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Hee Yeon Cho, Lawrence T. Scott*

Department of Chemistry, Merkert Chemistry Center, Boston College, 2609 Beacon Street, Chestnut Hill, MA 02467-3860, USA

ARTICLE INFO

Article history:

Received
Received in revised form
Accepted
Available online

Keywords:

Oxidative cyclotrimerization
Scholl-type oxidation
Central benzene moiety
Triphenylene synthesis
Regioselective coupling

ABSTRACT

Intermolecular oxidative cyclotrimerization reactions of alkenes and aromatic compounds with DDQ and trifluoromethanesulfonic acid are described. Scholl-type oxidation reactions involving alkenes have not previously been demonstrated. Moreover, the DDQ/acid system has never been used for intermolecular oxidative cyclization reactions. This convenient, metal-free reagent system (DDQ/TfOH) is advantageous with respect to metal-based Scholl-type oxidants because it eliminates the possibility of halogenation of aromatic compounds as a competing side reaction.

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Introduction

Carbon–carbon bond forming reactions between aromatic rings are fundamentally important reactions in organic, medicinal, and materials chemistry. Such transformations have been achieved by chemical,¹ photochemical,² and electrochemical³ methods. Among these, the chemical method for such transformations has a long history going back for more than a century. With regard to the construction of polycyclic aromatic compounds, the Scholl reaction (oxidative coupling) is the most widely employed (e.g., Scheme 1).

Scheme 1 Scholl Reaction (original report by Scholl)

The Scholl reaction (or Scholl oxidation) is one of the oldest C–C bond forming reactions in organic chemistry and involves dehydrogenative condensation between aromatic rings.⁴ The first such reaction reported by Scholl was the synthesis of meso-naphthodianthrone from helianthrone with aluminum chloride (Scheme 1).⁵ Balaban and Nenitzescu defined the Scholl reaction as *the elimination of two aryl-bound hydrogens accompanied by the formation of an aryl–aryl bond under the influence of Friedel–Crafts catalysts*.⁶ This Scholl-type process has been

heavily used in the synthesis of large polyaromatic hydrocarbon systems.

Scholl-type coupling with metal cations

After the original report by Scholl, a number of Scholl-type oxidative C–C bond forming reactions with metal cations were developed. One of the most common metals employed in these reactions has been aluminum. Wynberg and co-workers demonstrated that the Scholl oxidation with AlCl_3 can cyclize heterohelicenes to furnish dehydrohelicenes.⁷ In this system, a heterohelicene was mixed with AlCl_3 and NaCl at 140 °C to afford dehydrohelicenes in 93% yield. The Scholl-type oxidation reactions with copper–aluminum oxidants have been extensively examined by Müllen and co-workers.⁸ Under these milder Lewis acid oxidation conditions, large polycyclic aromatic hydrocarbons (PAHs) have been prepared.

The Bushby group reported that iron(III)-mediated intermolecular Scholl oxidations can afford triphenylene derivatives.⁹ When tetrahexyloxybiphenyl is mixed with 1-fluoro-2,3-dihexyloxybenzene in the presence of iron(III) chloride (ferric chloride), the desired Scholl product is produced in 69% yield. Another oxidant sometimes used for Scholl-type reactions in the synthesis of PAHs is molybdenum(V). The Waldvogel group has demonstrated that an intramolecular Scholl reaction can be promoted by molybdenum(V) chloride to afford a desired eight-membered ring system in 89% yield.¹⁰

Scholl-type oxidation reactions involving antimony(V) have been demonstrated by several research groups. The Kochi group has been particularly interested in a masked form of SbCl_5 as

* Corresponding author. Tel.: +1-617-447-1237; fax: +1-617-552-2705; e-mail: lawrence.scott@bc.edu

trialkylxonium hexachloroantimonate(V) salts. In the presence of this antimony(V) reagent, 1-methoxynaphthalene is readily oxidized to the corresponding dehydrogenated dimer in quantitative yield.¹¹ It has been observed that a thallium(III) reagent can likewise transform a variety of aromatic compounds into dehydrogenated coupling products. McKillop *et al.* have demonstrated that 1,3-bis(3,4-dimethoxyphenyl)propane can be converted into the corresponding bridged biphenyl in the presence of thallium(III) trifluoroacetate (TTFA) in trifluoroacetic acid (81% yield).¹²

Scholl-type coupling with DDQ/acid

Intramolecular oxidative C–C bond forming reactions involving non-metallic reagents have been demonstrated by the Rathore group.¹³ In this process, the DDQ/methanesulfonic acid system promotes six new intramolecular carbon–carbon bond formations, leading to a hexa-*peri*-hexabenzocoronene (HBC) in excellent yield. In addition, Chen and Liu demonstrated that a dibenzochrysene derivative can be transformed to a planar polycyclic aromatic hydrocarbon.¹⁴ In their system, a dibenzochrysene derivative possesses two non-planar fjord regions, which are transformed to closed ring systems under the DDQ/methanesulfonic acid system in 91% yield.

A recent report by the Johnson group demonstrated that quaterylene can be prepared by a Scholl-type oxidative dimerization using triflic acid and DDQ or molecular oxygen.¹⁵ The authors reported an efficient synthetic route to quaterylene from perylene utilizing DDQ/acid as well as a solution-phase ¹H NMR spectrum of the quaterylene dication.

Oxidative Cyclotrimerization of Alkene

During our investigations on circumtrindene, we have conducted triple aldol condensation reactions to obtain the FVP precursors to circumtrindene (Scheme 2).¹⁶ These reactions usually require harsh reaction conditions and are conducted in high-boiling organic solvents. Moreover, the precursors to the aldol condensation usually require multiple synthetic steps to install the ketone functionality. So far, very few synthetic methods to access the carbon skeletons (*i.e.* triply-annulated central benzene rings) that are required for circumtrindene precursors have been reported. In this regard, we were interested in developing a new methodology to construct a central benzene ring by intermolecular trimerization of simple hydrocarbons.

Scheme 2 Triple Aldol Condensation

We envisioned that alkenes might be trimerized to give a central benzene system under suitable oxidative reaction conditions. Notably, this method would eliminate the necessity to functionalize the substrate (*e.g.* preparing ketones); simple hydrocarbons would be directly oxidized to form new C–C bonds. Under the commonly used Scholl oxidation conditions, however, no alkenes had ever been cyclotrimerized. Considering our projects in polycyclic aromatic hydrocarbon (PAH) synthesis, we were particularly interested in cyclic alkenes, such as acenaphthylenes.

The initial experiments were carried out with 1 equivalent of 4,7-di-*tert*-butylacenaphthylene (**1**), 3 equivalents of DDQ, and 3

equivalents (1.4% v/v) of trifluoromethanesulfonic acid in dichloromethane at ambient temperature. To our great pleasure, the desired product (2,5,8,11,14,17-hexa-*tert*-butyldecacyclene, **2**) was afforded from 4,7-di-*tert*-butylacenaphthylene (**1**) under the oxidation conditions in good yield (48% yield, Scheme 3). The product was soluble enough in common organic solvents to be purified and to be fully characterized.

Scheme 3 Oxidative Cyclization of an Acenaphthylene

The effects of the concentration of the substrate and the reagents on the efficiency of the reaction were examined. When 3 equivalents of DDQ and 3 equivalents (1.4% v/v) of triflic acid were employed, the reaction having 0.02 M concentration (with regard to the substrate) afforded the desired product in 48% yield. When a more concentrated condition (0.10 M) was used, the efficiency of the reaction did not change significantly, giving the trimer in 40% yield. However, the yield of the reaction was more dependent on the concentration of the reagents (both the oxidant and the acid). When 1 equivalent of DDQ and 1 equivalent (0.46% v/v) of triflic acid were employed, the reaction with 0.02 M substrate concentration furnished the product in an improved yield of 68%. The cyclized trimeric product was not obtained, however, when 7 equivalents of DDQ and triflic acid were employed in a 0.02 M solution of **1**. To the best of our knowledge, this is the first example of an intermolecular oxidative cyclotrimerization of an alkene to form a triply fused benzene ring.

Conventional Routes to Triphenylene Cores

Conjugated materials have attracted significant interest in material sciences owing to their utilities in various types of devices.¹⁷ Throughout the history of organic semiconductors and electronics, conjugated polymers have been the main types of the materials in those fields. Among these, star-shaped oligomers bearing triphenylene cores are the most relevant to our studies; thus, they will be briefly introduced in this section.

One of the classic methods for the synthesis of triphenylene is the oxidative cyclotrimerization of benzene. Several oxidants can be employed for this process; iron(III) chloride is one of the most commonly used (Scheme 4).¹⁸ In addition, molybdenum(V) chloride¹⁹ or vanadium(V) chloride²⁰ can also participate in this process as an oxidant. Furthermore, Sato and co-workers demonstrated that photocyclization (with UV light) of *ortho*-terphenyl can afford triphenylene in the presence of iodine.²¹

Scheme 4 Synthesis of Triphenylene by Oxidative Cyclotrimerization

Transition-metal catalyzed reactions also have been developed to prepare the triphenylene skeleton from benzyne. Pérez and Guitián have shown that triphenylene can be synthesized by the cyclotrimerization of benzyne generated from 2-(trimethylsilyl)-

phenyl triflate *in situ* in the presence of a palladium(0) catalyst and cesium fluoride (83% yield, Scheme 5).²² This catalytic method has been applied to the synthesis of various substituted triphenylenes.²³

Scheme 5 Trimerization of Benzyne

Oxidative Cyclotrimerization of Benzene Derivatives

Even though it is known that aromatic compounds undergo cyclotrimerization reactions under Scholl-type oxidation conditions, as outlined in the previous section, the cyclotrimerization reaction has never been carried out with *non-metallic* Scholl reagents. Thus, we examined a number of aromatic compounds for the oxidative cyclotrimerization reactions; coupling reactions of these compounds would lead to construction of the triphenylene carbon skeleton.

Symmetrical 1,2-dialkoxybenzenes

When veratrole (1,2-dimethoxybenzene) was subjected to the DDQ/acid oxidation reaction, the corresponding trimer (**3**) was afforded in 82% yield (Scheme 6). A similar substrate with longer alkyl chains was also a competent substrate for this coupling reaction; the reaction with 1,2-bis(octyloxy)benzene also furnished the desired product (**4**) in 82% yield. Additionally, when 1,2-diethoxybenzene was subjected to the DDQ/triflic acid oxidation reaction, the corresponding coupling product (**5**) was formed in good yield (79% yield).

Scheme 6 Oxidative Cyclotrimerization of 1,2-dialkoxybenzenes

When 1,2-bis(decyloxy)benzene was subjected to the DDQ/acid oxidation reaction, the desired trimer (**6**) was furnished in good yield (60% yield). The reaction with 1,2-bis(hexyloxy)benzene afforded the corresponding trimerized product (**7**) in 56% yield. We also investigated the reactivity of several benzodioxole derivatives toward the oxidative cyclotrimerization reactions. When 1,4-benzodioxane was subjected to the DDQ/acid oxidation reaction, the corresponding trimer (**8**) was afforded in 34% yield.

Unsymmetrical 2-haloalkoxybenzenes

During our investigations on these oxidative cyclotrimerization reactions, we were also interested in employing substrates containing two different substituents. The reactions of a monomer containing two different substituents would afford either a C_3 symmetrical trimer or an unsymmetrical trimer.

Our initial investigations involved oxidation reactions to give halogenated triphenylene derivatives. We chose halogenated anisoles as a starting material, because they have both an electron-donating methoxy group and a halogen that can be further functionalized. When 2-chloroanisole was subjected to the DDQ/TfOH oxidation reaction (1 equiv of DDQ and 1.4% v/v of trifluoromethanesulfonic acid), the unsymmetrical trimer (**9**) was obtained in 82% yield (Scheme 7). The reaction was highly regioselective; we did not observe the formation of any symmetrical trimer from this process.

We also examined other halogenated anisoles and halogenated phenetoles (ethoxy benzenes). Scheme 7 summarizes our results. Unsymmetrical trimers were obtained in every case, which is consistent with an initial oxidative coupling between the electron-rich positions *para* to the methoxy groups.

Scheme 7 Oxidative Cyclotrimerization of 2-Haloalkoxybenzenes

Oxidative Cyclotrimerization of Benzothiophene

We were also interested in determining whether or not heterocyclic aromatic compounds, such as benzofuran, benzothiophene, and indole, would participate in this type of process. The oxidative cyclotrimerization reactions with these heterocycles could afford either symmetric heterotruxene derivatives or unsymmetrical isotruxene heterocycles, either of which might be useful as building blocks for various organic materials.

When an alkylated heteroaromatic compound, 5-methyl-1-benzothiophene, was subjected to the DDQ/triflic acid oxidation reaction, the corresponding cyclic trimer (**15**) was furnished in 43% yield (Scheme 8). This process was highly regioselective and produced exclusively the unsymmetrical trimer. Unfortunately, other heterocyclic aromatic compounds (e.g. benzofuran, indole, thiophene, etc.) did not give cyclic trimers under these oxidative reaction conditions.

Scheme 8 Oxidative Cyclotrimerization of an Aromatic Heterocycle

Conclusions

The first intermolecular oxidative cyclotrimerization reactions of alkenes and aromatic compounds with DDQ and trifluoromethanesulfonic acid have been described. Intermolecular Scholl-type oxidation reactions involving alkenes have never been demonstrated before. Moreover, the DDQ/acid system has never been used for intermolecular oxidative cyclotrimerization reactions. This convenient, metal-free reagent system (DDQ/TfOH) is advantageous with respect to metal-based Scholl-type oxidants because it eliminates the possibility of halogenation of aromatic compounds as a competing side reaction. Furthermore, the regioselective formation of cyclic trimers from substituted benzenes and heteroaromatic compounds is demonstrated. This DDQ/TfOH method provides a simple and convenient synthetic route toward star-shaped oligomers containing triphenylene or isotruxene cores.

Acknowledgments

This work was supported by the National Science Foundation. H.Y.C. is thankful for a Fellowship from the ACS Division of Organic Chemistry (sponsored by Roche).

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