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An Annulative Synthetic Strategy for Building Triphenylene Frameworks by Multiple C–H Bond Activations

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Dedicated to Professor Peter H. Seeberger on the occasion of his 50th birthday

Abstract: C-H activation is a versatile tool for appending aryl groups to aromatic systems. However, heavy demands on multiple catalytic cycle operations and site-selectivity have limited its use for graphene segment synthesis. A Pd-catalyzed one-step synthesis of functionalized triphenylene frameworks is disclosed, which proceeds by 2- or 4-fold C-H arylation of unactivated benzene derivatives. A $Pd_2(dibenzylideneacetone)_3$ catalytic system, using cyclic diaryliodonium salts as π -extending agents, leads to site-selective inter- and intramolecular tandem arylation sequences. Moreover, N-substituted triphenylenes are applied to a field-effect transistor sensor for rapid, sensitive, and reversible alcohol vapor detection.

Graphene is a fundamentally and industrially important synthetic carbon allotrope that has been applied to a vast array of applications since its isolation by Geim and Novoselov in 2004.^[1-4] The development of synthetic methods for accessing (functionalized) graphene and its molecular segment has been a recent theme for synthetic chemists in pursuit of two-dimensional nanostructures with finely tuned properties.^[1] Although top-down synthetic routes are wellestablished for producing large-scale graphene materials, bottom-up synthetic approaches, including the Diels–Alder reaction, cross-coupling reactions, surface-mediated

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synthesis, and C–H activation, are logical choices to access atomically precise graphene segments—also known as poly-cyclic aromatic hydrocarbons (PAHs).^[1,5–11]

Among the 35 parent structural units of PAHs, triphenylene belongs to a branched all-benzoid category.^[12] Pdcatalyzed annulation approaches to triphenylene moieties are based on aryne chemistry.^[13–17] For example, Pérez et al. have reported [2+2+2] cyclotrimerization of benzynes (Scheme 1 a).^[16] The Larock group introduced annulation of arynes using 2-halobiaryls.^[17] Alternatively, Nishihara et al. have reported a non-benzyne route using *o*-bromobenzyl alcohol as an annulating agent (route A, Scheme 1 b).^[18] Yorimitsu et al. developed a multi-step transformation approach from dibenzothiophenes (route B, Scheme 1 b).^[19] Shimizu and coworkers introduced [4+2]-type aromatic annulation between 9-stannafluorenes and di-/tetra-halogenated compounds (route C, Scheme 1 b).^[20] However, these methods for



Scheme 1. Synthesis of triphenylene frameworks.

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tailored triphenylene synthesis typically require laborious prefunctionalization steps. Therefore, the development of concise synthetic strategies to provide triphenylene frameworks from unactivated substrates is an important synthetic goal in graphene chemistry.

Herein, we show that unactivated and readily available arene substrates can undergo Pd-catalyzed 2- or even 4-fold C–H arylation to afford substituted triphenylenes **3** or phenanthro[9,10-*b*]triphenylenes **4**, respectively (Scheme 1 c). To our knowledge, this is the first example of a straightforward π -extension strategy utilized to provide triphenylene frameworks from acetanilides and benzamides. The *N*-substituted triphenylenes obtained are incorporated into an alcohol fieldeffect transistor (FET) sensor, which exhibits a rapid and reversible response.

Over the last few decades, direct arylation methods have emerged aided by bench-stable hypervalent iodine compounds.^[21,22] It was anticipated that **2**, with cyclic geometry, has the potential for 2-fold C–H arylation of **1** toward aromatic annulation (Figure 1). Simple amide moieties were chosen as the directing groups (DGs) owing to 1) their wide prevalence in natural products and functional organic materials, 2) the effective facilitation of sp² C–H activation,



Figure 1. Proposed 2-fold C–H arylation mechanism.

and 3) increased processability for FET applications. In cycle I, cyclic diaryliodonium salt **2** undergoes successive single-electron reductions by Pd^0 to form X- Pd^{II} -aryl complex **A**, as previously suggested by the Glorius group.^[23] Subsequently, cyclopalladation of arene **1** would afford **C**, which can undergo reductive elimination to give aryl iodide **D**. In cycle II, oxidative addition, concerted metalation–deprotonation, and subsequent reductive elimination, regenerate Pd^0 and afford the desired product **3**.

To examine the feasibility of this strategy, various reaction parameters were surveyed. The optimized conditions provided annulated product **3aa** in 85% yield (Table 1). In the absence of catalyst (entry 2), there was no reactivity. Changes in the palladium source or catalyst loading caused diminished yields (entries 3–5). A control reaction without NaOAc showed no reactivity (entry 6). Other weak bases, such as AgOAc and KOAc, were ineffective (entries 8 and 9). Addition of external oxidants, such as $K_2S_2O_8$ or air, led to Table 1: Optimization of 2-fold C-H arylation.[a]



[a] Reaction conditions: **1a** (0.228 mmol), **2a** (3.0 equiv), $Pd_2(dba)_3$ (5 mol%), NaOAc (5.0 equiv), ODCB (4 mL), 150 °C, 24 h under N₂ atmosphere; ODCB = 1,2-dichlorobenzene, dba = dibenzylidene-acetone. [b] Isolated yields. [c] Yield determined by GC using *n*-dodecane as an internal standard.

reduced yields (entries 10 and 11). The presence of radical scavengers (butylated hydroxytoluene (BHT) and 2,2,6,6tetramethyl-1-piperidinyloxy (TEMPO)) affected the reaction yields drastically (entries 12 and 13), indicating the potential involvement of a radical pathway. A probable thermal reduction of Pd(OAc)₂ to Pd⁰ may account for a moderate yield (55%, entry 5).^[23] However, an alternative mechanistic pathway involving a Pd^{II}/Pd^{IV} manifold cannot be ruled out completely.^[22,24] When other solvents were used, such as toluene or N,N-dimethylformamide (DMF), the reaction did not progress (entries 14 and 15). Reduction of the reaction volume (2 mL) only caused a moderate drop in yield (52%, entry 16). Finally, decreasing the concentration of 2a (1.5 equiv, entry 17) and reducing the reaction temperature (100°C, entry 18) led to moderate and poor yields, respectively.

With the optimized conditions in hand, our subsequent goal was to investigate the reaction scope. Arenes with *ortho*alkyl groups, including *i*Pr (**1a**), methyl (**1b**), and ethyl (**1c**), gave good yields of the corresponding triphenylenes. Functional groups with π -electron donors, such as *ortho*-phenyl (**1d**), *ortho*-fluoro (**1e**), and *ortho*-OMe (**1f**) were tolerated, furnishing the annulated products in moderate to good yields. However, electron-withdrawing trifluoromethyl, cyano, and nitro groups resulted in poorer reactivity (**3ha**, 30%; **3ia** and **3ja**, no product). Pivanilide (**1g**) with no *ortho*-substituent gave a poor yield (**3ga**, 25%). Subsequently, the 2-fold arylation was attempted with *meta*-substituted substrates with methyl and cyano groups (data not shown), but no product



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formation was observed. The para-substituted substrate 1k was subjected to the reaction conditions, but a poor isolated yield was obtained (26%). Additionally, the compatibility of this method with other simple but electron-deficient benzamide substrates was examined. Benzamide-based triphenylene derivatives (3na, 3oa, and 3pa) were obtained in moderate yields (56%, 40%, and 51%, respectively) with incomplete conversion of the corresponding substrates. Cyclic diaryliodonium salts **2b** and **2c** bearing difluoro and dimethyl groups provided good yields to afford 3ab and 3ac, respectively. Given the difficulties in constructing a diverse array of tailored triphenylenes, arising from the planar and (un)symmetrical structures,^[15,19] the reaction scope of this approach is comparable to that of previously reported methods.[16-20] Overall, the electronic nature of the substrates bearing amide DGs (and substituents) significantly affects the efficiency of the annulation.

With the aim of using alternative DGs, we reacted 1-phenylpyrrolidin-2-one (11) with 2a. Particularly noteworthy is the formation of phenanthro[9,10-*b*]triphenylene product 4la arising from 4-fold C–H arylation in 10% isolated yield along with product 3la (35% yield, Table 2). To enhance the yield of the bis-annulated (or 4-fold C–H arylated) product, we doubled the number of equivalents of 2a (6.0 equiv) and reduced the volume of 1,2-dichlorobenzene (ODCB; 2 mL), as shown in Scheme 2. With these

Table 2: Reaction scope.^[a]



[a] Standard conditions; isolated yields. [b] Reaction conditions: 1h (0.228 mmol), 2a (3.0 + 2.0 equiv), $Pd_2(dba)_3$ (5 + 2.5 mol%), NaOAc (5.0 equiv), ODCB (4 mL), 150°C, 48 h under N₂ atmosphere.

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changes, the yield of the bis-annulated product improved moderately to 40%. However, we still observed monoannulation with the reduced amount (18%). We performed additional reactions with 2b and 2c, and observed



Scheme 2. Synthesis of phenanthro[9,10-b]triphenylene 4 frameworks.

phenanthro[9,10-*b*]triphenylene derivative formation in 33% and 40% yields, respectively. Single-crystal X-ray diffraction analysis unambiguously confirmed the structure of **4lb**.^[25] Interestingly, chlorinated substrate **1q** gave bisannulated product **4qa**, albeit with a poor isolated yield (25%). The photophysical properties of compounds **4** were also studied (Supporting Information).

To highlight the applicability of substituted triphenylenes, readily soluble and processable 3aa was incorporated into graphene-based FETs for application as a chemical gas sensor as part of our ongoing research on the functionalization of nanostructured carbons.^[26-28] Graphene FETs were fabricated on a Si wafer as a bottom gate structure (gate: doped Si; dielectric layer: 300 nm-thick SiO₂), and then **3aa** was noncovalently immobilized on the graphene channel with π - π interactions, as shown in Figure 2a.^[26,29] Figure 2b presents the transfer curves of graphene FETs before and after 3aa coating (Supporting Information, Figure S60). The pristine FET showed ambipolar behavior consistent with the expected semimetallic characteristics of graphene,^[30-32] with a positive charge neutrality point of approximately 38 V (black curve in Figure 2b). The hole (electron) mobility of the graphene FET was 2940 cm² V⁻¹ s⁻¹ (2520 cm² V⁻¹ s⁻¹) for a channel length of 70 µm and width of 5 µm. After 3aa coating, the graphene FET showed a leftward V_{Dirac} shift because of its negative charge transfer effect, with negligible change in mobility. The similar slopes (trans-conductance (g_m)) of the two curves in Figure 2b indicate that graphene segment structured 3aa can induce charge transfer without causing additional scatterings on the graphene channel. Figure 2c reveals that the response of the 3aa-functionalized sensor to ethanol vapor at 1000 ppm is fast and completely reversible. The sensitivity was maintained upon multiple exposures. Hydrogen bonding with the amide functionality of 3aa may give rise to ethanol binding on





Figure 2. a) Interaction of **3 aa** with the graphene surface. b) Transfer characteristics ($V_D = 0.1 \text{ V}$). c) Real-time response. d) Sensor sensitivities.

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Conflict of interest

The authors declare no conflict of interest.

Keywords: arylation · C– H activation · diaryliodonium salt · palladium · triphenylene

the **3aa**-functionalized graphene channel, which effectively raises the Henry's law constant at the graphene surface (Figure 2a).^[33,34] Graphene without **3aa**-functionalization showed a weaker response and poor reversibility when exposed to ethanol vapor (Supporting Information, Figure S61). Figure 2d compares the sensitivities of the sensor to ethanol, NH₃, CO₂, and H₂ at room temperature (same concentration, 1000 ppm). The **3aa**-functionalized sensor is three to five times more sensitive to ethanol than to the other analytes.

In conclusion, a palladium-catalyzed 2- or 4-fold C–H arylation strategy to afford functionalized triphenylenes and phenanthro[9,10-*b*]triphenylenes from unactivated arenes was demonstrated for the first time. This annulative π -extension method features inter- and intramolecular tandem arylation sequences employing cyclic diaryliodonium salts by multiple C–H activations. *N*-substituted triphenylenes with good processability were incorporated into an alcohol FET sensor that showed a rapid and reversible response. This study is expected to bridge synthetic organic chemistry and nanoscience by providing a one-step synthetic route to access various triphenylene frameworks.

Experimental Section

General procedure for annulation: An oven-dried Schlenk tube was charged with 1 (0.228 mmol), 2 (3.0 or 6.0 equiv), NaOAc (5.0 equiv), and Pd₂(dba)₃ (5 mol%). The tube was evacuated and purged with N₂ repeatedly five times. To this mixture was added ODCB and the system stirred at 150°C for 24 h. Upon completion of the reaction, the mixture was diluted with dichloromethane and filtered through Celite. The solvents were removed in vacuo and the resulting mixture purified by flash column chromatography.

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Communications



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Synthesis and Application of Substituted Triphenylenes



Closing the circle: Palladium-catalyzed 2or 4-fold C-H arylation of unactivated arenes was developed to access substituted triphenylene frameworks.

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