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

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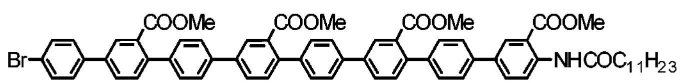
ABSTRACT



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.[1] These latter as well as related applications have inspired creative synthetic strategies and important property studies of a variety of conjugated oligomeric materials.[1,2] 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.[3] More recently, oligophenylenes have been transformed to planarized ladder-type materials[2h,4] and relatively large polycyclic aromatic hydrocarbons[5] as well as novel macrocycles.[6] Oligo(*p*-phenylene)s have also led to the discovery of a new mode of biomembrane recognition and depolarization[7] as well as fascinating biomimetic barrel-like folds,[8] ion channels[9] and amphiphilic materials[10] 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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(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.

(3) First efficient palladium-catalyzed synthesis of relatively long oligophenylene rods and references on earlier property studies, see: Galda, P.; Rehahn, M. *Synthesis* **1996**, 614.

(4) Grimme, J.; Scherf, U. *Macromol. Chem. Phys.* **1997**, *197*, 2297.

(5) Muller, M.; Iyer, V. S.; Kubel, C.; Enkelmann, V.; Mullen, K. *Angew. Chem, Int. Ed. Engl.* **1997**, *36*, 1607.

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(9) Baumeister, B.; Sakai, N.; Matile, S. *Angew. Chem., Int. Ed.* **2000**, *39*, 1955.

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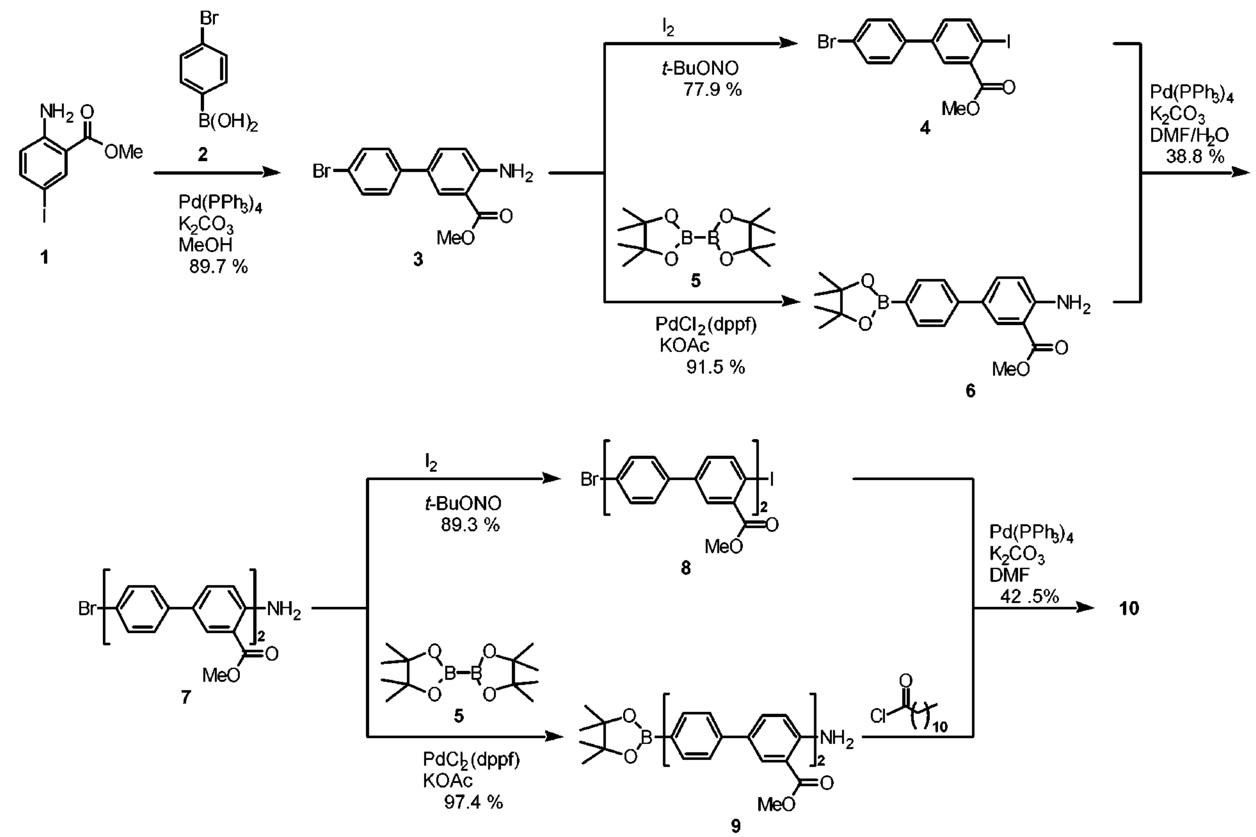
Scheme 1



isolation, and purification.[11] A recent major advance toward well-defined, relatively long oligo(*p*-phenylene)s in multigram amounts is based on repetitive growth strategies.[12] As part of our broader program which involves the discovery of new palladium-catalyzed coupling reactions[13] and the creation of three-dimensional oligoaromatic architectures[14] for optical and fluorescence bioanalytical sensing,[15] 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[12a] or Grignard chemistry.[12b] Each synthetic transformation is thus tolerant of pendant polar functional groups. The potentially troublesome isolation and characterization of aryl boronic acids[16] 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[17] of methyl ester **1**[18] (20 g, 0.0722 mol) to commercially available 4-bromophenylboronic acid **2** (16.0 g, 0.080 mol) in the presence of K_2CO_3 (22.5 g, 0.163 mol) and $Pd(PPh_3)_4$ (1.99 g, 1.72 mmol) in anhydrous MeOH deoxygenated by purging with N_2. The reaction mixture is heated at 60 °C for 12 h under N_2. After filtration through Celite, concentration of the filtrate, extraction, and removal of the solvent in vacuo, the residue is dissolved in CH_2Cl_2 and passed through a short silicagel plug to afford biaryl **3** (19.8 g), after drying, in 89.7% yield.[19] Compound **3** (3.02 g, 0.99 mmol) is transformed to the corresponding iodide upon dissolution in anhydrous PhH in the presence of I_2 (1.51 g, 5.94 mmol) and *t*-BuONO (90%, 1.40 mL, 10.6 mmol) at 0 °C.[20] After warming to 60 °C for 10 min, H_2O is added and the reaction mixture is extracted, dried, and concentrated.

(11) The difficulties associated with the synthesis of multiply substituted phenylenes have been very recently noted: Robert, F.; Winum, J.-Y.; Sakai, N.; Gerard, D.; Matile, S. *Org. Lett.* **2000**, *2*, 37.

(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.

(14) (a) Lewis, P. T.; Davis, C. J.; Saraiva, M.; Treleaven, D.; McCarley, T.; Strongin, R. M. *J. Org. Chem*. **1997**, *62*, 6110. (b) Lewis, P. T.; Strongin, R. M. *J. Org. Chem*. **1998**, *63*, 6065.

(15) (a) Davis, C. J.; Lewis, P. T.; McCarroll, M. E.; Read, M. W.; Cueto, R.; Strongin, R. M. *Org. Lett.* **1999**, *1*, 331. (b) Lewis, P. T.; Davis, C. J.; Cabell, L. A.; He, M.; Read, M. W.; McCarroll, M. E.; Strongin, R. M. *Org. Lett.* **2000**, *2*, 589.

(16) Hensel, V.; Schlüter, A.-D. *Liebigs Ann.* **1997**, 303.

(17) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457.

(18) Synthesis: Venuti, M. C.; Stephenson, R. A.; Alvarez, R.; Bruno, J. J.; Strosberg, A. M. *J. Med. Chem.* **1988**, *31*, 2136.

(19) Data for **3**: mp 138−139 °C. ^{1}H NMR ($CDCl_3$): 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). ^{13}C NMR ($CDCl_3$): 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 $C_{14}H_{12}BrNO_2$: 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.[21] 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 $PdCl_2$(dppf) (0.163 g, 0.290 mmol).[22] The mixture is heated at 60 °C for 12 h under N_2, filtered through Celite, extracted, and dried. The solid is redissolved in CH_2Cl_2 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.[23]

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_2O solution heated to 60 °C for 12 h under N_2 in the presence of K_2CO_3 (2.09 g, 15.1 mmol) and $Pd(PPh_3)_4$ (0.249 g, 0.216 mmol). After filtration, concentration of the filtrate, extraction, and drying, the residual solid is redissolved in CH_2Cl_2 and passed through a silica gel plug to afford **7** (1.44 g, 38.8%) after drying.[24] Compound **7** (0.300 g, 0.582 mmol) and I_2 (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_2O 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%).[25] 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 $PdCl_2$(dppf) (0.037 g, 0.067 mmol) in anhydrous DMF deoxygenated by purging with N_2. The solution is heated at 60 °C for 12 h under N_2 and cooled, the mixture is filtered, and the filtrate is concentrated, extracted, and dried. The residue is redissolved in CH_2Cl_2 and filtered through a silica gel plug and dried to afford **9** (0.702 g, 97.4%).[26]

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_2Cl_2 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_2CO_3 (0.226 g, 1.64 mmol), and $Pd(PPh_3)_4$ (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_2. The solution is filtered, the filtrate is concentrated, and the solid is washed with H_2O and MeOH, dissolved in 10% MeOH in CH_2Cl_2, and filtered through a short silicagel plug to afford 0.309 g (42.5%) of octamer **10** in overall 10.1% yield from **1**.[27]

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.[28] 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.[22c] 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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(21) Data for **4**: mp 99.5−101 °C. ^{1}H NMR ($CDCl_3$): 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). ^{13}C NMR ($CDCl_3$): 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 $C_{14}H_{10}BrIO_2$: 415.8909, found 415.8914.

(22) (a) Ishiyama, T.; Murata, M.; Miyaura, N. *J. Org. Chem.* **1995**, *60*, 7508. (b) Ishiyama, T.; Itoh, Y.; Kitano, T.; Miyaura, N. *Tetrahedron Lett.* **1997**, *38*, 3447. (c) Arylboronates from diboron pinacol used in one-pot cross-coupling reactions: Giroux, A.; Han, Y. X.; Prasit, P. *Tetrahedron Lett.* **1997**, *38*, 3841.

(23) Data for **6**: mp decomposed at 157.9−159 °C. ^{1}H NMR ($CDCl_3$): 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). ^{13}C NMR ($CDCl_3$): 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 $C_{20}H_{24}BNO_4$: 353.1798, found 353.1780.

(24) Data for **7**: mp decomposed at 192−195 °C. ^{1}H NMR ($CDCl_3$): 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). ^{13}C NMR ($CDCl_3$): 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 $C_{28}H_{22}BrNO_4$: 515.0732, found 515.0748.

(25) Data for **8**: mp 128−130 °C. ^{1}H NMR ($CDCl_3$): 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). ^{13}C NMR ($CDCl_3$): 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 $C_{28}H_{20}BrIO_4$: 625.9590, found 625.9587.

(26) Data for **9**: ^{1}H NMR ($CDCl_3$): 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). ^{13}C NMR ($CDCl_3$): 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 $C_{34}H_{34}BNO_6$: 563.2479, found 563.2488.

(27) Data for **10**: mp gels at 206−208 °C. ^{1}H NMR ($CDCl_3$): 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). ^{13}C NMR ($CDCl_3$): 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 $C_{68}H_{64}BrNO_9$: 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}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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