ORGANIC
LETTERS

2009
Vol. 11, No. 22
5146−5149

Corannulene Ethers via Ullmann Condensation

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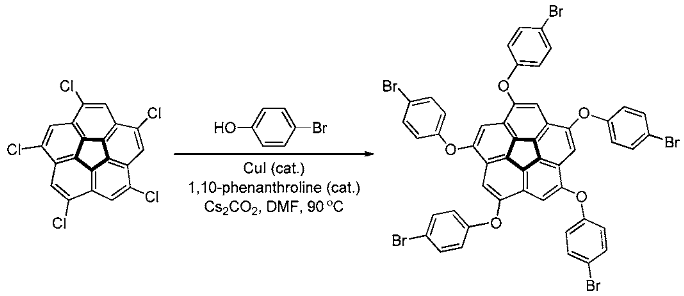
Received July 26, 2009

ABSTRACT



Penta-aryloxycorannulene derivatives, which were previously considered difficult synthetic targets, are efficiently achieved via the Cu(I)-catalyzed Ullmann condensation reaction between 1,3,5,7,9-pentachlorocorannulene and a broad variety of substituted phenols. The reaction proceeds under air and mild conditions that are compatible even with 4-bromophenol. These findings open new avenues for easy preparation of other symmetrically substituted pentagonal building blocks that can be used for the preparation of new materials and new supramolecular architectures.

The construction of large molecular and supramolecular architectures of pentagonal symmetry is a nontrivial task due to the scarcity of C_5-symmetrical organic molecules, unlike those having C_2, C_3, C_4, and C_6 symmetries.[1] The few known pentagonal compounds include mainly conformationally flexible macrocycles, such as calix[5]arenes,[2] calix[5]furans, calix[5]pyrroles,[3] crown ethers, and aza-crown ethers,[4] as well as a few conformationally rigid molecules.[5] In contrast, pentagonal symmetry is quite abundant in the realm of inorganic materials and metal coordination complexes[6] and in natural biomolecules, such as protein pentameric structures and DNA.[7]

This background renders the corannulene molecule,[8] which is characterized by a C_5-symmetrical bowl shape and rigid polycyclic aromatic nature, a unique building block. Peripheral functionalization of this molecule can lead to large molecular[9] and supramolecular architectures having 5-fold symmetry, including quasicrystals,[10] discotic liquid crystals,[11] chemical capsids,[12] pentagonal dendrimers,[13,14] single-wall nanotubes,[15] light emitters,[16] and helical foldamers.[17]

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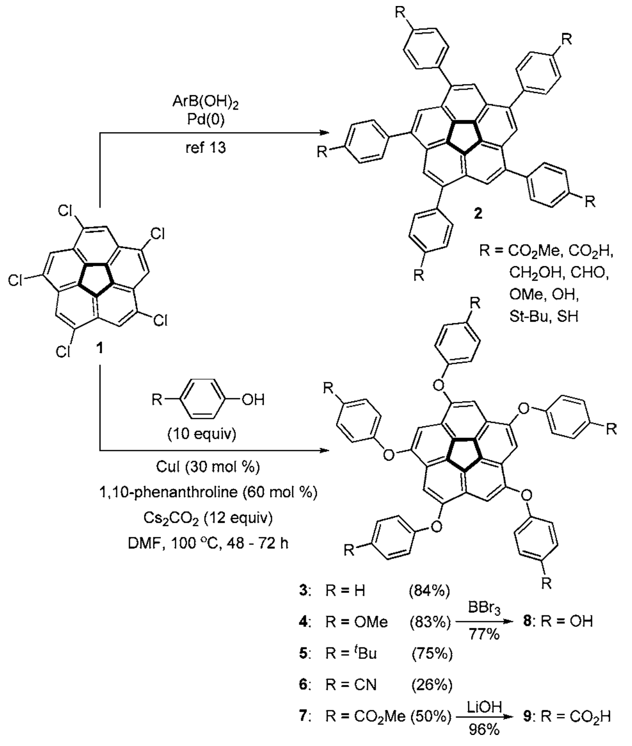
10.1021/ol902352k CCC: $40.75

For example, 12 pentagonal tiles equipped with "sticky edges" are required to construct a nonprotein molecular capsid. Such tiles can form a molecular capsule of icosahedral symmetry via self-assembly.[12] To meet this synthetic challenge, we have recently developed a general method for the cross-coupling of 1,3,5,7,9-pentachlorocorannulene, **1**, with aryl and heteroaryl boronic acids to produce pentaarylcorannulenes, **2** (Scheme 1). This approach has also yielded other unique structures, such as pentagonal dendrimers.[13] As the rigid, all-carbon molecular skeleton of **2** exhibits low solubility in most solvents, we envisioned that the corresponding pentaethers, **3**−**7**, would be much more soluble and easier to manipulate in organic solvents.

Scheme 1



An obvious approach to the formation of corannulene pentaethers was the direct substitution of **1** by alkoxide nucleophiles. Unfortunately, unlike substitution by thiolate anions,[18] the reaction with phenolate and alkoxide anions, which are less reactive nucleophiles, requires quite harsh conditions. For example, sym-pentakis(1,4,7-trioxaoctyl)-corannulene, which is the only reported pentaalkoxycorannulene thus far, was achieved by heating a solution of **1** with sodium diethyleneglycolate monomethyl ether at 180 °C for 2 days.[18,19] Our efforts to prepare compound **3** from **1** under similar conditions using 4-methoxyphenol with either NaH or K_2CO_3 (DMF, 110 °C) afforded low yields of complex mixtures of partially substituted corannulene derivatives.

In principle, the copper-catalyzed arylation of nucleophiles (Ullmann condensation) could solve this problem because the method has been widely used for the formation of C(aryl)−N, C(aryl)−C, and C(aryl)−O bonds.[20a] Furthermore, the special effect of bidentate *N*,*N*- and *N*,*O*- ligands on this reaction, which was discovered by Buchwald, has extended the synthetic scope and has allowed for substitution of aryl halides by phenols under mild conditions.[20] Unfortunately, the reaction was reported to be limited to aryl iodides and bromides and did not work well with aryl

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chlorides except for rare cases of highly electron-deficient substrates.[21]

Here we report that the synthesis of various pentaaryloxycorannulene derivatives can be achieved with high efficiency via the Cu(I)-catalyzed Ullmann condensation reaction under mild conditions that are compatible even with 4-chlorophenol and 4-bromophenol.

A typical procedure for this reaction[22] (Scheme 1) involves mixing **1** (0.1 mmol) in DMF (2 mL) together with the appropriate phenol (1 mmol, 10 equiv), CuI (0.03 mmol, 6% per site), 1,10-phenanthroline (0.06 mmol, 12% per site), and Cs_2CO_3 (1.2 mmol, 12 equiv). The mixture is stirred at 100 °C for 24−72 h, then cooled to room temperature, diluted with dichloromethane, and washed with aqueous NaOH, then with H_2SO_4, water, and brine. Removal of the solvent affords an orange-brown solid that can be purified either by chromatography or by recrystallization. For example, the reaction with 4-methoxyphenol affords, after purification, 1,3,5,7,9-pentakis(4-methoxyphenoxy)corannulene, **3**, in 83% yield. Considering the five reactive sites on the molecule, this overall yield reflects over 96% yield per site, which is quite remarkable for this type of nontrivial coupling. It is noteworthy that the reaction can be performed under air with no need for inert atmosphere.

Under these reaction conditions we have prepared a variety of pentaaryloxycorannulene derivatives, **3**−**9**, in satisfactory yields (Scheme 1), thus demonstrating the generality of the reaction with respect to phenols bearing either electron-withdrawing (CO_2Me, CN) or electron-donating (OMe, *tert*-Bu) groups. All products are highly soluble in chlorinated solvents, such as CH_2Cl_2 and $CHCl_3$ and partially soluble in other common organic solvents, including toluene, ethyl acetate, THF, and DMF. Consequently, most of these polyethers can be conveniently purified by silica-gel chromatography and easily characterized by NMR and MS. More importantly, unlike our previously described pentaarylcorannulenes, **2**, which are quite insoluble in most organic solvents,[13] the high solubility and ready availability of the pentaaryloxycorannulene derivatives render them excellent building blocks for pentagonal molecular and supramolecular architectures.

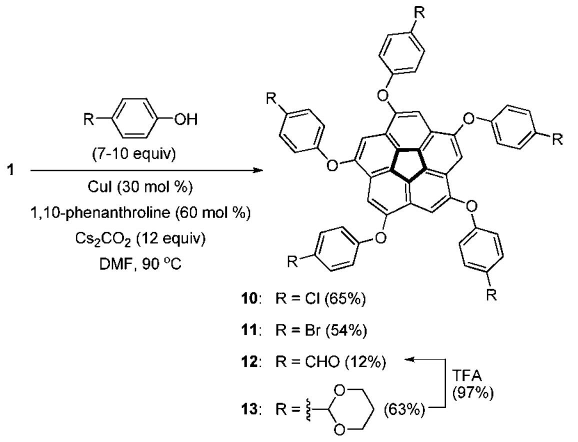
The new coupling products were found to be stable molecules that were easily transformed under straightforward conditions to other useful derivatives in high yields. For example, treatment of **4** with excess BBr_3 (CH_2Cl_2, rt, 24 h) afforded 1,3,5,7,9-pentakis(4-hydroxyphenoxy)corannulene, **8**, in 77% yield. The pentaester **7** was hydrolyzed (LiOH, THF−H_2O) to give 1,3,5,7,9-pentakis(4-carboxyphenoxy)corannulene, **9**, in 96% yield.

Of particular interest for synthetic applications is the remarkable scope of this transformation. Since it is commonly known that the copper(I)-catalyzed Ullmann condensation reaction between phenols and aryl halides works well with aryl iodides and bromides but not with aryl chlorides,[21,22] the high efficiency of the coupling between **1** and various phenols was quite surprising. Furthermore, one would expect that achieving penta-substitution under mild conditions would become increasingly difficult with the growing number of electron-donating substituents on the corannulene core. Increased electron density could diminish the reactivity of the remaining chloride groups.

Our counterintuitive observations could be explained by the unusual reactivity of **1**. It has already been reported that corannulene chlorides are more reactive than regular chloroaromatic compounds with respect to either nucleophilic substitution or oxidative addition to electron-rich transition metals.[9b] This unique reactivity could be explained by partial bond fixation in corannulene, which endows the aryl chloride functions in **1** with significant vinyl chloride character. Indeed, crystallographic data indicate that the rim double bond in corannulene is significantly shorter (1.38 Å) than an average aromatic bond (1.40 Å).[23]

In line with this enhanced reactivity was our observation that the copper-catalyzed substitution reaction proceeds in high chemoselectivity with 4-chlorophenol. The product, 1,3,5,7,9-pentakis(4-chlorophenoxy)corannulene, **10**, was obtained in 65% yield without any byproducts from either homocoupling of 4-chlorophenol or further reactions of **10** (Scheme 2). Even more remarkable was the chemoselectivity observed with 4-bromophenol, which produced 1,3,5,7,9-pentakis(4-bromophenoxy)corannulene, **11**, in 54% yield.

Scheme 2



The reaction conditions were found to be compatible with other sensitive functional groups, such as the free aldehyde in 4-hydroxybenzaldehyde, leading to 1,3,5,7,9-pentakis(4-formylphenoxy)corannulene, **12**, although in low yields (Scheme 2). Nevertheless, higher yields of **12** were achieved by adopting a two-step procedure: first coupling of **1** with 4-(1,3-dioxan-2-yl)phenol to produce 1,3,5,7,9-pentakis[4-(1,3-dioxan-2-yl)phenoxy]corannulene, **13**, and then acid-catalyzed hydrolysis (TFA, CH_2Cl_2−H_2O, rt, 16 h) to produce **12** in 63% overall yield from **1**.

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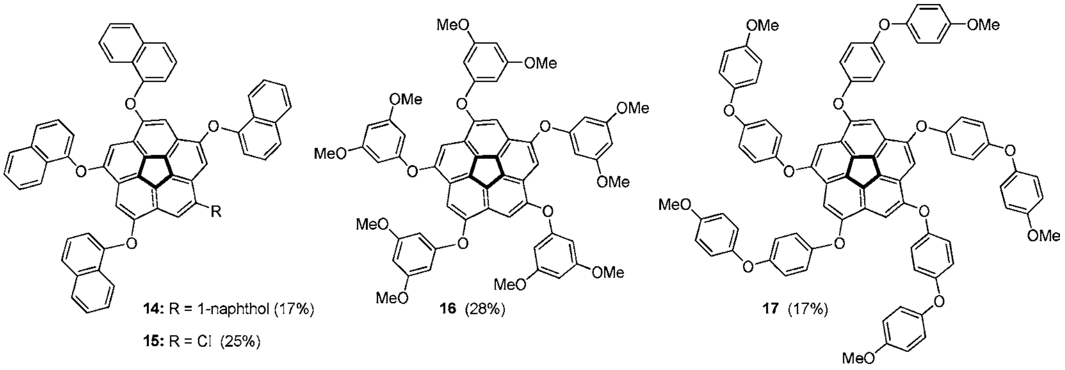

Figure 1. Structure of corannulene ethers **14**−**17**.

Further synthetic opportunities were explored with more sterically demanding phenols (Figure 1). However, with the highly sterically hindered α-naphthol the penta-substituted product, **14**, was obtained in 17% yield along with larger amounts of the tetrasubstituted product, 1-chloro-3,5,7,9-tetrakis(1-naphthoxy)corannulene, **15**, which was isolated in 25% yield.[24] The difficult substitution of the fifth position under our standard reaction conditions, and even when heated to 120 °C, can be understood in terms of steric shielding of the chloride atom in **15** by the two adjacent naphthalene groups. Coupling of phloroglucinol dimethyl ether with **1** afforded 1,3,5,7,9-pentakis(3,5-dimethoxyphenoxy)corannulene, **16**, in 28% yield. Compound **17** was isolated in relatively low yield (17%) due to partial decomposition upon purification by silica-gel chromatography.

In conclusion, this study has paved the way to a new class of pentaaryloxycorannulene derivatives, made readily available in good yields via the Ullmann condensation reaction between **1** and a broad variety of substituted phenols. The reaction can be performed under air with a catalyst loading of 6% per site.

The discovery that **1** is a reactive partner in the copper-catalyzed Ullmann condensation reactions opens new avenues for easy preparation of other corannulene derivatives that were previously considered difficult synthetic targets, thus setting the stage for the design and preparation of new materials and new supramolecular architectures on the basis of pentagonal building blocks. Various relevant applications are currently being investigated in our laboratories, including pentagonal discotic liquid crystals,[11a] pentagonal dendrimers,[13] potential binders of fullerenes,[19d,25] and molecular capsules.

Acknowledgment. This study was supported by the Israel Science Foundation, the German-Israeli Project Cooperation (DIP), the Institute of Catalysis Science and Technology, Technion, and the Skaggs Institute for Chemical Biology. E.K. is the incumbent of the Benno Gitter & Ilana Ben-Ami Chair of Biotechnology, Technion.

Supporting Information Available: General experimental procedures for the syntheses of compounds **3**−**17** and selected ^{1}H NMR, ^{13}C NMR, and UV spectra of compounds **3**−**17**. This material is available free of charge via the Internet at http://pubs.acs.org.

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[24] While the five identical corannulene protons in **14** resonate at 7.09 ppm, the inequivalent protons in **15** resonate at 7.88, 7.18, 7.16, 7.11, and 7.08 ppm.

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