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Modification of alkyne-functionalized asymmetric phthalocyanines by CuI-catalyzed azide-alkyne cycloaddition

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ABSTRACT

The use of asymmetric phthalocyanines (Pcs) as platforms for the preparation of several asymmetric hexatriazolyl-monohydroxyphthalocyanines via copper(I)-catalyzed azide-alkyne cycloaddition (CuAAC) reaction was investigated. Asymmetric Pcs **5a** and **5b** were prepared through statistical macrocyclization of phthalonitriles (Pns) **1a** and **2** to give PMB-protected **4a** and **4b**, which afforded asymmetric Pcs **5a** and **5b** after acidic cleavage. The 'ROMP-Capture-Release' method as a synthetic approach to prepare asymmetric Pc **5b** was also evaluated. TIPS-protection of the terminal alkynes was necessary to prevent cross-coupling during the ring-opening metathesis polymerization (ROMP) step. Zinc Pc **5b** was successfully used as a scaffold for functional modification under CuAAC conditions using several azides bearing hydrophobic, photo-crosslinkable, or electroactive moieties. Monitoring the CuAAC reaction by both UV/Vis and FTIR spectroscopies provided insight into the role of azide equivalent, reaction time, and catalyst on reaction progress.

1. Introduction

Pcs are 18 π-electron tetrapyrrolic macrocycles that have been applied in a number of advanced technologies including optical limiting devices,[1] photodynamic therapy (PDT),[2] organic field-effect transistors (OFETs),[3] and organic photovoltaic (OPV) devices.[4] Due to their physical and chemical properties,[5] effort has been dedicated to the development of structurally diverse Pcs. Of particular interest is the development of asymmetrically substituted AB_3 Pcs[6], which can possess improved photodynamic properties[7] and unique second-order nonlinear optical effects.[1d,8] Asymmetric AB_3 Pcs containing active functional groups in the odd quadrant such as hydroxy,[9] amino,[10] carboxylic acid,[10a,11] isothiocyanate,[12] azide,[13] and alkyne[14] serve as building blocks in the design of Pc-based molecular systems.[15] We have used asymmetric AB_3 Pcs as components of a model system to investigate charge capture at oxide interfaces from typical OPV donor materials.[16]

However, efficient production of Pc-based materials with structural diversity, including AB_3 asymmetry, still remains an open challenge, especially for Pcs with sensitive substituents that are not compatible with the conditions of cyclization of Pc precursors. The copper(I)-catalyzed azide-alkyne cycloaddition (CuAAC) reaction[17] has proven useful for the synthesis of novel materials,[18] and has been demonstrated by us[19] and others[20] as appropriate for Pc/Nc modification. We have previously demonstrated preparation of symmetric octaalkynyl Pcs as an effective platform for Pc chromophore modification through copper(I)-catalyzed azide-alkyne cycloaddition (CuAAC) reactions.[19] Herein we report the synthesis of asymmetric hexaalkynyl AB_3 Pcs **5a** and **5b** and subsequent post-cyclization modification with various azides to further demonstrate the utility of Pc modification through the CuAAC reaction.[21]

2. Results and discussion

In seeking to use the CuAAC reaction as a means of increasing structural diversity in asymmetric Pc chromophores, we identified bis(alkynyl) Pn **1a**,[19a] readily prepared from 4,5-bis(4′-hydroxyphenoxy)phthalonitrile and commercially available 1-hexyn-6-ol through a Mitsunobu reaction, as a suitable precursor. We have previously reported that macrocyclization of **1a** under basic Linstead conditions afforded octaalkynyl ZnPc **3b**, which possesses good solubility in common organic solvents such as THF, DCM, acetone, and Et_2O.[19a] Protection of the terminal alkyne moieties was not necessary during the macrocyclization reaction, providing a relatively simple way to incorporate acetylenic moieties into a Pc scaffold.

To use Pn **1a** in the preparation of asymmetric AB_3 Pcs, we needed to choose a strategy for asymmetric Pc synthesis. The preparation of asymmetrically substituted AB_3 Pcs can be achieved by solution phase statistical Linstead macrocyclization between

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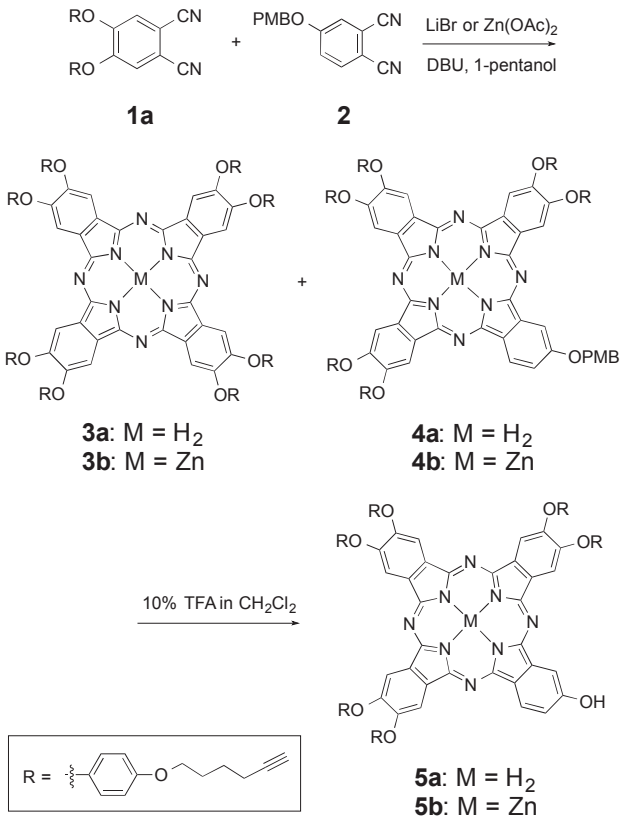
two different phthalonitriles or diiminoisoindolines.[22] Ready availability of precursors makes the statistical macrocyclization often a more effective and direct than other approaches such as solid-phase synthetic methods[23] and the 'sub-phthalocyanine' method.[24] The challenge of statistical macrocyclization is that it inherently yields a mixture of Pc products with minimal structural differences, making isolation of the desired Pcs often challenging.

However, we have recently reported statistical cyclization strategies but with modifications aimed at simplifying purification. We have described the synthesis of asymmetric AB_3 Pcs via: (1) statistical macrocyclization using 4-methoxybenzyl (PMB)-protected Pn[16a] to yield asymmetric AB_3 Pcs with a unique phenolic quadrant that aids in isolation once deprotected; and (2) a ROMP-Capture-Release[9b] strategy using a norbornyl-tagged Pn, again leading to an asymmetric AB_3 Pc with a phenolic unique quadrant. Both methods would potentially serve to produce asymmetric AB_3 Pcs with acetylenic moieties for post-synthetic modification by the CuAAC reaction.

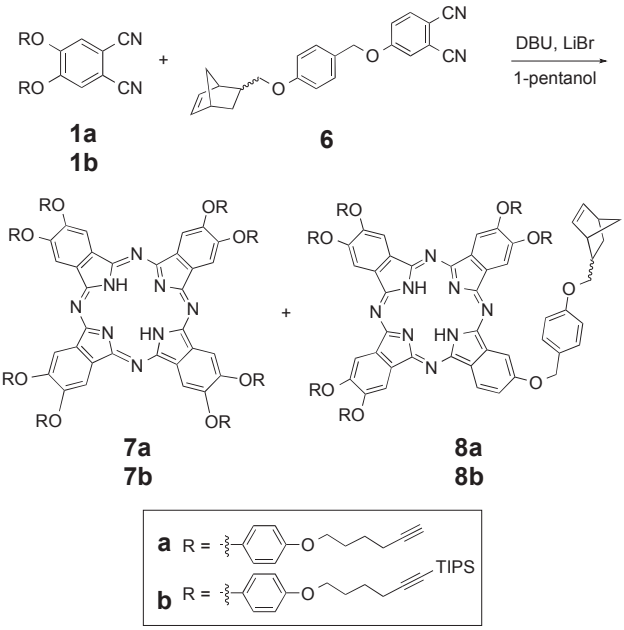
Employing the former method, statistical macrocyclization of **1a** and 4-methoxybenzyl (PMB)-protected Pn **2**[16a] (Pn **1a**:**2**=3:1) in the presence of 1,8-diazabicyclo-[5.4.0]undec-7-ene (DBU) as a base and either LiBr or $Zn(OAc)_2$ as metal template provided a mixture of symmetric and asymmetric Pcs (Scheme 1). The crude mixture was chromatographed to remove DBU and excess metal salt from the Pc mixture. MALDI mass spectral analysis of the resultant Pc mixtures revealed the presence of PMB-protected A_3B (**4a**/**4b**) and symmetric A_4 (**3a**/**3b**) Pcs. Subjecting the mixtures to PMB deprotection conditions yielded a mixture of asymmetric free hydroxyl A_3B (**5a**/**5b**) and symmetric A_4 (**3a**/**3b**) Pcs. Due to the increased polarity afforded by the unique phenolic quadrant in the asymmetric Pcs, this mixture was easily separable by flash chromatography to provide the desired macrocycles **5a**/**5b** in overall yields of 20 and 22% from Pn **2**, respectively.



Scheme 1. Synthesis of asymmetric Pc **5a** and **5b** by statistical macrocyclization followed by acidic cleavage.

We also evaluated the latter method, our previously reported 'ROMP-Capture-Release' strategy[9b] to synthesize asymmetric hexaalkynyl Pc **5a**. This method employs solution phase crossover-Linstead cyclization of a norbornyl-tagged Pn (A) with a second Pn (B), followed by selective capture of asymmetric norbornyl-tagged AB_3 Pc under ROMP conditions and acidic cleavage of the target asymmetric Pc from the ROMP polymer. While this method was successfully developed for the synthesis of an asymmetricAB_3 Pc with alkyl substituents,[9b] the concern of cross-coupling of free alkynes with the norbornyl tag during the ROMP process remained. Enyne metathesis[25] is well established to occur with ruthenium-based metathesis catalysts,[26] including the cross-metathesis of terminal alkynes with norbornene detivatives.[27] An unsuccessful attempt to ROMP a 7-oxanorbornene monomer with a pendant propargyl group was attributed to the competing enyne metathesis reaction.[28] If alkynes undergo ring-opening/ring-closing metathesis (ROM/RCM) with the norbornene moieties in the presence of Grubbs' catalyst, a protecting strategy can be employed to prevent competing metathesis with the alkyne moiety.

To provide a comparison, preparation of two Pcs with free and protected alkyne peripheries was conducted (Scheme 2) by ROMP-Capture-Release through statistical macrocyclization of norbornyl-tagged Pc **6** with both acetylenic Pn **1a** and its TIPS-protected analog **1b**. When the mixture of Pcs **7a** and **8a** was subjected to the previously established ROMP conditions,[9b] no polymer precipitate was observed. Modified conditions were also attempted, such as increasing the loading of crosslinker **9** and varying the reaction concentration and time, with similar negative results. Conversely, when the mixture of TIPS-protected Pcs **7b** and **8b** was subjected to the ROMP conditions in the presence of crosslinker **9** the corresponding cross-linked polymer was obtained after filtration and CH_2Cl_2 Soxhlet extraction (Scheme 3). Treatment of the resulting ROMP polymer **10** with 10% trifluoroacetic acid (TFA) in CH_2Cl_2 resulted in release of Pc **11**. Deprotection of Pc **11** using an excess of tetrabutylammonium fluoride (TBAF) afforded Pc **5a** in 7% overall yield from Pn **6**.



Scheme 2. Statistical macrocyclization of Pns **1a**, **1b**, and **6**.

Despite the successful isolation of Pc **5a** via the ROMP-Capture-Release strategy, including successful prevention of alkyne metathesis, the lengthy reaction route involving the additional protection and deprotection resulted in low yields of the desired