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Synthesis of a Bent, Twisted, and Chiral Phenanthrene via an Iodine Monochloride-Mediated, Strain-Inducing π-Extension Reaction

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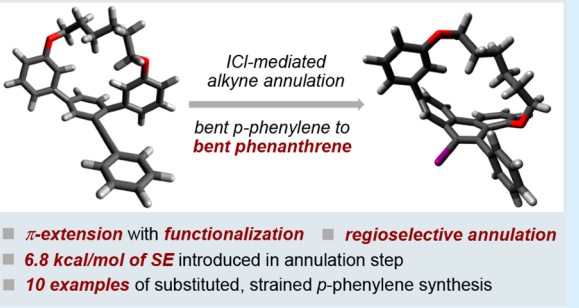
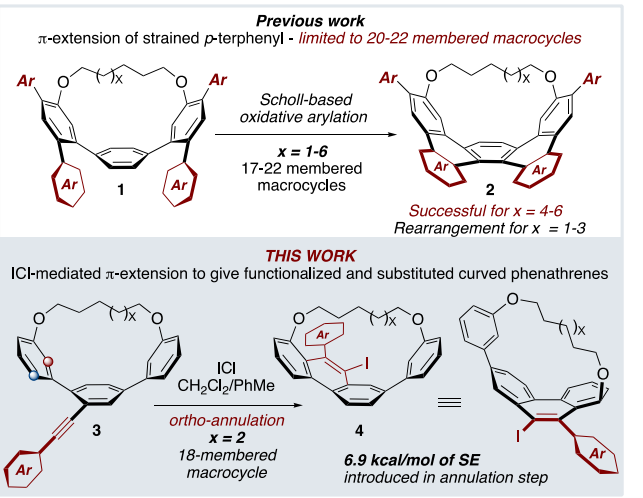
ABSTRACT: A strategy for the synthesis of substituted and strained *p*-phenylene units is reported. An oxidative allylic alcohol rearrangement, followed by organometallic addition to the resulting α-ketol and subsequent dehydrative aromatization, affords *p*-terphenyl-containing macrocycles in which the central *p*-phenylene has been selectively substituted. Ten 18-membered macrocycles have been synthesized, eight of which contain substituents that could enable π-extension. Only alkynylated derivatives were amenable to π-extension via an ICl-mediated reaction, affording a highly bent, twisted, and chiral phenanthrene.



The development of synthetic strategies that enable the preparation of atomically precise, carbon rich materials has been an important area of investigation for decades.[1] In particular, the synthesis of such materials that are curved, twisted, or bent has taken center stage in the field of nonplanar aromatic hydrocarbon synthesis.[2] Fascinating structures such as warped nanographenes,[3] twisted graphene nanoribbons (GNRs),[4] π-extended helicenes,[5] and carbon nanobelts (CNBs) have succumbed to chemical synthesis in recent years. In the case of the CNBs, approaches to their synthesis have been ongoing for more than 50 years, with their bottom up chemical syntheses being conquered by the groups of Itami and Miao independently in 2017 and 2019, respectively. The Itami approach to CNBs involved the synthesis of a macrocyclic precursor that contained strategically placed aryl bromides that would undergo a late stage Yamamoto reaction to furnish a fully conjugated, polycyclic aromatic hydrocarbon (PAH)-based CNB.[6] Miao and co-workers could capitalize on using cycloparaphenylene units as a diameter-defining templates for the synthesis of an armchair-based CNBs using a Scholl reaction to convert the benzenoid macrocycle to a PAH-based macrocycle.[7] In the case of the latter, π-extension of the carbon nanohoop was computed to be only slightly strain-inducing, and in some instances strain-relieving, which contributed to the success of the oxidative arylation-based approach.

Our group has been interested in developing synthetic strategies for enabling π-extension of strained benzenoid macrocycles to increasingly strained PAH-containing macrocycles, and in 2018, we reported an investigation of oxidative arylation reactions on a homlogous series of *p*-terphenyl-containing macrocycles. These studies demonstrated that the Scholl reaction can be employed in strain-induced π-extension reactons of curved macrocyclic templates, and ≤28 kcal/mol of strain energy (SE) could be imposed in the macrocyclic structure of **2** [i.e., **1** to **2**; x = 4 (Scheme 1A)]. While a considerable amount of SE can be induced during the Scholl

Scheme 1. π-Extension of *p*-Terphenyl-Containing Macrocycles via the Scholl Reaction (previous) and an ICl-Mediated Annulation (this work)



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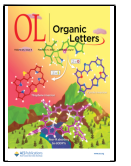

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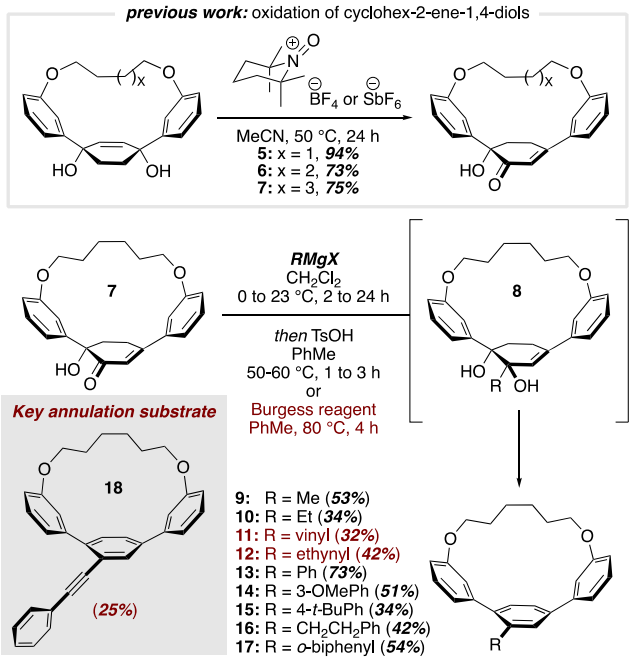
reaction, the amount of SE present in the benzenoid unit that is undergoing annulation is also an important consideration. Due to the acidic nature of the (Scholl) reaction conditions, strained benzenoid units, which comprise the *p*-terphenyl unit, are susceptible to 1,2-aryl migration reactions, which ultimately lead to strain relief (i.e., *p*-phenylene to *m*-phenylene migration).[8] Thus, only macrocycles that contained *p*-phenylene units with <4 kcal/mol of SE successfully underwent π-extension without rearrangements. To address this shortcoming of the Scholl reaction and to continue our program in the development of robust annulation methods that enable π-extension to increasingly strained aromatic systems, we report here the application of an iodine monochloride-mediated alkyne annulation reaction to furnish a bent, twisted, and chiral phenanthrene unit. This reaction not only leads to π-extension of a strained benzenoid/biphenyl fragment but also provides access to an arylated, functionalized, and curved PAH, from which subsequent skeletal building reactions can take place.

In 2020, we reported that macrocyclic cyclohex-2-ene-1,4-diols undergo oxidation upon treatment with oxoammonium salts derived from TEMPO to furnish α-ketol derivatives such as **5**–**7** (Scheme 2).[9] These substrates were viewed as

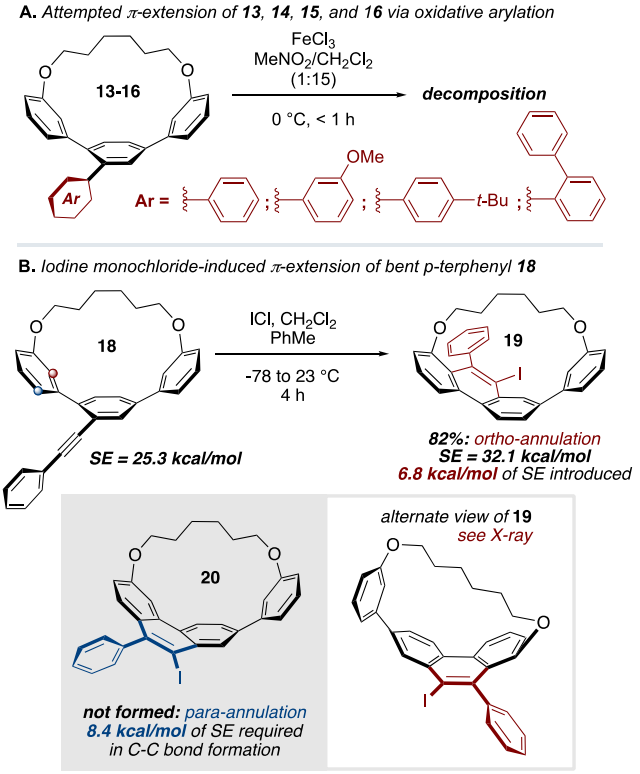
Scheme 2. Synthesis of Alkylated, Alkenylated, Alkynylated, and Arylated Bent *p*-Terphenyl-Containing Macrocycles



important building blocks for the synthesis of functionalized and substituted, strained *p*-phenylene units. Indeed, treatment of **7** with Grignard reagents afforded 1,2-diols, which were subsequently aromatized via dehydration with TsOH or the Burgess reagent[10] to afford alkylated (**9**, **10**, and **16**), alkenylated (**11**), alkynylated (**12** and **18**), and arylated (**13**–**15** and **17**) bent *p*-terphenyl-containing macrocycles in 25–73% overall yield (Scheme 2). The most interesting were the alkynylated and arylated derivatives, as these substrates could be subjected directly to π-extension reactions.

In the case of arylated derivatives **13**–**15** and **17**, subjecting these substrates to Scholl reaction conditions led to rapid decomposition of the macrocycles (Scheme 3A). While it was

Scheme 3. (A) Attempted π-Extension of 13–16 and (B) ICl-Mediated Strain-Induced, π-Extension of 18



anticipated that the desired π-extension reaction would be challenging using an oxidative arylation reaction, we were surprised to find that no tractable materials, either π-extended or rearranged, were afforded. Similarly, treatment of homobenzylically substituted derivative **16** with $FeCl_3$ led to decomposition of the starting material. At this stage, the π-extension of the strained *p*-terphenyl unit of alkynylated macrocycle **18** was investigated. Several groups have reported on alkyne annulation reactions that lead to π-extension of planar benzene rings and PAHs.[11] Chalifoux and co-workers have developed a powerful strategy for the synthesis of pyrene-based helicenes[12] and related warped nanographene-type materials.[13] While alkyne-based annulation reactions have been used to induce curvature in planar aromatic compounds, to the best of our knowledge, the application of such reactions has not been employed in the π-extension of preexisting curved and strained aromatic systems. Thus, when alkynylated macrocycle **18** was subjected to iodine monochloride in dichloromethane/toluene at −78 °C, we were delighted to find that π-extension of the strained *p*-terphenyl unit takes place to afford **19** in 82% yield (Scheme 3B).

π-Extended macrocycle **19** is the product of annulation at the carbon *ortho* to the alkyloxy bridging unit (colored red in Scheme 3B). DFT calculations indicate that an increase of 6.8 kcal in SE accompanies the formation of **19** and that annulation at the *para* carbon of **18** (colored blue in Scheme 3B) to afford **20** would result in an 8.4 kcal/mol increase (in SE). The latter was not observed or isolated in the reaction of **18** with ICl. To investigate whether electronic effects play a role in the regiochemical outcome of this reaction, a model, nonmacrocyclic *p*-terphenyl derivative was synthesized. Subjecting alkynylated *p*-terphenyl **21** (see the Supporting Information for details) to the same reaction conditions that

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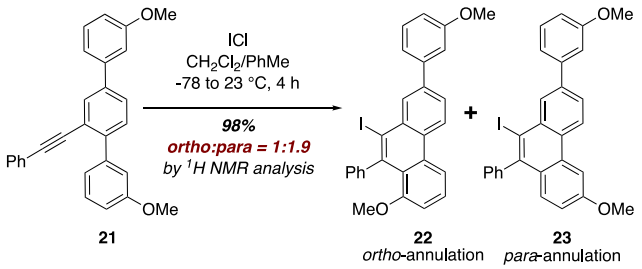
produced **19** gave a mixture of **22** and **23** (*r.r.* 1:1.9) in 98% yield (Scheme 4). Formation of **23** is favored when

Scheme 4. ICl-Mediated Annulation of *p*-Terphenyl 21



unperturbed dimethoxy-*p*-terphenyl **21** is subjected to ICl on the basis of steric hindrance, with annulation taking place via the least congested (*para*) mode of cyclization. In the case of **19**, the more congested (*ortho*) mode of cyclization takes place. This is likely due to conformational constraints imposed by the alkyloxy bridging group, resulting in preferential attack of the intermediate iodoniumm ion by the *ortho* carbon, furnishing the less strained phenanthrene-containing macrocycle (cf., **19** to **20**)

Initial assignment of the structure for the newly formed PAH-containing macrocycle was complicated by the appearance of only 13 (of 15) aromatic signals in its ^{1}H NMR spectrum at 25 °C. Variable-temperature NMR studies confirmed that the room-temperature spectrum of **19** is near the coalescence temperature of Ha and Hb, and at −30 °C, these signals are well resolved (Figure 1A). Fortunately, recrystallization of **19** from ethyl acetate and hexanes produced crystals suitable for X-ray analysis (Figure 1B). The solid-state structure of **19** corroborates the regiochemical outcome of the ICl-mediated annulation of the strained *p*-terphenyl unit of **18**. It also shows that the phenanthrene unit formed in this reaction is both bent and twisted. The end-to-end bend of the phenanthrene system in **19** (i.e., from C_b to C_i) is 28.5°, while the end-to-end bend of the entire aromatic unit of the cyclophane (i.e., the 2-phenylphenathrene system) is 53° (see the simplified subunit in Figure 1B). The high degree of twist about the PAH backbone is exemplified by the C_a−C_b−C_c−C_d, C_e−C_f−C_a−C_b, and C_g−C_e−C_f−C_h dihedral angles, which measure 5.4°, 16.0°, and 24.4°, respectively. The bay region of **19** is twisted by 8.2°. A comparison of the photophysical properties of **19** to the unperturbed 9-iodo-1,6-dimethoxy-10-phenylphenathrene (**22**) shows that there is a slight red shift in both the UV−vis and emission spectra of **19** relative to those of **22**. These results are consistent with reports on related twisted PAH systems, such as pero- and teropyrenes, albeit with much smaller bathochromic shifts.[14] Time-dependent DFT calculations (TD-DFT, B3LYP/6-31G* level theory) also predict a red shift in the electronic absorption spectra of **19** relative to those of **22**.[15] The UV−vis spectrum of **19** shows two major absorption bands with a λ_{max1} of 363 nm and a λ_{max2} of 380 nm, which are significantly broadened relative to those of **22** (λ_{max1} = 357 nm, and λ_{max2} = 375 nm). A similar result was observed for a constrained, π-extended helicene that we synthesized in 2018.[9] The broadening of these absorption bands may be do to "ring breathing" within the PAH of the constrained system. A temperature-dependent UV−vis study of **19** showed sharpening of these absorption bands at lower temperatures,[15] which supports this assertion. Finally, **19** was

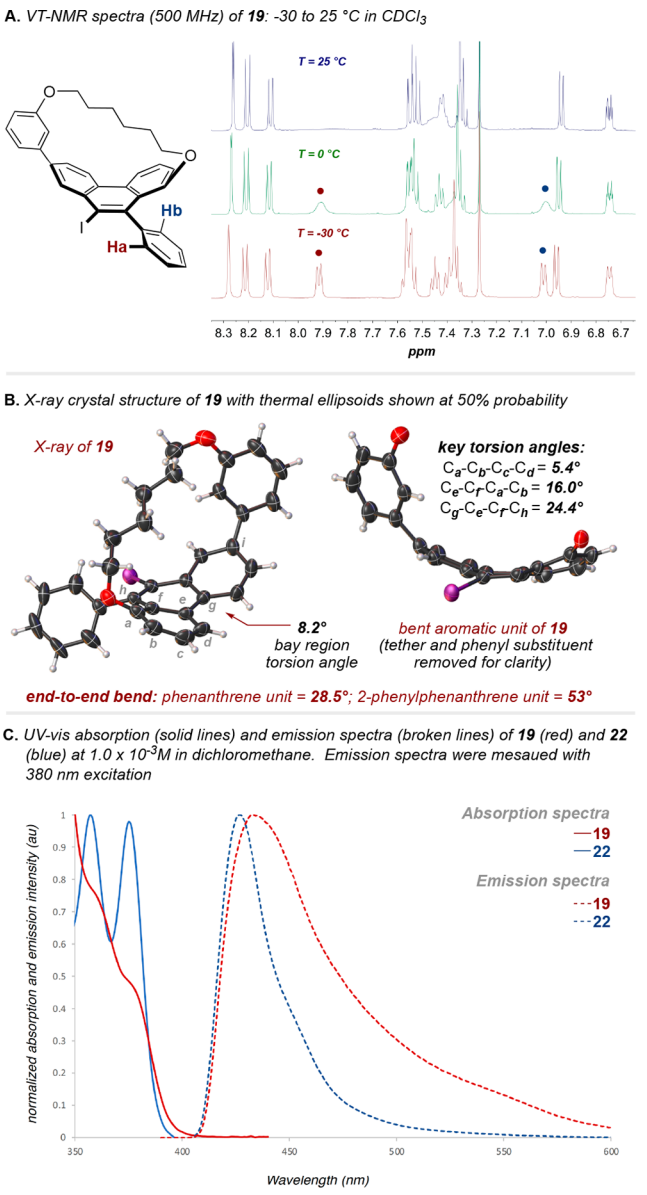


Figure 1. (A) Variable-temperature NMR spectra of **19**. (B) X-ray crystal structure of **19**. (C) UV−vis and fluorescence spectra of **19** and **21**.

produced as a pair of enantiomers, which were separated by preparative chiral HPLC, and their optical rotations were found to be −1.37° and 1.11°.[15]

In conclusion, a strategy for the synthesis of substituted, strained *p*-phenylenes, derived from an α-ketol arene surrogate, has been developed. In the case of the 18-membered, strained *p*-terphenyl-containing macrocycle investigated here, arylated derivatives proved to be poor substrates for π-extension to PAH-containing macrocycles; however, π-extension of an alkynylated derivative via an ICl-mediated reaction was accomplished.[16] The latter affords a highly bent and twisted phenanthrene unit, which contains vicinal iodide and phenyl substituents. The installation of these functional groups should enable future skeletal building reactions and subsequent π-extension to convert related macrocycles into wider PAH segments of CNBs. This ICl-mediated π-extension reaction enabled the introduction of 6.8 kcal/mol of SE into a preexisting strained arene unit (SE = 25.3 kcal/mol) and

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represents a rare example in which annulation can be achieved while increasing the SE of a macrocyclic benzenoid system. The application of this reaction to other strained *p*-terphenyl-containing macrocycles and subsequent π-extension of the functionalized strained phenanthrene units is currently under investigation in our laboratory. The results of these studies will be reported in due course.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.1c04233.

^{1}H and ^{13}C NMR spectra for all new compounds, crystallographic data, and DFT for compounds **18**−**20** (PDF)

Accession Codes

CCDC 2128704 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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