

## Practical synthesis of new functionalized tetraphenylenes

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The practical synthesis procedure of substituted tetraphenylene derivatives involving the synthesis of a precursor for 4,7-dimethoxyisobenzofuran and Diels-Alder addition of 4,7-dimethoxyisobenzofuran generated *in situ* to 5,6,11,12-tetrahydrodibenzo[a,e]cyclooctene, followed by a low valent titanium mediated deoxygenation to give 1,4,11,14-tetramethoxy-dibenzo[b,n]tetraphenylene, which can be further demethylated to the corresponding phenolic compound, which was acetylated to afford 1,4,11,14-tetraacetoxy-dibenzo[b,n]tetraphenylene.

**Keywords** Tetraphenylene, isobenzofuran, Diels-Alder addition

### Introduction

Tetraphenylene is a molecule of considerable interest. It can form clathrate inclusion compounds with a wide variety of guest species, ranging in size from methylene chloride to cyclohexane.<sup>1,2</sup> In order to obtain potential clathrate inclusion compounds containing guest species of larger sizes, a series of benzo-fused tetraphenylenes have been designed and synthesized.<sup>3</sup>

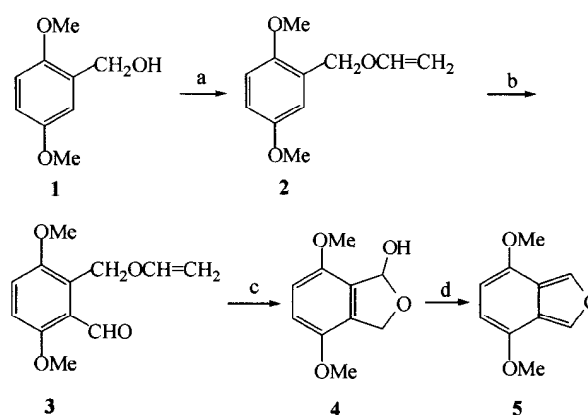
The functionalized tetraphenylene may have different feature of inclusion ability. In order to widen the inclusion capacity of the non-polar tetraphenylene and its derivatives, we would like to undertake the synthesis of substituted tetraphenylene derivatives with polar oxygenated functional groups. In this paper, the practical synthesis procedure of new functionalized tetraphenylene, 1,4,11,14-tetramethoxy-dibenzo[b,n]tetraphenylene and 1,4,11,14-tetraacetoxy-dibenzo[b,n]te-

traphenylene is reported.

### Results and discussion

The strategy for the assembly of new functionalized tetraphenylene derivatives is shown in Schemes 1 and 2. Protection of 2,5-dimethoxybenzyl alcohol with ethyl vinyl ether, followed by reaction with *n*-butyl lithium and *N,N*-dimethylformamide (DMF) gave the 2,5-dimethoxy-6-vinyloxymethylbenzaldehyde (**3**) in 18% yield for two steps.<sup>4</sup> 2,5-Dimethoxy-6-vinyloxymethylbenzaldehyde (**3**) was treated with mercury acetate to afford 4,7-dimethoxy-1-hydroxyphthalan (**4**) in 90% yield,<sup>4</sup> which was used after purification to synthesize 4,7-dimethoxyisobenzofuran (**5**).

Scheme 1



(a) EtOCH=CH<sub>2</sub>, Hg(OAc)<sub>2</sub>, reflux (60%); (b) *n*-BuLi, DMF (30%); (c) Hg(OAc)<sub>2</sub>, dioxane-H<sub>2</sub>O, r.t. (90%); (d) HOAc, CHCl<sub>3</sub>.

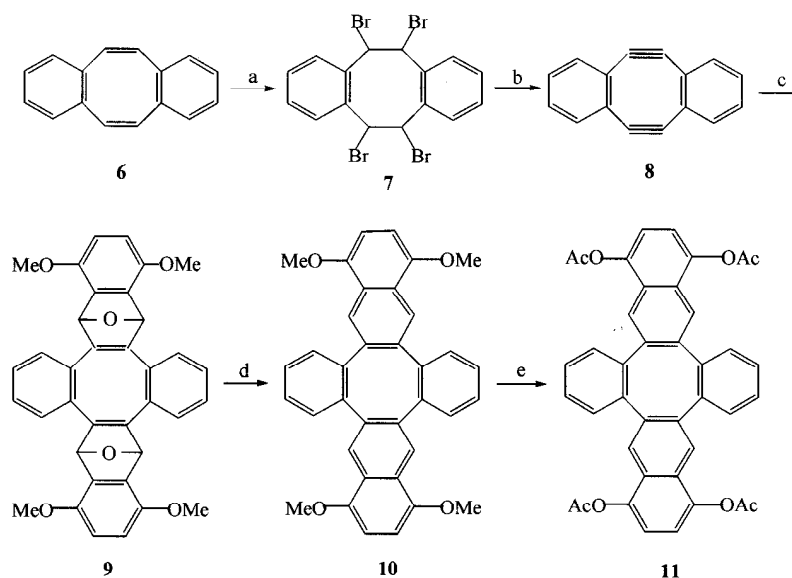
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Bromination of dibenzo[*a,e*]cyclooctene (**6**) at refluxing temperature afforded 5,6,11,12-tetrabromo-5,6,11,12-tetrahydrodibenzo[*a,e*]cyclooctene (**7**) in 65% yield.<sup>5</sup> Dehydrobromination of the tetrabromide (**7**) with potassium *t*-butoxide in tetrahydrofuran at room temperature resulted in elimination of four molecules of hydrogen bromide to give the diacetylene (**8**) as pale yellow crystals in 68% yield.<sup>6</sup> Diacetylene (**8**) was subjected to Diels-Alder cycloaddition with 4,7-dimethoxy-isobenzofuran (**5**) generated *in situ* from 4,7-dimethoxy-1-hydroxyphthalan (**4**) in acid conditions to afford endoxide

(**9**) in 85% yield. Deoxygenation of endoxide (**9**) with low-valent titanium gave 1,4,11,14-tetramethoxydibenzo[*b,n*]tetraphenylene (**10**) as colorless crystals in 89% yield. 1,4,11,14-Tetramethoxydibenzo[*b,n*]tetraphenylene (**10**) can be further demethylated using boron tribromide to give phenolic compound. However, the separation of this phenolic compound is difficult, so we converted it into 1,4,11,14-tetraacetoxy-dibenzo[*b,n*]tetraphenylene (**11**) (39% yield for two steps) by treating the crude phenol with acetic anhydride.

### Scheme 2



(a) Br<sub>2</sub>, CCl<sub>4</sub> reflux 12 h (65%); (b) *t*-BuOK, THF, r.t. (68%); (c) 4,7-dimethoxy-1-hydroxyphthalan, HOAc, CHCl<sub>3</sub> (85%); (d) TiCl<sub>4</sub>, AlLiH<sub>4</sub>, Et<sub>3</sub>N, THF (89%); (e) BBr<sub>3</sub>, CH<sub>2</sub>Cl<sub>2</sub>; Ac<sub>2</sub>O, NaOAc (39%).

The new compounds **9**, **10** and **11** were characterized by <sup>1</sup>H NMR, <sup>13</sup>C NMR, MS, elemental and X-ray single crystal diffraction analysis. The X-ray crystal structure of compound **10** is given in Fig. 1.

The above synthetic procedure can be applied to synthesize other tetraphenylenes substituted with other functional groups such as nitro or cyano group and halogens. These new functionalized tetraphenylenes can serve as new hosts for polar molecules, the further study of these molecules is undergoing and will be reported in forthcoming papers.

### Experimental

Melting points were measured on a hot-stage micro-

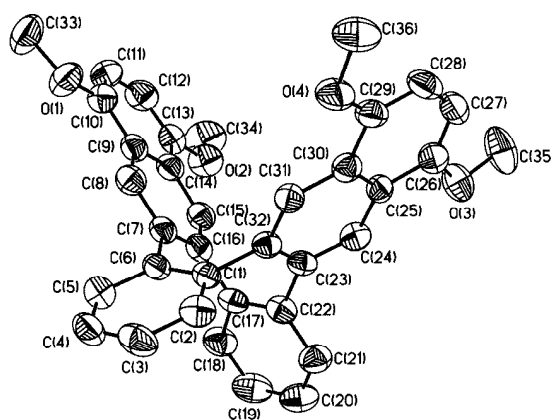


Fig. 1 Crystal structure of compound **10**.

scope and were uncorrected. Proton NMR spectra were

recorded on a Bruker ARX 300 MHz spectrometer with tetramethylsilane (TMS) as internal standard. Mass spectra were recorded on an HP 5989B spectrometer. Elemental analyses were measured with an Elementar Vario El instrument. Potassium *t*-butoxide was purified by sublimation under reduced pressure. Solvents used were purified and dried by standard procedures. All evaporation of solvents was carried out under reduced pressure by a rotary evaporator.

*Synthesis of 1,4,11,14-tetramethoxy-dibenzo[b,n]-1,4:9,12-diepoxy-1,4,9,12-tetrahydrotetraphenylene (9)*

A mixture of 4,7-dimethoxy-1-hydroxyphthalan (392 mg, 2 mmol) and acetic acid (0.3 mL) in chloroform (30 mL) was refluxed for 3 h under nitrogen before being cooled to room temperature. 5,6,11,12-Tetrahydrodibenzo[a,e]cyclooctene (**8**) (200 mg, 1 mmol) was then added and the mixture was refluxed for 6 h. After being cooled to room temperature, the mixture was filtered to afford **9** (475 mg, 85%) as a pale solid. mp > 340°C.  $\delta_{\text{H}}$  (DMSO-*d*<sub>6</sub>): 3.91(s, 12H, OCH<sub>3</sub>), 5.84(s, 4H, CH), 6.88(s, 4H, ArH), 7.02—7.05, 7.20—7.24 (A<sub>2</sub>B<sub>2</sub>, *J* = 4.0, 6.9 Hz, 8H, ArH). HRMS (*m/z*): measured M<sup>+</sup> 556.2011, Calcd. for C<sub>36</sub>H<sub>28</sub>O<sub>6</sub>: 556.1886. Anal. C<sub>36</sub>H<sub>28</sub>O<sub>6</sub>. Calcd: C, 77.68; H, 5.07. Found: C, 77.56; H, 5.36.

*Synthesis of 1,4,11,14-tetramethoxy-dibenzo[b,n]tetraphenylene (10)*

Lithium aluminum hydride (70 mg) was added to a solution of titanium(IV) chloride (0.26 mL) in tetrahydrofuran (15 mL) stirred under nitrogen, followed by a solution of triethylamine (0.13 mL) in tetrahydrofuran (2 mL). After 15 min of refluxing, a solution of endoxide (**9**) (85 mg, 0.15 mmol) in tetrahydrofuran (10 mL) was added. The mixture was then refluxed for 2 h. Saturated potassium carbonate solution (30 mL) was added, followed by extraction with chloroform (3 × 25 mL). The organic layer was dried over magnesium sulfate and concentrated to afford **10** (70 mg, 89%) as a colorless solid. mp > 340°C.  $\delta_{\text{H}}$  (CDCl<sub>3</sub>): 3.87 (s, 12H, OCH<sub>3</sub>), 6.59 (s, 4H, ArH), 7.27—7.34 (m, 8H, ArH), 7.97 (s, 4H, ArH).  $\delta_{\text{C}}$  (CDCl<sub>3</sub>): 55.57, 103.14, 121.96, 125.36, 127.28, 129.27, 140.08, 141.94, 149.34. CIMS (CH<sub>4</sub>): *m/z* 525 (M + 1).

Anal. C<sub>36</sub>H<sub>28</sub>O<sub>4</sub>. Calcd: C, 82.42; H, 5.38. Found: C, 82.25; H, 5.46.

*Synthesis of 1,4,11,14-tetraacetoxy-dibenzo[b,n]tetraphenylene (11)*

Boron tribromide (10 mL, 1.0 mol/L in dichloromethane) was added to a suspension of 1,4,11,14-tetramethoxy-dibenzo[b,n]tetraphenylene (**10**) (105 mg, 0.2 mmol) in dichloromethane (2 mL) stirred at 0°C under nitrogen. The mixture was allowed to warm up to room temperature and stirring was continued overnight. The mixture was then washed with water (10 mL) to hydrolyze excess reagent and boron complexes. The phenolic product was collected by extraction with dichloromethane (3 × 20 mL). The dichloromethane solution was dried and evaporated. The residue was treated with acetic anhydride (0.5 mL) and sodium acetate (50 mg) for 30 min with slightly warming (water-bath). Water (5 mL) and dichloromethane (3 × 15 mL) were added. The organic extracts were dried and evaporated. The residue was purified by column chromatography on silica gel (elution with dichloromethane) to afford the product, which crystallized from acetone-hexane to afford **11** (50 mg, 39%) as a colorless solid. mp > 340°C.  $\delta_{\text{H}}$  (CDCl<sub>3</sub>): 2.39 (s, 4H, OCH<sub>3</sub>), 7.20 (s, 4H, ArH), 7.26—7.30, 7.37—7.41 (AA'BB', *J* = 6.2, 3.2 Hz, 8H, ArH), 7.68 (s, 4H, ArH).  $\delta_{\text{C}}$  (CDCl<sub>3</sub>): 21.12, 117.85, 121.79, 126.88, 127.96, 129.53, 140.81, 141.12, 144.05, 169.18. CIMS (CH<sub>4</sub>): *m/z* 637 (M + 1). Anal. C<sub>40</sub>H<sub>28</sub>O<sub>8</sub>. Calcd: C, 75.46; H, 4.43. Found: C, 75.65; H, 4.25.

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