Synthesis of Saddle-Shape Octaaminotetraphenylene Octahydrochloride

Ishfaq Ahmad, Dongwook Kim, Rukhilllo Kodirov, Soo-Young Yu, Jeong-Min Seo, Javeed Mahmood,* and Jong-Beom Baek*

ABSTRACT: Apart from being experimentally and theoretically interesting, tetraphenylene has potential applications in different fields, including supramolecular chemistry, material science, and asymmetric catalysis. Although a wide range of substituted tetraphenynes have been reported, octaamine-based tetraphenylene derivatives have not been reported because of their instability. Here, stable octaaminotetraphenylene octahydrochloride is synthesized from the bromination of tetraphenylene to octabromotetraphenylene, which is subsequently aminated into octaaminotetraphenylene. Finally, the imino derivative is deprotected to yield octaaminotetraphenylene octahydrochloride.

INTRODUCTION

The material science experienced a significant revolution after the discovery of carbon allotropes such as zero-dimensional fullerene, one-dimensional carbon nanotubes, and two-dimensional graphene. In 1991, Mackay and Terrones proposed a new allotropic form - three-dimensional (3D) periodic carbon crystal with negative Gaussian curvature. These crystals formed triply regular trivalent networks with eight- and six-membered rings. Afterward, there were tremendous efforts to develop polyaromatic structures containing eight-membered rings. Generally, two approaches can be taken: constructing an octagonal structure at the late stage of synthesis or starting the synthesis from eight-membered building units to develop polyaromatics containing octagonal structures.

The development of nonplanar polyarenes has been one of the hotspot synthetic goals of the past few decades because of their unique molecular and electronic properties, which originate from their distorted structure. Their nonplanarity generally results from the insertion of nonhexagonal rings into the framework. Tetraphenylene is a nonplanar molecule with a saddle-shape conformation, containing four benzene rings attached to a rigid central octahedral ring due to orthoannulation. Each pair of phenyl rings are arranged alternately above and below the average plane of the molecule. Tetraphenylene fits the $D_{2d}$ symmetry point group. This exceptional geometry promotes unique 3D platforms suitable for unique molecular clathrates, supramolecular chemistry, materials science, asymmetric catalysis, helical $\pi$-system, and self-assembly building units. Because of their rigid conformations, tetraphenynes have unique molecular structures. However, despite their distinctive architectures, [8]circulenes have yet to attain serious consideration, likely because synthetic protocols to produce functionalized derivatives are scarce. The functionalization of these compounds furnishes a large variety of new building blocks.

For example, functionalization of the phenyl ring in tetraphenylene results in a large variety of unprecedented precursor molecules that can be employed in the design of different structures. Heterocyclic compounds, and specifically nitrogen-containing structures, are vital because of their diverse and exciting pharmaceutical functions. The formation of C–N bonds, and especially aromatic compounds containing nitrogen atoms, is crucial as it unlocks the window for inserting nitrogen in organic compounds.

Despite remarkable developments in this field, organic chemists still face challenges constructing C–N bonds, because in many cases, it involves a tedious multistep synthesis and difficult reaction conditions. Therefore, it is vital to find more appropriate and milder procedures for incorporating the amino groups into the C–H bonds. The synthesis of arylamines has become increasingly important in pharmaceutical and material research communities. ortho-Phenylenediamine (o-phenylendiamine), as a subdivision of arylamines, has emerged as an essential chemical building block for the synthesis of a wide variety of aromatic compounds such as benzotriazole.

Received: May 13, 2021
benzimidazole, and pyrazine derivatives. Tetraphenylene with an o-diamine in each benzene ring could be an essential building block for further modifications. For example, a variety of organic frameworks and heterocyclic functionalities can be synthesized by double-condensing o-phenylenediamine components with 1,2-dicarbonyl-containing moieties. The obstacle to using molecules containing o-phenylenediamine is their sensitivity toward moisture and air. Molecules containing o-diamine must be treated in an inert atmosphere or used immediately after the reduction of the o-dinitro precursors. An efficient and facile synthetic route to overcome this hurdle is highly desired. Here, we report a facile, air-stable, and high-yield synthetic route for octaaminotetraphenylene octahydrochloride.

**RESULTS AND DISCUSSION**

Currently, there are four main synthetic routes to constructing a tetraphenylene (2) skeleton. In this work, tetraphenylene was conveniently synthesized by the palladium-catalyzed homocoupling of 2-iodobiphenyl following a literature-reported procedure (Scheme 1).

Scheme 1. Synthesis of Tetraphenylene as a Precursor for Saddle-Shape Octaaminotetraphenylene Octahydrochloride

![Scheme 1](image1)

Given the exciting properties of tetraphenylene and its derivatives, the o-diamo derivative of tetraphenylene was designed and synthesized in four-step reactions (Scheme 2).

This saddle-shape tetraphenylene with cofacial benzene rings was subjected to electrophilic bromination with bromine in the presence of iron powder as a catalyst in chloroform at 80 °C, resulting in a quantitative yield of octabromotetraphenylene (3) (Figures S1–S3). Then, the palladium-catalyzed coupling reaction of compound 3 with benzophenone imine in toluene solution at 110 °C resulted in a high yield of (tetraphenylene-2,3,6,7,10,11,14,15-octayl)octakis(1,1-diphenylmethanimine) (4) (Figures S4–S6). Finally, the imine moiety was deprotected using an aqueous HCl (2 M) solution, resulting in a high yield of saddle-shape octaaminotetraphenylene octahydrochloride (5), which is an air-stable product allowing single-crystal study (vide infra) (Figures S7–S9).

To gain more insight into the molecular geometry of compound 5 and examine its solid-state packing, brownish needle-like crystals of compound 5 were grown by passing dry HCl gas through the compound 5 solution. The crystal growth was quite challenging due to color change in common organic solvents or water without HCl. Because of color change, the recovery of the materials was difficult. Furthermore, the heating of compound 5 in solvents makes it more difficult to grow crystals. Compound 5 shows better stability in acidic conditions, so we opted to grow the crystal in concentrated HCl. Compound 5 (500 mg) was dissolved in deionized water (5 mL), filtered through a polytetrafluoroethylene (PTFE) membrane (0.45 μm) to remove dust particles, if any, and concentrated HCl (45 mL) was added. Freshly prepared dry HCl was passed through the solution for about 20 min, and the vial was tightly sealed and placed in the freezer (−20 °C) until crystals developed; it takes about a week. The brown crystals...
were collected on a PTFE membrane, washed excessively with dichloromethane and hexane, and dried in the vacuum oven. The crystal structure was further confirmed by single-crystal X-ray crystallography. Compound S crystallizes in the orthorhombic form and belongs to the $Pmmn$ space group ($a = 13.04 \text{ Å}, b = 17.83 \text{ Å}, c = 8.98 \text{ Å}$) with two molecules per unit cell. The crystal structure exhibited a saddle-shape geometry with two phenyl rings oriented above and two others below the plane of the molecule with a dihedral angle of 122.9°. Protonated amine groups of the phenyl rings showed hydrogen-bonding interactions (both strong and weak) with different chlorine atoms. The N(1) atom of protonated amine has hydrogen-bonding interactions with four chlorine atoms, whereas the N(2) atom of the other protonated amine possesses hydrogen-bonding interactions with two chlorine atoms. Also, chlorine atoms possess strong anionic-$\pi$ interactions with the phenyl groups of compound S (Table S5). The molecular structure and crystal packing of compound S are shown in Figures S10 and S11. The crystallographic data and refinement results are provided in Tables S1–S5.

The synthesis of saddle-shape octaaminotetraphenylenedodehydrochloride is a facile and productive method with practical viability. The most important aspect of this synthesis is the crystal formation of air-stable octaaminotetraphenylenedodehydrochloride salt. Because of its suitable synthetic route, saddle-shape octaaminotetraphenylenedodehydrochloride (S) is a promising building block for various applications, including dendritic macromolecules and supramolecular structures, 3D covalent organic network structures, and rotaxanes. Specifically, it opens the possibility of generating porous negative curvature materials.

For concept verification, compound S was reacted with 1,2-diketone compounds, such as 4,4-dimethylbenzil, 4,4-dimethoxybenzil, and benzil in ethanol to produce compounds 6–8 (Scheme 3). The resultant compounds were analyzed by different characterization techniques (Figures S12–S20). The results demonstrate that a variety of materials can be synthesized by utilizing this stable saddle-shape octaaminotetraphenylenedodehydrochloride (S) as a precursor.

## CONCLUSIONS

In this study, we demonstrated a facile and efficient route for the synthesis of octaaminotetraphenylenedodehydrochloride. This ortho-diamine-containing tetraphenylenedodehydrochloride showed excellent stability, allowing purification using column chromatography. It was used as a versatile building block for the synthesis of functional heterocyclic derivatives. More importantly, it can be a potential building block for the bottom-up synthesis of well-defined negative curvature structures.

## EXPERIMENTAL SECTION

### Characterization Methods

All chemicals, including solvents and reagents, were purchased from Aldrich Chemical, Inc. unless otherwise stated. 2-Iodobiphenyl was purchased from Alfa Aesar. Tetraphenylenedodehydrochloride was synthesized following the literature procedure.

Proton ($\mathrm{H}$) and carbon ($\mathrm{^{13}\text{C}}$) nuclear magnetic resonance (NMR) studies were performed on an AVANCE III HD 400 MHz FT-NMR (Bruker) spectrometer. Melting point analysis was performed with a KSPIN automatic melting point meter (A. Krüss Optronic GmbH, Germany). Elemental analysis (EA) was conducted on a Thermofischer Scientific Flash 2000 Analyzer. High-resolution mass spectra (HR-MS) analyses were carried out using JEOL/JMS-700 (2) and AccuTOF 4G+ DART.

### Single-Crystal Structure Analyses

A crystal of octaaminotetraphenylenedodehydrochloride was coated with parabar oil, and the diffraction data were measured at 100 K with synchrotron radiation ($\lambda = 0.80000 \text{ Å}$) on a Rayonix MX225HS detector at BL2D-SMC with silicon (111) double crystal monochromator (DCM) at the Pohang Accelerator Laboratory, Korea. The PAL BL2D-SMD spectrometer was used for data collection, and HKL3000 was used for cell refinement, reduction, and absorption correction. The crystal structure of octaaminotetraphenylenedodehydrochloride was solved by the SHELX structure solution program and refined by full-matrix least-squares calculations with the SHELXL.

### Synthesis of 2,3,7,10,11,14,15-Octabromotetraphenylenedodehydrochloride (3)

A solution of tetraphenylenedodehydrochloride (0.5 g, 1.64 mmol) in distilled 198 chloroform (60 mL) and iron powder (67 mg, 1.20 mmol, catalytic amount) was charged into a three-necked round-bottom flask (500 mL), and bromine (3 mL, 59.04 mmol) was slowly added to the reaction flask and refluxed in an oil bath for 3 h. After completion, the solvent was concentrated by a rotary evaporator. Finally, the crude product was purified by column chromatography using pure hexane as an eluent to give a white solid (0.92 g, 60% yield). mp 220.5 °C. $\mathrm{^{1}H}$ NMR (400 MHz, CDCl$_3$) $\delta$ 7.42 (s, 8H) (Figure S1). $\mathrm{^{13}\text{C}}$ NMR (77.1 MHz, CDCl$_3$) $\delta$ 139.1, 133.9, 125.3 (Figure S2). Anal. calcd for $\text{C}_{21}\text{H}_{12}\text{Br}_4\text{Cl}$: C, 79.58; H, 3.01; Br, 21.02. Found: C, 79.05; H, 3.12; Br, 21.39. HRMS (DART) $m/z$: Calcd for $\text{C}_{21}\text{H}_{12}\text{Br}_4\text{Cl}$: 935.4008 ($[\text{M}-\text{Br}_4\text{Cl}]^+$) based on the relative mass abundance of bromine (79; 50.666% and 81; 49.314%); this value matches well the structure (Figure S3).

### Synthesis of (Tetraphenylenedodehydrochloride-octakis(1,1-diphenylmethanimine) (4)

A toluene solution (85 mL) of rac-2,2’-bis(diphenylphosphino)-1,1’-binaphthalene (BINAP, 1.3 g, 2.07 mmol) and tris(dibenzylideneacetone) dipalladium(0) (1 g, 2.16
Synthesis of Tetraphenyle-2,3,6,7,10,11,14,15-octammine (5). Aqueous HCl (2M, 5 mL) was added dropwise to a six-necked round-bottom flask containing compound 4 (0.22 g, 0.12 mmol) solution in tetrahydrofuran (THF) over 2 h, and the reaction mixture was stirred at room temperature for 6 h. Then, the mixture was diluted with CH2Cl2 and the product was collected by solvent evaporation and dried under reduced pressure (0.05 mmHg). Finally, the crude product was recrystallized from an aqueous HCl solution to give brown crystals (0.075 g, 83% yield); mp becomes dark at 265 °C.

The reaction mixture was stirred at room temperature for 12 h. After cooling, the reaction mixture was diluted with CH2Cl2, and the product was collected by solvent evaporation. Finally, the residue was purified by column chromatography (silica gel, hexane/EtOAc, 9/1, v/v) and further stirred in an oil bath at 110 °C for 15 h. After cooling, a yellow solid (4.50 g, 80%).

The reaction mixture was stirred at room temperature for 6 h. Then, the mixture was diluted with CH2Cl2, and the product was collected by solvent evaporation. Finally, the residue was purified by column chromatography (silica gel, hexane/EtOAc, 9/1, v/v) and further stirred in an oil bath at 110 °C for 15 h. After cooling, a yellow solid (4.50 g, 80%).

The reaction mixture was stirred at room temperature for 6 h. Then, the mixture was diluted with CH2Cl2, and the product was collected by solvent evaporation. Finally, the residue was purified by column chromatography (silica gel, hexane/EtOAc, 9/1, v/v) and further stirred in an oil bath at 110 °C for 15 h. After cooling, a yellow solid (4.50 g, 80%).


365 Center (SRC, 2016R1A5A1009405), and Young Researcher Initiative (CRI, 2014R1A3A2069102), Science Research This research was supported by the Creative Research precise carbon nanostructures. in Atomically Thin Carbon Films.

152, 14074. Complete contact information is available at: https://pubs.acs.org/10.1021/acs.joc.1c01127

346 Ulsan National Institute of Science and Technology (UNIST), Ulsan 44919, Republic of Korea
347 Jeong-Min Seo – School of Energy and Chemical Engineering, Center for Dimension-Controllable Organic Frameworks, Ulsan National Institute of Science and Technology (UNIST), Ulsan 44919, Republic of Korea

359 Center (SRC, 2016R1A5A1009405), and Young Researcher Initiative (CRI, 2014R1A3A2069102), Science Research This research was supported by the Creative Research


