

# Convenient Iterative Synthesis of an Octameric Tetracarboxylate-Functionalized Oligophenylene Rod with Divergent End Groups

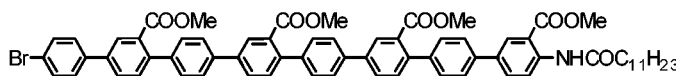
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## ABSTRACT



10

Oligo(*p*-phenylene) rigid rod 10 is synthesized via a functional group-tolerant molecular doubling approach. Preparative chromatographic methods, protecting groups, boronic acid isolations, and Grignard or organolithium reagents are not used. The convenient synthesis of well-defined, polar-functionalized oligophenylene rigid rods could afford ready access to a variety of useful electronic organic materials.

Well-defined conjugated oligomers are of current interest as nondefected structures for catalysis and electronic device fabrication, as models for property and characterization studies of their larger polymeric congeners, and as components of large-pocketed organic crystals.<sup>1</sup> These latter as well as related applications have inspired creative synthetic strategies and important property studies of a variety of conjugated oligomeric materials.<sup>1,2</sup> Oligo(*p*-phenylene)s are an important class of conjugated redox and chromophore materials that have found use, for example, as chain-stiffening building blocks in semiflexible polymers such as polyimides and aromatic polyesters and as models for rodlike polyaromatic and liquid crystalline materials.<sup>3</sup> More recently, oligophenylenes have been transformed to planarized ladder-

type materials<sup>2h,4</sup> and relatively large polycyclic aromatic hydrocarbons<sup>5</sup> as well as novel macrocycles.<sup>6</sup> Oligo(*p*-phenylene)s have also led to the discovery of a new mode of biomembrane recognition and depolarization<sup>7</sup> as well as fascinating biomimetic barrel-like folds,<sup>8</sup> ion channels<sup>9</sup> and amphiphilic materials<sup>10</sup> which form via supramolecular preorganization.

A barrier toward the realization of the full potential of soluble oligo(*p*-phenylene)s is their challenging synthesis,

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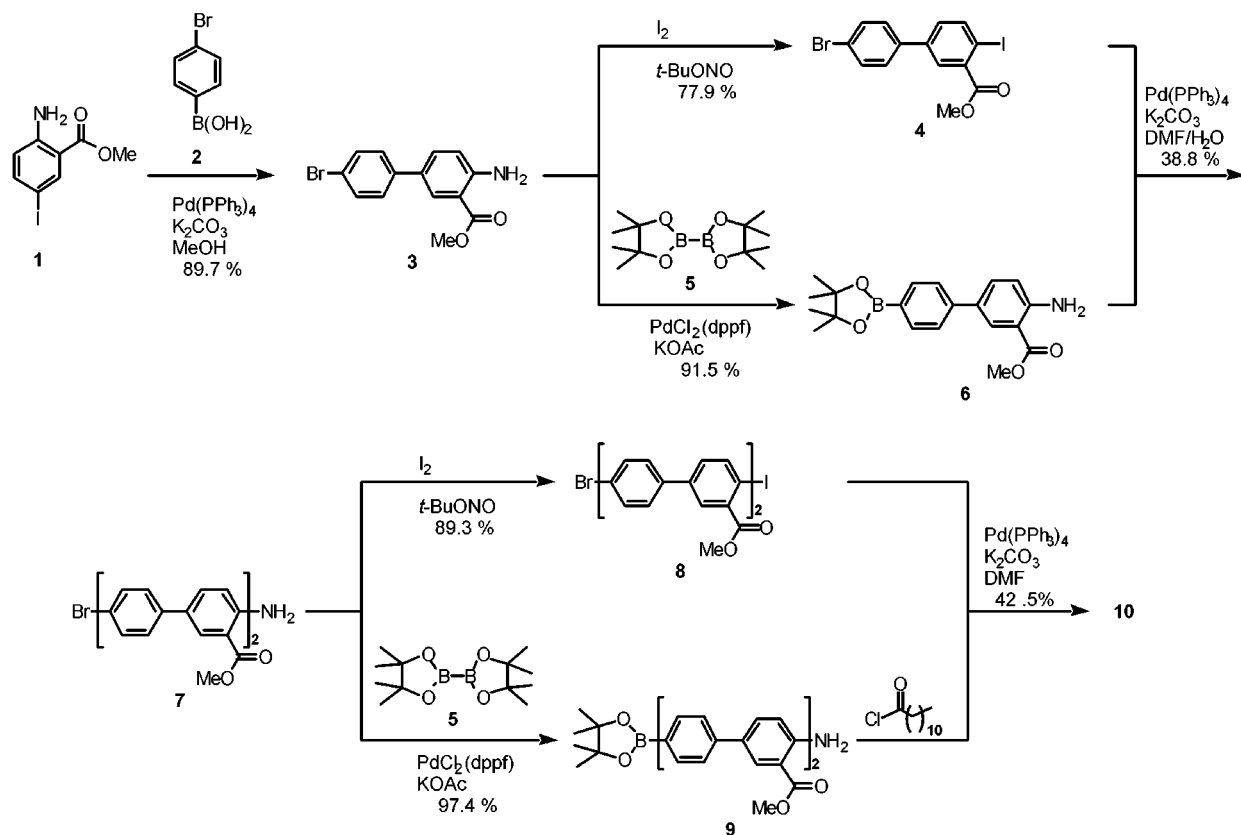
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(2) Reviews: (a) Moore, J. S. *Acc. Chem. Res.* **1997**, *30*, 402. (b) Roncali, J. *Chem. Rev.* **1997**, *97*, 173. (c) Feuerbacher, N.; Vogtle, F. *Top. Curr. Chem.* **1998**, *197*, 1. (d) Berresheim, A. J.; Muller, M.; Mullen, K. *Chem. Rev.* **1999**, *99*, 1747. (e) Kugler, T.; Logdlund, M.; Salaneck, W. R. *Acc. Chem. Res.* **1999**, *32*, 225. (f) Gao, Y. L. *Acc. Chem. Res.* **1999**, *32*, 2: 247. (g) Schwab, P. F. H.; Levin, M. D.; Michl, J. *Chem. Rev.* **1999**, *99*, 1863. (h) Scherf, U. *Top. Curr. Chem.* **1999**, *201*, 163.

Scheme 1



isolation, and purification.<sup>11</sup> A recent major advance toward well-defined, relatively long oligo(*p*-phenylene)s in multi-gram amounts is based on repetitive growth strategies.<sup>12</sup> As part of our broader program which involves the discovery of new palladium-catalyzed coupling reactions<sup>13</sup> and the creation of three-dimensional oligoaromatic architectures<sup>14</sup> for optical and fluorescence bioanalytical sensing,<sup>15</sup> we herein describe the synthesis of the new oligo(*p*-phenylene) rigid rod **10**. Compound **10** possesses divergent end groups for potential telechelic applications as well as readily interconvertible carboxylate side groups. The molecular doubling synthesis involves no formal protecting groups or organolithium<sup>12a</sup> or Grignard chemistry.<sup>12b</sup> Each synthetic transformation is thus tolerant of pendant polar functional groups. The potentially troublesome isolation and characterization of aryl boronic acids<sup>16</sup> is avoided. All of the intermediates

and the final target are purified without preparative thin layer or column chromatography.

The synthesis of **10** (Scheme 1) begins with the Suzuki coupling<sup>17</sup> of methyl ester **1**<sup>18</sup> (20 g, 0.0722 mol) to commercially available 4-bromophenylboronic acid **2** (16.0 g, 0.080 mol) in the presence of K<sub>2</sub>CO<sub>3</sub> (22.5 g, 0.163 mol) and Pd(PPh<sub>3</sub>)<sub>4</sub> (1.99 g, 1.72 mmol) in anhydrous MeOH deoxygenated by purging with N<sub>2</sub>. The reaction mixture is heated at 60 °C for 12 h under N<sub>2</sub>. After filtration through Celite, concentration of the filtrate, extraction, and removal of the solvent in vacuo, the residue is dissolved in CH<sub>2</sub>Cl<sub>2</sub> and passed through a short silicagel plug to afford biaryl **3** (19.8 g), after drying, in 89.7% yield.<sup>19</sup> Compound **3** (3.02 g, 0.99 mmol) is transformed to the corresponding iodide upon dissolution in anhydrous PhH in the presence of I<sub>2</sub> (1.51 g, 5.94 mmol) and *t*-BuONO (90%, 1.40 mL, 10.6 mmol) at 0 °C.<sup>20</sup> After warming to 60 °C for 10 min, H<sub>2</sub>O is added and the reaction mixture is extracted, dried, and concentrated.

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(12) (a) Liess, P.; Hensel, V.; Schlüter, A.-D. *Liebigs Ann.* **1996**, 1037. (b) A very different large scale synthesis of a sexiphenyl rod has also been reported: Kauffman, J. M. *Synthesis* **1999**, *6*, 918.

(13) For example, the cross-coupling of aniline-derived aryldiazonium tetrafluoroborate salts with arylboronic esters: Willis, D. M.; Strongin, R. M. *Tetrahedron Lett.* **2000**, *41*, 6271.

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(19) Data for **3**: mp 138–139 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 3.91 (s, 3H), 5.88 (bs, 2H), 6.78 (d, *J* = 8.56 Hz, 1H), 7.40 (d, *J* = 8.63 Hz, 2H), 7.51 (d, *J* = 8.59 Hz, 2H), 7.51 (dd, *J* = 2.31, 8.62 Hz, 1H), 8.09 (d, *J* = 2.28 Hz, 1H). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ: 51.3, 110.8, 117.2, 120.4, 127.7, 129.3, 131.7, 132.5, 139.3, 149.9. HRMS *m/z* calcd for C<sub>14</sub>H<sub>12</sub>BrNO<sub>2</sub>: 305.0051, found 305.0063.

(20) For a highly useful alternative for transforming anilines to aryl iodides, see: Moore, J. S.; Weinstein, E. J.; Wu, Z. Y. *Tetrahedron Lett.* **1991**, *32*, 2465.

The residual solid is triturated with hexanes to afford iodide **4** (3.18 g) in 77.9% yield.<sup>21</sup> Compound **3** (3.02 g, 9.86 mmol) is converted to boronate ester **6** via dissolution in a solution of anhydrous, deoxygenated DMF along with commercially available bis(pinacolato)diboron **5** (2.81 g, 11.1 mmol), KOAc (3.24 g, 33.0 mmol), and PdCl<sub>2</sub>(dppf) (0.163 g, 0.290 mmol).<sup>22</sup> The mixture is heated at 60 °C for 12 h under N<sub>2</sub>, filtered through Celite, extracted, and dried. The solid is redissolved in CH<sub>2</sub>Cl<sub>2</sub> and filtered through a short silicagel plug, dried, triturated with hexanes, and dried again to furnish biarylboronate **6** (3.17 g) in 91.5% yield.<sup>23</sup>

Tetrameric *p*-phenylene **7** is afforded via the coupling of **4** (3.00 g, 7.19 mmol) and **6** (2.80 g, 7.93 mmol) which are dissolved in a deoxygenated 4:1 DMF/H<sub>2</sub>O solution heated to 60 °C for 12 h under N<sub>2</sub> in the presence of K<sub>2</sub>CO<sub>3</sub> (2.09 g, 15.1 mmol) and Pd(PPh<sub>3</sub>)<sub>4</sub> (0.249 g, 0.216 mmol). After filtration, concentration of the filtrate, extraction, and drying, the residual solid is redissolved in CH<sub>2</sub>Cl<sub>2</sub> and passed through a silica gel plug to afford **7** (1.44 g, 38.8%) after drying.<sup>24</sup> Compound **7** (0.300 g, 0.582 mmol) and I<sub>2</sub> (0.092 g, 0.36 mmol) are dissolved in anhydrous PhH. *t*-BuONO (90%, 1.40 mL, 10.6 mmol) is added to the solution cooled to 0 °C. The solution is warmed to rt, stirred for 12 h, and heated at 60 °C for 10 min. After H<sub>2</sub>O addition, the reaction mixture is extracted, dried, and concentrated. The residual solid is triturated with hexanes to afford iodide **8** (0.364 g, 89.3%).<sup>25</sup> The corresponding boronate **9** is synthesized by dissolving **7** (0.603 g, 1.17 mmol), **5** (0.370 g, 1.45 mmol), KOAc (0.478 g, 4.87 mmol), and PdCl<sub>2</sub>(dppf) (0.037 g, 0.067 mmol) in anhydrous DMF deoxygenated by purging with N<sub>2</sub>. The solution is heated at 60 °C for 12 h under N<sub>2</sub> and cooled, the mixture is filtered, and the filtrate is concentrated, extracted, and dried. The residue is redissolved in CH<sub>2</sub>Cl<sub>2</sub> and filtered through a silica gel plug and dried to afford **9** (0.702 g, 97.4%).<sup>26</sup>

(21) Data for **4**: mp 99.5–101 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ: 3.96 (s, 3H), 7.33 (dd, *J* = 2.26, 8.25 Hz, 1H), 7.44 (d, *J* = 8.38 Hz, 2H), 7.58 (d, *J* = 8.41 Hz, 2H), 7.98 (d, *J* = 2.32 Hz, 1H), 8.05 (d, *J* = 8.25 Hz, 1H). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ: 52.6, 93.0, 122.5, 128.4, 129.3, 130.8, 132.1, 135.6, 138.0, 140.0, 141.9, 156.8. HRMS *m/z* calcd for C<sub>14</sub>H<sub>10</sub>BrIO<sub>2</sub>: 415.8909, found 415.8914.

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(23) Data for **6**: mp decomposed at 157.9–159 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ: 1.29 (s, 12H), 3.84 (s, 3H), 6.71 (d, *J* = 8.55 Hz, 1H), 7.48 (d, *J* = 8.24 Hz, 2H), 7.54 (dd, *J* = 2.27, 8.49 Hz, 1H), 7.78 (d, *J* = 8.24 Hz, 2H), 8.09 (d, *J* = 2.23 Hz, 1H). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ: 24.9, 51.7, 83.7, 111.2, 117.5, 125.4, 129.5, 129.6, 132.9, 135.3, 142.9, 149.2, 168.5. HRMS *m/z* calcd for C<sub>20</sub>H<sub>24</sub>BNO<sub>4</sub>: 353.1798, found 353.1780.

(24) Data for **7**: mp decomposed at 192–195 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ: 3.64 (s, 3H), 3.85 (s, 3H), 6.72 (d, *J* = 8, 54 Hz, 1H), 7.30–7.57 (m, 10H), 7.66 (dd, *J* = 2.06, 8.03 Hz, 1H), 7.95 (d, *J* = 1.96 Hz, 1H), 8.13 (d, *J* = 2.22 Hz, 1H). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ: 51.7, 52.2, 111.4, 117.0, 122.1, 125.9, 127.2, 127.4, 128.3, 128.6, 128.8, 128.9, 129.5, 131.4, 131.9, 132.1, 132.8, 138.6, 138.9, 141.3, 168.5, 169.1. HRMS *m/z* calcd for C<sub>28</sub>H<sub>22</sub>BrNO<sub>4</sub>: 515.0732, found 515.0748.

(25) Data for **8**: mp 128–130 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ: 3.73 (s, 3H), 3.97 (s, 3H), 7.42 (d, *J* = 8.29 Hz, 1H), 7.44 (d, *J* = 8.21 Hz, 2H), 7.47 (d, *J* = 8.01 Hz, 1H), 7.52 (d, *J* = 8.52 Hz, 3H), 7.60 (d, *J* = 8.52 Hz, 2H), 7.64 (d, *J* = 8.28 Hz, 2H), 7.73 (dd, *J* = 2.02, 7.97 Hz, 1H), 8.06 (d, *J* = 8.02 Hz, 1H), 8.08 (dd, *J* = 2.32, 8.68 Hz, 1H). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ: 52.2, 52.5, 92.7, 122.2, 126.6, 128.3, 128.4, 128.6, 129.0, 129.5, 129.6, 131.0, 131.4, 132.1, 135.5, 137.9, 138.5, 139.2, 140.6, 140.7, 141.0, 141.8, 166.9, 168.7. HRMS *m/z* calcd for C<sub>28</sub>H<sub>20</sub>BrIO<sub>4</sub>: 625.9590, found 625.9587.

To overcome potential solubility problems anticipated for longer phenylenes, we functionalized the tetrameric boronate with a lauryl moiety. Compound **9** (0.477 g, 0.85 mmol), di-*tert*-butylpyridine (0.25 mL, 1.25 mmol), and lauroyl chloride (0.26 mL, 1.12 mmol) are dissolved in CH<sub>2</sub>Cl<sub>2</sub> at 0 °C, warmed to rt, and stirred for 12 h. After extraction, the crude amide is directly coupled to iodide **8**.

The lauryl amide of **9** (0.589 g, 0.79 mmol), compound **8** (0.408 g, 0.650 mmol), K<sub>2</sub>CO<sub>3</sub> (0.226 g, 1.64 mmol), and Pd(PPh<sub>3</sub>)<sub>4</sub> (0.032 g, 0.0278 mmol) are mixed in DMF, and the solution is deoxygenated and heated at 60 °C for 12 h under N<sub>2</sub>. The solution is filtered, the filtrate is concentrated, and the solid is washed with H<sub>2</sub>O and MeOH, dissolved in 10% MeOH in CH<sub>2</sub>Cl<sub>2</sub>, and filtered through a short silicagel plug to afford 0.309 g (42.5%) of octamer **10** in overall 10.1% yield from **1**.<sup>27</sup>

In conclusion, we have efficiently synthesized a highly functional octameric oligo(*p*-phenylene) using a molecular doubling approach. Transesterification of the side groups to, for instance, glycolate esters at the tetramer stage or earlier should allow the repetitive scheme to continue without end group functionalization with a solubilizing moiety, thereby affording longer rigid rods if needed.<sup>28</sup> Decarboxylation to remove the side groups would furnish novel telechelic rigid rod phenylenes with unsubstituted repeat units. The use of **5** in this scheme also allows for further synthetic streamlining via the application of one-pot arylborylation/cross-coupling methods.<sup>22c</sup> Further successful synthetic transformations and the incorporation of new rigid rod oligo(*p*-phenylene)s into unique, well-defined nanoscale oligoaromatic architectures has now also been achieved in our laboratory and will be reported in due course.

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(26) Data for **9**: <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ: 1.26 (s, 12H), 3.71 (s, 3H), 3.92 (s, 3H), 6.79 (d, *J* = 8.52 Hz, 1H), 7.40 (d, *J* = 8.28 Hz, 2H), 7.49 (d, *J* = 7.98 Hz, 1H), 7.61 (d, *J* = 8.25 Hz, 2H), 7.62 (dd, *J* = 2.28, 8.48 Hz, 1H), 7.68 (d, *J* = 8.10 Hz, 2H), 7.78 (dd, *J* = 1.99, 8.00 Hz, 1H), 7.92 (d, *J* = 8.51 Hz, 2H), 8.09 (d, *J* = 1.93 Hz, 1H), 8.20 (d, *J* = 2.24 Hz, 1H). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ: 24.9, 51.7, 52.2, 83.9, 111.2, 117.5, 125.9, 126.3, 127.1, 128.5, 128.8, 128.9, 129.0, 129.5, 129.9, 131.3, 132.7, 135.4, 139.0, 139.3, 139.9, 141.1, 142.2, 149.4, 168.5, 169.2. HRMS *m/z* calcd for C<sub>34</sub>H<sub>34</sub>BNO<sub>6</sub>: 563.2479, found 563.2488.

(27) Data for **10**: mp gels at 206–208 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ: 0.88 (t, *J* = 6.85 Hz, 3H), 1.26 (m, 16H), 1.78 (p, *J* = 7.12 Hz, 2H), 2.48 (t, *J* = 7.32 Hz, 2H), 3.73 (s, 3H), 3.75 (s, 6H), 3.98 (s, 3H), 7.45–7.88 (m, 23H), 8.06 (d, *J* = 1.92 Hz, 1H), 8.17 (d, *J* = 1.74 Hz, 2H), 8.35 (d, *J* = 2.22 Hz, 1H), 8.86 (d, *J* = 8.84 Hz, 1H), 11.01 (bs, 1H). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ: 14.1, 22.7, 25.6, 29.2, 29.3, 29.5, 29.6, 31.9, 38.8, 52.2, 52.4, 115.1, 120.9, 122.2, 126.4, 126.8, 127.6, 128.4, 128.6, 129.0, 129.1, 129.6, 129.8, 131.2, 131.4, 132.1, 133.1, 134.6, 138.6, 139.2, 139.8, 140.1, 140.4, 140.5, 140.9, 141.1, 168.8, 168.9, 172.4. HRMS *m/z* calcd for C<sub>68</sub>H<sub>64</sub>BrNO<sub>9</sub>: 1117.3764, found 1117.3748.

(28) For the properties of glycol-functionalized oligo(phenylene ethynylene), see, for example: Prince, R. B.; Saven, J. G.; Wolynes, P. G.; Moore, J. S. *J. Am. Chem. Soc.* **1999**, *121*, 3114.

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**Supporting Information Available:**  $^1\text{H}$  NMR spectra and detailed experimental procedures for the preparation of **3**, **4**, and **6–10**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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