Synthetic Methods

DOI: 10.1002/ange.201105105

Highly Twisted Arenes by Scholl Cyclizations with Unexpected Regioselectivity

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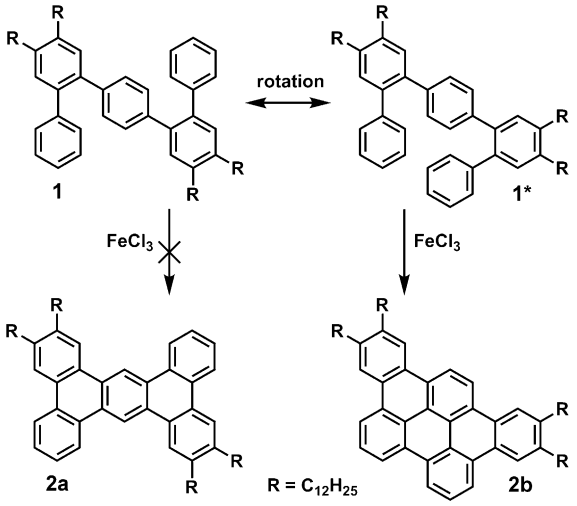
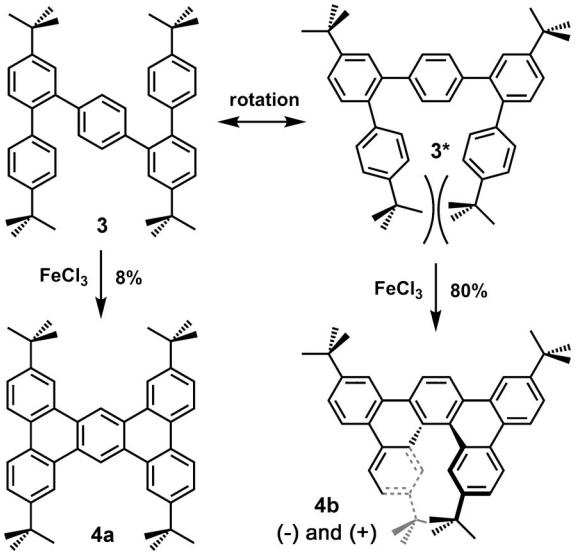
Polycyclic aromatic hydrocarbons (PAHs) have been an important focus of organic synthesis for over a century.[1] Current interest in PAHs is centered on their value as building blocks for carbon nanoribbons[2] and graphenes,[3] mainly because of their known or foreseen utility in organic electronics.[4] Whereas innovative, top-down syntheses allow the formation of giant graphene molecules,[5] bottom-up strategies are preferred for the reproducible synthesis of monodisperse and physically homogeneous nanographenes.[6] Whatever the global synthetic strategy, in most cases the last step is similar: a highly conjugated but flexible molecule has to be "graphenized", that is, transformed into a rigid, polycyclic, aromatic plate by the formation of several C–C bonds between adjacent aromatic rings. Photocyclization of stilbene-based precursors seems to be a satisfying solution for small substrates,[7] but subsequent reactivity with bigger molecules is rarely predictable. Therefore, intramolecular Scholl reactions, that is dehydrocyclizations with acidic oxidants such as $FeCl_3$[8] or $DDQ/MeSO_3H$,[9] are usually preferred.

The reactivity and regioselectivity of intramolecular Scholl reactions remain only partially predictable. Not every polyphenylene configuration can be graphenized, mainly because of incomplete reactions,[10] and sometimes because of unexpected rearrangements.[11] In addition, some experimentally determined regioselectivity remains unexplained (Scheme 1).[12] Despite a slightly higher steric hindrance, the intramolecular Scholl condensation of compound **1** was reported to lead exclusively to tribenzoperylene **2b**, instead of the benzenoid tetrabenzanthracene **2a**.

To form the tetrabenzanthracene core by forcing a *transoid* double cyclization through steric hindrance, we synthesized the tetrasubstituted quinquephenyl **3**.[13] In this case, the bulky *tert*-butyl groups generate strong steric hindrance when the molecule is in the *cisoid* conformation (Scheme 2). We were puzzled to find that this considerable steric hindrance seemed to have only a weak, if any, influence on the regioselectivity of this particular Scholl reaction. Tetrabenzanthracene **4a** was formed in only 8% yield, whereas dibenzopicene (or dibenzo[5]helicene) **4b** was obtained in 80% yield. Relative to the case described in Scheme 1, the only striking effect of steric hindrance in the



Scheme 1. Regioselectivity of the Scholl cyclization of the *o*,*p*,*o*-quinquephenyl derivative **1**, recently reported by Müllen and co-workers.[12]



Scheme 2. Unexpected regioselectivity of a Scholl reaction in favor of a highly congested [5]helicene.

Scholl reaction of **3** is the absence of the third dehydrocyclization to form a tribenzoperylene. This result was confirmed by ^1H NMR spectroscopy. Compound **4a** is more symmetrical than **4b**, and a significant shielding effect (an upfield shift of $\delta = 0.4$ ppm) was detected for the resonance of the protons of the two *tert*-butyl groups at the helicene bay entrance of **4b**. This shift suggests that the two *tert*-butyl substituents are facing an aromatic ring.

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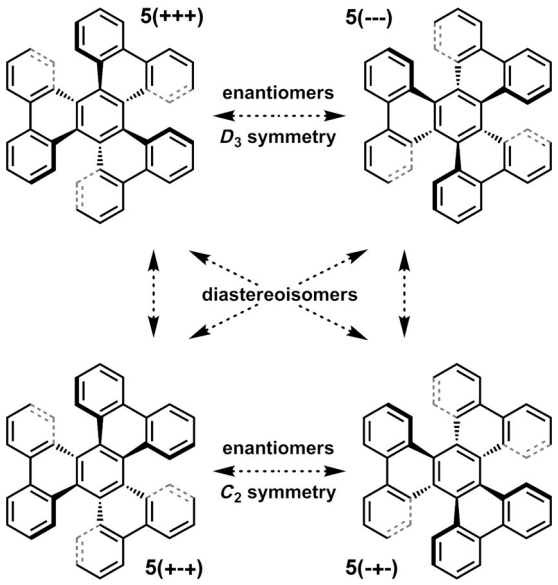
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201105105.

To take advantage of this unexpected reactivity, and to explore the limits of this path for accessing highly distorted polycyclic aromatic cores, we turned our attention to molecules incorporating several helicene units, in particular hexabenzotriphenylene (HBTP, **5**). HBTP is the smallest molecule that contains three [5]helicene units. As a result of its triple helicity, HBTP has four stereoisomers (Scheme 3).[14b,e] When the three helicene fragments have the same configuration, (+) or (−), HBTP has D_3 symmetry,



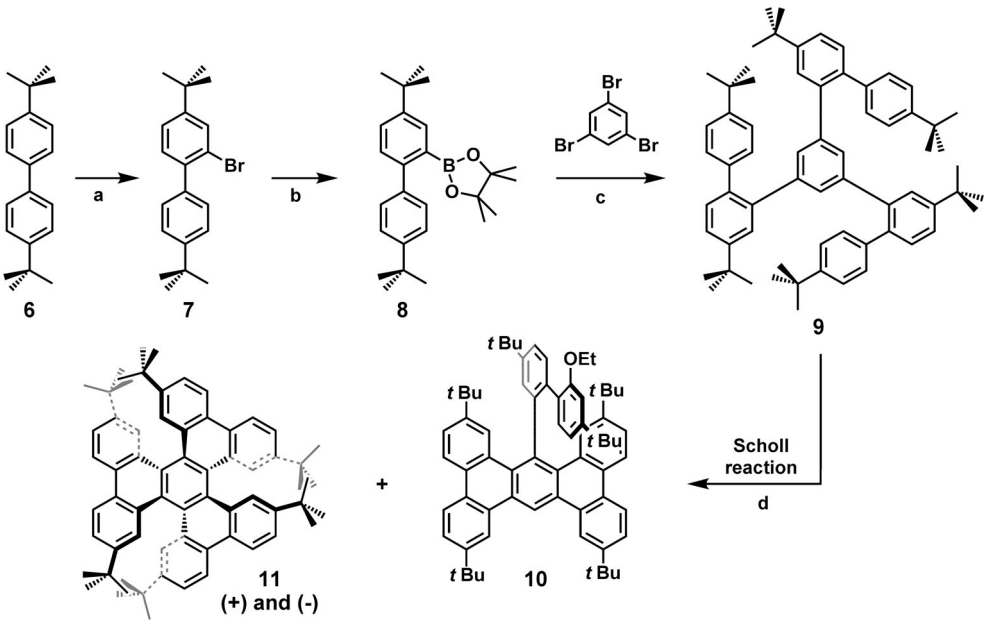
Scheme 3. The four isomers of hexabenzotriphenylene (HBTP).

and these two enantiomers are propeller-shaped molecules. When one helicene unit is different from the two others, the resulting two HBTP enantiomers have C_2 symmetry.

The synthesis of unsubstituted HBTP has already been described.[14] The most efficient method is a strategy based on cyclotrimerization of a polycyclic aryne.[14d] Substituted HBTPs have not yet been reported, and partial graphenizations of hexaphenylbenzene-based species have never led to HBTP.[10,15]

Hexa-*tert*-butylhexabenzotriphenylene (tBu$_6$-HBTP) **11** was obtained after a four-step synthesis, starting from commercially available compounds (Scheme 4). 4,4′-Di-*tert*-butylbiphenyl (**6**) was brominated with bromine in chloroform at 70 °C without any catalyst, to give 2-bromo-4,4′-di-*tert*-butylbiphenyl (**7**) in a high yield. Through an organolithium-mediated procedure, the bromo substituent was then replaced by a boronic ester function, to give compound **8**. Compound **8** was then treated with 1,3,5-tribromobenzene and a catalytic amount of [Pd(PPh$_3$)$_4$] to give **9** in good yield (76 %), despite the three Suzuki cross-coupling reactions. Finally, **9** was dissolved in anhydrous, degassed dichloromethane and a solution of $FeCl_3$ in nitromethane was added slowly, with argon vigorously bubbling through the solution to remove HCl from the mixture. After one hour, the reaction was quenched with an alcohol (methanol or ethanol) and the crude product was purified by column chromatography. Two very closely eluting products were isolated and identified. The major product was a racemic mixture of pure **11**, which was obtained in 63 % yield. The three-bladed propeller shape of **11** had D_3 symmetry, which made it easy to identify through its ^{1}H NMR spectrum of only four signals. Surprisingly, isomers of **11** with C_2 symmetry were not obtained. Such isomers were isolated in metal-catalyzed syntheses of unsubstituted HBTP,[14c–e] and were shown by NMR spectroscopy to convert into the more stable D_3 species when heated.[14d] However, in the case of the more hindered **11**, such a conversion may be sterically impeded at room temperature, making it unlikely that the C_2 species is formed initially. It follows that the topological path of the Scholl reaction is distinctively different from that of the metal-catalyzed cyclotrimerization of polycyclic arynes.

The minor product **10**, which was obtained impure with an estimated yield of 25 % for the last step, is a tetrabenzanthracene which resulted from a *transoid* second dehydrocyclization. This structure was determined by 2D ^{1}H NMR



Scheme 4. Synthesis of highly distorted tBu$_6$-HBTP (**11**): a) Br_2, $CHCl_3$, 70 °C, 16 h, 69 % yield. b) BuLi, THF, −78 °C, 15 min, then B(OMe)(pinacol), THF, −78 °C to RT, 1 h, 75 % yield. c) [Pd(PPh$_3$)$_4$], Na_2CO_3, PhMe, H_2O, EtOH, 90 °C, 48 h, 76 % yield. d) $FeCl_3$, $MeNO_2$, CH_2Cl_2, bubbling Ar, RT, 1 h, EtOH, 63 % yield of isolated **11**, 25 % yield of **10** (estimated by NMR spectroscopy).

(COSY and NOESY) spectroscopy. This side product was substituted with an alkoxy group during the quenching of the reaction with an alcohol. The origin of this substituent was confirmed by changing the nature of the quenching alcohol, which led to the incorporation of a different alkoxy group.

Monocrystals of **11** were obtained as large yellow needles by slow diffusion of methanol in dichloromethane. Analysis of these crystals by X-ray diffraction showed the distortion of **11** in the solid state (Figure 1). In single crystals of **11**·3CH_2Cl_2

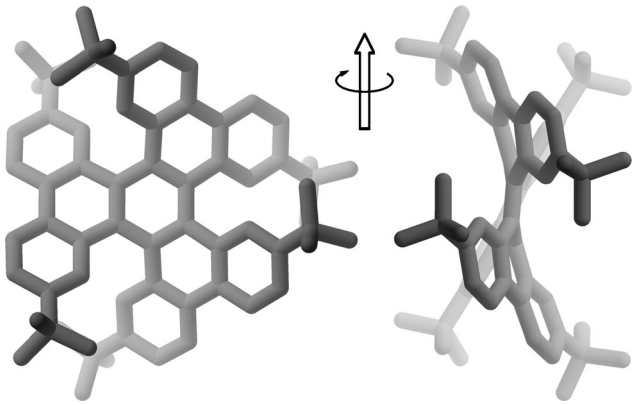


Figure 1. Crystal structure of *t*Bu_6-HBTP (**11**): two different views of a single molecule.

the compound crystallized in a centrosymmetric $P\bar{3}c1$ space group, and was composed of a racemic mixture of the two enantiomers. The structure of the molecule is similar to the one reported for the parent unsubstituted HBTP. The center of the molecule is on a threefold crystallographic axis. Each mean plane formed by the "propeller blade" is tilted by an angle of approximately 47° with respect to each other. Surprisingly, despite the presence of bulky *tert*-butyl groups, this tilt angle is very similar to the tilt angle in unsubstituted HBTP (49–50°).[14b] The bond lengths are consistent with six peripheral aromatic rings (C–C lengths between 1.368(4) Å and 1.414(4) Å, and dihedral angles C-C-C-C less than 1.6°) connected to a distorted central benzene ring (C–C lengths of 1.403(5) Å and 1.439(5) Å and dihedral angles up to 19.2°) by quite long C–C bonds. The lengths of these long bonds are consistent with single bonds (1.471(3) Å). The three resulting six-membered rings are twisted, with C-C-C-C dihedral angles of up to 31.3°. Another solvate of **11** (**11**·AcOEt·2H_2O) was also obtained and characterized by X-ray diffraction. A further description of the crystal structures is given in the Supporting Information.

In conclusion, to gain better insight into the well-known, but still only partially understood, Scholl reaction, its regioselectivity was investigated by using test molecules functionalized with bulky *tert*-butyl substituents. These compounds offered competing cyclization pathways to noncongested *transoid* products and highly congested *cisoid* alternatives, which had no apparent difference in their (all-benzenoid) aromatic stabilization. Against all expectation, even such strong steric hindrance had no marked effect on the regioselectivity. Highly twisted, polycyclic aromatic hydrocarbons were preferentially formed, whereas the corresponding flat and more symmetrical isomers were only obtained as minor by-products. These results indicate that trying to influence the regioselectivity of Scholl reactions by incorporating bulky groups into the flexible polyphenylene precursors may not be as efficient as expected. In addition, particular attention must be paid when analyzing products of dehydrocyclizations, and no isomer should be neglected as a possibility when adjacent benzene rings can react in several ways. Our results, especially the efficient Scholl synthesis of highly twisted, triply helical **11**, suggest that the Scholl reaction can be considered for the synthesis of helicenes and other highly strained polycyclic aromatic hydrocarbons, which have recently become the targets of considerable synthetic efforts.[16]

Received: July 20, 2011
Revised: October 6, 2011
Published online: November 4, 2011

Keywords: arenes · helicenes · polycycles · regioselectivity · Scholl reaction

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