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Electrophilic Activation of P-Alkynes in the Synthesis of P-Substituted and P-Centered Heterocycles

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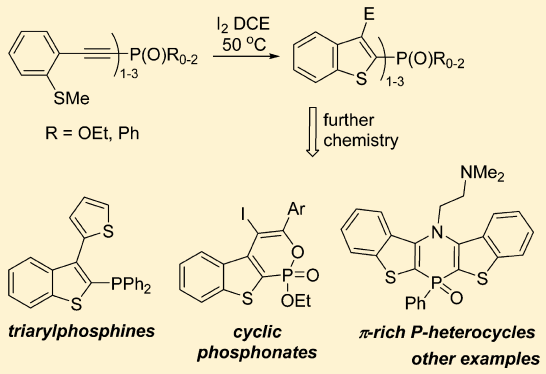
Supporting Information

ABSTRACT: Electrophilic activation of alkynylphosphine oxides and phosphonates provides a novel approach to the synthesis of P-substituted and P-centered heterocycles. Iodocyclization affords a heteroaryl iodide that can, among other things, be used in reiterative alkyne coupling and iodocyclization to give cyclic phosphonates and other cyclization reactions to give π-rich P-heterocycles.



INTRODUCTION

Phosphines and phosphonates have long played important roles in synthetic chemistry as reagents, catalysts, and ligands, and are finding increasing applications in drug discovery (e.g., fosinoprilat **1**[1]) and materials science (e.g., near-infrared fluorescence imaging agent, P-rhodamine **2**[2]) (Figure 1).[3,4] In

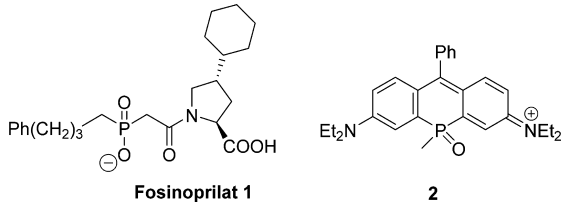


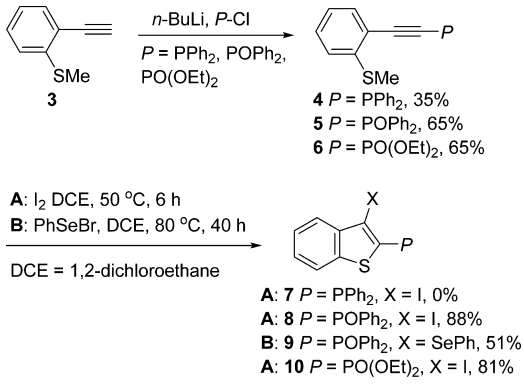
Figure 1. Use of phosphorus in drug discovery and materials science.

1 and **2** the P-group plays a central role in their function. In **1** the phosphinate serves as a mimetic of the tetrahedral-intermediate involved in peptidase amidolysis and in **2** the unique photophysical properties of the phosphine oxide group serve to significantly increase its bathometric shift relative to the parent rhodamine.[1,2] Over the past 15 years, electrophilic activation of alkynes bearing heteroatomic nucleophiles has emerged as a versatile method for the formation of numerous heterocycles.[5,6] The synthetic utility of this reaction has led to a number of applications in both drug discovery and materials science.[7,8] Herein, we describe our efforts to overcome inherent limitations in the electrophilic activation of alkynyl phosphines and phosphonates, providing new access to a range of P-substituted and P-centered heterocycles of potential benefit to ligand/catalyst design, drug discovery, and materials science.

RESULTS AND DISCUSSION

Our study commenced with the electrophilic cyclization of 2-alkynylphenyl methyl sulfides (**3**) bearing a diphenylphosphine **4**, diphenylphosphine oxide **5**, or diethyl phosphonate **6** on the alkyne (Scheme 1). All three P-alkynes were prepared by

Scheme 1. Electrophile Promoted 5-Endodigonal Cyclization of P-Alkynes



reaction of the corresponding P-chloride with the lithiated alkyne **3**, giving **4** (35%), **5** (65%), and **6** (65%). The low yield of the alkynylphosphine **4** (35%) is largely associated with the difficulties encountered in reaction workup and purification, where a considerable proportion of **4** was oxidized to the phosphine oxide **5**.

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Attempted iodocyclization of **4** failed, giving only **5** (room temperature reaction). Presumably, I_2 reacts at phosphine center instead of the alkyne to give a PI_2 complex **11** (Figure 2)

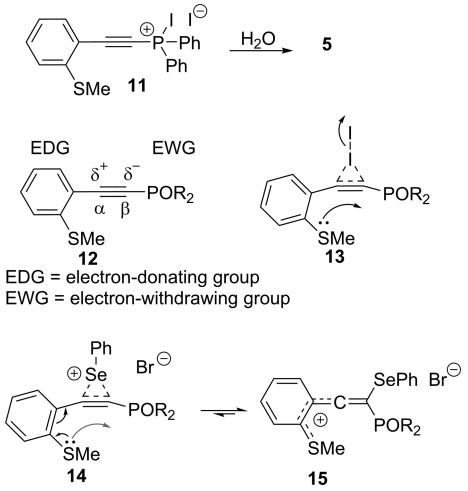
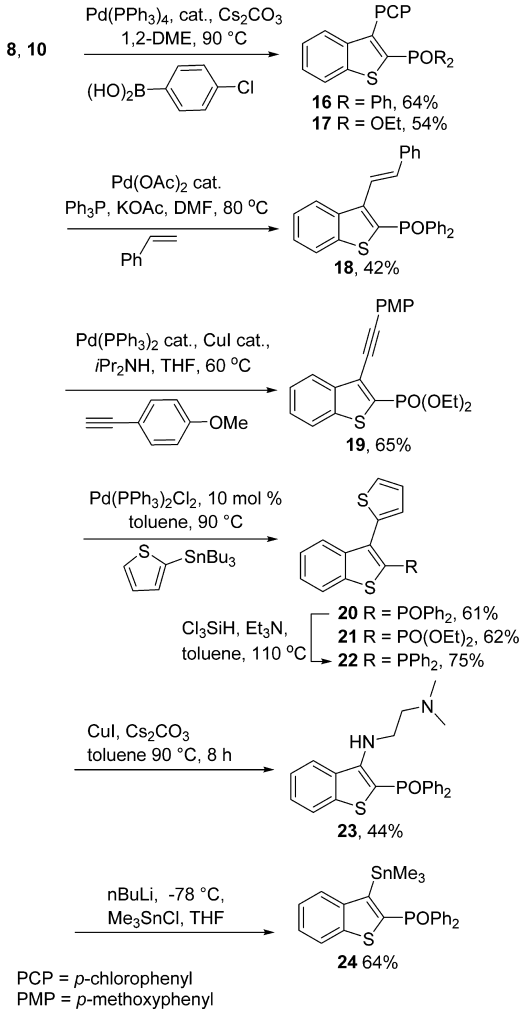


Figure 2. Mechanistic consideration for electrophilic activation of P-alkynes.

that reacts with water upon workup to give P=O (**5**). Successful iodocyclizations of **5** and **6** to **8** (88%) and **10** (81%), respectively, were achieved under quite mild conditions (A: I_2, 50 °C, 6 h; Scheme 1), especially considering unfavorable electronic bias of these alkynes.[9] Alkynes bearing an electron-donating aromatic ring and/or an electron-withdrawing β-substituent (e.g., P=O) as in **12** are resistant to 5-endodigonal cyclization.[9] In contrast to I_2, the more powerful electrophile PhSeBr required more forcing conditions (B: PhSeBr, 80 °C, 40 h; Scheme 1) in the cyclization of **5** to **9** (51%). This is consistent with our recently described mechanistic model for electrophile-promoted cyclization of alkynes, where I_2 and charged electrophiles have quite different effects on polarized alkynes.[9] The capacity of I_2 to form a charge neutral I_2-alkyne complex **13** ameliorates the unfavorable polarization of the alkyne **12**. This complex provides suitable electrophilic activation of the β-position to promote nucleophilic attack, enabling 5-endodiagonal cyclization. On the other hand, while the PhSe cation can in principle form a similar bridged intermediate **14**, for polarized alkynes these are disfavored relative to the allenic cation **15**, thus exacerbating the electronic bias imposed by the P=O group and disfavoring 5-endodigonal cyclization. The bridged species **14** is likely to only emerge as a transition state of cyclization attained at higher temperatures (**14** gray arrow).

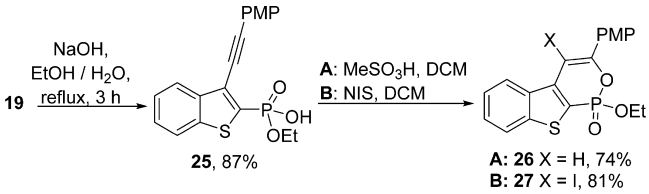
As expected, the introduction of a 3-iodo group provides a useful handle for the further synthetic manipulation of **8** and **10**. It can be used in Pd-mediated couplings, including Miyaura–Suzuki, Heck, Sonogashira, and Stille–Scott couplings, to give 3-(aryl-, alkenyl-, and alkynyl)-2-P-benzo[*b*]-thiophenes **16**–**21** (Scheme 2). 3-Amino groups can be introduced through Ullman coupling **8** → **23** (44%) and lithiation of the iodo group can also be undertaken to introduce other substituents as demonstrated in the preparation of trimethystannyl compound **24** (64%). The phosphine oxide group can serve as a masked phosphine that is revealed through reduction (using trichlorosilane (Cl_3SiH)), as exemplified in the conversion of **20** to **22** (75%).

Scheme 2. 3-Iodo Substitutions



The 3-alkynyl system **19** was used in an iterative approach to cyclic phosphonates **26** and **27** through subsequent electrophilic cyclization (Scheme 3). This required initial hydrolysis of

Scheme 3. Iterative Iodocyclization To Give Benzothiopheno-Fused Oxaphosphinines



the ester **19** to give **25** (87%), followed by reaction with either methanesulfonic acid ($MeSO_3H$; conditions **A**) or *N*-iodosuccinimide (NIS; conditions **B**) to give benzo[4,5]thieno-[2,3-*c*][1,2]oxaphosphinines **26** (74%) and **27** (81%), respectively (Scheme 3).

We next turned our attention to electrophilic activation of dialkynylphosphine oxides (Scheme 4). In this case, we experimented with an alternative means of preparing the iodocyclization substrate **30** by undertaking a Sonogashira coupling between **28** and the diethynylphosphine oxide **29**[10] to give **30** (50%). This material underwent efficient iodocyclization to the bis(3-iodobenzo[*b*]thiophen-2-yl) (phenyl)-

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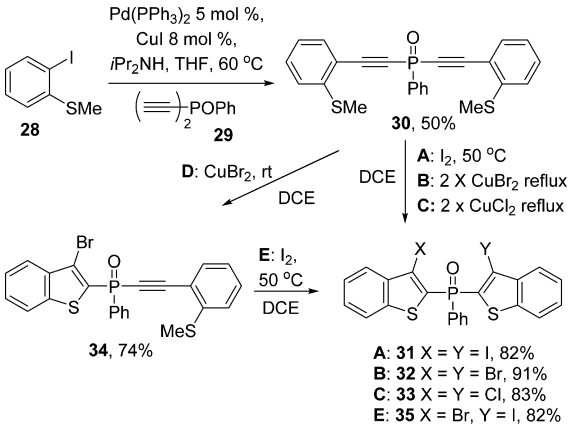
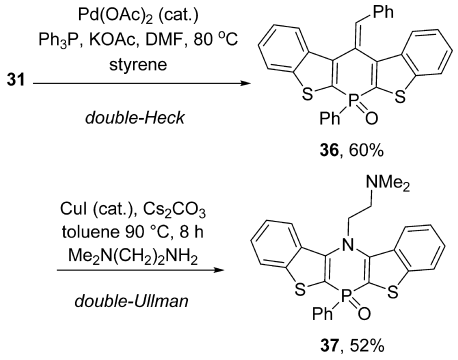
Scheme 4. Halocyclization of Dialkynylphosphine Oxide



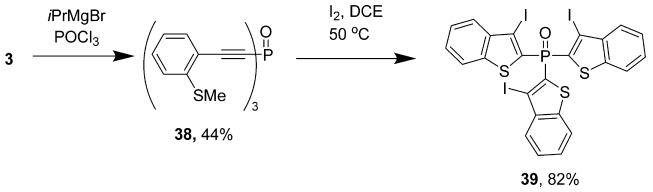
phosphine oxide **31** (82%). We also used copper(II) bromide ($CuBr_2$) and copper(II) chloride ($CuCl_2$) to achieve bromo- and chlorocyclizations of **30** to **32** (91%) and **33** (83%), respectively.[6c] We noted that in these reactions the first halocyclization proceeded at room temperature but the second required heating. This was taken advantage of in the preparation of the unsymmetrical bromo-iodo system **35**, where monobromocyclization to give **34** (74%) was followed by iodocyclization to give **35** (82%). Interestingly, attempted bromocyclization of **30** with a source of bromonium ion, such as *N*-bromosuccinimide, failed, even at elevated temperatures. Presumably, the bromonium ion exacerbates the unfavorable polarization, similar to PhSeBr **15** (Figure 2).[11] Possibly $CuBr_2$ proceeds through a charge neutral $CuBr_2$-alkyne complex[6a] where this polarization is ameliorated, as for I_2 **13** (Figure 2). The bis(3-iodobenzo[*b*]thiophenyl) (phenyl)phosphine oxide **31** was converted into two novel polyfused P-centered heterocycles through a double-Heck with styrene to give **36** (60%) and a double-Ullman to give **37** (52%) (Scheme 5). Compounds **36** and **37** absorb UV−vis light at significantly longer wavelengths than their uncyclized counterparts **31**-**35**.[12]

Scheme 5. Double-Heck and Double-Ullman Cyclization Reactions of Bis(3-iodobenzo[*b*]thiophen-2-yl) (Phenyl)phosphine Oxide 31



Finally, we also formed the trialkynylphosphine oxide substrate **38** by magnesiation of **3** (using iPrMgBr) followed by its reaction with $POCl_3$. This material underwent efficient iodocyclization to the tris(3-iodobenzo[*b*]thiophen-2-yl)-phosphine oxide **39** (82%) (Scheme 6).

Scheme 6. Formation of Tris(3-iodobenzo[*b*]thiophen-2-yl)phosphine Oxide 39



CONCLUSIONS

In conclusion, the electrophilic cyclization of (2-(methylthiophenyl)ethynyl)phosphine oxides and phosphonates and the subsequent applications of these to iterative and convergent methods of ring formation provides a valuable proof-of-concept for the use of this reaction class in the synthesis of novel P-substituted and P-centered heterocycles. The extension of this reaction to electrophilic activation using other electrophile and nucleophile combinations and its application to new materials is currently underway in our laboratories.

EXPERIMENTAL SECTION

All reactions were performed under an inert atmosphere of anhydrous N_2 (g), unless otherwise stated. Solvents used for various reactions were dried using a commercial solvent purification system. 1,2-Dichloroethane (DCE) was purchased in an anhydrous form and stored under nitrogen. Solvents used in reaction extractions and chromatography and all other reagents were used as supplied by commercial vendors without further purifications or drying. Thin layer chromatography (TLC) was performed using 0.25 mm thick plates precoated with silica gel (40−60 μm, F_{254}) and visualized using UV light (254 and 365 nm). Petroleum spirits with a boiling point range of 40−60 °C was used in chromatography. Column (flash) chromatography was performed on either 40−60 or 20−40 μm silica gel. ^{1}H NMR spectra were recorded at 300 or 400 MHz, as indicated. The following abbreviations were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, dd = doublet of doublets, and dt = doublet of triplets. ^{13}C NMR spectra were recorded at 75 or 101 MHz, as indicated. ^{77}Se NMR and ^{31}P NMR spectra were recorded at 76.3 and 162 MHz, respectively. Triphenylphosphine selenide and phosphoric acid were used as reference standards for ^{77}Se and ^{31}P NMR spectra. ^{1}H and ^{13}C chemical shifts were calibrated using residual nondeuterated solvent as an internal reference and are reported in parts per million (δ) relative to trimethylsilane (δ = 0). Melting points were measured using a digital melting point apparatus. For high-resolution mass spectra (HRMS), atmospheric-pressure chemical ionization (APCI) experiments were carried out on FTMS, ionizing by APCI from an atmospheric solids analysis probe (ASAP). The UV−vis spectra of compounds **31**−**37** are provided in the Supporting Information.

((2-(Methylthio)phenyl)ethynyl)diphenylphosphine Oxide (5). *n*-Butyllithium (3.72 mL, 7.43 mmol (2.0 M solution in hexanes)) was added dropwise to a solution of (2-ethynylphenyl) (methyl)-sulfane (1.00 g, 6.75 mmol) in anhydrous tetrahydrofuran (THF) (10.0 mL) at −78 °C (dry ice-acetone bath) and the resultant yellow suspension left to stir at this temperature for 0.5 h. The dry ice-acetone bath was replaced with ice-bath and the reaction mixture was allowed to warm to 0 °C and stirred for 0.5 h at this temperature. The reaction mixture was placed back in dry ice-acetone bath and diphenylphosphinic chloride (1.75 g, 7.43 mmol) in THF was added dropwise and the resulting mixture was left to stir overnight. Saturated ammonium chloride (40 mL) and diethyl ether (50 mL) were added to the reaction mixture and the organic layer was separated. Organic layer was washed with water (2 × 30 mL) followed by brine (30 mL), dried over anhydrous $MgSO_4$, and concentrated to a dark yellow oil which was subjected to chromatography on silica eluting with 50% diethyl

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ether in petroleum spirits followed by 100% diethyl ether providing **5** as a yellow oil (1.50 g, 65% yield). R_f (100% diethyl ether): 0.35; ^{31}P NMR (162 MHz, $CDCl_3$): δ 8.49; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01−7.95 (m, 4H), 7.56−7.46 (m, 7H), 7.42−7.37 (m, 1H), 7.22−7.20 (m, 1H), 7.15−7.11 (m, 1H), 2.50 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 143.8 (d, J = 1.7 Hz), 133.9 (d, J = 1.9 Hz), 133.8 (s), 132.6 (s), 132.3 (d, J = 2.9 Hz), 131.3 (d, J = 11.3 Hz), 131.1 (s), 128.7 (d, J = 13.6 Hz), 124.7 (d, J = 18.3 Hz), 118.5 (d, J = 4.0 Hz), 102.8 (d, J = 29.8 Hz), 88.8 (d, J = 168.9 Hz), 15.5 (s); HRMS (APCI): calculated for $C_{21}H_{17}OPS$ $[M]^+$ (m/z) 348.0732; found = 348.0740.

Diethyl ((2-(Methylthio)phenyl)ethynyl)phosphonate (6). This material was prepared using the procedure described above for **5** using (2-ethynylphenyl) (methyl)sulfane (2.00 g, 13.51 mmol), *n*-butyllithium (7.43 mL, 14.8 mmol (2.0 M solution in hexanes)), and diethyl phosphorochloridate (2.55 g, 14.8 mmol). The crude product was subjected to column chromatography on silica gel eluting with 100% diethyl ether providing **6** as a light yellow oil (2.5 g, 65% yield). R_f (100% diethyl ether): 0.58; ^{31}P NMR: δ −6.24 ppm; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53−7.51 (m, 1H), 7.42−7.38 (m, 1H), 7.20−7.18 (m, 1H), 7.14−7.10 (m, 1H), 4.30−4.22 (m, 4H), 2.50 (s, 3H), 1.43−1.40 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 143.7 (d, J = 2.3 Hz), 133.8 (d, J = 2.6 Hz), 131.1 (s), 124.6 (s), 124.5 (s), 117.8 (d, J = 5.7 Hz), 96.5 (d, J = 52.1 Hz), 84.4 (d, J = 295.6 Hz), 63.5 (d, J = 5.5 Hz), 16.3 (d, J = 7.1 Hz), 15.2 (s); HRMS (APCI): calculated for $C_{13}H_{18}O_3PS$ $[M + H]^+$ (m/z) 285.0709; found = 285.0717.

(3-Iodobenzo[*b*]thiophen-2-yl)diphenylphosphine Oxide (8). Compound **5** (1.20 g, 3.45 mmol) was dissolved in anhydrous dichloroethane (15.0 mL), and iodine (1.76 g, 6.95 mmol) was added at room temperature. The reaction mixture was stirred at 50 °C for 5 h, cooled to room temperature and was quenched with saturated $Na_2S_2O_3$ (20.0 mL). The organic layer was separated, washed with brine, dried over anhydrous $MgSO_4$, and recovered to get **8** as a light brown solid (1.40 g, 88% yield). mp = 180−181 °C; ^{31}P NMR: δ 22.71; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90−7.87 (m, 1H), 7.84−7.76 (m, 5H), 7.64−7.59 (m, 2H), 7.54−7.45 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 143.1 (d, J = 11.4 Hz), 141.5 (d, J = 5.4 Hz), 133.6 (s), 132.7 (d, J = 2.8 Hz), 132.4 (d, J = 10.3 Hz), 132.0 (s), 130.9 (s), 128.7 (d, J = 12.8 Hz), 127.1 (d, J = 47.1 Hz), 126.1 (s), 122.3 (d, J = 1.5 Hz), 90.6 (d, J = 6.1 Hz); HRMS (APCI): calculated for $C_{20}H_{14}OIPS$ $[M]^+$ (m/z) 459.9542; found = 459.9546.

Diphenyl(3-(phenylselanyl)benzo[*b*]thiophen-2-yl)-phosphine Oxide (9). Compound **5** (250 mg, 0.72 mmol) was dissolved in anhydrous dichloroethane (5.0 mL), and phenylselenyl bromide (222 mg, 0.94 mmol) was added at room temperature. The reaction mixture was refluxed for 48 h, cooled to room temperature, diluted with dichloromethane, and quenched with saturated $Na_2S_2O_3$ (15.0 mL). The organic layer was separated, washed with brine, dried over anhydrous $MgSO_4$, and recovered to get crude material which was subjected to chromatography on silica gel eluting with 50% diethyl ether in petroleum spirits followed by 100% diethyl ether providing **9** as an off-white solid (180 mg, 51% yield). R_f (100% diethyl ether): 0.40; mp = 62−63.1 °C; ^{77}Se NMR ($CDCl_3$, 76.3 MHz): δ 294.90; ^{31}P NMR ($CDCl_3$, 162 MHz): δ 21.60; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86−7.79 (ddt, J = 11.5, 7.8, 2.7 Hz, 6H), 7.55−7.50 (m, 2H), 7.44−7.39 (m, 5H), 7.36−7.32 (ddd, J = 8.1, 7.1, 1.1 Hz, 1H), 7.07−6.99 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 142.6 (d, J = 8.2 Hz), 142.5 (d, J = 2.3 Hz), 139.9 (d, J = 108.8 Hz), 132.9 (s), 132.4 (d, J = 2.8 Hz), 132.2 (d, J = 10.3 Hz), 131.8 (s), 131.5 (s), 130.5 (s), 129.1 (s), 128.7 (s), 128.6 (m), 128.5 (d, J = 12.7 Hz), 126.7 (d, J = 13.0 Hz), 125.6 (d, J = 13.2 Hz), 122.5 (d, J = 1.7 Hz); HRMS (APCI): calculated for $C_{26}H_{20}OPSSe$ $[M + H]^+$ (m/z) 491.0132; found = 491.0140.

Diethyl (3-Iodobenzo[*b*]thiophen-2-yl)phosphonate (10). Compound **6** (800 mg, 2.82 mmol) was dissolved in anhydrous dichloroethane (10.0 mL), and iodine (1.43 g, 5.64 mmol) was added at room temperature. The reaction mixture was stirred at 50 °C for 5 h, cooled to room temperature, diluted with dichloromethane (15.0 mL), and quenched with saturated $Na_2S_2O_3$ (20.0 mL). The organic layer was separated, washed with brine, dried over anhydrous $MgSO_4$, and recovered to get **10** as a yellow solid (900 mg, 81% yield). mp = 81−82 °C; ^{31}P NMR: δ 8.98 ppm; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92−7.85 (m, 2H), 7.53−7.48 (m, 2H), 4.30−4.17 (m, 4H), 1.41−1.38 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 142.5 (d, J = 16.7 Hz), 141.5 (d, J = 7.4 Hz), 129.6 (d, J = 208.0 Hz), 127.4 (s), 127.3 (d, J = 0.6 Hz), 126.0 (d, J = 0.9 Hz), 122.5 (d, J = 2.4 Hz), 88.6 (d, J = 8.1 Hz), 63.5 (d, J = 5.3 Hz), 16.4 (d, J = 6.8 Hz); HRMS (APCI): calculated for $C_{12}H_{14}IO_3PS$ $[M]^+$ (m/z) 395.9440; found = 395.9448.

(3-(4-Chlorophenyl)benzo[*b*]thiophen-2-yl)-diphenylphosphine Oxide (16). Compound **8** (150 mg, 0.33 mmol) and (4-chlorophenyl)boronic acid (78 mg, 0.50 mmol) were added in 1,2-dimethoxyethane (10.0 mL) in a 50 mL round-bottom flask followed by the addition of cesium carbonate (162 mg, 0.50 mmol) at room temperature. The reaction suspension was degassed for 10 min followed by the addition of tetrakis(triphenylphosphine)-palladium(0) (58 mg, 0.05 mmol) at room temperature. The resulting yellow suspension was refluxed overnight and solvent was evaporated off to get crude solid, which was subjected to column chromatography on silica (100% diethyl ether) to afford title compound **16** (95 mg, 64%) as a light yellowish solid. R_f (100% diethyl ether): 0.52; mp = 197−199 °C; ^{31}P NMR: δ 19.53; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86−7.81 (m, 1H), 7.73−7.65 (m, 4H), 7.54−7.34 (m, 9H), 7.27−7.21 (m, 2H), 7.18−7.13 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 145.6 (d, J = 7.7 Hz), 142.2 (d, J = 6.5 Hz), 140.8 (d, J = 12.3 Hz), 134.2 (s), 133.1 (s), 132.5 (d, J = 3.1 Hz), 132.2 (d, J = 2.9 Hz), 132.1 (s), 132.0 (s), 131.8 (d, J = 4.7 Hz), 131.1 (s), 128.5 (s), 128.3 (d, J = 10.8 Hz), 126.7 (s), 124.8 (d, J = 70.6 Hz), 122.4 (d, J = 1.7 Hz); HRMS (APCI): calculated for $C_{26}H_{17}ClOPS$ $[M-H]^+$ (m/z) 443.0421; found = 443.0425.

Diethyl (3-(4-Chlorophenyl)benzo[*b*]thiophen-2-yl)-phosphonate (17). This material was prepared using the procedure described above for **16** using compound **10** (250 mg, 0.63 mmol), (4-chlorophenyl)boronic acid (177 mg, 1.13 mmol), and cesium carbonate (409 mg, 1.26 mmol). The crude solid was subjected to column chromatography on silica (100% diethyl ether) to afford title compound **17** (130 mg, 54%) as a light yellow oil. R_f (100% diethyl ether): 0.62; ^{31}P NMR ($CDCl_3$, 162 MHz): δ 10.83; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95−7.90 (m, 1H), 7.56 (dd, J = 8.1, 0.8 Hz, 1H), 7.50−7.44 (m, 5H), 7.38 (ddd, J = 8.1, 5.6, 1.1 Hz, 1H), 4.13−3.94 (m, 4H), 1.24−1.18 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 143.9 (d, J = 11.0 Hz), 142.1 (d, J = 8.3 Hz), 140.2 (d, J = 18.1 Hz), 134.6 (s), 132.9 (d, J = 3.4 Hz), 131.5 (d, J = 1.0 Hz), 128.5 (s), 126.9 (s), 126.7 (s), 125.1 (d, J = 1.0 Hz), 124.9 (s), 124.6 (d, J = 1.1 Hz), 122.5 (d, J = 2.6 Hz), 62.9 (d, J = 5.7 Hz), 16.3 (d, J = 6.8 Hz); HRMS (APCI): calculated for $C_{18}H_{18}ClO_3PS$ $[M]^+$ (m/z) 380.0397; found =380.0404.

(*E*)-Diphenyl(3-styrylbenzo[*b*]thiophen-2-yl)phosphine Oxide (18). Compound **8** (100 mg, 0.22 mmol) was dissolved in dimethylformamide (3.0 mL) at room temperature under N_2(g) atmosphere. To this solution was added $Pd(OAc)_2$ (22 mg, 0.10 mmol), triphenylphosphine (78 mg, 0.30 mmol), potassium acetate (212 mg, 2.17 mmol), and styrene (45 mg, 0.43 mmol), and the resulting reaction mixture was stirred at 80 °C for 18 h. The reaction mixture was cooled to room temperature, diluted with water (10 mL), and extracted with ethyl acetate (2 × 15 mL). The organic layer was washed with water followed by brine, dried (anhydrous $MgSO_4$), and concentrated to get reddish-brown solid which was subjected to column chromatography on silica (100% diethyl ether) to get **18** (40 mg, 42%) as a dark red solid. R_f (100% diethyl ether): 0.60; mp = 137−138.3 °C; ^{31}P NMR: δ 21.81; ^{1}H NMR (400 MHz, $CDCl_3$: δ 8.19−8.14 (m, 1H), 7.84−7.76 (m, 5H), 7.58−7.42 (m, 9H), 7.34−7.26 (m, 4H), 7.26−7.19 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 143.3 (d, J = 7.0 Hz), 142.8 (d, J = 6.9 Hz), 139.3 (d, J = 12.3 Hz), 137.1 (s), 135.1 (s), 133.3 (s), 132.4 (d, J = 2.8 Hz), 132.1 (d, J = 10.3 Hz), 128.8 (s), 128.7 (d, J = 46.3 Hz), 128.6 (d, J = 3.7 Hz), 128.1 (s), 127.4 (d, J = 168.8 Hz), 126.9 (s), 125.8 (d, J = 110.1 Hz), 124.9 (d, J = 58.4 Hz), 122.7 (d, J = 1.8 Hz), 121.5 (d, J = 4.2 Hz); HRMS (APCI): calculated for $C_{28}H_{21}OPS$ $[M]^+$ (m/z) 436.1045; found = 436.1046.

Diethyl (3-((4-Methoxyphenyl)ethynyl)benzo[*b*]thiophen-2-yl)phosphonate (19). Compound **10** (285 mg, 0.72 mmol) was

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dissolved in 1:1 solvent mixture of diisopropylamine and THF (total volume =10.0 mL). To this mixture was added $Pd(PPh_3)Cl_2$ (140 mg, 0.2 mmol) and CuI (57 mg, 0.3 mmol), and the resulting suspension was stirred for 15 min while N_2 was bubbled through the mixture. The reaction mixture was heated to 60 °C and 1-ethynyl-4-methoxybenzene (237 mg, 1.80 mmol) in THF (5.0 mL) was added to the stirred solution dropwise over 2 h and left to stir overnight. The mixture was filtered and concentrated to a residue that was taken in diethyl ether (30.0 mL), washed with water (50.0 mL) followed by brine, dried over anhydrous $MgSO_4$, and concentrated to a brown liquid which was subjected to column chromatography on silica (100% diethyl ether) to afford title compound **19** (190 mg, 65%) as a dark brown oil. R_f (100% diethyl ether): 0.55; ^{31}P NMR: δ 9.76; ^1H NMR (400 MHz, $CDCl_3$): δ 8.12−8.08 (m, 1H), 7.90−7.86 (m, 1H), 7.60−7.57 (m, 2H), 7.53−7.48 (m, 2H), 6.94−6.91 (m, 2H), 4.34−4.19 (m, 4H), 3.86 (s, 3H), 1.39−1.36 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 160.3 (s), 141.5 (d, J = 8.5 Hz), 140.3 (d, J = 16.5 Hz), 133.5 (s), 131. 6−131.3 (m), 129.6−129.3 (m), 127.1 (s), 125.7 (d, J = 8.3 Hz), 125.4 (s), 124.5 (s), 122.6 (d, J = 2.5 Hz), 114.9 (s), 114.3 (s), 97.5 (s), 81.2 (d, J = 5.1 Hz), 63.3 (d, J = 5.3 Hz), 55.5 (s), 16.5 (d, J = 6.8 Hz); HRMS (APCI): calculated for $C_{21}H_{21}O_4PS$ $[M]^+$ (m/z) 400.0893; found = 400.0890.

Diphenyl(3-(thiophen-2-yl)benzo[*b*]thiophen-2-yl)-phosphine Oxide (20). Compound **8** (400 mg, 0.87 mmol) was dissolved in toluene (10.0 mL) in a 100 mL round-bottom flask followed by the addition of tributyl(thiophen-2-yl)stannane (488 mg, 1.31 mmol) at room temperature. The resulting solution was degassed for 0.5 h followed by the addition of bis(triphenylphosphine)-palladium(II) dichloride (140 mg, 0.20 mmol) at room temperature. The yellowish-orange reaction mixture was heated to reflux overnight. Solvent was evaporated under reduced pressure and the residue was purified by silica gel chromatography (100% diethyl ether) to get 220 mg (61%) of **20** as a brown solid. R_f (100% diethyl ether): 0.36; mp = 146.8−148.2 °C; ^{31}P NMR: δ 20.05; ^1H NMR (400 MHz, $CDCl_3$): δ 7.91−7.87 (m, 1H), 7.84−7.80 (m, 1H), 7.74−7.67 (m, 4H), 7.53−7.36 (m, 8H), 7.29 (dd, J = 3.6, 1.2 Hz, 1H), 7.22 (dd, J = 5.1, 1.2 Hz, 1H), 6.86 (dd, J = 5.1, 3.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 142.1 (d, J = 6.7 Hz), 140.9 (d, J = 11.8 Hz), 139.0 (d, J = 7.2 Hz), 133.7 (d, J = 3.6 Hz), 132.9 (s), 132.6−132.5 (m), 132.2 (d, J = 2.9 Hz), 132.0 (s), 131.9 (d, J = 10.1 Hz), 131.8 (s), 130.9 (s), 128.4 (d, J = 12.6 Hz), 127.3 (d, J = 20.0 Hz), 126.7 (s), 125.1 (d, J = 39.1 Hz) 122.3 (d, J = 1.8 Hz); HRMS (APCI): calculated for $C_{24}H_{17}OPS_2$ $[M]^+$ (m/z) 416.0453; found = 416.0446.

Diethyl (3-(Thiophen-2-yl)benzo[*b*]thiophen-2-yl)-phosphonate (21). This material was prepared using the procedure described above for **20** using compound **10** (200 mg, 0.50 mmol), tributyl(thiophen-2-yl)stannane (377 mg, 1.01 mmol), and bis-(triphenylphosphine)palladium(II) dichloride (70 mg, 0.10 mmol). The crude residue was purified by silica gel chromatography (100% diethyl ether) to get 110 mg (62%) of **21** as a light brown oil. R_f (100% diethyl ether): 0.65; ^{31}P NMR ($CDCl_3$, 162 MHz): δ 10.60; ^1H NMR (400 MHz, $CDCl_3$): δ 7.94−7.84 (m, 2H), 7.52−7.35 (m, 4H), 7.18 (dt, J = 7.9, 3.9 Hz, 1H), 4.16−3.97 (m, 4H), 1.23 (td, J = 7.1, 0.5 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 141.9−141.8 (m), 140.6−140.4 (m), 137.4−137.3 (m), 133.9 (d, J = 3.9 Hz), 129.6 (t, J = 10.9 Hz), 128.3 (d, J = 8.7 Hz), 127.2 (d, J = 16.7 Hz), 126.7 (s), 126.3 (d, J = 4.3 Hz), 125.1 (d, J = 1.2 Hz), 124.9 (d, J = 1.1 Hz), 122.4 (d, J = 2.6 Hz), 62.9 (d, J = 5.5 Hz), 16.2 (d, J = 7.0 Hz); HRMS (APCI): calculated for $C_{16}H_{17}O_3PS_2$ $[M]^+$ (m/z) 352.0351; found = 352.0354.

Diphenyl(3-(thiophen-2-yl)benzo[*b*]thiophen-2-yl)-phosphane (22). Compound **20** (200 mg, 0.48 mmol) was dissolved in toluene (5.0 mL) in a two-neck, 50 mL round-bottom flask followed by the addition of trichlorosilane (0.48 mL, 4.8 mmol) and triethylamine (0.66 mL, 4.8 mmol) at room temperature. The reaction mixture was then stirred vigorously at reflux for 18 h under N_2 stream. The reaction mixture was cooled to ambient temperature and diluted with deoxygenated ethyl acetate and $NaHCO_3$ solutions. The organic layer was separated, washed with deoxygenated $NaHCO_3$ followed by deoxygenated brine, dried over anhydrous $MgSO_4$, and recovered to get 145 mg (75.5%) of **22** as a light brown solid. mp = 125−127 °C; ^{31}P NMR: δ −23.65, ^1H NMR (400 MHz, $CDCl_3$): δ 7.93−7.89 (m, 1H), 7.77−7.73 (m, 1H), 7.45−7.32 (m, 13H), 7.12 (dd, J = 5.1, 3.5 Hz, 1H), 7.05 (dt, J = 3.5, 1.2 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 142.8 (s), 140.6 (d, J = 4.5 Hz), 138.5 (s), 138.2 (s), 137.9 (s), 137.7 (s), 137.4 (d, J = 9.2 Hz), 135.5 (d, J = 4.8 Hz), 133.7 (d, J = 19.9 Hz), 129.2 (s), 128.8 (d, J = 3.9 Hz), 128.7 (d, J = 7.1 Hz), 126.9 (d, J = 56.2 Hz), 124.9 (d, J = 62.0 Hz), 123.8 (s), 122.3 (s); HRMS (APCI): calculated for $C_{24}H_{18}PS_2$ $[M + H]^+$ (m/z) 401.0582; found = 401.0587.

(3-((2-(Dimethylamino)ethyl)amino)benzo[*b*]thiophen-2-yl)-diphenylphosphine Oxide (23). Compound **8** (200 mg, 0.43 mmol) was dissolved in toluene (5.0 mL). To this mixture was added Cs_2CO_3 (211 mg, 0.65 mmol) and CuI (38.0 mg, 0.20 mmol), and the resulting suspension was stirred for 15 min while N_2 (g) was bubbled through the mixture. Then *N*,*N*-dimethylethane-1,2-diamine (265 mg, 3.0 mmol) was added to the stirred solution and the resulting reaction mixture was refluxed overnight. The mixture was diluted with ethyl acetate (20.0 mL) and washed with water (2 × 30.0 mL) followed by brine (30.0 mL). The organic layer was dried ($MgSO_4$) and concentrated to get crude brown oil which was subjected to column chromatography on silica (20% methanol/ethyl acetate) to afford title compound **23** (80 mg, 44%) as a light brown oil. R_f (20% methanol/ethyl acetate): 0.30; ^{31}P NMR: δ 25.34; ^1H NMR (400 MHz, $CDCl_3$): δ 7.95 (dd, J = 6.6, 2.3 Hz, 1H), 7.80−7.73 (m, 4H), 7.66−7.62 (m, 1H), 7.59−7.52 (m, 2H), 7.50−7.44 (m, 4H), 7.39−7.31 (m, 2H), 6.28 (s, 1H), 3.62−3.52 (m, 2H), 2.47 (t, J = 6.4 Hz, 2H), 2.20 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 153.1 (d, J = 5.6 Hz), 142.0 (d, J = 7.7 Hz), 134.6 (d, J = 11.3 Hz), 133.8 (d, J = 109.3 Hz), 132.2 (d, J = 2.8 Hz), 132.0 (d, J = 10.4 Hz), 128.6 (d, J = 12.5 Hz), 126.7 (s), 124.1 (s), 123.6 (s), 122.9 (d, J = 2.1 Hz), 100.5 (d, J = 114.3 Hz), 59.4 (s), 45.4 (s), 45.3 (s); HRMS (APCI): calculated for $C_{24}H_{26}ON_2PS$ $[M + H]^+$ (m/z) 421.1498; found = 421.1495.

Diphenyl(3-(trimethylstannyl)benzo[*b*]thiophen-2-yl)-phosphine Oxide (24). Compound **8** (50 mg, 0.11 mmol) was dissolved in anhydrous THF (5.0 mL) and the reaction solution was cooled to −78 °C (dry ice-acetone bath) under N_2. The yellow solution was left to stir at this temperature for 30 min followed by the addition of *n*-butyllithium (0.06 mL (2.0 M solution in hexanes), 0.12 mmol). After stirring for 5 min, chlorotrimethylstannane (26 mg 0.13 mmol) was added dropwise and the dark yellow solution was stirred for 10 min at this temperature. The dry ice-acetone bath was removed and the reaction mixture was allowed to warm to room temperature and stirred for 30 min at this temperature. Saturated ammonium chloride (15 mL) and diethyl ether (20 mL) were added to the reaction mixture and the organic layer was separated. Organic layer was washed with brine (15 mL), dried over anhydrous $MgSO_4$, and concentrated to a dark yellow oil which was subjected to chromatography on silica gel eluting with 100% diethyl ether providing **24** as a yellow oil (35 mg, 64% yield). R_f (100% diethyl ether): 0.70; ^{31}P NMR: δ 23.64; ^1H NMR (400 MHz, $CDCl_3$): δ 8.17−8.13 (m, 1H), 7.87−7.84 (m, 1H), 7.77−7.70 (m, 4H), 7.59−7.53 (m, 2H), 7.50−7.43 (m, 4H), 7.43−7.36 (m, 2H), 0.42 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 152.1 (d, J = 16.0 Hz), 146.8 (d, J = 18.8 Hz), 144.3 (d, J = 4.3 Hz), 138.8 (d, J = 116.5 Hz), 133.7 (d, J = 107.5 Hz), 132.3 (d, J = 2.8 Hz), 132.1 (d, J = 10.3 Hz), 128.6 (d, J = 12.5 Hz), 127.0 (s), 125.8 (s), 124.6 (s), 122.3 (s), 1.1 (s); HRMS (APCI): calculated for $C_{23}H_{24}OPS[120]Sn$ $[M + H]^+$ (m/z) 499.0302; found =499.0301; calculated for $C_{23}H_{24}OPS[116]Sn$ $[M + H]^+$ (m/z) 495.0297; found = 495.0297.

Ethyl Hydrogen (3-((4-Methoxyphenyl)ethynyl)benzo[*b*]-thiophen-2-yl)phosphonate (25). Compound **19** (160 mg, 0.40 mmol) was dissolved in ethanol (2.0 mL), and NaOH (aq) (1.0 M, 2.4 mL) solution was added at room temperature. The resulting reaction mixture was refluxed for 3 h, cooled to room temperature, diluted with conc. HCl (aq) (2.0 mL), and extracted with ethyl acetate (20.0 mL). The organic layer was washed with water (2 × 20.0 mL) followed by brine, dried over anhydrous $MgSO_4$, and concentrated to a brown liquid (130 mg, 87%) which was used as such. ^{31}P NMR: 12.76; ^1H NMR (400 MHz, $CDCl_3$): δ 8.05−8.00 (m, 1H), 7.79−7.75 (m, 1H), 7.59−7.50 (m, 2H), 7.49−7.38 (m, 2H), 6.84−6.74 (m, 2H), 4.28−

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4.15 (m, 2H), 3.77 (s, 3H), 1.33 (t, J = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 160.0 (s), 141.2 (d, J = 8.5 Hz), 140.2 (d, J = 16.2 Hz), 133.5 (s), 132.2 (d, J = 10.0 Hz), 132.1 (d, J = 2.5 Hz), 128.6 (d, J = 12.2 Hz), 126.9 (s), 125.1 (s), 124.4 (s), 122.4 (s), 115.0 (s), 114.0 (s), 97.7 (s), 63.2 (d, J = 4.7 Hz), 55.3 (s), 16.3 (d, J = 6.7 Hz); HRMS (APCI): calculated for $C_{19}H_{17}O_4PS$ $[M]^+$ (m/z) 372.0580; found = 372.0581.

1-Ethoxy-3-(4-methoxyphenyl)benzo[4,5]thieno[2,3-*c*][1,2]-oxaphosphinine 1-Oxide (26). Compound **25** (38 mg, 0.102 mmol) was dissolved in anhydrous dichloromethane (1.5 mL), and methanesulfonic acid (0.01 mL, 0.20 mmol) was added at room temperature. The reaction mixture was stirred overnight at room temperature, diluted with water (3.0 mL), and extracted with dichloromethane (10.0 mL). The organic layer was separated, washed with water (10.0 mL) followed by brine, dried over anhydrous $MgSO_4$, and concentrated to get crude solid which was subjected to column chromatography on silica (100% diethyl ether) to get **26** (28 mg, 74%) as a brown solid. R_f (100% diethyl ether): 0.52; mp = 122−123 °C; ^{31}P NMR: δ 7.49; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05−8.00 (m, 1H), 7.98−7.94 (m, 1H), 7.83−7.77 (m, 2H), 7.58−7.50 (m, 2H), 7.01−6.95 (m, 3H), 4.27−4.16 (m, 2H), 3.88 (s, 3H), 1.36 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 161.2 (s), 152.9 (d, J = 11.5 Hz), 143.1 (d, J = 10.4 Hz), 142.4 (d, J = 8.4 Hz), 135.7 (d, J = 15.4 Hz), 127.8 (s), 126.8 (s), 125.4 (d, J = 7.5 Hz), 125.2 (d, J = 1.1 Hz), 123.3 (d, J = 3.0 Hz), 122.8 (d, J = 1.2 Hz), 116.4 (s), 114.3 (s), 95.4 (d, J = 10.4 Hz), 64.1 (d, J = 6.6 Hz), 55.6 (s), 16.5 (d, J = 6.3 Hz); HRMS (APCI): calculated for $C_{19}H_{17}O_4PS$ $[M]^+$ (m/z) 372.0580; found = 372.0584.

1-Ethoxy-4-iodo-3-(4-methoxyphenyl)benzo[4,5]thieno[2,3-*c*][1,2]oxaphosphinine 1-Oxide (27). Compound **25** (30 mg, 0.08 mmol) was dissolved in anhydrous dichloromethane (1.5 mL), and *N*-iodosuccinimide (36 mg, 0.16 mmol) was added at room temperature. The resulting reaction solution was stirred overnight at room temperature, quenched with saturated sodium thiosulfate (3.0 mL), and extracted with dichloromethane (5.0 mL). The organic layer was separated, washed with brine, dried over anhydrous $MgSO_4$, and concentrated to afford title compound **27** (32 mg, 81% yield) as a greenish-brown solid. mp > 110 °C (decomposed); ^{31}P NMR: δ 6.08; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.11−9.06 (m, 1H), 7.97−7.93 (m, 1H), 7.71−7.66 (m, 2H), 7.58−7.51 (m, 2H), 7.01−6.96 (m, 2H), 4.38−4.28 (m, 2H), 3.89 (s, 3H), 1.42 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 161.1 (s), 151.6 (d, J = 11.0 Hz), 143.3 (d, J = 10.6 Hz), 140.4 (d, J = 8.1 Hz), 137.1 (d, J = 14.5 Hz), 132.2 (d, J = 9.9 Hz), 132.1 (s), 128.6 (d, J = 12.1 Hz), 128.4 (d, J = 5.8 Hz), 127.2 (s), 125.4 (d, J = 266.6 Hz), 123.2 (d, J = 3.3 Hz), 120.6 (d, J = 198.9 Hz), 113.5 (s), 65.2 (d, J = 10.9 Hz), 64.6 (d, J = 6.5 Hz), 16.6 (d, J = 6.1 Hz); HRMS (APCI): calculated for $C_{19}H_{16}IO_4PS$ $[M]^+$ (m/z) 497.9552; found = 497.9549.

Bis((2-(methylthio)phenyl)ethynyl) (Phenyl)phosphine Oxide (30). 2-Iodothioanisole (1.32 g, 5.3 mmol) was dissolved in 1:1 solvent mixture of diisopropylamine and THF (total 20.0 mL). To this mixture was added $Pd(PPh_3)Cl_2$ (175 mg, 0.25 mmol) and CuI (95 mg, 0.50 mmol), and the resulting suspension was stirred for 30 min while N_2 was bubbled through the mixture. The reaction mixture was heated to 60 °C and diethynyl(phenyl)phosphine oxide (400 mg, 2.3 mmol) in THF (6.0 mL) was added to the stirred solution dropwise over 2.5 h and left to stir overnight. The mixture was filtered and concentrated to a residue that was taken in diethyl ether (50.0 mL), washed with water (50.0 mL) followed by brine, dried over anhydrous $MgSO_4$, and concentrated to a dark brown mass which was subjected to column chromatography on silica (100% diethyl ether) to afford title compound **30** (480 mg, 50%) as a light brown semisolid. R_f (100% diethyl ether): 0.45; ^{31}P NMR ($CDCl_3$, 162 MHz): δ −19.45; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.22−8.16 (m, 2H), 7.61−7.53 (m, 5H), 7.40−7.36 (m, 2H), 7.21−7.19 (m, 2H), 7.14−7.10 (m, 2H), 2.47 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 144.1 (d, J = 2.0 Hz), 133.9 (d, J = 2.1 Hz), 133.7, 132.7 (d, J = 3.1 Hz), 131.1, 130.9 (d, J = 12.8 Hz), 128.8 (d, J = 15.1 Hz), 125.0, 124.6, 118.4 (d, J = 4.5 Hz), 101.3 (d, J = 37.7 Hz), 89.3 (d, J = 201.5 Hz), 15.5; HRMS (APCI): calculated for $C_{24}H_{19}OPS_2$ $[M]^+$ (m/z) 418.0609; found = 418.0623.

Bis(3-iodobenzo[*b*]thiophen-2-yl) (Phenyl)phosphine Oxide (31). Compound **30** (70 mg, 0.17 mmol) was dissolved in anhydrous dichloroethane (5.0 mL), and iodine (215 mg, 0.85 mmol) was added at room temperature. The reaction mixture was stirred at 50 °C for 6 h, cooled to room temperature, diluted with dichloromethane (10.0 mL), and quenched with saturated $Na_2S_2O_3$ (15.0 mL). The organic layer was separated, washed with brine, dried over anhydrous $MgSO_4$, and recovered to get **31** as a light brown solid (85 mg, 82% yield). R_f (100% diethyl ether, for TLC): 0.69; mp = 236−238 °C; ^{31}P NMR ($CDCl_3$, 162 MHz): δ 15.65; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.00−7.92 (m, 4H), 7.83−7.79 (m, 2H), 7.70−7.65 (m, 1H), 7.58−7.48 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 143.1 (d, J = 12.3 Hz), 141.9 (d, J = 6.0 Hz), 133.3 (d, J = 3.0 Hz), 132.7 (s), 132.6 (d, J = 10.8 Hz), 131.3 (s), 130.1 (s), 128.8−128.7 (d, J = 13.4 Hz), 127.6−127.2 (d, J = 44.3 Hz), 126.1 (s), 122.5 (d, J = 1.7 Hz), 91.5−91.4 (d, J = 6.5 Hz); HRMS (APCI): calculated for $C_{22}H_{13}OI_2PS_2$ $[M]^+$ (m/z) 641.8229; found = 641.8235.

Bis(3-bromobenzo[*b*]thiophen-2-yl) (Phenyl)phosphine Oxide (32). Compound **30** (100 mg, 0.24 mmol) was dissolved in anhydrous dichloroethane (5.0 mL), and cupric bromide (268 mg, 1.20 mmol) was added at room temperature. The reaction mixture was refluxed for 48 h, cooled to room temperature, quenched with saturated $Na_2S_2O_3$ (10.0 mL), and diluted with dichloromethane (10.0 mL). The organic layer was separated, dried over anhydrous $MgSO_4$, and concentrated to a light green mass which was subjected to column chromatography on silica (100% diethyl ether) to afford title compound **32** (120 mg, 91%) as a light green solid. R_f (100% diethyl ether): 0.61; mp = 222−224 °C; ^{31}P NMR ($CDCl_3$, 162 MHz): δ 13.31; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.02−7.93 (m, 4H), 7.85−7.81 (m, 2H), 7.70−7.66 (m, 1H), 7.58−7.50 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 141.5 (d, J = 6.4 Hz), 139.5 (d, J = 10.8 Hz), 133.4 (d, J = 2.5 Hz), 132.3 (d, J = 11.0 Hz), 130.6 (d, J = 119.8 Hz), 128.8 (d, J = 13.5 Hz), 128.2 (s), 127.7 (s), 125.9 (s), 124.7 (s), 122.6 (s), 117.8 (d, J = 4.7 Hz); HRMS (APCI): calculated for $C_{22}H_{13}OBr_2PS_2$ $[M]^+$ (m/z) 545.8507; found = 545.8510.

Bis(3-chlorobenzo[*b*]thiophen-2-yl) (phenyl)phosphine Oxide (33). This material was prepared using the procedure described above for **32** using compound **30** (90 mg, 0.21 mmol) and anhydrous cupric chloride (113 mg, 0.84 mmol). The crude solid was subjected to column chromatography on silica eluting with 100% diethyl ether providing **33** as an off white solid (80 mg, 83% yield). R_f (100% diethyl ether): 0.60; mp = 207−209 °C; ^{31}P NMR ($CDCl_3$, 162 MHz): δ 11.32; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02−7.92 (m, 4H), 7.85−7.81 (m, 2H), 7.69−7.65 (m, 1H), 7.58−7.50 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 141.1 (d, J = 7.0 Hz), 137.8 (d, J = 10.2 Hz), 133.4 (d, J = 3.0 Hz), 132.0 (d, J = 11.2 Hz), 130.7 (d, J = 119.9 Hz), 129.8 (d, J = 4.1 Hz), 128.8 (d, J = 13.7 Hz), 127.7 (s), 127.0 (d, J = 116.9 Hz), 125.7 (s), 123.4 (s), 122.8 (d, J = 1.9 Hz); HRMS (APCI): calculated for $C_{22}H_{13}OCl_2PS_2$ $[M]^+$ (m/z) 457.9517; found = 457.9521.

(3-Bromobenzo[*b*]thiophen-2-yl)((2-(methylthio)phenyl)-ethynyl) (Phenyl)phosphine Oxide (34). Compound **30** (70 mg, 0.17 mmol) was dissolved in anhydrous dichloroethane (5.0 mL), and cupric bromide (76 mg, 0.34 mmol) was added at room temperature. The reaction mixture was stirred overnight at room temperature, diluted with dichloromethane (10.0 mL), and quenched with saturated $Na_2S_2O_3$ (10.0 mL). The organic layer was separated, dried over anhydrous $MgSO_4$, and concentrated to a light brown crude mass which was subjected to column chromatography on silica (100% diethyl ether) to afford title compound **34** (60 mg, 74%) as a light brown oil. R_f (100% diethyl ether): 0.52; ^{31}P NMR ($CDCl_3$, 162 MHz): δ −1.33; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.16−8.10 (m, 2H), 7.91−7.85 (m, 2H), 7.62−7.59 (m, 2H), 7.55−7.47 (m, 4H), 7.44−7.39 (m, 1H), 7.24−7.22 (m, 1H), 7.17−7.13 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 144.2 (s), 141.2 (s), 141.2−141.1 (m), 139.7 (d, J = 11.4 Hz), 134.2 (s), 132.9 (s), 132.4 (s), 131.7 (d, J = 12.2 Hz), 131.4 (s), 131.1 (s), 128.7 (d, J = 14.5 Hz), 127.4 (s), 125.7 (s), 124.9 (s), 124.6 (s), 124.3 (s), 122.7 (s), 118.1 (s), 115.9−115.7 (m), 104.0−103.3 (m), 86.8 (s), 15.5 (s); HRMS (APCI): calculated for $C_{23}H_{16}OBrPS_2$ $[M]^+$ (m/z) 481.9558; found = 481.9561.

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(3-Bromobenzo[*b*]thiophen-2-yl)(3-iodobenzo[*b*]thiophen-2-yl) (phenyl)phosphine Oxide (35). Compound **34** (50 mg, 0.103 mmol) was dissolved in anhydrous dichloroethane (5.0 mL), and iodine (53 mg, 0.21 mmol) was added at room temperature. The reaction mixture was stirred at 50 °C for 6 h, cooled to room temperature, diluted with dichloromethane (10.0 mL), and quenched with saturated $Na_2S_2O_3$ (10.0 mL). The organic layer was separated, washed with brine, dried over anhydrous $MgSO_4$, and recovered to get **35** as a light yellow solid (50 mg, 82% yield). R_f (100% diethyl ether, for TLC): 0.62; mp = 242−245 °C; ^{31}P NMR ($CDCl_3$, 162 MHz): δ 14.44; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.01−7.90 (m, 4H), 7.85−7.78 (m, 2H), 7.69−7.65 (m, 1H), 7.58−7.48 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 143.0 (d, J = 12.3 Hz), 141.8 (d, J = 6.1 Hz), 141.6 (d, J = 6.4 Hz), 139.6 (d, J = 10.9 Hz), 133.3 (d, J = 2.9 Hz), 132.6 (s), 132.4 (d, J = 10.9 Hz), 131.4 (s), 131.3 (s), 130.1 (s), 128.9 (d, J = 117.9 Hz), 128.8 (d, J = 13.5 Hz), 127.6 (d, J = 1.6 Hz), 127.2 (s), 126.0 (d, J = 22.0 Hz), 124.7 (s), 122.7 (d, J = 1.7 Hz), 122.4 (d, J = 1.7 Hz), 117.8 (d, J = 4.7 Hz), 91.2 (d, J = 6.6 Hz); HRMS (APCI): calculated for $C_{22}H_{13}OBrIPS_2$ $[M]^+$ (m/z) 593.8368; found = 593.8375.

Bis(benzo[*b*]thiophen-2-yl)-1-phosphinine-4-(2-phenylethene-1,1-diyl)-1-oxide (36). This material was prepared using the procedure described above for **18** using compound **31** (42 mg, 0.07 mmol), styrene (29 mg, 0.28 mmol), $Pd(OAc)_2$ (6.7 mg, 0.03 mmol), triphenylphosphine (31 mg, 0.12 mmol), and potassium acetate (69 mg, 0.70 mmol). The crude mass was subjected to column chromatography on silica eluting with 100% diethyl ether providing **36** as an off white solid (21 mg, 60% yield). R_f (100% diethyl ether): 0.43; ^{31}P NMR ($CDCl_3$, 162 MHz): δ 8.44; We observed this material as a mixture of isomers. HRMS (APCI): calculated for $C_{30}H_{19}OPS_2$ $[M]^+$ (m/z) 490.0609; found = 490.0613.

12-(2-(Dimethylamino)ethyl)-6-phenyl-12H-benzo[4,5]-thieno[3,2-*b*]benzo[4,5]thieno[2,3-*e*][1,4]azaphosphinine 6-Oxide (37). Compound **31** (51 mg, 0.08 mmol) was dissolved in dry toluene (5.0 mL). To this mixture was added Cs_2CO_3 (65 mg, 0.20 mmol) and CuI (38.0 mg, 0.20 mmol), and the resulting suspension was stirred for 15 min while N_2 (g) was bubbled through the mixture. Then *N*,*N*-dimethylethane-1,2-diamine (56 mg, 0.64 mmol) was added to the stirred solution and the resulting reaction mixture was stirred overnight at 100 °C. The reaction mixture was cooled to room temperature, diluted with ethyl acetate (20.0 mL), and washed with water (2 × 20.0 mL) followed by brine (20.0 mL). The organic layer was dried ($MgSO_4$) and concentrated to get crude brown mass which was subjected to column chromatography on silica (20% methanol/diethyl ether) to afford title compound **37** (20 mg, 52%) as an off white solid. R_f (20% methanol/diethyl ether): 0.30; mp = 156−158 °C; ^{31}P NMR ($CDCl_3$, 162 MHz): δ 0.52; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.24 (d, J = 7.7 Hz, 2H), 7.87−7.80 (m, 4H), 7.56−7.44 (m, 7H), 4.83−4.79 (m, 2H), 2.34−2.29 (m, 2H), 1.99 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 147.6 (d, J = 5.3 Hz), 142.0 (d, J = 8.6 Hz), 132.8 (s), 132.7 (s), 132.6 (s), 132.5 (s), 132.4 (s), 128.6 (d, J = 13.6 Hz), 127.2 (s), 126.9−126.8 (m), 125.0 (s), 124.1 (s), 124.1−124.0 (m), 123.7 (s), 70.8−70.4 (m), 56.3−56.2 (m), 45.1 (s); HRMS (APCI): calculated for $C_{26}H_{24}ON_2PS_2$ $[M + H]^+$ (m/z) 475.1062; found = 475.1067.

Tris((2-(methylthio)phenyl)ethynyl)phosphine Oxide (38). Isopropylmagnesium bromide solution (3.30 mL, 3.30 mmol (1.0 M solution in THF)) was added dropwise to a solution of (2-ethynylphenyl) (methyl)sulfane (592 mg, 4.00 mmol) in anhydrous THF (10.0 mL) at −20 °C, and the resulting off-white suspension was left to stir at this temperature for 2 h. Phosphorus(V) oxychloride (153 mg, 1 mmol) in THF was added at −20 °C and the reaction mixture was stirred for 2 h. Saturated ammonium chloride (20 mL) and diethyl ether (30 mL) were added to the reaction mixture and the organic layer was separated. The organic layer was washed with water (2 × 20 mL) followed by brine (20 mL), dried over anhydrous $MgSO_4$, and concentrated to an off-white solid which was subjected to chromatography on silica eluting with 100% diethyl ether providing **38** as an off-white crystalline solid (215 mg, 44% yield). R_f (100% diethyl ether): 0.47; mp = 126−127.7 °C; ^{31}P NMR ($CDCl_3$, 162 MHz): δ −52.34; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (dd, J = 7.7, 1.4 Hz, 3H), 7.39 (td, J = 7.9, 1.5 Hz, 3H), 7.22 (d, J = 7.9 Hz, 3H), 7.14 (td, J = 7.6, 1.1 Hz, 3H), 2.51 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 144.5 (d, J = 2.1 Hz), 134.1 (d, J = 2.3 Hz), 131.2 (s), 125.3 (s), 124.6 (s), 118.3 (d, J = 5.2 Hz), 100.1 (d, J = 46.8 Hz), 89.3 (d, J = 239.9 Hz), 15.6 (s); HRMS (APCI): calculated for $C_{27}H_{21}OPS_3$ $[M]^+$ (m/z) 488.0487; found = 488.0489.

Tris(3-iodobenzo[*b*]thiophen-2-yl)phosphine Oxide (39). This material was prepared using the procedure described above for **31** using compound **38** (50 mg, 0.10 mmol) and iodine (254 mg, 1 mmol). Flash chromatography of the crude mixture using diethyl ether as eluent afforded **39** (68 mg, 82%) as an off white solid. R_f (100% diethyl ether): 0.76; mp > 300 °C; ^{31}P NMR ($CDCl_3$, 162 MHz): δ 8.69; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00−7.96 (m, 3H), 7.84−7.80 (m, 3H), 7.57−7.49 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$); δ 143.0 (d, J = 13.2 Hz), 142.2 (d, J = 6.6 Hz), 131.0 (d, J = 130.4 Hz), 127.9 (s), 127.5 (s), 126.2 (s), 122.6 (d, J = 1.9 Hz), 92.2 (d, J = 7.3 Hz); HRMS (APCI): calculated for $C_{24}H_{12}OI_3PS_3$ $[M]^+$ (m/z) 823.6916; found = 823.6918.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00262.

UV−vis spectra of compounds **31**−**37** and the ^{1}H, ^{13}C, ^{31}P, and ^{77}Se NMR spectra of all newly synthesized compounds (PDF)

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Notes

The authors declare no competing financial interest.

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(12) See Supporting Information.

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