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Functionalization of Diynes. Preparation of Bis(alkynyl) Ditosylate and Dibenzoate Esters and Bis(alkynyl) Dithiocyanates Via Alkynyl Iodonium Chemistry

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Abstract: The synthesis and characterization of the title compounds from the interaction of nucleophiles and bis[(phenyl) iodonium] diyne salts is described

The carbon-carbon triple bond has found application in a diverse array of organic transformations including cycloadditions,[1,2] radical chemistry,[3,4] addition reactions[5] and cyclizations [6-8] This wide variety of reactivity has fostered continued enthusiasm for the preparation and functionalization of acetylenes

More specifically, alkynyl thiocyanates are employed in the synthesis of 1,3-thiazoles[9] and sulfenamides,[10] while alkynyl esters have been shown to be synthetically intriguing compounds[11] and are also known to be potent enzyme inhibitors [12] Traditional methods for the functionalization of acetylenes such as reaction of metal acetylide complexes, substitution or elimination reactions[13] proved ineffective for the synthesis of alkynyl esters[11] and requires the use of undesirable, highly toxic starting materials for the synthesis of alkynyl thiocyanates [9,14]

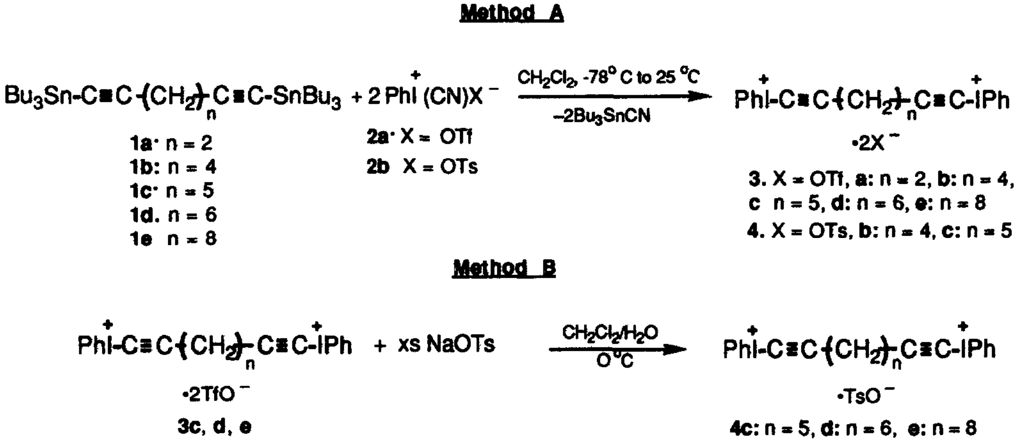
In this paper, we wish to report the synthesis and characterization of two new types of difunctionalized acetylenes, bis(alkynyl) diesters and bis(alkynyl) dithiocyanates, via the reaction of bis(alkynyl) iodonium salts[15,16] with tosylate, benzoate and thiocyanate anions,[17] respectively Additionally, the formation of bis[(phenyl) iodonium] diyne tosylate salts via two different methods is described

RESULTS AND DISCUSSION

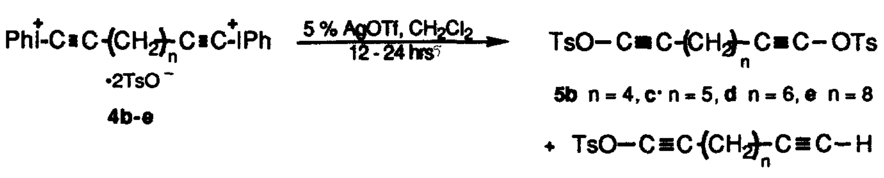
The metal mediated decomposition of alkynyl(phenyl) iodonium tosylate salts[18] has been shown to be an effective method for the formation of alkynyl tosylate esters [19] The application of this chemistry to the preparation of ditosylate esters first required the formation of the bis(iodonium) diyne tosylate precursors (Scheme 1) This may be accomplished via two different but related procedures Method A involves a direct synthesis via the interaction of the bis(tributylstannyl) diacetylenes **1b-c** and the iodonium transfer reagent

2b[20] affording the bis[(phenyl)iodonium] diyne tosylates **4b-c** in a manner analogous to the formation of the bis(iodonium) triflates[21] **3a-e**. Alternatively, iodonium tosylate formation can be accomplished via an ion exchange reaction (Method B). Subjecting a cooled solution of the iodonium triflate salts (CH_2Cl_2) to an aqueous solution of sodium tosylate results in triflate exchange and, following work-up, the isolation of bis[(phenyl)iodonium] diyne tosylates **4c-e**. Both methods yield the desired tosylate salts in good yield as stable solids which can be stored indefinitely under refrigeration

Subsequent decomposition of **4b-e** is accomplished by the addition of a catalytic amount of silver triflate (0 05 - 0 10 eq) to a stirred solution of the corresponding iodonium tosylate salt in CH_2Cl_2 or CH_3CN (Scheme 2) Radial chromatography of the resulting product mixture gives 18-26% yield of the respective ditosylate esters **5b-e** The reaction mixture of **4b-e** also yields smaller amounts of the mono ester as a result of either the alkynyl iodonium salt itself or of one of the ester moietys of the product being reduced to the terminal acetylene during the course of the reaction.[22] This reduced product is generally observed in 5-15% yields and is formed by an unknown mechanism [23] With the exception of **5c**, which is an oil, the ditosylate esters are stable white solids and all exhibit similar spectral properties to previously reported alkynyl sulfonate esters [19a]

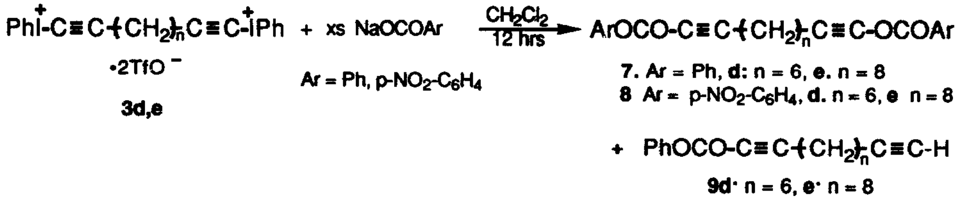


Scheme 1



Scheme 2

The interaction of bis(alkynyl) iodonium triflates **3d-e** with sodium benzoate and sodium *p*-(nitro) benzoate[24] (Scheme 3) affords the bis(alkynyl) diesters **7d-e, 8d-e** without isolation of the presumed iodonium benzoate salt intermediates. Unlike the disulfonate esters, the dibenzoate esters exhibit considerable instability and are extremely prone to hydration of the diyne triple bonds while in solution and to a lesser extent in the solid state making isolation and characterization difficult. Esters **7d-e, 8d-e** have, however, been isolated by radial chromatography in 6-18% isolated yield as white solids and characterized by IR, ^1H and ^{13}C NMR The IR spectra exhibit the expected *C≡C* absorption at 2278-2284 cm^{-1} and a strong *C=O* absorption at 1772-1779 cm^{-1} The ^{13}C NMR is equally characteristic, showing the α-acetylenic carbon at 79-80 ppm and the β-acetylenic carbon at 52-53 ppm In general, the *p*-(nitro) benzoate esters are slightly more stable in the solid state as well as in solution than the parent benzoate esters, facilitating characterization and handling



3d,e

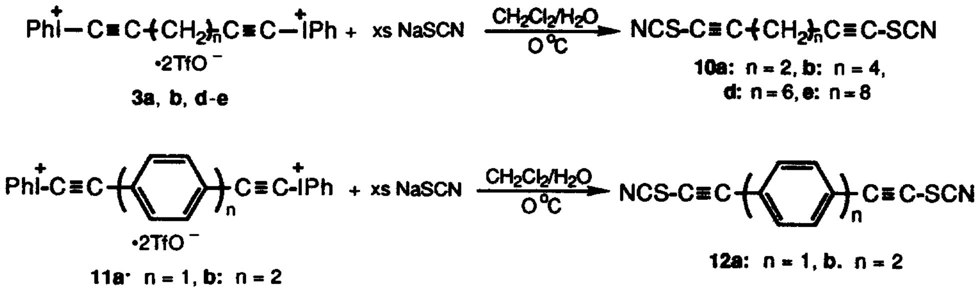
7. Ar = Ph, **d:** n = 6, **e.** n = 8
8 Ar = p-NO₂-C₆H₄, **d.** n = 6, **e** n = 8

9d· n = 6, **e**· n = 8

Scheme 3

As with the formation of the disulfonate esters, formation of the monobenzoate esters **9d-e** in 9-21% yields was observed, while small amounts (< 5%) of the monoesters were also detected during the formation of **8d-e**

Bis(alkynyl) dithiocyanates **10** and **12** were prepared by aqueous exchange reactions by shaking a solution (CH_2Cl_2/CH_3CN) of the respective iodonium triflate salt in a separatory funnel with an aqueous solution of sodium thiocyanate (Scheme 4) The nucleophilic thiocyanate anion easily displaces the triflate



3a, b, d-e

10a: n = 2, **b:** n = 4, **d:** n = 6, **e:** n = 8

11a· n = 1, **b:** n = 2

12a: n = 1, **b.** n = 2

Scheme 4

group of the alkynyl iodonium salt, and the subsequent decomposition of this intermediate affords the desired dithiocyanates in 68-80% yields after work-up and isolation by chromatography. Dithiocyanates **10a** and **12a-b** were isolated as light sensitive solids while **10b, d, e** were clear, light orange oils and were also found to be light sensitive The IR spectra are characteristic, showing a strong *C≡C* stretch between 2203-2208 cm^{-1} and a strong *C≡N* absorbance between 2163-2165 cm^{-1}, while the ^{13}C NMR shows the α-acetylenic carbon at 98-102 ppm and the β-carbon at 52-66 ppm

CONCLUSIONS

The interaction of nucleophiles with bis-[(phenyl)iodonium] diyne salts has been employed to synthesize the first known examples of bis(alkynyl) disulfonate and dibenzoate esters, as well as a number of bis(alkynyl) dithiocyanates. The disulfonate esters and dithiocyanates are obtained as relatively stable solids or oils, while the dibenzoate esters are unstable solids, prone to hydration both in solution and as solids

Experimental Section

General Methods Melting points (uncorrected) were obtained with a Mel-Temp® capillary melting point apparatus Radial chromatography was performed with a Harrison Research Chromatatron®, model 7924T Infrared spectra were recorded on a Mattson FT-IR spectrophotometer NMR spectra were recorded on a Varian XL 300 spectrometer at 300 MHz (^1H NMR), 75 MHz (^{13}C NMR) and 282 MHz (^{19}F NMR) Chemical shifts for ^1H and ^{13}C NMR are reported in parts per million (ppm) relative to internal tetramethylsilane or the proton resonance due to the residual protons in the deuterated NMR solvent, the chemical shifts for ^{19}F are relative to external $CFCl_3$ Mass spectra were obtained with a VG Micromass 7050E double focusing high resolution mass spectrometer with the VG data system 2000 under positive ion fast atom bombardment (FAB) conditions at 8 keV or positive methane chemical ionization (CI) at 150 eV 3-Nitrobenzyl alcohol was used as a matrix in CH_2Cl_2 or $CHCl_3$ as solvent, polypropylene glycol was used as a reference for peak matching Microanalysis were performed by Atlantic Microlab Inc, Norcross, Georgia

Materials All commercial reagents were ACS reagent grade and used without further purification Bis(tributyltin) diacetylenes **1d-e** were prepared by a known[25] method from the corresponding diacetylenes, *n*-butyl lithium and tri-butyltin chloride Sodium *p*-(nitro) benzoate was prepared by deprotonation of the acid with sodium hydroxide and recrystallized from water by the addition of ethanol 1,9-decadiyne, silver triflate, sodium p-toluenesulfonate, and sodium benzoate were purchased from Aldrich, 1,11-dodecadiyne was purchased from Lancaster, and sodium thiocanate was purchased from Mallinckrodt All solvents used were dried by distillation over CaH_2 The reaction flasks were flame-dried and flushed with nitrogen prior to use

1,10-Bis[phenyl[(trifluoromethanesulfonyl)oxy]iodo]-1,9-decadiyne 3d Reaction of 1,10-bis(tributylstannyl)-1,9-dodecadiyne **1d** (7 11 g, 10 mmol) with reagent **2a** (7 6 g, 20 mmol) gave 7 5 g (89%) of **3d** as a white microcrystalline solid, mp 108-111 °C dec, IR (CCl_4) 3066, 2937, 2183 (C≡C), 1286, 1227, 1169, 1018 cm^{-1}, ^1H NMR ($CDCl_3$) δ 8 03 (d, J = 8 5 Hz, 4H), 7 62 (t, J = 7 5 Hz, 2H), 7 49 (t, J = 7 8 Hz, 4H), 2 54 (t, J = 6 8 Hz, 4H), 1.53 (t, J = 6.9 Hz, 4H), 1 34 (m, 4H); ^{19}F NMR (CDCl$_3$) δ -78 55 (s, CF$_3$SO$_3^-$), ^{13}C NMR (CDCl$_3$)· δ 134 0, 132 5, 132 3, 116.2 (all Ph), 119.8 (q, J = 320 Hz, CF$_3$SO$_3^-$), 111.0 ($\underline{C}{\equiv}CI^+$), 27 8 (CH$_2$), 27.2 (CH$_2$), 21.7 ($C{\equiv}\underline{C}I^+$), 20 5 (CH$_2$), Anal. Calcd for C$_{24}H_{22}F_6I_2O_6S_2$. C, 34 37, H 2 63, S, 7 65. Found: C, 34.59; H, 2 69, S, 7 78.

1,12-Bis[phenyl[(trifluoromethanesulfonyl)oxy]iodo]-1,11-dodecadiyne 3e Reaction of 1,12-bis(tributylstannyl)-1,11-dodecadiyne **1e** (15 3 g, 20.7 mmol) with reagent **2a** (15 67 g, 41 4 mmol) gave 16 1 g (90%) of **3e** as a white microcrystalline solid, mp 141-143 °C dec, IR (CCl$_4$): 3056, 2921, 2185 (C≡C), 1296, 1220, 1160, 1023 cm^{-1}; ^{1}H NMR (CD$_3$CN). δ 8 12 (d, J = 8 5 Hz, 4H), 7 73 (t, J = 7 5 Hz, 2H), 7 57 (t, J = 7 6 Hz, 4H), 2.58 (t, J = 6.9 Hz, 4H), 1.48 (m, 4H), 1 27 (m, 4H), 1 20 (m, 4H), ^{19}F NMR (CD$_3$CN) δ -78 18 (s, CF$_3$SO$_3^-$), ^{13}C NMR (CD$_3$CN) δ 135 6, 133 9, 133 3, 117 2 (all Ph), 121 5 (q, J = 320 Hz, CF$_3$SO$_3^-$), 112 2 ($\underline{C}{\equiv}CI^+$), 29 3 (CH$_2$), 29 1 (CH$_2$), 28 2 (CH$_2$), 21 3 ($C{\equiv}\underline{C}I^+$), 20 9 (CH$_2$), Anal Calcd for C$_{26}H_{26}F_6I_2O_6S_2$ C, 36.04, H 3 02, S, 7 40 Found C, 36 15; H, 3 00, S, 7 49

General Procedure for Synthesis of Bis[(phenyl)iodonium] Diyne Tosylates. Method A: Reagent **2b** (2 35 g, 5 8 mmoles) was added at -78 °C under nitrogen to a stirred solution of the appropriate bis(tributyltin) diacetylene **1b-c** (2 9 mmoles) in CH$_2$Cl$_2$ (60 mL) The mixture was allowed to warm to 25 °C and stirred for 10 min until the formation of a clear solution The reaction mixture was concentrated to 10 mL *in vacuo* and ether was added to effect crystallization Hexane was added to complete precipitation and the solid was filtered under nitrogen, washed with dry hexane (100 mL) and dried *in vacuo* Analytically pure materials were obtained by recrystallization from a concentrated solution of the iodonium salt in CH$_2$Cl$_2$ by addition of ether **Method B:** A solution of the appropriate bis[(phenyl)iodonium] diyne triflate salt **3d-f** (0 93-2 3 mmoles) in CH$_2$Cl$_2$/CH$_3$CN (30 mL/20 mL) was shaken with an aqueous solution of sodium tosylate (7 4-18 4 mmoles in 100 mL of H$_2$O) in three portions of 33 mL at 0 °C The layers were separated and the combined aqueous layers were extracted once with 25 mL of CH$_2$Cl$_2$ The combined organic extracts were dried over anhydrous MgSO$_4$, filtered, and the volume reduced *in vacuo* Addition of ether and then hexanes effected the precipitation of **4c-e**, which were filtered and dried *in vacuo*

1,8-Bis[phenyl[(para-toluenesulfonyl)oxy]iodo]-1,7-octadiyne 4b Reaction of **1b** (2 0 g, 2 9 mmol) with reagent **2b** (2 35 g, 2 9 mmol) gave 1 50 g (61%) of **4b** as a white microcrystalline solid, mp 119-120 °C dec, IR (CCl$_4$) 3061, 2936, 2180 (C≡C), 1236, 1156, 1003 cm^{-1}, ^{1}H NMR (CDCl$_3$) δ 8 04 (d, J = 8 2 Hz, 4H), 7 60 (d, J = 8 0 Hz, 4H), 7 53 (t, J = 7 5 Hz, 2H), 7 39 (t, J = 7 5 Hz, 4H), 7 08 (d, J = 7 5 Hz, 4H), 2 46 (m, 4H), 2 32 (s, 6H), 1 58 (m, 4H), ^{13}C NMR (CDCl$_3$) δ 141 2, 137 4, 133 8, 131 9, 131 8, 128 7, 126 0, 118 0 (all Ph), 107 4 ($\underline{C}{\equiv}CI^+$), 29 1 (CH$_2$), 26 7 ($C{\equiv}\underline{C}I^+$), 21 4, 21 0 FAB HRMS m/z 683 964362 [M - TsO$^-$]$^+$, calcd for C$_{27}$H$_{26}$SI$_{26}$O$_3$ 683 968971

1,9-Bis[phenyl[(para-toluenesulfonyl)oxy]iodo]-1,8-nonadiyne 4c Method A Reaction of **1c** (2 0 g, 2 9 mmol) with reagent **2b** (2 35 g, 2 9 mmol) gave 1 68 g (67%) of **4c** as a white microcrystalline solid, mp 118-121 °C dec **Method B** Reaction of **3c** (1 0 g, 1 2 mmol) with aqueous NaOTs (2 20 g, 11 3 mmol, 100 mL) gave 0 76 g (72%) of **4c** as a white microcrystalline solid, mp 120-121 °C dec, IR (CCl$_4$) 3088, 3068, 2941, 2177 (C≡C), 1235, 1162, 1120, 1003 cm^{-1}, ^{1}H NMR (CDCl$_3$) δ 8 02 (d, J = 8 5 Hz, 4H), 7 55 (d, J = 8 1 Hz, 4H), 7 41 (t, J = 7 5 Hz, 2H), 7 37 (t, J = 8 1 Hz, 4H), 7 06 (d, J = 7 9 Hz, 4H), 2 44 (t, J = 6 6 Hz, 4H), 2 30 (s, 6H), 1 25-1 15 (m, 8H), ^{13}C NMR (CDCl$_3$) δ

142 1, 141 2, 135 0, 133 1, 132 7, 129 4, 126 3, 118 0 (all Ph), 109.9 ($\underline{C}$≡CI$^+$), 27.8, 27 4, 25.3 (C≡$\underline{C}$I$^+$), 21 3, 20 6 FAB HRMS m/z 697 978096 [M - TsO$^-$]$^+$, calcd for $C_{28}H_{27}SI_2O_3$ 697 976796.

1,10-Bis[phenyl[(para-toluenesulfonyl)oxy]iodo]-1,9-decadiyne 4d Reaction of **3d** (0.78 g, 0.93 mmol) with aqueous NaOTs (1 55 g, 7 8 mmol, 100 mL) gave 0.61 g (74%) of **4d** as a white microcrystalline solid, mp 119-121 °C dec, IR (CCl_4) 3058, 2933, 2181 (C≡C), 1228, 1151, 1003 cm^{-1}, ^{1}H NMR ($CDCl_3$) δ 7 99 (d, J = 7 6 Hz, 4H), 7 52 (d, J = 8 0 Hz, 4H), 7 50 (t, J = 7.3 Hz, 2H), 7 36 (t, J = 7 8 Hz, 4H), 7 05 (d, J = 7 8 Hz, 4H), 2 39 (t, J = 6 9 Hz, 4H), 2.29 (s, 6H), 1 40 (m, 4H), 1 22 (m, 4H) , ^{13}C NMR ($CDCl_3$)· δ 141 3, 140 1, 133 8, 131 7, 128 6, 125 9, 117 8 (all Ph), 108 3 ($\underline{C}$≡CI$^+$), 27 8, 27 3, 27 3 (C≡$\underline{C}$I$^+$), 21 3, 20 3. FAB HRMS m/z 711 993074 [M - TsO$^-$]$^+$, calcd for $C_{29}H_{29}SI_2O_3$ 711 992446

1,12-Bis[phenyl[(para-toluenesulfonyl)oxy]iodo]-1,11-dodecadiyne 4e Reaction of **3e** (2 0 g, 2 3 mmol) with aqueous NaOTs (2 6 g, 13 4 mmol) gave 1 75 g (83%) of **4e** as a white microcrystalline solid, mp 89-92 °C dec, IR (CCl_4) 3077, 2929, 2857, 2182 (C≡C), 1239, 1148, 1003 cm^{-1}, ^{1}H NMR (CD_3CN) δ 8 02 (d, J = 7 6 Hz, 4H), 7 54 (t, J = 7 3 Hz, 2H), 7 48 (m, 8H), 7 10 (d, J = 7 9 Hz, 4H), 2 46 (t, J = 7 0 Hz, 4H), 2 32 (s, 6H), 1 44 (m, 4H), 1 26-1 17 (m, 8H), ^{13}C NMR ($CDCl_3$) δ 141 2, 140 3, 133 8, 131 8, 128 7, 125 8, 117 3 (all Ph), 109 4 ($\underline{C}$≡CI$^+$), 28 6, 28 4, 27 5, 25 5 (C≡$\underline{C}$I$^+$), 21 3, 20 5, FAB HRMS m/z 739 021393 [M - TsO$^-$]$^+$, calcd for $C_{31}H_{33}SI_2O_3$ 739.023746

General procedure for the synthesis of Bis(tosyl) Diynes.[26] Silver triflate was added to a stirred solution of the appropriate bis[(phenyl)iodonium] diyne tosylate salt **4b-e** (0 55-2 3 mmoles) in CH_2Cl_2 (50-100 mL) at 25 °C and allowed to react until the iodonium salt *C≡C* IR absorption was no longer observed The volume was reduced via rotary evaporator and after flash silica gel (200-400 mesh, 5 g) chromatography (ether) and concentration of the solution to 2 mL, final separation was achieved via radial chromatography (2 mm, 10 1 hexanes/ethyl acetate) Removal of the solvent via rotary evaporator gave **5c** and **6b** as oils and **5b, d-e** as solids which could be purified by recrystallization from ether by the addition of hexanes

1,8-Bis(p-toluenesulfonyl)-1,7-octadiyne 5b. Reaction of **4b** (0 80 g, 0 94 mmol) with $AgOSO_2CF_3$ (0 03 g, 0 11 mmol) gave 88 mg (21%) of **5b** and 57 mg (21%) of **6b**

5b white solid, mp 53 °C, IR (neat) 3070, 2942, 2276 (C≡C), 1399, 1195, 1091 cm^{-1}, ^{1}H NMR ($CDCl_3$) δ 7 85 (d, J = 8 3 Hz, 4H), 7 38 (d, J = 8 6 Hz, 4H), 2 47 (s, 6H), 2 06 (t, J = 6 2 Hz, 4H), 1 37 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 147 0, 130 0, 129 0, 78 9 (C≡$\underline{C}$O), 47 5 ($\underline{C}$≡CO), 27 4, 21 9, 16 5 Anal Calcd for $C_{22}H_{22}O_6S_2$ C, 59 12, H, 4 93 Found C, 59 07, H, 4 97

6b: 1-(p-toluenesulfonyl)-1,7-octadiyne. pale yellow oil, IR (CCl_4) 3301, 3070, 2942, 2277 (C≡C), 2117 C≡CH 1399, 1195 cm^{-1}, ^{1}H NMR ($CDCl_3$) δ 7 85 (d, J = 8 2 Hz, 2H), 7 38 (d, J = 8 4 Hz, 2H), 2 47 (s, 3H), 2 12 (m, 4H), 1 93 (t, J = 2 7 Hz, 1H), 1 50 (m, 4H), ^{13}C NMR ($CDCl_3$) δ 146 9, 129 9, 129 1, 84 0 ($\underline{C}$≡CH), 78 7 (C≡$\underline{C}$O), 68 5 (C≡$\underline{C}$H), 47 3 ($\underline{C}$≡CO), 27 5, 27 3, 21 9, 17 9, 16 5

1,9-Bis(p-toluenesulfonyl)-1,8-nonadiyne 5c. Reaction of **4c** (1 40 g, 1 64 mmol) with $AgOSO_2CF_3$ (0 04 g, 0 16 mmol) gave 0 135 g (18%) of **5c** as a pale yellow oil, IR (neat) 3073, 2937, 2277 (C≡C), 1395, 1195, 1003, cm^{-1}, ^{1}H NMR ($CDCl_3$) δ 7 79 (d, J = 8 4 Hz, 4H), 7 32 (d, J = 8 4 Hz, 4H), 2 40 (s, 6H), 2 00 (t, J = 6.8 Hz, 4H), 1 28 (dq, J_1 = 6 6 Hz, J_2 = 3 1 Hz,4H), 1.20 (m, 4H); ^{13}C NMR ($CDCl_3$). δ 146.9, 130.0, 129 9, 129 0, 78 9 (C≡$\underline{C}$O), 47 5 ($\underline{C}$≡CO), 28 0, 27 6,, 21.8, 16 8.

1,10-Bis(p-toluenesulfonyl)-1,9-decadiyne 5d. Reaction of **4d** (0 50 g, 0 55 mmol) with $AgOSO_2CF_3$ (0 035 g, 0.137 mmol) gave 68 mg (26%) of **5d** as white solid, mp 49-50 °C; IR (CCl_4) 3070, 2932, 2276 (C≡C), 1194, 1092 cm^{-1}, ^{1}H NMR ($CDCl_3$) δ 7 86 (d, J = 8 4 Hz, 4H), 7 38 (d, J = 8 6 Hz, 4H), 2 47 (s, 6H), 2 08 (t, J = 7 0 Hz, 4H), 1 35 (m, 4H), 1 24 (m, 4H), ^{13}C NMR ($CDCl_3$)· δ 146 8, 130 0, 129 9, 129.0, 78 7 (C≡$\underline{C}$O), 47.7 ($\underline{C}$≡CO), 28 4, 28 0, 21 9, 16 9 Anal. Calcd for $C_{24}H_{26}O_6S_2$· C, 60 73, H, 5 48, S, 13 54 Found C, 60 67, H, 5 52, S, 13 60.

1,12-Bis(p-toluenesulfonyl)-1,11-dodecadiyne 5e. Reaction of **4e** (2 1 g, 2 3 mmol) with $AgOSO_2CF_3$ (0 06 g, 0 23 mmol) gave 0 18 g (16%) of **5e** as a white solid, mp 42-43 °C , IR (CCl_4) 3058, 2931, 2276 (C≡C), 1398, 1195, 1091 cm^{-1}, ^{1}H NMR ($CDCl_3$) δ 7 86 (d, J = 8 3 Hz, 4H), 7 37 (d, J = 8 3 Hz, 4H), 2 47 (s, 6H), 2 08 (t, J = 6 9 Hz, 4H), 1 38 (m, 4H), 1 21 (m, 8H), ^{13}C NMR ($CDCl_3$) δ 146 8, 130 0, 129 9, 129 1, 78 6 (C≡$\underline{C}$O), 47 8 ($\underline{C}$≡CO), 28 9, 28 5, 21 8, 16 9 Anal Calcd for $C_{26}H_{30}S_2O_6$ C, 62 13; H 6 02, S, 12 76 Found C, 62 01, H, 6 04, S, 12 93

General procedure for the synthesis of Bis(benzoyl) Diynes.[26] Sodium benzoate or sodium *p*-(nitro) benzoate (2 2-2 5 eq) was added to a stirred solution of the appropriate bis[(phenyl)iodonium] diyne triflate salt **3d-e** (1 2-1 4 mmoles) in CH_2Cl_2 (150 mL) at -78 °C and then was allowed to warm to 25 °C and react until the iodonium salt *C≡C* IR absorption was no longer observed The volume was reduced via rotary evaporator and after flash silica gel (200-400 mesh, 5 g) chromatography (ether) and concentration of the solution to 2 mL, final separation was achieved via radial chromatography (2 mm, 10 1 hexanes/ethyl acetate) Removal of the solvent via rotary evaporator gave **7d-e, 8d-e** as solids and **9d-e** as oils Both **7d-e** and **8d-e** are relatively stable as solids under refrigeration, but decompose slowlyat room temperature as solids (1-2 days), and quickly while in solution (less than 24 hrs)

1,10-Bis(benzoyl)-1,9-decadiyne 7d. Reaction of **3d** (1 0 g, 1 2 mmol) with NaOCOPh (0 38 g, 2 6 mmol) gave 22 mg (6%) of **7d** and 65 mg (21%) of **9d**,

7d: White solid, mp 91 °C, IR (CCl_4) 3071, 2937, 2283 (C≡C), 1779 (C=O), 1213, 998, ^{1}H NMR ($CDCl_3$) δ 8 03 (d,J = 7 4 Hz, 4H), 7 63 (t, J = 7 4 Hz, 2H), 7 46 (t, J = 7 9 Hz, 4H), 2 31 (t, J = 6 8 Hz, 4H), 1 58 (m, 4H), 1 47 (m, 4H), ^{13}C NMR ($CDCl_3$) δ 163 2 (C=O), 134 5, 130 4, 128 8, 126 6, 79 3 (C≡$\underline{C}$O), 51 7 ($\underline{C}$≡CO), 28 9, 28 4, 17 4

9d: 1-benzoyl-1,9-decadiyne Clear oil, IR (neat) 3300, 3067, 2961, 2284 (BzOC≡C), 2116 (C≡CH), 1769 (C=O), 1214, 1001 cm^{-1}, ^{1}H NMR ($CDCl_3$) δ 8 04 (d, J = 7 2 Hz, 2H), 7 63 (t, J = 7 6 Hz, 1H), 7 47 (t, J = 7 6 Hz, 2H), 2 30 (t, J = 6 8 Hz, 2H), 2 19 (m, 2H), 1 93 (t, J = 2 6 Hz, 1H), 1 57 (m, 4H), 1 42 (m, 4H), ^{13}C NMR ($CDCl_3$) δ 163 2, 134 5, 130 4, 128 8, 126 5, 84 6 ($\underline{C}$≡CH), 79 3 (C≡$\underline{C}$O), 68 1 (C≡$\underline{C}$H), 51 7 ($\underline{C}$≡CO), 28 8, 28 4, 28 3, 18 4, 17 4 CI HRMS m/z 255 136707 $[M + 1]^+$, calcd for $C_{17}H_{19}O_2$ 255 138505

1,12-Bis(benzoyl)-1,11-dodecadiyne 7e. Reaction of **3e** (1 22 g, 1.4 mmol) with NaOCOPh (0 50 g, 3 5 mmol) gave 83 mg (15%) of **7e** and 31 mg (9%) of **9e**

7e: White solid, mp 93 °C, IR (CCl_4) 3073, 2932, 2278 (C≡C), 1772 (C=O), 1214, 1003 cm^{-1}, ^{1}H NMR

($CDCl_3$) δ 8.04 (d, J = 7 3 Hz, 4H), 7 62 (t, J = 7 5 Hz, 2H), 7 47 (t, J = 7 4 Hz, 4H), 2.30 (t, J = 7 0 Hz, 4H), 1 37 (m, 4H), 1 43 (m, 4H), 1 33 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 163.2, 134 5, 130 4, 128.8, 126 6, 79 2 ($C\equiv\underline{C}O$), 51 8 ($\underline{C}\equiv CO$), 29 1, 29 0, 28.9, 17 4

9e: 1-benzoyl-1,11-dodecadiyne. Clear oil, IR (neat) 3306, 2931, 2284 ($C\equiv CO$), 2116 ($C\equiv CH$) 1772 ($C=O$), 1214, 1001 cm^{-1}, ^1H NMR ($CDCl_3$) δ 8 04 (d, J = 7 2 Hz, 2H), 7 63 (t, J = 7 5 Hz, 1H), 7.47 (t, J = 7 8 Hz, 2H), 2 89 (t, J = 7 8 Hz, 2H), 2 19 (dt, J_1 = 7 1 Hz, J_2 = 2 7 Hz, 2H), 1 92 (t, J = 2 7 Hz, 1H), 1 53 (m, 4H), 1 41 (m, 4H), 1 32 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 163 2, 134 5, 130 4, 128 8, 126 5, 84 8 ($\underline{C}\equiv CH$), 79 2 ($C\equiv\underline{C}O$), 68 1 ($C\equiv\underline{C}H$), 51 8 ($\underline{C}\equiv CO$), 29.0, 28 9, 28 8, 28 7, 28 5, 28.4, 18 4, 17 4

1,10-Bis[*p*-(nitro)-benzoyl]-1,9-decadiyne 8d. Reaction of **3d** (0.30 g, 0.36 mmol) with $NaOCO(p\text{-}NO_2\text{-}C_6H_4)$ (0 15 g, 0 88 mmol) gave 11 mg (6%) of **8d** as a white solid, mp. 137-139 °C, IR (CCl_4) 3122, 3084, 2933, 2278 ($C\equiv C$), 1773 ($C=O$), 1540 (NO_2), 1234, 1004 cm^{-1}; ^1H NMR ($CDCl_3$)· δ 8 32 (d, J = 8.5 Hz, 4H), 8 23 (d, J = 8 7 Hz, 4H), 2 32 (t, J = 6 9 Hz, 4H), 1 59 (m, 4H), 1 49 (m, 4H), ^{13}C NMR ($CDCl_3$) δ 161 7, 151 3, 131 9, 131 5, 124 0, 78 7 ($C\equiv\underline{C}O$), 53 0 ($\underline{C}\equiv CO$), 28 7, 28 3, 17 3

1,12-Bis[*p*-(nitro)-benzoyl]-1,11-dodecadiyne 8e. Reaction of **3e** (0 60 g, 71 mmol) with $NaOCO(p\text{-}NO_2\text{-}C_6H_4)$ (0 3 g, 1 76 mmol) gave 0 044 g (14 %) of **8e** as a white solid, mp 120-121 °C, IR (CCl_4) 3123, 3060, 2282 ($C\equiv C$), 1779 ($C=O$), 1547 (NO_2), 1235, 1008 cm^{-1}, ^1H NMR ($CDCl_3$) δ 8 32 (d, J = 8 7 Hz, 4H), 8 23 (d, J = 8 7 Hz, 4H), 2 30 (t, J = 6 9 Hz, 2H), 1 55 (m, 4H), 1 43 (m, 4H), 1 35 (m, 4H), ^{13}C NMR ($CDCl_3$) δ 161 7, 151 3, 131 9, 131 5, 123 9, 78 6 ($C\equiv\underline{C}O$), 53 0 ($\underline{C}\equiv CO$), 29 0, 28 8, 17 3

General Procedure for the Synthesis of Bis(alkynyl) dithiocyanates A solution of the appropriate bis[(phenyl)iodonium] diyne triflate salt **3a, b, d, e, 11a, b** (0 10-1 6 mmoles) in CH_2Cl_2/CH_3CN (30 mL/20 mL) was shaken with an aqueous solution of sodium thiocyanate (0 30-4.0 mmoles in 50 mL of H_2O) at 0 °C The layers were seperated and the aqueous layer was extracted once with 25 mL of CH_2Cl_2 The combined organic extracts were dried over anhydrous $MgSO_4$, filtered, and the volume reduced *in vacuo* Flash silica gel (200-400 mesh, 25 g) chromatography (5 1 hexanes/ethyl acetate) and removal of the solvent via rotary evaporator yielded **10b,d,e** as oils and **10a, 12a-b** as solids which could be purified by recrystallization from ether by the addition of hexanes

1,6-Bis(thiocyanato)-1,5-hexadiyne 10a. Reaction of **3a** (0 75 g, 0 96 mmol) with aqueous NaSCN (0 18 g, 2 2 mmol, 100 mL) gave 0 13 g (72%) of **10a** as a white solid, mp 49 °C, IR (CCl_4) 2932, 2208 ($C\equiv C$), 2165 ($C\equiv N$), 1428, 1259, 1059 cm^{-1}, ^1H NMR ($CDCl_3$) δ 2 62 (s, 4H), ^{13}C NMR ($CDCl_3$) δ 106.5 (NCS), 98 8 ($C\equiv\underline{C}\text{-}S$), 55 4 ($\underline{C}\equiv C\text{-}S$), 19 4, Anal Calcd for $C_8H_4N_2S_2$ C, 49 98, H 2 10, S, 33 35 Found C, 50 09, H, 2 11, S, 33 17

1,8-Bis(thiocyanato)-1,7-octacadiyne 10b. Reaction of **3b** (1 3 g, 1 6 mmol) with aqueous NaSCN (0 33 g, 4 mmol, 100 mL) gave 0 24 g (69%) of **10b** as a light orange oil, IR (neat) 2956, 2204 ($C\equiv C$), 2165 ($C\equiv N$), 1260, 1092, 1018 cm^{-1}, ^1H NMR ($CDCl_3$) δ 2 40 (t, J = 6 7 Hz, 4H), 1 65 (t, J = 6 7 Hz, 4H), ^{13}C NMR ($CDCl_3$) δ 107 1 (NCS), 101 2 ($C\equiv\underline{C}\text{-}S$), 53 4 ($\underline{C}\equiv C\text{-}S$), 26 7, 19 6 Anal Calcd for $C_{10}H_8N_2S_2$ C, 54 55, H 3 64, S, 29.09 Found C, 54 26, H, 3 83, S, 28 84

1,10-Bis(thiocyanato)-1,9-decacadiyne 10d. Reaction of **3d** (0 25 g, 0 30 mmol) with aqueous NaSCN (0 053 g, 0 65 mmol) gave 59 mg (80%) of **10d** as a light orange oil, IR (neat) 2938, 2203 ($C\equiv C$), 2165 (C≡N), 1457, 1086 cm^{-1}, ^{1}H NMR (CDCl$_3$)· δ 2.36 (t, J = 6 9 Hz, 4H), 1.56 (t, J = 6 8 Hz, 4H), 1 39 (m, 4H), ^{13}C NMR (CDCl$_3$) δ 107 3 (NCS), 102 1 (C≡$\underline{C}$-S), 52 7 ($\underline{C}$≡C-S), 28.2, 27 5, 20.0 CI HRMS m/z 249 052040 [M + 1]$^+$, calcd for $C_{12}H_{13}S_2N_2$ 249 052019

1,12-Bis(thiocyanato)-1,11-decacadiyne 10e. Reaction of **3e** (1 0 g, 1.2 mmol) with aqueous NaSCN (0 25 g, 3 1 mmol, 100 mL) gave 0 22 g (68%) of **10e** as a light orange oil, IR (neat) 2933, 2203 (C≡C), 2165 (C≡N), 1463 cm^{-1}, ^{1}H NMR (CDCl$_3$) δ 2.33 (t, J = 6 9 Hz, 4H), 1.53 (t, J = 7 4 Hz, 4H), 1 4-1 7 (m, 8H), ^{13}C NMR (CDCl$_3$)· δ 107 2 (NCS), 102 3 (C≡$\underline{C}$-S), 52 3 ($\underline{C}$≡C-S), 28 7, 28 6, 27 6, 20 0 Anal Calcd for $C_{14}H_{16}N_2S_2$ C, 60 83, H, 5 83, S, 23 20 Found. C, 60 91, H, 5 87, S, 23 10

1,4-Bis[(thiocyanato)ethynyl]benzene 12a. Reaction of **11a** (0 30 g, 0 36 mmol) with aqueous NaSCN (0 073 g, 0 90 mmol, 100 mL) gave 0 057 g (66%) of **12a** as a light orange solid, mp 118-120 °C dec, IR (CCl$_4$) 3083, 2180 (C≡C), 2163 (C≡N), 1261, 1015, 832 cm^{-1}, ^{1}H NMR (CDCl$_3$) δ 7 47 (s, 4H), ^{13}C NMR (CDCl$_3$)· δ 132 2, 122 2, 105 7 (NCS), 98 2 (C≡$\underline{C}$-S), 65 5 ($\underline{C}$≡C-S), CI HRMS m/z 240 9883 [M + 1]$^+$, calcd for $C_{12}H_5S_2N_2$ 240 9884

4,4'-Bis[(thiocyanato)ethynyl]biphenyl 12b. Reaction of **11b** (0 090 g, 0 10 mmol) with aqueous NaSCN (0 025 g, 0 30 mmol, 100 mL) gave 26 mg (75%) of **12b** as a light orange solid, mp 159-161 °C dec, IR (CCl$_4$) 3040, 2179 (C≡C), 2165 (C≡N), 1602, 1489, 1003 cm^{-1}, ^{1}H NMR (CDCl$_3$) δ 7 57 (s, 8H), ^{13}C NMR (CDCl$_3$) δ 141 5, 132 9, 127 2,120 2, 106 2 (NCS), 99 0 (C≡$\underline{C}$-S), 63 3 ($\underline{C}$≡C-S), EI HRMS m/z 316 0188 M$^+$, calcd for $C_{18}H_8S_2N_2$ 316 0129

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26 Caution A number of alkynyl esters are known to be potent enzyme inhibitors, therefore proper precautions should be taken to prevent inhalation or absorption through the skin [12]