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Construction of Benzo-1,2,3-thiazaphosphole Heterocycles by Annulations of *ortho*-Phosphinoarenesulfonyl Fluorides with Trimethylsilyl Azide

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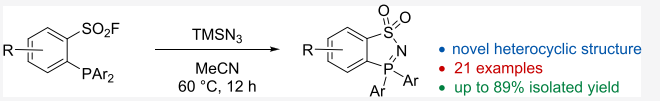
ABSTRACT: Annulations of *ortho*-phosphinoarenesulfonyl fluorides with trimethylsilyl azide were developed to access an unprecedented benzo-1,2,3-thiazaphosphole heterocycle. A corresponding reaction mechanism was proposed and further elucidated by experimental and computational studies. The reaction proceeds through a Staudinger-type iminophosphorane intermediate followed by intramolecular trapping with sulfonyl fluoride.

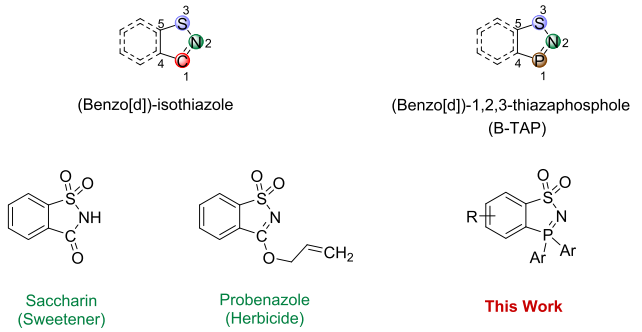


Heterocyclic compounds are widely distributed in Nature and play important roles in the biological world.[1] Heterocyclic compounds also contribute substantially to commercial drugs and drug candidates. Over 80% of top-selling US FDA-approved drugs contain a heterocyclic fragment, and 59% of marketed drugs contain one or more nitrogen heterocycles.[2] Aside from the heterocycles found in Nature, synthetic heterocycles have recently drawn much attention due to their metabolic stability and unique biological profiles.[3] In terms of structural diversity, it is highly desirable to explore novel heterocyclic scaffolds. Replacement of carbon with phosphorus represents an effective strategy to design novel phosphorus heterocycles,[4] since phosphorus is generally regarded as a "carbon copy"[5] but possesses some unique properties.[4,6] Herein, we report that the (benzo[*d*])-1,2,3-thiazaphosphole (B-TAP) heterocycle, a newborn cousin of (benzo[*d*])-isothiazole, can be effectively synthesized in one-step annulation reactions (Scheme 1).

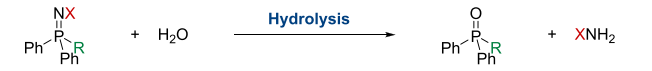
The original goal of this project was to seek a Staudinger-type intermediate $R_3P{=}NX$[7] with enhanced hydrolytic stability. Preliminary computational results indicated that an electron-withdrawing substituent on the nitrogen atom will stabilize the P═N double bond thermodynamically (Scheme 2). In addition, we speculated that a heterocycle like **2** or **3a** will further increase the stability of the P═N double bond by lowering the entropy term in the Gibbs free energy equation.

The designed (benzo[*d*])-1,2,3-thiazaphosphole (B-TAP) **3a** was initially prepared by a lithiation−deprotection−oxidation sequence (Scheme 3, top).[8] However, harsh

Scheme 1. Discovery of New Phosphorus Heterocycles



Scheme 2. Calculated Hydrolytic Stabilities of Iminophosphoranes



B3LYP/6-31g(d)	NMe (**1a**)	NPh (**1b**)	NAc (**1c**)
ΔG kcal/mol	-35.4	-34.4	-30.1
ΔH kcal/mol	-34.8	-33.4	-28.1
TΔS kcal/mol	+0.6	+1.0	+2.0
	NTs (**1d**)	O_2 (**2**)	O_2 (**3a**)
ΔG kcal/mol	-27.0	-25.0	-21.3
ΔH kcal/mol	-22.8	-33.7	-32.8
TΔS kcal/mol	+4.2	-8.7	-11.5

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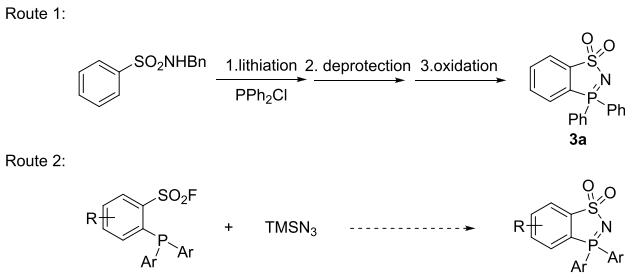
lithiation conditions (excessive *n*-BuLi) and unsatisfactory yields (10−30% yield in 3 steps) disallowed us to access other analogues using the same method.

Scheme 3. Synthetic Routes of B-TAP 3a



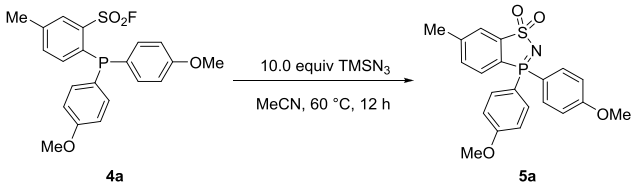
A second route was proposed to streamline the synthesis of **3a** and its analogues (Scheme 3, bottom). *ortho*-Phosphinoarenesulfonyl fluoride **4a** was selected as a model substrate since it has been readily prepared on a multigram scale by our protocol.[9] The proposed annulation was thought to be challenging due to the steric hindrance exerted by both the $-SO_2F$ and $-PPh_2$ groups. We speculated that the formation of nitrogen gas and trimethyl fluoride might compensate for the steric repulsion. Fortunately, preliminary experiments identified that trimethylsilyl azide was a suitable partner and the desired product was obtained. The azide group acts as both an oxidant and a nitrogen source while the trimethylsilyl group traps fluoride ions.

Further optimization suggested that there was a solvent effect in the annulation (Table 1). Acetonitrile was the optimal solvent in terms of rate and yield. Generally, either nonpolar solvents or solvents with high polarity were detrimental to the reaction. Although excessive trimethylsilyl azide was not required for product formation (entries 11−14, Table 1), the use of 10.0 equiv of $TMSN_3$ suppressed the formation of side products. The product **5a** is relatively stable in water but unstable on silica gel for an extended period. The hydrolytic stability of **5a** was tested in a 50% aqueous THF solution for 60 h, and only 10% **5a** was hydrolyzed. Fortunately, repeated precipitation afforded pure **5a** which was fully characterized by NMR and HRMS. Furthermore, the solid-state structure of **5a** was obtained by X-ray crystallography.

With the optimized conditions in hand, we evaluated the substrate scope with various *ortho*-phosphinoarenesulfonyl fluorides. As shown in Table 2, a set of substrates with diverse substituents were well-tolerated and the corresponding heterocycles were obtained in good to excellent yields. A marked electronic effect has been observed.

Substrates bearing an electron-withdrawing substituent required elevated temperature and a longer reaction time but gave cleaner reactions. In contrast, electron-rich substrates reacted faster but generated more side products. In addition, the reaction is sensitive to steric hindrance around the phosphorus atom. The substrates **4q** and **4r** remained intact under our standard conditions. Moderate yields were obtained

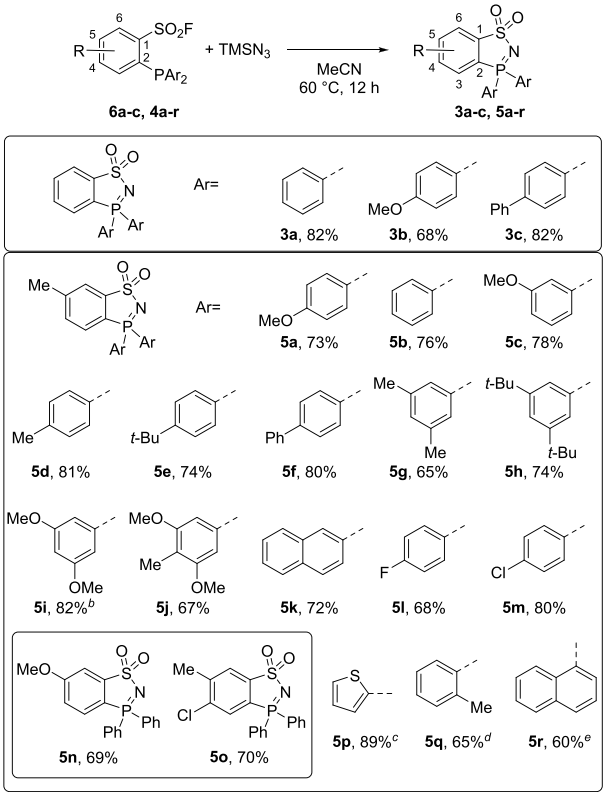
Table 1. Optimization of Reaction Conditions[a]



entry	change in condition from scheme	yield[b] (%)
1	none	82 (80)[c]
2	Toluene instead of CH_3CN	52
3	MTBE instead of CH_3CN	11
4	THF instead of CH_3CN	58
5	DMF instead of CH_3CN	73
6	DMSO instead of CH_3CN	38
7	EtOAc instead of CH_3CN	72
8	$CHCl_3$ instead of CH_3CN	80
9	30 °C instead of 60 °C	72
10	40 °C instead of 60 °C	73
11	1.0 equiv instead of 10.0 equiv of $TMSN_3$	66
12	2.0 equiv instead of 10.0 equiv of $TMSN_3$	76
13	3.0 equiv instead of 10.0 equiv of $TMSN_3$	76
14	5.0 equiv instead of 10.0 equiv of $TMSN_3$	79
15	0.05 M instead of 0.10 M	80
16	0.20 M instead of 0.10 M	81

[a]Reactions were run on a 0.05 mmol scale in 0.5 mL of anhydrous solvent under an N_2 atmosphere for 12 h. [b]Yields were determined by ^{31}P NMR. [c]Yield in parentheses was for the reactions in 2 h.

Table 2. Substrate Scope of Annulations with $TMSN_3$[a]



[a]Reactions were run with *ortho*-phosphinoarenesulfonyl fluoride (1.0 mmol), $TMSN_3$ (10.0 mmol), and anhydrous CH_3CN (10 mL) under a N_2 atmosphere at 60 °C for 12 h. All yields were isolated yields. [b]Reaction was run on a 0.5 mmol scale. [c]Reaction was run in 2.5 mL of CH_3CN at 70 °C for 48 h. [d]Reaction was run in 10 mL of *N,N*-dimethylformamide and 0.4 mL of dimethyl sulfoxide at 75 °C for 48 h. [e]Reaction was run on a 0.5 mmol scale in 5.0 mL of dimethyl sulfoxide at 75 °C for 48 h.

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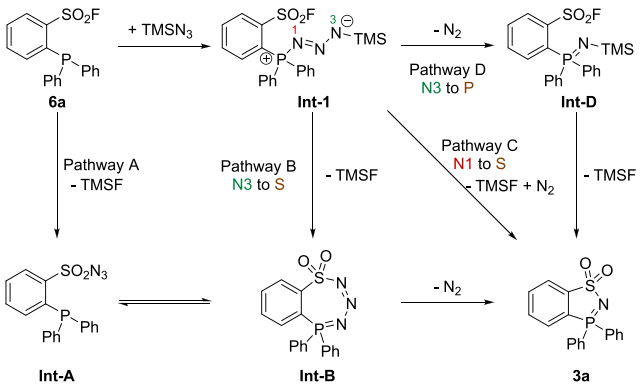
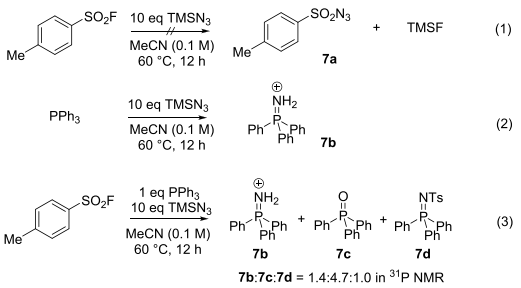
when the reactions were conducted in more polar solvents at 75 °C.

To probe the possible reaction mechanism (Scheme 4), a number of experiments with truncated fragments of **6a** have been conducted under our standard annulation conditions. Pathway A was ruled out due to no formation of the expected tosyl azide **7a** (Scheme 5, eq 1). Moreover, the detection of iminophosphorane **7b** suggested that a Staudinger-type intermediate was likely involved (Scheme 5, eq 2), which supported pathway D.[10] Additional evidence was brought from a trapping experiment in which the product **7d** was obtained (Scheme 5, eq 3).

Scheme 4. Proposed Reaction Pathways



Scheme 5. Control Experiments Mechanistic Probes



Computational studies have also been conducted to disclose more mechanistic insights.[11] Transition states involving pathways A–C are generally 20 kcal/mol higher than pathway D and thus less likely to be operative (Figure 1). The formation of iminophosphorane **Int-D** was the rate-determining step while the cyclization step had a lower activation energy. This can be understood by the fact that an *ortho*-fluorosulfonyl group is able to destabilize the four-membered ring **TS-D1** both electronically and sterically. We have also seen that **Int-D** and the final product are thermodynamically quite stable and hence drive the annulation reaction to completion. Although more complicated mechanisms cannot be ruled out at this time, combined results suggested that pathway D is plausible and the rate-determining step is the formation of **Int-D** from **Int-1**.

In conclusion, we have reported a facile synthesis of the novel (benzo[*d*])-1,2,3-thiazaphosphole heterocycle by the annulation of *ortho*-phosphinoarenesulfonyl fluorides with trimethylsilyl azide. Mechanistic studies suggest that the formation of an iminophosphorane intermediate is likely the rate-determining step for the annulation. Comprehensive chemical properties and synthetic applications of (benzo[*d*])-1,2,3-thiazaphosphole heterocycles will be investigated and reported in due course.

EXPERIMENTAL SECTION

General Information. Acetonitrile was dried by refluxing over CaH_2 and then distilled before use. Other solvents were purified according to standard procedures.[12] Analytical thin-layer chromatography was performed on 0.20 mm silica gel HSGF-254 plates (Huanghai, China). Visualization was accomplished with UV light, and/or potassium permanganate stain followed by heating. Flash column chromatography was performed on 200–300 mesh silica gel (Huanghai, China). Unless otherwise stated, all reagents were purchased from commercial sources and used without further purification. All reactions were conducted under an atmosphere of nitrogen in oven-dried glassware unless otherwise noted. 2-Iodoarenesulfonyl fluorides were prepared according to the literature methods.[13] Diarylphosphines were synthesized according to the literature methods.[14]

Instrumentation. High-resolution mass spectra (HRMS) were recorded on a Thermo Fisher Scientific's Q Exactive UHMR Hybrid Quadrupole-Orbitrap Mass Spectrometer LC/MS (ESI); melting points were obtained with INESA WRS-3 apparatus; ^{1}H, ^{19}F, ^{31}P, and ^{13}C NMR spectra were recorded on a Bruker AVANCE III 400 MHz spectrometer at 298 K and referenced to residual protium in the NMR solvent ($CHCl_3$, δ 7.26 in ^{1}H NMR) and the carbon resonances of the solvent ($CDCl_3$, δ 77.16 in ^{13}C NMR). Chemical shifts were reported in parts per million (ppm, δ) downfield from tetramethylsilane. NMR peaks are described as singlet (s), doublet (d), triplet (t), multiplet (m), complex (comp), approximate (app), and broad (br).

General Procedures for Synthesis of 2-(Diarylphosphaneyl)-arylsulfonyl Fluoride.[9,15] *Method A (for Compounds **6a, 6c, 4b–4k, and 4p**).* Under a N_2 atmosphere, a mixture of 2-iodoarenesulfonyl fluoride (5.00 mmol), diarylphosphine (5.50 mmol), $Pd(PPh_3)_4$ (289.8 mg, 0.25 mmol), Xantphos (145 mg, 0.25 mmol), and potassium phosphate (1.58 g, 7.5 mmol) in anhydrous toluene (10.0 mL) was stirred at 60 °C in an oil bath for 12 h. The reaction mixture was cooled to room temperature and quenched with 3 M hydrochloric acid (20.0 mL). The resulting mixture was extracted with dichloromethane (3 × 30.0 mL). The organic layer was dried over anhydrous sodium sulfate, filtered, and dried *in vacuo*. The crude product was purified by flash column chromatography to afford the product as a white solid.

*Method B (for Compounds **6c, 4a, 4n, and 4r**).* Under a N_2 atmosphere, a mixture of 2-iodoarenesulfonyl fluoride (5.00 mmol), diarylphosphine (5.50 mmol), $PdCl_2$(dppf) (182.8 mg, 0.25 mmol), and *N,N*-diisopropylethylamine (1.29 g, 10.0 mmol) in anhydrous toluene (10 mL) was stirred at 60 °C in an oil bath for 12 h. The reaction mixture was cooled to room temperature and quenched with 3 M hydrochloric acid (20.0 mL). The resulting mixture was extracted with dichloromethane (3 × 30.0 mL). The organic layer was dried over anhydrous sodium sulfate, filtered, and dried *in vacuo*. The crude product was purified by flash column chromatography to afford the product as a white solid.

*Method C (for Compounds **4l and 4m**).* Under a N_2 atmosphere, a mixture of $Pd(OAc)_2$ (112.2 mg, 0.50 mmol) and dppb (213.2 mg, 0.50 mmol) in anhydrous toluene (10.0 mL) was stirred at room temperature for 20 min followed by the addition of diarylphosphine (5.50 mmol), 2-iodoarenesulfonyl fluoride (5.00 mmol), and potassium carbonate (1.04 g, 7.50 mmol). The reaction mixture was stirred at 60 °C in an oil bath for 12 h, then was cooled to room temperature, and quenched with 3 M hydrochloric acid (20.0 mL). The resulting mixture was extracted with dichloromethane (3 × 30.0 mL). The organic layer was dried over anhydrous sodium sulfate, filtered and dried in vacuo. The crude product was purified by flash column chromatography to afford the product as a white solid.

*Method D (for Compounds **4o and 4q**).* Under a N_2 atmosphere, a solution of 2-iodoarenesulfonyl fluoride (10.0 mmol) in anhydrous tetrahydrofuran (40.0 mL) was cooled to −40 °C. To the stirred

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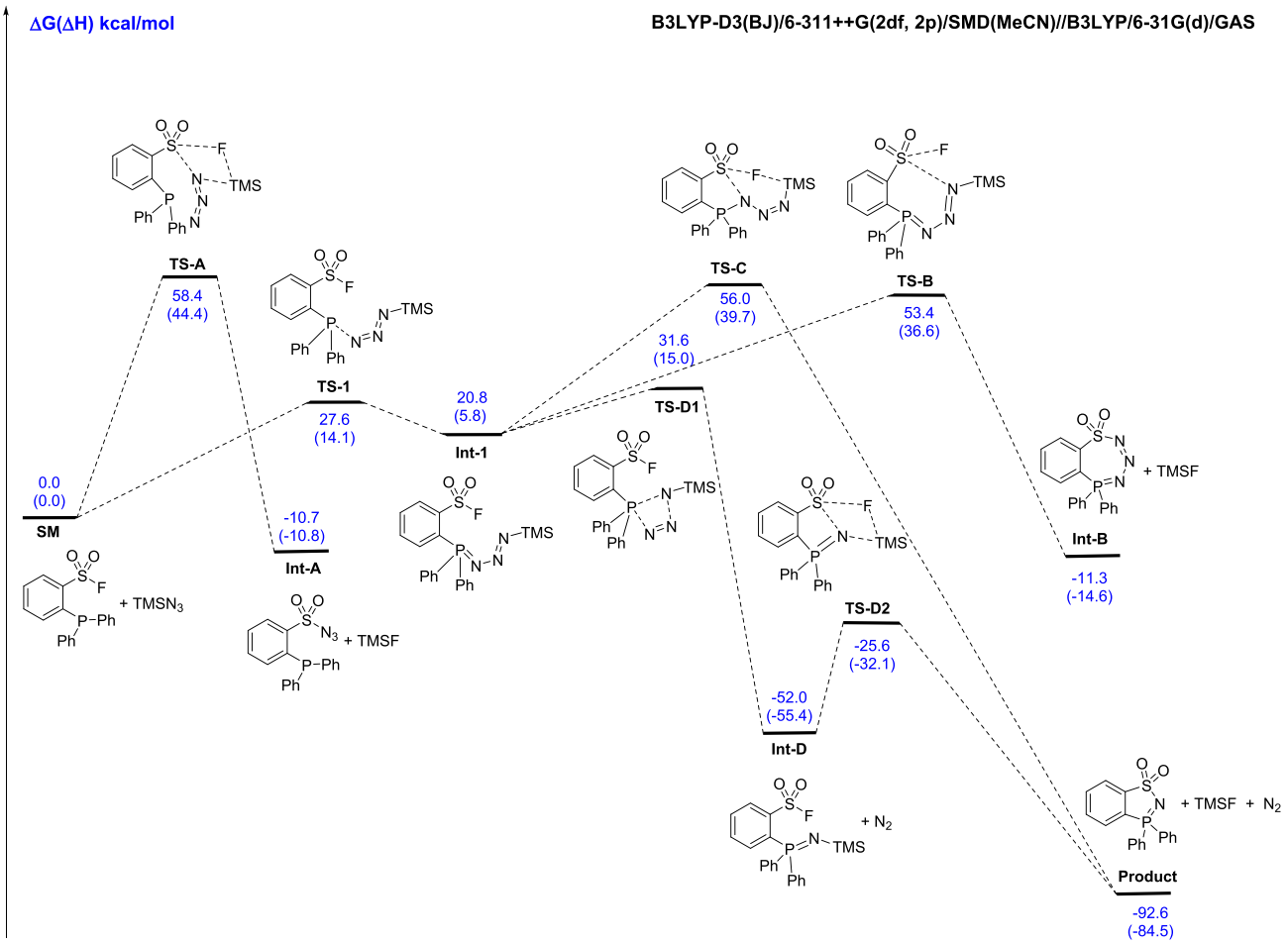

Figure 1. Calculated reaction pathways.

solution was added a solution of isopropylmagnesium chloride lithium chloride complex (9.20 mL, 12.0 mmol, 1.3 M) dropwise via syringe. The mixture was stirred at −20 °C for 1 h followed by the slow addition of a solution of chlorodiphenylphosphine (2.42 g, 11.0 mmol) in anhydrous tetrahydrofuran (10.0 mL) over 10 min. The reaction mixture was allowed to warm to room temperature and stirred for 8 h. After completion, the reaction was quenched by the careful addition of saturated aqueous ammonium chloride solution (20.0 mL). The upper layer was separated, and the aqueous layer was extracted with diethyl ether (40.0 mL). The organic layer was dried over anhydrous sodium sulfate, filtered, and dried *in vacuo*. The crude product was purified by flash column chromatography to afford the product as a white solid.

*2-(Diphenylphosphaneyl)benzenesulfonyl Fluoride (**6a**).* Compound **6a** was synthesized according to method A. Appearance: white solid (82%, 1.41 g), R_f = 0.55 (*n*-hexane/ethyl acetate, 10:1 v/v), mp 95−97 °C (dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (ddd, J = 7.7, 3.3, 1.6 Hz, 1H), 7.66−7.51 (comp, 2H), 7.42−7.30 (comp, 6H), 7.33−7.22 (comp, 5H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 140.2 (d, J_{C-P} = 33.6 Hz), 138.1 (dd, $J_{C-P+C-F}$ = 26.2, 22.3 Hz), 136.8, 135.3 (d, J_{C-P} = 11.4 Hz, 2C), 134.8, 133.9 (d, J_{C-P} = 20.7 Hz, 4C), 130.9 (d, J_{C-P} = 3.3 Hz), 129.5, 129.3 (2C), 128.8 (d, J_{C-P} = 6.8 Hz, 4C). ^{19}F NMR (377 MHz, $CDCl_3$) δ 64.63 (d, J_{F-P} = 39.4 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ −8.69 (d, J_{P-F} = 39.5 Hz). HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{18}H_{15}FO_2PS$ 345.0514; Found 345.0507.

*2-(Bis(4-methoxyphenyl)phosphaneyl)benzenesulfonyl Fluoride (**6b**).* Compound **6b** was synthesized according to method B. Appearance: white solid (75%, 1.15 g), R_f = 0.28 (*n*-hexane/ethyl acetate, 10:1 v/v), mp 98 °C (dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (ddd, J = 7.9, 3.4, 1.4 Hz, 1H), 7.62−7.56 (m, 1H), 7.53 (app t, J = 7.6 Hz, 1H), 7.28−7.23 (m, 1H), 7.25−7.15 (m, 4H), 6.89 (d, J = 8.5 Hz, 4H), 3.80 (s, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 160.6 (2C), 141.5 (d, J_{C-P} = 34.3 Hz), 137.6 (dd, $J_{C-P+C-F}$ = 25.2, 22.4 Hz), 136.3, 135.4 (d, J_{C-P} = 22.2 Hz, 4C), 134.6, 130.9, 129.1, 126.3 (d, J_{C-P} = 8.3 Hz), 114.5 (d, J_{C-P} = 8.1 Hz, 4C), 55.2 (2C). ^{19}F NMR (377 MHz, $CDCl_3$) δ 64.50 (d, J_{F-P} = 37.6 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ −11.28 (d, J_{P-F} = 37.4 Hz). HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{20}H_{19}FO_4PS$ 405.0726; Found 405.0716.

*2-(Di([1,1′-biphenyl]-4-yl)phosphaneyl)benzenesulfonyl Fluoride (**6c**).* Compound **6c** was synthesized according to method A. Appearance: white solid (46%, 1.17 g), R_f = 0.45 (*n*-hexane/ethyl acetate, 10:1 v/v), mp 149−150 °C (dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (dd, J = 8.4, 3.3 Hz, 1H), 7.73−7.50 (comp, 10H), 7.44 (app t, J = 7.5 Hz, 4H), 7.41−7.31 (comp, 7H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 142.1 (2C), 140.3 (2C), 140.2 (d, J_{C-P} = 33.7 Hz), 138.2 (dd, $J_{C-P+C-F}$ = 26.9, 21.4 Hz), 136.9, 134.9, 134.3 (d, J_{C-P} = 20.8 Hz, 4C), 134.2 (d, J_{C-P} = 10.7 Hz, 2C), 130.9 (d, J_{C-P} = 3.4 Hz), 129.6, 128.9 (4C), 127.8 (2C), 127.5 (d, J_{C-P} = 7.2 Hz, 4C), 127.1 (4C). ^{19}F NMR (377 MHz, $CDCl_3$) δ 64.67 (d, J_{F-P} = 39.7 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ −9.98 (d, J_{P-F} = 39.9 Hz). HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{30}H_{23}FO_2PS$ 497.1140; Found 497.1122.

*2-(Bis(4-methoxyphenyl)phosphaneyl)-5-methylbenzenesulfonyl Fluoride (**4a**).* Compound **4a** was synthesized according to method B. Appearance: white solid (80%, 2.01 g), R_f = 0.26 (*n*-hexane/ethyl acetate, 10:1 v/v), mp 124 °C (dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (app s, 1H), 7.38 (app d, J = 7.6 Hz, 1H), 7.24−7.14 (m, 4H), 7.13 (dd, $J_{H-H+H-P}$ = 7.8, 3.0 Hz, 1H), 6.88 (d, J = 8.0 Hz, 4H), 3.80 (s, 6H), 2.43 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 160.5 (2C), 139.9, 137.7 (d, J_{C-P} = 32.7 Hz), 137.4 (dd,

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$J_{C-P+C-F}$ = 25.8, 21.8 Hz), 136.4, 135.4, 135.3 (d, J_{C-P} = 22.0 Hz, 4C), 131.3 (d, J_{C-P} = 3.1 Hz), 126.7 (d, J_{C-P} = 8.3 Hz, 2C), 114.4 (d, J_{C-P} = 8.0 Hz, 4C), 55.2 (2C), 21.0. ^{19}F NMR (377 MHz, $CDCl_3$) δ 64.62 (d, J_{F-P} = 38.2 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ −12.52 (d, J_{P-F} = 38.3 Hz). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{21}FO_4PS$ 419.0882; Found 419.0872.

*2-(Diphenylphosphaneyl)-5-methylbenzenesulfonyl Fluoride (**4b**).* Compound **4b** was synthesized according to method A. Appearance: white solid (85%, 1.52 g), R_f = 0.59 (*n*-hexane/ethyl acetate, 10:1 v/v), mp 132−133 °C (dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (app s, 1H), 7.39 (app d, J = 8.1 Hz, 1H), 7.38−7.29 (comp, 6H), 7.30−7.21 (m, 4H), 7.14 (dd, $J_{H-H+H-P}$ = 7.9, 2.9 Hz, 1H), 2.44 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 140.3, 137.9 (dd, $J_{C-P+C-F}$ = 26.9, 21.9 Hz), 136.9, 136.4 (d, J_{C-P} = 32.0 Hz), 135.7 (d, J_{C-P} = 11.4 Hz, 2C), 135.5, 133.8 (d, J_{C-P} = 20.6 Hz, 4C), 131.3 (d, J_{C-P} = 3.3 Hz), 129.2 (2C), 128.7 (d, J_{C-P} = 7.0 Hz, 4C), 21.1. ^{19}F NMR (377 MHz, $CDCl_3$) δ 64.73 (d, J_{F-P} = 40.1 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ −9.95 (d, J_{P-F} = 40.0 Hz). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{17}FO_2PS$ 359.0671; Found 359.0664.

*2-(Bis(3-methoxyphenyl)phosphaneyl)-5-methylbenzenesulfonyl Fluoride (**4c**).* Compound **4c** was synthesized according to method A. Appearance: white solid (80%, 1.67 g), R_f = 0.35 (*n*-hexane/ethyl acetate, 10:1 v/v), mp 82 °C (dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (app s, 1H), 7.40 (app d, J = 7.6 Hz, 1H), 7.31−7.22 (m, 2H), 7.16 (dd, $J_{H-H+H-P}$ = 7.8, 2.9 Hz, 1H), 6.93−6.86 (m, 2H), 6.86−6.77 (comp, 4H), 3.73 (s, 6H), 2.44 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 159.6 (d, J_{C-P} = 8.8 Hz, 2C), 140.4, 137.9 (dd, $J_{C-P+C-F}$ = 26.8, 21.7 Hz), 137.1 (d, J_{C-P} = 11.9 Hz, 2C), 136.9, 136.0 (d, J_{C-P} = 31.7 Hz), 135.5, 131.3 (d, J_{C-P} = 3.3 Hz), 129.7 (d, J_{C-P} = 7.7 Hz, 2C), 126.0 (d, J_{C-P} = 19.6 Hz, 2C), 119.2 (d, J_{C-P} = 23.0 Hz, 2C), 114.6 (2C), 55.2 (2C), 21.1.^{19}F NMR (377 MHz, $CDCl_3$) δ 64.90 (d, J_{F-P} = 39.7 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ −8.67 (d, J_{P-F} = 39.8 Hz). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{21}FO_4PS$ 419.0882; Found 419.0873.

*2-(Di-p-tolylphosphaneyl)-5-methylbenzenesulfonyl Fluoride (**4d**).* Compound **4d** was synthesized according to method A. Appearance: white solid (80%, 1.54 g), R_f = 0.61 (*n*-hexane/ethyl acetate, 10:1 v/v), mp 109−110 °C (dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (app s, 1H), 7.38 (app d, J = 7.6 Hz, 1H), 7.24−7.03 (comp, 9H), 2.43 (s, 3H), 2.35 (s, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 140.0, 139.2 (2C), 137.8 (dd, $J_{C-P+C-F}$ = 26.5, 21.8 Hz), 137.1 (d, J_{C-P} = 32.5 Hz), 136.7, 135.4, 133.8 (d, J_{C-P} = 20.9 Hz, 4C), 132.3 (d, J_{C-P} = 10.0 Hz, 2C), 131.2 (d, J_{C-P} = 3.4 Hz), 129.5 (d, J_{C-P} = 7.2 Hz, 4C), 21.3 (2C), 21.0. ^{19}F NMR (377 MHz, $CDCl_3$) δ 64.62 (d, J_{F-P} = 39.9 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ −11.37 (d, J_{P-F} = 40.0 Hz). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{21}FO_2PS$ 387.0984; Found 387.0975.

*2-(Bis(4-(tert-butyl)phenyl)phosphaneyl)-5-methylbenzenesulfonyl Fluoride (**4e**).* Compound **4e** was synthesized according to method A. Appearance: white solid (80%, 0.94 g), R_f = 0.69 (*n*-hexane/ethyl acetate, 10:1 v/v), mp 220−221 °C (dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (app s, 1H), 7.40 (app d, J = 7.8 Hz, 1H), 7.35 (d, J = 7.2 Hz, 4H), 7.22−7.11 (comp, 5H), 2.43 (s, 3H), 1.30 (s, 18H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 152.2 (2C), 140.0, 137.9 (d, $J_{C-P+C-F}$ = 26.9, 21.6 Hz), 137.2 (d, J_{C-P} = 32.3 Hz), 136.9, 135.4, 133.5 (d, J_{C-P} = 20.6 Hz, 4C), 132.3 (d, J_{C-P} = 10.0 Hz, 2C), 131.1 (d, J_{C-P} = 3.5 Hz), 125.7 (d, J_{C-P} = 7.1 Hz, 4C), 34.7 (2C), 31.2 (6C), 21.0. ^{19}F NMR (377 MHz, $CDCl_3$) δ 64.70 (d, J_{F-P} = 41.8 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ −12.22 (d, J_{P-F} = 41.8 Hz). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{27}H_{33}FO_2PS$ 471.1923; Found 471.1917.

*2-(Di([1,1′-biphenyl]-4-yl)phosphaneyl)-5-methylbenzenesulfonyl Fluoride (**4f**).* Compound **4f** was synthesized according to method A. Appearance: white solid (69%, 1.74 g), R_f = 0.54 (*n*-hexane/ethyl acetate, 10:1 v/v), mp 110−112 °C (dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (app s, 1H), 7.59 (app d, J = 7.6 Hz, 8H), 7.47−7.41 (comp, 5H), 7.39−7.32 (comp, 6H), 7.27 (dd, $J_{H-H+H-P}$ = 7.9, 3.0 Hz, 1H), 2.46 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 142.0 (2C), 140.5, 140.3 (2C), 138.0 (dd, $J_{C-P+C-F}$ = 26.9, 21.6 Hz), 137.0, 136.3 (d, J_{C-P} = 31.9 Hz), 135.7, 134.5 (d, J_{C-P} = 11.4 Hz, 2C), 134.2 (d, J_{C-P} = 20.7 Hz, 4C), 131.4 (d, J_{C-P} = 3.9 Hz), 128.9 (4C), 127.7 (2C), 127.4 (d, J_{C-P} = 7.2 Hz, 4C), 127.1 (4C), 21.1. ^{19}F NMR (377 MHz, $CDCl_3$) δ 64.80 (d, J_{F-P} = 40.3 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ −11.23 (d, J_{P-F} = 40.2 Hz). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{31}H_{25}FO_2PS$ 511.1297; Found 511.1275.

*2-(Bis(3,5-dimethylphenyl)phosphaneyl)-5-methylbenzenesulfonyl Fluoride (**4g**).* Compound **4g** was synthesized according to method A. Appearance: white solid (85%, 1.75 g), R_f = 0.63 (*n*-hexane/ethyl acetate, 10:1 v/v), mp 162−165 °C (dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (app s, 1H), 7.39 (app d, J = 7.8 Hz, 1H), 7.18 (dd, $J_{H-H+H-P}$ = 7.9, 2.9 Hz, 1H), 6.98 (s, 2H), 6.85 (d, J_{H-P} = 8.3 Hz, 4H), 2.44 (s, 3H), 2.25 (s, 12H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 140.0, 138.0 (d, J_{C-P} = 7.4 Hz, 4C), 138.0 (dd, $J_{C-P+C-F}$ = 26.5, 22.1 Hz), 137.1, 136.9 (d, J_{C-P} = 32.4 Hz), 135.5 (d, J_{C-P} = 10.9 Hz, 2C), 135.5, 131.4 (d, J_{C-P} = 20.7 Hz, 4C), 131.1 (d, J_{C-P} = 3.4 Hz), 130.9 (2C), 21.3 (4C), 21.1. ^{19}F NMR (377 MHz, $CDCl_3$) δ 64.64 (d, J_{F-P} = 41.4 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ −9.92 (d, J_{P-F} = 41.4 Hz). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{23}H_{25}FO_2PS$ 415.1297; Found 415.1289.

*2-(Bis(3,5-ditert-butylphenyl)phosphaneyl)-5-methylbenzenesulfonyl Fluoride (**4h**).* Compound **4h** was synthesized according to method A. Appearance: white solid (72%, 2.10 g), R_f = 0.40 (*n*-hexane/ethyl acetate, 40:1 v/v), mp 160−162 °C (dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (app s, 1H), 7.42−7.36 (comp, 3H), 7.13 (dd, $J_{H-H+H-P}$ = 7.9, 2.8 Hz, 1H), 7.08 (dd, $J_{H-H+H-P}$ = 8.4, 1.6 Hz, 4H), 2.44 (s, 3H), 1.22 (s, 36H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 150.7 (d, J_{C-P} = 6.7 Hz, 4C), 139.7, 138.0 (d, J_{C-P} = 33.6 Hz), 137.8 (dd, $J_{C-P+C-F}$ = 25.8, 21.6 Hz), 136.6, 135.1, 134.9 (d, J_{C-P} = 10.2 Hz, 2C), 131.1 (d, J_{C-P} = 3.4 Hz), 128.1 (d, J_{C-P} = 21.0 Hz, 4C), 122.9 (2C), 34.9 (4C), 31.4 (12C), 21.0. ^{19}F NMR (377 MHz, $CDCl_3$) δ 65.33 (d, J_{F-P} = 39.3 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ −7.03 (d, J_{P-F} = 39.2 Hz). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{35}H_{49}FO_2PS$ 583.3175; Found 583.3166.

*2-(Bis(3,5-dimethoxyphenyl)phosphaneyl)-5-methylbenzenesulfonyl Fluoride (**4i**).* Compound **4i** was synthesized according to method A. Appearance: white solid (71%, 1.69 g), R_f = 0.22 (*n*-hexane/ethyl acetate, 10:1 v/v), mp 104−105 °C (dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14−7.90 (m, 1H), 7.41 (app d, J = 7.9 Hz, 1H), 7.20 (dd, $J_{H-H+H-P}$ = 7.8, 3.0 Hz, 1H), 6.44 (t, J = 2.3 Hz, 2H), 6.40 (dd, $J_{H-P+H-H}$ = 8.4, 2.3 Hz, 4H), 3.72 (s, 12H), 2.45 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 161.0 (d, J_{C-P} = 9.9 Hz, 4C), 140.5, 138.0 (dd, $J_{C-P+C-F}$ = 26.7, 21.8 Hz), 137.7 (d, J_{C-P} = 11.8 Hz, 2C), 136.9, 135.6 (d, J_{C-P} = 31.5 Hz), 135.6, 131.3 (d, J_{C-P} = 3.6 Hz), 111.6 (d, J_{C-P} = 22.3 Hz, 4C), 101.2 (2C), 55.3 (4C), 21.1. ^{19}F NMR (377 MHz, $CDCl_3$) δ 65.07 (d, J_{F-P} = 39.2 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ −6.39 (d, J_{P-F} = 39.3 Hz). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{23}H_{25}FO_6PS$ 479.1093; Found 479.1074.

*2-(Bis(4-methoxy-3,5-dimethylphenyl)phosphaneyl)-5-methylbenzenesulfonyl Fluoride (**4j**).* Compound **4j** was synthesized according to method A. Appearance: white solid (70%, 1.65 g), R_f = 0.49 (*n*-hexane/ethyl acetate, 10:1 v/v), mp 184 °C (dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (app s, 1H), 7.41 (app d, J = 7.8 Hz, 1H), 7.17 (dd, $J_{H-H+H-P}$ = 7.8, 2.9 Hz, 1H), 6.87 (d, J_{H-P} = 7.9 Hz, 4H), 3.72 (s, 6H), 2.45 (s, 3H), 2.22 (s, 12H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 157.9 (2C), 139.9, 137.8 (dd, $J_{C-P+C-F}$ = 26.6, 21.4 Hz), 137.3 (d, J_{C-P} = 32.5 Hz), 136.9, 135.4, 134.3 (d, J_{C-P} = 21.7 Hz, 4C), 131.2 (d, J_{C-P} = 8.2 Hz, 4C), 131.1 (d, J_{C-P} = 3.8 Hz), 130.4 (d, J_{C-P} = 9.9 Hz, 2C), 59.6 (2C), 21.1, 16.2 (4C). ^{19}F NMR (377 MHz, $CDCl_3$) δ 64.58 (d, J_{F-P} = 40.9 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ −11.64 (d, J_{P-F} = 41.0 Hz). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{25}H_{29}FO_4PS$ 475.1508; Found 475.1503.

*2-(Di(naphthalen-2-yl)phosphaneyl)-5-methylbenzenesulfonyl Fluoride (**4k**).* Compound **4k** was synthesized according to method A. Appearance: white solid (79%, 1.80 g), R_f = 0.57 (*n*-hexane/ethyl acetate, 10:1 v/v), mp 201−202 °C (dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (app s, 1H), 7.87−7.80 (comp, 4H), 7.77 (d, J_{H-P} = 8.5 Hz, 2H), 7.72 (d, J = 7.9 Hz, 2H), 7.55−7.43 (comp, 4H), 7.41−7.33 (comp, 3H), 7.28−7.24 (m, 1H), 2.50 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 140.5, 138.2 (dd, $J_{C-P+C-F}$ =

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27.0, 22.0 Hz), 137.2, 136.1 (d, J_{C-P} = 31.7 Hz), 135.6, 134.5 (d, J_{C-P} = 21.9 Hz, 2C), 133.5 (2C), 133.3 (d, J_{C-P} = 7.8 Hz, 2C), 133.1 (d, J_{C-P} = 11.5 Hz, 2C), 131.4 (d, J_{C-P} = 3.6 Hz), 129.8 (d, J_{C-P} = 20.0 Hz, 2C), 128.3 (d, J_{C-P} = 7.5 Hz, 2C), 128.2 (2C), 127.8(2C), 127.0(2C), 126.5(2C), 21.1. ^{19}F NMR (377 MHz, $CDCl_3$) δ 64.94 (d, J_{F-P} = 40.2 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ −9.02 (d, J_{P-F} = 40.1 Hz). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{27}H_{21}FO_2PS$ 459.0984; Found 459.0975.

*2-(Bis(4-fluorophenyl)phosphaneyl)-5-methylbenzenesulfonyl Fluoride (**4l**).* Compound **4l** was synthesized according to method C. Appearance: white solid (70%, 1.33 g), R_f = 0.57 (*n*-hexane/ethyl acetate, 10:1 v/v), mp 103 °C (dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (app s, 1H), 7.43 (app d, J = 7.7 Hz, 1H), 7.34−7.16 (m, 4H), 7.17−6.93 (comp, 5H), 2.46 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 163.6 (d, J_{C-F} = 250.2 Hz, 2C), 140.6, 137.7 (dd, $J_{C-P+C-F}$ = 31.7, 21.8 Hz), 136.3, 136.1(d, J_{C-P} = 32.1 Hz), 135.7 (dd, $J_{C-P+C-F}$ = 21.4, 9.4 Hz, 4C), 135.7, 131.6 (d, J_{C-P} = 3.1 Hz), 131.0 (dd $J_{C-P+C-F}$ = 11.2, 3.4 Hz, 2C), 116.1 (dd, $J_{C-P+C-F}$ = 21.1, 7.9 Hz, 4C), 21.1. ^{19}F NMR (377 MHz, $CDCl_3$) δ 68.93 (d, J_{F-P} = 38.0 Hz), −106.97 (d, J_{F-P} = 4.7 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ −7.82 (dt, J_{P-F} = 37.8, 4.6 Hz). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{15}F_3O_2PS$ 394.0404; Found 395.0475.

*2-(Bis(4-chlorophenyl)phosphaneyl)-5-methylbenzenesulfonyl Fluoride (**4m**).* Compound **4m** was synthesized according to method C. Appearance: white solid (69%, 1.47 g), R_f = 0.62 (*n*-hexane/ethyl acetate, 10:1 v/v), mp 118 °C (dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (app s, 1H), 7.43 (app d, J = 7.8 Hz, 1H), 7.37−7.29 (m, 4H), 7.22−7.12 (m, 4H), 7.09 (dd, $J_{H-H+H-P}$ = 7.8, 3.0 Hz, 1H), 2.46 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 140.9, 137.9 (dd, $J_{C-P+C-F}$ = 26.9, 22.2 Hz), 136.5, 135.9 (2C), 135.8, 135.4, 135.0 (d, J_{C-P} = 21.4 Hz, 4C), 133.9 (d, J_{C-P} = 12.5 Hz, 2C), 131.6 (d, J_{C-P} = 3.3 Hz), 129.1 (d, J_{C-P} = 7.7 Hz, 4C), 21.1. ^{19}F NMR (377 MHz, $CDCl_3$) δ 64.75 (d, J_{F-P} = 38.6 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ −11.74 (d, J_{P-F} = 38.6 Hz). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{15}Cl_2FO_2PS$ 426.9891 (^{35}Cl), 428.9862 (^{37}Cl); Found 426.9883 (^{35}Cl), 428.9855 (^{37}Cl).

*2-(Diphenylphosphaneyl)-5-methoxybenzenesulfonyl Fluoride (**4n**).* Compound **4n** was synthesized according to method B. Appearance: white solid (75%, 1.40 g), R_f = 0.49 (*n*-hexane/ethyl acetate, 10:1 v/v), mp 127−129 °C (dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (app t, J = 2.7 Hz, 1H), 7.41−7.30 (comp, 6H), 7.29−7.21 (m, 4H), 7.18 (dd, $J_{H-H+H-P}$ = 8.6, 2.7 Hz, 1H), 7.11 (dd, J = 8.6, 2.7 Hz, 1H), 3.87 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 160.2, 139.4 (dd, $J_{C-P+C-F}$ = 28.5, 22.4 Hz), 138.5, 136.0 (d, J_{C-P} = 11.5 Hz, 2C), 133.6 (d, J_{C-P} = 20.5 Hz, 4C), 129.8 (d, J_{C-P} = 30.6 Hz), 129.1 (2C), 128.7 (d, J_{C-P} = 6.9 Hz, 4C), 120.7, 116.0 (d, J_{C-P} = 3.2 Hz), 55.9. ^{19}F NMR (377 MHz, $CDCl_3$) δ 64.32 (d, J_{F-P} = 43.3 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ −11.24 (d, J_{P-F} = 43.2 Hz). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{17}FO_3PS$ 375.0620; Found 375.0612.

*4-Chloro-2-(diphenylphosphaneyl)-5-methylbenzenesulfonyl Fluoride (**4o**).* Compound **4o** was synthesized according to method D. Appearance: white solid (67%, 2.64 g), R_f = 0.71 (*n*-hexane/ethyl acetate, 10:1 v/v), mp 153−154 °C (dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J_{H-P} = 3.2 Hz, 1H), 7.43−7.32 (comp, 6H), 7.31−7.22 (m, 4H), 7.14 (app s, 1H), 2.45 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 142.1 (d, J_{C-P} = 2.6 Hz), 139.2 (d, J_{C-P} = 36.7 Hz), 138.4, 136.9, 135.9 (dd, $J_{C-P+C-F}$ = 26.1, 22.8 Hz), 134.9 (d, J_{C-P} = 11.4 Hz, 2C), 133.8 (d, J_{C-P} = 20.9 Hz, 4C), 133.1 (d, J_{C-P} = 3.2 Hz), 129.5 (2C), 128.9 (d, J_{C-P} = 7.1 Hz, 4C), 19.9. ^{19}F NMR (377 MHz, $CDCl_3$) δ 65.38 (d, J_{F-P} = 38.0 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ −9.33 (d, J_{P-F} = 37.7 Hz). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{16}ClFO_2PS$ 393.0281 (^{35}Cl), 395.0252 (^{37}Cl); Found 393.0261 (^{35}Cl), 395.0230 (^{37}Cl).

*2-(Di(thiophen-2-yl)phosphaneyl)-5-methylbenzenesulfonyl Fluoride (**4p**).* Compound **4p** was synthesized according to method A. Appearance: white solid (42%, 0.78 g), R_f = 0.53 (*n*-hexane/ethyl acetate, 10:1 v/v), mp 83−84 °C (dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (app d, J = 3.6 Hz, 1H), 7.61 (app d, J = 4.9 Hz, 2H), 7.53−7.38 (comp, 2H), 7.30 (ddd, $J_{H-H+H-P}$ = 5.8, 3.5, 1.1 Hz, 2H), 7.13 (ddd, $J_{H-H+H-P}$ = 4.9, 3.5, 1.4 Hz, 2H), 2.45 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 140.7, 137.3 (d, J_{C-P} = 28.4 Hz), 136.4 (d, J_{C-P} = 23.7 Hz, 2C), 136.4 (dd, $J_{C-P+C-F}$ = 25.2, 24.0 Hz), 136.3 (d, J_{C-P} = 27.0 Hz, 2C), 135.7, 135.3, 132.4 (d, J_{C-P} = 1.6 Hz, 2C), 131.4 (d, J_{C-P} = 3.4 Hz), 128.4 (d, J_{C-P} = 8.1 Hz, 2C), 21.1. ^{19}F NMR (377 MHz, $CDCl_3$) δ 65.47 (d, J_{F-P} = 36.0 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ −37.72 (d, J_{P-F} = 36.1 Hz). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{13}FO_2PS_3$ 370.9799; Found 370.9779.

*2-(Di-o-tolylphosphaneyl)-5-methylbenzenesulfonyl Fluoride (**4q**).* Compound **4q** was synthesized according to method D. Appearance: white solid (60%, 2.30 g), R_f = 0.62 (*n*-hexane/ethyl acetate, 10:1 v/v), mp 180−181 °C (dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (app s, 1H), 7.41 (app d, J = 7.7 Hz, 1H), 7.31−7.17 (comp, 4H), 7.16−7.05 (comp, 3H), 6.67 (dd, J = 7.4, 4.2 Hz, 2H), 2.49 (s, 3H), 2.40 (s, 6H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 142.5 (d, J_{C-P} = 27.6 Hz, 2C), 140.3, 138.4 (dd, $J_{C-P+C-F}$ = 28.1, 21.5 Hz), 137.2, 135.5, 135.5 (d, J_{C-P} = 30.6 Hz), 133.9 (d, J_{C-P} = 11.8 Hz, 2C), 133.0 (2C), 131.4 (d, J_{C-P} = 3.0 Hz), 130.4 (d, J_{C-P} = 4.8 Hz, 2C), 129.2 (2C), 126.2 (2C), 21.3, 21.1 (d, J_{C-P} = 2.6 Hz, 2C). ^{19}F NMR (377 MHz, $CDCl_3$) δ 63.39 (d, J_{F-P} = 41.9 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ −24.66 (d, J_{P-F} = 42.0 Hz). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{21}FO_2PS$ 387.0984; Found 387.0961.

*2-(Di(naphthalen-1-yl)phosphaneyl)-5-methylbenzenesulfonyl Fluoride (**4r**).* Compound **4r** was synthesized according to method B. Appearance: white solid (70%, 1.60 g), R_f = 0.49 (*n*-hexane/ethyl acetate, 10:1 v/v), mp 213 °C (dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (dd, $J_{H-H+H-P}$ = 8.2, 4.5 Hz, 2H), 8.07 (app s, 1H), 7.91−7.81 (comp, 4H), 7.53−7.39 (comp, 4H), 7.33−7.23 (comp, 3H), 7.06 (dd, $J_{H-H+H-P}$ = 7.8, 3.0 Hz, 1H), 6.88 (ddd, $J_{H-H+H-P}$ = 7.0, 4.6, 1.2 Hz, 2H), 2.42 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 140.6, 138.2 (dd, $J_{C-P+C-F}$ = 27.9, 22.0 Hz), 137.9, 135.7, 135.3 (d, J_{C-P} = 24.4 Hz, 2C), 134.8 (d, J_{C-P} = 28.5 Hz), 133.6 (d, J_{C-P} = 4.8 Hz, 2C), 133.0 (2C), 132.3 (d, J_{C-P} = 12.7 Hz, 2C), 131.6 (d, J_{C-P} = 4.1 Hz), 130.1 (2C), 128.7 (d, J_{C-P} = 2.1 Hz, 2C), 126.6 (d, J_{C-P} = 2.5 Hz, 2C), 126.2 (2C), 126.2 (d, J_{C-P} = 28.1 Hz, 2C), 125.6 (2C), 21.1. ^{19}F NMR (377 MHz, $CDCl_3$) δ 63.91 (d, J_{F-P} = 41.8 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ −26.25 (d, J_{P-F} = 42.0 Hz). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{27}H_{21}FO_2PS$ 459.0984; Found 459.0958.

General Procedures for Synthesis of 3,3-Diaryl-3λ^5-aryl Benzo[2,3-*d*][1,2,3]thiazaphosphole 1,1-Dioxide (*Caution: A safety shield is required since the reaction accumulates pressure when conducted in a sealed vessel*). *Method A (for Compounds **3a−c**, **5a−p**).* To a solution of *ortho*-phosphinoarenesulfonyl fluoride (1.00 mmol) in anhydrous acetonitrile (10.0 mL) was added trimethylsilyl azide (1.15 g, 10.0 mmol). The reaction mixture was stirred at 60 °C in an aluminum heating block for 12 h. Then, the solvent was evaporated *in vacuo*. Repeated precipitation with ethyl acetate and petroleum ether afforded the product.

*Method B (for Compound **5q** and **5r**).* To a solution of *ortho*-phosphinoarenesulfonyl fluoride (1.00 mmol) in anhydrous *N,N*-dimethylformamide (10.0 mL) and dimethyl sulfoxide (0.4 mL) was added trimethylsilyl azide (1.15 g, 10.0 mmol). The reaction mixture was stirred at 75 °C in an aluminum heating block for 48 h and then concentrated *in vacuo*. The reaction mixture was diluted with dichloromethane (50 mL) and washed with half-saturated brine (20 mL × 5). The organic layer was dried over anhydrous sodium sulfate and concentrated *in vacuo*. The crude product was purified by flash column chromatography over silica gel (eluent: 1:1:1 petroleum ether/dichloromethane/ethyl acetate) to afford the product.

*3,3-Diphenyl-3λ^5-benzo[d][1,2,3]thiazaphosphole 1,1-Dioxide (**3a**).* Compound **3a** was synthesized according to method A. Appearance: white solid (82%, 277.6 mg), R_f = 0.62 (*n*-hexane/dichloromethane/ethyl acetate, 1:1:1 v/v/v), mp 256−257 °C (dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (*d*, J = 7.8 Hz, 1H), 7.88−7.75 (comp, 5H), 7.74−7.63 (comp, 4H), 7.60−7.51 (m, 4H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 150.5 (d, J_{C-P} = 11.7 Hz), 134.3 (d, J_{C-P} = 2.7 Hz), 134.2 (d, J_{C-P} = 2.9 Hz, 2C), 132.5 (d, J_{C-P} = 11.7 Hz, 4C), 132.2 (d, J_{C-P} = 10.1 Hz), 129.5 (d, J_{C-P} = 13.7 Hz, 4C), 128.2 (d, J_{C-P} = 6.4 Hz), 125.1 (d, J_{C-P} = 78.9

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Hz), 124.9 (d, J_{C-P} = 109.1 Hz, 2C), 123.6 (d, J_{C-P} = 14.5 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ 25.71. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{14}NNaO_2PS$ 362.0381; Found 362.0373.

*3,3-Bis(4-methoxyphenyl)-3λ^5-benzo[d][1,2,3]thiazaphosphole 1,1-Dioxide (**3b**).* Compound **3b** was synthesized according to method A. Appearance: white solid (68%, 270.0 mg), R_f = 0.25 (*n*-hexane/dichloromethane/ethyl acetate, 1:1:1 v/v/v), mp 183−184 °C (dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 7.8 Hz, 1H), 7.80−7.75 (m, 1H), 7.71 (dd, $J_{H-P+H-H}$ = 13.3, 8.8 Hz, 4H), 7.66−7.59 (comp, 2H), 7.02 (dd, $J_{H-H+H-P}$ = 8.9, 2.7 Hz, 4H), 3.86 (s, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 164.2 (d, J_{C-P} = 2.9 Hz, 2C), 150.3 (d, J_{C-P} = 11.8 Hz), 134.7 (d, J_{C-P} = 13.3 Hz, 4C), 133.9 (d, J_{C-P} = 2.5 Hz), 132.0 (d, J_{C-P} = 10.1 Hz), 128.0 (d, J_{C-P} = 6.5 Hz), 126.4 (d, J_{C-P} = 80.4 Hz), 123.4 (d, J_{C-P} = 14.5 Hz), 115.5 (d, J_{C-P} = 116.7 Hz, 2C), 115.1 (d, J_{C-P} = 15.2 Hz, 4C), 55.6 (2C). ^{31}P NMR (162 MHz, $CDCl_3$) δ 25.31. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{20}H_{18}NNaO_4PS$ 422.0592; Found 422.0582.

*3,3-Di([1,1′-biphenyl]-4-yl)-3λ^5-benzo[d][1,2,3]thiazaphosphole 1,1-Dioxide (**3c**).* Compound **3c** was synthesized according to method A. Appearance: white solid (82%, 405.0 mg), R_f = 0.42 (*n*-hexane/dichloromethane/ethyl acetate, 2:2:1 v/v/v), mp 201−203 °C (dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 7.8 Hz, 1H), 7.91 (dd, $J_{H-P+H-H}$ = 13.6, 8.4 Hz, 4H), 7.88−7.79 (m, 1H), 7.80−7.73 (comp, 5H), 7.75−7.66 (m, 1H), 7.63−7.56 (m, 4H), 7.53−7.38 (comp, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 150.5 (d, J_{C-P} = 11.9 Hz), 147.2 (d, J_{C-P} = 3.0 Hz, 2C), 139.1 (2C), 134.3 (d, J_{C-P} = 2.9 Hz), 133.1 (d, J_{C-P} = 12.1 Hz, 4C), 132.2 (d, J_{C-P} = 10.2 Hz), 129.2 (4C), 128.8 (2C), 128.2 (d, J_{C-P} = 6.7 Hz), 128.2 (d, J_{C-P} = 14.0 Hz, 4C), 127.4 (4C), 125.4 (d, J_{C-P} = 79.4 Hz), 123.7 (d, J_{C-P} = 14.6 Hz), 123.2 (d, J_{C-P} = 111.2 Hz, 2C). ^{31}P NMR (162 MHz, $CDCl_3$) δ 25.66. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{30}H_{22}NNaO_2PS$ 514.1007; Found 514.0993.

*3,3-Bis(4-methoxyphenyl)-6-methyl-3λ^5-benzo[d][1,2,3]thiazaphosphole 1,1-Dioxide (**5a**).* Compound **5a** was synthesized according to method A. Appearance: white solid (73%, 300.6 mg), R_f = 0.35 (*n*-hexane/dichloromethane/ethyl acetate, 1:1:1 v/v/v), mp 188−189 °C (dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.69 (dd, $J_{H-P+H-H}$ = 13.2, 8.8 Hz, 4H), 7.55−7.48 (m, 1H), 7.43 (dd, $J_{H-H+H-P}$ = 7.6, 3.7 Hz, 1H), 7.00 (dd, $J_{H-H+H-P}$ = 8.9, 2.7 Hz, 4H), 3.85 (s, 6H), 2.49 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 164.1 (d, J_{C-P} = 2.8 Hz, 2C), 150.6 (d, J_{C-P} = 12.2 Hz), 145.5 (d, J_{C-P} = 2.7 Hz), 134.6 (d, J_{C-P} = 13.3 Hz, 4C), 133.0 (d, J_{C-P} = 10.7 Hz), 127.8 (d, J_{C-P} = 6.8 Hz), 123.7 (d, J_{C-P} = 14.9 Hz), 123.1 (d, J_{C-P} = 82.7 Hz), 115.9 (d, J_{C-P} = 116.7 Hz, 2C), 115.1 (d, J_{C-P} = 14.9 Hz, 4C), 55.6 (2C), 21.7. ^{31}P NMR (162 MHz, $CDCl_3$) δ 25.31. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{21}H_{20}NNaO_4PS$ 436.0748; Found 436.0741.

*6-Methyl-3,3-diphenyl-3λ^5-benzo[d][1,2,3]thiazaphosphole 1,1-Dioxide (**5b**).* Compound **5b** was synthesized according to method A. Appearance: white solid (76%, 210.0 mg), R_f = 0.53 (*n*-hexane/dichloromethane/ethyl acetate, 1:1:1 v/v/v), mp 297−298 °C (dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.79 (dd, $J_{H-H+H-P}$ = 14.0, 7.4 Hz, 4H), 7.72−7.62 (m, 2H), 7.61−7.50 (comp, 5H), 7.47 (dd, $J_{H-H+H-P}$ = 7.5, 3.7 Hz, 1H), 2.51 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 150.8 (d, J_{C-P} = 12.1 Hz), 145.9 (d, J_{C-P} = 2.7 Hz), 134.0 (d, J_{C-P} = 2.9 Hz, 2C), 133.2 (d, J_{C-P} = 10.6 Hz), 132.5 (d, J_{C-P} = 11.7 Hz, 4C), 129.5 (d, J_{C-P} = 13.7 Hz, 4C), 127.9 (d, J_{C-P} = 6.8 Hz), 125.2 (d, J_{C-P} = 109.0 Hz, 2C), 124.0 (d, J_{C-P} = 14.9 Hz), 121.9 (d, J_{C-P} = 81.3 Hz), 21.8. ^{31}P NMR (162 MHz, $CDCl_3$) δ 25.72. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{16}NNaO_2PS$ 376.0537; Found 376.0530.

*3,3-Bis(3-methoxyphenyl)-6-methyl-3λ^5-benzo[d][1,2,3]thiazaphosphole 1,1-Dioxide (**5c**).* Compound **5c** was synthesized according to method A. Appearance: white solid (78%, 321.2 mg), R_f = 0.44 (*n*-hexane/dichloromethane/ethyl acetate, 1:1:1 v/v/v), mp 185−186 °C (dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.59 (app t, J = 8.3 Hz, 1H), 7.51−7.39 (comp, 3H), 7.37−7.27 (comp, 4H), 7.16 (d, J = 8.4 Hz, 2H), 3.80 (s, 6H), 2.51 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 160.1 (d, J_{C-P} = 17.1 Hz, 2C), 150.7 (d, J_{C-P} = 12.2 Hz), 145.9 (d, J_{C-P} = 2.6 Hz), 133.2 (d, J_{C-P} = 10.6 Hz), 130.7 (d, J_{C-P} = 16.4 Hz, 2C), 128.0 (d, J_{C-P} = 6.7 Hz), 126.4 (d, J_{C-P} = 108.5 Hz, 2C), 124.4 (d, J_{C-P} = 11.8 Hz, 2C), 123.9 (d, J_{C-P} = 14.9 Hz), 121.8 (d, J_{C-P} = 81.4 Hz), 120.0 (d, J_{C-P} = 2.8 Hz, 2C), 117.3 (d, J_{C-P} = 12.9 Hz, 2C), 55.6 (2C), 21.8. ^{31}P NMR (162 MHz, $CDCl_3$) δ 25.98. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{21}H_{20}NNaO_4PS$ 436.0748; Found 436.0741.

*6-Methyl-3,3-di-p-tolyl-3λ^5-benzo[d][1,2,3]thiazaphosphole 1,1-Dioxide (**5d**).* Compound **5d** was synthesized according to method A. Appearance: white solid (81%, 309.0 mg), R_f = 0.59 (*n*-hexane/dichloromethane/ethyl acetate, 1:1:1 v/v/v), mp 222−223 °C (dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.66 (dd, $J_{H-P+H-H}$ = 13.7, 8.1 Hz, 4H), 7.52 (app t, J = 8.3 Hz, 1H), 7.44 (dd, $J_{H-H+H-P}$ = 8.0, 3.6 Hz, 1H), 7.33 (dd, $J_{H-H+H-P}$ = 8.0, 3.2 Hz, 4H), 2.51 (s, 3H), 2.42 (s, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 150.7 (d, J_{C-P} = 12.0 Hz), 145.6 (d, J_{C-P} = 2.6 Hz), 145.0 (d, J_{C-P} = 2.9 Hz, 2C), 133.0 (d, J_{C-P} = 10.6 Hz), 132.5 (d, J_{C-P} = 12.1 Hz, 4C), 130.1 (d, J_{C-P} = 14.2 Hz, 4C), 127.8 (d, J_{C-P} = 6.7 Hz), 123.9 (d, J_{C-P} = 14.8 Hz), 122.5 (d, J_{C-P} = 81.5 Hz), 122.0 (d, J_{C-P} = 111.6 Hz, 2C), 21.8 (2C), 21.7. ^{31}P NMR (162 MHz, $CDCl_3$) δ 25.82. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{21}H_{20}NNaO_2PS$ 404.0850; Found 404.0842.

*3,3-Bis(4-(tert-butyl)phenyl)-6-methyl-3λ^5-benzo[d][1,2,3]thiazaphosphole 1,1-Dioxide (**5e**).* Compound **5e** was synthesized according to method A. Appearance: white solid (74%, 346.7 mg), R_f = 0.80 (*n*-hexane/dichloromethane/ethyl acetate, 1:1:1 v/v/v), mp 263 °C (dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.72 (dd, $J_{H-P+H-H}$ = 13.6, 8.4 Hz, 4H), 7.61−7.51 (comp, 5H), 7.45 (dd, $J_{H-H+H-P}$ = 7.5, 3.6 Hz, 1H), 2.51 (s, 3H), 1.32 (s, 18H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 157.9 (d, J_{C-P} = 3.0 Hz, 2C), 150.8 (d, J_{C-P} = 12.0 Hz), 145.6 (d, J_{C-P} = 2.7 Hz), 133.0 (d, J_{C-P} = 10.6 Hz), 132.5 (d, J_{C-P} = 12.1 Hz, 4C), 127.9 (d, J_{C-P} = 6.8 Hz), 126.5 (d, J_{C-P} = 13.9 Hz, 4C), 123.9 (d, J_{C-P} = 14.8 Hz), 122.6 (d, J_{C-P} = 81.7 Hz), 121.9 (d, J_{C-P} = 111.3 Hz, 2C), 35.3 (2C), 31.0 (6C), 21.7. ^{31}P NMR (162 MHz, $CDCl_3$) δ 25.42. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{27}H_{32}NNaO_2PS$ 488.1789; Found 488.1780.

*3,3-Di([1,1′-biphenyl]-4-yl)-6-methyl-3λ^5-benzo[d][1,2,3]thiazaphosphole 1,1-Dioxide (**5f**).* Compound **5f** was synthesized according to method A. Appearance: white solid (80%, 403.4 mg), R_f = 0.55 (*n*-hexane/dichloromethane/ethyl acetate, 2:2:1 v/v/v), mp 198−201 °C (dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97−7.83 (comp, 5H), 7.74 (dd, $J_{H-H+H-P}$ = 8.3, 3.2 Hz, 4H), 7.67 (app t, J = 8.4 Hz, 1H), 7.57 (d, J = 7.6 Hz, 4H), 7.53−7.37 (comp, 7H), 2.50 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 150.8 (d, J_{C-P} = 12.1 Hz), 147.0 (d, J_{C-P} = 3.0 Hz, 2C), 145.9 (d, J_{C-P} = 2.7 Hz), 139.1 (2C), 133.3 (d, J_{C-P} = 10.7 Hz), 133.0 (d, J_{C-P} = 12.1 Hz, 4C), 129.1 (4C), 128.8 (2C), 128.1 (d, J_{C-P} = 14.0 Hz, 4C), 128.0 (d, J_{C-P} = 7.0 Hz), 127.3 (4C), 123.9 (d, J_{C-P} = 14.8 Hz), 123.5 (d, J_{C-P} = 110.9 Hz, 2C), 122.1 (d, J_{C-P} = 81.6 Hz), 21.8. ^{31}P NMR (162 MHz, $CDCl_3$) δ 25.66. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{31}H_{24}NNaO_2PS$ 528.1163; Found 528.1143.

*3,3-Bis(3,5-dimethylphenyl)-6-methyl-3λ^5-benzo[d][1,2,3]thiazaphosphole 1,1-Dioxide (**5g**).* Compound **5g** was synthesized according to method A. Appearance: white solid (65%, 266.6 mg), R_f = 0.70 (*n*-hexane/dichloromethane/ethyl acetate, 1:1:1 v/v/v), mp 256−257 °C (dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.59 (app t, J = 8.3 Hz, 1H), 7.48 (dd, $J_{H-H+H-P}$ = 7.6, 3.6 Hz, 1H), 7.36 (d, J_{H-P} = 14.4 Hz, 4H), 7.26 (s, 2H), 2.50 (s, 3H), 2.33 (s, 12H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 150.6 (d, J_{C-P} = 12.0 Hz), 145.6 (d, J_{C-P} = 2.7 Hz), 139.4 (d, J_{C-P} = 14.5 Hz, 4C), 135.8 (d, J_{C-P} = 3.0 Hz, 2C), 133.1 (d, J_{C-P} = 10.6 Hz), 129.8 (d, J_{C-P} = 11.6 Hz, 4C), 128.1 (d, J_{C-P} = 6.7 Hz), 125.1 (d, J_{C-P} = 107.6 Hz, 2C), 123.8 (d, J_{C-P} = 14.8 Hz), 122.2 (d, J_{C-P} = 80.9 Hz), 21.7, 21.3 (4C). ^{31}P NMR (162 MHz, $CDCl_3$) δ 26.49. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{23}H_{24}NNaO_4PS$ 432.1163; Found 432.1143.

*3,3-Bis(3,5-di-tert-butylphenyl)-6-methyl-3λ^5-benzo[d][1,2,3]-thiazaphosphole 1,1-Dioxide (**5h**).* Compound **5h** was synthesized according to method A. Appearance: white solid (74%, 429.9 mg), R_f = 0.45 (*n*-hexane/dichloromethane/ethyl acetate, 10:10:1 v/v/v), mp 259−261 °C (dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.73−7.67(app q, J = 1.7 Hz, 2H), 7.60 (dd, $J_{H-P+H-H}$ =

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14.8, 1.7 Hz, 4H), 7.53 (app t, J = 8.2 Hz, 1H), 7.46 (dd, $J_{H-H+H-P}$ = 7.5, 3.7 Hz, 1H), 2.51 (s, 3H), 1.29 (s, 36H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 152.2 (d, J_{C-P} = 13.3 Hz, 4C), 150.7 (d, J_{C-P} = 12.0 Hz), 145.4 (d, J_{C-P} = 2.6 Hz), 132.9 (d, J_{C-P} = 10.4 Hz), 128.2 (d, J_{C-P} = 2.9 Hz, 2C), 127.6 (d, J_{C-P} = 6.7 Hz), 126.7 (d, J_{C-P} = 12.4 Hz, 4C), 124.4 (d, J_{C-P} = 107.4 Hz, 2C), 123.9 (d, J_{C-P} = 14.6 Hz), 123.2 (d, J_{C-P} = 80.4 Hz), 35.2 (4C), 31.2 (12C), 21.7. ^{31}P NMR (162 MHz, $CDCl_3$) δ 27.39. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{35}H_{48}NNaO_2PS$ 600.3041; Found 600.3025.

*3,3-Bis(3,5-dimethoxyphenyl)-6-methyl-3λ⁵-benzo[d][1,2,3]-thiazaphosphole 1,1-Dioxide (**5i**).* Compound **5i** was synthesized according to method A on a 0.50 mmol scale. Appearance: white solid (82%, 390.1 mg), R_f = 0.47 (*n*-hexane/dichloromethane/ethyl acetate, 1:1:1 v/v/v), mp 239−240 °C (dichloromethane); ^1H NMR (400 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.58 (app t, J = 8.3 Hz, 1H), 7.47 (dd, $J_{H-H+H-P}$ = 7.2, 3.7 Hz, 1H), 6.89 (dd, $J_{H-P+H-H}$ = 15.5, 1.8 Hz, 4H), 6.67 (app s, 2H), 3.78 (s, 12H), 2.51 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 161.5 (d, J_{C-P} = 20.5 Hz, 4C), 150.7 (d, J_{C-P} = 12.1 Hz), 146.0 (d, J_{C-P} = 2.7 Hz), 133.1 (d, J = 10.6 Hz), 128.0 (d, J = 6.6 Hz), 127.0 (d, J_{C-P} = 109.2 Hz, 2C), 124.0 (d, J_{C-P} = 14.9 Hz), 121.6 (d, J_{C-P} = 81.6 Hz), 110.0 (d, J_{C-P} = 13.1 Hz, 4C), 105.8 (d, J_{C-P} = 2.4 Hz 2C), 55.8 (4C), 21.8. ^{31}P NMR (162 MHz, $CDCl_3$) δ 26.94. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{23}H_{24}NNaO_6PS$ 496.0960; Found 496.0951.

*3,3-Bis(4-methoxy-3,5-dimethylphenyl)-6-methyl-3λ⁵-benzo[d]-[1,2,3]thiazaphosphole 1,1-Dioxide (**5j**).* Compound **5j** was synthesized according to method A. Appearance: white solid (67%, 313.6 mg), R_f = 0.61 (*n*-hexane/dichloromethane/ethyl acetate, 1:1:1 v/v/v), mp 218 °C (dichloromethane); ^1H NMR (400 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.56 (app t, J = 8.3 Hz, 1H), 7.47 (dd, $J_{H-P+H-H}$ = 7.6, 3.6 Hz, 1H), 7.40 (d, J_{H-P} = 13.9 Hz, 4H), 3.75 (s, 6H), 2.51 (s, 3H), 2.29 (s, 12H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 162.0 (d, J_{C-P} = 3.5 Hz, 2C), 150.6 (d, J_{C-P} = 12.1 Hz), 145.6 (d, J_{C-P} = 2.6 Hz), 133.1 (d, J_{C-P} = 12.5 Hz, 4C), 133.1 (d, J = 10.3 Hz), 132.8 (d, J_{C-P} = 15.2 Hz, 4C), 128.0 (d, J_{C-P} = 6.7 Hz), 123.8 (d, J_{C-P} = 14.8 Hz), 122.6 (d, J_{C-P} = 81.6 Hz), 119.8 (d, J_{C-P} = 111.1 Hz, 2C), 59.7 (2C), 21.7, 16.3 (4C). ^{31}P NMR (162 MHz, $CDCl_3$) δ 25.67. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{25}H_{28}NNaO_4PS$ 492.1374; Found 492.1365.

*6-Methyl-3,3-di(naphthalen-2-yl)-3λ⁵-benzo[d][1,2,3]thiaza-phosphole 1,1-Dioxide (**5k**).* Compound **5k** was synthesized according to method A. Appearance: white solid (72%, 326.1 mg), R_f = 0.62 (*n*-hexane/dichloromethane/ethyl acetate, 1:1:1 v/v/v), mp 276−277 °C (dichloromethane); ^1H NMR (400 MHz, $CDCl_3$) δ 8.43 (d, J_{H-P} = 16.1 Hz, 2H), 8.03−7.95 (comp, 3H), 7.91 (comp, 4H), 7.79−7.64 (comp, 5H), 7.60 (app t, J = 7.6 Hz, 2H), 7.49 (dd, $J_{H-H+H-P}$ = 8.2, 3.8 Hz, 1H), 2.53 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 150.9 (d, J_{C-P} = 11.9 Hz), 146.0 (d, J_{C-P} = 2.9 Hz), 135.5 (d, J_{C-P} = 2.9 Hz, 2C), 135.4 (d, J_{C-P} = 11.2 Hz, 2C), 133.2 (d, J_{C-P} = 10.7 Hz), 132.5 (d, J_{C-P} = 15.1 Hz, 2C), 129.6 (d, J_{C-P} = 13.8 Hz, 2C), 129.5 (2C), 129.2 (2C), 128.1 (d, d, J_{C-P} = 5.3 Hz), 128.0 (2C), 127.8 (2C), 126.0 (d, J_{C-P} = 12.6 Hz, 2C), 124.1 (d, J_{C-P} = 14.9 Hz), 122.2 (d, J_{C-P} = 109.8 Hz, 2C), 122.1 (d, J_{C-P} = 81.5 Hz), 21.8. ^{31}P NMR (162 MHz, $CDCl_3$) δ 26.29. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{27}H_{20}NNaO_2PS$ 476.0850; Found 476.0842.

*3,3-Bis(4-fluorophenyl)-6-methyl-3λ⁵-benzo[d][1,2,3]thiaza-phosphole 1,1-Dioxide (**5l**).* Compound **5l** was synthesized according to method A. Appearance: white solid (68%, 263.2 mg), R_f = 0.55 (*n*-hexane/dichloromethane/ethyl acetate, 1:1:1 v/v/v), mp 263−267 °C (dichloromethane); ^1H NMR (400 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.88−7.71 (m, 4H), 7.64−7.55 (m, 1H), 7.51 (dd, $J_{H-H+H-P}$ = 7.6, 3.9 Hz, 1H), 7.30−7.20 (m, 4H), 2.53 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 166.4 (dd, $J_{C-P+C-F}$ = 258.2, 3.4 Hz, 2C), 150.8 (d, J_{C-P} = 12.2 Hz), 146.3 (d, J_{C-P} = 2.7 Hz), 135.2 (dd, $J_{C-P+C-F}$ = 13.5, 9.4 Hz, 4C), 133.5 (d, J_{C-P} = 10.7 Hz), 127.8 (d, J_{C-P} = 6.8 Hz), 124.1 (d, J_{C-P} = 15.0 Hz), 121.5 (d, J_{C-P} = 82.3 Hz), 121.0 (dd, $J_{C-P+C-F}$ = 113.7, 3.6 Hz, 2C), 117.3 (dd, $J_{C-P+C-F}$ = 21.9, 15.2 Hz, 4C), 21.8. ^{19}F NMR (377 MHz, $CDCl_3$) δ −101.79 (d, J_{F-P} = 1.5 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ 24.50. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{14}F_2NNaO_2PS$ 412.0349; Found 412.0341.

*3,3-Bis(4-chlorophenyl)-6-methyl-3λ⁵-benzo[d][1,2,3]thiaza-phosphole 1,1-Dioxide (**5m**).* Compound **5m** was synthesized according to method A. Appearance: white solid (80%, 339.5 mg), R_f = 0.68 (*n*-hexane/dichloromethane/ethyl acetate, 1:1:1 v:v:v), mp 240−241 °C (dichloromethane); ^1H NMR (400 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.78−7.65 (m, 4H), 7.62−7.43 (comp, 6H), 2.53 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 151.0 (d, J_{C-P} = 12.2 Hz), 146.5 (d, J_{C-P} = 2.5 Hz), 141.4 (d, J_{C-P} = 3.6 Hz, 2C), 133.7 (d, J_{C-P} = 12.7 Hz, 4C), 133.5 (d, J_{C-P} = 10.6 Hz), 130.1 (d, J_{C-P} = 14.4 Hz, 4C), 127.7 (d, J_{C-P} = 6.7 Hz), 124.2 (d, J_{C-P} = 15.0 Hz), 123.4 (d, J_{C-P} = 111.8 Hz, 2C), 121.0 (d, J_{C-P} = 82.3 Hz), 21.8. ^{31}P NMR (162 MHz, $CDCl_3$) δ 24.69. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{14}Cl_2NNaO_2PS$ 443.9758 (^{35}Cl), 445.9728 (^{37}Cl); Found 443.9748 (^{35}Cl), 445.9715 (^{37}Cl).

*6-Methoxy-3,3-diphenyl-3λ⁵-benzo[d][1,2,3]thiazaphosphole 1,1-Dioxide (**5n**).* Compound **5n** was synthesized according to method A. Appearance: white solid (69%, 256.3 mg), R_f = 0.42 (*n*-hexane/dichloromethane/ethyl acetate, 1:1:1 v/v/v), mp 227−228 °C (dichloromethane); ^1H NMR (400 MHz, $CDCl_3$) δ 7.84−7.73 (m, 4H), 7.71−7.62 (m, 2H), 7.59−7.49 (comp, 6H), 7.17 (ddd, $J_{H-H+H-P}$ = 8.4, 3.3, 2.2 Hz, 1H), 3.92 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 164.9 (d, J_{C-P} = 2.6 Hz), 153.3 (d, J_{C-P} = 13.2 Hz), 134.0 (d, J_{C-P} = 3.0 Hz, 2C), 132.4 (d, J_{C-P} = 11.7 Hz, 4C), 129.4 (d, J_{C-P} = 13.7 Hz, 4C), 129.1 (d, J_{C-P} = 8.1 Hz), 125.4 (d, J_{C-P} = 109.3 Hz, 2C), 120.8 (d, J_{C-P} = 11.2 Hz), 115.2 (d, J_{C-P} = 85.4 Hz), 106.8 (d, J_{C-P} = 15.9 Hz), 56.2. ^{31}P NMR (162 MHz, $CDCl_3$) δ 25.57. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{16}NNaO_3PS$ 392.0486; Found 392.0478.

*5-Chloro-6-methyl-3,3-diphenyl-3λ⁵-benzo[d][1,2,3]thiaza-phosphole 1,1-Dioxide (**5o**).* Compound **5o** was synthesized according to method A. Appearance: white solid (70%, 272.6 mg), R_f = 0.44 (*n*-hexane/dichloromethane/ethyl acetate, 2:2:1 v/v/v), mp 308−309 °C (dichloromethane); ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.80 (dd, $J_{H-P+H-H}$ = 14.1, 7.7 Hz, 4H), 7.70 (t, J = 7.6 Hz, 2H), 7.66−7.53 (comp, 5H), 2.52 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 148.9 (d, J_{C-P} = 11.6 Hz), 143.8 (d, J_{C-P} = 2.6 Hz), 138.9 (d, J_{C-P} = 13.8 Hz), 134.4 (d, J_{C-P} = 2.9 Hz, 2C), 132.5 (d, J_{C-P} = 11.8 Hz, 4C), 129.6 (d, J_{C-P} = 13.8 Hz, 4C), 128.0 (d, J_{C-P} = 7.6 Hz), 125.5 (d, J_{C-P} = 15.9 Hz), 124.5 (d, J_{C-P} = 79.4 Hz), 124.5 (d, J_{C-P} = 109.3 Hz, 2C), 20.9. ^{31}P NMR (162 MHz, $CDCl_3$) δ 24.35. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{15}ClNNaO_2PS$ 410.0147 (^{35}Cl), 412.0118 (^{37}Cl); Found 410.0128 (^{35}Cl), 412.0092 (^{37}Cl).

*6-Methyl-3,3-di(thiophen-2-yl)-3λ⁵-benzo[d][1,2,3]thiaza-phosphole 1,1-Dioxide (**5p**).* Compound **5p** was synthesized according to method A except that the reaction was run in anhydrous acetonitrile (2.5 mL) at 70 °C for 48 h. Appearance: white solid (89%, 325.2 mg), R_f = 0.22 (*n*-hexane/dichloromethane/ethyl acetate, 2:2:1 v/v/v), mp 244−245 °C (dichloromethane); ^1H NMR (400 MHz, $CDCl_3$) δ 7.97−7.89 (comp, 3H), 7.84 (dd, $J_{H-P+H-H}$ = 8.8, 3.7 Hz, 2H), 7.60 (dd, $J_{H-P+H-H}$ = 10.6, 7.8 Hz, 1H), 7.49 (dd, $J_{H-H+H-P}$ = 8.0, 4.1 Hz, 1H), 7.34−7.24 (m, 2H), 2.52 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 150.5 (d, J_{C-P} = 13.6 Hz), 146.3 (d, J_{C-P} = 2.9 Hz), 140.2 (d, J_{C-P} = 12.4 Hz, 2C), 137.6 (d, J_{C-P} = 6.6 Hz, 2C), 133.3 (d, J_{C-P} = 11.6 Hz), 129.6 (d, J_{C-P} = 16.6 Hz, 2C), 127.8 (d, J_{C-P} = 7.0 Hz), 125.6 (d, J_{C-P} = 132.4 Hz, 2C), 123.8 (d, J_{C-P} = 16.1 Hz), 122.9 (d, J_{C-P} = 90.8 Hz), 21.8. ^{31}P NMR (162 MHz, $CDCl_3$) δ 10.34. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{12}NNaO_2PS_3$ 387.9665; Found 387.9652.

*6-Methyl-3,3-di-o-tolyl-3λ⁵-benzo[d][1,2,3]thiazaphosphole 1,1-Dioxide (**5q**).* Compound **5q** was synthesized according to method B. Appearance: white solid (65%, 247.9 mg), R_f = 0.38 (*n*-hexane/dichloromethane/ethyl acetate, 2:2:1 v/v/v), mp 209−210 °C (dichloromethane); ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (s, 1H), 7.76−7.58 (comp, 3H), 7.57−7.46 (comp, 3H), 7.38−7.24 (comp, 4H), 2.54 (s, 3H), 2.40 (s, 6H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 151.1 (d, J_{C-P} = 12.9 Hz), 145.8 (d, J_{C-P} = 2.8 Hz), 142.9 (d, J_{C-P} = 9.5 Hz, 2C), 133.9 (d, J_{C-P} = 3.0 Hz, 2C), 133.0 (d, J_{C-P} = 14.1 Hz, 2C), 132.9 (d, J_{C-P} = 10.2 Hz), 132.6 (d, J_{C-P} = 11.8 Hz, 2C), 128.6 (d, J_{C-P} = 6.3 Hz), 126.6 (d, J_{C-P} = 14.3 Hz, 2C), 124.5 (d, J_{C-P} =

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14.7 Hz), 124.5 (d, J_{C-P} = 106.2 Hz, 2C), 121.5 (d, J_{C-P} = 79.5 Hz), 21.8 (d, J_{C-P} = 4.8 Hz, 2C), 21.7. ^{31}P NMR (162 MHz, $CDCl_3$) δ 28.56. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{21}H_{20}NNaO_2PS$ 404.0850; Found 404.0825.

*6-Methyl-3,3-di(naphthalen-1-yl)-3λ^5-benzo[d][1,2,3]thiazaphosphole 1,1-Dioxide (**5r**).* Compound **5r** was synthesized according to method B except that the reaction was run on a 0.50 mmol scale in anhydrous dimethyl sulfoxide (5.0 mL). Appearance: white solid (60%,136.0 mg), R_f = 0.42 (*n*-hexane/dichloromethane/ethyl acetate, 2:2:1 v/v/v), mp 302−304 °C (dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, J = 8.5 Hz, 2H), 8.19−8.09 (comp, 4H), 8.02 (s, 1H), 7.92 (app d, J = 8.2 Hz, 2H), 7.74 (app t, J = 8.3 Hz, 1H), 7.63−7.47 (comp, 4H), 7.49−7.38 (comp, 3H), 2.51 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 150.6 (d, J_{C-P} = 12.8 Hz), 146.1 (d, J_{C-P} = 2.9 Hz), 135.3 (d, J_{C-P} = 3.3 Hz, 2C), 134.4 (d, J_{C-P} = 12.6 Hz, 2C), 134.0 (d, J_{C-P} = 10.4 Hz, 2C), 133.0 (d, J_{C-P} = 10.5 Hz), 132.6 (d, J_{C-P} = 10.0 Hz, 2C), 129.5 (d, J_{C-P} = 1.8 Hz, 2C), 128.6 (d, J_{C-P} = 6.4 Hz), 128.4 (2C), 127.1 (2C), 125.4 (d, J_{C-P} = 6.3 Hz, 2C), 125.0 (d, J_{C-P} = 16.0 Hz, 2C), 124.7 (d, J_{C-P} = 15.0 Hz), 122.8 (d, J_{C-P} = 106.6 Hz, 2C), 122.0 (d, J_{C-P} = 80.8 Hz), 21.7. ^{31}P NMR (162 MHz, $CDCl_3$) δ 28.05. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{27}H_{20}NNaO_2PS$ 476.0850; Found 476.0826.

Computational Details. The calculations were carried out with the Gaussian 09 software package.[11] The structures were optimized by the density functional theory (DFT)[16] with the B3LYP functional[17] with basis set 6-31G(d)[18] in the gas phase. Frequency analysis was conducted at the same level of theory to verify the stationary points to be real minima or saddle points and to obtain the thermodynamic energy corrections at 298.15 K. Intrinsic reaction coordinate (IRC)[19] calculations were performed to confirm the connection between two correct minima for a transition state. More accurate electronic energy results were refined by calculating the single-point energy at the B3LYP-D3(BJ)[20]/6-311++G(2df, 2p)[18] level of theory with the SMD model[21] (solvent = acetonitrile).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c01309.

NMR spectra of **3a−c**, **4a−r**, **5a−r**, and **6a−c**, crystal data and structure refinement for compound of **5a**, and geometries and energies for all chemical structures in Figure 1 (PDF)

X-ray crystal structure for **5a** (CCDC 1997095) (CIF)

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Notes

The authors declare the following competing financial interest(s): Sun Yat-sen University has filed a patent application.

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■ REFERENCES

(1) (a) Eicher, T.; Hauptmann, S.; Speicher, A. *The Chemistry of Heterocycles*, 3rd ed., Wiley-VCH: Weinheim, 2012. (b) Katritzky, A. R.; Ramsden, C. A.; Joule, J. A.; Zhdankin, V. V. *Handbook of Heterocyclic Chemistry*, 3rd ed.; Pergamon: Amsterdam, 2010. (c) Joule, J. A.; Mills, K. *Heterocyclic Chemistry*, 4th ed.; Blackwell: Oxford, 2000.

(2) (a) Zhang, T. Y. The Evolving Landscape of Heterocycles in Drugs and Drug Candidates. *Adv. Heterocycl. Chem.* **2017**, *121*, 1. (b) Vitaku, E.; Smith, D. T.; Njardarson, J. T. Analysis of the Structural Diversity, Substitution Patterns, and Frequency of Nitrogen Heterocycles among U.S. FDA Approved Pharmaceuticals. *J. Med. Chem.* **2014**, *57*, 10257. (c) Li, J. J. *Heterocyclic Chemistry in Drug Discovery*; Wiley: Hoboken, 2013. (d) Gomtsyan, A. Heterocycles in Drugs and Drug Discovery. *Chem. Heterocycl. Compd.* **2012**, *48*, 7.

(3) (a) Cabrele, C.; Reiser, O. The Modern Face of Synthetic Heterocyclic Chemistry. *J. Org. Chem.* **2016**, *81*, 10109. (b) Garcia-Castro, M.; Zimmermann, S.; Sankar, M. G.; Kumar, K. Scaffold Diversity Synthesis and Its Application in Probe and Drug Discovery. *Angew. Chem., Int. Ed.* **2016**, *55*, 7586. (c) St. Jean, D. J., Jr.; Fotsch, C. Mitigating Heterocycle Metabolism in Drug Discovery. *J. Med. Chem.* **2012**, *55*, 6002. (d) Dua, R.; Shrivastava, S.; Sonwane, S. K.; Srivastava, S. K. Pharmacological Significance of Synthetic Heterocycles Scaffold: A Review. *Adv. Biol. Res.* **2011**, *5*, 120.

(4) Iaroshenko, V. *Organophosphorus Chemistry*; Wiley-VCH: Weinheim, 2019.

(5) Dillon, K. B.; Mathey, F.; Nixon, J. F. *Phosphorus: The Carbon Copy*; Wiley: Chichester, 1998.

(6) (a) Rodriguez, J. B.; Gallo-Rodriguez, C. The Role of the Phosphorus Atom in Drug Design. *ChemMedChem* **2018**, *14*, 190. (b) Demkowicz, S.; Rachon, J.; Daśko, M.; Kozak, W. Selected Organophosphorus Compounds with Biological Activity. Applications in Medicine. *RSC Adv.* **2016**, *6*, 7101. (c) Westheimer, F. H. Why Nature Chose Phosphates. *Science* **1987**, *235*, 1173. (d) Yamashita, M. Preparation, Structure, and Biological Properties of Phosphorus Heterocycles with a C−P Ring System. In *Bioactive Heterocycles II*; Eguchi, S., Eds.; Topics in Heterocyclic Chemistry, *Vol. 8*; Springer: Berlin, Heidelberg, 2007; pp 173−222. (e) Suter, R.; Benkő, Z.;

Bispinghoff, M.; Grützmacher, H. Annulated 1,3,4-Azadiphospholides: Heterocycles with Widely Tunable Optical Properties. *Angew. Chem., Int. Ed.* **2017**, *56*, 11226. (f) Romero-Nieto, C.; López-Andarias, A.; Egler-Lucas, C.; Gebert, F.; Neus, J.-P.; Pilgram, O. Paving the Way to Novel Phosphorus-Based Architectures: A Noncatalyzed Protocol to Access Six-Membered Heterocycles. *Angew. Chem., Int. Ed.* **2015**, *54*, 15872. (g) Loibl, A.; de Krom, I.; Pidko, E. A.; Weber, M.; Wiecko, J.; Müller, C. Tuning the Electronic Effects of Aromatic Phosphorus Heterocycles: An Unprecedented Phosphinine with Significant P(π)-donor Properties. *Chem. Commun.* **2014**, *50*, 8842.

(7) (a) Kürti, L.; Czakó, B. *Strategic Applications of Named Reactions in Organic Synthesis*; Elsevier: Dorecht, 2005. (b) Li, J. J. Name Reactions. *A Collection of Detailed Reaction Mechanisms*, 2nd ed.; Springer: Heidelberg, 2003. (c) Tian, W. Q.; Wang, Y. A. Mechanisms of Staudinger Reactions within Density Functional Theory. *J. Org. Chem.* **2004**, *69*, 4299. (d) Leffler, J. E.; Temple, R. D. The Staudinger Reaction between Triarylphosphines and Azides. A Study of the Mechanism. *J. Am. Chem. Soc.* **1967**, *89*, 5235. Selected publications on the synthesis of heterocycles through an iminophosphorane intermediate: (e) Wang, Y.; Zhang, C. Progress in Reactions of N-Isocyanoiminotriphenylphosphorane. *ChemistrySelect* **2020**, *5*, 171. (f) Ramazani, A.; Rezaei, A. Novel One-Pot, Four-Component Condensation Reaction; An Efficient Approach for the Synthesis of 2,5-Disubstituted 1,3,4-Oxadiazole Derivatives by a Ugi-4CR/*aza*-Wittig Sequence. *Org. Lett.* **2010**, *12*, 2852.

(8) (a) Jian, Z.; Falivene, L.; Wucher, P.; Roesle, P.; Caporaso, L.; Cavallo, L.; Goettker-Schnetmann, I.; Mecking, S. Insights into Functional-Group-Tolerant Polymerization Catalysis with Phosphine-Sulfonamide Palladium(II) Complexes. *Chem. - Eur. J.* **2015**, *21*, 2062. (b) Bennett, J. L.; Brookhart, M. S., III; Johnson, L. K.; Killian, C. M. *PCT Int. Appl.* WO 9830610 A1, July 16, 1998.

(9) (a) Li, L.; Liang, D.; Cao, X.; Wang, Z. *PCT Int. Appl.* WO 2019206166 A1, October 31, 2019. (b) Li, L.; Liang, D.; Cao, X. *Faming Zhuanli Shenqing* CN 108484668 A, September 4, 2018. (c) Li, L.; Liang, D.; Wang, Z. *Faming Zhuanli Shenqing* CN 108467409 A, August 31, 2018.

(10) (a) Rhine, M. A.; Rodrigues, A. V.; Urbauer, R. J. B.; Urbauer, J. L.; Stemmler, T. L.; Harrop, T. C. Proton-Induced Reactivity of NO− from a $\{CoNO\}^8$ Complex. *J. Am. Chem. Soc.* **2014**, *136*, 12560. (b) Lacour, M.-A.; Zablocka, M.; Duhayon, C.; Majoral, J.-P.; Taillefer, M. Efficient Phosphorus Catalysts for the Halogen-Exchange (Halex) Reaction. *Adv. Synth. Catal.* **2008**, *350*, 2677. (c) Yavari, I.; Zabarjad-Shiraz, N.; Bijanzadeh, H. R. Synthesis of Sulfur-Containing Aryliminophosphoranes. *Phosphorus, Sulfur Silicon Relat. Elem.* **2004**, *179*, 1381. (d) Stephan, D. W.; Stewart, J. C.; Guérin, F.; Courtenay, S.; Kickham, J.; Hollink, E.; Beddie, C.; Hoskin, A.; Graham, T.; Wei, P.; Spence, R. E. v. H.; Xu, W.; Koch, L.; Gao, X.; Harrison, D. G. An Approach to Catalyst Design: Cyclopentadienyl-Titanium Phosphinimide Complexes in Ethylene Polymerization. *Organometallics* **2003**, *22*, 1937. (e) Cherryman, J. C.; Harris, R. K.; Davidson, M. G.; Price, R. D. Structural and Electronic Information on Two Solid Iminophosphoranes, Obtained from NMR. *J. Braz. Chem. Soc.* **1999**, *10*, 287.

(11) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, Jr., J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Keith, T.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, O.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. *Gaussian 09, Revision D.01*; Gaussian, Inc.: Wallingford, CT, 2013.

(12) Armarego, W. L. F.; Perrin, D. D. *Purification of Laboratory Chemicals*, 4th ed.; Butterworth-Heinemann: Oxford, 1997.

(13) Zheng, Q.; Woehl, J. L.; Kitamura, S.; Santos-Martins, D.; Smedley, C. J.; Li, G.; Forli, S.; Moses, J. E.; Wolan, D. W.; Sharpless, K. B. SuFEx-Enabled, Agnostic Discovery of Covalent Inhibitors of Human Neutrophil Elastase. *Proc. Natl. Acad. Sci. U. S. A.* **2019**, *116*, 18808.

(14) (a) Busacca, C. A.; Lorenz, J. C.; Grinberg, N.; Haddad, N.; Hrapchak, M.; Latli, B.; Lee, H.; Sabila, P.; Saha, A.; Sarvestani, M.; Shen, S.; Varsolona, R.; Wei, X. D.; Senanayake, C. H. A Superior Method for the Reduction of Secondary Phosphine Oxides. *Org. Lett.* **2005**, *7*, 4277. (b) Stankevič, M.; Pietrusiewicz, M. An Expedient Reduction of *sec*-Phosphine Oxides to *sec*-Phosphine-Boranes by $BH_3{\cdot}SMe_2$. *Synlett* **2003**, 1012. (c) Senda, Y.; Ogasawara, O.; Hayashi, T. Rhodium-Catalyzed Asymmetric 1,4-Addition of Organoboron Reagents to 5,6-Dihydro-2(*1H*)-pyridinones. Asymmetric Synthesis of 4-Aryl-2-piperidinones. *J. Org. Chem.* **2001**, *66*, 6852. (d) Hobbs, C. F.; Knowles, W. S. Asymmetric Hydroformylation of Vinyl Acetate with DIOP-Type Ligands. *J. Org. Chem.* **1981**, *46*, 4422.

(15) (a) Hou, M. Q.; Deng, R. X.; Gu, Z. H. Cu-Catalyzed Enantioselective Atropisomer Synthesis via Thiolative Ring Opening of Five-Membered Cyclic Diaryliodoniums. *Org. Lett.* **2018**, *20*, 5779. (b) Bloomfield, A. J.; Herzon, S. B. Room Temperature, Palladium-Mediated P−Arylation of Secondary Phosphine Oxide. *Org. Lett.* **2012**, *14*, 4370. (c) Julienne, D.; Lohier, J.-F.; Delacroix, O.; Gaumont, A.-C. Palladium-Catalyzed C−P Coupling Reactions between Vinyl Triflates and Phosphine−Boranes: Efficient Access to Vinylphosphine−Boranes. *J. Org. Chem.* **2007**, *72*, 2247. (d) Herd, O.; Heβler, A.; Hingst, M.; Tepper, M.; Stelzer, O. Water Soluble Phosphines VIII. Palladium-Catalyzed P−C Cross Coupling Reactions between Primary or Secondary Phosphines and Functional Aryliodides — a Novel Synthetic Route to Water Soluble Phosphines. *J. Organomet. Chem.* **1996**, *522*, 69. (e) Uozumi, Y.; Tanahashi, A.; Lee, S. P.; Hayashi, T. Synthesis of Optically Active 2-(Diarylphosphino)-1,1′-binaphthyls, Efficient Chiral Monodentate Phosphine Ligands. *J. Org. Chem.* **1993**, *58*, 1945. (f) Kurz, L.; Lee, G.; Morgans, D., Jr.; Waldyke, M. J.; Ward, T. Stereospecific Functionalization of (R)-(−)-1,1′-Bi-2-naphthol Triflate. *Tetrahedron Lett.* **1990**, *31*, 6321.

(16) Koch, W.; Holthausen, M. C. *A Chemist's Guide to Density Functional Theory*; Wiley: New York, 2001.

(17) (a) Becke, A. D. Becke's Three Parameter Hybrid Method Using the LYP Correlation Functional. *J. Chem. Phys.* **1993**, *98*, 5648. (b) Lee, C. T.; Yang, W. T.; Parr, R. G. Development of the ColleSalvetti Correlation-Energy Formula into a Functional of the Electron Density. *Phys. Rev. B: Condens. Matter Mater. Phys.* **1988**, *37*, 785.

(18) (a) Hariharan, P. C.; Pople, J. A. The Influence of Polarization Functions on Molecular Orbital Hydrogenation Energies. *Theoret. Chimica Acta* **1973**, *28*, 213. (b) Rassolov, V.; Pople, J. A.; Ratner, M.; Windus, T. L. 6-31G* Basis Set for Atoms K through Zn. *J. Chem. Phys.* **1998**, *109*, 1223.

(19) (a) Fukui, K. Formulation of the Reaction Coordinate. *J. Phys. Chem.* **1970**, *74*, 4161. (b) Gonzalez, C.; Schlegel, H. B. An Improved Algorithm for Reaction Path Following. *J. Chem. Phys.* **1989**, *90*, 2154. (c) Gonzalez, C.; Schlegel, H. B. Reaction Path Following in Mass-Weighted Internal Coordinates. *J. Phys. Chem.* **1990**, *94*, 5523.

(20) Grimme, S.; Ehrlich, S.; Goerigk, L. Effect of the Damping Function in Dispersion Corrected Density Functional Theory. *J. Comput. Chem.* **2011**, *32*, 1456.

(21) Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. Universal Solvation Model Based on Solute Electron Density and on a Continuum Model of the Solvent Defined by the Bulk Dielectric Constant and Atomic Surface Tensions. *J. Phys. Chem. B* **2009**, *113*, 6378.

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