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Deca-heterosubstituted corannulenes†

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The Cu(1)-catalyzed Ullmann condensation reaction between aliphatic alcohols and *sym*-pentachlorocorannulene provides a convenient entry to 1,3,5,7,9-pentaalkoxycorannulenes. The latter are easily converted to novel deca-heterosubstituted derivatives, such as 1,3,5,7,9-penta-X-2,4,6,8,10-penta-Y-corannulenes by electrophilic aromatic substitution.

Small molecules with pentagonal symmetry are essential components for the synthesis and assembly of large molecular¹ and supramolecular architectures having 5-fold symmetry, including icosahedral capsids,² pentagonal dendrimers,^{3,4} single-wall nanotubes,^{5,6} quasi-periodic crystals,⁷ discotic liquid crystals,⁸ other curved graphene structures,⁵ light emitters,⁹ and helical foldamers.¹⁰ Unfortunately, small, rigid organic molecules having pentagonal symmetry are quite rare, and most of them are based on the core structure of either metallocene or corannulene.^{11,12} Large, non-rigid pentagonal macrocycles¹³ are more abundant, including calix[5]arenes,¹⁴ calix[5]furans, calix[5]pyrroles,¹⁵ crown ethers, aza-crown ethers,¹⁶ cucurbit[5]urils,¹⁷ as well as pentameric proteins¹⁸ and DNA.¹⁹

The rigid polycyclic aromatic core of the corannulene molecule can serve as an attractive building block for the abovementioned variety of applications provided that an efficient methodology is available for the functionalization of its molecular periphery.²⁰ Of particular significance would be the ability to achieve multiple functionalization and heterogeneous substitution patterns. For example, for the synthesis of condensed aromatic polycyclic structures⁵ all ten positions of the corannulene core should be substituted and become available for further chemical transformations. Heterogeneous substitution patterns and diversity of functional groups could offer much flexibility in the synthetic design of complex structures.

Deca-chlorocorannulene, **1**, is an attractive starting material for highly substituted corannulene derivatives.²¹



However, although a few deca-homo-substituted corannulenes have been prepared from **1** (Scheme 1), this compound cannot be used for the synthesis of heterogeneously substituted symmetrical corannulene derivatives.

Here we report on a selective entry into novel decaheterosubstituted corannulene derivatives from *sym*pentachlorocorannulene, **2**. The general structure and C-5 symmetry of 1,3,5,7,9-penta-X-2,4,6,8,10-penta-Y-corannulene were accomplished using the Ullmann condensation reaction for the preparation of penta-alkoxycorannulenes and subsequent substitution at the remaining five rim positions with different functional groups. We also report here that the degree of substitution of **2** by aliphatic alcohols can be controlled by the appropriate choice of reaction conditions to produce either tri-, tetra- or penta-alkoxy corannulene derivatives.

We have previously reported on an efficient approach to 1,3,5,7,9-pentaarylcorannulenes, **3**, from **2** by the palladiumcatalyzed Suzuki cross coupling reaction (Scheme 2).^{3,22} Furthermore, we achieved 1,3,5,7,9-pentaaryloxycorannulene derivatives, **4**, *via* the Cu(1)-catalyzed Ullmann condensation reaction²³ between **2** and a broad variety of substituted phenols.²⁴

The reaction proceeded under air with mild conditions that were compatible even with 4-bromophenol. These synthetic transformations opened the way to easy preparation of other symmetrically substituted pentagonal building blocks. On the basis of these findings, and the relatively high reactivity of chloro-corannulenes in the Ullmann condensation reaction in comparison with regular chloroarenes,²⁴ we assumed that the

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reaction might work also with aliphatic alcohols under similar conditions.

Indeed, heating **2** to 110 °C in DMF for 24 h with excess methanol, CuI (0.5 equiv.), 1,10-phenanthroline (1 equiv.) and Cs_2CO_3 (12 equiv., 2.4 equiv. per site) afforded a mixture of two inseparable isomers, 1,3-dichloro-5,7,9-trimethoxycorannulene, **5a**, and 1,5-dichloro-3,7,9-trimethoxycorannulene, **6a**, in a 1 : 4 ratio and a combined yield of 34% (Scheme 3 and Table 1, entry 1).

The structural assignment of these isomers was based on their ¹H and ¹³C NMR spectra. Typically, upon substitution of a chloride by an alkoxide group, the *ortho* proton is shifted from *ca*. 7.8 to *ca*. 7.1 ppm. For example, **6a** exhibited two downfield protons at 7.8 and 7.85 ppm and three upfield protons at *ca*. 7.1, 7.15 and 7.2 ppm. The exact substitution pattern was elucidated by 2D $^{1}H^{-13}C$ correlation experiments, HMQC and HMBC.²⁵

We found that the degree of substitution can be efficiently controlled to produce exclusive products by changing the reaction conditions, such as base concentration, solvent and



temperature. Using 12 equiv. of Cs_2CO_3 and heating to 150 °C for 48 h in polar solvents, either *N*-methylpyrrolidinone (NMP) or 1,3-dimethylimidazolidinone (DMI) or dimethylacetamide, resulted in 1-chloro-3,5,7,9-tetramethoxycorannulene, **7a**, as the main product in 64% yield (entry 2). A further increase in the base concentration to 30 equiv. (6 equiv. per site) produced 1,3,5,7,9-pentamethoxycorannulene, **8a**, in 89% yield (entry 3).

The reactions with higher aliphatic alcohols also produced the fully substituted products, **8b** and **8c**, but in lower yields, requiring higher temperatures and extended reaction times. Microwave irradiation was found to significantly facilitate the reaction in most cases (entries 4, 6, and 8). For example, the reaction of **2** with ethanol in DMSO at 155 °C took 4 days to produce **7b** and **8b** in 32% and 16% yields, respectively (entry 5). In contrast, under microwave irradiation in DMF at 200 °C the reaction was complete in 2 h, affording **8b** in 57% yield (entry 6). However, the microwave irradiation facilitated not only the substitution reaction, but also the competing Cu-catalyzed reductive dechlorination reaction, leading to substantial amounts of 1,3,5,7-tetraethoxycorannulene **9b** (40% yield, entry 6).

Similarly, the reaction with heptanol in DMI (200 °C, 74 h) afforded **8c** and 1,3,5,7-tetraheptyloxycorannulene, **9c** in 30% and 22% yields, respectively (entry 7). The same reaction proceeded much faster (2.5 h) under microwave irradiation, producing **8c** and **9c** in 40% and 25% (entry 8). Expectedly, isopropanol reacted much slower than the primary alcohols, producing 1-chloro-3,5,7,9-tetraisopropyloxy-corannulene, **7d**, in 24% yield (entry 9). Under microwave irradiation, this reaction afforded predominantly reductive dechlorination products, including unsubstituted corannulene, mono- and dichlorocorannulene. This tendency was even more pronounced in the reaction with *tert*-butanol under microwave irradiation, which produced only unsubstituted corannulene in 71% yield.

The pentaalkoxycorannulenes, **8a–c**, represent a new family of useful intermediates for further functionalization of the core structure. The increased electron density on the unsubstituted aromatic carbon atoms offers attractive opportunities for electrophilic aromatic substitution to produce deca-heterosubstituted corannulenes under mild conditions (Scheme 4).

Indeed, treatment of either **8a** or **8c** with excess Br_2 in DCM (from 0 °C to room temperature) afforded 1,3,5,7,9-pentaalkoxy-2,4,6,8,10-pentabromocorannulene, **10a** or **10c** in 87% and 42% yield, respectively. Similarly, refluxing either **8a** or **8c** in thionyl chloride in the presence of catalytic amounts of DMF resulted in full chlorination of all free aromatic positions to produce 1,3,5,7,9-pentaalkoxy-2,4,6,8,10-pentachlorocorannulene, **11a** and **11c**, in 78% and 62% yields, respectively.

 Table 1
 Multiple substitution of 2 by aliphatic alcohols. All reactions were carried out with excess alcohol (>100 equiv.), CuI (0.5 equiv.) and 1,10-phenanthroline (1 equiv.); see the ESI for experimental details. All yields are of isolated products, nd: not determined

Entry	ROH	Cs ₂ CO ₃ (equiv.)	Solvent	<i>T</i> (°C)	Microwave	Time	5+6	7	8	9
1	MeOH	12	DMF	110	_	24 h	34%	_	_	
2	MeOH	12	NMP	150	_	48 h	_	64%	_	
3	MeOH	30	NMP	140	_	48 h	_		89%	
4	MeOH	30	DMSO	150	+	20 min	_		92%	
5	EtOH	30	DMSO	155	_	4 d	_	32%	16%	
6	EtOH	30	DMF	200	+	2 h	_		57%	40%
7	Heptanol	30	DMI	200	_	74 h	_		30%	22%
8	Heptanol	30	DMI	200-220	+	2.5 h	_		40%	25%
9	iPrOH	30	DMSO	165	_	5 d	nd	24%	—	



radicals and molecular chlorine, which could result from thermal decomposition of thionyl chloride.²⁶ A third mechanism could involve electrophilic aromatic substitution by thionyl chloride itself followed by rearrangement.27 The Cu(I)-catalyzed Ullmann condensation reaction provides a convenient entry to 1,3,5,7,9-pentaalkoxycorannulenes, 8, from various aliphatic alcohols and sym-pentachlorocorannulene, 2. The degree of substitution of 2 by aliphatic alcohols can be controlled by the appropriate choice of reaction conditions to

Scheme 4

RC

Rό

8

OR

DR

SOCI2

DMF (cat)

80 °C

С

CI

RO

RC

RÓ

a) R = Me

OR

78%

ċι

11

c) R = heptyl 62%

produce trialkoxydichloro and tetraalkoxychloro corannulene derivatives, 5, 6 and 7. The availability of these heterosubstituted compounds offers interesting opportunities for substitution with other groups to produce hetero-substituted corannulenes. Furthermore, deca-hetero-substituted corannulene derivatives of the general structure of 1,3,5,7,9-penta-X-2,4,6,8,10-penta-Y-corannulene are now readily available from 8 by electrophilic aromatic substitution. The synthetic applications of these new corannulene derivatives are currently explored in our laboratories.

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