

REPORT

ORGANIC CHEMISTRY

Synthesis of partially and fully fused polyaromatics by annulative chlorophenylene dimerization

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Since the discovery by Ullmann and Bielecki in 1901, reductive dimerization (or homocoupling) of aryl halides has been extensively exploited for the generation of a range of biaryl-based functional molecules. In contrast to the single-point connection in these products, edge-sharing fused aromatic systems have not generally been accessible from simple aryl halides via annulation cascades. Here we report a single-step synthesis of fused aromatics with a triphenylene core by the palladium-catalyzed annulative dimerization of structurally and functionally diverse chlorophenylenes through double carbon-hydrogen bond activation. The partially fused polyaromatics can be transformed into fully fused, small graphene nanoribbons, which are otherwise difficult to synthesize. This simple, yet powerful, method allows access to functional π -systems of interest in optoelectronics research.

The reductive dimerization (or homocoupling) of aryl halides (*1*) has been extensively exploited in organic synthesis since Ullmann and Bielecki's discovery of the copper-mediated dimerization of aryl halides in 1901 (*2*) (Fig. 1A). This reaction has proved to be particularly useful in the synthesis of biaryl-based functional molecules, including pharmaceuticals, biologically active natural products, optoelectronic π -conjugated materials, and polymers. Although this textbook reaction is a powerful technique for the single-point connection of

two aromatic nuclei, methods to access fused aromatic systems from simple aryl halides, via annulation cascades, have not been developed (Fig. 1A). Such fused polycyclic aromatics represent an emerging class of π -conjugated molecules in optoelectronic devices, nanographene materials (*3*), ultrashort carbon nanotubes (*4*), and carbon nanobelts (*5*). Their optoelectronic properties are susceptible to structural perturbations based on shape, width, edge topology, and degree of π -extension. Thus, a method to synthesize fused aromatics in a bottom-up fashion with atom-by-

atom precision is in high demand (*3–7*). In particular, methods that involve C–H functionalization (*8, 9*), a direct molecular activation-transformation technology, are attractive not only to streamline overall synthesis but also to unlock opportunities for markedly different reactivity and selectivity. On the basis of our single-step π -extension strategy for making new nanocarbon molecules by C–H functionalization (*10, 11*), we envisioned that ortho-C–H bonds of aryl halides might be activated for annulative dimerization processes to access π -extended, fused polyaromatic systems (Fig. 1A).

Here we report a single-step synthesis of triphenylene-cored, fused aromatics by the palladium-catalyzed annulative dimerization of structurally and functionally diverse chlorophenylenes (*12, 13*) through double C–H activation (Fig. 1B). The overall reaction is redox-neutral, such that stoichiometric reductant is not required. Chlorinated aromatic reagents are readily available. This simple, yet powerful, dimerization allows for the fusion of two functional aromatic nuclei to directly access triphenylene-cored π -systems that are known as privileged structures for materials in organic light-emitting diodes (OLEDs) (*14–17*). Moreover, the thus-generated partially fused aromatics can be transformed into fully fused, small graphene nanoribbons, which are otherwise difficult to synthesize.

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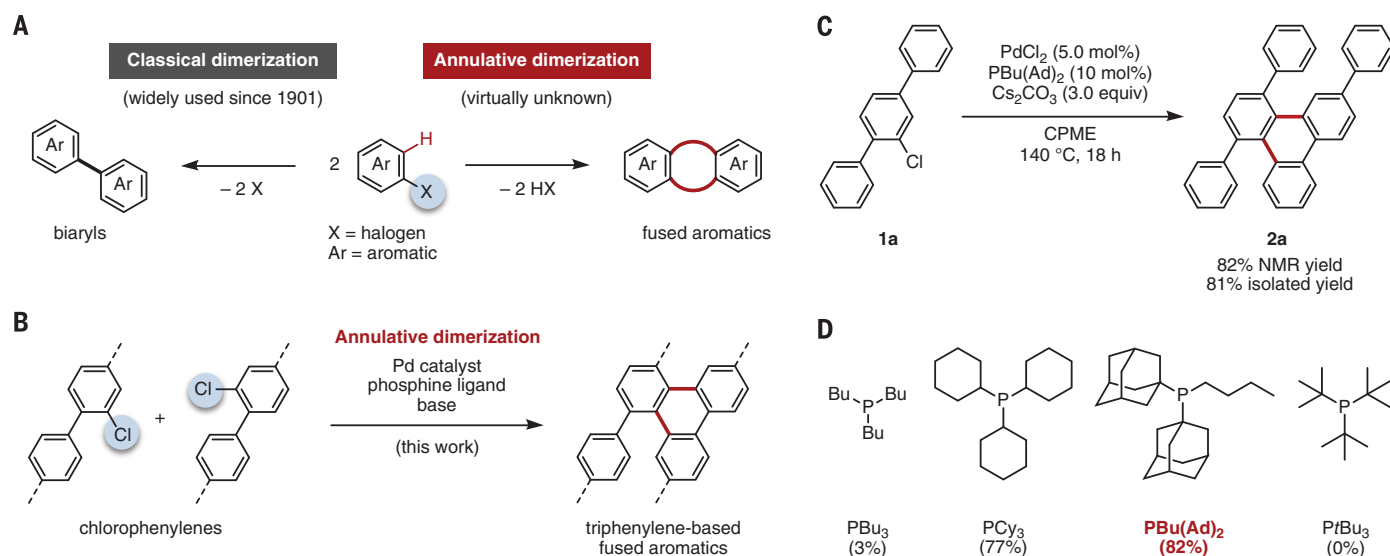


Fig. 1. Potential of annulative dimerization of aryl halides. (A) Classical reductive dimerization and annulative dimerization. (B) Pd-catalyzed annulative dimerization of chlorophenylenes to give triphenylene-based fused aromatics. (C) Optimized reaction conditions: **1a** (1.0 equivalent), PdCl₂ (5.0 mol %), PBu(Ad)₂ (10 mol %), Cs₂CO₃ (3.0 equivalents), CPME, 140 °C, 18 hours. (D) Effect of phosphine ligands. Conditions: **1a** (1.0 equivalent), PdCl₂ (5.0 mol %), ligand (10 mol %), Cs₂CO₃ (3.0 equivalents), CPME, 140 °C, 18 hours. ¹H NMR yields of **2a** are given in parentheses. Red bonds indicates those that are newly formed.

We began our campaign by establishing the conditions for the annulative dimerization reaction using 2'-chloro-1,1':4',1''-terphenyl (**1a**) as a representative chlorinated oligophenylene. Through extensive screening of various catalysts and additives, we identified the optimized reaction conditions: Treatment of **1a** (1.0 equivalent) with PdCl₂ [5.0 mole % (mol %)], PBU(Ad)₂ (10 mol %; Bu, *n*-butyl; Ad, 1-adamantyl), and cesium carbonate (3.0 equivalents) in cyclopentyl methyl ether (CPME) at 140°C for 18 hours afforded the annu-

lative dimerization product **2a** in 81% isolated yield (Fig. 1C). The structure of **2a** was unambiguously confirmed by x-ray crystallographic analysis. The ligand had a critical effect on the reaction efficiency; representative results are shown in Fig. 1D. The use of less bulky PBu₃ hindered the reaction. Moderately large trialkylphosphines PCy₃ (Cy, cyclohexyl) and PBU(Ad)₂ afforded the best results (77 and 82%), whereas much bulkier PtBu₃ (*t*Bu, *tert*-butyl) did not facilitate the dimerization. Other phosphine ligands P(*o*-tol)₃ (*o*-tol, *o*-CH₃C₆H₄)

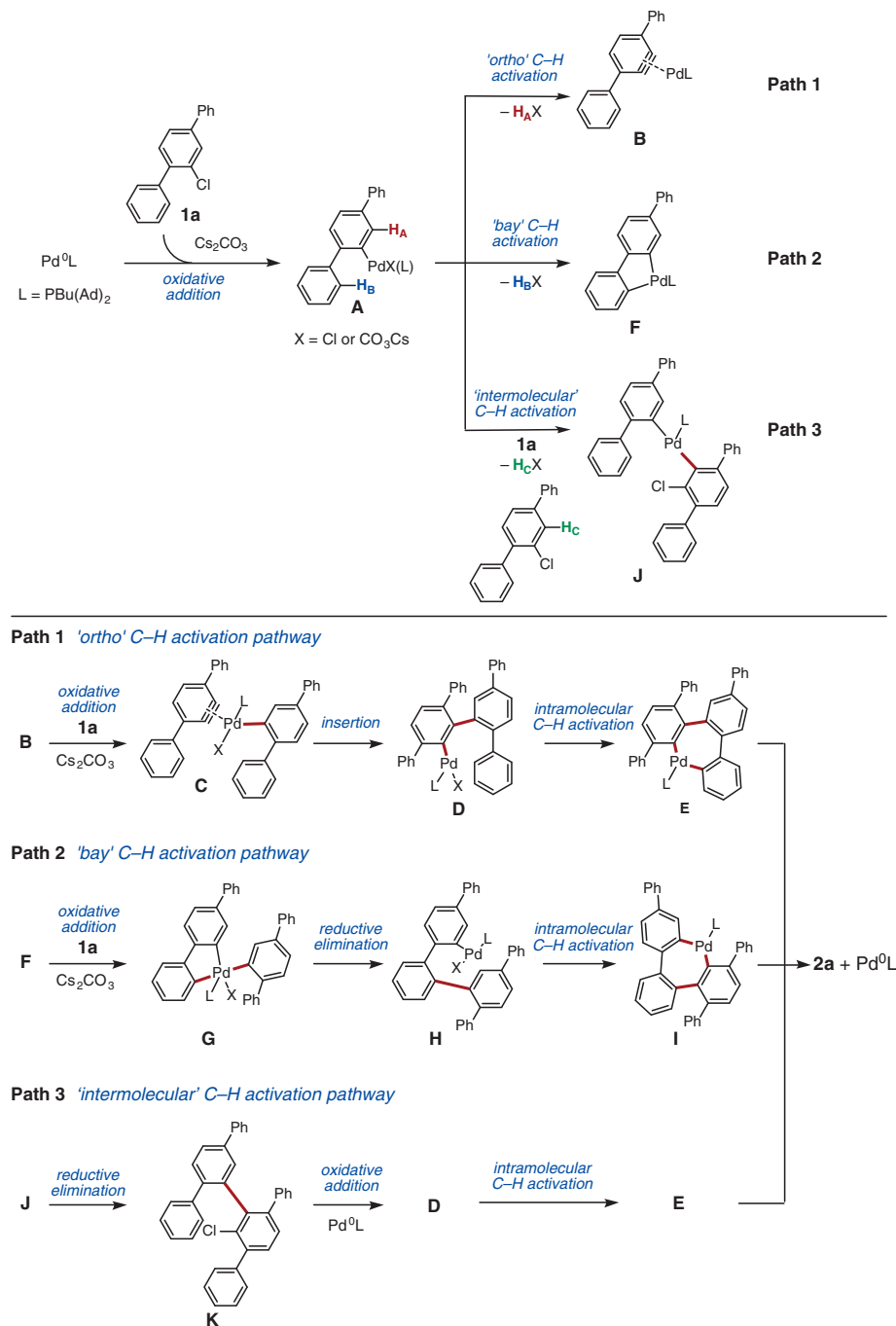


Fig. 2. Possible reaction pathways. Three pathways are shown: path 1, ortho C-H activation pathway; path 2, bay C-H activation pathway; and path 3, intermolecular C-H activation pathway. Ph, phenyl; L, PBU(Ad)₂; X, Cl or CO₃Cs.

and 1,2-bis(dicyclohexylphosphino)ethane, as well as *N*-heterocyclic carbene ligands, were not effective for the reaction.

Although the exact mechanism of the annulative dimerization remains unclear, our current assumption is shown in Fig. 2. An in situ-generated, phosphine-bound Pd(0) species Pd⁰L [L, PBU(Ad)₂] undergoes the first oxidative addition with chloroterphenyl **1a** to give arylpalladium **A**. The resulting arylpalladium **A** can abstract three hydrogen atoms via path 1, intramolecular H_A (red); path 2, intramolecular H_B (blue); or path 3, intermolecular H_C (green). Path 1 initiates from intramolecular ortho-C-H activation (18) from **A** to give Pd-aryne **B** (**19**). Oxidative addition of **1a** to **B** provides **C**, which undergoes an insertion (carbopalladation) across the aryne moiety to give arylpalladium **D**. Subsequent intramolecular C-H palladation affords seven-membered palladacycle **E**, which then undergoes reductive elimination to provide triphenylene product **2a** and Pd⁰L, completing the catalytic cycle. As an alternative to the Pd-aryne pathway (path 1), the Pd(IV) pathway (path 2) might also be possible (20). For example, intramolecular C-H activation of **A** at the baylike region affords palladacycle intermediate **F**. Subsequent oxidative addition of **1a** generates Pd(IV) intermediate **G**, which then undergoes biaryl-forming reductive elimination to yield arylpalladium **H**. Intramolecular C-H activation affords **I**, which finally gives **2a** and Pd⁰L. Path 3 involves intermolecular C-H activation of **A** with **1a**, whereby the C-H bond ortho to the chlorine atom is activated, to give intermediate **J**, which then provides **K**. Subsequent intramolecular C-H arylation of **K** affords **2a** through intermediates **D** and **E**.

With the optimal conditions for the annulative dimerization in hand, the scope of the reaction was investigated with a range of structurally and functionally diverse chlorophenylenes (Fig. 3A). Terphenyl **1b** with a *t*Bu group was converted into the corresponding triphenylene derivative **2b** in 77% isolated yield. Terphenyls with an electron-donating methoxy, trifluoromethoxy, methylsulfanyl, or electron-withdrawing trifluoromethyl group (**1c** to **1f**) were smoothly converted into **2c** to **2f** in good to high yields (85, 68, 49, and 64%, respectively). The methylsulfanyl group can be transformed through metal-catalyzed cross-coupling reactions as a halogen equivalent. Silyl groups, which can be used for further derivatizations, were also tolerated, and **2g** was obtained in 66% yield. In the reaction of **1h**, the methoxycarbonyl group remained intact to give **2h**. A small amount of isomer **2h'** was also generated, presumably because the ester group increased the acidity of the C-H bond on the arene to induce an unwanted palladium migration through the palladacycle intermediate (21). The reaction of **1i** afforded carbazole-containing triphenylene **2i** that could have potential as a hole-transporting material. *m*-Methyl- or *m*-phenyl-substituted **1j** and **1k** reacted smoothly to give **2j** and **2k** in 85 and 58% yields, respectively. Chlorobenzene derivatives with two naphthalene rings (**1l** and **1m**) dimerized to give fused π -extended systems **2l**

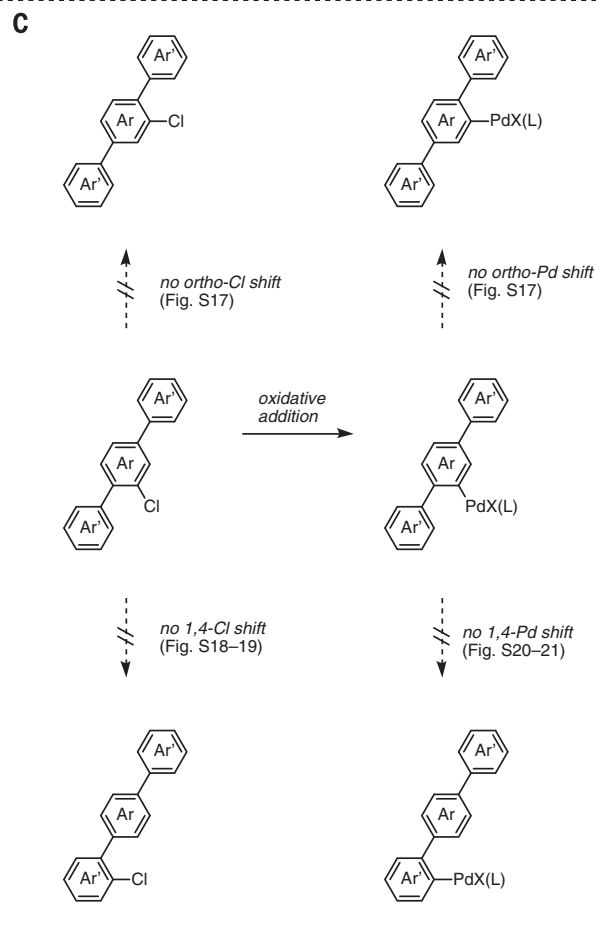
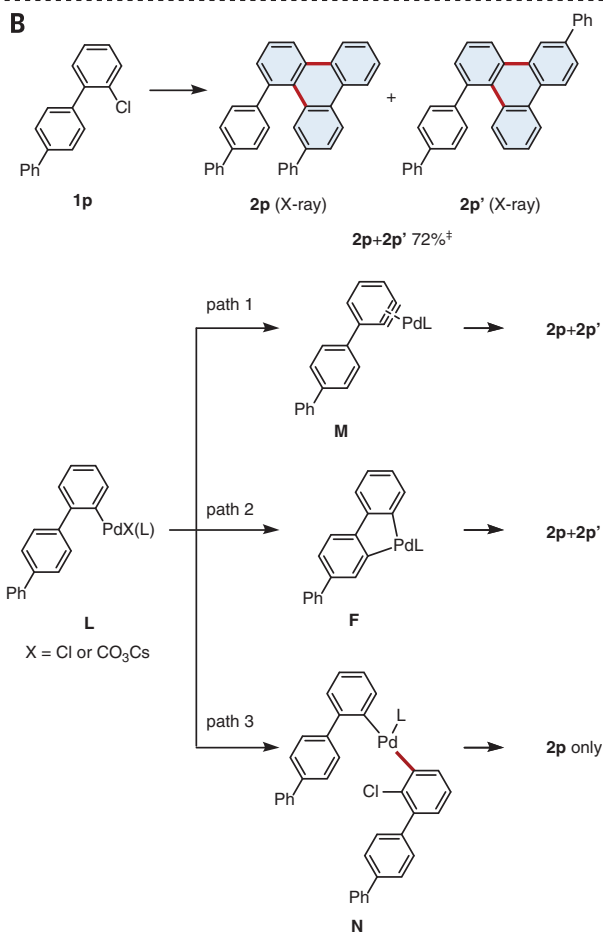
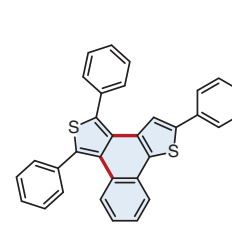
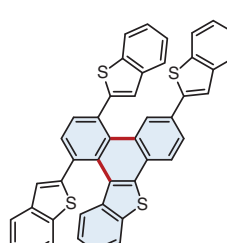
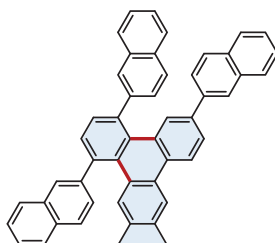
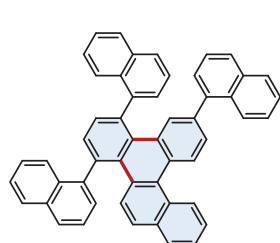
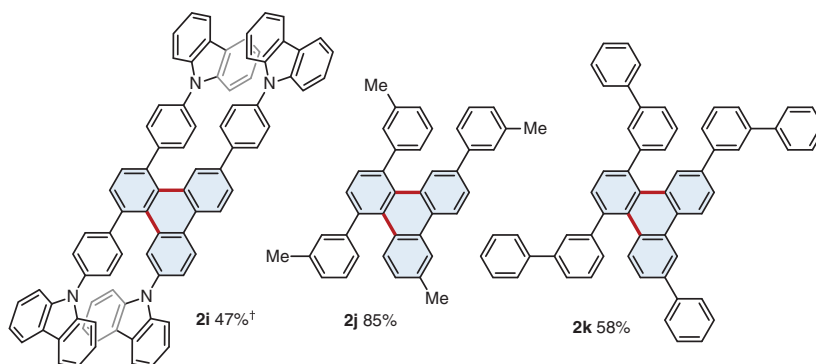
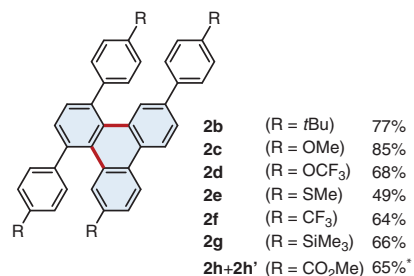
A Representative products: **2** isolated yield

Fig. 3. Annulative dimerization with various substrates. Optimized reaction conditions: **1** (1.0 equivalent), PdCl₂ (5.0 mol %), PBu(Ad)₂ (10 mol %), Cs₂CO₃ (3.0 equivalents), CPME, 140°C, 18 hours. **(A)** Scope to examine functional group compatibility and structural diversity. *Ratio of **2h**

to **2h'** is 3:1. For the structure of **2h'**, see supplementary materials. †CsF (3.0 equivalents) was used instead of Cs₂CO₃. Me, methyl. **(B)** Reaction of **1p**. ‡Ratio of **2p** to **2p'** is 3:1. **(C)** No chloride or palladium migration occur. L, PBu(Ad)₂; Ar, aromatic; X, Cl or CO₃Cs.

and **2m** in 73 and 91% yields with virtually complete regioselectivity. No further dehydrocyclization was observed. Benzothiophene-substituted derivative **1n** also reacted to give thiophene-benzene fused system **2n**. Chlorinated thiophene derivative **1o** also underwent annulative dimerization to give **2o** in 33% yield.

By applying various chloroarene substrates to the present annulative dimerization, mechanistic insights were also obtained. An overview of possible reaction pathways and the mechanistic experiments are provided in the supplementary materials. For example, chloroterphenyl **1p** is

useful as a mechanistic probe (Fig. 3B). The reaction of **1p** resulted in the formation of a mixture of **2p** and **2p'**, structures of which were confirmed by x-ray crystallographic analysis. This shows that either path 1 or 2 was dominant and that the mixture of **2p** and **2p'** was generated through Pd-aryne intermediate **M** or palladacycle intermediate **F** (Fig. 3B). Intermediate **M** or **F** then reacted with **1p** to give two regioisomers. On the other hand, if path 3 had been dominant, the reaction would have resulted in the exclusive formation of **2p** via intermediate **N**. Importantly, this discussion is based on the hypothesis that no

chloride or palladium migration occurs in the substrate and/or intermediates (Fig. 3C). From extensive experiments, we confirmed that such chloride or palladium migration is not taking place under the present reaction conditions (figs. S17 to S21). Taken together, we conclude that the intermolecular C–H activation pathway (path 3) is unlikely. Because both possible pathways, paths 1 and 2, involve previously unappreciated elementary reactions [the formation of Pd-aryne via ortho-C–H activation of arylpalladium or the oxidative addition of an aryl chloride to a palladacycle (**22**)], the mechanism of the present reaction is of great interest in its own right.

The construction of polycyclic aromatics has garnered considerable attention owing to their applicability in a range of functional materials. It is particularly important to synthesize these materials in a controlled fashion, because their structure profoundly affects their properties. In this study, all triphenylene-cored, π -extended compounds **2** display blue fluorescence with reasonably sharp spectral widths. The photophysical properties (ultraviolet through visible absorption spectra, fluorescence spectra, and fluorescence quantum yields) of **2** are provided in figs. S30 to S48. Coupled with their nonplanar molecular structures, these new molecules should have considerable potential as materials for OLEDs (*14–17*). For example, as reported by Adachi, triphenylene-based molecules with bipyridine substituents are high-molecular orientation electron-transport materials (*15, 16*) that have become one of the standard materials for OLEDs (*17*).

In addition to their potential use as optoelectronic materials, the annulation products also serve as partially fused polyaromatics and may be useful soluble precursors for the synthesis of fully fused, graphene nanoribbon substrates via Scholl-type dehydrocyclizations (**23**) (Fig. 4A). As a proof-of-concept, we used the annulative dimerization-dehydrocyclization sequence for the synthesis of fully fused nanographenes (Fig. 4B). Triphenylene **2a** was treated with FeCl_3 in CH_2Cl_2 at 0°C (standard conditions for the Scholl reaction), and **3** was obtained in 77% yield (62% two-step yield from **1a**). The clean, high-yielding formation of **3** without any optimization was quite surprising. It is well known that unwanted side reactions such as arene rearrangement (**24**) and aromatic chlorination often take place with polyaromatic compounds (**23**) in Scholl chemistry. For example, when polyphenylene **4**, which can be prepared by the nickel-catalyzed reductive dimerization of **1a** (**25**), was subjected to the standard Scholl conditions (FeCl_3 , CH_2Cl_2 , 0°C), the fully fused product **3** was not obtained; instead, a complex mixture of various unidentified products (most likely arene rearrangement products) was obtained. Thus, there is a clear advantage of the present reaction, accessing partially fused structures (triphenylene substrates in this case), to ensure that subsequent dehydrocyclization occurs successfully. This ring-fusing sequence, enabled by the annulative dimerization reaction, facilitates the synthesis of privileged fused π -conjugated systems, which are otherwise difficult to synthesize.

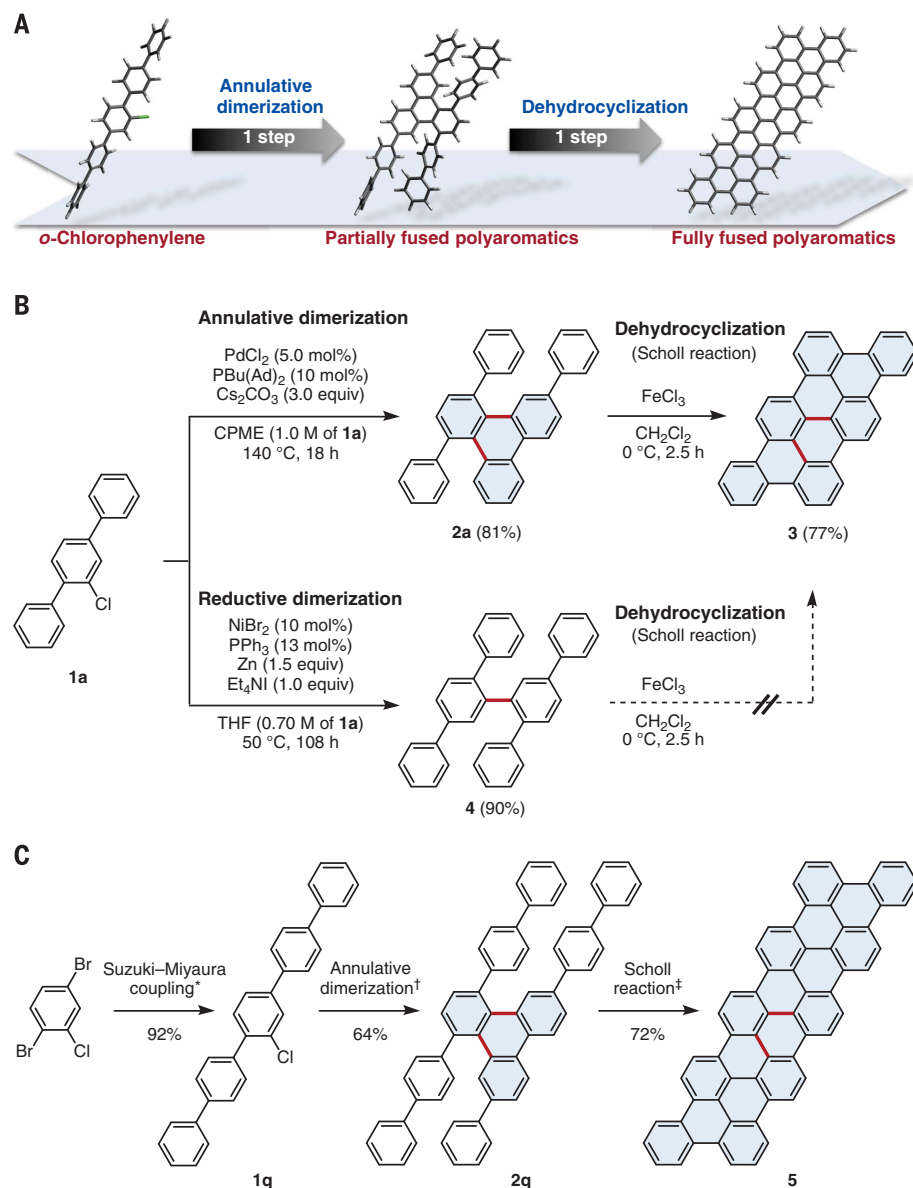


Fig. 4. Access to graphene nanoribbon structures. (A) Rapid synthesis of partially and fully fused polyaromatics enabled by annulative dimerization of chlorophenylenes. (B) Advantage of annulative dimerization over classical reductive dimerization in the synthesis of fully fused phenylene **3**. THF, tetrahydrofuran; Et, ethyl. (C) Synthesis of graphene nanoribbon structure **5**. Reaction conditions: *1,4-dibromo-2-chlorobenzene (1.0 equivalent), 4-biphenylboronic acid (2.4 equivalents), $\text{PdCl}_2(\text{PPh}_3)_2$ (2.0 mol %), K_2CO_3 (5.0 equivalents), toluene/ H_2O /ethanol, 80°C , 18 hours, 92%. † PdCl_2 (5.0 mol %), $\text{PBu}(\text{Ad})_2$ (10 mol %), Cs_2CO_3 (3.0 equivalents), CPME (1.0 M of **1q**), 140°C , 18 hours, 64%. ‡**2q** (0.010 mmol), FeCl_3 (0.47 mmol), CH_2Cl_2 (2.0 ml), room temperature, 42 hours, 72%.

To further demonstrate the utility of the present strategy, the rapid and convergent synthesis of an armchair-edged graphene nanoribbon segment (3, 26–31) was carried out (Fig. 4C). 1,4-Dibromo-2-chlorobenzene was treated with *p*-biphenylboronic acid in the presence of a palladium catalyst (Suzuki-Miyaura cross-coupling) to give chloropentaphenyl **1q** (92% yield). The palladium-catalyzed annulative dimerization of **1q** afforded partially fused product **2q** (64% yield). Finally, the Scholl reaction of **2q** gave small graphene nanoribbon segment C₆₀H₂₆ (**5**) in 72% yield. Notably, this 60-carbon nanoribbon **5** was obtained from 1,4-dibromo-2-chlorobenzene in three steps in 42% overall yield. The Raman and Fourier transform infrared spectra of small nanoribbon **5** were quite similar to the calculated spectra, supporting the formation of the expected nanoribbon structure (see figs. S7, S12, and S13 for details). This represents a very rare example of access to fully fused planar nanographenes without any solubilizing substituents under solution-phase conditions (32–34). Overall, the annulative dimerization reaction sequence reported here should drastically alter the execution of partially and fully fused polyaromatics, as chlorine and ortho hydrogen atoms on aromatic nuclei can now be considered ring-fusing handles.

REFERENCES AND NOTES

- J. Hassan, M. Sévignon, C. Gozzi, E. Schulz, M. Lemaire, *Chem. Rev.* **102**, 1359–1470 (2002).
- F. Ullmann, J. Bielecki, *Chem. Ber.* **34**, 2174–2185 (1901).
- L. Chen, Y. Hernandez, X. Feng, K. Müllen, *Angew. Chem. Int. Ed.* **51**, 7640–7654 (2012).
- L. T. Scott *et al.*, *J. Am. Chem. Soc.* **134**, 107–110 (2012).
- G. Povie, Y. Segawa, T. Nishihara, Y. Miyauchi, K. Itami, *Science* **356**, 172–175 (2017).
- M. G. Schwab *et al.*, *J. Am. Chem. Soc.* **134**, 18169–18172 (2012).
- Y. Segawa, H. Ito, K. Itami, *Nat. Rev. Mater.* **1**, 15002 (2016).
- L. Ackermann, R. Vicente, A. R. Kapdi, *Angew. Chem. Int. Ed.* **48**, 9792–9826 (2009).
- Y. Segawa, T. Maekawa, K. Itami, *Angew. Chem. Int. Ed.* **54**, 66–81 (2015).
- H. Ito, K. Ozaki, K. Itami, *Angew. Chem. Int. Ed.* **56**, 11144–11164 (2017).
- K. Ozaki, K. Kawasumi, M. Shibata, H. Ito, K. Itami, *Nat. Commun.* **6**, 6251 (2015).
- C.-W. Li, C.-I. Wang, H.-Y. Liao, R. Chaudhuri, R.-S. Liu, *J. Org. Chem.* **72**, 9203–9207 (2007).
- R. K. Mohamed *et al.*, *Angew. Chem. Int. Ed.* **55**, 12054–12058 (2016).
- P.-Y. Chou *et al.*, *Chem. Commun. (Camb.)* **50**, 6869–6871 (2014).
- K. Togashi, S. Nomura, N. Yokoyama, T. Yasuda, C. Adachi, *J. Mater. Chem.* **22**, 20689–20695 (2012).
- K. Togashi, Y. Sagara, T. Yasuda, C. Adachi, *Chem. Lett.* **42**, 651–653 (2013).
- C. Adachi, K. Togashi, N. Yokoyama, S. Nomura, Patent WO 2012/114745 (2012).
- S. L. Buchwald, B. T. Watson, J. C. Huffman, *J. Am. Chem. Soc.* **108**, 7411–7414 (1986).
- D. A. Watson *et al.*, *Science* **325**, 1661–1664 (2009).
- H. Jiang, Y. Zhang, D. Chen, B. Zhou, Y. Zhang, *Org. Lett.* **18**, 2032–2035 (2016).
- M. A. Campo *et al.*, *J. Am. Chem. Soc.* **129**, 6298–6307 (2007).
- L.-M. Xu, B.-J. Li, Z. Yang, Z.-J. Shi, *Chem. Soc. Rev.* **39**, 712–733 (2010).
- M. Grzybowski, K. Skonieczny, H. Butenschön, D. T. Gryko, *Angew. Chem. Int. Ed.* **52**, 9900–9930 (2013).
- J. He *et al.*, *Chem. Commun. (Camb.)* **51**, 7245–7248 (2015).
- M. F. Semmelhack, P. M. Helquist, L. D. Jones, *J. Am. Chem. Soc.* **93**, 5908–5910 (1971).
- K. Müllen, *ACS Nano* **8**, 6531–6541 (2014).
- A. Narita *et al.*, *Nat. Chem.* **6**, 126–132 (2014).
- L. T. Scott *et al.*, *Pure Appl. Chem.* **71**, 209–219 (1999).
- V. M. Tsefrikas, L. T. Scott, *Chem. Rev.* **106**, 4868–4884 (2006).
- J. Cai *et al.*, *Nature* **466**, 470–473 (2010).
- M. Treier *et al.*, *Nat. Chem.* **3**, 61–67 (2011).
- C. D. Simpson *et al.*, *Chem. Eur. J.* **8**, 1424–1429 (2002).
- B. Schuler *et al.*, *Angew. Chem. Int. Ed.* **53**, 9004–9006 (2014).
- Z. Wang *et al.*, *J. Am. Chem. Soc.* **126**, 7794–7795 (2004).

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SUPPLEMENTARY MATERIALS

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Materials and Methods
Figs. S1 to S188
Table S1
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Synthesis of partially and fully fused polyaromatics by annulative chlorophenylene dimerization

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How to get two bonds for the price of one

For more than a century, we have known how to couple aryl chlorides at the sites of their C-Cl bonds to form a single C-C bond. Koga *et al.* found that palladium catalysis can instead activate these C-Cl bonds to attack nearby aromatic C-H bonds in a terphenyl molecular framework. The reaction thereby produces a new ring, fused to the original rings on either side. Polycyclic compounds of this sort are of particular interest in optoelectronics research because of their expansive electron delocalization.

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