The Purported Synthesis of "Holey Graphyne" Fails Replication

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In their recent Article, Ryu, Lee, and coworkers assert that they have synthesized "holey graphyne," a highly unusual sp\(^2\)/sp\(^1\) carbon lattice featuring a repeating dibenzo-1,5-cyclooctadiene-3,7-diyn motif. Here, we replicate the key experiments from this work and show that the described conditions do not lead to the formation of "holey graphyne." Furthermore, we demonstrate that the claimed palladium-free Sonogashira-type cross-coupling chemistry is unattainable, even with model substrates.

We synthesized the 1,3,5-tribromo-2,4,6-triethynylbenzene (TBTEB) monomer using a procedure previously reported by us and others. Our synthesis required fewer steps and was less laborious than the seven-step sequence described by Ryu and Lee. The product we obtained was spectroscopically identical to theirs. Subsequently, we replicated the key biphasic polymerization experiment as closely as possible by following the reported procedure.

The original Article fails to provide a clear and complete description of the polymerization experiment. Although the volumes of water and dichloromethane are specified, the concentrations of the reagents are not. The authors mention introducing a "buffer layer" of water to prevent "random encounters" between TBTEB and copper acetate (CuOAc). It is not feasible to introduce two separate, stable aqueous layers into a biphasic mixture of dichloromethane and water, and encounters between molecules are always random. Despite these ambiguities, we were able to replicate the experiment using Fig. S10a from the original Supplementary Information as a guide. Our CuOAc concentration is similar to that used in the original Article, as evidenced by the closely matching colors of the aqueous layers (Fig. S3, SI). For our experiment, we employed a 20 mM concentration of TBTEB, which falls within the range of concentrations previously used for similar 2D polymerizations.

Figure 1. SEM and EDS analysis of the dark substance produced by Cu-mediated reaction of TBTEB. (A) Representative SEM image of a piece of the material. (B) EDS analysis of the region highlighted by the green square in A.
After 48 hours of reaction time, a dark, filmy substance formed at the boundary between the organic and aqueous layers, consistent with the description in the original Article. We washed this material by repeatedly exchanging the solvent in each layer, and then collected and deposited it onto a silicon wafer using the same method as shown in the original Supplementary Fig. S10b. The visual appearance of the dark material closely resembled the magnified image depicted in the original Supplementary Fig. S10a. It's worth noting that the yield of this substance was small - a maximum of 2-3 mg from a typical reaction in a 20 mL vial. As such, it remains unclear how certain experiments described in the original article, such as solid-state NMR, were conducted, as they typically require larger amounts of material.

Using scanning electron microscopy (SEM), we examined the substance and found that it was amorphous without any discernible structure (see Fig. 1A). Energy-dispersive X-ray spectroscopy (EDS) analysis of the isolated material indicated that it contained more than 20 atomic percent (at%) of both Cu and Br (see Fig. 1B, as well as Fig. S25 and Table S2, SI). The composition of the film was highly inhomogeneous, with oxygen content varying between roughly 13 at% and 24 at% in different areas (Fig. S25 and Table S2, SI). Carbon content in the film never exceeded 39 at% in any of the observed regions. As EDS has a typical penetration depth of several μm, the composition determined in this experiment is representative of the bulk material, not just the surface of the film. Moreover, since Br species make up ~20 at% of TBTEB, it seems that few, if any, of these atoms were lost during the reaction.

The Raman spectrum of the dark material (Fig. S24, SI) was complex, with significant bands observed between ~850 cm⁻¹ and 1500 cm⁻¹. Some of these bands, such as 1481 cm⁻¹, could be attributed to the substituted aromatic rings. A sharp, low-intensity band at 2116 cm⁻¹ corresponded to the C≡C stretch of a terminal triple bond, such as that found in TBTEB.² However, the complex composition of the material prevented a more comprehensive assignment of Raman bands. Our Raman spectrum did not match that reported by Ryu and Lee, which may be due to differences in excitation wavelengths (632.8 nm in this study, 532 nm in the original Article) or photochemical decomposition of the film triggered by one of these wavelengths.² The extreme heterogeneity of the product suggested by the SEM/EDS analysis above could also be a factor. Regardless, the Raman band assignment in the original Article is entirely based on modeling and speculation and is inadequate as structural evidence. Some of the major bands in this original Raman spectrum, such as 950 cm⁻¹ and 474 cm⁻¹, could correspond to complex hydrated Cu(II) acetates.⁵

Based on the evidence above, we concluded that the material we obtained could not possibly be the claimed “holey graphyne”. However, we were still curious about the chemical reaction that led to the formation of the dark film. After all, the most notable assertion of the original Article is not the structure of “holey graphyne” itself, but rather the claim of a Sonogashira-type sp¹/sp² cross-coupling that is incredibly efficient even for aryl bromides and is both palladium- and phosphine-free. Since the solid residue resulting
from the exposure of TBTEB to CuOAc was highly disordered and impure, we conducted several control reactions between phenylacetylene and bromobenzene (see Fig. 2A, as well as Fig. S1, S2, SI) to investigate the possible transformations and products under the conditions described in the original Article.

**Figure 2.** Analysis of Cu-mediated reactions between phenylacetylene and bromobenzene. (A) General reaction scheme showing two possible products. Diphenylacetylene is never formed under the conditions we surveyed. (B) A $^{13}$C NMR spectrum of a mixture of phenylacetylene and bromobenzene in CDCl$_3$. The peaks are color-coded for each of the reactants. (C) A $^{13}$C NMR spectrum of the reaction mixture in B 24 hours after adding copper acetate. (D) A $^{13}$C NMR spectrum of a reaction like that in C but performed in a biphasic mixture of CDCl$_3$ and water.

We first performed a reaction between phenylacetylene and bromobenzene in the presence of CuOAc and pyridine in pure CDCl$_3$. This allowed us to directly monitor the reaction by NMR, eliminating any
errors that could be introduced during workup and product extraction. After 24 hours, $^{13}$C NMR indicated the formation of 1,4-diphenylbuta-1,3-diyne, the product of Glaser-type homocoupling of phenylacetylene (Fig. 1B, 1C). No diphenylacetylene was detected. $^1$H NMR showed that only phenylacetylene was consumed in the reaction (see Fig. S11, S12, SI). This strongly suggests that CuOAc cannot activate aryl bromides under the relatively mild conditions employed here and in the original Article.

In the second control experiment, we conducted the reaction under conditions similar to those in the original Article. Phenylacetylene and bromobenzene were dissolved in chloroform, and an aqueous solution of CuOAc and pyridine was added to the organic layer. After 24 hours, no new products were observed in the $^{13}$C NMR spectrum, only unreacted phenylacetylene and bromobenzene (Fig. 1D). Therefore, it can be concluded that the reaction between phenylacetylene and bromobenzene does not occur under the conditions described by Ryu and Lee. These results, combined with the EDS analysis above, suggest that the solid residue from the biphasic homocoupling of TBTEB is primarily composed of the corresponding Cu acetylides, possibly with some diyne crosslinks formed through Glaser-type chemistry.

Our findings align with the extensive literature on copper-catalyzed cross-coupling reactions involving aryl halides. The copper-catalyzed Ullmann-type sp$^2$/sp$^2$ couplings of aryl bromides consistently demand elevated temperatures, indicating a substantial kinetic barrier for the activation of (sp$^2$)C-Br bonds with Cu. In the context of our current discussion, copper can indeed be employed for Pd-free sp$^1$/sp$^2$ cross-couplings, with some protocols being catalytic. However, the scope of these Cu-mediated cross-couplings is limited in comparison with conventional Pd/Cu Sonogashira coupling methodology, showing a strong preference for aryl iodides over bromides as the coupling substrates. Furthermore, even the most promising examples of these Pd-free reactions require temperatures exceeding 100 °C and the use of strongly coordinating ligands for Cu, such as phosphines or privileged multidentate nitrogen species. These ligands are necessary to assist the depolymerization of the stubborn and otherwise unreactive copper acetylides. Dilute aqueous pyridine at room temperature as employed by Ryu and Lee would not be adequate for this task, especially for a poorly soluble multifunctional substrate such as TBTEB. Finally, it is worth noting that Ryu and Lee incorrectly refer to their claimed coupling chemistry as a “Stevens-Castro reaction”. Conventional Stevens-Castro reactions require stoichiometric loadings of pre-made copper acetylides, which is fundamentally impossible for a homopolymerization of an A$_3$B$_3$-type bifunctional monomer such as TBTEB.

In conclusion, we urge extreme caution in the interpretation of the data in the original Article. It appears that the key experiments are not reproducible, and much of the reported characterization is artifactual. Furthermore, the claimed chemistry demonstrably fails even for simple model substrates. Thus, the claimed “holey graphyne” structure is highly unlikely to be realistic. Nevertheless, we share the authors’ enthusiasm
for sp\(^1\)/sp\(^2\) allotropes of carbon. We hope that this contribution helps to clarify some of the pitfalls in the characterization of nonbenzenoid carbon allotropes.

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Competing Interests

The authors declare no competing interests.

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