Supporting Information for

Substituted Alkyne Synthesis Under Non-basic Conditions – Copper Carboxylate-mediated, Palladium-catalyzed Thioalkyne–Boronic Acid Cross-Coupling

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GENERAL METHODS

^{1}H, ^{13}C and ^{19}F NMR spectra were recorded on a Varian Mercury 300 MHz (300 MHz ^{1}H, 75.0 MHz ^{13}C) or Varian Inova 400 MHz (400 MHz ^{1}H, 100.0 MHz ^{13}C, 376.3 MHz ^{19}F) spectrometer in deuteriochloroform ($CDCl_3$) or deuterio-DMSO ($(CD_6)_2SO$) with either tetramethylsilane (TMS) (0.00 ppm ^{1}H, 0.00 ppm) or chloroform (7.26 ppm ^{1}H, 77.00 ppm) or DMSO (2.50 ppm, ^{1}H) or DMS (2.09 ppm, ^{1}H) as internal reference unless otherwise stated. ^{19}F NMR spectra were referenced with trifluoromethyltoluene in benzene (-63.7 ppm) as external standard. ^{31}P NMR spectra were referenced with 85% H_3PO_4 in benzene (0.0 ppm) as external standard. Data are reported in the following order: chemical shifts are given (δ); multiplicities are indicated (br (broadened), s (singlet), d (doublet), t (triplet), q (quartet), pent (pentuplet), hex (hextet), hept (heptet), m (multiplet), exch (exchangeable), app (apparent)); coupling constants, *J*, are reported (Hz); integration is provided. Infrared spectra were recorded on a Nicolet 510 FT-IR spectrometer with a resolution of 4 cm^{-1} or ASI ReactIR 1000FT-IR spectrometer with a silicone probe. Peaks are reported (cm^{-1}) with the following relative intensities: s (strong, 67-100%), m (medium, 40-67%), w (weak, 20-40%) and br (broad). GC-MS spectra were recorded on a Shimadzu Gas Chromatograph GC-17A, Mass Spectrometer QP-5000. GC/MS analysis was carried out on a bonded 5% diphenylsiloxane capillary

column (30 m, 0.25 mm id, 0.25 μm df). Elementary analyses were performed by Atlantic Microlab, Inc., Norcross, Georgia. Melting points were taken on a Thomas-Hoover melting point apparatus in open capillary tubes and are uncorrected. Analytical thin-layer chromatography (TLC) was performed on Merck silica gel 60 plates, 0.25 mm thick with F-254 indicator. Visualization was accomplished by UV light, 5% phosphomolybdic acid solution in ethanol. Flash column chromatography was performed by the method of Still with 32-63 μm silica gel (Woelm). Rotatory chromatography was performed with a Chromatotron™ from Harrison Research using 4 mm PF-254 silica rotors. Preparative plate chromatography was performed on Merck silica gel 60 plates, 0.5 mm thick with F-254 indicator. Solvents for extraction and chromatography were reagent grade and used as received. Dried solvents (THF, toluene, CH_3CN, benzene, DMA) used as reaction media were purchased from Aldrich and dried over 4A molecular sieves and titrated for water level prior to use with a Fisher Coulomatic K-F titrator. Et_3N and pyridine were dried over 4A molecular sieves. All solvents, unless otherwise noted were sparged with nitrogen for several hr. All reactions were performed under a dry nitrogen in oven- and/or flame-dried glassware, except for those reactions utilizing water as a solvent, which were run under air. "Brine" refers to a saturated aqueous solution of NaCl. Unless otherwise specified, solutions of HCl, NH_4Cl, $NaHCO_3$ refer to aqueous solutions.

STARTING MATERIALS

N-Chlorosuccinimide, thiocresol, methyldisulfide, 3-methylsalicylic acid, thiophene-2-carboxylic acid, phenylboronic acid, Cu_2O, $Pd(dppf)Cl_2$, $Pd(PPh_3)_4$, $Pd(OAc)_2$ P(*o*-tolyl)$_3$, $P(OEt)_3$, *n*-BuLi (1.4-1.6 M in hexanes), ethynylmagnesium chloride (0.5 M in THF), ethynylbenzene, (cyclohex-1-enyl)ethyne, propynoic acid ethyl ester, hex-1-yne, and 17-ethynyl-3-methoxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[a]phenanthren-17-ol, 3-methoxypropyne were purchased from Aldrich Chemical Co. and used as received. Boronic acid reagents were obtained from Frontier Scientific. CuTC was prepared as previously described.[1]

Copper (I)-3-methylsalicylate, CuMeSal. Cu_2O (6.9 g, 0.09 mol of Cu, 1.0 equiv) and 3-methylsalicylic acid (23.0 g, 0.15 mol, 1.6 equiv) were introduced into a 1000 mL round-bottomed flask, which was equipped with a Dean-Stark apparatus. Under argon,

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[1] (a) Zhang, S.; Zhang, D.; Liebeskind, L. S. *J. Org. Chem.* **1997**, *62*, 2312-2313.

dry and degassed toluene (200 mL) was added and the mixture was refluxed for 2 days. CuMeSal was filtered under argon, washed with dry and degassed toluene (2 x 100 mL), MeOH (50 mL), ether (200 mL) and dried for 2 h. CuMeSal (16.7 g, 0.08 mol, 88%) was obtained as a beige powder. Mp 205 ^{o}C (decomp). IR (KBr pellet, cm^{-1}): 3210 (br), 1873 (s), 1734 (s), 1597 (s). ^{1}H NMR (d_6 DMS, 400 MHz): 14.35 (br s, 1 H), 7.75 (d, *J* = 6.8 Hz,1 H), 7.08 (d, *J* = 6.4 Hz,1 H), 6.58 (t, *J* = 6.8 Hz, 1 H), 2.21 (s, 3 H). Anal. Calcd for $C_8H_7O_3Cu$: C, 44.75; H, 3.29; O, 22.36; Found: C, 44.55; H, 3.18; O, 22.22.

***N*-(*p*-Tolylthio)succinimide** was prepared by a literature procedure.[2] TLC (CH_2Cl_2-ethanol, 20:1, R_f =0.74) Mp 111-112 ^{o}C (ethanol; lit.{113 ^{o}C,[2] 114-115 ^{o}C [3]}; IR (CCl_4, KCl, cm^{-1}): 2914 (w), 2848 (m), 1731 (s). ^{1}H NMR ($CDCl_3$, 400 MHz): 7.59 (d, *J* = 8.4 Hz, 2 H), 7.15 (d, *J* = 8.4 Hz, 2 H), 2.78 (s, 3 H), 2.24 (s, 4 H).

(Hex-1-ynyl)methyl sulfide, 1 was prepared by the procedure of Narasaka.[4] Bp 95 ^{o}C (7 mm Hg, short-path distillation); IR (neat, KCl, cm^{-1}): 2197 (w). ^{1}H NMR ($CDCl_3$, 300 MHz): 2.29 (s, 3 H), 2.24 (t, *J* = 7.2 Hz, 2 H), 1.44-1.34 (m, 4 H), 0.86 (t, *J* = 7.2 Hz, 3 H).

PREPARATION OF THIOALKYNE DERIVATIVES.

General Procedure. The terminal alkyne (1.0 equiv) in dry and degassed THF was treated with *n*-BuLi (1.4-1.6 M in hexanes, 1.0-1.1 equiv) at -78 ^{o}C under argon for 30-90 min. *p*-Tolylthiosuccinimide (1.0-1.1 equiv) in dry and degassed THF was then added to the reaction mixture at -78 ^{o}C. After warming to room temperature, the reaction was monitored by TLC and GC/MS analysis. Upon completion of the reaction, hexanes was added to the reaction mixture, which was then filtered (except for thioalkyne **7**, see details). The filtrate was evaporated to dryness to afford the desired product. Most were of sufficient purity for subsequent use, but some of the products needed aqueous work-up and/or further purification by chromatography. (Chromatotron™, 4mm thick plate of

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[2] Reaction of disulfide and trisulfide with *N*-chlorocarboxamide. Furukawa, M.; Fujino, Y.; Kojima, Y.; Ono, M.; Hayashi, S. *Chem. Pharm. Bull.* **1972**, *26*, 9, 2024-2028.

[3] The preparation of *N*-(alkylthio)- and *N*-(arylthio)succinimide. Abe, Y.; Nakabayashi, T.; Tsurugi, J. *Bull. Chem. Soc. Jap.* **1973,** *46*, 1898-1899.

[4] Chiral Ti catalyst in asymmetric cycloaddition. Narasaka, K.; Hayashi, Y.; Shimadzu, H.; Niihata, S. *J. Am. Chem. Soc.* **1992**, *114*, 23, 8869-8885.

silica gel, hexanes as eluent). The reaction time and conditions were not optimized, and reactions were run only once.

(Phenylethynyl) (*p*-tolyl) sulfide, 2.[5] Following the typical procedure, ethynylbenzene (702 mg, 6.9 mmol, 1.0 equiv) in THF (12 mL) was treated at -78 °C with 1.6 M *n*-BuLi (4.20 mL, 6.7 mmol, 1.0 equiv) for 90 min, and then *p*-tolylthiosuccinimide (1.50 g, 6.8 mmol, 1.0 equiv) in THF (10 mL) was added. After addition of hexanes (70 mL), filtration of the reaction mixture, and evaporation of the filtrate to dryness, **2** (1.32 g, 5.9 mmol, 88 %) was obtained as a white solid. TLC (hexanes, R_f = 0.45); Mp 46-47 °C (ethanol; lit.{45-46 °C[5b]}); IR (neat, cm^{-1}): 2171 (m), 1596 (m). ^{1}H NMR ($CDCl_3$, 400 MHz): 7.53-7.51 (m, 2 H), 7.40 (d, *J* = 8.0 Hz, 2 H), 7.36-7.34 (m, 3 H), 7.18 (d, *J* = 8.0 Hz, 2 H), 2.36 (s, 3 H).

(3-Methoxyprop-1-ynyl)- *p*-tolyl sulfide, 3.[6] Following the typical procedure, 3-methoxypropyne (0.58 mL, 6.9 mmol, 1.0 equiv) in THF (12 mL) was treated at -78 °C with 1.6 M *n*-BuLi (4.20 mL, 6.7 mmol, 1.0 equiv) for 90 min, and then *p*-tolylthiosuccinimide (1.50 g, 6.8 mmol, 1.0 equiv) in THF (10 mL) was added. After addition of hexanes (70 mL), filtration of the reaction mixture, and evaporation of the filtrate to dryness, **3** (1.13 g, 5.9 mmol, 85 %) was obtained as a colorless oil. TLC (hexanes-ether, 2:1, R_f = 0.58); IR (neat, KCl, cm^{-1}): 2182 (m). ^{1}H NMR ($CDCl_3$, 400 MHz): 7.32 (d, *J* = 8.0 Hz, 2 H), 7.15 (d, *J* = 8.0 Hz, 2 H), 4.32 (s, 2 H), 3.42 (s, 3 H), 2.33 (s, 3 H). ^{13}C NMR ($CDCl_3$, 100 MHz): 136.8, 130.0, 128.6, 126.7, 94.5, 74.2, 60.7, 57.5, 21.0.

3-(*p*-Tolylthio)propynoic acid ethyl ester 4. Following the typical procedure, propynoic acid ethyl ester (0.5 mL, 4.9 mmol, 1.0 equiv) in THF (13 mL) was treated at -78 °C with 1.6 M *n*-BuLi (2.95 mL, 4.7 mmol, 1.0 equiv) for 75 min, and then *p*-tolylthiosuccinimide (1.09 g, 4.9 mmol, 1.0 equiv) in THF (7 mL) was added. After

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[5] (a) Nucleophilic substitution at an acetylenic carbon. Miller, S. I.; Orzech, C. E.; Welch, C. A.; Ziegler, G. R.; Dickstein, J. I. *J. Am. Chem. Soc.* **1962**, *84*, 2020-2021. (b) Kinetics and mechanism of the nucleophilic substitution of arylhalogeno acetylenes by sodium toluene-*p*-thiolate in N, N-dimethylformamide. Beltrame, P. L.; Cattania, M. G.; Simonetta, M. *J. Chem. Soc. Perkin Trans 2* **1973**, 63-66.

[6] Asymmetric approaches to cyclopentenones in the Ni(0)-promoted cyclocarbonylation reaction of allyl halides and acetylenes. Villar, J. M.; Degado, A.; Llebaria, A.; Moreto, J. M.; Molins, E.; Miravitlles, C. *Tetrahedron* **1996**, *52*, 31, 10525-10546.

addition of hexanes (80 mL), filtration of the reaction mixture, evaporation of the filtrate to dryness, and chromatography by Chromatotron™ (hexanes), **4** (796 mg, 3.6 mmol, 73 %) was obtained as a colorless oil. TLC (hexanes-ether, 2:1, R_f = 0.67); IR (neat, KCl, cm^{-1}): 2156 (s), 1706 (s). ^{1}H NMR ($CDCl_3$, 400 MHz): 7.36 (d, *J* = 8.4 Hz, 2 H), 7.19 (d, *J* = 8.0 Hz, 2 H), 4.26 (q, *J* = 7.2 Hz, 2 H), 2.35 (s, 3 H), 1.32 (t, *J* = 7.2 Hz, 3 H). ^{13}C NMR ($CDCl_3$, 100 MHz): 153.0, 138.2, 130.4, 127.9, 125.6, 90.9, 80.7, 61.9, 21.1, 14.1. Anal. Calcd for $C_{12}H_{12}O_2S$: C, 65.43; H, 5.49; S, 14.56; Found: C, 65.50; H, 5.50; S, 14.33.

Bis(*p*-tolylthio)ethyne 5.[7] Ethynylmagnesium chloride (0.5 M in THF, 0.45 mL, 0.23 mmol, 1.0 equiv) was added to a solution of *p*-tolylthiosuccinimide (53 mg, 0.24 mmol, 1.0 equiv) in THF (1 mL) at 0 °C. After stirring for one hour at 0-5 °C, completion of the reaction was checked by TLC and GC/MS. Then, at 0 °C 1.4 M *n*-BuLi (0.17 mL, 0.24 mmol, 1.0 equiv) was added and, after stirring for 30 min at 0 °C, *p*-tolylthiosuccinimide (53 mg, 0.24 mmol, 1.0 equiv) was added. The reaction mixture was stirred for 2 hr and allowed to warm to room temperature. After addition of hexanes (20 mL), filtration of the reaction mixture, and evaporation of the filtrate to dryness, **5** (46 mg, 0.17 mmol, 75 %) was obtained as white needles. TLC (hexanes-ether, 2:1, R_f = 0.80); Mp 99-100 °C (ethanol; lit.{98-99 °C [7]}); IR (CCl_4, KCl, cm^{-1}): 1905 (m). ^{1}H NMR ($CDCl_3$, 400 MHz): 7.34 (d, *J* = 8.0 Hz, 4 H), 7.16 (d, *J* = 8.0 Hz, 4 H), 2.33 (s, 6 H).

[2-(Cyclohex-1-enyl)ethynyl] (*p*-tolyl) sulfide, 6. Following the typical procedure, (cyclohex-1-enyl)ethyne (0.52 mL, 4.6 mmol, 1.0 equiv) in THF (16 mL) was treated at -78 °C with 1.6M *n*-BuLi (3.0 mL, 4.8 mmol, 1.0 equiv) for 2 h, and then *p*-tolylthiosuccinimide (1.11 g, 5.0 mmol, 1.1 equiv) in THF (6 mL) was added. After addition of hexanes (50 mL), filtration of the reaction mixture, and evaporation of the filtrate to dryness, **6** (0.98 g, 4.3 mmol, 93 %) was obtained as a colorless oil. TLC (hexanes, R_f = 0.40); IR (neat, KCl, cm^{-1}): 2146 (m), 1890 (m). ^{1}H NMR ($CDCl_3$, 400 MHz): 7.31 (dt, *J* = 8.0, 2.0 Hz, 2 H), 7.14 (d, *J* = 8.0 Hz, 2 H), 6.20 (pent, *J* = 2.0 Hz, 1 H), 2.32 (s, 3 H), 2.21-2.17 (m, 2 H), 2.16-2.11 (m, 2 H), 1.68-1.59 (m, 4 H). ^{13}C NMR ($CDCl_3$, 100 MHz): 136.1, 135.8, 129.8, 129.8, 126.1, 120.7, 99.4, 72.4, 29.1, 25.7, 22.2,

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[7] Nucleophilic substitution at an acetylenic carbon: acetylenic thioethers from haloalkynes and sodium thiolates. Ziegler, G. R.; Welch, C. A.; Orzech, C. E.; Kikkawa, S.; Miller, S. I. *J. Am. Chem. Soc.* **1963**, *85*, 1648-1650.

21.4, 20.9. Anal. Calcd for $C_{15}H_{16}S$: C, 78.90; H, 7.06; S, 14.04 Found: C, 79.00; H, 7.11; S, 13.91.

3-Methoxy-13-methyl-17-[(*p*-tolylthio)ethynyl]-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-17-ol, 7. 17-Ethynyl-3-methoxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[a]phenanthren-17-ol (101 mg, 0.33 mmol, 1.0 equiv) in THF (2 mL) was treated at -78 ^{o}C with 1.6 M *n*-BuLi (0.4 mL, 0.64 mmol, 2.0 equiv) for 120 min (-78 ^{o}C to -40 ^{o}C). Then *p*-tolylthiosuccinimide (102 mg, 0.46 mmol, 1.4 equiv) was added. After stirring for 2 h, the temperature was allowed to warm to room temperature and CH_2Cl_2 (40 mL) was added. The organic layer was extracted with 2N HCl (20 mL), dried (Na_2SO_4), filtered and evaporated. After chromatography (Chromatotron™, CH_2Cl_2), **7** (100 mg, 0.23 mmol, 70 %) was obtained as white crystals. TLC (CH_2Cl_2, R_f = 0.52); Mp 58-59 ^{o}C; IR (neat, cm^{-1}): 3435 (br, m), 2165 (w). ^{1}H NMR ($CDCl_3$, 400 MHz): 7.35 (d, *J* = 8.0 Hz, 2 H), 7.23 (d, *J* = 8.4 Hz, 1 H), 7.16 (d, *J* = 8.0 Hz, 2 H), 6.74 (dd, *J* = 8.4, 2.8 Hz, 1 H), 6.66 (d, *J* = 2.8 Hz, 1 H), 3.80 (s, 3 H), 2.90-2.86 (m, 2 H), 2.42-2.34 (m, 2 H), 2.35 (s, 3 H), 2.24-2.11 (m, 3 H), 1.91-1.76 (m, 5 H), 1.53-1.40 (m, 4 H), 0.94 (s, 3 H). ^{13}C NMR ($CDCl_3$, 100 MHz): 157.4, 137.9, 136.5, 132.5, 130.0, 129.1, 126.3, 113.7, 111.4, 101.7, 81.0, 72.9, 55.1, 49.7, 47.7, 43.5, 39.4, 39.2, 33.1, 29.8, 27.2, 26.4, 22.9, 20.9, 12.8. LRMS (FAB): 432 ([M^+], 76), 415 (100), 283 (37). HRMS (EI) Calcd for $C_{28}H_{32}O_2S$: 432.2123. Found: 432.2112 ([M^+], error -2.5 ppm). Anal. Calcd for $C_{28}H_{32}O_2S$: C, 77.74; H, 7.46; S, 7.41; Found: C, 77.13; H, 7.39; S, 7.32. $[\alpha]^{25}_{D}$ = -41.6 (c 0.49 in CH_2Cl_2).

CROSS-COUPLING OF THIOALKYNE DERIVATIVES

General Procedure. The organoboron reagent (1.0-1.5 equiv), Pd catalyst (3-10%), copper salt (CuTC, or CuMeSal, 1.0-1.5 equiv) and thioalkyne (1.0 equiv) were placed in a 25 mL Schlenk tube. After a vacuum and argon cycle, dry and degassed solvent was added. The reaction mixture was stirred for 3-18 h at 45-50 ^{o}C and monitored by GC/MS and TLC. When one of the starting materials was an oil, all the solids were first placed in a Schlenk tube, and after vacuum and argon cycle, the solvent was added followed by the addition of the oil by a syringe. After completion of the reaction, diethyl ether or CH_2Cl_2 (depending on the solubility of the substrate) was added to the reaction mixture and the organic layer was then extracted with 2N HCl or NH_4Cl, and then with $NaHCO_3$ or NH_4OH. The aqueous layer was then washed once with ether or CH_2Cl_2. The organic layer was dried (Na_2SO_4), filtered, and concentrated to a viscous oil or solid. The residue

was purified by preparative thin layer chromatography (silica, 0.5 mm thick plate) or Chromatotron™ (silica, 4 mm thick plate) to give the desired product, some being further recrystallized.

1-(Hex-1-ynyl)-2-methoxybenzene 8.[8] Following the typical procedure, (hex-1-ynyl)methyl sulfide **1** (111 mg, 0.87 mmol, 1.0 equiv) was added to a mixture of CuTC (200 mg, 1.05 mmol, 1.2 equiv), 2-methoxyphenylboronic acid (146 mg, 0.96 mmol, 1.1 equiv) and $Pd(PPh_3)_4$ (47 mg, 0.04 mmol, 5%) in dry and degassed THF (5 mL). The reaction mixture was stirred for 14 h at 50 ^oC; **8** (111 mg, 0.59 mmol, 68 %) was obtained as a colorless oil after chromatography (Chromatotron™, hexanes). TLC (hexanes-ether, 2:1, R_f = 0.55). IR (neat, KCl, cm^{-1}): 2054 (w). ^1H NMR ($CDCl_3$, 400 MHz): 7.38 (dd, *J* = 7.6, 1.6 Hz, 1 H), 7.24 (dt, *J* = 8.4, 1.6 Hz, 1 H), 6.90-6.84 (m, 2 H), 3.87 (s, 3 H), 2.48 (t, *J* = 7.2 Hz, 2 H), 1.62 (pent, *J* = 7.2 Hz, 2 H), 1.51 (pent, *J* = 7.2 Hz, 2 H), 0.95 (t, *J* = 7.2 Hz, 3 H). ^{13}C NMR ($CDCl_3$, 100 MHz): 159.7, 133.6, 128.8, 120.3, 113.0, 110.4, 94.6, 76.5, 55.7, 30.9, 22.0, 19.4, 13.6.

3-E-1,4-Diphenyl-3-buten-1-yne 9.[9] Following the typical procedure, dry and degassed THF (2.5 mL) was added to (phenylethynyl) (*p*-tolyl) sulfide **2** (99 mg, 0.44 mmol, 1.0 equiv), CuMeSal (103 mg, 0.48 mmol, 1.1 equiv), *trans*-ß-styrylboronic acid (72 mg, 0.40 mmol, 1.1 equiv) and $Pd(PPh_3)_4$ (20 mg, 0.02 mmol, 4%). The reaction mixture was stirred for 14 h at 45 ^oC. After preparative plate chromatography (hexanes) and recrystallization from ethanol, **9** (61 mg, 0.30 mmol, 68 %) was obtained as a white solid. TLC (hexanes, R_f = 0.60). Mp 95-96 ^oC (ethanol; lit.{95-96 ^oC[9b]}); IR (neat, cm^{-1}): 1957 (w), 1887 (w). ^1H NMR ($CDCl_3$, 400 MHz): 7.42-7.49 (m, 4 H), 7.29-7.37 (m, 6 H), 7.05 (d, *J* = 16.4 Hz, 1 H), 6.39 (d, *J* = 16.4 Hz, 1 H).

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[8] A new synthesis of 2-substituted benzofurans and benzothiophens: novel fragmentation reactions of simple alkyl groups. Aitken, R. A.; Burns, G. *Tetrahedron Lett.* **1987**, *28*, 32, 3717-3718.

[9] (a) Palladium-catalyzed coupling of organostannanes with hypervalent iodonium salts. Kang, S-H.; Lee, H-W.; Jang, S-B.; Kim, T-H.; Kim, J-S. *Synth. Commun.* **1996**, *26*, 23, 4311-4318. (b) Synthesis of (E)-1, 4-bis(organyl)but-1-en-3-ynes by lithium-tellurium exchange reaction on (Z)-1-butyltelluro-1,4-bis(organyl)but-1-en-3ynes. Dabdoub, M. J.; Dabdoub, V. B.; Comasseto, J. V. *Tetrahedron Lett.* **1992**, *33*, 17, 2261-2264.

5-Methyl-2-(phenylethynyl)thiophene 10.[10] Following the typical procedure, dry and degassed THF (3.5 mL) was added to (phenylethynyl) (*p*-tolyl) sulfide **2** (53 mg, 0.24 mmol, 1.0 equiv), CuTC (61.0 mg, 0.32 mmol, 1.3 equiv), 5-methylthiophene-2-boronic acid (45 mg, 0.32 mmol, 1.3 equiv), $Pd(PPh_3)_4$ (13 mg, 0.01 mmol, 5%). The reaction mixture was stirred for 15 h at room temperature. After preparative plate chromatography (hexanes) and recrystallization from methanol, **10** (41 mg, 0.21 mmol, 87 %) was obtained as a yellowish solid. TLC (hexanes, R_f = 0.37). Mp 56-57 ^oC (methanol; lit.{57-58 ^oC[10]}); IR (CCl_4, KCl, cm^{-1}): 2208 (m), 1962 (w), 1941 (w), 1803 (w), 1747 (w). ^1H NMR ($CDCl_3$, 400): 7.51-7.48 (m, 2 H), 7.34-7.32 (m, 3 H), 7.08 (d, *J* = 3.6 Hz, 1 H), 6.66 (dd, *J* = 3.6, 0.8 Hz, 1 H), 2.49 (s, 3 H).

[2,4-Bis(benzyloxy)pyrimidin-5-yl](phenyl)ethyne 11. Following the typical procedure, dry and degassed THF (3 mL) was added to (phenylethynyl) (*p*-tolyl) sulfide **2** (71 mg, 0.32 mmol, 1.0 equiv), CuMeSal (102 mg, 0.48 mmol, 1.5 equiv), 2,4-bis(benzyloxy)pyrimidinyl-5-boronic acid (166 mg, 0.49 mmol, 1.5 equiv) and $Pd(PPh_3)_4$ (24 mg, 0.02 mmol, 6%). The reaction mixture was stirred for 24 h at 45 ^oC. After preparative plate chromatography (CH_2Cl_2), **11** (49 mg, 0.12 mmol, 39 %) was obtained as a yellowish solid. TLC (hexanes: CH_2Cl_2, 1:1, R_f = 0.53). Mp 94-96 ^oC; IR (neat, cm^{-1}): 2223 (w). ^1H NMR ($CDCl_3$, 400 MHz): 8.44 (s, 1 H), 7.51-7.46 (m, 6 H), 7.41-7.33 (m, 9 H), 5.52 (s, 2 H), 5.44 (s, 2 H). ^{13}C NMR ($CDCl_3$, 100 MHz): 169.9, 163.4, 161.3, 136.2, 135.9, 131.5, 128.5, 128.5, 128.3, 128.1, 128.1, 127.5, 122.9, 100.6, 95.7, 80.7, 69.6, 68.6; Anal. Calcd for $C_{26}H_{20}O_2N_2$: C, 79.57; H, 5.14; N, 7.14; O, 8.15; Found: C, 79.51; H, 5.31; N, 7.06; O, 7.91.

1-(3-Methoxyprop-1-ynyl)-3-nitrobenzene 12. Following the typical procedure, (3-methoxyprop-1-ynyl (*p*-tolyl) sulfide **3** (42 mg, 0.22 mmol, 1.0 equiv) was added to a mixture of CuTC (54 mg, 0.28 mmol, 1.3 equiv), 3-nitrophenylboronic acid (42 mg, 0.25 mmol, 1.1 equiv), and $Pd(PPh_3)_4$ (13 mg, 0.01 mmol, 4%) in dry and degassed THF (5 mL). The reaction mixture was stirred for 14 h at 45 ^oC. After preparative plate chromatography (hexanes-ether, 2:1), **12** (36 mg, 0.19 mmol, 86 %) was obtained as a colorless oil. TLC (hexanes-ether, 2:1, R_f = 0.50); IR (CCl_4, KCl, cm^{-1}): 2100 (w), 1782 (w), 1731 (w). ^1H NMR ($CDCl_3$, 400 MHz): 8.29 (t, *J* = 2.0 Hz, 1 H), 8.17 (ddd, *J* = 8.4, 2.4, 1.2 Hz, 1 H), 7.74 (td, *J* = 7.6, 1.2 Hz, 1 H), 7.50 (t, *J* = 8.0 Hz, 1 H), 4.34 (s, 2 H),

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[10] Thiophene aus alkinen. Schulte, K. E.; Reisch, J.; Horner, L. *Chem. Ber.* **1962**, *95*, 1943-1952.

3.46 (s, 3 H). ^{13}C NMR ($CDCl_3$, 100 MHz): 148.0, 137.3, 129.3, 126.6, 124.4, 123.2, 87.7, 83.9, 60.2, 57.9. Anal. Calcd for $C_{10}H_9NO_3$: C, 62.82; H, 4.74; N, 7.33; Found: C, 62.68; H, 4.73; N, 7.24.

3-(3,4-Methylenedioxyphenyl)propynoic acid ethyl ester 13.[11] Following the typical procedure, 3-(*p*-tolylthio)propynoic acid ethyl ester **4** (28 mg, 0.13 mmol, 1.0 equiv) was added to a mixture of CuTC (31 mg, 0.16 mmol, 1.2 equiv), 3,4-methylenedioxyphenylboronic acid (26 mg, 0.16 mmol, 1.2 equiv) and $Pd(PPh_3)_4$ (8 mg, 0.01 mmol, 5%) in dry and degassed THF (3.5 mL). The reaction mixture was stirred for 14 h at 45 ^{o}C. After preparative plate chromatography (hexanes-ether, 2:1) and recrystallization from ether-hexanes, **13** (26 mg, 0.12 mmol, 91 %) was obtained as a white solid. TLC (hexanes-ether, 2:1, R_f = 0.60); Mp 79-80 ^{o}C (ether-hexanes; lit.{ethanol, 75-76 ^{o}C [11]}); IR (CCl_4, KCl, cm^{-1}): 2213 (s), 1706 (s). ^{1}H NMR ($CDCl_3$, 400 MHz): 7.16 (dd, *J* = 8.0, 1.6 Hz, 1 H), 7.00 (d, *J* = 1.6 Hz, 1 H), 6.80 (d, *J* = 8.0 Hz, 1 H), 6.02 (s, 2 H), 4.28 (q, *J* = 7.2 Hz, 2 H), 1.35 (t, *J* = 7.2 Hz, 3 H).

(*p*-Tolyl)[(3-trifluoromethylphenyl)ethynyl] sulfide 14. Following the typical procedure, dry and degassed THF (4 mL) was added to bis(*p*-tolylthio)ethyne **5** (89 mg, 0.33 mmol, 1.0 equiv), CuMeSal (88 mg, 0.41 mmol, 1.3 equiv), 3-trifluoromethylphenylboronic acid (62 mg, 0.33 mmol, 1.0 equiv) and $Pd_2(dba)_3$•$CHCl_3$ (9 mg, 0.01 mmol of Pd, 3% of Pd) and $SbPh_3$ (26 mg, 0.07 mmol, 22%). The reaction mixture was stirred for 14 h at 45 ^{o}C. After preparative plate chromatography (hexanes) and recrystallization from ethanol, **14** (52 mg, 0.18 mmol, 54 %) was obtained as a white solid. TLC (hexanes, R_f = 0.46); Mp 59-60 ^{o}C (ethanol); IR (neat, cm^{-1}): 2173 (m), 1494 (m). ^{1}H NMR ($CDCl_3$, 400 MHz): 7.73 (br s, 1 H), 7.64 (d, *J* = 7.6 Hz, 1 H), 7.57 (d, *J* = 8.0 Hz, 1 H), 7.46 (t, *J* = 7.6 Hz, 1 H), 7.38 (dt, *J* = 8.0, 2.0 Hz, 2 H), 7.19 (d, *J* = 8.0 Hz, 2 H), 2.35 (s, 3 H). ^{13}C NMR ($CDCl_3$, 100 MHz): 137.1, 134.5, 130.2, 128.9, 128.4, 128.2 (q, *J* = 3.6 Hz), 127.0, 124.9 (q, *J* = 3.6 Hz), 123.9, 95.4, 78.7, 21.3 (the signals of the C of CF_3 and in alpha of CF_3 were not observed under the conditions of the experiment). ^{19}F NMR ($CDCl_3$, 376 MHz): - 64.3 (s). Anal. Calcd for $C_{16}H_{11}SF_3$: C, 65.74; H, 3.79; S, 10.97; Found: C, 65.49; H, 3.89; S, 10.87.

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[11] Synergists of insecticides IV. Polarography of some 4-substituted 1,2-(methylenedioxy)benzenes. Lurik, B. B.; Marinova, R. I.; Volkov, Y. P. *J. Gen. Chem. USSR* **1975,** 2246-2249.

Bis(3-trifluoromethylphenyl)ethyne 15.[12] Following the typical procedure, dry and degassed THF (3 mL) was added to bis(*p*-tolylthio)ethyne **5** (34 mg, 0.13 mmol, 1.0 equiv), CuMeSal (92 mg, 0.43 mmol, 3.3 equiv), 3-trifluoromethylphenylboronic acid (77 mg, 0.41 mmol, 3.1 equiv), $Pd(PPh_3)_4$ (13 mg, 0.01 mmol, 10%). The reaction mixture was stirred for 14 h at 45 °C. After preparative plate chromatography (hexanes) and recrystallization from ethanol, **15** (30 mg, 0.10 mmol, 74 %) was obtained as a white solid. TLC (hexanes, R_f = 0.64); Mp 85-86 °C (ethanol; lit.{85-87 °C [12]}); IR (neat, cm^{-1}): 1729 (m). ^{1}H NMR ($CDCl_3$, 400 MHz): 7.81 (br s, 2 H), 7.71 (d, *J* = 7.6 Hz, 2 H), 7.61 (d, *J* = 7.6 Hz, 2 H), 7.50 (t, *J* = 7.6 Hz, 2 H). ^{19}F NMR ($CDCl_3$, 376 MHz): -64.3 (s).

Bis(4-methoxyphenyl)ethyne 16.[13] Following the typical procedure, dry and degassed THF (3 mL) was added to bis(*p*-tolylthio)ethyne **5** (53 mg, 0.20 mmol, 1.0 equiv), CuTC (87 mg, 0.46 mmol, 2.3 equiv), 4-methoxyphenylboronic acid (78 mg, 0.51 mmol, 2.6 equiv), $Pd_2(dba)_3$•$CHCl_3$ (5 mg, 0.01 mmol of Pd, 5% of Pd) and tris-2-furylphosphine (3 mg, 0.01 mmol, 6%). The reaction mixture was stirred for 12 h at 50 °C. After chromatography (Chromatotron™, hexanes) and recrystallization from ethanol, **16** (30 mg, 0.13 mmol, 65 %) was obtained as a white solid. TLC (hexanes-ether, 2:1, R_f = 0.39); Mp 140-141 °C (ethanol; lit.{141-143 °C[13b]}); ^{1}H NMR ($CDCl_3$, 400 MHz): 7.45 (td, *J* = 8.4, 2.8 Hz, 4 H), 6.87 (td, *J* = 8.4, 2.8 Hz, 4 H), 3.83 (s, 6 H).

1-[(Cyclohex-1-enyl)ethynyl]-4-methoxybenzene 17. Following the typical procedure, [2-(cyclohex-1-enyl)ethynyl] (*p*-tolyl) sulfide **6** (29 mg, 0.13 mmol, 1.0 equiv) was added to a mixture of CuTC (30 mg, 0.16 mmol, 1.2 equiv), 4-methoxyphenyl boronic acid (26 mg, 0.17 mmol, 1.3 equiv) and $Pd(PPh_3)_4$ (7 mg, 0.01 mmol, 5%) in dry and degassed THF (4 mL). The reaction mixture was stirred for 14 h at 50 °C. After preparative plate chromatography (hexanes) and recrystallization from ethanol, **17** (20 mg, 0.09 mmol, 74 %) was obtained as a white solid. TLC (hexanes, R_f = 0.15); Mp 52-53 °C (ethanol); IR (CCl_4, KCl, cm^{-1}): 2197 (m), 1731 (m). ^{1}H NMR ($CDCl_3$, 400 MHz): 7.36 (d, *J* = 8.8 Hz, 2 H), 6.83 (d, *J* = 8.8 Hz, 2 H), 6.17 (pent, *J* = 2.0 Hz, 1 H), 3.80 (s, 3 H), 2.22-2.19 (m, 2

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[12] Oxidation of aromatic compounds VI. Oxidation of unsymmetrical diarylacetylenes in the CF_3COOH-CH_2Cl_2-PbO_2 system. Vasil'ev, A.V.; Rudenko, A.P *Russ. J. Org. Chem.* **1997**, *33*, 11, 1555-1584.

[13] (a) Synthesis of aryl cluster glycosides by cyclotrimerization of 2-propynyl carbohydrate derivatives. Kaufman, R. J.; Sidhu, R. S. *J. Org. Chem.* **1982**, *47*, 25, 4941-4947. (b) Rudenko, A. P.; Vasil'ev, A. V. *Russ. J. Org. Chem.* **1995**, *31*, 10, 1360-1379.

H), 2.15-2.12 (m, 2 H), 1.70-1.59 (m, 4 H). ^{13}C NMR ($CDCl_3$, 100 MHz): 159.2, 134.5, 132.8, 120.8, 115.8, 113.8, 89.8, 86.6, 55.2, 29.3, 25.7, 22.3, 21.5. LRMS (EI), m/e (relative intensity) 212 (M^+, 100), 184, 165, 115, 57. HRMS (EI) Calcd for $C_{15}H_{16}O$: 212.1201. Found: 212.1203 (M^+, error - 0.8 ppm). Anal. Calcd for $C_{15}H_{16}O$: C, 84.87; H, 7.60; Found: C, 84.02; H, 7.58.

3-Methoxy-13-methyl-17-[(4-methoxyphenyl)ethynyl]-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-17-ol 18.[14] Following the typical procedure, dry and degassed THF (2.5 mL) was added to **7** (50 mg, 0.11 mmol, 1.0 equiv), CuMeSal (26 mg, 0.12 mmol, 1.1 equiv), *p*-methoxyphenylboronic acid (20 mg, 0.13 mmol, 1.1 equiv) and $Pd(PPh_3)_4$ (7 mg, 0.01 mmol, 5%). The reaction mixture was stirred for 14 h at 45 ^{o}C. After preparative plate chromatography (CH_2Cl_2), **18** (37 mg, 0.09 mmol, 81 %) was obtained as white crystals. TLC (CH_2Cl_2, R_f = 0.30). Mp 59-60 ^{o}C (lit.{60-62 ^{o}C[14]}); IR (neat, cm^{-1}): 3466 (br m), 2290 (w), 1606 (s). ^{1}H NMR ($CDCl_3$, 400 MHz): 7.39 (td, *J* = 8.8, 2.8 Hz, 2 H), 7.23 (d, *J* = 8.8 Hz, 1 H), 6.84 (td, *J* = 8.8, 2.8 Hz, 2 H), 6.72 (dd, *J* = 8.8, 2.8 Hz, 1 H), 6.63 (d, *J* = 2.8 Hz, 1 H), 3.81 (s, 3 H), 3.78 (s, 3 H), 2.90-2.84 (m, 2 H), 2.46-1.30 (m, 14 H), 0.93 (s, 3 H). ^{13}C NMR ($CDCl_3$, 100 MHz): 159.5, 157.4, 138.0, 133.1, 132.6, 115.0, 113.9, 113.7, 111.5, 91.3, 85.8, 80.3, 55.3, 55.2, 49.7, 47.6, 43.6, 39.5, 39.0, 33.0, 29.8, 27.2, 26.5, 22.9, 12.9. LRMS (FAB), m/e (relative intensity) 424 ([M^++H+Li], 31), 423 ([M^++Li], 100), 405 (26), 378 (17), 377 (26), 313 (31), 301 (24), 294 (67). HRMS (FAB) Calcd for $C_{28}H_{32}O_3Li$: 423.2511. Found: 423.2507 ([M^++Li], error –1.1 ppm). $[\alpha]^{25}_D$ = -41.0 (c 0.24 in CH_2Cl_2).

CONTROL EXPERIMENTS.

Synthesis of $Pd(PPh_3)_2$(S-*p*-tolyl)(CCC_6H_5) (II) 19. (Phenylethynyl) (*p*-tolyl) sulfide **2** (101 mg, 0.45 mmol, 1.0 equiv) was mixed with $Pd(PPh_3)_4$ (502 mg, 0.43 mmol, 1.0 equiv) in dry and degassed benzene (11 mL) at room temperature in the dark under argon. After 10 h, pentane (60 mL), was added and an orange solid precipitated. After filtration of the solid, the palladium complex **19** (230 mg, 0.27 mmol, 63 %) was obtained as a light orange solid. The filtrate contained PPh_3 but no (phenylethynyl)(p-tolyl)sulfide **2**. Complex **19** decomposes if left in solution at room temperature. Mp 95-108 ^{o}C (decomp); IR (neat, cm^{-1}): 2115 (m). ^{31}P NMR (benzene, 162 MHz): 27.73 ppm. LRMS

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[14] The palladium-catalyzed reductive addition of aryl iodides to propargyl alcohols: a route to γ,γ-diarylallylic alcohols. Arcadi, A.; Cacchi, S.; Marinelli, F.*Tetrahedron* **1985**, *41*, 22, 5121-5131.

(FAB), m/e (relative intensity) 731 ([M^+-(S-*p*-tolyl)], 10), 661 (2), 630 (2). HRMS (FAB) Calcd for $C_{44}H_{35}P_2Pd$ ([M^+-(S-*p*-tolyl)]: 731.1249. Found: 731.1285 (error +5.0 ppm). Anal. Calcd for $C_{51}H_{42}P_2PdS$: C, 71.62; H, 4.95; S, 3.75; Anal. Calcd for $C_{51}H_{42}P_2PdS.1/2\ H_2O$: C, 70.87; H, 5.01; S, 3.71; Found: C, 70.61; H, 5.00; S, 3.55.

*Cross-coupling of (phenylethynyl) (p-tolyl) sulfide **2** and $PhB(OH)_2$ with NaTC in the absence of Cu(I)*

Following the typical procedure, dry and degassed THF (1 mL) was added to (phenylethynyl) (p-tolyl) sulfide **2** (29 mg, 0.13 mmol, 1.0 equiv), NaTC (28 mg, 0.19 mmol, 1.4 equiv), phenylboronic acid (22 mg, 0.18 mmol, 1.4 equiv) and $Pd(PPh_3)_4$ (7 mg, 0.01 mmol, 7%). The reaction mixture was stirred for 24 h at 45 ^oC. No product was detected by GC/MS (octadecane (33 mg, 0.13 mmol) was used as internal standard).

*Cross-coupling of palladium complex **19** and $PhB(OH)_2$ with CuMeSal(I).*

Following the typical procedure, dry and degassed THF (0.8 mL) was added to complex **19** (11 mg, 0.01 mmol, 1.0 equiv), CuMeSal (3 mg, 0.01 mmol, 1.1 equiv), and phenylboronic acid (3 mg, 0.02 mmol, 1.9 equiv). The reaction mixture was stirred for 24 h at 45 ^oC. Diphenylacetylene was detected by GC/MS [octadecane (3 mg, 0.01 mmol) was used as internal standard].

*Cross-coupling of palladium complex **19** and $PhB(OH)_2$ without Cu(I) cofactor.*

Following the typical procedure, dry and degassed THF (1 mL) was added to complex **19** (11 mg, 0.01 mmol, 1.0 equiv) and phenylboronic acid (3 mg, 0.02 mmol, 1.9 equiv). The reaction mixture was stirred for 24 h at 50 ^oC. No product was detected by GC/MS [octadecane (3 mg, 0.01 mmol) was used as internal standard].

*Cross-coupling of palladium complex **19** and $PhB(OH)_2$ without Cu(I) cofactor and with NaOAc as a base.*

Following the typical procedure, dry and degassed THF (1 mL) was added to complex **19** (10 mg, 0.01 mmol, 1.0 equiv), phenylboronic acid (3 mg, 0.02 mmol, 1.9 equiv) and NaOAc (6 mg, 0.07 mmol, 6.0 equiv). The reaction mixture was stirred for 24 h at 50 ^oC. No product was detected by GC/MS [octadecane (3 mg, 0.01 mmol) was used as internal standard].