DOI: 10.1002/ejoc.201500496

Propeller-Shaped D_{3h}-Symmetric Macrocycles with Three 1,8-Diazaanthracene Blades as Building Blocks for Photochemically Induced Growth Reactions

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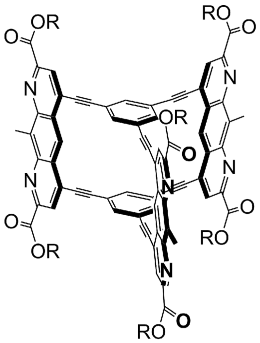
Keywords: Functional materials / Propellers / Cyclophanes / Photochemistry / Cross-coupling / Cycloaddition

The efficient synthesis of new D_{3h}-symmetric propeller-shaped, double-decker compounds with three vertically standing diazaanthracene units arranged so as to allow for photochemically induced intermolecular growth reaction by [4+4] cycloaddition is presented. The propellers bear alkyl chains of four different lengths (ethyl, propyl, hexyl, dodecyl) to have flexibility in creating ordered arrays by packing them into single crystals, onto solid substrates or into mesophases. All propellers are obtained in only six steps and on a 50–200 mg scale. The sequence passes through the ditriflated 1,8-diazaanthracene derivatives **6** which are a very versatile building block for many purposes and were therefore synthesized on a 30 g scale.

Introduction

Shape-persistent compounds with two or three photosensitive anthracene (A) or 1,8-diazaanthracene (DAA) units in the proper geometric relation have been reported as attractive monomers for photochemically induced polymerizations in single crystals as well as in monolayers spread at the air/water interface. Two-dimensional polymers (2DP),[1] covalent monolayer sheets[2] and a novel rigid rod polymer[3] were obtained this way. The growth chemistry in these cases was mainly [4+4] cycloaddition between either two A and two DAA units, or one A and one DAA unit. In a particular case [4+2] cycloaddition between an A unit and an acetylene also proved successful. Fascinated by the fact that this growth chemistry can pave the way to two-dimensionally extended entities, may it be 2DPs[4] or covalent monolayer sheets,[5] and in combination with the present interest in 2D materials,[6] we decided to work on a broad synthetic access to more such building blocks in order to explore the area of rational and mild sheet synthesis more systematically. This shall in future enable us to investigate the use of covalent sheets with high degrees of internal order for applications such as ultra-selective membranes, ultra-sensitive pressure sensors, scratch-resistant surface coatings, novel ferroelectric materials, scaffoldings for novel catalyst systems and the like.

At the same time, we are interested in providing access not only to building blocks (monomers) that can mediate growth in confined geometries such as in single crystals, at the air/water interface or on solid substrates, but also in liquid crystalline phases and possibly even in homogeneous solution. We were therefore interested in having a series of versatile monomers at hand, all sharing the same structural skeleton but differing in their functionalities to meet the respective requirements for these different methods of polymerization. In the present work, we introduce D_{3h}-symmetric propeller-shaped compounds of type **1** (Figure 1) with three photoreactive blades, spaced by acetylene moieties and connected to two central orthogonal benzene cores. The persistent molecular geometry ensures that the blades, which are spatially separated from each other by 120°, cannot react intramolecularly. In addition, intermolecular *syn*-alignment of the blades[7] is impossible. Consequently, reactions of compounds **1** are preset for the intermolecular, *anti*-selective [4+4] cycloaddition, supposed a face-to-face



1
a: $R = C_2H_5$
b: $R = C_3H_7$
c: $R = C_6H_{13}$
d: $R = C_{12}H_{25}$

Figure 1. Chemical structure of the D_{3h}-symmetric cyclophane propellers **1a**–**d** synthesized in the present study. All compounds carry six esters with differently long alkyl groups.

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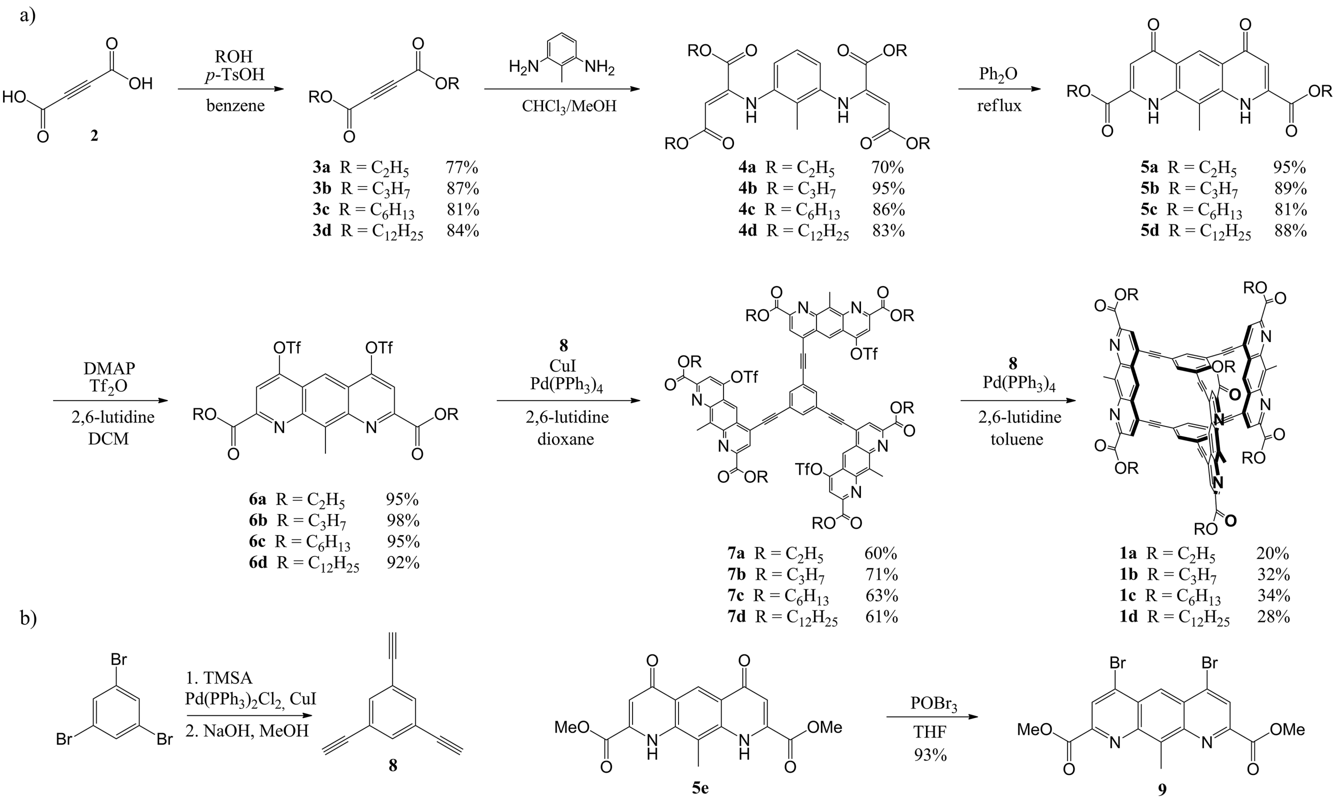
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201500496.

(*ftf*) arrangement can be realized. Compounds **1a–d** are formally cyclophanes[8] bearing six ester groups each with differently long alkyl chains (ethyl to dodecyl). Functional groups that could disturb the desired anthracene π-π interactions (such as H-bond acceptors/donors) have been avoided. It is noted that similar cyclophanes have already been realized by Moore[9] and Zhang.[10] However either the "blades" consist of phenylene-ethynylene units (rather than anthracenes) which were not designed for intermolecular reactions or the compound was not shape-persistent which reduces the probability for an intermolecular *ftf* packing as required for topochemistry.[1,11] Here we report the efficient synthesis of a series of compounds **1a–d** following a few-steps procedure and passing through the novel ditriflates **6a–d** which are a particularly potent building block for cross-coupling reactions and nucleophilic substitutions.

Results and Discussion

The synthesis of the propeller-shaped compounds **1a–d** is depicted in Scheme 1 (a). 2,7-Disubstituted 1,8-diazaanthracene-4,5-ditriflates **6a–d** were selected as key building blocks constituting the blades for monomers **1a–d**, respectively. They were then assembled into the propeller-shaped cyclophanes by Pd-mediated cross-coupling reactions. The sequence starts off with the commercially available acetylenedicarboxylic acid **2**. The acid was first esterified with the corresponding alcohol (a: ethanol, b: *n*-propanol, c: *n*-hexanol, d: *n*-dodecanol) using TsOH as catalyst under azeotropic removal of water in benzene and afforded the diesters **3a–d**. **3a** and **3b** were conveniently purified by distillation, while the higher esters **3c** and **3d** were purified by column chromatography. Inspired by the procedure published by Molock and Boykin,[12] the diesters were then subjected to double aza-Michael additions with 2,6-diaminotoluene as nucleophile in mixtures of $CHCl_3$ and a protic solvent such as MeOH (for **3a–c**) or EtOH (for **3d**), to selectively ensure (*Z*)-isomer formation.[13] This resulted in fast and high-yielding formation of compounds **4a–d**, which were purified by column chromatography (**4c–d**), while the lower congeners precipitated out during the reaction and could be used without further treatment. Double intramolecular cyclization under dilute conditions in refluxing diphenyl ether afforded the pyridoquinolone derivatives **5a–d** in good yields ranging from 81 % to 91 %. In particular, the steric bulk provided by longer alkyl chains such in the case of **5b–d** was beneficial for the scale-up of the reactions. It prevented intermolecular reactions and allowed using more concentrated solutions (e.g. 118 mM instead of 43 mM), though this effect was not fully investigated. Triflation of **5a–d** by treatment with Tf_2O, 2,6-lutidine as base and DMAP as catalyst in dry DCM afforded quantitatively the ditriflates **6a–d** on a multi-gram scale without the need of column chromatography. The ditriflates turned out to be quite stable in the solid state under ambient conditions, but due to their photoreactive nature they needed to be stored in the dark. In solution, the compounds **6a–d** are also quite activated towards nucleophilic aromatic substitution



Scheme 1. (a) The synthetic sequence to the propeller-shaped monomers **1a–d**. (b) Synthesis of building block **8** and dibromide **9**.

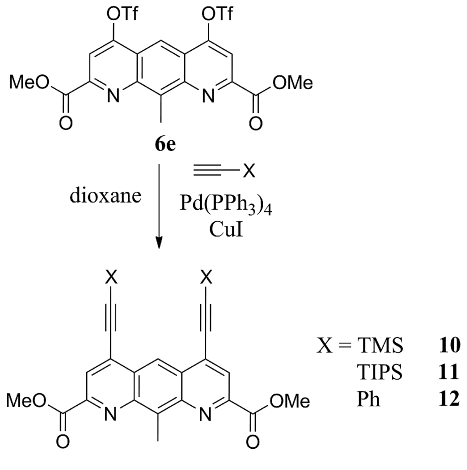
through loss of the triflate moiety, as evidenced by their immediate reaction with secondary amines such as piperidine. 2,6-Lutidine being non-nucleophilic and sterically hindered, proved to be the optimal choice as mild base for working with these compounds. In the next step, the direct target precursors were assembled. For this purpose the ditriflates **6a**–**d** were coupled in excess with 1,3,5-triethynylbenzene **8** (Scheme 1, b) under standard Sonogashira conditions with $Pd(PPh_3)_4$ and CuI as catalyst and co-catalysts, respectively, and 2,6-lutidine as base to afford the monomer precursors **7a**–**d** in yields ranging from 50–70%.

It needs to be mentioned here that while compounds **7c** and **7d** could be easily purified by *r*GPC (recycling gel permeation chromatography), their lower molar mass congeners **7a** and **7b** were poorly soluble which caused difficulty in purification. Despite washings and recrystallizations these two compounds could not be obtained in pure form and were used as obtained. If strictly necessary, these compounds can be nevertheless purified by *r*GPC in small amounts. The NMR spectra of these two compounds in the highest achieved purity are displayed in the SI. Column chromatography was not considered an option due to the six nitrogen functionalities and the sensitivity of the three triflate groups. The excess of the ditriflates **6a**–**d** could be recovered virtually quantitatively by precipitation from the reaction mixture with MeOH and subsequent filtration through a silica plug.

Compound **8** is commercially available but was nevertheless synthesized on the 10 g scale from 1,3,5-tribromobenzene following literature procedures (Scheme 1, b).[14] For the final step to the propellers **1a**–**d**, the precursors **7a**–**d** were subjected to the complex cyclization required which involved one inter- and two intramolecular consecutive reaction steps. For these steps copper-free Sonogashira conditions were applied under high-dilution (1–2 mM) with **8** as stoichiometric coupling partner. Due to the inconvenience of degassing the large volumes of solvent employed for these reactions, the use of copper iodide was avoided in order to reduce the formation of oligomers due to Glaser coupling. Considering the complexity of this step, yields ranging from 20–34% were quite satisfactory. Compounds **1a**–**c** precipitated out during the reaction while the relatively highly soluble **1d** was best purified by *r*GPC. In the latter case, the polarity of the intermediates is dominated by the dodecyl chains, making difficult to separate the desired compounds from the side products by silica gel column chromatography. The waxy consistency of all these compounds was also an undesirable characteristic in terms of purification and for analytical purposes. Nevertheless, this compound could be obtained in pure form. The overall yields to the ditriflates **6a**–**d** were between 49% and 72%, those to the final propellers **1a**–**1d** were between 6% and 16% over all steps.

Given the high symmetry of the compounds, analysis by NMR spectroscopy was simple; full characterization by ^{1}H-NMR- and ^{13}C-NMR spectroscopy as well as high-resolution mass spectrometry (HRMS) confirmed the proposed structure of rotors **1c**–**d**. For **1a**–**b**, a ^{13}C-NMR spectrum could not be obtained even by measuring at 80 °C because of insufficient solubility. It is noted that the poor solubility of these two compounds is a key element of their structure design as it will help force these propellers into the crystalline state. Thus, their structure proof rests only on HRMS and the ^{1}H-NMR spectra, the latter of which are virtually superimposable to that of their soluble congeners (see Supporting Information). Compounds **1a**–**b** can be crystallized from *o*-dichlorobenzene to form crystals of up to 100 µm of various shapes, the structures of which is presently under investigation. The melting points are above decomposition temperature. The UV/Vis absorption of all the monomers are virtually superimposable and therefore the propyl series was chosen as representative for the characterization. Cross-talk between the DAA units in the same compound is minor as the comparison with model compound **12** shows [λ_{max}(**1b**) = 422 nm; λ_{max}(**12**) = 431 nm]. The fluorescence spectra were also measured for the propyl representatives by diluting the same solutions used for the UV/Vis study and do not display any particular feature (Figure S34). Finally, compounds **1a**–**d** were found to be stable up to approximately 300 °C (heating rate: 10 °C/min) by thermogravimetric analysis.

Anthracene and DAA units which can be incorporated into building blocks via their C-1, C-8 positions are particularly attractive for photochemical dimerization reactions because shrinkage can be prevented between the compounds that are connected to one another. This made us explore the reactivity of ditriflates **6** towards Sonogashira cross-couplings. As substrate, we decided to use the not yet discussed derivative **6e** which carries methyl ester groups. The compound was initially synthesized in order to achieve the methyl ester monomer **1e** (see Scheme S1), however synthesis of the latter failed most likely due to severe solubility problems at the precursor stage **7e**. As coupling partners for **6e**, we chose phenylacetylene and the two silylated acetylenes trimethylsilylacetylene and triisopropylsilylacetylene (Scheme 2). In all cases high yields of the doubly substituted products **10**, **11** and **12** were obtained under mild conditions. For product **12**, a single crystal structure was ob-



Scheme 2. Sonogashira cross-coupling reactions of the ditriflate **6e**.

tained (displayed in Figure S36), displaying a rare case of DAA face-to-face stacking. The two units of **12** are engaged in this stack not in the expected anti-parallel,[15] but rather a parallel yet slightly set-off fashion. The crystals do not contain solvent molecules, which proves the efficiency of the packing. It is noted that the ditriflates **6** are clearly superior to the dibromide **9** mentioned in Scheme 1 (b). While the latter would perhaps have been the natural choice for transformations as described in this paper, it proved to be so poorly soluble and unreactive, that even under forcing conditions such as microwave treatment at 150 °C, no coupling products could be obtained (not further described).

Conclusions

In summary, by using the very potent ditriflates **6a–d** a variety of propeller-shaped compounds were made available in short sequences with reasonable overall yields and reasonable overall effort. These propellers will be important building blocks for laterally extended covalent structures derived from photochemically induced DAA dimerization reactions. Future reports will be devoted to this.

Experimental Section

General: Details about the experimental procedures, including characterization, can be found in the Supporting Information.

General Procedure for Esterification to Compounds 3a–d: Acetylenedicarboxylic acid **2** (1 equiv.) was refluxed with the corresponding alcohol (2.2 equiv.) and *p*-toluenesulfonic acid (0.1 equiv.) in benzene using a Dean–Stark trap until the theoretical amount of water was distilled off. The reaction mixture was concentrated and the products were isolated by vacuum distillation in the case of **3a–b**, while silica gel column chromatography was employed for the higher congeners **3c–d**.

General Procedure for Aza-Michael Addition to Compounds 4a–d: A solution of 2,6-diaminotoluene (1 equiv.) in MeOH was added dropwise to a solution of diesters **3a–d** (2 equiv.) in MeOH/$CHCl_3$ at 0 °C. The reaction mixture was stirred at room temperature for additional 16 h. The products **4a–b** were isolated in pure form by filtration and subsequent rinsing with MeOH, while for **4c–d**, the reaction mixture was concentrated and the oily residue was purified by silica gel column chromatography.

General Procedure for Double Intramolecular Cyclisation to Compounds 5a–d: Compounds **4a–d** were refluxed for 1.5 h in degassed diphenyl ether under high diluted conditions (ranging from 43 to 118 mM). In the case of **5a–c**, the product precipitated out of the solution upon cooling to room temperature; hexane was added to complete precipitation and the obtained solid was then filtered and thoroughly washed with additional hexane in order to eliminate all traces of diphenyl ether. For the isolation of **5d**, the solvent was removed by vacuum distillation and the residue purified by silica gel column chromatography.

General Procedure for Triflation to Compounds 6a–d: Compounds **5a–d** (1 equiv.) were suspended/dissolved in dry DCM along with DMAP (0.4 equiv.) and 2,6-lutidine (3 equiv.). The reaction mixture was cooled to 0 °C and triflic anhydride (3 equiv.) was added dropwise over 10 min. After addition, the mixture was warmed to room temperature and stirred for additional 6 h. The solvent was evaporated in vacuo and the obtained residue was washed with warm MeOH to obtain a yellow suspension. The solid was filtered and rinsed with additional MeOH to afford pure **6a–d** as a yellow fluffy solid.

General Procedure for Monomer Precursors 7a–d: An excess of triflates **6a–d** (6 equiv.) was suspended/dissolved in dry dioxane with 1,3,5-triethynylbenzene **8** (1 equiv.) and 2,6-lutidine (6 equiv.). The reaction mixture was degassed and then the catalysts $Pd(PPh_3)_4$ (0.05 equiv.) and CuI (0.05 equiv.) were added. The reaction mixture was then heated under nitrogen in the dark at 65 °C for 2 d. For the isolation of **7a–b**, the reaction mixture was filtered and the obtained yellow solid was washed with dioxane and acetonitrile to eliminate any excess of starting material and then washed with MeOH. The obtained solid was isolated in purities high enough for the next step. To recover the excess of ditriflate, MeOH was added to the filtrate and the obtained precipitate was dissolved in little DCM and passed through a short silica plug (eluent 20% ethyl acetate in hexanes) to obtain **6a–b**. For the isolation of **7c–d**, MeOH was added to the reacton mixture and the resulting yellowish precipitate was collected by filtration and purified by *r*GPC to afford the products as yellow solids and recover the excess starting material.

General Procedure for Synthesis of the Monomers 1a–d: Precursors **7a–d** (1 equiv.) were suspended in dry toluene (concentrations ranging from 1 mM to 2 mM) with **8** (1 equiv.) and 2,6-lutidine (100 equiv.). The suspension was degassed, then $Pd(PPh_3)_4$ (0.6 equiv.) was added. The reaction mixture was heated in the dark at 80 °C under argon for 7 d. To isolate **1a–b**, the reaction mixture was filtered and the obtained brown solid was washed with toluene and MeOH. It was then suspended in chloroform and passed through a pad of celite to obtain yellow solution. The solution was concentrated to saturation and put in the fridge to let the product precipitate out as a fluffy yellow solid. Filtration afforded pure monomers **1a–b**. To isolate **1c–d**, the reaction mixture was concentrated to about ¼ of its volume, MeOH was added and the obtained yellow solid was collected by filtration. Purification by *r*GPC afforded the desired compounds.

General Procedure for Sonogashira Cross-coupling Reactions to Compounds 10, 11 and 12: Ditriflate **6e** (1 equiv.) was suspended in dry dioxane with the corresponding acetylenic coupling partner (2.5 equiv.) and 2,6-lutidine (3 equiv.). The suspension was degassed, then $Pd(PPh_3)_4$ (0.03 equiv.) and CuI (0.03 equiv.) were added and the reaction mixture was heated to 65 °C under nitrogen for 16 to 24 h, depending on the coupling partner. For the isolation of **10**, the reaction mixture was passed through a celite pad and concentrated; the residue was dissolved in little DCM, then MeOH was added and the formed yellow precipitate was collected and recrystallized from acetonitrile to afford pure **10** as yellow needles. To isolate **11**, the reaction mixture was passed through a celite pad and concentrated; the residue was subjected to silica gel chromatography (10% EtOAc in hexane) to afford the pure product. Compound **12** precipitated out during the reaction as a yellow solid; filtration and subsequent recrystallization from boiling *o*-dichlorobenzene, afforded the target compound as yellow needles, suitable for SC-XRD analysis.

Acknowledgments

This work was supported by the ETH Zürich, Switzerland (grant number ETH-26 10-2). The authors thank Chiara Gstrein for her competent help with UV/Vis measurements, Dr. Bernd Schweizer (D-CHAB, ETHZ) for solving the X-ray crystal structure and Rolf

Häfliger (Laboratory of Organic Chemistry, ETHZ) for the high-resolution mass spectrometry measurements. The authors thank Dr. Yoan Simon (Adolphe Merkle Institute, Fribourg, Switzerland) and Dr. Animesh Saha for their kind help with first reaction steps shown in Scheme 2.

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Received: April 20, 2015