ORGANIC LETTERS

2002
Vol. 4, No. 5
745−748

Synthesis of Monodisperse Oligo-*p*-phenylenes via Rhodium-Catalyzed Alkyne Cyclotrimerization

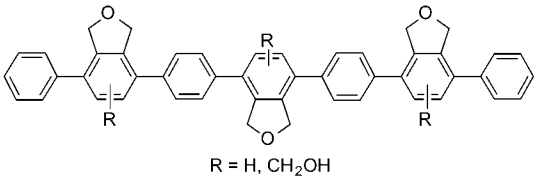
Frank E. McDonald* and Vladimir Smolentsev

Department of Chemistry, Emory University, 1515 Pierce Drive, Atlanta, Georgia 30322

fmcdona@emory.edu

Received December 8, 2001

ABSTRACT



A novel synthesis of monodisperse oligo-*p*-phenylenes is described that features alkyne cyclotrimerization of ether-linked *p*-dialkynylarenes. This route introduces solubilizing dihydrofuran and alcohol functional groups that may improve processing of the corresponding polymeric *p*-phenylene materials.

Poly-*p*-phenylenes (PPPs) have been extensively studied as organic conducting and light-emitting polymers.[1] The potential for the parent PPP, poly-*p*-benzene, to serve in this regard has been hampered by the insolubility of this PPP, which prevents practical processing of the conducting material into thin films or fibers. To this end, substituted PPPs have been synthesized that bear solubilizing substituents, including alkyl substituents,[2] acyclic ethers,[3] and carboxylic acid[4] and ester[5] functional groups.

We sought to develop a novel synthesis of substituted oligo-*p*-phenylenes that would permit the introduction of solubilizing functional groups as well as the preparation of polyphenylenes of low monodispersity[6] (precise length and constitution). Our approach would specifically involve a sequence of carbon−carbon bond coupling[7] between α,ω-diynes and para-substituted aryl electrophiles, followed by alkyne cyclotrimerization[8] methodology to construct some or all of the benzenoid rings.

The reaction conditions for cyclotrimerization were developed with a model system based on 1,7-diphenyl-4-oxa-1,6-heptadiyne (**1**).[9] Of several catalyst systems evaluated for cyclotrimerization of this diyne, the Wilkinson catalyst [$(Ph_3P)_3RhCl$] method pioneered by Müller[10] and Grigg[11] and subsequently explored by others[12] was the catalyst of choice

(1) Reviews: (a) Kovacic, P.; Jones, M. B. *Chem. Rev.* **1987**, *87*, 357. (b) Gin, D. L.; Conticello, V. P. *Trends Polym. Sci.* **1996**, *4*, 217. (c) Kraft, A.; Grimsdale, A. C.; Holmes, A. B. *Angew. Chem., Int. Ed.* **1998**, *37*, 102. (d) Scherf, U. *Top. Curr. Chem.* **1999**, *201*, 163. (e) Berresheim, A. T.; Müller, M.; Müllen, K. *Chem. Rev.* **1999**, *99*, 1747.

(2) Rehahn, M.; Schlüter, A.-D.; Wegner, G.; Feast, W. J. *Polymer* **1989**, *30*, 1054, 1060.

(3) Robert, F.; Winum, J.-Y.; Sakai, N.; Gerard, D.; Matile, S. *Org. Lett.* **2000**, *2*, 37.

(4) Wallow, T. I.; Novak, B. M. *J. Am. Chem. Soc.* **1991**, *113*, 7411.

(5) (a) Chaturvedi, V.; Tanaka, S.; Kaeriyama, K. *Macromolecules* **1993**, *26*, 2607. (b) Read, M. W.; Escobedo, J. O.; Willis, D. M.; Beck, P. A.; Strongin, R. M. *Org. Lett.* **2000**, *2*, 3201.

(6) Tour, J. M. *Chem. Rev.* **1996**, *96*, 537.

(7) (a) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, 4467. (b) Zhang, J.; Pesak, D. J.; Ludwick, J. L.; Moore, J. S. *J. Am. Chem. Soc.* **1994**, *116*, 4227. (c) Schumm, J. S.; Pearson, D. L.; Tour, J. M. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1360.

(8) Reviews: (a) Saito, S.; Yamamoto, Y. *Chem. Rev.* **2000**, *100*, 2901. (b) Vollhardt, K. P. C. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 539.

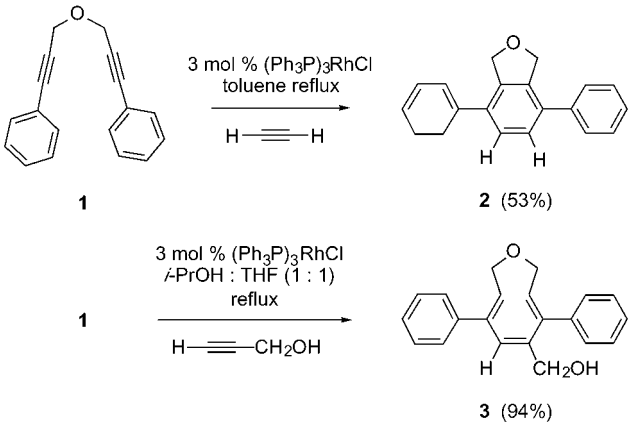
(9) Iwai, I.; Ide, J. *Chem. Pharm. Bull.* **1964**, *12*, 1094.

(10) Müller, E. *Synthesis* **1974**, 761.

(11) (a) Grigg, R.; Scott, R.; Stevenson, P. J. *Tetrahedron Lett.* **1982**, *23*, 2691. (b) Grigg, R.; Scott, R.; Stevenson, P. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1357. (c) Grigg, R.; Sridharan, V.; Wang, J.; Xu, J. *Tetrahedron* **2000**, *56*, 8967.

10.1021/ol0171970 CCC: $22.00
Published on Web 02/08/2002

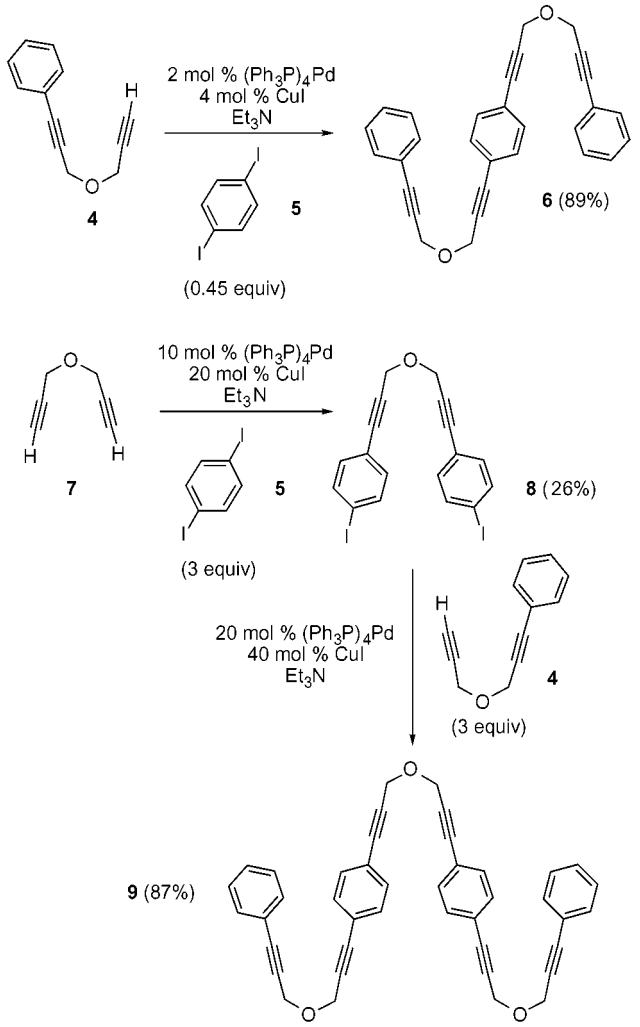
Scheme 1. Cyclotrimerizations of **1** with Acetylene and Propargyl Alcohol



in reactions with simple alkynes, affording the triphenylene products **2**[13,14] and **3**[15] from acetylene and propargyl alcohol, respectively (Scheme 1). Optimal yields of the cyclotrimerization product **2** from acetylene were obtained in refluxing toluene, whereas the ideal solvent system for the synthesis of **3** from propargyl alcohol was found to be a mixture of 2-propanol and tetrahydrofuran.

Construction of a tetrayne precursor to a pentaphenylene was accomplished by Sonogashira coupling[6] of 1-phenyl-4-oxa-1,6-heptadiyne (**4**)[16] with 0.45 equiv of *p*-diiodobenzene (**5**) to give the triphenyl-tetrayne **6** (Scheme 2).[17] Sequential Sonogashira couplings of 4-oxa-1,6-heptadiyne (**7**) with 3 equiv of *p*-diiodobenzene **5** provided the diiodide **8**, which upon coupling with 3 equiv of 1-phenyl-4-oxa-1,6-heptadiyne (**4**) afforded a short route to the tetraphenyl-hexayne substrate

Scheme 2. Sonogashira Coupling Syntheses of Tetrayne **6** and Hexayne **9**



9.[18] The polyalkyne substrates **6** and **9** did not exhibit any unusual solubility problems and were purified by silica gel chromatography using hexane/ethyl acetate eluent mixtures.

Cyclotrimerization of the tetrayne **6** with acetylene provided the penta-*p*-phenylene **10**[19] bearing two dihydrofuran substituents, for which a pure sample was obtained by crystallization from tetrahydrofuran (Scheme 3). The corresponding cyclotrimerization reaction of **6** with propargyl alcohol afforded the more soluble penta-*p*-phenylene **11**[20] as an inseparable mixture of all three possible regioisomers.

(12) (a) Magnus, P.; Witty, D.; Stamford, A. *Tetrahedron Lett.* **1993**, *34*, 23. (b) McDonald, F. E.; Zhu, H. Y. H.; Holmquist, C. R. *J. Am. Chem. Soc.* **1995**, *117*, 6605. (c) Witulski, B.; Stengel, T. *Angew. Chem., Int. Ed.* **1999**, *38*, 2426. (d) Kotha, S.; Mohanraja, K.; Durani, S. *Chem. Commun.* **2000**, 1909.

(13) Compound **2** was previously prepared by *stoichiometric* reaction of diyne **1** with $ClRh(PPh_3)_3$ followed by reaction with acetylene: Scheller, A.; Winter, W.; Müller, E. *Liebigs Ann. Chem.* **1976**, 1448.

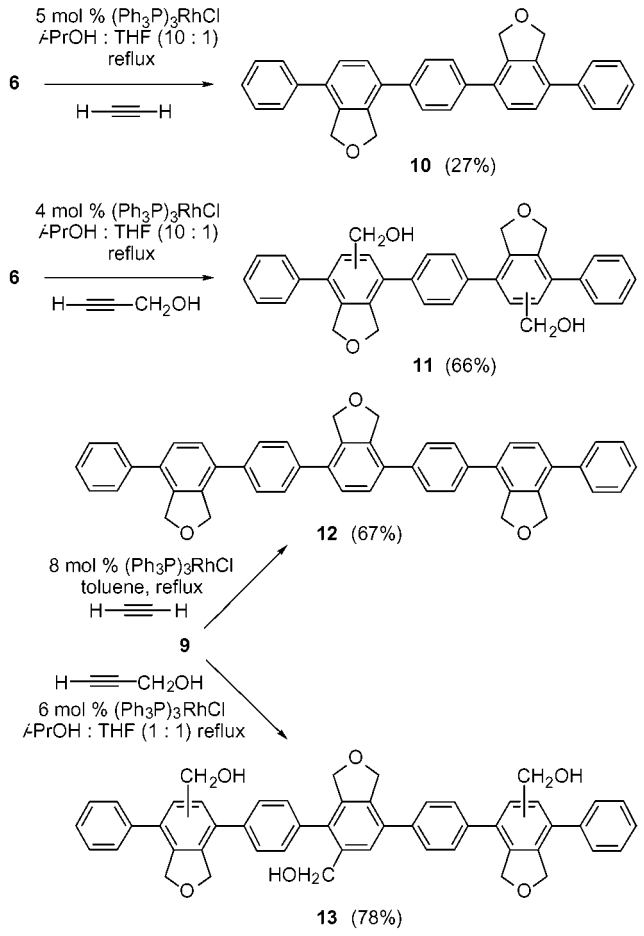
(14) Procedure for **2**: Diyne (**1**) (150 mg, 0.60 mmol), $ClRh(PPh_3)_3$ (16 mg, 17 μmol), and anhydrous toluene (10 mL) were added to an oven-dried 25 mL Schlenk flask equipped with a spin bar, reflux condenser, and acetylene inlet. The reaction mixture was sparged with acetylene, heated to reflux, and incubated in an atmosphere of acetylene at reflux for 22 h. Upon completion of the reaction, the reaction mixture was filtered through a short pad of silica gel, eluting with boiling benzene. The solution was concentrated by rotary evaporation. The solid residue was placed onto a fine mesh glass filter and washed several times with hexanes. The remaining solid was collected and dried in vacuo to yield compound **2** (87.5 mg, 53% yield): IR not active; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52−7.36 (m, 12H), 5.27 (s, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.1, 138.1, 135.2, 128.9, 128.4, 128.1, 127.8, 73.9; HRMS (EI$^+$) calcd for $C_{20}H_{16}O$ 272.1201, found 272.1207.

(15) Procedure for **3**: Diyne (**1**) (200 mg, 0.81 mmol), $ClRh(PPh_3)_3$ (12 mg, 13 μmol), distilled propargyl alcohol (300 μL, 5 mmol), anhydrous 2-propanol (5 mL), and THF (5 mL) were placed into a 25 mL Schlenk flask equipped with a spin bar and reflux condenser. The reaction mixture was heated to reflux for 14 h. Upon completion of the reaction, the reaction mixture was filtered through a short pad of silica gel, eluting with THF. The solution was concentrated by rotary evaporation, and the residue was further purified by silica gel chromatography (4:1 eluent hexane/THF) to afford compound **3** (230 mg, 94% yield): IR 3324, 2952, 2861, 1602, 1470, 1398, 1367, 1191, 1058 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49−7.30 (m, 11H), 5.28 (t, 2H), 4.94 (d, 2H), 4.59 (d, 2H); HRMS calcd for $C_{21}H_{18}O_2$ 302.1307, found 302.1294 (−4.3 ppm).

(16) Xiong, Y.; Xia, H.; Moore, H. W. *J. Org. Chem.* **1995**, *60*, 6460.

(17) Procedure for **6**: Diyne (**4**) (374 mg, 2.2 mmol), 1,4-diiodobenzene **5** (330 mg, 1.0 mmol), $(Ph_3P)_4Pd$ (40 mg, 40 μmol), CuI (16 mg, 80 μmol), and Et_3N (5 mL) were placed into a 10 mL flask and stirred at room temperature for 8 h. The reaction mixture was then filtered through a medium frit glass filter eluting with diethyl ether, concentrated by rotary evaporation, and dried in vacuo. Purification by column chromatography (hexanes/ethyl acetate, gradient from 16:1 to 8:1) afforded pure product **6** as a red-brown solid (395.5 mg, 89% yield): IR 3124, 2883, 2856, 1504, 1490, 1402, 1346, 1068 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52−7.48 (m, 4H), 7.43 (s, 4H), 7.35−7.33 (m, 6H), 4.58 (d, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 131.9, 131.8, 128.7, 128.4 (2 signals), 122.7, 122.5, 87.0, 86.5, 86.4, 84.4, 57.6, 57.5; MS (FAB + Li$^+$) 422 (M + Li$^+$ + H$^+$, 10), 421 (30), 397 (16), 320 (10), 314 (25), 313 (100). Anal. Calcd for $C_{30}H_{22}O_2$: C, 86.96; H, 5.31. Found: C, 86.74; H, 5.49.

Scheme 3. Cyclotrimerization Syntheses of Oligo-*p*-phenylenes **10**−**13**



This mixture was purified from other materials by silica gel chromatography and elution with hexane/THF mixtures.

The hexayne substrate **9** underwent cyclotrimerization with acetylene and propargyl alcohol to give the corresponding heptaphenylene products **12**[21] and **13**,[22] respectively. The solvent conditions for the cyclotrimerization syntheses of **12** and **13** were individually optimized for each product largely on the basis of our results with diyne substrate **1**.

The potential of the dihydrofuran-substituted oligophenylenes as conducting materials was evaluated by measuring the wavelength of the maximum absorption for

(18) Procedure for **9**: 1,4-diiodobenzene **5** (3.0 g, 9.1 mmol), $(Ph_3P)_4Pd$ (350 mg, 0.303 mmol), CuI (84 mg, 0.44 mmol), benzene (10 mL), and Et_3N (20 mL) were placed into a 100 mL flask and stirred at room temperature for 15 min. Then, a solution of 4-oxa-1,6-heptadiyne (**7**) (312 μL, 3.0 mmol) in Et_3N (10 mL) was added via a syringe pump (rate = 1.2 mL/h). Upon completion of the addition, the reaction mixture was stirred for an additional 6 h. The reaction mixture was then filtered through a medium glass filter, washing with benzene, and the filtrant was concentrated by rotary evaporation and dried in vacuo. Purification by column chromatography (16:1 hexanes/ethyl acetate) afforded pure product **8** as a yellow solid (387 mg, 26% yield): IR 3122, 2919, 2858, 2347, 1483, 1469, 1400, 1344, 1068, 1058, 815 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.67−7.64 (d, 4H), 7.19−7.16 (d, 4H), 4.52 (s, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.7, 133.4, 122.1, 94.8, 86.1, 85.9, 57.7. Diiodide **8** (387 mg, 0.77 mmol), 1-phenyl-4-oxa-1,6-heptadiyne (**4**) (396 mg, 2.33 mmol), $(Ph_3P)_4Pd$ (178 mg, 0.154 mmol), CuI (58.5 mg, 0.308 mmol), Et_3N (5 mL), and benzene (7 mL) were placed into a 25 mL flask, and the mixture was stirred for 30 h. The reaction mixture was then filtered through a medium glass filter, and the solid filtrate was washed with dichloromethane. The combined liquid filtrant fractions were concentrated by rotary evaporation and dried in vacuo to give the crude product. Purification by column chromatography (16:1 hexanes/ethyl acetate) afforded pure product **9** as a red-brown solid (396 mg, 88% yield): IR 3122, 2883, 2856, 1504, 1490, 1400, 1346, 1070 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.51−7.46 (m, 4H), 7.42 (s, 8H), 7.36−7.30 (m, 6H), 4.58−4.54 (d, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 132.0, 131.8 (2 signals), 128.7, 128.5, 122.9, 122.7, 122.6, 87.1, 86.54, 85.52, 86.4 (2 signals), 84.4, 57.7, 57.6, 57.5; MS (FAB + Li^+) 590 (M + Li^+, 4), 447 (16), 397 (15), 314 (25), 313 (100).

(19) Procedure for **10**: Tetrayne **6** (600 mg, 0.81 mmol) was dissolved in 2-propanol (30 mL) and THF (3 mL) in a 50 mL Schlenk flask equipped with a spin bar, reflux condenser, and acetylene inlet. This solution was degassed by bubbling acetylene through it for 15 min. $ClRh(PPh_3)_3$ (37 mg, 40 μmol) was added, and the reaction mixture was heated to reflux for 19 h. Upon completion of the reaction, the reaction mixture was filtered through a short pad of silica gel, eluting with hot chloroform. The solution was concentrated by rotary evaporation and dried in vacuo to provide **10** (700 mg crude weight). This product was further purified by recrystallization from hot THF (170 mg, 27% yield): IR not active; ^1H NMR (300 MHz, $CDCl_3$) δ 7.59−7.46 (m, 18H), 5.34 (s, 4H), 5.29 (s, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 129.0, 128.5, 128.4 (several overlapping C), 128.1, 73.9 (4 overlapping benzylic C); MS (FAB + Li^+) 466 (M^+, 4), 447 (16), 377 (11), 320 (11), 314 (25), 313 (100).

(20) Procedure for **11**: Tetrayne **6** (140 mg, 0.34 mmol), distilled propargyl alcohol (300 μL, 5 mmol), anhydrous 2-propanol (10 mL), and THF (1 mL) were placed into a 25 mL Schlenk flask equipped with a spin bar and reflux condenser. The reaction mixture was degassed by bubbling Ar through the solution for 15 min. Then, $ClRh(PPh_3)_3$ (13.3 mg, 14 μmol) was added, and the reaction mixture was heated to reflux for 12 h. Upon completion of the reaction, the reaction mixture was filtered through a short pad of silica gel, eluting with THF. The solution was concentrated by rotary evaporation and dried in vacuo. The residue was purified by silica gel chromatography (eluent hexane/THF, gradient from 1:1 to pure THF) to give compound **11** (118 mg, 66% yield) as an inseparable mixture of all three regioisomers: IR 3392, 2923, 2852, 1623, 1400, 1193, 1099, 1051 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.64−7.32 (m, 16H), 5.34 (s, 2H), 5.30 (s, 2H), 5.01 (s, 2H), 4.96 (s, 2H), 4.65 (s, 2H), 4.61 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 129.3, 129.1, 129.0, 128.9, 128.8, 128.4, 128.3, 128.2, 128.1, 127.9, 74.14, 74.13, 73.7, 62.9; HRMS (FAB + Li^+) calcd for $C_{36}H_{30}O_4Li$ 533.2304, found 533.2314 (+1.9 ppm).

(21) Procedure for **12**: Hexayne **9** (150 mg, 0.258 mmol), $ClRh(PPh_3)_3$ (19 mg, 21 μmol), and anhydrous toluene (20 mL) were added to an oven-dried 50 mL Schlenk flask equipped with a spin bar, reflux condenser, and acetylene inlet. The reaction mixture was sparged with acetylene for 15 min, heated to reflux, and incubated in an atmosphere of acetylene at reflux for 22 h. Upon completion of the reaction, the reaction mixture was filtered through a short pad of silica gel, eluting with chloroform. The solution was concentrated by rotary evaporation and dried in vacuo. The solid residue was placed onto a fine mesh glass filter and washed sequentially with water (25 mL), aqueous 10% $NaHCO_3$ (25 mL), water (25 mL), 1 M HCl (25 mL), water (25 mL), and acetone (30 mL). The remaining solid was collected and dried in vacuo to yield compound **12** (114 mg, 67% yield): IR not active; ^1H NMR (400 MHz, $CDCl_3$) δ 7.59−7.46 (m, 24H), 5.36 (s, 4H), 5.34 (s, 4H), 5.29 (s, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 135.5, 132.3, 132.2, 129.0, 128.4 (several overlapping C), 128.1, 73.9 (1 apparent peak for all benzylic C); MS (FAB + Li^+) 670 (M + Li^+ + $3H^+$, 4), 563 (3), 368 (19), 286 (21), 285 (100). Product **12** retained water even after drying in vacuo as indicated by ^1H NMR and elemental analysis, which was consistent with the formula $C_{48}H_{36}O_3 \cdot 2H_2O$. Calcd: C, 82.73; H, 5.79. Found C, 82.47; H, 5.28. This compound was also analyzed for Cl (found trace, <0.5%) and N (found 0.0%), indicating that no significant contamination from Wilkinson's catalyst was present.

(22) Procedure for **13**: Hexayne **9** (150 mg, 0.258 mmol), distilled propargyl alcohol (300 μL, 5 mmol), anhydrous 2-propanol (5 mL), and THF (5 mL) were placed into a 25 mL Schlenk flask equipped with a spin bar and reflux condenser. The reaction mixture was degassed by bubbling Ar through the solution for 15 min. Then, $ClRh(PPh_3)_3$ (15.3 mg, 17 μmol) was added, and the reaction mixture was heated to reflux for 24 h. At this stage, 11.6 mg of additional $ClRh(PPh_3)_3$ was added, and the reaction was refluxed for additional 20 h. Upon completion of the reaction, the reaction mixture was filtered through a short pad of silica gel, eluting with boiling THF. The solution was concentrated by rotary evaporation and dried in vacuo. The product was purified by silica gel chromatography (eluent hexane/THF, gradient from 1:1 to pure THF) to afford compound **13** (150 mg, 78% yield): IR 3395, 3324, 2925, 2857, 1430, 1194 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.69−7.31 (m, 21H), 5.35 (br s, 4H), 5.30 (s, 2H), 5.02 (br s, 4H), 4.96 (s, 2H), 4.67 (br d, 4H), 4.61 (s, 2H); MS (FAB + Li^+) 757 (M + Li^+, 2), 581 (3), 466 (4), 447 (16), 314 (25), 313 (100). Product **13** retained water even after drying in vacuo as indicated by ^1H NMR and elemental analysis, which was consistent with the formula $C_{51}H_{42}O_6 \cdot 9H_2O$. Calcd: C, 67.09; H, 6.62. Found: C, 66.76; H, 6.58.

comparison with that of the parent polybenzene ($\lambda_{max} = 336$ nm). The trend for increasing wavelength with λ_{max} of the dihydrofuranyl-oligophenylenes **2**, **10**, and **12** obtained from cyclotrimerization with acetylene is promising. However, the more highly substituted oligophenylenes **3**, **11**, and **13** show little increase in λ_{max} with increasing polyarene chain length, suggesting that there is little or no conjugation between aromatic rings in these pentasubstituted arenes (Table 1).

Table 1. λ_{max} for Oligophenylenes

	no. of aromatic rings		
	3	5	7
oligophenylenes **2**, **10**, **12**	274 nm	305 nm	306 nm
hydroxymethyl **3**, **11**, **13**	274 nm	278 nm	284 nm

In summary, these studies demonstrate that rhodium-catalyzed alkyne cyclotrimerization is effective for substrates bearing multiple 1,6-diyne moieties, providing a novel synthetic route to dihydrofuran-substituted oligophenylenes.

Acknowledgment. Unrestricted seed funding for research programs in our laboratory is provided from Novartis Pharmaceuticals (Grant Program for the Support of Academic Research in Synthetic Organic Chemistry). We gratefully acknowledge the use of shared instrumentation (NMR spectroscopy, mass spectrometry) provided by grants from the National Institutes of Health, National Science Foundation, and the Georgia Research Alliance. We also thank Prof. Vincent Conticello for a critical reading of the manuscript and Ms. Svetlana Burova for her assistance in obtaining ^{13}C NMR spectra for several compounds.

Supporting Information Available: Experimental procedures for substrate preparation and alkyne cyclotrimerization, compound characterization for compounds **2**−**3**, **6**, **8**−**13**. This material is available free of charge via the Internet at http://pubs.acs.org.

OL0171970