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ORIGINAL PAPER

Pinacolophanes as versatile precursor for the practical synthesis of tolanophanes

Hossein Reza Darabi[1] · Saeed Rastgar[1] · Kioumars Aghapoor[1] · Farshid Mohsenzadeh[1]

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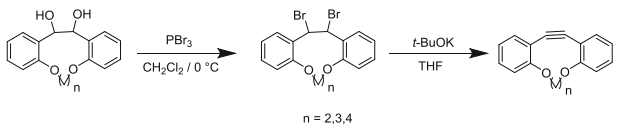
Abstract

A new strategy for the synthesis of tolanophanes was investigated. The coupling of bridged dialdehydes gave selectively the corresponding monomer of pinacolophanes in quantitative yields under a simple and clean reaction condition. Without any further purification, pinacolophanes were quantitatively converted to tolanophanes using a two-step bromination–dehydrobromination process. The overall yield of this practical protocol is upper than 90%. This precursor is highly advantageous compared to the reported stilbenophane in terms of safety, operational simplicity, easy workup, and high efficiency.

Graphical abstract



Keywords Cyclophanes · Strained molecules · Alkynes · Methodology · Bromination

Introduction

The diarylacetylenes are extensively utilized for the synthesis of larger ethynylated aromatic systems. Many ethynylated aromatic systems, such as 1,4-bis(phenylethynyl)benzenes, 9,10-bis(phenylethynyl)anthracenes, 2,5-bis(phenylethynyl)thiophenes, and 2,5-bis(phenylethynyl)metallacylopentadienes, exhibit interesting structural, optoelectronic, luminescent properties, and have the potential to be incorporated into nonlinear optical devices and chemical probes [1–3].

Diarylacetylenes are also important building blocks for the production of hexaarylbenzenes [4]. Hexaarylbenzene derivatives are important organic precursors for fabrication of semiconducting materials [5, 6], graphene fragments [7], and advanced polymers [8], and have been found to be of importance in crystal engineering [9–11] and photovoltaic devices [12]. Despite various approaches to their synthesis, the conventional method remains in catalytic cyclotrimerization of 1,2-disubstituted alkynes in the presence of activated transition metal complex [13]. However, this methodology has the drawback of producing multiple rotamers due to the restricted rotation around the C–C bonds between the six peripheral aryl rings and central benzene ring [14]. Recently, Rathore and coworkers reported the synthesis of hexaarylbenzenes from bridged diarylacetylenes (tolanophanes) leading to solely two isomers [15].

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✉ Hossein Reza Darabi
darabi@ccerci.ac.ir; r_darabi@yahoo.com

[1] Nano and Organic Synthesis Laboratory, Chemistry and Chemical Engineering Research Center of Iran, Pajoohesh Blvd., 17th Km of Tehran-Karaj Highway, Tehran 14968-13151, Iran

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Tolanophanes (cyclic diarylacetylenes) are cyclophanes in which the rotation of tolan moiety around the alkynyl–aryl single bond is restricted. In this regard, the small-sized sterically constrained *ortho*-alkoxy cyclic diarylacetylenes, namely tolanophanes **3**, are promising targets applicable in synthetic methodology [16–18], dynamic conformation [18–20], building blocks for the production of hexaarylbenzenes [15], as well as host–guest chemistry [21].

Tolanophanes have been so far prepared by three approaches, as shown in Scheme 1. Bunz and coworkers recently reported the synthesis of some tolanophanes by ring-closing metathesis of alkynes at 130 °C (method A) [18]. Crisp and coworkers reported synthesis of tolanophanes by Heck–Cassar–Sonogashira–Hagihara coupling of aryl halides with alkynes in the presence of palladium salts (method B) [20]. As shown in Scheme 1, despite the usefulness of these methods to prepare acyclic tolans, the synthesis of the tolanophanes **3** from both procedures was possible only in very poor yields. Therefore, we recently developed a practical method as third route to access these compounds in which bromination/dehydrobromination of stilbenophanes led to the formation of **3** in high yields (method C) [16]. However, the preparation of precursors, i.e., stilbenophanes, suffers from some drawbacks, such as using of bromine, harsh reaction condition, and cumbersome isolation of monomers and dimers which their separation from the reaction mixture required time-consuming column. Moreover, the formation of dimers led to the lower formation of monomers **3**.

Taking into account the importance of tolanophanes as potential precursors for hexaarylbenzene derivatives [15] and our interest to their potential application [19, 21], herein, we introduce a facile, practical, and convenient two-step method for the preparation of tolanophanes from pinacolophanes that, to the best of our knowledge, has not yet been reported.

Results and discussion

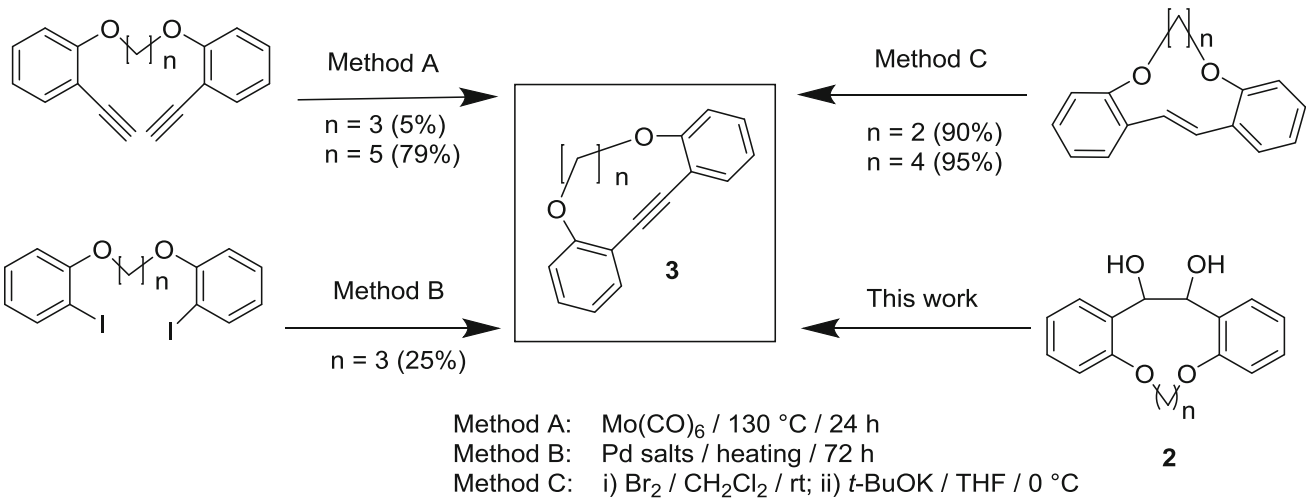
Our new strategy to obtain tolanophanes **3** with the highest efficiency and convenient reaction condition from salicylaldehyde includes four steps. First, one-pot reaction of salicylaldehyde with dihaloalkanes and potassium hydroxide in THF/DMSO gave bridged dialdehydes **1a–1c** as crystalline solids in high yield (95%) (Scheme 2).

We recently achieved the synthesis of the pinacolophanes **2** by the coupling of the corresponding dialdehydes **1** at room temperature under low-valent titanium reaction condition (Scheme 3). The method gave; however, a mixture of monomer and dimer in which the obtained isomers were difficult to separate, leading to lower yield of the desired monomers **2** [22].

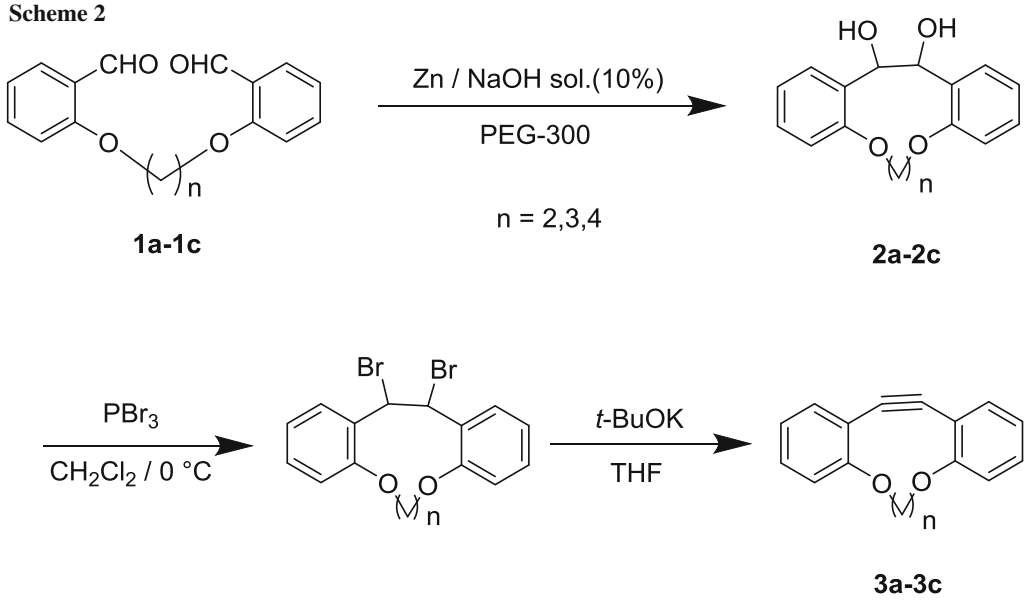
To get a sole monomer, an intramolecular coupling of compounds **1a–1c** was carried out in the presence of Zn, NaOH solution, and PEG-300 following a modified methodology established by Tashiro and coworkers [23]. A quantitative conversion of **1a–1c** was observed (Scheme 2) and it was found that the use of PEG-300 instead of ethanol resulted in almost a sole monomer in excellent yields (**2a** = 92%, **2b** = 94%, and **2c** = 95%).

A literature survey revealed the conversion of hydrobenzoin to 1,2-dibromo-1,2-diphenylethane in the presence of phosphorous tribromide [24]. Considering its effectiveness, it was thought that PBr_3 might satisfactorily convert pinacolophanes to their corresponding dibromo compounds, and indeed, this was observed. The reaction took place rapidly and was completed in 10 min. The

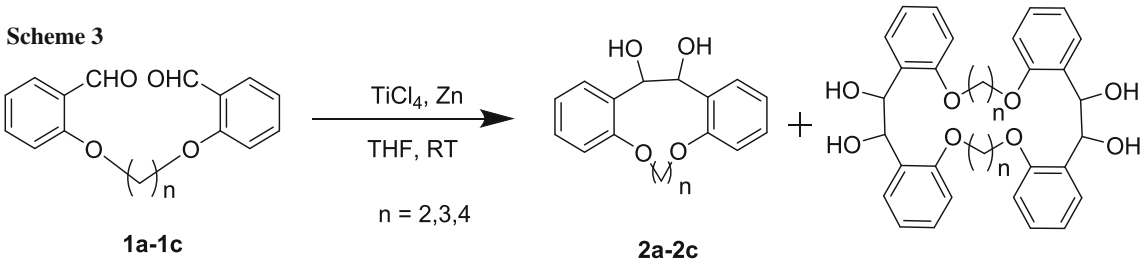
Scheme 1



Scheme 2



Scheme 3



conversion was quantitative and no byproduct was observed. These dibromo compounds were subjected to dehydrobromination to produce tolanophanes **3a**–**3c** quantitatively (Scheme 2). NMR spectroscopy data confirmed the formation of tolanophanes **3a**–**3c** [16, 18].

Conclusion

A simple, clean, efficient, and improved protocol is introduced for the preparation of pinacolophanes. These precursors were quantitatively converted to tolanophanes using a two-step dibromination–dehydrobromination process. The overall yield of this protocol is upper than 90%. The important features of this efficient protocol are the operational simplicity and easy product isolation and purification. This procedure towards tolanophanes is highly advantageous compared to the reported methods in terms of operational simplicity, easy workup, and high efficiency.

Further investigations on various aromatic diols, the substrate generality, and the scope and limitations of the present protocol are currently underway in our lab to elucidate the reaction pathway.

Experimental

2-Hydroxybenzaldehyde (99%, Merck-800640), potassium carbonate (99.5%, Merck-104924), zinc (95%, Merck-108789), phosphorous tribromide (98%, Merck-822321), PEG-300 (Merck-807484), potassium *tert*-butylate (Merck-804918), silica gel 60 (230–400 mesh ASTM, Merck-109385), 1,2-dibromoethane (Merck-800952), 1,3-dibromopropane (Merck-803279), and 1,4-dibromobutane (Merck-803275) were used as received. All other chemicals (KOH, NaOH, and organic solvents) were of analytical quality, and water was purified in an SG Water purification system (Germany). ^{1}H and ^{13}C NMR were recorded on a Bruker 500 MHz spectrometer using TMS as internal standard and $CDCl_3$ as solvent.

General procedure for synthesis of compounds 1a–1c

Salicylaldehyde (200 mmol), KOH (240 mmol), 50 cm^3 THF, and 10 cm^3 DMSO were placed in a 250 cm^3 two-necked round-bottom flask provided with a reflux condenser. The obtained mixture was refluxed for 30 min under continuous stirring. A solution of 100 mmol of 1,2-dibromoethane, 1,3-dibromopropane, or 1,4-dibromobutane was dissolved in 10 cm^3 of THF/DMSO (9:1) and added slowly to the reaction mixture using a dropping funnel. After the addition, the mixture was kept under reflux for 16 h. After completion of the reaction [monitored by TLC using ethyl acetate/hexane (1:3 v/v)], the resulting mixture was cooled to room temperature and washed with 250 cm^3 water. The pale yellow precipitate was filtered off and recrystallized in ethanol to afford pure products **1a**–**1b** as colorless crystalline solids. (**1a**: 25 g, yield: 92%; **1b**: 27 g, yield: 95%; **1c**: 28.8 g, yield: 97%) [22, 23].

General procedure for synthesis of compounds 2a–2c

Zn dust (53 mmol) was added to a solution of NaOH (62 mmol) in 80 cm^3 water and the resulting mixture was refluxed for 1 h. Dialdehydes **1a**–**1c** (10 mmol) were solubilized in 20 cm^3 hot PEG-300 and added to the above mixture and refluxed for 8 h. After completion of the reaction [monitored by TLC using ethyl acetate/hexane (1:2 v/v)], the resulting mixture was cooled to room temperature and filtered. The filtrate mixture was extracted with ethyl acetate (5 × 150 cm^3). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and evaporated to afford the crude products. The crude reaction mixture was purified by flash column chromatography on dry silica gel using a short column [eluent:ethyl acetate/hexane (1:9 v/v)] to afford pure products **2a**–**2c** as colorless solids. (**2a**: 2.56 g, yield: 94%; **2b**: 2.7 g, yield: 94%; **2c**: 2.85 g, yield: 95%) [22, 23].

General procedure for synthesis of compounds 3a–3c

Phosphorous tribromide (15 mmol) was added dropwise to a solution of pinacolophanes **2a**–**2c** (10 mmol) in 50 cm^3 dichloromethane at 0 °C. The reaction mixture was stirred for 15 min at 0 °C. After the completion of the reaction, the obtained solution was washed with 10% aqueous sodium carbonate (2 × 20 cm^3) and poured into 200 cm^3 water. The resulting mixture was extracted with dichloromethane (3 × 50 cm^3) and dried over anhydrous Na_2SO_4. Evaporation of the solvent afforded a quantitative yield of the corresponding dibromo compounds, which was used in the next step without further purification.

Dibromo compounds (10 mmol), 40 cm^3 THF, and potassium *tert*-butoxide (50 mmol) were placed in a round-bottom flask and stirred at room temperature for 15 min. After the completion of the reaction, the obtained solution poured into 200 cm^3 water. The resulting mixture was extracted with dichloromethane (4 × 30 cm^3). The organic medium was removed with rotary evaporator to afford pure tolanophanes **3a**–**3c** in quantitative yields [16, 18].

The crude reaction mixture was purified by flash column chromatography on dry silica gel using a short column (eluent: hexane) to afford pure products **3a**–**3c** (**3a**: 2.21 g, 94%; **3b**: 2.34 g, 94%; **2c**: 2.5 g, 95%).

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