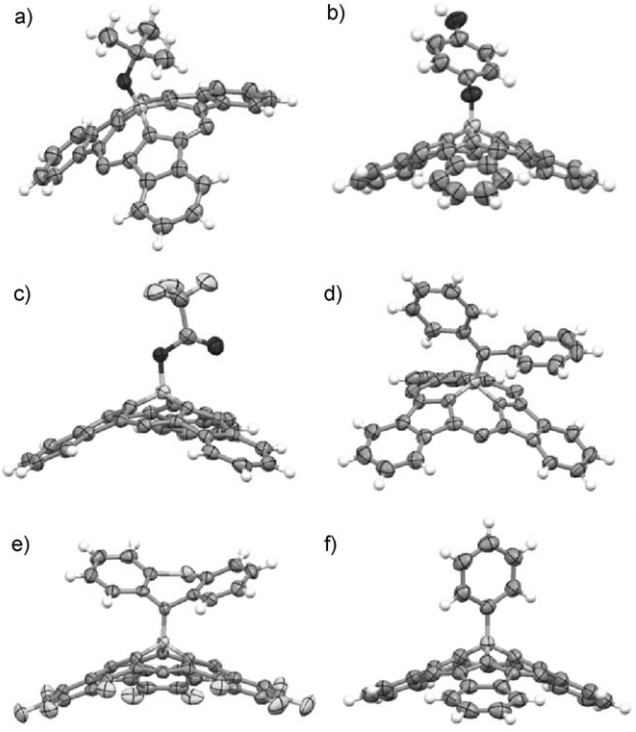


Figure 2. ORTEP drawing (90% probability level) of the molecular structure of SubPcs: a) **5**, b) **8**, c) **10**, d) **23**, e) **28**, f) **27** in the crystal, as determined from X-ray diffraction analysis (C gray, H white, O black).

In summary, we have described the straightforward generation of highly activated "SubPcB$^+$" species in the presence of inexpensive and commercially available AgOTf or Me_3SiOTf reagents. These intermediates are universal substrates for efficient axial substitution reactions with oxygen, sulfur, nitrogen, and carbon nucleophiles. Moreover, this novel methodology can be generalized for SubPcs with diverse peripheral substituents and could also be applied to SubPzs and SubPors.[15] The high reactivities observed, which allow working at room temperature, render this method ideal for the incorporation of these singular chromophores into

systems of increasing complexity. Future work will be focused on this direction, as well as on the detailed study of the reaction mechanism, which, because of the particular boron coordination in submacrocycles, is quite unusual for boron compounds.[3e]

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[4] Submacrocycles are versatile active chromophores that can function as energy donors (Refs. [7a,b,d,g]), energy acceptors (Ref. [7e]) electron donors (Refs. [7a,d]), or electron acceptors (Refs. [7b,c,h]): a) D. González-Rodríguez, T. Torres, D. M. Guldi, J. Rivera, M. A. Herranz, L. Echegoyen, *J. Am. Chem. Soc.* **2004**, *126*, 6301 – 6313; b) D. González-Rodríguez, C. G. Claessens, T. Torres, S.-G. Liu, L. Echegoyen, N. Vila, S. Nonell, *Chem. Eur. J.* **2005**, *11*, 3881 – 3893; c) D. González-Rodríguez, T. Torres, M. M. Olmstead, J. Rivera, M. A. Herranz, L. Echegoyen, C. Atienza Castellanos, D. M. Guldi, *J. Am. Chem. Soc.* **2006**, *128*, 10680 – 10681; d) D. González-Rodríguez, T. Torres, M. A. Herranz, L. Echegoyen, E. Carbonell, D. M. Guldi, *Chem. Eur. J.* **2008**, *14*, 7670 – 7679; e) J.-Y. Liu, H.-S. Yeung, W. Xu, X. Li, D. K. P. Ng, *Org. Lett.* **2008**, *10*, 5421 – 5424; f) Y. Inokuma, S. Easwaramoorthi, Z. Seok Yoon, D. Kim, A. Osuka, *J. Am. Chem. Soc.* **2008**, *130*, 12234 – 12235; g) R. Ziessel, G. Ulrich, K. J. Elliott, A. Harriman, *Chem. Eur. J.* **2009**, *15*, 4980 – 4984; h) M. E. El-Khouly, J. B. Ryu, K.-Y. Kay, O. Ito, S. Fukuzumi, *J. Phys. Chem. C* **2009**, *113*, 15444 – 15453; i) D. González-Rodríguez, E. Carbonell, D. M. Guldi, T. Torres, *Angew. Chem.* **2009**, *121*, 8176 – 8180; *Angew. Chem. Int. Ed.* **2009**, *48*, 8032 – 8036; j) D. González-Rodríguez, E. Carbonell, G. de Miguel Rojas, C. Atienza Castellanos, D. M. Guldi, T. Torres, *J. Am. Chem. Soc.* **2010**, *132*, 16488 – 16500.

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[8] T. Kato, F. S. Tham, P. D. W. Boyd, C. A. Reed, *Heteroat. Chem.* **2006**, *17*, 209 – 216.

[9] See the Supporting Information for further details.

[10] Likely formed by reaction between SubPcBOH and SubPcBOTf. See: a) M. Geyer, F. Plenzig, J. Rauschnabel, M. Hanack, B. del Rey, A. Sastre, T. Torres, *Synthesis* **1996**, 1139; b) N. Kobayashi, T. Ishizaki, K. Ishii, H. Konami, *J. Am. Chem. Soc.* **1999**, *121*, 9096 – 9110.

[11] The yields reported in Tables 1 and 2 were calculated with respect to the starting SubPcBCl. It is important to note that the yields calculated with respect to the nucleophile are close to quantitative when an excess of SubPcBOTf is employed, which renders this method ideal for the complete derivatization of systems with multiple functionalizable sites, such as polymers or reactive surfaces.

[12] The reaction of SubPcBCl with alkynyl magnesium bromides was studied recently, see: F. Camerel, G. Ulrich, P. Retailleau, R. Ziessel, *Angew. Chem.* **2008**, *120*, 9008 – 9012; *Angew. Chem. Int. Ed.* **2008**, *47*, 8876 – 8880.

[13] Compound **27** was previously prepared by reaction of phthalonitrile in the presence of BPh_3 and DBU. It could also be detected in the reaction between SubPcBCl and PhLi, but the yield was very low. X-ray diffraction showed an axial B–C distance of 1.605 Å. See ref. [10a].

[14] CCDC 798228, 798229, 798230, 798231 and 798232 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[15] Although SubPors are usually synthesized as −OH (or −OMe) derivatives, these axial ligands should also be prone to react with, for instance, Me_3SiOTf, to generate activated triflate-SubP intermediates.

