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Synthesis of a Triaza Analogue of Crushed-Fullerene by Intramolecular Palladium-Catalyzed Arylation

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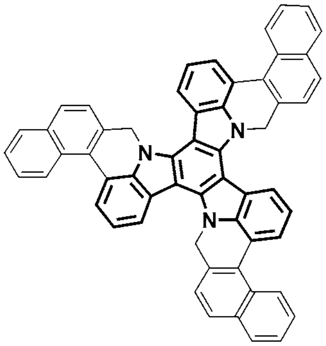
ABSTRACT



Alkylation and intramolecular palladium-catalyzed arylation allows for the ready synthesis of $C_{57}H_{33}N_3$ from symmetrical triindole, a triaza analogue of truxene.

Azafullerenes have attracted much interest.[1] Theoretical studies have predicted several stable $C_{60-2n}N_{2n}$ structures,[2] whose detection has been reported under different conditions.[3,4] Wudl and Hirsch attempted independently the synthesis of azafullerene $C_{59}N$ starting from different azide adducts of C_{60}.[5,6] The substitution of one carbon atom of the fullerene framework with nitrogen leads to a reactive $C_{59}N$ radical that has been detected in MS experiments and that can only be isolated as the dimer $(C_{59}N)_2$.[6,7] The corresponding cation, $C_{59}N^+$, has been detected by fragmentation of suitable precursors.[6,8] Salts of the cation[9,10] and the anion[5,11] have been isolated. Several monomeric substituted azafullerenes have also been obtained.[12] However, no azafullerene has yet been synthesized from a nonfullerene

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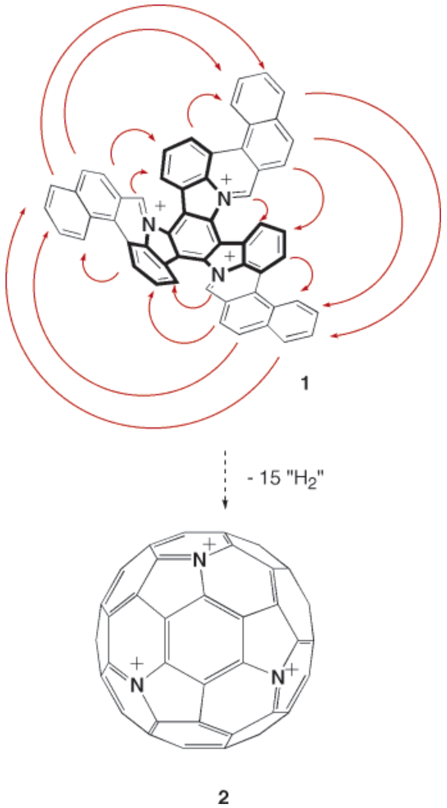
precursor where more than one carbon atom is replaced by nitrogen atoms. An attempt toward a rational synthesis of diazafullerene has been reported by Tobe. In this approach, a pyridinophane was synthesized as a precursor to $C_{58}N_2$, whose anion $C_{58}N_2^-$ was detected in a LD-TOF mass experiment.[13]

Scheme 1



We have previously completed a synthesis of tribenzo*l*:*l′*:*l″*benzo1,2-*e*:3,4-*e′*:5,6-*e″*triacephenanthrylene ($C_{60}H_{30}$) by using a palladium-catalyzed intramolecular arylation reaction in the key step;[14] $C_{60}H_{30}$ suffers by multiple intramolecular cyclodehydrogenation reactions in LDI-TOF-MS.[15] We decided to apply the palladium-catalyzed intramolecular arylation approach[16] to the synthesis of a tricationic **1**. This cationic species could form triazafullerene $C_{57}N_3^{3+}$ (**2**) (triaza60fulleronium) by pyrolysis or under the conditions of LDI-TOF-MS by formal 15-fold H_2 losses (Scheme 1).

We report the ready synthesis of **3** ($C_{57}H_{33}N_3$), the neutral precursor of **1**, by a triple palladium-catalyzed intramolecular arylation, as well as lower analogues. We also address the issue of the regioselectivity of this reaction, which could shed light on the mechanism of this palladium-catalyzed C−H functionalization process.[17]

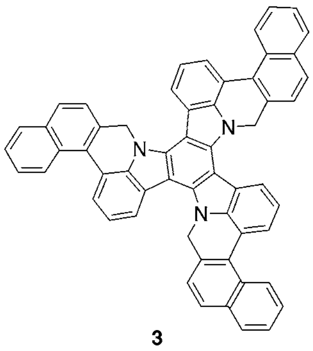
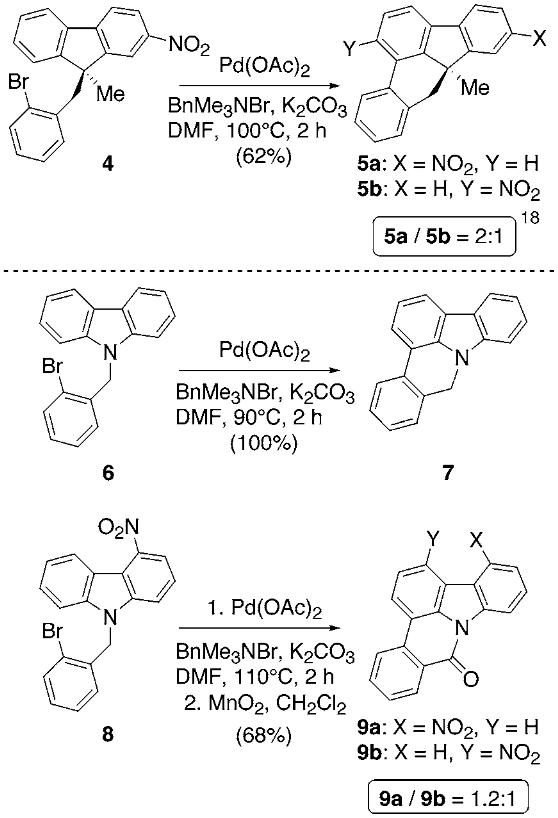


Figure 1.

We have previously found that the arylation reaction on nitrofluorene **4** gives a 2:1 ratio of nitrofluorenes **5a,b** (Scheme 2).[18] This low selectivity is difficult to reconcile with a palladation proceeding by an electrophilic aromatic substitution and was alternatively interpreted as due to the

Scheme 2



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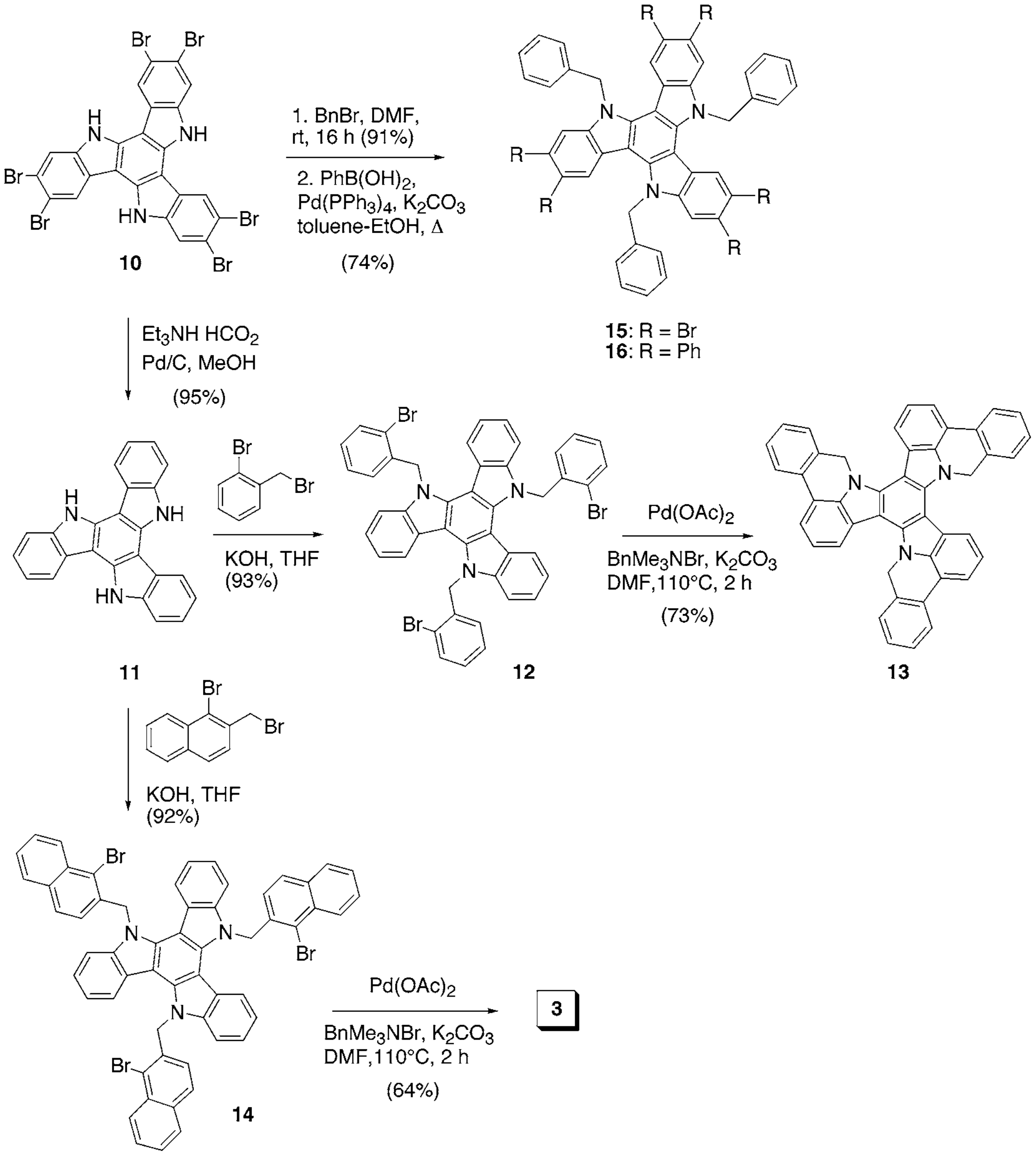
Scheme 3



steric effect of the nitro group. We decided to try the intramolecular arylation on carbazole **8**,[19] a more appropriate substrate for the analysis of the effect of the nitro group. First, the arylation reaction was assayed on simple *N*-[(2-bromophenyl)methyl]carbazole (**6**). Reaction of **6** with $Pd(OAc)_2$ (15 mol %) as the catalyst in DMF, in the presence of K_2CO_3 as the base and $BnMe_3NBr$ as a bromide source, gave 9*H*-indolo(3,2,1-*de*)phenanthridine (8*H*-7b-aza-benzo-[*e*]acephenanthrylene) **7**[20] in quantitative yield. It is interesting to note that no benzylic oxidation of **7** occurs under these conditions, whereas 9-[(2-bromophenyl)methyl]fluorene gives fully aromatic benzo[*e*]acephenanthrylene in the palladium-catalyzed intramolecular arylation.[18]

Under conditions similar to those used in the cyclization of **6**, carbazole **8** gave a mixture of two arylated derivatives along with the corresponding lactames resulting from benzylic oxidation. To quantify the regioisomeric mixture, the crude product was directly treated with MnO_2 in CH_2Cl_2 at room temperature to give a 1.2:1 mixture of 9*H*-indolo[3,2,1-*de*]phenanthridin-9-ones **9a,b** in 68% overall yield. Although the major regiosiomer is the one resulting from arylation at the unsubstituted arene ring,[21] a substantial amount of product

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[21] The regiochemical assignment for **9a** and **9b** is supported by COSY and HMBC spectra of **9a** and by comparison of the ^{1}H NMR spectra with that of unsubstituted 9*H*-indolo[3,2,1-*de*]phenanthridin-9-one. See Supporting Information for details.

is formed by reaction at the position *para* to a nitro group. This low sensitivity to the effect of such a strong electron-withdrawing group raises additional doubts on the proposal of a conventional electrophilic aromatic substitution mechanism for this reaction.

The synthesis of **13**, a lower analogue of **3**, was carried out from known symmetrical hexabromotriindole **10**, which is readily available by reaction of indole with Br_2[22] (Scheme 3). Reductive debromination of **10** with triethylammonium formate and Pd/C yielded **11** (95%). This preparation of symmetrical triindole **11** is more convenient than that previously reported based on the acid-catalyzed reaction between indole and 3-bromoindole, which furnishes a complex mixture of indole dimers and trimers from which **11** could be only obtained in low yield.[23] N-Alkylation with 1-bromo-2-(bromomethyl)benzene gave **12** (93%), which under the conditions of the palladium-catalyzed intramolecular arylation gave **13** in 73% yield as a white powder insoluble in all NMR solvents. When the reaction was performed in *N*,*N*-dimethylacetamide with Cs_2CO_3 as base, partially oxidized **13** was obtained. On the other hand, palladium-catalyzed reaction of the triamide analogue of **12**, prepared by reaction of **11** with *o*-bromobenzoyl chloride in 44% yield, failed to provide the desired arylation derivative.

The synthesis of **3** ($C_{57}N_3H_{33}$) was similarly carried out in two steps from triindole **11** (Scheme 3). Alkylation of **11** with 1-bromo-2-bromomethylnaphthalene gave **14** (92%), which underwent a triple palladium-catalyzed arylation under the standard conditions to give **3** in 64% yield as a yellow powder. In contrast with **13**, **3** is soluble in $CDCl_3$ and acetone-d_6, although a well-resolved ^{1}H NMR spectrum was best obtained in 1,1,2,2-tetrachloroethane-d_2 at 100 °C. Solid compounds **3**, **7**, and **13** suffer oxidation by oxygen at the methylenes to give the corresponding lactames and must be kept under Ar.

Taking advantage of the presence of six bromo substituents in **10**, palladium-catalyzed functionalization could provide a variety of hexasubstituted derivatives with C_{3h} symmetry. Thus, for example,[24] N-benzylation of **11** in (DMF, rt, 16 h) provided **15** in 91% yield, which was coupled with phenylboronic acid to give **16** (74%), displaying nine phenyl groups surrounding a triindole nucleus.

In summary, we have shown that now readily available symmetrical triindole **11** can be used for the ready construction of large triazapolyarenes such as **3** based on the intramolecular palladium-catalyzed arylation reaction. Triindole **11** is a triaza analogue of truxene, a useful scaffold for the synthesis of complex polyarenes.[14,16] The nonselective arylation on carbazole **8** is not consistent with an electrophilic aromatic substitution reaction for this process. Substitution at the periphery of triindole **11** can also be carried out by palladium-catalyzed coupling reactions. Work along these lines is underway for the synthesis of related systems.

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Supporting Information Available: Experimental procedures and characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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