

Solid-Phase Synthesis of Phenylacetylene Oligomers Utilizing a Novel 3-Propyl-3-(benzyl-supported) Triazene Linkage

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Sequence-specific phenylacetylene oligomers consisting of functionalized monomers (hexyl benzoate, hexyl phenyl ether, benzonitrile, and *tert*-butylphenyl) are synthesized in gram quantities using solid-phase methods. Growing oligomers are attached to a divinylbenzene cross-linked polystyrene support by the 1-aryl-3-propyl-3-(benzyl-supported) triazene moiety. This linkage is obtained by reaction of arenediazonium tetrafluoroborate salts with a *n*-propylamino-modified Merrifield resin. Condensation strategies are described, producing oligomers with higher yields and simplified procedures compared to solution-phase methods. Terminal acetylene is protected with a trimethylsilyl group. After deprotection of the resin-bound terminal acetylene, an aryl iodide monomer or an aryl iodide-terminated oligomer is coupled to the supported oligomer using a palladium(0) catalyst. The cycle can be repeated to produce sequence-specific oligomers of varying length and functionality. The resulting oligomers are liberated from the polymer support by cleavage of the 1-aryl-3-propyl-3-(benzyl-supported) triazene group by reaction with iodomethane producing an aryl iodide.

Introduction

Well-defined phenylacetylene oligomers are valuable as precursors to shape-persistent macrocycles¹ and as linear chain molecules with extended conjugation.² The phenylacetylene construction has been used to produce molecules which exhibit a variety of interesting properties such as liquid crystallinity, nanoporosity, conformational bistability, and solution aggregation.^{3–6} The phenylacetylene construction is unique in that it allows for the production of monodisperse site-specifically functionalized oligomers comprised of an all carbon backbone. We have reported solution-based synthetic routes to precisely defined phenylacetylene oligomers⁷ as well as communicated the solid-phase preparation of these oligomers.⁸ Here we present full details of the solid-phase method.

Solid-phase synthetic methods are utilized extensively for the synthesis of oligopeptides, oligonucleotides, and recently, many small molecules.^{9–12} Solid-phase applications are widespread owing to the ease of workup, purification, and to their natural incorporation into repetitive coupling schemes. Solid-phase methodologies

have been utilized in combinatorial and automated strategies involving the simultaneous preparation of as many as 10⁶ different peptides.^{13,14} When the combinatorial approach is combined with an effective screening protocol, a wide variety of substrates can be tested for a desired property or activity. Because this approach has yielded rich rewards in the biomolecular field, it is reasonable to expect analogous benefits when it is applied to the study of more broadly defined supramolecular interactions. To this end, we describe solid-phase methodology for the preparation of phenylacetylene oligomers.

In this article we present full details and describe further developments in the solid-phase synthesis of phenylacetylene oligomers including a novel 3-propyl-3-(benzyl-supported) triazene linkage. We report the preparation and characterization of the polymeric support, methods for attaching substrates, repetitive methods involved in oligomeric growth, liberation of the oligomer from the support to produce aryl iodide terminated oligomers, and a nondestructive IR method for tracking oligomer synthesis. Finally, we compare and contrast the yields and purities of oligomers obtained by this solid-phase method with oligomers produced by solution methods.

Results and Discussion

The synthesis of oligomers utilizes a polymer-bound terminal acetylene that is masked with a trimethylsilyl group. After removal of the trimethylsilyl protecting group, an aryl iodide is coupled to the polymer-supported terminal acetylene using a palladium(0) catalyst. This cycle is repeated producing oligomers of varying length and functionality. The resulting oligomer is liberated from the polymer support by cleavage of the 1-aryl-3-propyl-3-(benzyl-supported) triazene group by reaction with iodomethane to produce an oligomer terminated at one end by an aryl iodide and at the other end by

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(1) Zhang, J.; Pesak, D. J.; Ludwick, J. L.; Moore, J. S. *J. Am. Chem. Soc.* **1994**, *116*, 4227–4239.

(2) Tour, J. M. *Chem. Rev.* **1996**, *96*, 537–553.

(3) Venkataraman, D.; Lee, S.; Zhang, J.; Moore, J. S. *Nature* **1994**, *371*, 591–593.

(4) Bedard, T. C.; Moore, J. S. *J. Am. Chem. Soc.* **1995**, *117*, 10662–10671.

(5) Shetty, A. S.; Zhang, J.; Moore, J. S. *J. Am. Chem. Soc.* **1996**, *118*, 1019–1027.

(6) Zhang, J.; Moore, J. S. *J. Am. Chem. Soc.* **1994**, *116*, 2655–2656.

(7) Zhang, J.; Moore, J. S.; Xu, Z.; Aguirre, R. A. *J. Am. Chem. Soc.* **1992**, *114*, 2273–2274.

(8) Young, J. K.; Nelson, J. C.; Moore, J. S. *J. Am. Chem. Soc.* **1994**, *116*, 10841–10842.

(9) Hermkens, P. H. H.; Ottenheijm, H. C. J.; Rees, D. *Tetrahedron* **1996**, *52*, 4527–4554.

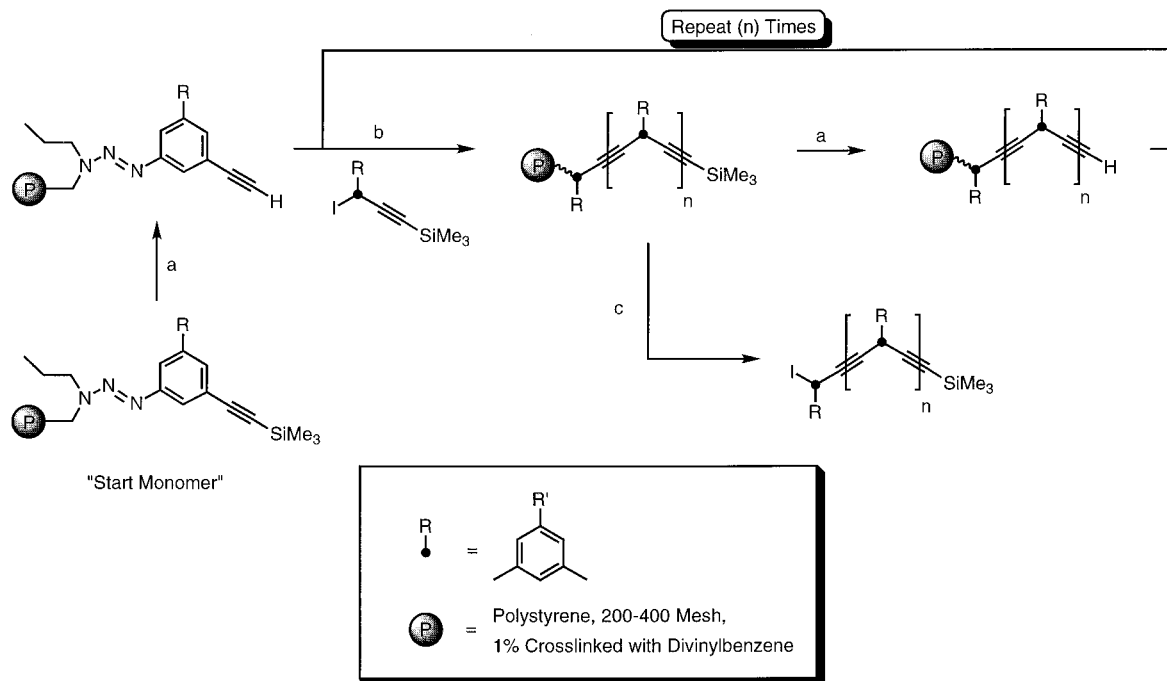
(10) Früchtel, J. S.; Jung, G. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 17–42.

(11) Lloyd-Williams, P.; Albericio, F.; Giralt, E. *Tetrahedron* **1993**, *49*, 11065–11133.

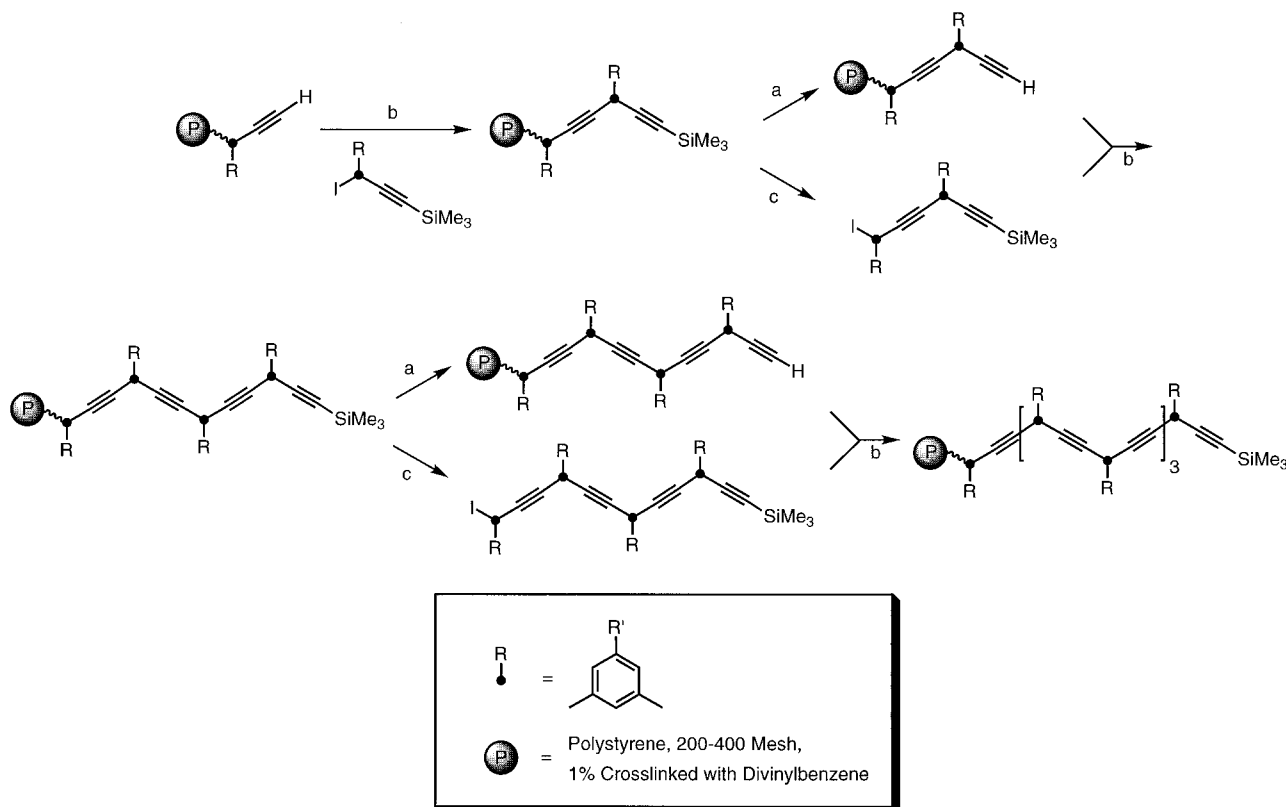
(12) Merrifield, R. B. *J. Am. Chem. Soc.* **1963**, *85*, 2149–2154.

(13) Terrett, N. K.; Gardner, M.; Gordon, D. W.; Kobylecki, R. J.; Steele, J. *Tetrahedron* **1995**, *51*, 8135–8173.

(14) Thompson, L. A.; Ellman, J. A. *Chem. Rev.* **1996**, *96*, 555–600.

Scheme 1. A Stepwise Addition Approach to Oligomeric Chain Growth^a

^a Reagents: (a) tetrabutylammonium fluoride, THF, rt, 5 min; (b) Pd₂(dba)₃, CuI, PPh₃, triethylamine, 65 °C, 12 h; (c) MeI, 110 °C, 6–48 h.

Scheme 2. Fragment Addition Approach^a

^a Reagents: (a) tetrabutylammonium fluoride, THF, rt, 5 min; (b) Pd₂(dba)₃, CuI, PPh₃, triethylamine, 65 °C, 12 h; (c) MeI, 110 °C, 6–48 h.

(trimethylsilyl)acetylene. Overviews of the repetitive chemistry used for oligomer synthesis are shown in Schemes 1 and 2. As shown in Scheme 1, the polymer-supported trimethylsilyl monomer is deprotected and then coupled with monomer to produce a trimethylsilyl dimer. By repeating trimethylsilyl deprotection and

monomer coupling, oligomers are prepared in a sequential fashion. This stepwise addition of monomers is useful in the preparation of small nonrepeating oligomers. Alternatively, a fragment condensation strategy may be useful for the preparation of large repeating oligomers (Scheme 2). Fragment condensation strategies

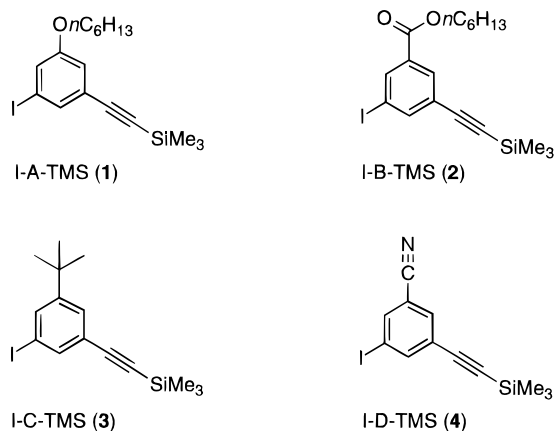


Figure 1. Functionalized monomers.

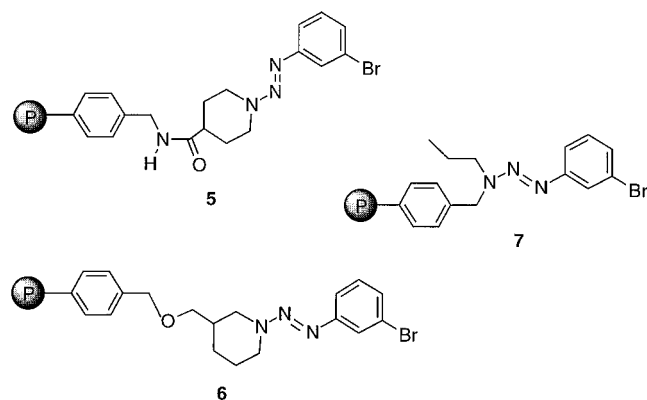


Figure 2. Chemical structures of triazene tethers. **5:** peptide linkage of acid triazene. **6:** ether linkage of alcohol triazene. **7:** direct triazene linkage of benzenediazonium tetrafluoroborate.

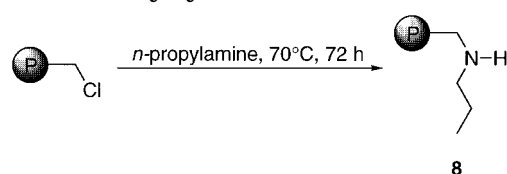
enhance the overall yield and purity of an oligomer by reducing the number of coupling and deprotection steps required during the synthesis, relative to the sequential strategy.

The difunctional monomers are based on aryl iodides and terminal acetylenes protected as their corresponding trimethylsilyl derivatives and aryl iodides. The monomers used in this investigation are summarized in Figure 1 and abbreviated hexyl phenyl ether (A), hexyl benzoate (B), *tert*-butylphenyl (C), benzonitrile (D), aryl bromide (Br), aryl iodide (I), and (trimethylsilyl)acetylene (TMS). All four monomers are readily synthesized from commercially available materials as described in the supporting information.

Linkage. Three separate linkages to the polymer support are shown in Figure 2. Peptide coupling of a triazene derivative of nipecotic acid to *p*-aminomethyl polystyrene:1% divinylbenzene copolymer beads gives **5**. Etherification of a triazene derivative of 3-piperidinemethanol to chloromethyl polystyrene:1% divinylbenzene copolymer beads gives **6**. Direct triazene link to propylaminomethyl polystyrene:1% divinylbenzene copolymer beads gives **7**.⁸ Linkage **7** is preferred as it allows for facile infrared monitoring at every reaction step, can easily be adapted to base sensitive functionality, and eliminates the need to synthesize the triazene derivatives required for the other two linking strategies.

Propylaminomethyl polystyrene:1% divinylbenzene copolymer beads (resin, **8**) are prepared by heating a suspension of chloromethylated polystyrene resin with

Scheme 3. Conversion of Chloromethylated Polystyrene to Resin (**8**)



neat *n*-propylamine in a sealed vessel under nitrogen at 70 °C for 3 days (Scheme 3). The resulting resin is washed according to a literature procedure to remove noncovalently bound material.¹⁵ Characterization of the resin includes gel-phase ¹³C NMR, IR, elemental analysis (C, H, N, and Cl), and swelling ratios. A comparison of the ¹³C NMR spectra of the chloromethyl polymer and resin **8** indicate complete substitution of the benzyl chloride for the benzylpropylamino group. Elemental analyses data show a chlorine null and approximately 1% nitrogen incorporation, consistent with the expected value based on the chloride loading of the unmodified support. Swelling ratios in dichloromethane of the starting polymer and resin **8** are identical, indicating that no significant cross-linking occurs during the propylamination.¹⁶

Determination of the degree of substitution σ_o (mequiv/g of resin) of the resin is accomplished by two methods: (1) elemental analysis (eq 1), where A is the percent of chlorine or nitrogen obtained from combustion analysis and M_A is atomic weight of chlorine or nitrogen, (2) recording the weight change of resin after a particular reaction (eq 2), where W is weight of resin in grams and ΔM is change in molecular weight for the added fragment. Method 1 is utilized to determine the substitution of resin **8**. This method is only accurate to within ca. 20% due to the small percentage of chlorine or nitrogen measured (Cl, 2.5%, and N, 1%), as a result the substitution of resin **8** varies from 0.5 mequiv/g to 0.7 mequiv/g of nitrogen using method 1. Method 2 is used to determine the substitution of resin-bound aryl bromide monomers. Method 2 is accurate to within 1%, because weight increases of up to 15% are associated with the linkage reaction. All subsequent substitutions (σ) are calculated based on σ_o (obtained from method 2 for resin-bound aryl bromide monomers) using eq 3. Constants are added in order to obtain the units of mequiv/g of support.

$$\sigma_o = 10A/M_A \quad (1)$$

$$\sigma_o = 1000\Delta W_{\text{conversion}}/\Delta M_{\text{conversion}} W_{\text{support}} \quad (2)$$

$$\sigma = 1000\sigma_o/(\sigma_o\Delta M_{\text{conversion}} + 1000) \quad (3)$$

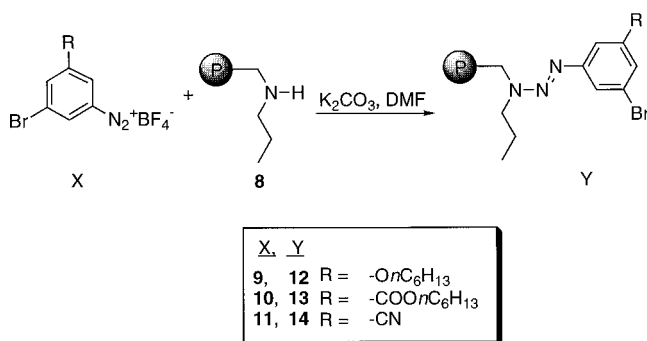
Functionalized aryl bromide monomers are linked to the resin by reaction of the corresponding benzenediazonium tetrafluoroborate salts with resin **8** suspended in DMF containing finely ground potassium carbonate at 0 °C (Scheme 4). The functionalized benzenediazonium tetrafluoroborate salts **9**, **10**, and **11** are prepared analytically pure in high yield from the corresponding anilines using the method of Doyle et al.¹⁷ The linkage

(15) Patterson, J. A. *Biochemical Aspects of Reactions on Solid Supports*; Academic Press: New York, 1971.

(16) Rich, D. H.; Gurwara, S. K. *J. Am. Chem. Soc.* **1975**, *97*, 1575–1579.

(17) Doyle, M. P.; Bryker, W. J. *J. Org. Chem.* **1979**, *44*, 1572–1574.

Scheme 4. Attachment of Benzenediazonium Salts to Resin (8)



reaction is accomplished by the portionwise addition of solid benzenediazonium to the DMF suspension. A convenient way to monitor this reaction is by indirect analysis of the supernatant DMF solution. Removal of an aliquot of this solution followed by quenching with diethylamine produces a 3,3-diethyltriazene which is analyzed by GC. Once 3,3-diethyltriazene is detected, no more benzenediazonium is added and the reaction is complete. Figure 3 shows the 3,3-diethyltriazene concentration after each addition of benzenediazonium. The end point is apparent by the jump in concentration of the triazene. This method allows for the minimization of reaction time as well as the efficient use of the benzenediazonium tetrafluoroborate. The product resin is filtered, washed with DMF to remove excess benzenediazonium, washed with water to remove excess carbonate, and then washed with methanol to collapsed the resin to an easily transferable form. IR analysis of the resin-bound aryl bromides (P = resin) P-A-Br (**12**), P-B-Br (**13**), P-D-Br (**14**) in all cases reveals a weak band at 1405 cm^{-1} which is assigned to the triazene N=N stretch.¹⁸ Resin **13** reveals a band at 1721 cm^{-1} which is assigned to the carbonyl stretch of the COOnC₆H₁₃ group, and resin **14** reveals a band at 2233 cm^{-1} which is assigned to the carbon–nitrogen stretch of the CN group.

Resin-bound aryl bromides **12–14** are coupled with (trimethylsilyl)acetylene to produce resin-bound “start-monomers” P-A-TMS (**15**), P-B-TMS (**16**), P-D-TMS (**17**) using a Pd₂(dba)₃ (2.5 mM)/PPh₃ (20 mM)/CuI (4 mM) catalyst solution in triethylamine. This catalyst solution is prepared oxygen free and heated with stirring at 70 °C for 2 h prior to use. The supernate of the resulting heterogeneous mixture (some undissolved palladium and copper iodide remains) is cannula transferred under an inert atmosphere onto the resin-bound aryl bromide followed by addition of oxygen free (trimethylsilyl)acetylene. The resulting suspension is heated in a sealed vessel in an oven at 65 °C without stirring and is agitated periodically to remix resin beads stuck to the side of the reaction vessel. A typical coupling reaction proceeds in 24–48 h at 65 °C.¹⁹ In our original report, the catalyst was prepared homogeneously in a 1:1 DMF:triethylamine solution.⁸ The problem associated with this catalyst system was its instability, resulting in palladium metal deposition and darkening of the resin. At the completion of the coupling reaction, the resin-bound monomer is filtered, washed with CH₂Cl₂ (to remove the catalyst

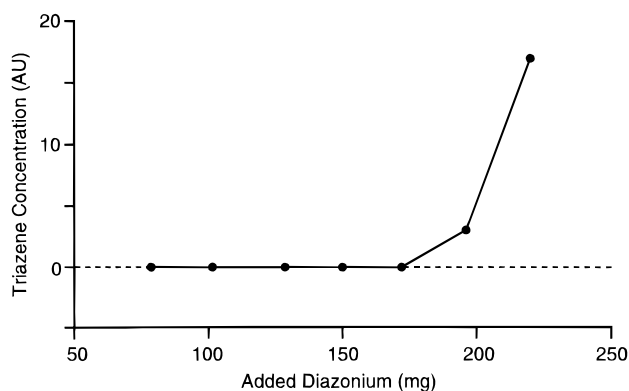


Figure 3. Portionwise addition of solid benzenediazonium salt to the DMF/resin suspension followed by removal of an aliquot of this solution and quenching with diethylamine produces a 3,3-diethyltriazene that can be analyzed by GC. When the concentration of triazene increases (ca. 200 mg addition), the reaction is complete.

components, excess (trimethylsilyl)acetylene, and triethylamine hydroiodide byproduct), washed with DMF (in preparation for the next wash), washed with a 0.05 M solution of sodium diethyl dithiocarbamate in 99/1 DMF/diisopropylethylamine (to remove any Cu(I), Cu(II) or Pd(II) trapped in the resin),²⁰ washed with DMF (to remove excess sodium diethyl dithiocarbamate from the previous wash), washed with CH₂Cl₂ (to remove DMF from previous wash), washed with methanol to collapsed the resin to an easily transferable, and dried to a constant mass in *vacuo*. The (trimethylsilyl)acetylene coupling reaction is monitored by liberating a small portion of the resin-bound monomer with iodomethane followed by GC analysis of the resulting aryl iodide.

Resin-bound monomers P-A-TMS (**15**), P-B-TMS (**16**), P-D-TMS (**17**) are deprotected by treatment of the resin-bound (trimethylsilyl)acetylene group with a solution of tetrabutylammonium fluoride in wet (5 wt % H₂O) tetrahydrofuran at room temperature. This deprotection reaction was originally accomplished by treatment of the resin with a suspension of potassium hydroxide, methanol, and tetrahydrofuran at 75 °C for 1–24 h. These initial conditions, in addition to being slow, were unsuitable for resin-bound monomers **16** and **17**, resulting in the formation of hydrolysis products. When using tetrabutylammonium fluoride, the trimethylsilyl group of **2** is removed cleanly, whereas under the potassium hydroxide conditions transesterification and hydrolysis of the hexyl benzoate of **2** occurred. When the tetrabutylammonium fluoride method is applied to the deprotection of resin-bound monomers **16** and **17**, no hydrolysis was observed as evidenced by infrared analysis of resin-bound deprotected monomers (no additional band was observed in 3200–3450 cm^{-1} region). The resin-bound terminal acetylene is filtered, washed with THF to remove excess tetrabutylammonium fluoride, washed with methanol to collapse the resin to an easily transferable form, and dried to a constant mass in *vacuo*. (Trimethylsilyl)acetylene deprotection is monitored by infrared analysis of the dried resin, as described below.

Null-to-Null Infrared Monitoring. A simple, non-destructive method was developed to monitor oligomer synthesis. Infrared analysis of the resin is accomplished by placing approximately 1 mg of the resin between two

(18) Zimmermann, F.; Lippert, T.; Beyer, C.; Stebani, J.; Nuyken, O.; Wokaun, A. *Appl. Spectrosc.* **1993**, *47*, 986–993.

(19) Alami, M.; Ferri, F.; Linstrumelle, G. *Tetrahedron Lett.* **1993**, *34*, 6403–6406.

(20) Briscoe, G. B.; Humphries, S. *Talanta* **1969**, *16*, 1403–1419.

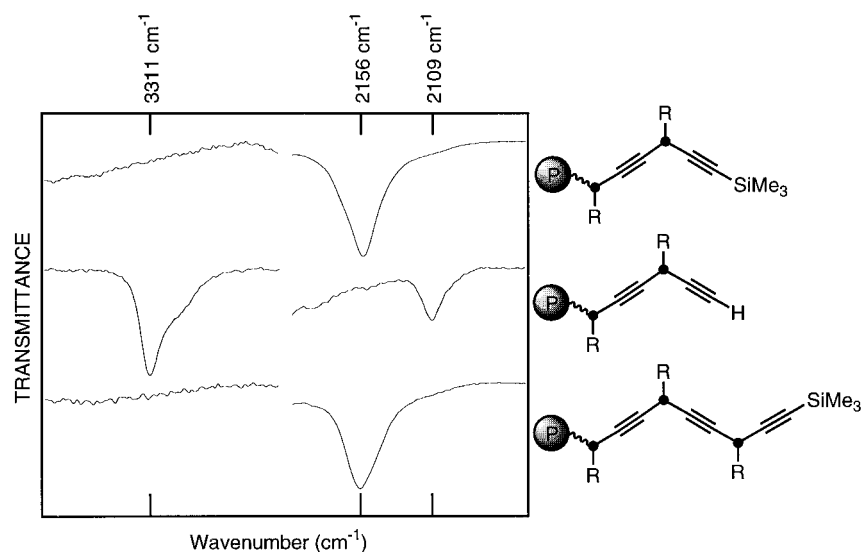


Figure 4. Infrared spectra used to monitor cross-coupling and deprotection reactions on the resin-bound oligomer. Observation of a null at 3311 cm^{-1} and 2156 cm^{-1} corresponds to complete acetylene coupling and (trimethylsilyl)acetylene deprotection, respectively.

NaCl plates, swelling the beads by adding a drop of carbon tetrachloride, and immediately recording an FTIR spectrum. Failure to swell the beads yields no useful signal. The resulting IR spectra have the characteristic polystyrene absorptions in addition to the diagnostic bands, assigned as follows, to the resin-bound functional groups: 3311 cm^{-1} (strong) terminal acetylenic carbon–hydrogen stretch; 2109 cm^{-1} (weak) terminal acetylenic carbon–carbon stretch; 2156 cm^{-1} (medium) carbon–carbon stretch of acetylene with trimethylsilyl group; 2233 cm^{-1} (medium) benzonitrile carbon–nitrogen triple bond stretch; 1721 cm^{-1} (strong) benzoate carbonyl stretch; 1405 cm^{-1} (weak) triazene (N=N) stretch.^{18,21} The trimethylsilyl deprotection step is monitored by the complete disappearance (null signal) of the 2156 cm^{-1} band and the appearance of the 3311 cm^{-1} band (Figure 4). The coupling of resin-bound terminal acetylene (described below) is monitored by the complete disappearance (null signal) of the 3311 cm^{-1} band and the appearance of the 2156 cm^{-1} band. The reliability of this “null-to-null” infrared monitoring was confirmed by removal and characterization of a trimethylsilyl deprotected product and is believed to be sensitive to a level of detection of at least 5% unreacted material. Liberation of resin-bound oligomers (described below) is monitored by the disappearance of IR bands attributed to the oligomer.

Treatment of resin-bound aryl bromide monomers **12** and **13** and resin-bound monomers **15** and **16** with iodomethane in a sealed reaction flask at $110\text{ }^{\circ}\text{C}$ for 12 h affects the liberation of monomers **18**, **19**, **1**, and **2**. As shown in Table 1 all monomers are recovered in greater than 90% yield with a greater than 90% purity. The liberated monomers are recovered from the resin by filtration and repeated washing with CH_2Cl_2 . The completeness of this reaction is assessed by infrared analysis. In all cases, small amounts (approximately 5%) of monomer remain attached to the resin. Complete removal of the monomer can be achieved by increasing the reaction time; however, products obtained after long

Table 1. Yields and Purity of Monomers

| oligomer | polymer support (mg) | isolated product (mg) | yield ^a | purity ^b |
|----------------------|----------------------|-----------------------|--------------------|---------------------|
| I-A-Br (18) | 610.4 | 85.0 | 98 | 98 |
| I-B-Br (19) | 597.2 | 83.8 | 90 | 95 |
| I-A-TMS (1) | 647.1 | 93.3 | 94 | 97 |
| I-B-TMS (2) | 651.1 | 90.3 | 98 | 94 |

^a Overall yield calculated from weight increase of initial polymer-supported aryl bromide monomer. ^b Purity assessed by GC after filtration through silica gel.

reaction times (48–72 h) are less pure. The resin obtained at the end of the reaction is dark brown in color and partially decomposed, as evidenced by examination of the spent resin under an optical microscope. Treatment of unmodified chloromethylated polystyrene with iodomethane at $110\text{ }^{\circ}\text{C}$ also results in partially decomposed polymer beads.

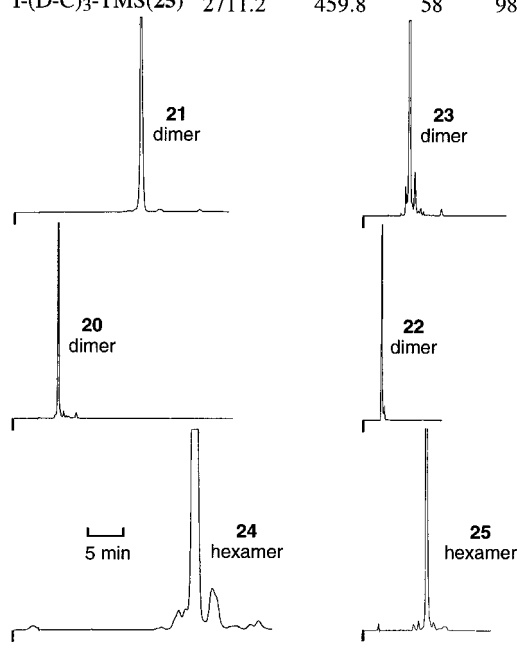
Oligomer Synthesis. Dimers I-A-B-TMS (**20**) and I-B-B-TMS (**21**) are prepared by coupling monomer **2** to resin-bound monomers **15** and **16**, respectively, followed by liberation from the support. Dimers I-A-A-TMS (**22**) and I-B-A-TMS (**23**) are prepared by coupling monomer **1** to resin-bound monomers **15** and **16**, respectively, followed by liberation from the support. The couplings are accomplished using the palladium(0) catalyst system described above. The triethylamine supernatant is added to the resin/aryl halide mixture with the aryl halide in 10% excess. The resulting suspension is heated in a sealed vessel in an oven at $65\text{ }^{\circ}\text{C}$ without stirring and is agitated periodically to remix resin beads stuck to side of the vessel. A typical coupling reaction proceeds in 12 h at $65\text{ }^{\circ}\text{C}$. The product resin is washed as above and excess monomer is recovered from the first CH_2Cl_2 wash. As shown in Table 2 all dimers are obtained in greater than 75% yield with a purity greater than 91%. All cross-coupling and (trimethylsilyl)acetylene deprotection reactions were monitored by IR analysis. As before, the resin obtained after liberation with iodomethane is dark brown, and small amounts (approximately 5%) of dimer remain resin bound.

The synthesis of the hexameric oligomer I-B-B-B-A-A-TMS (**24**) is accomplished by the stepwise addition of single monomer units (Scheme 1). Two repetitive cycles

(21) Grindley, T. B.; Johnson, K. F.; Katritzky, A. R.; Keogh, H. J.; Thirkettle, C.; Topsom, R. D. *J. Chem. Soc., Perkin Trans. 2* **1974**, 3, 282–288.

Table 2. Yields and Purity of Dimers and Hexamers

| oligomer | polymer support(mg) | isolated product(mg) | yield ^a | purity ^b |
|--|---------------------|----------------------|--------------------|---------------------|
| I-A-B-TMS(20) | 596.7 | 116.9 | 88 | 94 |
| I-B-B-TMS(21) | 674.0 | 134.4 | 75 | 96 |
| I-A-A-TMS(22) | 751.4 | 135.7 | 84 | 95 |
| I-B-A-TMS(23) | 560.6 | 110.7 | 76 | 91 |
| I-B ₃ -A ₃ -TMS(24) | 7373.0 | 1587.0 | 48 | 92 |
| I-(D-C) ₃ -TMS(25) | 2711.2 | 459.8 | 58 | 98 |

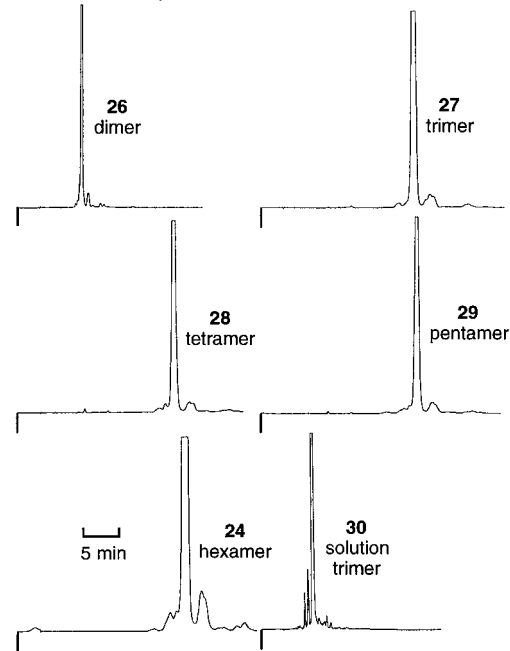


^aOverall yield calculated from weight increase of initial polymer-supported aryl bromide monomer. ^bPurity assessed by HPLC with UV detection after filtration through silica gel.

of deprotection and coupling using monomer **2** to resin-bound monomer **16** followed by three repetitive cycles of deprotection and coupling with monomer **1** and finally liberation with iodomethane gave **24** in overall yield of 48%. All stages of this 10-step sequence are monitored by IR analysis. All cross-coupling reactions were complete after 12 h at 65 °C and all (trimethylsilyl)acetylene deprotection reactions were finished within 5 min at room temperature. During the synthesis, small portions (5 mg) of the intermediate dimer, trimer, tetramer, and pentamer were liberated from the resin and analyzed by HPLC. As can be seen in Table 3, the purity of intermediate dimer **26**, trimer **27**, tetramer **28**, pentamer **29**, and hexamer **24** are all similar. This constant qualitative purity level suggests that most of the impurities arise from the liberation step rather than being a result of the repetitive couplings or (trimethylsilyl)acetylene deprotections, as this would result in a decrease in purity with each repetitive cycle. Included in Table 3 is the HPLC trace of methyl benzoate trimer **30** (R = methyl) prepared by solution-phase methods. As can be seen, the purity of trimer **30** is similar to trimer **27** which was prepared with the solid-phase method. The hexameric oligomer **24** prepared on a 2 g scale by the solid-phase method was compared with authentic sample synthesized in solution. The solid-phase method resulted in an overall yield of 48% as compared to 39% using the solution-phase method. The solid-phase method from monomer to hexamer required 11 synthetic steps taking 6 days to

Table 3. HPLC of Crude Oligomeric Products

| oligomer | solvent conditions | retention time (min) | purity ^a |
|--|--------------------|----------------------|---------------------|
| I-B-B-TMS(26) | 40/60 ^b | 9.6 | 94 |
| I-B ₃ -TMS(27) | 40/60 ^b | 21.9 | 95 |
| I-B ₃ -A-TMS(28) | 40/60 ^b | 22.8 | 91 |
| I-B ₃ -A ₂ -TMS(29) | 40/60 ^b | 22.5 | 88 |
| I-B ₃ -A ₃ -TMS(24) | 40/60 ^b | 23.7 | 92 |
| I-B ₃ -TMS(methyl, 30) ^d | 10/90 ^c | 7.5 | 95 |

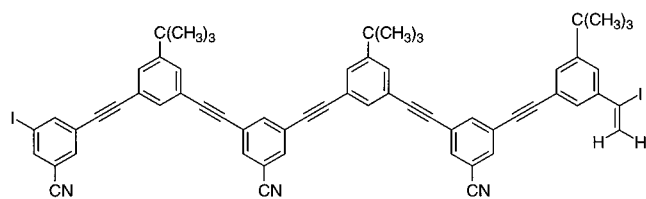


^aPurity assessed by HPLC with UV detection after filtration through silica gel. ^bDichloromethane/hexanes. ^cEthylacetate/hexanes. ^dPrepared by solution-phase methods.

complete. The solution-phase method from the monomer required 13 synthetic steps taking approximately 14 days to complete.

Hexamer I-B-B-B-A-A-TMS (**24**) prepared using the solid-phase method was cyclized to the corresponding phenylacetylene macrocycle using previously described methods.¹ The macrocycle derived from the hexamer prepared using the solid-phase method was compared to authentic macrocycle derived from a hexamer prepared by solution-phase methods. Both HPLC and ¹H NMR data were identical for both macrocycles. Thus, in the hexyl benzoate/hexyl phenyl ether system, the solid-phase method is far less laborious and is superior to the solution-phase method, giving enhanced yields and resulting in products of similar purity. In addition, this solid-phase method allows for simplified workup and purification by allowing for filtration and washing of insoluble intermediates.

The synthesis of the hexameric oligomer I-D-C-D-C-D-C-TMS (**25**) is accomplished by the repetitive process of coupling and deprotection with alternate addition of monomer **3** and monomer **4** to resin-bound monomer **17**. Liberation of **25** from the support was relatively slow due to the electron-withdrawing nature of the nitrile group on resin-bound monomer **17**. The purity of hexamer **25** was found to be greatly effected by the reaction time of cleavage. If the reaction was allowed to proceed for 48 h, a product was obtained which contained 20% of a relatively polar impurity as assessed by HPLC. If the



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Figure 5. Isolated impurity **31** produced during the cleavage of oligomer **25** after 48 h reaction time.

reaction time was minimized to 8–12 h at 110 °C a product which was 98% pure resulted (Table 2). A small quantity (3 mg) of impurity **31** was isolated by preparative HPLC. Characterization by mass spectrometry and ¹H NMR indicated **31** to be a result of the (trimethylsilyl)-acetylene moiety reacting with advantageous HI produced under cleavage conditions (Figure 5). Attempts to quench HI, *in situ*, by the addition of propylene oxide or potassium carbonate resulted in slow or no reaction. This observation supports an acid-catalyzed mechanism for the decomposition of aryl triazenes in iodomethane at 110 °C.²² It is believed that the primary source of impurities come from the side reaction with HI. Hexamer **25** was also synthesized utilizing solution-phase methods, thus providing a comparison. The solid-phase method resulted in an overall yield of 58% as compared to 40% using solution-phase methods, with both methods giving products of similar purity. The solid-phase method from monomer to hexamer required 11 synthetic steps taking 6 days to complete. The solution-phase method from the monomer required 9 synthetic steps taking approximately 14 days to complete.

Conclusion

The 3-propyl-3-(benzyl-supported) triazene linkage can be used for a variety of functionalized monomers (e.g., esters, ethers, nitriles). This linkage is achieved by direct reaction of benzenediazonium salts with resin **8**. Oligomers consisting of functionalized monomers have been synthesized in gram quantities, in higher yields, and employing simplified procedures as compared to solution-phase methods. Purity levels are comparable or better than those obtained using solution-phase methods. Using tetrabutylammonium fluoride to deprotect resin-bound (trimethylsilyl)acetylene results in facile removal (5 min) of the silyl group in the presence of base sensitive functionality such as benzoate and benzonitrile. By utilizing a premade catalyst solution in triethylamine decomposition of the palladium(0) catalyst, which results in the decomposition of palladium metal on the support, can be avoided. The development of this solid-phase method is the first step toward the combinatorial synthesis of phenylacetylene oligomers and is the first report to describe direct attachment of benzenediazonium salts producing a triazene linker.

Experimental Section

General. Unless otherwise noted, all starting materials were obtained from commercial suppliers and were used without further purification. Melting points were obtained in open capillary tubes and are uncorrected. Analytical thin layer

chromatography (TLC) was performed on precoated sheets of silica gel 60, and flash column chromatography was carried out with silica gel 60 (230–400 mesh). Dry triethylamine was obtained by vacuum transfer from calcium hydride. Dry tetrahydrofuran (THF) was obtained by vacuum transfer from sodium and benzophenone. The ¹H, ¹³C, and gel-phase ¹³C NMR spectra were recorded at 400 and 100 MHz. Gel-phase ¹³C NMR samples were prepared by swelling the polymer support in CDCl₃ and removing excess solvent by evaporation. Chemical shifts are expressed in parts per million (δ) using residual solvent protons as internal standard. Low and high resolution electron impact mass spectra were obtained operating at 70 eV. Low and high resolution fast atom bombardment (FAB) mass spectra were obtained on VG ZAB-SE and VG 70-SE-4F spectrometers. Gas-liquid chromatography (GC) was performed with a 12.5 m x 0.2 mm x 0.5 μm HP-1 methyl silicone column, with helium carrier gas, and a flame ionization detector. Elemental analyses were performed by the University of Illinois Micro Analytical Service Laboratory. Infrared spectra were recorded on an Mattson, galaxy series FTIR 5000 Spectrometer; absorptions are reported in cm⁻¹. Infrared analysis of the polymer support was accomplished by placing approximately 1 mg of the support between two NaCl plates, swelling the beads by adding a drop of carbon tetrachloride and immediately recording an FTIR spectrum. HPLC analysis was accomplished using a UV absorbance detector and a silica column (4.6 mm x 25 cm). Swelling ratios were measured by using an optical microscope fitted with a camera and video recorder. The beads were repeatedly swollen and shrunk to obtain a statistical average of change in bead diameter. 3-*tert*-Butyl-5-(2-(trimethylsilyl)ethynyl)iodobenzene (**3**) was prepared following the reported procedure.¹

Propylaminomethylated Polystyrene (0.7 mequiv/g of nitrogen, 1% crosslinked with divinylbenzene, 200–400 mesh) (8). A suspension of chloromethyl polystyrene:1% divinylbenzene copolymer beads (20.0 g, 0.700 mequiv/g of chlorine, 200–400 mesh) and *n*-propylamine (100 mL, 1.22 mol) were degassed and heated at 70 °C for 3 days in a sealed tube and agitated periodically. The polymer was transferred to a coarse sintered glass filter using CH₂Cl₂ and washed with CH₂Cl₂ (400 mL). The resin was thoroughly washed according to the following protocol to remove noncovalently-bound material:¹⁵ the resin was placed in a 1-L round-bottom flask and fitted with a magnetic stirrer and reflux condenser at 70 °C. The resin was stirred slowly with dioxane/2 N NaOH (1/1, v/v, 400 mL) for 30 min, and the solvent was removed by aspiration through a coarse sintered glass filter. This was repeated once more with dioxane/2 N NaOH (1/1, v/v, 400 mL), twice each with dioxane/H₂O (1/1, v/v, 400 mL), DMF (400 mL), methanol (400 mL), and finally benzene (400 mL). The resin was then rinsed with hot methanol (400 mL), hot benzene (400 mL), hot methanol (400 mL), hot CH₂Cl₂ (400 mL), and 200 mL of methanol and dried *in vacuo* to a constant mass to give 19.58 g of propylaminomethyl polystyrene:1% divinylbenzene copolymer beads (**8**) (0.689 mequiv/g of nitrogen, 200–400 mesh). Anal. Found: C, 90.44; H, 7.87; N, 0.95; Cl, 0.01. Swelling ratio using CH₂Cl₂, chloromethyl polystyrene:1% divinylbenzene copolymer beads (4.64, σ = 0.50), propylaminomethyl polystyrene:1% divinylbenzene copolymer beads (**8**) (4.25, σ = 0.13).

3-Bromo-5-(hexyloxy)benzenediazonium Tetrafluoroborate (9). To a three-neck round-bottom flask fitted with addition funnel and nitrogen inlet was added boron trifluoride etherate (8.1 mL, 66.2 mmol) which was then chilled in an ice–acetone bath (–20 °C). To the reaction flask was added dropwise over 5 min a solution of 3-bromo-5-(hexyloxy)aniline (**32**, 4.5 g, 16.5 mmol) in dry THF (67 mL). To the chilled reaction mixture was added dropwise over 30 min a solution of *tert*-butyl nitrite (6.9 mL, 57.9 mmol) in dry THF (54 mL). The chilled mixture was stirred an additional 10 min, and the cold bath was allowed to warm to 5 °C over 20 min (during which time a white solid precipitated). To the mixture was added diethyl ether (300 mL), and the mixture was chilled in an ice-bath for 15 min. The solid was collected by filtration, washed with chilled (0–5 °C) diethyl ether (20 mL), and dried *in vacuo* to give 5.62 g, (15.22 mmol, 92%) of 3-bromo-5-

(22) Moore, J. S.; Weinstein, E. J.; Wu, Z. *Tetrahedron Lett.* **1991**, 32, 2465–2466.

(hexyloxy)benzenediazonium tetrafluoroborate (**9**) as a yellow powder. Anal. Calcd for $C_{12}H_{16}N_2BBrF_4O$: C, 38.85; H, 4.35; N, 7.55. Found: C, 39.21; H, 4.53; N, 7.31.

3-Bromo-5-(hexyloxy)benzenediazonium Tetrafluoroborate (10). Using the procedure for **9**, 6.35 g (15.93 mmol, 95%) of 3-bromo-5-(hexyloxy)benzenediazonium tetrafluoroborate (**10**) was produced as a white powder from hexyl 3-bromo-5-aminobenzoate (**33**, 5.0 g, 16.7 mmol). Anal. Calcd for $C_{13}H_{16}N_2BBrO_2F_4$: C, 39.13; H, 4.04; N, 7.02. Found: C, 39.19; H, 3.90; N, 6.99.

3-Bromo-5-cyanobenzenediazonium Tetrafluoroborate (11). Using the procedure for **9**, 7.23 g (24.4 mmol, 96%) of 3-bromo-5-cyanobenzenediazonium tetrafluoroborate (**11**) was produced as a white powder from 3-bromo-5-aminobenzonitrile (**34**, 5.0 g, 25.4 mmol): 172–174 °C dec. Anal. Calcd for $C_7H_7N_3BBrF_4$: C, 28.42; H, 1.02; N, 14.20. Found: C, 28.76; H, 1.13; N, 14.12.

1-(3-Bromo-5-(hexyloxy)phenyl)-3-propyl-3-(benzyl-supported) Triazene (12). To a chilled (0 °C) suspension of propylaminomethyl polystyrene:1% divinylbenzene copolymer beads (**8**, 4.32 g, 0.522 mequiv/g of nitrogen, 200–400 mesh), finely ground potassium carbonate (590 mg, 4.5 mmol), and DMF (50 mL) was added 3-bromo-5-(hexyloxy)benzenediazonium tetrafluoroborate (**9**, 1.0 g, 2.69 mmol) in portions over 1 h. After each addition, an aliquot of the DMF supernatant was diluted in diethylamine and analyzed by GC. After diethyltriazene was detected, the additions were ceased and the suspension was transferred to a fritted filter using DMF and washed sequentially with 120 mL of the following solvents: MeOH, H₂O, MeOH, THF, MeOH, and dried *in vacuo* to a constant mass to give 4.85 g (0.389 mequiv/g, 84%) of 1-(3-bromo-5-(hexyloxy)phenyl)-3-propyl-3-(benzyl-supported) triazene (**12**) as light yellow polymer beads.

1-(3-Bromo-5-(hexyloxy)phenyl)-3-propyl-3-(benzyl-supported) Triazene (13). Using the procedure for **12**, 3-bromo-5-(hexyloxy)benzenediazonium tetrafluoroborate (**10**, 2.06 g, 5.16 mmol), potassium carbonate (1.13 g, 8.60 mmol), propylaminomethyl polystyrene:1% divinylbenzene copolymer beads (**8**, 8.30 g, 0.522 mequiv/g of nitrogen, 200–400 mesh) and DMF (60 mL) were allowed to react to produce 9.66 g (0.452 mequiv/g, 100%) of 1-(3-bromo-5-(hexyloxy)phenyl)-3-propyl-3-(benzyl-supported) triazene (**13**) as light yellow polymer beads.

1-(3-Bromo-5-cyanophenyl)-3-propyl-3-(benzyl-supported) Triazene (14). Using the procedure for **12**, 3-bromo-5-cyanobenzenediazonium tetrafluoroborate (**11**, 1.85 g, 6.26 mmol), potassium carbonate (1.37 g, 10.4 mmol), propylaminomethyl polystyrene:1% divinylbenzene copolymer beads (**8**, 10.03 g, 0.522 mequiv/g of nitrogen, 200–400 mesh), and DMF (75 mL) were allowed to react to produce 10.82 g (0.351, 73%) of 1-(3-bromo-5-cyanophenyl)-3-propyl-3-(benzyl-supported) triazene (**14**) as light yellow polymer beads.

1-(3-(Hexyloxy)-5-(2-(trimethylsilyl)ethynyl)phenyl)-3-propyl-3-(benzyl-supported) Triazene (15). To a heavy-walled flask equipped with nitrogen inlet was added 1-(3-bromo-5-(hexyloxy)phenyl)-3-propyl-3-(benzyl-supported) triazene (**12**, 3.00 g, 0.389 mequiv/g). The flask was evacuated and back-filled with dry nitrogen three times. In a separate flask a catalyst solution consisting of tris(dibenzylideneacetone)dipalladium(0) (2.5 mM), copper(I) iodide (4 mM), and triphenylphosphine (20 mM) in dry triethylamine was degassed and stirred at 70 °C for 2 h. The supernatant from this catalyst (18 mL) was transferred via cannula to the reaction flask containing the resin-bound aryl bromide. To the mixture was added dry, degassed (trimethylsilyl)acetylene (1.0 mL, 7.2 mmol). The flask was sealed and kept at 65 °C for 48 h and agitated periodically to remix polymer beads stuck on flask walls. The polymer was transferred to a fritted filter using CH₂Cl₂ and washed sequentially with 30 mL of the following solvents: CH₂Cl₂, DMF, 0.05 M solution of sodium diethyl dithiocarbamate in 99/1 DMF/diisopropylethylamine,²⁰ DMF, CH₂Cl₂, MeOH, and dried *in vacuo* to constant mass to give 2.96 g (0.386 mequiv/g) of 1-(3-(hexyloxy)-5-(2-(trimethylsilyl)ethynyl)phenyl)-3-propyl-3-(benzyl-supported) triazene (**15**) as light yellow polymer beads.

1-(3-(Hexyloxy)carbonyl)-5-(2-(trimethylsilyl)ethynyl)phenyl)-3-propyl-3-(benzyl-supported) Triazene (16). Using the procedure for **15**, 1-(3-bromo-5-(hexyloxy)carbonyl)phenyl)-3-propyl-3-(benzyl-supported) triazene (**13**, 5.45 g, 0.452 mequiv/g) and (trimethylsilyl)acetylene (1.0 mL, 7.2 mmol) were allowed to react to produce 5.24 g (0.448 mequiv/g) of 1-(3-(hexyloxy)carbonyl)-5-(2-(trimethylsilyl)ethynyl)phenyl)-3-propyl-3-(benzyl-supported) triazene (**16**) as light yellow polymer beads.

1-(3-Cyano-5-(2-(trimethylsilyl)ethynyl)phenyl)-3-propyl-3-(benzyl-supported) Triazene (17). Using the procedure for **15**, 1-(3-bromo-5-cyanophenyl)-3-propyl-3-(benzyl-supported) triazene (**14**, 9.00 g, 0.351 mequiv/g) and (trimethylsilyl)acetylene (3.0 mL, 21.6 mmol) were allowed to react to produce 8.99 g (0.349 mequiv/g) of 1-(3-cyano-5-(2-(trimethylsilyl)ethynyl)phenyl)-3-propyl-3-(benzyl-supported) triazene (**17**) as light yellow polymer beads.

3-Bromo-5-(hexyloxy)iodobenzene (18). A suspension of 1-(3-bromo-5-(hexyloxy)phenyl)-3-propyl-3-(benzyl-supported) triazene (**12**, 610.4 mg, 0.389 mequiv/g) and iodomethane (6.1 mL) was degassed and heated at 110 °C in a sealed tube for 24 h. After the iodomethane was removed *in vacuo*, the product was extracted from the resin using hot CH₂Cl₂. The resulting solution was cooled and filtered through a plug of silica gel, and the CH₂Cl₂ was removed *in vacuo* to give a brown oily residue. The residue was purified by filtration through a plug of silica gel in hexanes to give 85 mg (0.23 mmol, 98%) of 3-bromo-5-(hexyloxy)iodobenzene (**18**) as a colorless oil: *R*_f 0.53 (hexanes); MS (EI) *m/e* 384 (21), 382 (22), 300 (67), 298 (70). Anal. Calcd for $C_{12}H_{16}BrIO$: C, 37.63; H, 4.21. Found: C, 37.70; H, 4.42.

Hexyl 3-Bromo-5-iodobenzoate (19). Using the procedure for **18**, 1-(3-bromo-5-(hexyloxy)phenyl)-3-propyl-3-(benzyl-supported) triazene (**13**, 597.2 mg, 0.411 mequiv/g) and iodomethane (6.0 mL) were allowed to react to give a brown residue. The residue was purified by filtration through a plug of silica gel in hexanes to give 83.8 mg (0.22 mmol, 90%) of hexyl 3-bromo-5-iodobenzoate (**19**) as a white solid: mp 43.1–45.0 °C; *R*_f 0.34 (20:80 (v/v), dichloromethane: hexanes); MS (EI) *m/e* 412 (9), 410 (10), 328 (98), 326 (100). Anal. Calcd for $C_{13}H_{16}BrIO_2$: C, 37.98; H, 3.92. Found: C, 37.98; H, 4.11.

3-(Hexyloxy)-5-(2-(trimethylsilyl)ethynyl)iodobenzene (1). Using the procedure for **18**, 1-(3-(hexyloxy)-5-(2-(trimethylsilyl)ethynyl)phenyl)-3-propyl-3-(benzyl-supported) triazene (**15**, 11.0 g, 0.316 mequiv/g) and iodomethane (95 mL) were allowed to react to give a brown residue. The residue was purified by flash chromatography (hexanes) to give 1.31 g (3.26 mmol, 94%) of 3-(hexyloxy)-5-(2-(trimethylsilyl)ethynyl)iodobenzene (**1**) as a white solid: mp 28.3–30.1 °C; *R*_f 0.40 (hexanes); MS (EI) *m/e* 400 (58), 385 (60). Anal. Calcd for $C_{17}H_{25}IOSi$: C, 51.00; H, 6.29. Found: C, 51.22; H, 6.04.

Hexyl 3-Iodo-5-(2-(trimethylsilyl)ethynyl)benzoate (2). Using the procedure for **18**, 1-(3-(hexyloxy)phenyl)-5-(2-(trimethylsilyl)ethynyl)phenyl)-3-propyl-3-(benzyl-supported) triazene (**16**, 10.0 g, 0.300 mequiv/g) and iodomethane (90 mL) were allowed to react to give a brown residue. The residue was purified by flash chromatography (25/75, dichloromethane/hexanes) to give 1.26 g (2.90 mmol, 98%) of hexyl 3-iodo-5-(2-(trimethylsilyl)ethynyl)benzoate (**2**) as a white solid: mp 46.9–48.3 °C; *R*_f 0.28 (25:75 (v/v), dichloromethane: hexanes); MS (EI) 428 (38), 413 (100), 344 (16), 329 (20). Anal. Calcd for $C_{18}H_{25}IO_2Si$: C, 50.47; H, 5.88. Found: C, 50.74; H, 6.05.

Deprotection of Resin-Bound (Trimethylsilyl)acetylenes. To a suspension of resin-bound (trimethylsilyl)acetylene (1.0 equiv) and THF (9 mL/g of polymer) was added a solution of tetrabutylammonium fluoride (1.0 M) in wet (5 wt % H₂O) THF (2.0 equiv). The suspension was stirred periodically for 5 min. The polymer was transferred to a fritted filter using THF and washed sequentially (30 mL/g of polymer) with THF followed by MeOH and dried *in vacuo* to constant mass to give the resin-bound terminal acetylene as light yellow polymer beads.

Cross-Coupling of Resin-Bound Terminal Acetylenes with Aryl Halide Monomers. To a heavy-walled flask equipped with nitrogen inlet side arm were added resin-bound

terminal acetylene (1.0 equiv) and aryl iodide (1.1 equiv). The flask was evacuated and back-filled with dry nitrogen three times. In a separate flask a catalyst solution consisting of tris(dibenzylideneacetone)dipalladium(0) (2.5 mM), copper(I) iodide (4 mM), and triphenylphosphine (20 mM) in dry triethylamine was degassed and stirred at 70 °C for 2 h. The supernatant from this catalyst (6 mL/g of resin) was transferred via cannula to the reaction flask containing the resin-bound terminal acetylene. The flask was sealed and kept at 65 °C for 12 h and agitated periodically to remix polymer beads stuck on flask walls. The polymer was transferred to a fritted filter using CH₂Cl₂ and washed with CH₂Cl₂ (30 mL/g of resin). Excess aryl iodide can be recovered from the first CH₂Cl₂ wash. The resin was washed sequentially (30 mL/g of resin) with the following solvents: DMF, 0.05 M solution of sodium diethyl dithiocarbamate in 99/1 DMF/diisopropylethylamine, DMF, CH₂Cl₂, MeOH, and dried *in vacuo* to constant mass to give resin-bound oligomer as light yellow to brown polymer beads.

I-A-B-TMS (20). Using the above procedures, monomer **2** was coupled with deprotected monomer **15** (0.386 mequiv/g) to produce polymer-supported dimer P-A-B-TMS. Using the procedure for **18**, polymer-supported dimer P-A-B-TMS (596.7 mg, 0.355 mequiv/g) and iodomethane (5.0 mL) were allowed to react to give a brown residue. The crude residue was filtered through a plug of silica eluting with 25/75 (v/v), dichloromethane/hexanes, to give 116.9 mg (0.19 mmol, 88%) of I-A-B-TMS (**20**) as a clear oil: *R_f* 0.24 (25:75 (v/v), dichloromethane:hexanes); MS (EI) 628 (100), 613 (10). Anal. Calcd for C₃₂H₄₁IO₂Si: C, 61.14; H, 6.57. Found: C, 61.47; H, 6.47.

I-B-B-TMS (21). Using the above procedures, monomer **2** was coupled with deprotected monomer **16** (0.448 mequiv/g) to produce polymer-supported dimer P-B-B-TMS. Using the procedure for **18**, polymer-supported dimer P-B-B-TMS (674.0 mg, 0.407 mequiv/g) and iodomethane (5.0 mL) were allowed to react to give a brown residue. The crude residue was filtered through a plug of silica eluting with 40/60 (v/v), dichloromethane/hexanes, to give 134.4 mg (0.20 mmol, 75%) of I-B-B-TMS (**21**) as a white solid: mp 51.2–53.3 °C; *R_f* 0.42 (40:60 (v/v), dichloromethane:hexanes); MS (EI) *m/e* 659 (3), 658 (13), 657 (43), 656 (100), 572 (12). Anal. Calcd for C₃₃H₄₁IO₂Si: C, 60.36; H, 6.29. Found: C, 60.43; H, 6.47.

I-A-A-TMS (22). Using the above procedures, monomer **1** was coupled with deprotected monomer **15** (0.386 mequiv/g) to produce polymer-supported dimer P-A-A-TMS. Using the procedure for **18**, polymer-supported dimer P-A-A-TMS (751.4 mg, 0.359 mequiv/g) and iodomethane (5.0 mL) were allowed to react to give a brown residue. The crude residue was filtered through a plug of silica eluting with 10/90 (v/v), dichloromethane/hexanes, to give 135.7 mg (0.23 mmol, 84%) of I-A-A-TMS (**22**) as a white solid: mp 39.3–40.8 °C; *R_f* 0.24 (10:90 (v/v), dichloromethane:hexanes); MS (EI) *m/e* 603 (1), 602 (6), 601 (22), 600 (55), 585 (5). Anal. Calcd for C₃₁H₄₁IO₂Si: C, 61.99; H, 6.88. Found: C, 61.78; H, 6.86.

I-B-A-TMS (23). Using the above procedures, monomer **1** was coupled with deprotected monomer **16** (0.448 mequiv/g) to produce polymer-supported dimer P-B-A-TMS. Using the procedure for **18**, polymer-supported dimer P-B-A-TMS (560.6 mg, 0.412 mequiv/g) and iodomethane (5.0 mL) were allowed to react to give a brown residue. The crude residue was filtered through a plug of silica eluting with 25/75 (v/v), dichloromethane/hexanes, to give 110.7 mg (0.18 mmol, 76%) of I-B-A-TMS (**23**) as a white solid: mp 45.5–47.5 °C; *R_f* 0.22 (25:75 (v/v), dichloromethane:hexanes); MS (EI) *m/e* 631 (1), 630 (5), 629 (17), 628 (41). Anal. Calcd for C₃₂H₄₁IO₂Si: C, 61.14; H, 6.57. Found: C, 61.29; H, 6.55.

I-B-B-A-A-TMS (24) and I-B-B-A-A-H (36). Using the above procedures, monomer **1** and monomer **2** were coupled with deprotected monomer **16** (0.448 mequiv/g) to produce polymer-supported hexamer P-B-B-A-A-A-TMS. Using the procedure for **18**, polymer-supported hexamer P-B-B-A-A-A-TMS (7.37 g, 0.304 mequiv/g) and iodomethane (50.0 mL) were allowed to react to give a brown residue. The crude residue was filtered through a plug of silica in 50:50

(v/v), dichloromethane:hexanes, to give I-B-B-B-A-A-A-TMS (**24**) as a white powder. The crude powder was purified by precipitation from CH₂Cl₂ using MeOH to give 1.587 g (1.07 mmol, 48%) of I-B-B-B-A-A-A-TMS (**24**) as a white solid. To a solution of **24** (611 mg, 0.41 mmol) in THF (16 mL) was added a solution of tetrabutylammonium fluoride (1.0 M) in wet (5 wt % H₂O) THF (0.8 mL), and the mixture was stirred at room temperature for 5 min. The mixture was diluted with diethyl ether (100 mL) and washed with water (3 × 50 mL) and brine (2 × 50 mL). The organic phase was dried over MgSO₄, filtered, and concentrated *in vacuo* to give a light yellow solid residue. The residue was purified by flash chromatography (40:60 (v/v), dichloromethane:hexanes) to give 580 mg (0.41 mmol, 99%) of I-B-B-B-A-A-A-H (**36**) as a white solid: mp >250 °C dec; *R_f* 0.28 (40:60 (v/v), dichloromethane:hexanes); MS (FAB) 1413.6 (100). Anal. Calcd for C₈₇H₉₇IO₉: C, 73.92; H, 6.92. Found: C, 73.81; H, 6.99.

Oligomers 26 through 30. Oligomers (I-B-B-TMS (**26**), I-B-B-B-TMS (**27**), I-B-B-B-A-TMS (**28**), I-B-B-B-A-A-TMS (**29**)) were prepared on a 5 mg scale by liberation of the corresponding resin-bound oligomers and analyzed by HPLC (Table 2). Methyl benzoate trimer **30** (I-B-B-B-TMS (**30**), R = methyl) was prepared by solution-phase methods and was analyzed by HPLC (Table 2).

I-D-C-D-C-D-C-TMS (25). Using the above procedures, monomer **3** and monomer **4** were coupled with deprotected monomer **17** (0.349 mequiv/g) to produce polymer-supported hexamer P-D-C-D-C-D-C-TMS. Using the procedure for **18**, polymer-supported hexamer P-D-C-D-C-D-C-TMS (2.71 g, 0.279 mequiv/g) and iodomethane (27.0 mL) were allowed to react for 12 h to give a brown residue. The crude residue was filtered through a plug of silica eluting with dichloromethane to give 459.8 mg (0.44 mmol, 58%) of I-D-C-D-C-D-C-TMS (**25**) as a white powder: mp 306.0–309.0 °C; *R_f* 0.25 (1:1 (v/v), dichloromethane:hexanes); MS (FAB) *m/e* 1044.8 (10). Anal. Calcd for C₆₆H₅₄N₃ISi: C, 75.92; H, 5.21; N, 4.02. Found: C, 76.15; H, 5.61; N, 3.77.

3-Iodo-5-(2-(trimethylsilyl)ethynyl)benzotrile (4). To a sealed tube was added 1-(3-(2-(trimethylsilyl)ethynyl)-5-cyanophenyl)-3,3-diethyltriazene (**35**, 7.26 g, 24.3 mmol), iodine (1.24 g, 4.9 mmol), and iodomethane (50 mL). The mixture was degassed three times by evacuation, sealed, and kept at 110 °C for 29 h. The excess iodomethane was removed by vacuum transfer leaving a brown residue. The residue was dissolved in CH₂Cl₂ (100 mL) and filtered through a plug of silica gel. The organic layer was washed with a half saturated solution of sodium meta bisulfite (100 mL), and brine (100 mL), dried over anhydrous MgSO₄, filtered, and concentrated *in vacuo* to give a light brown residue. The residue was purified by flash chromatography (20/80, dichloromethane/hexanes) to give 7.19 g (22.1 mmol, 91%) of 3-iodo-5-(2-(trimethylsilyl)ethynyl)benzotrile (**4**) as a white solid: mp 64.2–65.3 °C; *R_f* 0.24 (20:80 (v/v), dichloromethane:hexanes); MS (EI) *m/e* 327 (1), 326 (4), 325 (20), 310 (100). Anal. Calcd for C₁₂H₁₂NISi: C, 44.32; H, 3.72; N, 4.31. Found: C, 44.35; H, 3.82; N, 4.17.

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Supporting Information Available: Listings of ¹H NMR, ¹³C NMR, and IR spectra; preparative procedures for compounds **32–35** and precursors (12 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.