

Supporting Online Material for

Selective Halogenation of Pyridines Using Designed Phosphine Reagents

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1. General Information

Proton nuclear magnetic resonance (^1H NMR) spectra were recorded at ambient temperature on either a Bruker Ultrashield-400 (400 MHz) spectrometer, a Varian 400 MR (400 MHz) spectrometer or an Agilent Inova 400 (400 MHz) spectrometer. Chemical shifts (δ) are reported in ppm and quoted to the nearest 0.01 ppm relative to the residual protons in CDCl_3 (7.26 ppm), C_6D_6 (7.16 ppm), $(\text{CD}_3)_2\text{SO}$ (2.50 ppm), CD_3OD (3.31 ppm) or CD_3CN (1.94 ppm) and coupling constants (J) are quoted in Hertz (Hz). Data are reported as follows: Chemical shift (number of protons, multiplicity, coupling constants). Coupling constants were quoted to the nearest 0.1 Hz and multiplicity reported according to the following convention: s = singlet, d = doublet, t = triplet, q = quartet, qn = quintet, sext = sextet, sp = septet, m = multiplet, br = broad. Where coincident coupling constants have been observed, the apparent (app) multiplicity of the proton resonance has been reported. Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded at ambient temperature on either a Bruker Ultrashield-400 (400 MHz) spectrometer, a Varian 400 MR spectrometer (100 MHz) or an Agilent Inova 400 (100 MHz) spectrometer. Chemical shift (δ) was measured in ppm and quoted to the nearest 0.1 ppm relative to the residual solvent peaks in CDCl_3 (77.16 ppm), C_6D_6 (128.06 ppm), $(\text{CD}_3)_2\text{SO}$ (39.51 ppm), CD_3OD (49.00 ppm) or CD_3CN (1.32 ppm).

Low-resolution mass spectra (LRMS) were measured on an Agilent 6310 Quadrupole Mass Spectrometer. Infrared (IR) spectra were recorded on a Bruker Tensor 27 FT-IR spectrometer as either solids or neat films, either through direct application or deposited in CHCl_3 , with absorptions reported in wavenumbers (cm^{-1}).

Analytical thin layer chromatography (TLC) was performed using pre-coated Merck glass backed silica gel plates (Silicagel 60 F254). Flash column chromatography was undertaken on Fluka or Material Harvest silica gel (230–400 mesh) under a positive pressure of air. Visualization was achieved using ultraviolet light (254 nm) and chemical staining with ceric ammonium molybdate or basic potassium permanganate solutions as appropriate.

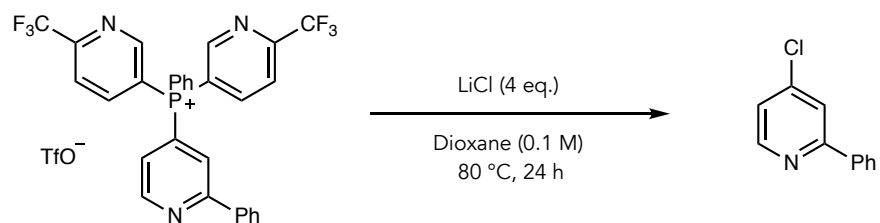
Tetrahydrofuran (THF), toluene, hexane, diethyl ether and dichloromethane were dried and distilled using standard methods.¹ Ethyl acetate (EtOAc), 1,2-Dichloroethane (DCE), chloroform, and acetone were purchased anhydrous from Sigma Aldrich chemical company. All reagents were purchased at the highest commercial quality and used without further purification. Reactions were carried out under an atmosphere of nitrogen unless otherwise stated. All reactions were monitored by TLC, ^1H NMR spectra taken from reaction samples, gas chromatography (GC) and gas chromatography-mass spectrometry (GCMS) using an Agilent 5977A fitted with an Agilent J&W HP-5ms Ultra Inert Column (30 m, 0.25 mm, 0.25 μm film) for MS analysis and an Agilent J&W VF-5ms column (10 m, 0.15 mm, 0.15 μm film) for FID analysis or liquid chromatography mass spectrometry (LCMS) using an Agilent 6310 Quadrupole Mass Spectrometer. Melting points (mp) were recorded using a Büchi B-450 melting point apparatus and are reported uncorrected.

Lithium halide salts were dried under vacuum at 120 °C before being stored in a glovebox. HCl (4.0 M in Dioxane) and trifluoromethanesulfonic acid (98%) were purchased from Sigma Aldrich chemical company and used without further purification but were routinely stored in a –20 °C fridge. Anhydrous 1,4-Dioxane was purchased from EMD Millipore.

Chlorodiphenylphosphine was purchased from Strem Chemicals and stored in a glovebox. Dichlorophenylphosphine was purchased from BeanTown Chemical and stored in a glovebox. NEt₃ and DBU were distilled before use.

2. Optimization Studies

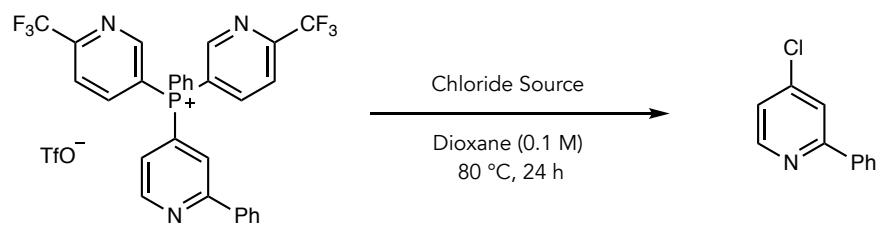
Table S1: Optimization of General Reaction Conditions^a



Entry	Change from Standard Conditions	Yield
1	None	70
2	100 °C	68
3	60 °C	36
4	EtOAc	45
5	EtOAc, 60 °C	12
6	Toluene	58
7	DME	38
8	DCE	n.d.
9	Dibutyl Ether	n.d.
10	EtOH	trace
11	1:1 Dioxane:EtOAc	52
12	0.05 M	62
13	0.2 M	49
14	0.5 M	25

^aYields by GCMS using 1,3,5-Trimethoxybenzene as an internal standard. Reactions run on 0.05 mmol scale.

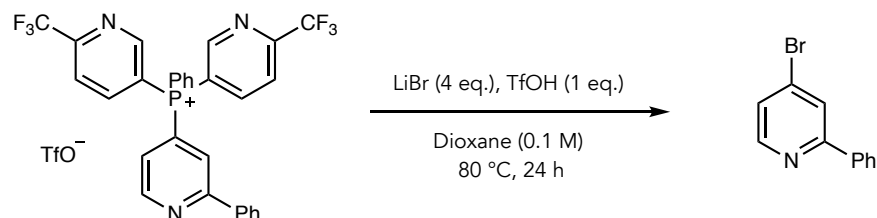
Table S2: Optimization of Chloride Source^a



Entry	Chloride Source	Yield
1	LiCl (4 eq.)	70
2	LiCl (4 eq.) + 12-crown-4 (2 eq.)	54
3	LiCl (4 eq.) + TBAC (2 eq.)	20
4	LiCl (4 eq.) + 4Å MS	3
5	LiCl + H ₂ O (5 eq.)	12
6	KCl (4 eq.)	11
7	KCl (4 eq.) + 18-crown-6 (2 eq.)	73
8	NaCl (4 eq.)	5
9	NaCl (4 eq.) at 100 °C	21
10	NaCl (4 eq.) + 15-crown-5 (2 eq.)	65
11	HCl in Dioxane (1 eq.)	81
12	TBAC (4 eq.)	20
13	CsCl	30

14 AgCl n.d.
^aYields determined by GCMS using 1,3,5-Trimethoxybenzene as an internal standard. Reactions run on 0.05 mmol scale.

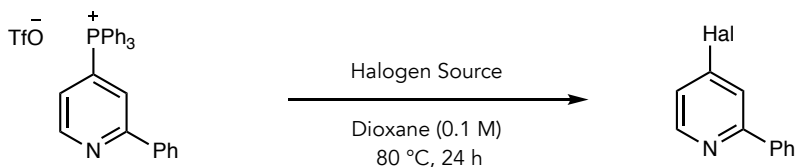
Table S3: Optimization of Bromination Conditions^a



Entry	Bromide Source	Yield
1	LiBr (4 eq.)	21
2	LiBr (4 eq.) at 120 °C	45
3	LiBr (4 eq.) + 12-crown-4 (2 eq.)	9
4	LiBr (4 eq.) + TfOH (1 eq.)	79
5	LiBr (4 eq.) + TfOH (1 eq.) + 12-crown-4 (2 eq.)	54
6	LiBr (4 eq.) + AcOH (1 eq.)	13
7	LiBr (4 eq.) + TFA (1 eq.)	9
8	KBr (4 eq.)	4
9	KBr (4 eq.) + 18-crown-6 (2 eq.)	23
10	TBAB	8

^aYields determined by ¹H NMR using 1,3,5-Trimethoxybenzene as an internal standard. Reactions run on 0.05 mmol scale.

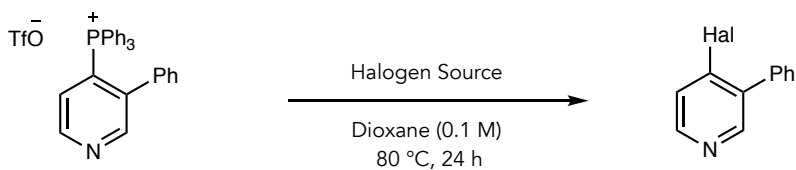
Table S4: Control Reactions on 2-phenylpyridine phosphonium salt^{a,b}



Entry	Halogen Source	Additive	Yield
1	LiCl (4 eq.)	-	n.d.
2	NaCl (4 eq.)	-	n.d.
3	KCl (4 eq.)	-	n.d.
4	TBAC (4 eq.)	-	1
5	HCl (1 eq.)	-	<1
7	LiBr (4 eq.)	TfOH (1 eq.)	n.d.
8 ^b	LiI (4 eq.)	TfOH (1 eq.)	n.d.

^aAll reactions run on 0.05 mmol scale. Yields determined by ¹H NMR using 1,3,5-trimethoxybenzene as an internal standard. ^bIodination Ran at 120 °C.

Table S5: Control Reactions on 3-phenylpyridine phosphonium salt^{a,b}



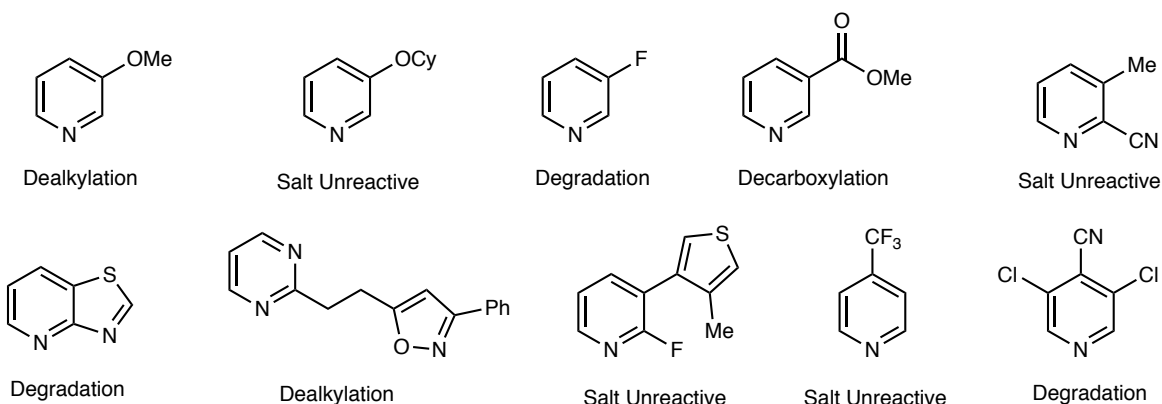
Entry	Halogen Source	Additive	Yield
1	LiCl (4 eq.)	-	5
2	NaCl (4 eq.)	-	1
3	KCl (4 eq.)	-	n.d.
4	TBAC (4 eq.)	-	7
5	HCl (1 eq.)	-	39
7	LiBr (4 eq.)	TfOH (1 eq.)	2
8 ^b	LiI (4 eq.)	TfOH (1 eq.)	n.d.

^aAll reactions run on 0.05 mmol scale. Yields determined by ¹H NMR using 1,3,5-trimethoxybenzene as an internal standard. ^bIodination Ran at 120 °C.

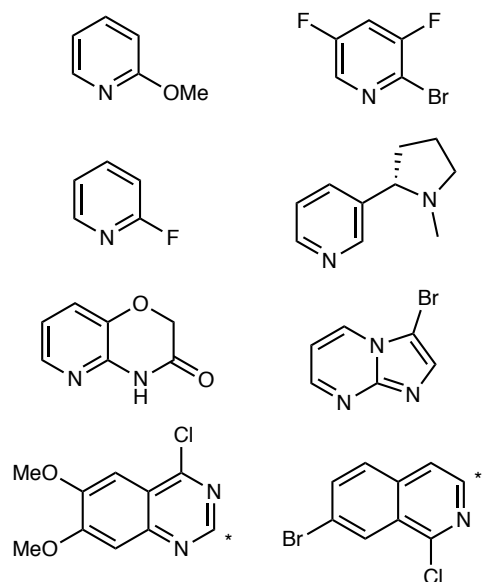
3. Problematic Substrates

Major Problems: Pyridines with fluorines, multiple electron-withdrawing groups, electron-donating groups (alkoxy), and substrates with basic amines anywhere on the molecule.

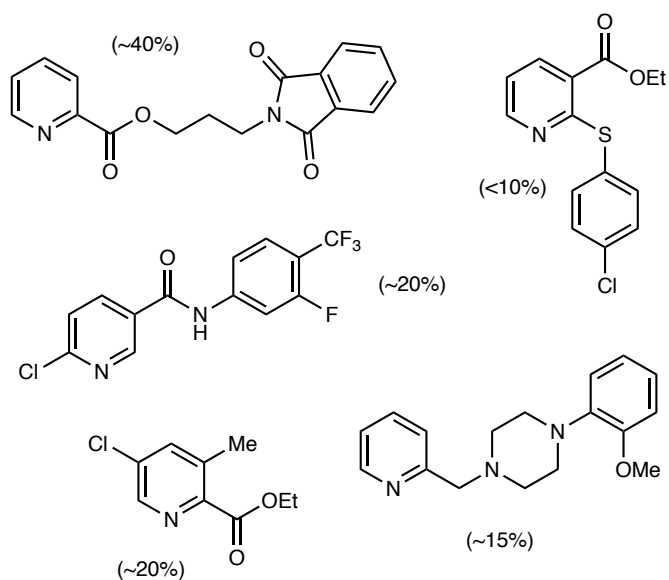
Phosphonium Salt Formation is Successful. Problems with Chlorination:



No Phosphonium Salt Formation:

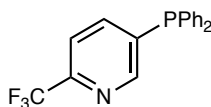


Low Phosphonium Salt Formation:



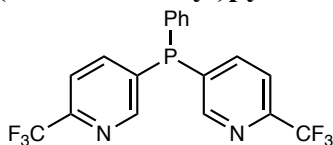
4. Preparation of Heterocyclic Phosphines

5-(diphenylphosphaneyl)-2-(trifluoromethyl)pyridine (3a)



An oven-dried 250mL round bottom flask was charged with 2-trifluoromethyl-5-bromo pyridine (4.97 g, 22.00 mmol) and diethyl ether (80 mL). The colorless solution was cooled to -78°C , and n-BuLi (1.6 M in Hexanes, 22.00 mmol 13.75 mL) was added dropwise. After 30 minutes, diphenylphosphine chloride (3.56 mL, 20.00 mmol) was added dropwise, and the flask was allowed to warm to room temperature. After 4 hours of stirring, the reaction was quenched with water (80 mL). The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried (MgSO_4), filtered and concentrated *in vacuo*. The crude material was purified by flash chromatography (silica gel: 2.5% EtOAc in Hexanes) to provide the title compound as a white solid (5.63 g, 17.01 mmol, 85% yield). mp $67\text{--}70^{\circ}\text{C}$. IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3058, 3013, 1479, 1433, 1331, 1142, 1073, 746, 695; ^1H NMR (400 MHz, CDCl_3) δ : 8.56 (1H, s), 7.72-7.66 (1H, m), 7.61 (1H, d, $J = 8.0$ Hz), 7.42-7.30 (10H, m); ^{13}C NMR (100 MHz, CDCl_3) δ : 153.94 (d, $J = 22.2$ Hz), 147.84 (q, $J = 34.8$ Hz), 142.07 (d, $J = 16.4$ Hz), 138.68 (d, $J = 20.1$ Hz), 134.72 (d, $J = 9.8$ Hz), 134.05 (d, $J = 20.5$ Hz), 129.83, 129.15 (d, $J = 7.2$ Hz), 121.68 (q, $J = 274.0$ Hz), 120.20-120.05 (m); ^{19}F NMR (365 MHz, CDCl_3) δ : -68.07 ; ^{31}P NMR (162 MHz, CDCl_3) δ : -11.63 ; m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 332.1, $\text{C}_{18}\text{H}_{14}\text{F}_3\text{NP}^+$ requires 332.1.

5,5'-(phenylphosphanediyl)bis(2-(trifluoromethyl)pyridine) (3b)

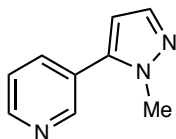


An oven-dried 250 mL round bottom flask was charged with 2-trifluoromethyl-5-bromo pyridine (16.65 g, 73.68 mmol) and diethyl ether (60 mL). The colorless solution was cooled to -78°C , n-BuLi (2.5 M in hexanes, 73.68 mmol, 29.5 mL) was added dropwise. After 30 minutes, dichlorophenylphosphine (4.76 mL, 35.10 mmol) was added dropwise, and the flask was allowed to warm to room temperature. After 8 hours of stirring, the reaction was quenched with water (80 mL), organic layer separated, and aqueous layer extracted with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried (MgSO_4), filtered and concentrated *in vacuo*. The crude material was purified by flash chromatography (silica gel: 5% EtOAc in Hexanes) to provide the title compound as a white solid (12.06 g, 30.10 mmol, 86% yield). mp $65\text{--}66^{\circ}\text{C}$. IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3076, 1368, 1331, 1234, 1128, 1070, 834, 713; ^1H NMR (400 MHz, CDCl_3) δ : 8.61 (2H, app t, $J = 2.4$ Hz), 7.75 (2H, ddd, $J = 7.9, 6.1, 1.9$ Hz), 7.68 (2H, d, $J = 8.0$ Hz), 7.52-7.43 (3H, m), 7.40-7.33 (2H, m); ^{13}C NMR (100 MHz, CDCl_3) δ : 153.95 (d, $J = 24.0$ Hz), 148.79 (q, $J = 35.3$ Hz), 142.33 (d, $J = 16.6$ Hz), 136.10 (d, $J = 19.0$ Hz), 134.20 (d, $J = 21.3$ Hz), 132.05 (d, $J = 9.1$ Hz), 130.81, 129.67 (d, $J = 8.0$ Hz), 121.43 (q, $J = 121.4$ Hz), 120.62-120.45 (m); ^{19}F

NMR (365 MHz, CDCl₃) δ : -68.20; ³¹P NMR (162 MHz, CDCl₃) δ : -18.24; m/z LRMS (ESI + APCI) found [M + H]⁺ 401.2, C₁₈H₁₂F₆N₂P⁺ requires 401.1.

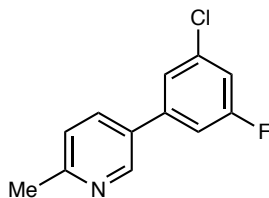
5. Preparation of Heterocyclic Phosphonium Salt Precursors

3-(1-Methyl-1*H*-pyrazol-5-yl)pyridine



An oven-dried 250 mL round bottom flask was charged with 3-bromopyridine (771 μ L, 8.00 mmol), 1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-pyrazole (2.33 g, 11.20 mmol), Pd(PPh₃)₄ (462 mg, 0.40 mmol), K₃PO₄ (3.06 g, 14.40 mmol), DMF (80 mL), and H₂O (780 μ L). The reaction was heated at 80 °C for 24 hours. After cooling to room temperature, the reaction was diluted with EtOAc and H₂O and the organic layer was separated. The aqueous layer was extracted from with EtOAc (2 x 50 mL). The combined organic layers were then washed with H₂O (5 x 50 mL), dried over MgSO₄, concentrated *in vacuo*, and purified by flash chromatography (silica gel gradient elution: 50% EtOAc in Hexanes to 100% EtOAc) to provide the title compound as a clear oil (484 mg, 3.04 mmol, 38% yield). IR ν_{max} /cm⁻¹ (film): 3032, 2946, 2226, 1717, 1470, 1409, 927, 711; ¹H NMR (400 MHz, CDCl₃) δ : 8.71 (1H, dd, *J* = 2.2, 0.7 Hz), 8.66 (1H, dd, *J* = 4.8, 1.6 Hz), 7.74 (1H, ddd, *J* = 7.8, 5.7, 1.8 Hz), 7.55 (1H, d, *J* = 1.9 Hz), 7.40 (1H, ddd, *J* = 7.8, 3.0, 0.8 Hz), 6.38 (1H, d, *J* = 1.9 Hz), 3.91 (3H, s); ¹³C NMR (100 MHz, CDCl₃) δ : 149.63, 149.45, 140.15, 138.92, 135.96, 126.96, 123.52, 106.88, 37.65; m/z LRMS (ESI + APCI) found [M + H]⁺ 160.1, C₉H₁₀N₃⁺ requires 160.1.

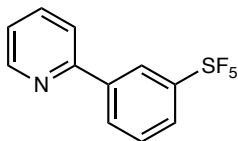
5-(3-Chloro-5-fluorophenyl)-2-methylpyridine



An oven-dried 25 mL sealed tube was charged with 5-bromo-2-methylpyridine (860 mg, 5.00 mmol), (3-chloro-5-fluorophenyl)boronic acid (870 mg, 7.50 mmol), Pd(PPh₃)₄ (58 mg, 0.05 mmol), K₂CO₃ (1.38 g, 10.00 mmol), EtOH (10 mL). The reaction was heated at 100 °C for 17 hours. After cooling to room temperature, the reaction was diluted with EtOAc and H₂O and the organic layer was separated. The aqueous layer was extracted from with EtOAc (2 x 20 mL). The combined organic layers were then washed with H₂O, dried over MgSO₄, concentrated *in vacuo*, and purified by flash chromatography (silica gel gradient elution: 25% EtOAc in Hexanes) to provide the title compound as a white solid (946 mg, 4.28 mmol, 86% yield). mp 80-81 °C; IR ν_{max} /cm⁻¹ (film): 3023, 1608, 1497, 1430, 1366, 1183, 918, 842, 779; ¹H NMR (400 MHz, CDCl₃) δ : 8.68 (1H, dd, *J* = 2.5, 0.8 Hz), 7.73 (1H, dd, *J* = 8.0, 2.5 Hz), 7.34 (1H, td, *J* = 1.7, 0.6 Hz), 7.26-7.21 (2H, m), 7.17 (1H, ddd, *J* = 9.3, 2.4, 1.5 Hz), 7.13-7.02 (1H, m), 2.62 (3H, s); ¹³C NMR (100 MHz, CDCl₃) δ : 163.13 (d, *J* = 249.8 Hz), 158.76, 147.44 (d, *J* = 2.1 Hz), 141.31 (d,

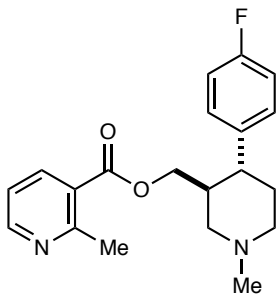
$J = 8.6$ Hz), 135.79 (d, $J = 11.3$ Hz), 134.69 (d, $J = 3.9$ Hz), 131.48, 123.41 (d, $J = 2.0$ Hz), 123.07 (d, $J = 3.3$ Hz), 115.47 (d, $J = 25.0$ Hz), 112.50 (d, $J = 22.0$ Hz), 24.29; ^{19}F NMR (365 MHz, CDCl_3) δ : -110.19; m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 222.1, $\text{C}_{12}\text{H}_{10}\text{ClFN}^+$ requires 222.0.

2-(3-(Pentafluoro- λ^6 -sulfaneyl)phenyl)pyridine



An oven-dried 50 mL round bottom flask was charged with (3-bromophenyl)pentafluoro- λ^6 -sulfane (546 μL , 3.53 mmol), 2-(tributylstannyl)pyridine (1.37 mL, 4.24 mmol), $\text{Pd}(\text{PPh}_3)_4$ (205 mg, 0.18 mmol), and toluene (15 mL). The reaction was refluxed for 40 hours. After cooling to room temperature, the mixture was concentrated *in vacuo*. Flash chromatography (silica gel gradient elution: 33% CH_2Cl_2 in Hexanes to 50% CH_2Cl_2 in Hexanes) followed by a second and third flash chromatography column (silica gel gradient elution: 100% Hexanes to 50% CH_2Cl_2 in Hexanes) afforded the title compound (761 mg, 2.70 mmol, 77% yield) as an amorphous solid. IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3086, 3011, 1588, 1462, 1113, 832, 648, 595; ^1H NMR (400 MHz, CDCl_3) δ : 8.72 (1H, d, $J = 4.8$ Hz), 8.50 (1H, app t, $J = 1.9$ Hz), 8.11 (1H, d, $J = 7.8$ Hz), 7.82-7.70 (3H, m), 7.54 (1H, app t, $J = 8.0$ Hz), 7.28 (1H, ddd, $J = 7.3, 5.2, 1.2$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 155.22, 154.63 (qn, $J = 16.8$ Hz), 149.99, 140.46, 137.09, 129.75, 129.13, 126.17 (qn, $J = 4.5$ Hz), 124.61 (qn, $J = 4.7$ Hz), 123.09, 120.58; ^{19}F NMR (365 MHz, CDCl_3) δ : (84.27 (1F, qn, $J = 151.2$ Hz), 62.72 (4F, d, $J = 150.1$ Hz); m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 282.1, $\text{C}_{11}\text{H}_9\text{F}_5\text{NS}^+$ requires 282.0.

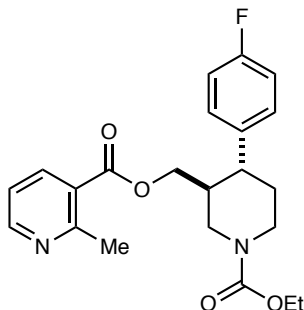
((3*S*,4*R*)-4-(4-Fluorophenyl)-1-methylpiperidin-3-yl)methyl 2-methylnicotinate



An oven-dried 100 mL round bottom flask was charged with 2-methylnicotinic acid (686 mg, 5.00 mmol), ((3*S*,4*R*)-4-(4-fluorophenyl)-1-methylpiperidin-3-yl)methanol (1.23 g, 5.50 mmol), $\text{N,N}'$ -Dicyclohexylcarbodiimide (1.13 g, 5.50 mmol), DMAP (61 mg, 0.50 mmol), and CH_2Cl_2 (25 mL). After 20 hours of stirring at room temperature, the reaction was concentrated *in vacuo*, and purified by flash chromatography (silica gel: 10% MeOH in CH_2Cl_2) to provide the title compound as a clear oil (1.25 g, 3.65 mmol, 73% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2936, 2785, 1721, 1510, 1244, 1077, 754; ^1H NMR (400 MHz, CDCl_3) δ : 8.61 (1H, dd, $J = 4.8, 1.8$ Hz), 8.03 (1H, dd, $J = 7.9, 1.8$ Hz), 7.22-7.14 (3H, m), 7.02-6.95 (2H, m), 4.09-4.05 (1H, m), 3.94-3.88 (1H, m), 3.17 (1H, d, $J = 11.7$ Hz), 3.00 (1H, d, $J = 10.3$ Hz), 2.80 (3H, s), 2.42-2.30 (5H, m), 2.13-1.80 (4H, m); ^{13}C NMR (100 MHz, CDCl_3) δ : 163.33, 161.78 (d, $J = 244.6$ Hz), 160.03, 152.04,

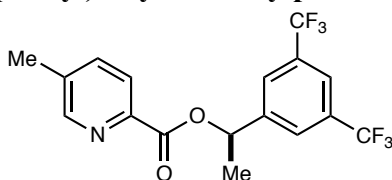
139.25, 138.39, 128.87 (d, $J = 7.8$ Hz), 125.30, 120.99, 115.76 (d, $J = 21.3$ Hz), 66.30, 59.64, 56.26, 46.57, 44.44, 41.50, 34.70, 25.10; ^{19}F NMR (365 MHz, CDCl_3) δ : -116.2; m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 343.2, $\text{C}_{20}\text{H}_{24}\text{FN}_2\text{O}_2^+$ requires 343.2.

((3*S*,4*R*)-1-(Ethoxycarbonyl)-4-(4-fluorophenyl)piperidin-3-yl)methyl 2-methylnicotinate



An oven-dried 50 mL round bottom flask was charged with ((3*S*,4*R*)-4-(4-fluorophenyl)-1-methylpiperidin-3-yl)methyl 2-methylnicotinate (1.10 g, 3.20 mmol), Na_2CO_3 (34 mg, 0.032 mmol), ethyl chloroformate (609 μL , 6.40 mmol), and toluene (16 mL). The reaction was heated at 80 $^\circ\text{C}$ for 1 hour. After cooling down to room temperature, the reaction was diluted with EtOAc, poured into H_2O , and extracted with EtOAc (3 x 20 mL). The combined organic layers were dried over MgSO_4 , concentrated *in vacuo*, and purified by flash chromatography (silica gel gradient elution: 50% EtOAc in Hexanes to 100% EtOAc) to provide the title compound as a colorless oil (1.01 g, 2.52 mmol, 79% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2939, 2859, 2250, 1692, 1437, 1222, 910, 728; ^1H NMR (400 MHz, CDCl_3) δ : 8.59 (1H, dd, $J = 4.8, 1.6$ Hz), 8.06 (1H, dd, $J = 7.9, 1.7$ Hz), 7.20-7.10 (3H, m), 7.01-6.95 (2H, m), 4.50 (1H, br s), 4.38-4.05 (4H, m), 3.89 (1H, dd, $J = 11.4, 7.7$ Hz), 2.93-2.65 (5H, m), 2.54 (1H, td, $J = 11.7, 3.8$), 2.21-2.09 (1H, m), 1.85-1.76 (1H, m), 1.69 (1H, qd, $J = 12.9, 4.2$), 1.26 (3H, t, $J = 7.1$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 166.20, 161.80 (d, $J = 245.3$ Hz), 159.61, 155.48, 152.03, 138.60 (d, $J = 3.2$ Hz), 138.39, 128.70 (d, $J = 7.9$ Hz), 125.13, 120.99, 115.83 (d, $J = 21.3$), 65.69, 61.60, 47.30, 45.01, 44.41, 41.11, 34.25, 25.08, 14.76; ^{19}F NMR (365 MHz, CDCl_3) δ : -115.66-(-115.74); m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 401.3, $\text{C}_{22}\text{H}_{26}\text{FN}_2\text{O}_4^+$ requires 401.2.

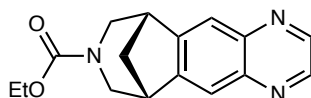
(*R*)-1-(3,5-Bis(trifluoromethyl)phenyl)ethyl 5-methylpicolinate



An oven-dried 100 mL round bottom flask was charged with 5-methylpicolinic acid (686 mg, 5.00 mmol), (*R*)-1-(3,5-bis(trifluoromethyl)phenyl)ethan-1-ol (1.42 g, 5.50 mmol), $\text{N,N}'$ -Dicyclohexylcarbodiimide (1.13 g, 5.50 mmol), DMAP (61 mg, 0.50 mmol), and CH_2Cl_2 (25 mL). After 18 hours of stirring at room temperature, the reaction was concentrated *in vacuo*, and purified by flash chromatography (silica gel: 15% EtOAc in Hexanes) to provide the title compound as a colorless oil (596 mg, 1.58 mmol, 32% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2988, 2234, 1723, 1383, 1277, 1131, 607, 728; ^1H NMR (400 MHz, CDCl_3) δ : 8.63-8.60 (1H, m), 8.02 (1H, d, $J = 8.0$ Hz), 7.92 (2H, s), 7.82 (1H, s), 7.66-7.63 (1H, m), 6.26 (1H, q, $J = 6.7$ Hz), 2.43 (3H,

s), 1.77 (3H, d, $J = 6.7$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 164.57, 150.85, 145.18, 144.19, 137.95, 137.46, 132.13 (q, $J = 33.3$ Hz), 126.76-126.55 (m), 125.17, 123.32 (q, $J = 272.8$ Hz), 122.30-122.08 (m), 72.31, 22.26, 18.85; ^{19}F NMR (365 MHz, CDCl_3) δ : -62.87 (m); m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 378.1, $\text{C}_{17}\text{H}_{14}\text{F}_6\text{NO}_2^+$ requires 378.1.

Ethyl (6R,10S)-6,7,9,10-tetrahydro-8H-6,10-methanoazepino[4,5-g]quinoxaline-8-carboxylate



A 25 mL round bottom flask was charged with varenicline tartrate (488 mg, 1.35 mmol), DMAP (17 mg, 0.14 mmol), and CH_2Cl_2 (10 mL). Ethyl Chloroformate (257 μL , 2.70 mmol) and *N,N*-Diisopropylethylamine (941 μL , 5.40 mmol) were added dropwise. After stirring at room temperature for 16 hours, the reaction was concentrated *in vacuo* and purified by flash chromatography (80% EtOAc in Hexanes) to afford the title product as an amorphous solid (314 mg, 1.11 mmol, 82% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2952, 2866, 1687, 1417, 1212, 1113, 914, 731; ^1H NMR (400 MHz, CDCl_3) δ : 8.76 (2H, d, $J = 3.9$ Hz), 7.87 (2H, d, $J = 6.9$ Hz), 4.16-3.78 (4H, m), 3.50-3.27 (4H, m), 2.45-2.37 (1H, m), 2.00 (1H, d, $J = 11.1$ Hz), 1.03 (3H, t, $J = 7.1$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 156.73, 148.69 (d, $J = 2.7$ Hz), 144.00 (d, $J = 6.8$ Hz), 143.50 (d, $J = 8.3$ Hz), 122.35 (d, $J = 46.4$ Hz), 61.26, 49.75 (d, $J = 27.4$ Hz), 41.22, 40.00 (d, $J = 1.4$ Hz), 14.55; m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 284.1, $\text{C}_{16}\text{H}_{18}\text{N}_3\text{O}_2^+$ requires 284.1.

6. Preparation of Heterocyclic Phosphonium Salts

Preparation of Heterocyclic Phosphonium Salts

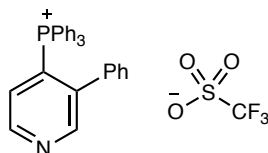
General Procedure A:

An oven dried round bottom flask equipped with a stir bar was charged with the heterocycle (1.0 equiv), phosphine (1.1 equiv), and placed under a nitrogen atmosphere. CH_2Cl_2 (0.1 M) was added, the reaction vessel cooled to $-50\text{ }^\circ\text{C}$ and Tf_2O (1.0 equiv) was added dropwise. After stirring for 1 hour, the reaction was cooled to $-78\text{ }^\circ\text{C}$ and DBU (1.0 equiv) was added dropwise via syringe. The cooling bath was removed and the reaction was allowed to warm to room temperature while stirring (approximately 20-30 minutes). The reaction mixture was diluted with CH_2Cl_2 and washed with H_2O (3x). The organic layer was dried (MgSO_4), filtered and concentrated *in vacuo* to approximately 2-5 mL (depending on the scale of the reaction). The concentrated reaction mixture was added dropwise to an excess of a 50:50 Et_2O :Hexanes solution that was then placed in a $-20\text{ }^\circ\text{C}$ refrigerator until the solid has settled to the bottom of the flask. The suspension was filtered on a frit, the solid washed with chilled Et_2O ($0\text{ }^\circ\text{C}$) and dried *in vacuo* to provide the pure product.

Notes.

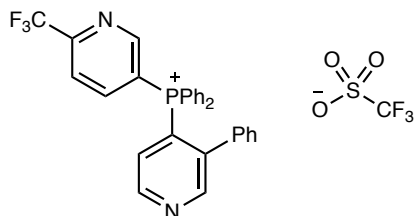
- 1) To maximize the yield, vigorous stirring is required.
- 2) For long term storage (>2 weeks) it is best to keep the heteroaryl phosphonium salt product in a $-20\text{ }^\circ\text{C}$ fridge.

Triphenyl(3-phenylpyridin-4-yl)phosphonium trifluoromethanesulfonate (1a)



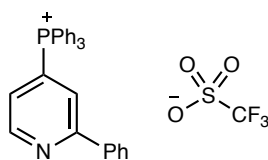
Prepared according to our previous report.¹ ^1H NMR (400 MHz, CDCl_3): 8.95 (1H, app t, $J = 4.7$ Hz), 8.74 (1H, d, $J = 6.8$ Hz), 7.85- 7.73 (3H, m), 7.73-7.40 (13H, m), 7.11 (1H, t, $J = 7.6$ Hz), 6.91 (2H, app t, $J = 7.6$ Hz), 6.71 (2H, d, $J = 7.5$ Hz); ^{13}C NMR (100 MHz, CDCl_3): 153.63 (d, $J = 8.0$ Hz), 149.97 (d, $J = 10.4$ Hz), 141.68 (d, $J = 7.3$ Hz), 135.43 (d, $J = 3.0$ Hz), 134.41 (d, $J = 4.5$ Hz), 134.18 (d, $J = 10.3$ Hz), 130.59 (d, $J = 13.0$ Hz), 129.21, 128.89, 128.30, 128.20, 126.35 (d, $J = 83.4$ Hz), 120.82 (q, $J = 321.2$ Hz), 116.89 (d, $J = 89.2$ Hz); ^{19}F NMR (365 MHz, CDCl_3): -77.68 ; ^{31}P NMR (162 MHz, CDCl_3): 21.73. The spectroscopic data is in agreement with our reported synthesis.

Diphenyl(3-phenylpyridin-4-yl)(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1a')



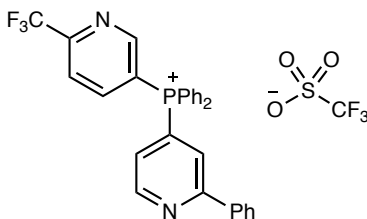
Prepared according to general procedure A, using 3-phenylpyridine (282 μL , 2.00 mmol), TiF_2O (336 μL , 2.00 mmol), 5-(diphenylphosphaneyl)-2-(trifluoromethyl)pyridine (728 mg, 2.20 mmol), DBU (298 μL , 2.00 mmol), and CH_2Cl_2 (20 mL). After purification by the standard procedure (except that two crash-outs were required), the title compound was isolated as a white solid (964 mg, 1.52 mmol, 76% yield). mp 54-57 $^\circ\text{C}$. IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3064, 1440, 1336, 1258, 1140, 1029, 722, 635; ^1H NMR (400 MHz, CDCl_3) δ : 8.99 (1H, app t, $J = 4.0$ Hz), 8.89-8.70 (2H, m), 8.38 (1H, dd, $J = 5.9$ Hz, 2.1 Hz), 7.97-7.87 (3H, m), 7.82-7.70 (8H, m), 7.49 (1H, d, $J = 15.4$, 5.2 Hz), 7.17 (1H, app t, $J = 7.5$ Hz), 6.96 (2H, app t, $J = 8.0$ Hz), 6.80 (2H, dd, $J = 8.3$, 1.3 Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 153.70 (d, $J = 7.9$ Hz), 152.74 (d, $J = 12.6$ Hz), 151.94 (qd, $J = 35.8$, 2.4 Hz), 150.22 (d, $J = 10.6$ Hz), 145.12 (d, $J = 9.3$ Hz), 141.69 (d, $J = 7.0$ Hz), 136.38 (d, $J = 3.1$ Hz), 134.63 (d, $J = 10.7$ Hz), 134.33 (d, $J = 4.6$ Hz), 131.20 (d, $J = 13.4$ Hz), 129.55, 129.41, 128.64, 128.30 (d, $J = 3.1$ Hz), 124.81 (d, $J = 84.7$ Hz), 122.00-121.78 (m), 120.72 (q, $J = 321.0$ Hz), 120.44 (qd, $J = 275.3$, 1.7 Hz), 119.15 (d, $J = 86.4$ Hz), 115.33 (d, $J = 89.3$ Hz); ^{19}F NMR (365 MHz, CDCl_3) δ : -68.89, -78.29; ^{31}P NMR (162 MHz, CDCl_3) δ : 19.31; m/z LRMS (ESI + APCI) found $[\text{M} - \text{OTf}]^+$ 485.2, $\text{C}_{27}\text{H}_{21}\text{F}_3\text{N}_4\text{P}^+$ requires 485.1.

Triphenyl(2-phenylpyridin-4-yl)phosphonium trifluoromethanesulfonate (1b)



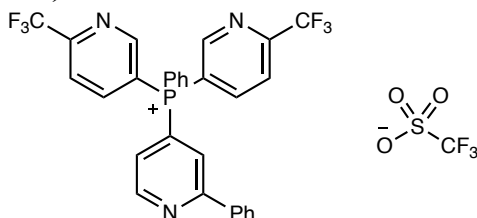
Prepared according to our previous report. ^1H NMR (400 MHz, CDCl_3): 9.01 (1H, app t, $J = 5.1$ Hz), 7.93-7.54 (18H, m), 7.50 (1H, ddd, $J = 17.8$, 5.1, 1.1 Hz), 7.42-7.36 (3H, m); ^{13}C NMR (100 MHz, CDCl_3): 159.09 (d, $J = 9.9$ Hz), 151.63 (d, $J = 10.7$ Hz), 136.74 (d, $J = 1.5$ Hz), 136.14 (d, $J = 3.2$ Hz), 134.30 (d, $J = 9.8$ Hz), 130.91 (d, $J = 13.0$ Hz), 130.35, 129.23 (d, $J = 84.1$ Hz), 128.98, 127.00, 125.25 (d, $J = 7.8$ Hz), 123.08, (d, $J = 8.4$ Hz), 120.68 (q, $J = 321.1$ Hz), 115.49 (d, $J = 89.1$ Hz); ^{19}F NMR (365 MHz, CDCl_3): -78.1; ^{31}P NMR (162 MHz, CDCl_3): 22.7. The spectroscopic data is in agreement with our reported synthesis.

Diphenyl(2-phenylpyridin-4-yl)(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1b')



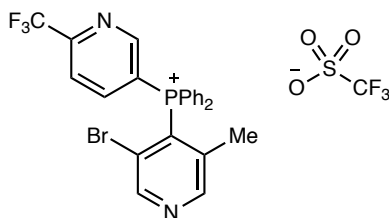
Prepared according to general procedure A, using 2-phenylpyridine (571 μL , 4.00 mmol), TiF_2O (676 μL , 4.00 mmol), 5-(diphenylphosphaneyl)-2-(trifluoromethyl)pyridine (1.460 g, 4.40 mmol), DBU (598 μL , 4.00 mmol), and CH_2Cl_2 (40 mL). After purification by the standard procedure (except that two crash-outs were required), the title compound was isolated as a white solid (1.906 g, 3.00 mmol, 75% yield). mp 68-72 $^\circ\text{C}$. IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3063, 1573, 1440, 1258, 1141, 1029, 724, 635; ^1H NMR (400 MHz, CDCl_3) δ : 9.07 (1H, app t, $J = 5.3$ Hz), 8.83 (1H, dd, $J = 6.1, 1.5$ Hz), 8.68 (1H, ddd, $J = 12.7, 8.5, 2.2$ Hz), 8.18 (1H, dd, $J = 8.3, 1.2$ Hz), 7.98-7.68 (13H, m), 7.56 (1H, ddd, $J = 13.3, 5.1, 1.1$ Hz), 7.47-7.42 (3H, m); ^{13}C NMR (100 MHz, CDCl_3) δ : 159.40 (d, $J = 10.8$ Hz), 153.29 (d, $J = 13.0$ Hz), 153.11 (qd, $J = 36.1, 2.7$ Hz), 151.90 (d, $J = 11.0$ Hz), 145.70 (d, $J = 9.4$ Hz), 136.71 (d, $J = 2.0$ Hz), 134.57 (d, $J = 11.0$ Hz), 131.25 (d, $J = 13.4$ Hz), 130.45, 129.01, 127.97, 127.13, 125.36 (d, $J = 8.5$ Hz), 123.24 (d, $J = 9.2$ Hz), 122.57-122.35 (m), 120.51 (q, $J = 321.2$ Hz), 120.42 (qd, $J = 275.2, 1.7$ Hz), 118.00 (d, $J = 87.4$ Hz), 113.83 (d, $J = 89.9$ Hz); ^{19}F NMR (365 MHz, CDCl_3) δ : -68.53, -78.34; ^{31}P NMR (162 MHz, CDCl_3) δ : 20.38; m/z LRMS (ESI + APCI) found $[\text{M} - \text{OTf}]^+$ 485.2, $\text{C}_{27}\text{H}_{21}\text{F}_3\text{N}_4\text{P}^+$ requires 485.1.

Phenyl(2-phenylpyridin-4-yl)bis(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1b'')



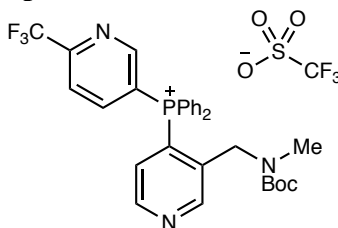
Prepared according to general procedure A, using 2-phenylpyridine (282 μL , 2.00 mmol), TiF_2O (336 μL , 2.00 mmol), 5,5'-(phenylphosphanediy)bis(2-(trifluoromethyl)pyridine (881 mg, 2.20 mmol), DBU (299 μL , 2.00 mmol), and CH_2Cl_2 (20 mL). After purification by the standard procedure (except that two crash-outs were required), the title compound was isolated as a white solid (1.146 g, 1.64 mmol, 81% yield). mp 85-88 $^\circ\text{C}$. IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3063, 1573, 1333, 1139, 1075, 1029, 725, 635; ^1H NMR (400 MHz, CDCl_3) δ : 9.05 (1H, app t, $J = 5.3$ Hz), 8.90 (2H, dd, $J = 6.1, 1.7$ Hz), 8.60 (2H, ddd, $J = 13.2, 8.4, 2.1$ Hz), 8.09 (2H, dd, $J = 8.3, 1.9$ Hz), 7.99-7.90 (4H, m), 7.85-7.71 (4H, m), 7.55 (1H, ddd, $J = 13.7, 5.0, 1.3$ Hz), 7.45-7.38 (3H, m); ^{13}C NMR (100 MHz, CDCl_3) δ : 159.82 (d, $J = 11.0$ Hz), 153.69 (d, $J = 13.4$ Hz), 153.62 (qd, $J = 35.8, 2.4$ Hz), 152.16 (d, $J = 11.5$ Hz), 145.95 (d, $J = 9.9$ Hz), 137.34 (d, $J = 2.9$ Hz), 136.64 (d, $J = 1.7$ Hz), 134.89 (d, $J = 11.2$ Hz), 131.61 (d, $J = 13.6$ Hz), 130.75, 129.15, 127.45, 126.09 (d, $J = 85.4$ Hz), 125.43 (d, $J = 8.9$ Hz), 123.47 (d, $J = 9.4$ Hz), 122.62-122.35 (m), 120.47 (qd, $J = 275.7, 2.1$ Hz), 120.32 (q, $J = 320.7$ Hz), 116.62 (d, $J = 88.4$ Hz), 112.45 (d, $J = 90.2$ Hz); ^{19}F NMR (365 MHz, CDCl_3) δ : -68.74, -78.74; ^{31}P NMR (162 MHz, CDCl_3) δ : 18.52; m/z LRMS (ESI + APCI) found $[\text{M} - \text{OTf}]^+$ 554.2, $\text{C}_{27}\text{H}_{21}\text{F}_3\text{N}_4\text{P}^+$ requires 554.1.

(3-Bromo-5-methylpyridin-4-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1c')



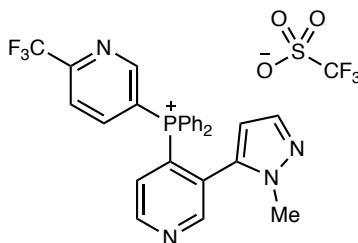
Prepared according to general procedure A, using 3-bromo-5-methylpyridine (116 μL , 1.00 mmol), TF_2O (168 μL , 1.00 mmol), 5-(diphenylphosphan-2-yl)-2-(trifluoromethyl)pyridine (364 mg, 1.10 mmol), DBU (149 μL , 1.00 mmol), and CH_2Cl_2 (10 mL). After purification by the standard procedure (except that two crash-outs were required), the title compound was isolated at 95% purity as a white solid (172 mg, 0.26 mmol, 26% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3065, 1336, 1258, 1138, 1075, 1029, 720, 635; ^1H NMR (400 MHz, CDCl_3) δ : 8.97-8.87 (2H, m), 8.84 (1H, d, $J = 5.7$ Hz), 8.67 (1H, d, $J = 6.0$ Hz), 8.19-8.15 (1H, m), 7.96-7.77 (10H, m), 1.92 (3H, s); ^{13}C NMR (100 MHz, CDCl_3) δ : 154.17 (d, $J = 8.6$ Hz), 153.18 (d, $J = 6.1$ Hz), 152.86 (d, $J = 12.7$ Hz), 152.84 (qd, $J = 36.0, 2.7$ Hz), 145.69 (d, $J = 9.3$ Hz), 142.66 (d, $J = 7.4$ Hz), 136.56 (d, $J = 3.3$ Hz), 134.80 (d, $J = 11.0$ Hz), 131.47 (d, $J = 13.7$ Hz), 125.06 (d, $J = 8.5$ Hz), 124.60 (d, $J = 94.1$ Hz), 122.70-122.46 (m), 121.06 (d, $J = 87.7$ Hz), 120.75 (q, $J = 321.0$ Hz), 120.60 (qd, $J = 275.6, 2.2$ Hz), 116.62 (d, $J = 89.1$ Hz), 20.85 (d, $J = 4.2$ Hz); ^{19}F NMR (365 MHz, CDCl_3) δ : -68.55, -78.39; ^{31}P NMR (162 MHz, CDCl_3) δ : 19.35; m/z LRMS (ESI + APCI) found $[\text{M} - \text{OTf}]^+$ 501.1, $\text{C}_{27}\text{H}_{21}\text{F}_3\text{N}_4\text{P}^+$ requires 501.0.

(3-(((*Tert*-butoxycarbonyl)(methyl)amino)methyl)pyridin-4-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1d')



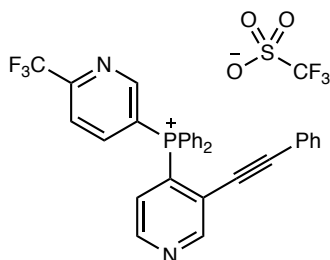
Prepared according to general procedure A, using *tert*-butyl methyl(pyridin-3-ylmethyl)carbamate (222 mg, 1.00 mmol), TF_2O (168 μL , 1.00 mmol), 5-(diphenylphosphan-2-yl)-2-(trifluoromethyl)pyridine (364 mg, 1.10 mmol), DBU (149 μL , 1.00 mmol), and CH_2Cl_2 (10 mL). After purification by the standard procedure, the title compound was isolated as a brown solid (560 mg, 0.80 mmol, 80% yield). mp 83-87 $^\circ\text{C}$. IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2978, 2932, 1690, 1260, 1140, 1029, 723, 636; ^1H NMR (400 MHz, CDCl_3) δ : 8.88-8.70 (3H, m), 8.62 (1H, ddd, $J = 12.8, 8.4, 2.1$ Hz), 8.12 (1H, d, $J = 7.6$ Hz), 7.95-7.88 (2H, m), 7.85-7.76 (8H, m), 7.23 (1H, d, $J = 15.3$ Hz), 3.90 (2H, s), 2.61 (3H, s), 1.34 (9H, s); ^{13}C NMR (100 MHz, CDCl_3) δ : 155.57, 153.43 (d, $J = 12.7$ Hz), 153.33 (qd, $J = 36.1, 2.3$ Hz), 150.84, 150.35, 146.04 (d, $J = 9.6$ Hz), 137.30-136.55 (2C, m), 134.47 (d, $J = 11.0$ Hz), 131.66 (d, $J = 13.4$ Hz), 128.78, 124.12 (d, $J = 82.5$ Hz), 122.90-122.52 (m), 120.64 (q, $J = 321.0$ Hz), 120.49 (qd, $J = 275.6, 1.7$ Hz), 118.30 (d, $J = 86.8$ Hz), 114.14 (d, $J = 88.3$ Hz), 81.09, 50.42, 35.62, 28.17; ^{19}F NMR (365 MHz, CDCl_3) δ : -68.63, -78.40; ^{31}P NMR (162 MHz, CDCl_3) δ : 18.92; m/z LRMS (ESI + APCI) found $[\text{M} - \text{OTf}]^+$ 552.2, $\text{C}_{30}\text{H}_{30}\text{F}_3\text{N}_3\text{O}_2\text{P}^+$ requires 552.2.

(3-(1-Methyl-1*H*-pyrazol-5-yl)pyridin-4-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1e')



Prepared according to general procedure A, using 3-(1-methyl-1*H*-pyrazol-5-yl)pyridine (159 mg, 1.00 mmol), TF_2O (168 μL , 1.00 mmol), 5-(diphenylphosphaneyl)-2-(trifluoromethyl)pyridine (364 mg, 1.10 mmol), DBU (149 μL , 1.00 mmol), and CH_2Cl_2 (10 mL). After purification by the standard procedure (except that two crash-outs were required), the title compound was isolated as a white solid (362 mg, 0.57 mmol, 57% yield). mp 154-149 $^\circ\text{C}$. IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3066, 1440, 1259, 1142, 1029, 722, 636; ^1H NMR (400 MHz, CDCl_3) δ : 9.06 (1H, app t, $J = 4.6$ Hz), 8.89-8.76 (2H, m), 8.64 (1H, d, $J = 5.8$ Hz), 8.08 (1H, d, $J = 8.2$ Hz), 7.96-7.66 (10H, m), 7.57 (1H, dd, $J = 15.4, 4.8$ Hz), 7.11 (1H, s), 5.68 (1H, s), 3.28 (3H, s); ^{13}C NMR (100 MHz, CDCl_3) δ : 153.54 (d, $J = 7.4$ Hz), 153.04 (d, $J = 12.8$ Hz), 152.58 (qd, $J = 36.1, 2.2$ Hz), 152.11 (d, $J = 10.5$ Hz), 145.11 (d, $J = 9.2$ Hz), 138.58, 136.50 (d, $J = 2.7$ Hz), 134.51 (d, $J = 10.7$ Hz), 134.29 (d, $J = 4.9$ Hz), 131.13 (d, $J = 13.4$ Hz), 130.10 (d, $J = 6.2$ Hz), 129.37 (d, $J = 9.3$ Hz), 127.33 (d, $J = 85.8$ Hz), 121.90-121.60 (m), 120.59 (q, $J = 320.7$ Hz), 120.45 (q, $J = 275.0$ Hz), 118.59 (d, $J = 87.0$ Hz), 114.53 (d, $J = 89.3$ Hz), 110.88, 37.03; ^{19}F NMR (365 MHz, CDCl_3) δ : -68.69, -78.36; ^{31}P NMR (162 MHz, CDCl_3) δ : 19.01; m/z LRMS (ESI + APCI) found $[\text{M} - \text{OTf}]^+$ 489.2, $\text{C}_{27}\text{H}_{21}\text{F}_3\text{N}_4\text{P}^+$ requires 489.1.

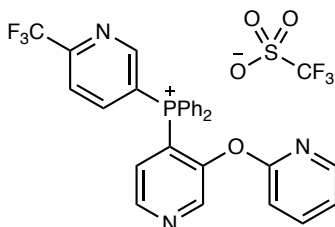
Diphenyl(3-(phenylethynyl)pyridin-4-yl)(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1f')



Prepared according to general procedure A, using 3-(phenylethynyl)pyridine (179 mg, 1.00 mmol), TF_2O (168 μL , 1.00 mmol), 5-(diphenylphosphaneyl)-2-(trifluoromethyl)pyridine (364 mg, 1.10 mmol), DBU (149 μL , 1.00 mmol), and CH_2Cl_2 (10 mL). After purification by the standard procedure, the title compound was isolated as a brown solid (444 mg, 0.67 mmol, 67% yield). mp 69-72 $^\circ\text{C}$. IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3062, 2361, 2213, 1439, 1335, 1259, 1142, 722, 563; ^1H NMR (400 MHz, CDCl_3) δ : 9.10 (1H, d, $J = 6.2$ Hz), 8.93 (1H, app t, $J = 4.8$ Hz), 8.85 (1H, dd, $J = 6.1, 2.1$ Hz), 8.79 (1H, ddd, $J = 12.9, 4.5, 2.0$ Hz), 8.11 (1H, dd, $J = 7.7, 1.5$ Hz), 7.95-7.87 (2H, m), 7.84-7.76 (8H, m), 7.42-7.30 (2H, m), 7.22-7.17 (2H, m), 6.69-6.65 (2H, m); ^{13}C NMR (100 MHz, CDCl_3) δ : 154.64 (d, $J = 6.7$ Hz), 153.20 (d, $J = 12.9$ Hz), 153.00 (qd, $J = 35.9, 2.5$ Hz), 150.62 (d, $J = 10.5$ Hz), 145.73 (d, $J = 9.5$ Hz), 136.54 (d, $J = 3.1$ Hz), 134.65 (d, $J = 11.0$ Hz), 131.23 (d, $J = 13.5$ Hz), 131.01, 130.58, 129.06 (d, $J = 9.1$ Hz), 128.68, 127.07 (d, $J = 87.6$ Hz), 123.39 (d, $J = 4.6$ Hz), 122.50 – 122.30 (m), 120.68 (q, $J = 321.0$ Hz), 120.49 (qd, $J = 275.4, 2.0$ Hz), 119.38, 118.24 (d, $J = 88.3$ Hz), 114.00 (d, $J = 90.8$ Hz), 105.23, 84.14 (d, $J =$

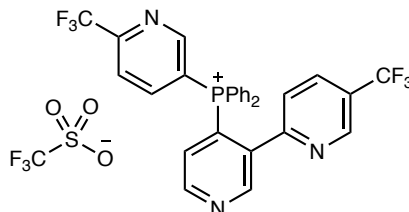
6.5 Hz); ^{19}F NMR (365 MHz, CDCl_3) δ : -68.68, -78.31; ^{31}P NMR (162 MHz, CDCl_3) δ : 20.23; m/z LRMS (ESI + APCI) found $[\text{M} - \text{OTf}]^+$ 509.2, $\text{C}_{31}\text{H}_{21}\text{F}_3\text{N}_2\text{P}^+$ requires 509.1.

Diphenyl(3-(pyridin-2-yloxy)pyridin-4-yl)(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1g')



Prepared according to general procedure A, using 2-(pyridin-3-yloxy)pyridine (258 mg, 1.50 mmol), Ti_2O (252 μL , 1.50 mmol), 5-(diphenylphosphanyl)-2-(trifluoromethyl)pyridine (547 mg, 1.65 mmol), DBU (224 μL , 1.50 mmol), and CH_2Cl_2 (15 mL). After purification by the standard procedure, the title compound was isolated as a white solid (870 mg, 1.34 mmol, 89% yield). mp 50-55 $^\circ\text{C}$. IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3064, 2248, 1430, 1529, 1140, 1029, 723, 635; ^1H NMR (400 MHz, CDCl_3) δ : 8.79-8.74 (2H, m), 8.68 (1H, app t, $J = 4.3$ Hz), 8.51 (1H, ddd, $J = 13.1, 8.2, 2.2$ Hz), 7.97 (1H, ddd, $J = 8.3, 2.1, 0.7$ Hz), 7.88 (1H, ddd, $J = 5.0, 2.0, 0.7$ Hz), 7.83-7.76 (2H, m), 7.72-7.64 (8H, m), 7.49 (1H, ddd, $J = 8.2, 7.3, 2.0$ Hz), 7.32 (1H, dd, $J = 14.5, 5.1$ Hz), 6.98 (1H, ddd, $J = 7.3, 5.0, 0.8$ Hz), 6.33 (1H, d, $J = 8.3$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 159.60, 153.01 (d, $J = 13.2$ Hz), 152.77 (qd, $J = 34.7, 2.7$ Hz), 151.17, 146.90, 146.89 (d, $J = 10.8$ Hz), 146.45 (d, $J = 4.7$ Hz), 145.22 (d, $J = 9.7$ Hz), 140.60, 136.34 (d, $J = 3.1$ Hz), 134.27 (d, $J = 11.4$ Hz), 131.07 (d, $J = 13.6$ Hz), 127.96 (d, $J = 7.3$ Hz), 122.31-122.10 (m), 121.17, 120.65 (q, $J = 321.0$ Hz), 120.37 (qd, $J = 275.7$ Hz, 2.2 Hz), 118.30 (d, $J = 87.2$ Hz), 118.19 (d, $J = 89.3$ Hz), 113.97 (d, $J = 91.3$ Hz), 111.22; ^{19}F NMR (365 MHz, CDCl_3) δ : -68.57, -78.30; ^{31}P NMR (162 MHz, CDCl_3) δ : 18.70; m/z LRMS (ESI + APCI) found $[\text{M} - \text{OTf}]^+$ 502.2, $\text{C}_{28}\text{H}_{20}\text{F}_3\text{N}_3\text{OP}^+$ requires 502.1.

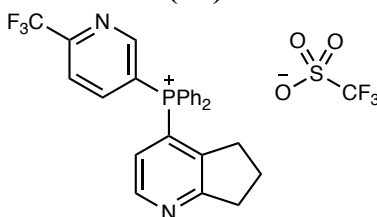
Diphenyl(5-(trifluoromethyl)-[2,3'-bipyridin]-4'-yl)(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1h')



Prepared according to general procedure A using 5-(trifluoromethyl)-2,3'-bipyridine (336 mg, 1.50 mmol), Ti_2O (252 μL , 1.50 mmol), 5-(diphenylphosphanyl)-2-(trifluoromethyl)pyridine (546 mg, 1.65 mmol), DBU (222 μL , 1.50 mmol) and CH_2Cl_2 (15 mL). After purification by the standard procedure, the title compound was isolated as a yellow solid (720 mg, 1.03 mmol, 69% yield). mp 72-76 $^\circ\text{C}$; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 1606, 1581, 1440, 1329, 1259, 1134, 1076, 1029, 719, 635; ^1H NMR (400 MHz, CDCl_3) δ : 9.55 (1H, d, $J = 7.1$ Hz), 9.02 (1H, t, $J = 4.9$ Hz), 8.82 (1H,

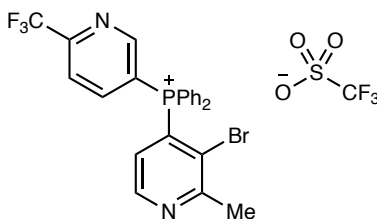
dd, $J = 5.9, 2.2$ Hz), 8.60 (1H, ddd, $J = 12.8, 8.2, 2.3$ Hz), 8.28 (1H, d, $J = 8.4$ Hz), 8.07-7.94 (2H, m), 7.79 (3H, qq, $J = 4.3, 2.0$ Hz), 7.73-7.61 (8H, m), 7.39 (1H, dd, $J = 16.7, 5.1$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 152.87 (d, $J = 11.8$ Hz), 152.70, 151.79 (q, $J = 35.8$ Hz), 151.24 (d, $J = 6.5$ Hz), 144.60 (d, $J = 8.8$ Hz), 143.43, 135.80 (d, $J = 3.7$ Hz), 135.08 (d, $J = 3.1$ Hz), 135.01, 133.03 (dd, $J = 10.4, 2.7$ Hz), 131.45 (d, $J = 10.6$ Hz), 130.57 (d, $J = 13.6$ Hz), 126.97 (q, $J = 33.8$ Hz), 124.47, 123.28 (d, $J = 57.7$ Hz), 122.21 (d, $J = 273.0$ Hz), 122.14, 121.73 (d, $J = 10.1$ Hz), 120.85, 120.54 (q, $J = 321.1$ Hz), 120.43 (qd, $J = 275.1, 1.9$ Hz), 119.05 (d, $J = 95.5$ Hz); ^{19}F NMR (365 MHz, CDCl_3) δ : -63.06, -68.64, -78.39; ^{31}P NMR (162 MHz, CDCl_3) δ : 24.41; m/z LRMS (ESI + APCI) found $[\text{M} - \text{OTf}]^+ 554.2$, $\text{C}_{29}\text{H}_{19}\text{F}_6\text{N}_3\text{P}^+$ requires 554.1.

(6,7-Dihydro-5H-cyclopenta[b]pyridin-4-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1i')



Prepared according to general procedure A using 6,7-dihydro-5H-cyclopenta[b]pyridine (119 mg, 1.00 mmol), Ti_2O (169 μL , 1.00 mmol), 5-(diphenylphosphanyl)-2-(trifluoromethyl)pyridine (364 mg, 1.10 mmol), DBU (147 μL , 1.00 mmol) and CH_2Cl_2 (10 mL). After purification by the standard procedure, the title compound was isolated as a white solid (300 mg, 0.50 mmol, 50% yield). mp 65-68 $^\circ\text{C}$; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 1587, 1440, 1335, 1260, 1139, 1076, 1029, 724, 636; ^1H NMR (400 MHz, CDCl_3) δ : 8.87-8.64 (3H, m), 8.25 (1H, ddd, $J = 8.0, 2.2, 1.1$ Hz), 8.02-7.90 (2H, m), 7.84 (4H, td, $J = 7.8, 3.9$ Hz), 7.80-7.67 (4H, m), 7.02 (1H, dd, $J = 14.5, 5.2$ Hz), 3.17 (2H, t, $J = 7.6$ Hz), 2.37-2.23 (2H, m), 2.09 (2H, q, $J = 7.5$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 169.60 (d, $J = 8.8$ Hz), 153.22 (qd, $J = 36.1, 2.5$ Hz), 153.16 (d, $J = 13.0$ Hz), 150.00 (d, $J = 9.9$ Hz), 145.82 (d, $J = 9.4$ Hz), 140.92 (d, $J = 7.5$ Hz), 136.65 (d, $J = 3.2$ Hz), 134.32 (d, $J = 10.9$ Hz), 131.49 (d, $J = 13.4$ Hz), 124.64 (d, $J = 9.8$ Hz), 122.80 (dd, $J = 10.1, 2.6$ Hz), 121.87 (d, $J = 83.9$ Hz), 120.63 (q, $J = 321.0$ Hz), 120.47 (qd, $J = 275.4, 1.9$ Hz), 118.13 (d, $J = 86.5$ Hz), 113.93 (d, $J = 89.1$ Hz), 33.85 (d, $J = 1.6$ Hz), 32.39 (d, $J = 2.5$ Hz), 22.87; ^{19}F NMR (365 MHz, CDCl_3) δ : -68.60, -78.37; ^{31}P NMR (162 MHz, CDCl_3) δ : 17.86; m/z LRMS (ESI + APCI) found $[\text{M} - \text{OTf}]^+ 449.2$, $\text{C}_{26}\text{H}_{21}\text{F}_3\text{N}_2\text{P}^+$ requires 449.1.

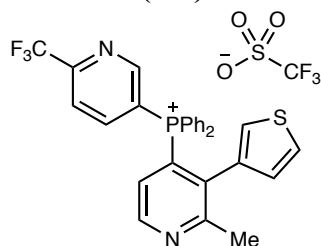
(3-Bromo-2-methylpyridin-4-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1j')



Prepared according to general procedure A using 3-bromo-2-methylpyridine (172 mg, 1.0 mmol), Ti_2O (169 μL , 1.00 mmol), 5-(diphenylphosphanyl)-2-(trifluoromethyl)pyridine (364 mg, 1.10 mmol), DBU (147 μL , 1.00 mmol) and CH_2Cl_2 (10 mL). After purification by the standard

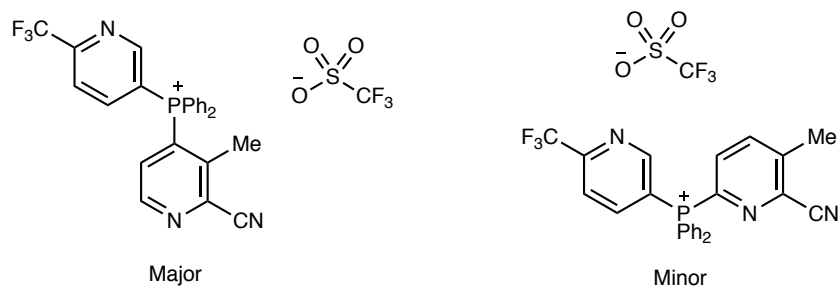
procedure, the title compound was isolated as a yellow solid (360 mg, 0.56 mmol, 56% yield). mp 56-60 °C; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3064, 1440, 1335, 1185, 1142, 1076, 1028, 722, 635; ^1H NMR (400 MHz, CDCl_3) δ : 8.93-8.78 (3H, m), 8.27-8.17 (1H, m), 7.99-7.90 (2H, m), 7.86-7.72 (8H, m), 7.12 (1H, dd, $J = 15.0, 4.9$ Hz), 2.83 (3H, s); ^{13}C NMR (100 MHz, CDCl_3) δ : 161.86 (d, $J = 6.1$ Hz), 153.18 (d, $J = 12.9$ Hz), 152.88 (qd, $J = 36.1, 2.5$ Hz), 149.86 (d, $J = 11.6$ Hz), 145.70 (d, $J = 9.4$ Hz), 136.41 (d, $J = 3.2$ Hz), 134.45 (d, $J = 10.9$ Hz), 131.25 (d, $J = 13.7$ Hz), 129.34 (d, $J = 9.9$ Hz), 127.96 (d, $J = 91.4$ Hz), 124.75 (d, $J = 3.4$ Hz), 122.51 (dd, $J = 10.4, 2.9$ Hz), 120.54 (q, $J = 321.1$ Hz), 120.44 (qd, $J = 275.2, 1.6$ Hz), 118.20 (d, $J = 88.6$ Hz), 114.04 (d, $J = 91.0$ Hz), 25.76 (d, $J = 2.2$ Hz); ^{19}F NMR (365 MHz, CDCl_3) δ : -68.60, -78.36; ^{31}P NMR (162 MHz, CDCl_3) δ : 23.10; m/z LRMS (ESI + APCI) found $[\text{M} - \text{OTf}]^+$ 501.1, $\text{C}_{24}\text{H}_{28}\text{BrF}_3\text{N}_2\text{P}^+$ requires 501.0.

(2-Methyl-3-(thiophen-3-yl)pyridin-4-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1k')



Prepared according to general procedure A, using 2-methyl-3-(thiophen-3-yl)pyridine (263 mg, 1.50 mmol), TF_2O (252 μL , 1.50 mmol), 5-(diphenylphosphaneyl)-2-(trifluoromethyl)pyridine (547 mg, 1.65 mmol), DBU (224 μL , 1.50 mmol), and CH_2Cl_2 (15 mL). After purification by the standard procedure (except that two crash-outs were done), the title compound was isolated as a white solid (489 mg, 0.75 mmol, 50% yield). mp 66-71 °C. IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3066, 3013, 2248, 1439, 1260, 1144, 1029, 721, 663; ^1H NMR (400 MHz, CDCl_3) δ : 8.78 (1H, app t, $J = 5.1$ Hz), 8.57 (1H, ddd, $J = 12.5, 8.5, 2.0$ Hz), 8.49 (1H, d, $J = 5.7$ Hz), 8.01-7.96 (1H, m), 7.91-7.82 (2H, m), 7.81-7.70 (4H, m), 7.70-7.61 (4H, m), 7.20 (1H, dd, $J = 15.1, 5.2$ Hz), 6.84 (1H, ddd, $J = 4.9, 2.9, 0.4$ Hz), 6.69-6.66 (1H, m), 6.27 (1H, d, $J = 5.0$ Hz), 2.27 (3H, s); ^{13}C NMR (100 MHz, CDCl_3) δ : 162.36 (d, $J = 8.0$ Hz), 152.31 (d, $J = 12.5$ Hz), 151.86 (qd, $J = 35.7, 2.4$ Hz), 149.81 (d, $J = 11.9$ Hz), 144.77 (d, $J = 9.2$ Hz), 136.24 (d, $J = 5.1$ Hz), 135.92 (d, $J = 7.1$ Hz), 134.94 (d, $J = 5.5$ Hz), 134.39 (d, $J = 10.5$ Hz), 131.15 (d, $J = 13.2$ Hz), 128.36, 126.95 (d, $J = 66.1$ Hz), 126.14 (d, $J = 86.2$ Hz), 126.02 (d, $J = 10.7$ Hz), 122.14-121.92 (m), 120.72 (q, $J = 321.0$ Hz), 120.51 (qd, $J = 275.2, 2.2$ Hz), 119.61 (d, $J = 87.0$ Hz), 116.15 (d, $J = 83.1$ Hz), 115.26 (d, $J = 83.9$ Hz), 23.70 (d, $J = 2.4$ Hz); ^{19}F NMR (365 MHz, CDCl_3) δ : -68.73, -78.30; ^{31}P NMR (162 MHz, CDCl_3) δ : 19.25; m/z LRMS (ESI + APCI) found $[\text{M} - \text{OTf}]^+$ 505.2, $\text{C}_{28}\text{H}_{21}\text{F}_3\text{N}_2\text{PS}^+$ requires 515.1.

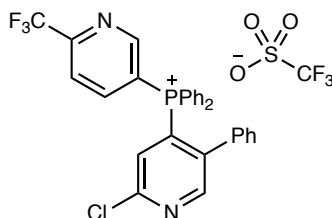
(2-Cyano-3-methylpyridin-4-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1l')



Major : Minor = 17:1

Prepared according to general procedure A, using 3-methylpicolinonitrile (118 mg, 1.00 mmol), TF_2O (168 μL , 1.00 mmol), 5-(diphenylphosphaneyl)-2-(trifluoromethyl)pyridine (364 mg, 1.10 mmol), DBU (149 μL , 1.00 mmol), and CH_2Cl_2 (10 mL). After purification by the standard procedure, the title compound was isolated as a yellow solid (490 mg, 0.82 mmol, 82% yield); Major Isomer ^1H NMR (400 MHz, CDCl_3) δ : 8.86-8.80 (2H, m), 8.69 (1H, ddd, $J = 13.0, 8.4, 2.2$ Hz), 8.17 (1H, dd, $J = 8.3, 1.8$ Hz), 8.00-7.93 (2H, m), 7.87-7.75 (8H, m), 7.51 (1H, dd, $J = 15.7, 5.0$ Hz), 2.23 (3H, s); ^{13}C NMR (100 MHz, CD_3CN) δ : 155.16 (d, $J = 13.2$ Hz), 153.48 (d, $J = 35.6, 2.4$ Hz), 150.93 (d, $J = 11.7$ Hz), 146.62 (d, $J = 9.6$ Hz), 142.65 (d, $J = 8.2$ Hz), 138.83 (d, $J = 11.1$ Hz), 137.53 (d, $J = 3.2$ Hz), 135.81 (d, $J = 11.2$ Hz), 134.32 (d, $J = 10.4$ Hz), 132.05 (d, $J = 13.9$ Hz), 128.52 (d, $J = 86.3$ Hz), 123.22-123.30 (m), 122.00 (q, $J = 321.0$ Hz), 121.89 (qd, $J = 276.0, 3.2$ Hz), 119.14 (d, $J = 87.89$ Hz), 116.41 (d, $J = 7.6$ Hz), 115.94 (d, $J = 86.0$ Hz), 21.14 (d, $J = 5.3$ Hz); ^{19}F NMR (365 MHz, CD_3CN) δ : -69.19, -79.20; ^{31}P NMR (162 MHz, CD_3CN) δ : 20.21 (Major Isomer), 14.58 (Minor Isomer); m/z LRMS (ESI + APCI) found $[\text{M} - \text{OTf}]^+ 448.2$, $\text{C}_{25}\text{H}_{18}\text{F}_3\text{N}_3\text{P}^+$ requires 448.1.

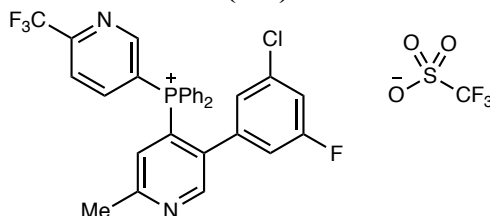
(2-Chloro-5-phenylpyridin-4-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1m')



Prepared according to general procedure A, using 2-chloro-5-phenylpyridine (114 mg, 0.60 mmol), TF_2O (101 μL , 0.60 mmol), 5-(diphenylphosphaneyl)-2-(trifluoromethyl)pyridine (219 mg, 0.66 mmol), DBU (90 μL , 0.60 mmol), and CH_2Cl_2 (6 mL). After purification by the standard procedure, the title compound was isolated as an amorphous solid (292 mg, 0.44 mmol, 73% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3604, 3013, 1560, 1441, 1259, 1029, 722, 666; ^1H NMR (400 MHz, CDCl_3) δ : 8.80 (1H, ddd, $J = 12.8, 8.2, 2.1$ Hz), 8.54 (1H, d, $J = 7.1$ Hz), 8.35 (1H, dd, $J = 5.9, 1.9$ Hz), 7.97-7.91 (3H, m), 7.86-7.74 (8H, m), 7.38 (1H, d, $J = 15.2$ Hz), 7.16 (1H, app td, $J = 7.5, 1.0$ Hz), 6.96 (2H, app t, $J = 7.6$ Hz), 6.81 (2H, dd, $J = 8.0, 0.9$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 153.88 (d, $J = 9.1$ Hz), 152.63 (d, $J = 12.8$ Hz), 152.36 (d, $J = 15.7$ Hz), 152.09 (qd, $J = 36.4, 2.7$ Hz), 145.49 (d, $J = 9.5$ Hz), 140.46 (d, $J = 7.2$ Hz), 136.61 (d, $J = 3.1$ Hz), 134.73 (d, $J = 10.6$ Hz), 133.24 (d, $J = 3.9$ Hz), 131.90 (d, $J = 10.2$ Hz), 131.32 (d, $J = 13.4$ Hz), 129.80, 129.10 (d, $J = 80.9$ Hz), 128.69 (d, $J = 11.7$ Hz), 128.15 (d, $J = 84.9$ Hz), 122.07-121.82 (m),

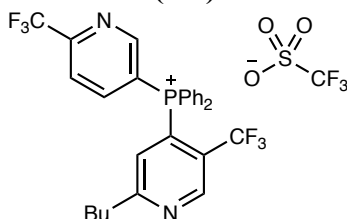
120.70 (q, $J = 320.9$ Hz), 120.37 (qd, $J = 275.5, 2.3$ Hz), 118.39 (d, $J = 87.4$ Hz), 114.86 (d, $J = 89.3$ Hz); ^{19}F NMR (365 MHz, CDCl_3) δ : -68.97, -78.33; ^{31}P NMR (162 MHz, CDCl_3) δ : 19.20; m/z LRMS (ESI + APCI) found $[\text{M} - \text{OTf}]^+$ 519.2, $\text{C}_{29}\text{H}_{20}\text{ClF}_3\text{N}_2\text{P}^+$ requires 519.1.

(5-(3-Chloro-5-fluorophenyl)-2-methylpyridin-4-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1n')



Prepared according to general procedure A using (3-chloro-5-fluorophenyl)-2-methylpyridine (221 mg, 1.00 mmol), TiF_4 (169 μL , 1.00 mmol), 5-(diphenylphosphanyl)-2-(trifluoromethyl)pyridine (364 mg, 1.10 mmol), DBU (147 μL , 1.00 mmol) and CH_2Cl_2 (10 mL). After purification by the standard procedure, the title compound was isolated as a white solid (434 mg, 0.62 mmol, 62% yield). mp 100-102 $^\circ\text{C}$; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 1581, 1439, 1335, 1259, 1143, 1075, 1029, 722, 636; ^1H NMR (400 MHz, CDCl_3) δ : 9.00-8.83 (1H, m), 8.63 (1H, d, $J = 7.5$ Hz), 8.52 (1H, dd, $J = 6.0, 1.9$ Hz), 8.10 (1H, dd, $J = 8.2, 2.1$ Hz), 7.98-7.86 (2H, m), 7.86-7.69 (8H, m), 7.32 (1H, d, $J = 16.2$ Hz), 6.85 (1H, dt, $J = 8.2, 2.0$ Hz), 6.54 (1H, t, $J = 1.7$ Hz), 6.44 (1H, dt, $J = 8.3, 1.9$ Hz), 2.72 (3H, s); ^{13}C NMR (100 MHz, CDCl_3) δ : 161.68 (d, $J = 254.1$ Hz), 161.34 (d, $J = 10.5$ Hz), 153.16-152.26 (m), 152.55 (qd, $J = 36.0, 2.4$ Hz), 145.68 (d, $J = 9.3$ Hz), 137.60 (dd, $J = 8.9, 4.4$ Hz), 136.49 (d, $J = 3.2$ Hz), 135.85-135.18 (m), 134.63 (d, $J = 10.7$ Hz), 131.90 (d, $J = 10.3$ Hz), 131.22 (d, $J = 13.3$ Hz), 129.04 (d, $J = 12.5$ Hz), 128.10 (d, $J = 9.7$ Hz), 126.19 (d, $J = 3.3$ Hz), 124.95 (d, $J = 84.2$ Hz), 122.06 (d, $J = 10.1$ Hz), 120.69 (q, $J = 320.8$ Hz, 1H), 120.46 (qd, $J = 275.2, 1.9$ Hz), 119.42 (d, $J = 65.1$ Hz), 117.08 (d, $J = 24.3$ Hz), 115.58 (d, $J = 22.6$ Hz), 114.98 (d, $J = 89.0$ Hz), 24.62 (d, $J = 1.2$ Hz); ^{19}F NMR (365 MHz, CDCl_3) δ : -68.80, -78.37, -108.46; ^{31}P NMR (162 MHz, CDCl_3) δ : 18.93; m/z LRMS (ESI + APCI) found $[\text{M} - \text{OTf}]^+$ 551.2, $\text{C}_{30}\text{H}_{21}\text{ClF}_4\text{N}_2\text{P}^+$ requires 551.1.

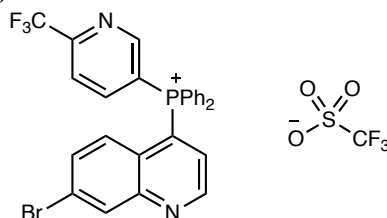
(2-Butyl-5-(trifluoromethyl)pyridin-4-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1o')



Prepared according to general procedure A, using 2-butyl-5-(trifluoromethyl)pyridine (305 mg, 1.50 mmol), TiF_4 (252 μL , 1.50 mmol), 5-(diphenylphosphanyl)-2-(trifluoromethyl)pyridine (547 mg, 1.65 mmol), DBU (224 μL , 1.50 mmol), and CH_2Cl_2 (15 mL). After purification by the standard procedure (except that two crash-outs were required), the title compound was isolated as a white solid (723 mg, 1.06 mmol, 71% yield). mp 58-60 $^\circ\text{C}$. IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2962, 2874, 1578, 1259, 1137, 1029, 722, 636; ^1H NMR (400 MHz, CDCl_3) δ : 9.19 (1H, d, $J = 7.4$ Hz), 8.83-8.76 (2H, m), 8.21-8.16 (1H, m), 7.97-7.91 (2H, m), 7.85-7.69 (8H, m), 7.22 (1H, d, $J = 17.6$ Hz), 2.95 (2H, t, $J = 7.8$ Hz), 1.72-1.63 (2H, m), 1.37-1.27 (2H, m), 0.87 (3H, t, $J = 7.3$ Hz); ^{13}C

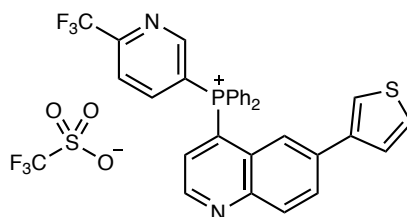
NMR (100 MHz, CDCl₃) δ : 170.61 (d, J = 9.9 Hz), 153.23 (qd, J = 35.5, 2.5 Hz), 153.16 (d, J = 13.1 Hz), 150.35-150.11 (m), 146.26 (d, J = 9.5 Hz), 136.69 (d, J = 3.0 Hz), 134.74 (d, J = 11.0 Hz), 131.21 (d, J = 13.7 Hz), 130.34 (d, J = 8.7 Hz), 124.06 (d, J = 80.8 Hz), 124.05 (qd, J = 33.2, 3.9 Hz), 122.64 (qd, J = 274.8, 2.5 Hz), 122.57-122.35 (m), 120.65 (q, J = 321.0 Hz), 120.54 (qd, J = 273.2, 2.1 Hz), 118.87 (d, J = 88.1 Hz), 114.85 (d, J = 90.5 Hz), 38.10, 30.37, 22.29, 13.73; ¹⁹F NMR (365 MHz, CDCl₃) δ : -53.49, -68.68, -78.48; ³¹P NMR (162 MHz, CDCl₃) δ : 25.06; m/z LRMS (ESI + APCI) found [M - OTf]⁺ 533.2, C₂₈H₂₄F₆N₂P⁺ requires 533.2.

(7-Bromoquinolin-4-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1p')



Prepared according to general procedure A (except that the reaction mixture was stirred for 60 min at -30 °C instead of -50 °C) using 7-bromoquinoline (208 mg, 1.0 mmol), Tf₂O (169 μ L, 1.0 mmol), 5-(diphenylphosphanyl)-2-(trifluoromethyl)pyridine (364 mg, 1.1 mmol), DBU (147 μ L, 1.0 mmol) and CH₂Cl₂ (10 mL). After the purification procedure, the title compound was isolated as a white solid (560 mg, 0.82 mmol, 82% yield). mp 134-137 °C; IR ν_{max} /cm⁻¹ (film): 1488, 1439, 1135, 1260, 1141, 1076, 1029, 723, 636; ¹H NMR (400 MHz, CDCl₃) δ : 9.22 (1H, t, J = 4.4 Hz), 8.82-8.70 (2H, m), 8.56 (1H, t, J = 2.0 Hz), 8.23-8.15 (1H, m), 7.98-7.89 (2H, m), 7.86-7.70 (8H, m), 7.61-7.50 (2H, m), 7.20 (1H, d, J = 9.0 Hz); ¹³C NMR (100 MHz, CDCl₃) δ : 153.39 (qd, J = 36.2, 2.4 Hz), 153.37 (d, J = 13.1 Hz), 151.65 (d, J = 12.3 Hz), 149.27 (d, J = 7.2 Hz), 145.97 (d, J = 9.6 Hz), 136.79 (d, J = 3.2 Hz), 134.57 (d, J = 11.0 Hz), 134.34 (d, J = 2.3 Hz), 133.16, 131.78 (d, J = 9.1 Hz), 131.55 (d, J = 13.5 Hz), 126.39 (d, J = 6.5 Hz), 125.71, 124.33 (d, J = 6.7 Hz), 122.76 (dd, J = 10.3, 2.7 Hz), 122.33 (d, J = 29.9 Hz), 120.59 (q, J = 321.0 Hz), 120.49 (qd, J = 275.3, 1.8 Hz), 118.54 (d, J = 87.2 Hz), 114.58 (d, J = 89.1 Hz); ¹⁹F NMR (365 MHz, CDCl₃) δ : -68.63, -78.39; ³¹P NMR (162 MHz, CDCl₃) δ : 19.40; m/z LRMS (ESI + APCI) found [M - OTf]⁺ 537.1, C₂₇H₂₈BrF₃N₂P⁺ requires 537.0.

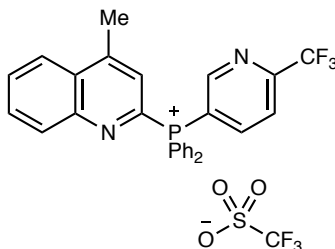
Diphenyl(6-(thiophen-3-yl)quinolin-4-yl)(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1q')



Prepared according to general procedure A using 6-(thiophen-3-yl)quinoline (211 mg, 1.00 mmol), Tf₂O (169 μ L, 1.00 mmol), 5-(diphenylphosphanyl)-2-(trifluoromethyl)pyridine (382 mg, 1.10 mmol), DBU (147 μ L, 1.00 mmol) and CH₂Cl₂ (10 mL). After purification by the

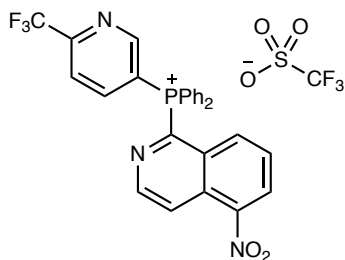
standard procedure, the title compound was isolated as a yellow solid (418 mg, 0.61 mmol, 61% yield). mp 95-99 °C; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 1616, 1439, 1334, 1260, 1140, 1075, 1029, 723, 635; ^1H NMR (400 MHz, CDCl_3) δ : 9.16 (1H, t, $J = 4.5$ Hz), 8.86-8.72 (2H, m), 8.38 (1H, dd, $J = 8.8$, 2.2 Hz), 8.21 (1H, dd, $J = 8.7$, 2.3 Hz), 8.10 (1H, dd, $J = 8.8$, 1.9 Hz), 7.95 (2H, ddt, $J = 11.2$, 6.1, 2.8 Hz), 7.88-7.76 (8H, m), 7.53 (1H, dd, $J = 17.6$, 4.4 Hz), 7.39 (1H, d, $J = 1.9$ Hz), 7.30 (1H, dd, $J = 5.1$, 2.9 Hz), 7.12 (1H, dd, $J = 2.9$, 1.4 Hz), 6.68 (1H, dd, $J = 5.1$, 1.4 Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 153.47 (d, $J = 13.0$ Hz), 153.36 (d, $J = 35.5$ Hz), 149.91 (d, $J = 12.4$ Hz), 148.01 (d, $J = 7.1$ Hz), 146.09 (d, $J = 9.5$ Hz), 139.43, 136.78, 136.73 (d, $J = 3.1$ Hz), 134.42 (d, $J = 11.0$ Hz), 132.63 (d, $J = 2.3$ Hz), 131.72, 131.56 (d, $J = 13.3$ Hz), 130.47, 127.80, 126.27 (d, $J = 6.5$ Hz), 125.29, 123.23, 122.79 (d, $J = 10.4$ Hz), 121.38, 121.29 (d, $J = 4.0$ Hz), 120.65 (q, $J = 321.1$ Hz), 120.48 (q, $J = 275.6$ Hz), 118.71 (d, $J = 68.3$ Hz), 114.88 (d, $J = 88.9$ Hz); ^{19}F NMR (365 MHz, CDCl_3) δ : -68.62, -78.35; ^{31}P NMR (162 MHz, CDCl_3) δ : 19.32; m/z LRMS (ESI + APCI) found $[\text{M} - \text{OTf}]^+$ 541.2, $\text{C}_{31}\text{H}_{21}\text{F}_3\text{N}_2\text{PS}^+$ requires 541.1.

(4-Methylquinolin-2-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1r')



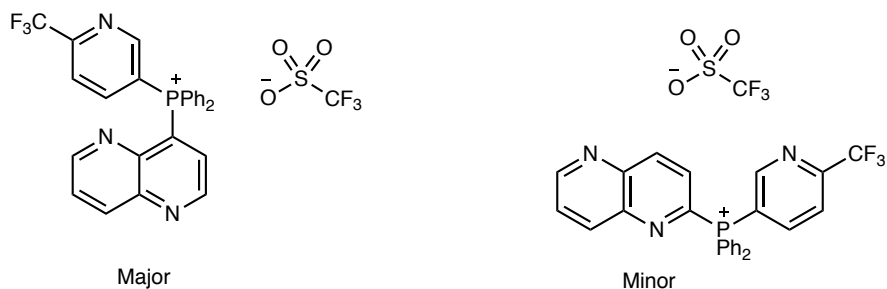
Prepared according to general procedure A, using 4-methylquinoline (132 μL , 1.00 mmol), Tf_2O (168 μL , 1.00 mmol), 5-(diphenylphosphanyl)-2-(trifluoromethyl)pyridine (364 mg, 1.10 mmol), DBU (149 μL , 1.00 mmol), and CH_2Cl_2 (10 mL). After purification by the standard procedure, the title compound was isolated as a yellow solid (510 mg, 0.82 mmol, 82% yield). mp 64-67 °C. IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3065, 1576, 1334, 1259, 1140, 1029, 724, 635; ^1H NMR (400 MHz, CDCl_3) δ : 9.08 (1H, dd, $J = 5.5$, 1.7 Hz), 8.63 (1H, ddd, $J = 12.4$, 8.5, 2.1 Hz), 8.19-8.15 (2H, m), 8.13 (1H, dd, $J = 8.3$, 1.9 Hz), 7.95-7.87 (3H, m), 7.85-7.71 (9H, m), 7.65 (1H, d, $J = 4.9$ Hz), 2.83 (3H, s); ^{13}C NMR (100 MHz, CDCl_3) δ : 154.16 (d, $J = 11.7$ Hz), 152.97 (qd, $J = 36.2$, 2.4), 149.47 (d, $J = 11.1$ Hz), 148.71 (d, $J = 23.0$), 145.90 (d, $J = 8.8$ Hz), 143.45, 142.27, 136.46 (d, $J = 3.0$ Hz), 134.89 (d, $J = 10.6$ Hz), 132.05, 131.16 (d, $J = 13.1$ Hz), 130.81 (d, $J = 12.6$ Hz), 129.22 (d, $J = 3.1$ Hz), 125.20 (d, $J = 109.5$ Hz), 125.08 (d, $J = 82.0$ Hz), 122.23-122.00 (m), 120.82 (q, $J = 321.0$), 120.71 (qd, $J = 274.7$, 1.7 Hz), 119.79 (d, $J = 87.3$ Hz), 115.53 (d, $J = 88.3$ Hz), 19.34; ^{19}F NMR (365 MHz, CDCl_3) δ : -68.71, -78.51; ^{31}P NMR (162 MHz, CDCl_3) δ : 12.41; m/z LRMS (ESI + APCI) found $[\text{M} - \text{OTf}]^+$ 473.3, $\text{C}_{28}\text{H}_{21}\text{F}_3\text{N}_3\text{P}^+$ requires 473.1.

(5-Nitroisoquinolin-1-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1s')



Prepared according to general procedure A, using 5-nitroisoquinoline (174 mg, 1.00 mmol), $\text{ Tf}_2\text{O}$ (168 μL , 1.00 mmol), 5-(diphenylphosphanyl)-2-(trifluoromethyl)pyridine (364 mg, 1.10 mmol), DBU (149 μL , 1.00 mmol), and CH_2Cl_2 (10 mL). After purification by the standard procedure, the title compound was isolated as an amorphous solid (471 mg, 0.72 mmol, 72% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3067, 3013, 1530, 1335, 1262, 1029, 747, 636; ^1H NMR (400 MHz, CDCl_3) δ : 9.02 (1H, d, J = 5.9 Hz), 8.89 (1H, dd, J = 5.6, 2.4 Hz), 8.83 (1H, d, J = 4.7 Hz), 8.57 (1H, d, J = 7.7 Hz), 8.44 (1H, app t, J = 9.7 Hz), 8.05 (1H, d, J = 8.1 Hz), 7.89-7.88 (3H, m), 7.82-7.74 (9H, m); ^{13}C NMR (100 MHz, CDCl_3) δ : 154.48 (d, J = 12.1 Hz), 152.75 (qd, J = 35.6, 2.4 Hz), 146.28 (d, J = 42.7 Hz), 146.18 (d, J = 3.3 Hz), 146.13 (d, J = 29.4 Hz), 143.64 (d, J = 121.2 Hz), 136.81 (d, J = 3.1 Hz), 134.61 (d, J = 10.8 Hz), 131.66 (d, J = 13.3 Hz), 131.30 (d, J = 25.9 Hz), 130.84 (d, J = 2.2 Hz), 130.01-129.85 (2C, m), 129.11 (d, J = 12.6 Hz), 122.33 (d, J = 3.8 Hz), 121.97-121.73 (m), 120.71 (qd, J = 272.9, 2.3 Hz), 120.69 (q, J = 321.7 Hz), 120.43 (d, J = 92.7 Hz), 115.16 (d, J = 85.7 Hz); ^{19}F NMR (365 MHz, CDCl_3) δ : -68.58, -78.37; ^{31}P NMR (162 MHz, CDCl_3) δ : 19.30; m/z LRMS (ESI + APCI) found $[\text{M} - \text{OTf}]^+$ 504.2, $\text{C}_{27}\text{H}_{18}\text{F}_3\text{N}_3\text{O}_2\text{P}^+$ requires 504.1.

(1,5-Naphthyridin-4-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1t')

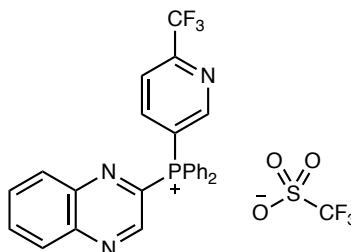


Major : Minor = 7:1

Prepared according to general procedure A using 1,5-naphthyridine (130 mg, 1.0 mmol), $\text{ Tf}_2\text{O}$ (169 μL , 1.0 mmol), 5-(diphenylphosphanyl)-2-(trifluoromethyl)pyridine (382 mg, 1.1 mmol), DBU (147 μL , 1.0 mmol) and CH_2Cl_2 (10 mL). After the purification procedure, the title compound was isolated as a yellow solid (440 mg, 0.73 mmol, 73% yield, combined yield). mp 95-99 $^{\circ}\text{C}$; Both isomers, IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 1622, 1519, 1324, 1265, 1240, 1175, 942, 729, 636; Major isomer, ^1H NMR (400 MHz, CDCl_3) δ : 9.36 (1H, t, J = 4.6 Hz), 8.88 (1H, dd, J = 6.4, 2.1 Hz), 8.74- 8.62 (3H, m), 7.89 (3H, dq, J = 14.3, 3.3, 2.2 Hz), 7.84-7.64 (10H, m); ^{13}C NMR (100 MHz, CDCl_3) δ : 153.16 (d, J = 13.2 Hz), 152.04, 151.73 (d, J = 12.2 Hz), 145.06 (d, J = 9.6 Hz), 144.54 (d, J = 5.8 Hz), 141.02 (d, J = 3.6 Hz), 138.63 (d, J = 2.4 Hz), 135.77 (d, J = 3.3 Hz), 134.24 (d, J = 11.0 Hz), 133.24 (d, J = 7.7 Hz), 131.05 (d, J = 13.3 Hz), 130.70 (d, J = 13.6 Hz),

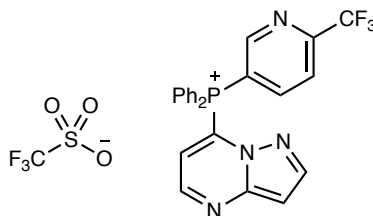
126.71, 126.14 (d, $J = 86.6$ Hz), 123.18-121.21 (m), 120.56 (qd, $J = 275.5, 2.0$ Hz), 120.47 (q, $J = 321.1$ Hz), 119.95 (d, $J = 90.1$ Hz), 115.65 (d, $J = 91.9$ Hz); ^{19}F NMR (365 MHz, CDCl_3) δ : -68.59, -78.40; ^{31}P NMR (162 MHz, CDCl_3) δ : 20.96, 13.58; m/z LRMS (ESI + APCI) found $[\text{M} - \text{OTf}]^+$ 460.2, $\text{C}_{26}\text{H}_{18}\text{F}_3\text{N}_3\text{P}^+$ requires 460.1.

Diphenyl(quinoxalin-2-yl)(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1u')



Prepared according to general procedure A, using quinoxaline (130 mg, 1.00 mmol), TF_2O (168 μL , 1.00 mmol), 5-(diphenylphosphaneyl)-2-(trifluoromethyl)pyridine (364 mg, 1.10 mmol), DBU (149 μL , 1.00 mmol), and CH_2Cl_2 (10 mL). After purification by the standard procedure, the title compound was isolated as a white solid (562 mg, 0.92 mmol, 92% yield). mp 172-175 $^\circ\text{C}$. IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3065, 2922, 1440, 1260, 1141, 1029, 724, 634; ^1H NMR (400 MHz, CDCl_3) δ : 9.11-9.04 (2H, m), 8.74 (1H, ddd, $J = 12.3, 8.6, 1.4$ Hz), 8.28-8.22 (2H, m), 8.17-8.11 (1H, dd, $J = 8.2, 1.1$ Hz), 8.11-7.90 (4H, m), 7.87-7.75 (8H, m); ^{13}C NMR (100 MHz, CDCl_3) δ : 153.97 (d, $J = 12.1$ Hz), 153.28 (qd, $J = 35.7, 2.4$ Hz), 146.44 (d, $J = 7.3$ Hz), 146.30 (d, $J = 10.0$ Hz), 143.85 (d, $J = 2.9$ Hz), 142.88 (d, $J = 17.5$ Hz), 139.52 (d, $J = 114.1$ Hz), 136.86 (d, $J = 3.1$ Hz), 135.37, 135.05 (d, $J = 10.9$ Hz), 133.29, 131.42 (d, $J = 13.4$ Hz), 130.30 (d, $J = 1.0$ Hz), 130.16 (d, $J = 2.6$ Hz), 122.48-122.26 (m), 120.68 (qd, $J = 275.2, 1.7$ Hz), 120.65 (q, $J = 321.0$ Hz), 118.75 (d, $J = 88.0$ Hz), 114.55 (d, $J = 88.6$ Hz); ^{19}F NMR (365 MHz, CDCl_3) δ : -68.62, -78.46; ^{31}P NMR (162 MHz, CDCl_3) δ : 11.78; m/z LRMS (ESI + APCI) found $[\text{M} - \text{OTf}]^+$ 460.2, $\text{C}_{26}\text{H}_{18}\text{F}_3\text{N}_3\text{P}^+$ requires 460.1.

Diphenyl(pyrazolo[1,5-a]pyrimidin-7-yl)(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1w')

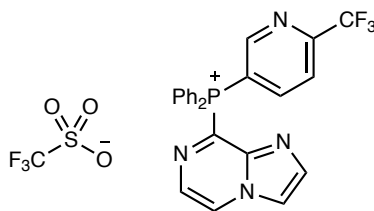


>20:1 (Major:Unidentified Phosphonium) Mixture of Isomers

Prepared according to general procedure A using pyrazolo[1,5-a]pyrimidine (179 mg, 1.50 mmol), TF_2O (252 μL , 1.50 mmol), 5-(diphenylphosphaneyl)-2-(trifluoromethyl)pyridine (546 mg, 1.65 mmol), DBU (224 μL , 1.50 mmol), and CH_2Cl_2 (15 mL). After purification by the standard procedure, the title compound was isolated as a yellow solid (739 mg, 1.23 mmol, 82% yield). Both Isomers, IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3066, 2925, 1726, 1603, 1260, 1121, 840, 766; Major

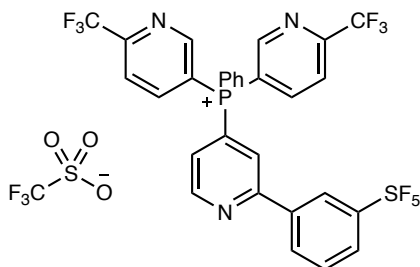
Isomer: ^1H NMR (400 MHz, CDCl_3) δ : 8.95 (1H, d, J = 6.4, 2.1 Hz), 8.78-8.70 (2H, m), 8.07 (1H, ddd, J = 8.3, 6.1, 0.7 Hz), 7.98-7.91 (3H, m), 7.82-7.74 (8H, m), 7.29 (1H, dd, J = 12.1, 4.2 Hz), 6.93 (1H, app t, J = 2.4 Hz); Major Isomer: ^{13}C NMR (100 MHz, CDCl_3) δ : 153.78 (d, J = 14.1 Hz), 153.51 (qd, J = 36.4, 2.8 Hz), 149.19 (d, J = 8.6 Hz), 148.85 (d, J = 1.4 Hz), 146.03 (d, J = 9.8 Hz), 145.42, 137.03 (d, J = 3.2 Hz), 134.77 (d, J = 11.3 Hz), 131.39 (d, J = 14.2 Hz), 126.70 (d, J = 99.5 Hz), 122.42-122.20 (m), 121.31 (d, J = 8.8 Hz), 120.66 (q, J = 320.7 Hz), 120.61 (qd, J = 275.7, 2.3 Hz), 116.83 (d, J = 90.9 Hz), 112.77 (d, J = 92.7 Hz), 100.2; ^{19}F NMR (365 MHz, CDCl_3) δ : -68.65, -78.43; ^{31}P NMR (162 MHz, CDCl_3) δ : 18.10 (Major Isomer), 14.6 (Minor Isomer); m/z LRMS (ESI + APCI) found $[\text{M} - \text{OTf}]^+$ 449.3, $\text{C}_{24}\text{H}_{17}\text{F}_3\text{N}_4\text{P}^+$ requires 449.1.

Imidazo[1,5-*a*]pyrazin-8-ylphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1x'**)**



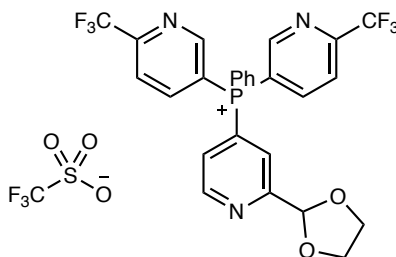
Prepared according to general procedure A, using imidazo[1,2-*a*]pyrazine (179 mg, 1.50 mmol), Tf_2O (252 μL , 1.50 mmol), 5-(diphenylphosphaneyl)-2-(trifluoromethyl)pyridine (547 mg, 1.65 mmol), DBU (224 μL , 1.50 mmol), and CH_2Cl_2 (15 mL). After purification by the standard procedure (except that two crash-outs were done), the title compound was isolated as an amorphous solid (321 mg, 0.54 mmol, 36% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3101, 3064, 2249, 1588, 1439, 1259, 1142, 1029, 724; ^1H NMR (400 MHz, CDCl_3) δ : 9.04 (1H, app t, J = 4.3 Hz), 8.99 (1H, dd, J = 5.9, 2.1 Hz), 8.60 (1H, ddd, J = 12.5, 8.1, 2.2 Hz), 8.35 (1H, dd, J = 1.7, 1.2 Hz), 8.24 (1H, dd, J = 4.4, 1.0 Hz), 8.06 (1H, ddd, J = 8.3, 2.1, 0.8 Hz), 7.93-7.87 (2H, m), 7.87-7.70 (9H, m); ^{13}C NMR (100 MHz, CDCl_3) δ : 154.61 (d, J = 12.5 Hz), 153.09 (qd, J = 36.2, 2.4 Hz), 146.05 (d, J = 9.3 Hz), 140.46 (d, J = 33.9 Hz), 137.89, 136.46 (d, J = 3.1 Hz), 134.96 (d, J = 11.1 Hz), 133.77, 130.85 (d, J = 13.7 Hz), 130.58 (d, J = 22.1 Hz), 125.67 (d, J = 3.3 Hz), 121.73-121.52 (m), 120.80 (q, J = 320.7 Hz), 120.69 (qd, J = 275.2, 1.6 Hz), 118.55 (d, J = 89.3 Hz), 116.90, 114.82 (d, J = 90.6 Hz); ^{19}F NMR (365 MHz, CDCl_3) δ : -68.62, -78.39; ^{31}P NMR (162 MHz, CDCl_3) δ : 16.40; m/z LRMS (ESI + APCI) found $[\text{M} - \text{OTf}]^+$ 449.2, $\text{C}_{24}\text{H}_{17}\text{F}_3\text{N}_4\text{P}^+$ requires 449.1.

(2-(3-(Pentafluoro- λ^6 -sulfaneyl)phenyl)pyridin-4-yl)(phenyl)bis(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1y''**)**



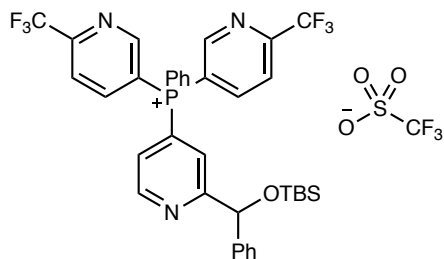
Prepared according to general procedure A (except that Et₃N was used as the base), using, 2-(3-(pentafluoro- λ 6-sulfaneyl)phenyl)pyridine (422 mg, 1.50 mmol), Tf₂O (252 μ L, 1.50 mmol), 5,5'-(phenylphosphanediyl)bis(2-(trifluoromethyl)pyridine) (660 mg, 1.65 mmol), Et₃N (209 μ L, 1.50 mmol), and CH₂Cl₂ (15 mL). After purification by the standard procedure (except that a second crash-out using 100% diethyl ether was required), the title compound was isolated as a white solid (1.01 g, 1.22 mmol, 80% yield). mp 82-86 °C. IR ν_{max} /cm⁻¹ (film): 3066, 1586, 1441, 1334, 1075, 1029, 839, 635; ¹H NMR (400 MHz, CDCl₃) δ : 9.09 (1H, app t, *J* = 5.4 Hz), 8.92 (2H, dd, *J* = 6.1, 1.7 Hz), 8.60 (2H, ddd, *J* = 13.1, 4.8, 2.0 Hz), 8.47 (1H, app t, *J* = 1.6 Hz), 8.13-8.06 (4H, m), 8.01-7.94 (1H, m), 7.87-7.72 (5H, m), 7.60 (1H, ddd, *J* = 13.7, 8.7, 1.4 Hz), 7.52 (1H, app t, *J* = 8.0 Hz); ¹³C NMR (100 MHz, CDCl₃) δ : 158.14 (d, *J* = 12.0 Hz), 155.06 – 154.40 (m), 154.07 (qd, *J* = 36.3, 2.4 Hz), 153.75 (d, *J* = 13.5 Hz), 152.34 (d, *J* = 11.3 Hz), 146.14 (d, *J* = 10.0 Hz), 137.67, 137.55 (d, *J* = 3.0 Hz), 134.98 (d, *J* = 11.1 Hz), 131.77 (d, *J* = 13.7 Hz), 130.69, 129.92, 128.00-127.80 (m), 126.76 (d, *J* = 86.1 Hz), 126.26 (d, *J* = 8.9 Hz), 125.38-125.16 (m), 124.11 (d, *J* = 9.5 Hz), 122.75-122.50 (m), 120.50 (qd, *J* = 275.8, 2.2 Hz), 120.36 (q, *J* = 320.3 Hz), 116.48 (d, *J* = 88.5 Hz), 112.61 (d, *J* = 86.2 Hz); ¹⁹F NMR (365 MHz, CDCl₃) δ : 83.61 (1F, qn, *J* = 150.6 Hz), 62.55 (4F, d, *J* = 150.0 Hz), -68.78, -78.80; ³¹P NMR (162 MHz, CDCl₃) δ : 18.64; m/z LRMS (ESI + APCI) found [M - OTf]⁺ 680.2, C₂₉H₁₈F₁₁N₃PS⁺ requires 680.1.

(2-(1,3-Dioxolan-2-yl)pyridin-4-yl)(phenyl)bis(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1z'')



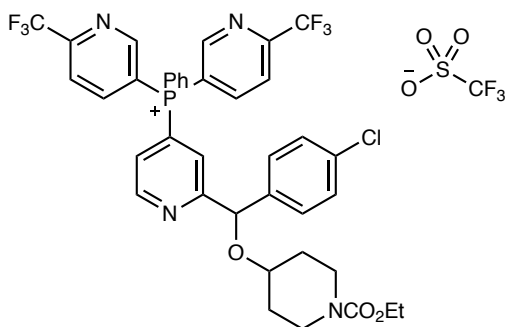
Prepared according to general procedure A, using 2-(1,3-dioxolan-2-yl)pyridine (151 mg, 1.00 mmol), Tf₂O (168 μ L, 1.00 mmol), 5,5'-(phenylphosphanediyl)bis(2-(trifluoromethyl)pyridine) (440 mg, 1.10 mmol), DBU (149 μ L, 1.00 mmol), and CH₂Cl₂ (10 mL). After purification by the standard procedure (except that two crash-outs were done), the title compound was isolated as a brown solid (330 mg, 0.47 mmol, 47% yield). mp 67-72 °C. IR ν_{max} /cm⁻¹ (film): 3066, 2900, 1334, 1258, 1138, 1074, 725, 636; ¹H NMR (400 MHz, CDCl₃) δ : 8.99 (1H, app t, *J* = 4.9 Hz), 8.87 (2H, d, *J* = 5.0 Hz), 8.57 (2H, ddd, *J* = 13.1, 8.4, 1.7 Hz), 8.10 (2H, dd, *J* = 8.3, 1.3 Hz), 7.98 (1H, app t, *J* = 7.7 Hz), 7.86-7.78 (2H, m), 7.77-7.69 (4H, m), 5.86 (1H, s), 4.07-3.95 (4H, m); ¹³C NMR (100 MHz, CDCl₃) δ : 160.37 (d, *J* = 10.1 Hz), 153.94 (qd, *J* = 36.2, 2.6 Hz), 153.72 (d, *J* = 13.5 Hz), 152.12 (d, *J* = 10.7 Hz), 146.14 (d, *J* = 9.8 Hz), 137.52 (d, *J* = 3.1 Hz), 135.00 (d, *J* = 11.3 Hz), 131.74 (d, *J* = 13.6 Hz), 128.06 (d, *J* = 9.0 Hz), 126.33 (d, *J* = 85.5 Hz), 123.90 (d, *J* = 9.6 Hz), 122.57-122.55 (m), 122.55 (qd, *J* = 275.3, 2.2 Hz), 120.39 (q, *J* = 320.8 Hz), 116.48 (d, *J* = 88.5 Hz), 112.44 (d, *J* = 90.2 Hz), 101.23 (d, *J* = 1.9 Hz), 65.85; ¹⁹F NMR (365 MHz, CDCl₃) δ : -68.78, -78.78; ³¹P NMR (162 MHz, CDCl₃) δ : 18.42; m/z LRMS (ESI + APCI) found [M - OTf]⁺ 550.2, C₂₆H₁₉F₆N₃O₂P⁺ requires 550.1.

(2-(((Tert-butyldimethylsilyl)oxy)(phenyl)methyl)pyridin-4-yl)(phenyl)bis(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1aa'')



Prepared according to general procedure A using 2-(((tert-butyldimethylsilyl)oxy)(phenyl)methyl)pyridine (300 mg, 1.00 mmol), TiF_4 (169 μL , 1.00 mmol), 5,5'-(phenylphosphanediy) bis(2-(trifluoromethyl)pyridine) (440 mg, 1.10 mmol), DBU (147 μL , 1.00 mmol) and CH_2Cl_2 (10 mL). After purification by the standard procedure, the title compound was isolated as a yellow solid (510 mg, 0.60 mmol, 60% yield). mp 70-74 $^\circ\text{C}$; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2954, 2932, 2859, 1373, 1333, 1257, 1142, 1075, 1029, 838, 725, 636; ^1H NMR (400 MHz, CDCl_3) δ : 9.07 (1H, t, $J = 5.2$ Hz), 8.94 (2H, ddd, $J = 8.3, 6.1, 2.0$ Hz), 8.87-8.74 (2H, m), 8.28 (2H, dt, $J = 8.4, 2.7$ Hz), 8.18-8.06 (1H, m), 8.00-7.77 (5H, m), 7.71 (1H, ddd, $J = 13.5, 5.1, 1.9$ Hz), 7.52-7.39 (5H, m), 6.08 (1H, s), 0.84 (9H, s), 0.07 (3H, s), 0.00 (3H, s); ^{13}C NMR (100 MHz, CDCl_3) δ : 167.44 (d, $J = 9.7$ Hz), 153.77 ($J = 35.8, 1.8$ Hz), 153.58 (d, $J = 13.4$ Hz), 151.68 (d, $J = 10.9$ Hz), 145.97 (dd, $J = 9.8, 1.9$ Hz), 142.05, 137.31 (d, $J = 3.2$ Hz), 134.85 (d, $J = 11.3$ Hz), 131.62 (d, $J = 13.8$ Hz), 128.66, 128.10, 126.47, 126.01 (d, $J = 84.9$ Hz), 125.94 (d, $J = 9.0$ Hz), 122.53 (d, $J = 10.1$ Hz), 120.45 (qd, $J = 275.4, 1.8$ Hz), 120.36 (q, $J = 320.7$ Hz), 116.54 (dd, $J = 88.3, 5.3$ Hz), 112.43 (d, $J = 90.2$ Hz), 77.23 (d, $J = 1.7$ Hz), 25.55, 17.94, -5.06 (d, $J = 39.0$ Hz); ^{19}F NMR (365 MHz, CDCl_3) δ : -68.70, -78.64; ^{31}P NMR (162 MHz, CDCl_3) δ : 18.49; m/z LRMS (ESI + APCI) found $[\text{M} - \text{OTf}]^+$ 698.3, $\text{C}_{36}\text{H}_{35}\text{F}_6\text{N}_3\text{OPSi}^+$ requires 698.2.

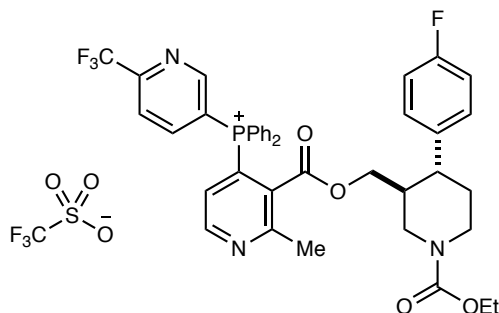
(2-((4-Chlorophenyl)((1-(ethoxycarbonyl)piperidin-4-yl)oxy)methyl)pyridin-4-yl)(phenyl)bis(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1ai'')



Prepared according to general procedure A using ethyl 4-((4-chlorophenyl) (pyridin-2-yl)methoxy)piperidine-1-carboxylate (450 mg, 1.20 mmol), TiF_4 (202 μL , 1.20 mmol), 5,5'-(phenylphosphanediy)bis(2-(trifluoromethyl)pyridine) (528 mg, 1.44 mmol), DBU (176 μL , 1.20 mmol) and CH_2Cl_2 (12 mL). After purification by the standard procedure, the title

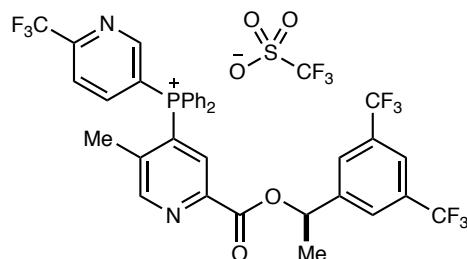
compound was isolated as a yellow solid (700 mg, 0.94 mmol, 63% yield). mp 103-105 °C; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3063, 2930, 1682, 1439, 1334, 1259, 1142, 1075, 1029, 725, 636; ^1H NMR (400 MHz, CDCl_3) δ : 9.01-8.80 (3H, m), 8.73-8.59 (2H, m), 8.14 (2H, dt, $J = 8.6, 2.2$ Hz), 8.07-7.93 (1H, m), 7.92-7.64 (5H, m), 7.57 (1H, ddd, $J = 13.5, 5.1, 1.7$ Hz), 7.36-7.28 (4H, m), 5.73 (1H, s), 4.10 (2H, q, $J = 7.1$ Hz), 3.72-3.44 (3H, m), 3.14 (2H, ddt, $J = 12.3, 7.6, 3.7$ Hz), 1.78-1.56 (3H, m), 1.45 (2H, dtd, $J = 12.4, 7.9, 3.8$ Hz), 1.24 (3H, t, $J = 7.1$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 165.12 (d, $J = 10.1$ Hz), 155.46, 153.89 (qd, $J = 36.3, 2.5$ Hz), 153.73 (d, $J = 13.4$ Hz), 151.68 (d, $J = 10.8$ Hz), 146.05 (d, $J = 9.7$ Hz), 138.51, 137.40 (d, $J = 3.2$ Hz), 134.95 (d, $J = 11.3$ Hz), 134.21, 131.61 (d, $J = 13.6$ Hz), 128.85 (d, $J = 26.9$ Hz), 126.31 (d, $J = 38.4$ Hz), 125.85 (d, $J = 38.0$ Hz), 123.73 (d, $J = 10.0$ Hz), 122.51 (d, $J = 10.5$ Hz), 120.48 (qd, $J = 275.6, 2.1$ Hz), 120.39 (q, $J = 320.8$ Hz), 116.53 (dd, $J = 88.3, 3.8$ Hz), 112.58 (d, $J = 90.3$ Hz), 79.95, 73.08, 61.37, 40.81 (d, $J = 6.0$ Hz), 30.91 (d, $J = 94.6$ Hz), 14.66; ^{19}F NMR (365 MHz, CDCl_3) δ : -68.74, -78.68; ^{31}P NMR (162 MHz, CDCl_3) δ : 18.51; m/z LRMS (ESI + APCI) found $[\text{M} - \text{OTf}]^+ 773.2$, $\text{C}_{38}\text{H}_{33}\text{ClF}_6\text{N}_4\text{O}_3\text{P}^+$ requires 773.2.

(3-(((3*S*,4*R*)-1-(ethoxycarbonyl)-4-(4-fluorophenyl)piperidin-3-yl)methoxy)carbonyl)-2-methylpyridin-4-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1aj')



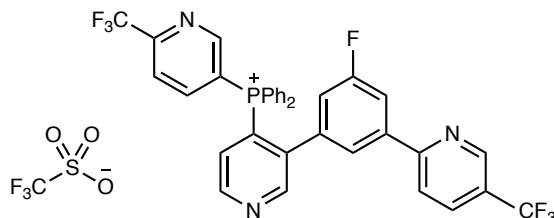
Prepared according to general procedure A, using ((3*S*,4*R*)-1-(ethoxycarbonyl)-4-(4-fluorophenyl)piperidin-3-yl)methyl 2-methylnicotinate (401 mg, 1.00 mmol), Ti_2O (169 μL , 1.00 mmol), 5-(diphenylphosphanyl)-2-(trifluoromethyl)pyridine (364 mg, 1.10 mmol), DBU (149 μL , 1.00 mmol), and CH_2Cl_2 (10 mL). After purification by the standard procedure, the title compound was isolated as a white solid (1st run: 525 mg, 0.60 mmol, 60% yield, 2nd run: 772 mg, 0.88 mmol, 88% yield, Average = 74%). mp 106-110 °C. IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3068, 2985, 1688, 1439, 1261, 1139, 1030, 636; ^1H NMR (400 MHz, CDCl_3) δ : 8.99 (1H, app t, $J = 4.9$ Hz), 8.69 (1H, dd, $J = 5.7, 1.7$ Hz), 8.59 (1H, app t, $J = 10.6$ Hz), 8.09 (1H, dd, $J = 8.1, 1.7$ Hz), 7.83-7.55 (10H, m), 7.30-7.22 (1H, m), 7.05-6.95 (4H, m), 4.33-4.16 (4H, m), 3.53-3.08 (2H, m), 2.97 (3H, s), 2.79 (1H, br s), 2.55-2.28 (2H, m), 1.92-1.50 (3H, m), 1.30 (3H, t, $J = 7.1$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 166.64, 166.61, 161.73 (d, $J = 245.5$ Hz), 161.65-161.43 (m), 155.43-155.14 (m), 153.45 (dd, $J = 40.4, 12.2$ Hz), 152.47 (qd, $J = 35.3, 2.2$ Hz), 145.88 (d, $J = 9.1$ Hz), 137.98 (d, $J = 2.7$ Hz), 135.69 (d, $J = 10.6$ Hz), 133.86 (dd, $J = 26.3, 10.5$ Hz), 130.97-130.53 (2C, m), 128.65 (d, $J = 7.8$ Hz), 127.50 (d, $J = 4.4$ Hz), 122.15-121.92 (m), 120.69 (q, $J = 321.0$ Hz), 120.69 (d, $J = 91.8$ Hz), 120.59 (qd, $J = 275.9, 1.6$ Hz), 116.98 (d, $J = 92.0$), 116.66 (d, $J = 92.9$ Hz), 115.75 (d, $J = 21.2$ Hz), 67.98, 61.54, 46.98, 44.10, 44.02, 40.36, 34.00, 26.16, 14.62; ^{19}F NMR (365 MHz, CDCl_3) δ : -68.55, -78.33, -115.40; ^{31}P NMR (162 MHz, CDCl_3) δ : 26.58; m/z LRMS (ESI + APCI) found $[\text{M} - \text{OTf}]^+ 730.3$, $\text{C}_{40}\text{H}_{37}\text{F}_4\text{N}_3\text{O}_4\text{P}^+$ requires 730.2.

(*R*)-2-((1-(3,5-Bis(trifluoromethyl)phenyl)ethoxy)carbonyl)-5-methylpyridin-4-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1ak')



Prepared according to general procedure A, using (*R*)-1-(3,5-bis(trifluoromethyl)phenyl)ethyl 5-methylpicolinate (596 mg, 1.58 mmol), Ti_2O (266 μL , 1.58 mmol), 5-(diphenylphosphaneyl)-2-(trifluoromethyl)pyridine (576 mg, 1.74 mmol), DBU (233 μL , 1.58 mmol), and CH_2Cl_2 (16 mL). After purification by the standard procedure (except that two crash-outs were required), the title compound was isolated as a white solid (1.04 g, 1.21 mmol, 77% yield). mp 106-108 $^\circ\text{C}$. IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3064, 1743, 1441, 1277, 1130, 1076, 724, 636; ^1H NMR (400 MHz, CDCl_3) δ : 8.93 (1H, d, J = 6.6 Hz), 8.83 (1H, d, J = 5.1 Hz), 8.69 (1H, app t, J = 9.2 Hz), 8.17 (1H, d, J = 7.9 Hz), 7.97-7.70 (14H, m), 6.10 (1H, q, J = 6.5 Hz), 2.15 (3H, s), 1.64 (3H, d, J = 6.5 Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 162.45, 154.56 (d, J = 8.5 Hz), 153.28 (q, J = 35.4 Hz), 153.23 (d, J = 12.9 Hz), 147.43 (d, J = 11.1 Hz), 145.89 (d, J = 9.5 Hz), 143.32, 141.39 (d, J = 7.1 Hz), 136.76 (d, J = 1.8 Hz), 134.39 (d, J = 11.0 Hz), 131.82 (q, J = 33.3 Hz), 131.56 (d, J = 13.7 Hz), 129.55 (d, J = 11.3 Hz), 126.64, 126.22 (d, J = 84.6 Hz), 123.05 (q, J = 272.7 Hz), 122.90-122.60 (m), 122.25-122.20 (m), 120.53 (q, J = 321.3 Hz), 120.42 (q, J = 275.1 Hz), 117.89 (d, J = 86.7 Hz), 113.78 (d, J = 89.1 Hz), 73.21, 21.46, 20.55 (d, J = 4.7 Hz); ^{19}F NMR (365 MHz, CDCl_3) δ : -62.68, -68.69, -78.50; ^{31}P NMR (162 MHz, CDCl_3) δ : 19.53; m/z LRMS (ESI + APCI) found $[\text{M} - \text{OTf}]^+$ 707.2, $\text{C}_{35}\text{H}_{25}\text{F}_9\text{N}_2\text{O}_2\text{P}^+$ requires 707.2.

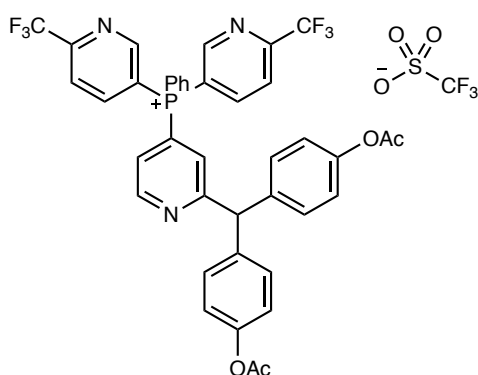
(3-(3-Fluoro-5-(5-(trifluoromethyl)pyridin-2-yl)phenyl)pyridin-4-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1am')



Prepared according to general procedure A, using 3-(3-fluoro-5-(5-(trifluoromethyl)pyridin-2-yl)phenyl)pyridine (318 mg, 1.50 mmol), Ti_2O (252 μL , 1.50 mmol), 5-(diphenylphosphaneyl)-2-(trifluoromethyl)pyridine (547 mg, 1.65 mmol), DBU (224 μL , 1.50 mmol), and CH_2Cl_2 (15 mL). After purification by the standard procedure (except that two crash-outs were required), the title compound was isolated as a white solid (1.04 g, 1.30 mmol, 87% yield). mp 106-110 $^\circ\text{C}$. IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3066, 1604, 1330, 1260, 1134, 1029, 722, 636; ^1H NMR (400 MHz, CDCl_3) δ : 8.93 (1H, app t, J = 4.8 Hz), 8.74 (1H, d, J = 7.1 Hz), 8.69-8.57 (3H, m), 7.97-7.67 (12H, m), 7.62 (1H, d, J = 8.4 Hz), 7.57-7.44 (3H, m), 6.64 (1H, d, J = 8.0 Hz); ^{13}C NMR (100 MHz,

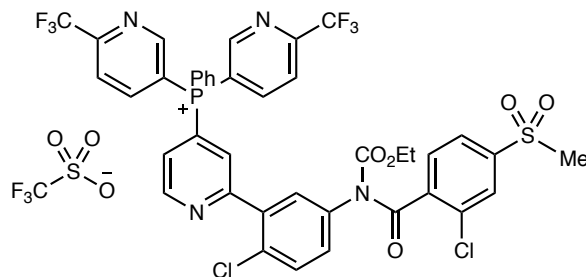
CDCl₃) δ : 162.37 (d, J = 250.7 Hz), 156.66, 153.26 (d, J = 7.8 Hz), 152.96 (d, J = 12.5 Hz), 152.14 (qd, J = 36.1, 2.4 Hz), 150.71 (d, J = 10.6 Hz), 146.26 (q, J = 3.9 Hz), 145.33 (d, J = 9.3 Hz), 140.13 (d, J = 8.1 Hz), 139.6 (dd, J = 6.8, 1.8 Hz), 137.02 (dd, J = 8.1, 4.5 Hz), 136.22 (d, J = 2.9 Hz), 134.45-134.80 (2C, m), 131.13 (d, J = 13.3 Hz), 128.54 (d, J = 9.8 Hz), 125.80 (q, J = 33.2 Hz), 125.54, 124.78-124.60 (m), 123.35 (q, J = 272.4 Hz), 121.90-121.62 (m), 120.65 (q, J = 320.9 Hz), 120.33, 120.30 (qd, J = 275.3, 2.2 Hz), 119.20 (d, J = 86.6 Hz), 117.57 (d, J = 23.1 Hz), 115.07 (d, J = 89.3 Hz), 115.00 (d, J = 22.9 Hz); ¹⁹F NMR (365 MHz, CDCl₃) δ : -62.49, -69.08, -78.38, -110.01 (1F, t, J = 8.9 Hz); ³¹P NMR (162 MHz, CDCl₃) δ : 19.24; m/z LRMS (ESI + APCI) found [M - OTf]⁺ 648.2, C₃₅H₂₂F₇N₃P⁺ requires 648.1.

(2-(Bis(4-acetoxyphenyl)methyl)pyridin-4-yl)(phenyl)bis(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1an'')



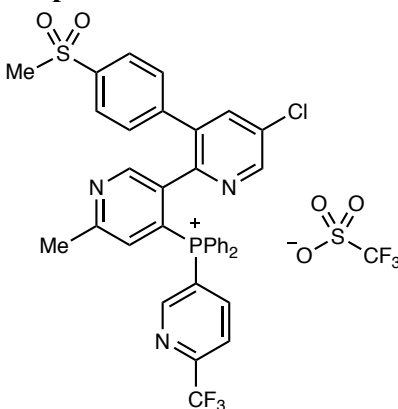
Prepared according to general procedure A using (pyridin-2-ylmethylene)bis(4,1-phenylene) diacetate (362 mg, 1.00 mmol), Tf₂O (169 μ L, 1.00 mmol), 5,5'-(phenylphosphanediy)bis (2-(trifluoromethyl)pyridine) (440 mg, 1.10 mmol), DBU (147 μ L, 1.00 mmol) and CH₂Cl₂ (10 mL). After purification by the standard procedure, the title compound was isolated as a white solid (610 mg, 0.64 mmol, 64% yield). mp 125-130 °C; IR ν_{max} /cm⁻¹ (film): 1751, 1505, 1372, 1335, 1260, 1194, 1076, 725, 637; ¹H NMR (400 MHz, CDCl₃) δ : 8.93 (1H, s), 8.75 (2H, d, J = 6.1 Hz), 8.57 (2H, s), 8.09 (2H, s), 7.94 (1H, d, J = 7.4 Hz), 7.77 (2H, s), 7.61 (2H, dd, J = 13.4, 7.2 Hz), 7.52 (1H, s), 7.24 (1H, s), 7.17 (4H, d, J = 8.0 Hz), 6.96 (4H, d, J = 8.0 Hz), 5.78 (1H, s), 2.25 (6H, s); ¹³C NMR (100 MHz, CDCl₃) δ : 169.54, 165.87 (d, J = 10.3 Hz), 153.72 (d, J = 13.6 Hz), 153.61 (qd, J = 36.0, 2.3 Hz), 151.89 (d, J = 11.0 Hz), 149.65, 145.81 (d, J = 9.7 Hz), 138.73, 137.29, 134.80 (d, J = 11.3 Hz), 131.53 (d, J = 13.7 Hz), 130.34, 126.89 (d, J = 9.4 Hz), 125.32 (d, J = 15.5 Hz), 122.37 (d, J = 10.5 Hz), 121.88, 120.57 (qd, J = 275.1, 1.9 Hz), 120.46 (d, J = 320.8 Hz), 119.88-118.09 (m), 116.46 (d, J = 88.4 Hz), 112.25 (d, J = 90.1 Hz), 57.54, 20.98; ¹⁹F NMR (365 MHz, CDCl₃) δ : -68.70, -78.58; ³¹P NMR (162 MHz, CDCl₃) δ : 18.19; m/z LRMS (ESI + APCI) found [M - OTf]⁺ 760.2, C₄₀H₂₉F₆N₃O₄P⁺ requires 760.2.

(2-(2-Chloro-5-(2-chloro-N-(ethoxycarbonyl)-4-(methylsulfonyl)benzamido)phenyl)pyridin-4-yl)(phenyl)bis(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1ao'')



Prepared according to general procedure A using ethyl (4-chloro-3-(pyridin-2-yl)phenyl) (2-chloro-4-(methylsulfonyl)benzoyl)carbamate (492 mg, 1.00 mmol), TiF_4 (169 μL , 1.00 mmol), 5,5'-(phenylphosphanediy)bis(2-(trifluoromethyl)pyridine) (440 mg, 1.10 mmol), DBU (147 μL , 1.00 mmol) and CH_2Cl_2 (10 mL). After purification by the standard procedure, the title compound was isolated as a white solid (500 mg, 0.49 mmol, 49% yield). mp 155-160 $^\circ\text{C}$; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 1750, 1689, 1373, 1335, 1259, 1148, 1075, 1030, 725, 637; ^1H NMR (400 MHz, CDCl_3) δ : 9.15 (1H, t, $J = 5.4$ Hz), 8.92 (2H, dd, $J = 6.3, 2.2$ Hz), 8.68 (2H, ddd, $J = 13.4, 8.3, 2.3$ Hz), 8.13 (2H, dd, $J = 8.4, 2.2$ Hz), 8.05-7.47 (12H, m), 7.35 (1H, dd, $J = 8.5, 2.6$ Hz), 4.09 (2H, q, $J = 7.1$ Hz), 3.06 (3H, s), 1.04 (3H, t, $J = 7.1$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 167.91, 157.40 (d, $J = 11.5$ Hz), 153.96 (dd, $J = 36.4, 2.3$ Hz), 153.85 (d, $J = 13.9$ Hz), 152.56 (d, $J = 11.3$ Hz), 152.45, 145.99 (d, $J = 9.9$ Hz), 142.26 (d, $J = 47.1$ Hz), 136.96 (d, $J = 114.0$ Hz), 135.03 (d, $J = 11.3$ Hz), 132.28 (d, $J = 5.4$ Hz), 131.72 (d, $J = 13.8$ Hz), 131.49, 131.31, 131.01 (d, $J = 14.5$ Hz), 129.62 (d, $J = 13.0$ Hz), 129.37, 128.98, 128.14, 127.99 (d, $J = 9.8$ Hz), 126.61 (d, $J = 8.5$ Hz), 126.10 (d, $J = 9.7$ Hz), 125.20, 122.60 (d, $J = 10.3$ Hz), 122.06, 121.89 (d, $J = 2.0$ Hz), 120.52 (qd, $J = 275.5, 2.0$ Hz), 120.47 (q, $J = 320.7$ Hz), 119.02 (d, $J = 29.4$ Hz), 116.48 (d, $J = 88.5$ Hz), 112.40 (d, $J = 90.3$ Hz), 64.43, 44.37, 13.77; ^{19}F NMR (365 MHz, CDCl_3) δ : -68.67, -78.62; ^{31}P NMR (162 MHz, CDCl_3) δ : 18.58; m/z LRMS (ESI + APCI) found $[\text{M} - \text{OTf}]^+ 891.1$, $\text{C}_{40}\text{H}_{28}\text{Cl}_2\text{F}_6\text{N}_4\text{O}_5\text{PS}^+$ requires 891.1.

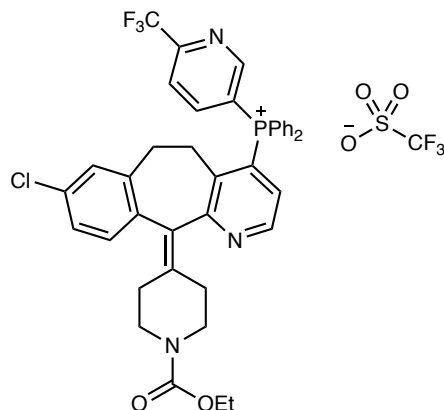
(5-Chloro-6'-methyl-3-(4-(methylsulfonyl)phenyl)-[2,3'-bipyridin]-4'-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1ap')



Prepared according to general procedure A using 5-chloro-6'-methyl-3-(4-(methylsulfonyl)phenyl)-2,3'-bipyridine (538 mg, 1.50 mmol), TiF_4 (252 μL , 1.50 mmol), 5-(diphenylphosphanyl)-2-(trifluoromethyl)pyridine (546 mg, 1.65 mmol), DBU (147 μL , 1.50 mmol) and CH_2Cl_2 (15 mL). After purification by the standard procedure, the title compound was isolated as a white solid (620 mg, 0.75 mmol, 50% yield). mp 160-164 $^\circ\text{C}$; IR $\nu_{\text{max}}/\text{cm}^{-1}$

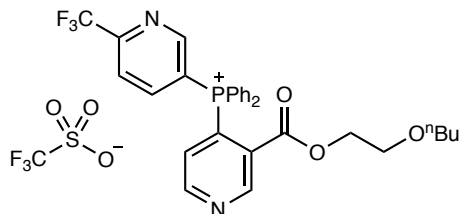
(film): 1576, 1437, 1336, 1260, 1068, 1030, 772, 720; ^1H NMR (400 MHz, CDCl_3) δ : 8.82 (2H, d, $J = 5.6$ Hz), 8.33 (1H, d, $J = 7.5$ Hz), 8.09 (3H, d, $J = 8.0$ Hz), 7.83 (6H, ddd, $J = 27.8, 10.5, 6.8$ Hz), 7.74-7.61 (5H, m), 7.60-7.44 (3H, m), 7.21 (1H, d, $J = 17.1$ Hz), 3.11 (3H, s), 2.55 (3H, s); ^{13}C NMR (100 MHz, CDCl_3) δ : 161.53 (d, $J = 11.5$ Hz), 153.68 (d, $J = 12.1$ Hz), 152.53 (d, $J = 7.4$ Hz), 152.24 (q, $J = 35.8$ Hz), 147.18 (d, $J = 2.3$ Hz), 146.13, 145.59 (d, $J = 8.8$ Hz), 141.39 (d, $J = 38.5$ Hz), 139.46, 136.06, 135.50 (d, $J = 3.1$ Hz), 134.05 (d, $J = 10.3$ Hz), 133.09 (d, $J = 3.5$ Hz), 132.59, 131.19 (d, $J = 10.3$ Hz), 130.57 (d, $J = 13.5$ Hz), 130.14, 128.80, 126.37 (d, $J = 88.2$ Hz), 122.66, 121.77, 120.78 (q, $J = 321.1$ Hz), 120.64 (q, $J = 275.2$ Hz), 118.07 (d, $J = 93.3$ Hz), 44.17, 24.67; ^{19}F NMR (365 MHz, CDCl_3) δ : -68.54, -78.27; ^{31}P NMR (162 MHz, CDCl_3) δ : 22.98; m/z LRMS (ESI + APCI) found $[\text{M} - \text{OTf}]^+$ 688.2, $\text{C}_{36}\text{H}_{27}\text{ClF}_3\text{N}_3\text{O}_2\text{PS}^+$ requires 688.1.

(8-Chloro-11-(1-(ethoxycarbonyl)piperidin-4-ylidene)-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-4-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1aq')



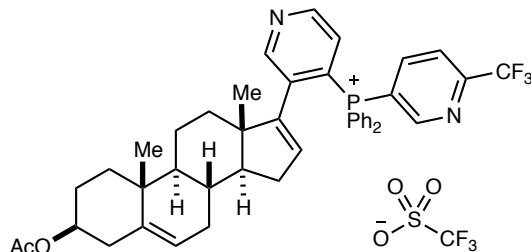
Prepared according to general procedure A using ethyl 4-(8-chloro-5,6-dihydro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-ylidene)piperidine-1-carboxylate (574.5 mg, 1.50 mmol), Tf_2O (252 μL , 1.50 mmol), 5-(diphenylphosphanyl)-2-(trifluoromethyl)pyridine (546 mg, 1.65 mmol), DBU (222 μL , 1.50 mmol) and CH_2Cl_2 (15 mL). After purification by the standard procedure, the title compound was isolated as a yellow solid (1.05 g, 1.21 mmol, 81% yield). mp 150-153 $^\circ\text{C}$; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2922, 1688, 1479, 1438, 1336, 1260, 1223, 1143, 1030, 724, 636; ^1H NMR (400 MHz, CDCl_3) δ : 8.94-8.69 (3H, m), 8.24 (1H, d, $J = 7.6$ Hz), 7.98 (2H, q, $J = 8.0$ Hz), 7.92-7.61 (8H, m), 7.19-7.07 (3H, m), 6.72 (1H, d, $J = 2.0$ Hz), 4.15 (2H, q, $J = 7.1$ Hz), 3.75 (2H, dd, $J = 12.5, 6.1$ Hz), 3.46-3.27 (3H, m), 2.81 (1H, d, $J = 17.5$ Hz), 2.61-2.32 (4H, m), 2.25 (1H, s), 1.53 (1H, ddd, $J = 17.0, 11.7, 4.9$ Hz), 1.26 (3H, t, $J = 7.1$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 163.79 (d, $J = 8.5$ Hz), 155.42, 153.35 (d, $J = 13.2$ Hz), 153.26 (q, $J = 36.2$ Hz), 149.47 (d, $J = 11.7$ Hz), 145.99 (d, $J = 9.5$ Hz), 139.68, 136.92-136.39 (m), 134.49 (d, $J = 10.9$ Hz), 134.30 (d, $J = 10.8$ Hz), 133.85 (d, $J = 33.8$ Hz), 132.24, 131.73, 131.54 (dd, $J = 13.3, 7.4$ Hz), 129.90, 127.53 (d, $J = 10.4$ Hz), 126.59, 125.27 (d, $J = 82.9$ Hz), 122.81 (d, $J = 10.2$ Hz), 120.64 (q, $J = 321.0$ Hz), 120.50 (qd, $J = 275.5, 2.1$ Hz), 118.76 (d, $J = 86.8$ Hz), 115.32 (d, $J = 55.2$ Hz), 114.44 (d, $J = 55.1$ Hz), 61.44, 44.72, 44.61, 30.55 (dd, $J = 15.1, 9.6$ Hz), 29.51, 14.64; ^{19}F NMR (365 MHz, CDCl_3) δ : -68.61, -78.38; ^{31}P NMR (162 MHz, CDCl_3) δ : 19.14; m/z LRMS (ESI + APCI) found $[\text{M} - \text{OTf}]^+$ 712.3, $\text{C}_{40}\text{H}_{35}\text{ClF}_3\text{N}_3\text{O}_2\text{P}^+$ requires 712.2.

(3-((2-Butoxyethoxy)carbonyl)pyridin-4-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1ar')



Prepared according to general procedure A using 2-butoxyethyl nicotinate (223 mg, 1.00 mmol), TiF_2O (169 μL , 1.00 mmol), 5-(diphenylphosphanyl)-2-(trifluoromethyl)pyridine (382 mg, 1.10 mmol), DBU (147 μL , 1.00 mmol) and CH_2Cl_2 (10 mL). After purification by the standard procedure, the title compound was isolated as a yellow solid (430 mg, 0.62 mmol, 62% yield). mp 54-56 $^\circ\text{C}$; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2960, 2872, 1712, 1440, 1336, 1259, 1142, 1076, 1029, 721, 636; ^1H NMR (400 MHz, CDCl_3) δ : 9.57 (1H, d, $J = 6.4$ Hz), 9.11 (1H, s), 8.77 (1H, dd, $J = 6.1$, 2.1 Hz), 8.48 (1H, ddd, $J = 13.2$, 8.2, 2.2 Hz), 8.05 (1H, dd, $J = 8.3$, 2.1 Hz), 7.93-7.51 (10H, m), 7.41 (1H, dd, $J = 16.2$, 5.0 Hz), 4.15-3.96 (2H, m), 3.50-3.39 (2H, m), 3.33 (2H, t, $J = 6.6$ Hz), 1.46 (2H, dq, $J = 8.4$, 6.7 Hz), 1.37-1.21 (2H, m), 0.85 (3H, t, $J = 7.4$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 164.38 (d, $J = 1.8$ Hz), 156.25 (d, $J = 10.9$ Hz), 153.24 (d, $J = 5.7$ Hz), 152.73 (d, $J = 12.8$ Hz), 152.23 (qd, $J = 35.9$, 2.5 Hz), 145.07 (d, $J = 9.3$ Hz), 135.61 (d, $J = 3.2$ Hz), 133.84 (d, $J = 10.7$ Hz), 131.54 (d, $J = 9.4$ Hz), 130.74 (d, $J = 13.6$ Hz), 127.88 (d, $J = 84.7$ Hz), 126.67, 121.95 (d, $J = 2.3$ Hz), 120.72 (d, $J = 92.9$ Hz), 120.62 (qd, $J = 283.1$, 2.3 Hz), 120.60 (q, $J = 321.0$ Hz), 116.98 (d, $J = 93.5$ Hz), 71.10, 67.51, 66.54, 31.45, 19.10, 13.78; ^{19}F NMR (365 MHz, CDCl_3) δ : -68.53, -78.36; ^{31}P NMR (162 MHz, CDCl_3) δ : 26.70; m/z LRMS (ESI + APCI) found $[\text{M} - \text{OTf}]^+$ 553.3, $\text{C}_{30}\text{H}_{29}\text{F}_3\text{N}_2\text{O}_3\text{P}^+$ requires 553.2.

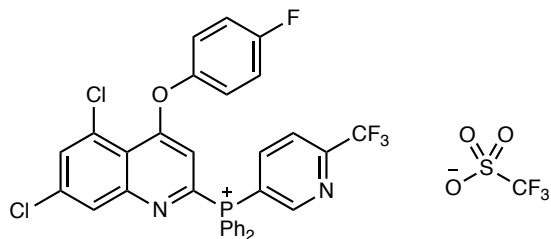
(3-((3*S*,8*R*,9*S*,10*R*,13*S*,14*S*)-3-acetoxy-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15-dodecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)pyridin-4-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1as')



Prepared according to general procedure A, using (3*S*,9*S*,10*R*,13*S*,14*S*)-10,13-dimethyl-17-(pyridin-3-yl)-2,3,4,7,8,9,10,11,12,13,14,15-dodecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl acetate (587 mg, 1.50 mmol), TiF_2O (252 μL , 1.50 mmol), 5-(diphenylphosphanyl)-2-(trifluoromethyl)pyridine (547 mg, 1.65 mmol), DBU (224 μL , 1.50 mmol), and CH_2Cl_2 (15 mL). After purification by the standard procedure (except that two crash-outs were required), the title compound was isolated as a white solid (898 mg, 1.03 mmol, 69% yield). mp 154-158 $^\circ\text{C}$. IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3503, 2940, 1726, 1258, 1144, 1030, 721, 636; ^1H NMR (400 MHz, CDCl_3) δ : 9.04 (1H, d, $J = 7.4$ Hz), 8.82-8.70 (3H, m), 8.18 (1H, d, $J = 6.9$ Hz), 7.94-7.87 (2H, m), 7.87-7.77 (6H, m), 7.73-7.68 (2H, m), 7.32 (1H, dd, $J = 16.3$, 5.1 Hz), 5.54 (1H, s), 5.28 (1H, d, $J =$

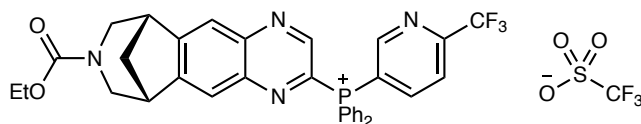
4.6 Hz), 4.57 (1H, m), 2.33-2.20 (2H, m), 2.00 (3H, s), 1.87-1.68 (5H, m), 1.63-1.32 (5H, m), 1.23-1.01 (5H, m), 0.95 (3H, s), 0.77 (1H, td, $J = 12.6, 4.1$ Hz), 0.59 (1H, td, $J = 11.3, 4.1$ Hz), -0.29 (1H, m); ^{13}C NMR (100 MHz, CDCl_3) δ : 170.56, 152.90 (qd, $J = 36.2, 2.3$ Hz), 152.82 (d, $J = 12.3$ Hz), 150.97 (d, $J = 7.6$ Hz), 149.67 (d, $J = 4.1$ Hz), 149.23 (d, $J = 11.0$ Hz), 145.67 (d, $J = 8.8$ Hz), 139.86 (d, $J = 20.9$ Hz), 137.54 (d, $J = 6.2$ Hz), 136.40 (dd, $J = 6.9, 3.1$ Hz), 134.65 (dd, $J = 28.9, 10.5$ Hz), 131.45 (dd, $J = 13.4, 8.8$ Hz), 130.28 (d, $J = 10.7$ Hz), 123.79 (d, $J = 84.9$ Hz), 123.02-122.75 (m), 121.65, 120.77 (q, $J = 321.0$ Hz), 120.62 (d, $J = 86.9$ Hz), 120.54 (qd, $J = 273.7, 1.8$ Hz), 116.96 (d, $J = 89.8$ Hz), 115.98 (d, $J = 90.0$ Hz), 73.73, 56.05, 49.70, 49.12, 38.06, 36.91, 36.59, 33.64, 32.64, 30.99, 22.90, 27.68, 21.47, 20.43, 19.14, 18.87; ^{19}F NMR (365 MHz, CDCl_3) δ : -68.33, -78.29; ^{31}P NMR (162 MHz, CDCl_3) δ : 20.59; m/z LRMS (ESI + APCI) found $[\text{M} - \text{OTf}]^+ 721.4$, $\text{C}_{44}\text{H}_{45}\text{F}_3\text{N}_2\text{O}_2\text{P}^+$ requires 721.3.

(5,7-Dichloro-4-(4-fluorophenoxy)quinolin-2-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1at')



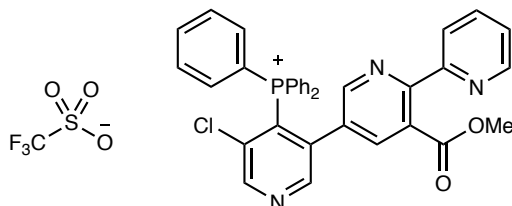
Prepared according to general procedure A (except that EtOAc was used instead of CH_2Cl_2), using 5,7-dichloro-4-(4-fluorophenoxy)quinoline (308 mg, 1.50 mmol), Tf_2O (252 μL , 1.50 mmol), 5-(diphenylphosphaneyl)-2-(trifluoromethyl)pyridine (547 mg, 1.65 mmol), DBU (224 μL , 1.50 mmol), and EtOAc (15 mL). After purification by the standard procedure, the title compound was isolated as a white solid (811 mg, 1.03 mmol, 69% yield). mp 143-145 $^\circ\text{C}$. IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3070, 2360, 1559, 1263, 1139, 1030, 930, 725; ^1H NMR (400 MHz, CDCl_3) δ : 8.98 (1H, d, $J = 5.0$ Hz), 8.64 (1H, ddd, $J = 12.5, 8.6, 1.8$ Hz), 8.08-8.02 (2H, m), 7.88-7.81 (2H, m), 7.75 (1H, d, $J = 1.9$ Hz), 7.72-7.65 (8H, m), 7.17-7.12 (2H, m), 7.05 (2H, app t, $J = 8.1$ Hz), 6.56 (1H, d, $J = 6.9$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 165.23 (d, $J = 14.2$ Hz), 160.71 (d, $J = 246.5$ Hz), 153.84 (d, $J = 12.1$ Hz), 153.16 (qd, $J = 35.8, 2.3$ Hz), 152.28 (d, $J = 25.3$ Hz), 148.23 (d, $J = 2.9$ Hz), 146.80 (d, $J = 120.3$ Hz), 145.97 (d, $J = 9.1$ Hz), 137.85, 136.47 (d, $J = 8.6$ Hz), 134.87 (d, $J = 10.8$ Hz), 132.91, 131.53 (d, $J = 1.5$ Hz), 131.08 (d, $J = 13.1$ Hz), 128.22, 123.07 (d, $J = 8.6$ Hz), 122.15-121.92 (m), 120.68 (q, $J = 321.1$ Hz), 120.64 (qd, $J = 274.4, 1.7$ Hz), 118.97 (d, $J = 87.4$ Hz), 118.42 (d, $J = 2.3$ Hz), 117.49 (d, $J = 23.7$ Hz), 114.66 (d, $J = 88.4$ Hz), 110.68 (d, $J = 30.2$ Hz); ^{19}F NMR (365 MHz, CDCl_3) δ : -68.69, -78.49, -115.18 (m); ^{31}P NMR (162 MHz, CDCl_3) δ : 12.91; m/z LRMS (ESI + APCI) found $[\text{M} - \text{OTf}]^+ 637.1$, $\text{C}_{33}\text{H}_{20}\text{Cl}_2\text{F}_4\text{N}_2\text{OP}^+$ requires 637.1.

((6S,10R)-8-(Ethoxycarbonyl)-7,8,9,10-tetrahydro-6H-6,10-methanoazepino[4,5-g]quinoxalin-2-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1au')



Prepared according to general procedure A, using ethyl (6R,10S)-6,7,9,10-tetrahydro-8H-6,10-methanoazepino[4,5-g]quinoxaline-8-carboxylate (185 mg, 0.65 mmol), TiF_4 (109 μL , 0.65 mmol), 5-(diphenylphosphaneyl)-2-(trifluoromethyl)pyridine (237 mg, 0.72 mmol), DBU (98 μL , 0.65 mmol), and CH_2Cl_2 (7 mL). After purification by the standard procedure (except that two crash-outs were required), the title compound was isolated as a yellow solid (413 mg, 0.54 mmol, 83% yield). mp 133 - 137 $^\circ\text{C}$. IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2958, 2870, 1683, 1260, 1142, 1029, 754, 636; ^1H NMR (400 MHz, CDCl_3) δ : 9.12-8.90 (2H, m), 8.86-8.68 (1H, m), 8.26-7.90 (5H, m), 7.88-7.70 (8H, m), 4.19-3.74 (4H, m), 3.60-3.30 (4H, m), 2.52-2.43 (1H, m), 2.07 (1H, d, J = 11.4 Hz), 1.06 (3H, t, J = 7.0 Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 156.44, 155.35, 153.79 (d, J = 12.1 Hz), 152.94 (qd, J = 36.1, 2.5 Hz), 152.80 (d, J = 15.3 Hz), 145.96 (dd, J = 12.7, 9.1 Hz), 145.42 (dd, J = 27.2, 7.6 Hz), 144.34 (d, J = 2.7 Hz), 143.29 (dd, J = 17.4, 3.8 Hz), 137.92, 136.85-136.57 (m), 134.95-134.65 (m), 131.22 (dd, J = 13.3, 3.7 Hz), 122.53-122.10 (2C, m), 120.56 (q, J = 321.0 Hz), 120.52 (qd, J = 275.2, 1.9 Hz), 118.80 (d, J = 87.8 Hz), 114.59 (d, J = 89.0 Hz), 114.30 (dd, J = 88.9, 7.6 Hz), 61.20 (d, J = 4.5 Hz), 49.72, 49.41 (d, J = 10.6 Hz), 40.65-39.80 (3C, m), 14.30; ^{19}F NMR (365 MHz, CDCl_3) δ : -68.57, -78.34; ^{31}P NMR (162 MHz, CDCl_3) δ : 11.45 (d, J = 7.2 Hz); m/z LRMS (ESI + APCI) found $[\text{M} - \text{OTf}]^+$ 613.3, $\text{C}_{34}\text{H}_{29}\text{F}_3\text{N}_4\text{O}_2\text{P}^+$ requires 613.2.

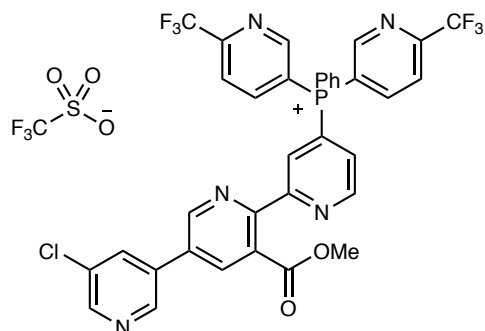
(5''-chloro-3'-(methoxycarbonyl)-[2,2':5',3''-terpyridin]-4''-yl)triphenylphosphonium trifluoromethanesulfonate (1av)



>20:1 (Major:Unidentified Phosphonium) Mixture of Isomers

Prepared according to our previous report.² Major isomer: ^1H NMR (400 MHz, CDCl_3) δ : 8.96 (1H, d, J = 4.5 Hz), 8.70 (1H, d, J = 3.1 Hz), 8.61 (1H, s), 8.28 (1H, s), 8.06-7.46 (18H, m), 7.40-7.29 (1H, m), 3.74 (3H, s); ^{13}C NMR (100 MHz, CDCl_3) δ : 167.6, 155.3 (d, J = 2.2 Hz), 154.7, 152.4 (d, J = 7.2 Hz), 151.9 (d, J = 4.8 Hz), 149.6, 148.6, 140.7 (d, J = 5.7 Hz), 136.9 (d, J = 10.9 Hz), 136.8, 136.1 (d, J = 2.3 Hz), 135.4 (d, J = 2.7 Hz), 134.0 (d, J = 10.6 Hz), 130.7 (d, J = 13.6 Hz), 130.0, 127.5, 125.5 (d, J = 88.0 Hz), 124.1, 122.6, 120.8 (q, J = 321.4 Hz), 116.9 (d, J = 89.1 Hz), 52.3; ^{19}F NMR (365 MHz, CDCl_3) δ : -78.17; ^{31}P NMR (162 MHz, CDCl_3) δ : 20.78.

(5''-Chloro-3'-(methoxycarbonyl)-[2,2':5',3''-terpyridin]-4-yl)(phenyl)bis(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1aw'')



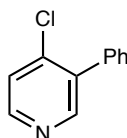
A 25 mL round bottom flask was charged with methyl 5''-chloro-[2,2':5',3''-terpyridine]-3'-carboxylate (260 mg, 0.80 mmol), 5,5'-(phenylphosphanediyl)bis(2-(trifluoromethyl)pyridine) (641 mg, 1.60 mmol, 2.0 equiv), and CH₂Cl₂ (8 mL). After being cooled to -50 °C, Tf₂O (269 μL, 1.60 mmol, 2.0 equiv) was added dropwise. After stirring for 90 minutes, the reaction was cooled to -78 °C and N,N-Dimethylcyclohexylamine (240 μL, 1.60 mmol, 2 equiv) was added dropwise. The reaction was warmed to room temperature before being quenched with H₂O. The organic layer was washed with H₂O (8 x 20 mL), dried over MgSO₄, concentrated in *vacuo*, and added dropwise to a 50/50 mixture of Et₂O/Hexanes before being placed in a -20 °C fridge. The mixture was filtered, redissolved in CH₂Cl₂, and the crash-out procedure was repeated a second and third time before affording the title compound as a yellow solid (362 mg, 0.41 mmol, 52% yield). mp 115 – 119 °C. IR ν_{max}/cm⁻¹ (film): 3061, 2955, 1726, 1440, 1334, 1258, 1029, 725; ¹H NMR (400 MHz, CDCl₃) δ: 9.02 (1H, app t, *J* = 4.9 Hz), 8.96 (2H, d, *J* = 5.3 Hz), 8.86 (1H, d, *J* = 1.5 Hz), 8.72 (1H, s), 8.67-8.59 (3H, m), 8.47 (1H, d, *J* = 14.4 Hz), 8.15-8.09 (3H, m), 7.99 (1H, app t, *J* = 6.5 Hz), 7.91 (1H, s), 7.87-7.77 (5H, m), 3.82 (3H, s); ¹³C NMR (100 MHz, CDCl₃) δ: 168.13, 157.52 (d, *J* = 11.0 Hz), 153.93 (qd, *J* = 36.0, 2.5 Hz), 153.81 (d, *J* = 13.5 Hz), 152.00 (d, *J* = 2.2 Hz), 151.42 (d, *J* = 11.0 Hz), 149.05, 148.73, 146.19 (d, *J* = 9.9 Hz), 145.81, 137.51 (d, *J* = 3.0 Hz), 135.77, 135.06 (d, *J* = 11.3 Hz), 134.24, 132.91, 132.79, 131.82, 131.69, 129.27, 127.82 (d, *J* = 9.0 Hz), 126.42 (d, *J* = 86.1 Hz), 125.82 (d, *J* = 9.8 Hz), 122.78-122.55 (m), 120.49 (qd, *J* = 275.5, 2.0 Hz), 120.40 (q, *J* = 320.8 Hz), 116.50 (d, *J* = 88.5 Hz), 112.45 (d, *J* = 90.2 Hz), 53.05; ¹⁹F NMR (365 MHz, CDCl₃) δ: -68.72, -78.70; ³¹P NMR (162 MHz, CDCl₃) δ: 18.51; m/z LRMS (ESI + APCI) found [M - OTf]⁺ 724.2, C₃₅H₂₂ClF₆N₅O₂P⁺ requires 724.1.

7. Preparation of Chlorinated Heterocycles

General Procedure B

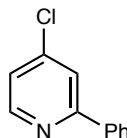
An 8 mL screw-cap vial equipped with a stir bar was charged with the phosphonium salt (1.0 equiv), LiCl (4.0 equiv), and placed under a nitrogen atmosphere. Dioxane (0.1M) was added with a syringe. The septa cap was quickly replaced with an unpierced one and the reaction was heated to 80 °C. After the stated time, the reaction was cooled to room temperature, concentrated in *vacuo*, and purified by column chromatography under the stated conditions to provide the chlorinated heterocycle.

4-Chloro-2-phenylpyridine (2a)



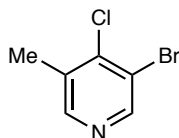
Prepared according to general procedure B, using diphenyl(3-phenylpyridin-4-yl)(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (32 mg, 0.05 mmol), LiCl (9 mg, 0.20 mmol), and Dioxane (0.5 mL). The reaction was heated to 80 °C for 24 hours. Flash column chromatography (silica gel: 10% EtOAc in Hexanes) was used to isolate a pure sample of the product (NMR Yield = 85%). ¹H NMR (400 MHz, CDCl₃) δ: 8.56 (1H, s), 8.48 (1H, d, *J* = 5.3 Hz), 7.52-7.41 (6H, m); ¹³C NMR (100 MHz, CDCl₃) δ: 151.55, 149.30, 142.41, 136.55, 135.58, 129.63, 128.59, 128.56, 124.94. The spectroscopic data is in agreement with the literature.³

4-Chloro-2-phenylpyridine (2b)



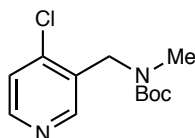
Prepared according to general procedure B, using phenyl(2-phenylpyridin-4-yl)bis(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (35 mg, 0.05 mmol), LiCl (9 mg, 0.20 mmol), and Dioxane (0.5 mL). The reaction was heated to 80 °C for 24 hours. Flash column chromatography (silica gel: 7.5% EtOAc in Hexanes) was used to isolate a pure sample of the product (GC Yield: 70%). ¹H NMR (400 MHz, CDCl₃) δ: 8.59 (1H, d, *J* = 5.3 Hz), 8.00-7.96 (2H, m), 7.74 (1H, d, *J* = 1.9 Hz), 7.52-7.42 (3H, m), 7.25 (1H, dd, *J* = 5.4, 1.9 Hz); ¹³C NMR (100 MHz, CDCl₃) δ: 159.17, 150.64, 144.89, 138.29, 129.75, 129.01, 127.13, 122.43, 121.03. The spectroscopic data is in agreement with the literature.⁴

3-Bromo-4-chloro-5-methylpyridine (2c)



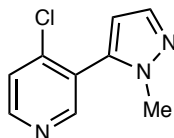
Prepared according to general procedure B using (3-bromo-5-methylpyridin-4-yl) triphenylphosphonium trifluoromethanesulfonate (175 mg, 0.30 mmol), LiCl (51 mg, 1.20 mmol), and Dioxane (3 mL). The reaction was heated at 80 °C for 24 hours. Flash column chromatography (silica gel: 33% EtOAc in Hexanes) afforded the title compound as a colorless oil (42 mg, 0.20 mmol, 68% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2921, 1584, 1458, 1422, 1146, 876; ^1H NMR (400 MHz, CDCl_3) δ : 8.58 (1H, s), 8.33 (1H, s), 2.41 (3H, s); ^{13}C NMR (100 MHz, CDCl_3) δ : 150.38, 149.46, 143.87, 134.05, 121.53, 18.00; m/z LRMS (ESI + APCI) found $[\text{M}+\text{H}]^+$ 206.0, $\text{C}_6\text{H}_6\text{BrClN}^+$ requires 205.9.

***Tert*-butyl ((4-chloropyridin-3-yl)methyl)(methyl)carbamate (2d)**



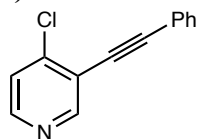
Prepared according to general procedure B, using (3-(((tert-butoxycarbonyl)(methyl)amino)methyl)pyridin-4-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (211 mg, 0.30 mmol), LiCl (51 mg, 1.20 mmol), and Dioxane (3 mL). The reaction was heated to 80 °C for 24 hours. Flash column chromatography (silica gel: 40% EtOAc in Hexanes) afforded the title compound as a colorless oil (43 mg, 0.17 mmol, 56% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2976, 2930, 1690, 1390, 1143, 729, 646; ^1H NMR (400 MHz, CDCl_3) δ : 8.41 (1H, s), 8.38 (1H, d, $J = 5.0$ Hz), 7.27 (1H, d, $J = 5.7$ Hz), 4.53 (2H, d, $J = 10.6$ Hz), 2.86 (3H, s), 1.42 (9H, d, $J = 14.7$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 155.73 (d, $J = 45.7$ Hz), 150.08, 149.40, 143.30 (d, $J = 12.6$ Hz), 131.52, 124.50, 80.33, 48.02 (d, $J = 71.8$ Hz), 34.68, 28.43; m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 257.1, $\text{C}_{12}\text{H}_{18}\text{ClN}_2\text{O}_2^+$ requires 257.1.

4-Chloro-3-(1-methyl-1H-pyrazol-5-yl)pyridine (2e)



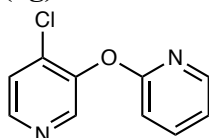
Prepared according to general procedure B, using (3-(1-methyl-1H-pyrazol-5-yl)pyridin-4-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (192 mg, 0.30 mmol), LiCl (51 mg, 1.20 mmol), and Dioxane (3 mL). The reaction was heated to 80 °C for 24 hours. Flash column chromatography (silica gel: 80% Et_2O in Hexanes) afforded the title compound as a clear oil (42 mg, 0.22 mmol, 73% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3038, 2920, 2231, 1551, 1391, 1095, 927, 729; ^1H NMR (400 MHz, CDCl_3) δ : 8.58 (1H, d, $J = 4.4$ Hz), 8.55 (1H, s), 7.59 (1H, s), 7.48 (1H, d, $J = 5.0$ Hz), 6.36 (1H, s), 3.76 (3H, s); ^{13}C NMR (100 MHz, CDCl_3) δ : 151.90, 151.03, 144.15, 138.78, 136.74, 126.73, 124.75, 108.13, 37.25; m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 194.1, $\text{C}_9\text{H}_9\text{ClN}_3^+$ requires 194.0.

4-Chloro-3-(phenylethynyl)pyridine (2f)



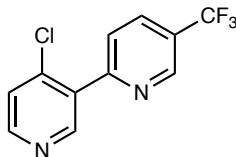
Prepared according to general procedure B, using diphenyl(3-(phenylethynyl)pyridin-4-yl)(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (198 mg, 0.30 mmol), LiCl (51 mg, 1.20 mmol), and Dioxane (3 mL). The reaction was heated to 80 °C for 48 hours. Flash column chromatography (silica gel: 2% Et₂O in Hexanes) afforded the title compound as a clear oil (41 mg, 0.19 mmol, 64% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3057, 2922, 2219, 1492, 1261, 851, 688, 564; ¹H NMR (400 MHz, CDCl₃) δ : 8.74 (1H, s), 8.42 (1H, d, J = 5.3 Hz), 7.61-7.56 (2H, m), 7.43-7.34 (4H, m); ¹³C NMR (100 MHz, CDCl₃) δ : 153.45, 149.03, 145.16, 131.95, 129.29, 128.59, 124.13, 122.31, 120.94, 97.78, 83.02; m/z LRMS (ESI + APCI) found $[M + H]^+$ 214.1, C₁₃H₉ClN⁺ requires 214.0.

4-Chloro-3-(pyridin-2-yloxy)pyridine (2g)



Prepared according to general procedure B, using diphenyl(3-(pyridin-2-yloxy)pyridin-4-yl)(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (195 mg, 0.30 mmol), LiCl (51 mg, 1.20 mmol), and Dioxane (3 mL). The reaction was heated to 80 °C for 48 hours. Flash column chromatography (silica gel: 50% EtOAc in Hexanes) afforded the title compound as a clear oil (24 mg, 0.12 mmol, 39% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3060, 2924, 2360, 2342, 1478, 1243, 776, 693; ¹H NMR (400 MHz, CDCl₃) δ : 8.51 (1H, s), 8.39 (1H, d, J = 5.2 Hz), 8.11 (1H, dd, J = 4.9, 1.8 Hz), 7.78- 7.72 (1H, m), 7.43 (1H, d, J = 5.2 Hz), 7.08-7.02 (2H, m); ¹³C NMR (100 MHz, CDCl₃) δ : 162.54, 147.44, 147.18, 146.82, 146.00, 139.93, 137.08, 125.36, 119.28, 111.26; m/z LRMS (ESI + APCI) found $[M + H]^+$ 207.1, C₁₀H₈ClN₂O⁺ requires 207.0.

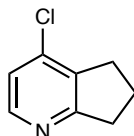
4'-Chloro-5-(trifluoromethyl)-2,3'-bipyridine (2h)



Prepared according to general procedure B using diphenyl(5-(trifluoromethyl)-[2,3'-bipyridin]-4'-yl) (6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (141 mg, 0.20 mmol), LiCl (34 mg, 0.80 mmol), and Dioxane (2 mL). The reaction was heated at 80 °C for 24 hours. Flash column chromatography (silica gel: 33% EtOAc in Hexanes) afforded the title compound as a white solid (32 mg, 0.13 mmol, 63% yield). mp 155-157 °C; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 1625, 1604, 1575, 1484, 1323, 1126, 1083, 1015, 835; ¹H NMR (400 MHz, CDCl₃) δ : 9.02 (1H, d, J = 2.2 Hz), 8.83 (1H, s), 8.73-8.47 (1H, m), 8.05 (1H, dd, J = 8.3, 2.4 Hz), 7.83 (1H, d, J =

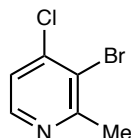
8.3 Hz), 7.46 (1H, d, $J = 5.4$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 157.24, 152.00, 150.86, 146.95 (q, $J = 4.0$ Hz), 142.14, 133.86, 133.61 (q, $J = 3.5$ Hz), 126.06 (q, $J = 33.2$ Hz), 125.15, 124.83, 123.52 (q, $J = 272.6$ Hz); ^{19}F NMR (365 MHz, CDCl_3) δ : -62.46; m/z LRMS (ESI + APCI) found $[\text{M}+\text{H}]^+$ 259.1, $\text{C}_{11}\text{H}_7\text{ClF}_3\text{N}_2^+$ requires 259.0.

4-Chloro-6,7-dihydro-5H-cyclopenta[b]pyridine (2i)



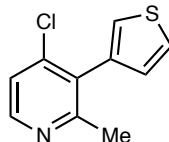
Prepared according to general procedure B using (6,7-dihydro-5H-cyclopenta [b]pyridin-4-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (120 mg, 0.20 mmol), LiCl (34 mg, 0.80 mmol), and Dioxane (2 mL). The reaction was heated at 80 °C for 40 hours. Flash column chromatography (silica gel: 33% EtOAc in Hexanes) afforded the title compound as a colorless oil (12 mg, 0.08 mmol, 41% yield, NMR yield is 66%). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2961, 2924, 2853, 1559, 1457, 1259, 1088, 798; ^1H NMR (400 MHz, CDCl_3) δ : 8.22 (1H, d, $J = 5.4$ Hz), 7.04 (1H, d, $J = 5.4$ Hz), 3.08 (2H, t, $J = 7.8$ Hz), 2.99 (2H, t, $J = 7.5$ Hz), 2.14 (2H, p, $J = 7.7$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 167.39, 148.63, 140.84, 135.96, 121.55, 35.15, 30.06, 22.14; m/z LRMS (ESI + APCI) found $[\text{M}+\text{H}]^+$ 154.1, $\text{C}_8\text{H}_9\text{ClN}^+$ requires 154.0.

3-Bromo-4-chloro-2-methylpyridine (2j)



Prepared according to general procedure B using (3-bromo-2-methylpyridin-4-yl) diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (130 mg, 0.20 mmol), LiCl (34 mg, 0.80 mmol), and Dioxane (2 mL). The reaction was heated at 80 °C for 40 hours. Flash column chromatography (silica gel: 33% EtOAc in Hexanes) afforded the title compound as a colorless oil (26 mg, 0.13 mmol, 63% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2921, 1547, 1424, 1384, 1182, 854, 706; ^1H NMR (400 MHz, CDCl_3) δ : 8.28 (1H, d, $J = 5.3$ Hz), 7.23 (1H, d, $J = 5.2$ Hz), 2.73 (3H, s); ^{13}C NMR (100 MHz, CDCl_3) δ : 160.11, 147.58, 144.62, 123.09, 122.01, 26.52; m/z LRMS (ESI + APCI) found $[\text{M}+\text{H}]^+$ 206.0, $\text{C}_6\text{H}_6\text{BrClN}^+$ requires 205.9.

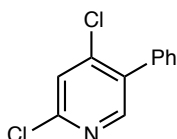
4-Chloro-2-methyl-3-(thiophen-3-yl)pyridine (2k)



Prepared according to general procedure B, using (2-methyl-3-(thiophen-3-yl)pyridin-4-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (196 mg, 0.30 mmol), LiCl (51 mg, 1.20 mmol), and Dioxane (3 mL). The reaction was heated to 80 °C

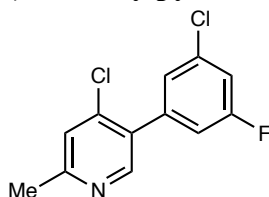
for 28 hours. Flash column chromatography (silica gel: 20% EtOAc in Hexanes) afforded the title compound as a yellow oil (54 mg, 0.26 mmol, 86% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3105, 2925, 2217, 1550, 1418, 907, 726, 656; ^1H NMR (400 MHz, CDCl_3) δ : 8.35 (1H, d, $J = 5.4$ Hz), 7.44 (1H, dd, $J = 4.9, 3.0$ Hz), 7.25 (1H, d, $J = 5.6$ Hz), 7.22 (1H, dd, $J = 3.0, 1.3$ Hz), 7.02 (1H, dd, $J = 5.0, 1.3$ Hz), 2.40 (3H, s); ^{13}C NMR (100 MHz, CDCl_3) δ : 159.37, 148.49, 144.11, 136.12, 131.37, 128.54, 125.93, 124.59, 122.33, 24.20; m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 210.1, $\text{C}_{10}\text{H}_8\text{ClNS}^+$ requires 210.1.

2,4-Dichloro-5-phenylpyridine (2m)



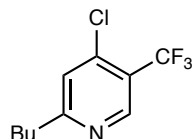
Prepared according to general procedure B, using (2-chloro-5-phenylpyridin-4-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (196 mg, 0.30 mmol), LiCl (51 mg, 1.20 mmol), and Dioxane (3 mL). The reaction was heated to 80 °C for 72 hours. Flash column chromatography (silica gel gradient elution: 2% Et_2O in Hexanes to 10% Et_2O in Hexanes) afforded the title compound as a white solid (32 mg, 0.14 mmol, 48% yield). mp 74-78 °C. IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3085, 2923, 1732, 1539, 1441, 1127, 826, 696; ^1H NMR (400 MHz, CDCl_3) δ : 8.34 (1H, s), 7.52-7.40 (6H, m); ^{13}C NMR (100 MHz, CDCl_3) δ : 150.77, 150.69, 144.25, 135.58, 134.42, 129.53, 128.89, 128.68, 124.87; m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 224.0, $\text{C}_{11}\text{H}_8\text{Cl}_2\text{N}^+$ requires 224.0.

4-Chloro-5-(3-chloro-5-fluorophenyl)-2-methylpyridine (2n)



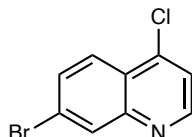
Prepared according to general procedure B using (5-(3-chloro-5-fluorophenyl)-2-methylpyridin-4-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (140 mg, 0.20 mmol), LiCl (34 mg, 0.80 mmol), and Dioxane (2 mL). The reaction was heated at 80 °C for 24 hours. Flash column chromatography (silica gel: 15% EtOAc in Hexanes) afforded the title compound as a white solid (33 mg, 0.13 mmol, 65% yield). mp 108-110 °C; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3027, 1608, 1577, 1449, 1407, 1335, 1220, 873, 794; ^1H NMR (400 MHz, CDCl_3) δ : 8.39 (1H, s), 7.29 (1H, s), 7.21 (1H, q, $J = 1.2, 0.7$ Hz), 7.15 (1H, dt, $J = 8.4, 2.1$ Hz), 7.06 (1H, ddd, $J = 9.0, 2.4, 1.5$ Hz), 2.58 (3H, s); ^{13}C NMR (100 MHz, CDCl_3) δ : 162.48 (d, $J = 250.2$ Hz), 159.79, 150.28, 142.28, 138.68 (d, $J = 9.1$ Hz), 135.22 (d, $J = 10.9$ Hz), 131.38 (d, $J = 2.3$ Hz), 125.76 (d, $J = 3.3$ Hz), 124.34, 116.19 (d, $J = 24.6$ Hz), 115.42 (d, $J = 22.3$ Hz), 24.12; ^{19}F NMR (365 MHz, CDCl_3) δ : -110.53; m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 256.1, $\text{C}_{12}\text{H}_9\text{Cl}_2\text{FN}^+$ requires 256.0.

2-Butyl-4-chloro-5-(trifluoromethyl)pyridine (2o)



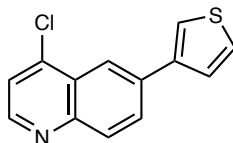
Prepared according to general procedure B, using (2-butyl-5-(trifluoromethyl)pyridin-4-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (205 mg, 0.30 mmol), LiCl (51 mg, 1.20 mmol), and Dioxane (3 mL). The reaction was heated to 80 °C for 24 hours. The ^1H NMR yield was measured using triphenylmethane (73 mg, 0.30 mmol, 1.0 equiv) as an internal standard (83% NMR yield). PTLC (2% Et₂O in Hexanes) was used to obtain approximately 25 mg of product (with solvent impurities) for characterization. IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2956, 2921, 1724, 1591, 1463, 1148, 1024; ^1H NMR (400 MHz, CDCl₃) δ : 8.75 (1H, s), 7.31 (1H, s), 2.83 (2H, t, J = 7.7 Hz), 1.77-1.67 (2H, m), 1.44-1.33 (2H, m), 0.95 (3H, t, J = 7.4 Hz); ^{13}C NMR (100 MHz, CDCl₃) δ : 168.15, 147.84 (q, J = 5.7 Hz), 142.64 (q, J = 1.6 Hz), 124.83, 122.70 (d, J = 273.0 Hz), 122.28 (q, J = 31.7 Hz), 37.95, 31.56, 22.50, 13.98; ^{19}F NMR (365 MHz, CDCl₃) δ : -62.15; m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 238.1, C₁₀H₁₂ClF₃N⁺ requires 238.1.

7-Bromo-4-chloroquinoline (2p)



Prepared according to general procedure B using (7-bromoquinolin-4-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (137.6 mg, 0.20 mmol), LiCl (34 mg, 0.8 mmol), and Dioxane (2.0 mL). The reaction was heated to 80 °C for 14 hours. Flash column chromatography (silica gel: 20% EtOAc in Hexanes) afforded the title compound as a white solid (36 mg, 0.15 mmol, 75% yield). mp 100-102 °C; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3080, 1602, 1551, 1483, 1059, 971, 812; ^1H NMR (400 MHz, CDCl₃) δ : 8.76 (1H, d, J = 4.7 Hz), 8.29 (1H, d, J = 1.9 Hz), 8.07 (1H, d, J = 9.0 Hz), 7.70 (1H, dd, J = 8.9, 2.0 Hz), 7.48 (1H, d, J = 4.7 Hz); ^{13}C NMR (100 MHz, CDCl₃) δ : 151.03, 149.77, 142.86, 132.23, 131.26, 125.70, 125.40, 124.89, 121.67; m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 242.0, C₉H₆BrClN⁺ requires 241.9.

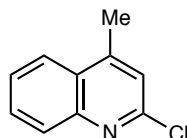
4-Chloro-6-(thiophen-3-yl)quinoline (2q)



Prepared according to general procedure B using diphenyl(6-(thiophen-3-yl)quinolin-4-yl)(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (138 mg, 0.20 mmol), LiCl (34 mg, 0.80 mmol), and Dioxane (2 mL). The reaction was heated at 80 °C for 17 hours. Flash column chromatography (silica gel: 33% EtOAc in Hexanes) afforded the title compound as a white solid (35 mg, 0.14 mmol, 72% yield). mp 114-116 °C; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3064, 1581,

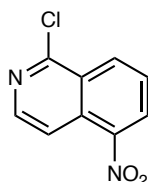
1556, 1500, 1432, 1366, 834, 821; ^1H NMR (400 MHz, CDCl_3) δ : 8.73 (1H, d, $J = 4.7$ Hz), 8.36 (1H, d, $J = 2.0$ Hz), 8.12 (1H, d, $J = 8.7$ Hz), 8.01 (1H, dd, $J = 8.8, 2.0$ Hz), 7.64 (1H, dd, $J = 3.0, 1.4$ Hz), 7.54 (1H, dd, $J = 5.0, 1.4$ Hz), 7.50-7.38 (2H, m); ^{13}C NMR (100 MHz, CDCl_3) δ : 149.61, 148.50, 142.59, 141.26, 135.07, 130.47, 129.62, 126.98, 126.88, 126.49, 122.06, 121.76, 120.72; m/z LRMS (ESI + APCI) found $[\text{M}+\text{H}]^+$ 246.0, $\text{C}_{13}\text{H}_9\text{ClNS}^+$ requires 246.0.

2-Chloro-4-methylquinoline (2r)



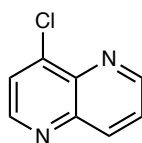
Prepared according to general procedure B, using (4-methylquinolin-2-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (187 mg, 0.30 mmol), LiCl (51 mg, 1.20 mmol), and Dioxane (3 mL). The reaction was heated to 80 °C for 72 hours. Flash column chromatography (silica gel: 2% Et_2O in Hexanes) afforded the title compound as a white solid (17 mg, 0.10 mmol, 32% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2924, 2853, 1730, 1558, 1291, 1099, 844, 756; ^1H NMR (400 MHz, CDCl_3) δ : 8.01 (1H, d, $J = 8.4$ Hz), 7.95 (1H, d, $J = 8.3$ Hz), 7.75-7.69 (1H, m), 7.60-7.54 (1H, m), 7.23 (1H, s), 2.68 (3H, s); ^{13}C NMR (100 MHz, CDCl_3) δ : 150.65, 147.84, 147.78, 130.36, 129.27, 127.08, 126.81, 123.94, 122.62, 18.73; m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 178.1, $\text{C}_{10}\text{H}_9\text{ClN}^+$ requires 178.0.

1-Chloro-5-nitroisoquinoline (2s)



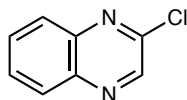
Prepared according to general procedure B, using (5-nitroisoquinolin-1-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (196 mg, 0.30 mmol), LiCl (51 mg, 1.20 mmol), and Dioxane (3 mL). The reaction was heated to 80 °C for 12 hours. Flash column chromatography (silica gel: 10% EtOAc in Hexanes) afforded the title compound as a yellow solid (48 mg, 0.23 mmol, 76% yield). mp 183 - 185 °C. IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3055, 2923, 1622, 1519, 1315, 1048, 813, 725; ^1H NMR (400 MHz, CDCl_3) δ : 8.73 (1H, d, $J = 8.5$ Hz), 8.55 (1H, d, $J = 7.7$ Hz), 8.48 (1H, d, $J = 6.1$ Hz), 8.39 (1H, d, $J = 6.1$ Hz), 7.81 (1H, app t, $J = 8.0$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 152.72, 145.45, 144.89, 133.40, 130.43, 129.03, 127.60, 127.12, 115.93; m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 209.0, $\text{C}_9\text{H}_6\text{ClN}_2\text{O}_2^+$ requires 209.0.

4-Chloro-1,5-naphthyridine (2t)



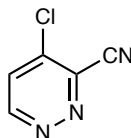
Prepared according to general procedure B using (1,5-naphthyridin-4-yl)diphenyl (6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (122 mg, 0.20 mmol), LiCl (34 mg, 0.8 mmol), and Dioxane (2.0). The reaction was heated at 80 °C for 34 hours. Flash column chromatography (silica gel: 50% EtOAc in Hexanes) afforded the title compound as a colorless oil (8 mg, 0.05 mmol, 25% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2961, 2855, 1560, 1457, 1160, 1088, 942, 796; ^1H NMR (400 MHz, CDCl_3) δ : 9.10 (1H, dd, $J = 4.2, 1.6$ Hz), 8.86 (1H, d, $J = 4.7$ Hz), 8.45 (1H, dd, $J = 8.5, 1.7$ Hz), 7.82-7.66 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ : 151.77, 150.85, 145.13, 144.29, 141.09, 138.18, 125.47, 124.67; m/z LRMS (ESI + APCI) found $[\text{M}+\text{H}]^+$ 164.1, $\text{C}_8\text{H}_5\text{ClN}_2^+$ requires 164.0.

2-Chloroquinoxaline (2u)



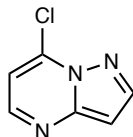
Prepared according to general procedure B, using diphenyl(quinoxalin-2-yl)(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (244 mg, 0.40 mmol), LiCl (68 mg, 1.60 mmol), and Dioxane (4 mL). The reaction was heated to 80 °C for 24 hours. Flash column chromatography (silica gel: 2% Et_2O in Hexanes) afforded the title compound as a white solid (36 mg, 0.24 mmol, 60% yield). mp 43-45 °C IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3048, 2920, 1542, 1153, 1092, 957, 758, 592; ^1H NMR (400 MHz, CDCl_3) δ : 8.77 (1H, s), 8.13-8.08 (1H, m), 8.04-7.98 (1H, m), 7.83-7.74 (2H, m); ^{13}C NMR (100 MHz, CDCl_3) δ : 147.47, 145.05, 142.11, 141.12, 131.35, 130.30, 129.43, 128.67; m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 165.1, $\text{C}_8\text{H}_6\text{ClN}_2^+$ requires 165.0.

4-Chloropyridazine-3-carbonitrile (2v)



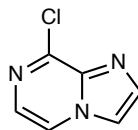
A 50 mL pressure tube was charged with pyridazine-3-carbonitrile (53 mg, 0.50 mmol), 5-(diphenylphosphaneyl)-2-(trifluoromethyl)pyridine (182 mg, 0.55 mmol), and EtOAc (5 mL). The pressure tube was cooled to -50 °C and Tf_2O (84 μL , 0.50 mmol) was added dropwise. After stirring for 1 hour, the flask was cooled to -78 °C, DBU (75 μL , 0.50 mmol) was added dropwise, and the flask was allowed to warm to room temperature. After 30 minutes, LiCl (85 mg, 2.00 mmol) was added, and the pressure tube was heated to 80 °C. After 5 hours, the reaction was cooled to room temperature, concentrated *in vacuo*, and purified by flash column chromatography (silica gel: 60% Et_2O in Hexanes) to afford the title compound as an amorphous solid (32 mg, 0.23 mmol, 45% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3101, 2921, 1531, 1081, 852, 818, 756, 732; ^1H NMR (400 MHz, CDCl_3) δ : 9.27 (1H, d, $J = 5.6$ Hz), 7.74 (1H, d, $J = 5.8$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 151.97, 141.34, 140.36, 126.88, 112.93; m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 140.1, $\text{C}_5\text{H}_3\text{ClN}_3^+$ requires 140.0.

7-Chloropyrazolo[1,5-a]pyrimidine (2w)



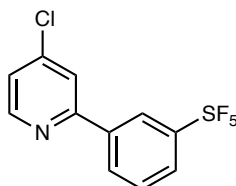
Prepared according to general procedure B, using diphenyl(pyrazolo[1,5-a]pyrimidin-7-yl)(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (180 mg, 0.30 mmol), LiCl (51 mg, 1.20 mmol), and Dioxane (3 mL). The reaction was heated to 80 °C for 48 hours. Flash column chromatography (silica gel: 50% EtOAc in Hexanes) afforded the title compound as a yellow solid (23 mg, 0.06 mmol, 21% yield). The NMR spectra obtained match the reported literature values.⁵ ¹H NMR (400 MHz, CDCl₃) δ: 8.40 (1H, d, *J* = 4.5 Hz), 8.25 (1H, d, *J* = 2.3 Hz), 6.99 (1H, d, *J* = 4.5 Hz), 6.84 (d, *J* = 2.3 Hz); ¹³C NMR (100 MHz, CDCl₃) δ: 150.15, 148.33, 145.61, 139.14, 108.16, 98.84; *m/z* LRMS (ESI + APCI) found [M + H]⁺ 154.1, C₆H₅ClN₃⁺ requires 154.0.

8-Chloroimidazo[1,5-*a*]pyrazine (2x)



Prepared according to general procedure B, using imidazo[1,5-*a*]pyrazin-8-yl diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (180 mg, 0.30 mmol), LiCl (51 mg, 1.20 mmol), and Dioxane (3 mL). The reaction was heated to 80 °C for 48 hours. Flash column chromatography (silica gel: 2% CH₃OH, 49% EtOAc, 49% Hexanes) afforded the title compound as a white solid (23 mg, 0.15 mmol, 50% yield). mp 175-176 °C. IR *v*_{max}/cm⁻¹ (film): 3120, 2922, 1613, 1431, 1329, 1197, 905, 738, 592; ¹H NMR (400 MHz, CDCl₃) δ: 8.06 (1H, d, *J* = 4.6 Hz), 7.82 (1H, d, *J* = 1.0 Hz), 7.77 (1H, d, *J* = 1.1 Hz), 7.67 (1H, d, *J* = 4.5 Hz); ¹³C NMR (100 MHz, CDCl₃) δ: 144.13, 138.17, 135.89, 128.08, 118.94, 115.72; *m/z* LRMS (ESI + APCI) found [M + H]⁺ 154.1, C₆H₅ClN₃⁺ requires 154.0.

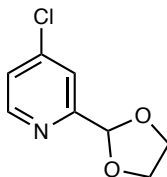
4-Chloro-2-(3-(pentafluoro-λ⁶-sulfaneyl)phenyl)pyridine (2y)



Prepared according to general procedure B, using (2-(3-(pentafluoro-λ⁶-sulfaneyl)phenyl)pyridin-4-yl)(phenyl)bis(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (249 mg, 0.30 mmol), LiCl (51 mg, 1.20 mmol), and Dioxane (3 mL). The reaction was heated to 80 °C for 48 hours. Flash column chromatography (silica gel: 20% CH₂Cl₂ in Hexanes, ran twice) afforded the title compound as an amorphous solid (76 mg, 0.24 mmol, 80% yield). IR *v*_{max}/cm⁻¹ (film): 3081, 2926, 1572, 1459, 1099, 827, 713, 595; ¹H NMR (400 MHz, CDCl₃) δ: 8.61 (1H, d, *J* = 5.2 Hz), 8.43 (1H, s), 8.10 (1H, d, *J* = 7.8 Hz), 7.82 (1H, d, *J* = 8.2 Hz), 7.72 (1H, s), 7.58 (1H, app t, *J* = 8.0 Hz), 7.33-7.29 (1H, m); ¹³C NMR (100

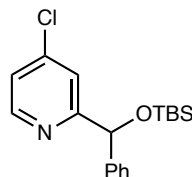
MHz, CDCl₃) δ : 156.92, 154.76 (m), 150.93, 145.30, 139.25, 129.89, 129.36, 126.95 (qn, J = 4.7 Hz), 124.88 (qn, J = 4.7 Hz), 123.37, 121.11; ¹⁹F NMR (365 MHz, CDCl₃) δ : 83.96 (1F, qn, J = 152.1 Hz), 62.70 (4F, d, J = 150.1 Hz); m/z LRMS (ESI + APCI) found $[M + H]^+$ 316.0, C₁₁H₈ClF₅NS⁺ requires 316.0.

4-chloro-2-(1,3-dioxolan-2-yl)pyridine (2z)



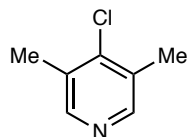
Prepared according to general procedure B, using 2-(1,3-dioxolan-2-yl)pyridin-4-yl(phenyl)bis(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (210 mg, 0.30 mmol), LiCl (51 mg, 1.20 mmol), and Dioxane (3 mL). The reaction was heated to 80 °C for 24 hours. Flash column chromatography (silica gel: 30% EtOAc in Hexanes) afforded the title compound as a yellow oil (34 mg, 0.18 mmol, 61% yield). IR $\nu_{\max}/\text{cm}^{-1}$ (film): 2956, 2889, 1578, 1382, 1227, 1113, 831, 670; ¹H NMR (400 MHz, CDCl₃) δ : 8.51 (1H, d, J = 5.3 Hz), 7.55 (1H, d, J = 1.8 Hz), 7.29 (1H, dd, J = 5.3, 2.0 Hz), 5.84 (1H, s), 4.19-4.04 (4H, m); ¹³C NMR (100 MHz, CDCl₃) δ : 158.94, 150.43, 145.07, 124.41, 121.38, 103.08, 65.77; m/z LRMS (ESI + APCI) found $[M + H]^+$ 186.1, C₈H₉ClNO₂⁺ requires 186.0.

2-(((Tert-butyldimethylsilyl)oxy)(phenyl)methyl)-4-chloropyridine (2aa)



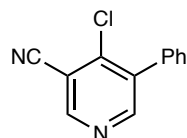
Prepared according to general procedure B using 2-(((tert-butyldimethylsilyl)oxy)(phenyl)methyl)pyridin-4-yl(phenyl)bis(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (85 mg, 0.10 mmol), LiCl (17 mg, 0.40 mmol), and Dioxane (1 mL). The reaction was heated at 80 °C for 44 hours. Flash column chromatography (silica gel: 15% EtOAc in Hexanes) afforded the title compound as a colorless oil (18 mg, 0.12 mmol, 62% yield). IR $\nu_{\max}/\text{cm}^{-1}$ (film): 2954, 2928, 2856, 1973, 1556, 1462, 1390, 1252, 1112, 1068, 863, 835, 702; ¹H NMR (400 MHz, CDCl₃) δ : 8.34 (1H, d, J = 5.3 Hz), 7.60 (1H, d, J = 2.1 Hz), 7.47-7.37 (2H, m), 7.31-7.25 (2H, m), 7.21 (1H, d, J = 7.3 Hz), 7.10 (1H, dd, J = 5.3, 2.1 Hz), 5.83 (1H, s), 0.91 (10H, s), -0.01 (6H, d, J = 8.7 Hz); ¹³C NMR (100 MHz, CDCl₃) δ : 166.33, 149.65, 144.97, 143.32, 128.46, 127.59, 126.36, 122.54, 120.57, 77.64, 25.97, 18.41, -4.71, -4.83; m/z LRMS (ESI + APCI) found $[M+H]^+$ 334.2, C₁₈H₂₅ClOSi⁺ requires 334.1.

4-Chloro-3,5-dimethylpyridine (2ab)



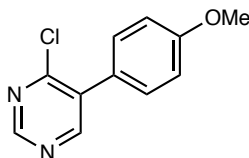
A 25 mL round bottom flask was charged with 3,5-dimethylpyridine (57 μ L, 0.50 mmol), triphenylphosphine (131 mg, 0.55 mmol), and CH_2Cl_2 (5 mL). The flask was cooled to -50°C and Ti_2O (84 μ L, 0.50 mmol) was added dropwise. After 1 hour, the flask was cooled to -78°C , DBU (75 μ L, 0.50 mmol) was added dropwise, and the flask was allowed to warm to room temperature. After 30 minutes, the reaction was quenched with H_2O and the organic layer was washed (3 x 10 mL). The organic layer was dried over MgSO_4 , concentrated in *vacuo*, and dried under high-vacuum for 20 minutes. Dioxane (5 mL) was added, followed by the dropwise addition of HCl (4M in Dioxanes, 125 μ L, 0.50 mmol). The reaction was heated at 80°C for 24 hours before being cooled to room temperature and quenched with aqueous NaHCO_3 . The aqueous layer was extracted from with CH_2Cl_2 (3 x 10 mL), and the organic extracts were dried with MgSO_4 and concentrated in *vacuo*. The ^1H NMR yield was measured using triphenylmethane (122 mg, 0.50 mmol, 1.0 equiv) as an internal standard (33% NMR yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3021, 2954, 1562, 1408, 1078, 880, 762; ^1H NMR (400 MHz, CD_3OD) δ : 8.23 (2H, s), 2.38 (6H, s); ^{13}C NMR (100 MHz, CDCl_3) δ : 148.87, 144.15, 131.58, 17.13; m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 142.1, $\text{C}_7\text{H}_9\text{ClN}^+$ requires 142.0.

4-Chloro-5-phenylnicotinonitrile (2ac)



Prepared according to general procedure B, using (3-cyano-5-phenylpyridin-4-yl)triphenylphosphonium trifluoromethanesulfonate (177 mg, 0.30 mmol), LiCl (51 mg, 1.20 mmol), and Dioxane (3 mL). The reaction was heated to 80°C for 40 hours. Flash column chromatography (silica gel: 20% EtOAc in Hexanes) afforded the title compound as a white solid (57 mg, 0.27 mmol, 89% yield). mp $64\text{--}66^\circ\text{C}$; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3035, 2921, 2360, 2236, 1544, 1422, 1095, 764, 698; ^1H NMR (400 MHz, CDCl_3) δ : 8.81 (1H, s), 8.72 (1H, s), 7.55–7.39 (5H, m); ^{13}C NMR (100 MHz, CDCl_3) δ : 154.15, 152.38, 144.48, 137.20, 133.66, 129.43, 129.35, 128.87, 114.28, 111.95; m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 215.0, $\text{C}_{12}\text{H}_8\text{ClN}_2^+$ requires 215.0.

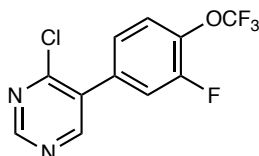
4-Chloro-5-(4-methoxyphenyl)pyrimidine (3ad)



Prepared according to general procedure B using (5-(4-methoxyphenyl)pyrimidin-4-yl)triphenylphosphonium trifluoromethanesulfonate (119 mg, 0.20 mmol), LiCl (34 mg, 0.80 mmol), and Dioxane (2 mL). The reaction was heated at 80°C for 40 hours. Flash column

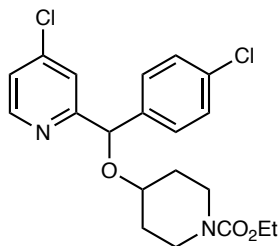
chromatography (silica gel: 15% EtOAc in Hexanes) afforded the title compound as a white solid (17 mg, 0.08 mmol, 40% yield). mp 90-91 °C; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2934, 1608, 1531, 1514, 1246, 1189, 1111, 1031, 824, 764, 885; ^1H NMR (400 MHz, CDCl_3) δ : 8.94 (1H, s), 8.64 (1H, s), 7.48-7.35 (2H, m), 7.10-6.93 (2H, m), 3.87 (3H, s); ^{13}C NMR (100 MHz, CDCl_3) δ : 160.47, 159.36, 158.11, 157.02, 134.67, 130.69, 125.75, 114.35, 55.52; m/z LRMS (ESI + APCI) found $[\text{M}+\text{H}]^+$ 221.1, $\text{C}_{11}\text{H}_{10}\text{ClN}_2\text{O}^+$ requires 221.0.

4-Chloro-5-(3-fluoro-4-(trifluoromethoxy)phenyl)pyrimidine (2ae)



Prepared according to general procedure B using (5-(3-fluoro-4-(trifluoromethoxy)phenyl)pyrimidin-4-yl)triphenylphosphonium (134 mg, 0.20 mmol), LiCl (34 mg, 0.80 mmol), and Dioxane (2 mL). The reaction was heated at 80 °C for 24 hours. Flash column chromatography (silica gel: 15% EtOAc in Hexanes) afforded the title compound as a colorless oil (44 mg, 0.15 mmol, 76% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 1625, 1567, 1530, 1506, 1396, 1249, 1210, 1169, 1101, 788, 687; ^1H NMR (400 MHz, CDCl_3) δ : 9.03 (1H, s), 8.64 (1H, s), 7.41 (1H, t, $J = 8.2$ Hz), 7.28-7.00 (2H, m); ^{13}C NMR (100 MHz, CDCl_3) δ : 160.77 (d, $J = 68.5$ Hz), 158.70 (d, $J = 1.7$ Hz), 158.60, 158.52, 150.93 (dd, $J = 11.1, 1.7$ Hz), 132.26 (d, $J = 1.7$ Hz), 128.74, 120.39 (q, $J = 259.3$ Hz), 120.13 (d, $J = 15.5$ Hz), 116.85 (d, $J = 3.3$ Hz), 109.54 (d, $J = 25.7$ Hz); ^{19}F NMR (365 MHz, CDCl_3) δ : -57.99, -109.03; m/z LRMS (ESI + APCI) found $[\text{M}+\text{H}]^+$ 293.1, $\text{C}_{11}\text{H}_6\text{ClF}_4\text{N}_2\text{O}^+$ requires 293.0.

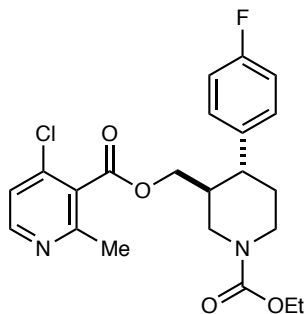
Ethyl 4-((4-chlorophenyl)(4-chloropyridin-2-yl)methoxy)piperidine-1-carboxylate (2ai)



Prepared according to general procedure B using (2-((4-chlorophenyl)((1-(ethoxycarbonyl)piperidin-4-yl)oxy)methyl)pyridin-4-yl)(phenyl)bis(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (185 mg, 0.20 mmol), LiCl (34 mg, 0.80 mmol), and Dioxane (2 mL). The reaction was heated at 80 °C for 24 hours. Flash column chromatography (silica gel: 33% EtOAc in Hexanes) afforded the title compound as a colorless oil (54 mg, 0.13 mmol, 66% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2929, 2867, 1692, 1572, 1431, 1383, 1227, 1085, 1029, 823, 756; ^1H NMR (400 MHz, CDCl_3) δ : 8.37 (1H, d, $J = 5.3$ Hz), 7.54 (1H, d, $J = 2.0$ Hz), 7.44-7.23 (4H, m), 7.15 (1H, dd, $J = 5.3, 2.1$ Hz), 5.57 (1H, s), 4.10 (2H, q, $J = 7.1$ Hz), 3.75 (2H, dt, $J = 11.6, 4.6$ Hz), 3.60 (1H, tt, $J = 7.6, 3.6$ Hz), 3.22-3.10 (2H, m), 1.81 (2H, ddd, $J = 11.6, 6.8, 3.4$ Hz), 1.63 (2H, ddd, $J = 13.1, 8.5, 4.3$ Hz), 1.23 (3H, t, $J = 7.1$ Hz); ^{13}C NMR (100 MHz,

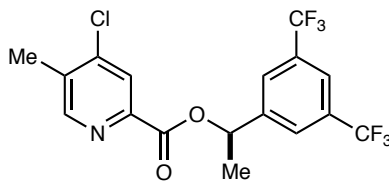
CDCl₃) δ : 163.72, 155.58, 149.97, 145.14, 139.50, 133.79, 128.80, 128.25, 123.00, 120.89, 80.51, 72.89, 61.38, 41.14, 41.08, 31.27, 30.96, 14.78; *m/z* LRMS (ESI + APCI) found [M+H]⁺ 409.2, C₂₀H₂₃Cl₂N₂O₃⁺ requires 409.1.

((3*S*,4*R*)-1-(Ethoxycarbonyl)-4-(4-fluorophenyl)piperidin-3-yl)methyl 4-chloro-2-methylnicotinate (2aj)



Prepared according to general procedure B, using (3-(((3*S*,4*R*)-1-(ethoxycarbonyl)-4-(4-fluorophenyl)piperidin-3-yl)methoxy)carbonyl)-2-methylpyridin-4-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (176 mg, 0.20 mmol), LiCl (34 mg, 0.80 mmol), and Dioxane (2 mL). The reaction was heated to 80 °C for 24 hours. Flash column chromatography (silica gel gradient elution: 40% EtOAc in Hexanes to 50% EtOAc in Hexanes) afforded the title compound as an amorphous solid (71 mg, 0.16 mmol, 82% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2920, 2864, 1689, 1438, 1273, 1222, 832, 726; ¹H NMR (400 MHz, CDCl₃) δ : 8.42 (1H, d, *J* = 5.3 Hz), 7.21 (1H, d, *J* = 5.4 Hz), 7.15 (2H, dd, *J* = 13.8 Hz, 5.5 Hz), 7.01 (2H, app t, *J* = 8.6 Hz), 4.49 (1H, br s), 4.27 (1H, br s), 4.19-4.09 (3H, m), 3.96 (1H, dd, *J* = 11.4, 7.3 Hz), 2.88-2.67 (2H, m), 2.60-2.44 (4H, m), 2.19-2.07 (1H, m), 1.81 (1H, m), 1.69 (1H, qd, *J* = 12.7, 4.2 Hz), 1.26 (3H, t, *J* = 7.1 Hz); ¹³C NMR (100 MHz, CDCl₃) δ : 166.01, 161.89 (d, *J* = 245.7 Hz), 156.93, 155.50, 150.38, 141.12, 138.43 (d, *J* = 3.2 Hz), 129.08, 128.80 (d, *J* = 7.8 Hz), 122.02, 115.87 (d, *J* = 21.3 Hz), 66.25, 61.64, 47.09, 44.47, 41.02, 41.00, 34.23, 23.07, 14.84; ¹⁹F NMR (365 MHz, CDCl₃) δ : -115.60 (m); *m/z* LRMS (ESI + APCI) found [M + H]⁺ 435.2, C₂₂H₂₅ClF₂N₂O₄⁺ requires 435.1.

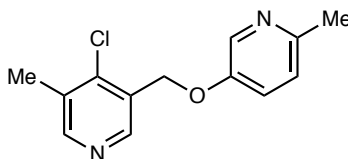
(*R*)-1-(3,5-Bis(trifluoromethyl)phenyl)ethyl 4-chloro-5-methylpicolinate (2ak)



Prepared according to general procedure B, using (*R*)-(2-((1-(3,5-bis(trifluoromethyl)phenyl)ethoxy)carbonyl)-5-methylpyridin-4-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (257 mg, 0.30 mmol), LiCl (51 mg, 1.20 mmol), and Dioxane (3 mL). The reaction was heated to 80 °C for 48 hours. Flash column chromatography (silica gel: 15% EtOAc in Hexanes) afforded the title compound as a clear oil (71 mg, 0.16 mmol, 82% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3469, 2976, 1724, 1276, 1130, 899, 754, 637; ¹H NMR (400 MHz, CDCl₃) δ : 8.58 (1H, s), 8.07 (1H, s), 7.91 (2H, s), 7.81 (1H,

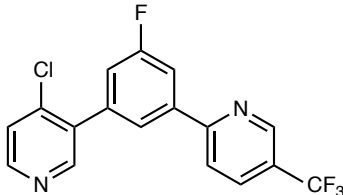
s), 6.24 (1H, q, $J = 6.7$ Hz), 2.43 (3H, s), 1.77 (3H, d, $J = 6.7$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 163.63, 151.69, 146.57, 145.15, 143.83, 136.51, 133.16 (q, $J = 33.6$ Hz), 126.70 (d, $J = 3.7$ Hz), 125.91, 123.27 (q, $J = 272.7$ Hz), 122.28 (m), 72.72, 22.07, 17.12; ^{19}F NMR (365 MHz, CDCl_3) δ : -62.93; m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 412.1, $\text{C}_{17}\text{H}_{13}\text{ClF}_6\text{NO}_2^+$ requires 412.1.

4-Chloro-3-methyl-5-(((6-methylpyridin-3-yl)oxy)methyl)pyridine (2al)



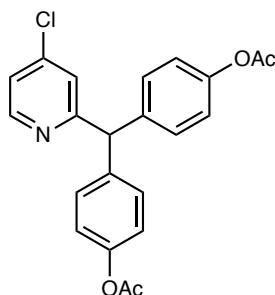
Prepared according to general procedure B using (3-methyl-5-(((6-methylpyridin-3-yl)oxy)methyl)pyridin-4-yl)triphenylphosphonium trifluoromethanesulfonate (125 mg, 0.20 mmol), LiCl (34 mg, 0.80 mmol), and Dioxane (2 mL). The reaction was heated to 80 °C for 24 hours. Flash column chromatography (silica gel: 33% EtOAc in Hexanes) afforded the title compound as a white solid (17 mg, 0.07 mmol, 34% yield). mp 88-90 °C; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2922, 2854, 1742, 1697, 1574, 1484, 1455, 1368, 1271, 1243, 1065, 814, 762; ^1H NMR (400 MHz, CDCl_3) δ : 8.55 (s, 1H), 8.44 (s, 1H), 8.29 (d, $J = 3.0$ Hz, 1H), 7.21 (dd, $J = 8.5, 3.0$ Hz, 1H), 7.09 (d, $J = 8.4$ Hz, 1H), 5.18 (s, 2H), 2.50 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 152.74, 151.39, 151.10, 147.83, 143.45, 136.73, 132.34, 129.81, 123.78, 123.03, 66.29, 23.31, 17.06; m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 249.1, $\text{C}_{13}\text{H}_{14}\text{ClN}_2\text{O}^+$ requires 249.1.

4-Chloro-3-(3-fluoro-5-(5-(trifluoromethyl)pyridin-2-yl)phenyl)pyridine (2am)



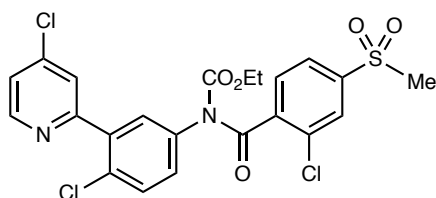
Prepared according to general procedure B, using (3-(3-fluoro-5-(5-(trifluoromethyl)pyridin-2-yl)phenyl)pyridin-4-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (239 mg, 0.30 mmol), LiCl (51 mg, 1.20 mmol), and Dioxane (3 mL). The reaction was heated to 80 °C for 24 hours. Flash column chromatography (silica gel: 15% EtOAc in Hexanes) afforded the title compound as a white solid (82 mg, 0.23 mmol, 78% yield). mp 112-113 °C. IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3044, 2924, 1596, 1328, 1114, 1082, 920, 838; ^1H NMR (400 MHz, CDCl_3) δ : 8.96 (1H, s), 8.62 (1H, s), 8.53 (1H, d, $J = 5.3$ Hz), 8.02 (1H, dd, $J = 8.3, 2.2$ Hz), 7.92 (1H, app t, $J = 8.3$ Hz), 7.89-7.83 (2H, m), 7.46 (1H, d, $J = 5.3$ Hz), 7.29 (1H, ddd, $J = 8.8, 6.4, 1.5$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 163.14 (d, $J = 247.5$ Hz), 158.73 (m), 151.28, 150.11, 146.94 (q, $J = 4.1$ Hz), 142.40, 140.48 (d, $J = 8.2$ Hz), 138.18 (d, $J = 8.1$ Hz), 135.06 (d, $J = 2.2$ Hz), 134.38 (q, $J = 3.6$ Hz), 125.84 (q, $J = 33.2$ Hz), 125.04, 124.26 (d, $J = 2.6$ Hz), 123.67 (q, $J = 274.3$ Hz), 120.23, 118.24 (d, $J = 22.9$ Hz), 114.44 (d, $J = 23.0$ Hz); ^{19}F NMR (365 MHz, CDCl_3) δ : -62.36, -111.67 (t, $J = 9.5$ Hz); m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 353.1, $\text{C}_{17}\text{H}_{10}\text{ClF}_4\text{N}_2^+$ requires 353.0.

((4-Chloropyridin-2-yl)methylene)bis(4,1-phenylene) diacetate (2an)



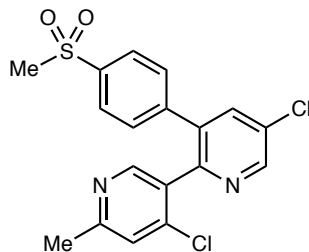
Prepared according to general procedure B using (2-(bis(4-acetoxyphenyl)methyl) pyridin-4-yl)(phenyl)bis(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (190 mg, 0.20 mmol), LiCl (34 mg, 0.80 mmol), and Dioxane (2 mL). The reaction was heated to 80 °C for 24 hours. Flash column chromatography (silica gel: 33% EtOAc in Hexanes) afforded the title compound as a colorless oil (51 mg, 0.13 mmol, 65% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 1754, 1572, 1555, 1503, 1368, 1191, 1164, 1016, 910, 733; ^1H NMR (400 MHz, CDCl_3) δ : 8.48 (1H, d, $J = 5.3$ Hz), 7.23-7.10 (6H, m), 7.10-6.96 (4H, m), 5.62 (1H, s), 2.27 (6H, s); ^{13}C NMR (100 MHz, CDCl_3) δ : 169.46, 164.40, 150.58, 149.58, 144.76, 139.33, 130.31, 124.14, 122.21, 121.72, 57.95, 21.22; m/z LRMS (ESI + APCI) found $[\text{M}+\text{H}]^+$ 396.2, $\text{C}_{22}\text{H}_{19}\text{ClNO}_4^+$ requires 396.1.

Ethyl (4-chloro-3-(4-chloropyridin-2-yl)phenyl)(2-chloro-4-(methylsulfonyl)benzoyl)carbamate (2ao)



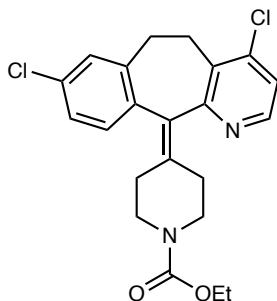
Prepared according to general procedure B using (2-(3-(2-chloro-N(ethoxycarbonyl)-4-(methylsulfonyl)benzoyl)phenyl)pyridin-4-yl)(phenyl)bis(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (208 mg, 0.20 mmol), LiCl (34 mg, 0.80 mmol), and Dioxane (2 mL). The reaction was heated at 80 °C for 26 hours. Flash column chromatography (silica gel: 50% EtOAc in Hexanes) afforded the title compound as a white solid (62 mg, 0.12 mmol, 59% yield). mp 104-105 °C; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2980, 2929, 1744, 1697, 1572, 1453, 1312, 1259, 1152, 1074, 919, 726, 667; ^1H NMR (400 MHz, CDCl_3) δ : 8.63 (1H, d, $J = 5.4$ Hz), 8.09-7.85 (2H, m), 7.76 (1H, s), 7.68-7.51 (3H, m), 7.38-7.28 (2H, m), 4.10 (2H, q, $J = 7.1$ Hz), 3.08 (3H, s), 1.07 (3H, t, $J = 7.1$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 167.85, 156.98, 152.76, 150.60, 144.18, 142.59, 142.11, 139.13, 135.77, 132.75, 131.45, 131.42, 131.08, 129.87, 128.94, 128.46, 126.15, 125.36, 123.29, 64.28, 44.55, 13.91; m/z LRMS (ESI + APCI) found $[\text{M}+\text{H}]^+$ 527.1, $\text{C}_{22}\text{H}_{18}\text{Cl}_3\text{N}_2\text{O}_5\text{S}^+$ requires 527.0.

4',5-Dichloro-6'-methyl-3-(4-(methylsulfonyl)phenyl)-2,3'-bipyridine (2ap)



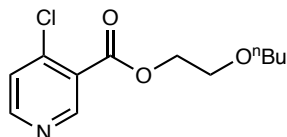
Prepared according to general procedure B using (5-chloro-6'-methyl-3-(4-(methylsulfonyl)phenyl)-[2,3'-bipyridin]-4'-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (168 mg, 0.20 mmol), LiCl (34 mg, 0.80 mmol), and Dioxane (2 mL). The reaction was heated to 80 °C for 24 hours. Flash column chromatography (silica gel: 70% EtOAc in Hexanes) afforded the title compound as a colorless oil (52 mg, 0.13 mmol, 66% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2923, 2852, 1587, 1538, 1431, 1311, 1149, 1088, 1011, 836, 785, 727; ^1H NMR (400 MHz, CDCl_3) δ : 8.71 (1H, d, $J = 2.4$ Hz), 8.34 (1H, s), 7.88-7.72 (3H, m), 7.38-7.30 (2H, m), 7.12 (1H, s), 3.03 (3H, s), 2.52 (3H, s); ^{13}C NMR (100 MHz, CDCl_3) δ : 160.20, 150.97, 150.71, 148.31, 142.95, 142.70, 140.29, 137.40, 137.20, 132.20, 131.21, 130.07, 127.71, 123.97, 44.50, 24.19; m/z LRMS (ESI + APCI) found $[\text{M}+\text{H}]^+$ 393.1, $\text{C}_{18}\text{H}_{15}\text{Cl}_2\text{N}_2\text{O}_2\text{S}^+$ requires 393.0.

Ethyl 4-(4,8-dichloro-5,6-dihydro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-ylidene)piperidine-1-carboxylate (2aq)



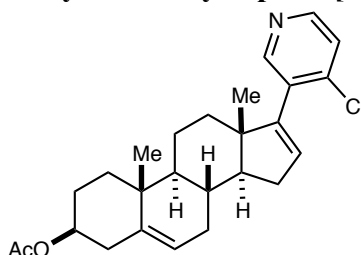
Prepared according to general procedure B using (8-chloro-11-(1-(ethoxycarbonyl) piperidin-4-ylidene)-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-4-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (172 mg, 0.20 mmol), LiCl (34 mg, 0.80 mmol), and Dioxane (2 mL). The reaction was heated to 80 °C for 24 hours. Flash column chromatography (silica gel: 50% EtOAc in Hexanes) afforded the title compound as a white solid (59 mg, 0.14 mmol, 70% yield). mp 140-142 °C; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2977, 2907, 1695, 1542, 1423, 1384, 1215, 1118, 1057, 836, 766; ^1H NMR (400 MHz, CDCl_3) δ : 8.27 (1H, d, $J = 5.3$ Hz), 7.25-6.93 (4H, m), 4.12 (2H, q, $J = 7.1$ Hz), 3.78 (2H, t, $J = 16.5$ Hz), 3.38 (1H, ddd, $J = 14.9, 10.3, 4.4$ Hz), 3.20 (3H, dddt, $J = 32.4, 13.4, 8.7, 4.4$ Hz), 3.03 (1H, ddd, $J = 16.7, 10.3, 4.5$ Hz), 2.82 (1H, ddd, $J = 15.0, 7.4, 4.5$ Hz), 2.48 (1H, ddd, $J = 14.0, 9.3, 4.6$ Hz), 2.31 (3H, pt, $J = 5.4, 2.9$ Hz), 1.23 (3H, t, $J = 7.1$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 158.53, 155.53, 147.03, 144.78, 139.46, 138.42, 137.60, 133.66, 133.31, 131.75, 130.35, 128.85, 126.48, 123.36, 61.43, 44.80, 30.80, 30.69, 29.34, 14.76; m/z LRMS (ESI + APCI) found $[\text{M}+\text{H}]^+$ 417.2, $\text{C}_{22}\text{H}_{23}\text{Cl}_2\text{N}_2\text{O}_2^+$ requires 417.1.

2-Butoxyethyl 4-chloronicotinate (2ar)



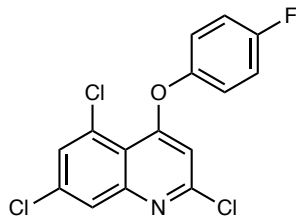
Prepared according to general procedure B using (3-((2-butoxyethoxy)carbonyl)pyridin-4-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (140 mg, 0.20 mmol), LiCl (34 mg, 0.80 mmol), and Dioxane (2 mL). The reaction was heated to 80 °C for 24 hours. Flash column chromatography (silica gel: 33% EtOAc in Hexanes) afforded the title compound as a colorless oil (34 mg, 0.13 mmol, 66% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2933, 2862, 1711, 1640, 1600, 1465, 1292, 1203, 1092, 819; ^1H NMR (400 MHz, CDCl_3) δ : 9.05 (1H, s), 8.58 (1H, s), 7.40 (1H, d, $J = 5.3$ Hz), 4.55–4.42 (2H, m), 3.83–3.69 (2H, m), 3.49 (2H, t, $J = 6.6$ Hz), 1.56 (2H, tt, $J = 8.5, 6.4$ Hz), 1.43–1.30 (2H, m), 0.89 (3H, t, $J = 7.4$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 163.95, 152.79, 152.50, 144.27, 126.25, 126.01, 71.33, 68.38, 65.12, 31.78, 19.35, 13.97; m/z LRMS (ESI + APCI) found $[\text{M}+\text{H}]^+$ 258.1, $\text{C}_{12}\text{H}_{17}\text{ClNO}_3^+$ requires 258.1.

(3*S*,8*R*,9*S*,10*R*,13*S*,14*S*)-17-(4-Chloropyridin-3-yl)-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15-dodecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl acetate (2as)



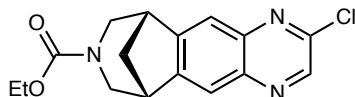
Prepared according to general procedure B, using (3-((3*S*,8*R*,9*S*,10*R*,13*S*,14*S*)-3-acetoxy-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15-dodecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)pyridin-4-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (218 mg, 0.25 mmol), LiCl (42 mg, 1.00 mmol), and Dioxane (2.5 mL). The reaction was heated to 80 °C for 24 hours. Flash column chromatography (silica gel: 15% EtOAc in Hexanes) afforded the title compound as a white solid (78 mg, 0.18 mmol, 73% yield). mp 188 - 190 °C. IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2942, 2911, 1730, 1367, 1235, 1036, 816, 729; ^1H NMR (400 MHz, CDCl_3) δ : 8.36–8.33 (2H, m), 7.32 (1H, d, $J = 5.2$ Hz), 5.83 (1H, s), 5.40 (1H, d, $J = 3.3$ Hz), 4.65–4.55 (1H, m), 2.38–2.26 (3H, m), 2.15–1.98 (5H, m), 1.89–1.79 (2H, m), 1.77–1.43 (8H, m), 1.25–0.84 (8H, m); ^{13}C NMR (100 MHz, CDCl_3) δ : 170.56, 150.70, 148.68, 148.43, 143.49, 140.11, 133.07, 132.53, 124.73, 122.37, 73.95, 56.92, 50.47, 49.82, 38.23, 37.02, 36.92, 34.81, 32.43, 31.68, 30.80, 27.83, 21.52, 20.80, 19.34, 16.38; m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 426.3, $\text{C}_{26}\text{H}_{32}\text{ClNO}_2^+$ requires 426.2.

2,5,7-Trichloro-4-(4-fluorophenoxy)quinolone (2at)



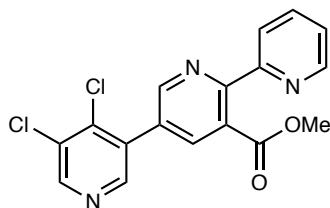
Prepared according to general procedure B, using (5,7-dichloro-4-(4-fluorophenoxy)quinolin-2-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (236 mg, 0.3 mmol), LiCl (51 mg, 1.20 mmol), and Dioxane (3 mL). The reaction was heated to 80 °C for 48 hours. Flash column chromatography (silica gel: 2% EtOAc in Hexanes) afforded the title compound as a white solid (42 mg, 0.12 mmol, 41% yield). Mp 143-145 °C. IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3095, 2923, 1560, 1365, 1189, 917, 767, 620; ^1H NMR (400 MHz, CDCl_3) δ : 7.88 (1H, d, $J = 2.0$ Hz), 7.58 (1H, d, $J = 2.0$ Hz), 7.23-7.10 (4H, m), 6.52 (1H, s); ^{13}C NMR (100 MHz, CDCl_3) δ : 164.16, 166.60 (d, $J = 248.0$ Hz), 153.02, 150.08, 149.16 (d, $J = 2.9$ Hz), 136.43, 130.78, 130.08, 127.15, 122.67 (d, $J = 8.7$ Hz), 117.55 (d, $J = 23.7$ Hz), 117.04, 106.97; ^{19}F NMR (365 MHz, CDCl_3) δ : -155.57(-155.65); m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 342.0, $\text{C}_{15}\text{H}_8\text{Cl}_3\text{FNO}^+$ requires 342.0.

Ethyl (6R,10S)-2-chloro-6,7,9,10-tetrahydro-8H-6,10-methanoazepino[4,5-g]quinoxaline-8-carboxylate (2au)



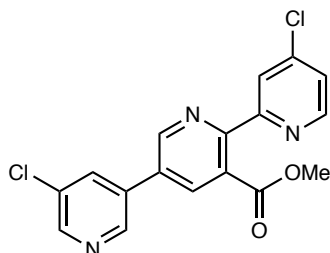
Prepared according to general procedure B, using ((6S,10R)-8-(ethoxycarbonyl)-7,8,9,10-tetrahydro-6H-6,10-methanoazepino[4,5-g]quinoxalin-2-yl)diphenyl(6-(trifluoromethyl)-114-pyridin-3-yl)phosphonium trifluoromethanesulfonate (191 mg, 0.25 mmol), LiCl (42 mg, 1.00 mmol), and Dioxane (2.5 mL). The reaction was heated to 80 °C for 72 hours. Flash column chromatography (silica gel: 50% EtOAc in Hexanes) afforded the title compound as a yellow oil (36 mg, 0.11 mmol, 46% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2955, 2867, 2245, 1686, 1213, 1094, 910, 727; ^1H NMR (400 MHz, CDCl_3) δ : 8.69 (1H, d, $J = 3.8$ Hz), 7.87 (1H, d, $J = 6.3$ Hz), 7.77 (1H, d, $J = 6.5$ Hz), 4.15-3.76 (4H, m), 3.48-3.25 (4H, m), 2.45-2.38 (1H, m), 2.00 (1H, d, $J = 11.1$ Hz), 1.04 (3H, t, $J = 7.1$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 156.63, 150.04, 148.86, 146.48 (d, $J = 1.9$ Hz), 143.69, 142.41 (d, $J = 7.2$ Hz), 141.38 (d, $J = 5.3$ Hz), 122.17 (d, $J = 43.9$ Hz), 141.43 (d, $J = 42.6$ Hz), 61.28, 49.74, 49.44, 41.22, 40.05, 39.37, 14.53; m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 318.2, $\text{C}_{16}\text{H}_{17}\text{ClN}_3\text{O}_2^+$ requires 318.1.

Methyl 4'',5''-dichloro-[2,2':5',3''-terpyridine]-3'-carboxylate (2av)



Prepared according to general procedure B, using (5''-chloro-3'-(methoxycarbonyl)-[2,2':5',3''-terpyridin]-4''-yl)triphenylphosphonium trifluoromethanesulfonate (147 mg, 0.20 mmol), LiCl (34 mg, 0.80 mmol), and Dioxane (2 mL). The reaction was heated to 80 °C for 72 hours. Flash column chromatography (silica gel: 70% EtOAc in Hexanes, run twice) afforded the title compound as an amorphous solid (24 mg, 0.07 mmol, 33% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2948, 2853, 1728, 1421, 1269, 1118, 908, 726; ^1H NMR (400 MHz, CDCl_3) δ : 8.83 (1H, d, $J = 2.2$ Hz), 8.71 (1H, s), 8.65 (1H, ddd, $J = 4.8, 3.1, 0.9$ Hz), 8.48 (1H, s), 8.23 (1H app dt, $J = 7.9, 1.0$ Hz), 8.06 (1H, d, $J = 2.2$ Hz), 7.88 (1H, app td, $J = 7.8, 1.8$ Hz), 7.36 (1H, ddd, $J = 7.6, 2.8, 1.1$ Hz), 3.84 (3H, s); ^{13}C NMR (100 MHz, CDCl_3) δ : 168.99, 155.60, 155.50, 150.29, 150.20, 148.78, 148.65, 141.04, 137.79, 137.07, 133.63, 131.99, 130.27, 128.40, 124.21, 122.95, 52.77; m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 360.1, $\text{C}_{17}\text{H}_{12}\text{Cl}_2\text{N}_3\text{O}_2^+$ requires 360.0.

Methyl 4,5''-dichloro-[2,2':5',3''-terpyridine]-3'-carboxylate (2aw)



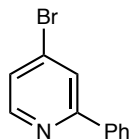
Prepared according to general procedure B, using (5''-chloro-3'-(methoxycarbonyl)-[2,2':5',3''-terpyridin]-4''-yl)(phenyl)bis(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (131 mg, 0.15 mmol), LiCl (25 mg, 0.60 mmol), and Dioxane (1.5 mL). The reaction was heated to 80 °C for 72 hours. Flash column chromatography (silica gel: 30% EtOAc in Hexanes) afforded the title compound as a white solid (28 mg, 0.08 mmol, 51% yield). mp 140-144 °C. IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2919, 2850, 1732, 1376, 1265, 1129, 891, 632; ^1H NMR (400 MHz, CDCl_3) δ : 8.95 (1H, d, $J = 2.3$ Hz), 8.80 (1H, d, $J = 2.0$ Hz), 8.67 (1H, d, $J = 2.3$ Hz), 8.52 (1H, d, $J = 5.3$ Hz), 8.28 (1H, d, $J = 1.9$ Hz), 8.13 (1H, d, $J = 2.3$ Hz), 7.95 (1H, app t, $J = 2.1$ Hz), 7.36 (1H, dd, $J = 5.3, 2.0$ Hz), 3.85 (3H, s); ^{13}C NMR (100 MHz, CDCl_3) δ : 168.85, 156.80, 153.91, 149.51, 148.92, 148.43, 145.93, 145.24, 135.49, 134.23, 133.39, 132.80, 131.90, 129.20, 124.38, 123.39, 52.83; m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 360.1, $\text{C}_{17}\text{H}_{12}\text{Cl}_2\text{N}_3\text{O}_2^+$ requires 360.0.

8. Preparation of Brominated Heterocycles

General Procedure C

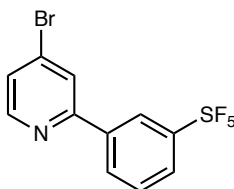
An 8 mL screw-cap vial equipped with a stir bar was charged with the phosphonium salt (1.0 equiv), LiBr (4.0 equiv), and placed under a nitrogen atmosphere. Dioxane (0.1M) was added, followed by a dropwise addition of TfOH (1.0 equiv). The septa cap was quickly replaced with an unpierced one and the reaction was heated to 80 °C. After the stated time, the reaction was quenched with a saturated aqueous solution of Na_2CO_3 and the aqueous layer was extracted with CH_2Cl_2 (3x). The combined organic extracts were dried (MgSO_4), filtered, and concentrated in *vacuo*. The residue was purified by flash column chromatography under the stated conditions to provide the brominated heterocycle.

4-Bromo-2-phenylpyridine (2b')



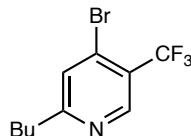
Prepared according to general procedure C, using phenyl(2-phenylpyridin-4-yl)bis(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (35 mg, 0.05 mmol), LiBr (17 mg, 0.20 mmol), TfOH (4 μ L, 0.05 mmol) and Dioxane (0.5 mL). The reaction was heated to 80 °C for 24 hours. Flash column chromatography (silica gel: 3% EtOAc in Hexanes) was used to isolate a pure sample of the product (NMR Yield: 79%). ^1H NMR (400 MHz, CDCl_3) δ : 8.50 (1H, dd, J = 5.3, 0.4 Hz), 7.99-7.95 (2H, m), 7.90 (2H, dd, J = 1.8, 0.5 Hz), 7.51-7.38 (4H, m); ^{13}C NMR (100 MHz, CDCl_3) δ : 159.05, 150.49, 138.20, 133.59, 129.73, 128.99, 127.14, 125.35, 124.02. The spectroscopic data is in agreement with the literature.⁴

4-Bromo-2-(3-(pentafluoro- λ^6 -sulfaneyl)phenyl)pyridine (2af)



Prepared according to general procedure C, using (2-(3-(pentafluoro- λ^6 -sulfaneyl)phenyl)pyridin-4-yl)(phenyl)bis(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (166 mg, 0.20 mmol), LiBr (69 mg, 0.80 mmol), TfOH (18 μ L, 0.20 mmol), and Dioxane (2 mL). The reaction was heated to 80 °C for 48 hours. Flash column chromatography (silica gel: 20% CH_2Cl_2 in Hexanes, ran twice) afforded the title compound as an amorphous solid (62 mg, 0.17 mmol, 86% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3084, 2927, 1566, 1369, 1100, 834, 694, 596; ^1H NMR (400 MHz, CDCl_3) δ : 8.53 (1H, d, J = 5.2 Hz), 8.42 (1H, app t, J = 1.9 Hz), 8.09 (1H, d, J = 7.9 Hz), 7.91 (1H, d, J = 1.4 Hz), 7.82 (1H, ddd, J = 8.3, 2.2, 0.8 Hz), 7.85 (1H, app t, J = 8.0 Hz), 7.47 (1H, dd, J = 7.0, 1.7 Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 156.79, 154.75 (m), 150.76, 139.14, 133.95, 129.91, 129.36, 126.95 (qn, J = 4.6 Hz), 126.36, 124.89 (qn, J = 4.7 Hz), 124.12; ^{19}F NMR (365 MHz, CDCl_3) δ : 83.99 (1F, qn, J = 151.7 Hz), 62.73 (4F, d, J = 150.0 Hz); m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 360.0, $\text{C}_{11}\text{H}_8\text{BrF}_5\text{NS}^+$ requires 359.9.

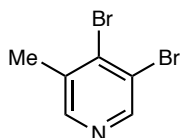
4-Bromo-2-butyl-5-(trifluoromethyl)pyridine (2ag)



Prepared according to general procedure C, using (2-butyl-5-(trifluoromethyl)pyridin-4-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (137 mg, 0.20 mmol), LiBr (69 mg, 0.80 mmol), TfOH (18 μ L, 0.20 mmol), and Dioxane (2 mL). The

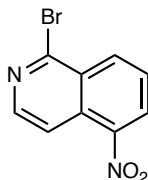
reaction was heated to 80 °C for 24 hours. The ^1H NMR yield was measured using triphenylmethane (49 mg, 0.20 mmol, 1.0 equiv) as an internal standard (90% NMR yield). PTLC (4% Et₂O in Hexanes) was used to obtain approximately 10 mg of product for characterization. IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2959, 2861, 1583, 1321, 1137, 1019, 870, 690; ^1H NMR (400 MHz, CDCl₃) δ : 8.72 (1H, s), 7.51 (1H, s), 2.82 (2H, t, J = 7.7 Hz), 1.76-1.67 (2H, m), 1.39 (2H, m, J = 7.5 Hz), 0.95 (3H, t, J = 7.3 Hz); ^{13}C NMR (100 MHz, CDCl₃) δ : 167.79, 147.70 (q, J = 5.9 Hz), 131.10 (q, J = 2.0 Hz), 128.37, 124.10 (q, J = 31.5 Hz), 122.90 (q, J = 273.1 Hz), 37.82, 31.59, 22.51, 13.97; ^{19}F NMR (365 MHz, CDCl₃) δ : -62.29; m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 282.0, C₁₀H₁₂BrF₃N⁺ requires 282.0.

3,4-Dibromo-5-methylpyridine (2ah)



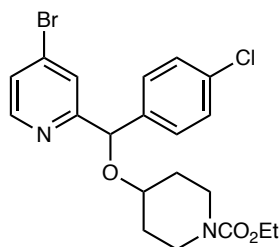
Prepared according to general procedure C using (3-bromo-5-methylpyridin-4-yl) triphenylphosphonium trifluoromethanesulfonate (175 mg, 0.30 mmol), LiBr (104 mg, 1.20 mmol), TfOH (26 μL , 0.3 mmol), and Dioxane (3 mL). The reaction was heated to 80 °C for 40 hours. Flash column chromatography (silica gel: 10% EtOAc in Hexanes) afforded the title compound as a colorless oil (60 mg, 0.24 mmol, 80% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2924, 1461, 1268, 1120, 1071, 1029; ^1H NMR (400 MHz, CDCl₃) δ : 8.52 (1H, s), 8.28 (1H, s), 2.43 (3H, s); ^{13}C NMR (100 MHz, CDCl₃) δ : 149.88, 148.66, 137.07, 136.38, 124.17, 21.21; m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 249.9, C₆H₆Br₂N⁺ requires 249.9.

1-Bromo-5-nitroisoquinoline



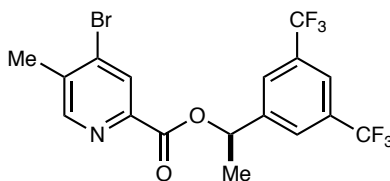
Prepared according to general procedure C, using (5-nitroisoquinolin-1-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (131 mg, 0.20 mmol), LiBr (69 mg, 0.80 mmol), TfOH (18 μL , 0.20 mmol), and Dioxane (2 mL). The reaction was heated to 80 °C for 24 hours. Flash column chromatography (silica gel: 20% CH₂Cl₂ in Hexanes, ran twice) afforded the title compound as a white solid (37 mg, 0.15 mmol, 70% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3050, 2923, 1622, 1522, 1311, 1037, 812, 717; ^1H NMR (400 MHz, CDCl₃) δ : 8.71 (1H, app dt, J = 8.5, 0.9 Hz), 8.55 (1H, dd, J = 7.7, 1.1 Hz), 8.46 (1H, d, J = 6.1 Hz), 8.40 (1H, dd, J = 6.1, 0.8 Hz), 7.81 (1H, app t, J = 8.0 Hz); ^{13}C NMR (100 MHz, CDCl₃) δ : 146.34, 145.45, 145.36, 135.78, 130.05, 129.40, 128.95, 127.26, 116.16; m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 253.0, C₉H₆Br₂N₂O₂⁺ requires 253.0.

Ethyl 4-((4-bromopyridin-2-yl)(4-chlorophenyl)methoxy)piperidine-1-carboxylate (2ai')



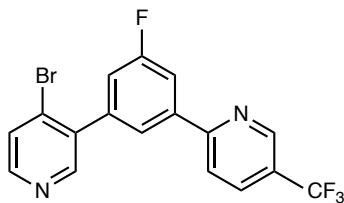
Prepared according to general procedure C using (2-((4-chlorophenyl) ((1-(ethoxycarbonyl)piperidin-4-yl)oxy)methyl)pyridin-4-yl)(phenyl)bis(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (185 mg, 0.20 mmol), LiBr (70 mg, 0.80 mmol), TfOH (18 μ L, 0.20 mmol), and Dioxane (2 mL). The reaction was heated at 80 °C for 40 hours. Flash column chromatography (silica gel: 50% EtOAc in Hexanes) afforded the title compound as a colorless oil (52 mg, 0.12 mmol, 58% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2929, 2866, 1691, 1566, 1431, 1381, 1226, 1085, 810; ^1H NMR (400 MHz, CDCl_3) δ : 8.28 (1H, d, J = 5.3 Hz), 7.69 (1H, d, J = 1.9 Hz), 7.41-7.18 (5H, m), 5.56 (1H, s), 4.10 (2H, q, J = 7.1 Hz), 3.75 (2H, t, J = 9.1 Hz), 3.60 (1H, dq, J = 7.9, 3.8 Hz), 3.17 (2H, ddd, J = 12.9, 8.5, 3.7 Hz), 1.81 (2H, ddd, J = 14.4, 7.1, 3.5 Hz), 1.63 (2H, ddt, J = 17.0, 12.9, 6.1 Hz), 1.23 (3H, t, J = 7.1 Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 163.54, 155.61, 149.85, 139.52, 133.91, 133.83, 128.84, 128.27, 126.02, 123.94, 80.51, 72.94, 61.42, 41.18, 41.11, 31.30, 31.00, 14.81; m/z LRMS (ESI + APCI) found $[\text{M}+\text{H}]^+$ 453.1, $\text{C}_{20}\text{H}_{23}\text{BrClN}_2\text{O}_3^+$ requires 453.1.

(R)-1-(3,5-Bis(trifluoromethyl)phenyl)ethyl 4-bromo-5-methylpicolinate (2ak')



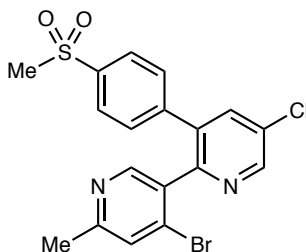
Prepared according to general procedure C, using (R)-(2-((1-(3,5-bis(trifluoromethyl)phenyl)ethoxy)carbonyl)-5-methylpyridin-4-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (171 mg, 0.20 mmol), LiBr (69 mg, 0.80 mmol), TfOH (18 μ L, 0.20 mmol), and Dioxane (2 mL). The reaction was heated to 80 °C for 24 hours. Flash column chromatography (silica gel: 15% EtOAc in Hexanes) afforded the title compound as a clear oil (72 mg, 0.16 mmol, 79% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2999, 2926, 1717, 1280, 1196, 1112, 900, 682; ^1H NMR (400 MHz, CDCl_3) δ : 8.55 (1H, s), 8.26 (1H, s), 7.91 (2H, s), 7.82 (1H, s), 6.25 (1H, q, J = 6.7 Hz), 2.45 (3H, s), 1.77 (3H, d, J = 6.7 Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 163.49, 151.13, 146.32, 143.82, 138.63, 135.93, 132.20 (q, J = 33.3 Hz), 129.22, 126.74 (d, J = 2.6 Hz), 123.29 (q, J = 27.2 Hz), 122.32 (qn, J = 3.6 Hz), 72.75, 22.11, 19.95; ^{19}F NMR (365 MHz, CDCl_3) δ : -62.88; m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 456.1, $\text{C}_{17}\text{H}_{13}\text{BrF}_6\text{NO}_2^+$ requires 456.0.

4-Bromo-3-(3-fluoro-5-(5-(trifluoromethyl)pyridin-2-yl)phenyl)pyridine (2am')



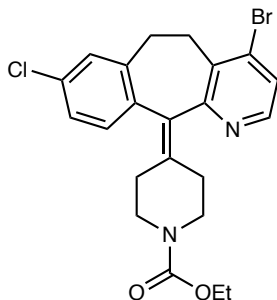
Prepared according to general procedure C, using (3-(3-fluoro-5-(5-(trifluoromethyl)pyridin-2-yl)phenyl)pyridin-4-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (239 mg, 0.30 mmol), LiBr (104 mg, 1.20 mmol), TfOH (27 μ L, 0.30 mmol), and Dioxane (3 mL). The reaction was heated to 80 $^{\circ}$ C for 48 hours. Flash column chromatography (silica gel: 20% EtOAc in Hexanes) afforded the title compound as a yellow solid (37 mg, 0.15 mmol, 70% yield). mp 115-118 $^{\circ}$ C. IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3038, 2924, 1603, 1329, 1109, 922, 840, 691; ^1H NMR (400 MHz, CDCl_3) δ : 8.96 (1H, s), 8.58 (1H, s), 8.43 (1H, d, J = 4.9 Hz), 8.03 (1H, d, J = 8.3 Hz), 7.92-7.84 (3H, m), 7.66 (1H, d, J = 4.9 Hz), 7.27 (1H, d, J = 7.6 Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 163.07 (d, J = 247.7 Hz), 158.71 (m), 150.80, 149.81, 146.94 (d, J = 4.0 Hz), 140.40 (d, J = 8.1 Hz), 139.80 (d, J = 8.4 Hz), 137.23 (d, J = 1.4 Hz), 134.38 (q, J = 3.4 Hz), 132.92, 128.30, 125.83 (q, J = 33.2 Hz), 124.20 (d, J = 2.6 Hz), 123.66 (q, J = 272.1 Hz), 120.23, 118.22 (d, J = 22.7 Hz), 114.4 (d, J = 23.0 Hz); ^{19}F NMR (365 MHz, CDCl_3) δ : -62.36 (3F, s), -111.63 (1F, t, J = 9.3 Hz); m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 397.1, $\text{C}_{17}\text{H}_{10}\text{BrF}_4\text{N}_2^+$ requires 397.0.

4'-Bromo-5-chloro-6'-methyl-3-(4-(methylsulfonyl)phenyl)-2,3'-bipyridine (2ap')



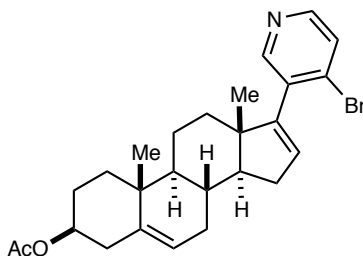
Prepared according to general procedure C using (5-chloro-6'-methyl-3-(4-(methylsulfonyl)phenyl)-[2,3'-bipyridin]-4'-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (168 mg, 0.20 mmol), LiBr (70 mg, 0.80 mmol), and Dioxane (2.0 mL). The reaction was heated at 80 $^{\circ}$ C for 36 hours. Flash column chromatography (silica gel: 50% EtOAc in Hexanes) afforded the title compound as a colorless oil (51 mg, 0.12 mmol, 58% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2924, 1581, 1431, 1399, 1311, 1284, 1149, 1090, 789, 727; ^1H NMR (400 MHz, CDCl_3) δ : 8.73 (1H, d, J = 2.3 Hz), 8.27 (1H, s), 7.89-7.75 (3H, m), 7.40-7.32 (3H, m), 3.04 (3H, s), 2.53 (3H, s); ^{13}C NMR (100 MHz, CDCl_3) δ : 159.91, 152.09, 150.58, 148.32, 142.91, 140.34, 137.49, 136.96, 133.26, 133.24, 132.23, 130.26, 127.75, 127.29, 44.55, 24.09; m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 437.1, $\text{C}_{18}\text{H}_{15}\text{BrClO}_2\text{N}_2\text{S}^+$ requires 437.0.

Ethyl 4-(4-bromo-8-chloro-5,6-dihydro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-ylidene) piperidine-1-carboxylate (2aq')



Prepared according to general procedure C using 8-chloro-11-(1-(ethoxycarbonyl) piperidin-4-ylidene)-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-4-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (172 mg, 0.20 mmol), LiBr (69 mg, 0.80 mmol), TfOH (18 μ L, 0.20 mmol), and Dioxane (2 mL). The reaction was heated to 80 °C for 36 hours. Flash column chromatography (silica gel: 50% EtOAc in Hexanes) afforded the title compound as a white solid (76 mg, 0.17 mmol, 83% yield). mp 143-144 °C; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2976, 2907, 1695, 1541, 1422, 1383, 1215, 1120, 995, 835, 767; ^1H NMR (400 MHz, CDCl_3) δ : 8.15 (1H, d, $J = 5.3$ Hz), 7.35 (1H, d, $J = 5.2$ Hz), 7.20-7.02 (3H, m), 4.11 (2H, q, $J = 7.1$ Hz), 3.86-3.70 (2H, m), 3.44-3.10 (4H, m), 3.02 (1H, ddd, $J = 16.3, 9.6, 4.5$ Hz), 2.82 (1H, ddd, $J = 15.3, 8.0, 4.5$ Hz), 2.46 (1H, ddd, $J = 14.0, 9.0, 4.4$ Hz), 2.39-2.22 (3H, m), 1.22 (3H, t, $J = 7.1$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 158.55, 155.49, 146.97, 139.22, 138.18, 137.20, 135.99, 133.70, 133.42, 133.28, 130.49, 128.99, 126.82, 126.39, 61.41, 44.77, 44.74, 32.07, 30.96, 30.76, 30.66, 14.73; m/z LRMS (ESI + APCI) found $[\text{M}+\text{H}]^+$ 461.2, $\text{C}_{22}\text{H}_{23}\text{ClBrN}_2\text{O}_2^+$ requires 461.1.

(3*S*,8*R*,9*S*,10*R*,13*S*,14*S*)-17-(4-Bromopyridin-3-yl)-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15-dodecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl acetate (2*as'*)



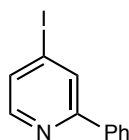
Prepared according to general procedure C, using using (3-((3*S*,8*R*,9*S*,10*R*,13*S*,14*S*)-3-acetoxy-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15-dodecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)pyridin-4-yl)diphenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (174 mg, 0.20 mmol), LiBr (69 mg, 0.80 mmol), TfOH (18 μ L, 0.20 mmol), and Dioxane (2 mL). The reaction was heated to 80 °C for 24 hours. Flash column chromatography (silica gel: 15% EtOAc in Hexanes) afforded the title compound as a white solid (78 mg, 0.17 mmol, 83% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2951, 2854, 1729, 1366, 1234, 1036, 815, 740; ^1H NMR (400 MHz, CDCl_3) δ : 8.32 (1H, s), 8.25 (1H, d, $J = 5.0$ Hz), 7.52 (1H, d, $J = 5.2$ Hz), 5.82 (1H, s), 5.41 (1H, d, $J = 4.8$ Hz), 4.66-4.56 (1H, m), 2.40-2.29 (3H, m), 2.15-2.00 (5H, m), 1.90-1.80 (2H, m), 1.77-1.45 (8H, m), 1.28-0.90 (8H, m); ^{13}C NMR (100 MHz, CDCl_3) δ : 170.59, 150.14, 149.95, 148.46, 140.13, 135.34, 134.47, 132.42, 128.05, 122.38, 73.95, 56.97, 50.47, 49.92, 38.24, 37.03, 36.94, 34.75, 32.38, 31.68, 30.83, 27.84, 21.54, 20.79, 19.35, 16.42; m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 470.3, $\text{C}_{26}\text{H}_{32}\text{BrNO}_2^+$ requires 470.2.

9. Preparation of Iodinated Heterocycles

General Procedure D

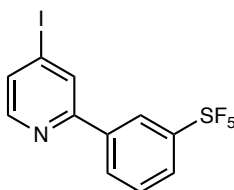
An 8 mL screw-cap vial equipped with a stir bar was charged with the phosphonium salt (1.0 equiv), LiI (4.0 equiv), and placed under a nitrogen atmosphere. Dioxane (0.1M) was added, followed by a dropwise addition of TfOH (1.0 equiv). The septa cap was quickly replaced with an unpierced one and the reaction was heated to 120 °C. After the stated time, the reaction was quenched with a saturated aqueous solution of Na₂CO₃ and the aqueous layer was extracted with CH₂Cl₂ (3x). The combined organic extracts were dried (MgSO₄), filtered, and concentrated in *vacuo*. The residue was purified by flash column chromatography under the stated conditions to provide the iodinated heterocycle.

4-Iodo-2-phenylpyridine (2b'')



Prepared according to general procedure B, using phenyl(2-phenylpyridin-4-yl)bis(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (1.06 g, 1.50 mmol), LiI (803 mg, 6.00 mmol), and Dioxane (15 mL). The reaction was heated to 120 °C for 63 hours. Flash column chromatography (silica gel: 5% EtOAc in Hexanes, then 3% EtOAc in Hexanes) afforded the title compound as a clear oil (320 mg, 1.14 mmol, 76% yield). IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3036, 2921, 1558, 1442, 1374, 1049, 771, 691, 632; ¹H NMR (400 MHz, CDCl₃) δ : 8.34 (1H, d, J = 5.1 Hz), 8.11 (1H, s), 7.59 (2H, d, J = 8.0 Hz), 7.60 (1H, d, J = 5.2 Hz), 7.50-7.41 (3H, m); ¹³C NMR (100 MHz, CDCl₃) δ : 158.52, 150.05, 138.07, 131.25, 130.06, 129.67, 128.97, 127.12, 106.26; m/z LRMS (ESI + APCI) found $[M + H]^+$ 282.0, C₁₁H₉IN⁺ requires 282.1.

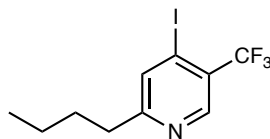
4-Iodo-2-(3-(pentafluoro- λ 6-sulfaneyl)phenyl)pyridine (2af')



Prepared according to general procedure D, using (2-(3-(pentafluoro- λ 6-sulfaneyl)phenyl)pyridin-4-yl)(phenyl)bis(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (166 mg, 0.20 mmol), LiI (107 mg, 0.80 mmol), TfOH (18 μ L, 0.20 mmol), and Dioxane (2 mL). The reaction was heated to 120 °C for 72 hours. Flash column chromatography (silica gel: 20% CH₂Cl₂ in Hexanes, ran twice) afforded the title compound as a white solid (50 mg, 0.12 mmol, 61% yield). mp 33-34 °C. IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 3086, 2923, 1560, 1364, 1100, 823, 781, 593; ¹H NMR (400 MHz, CDCl₃) δ : 8.41-8.36 (2H, m), 8.13-8.07 (2H, m), 7.82 (1H, ddd, J = 8.3, 6.0, 0.8 Hz), 7.68 (1H, dd, J = 5.1, 1.5 Hz), 7.58 (1H, app t, J = 8.1 Hz);

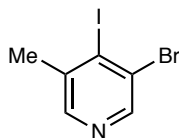
^{13}C NMR (100 MHz, CDCl_3) δ : 156.30, 154.90-154.45 (m), 150.30, 139.04, 132.27, 130.07, 129.92, 129.34, 126.89 (qn, $J = 4.6$ Hz), 124.86 (qn, $J = 4.7$ Hz), 106.49; ^{19}F NMR (365 MHz, CDCl_3) δ : 84.00 (1F, qn, $J = 150.8$ Hz), 62.67 (4F, d, $J = 150.0$ Hz); m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 408.0, $\text{C}_{11}\text{H}_8\text{F}_5\text{INS}^+$ requires 407.9.

2-Butyl-4-iodo-5-(trifluoromethyl)pyridine (2ag')



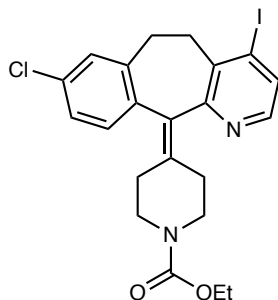
Prepared according to general procedure D, using 2-butyl-5-(trifluoromethyl)pyridine (136 mg, 0.20 mmol), LiI (107 mg, 0.80 mmol), TfOH (18 μL , 0.20 mmol), and Dioxane (2 mL). The reaction was heated to 120 $^\circ\text{C}$ for 24 hours. Flash column chromatography (silica gel: 5% CH_2Cl_2 in Toluene) afforded the title compound as a white solid (47 mg, 0.14 mmol, 71% yield). mp 44-46 $^\circ\text{C}$. IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2939, 2866, 1577, 1324, 1105, 1024, 937, 744; ^1H NMR (400 MHz, CDCl_3) δ : 8.65 (1H, s), 7.83 (1H, s), 2.78 (2H, t, $J = 7.7$ Hz), 1.75-1.66 (2H, m), 1.44-1.33 (2H, m), 0.95 (3H, t, $J = 7.3$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 166.87, 146.92 (q, $J = 6.2$ Hz), 135.53, 127.57 (q, $J = 31.0$ Hz), 122.78 (q, $J = 276.0$ Hz), 103.41, 37.47, 31.63, 22.54, 13.99; ^{19}F NMR (365 MHz, CDCl_3) δ : -62.61; m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 330.1, $\text{C}_{11}\text{H}_8\text{F}_5\text{INS}^+$ requires 330.0.

3-Bromo-4-iodo-5-methylpyridine (2ah')



Prepared according to general procedure D using (3-bromo-5-methylpyridin-4-yl) triphenylphosphonium trifluoromethanesulfonate (175 mg, 0.30 mmol), LiI (160 mg, 1.20 mmol), TfOH (26 μL , 0.30 mmol), and Dioxane (3 mL). The reaction was heated at 120 $^\circ\text{C}$ for 3 hours. Flash column chromatography (silica gel: 10% EtOAc in Hexanes) afforded the title compound as a white solid (60 mg, 0.13 mmol, 67% yield). mp 110-112 $^\circ\text{C}$; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2920, 1545, 1414, 1374, 1182, 1134, 854, 704; ^1H NMR (400 MHz, CDCl_3) δ : 8.44 (1H, s), 8.19 (1H, s), 2.49 (3H, s); ^{13}C NMR (100 MHz, CDCl_3) δ : 148.26, 146.61, 140.65, 129.48, 119.21, 27.11; m/z LRMS (ESI + APCI) found $[\text{M} + \text{H}]^+$ 297.9, $\text{C}_6\text{H}_6\text{BrIN}^+$ requires 297.9.

Ethyl 4-(8-chloro-4-iodo-5,6-dihydro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-ylidene)piperidine-1-carboxylate (2aq'')



Prepared according to general procedure D using 8-chloro-11-(1-(ethoxycarbonyl) piperidin-4-ylidene)-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-4-yl)diiodophenyl(6-(trifluoromethyl)pyridin-3-yl)phosphonium trifluoromethanesulfonate (172 mg, 0.20 mmol), LiI (107 mg, 0.80 mmol), TfOH (18 μ L, 0.2 mmol), and Dioxane (2 mL). The reaction was heated at 120 $^{\circ}$ C for 16 hours. Flash column chromatography (silica gel: 50% EtOAc in Hexanes) afforded the title compound as a white solid (64 mg, 0.13 mmol, 63% yield). mp 149-150 $^{\circ}$ C; IR $\nu_{\text{max}}/\text{cm}^{-1}$ (film): 2920, 2855, 1688, 1534, 1471, 1431, 1227, 1114, 997, 832; ^1H NMR (400 MHz, CDCl_3) δ : 7.93 (1H, d, $J = 5.2$ Hz), 7.64 (1H, d, $J = 5.2$ Hz), 7.20-7.03 (3H, m), 4.13 (2H, q, $J = 7.1$ Hz), 3.77 (2H, dd, $J = 19.7, 9.9$ Hz), 3.32 (2H, tdd, $J = 18.9, 8.6, 5.3$ Hz), 3.17 (tt, $J = 2\text{H}, 9.1, 4.6$ Hz), 3.01-2.76 (2H, m), 2.52-2.21 (4H, m), 1.24 (3H, t, $J = 7.1$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 157.68, 155.55, 146.89, 138.96, 137.83, 136.82, 136.57, 133.94, 133.66, 133.34, 130.78, 129.29, 126.39, 113.56, 61.46, 44.83, 44.76, 37.35, 31.33, 30.72, 14.79; m/z LRMS (ESI + APCI) found $[\text{M}+\text{H}]^+$ 509.1, $\text{C}_{22}\text{H}_{23}\text{ClIN}_2\text{O}_2^+$ requires 509.0.

10. Computational study

Technical details

The dispersion-corrected density functional theory (DFT) functional ω B97X-D was used with the Def2-SVP basis set in the optimization of geometries of all ground and transition structures. We carried out vibrational frequency calculations to obtain thermal corrections to Gibbs free energies (G). Additionally, these frequency calculations were used to confirm that stationary points were either minima or first-order saddle points on the potential energy surface. The connection between intermediates (**Int**) and their corresponding transition structures (**TS**) was studied using intrinsic reaction coordinate (IRC) calculations.⁶

G values included a correction for the change in standard state from gas phase at 1 atm to a 1 M solution. In all the individual calculations, quasi-harmonic (QHA) vibrational corrections were applied to entropies using a frequency cut-off value of 100.0 cm⁻¹, as proposed by Grimme.⁷ In a few cases, systems showed one persistent small imaginary frequency with $\nu_i < 50$ cm⁻¹. These imaginary frequencies were inverted to their respective positive values before the QHA entropic corrections were computed as seen in previous examples.⁸ All of these thermodynamic corrections were calculated and automatically applied to the computed results by the *GoodVibes* program using T = 353.15 K (80 °C).

Single-point energy calculations were used to refine electronic energies of optimized geometries. For this, DFT (ω B97X-D/Def2-QZVPP) was used. QHA G corrections calculated at the ω B97X-D/Def2-SVP level of theory were applied to these single point energies to obtain the final G values used to create energy profiles. This process was automated using the *GoodVibes* program.

All the optimizations, frequency and single-point energy calculations included solvent effects obtained with the integral equation formalism variant of the polarizable continuum model (IEF-PCM) with the SMD solvation model (solvent=1,4-dioxane).

A manual conformational search was carried out in all the steps, positioning the different units in multiple interaction sites. Additionally, the different functional groups were rotated in each of the different interaction sites (see section *Thermochemical data and absolute energy values* for more information about the number of conformers used).

*Gaussian 16*⁹ was used to perform all the DFT calculations with an “ultrafine” pruned (99,590) grid for numerical integration. Atomic charges and Wiberg bond orders (WBO) were computed using natural population analysis (NPA) with *NBO 6.0*¹⁰ interfaced to *Gaussian 16*. Molecular graphics were generated using *PyMol*;¹¹ Our display settings have been made openly accessible.¹² *NCIPlot* was used to generate the surfaces of noncovalent interactions using previously DFT-generated WFN files (at the optimization level of theory) and these surfaces were represented using *PyMOL*.

Structures of different initial reagents in step Int-II with halogen atoms

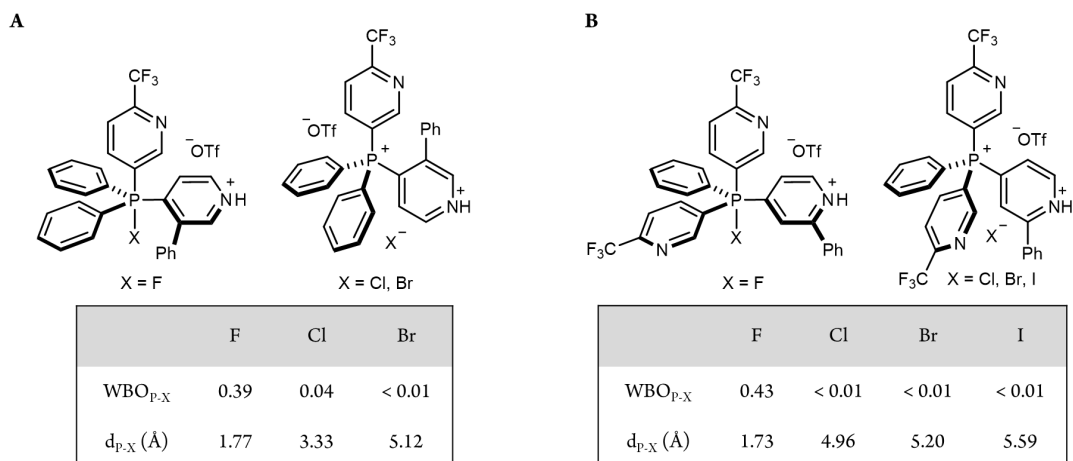


Figure S1. (A) **Int-II** step when using a phosphonium salt with 3-Ph-Py and one 3-(6-CF₃-Py) ring. (B) **Int-II** step when using a phosphonium salt with 2-Ph-Py and two 3-(6-CF₃-Py) rings.

Electrostatic potential at nucleus (EPN) studies to determine relative electrophilicity

EPN values have previously shown a correlation to the electrophilicity of acceptor atoms in different nucleophilic substitution reactions.¹³ As the EPN value of the acceptor atom becomes higher, the electrophilicity and, therefore, reactivity of that atom increases. As seen in Figure S2, including electron-withdrawing aromatic substituents in the phosphine and using acids that interact with the acceptor Py increase the relative electrophilicity of the acceptor Py.

EPN (kcal/mol): As EPN values becomes higher, electrophilicity increases

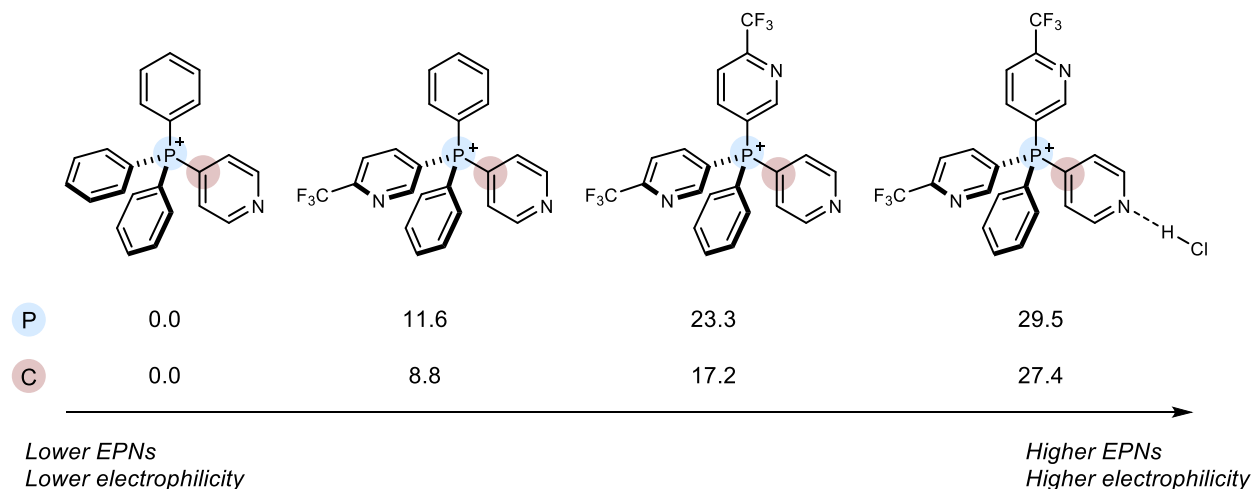


Figure S2. Relative EPN values (in kcal/mol) at the P central atom and the *para* C atom of the accepting pyridine group for different phosphines.

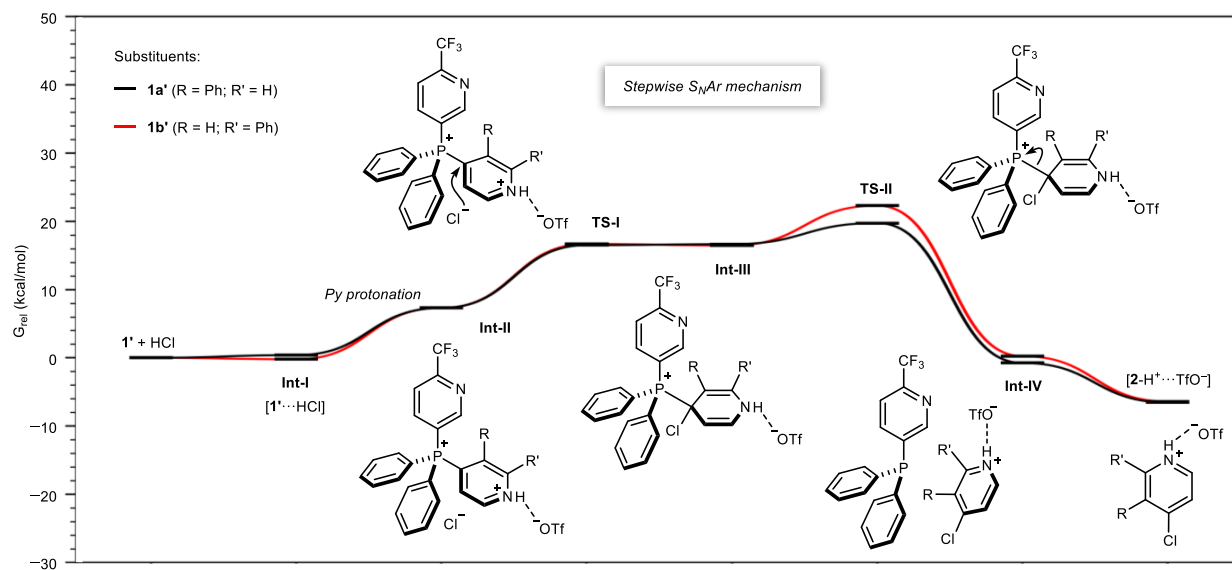
Computed reaction pathways

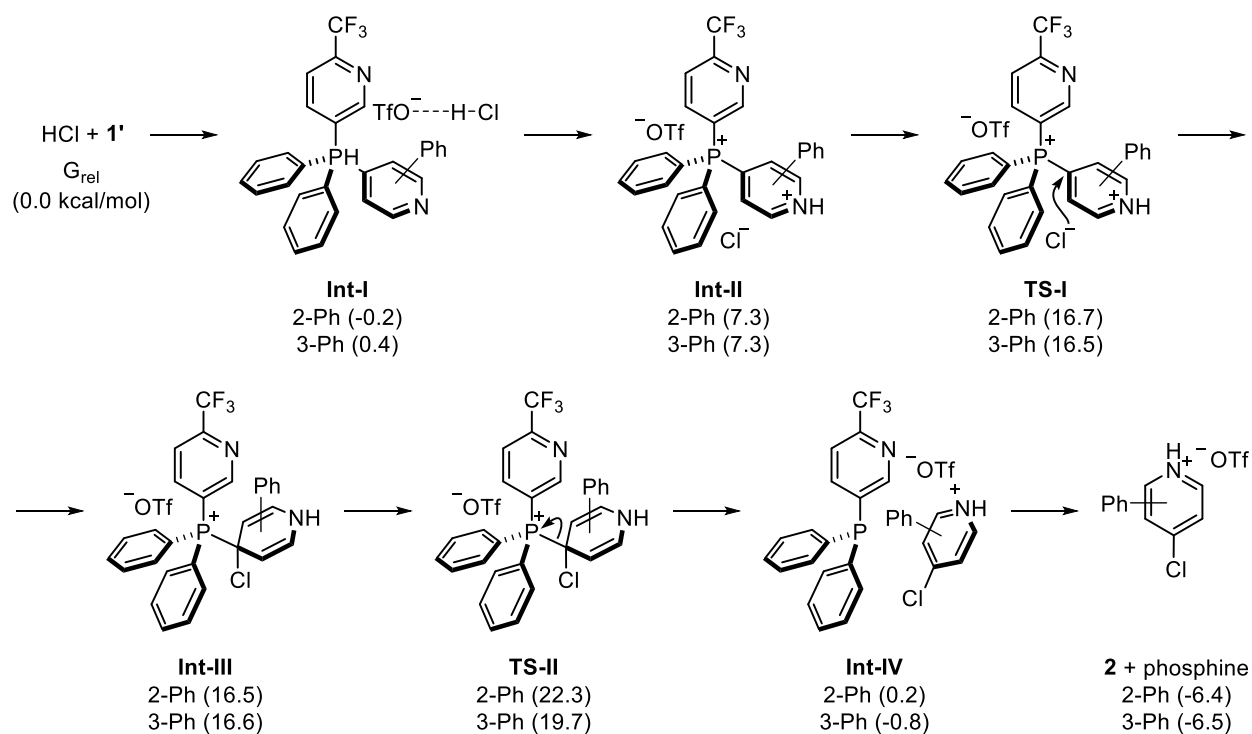
The names of the calculations included in the xyz and thermochemistry files (provided along with this ESI) contain suffixes that help understanding the type of system studied in each calculation. The suffixes used to separate the different pathways studied are represented in

reaction schemes below the energy profiles of this section. Also, for each reaction step, the different conformers were differentiated by using letters at the end of their names (i.e. **TS-I-Cl-2Ph_a**, **TS-I-Cl-2Ph_b**, and so on).

Computed reaction pathways for the chlorination of 3-Ph-Py (**1a'**) and 2-Ph-Py (**1b'**)

Charge: 0 Multiplicity: 1





Other names of the structures in the xyz file and thermochemistry data:

$\mathbf{1}'$ = Phosphonium_initial-2Ph/3Ph

$\mathbf{2}$ = Product-2Ph/3Ph

Phosphine byproduct = Phosphine-product

Figure S3. Top: G profiles of pathways with different selectivity in the chlorination of $\mathbf{1a'}$ and $\mathbf{1b'}$ to form product $\mathbf{2}$. G values are Boltzmann weighted G obtained using all the conformers found in each reaction step (see section *Thermochemical data and absolute energy values*). Bottom: Schematic representation of the reaction pathways studied.

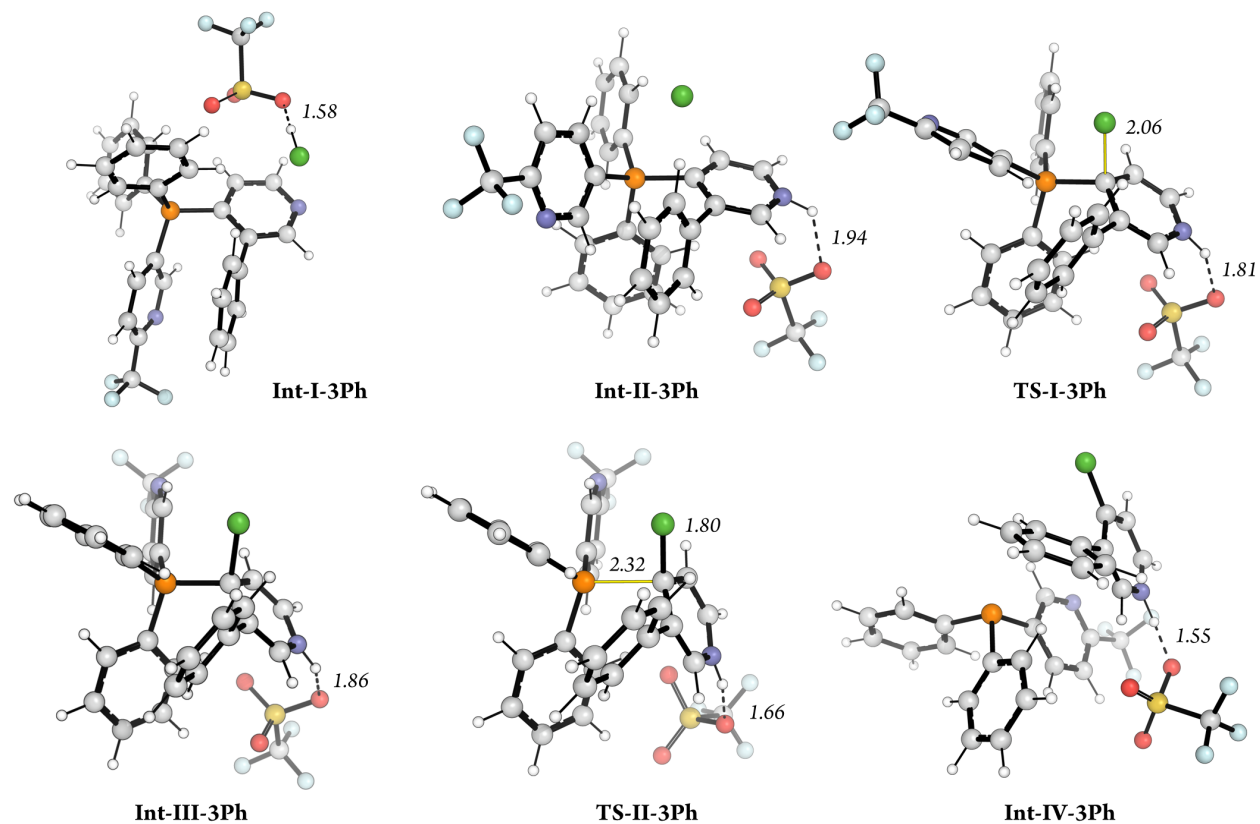


Figure S4. Representation of the most stable conformers of each reaction step when using **1a'** as the initial reagent (3-Ph). Bonds involved in the TS and hydrogen bonds are represented as yellow and dotted lines, respectively. Distances are shown in Å.

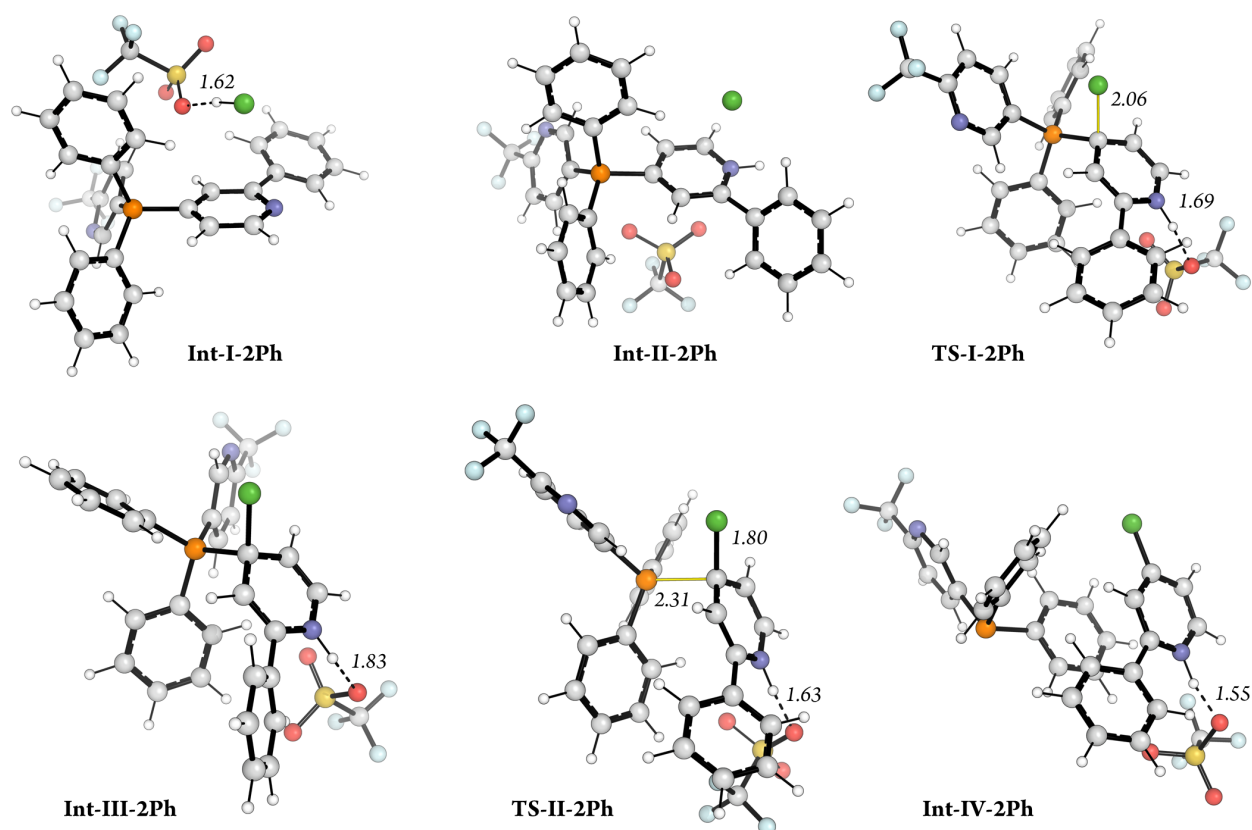


Figure S5. Representation of the most stable conformers of each reaction step when using **1b'** as the initial reagent (2-Ph). Bonds involved in the TS and hydrogen bonds are represented as yellow and dotted lines, respectively. Distances are shown in Å.

Computed reaction pathways for the chlorination of other substituted pyridines

Charge: 0 Multiplicity: 1

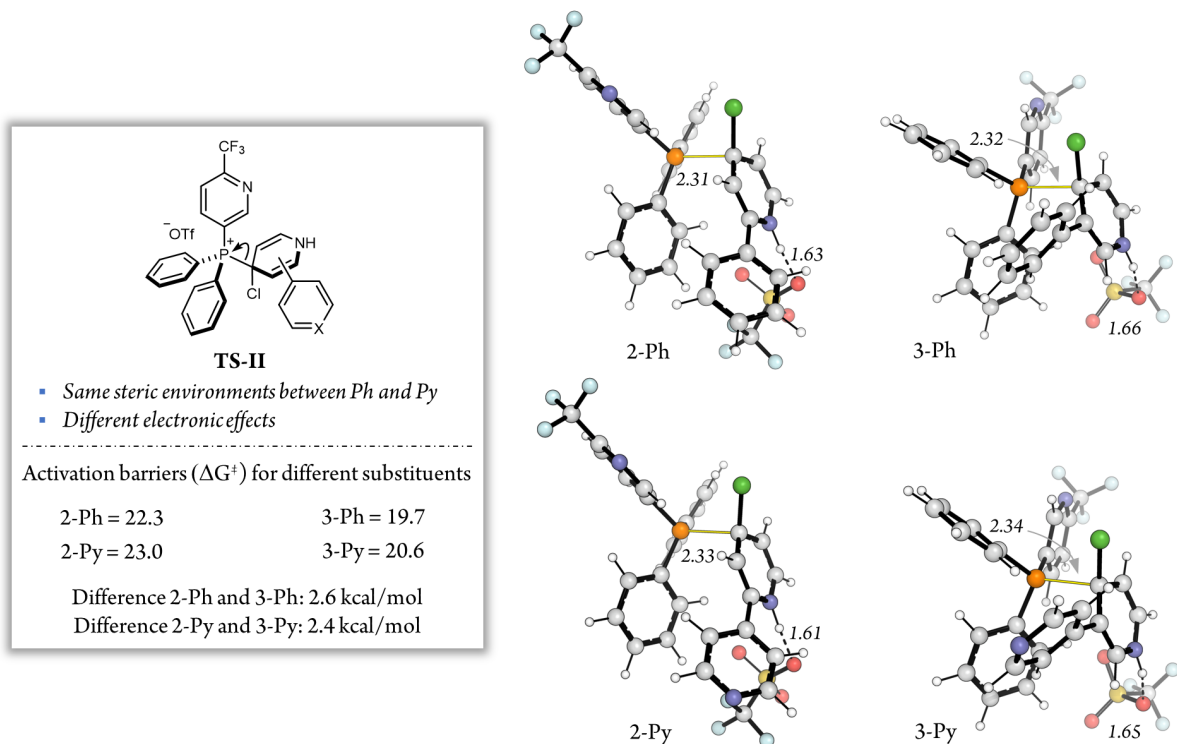
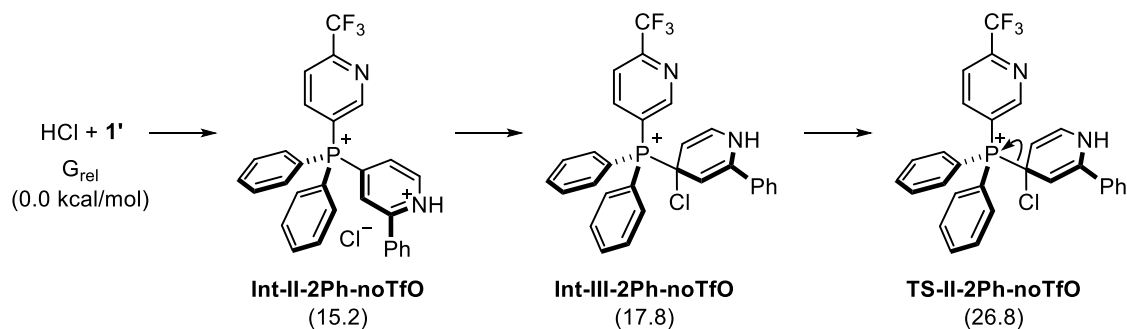


Figure S6. Boltzmann weighted G barriers from HCl + **1** to **TS-II** computed when using Ph and Py groups as substituents in the pyridine acceptors (for the G values of each conformer, see section *Thermochemical data and absolute energy values*). The geometries of the most stable conformers of **TS-II** are represented for each substituent. Bonds involved in the TS and hydrogen bonds are represented as yellow and dotted lines, respectively. Distances are shown in Å.

Computed reaction pathway without TfO⁻

Charge: 1 Multiplicity: 1

A model system that did not include the TfO⁻ counteranion was also modeled (Figure S7). In this model, the overall mechanism is similar to the mechanism of the complete system including the counteranion but there are reaction steps that are very difficult to model such as **TS-I**. One reason why **TS-I** is challenging to model might be the small energy difference between this step and steps **Int-II** and **Int-III**.



Name of the structures in the xyz file and thermochemistry data

$\mathbf{1}'$ = Phosphonium_initial-2Ph-noTfO

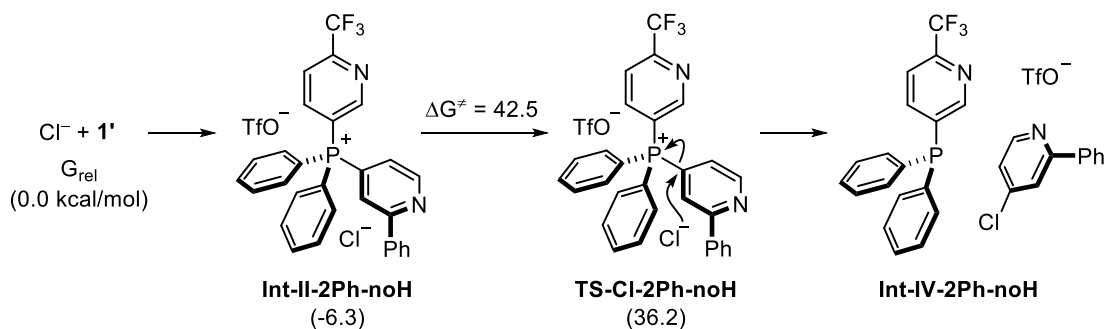
Figure S7. Boltzmann weighted G values obtained for the model reaction in which the TfO^- counteranion is not included.

Computed reaction pathway without TfOH and H^+

Charge: 0 Multiplicity: 1 (with no TfOH)

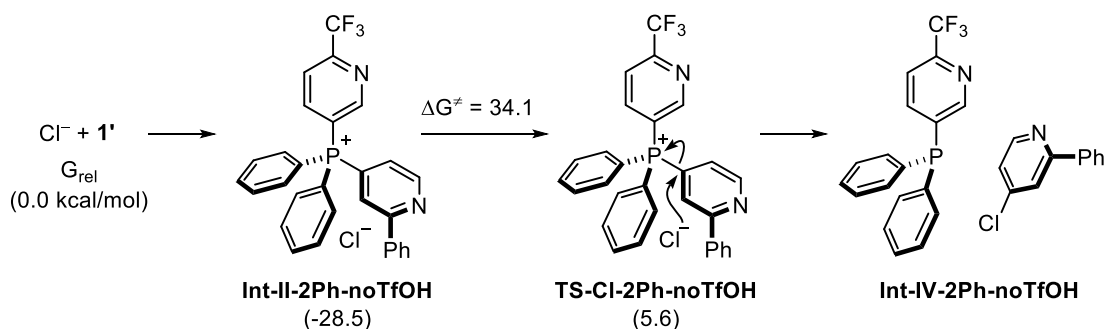
Charge: -1 Multiplicity: 1 (with no H^+)

Furthermore, model systems that did not include the H^+ source (excluding either TfOH or only H^+) were also employed to simulate the experimental reactions in which Cl anions are used without strong Lewis or Brønsted acids (i.e. NMe_4Cl). As seen in Figure S8, these reactions show high energy activation barriers that should not be possible to cross under the reaction temperature (80 °C).



Name of the structures in the xyz file and thermochemistry data

$\mathbf{1}'$ = Phosphonium_initial-2Ph



Name of the structures in the xyz file and thermochemistry data

$\mathbf{1}'$ = Phosphonium_initial-2Ph-noTfO

Figure S8. Boltzmann weighted G values obtained for reactions in which either TfOH or H^+ were excluded.

One notorious difference to the mechanism involving acid activation is the concerted nature of these $\text{S}_{\text{N}}\text{Ar}$ to nonactivated pyridine acceptors. Figure S9 shows that **Int-III** is not stable when there are not any H^+ sources, since this reaction goes directly from **Int-II** to **Int-IV** in a single transition step (compared to **TS-I**, **Int-III** and **TS-II** when a H^+ source is used).

Figure S9. IRC of the TS step of the Cl-Py coupling to nonactivated pyridines.

Studies using larger basis sets with diffuse functions

For the DFT benchmarking study, larger basis sets were employed for halide anions and P atoms (Def2-TZVPPD for F, Cl, Br and I atoms and Def2-TZVPP for P atoms) during the optimization process, which was followed by single-point energy corrections at the $\omega\text{B97X-D/Def2-QZVPP}$ level. Using a total of 24 calculations including the most stable conformers of the different reaction steps, the geometries and G values obtained were very similar compared to the initial

methodology (G mean absolute error (MAE) for both approaches was 0.4 ± 0.4 kcal/mol, Table S6 and Figure S10). Thus, it is preferred to use the initial approach since it requires less computation time, the input files are easier to make, and it avoids some SCF convergence problems encountered when using I atoms with Def2-TZVPPD. Additionally, we further tested the robustness of the initial approach to model this reaction by comparing the energy values obtained initially with the values obtained using single-point calculations with diffuse functions (ω B97X-D/Def2-QZVPPD). For this test, 20 structures chosen from different reaction steps were employed. In all the cases, the two approaches led to nearly identical results (MAE of calculated G with both methods was 0.04 ± 0.04 kcal/mol, Table S7) and, therefore, it is preferred to employ Def2-QZVPP over Def2-QZVPPD for single-point energy corrections since the calculation times required for both approaches differ considerably (average job CPU times were 176 ± 13 and 578 ± 107 hours for Def2-QZVPP and Def2-QZVPPD, respectively, Table S8).

Geometry optimization including diffuse functions¹⁴

In order to use the gen (or genecp when I atoms were included) option in *Gaussian* for the level ω B97X-D/Def2-SVP for C, H, N, O, F (selected atoms for CF₃) and S; Def2-TZVPPD for F, Cl, Br and I anions; and Def2-TZVPP for P, we used the following input to specify the basis sets:

Def2-SVP for C, O, S, F, N and H atoms:

C O S F N H O
def2SVP

Def2-TZVPP for P atoms:

P 0
def2TZVPP

Def2-TZVPPD for F atoms:

F 0
S 6 1.00
35479.1004410 0.21545014888D-03
5318.4728983 0.16700686527D-02
1210.4810975 0.86733211476D-02
342.85518140 0.35049933175D-01
112.01943181 0.11165320133
40.714740248 0.25988506647
S 2 1.00
16.039678111 0.39422966880
6.5038186740 0.24998238551
S 1 1.00
1.5440477509 1.0000000
S 1 1.00
0.61223452862 1.0000000
S 1 1.00
0.24027979698 1.0000000
S 1 1.00

0.90918446478D-01 1.0000000
P 4 1.00
80.233900483 0.63685999134D-02
18.594010743 0.44303143530D-01
5.6867902653 0.16867248708
1.9511006294 0.36166346255
P 1 1.00
0.66970211298 .44202901491
P 1 1.00
0.21651300410 .24319875730
P 1 1.00
0.59613282472D-01 1.0000000
D 1 1.00
3.10700000 1.0000000
D 1 1.00
0.85500000 1.0000000
D 1 1.00
0.18608388111 1.0000000
F 1 1.00
1.91700000 1.0000000

Def2-TZVPPD for Cl atoms:

Cl 0
S 7 1.00
69507.9909450 0.54314897497D-03
10426.1568800 0.41990463961D-02
2373.2334061 0.21592141679D-01
671.56420071 0.84598850094D-01

218.41999790	0.24757249724
77.572249714	0.47016930228
28.888815277	0.37436370716
S 3 1.00	
127.10527185	0.25182166603D-01
39.339582961	0.10786112456
7.6740679989	-0.27408821574
S 2 1.00	
3.8745627630	1.3213875014
1.8385832573	0.68636955368
S 1 1.00	
0.50229057542	1.00000000
S 1 1.00	
0.17962723420	1.00000000
S 1 1.00	
0.61133095854D-01	1.00000000
P 5 1.00	
666.50423284	0.23632663836D-02
157.64241690	0.18879300374D-01
50.262520978	0.87206341273D-01
18.536078105	0.25285612970
7.2940532777	0.43507154820
P 1 1.00	
2.9433248995	.35026513165
P 1 1.00	
1.0404970818	1.00000000
P 1 1.00	
0.38456415080	1.00000000
P 1 1.00	
0.13069642732	1.00000000
P 1 1.00	
0.35381580722D-01	1.00000000
D 1 1.00	
4.61000000	1.00000000
D 1 1.00	
1.01100000	1.00000000
D 1 1.00	
0.339000000	1.00000000
D 1 1.00	
0.99601358790D-01	1.00000000
F 1 1.00	
0.706000000	1.00000000

Def2-TZVPPD for Br atoms:

Br 0	
S 8 1.00	
565073.2525600	0.23660314690D-03
84701.7231790	0.18348332508D-02
19276.2719000	0.95465849860D-02
5456.4284576	0.38877142153D-01
1776.9503500	0.12718314231
639.19398276	0.30437662191
248.78823961	0.44490940497
98.678305494	0.24381643058

S 4 1.00	
606.07824568	-0.26527158709D-01
188.45598484	-0.12484584809
31.497144506	0.56468683559
13.736008320	0.55555268564
S 2 1.00	
21.203212766	-0.24940920493
3.7616420178	0.71213119743
S 1 1.00	
1.7735933962	1.00000000
S 1 1.00	
0.45197413664	1.00000000
S 1 1.00	
0.16613377099	1.00000000
S 1 1.00	
0.52769579657D-01	1.00000000
P 6 1.00	
3019.6955723	0.24971049798D-02
715.35481126	0.20419267596D-01
229.98328751	0.96897148309D-01
86.167844615	0.28053901252
34.667870802	0.44606390473
14.113870307	0.24410073923
P 4 1.00	
57.085653082	-0.21855950710D-01
8.8193845840	0.32707075320
3.9340302872	0.57855229520
1.7998830384	0.33570987698
P 1 1.00	
0.66899410512	1.00000000
P 1 1.00	
0.27136238231	1.00000000
P 1 1.00	
0.10083790243	1.00000000
P 1 1.00	
0.29005224647D-01	1.00000000
D 5 1.00	
168.85370257	0.89663981988D-02
49.977949919	0.62062059316D-01
18.274913338	0.21474732384
7.2455694631	0.40335336746
2.8562315025	0.42208813080
D 1 1.00	
1.0459621144	.17874813267
D 1 1.00	
0.56865655	1.00000000
D 1 1.00	
0.22031490	1.00000000
D 1 1.00	
0.75865567476D-01	1.00000000
F 1 1.00	
0.57083312	1.00000000

Def2-TZVPPD for I atoms:

I 0			0.17000000000	1.0000000
S 5 1.00			D 1 1.00	
5899.5791533	0.24188269271D-03		0.61341708807D-01	1.0000000
898.54238765	0.15474041742D-02		F 1 1.00	
200.37237912	0.42836684457D-02		2.1800000	1.0000000
31.418053840	-0.39417936275D-01		F 1 1.00	
15.645987838	0.96086691992		0.44141808	1.0000000
S 2 1.00			****	
11.815741857	0.75961524091		I 0	
6.4614458287	0.42495501835		I-ECP 3 28	
S 1 1.00			f potential	
2.3838067579	1.0000000		4	
S 1 1.00			2 19.45860900	-21.84204000
1.1712089662	1.0000000		2 19.34926000	-28.46819100
S 1 1.00			2 4.82376700	-0.24371300
0.32115875757	1.0000000		2 4.88431500	-0.32080400
S 1 1.00			s-f potential	
0.12387919364	1.0000000		7	
S 1 1.00			2 40.01583500	49.99429300
0.43491550641D-01	1.0000000		2 17.42974700	281.02531700
P 4 1.00			2 9.00548400	61.57332600
12.984316904	-0.49096186164D-01		2 19.45860900	21.84204000
3.6199503008	0.38914432482		2 19.34926000	28.46819100
2.0232273090	0.65610817262		2 4.82376700	0.24371300
1.0367490559	0.31803551647		2 4.88431500	0.32080400
P 3 1.00			p-f potential	
197.30030547	0.73951226905D-03		8	
20.061411349	0.66168450008D-01		2 15.35546600	67.44284100
9.7631460485	-0.28554662348		2 14.97183300	134.88113700
P 1 1.00			2 8.96016400	14.67505100
0.45937816000	1.0000000		2 8.25909600	29.37566600
P 1 1.00			2 19.45860900	21.84204000
0.19116532928	1.0000000		2 19.34926000	28.46819100
P 1 1.00			2 4.82376700	0.24371300
0.74878813023D-01	1.0000000		2 4.88431500	0.32080400
P 1 1.00			d-f potential	
0.21653491846D-01	1.0000000		10	
D 6 1.00			2 15.06890800	35.43952900
119.12671745	0.82596039573D-03		2 14.55532200	53.17605700
33.404240134	0.68377675770D-02		2 6.71864700	9.06719500
17.805918203	-0.10308158997D-01		2 6.45639300	13.20693700
4.8990510353	0.22670457658		2 1.19177900	0.08933500
2.4516753106	0.44180113937		2 1.29115700	0.05238000
1.1820693432	0.36775472225		2 19.45860900	21.84204000
D 1 1.00			2 19.34926000	28.46819100
0.52923110068	1.0000000		2 4.82376700	0.24371300
D 1 1.00			2 4.88431500	0.32080400

Even in the most difficult cases (i.e. modelling F anions),¹⁵ the geometries optimized with diffuse functions did not present substantial differences compared to the geometries obtained with the initial approach (ω B97X-D/Def2-SVP for all the atoms) (Figure S10). It is worth to mention that in all cases the geometries and P–halogen, P–C and other bond distances obtained when using

diffuse functions do not show significant changes that would affect any of the results obtained when optimizing with ω B97X-D/Def2-SVP.

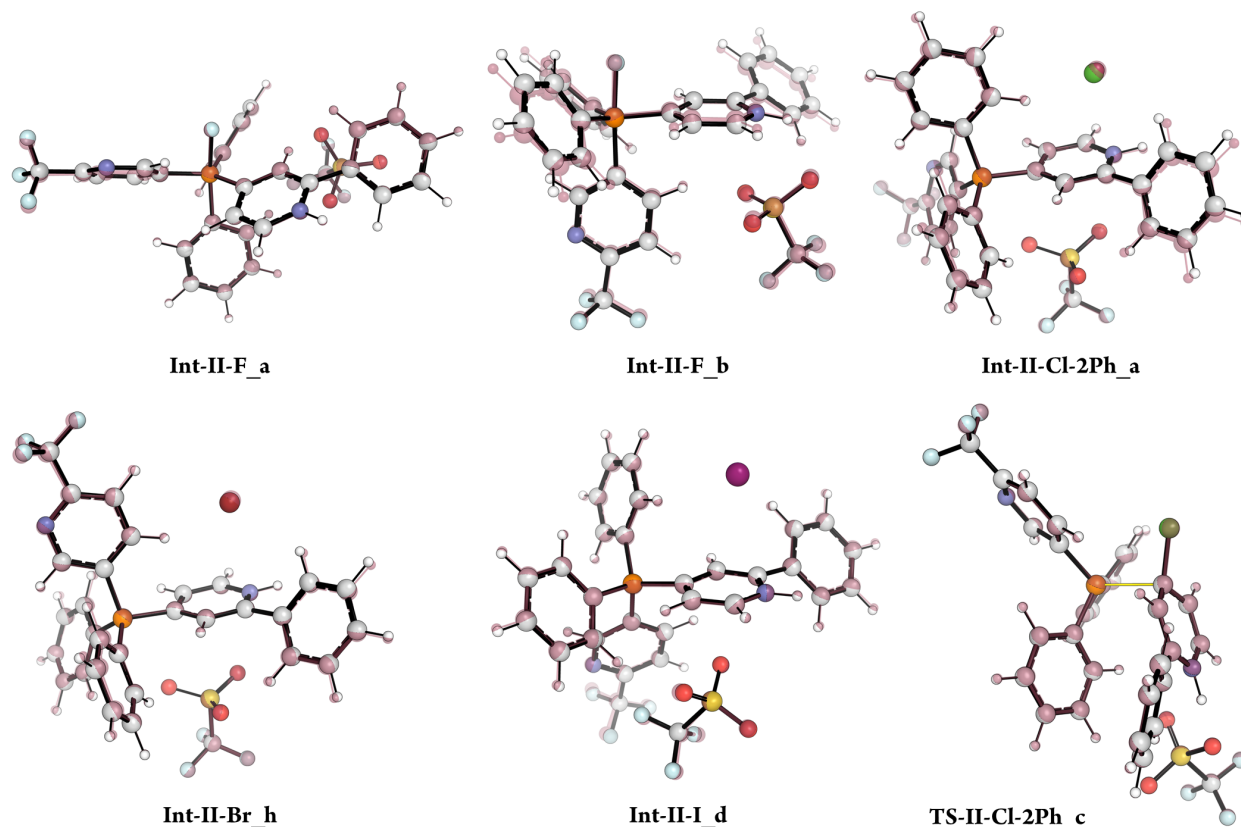


Figure S10. Overlay of geometries optimized with ω B97X-D/Def2-SVP for C, H, N, O, F (in CF_3) and S; Def2-TZVPPD for F, Cl, Br and I anions; and Def2-TZVPP for P (red color) and ω B97X-D/Def2-SVP (normal colors).

Table S6. Comparison of relative G obtained using (i) ω B97X-D/Def2-QZVPP// ω B97X-D/Def2-SVP for all atoms and (ii) ω B97X-D/Def2-QZVPP// ω B97X-D/Def2-SVP for C, H, N, O, F (in CF_3) and S; Def2-TZVPPD for F, Cl, Br and I anions; and Def2-TZVPP for P. The difference in the two relative G is also shown. It is worth to mention that the G values represented are the energy of individual conformers (not Boltzmann averages). MAE = mean absolute error. SD = standard deviation.

System	G_{rel} (kcal/mol) with ω B97X-D/Def2-QZVPP// ω B97X-D/Def2-SVP for all atoms	G_{rel} (kcal/mol) with ω B97X-D/Def2-QZVPP// ω B97X-D/Def2-SVP for C, H, N, O, F (in CF_3) and S; Def2-TZVPPD for F, Cl, Br and I anions; and Def2-TZVPP for P	Absolute G diff. (kcal/mol)
HCl + Phosphonium_initial-2Ph_h (reference for 2Ph)	0.0	0.0	-
HCl + Phosphonium_initial-3Ph_f (reference for 3Ph)	0.0	0.0	-
Int-I-Cl-2Ph_g	1.7	1.7	0.0

Int-I-Cl-3Ph_f	1.4	1.5	0.1
Int-II-Cl-2Ph_a	7.4	6.9	0.5
Int-II-Cl-2Ph_f	8.2	7.2	1.0
Int-II-Cl-3Ph_c	8.3	6.8	1.5
Int-III-Cl-2Ph_b	21.9	22.3	0.4
Int-III-Cl-2Ph_e	16.9	17.4	0.5
Int-III-Cl-3Ph_a	20.4	20.2	0.2
Int-III-Cl-3Ph_b	17.1	17.7	0.6
Int-IV-Cl-2Ph_e	0.2	0.9	0.7
Int-IV-Cl-3Ph_b	1.7	2.1	0.4
Int-IV-Cl-3Ph_c	-0.4	-0.3	0.1
HCl + Phosphonium_initial-2Ph_f	0.2	0.6	0.4
HCl + Phosphonium_initial-3Ph_k	4.5	3.9	0.6
Product-2Ph_a + Phosphine-product_b	-5.9	-5.8	0.1
Product-2Ph_b + Phosphine-product_b	-6.1	-6.1	0.0
Product-3Ph_a + Phosphine-product_b	-6.0	-6.0	0.0
Product-3Ph_c + Phosphine-product_b	-6.2	-6.0	0.2
TS-II-Cl-2Ph_c	23.5	23.5	0.0
TS-II-Cl-2Ph_g	22.4	22.0	0.4
TS-II-Cl-3Ph_c	20.1	21.6	1.5
TS-II-Cl-3Ph_h	22.0	22.2	0.2
MAE = 0.4 kcal/mol; SD = 0.4 kcal/mol			

Single-point energy calculations including diffuse functions

In order to use the gen option in *Gaussian* for the level ω B97X-D/Def2-QZVPPD for all the atoms, we used the following input to specify the basis sets:

Def2-QZVPPD for H atoms:

H 0

S 4 1.00

190.6916900 0.70815167D-03

28.6055320 0.54678827D-02

6.5095943 0.27966605D-01

1.8412455 0.10764538

S 1 1.00

0.59853725 1.0000000

S 1 1.00

0.21397624 1.0000000

S 1 1.00

0.80316286D-01 1.0000000

P 1 1.00

2.29200000 1.0000000

P 1 1.00

0.83800000 1.0000000

P 1 1.00

0.29200000 1.0000000

P 1 1.00

0.84063199228D-01 1.0000000

D 1 1.00

2.06200000 1.0000000

D 1 1.00

0.66200000 1.0000000

F 1 1.00

1.39700000 1.0000000

Def2-QZVPPD for C atoms:

```

C 0
S 8 1.00
  67025.0710290      0.38736308501D-04
  10039.9865380      0.30107917575D-03
  2284.9316911       0.15787918095D-02
  647.14122130       0.66087087195D-02
  211.09472335       0.23367123250D-01
  76.177643862       0.70420716898D-01
  29.633839163       0.17360344953
  12.187785081       0.32292305648
S 2 1.00
  53.026006299       0.74897404492D-01
  15.258502776       0.76136220983
S 1 1.00
  5.2403957464       1.00000000
S 1 1.00
  2.2905022379       1.00000000
S 1 1.00
  0.69673283006      1.00000000
S 1 1.00
  0.27599337363      1.00000000
S 1 1.00
  0.10739884389      1.00000000
S 1 1.00
  0.44981404899D-01  1.00000000
P 5 1.00
  105.12555082       0.84647553844D-03
  24.884461066       0.66274038534D-02
  7.8637230826       0.30120390419D-01
  2.8407001835       0.99951435476D-01
  1.1227137335       0.23826299282
P 1 1.00
  0.46050725555      1.00000000
P 1 1.00
  0.18937530913      1.00000000
P 1 1.00
  0.75983791611D-01  1.00000000
D 1 1.00
  1.84800000         1.00000000
D 1 1.00
  0.64900000         1.00000000
D 1 1.00
  0.22800000         1.00000000
D 1 1.00
  0.76889830417D-01  1.00000000
F 1 1.00
  1.41900000         1.00000000
F 1 1.00
  0.48500000         1.00000000
G 1 1.00
  1.01100000         1.00000000

```

Def2-QZVPPD for N atoms:

```

N 0
S 8 1.00
  90726.8892100      0.39257887368D-04
  13590.5288010      0.30513316455D-03
  3092.9883781       0.16000560446D-02
  875.99876362       0.66982937306D-02
  285.74469982       0.23690078765D-01
  103.11913417       0.71455405268D-01
  40.128556777       0.17632774876
  16.528095704       0.32677592815
S 2 1.00
  69.390960983       0.80052094386D-01
  20.428200596       0.78268063538
S 1 1.00
  7.1292587972       1.00000000
S 1 1.00
  3.1324304893       1.00000000
S 1 1.00
  0.98755778723      1.00000000
S 1 1.00
  0.38765721307      1.00000000
S 1 1.00
  0.14909883075      1.00000000
S 1 1.00
  0.62151630318D-01  1.00000000
P 5 1.00
  150.05742670       -0.86216165986D-03
  35.491599483       -0.68571273236D-02
  11.247864223       -0.31795688855D-01
  4.0900305195       -0.10537396822
  1.6220573146       -0.24519708041
P 1 1.00
  0.66442261530      1.00000000
P 1 1.00
  0.27099770070      1.00000000
P 1 1.00
  0.10688749984      1.00000000
D 1 1.00
  2.83700000         1.00000000
D 1 1.00
  0.96800000         1.00000000
D 1 1.00
  0.33500000         1.00000000
D 1 1.00
  0.10825280010      1.00000000
F 1 1.00
  2.02700000         1.00000000
F 1 1.00
  0.68500000         1.00000000
G 1 1.00
  1.42700000         1.00000000

```

Def2-QZVPPD for O atoms:

```

O  0
S  8  1.00
116506.4690800      0.40383857939D-04
17504.3497240      0.31255139004D-03
3993.4513230      0.16341473495D-02
1133.0063186      0.68283224757D-02
369.99569594      0.24124410221D-01
133.62074349      0.72730206154D-01
52.035643649      0.17934429892
21.461939313      0.33059588895
S  2  1.00
89.835051252      0.96468652996D-01
26.428010844      0.94117481120
S  1  1.00
9.2822824649      1.00000000
S  1  1.00
4.0947728533      1.00000000
S  1  1.00
1.3255349078      1.00000000
S  1  1.00
0.51877230787      1.00000000
S  1  1.00
0.19772676454      1.00000000
S  1  1.00
0.69638535104D-01      1.00000000
P  5  1.00
191.15255810      0.25115697705D-02
45.233356739      0.20039240864D-01
14.353465922      0.93609064762D-01
5.2422371832      0.30618127124
2.0792418599      0.67810501439
P  1  1.00
0.84282371424      1.00000000
P  1  1.00
0.33617694891      1.00000000
P  1  1.00
0.12863997974      1.00000000
P  1  1.00
0.43598162776D-01      1.00000000
D  1  1.00
3.77500000      1.00000000
D  1  1.00
1.30000000      1.00000000
D  1  1.00
0.44400000      1.00000000
D  1  1.00
0.12546378695      1.00000000
F  1  1.00
2.66600000      1.00000000
F  1  1.00
0.85900000      1.00000000
G  1  1.00
1.84600000      1.00000000
****

```

Def2-QZVPPD for F atoms:

```

F  0
S  8  1.00
132535.9734500      0.47387482743D-04
19758.1125880      0.37070120897D-03
4485.1996947      0.19450784713D-02
1273.8151020      0.80573291994D-02
418.93831236      0.27992880781D-01
152.55721985      0.82735120175D-01
59.821524823      0.19854169012
24.819076932      0.34860632233
S  2  1.00
100.74446673      0.10505068816
30.103728290      0.94068472434
S  1  1.00
10.814283272      1.00000000
S  1  1.00
4.8172886770      1.00000000
S  1  1.00
1.6559334213      1.00000000
S  1  1.00
0.64893519582      1.00000000
S  1  1.00
0.24778104545      1.00000000
S  1  1.00
0.87626236800D-01      1.00000000
P  5  1.00
240.96654114      0.30389933451D-02
57.020699781      0.24357738582D-01
18.126952120      0.11442925768
6.6457404621      0.37064659853
2.6375722892      0.79791551766
P  1  1.00
1.0638217200      1.00000000
P  1  1.00
0.41932562750      1.00000000
P  1  1.00
0.15747588299      1.00000000
P  1  1.00
0.46772400332D-01      1.00000000
D  1  1.00
5.01400000      1.00000000
D  1  1.00
1.72500000      1.00000000
D  1  1.00
0.58600000      1.00000000
D  1  1.00
0.15967986245      1.00000000
F  1  1.00
3.56200000      1.00000000
F  1  1.00
1.14800000      1.00000000
G  1  1.00
2.37600000      1.00000000

```

Def2-QZVPPD for P atoms:

```

P 0
S 10 1.00
1090561.7138000      0.12142449664D-04
163316.3946100      0.94395292614D-04
37166.6074510      0.49622262177D-03
10526.8809450      0.20900040747D-02
3433.9976028      0.75489230025D-02
1239.5360480      0.24010423937D-01
483.27456199      0.67231473697D-01
200.16911586      0.15978669881
86.960394829      0.29735906782
39.211283369      0.36187171850
S 3 1.00
336.75883662      0.19154721050D-01
103.72179793      0.17134079100
39.771861240      0.63689655985
S 1 1.00
17.888612952      1.0000000
S 1 1.00
6.9644556879      1.0000000
S 1 1.00
3.2198092087      1.0000000
S 1 1.00
1.4669943979      1.0000000
S 1 1.00
0.47765437532      1.0000000
S 1 1.00
0.21637789241      1.0000000
S 1 1.00
0.90235894336D-01      1.0000000
S 1 1.00
0.40836372978D-01      1.0000000
P 8 1.00
2019.6711374      0.21359172406D-03
478.60125090      0.18568771399D-02
155.14942504      0.10070690115D-01
58.816356575      0.39605153679D-01
24.544512785      0.11736067844
10.883571061      0.24950540642
4.9624791285      0.36421287984
2.3002912343      0.31764127123
P 2 1.00
59.371345016      0.39432918004
3.0694590986      -6.3522960431
P 1 1.00
1.0634401739      1.0000000
P 1 1.00
0.45022152161      1.0000000
P 1 1.00
0.18267271344      1.0000000
P 1 1.00
0.71610333771D-01      1.0000000

```

```

D 1 1.00
3.34300000      1.0000000
D 1 1.00
0.807000000      1.0000000
D 1 1.00
0.365000000      1.0000000
D 1 1.00
0.154000000      1.0000000
D 1 1.00
0.59687731846D-01      1.0000000
F 1 1.00
0.703000000      1.0000000
F 1 1.00
0.280000000      1.0000000
G 1 1.00
0.597000000      1.0000000
****

```

Def2-QZVPPD for S atoms:

```

S 0
S 10 1.00
1273410.9023000      0.11767088246D-04
190697.8300700      0.91478610166D-04
43397.8853300      0.48090078640D-03
12291.8096770      0.20257193592D-02
4009.7420824      0.73190096406D-02
1447.3531030      0.23300499900D-01
564.30102913      0.65386213610D-01
233.74506243      0.15614449910
101.56402814      0.29318563787
45.805907187      0.36287914289
S 3 1.00
394.27281503      0.18753305081D-01
121.72249591      0.16870726663
46.754125963      0.63806830653
S 1 1.00
20.923008254      1.0000000
S 1 1.00
8.2685567800      1.0000000
S 1 1.00
3.8629345671      1.0000000
S 1 1.00
1.7794684781      1.0000000
S 1 1.00
0.61064260103      1.0000000
S 1 1.00
0.27412269445      1.0000000
S 1 1.00
0.11325939107      1.0000000
S 1 1.00
0.44392624881D-01      1.0000000
P 8 1.00
2189.8930459      0.23912552864D-03
518.94596592      0.20772032158D-02
168.19560151      0.11242420571D-01

```

63.745282788	0.44069933941D-01
26.597033077	0.12918778608
11.774251449	0.26910820167
5.3534379024	0.37855928620
2.4701911802	0.29692134655
P 2 1.00	
82.120288349	-0.39420318847D-01
4.9523532869	0.64048403090
P 1 1.00	
1.0828262029	1.00000000
P 1 1.00	
0.49271277356	1.00000000
P 1 1.00	
0.20483450942	1.00000000
P 1 1.00	
0.80743615716D-01	1.00000000
P 1 1.00	
0.25661157833D-01	1.00000000
D 1 1.00	
4.159000000	1.00000000
D 1 1.00	
1.019000000	1.00000000
D 1 1.00	
0.464000000	1.00000000
D 1 1.00	
0.194000000	1.00000000
D 1 1.00	
0.67889829366D-01	1.00000000
F 1 1.00	
0.869000000	1.00000000
F 1 1.00	
0.335000000	1.00000000
G 1 1.00	
0.683000000	1.00000000

Def2-QZVPPD for Cl atoms:

Cl 0	
S 10 1.00	
1467459.0095000	0.11478257194D-04
219756.1643300	0.89234299775D-04
50010.7703010	0.46911086186D-03
14164.8239180	0.19762446133D-02
4620.7465525	0.71419937783D-02
1667.8991635	0.22753219445D-01
650.29199265	0.63959782953D-01
269.38037376	0.15331059238
117.06752106	0.28986952417
52.811766843	0.36348071452
S 3 1.00	
461.42769988	0.18019457578D-01
142.12665355	0.16489442314
54.437838768	0.63891587584
S 1 1.00	
24.160770219	1.00000000

S 1 1.00	
9.7083540306	1.00000000
S 1 1.00	
4.5640696733	1.00000000
S 1 1.00	
2.1194744832	1.00000000
S 1 1.00	
0.75722365394	1.00000000
S 1 1.00	
0.33747224597	1.00000000
S 1 1.00	
0.13860775149	1.00000000
S 1 1.00	
0.54234565513D-01	1.00000000
P 8 1.00	
2501.9457890	0.24242618410D-03
592.88059285	0.21079961749D-02
192.18089186	0.11432693869D-01
72.875710488	0.44956698060D-01
30.436358370	0.13197476145
13.490178902	0.27493639225
6.1478071413	0.38347236372
2.8450944820	0.28871943885
P 2 1.00	
105.39397936	-0.34311760144D-01
6.7369738513	0.64060818902
P 1 1.00	
1.2421095772	1.00000000
P 1 1.00	
0.55669714254	1.00000000
P 1 1.00	
0.23387801464	1.00000000
P 1 1.00	
0.93164490890D-01	1.00000000
P 1 1.00	
0.27256146018D-01	1.00000000
D 1 1.00	
5.191000000	1.00000000
D 1 1.00	
1.276000000	1.00000000
D 1 1.00	
0.583000000	1.00000000
D 1 1.00	
0.243000000	1.00000000
D 1 1.00	
0.83456538402D-01	1.00000000
F 1 1.00	
1.089000000	1.00000000
F 1 1.00	
0.423000000	1.00000000
G 1 1.00	
0.827000000	1.00000000

We calculated the relative G energies obtained with and without diffuse functions in the single-point energy corrections using a variety of structures from different reaction steps (Table S7). The G values obtained with both basis sets are nearly equal (MAE = 0.04 ± 0.04 kcal/mol over 20 structures) and the use of diffuse functions do not change any of the conclusions discussed in this study.

Table S7. Comparison of relative G obtained using (i) ω B97X-D/Def2-QZVPP// ω B97X-D/Def2-SVP and (ii) ω B97X-D/Def2-QZVPPD// ω B97X-D/Def2-SVP. It is worth to mention that the G values represented are the energy of individual conformers (not Boltzmann averages). MAE = mean absolute error. SD = standard deviation.

System	G _{rel} (kcal/mol) with ω B97X-D/Def2-QZVPP// ω B97X-D/Def2-SVP	G _{rel} (kcal/mol) with ω B97X-D/Def2-QZVPPD// ω B97X-D/Def2-SVP	Absolute G diff. (kcal/mol)
HCl + Phosphonium_initial-2Ph_f (reference for 2Ph and 3Ph)	0.00	0.00	-
Int-I-Cl-2Ph_a	5.37	5.39	0.02
Int-I-Cl-2Ph_b	2.40	2.47	0.07
Int-I-Cl-2Ph_c	2.34	2.35	0.01
Int-I-Cl-2Ph_d	1.65	1.72	0.07
Int-I-Cl-2Ph_e	2.03	2.06	0.03
Int-I-Cl-2Ph_g	1.56	1.57	0.01
Int-I-Cl-2Ph_h	3.01	3.02	0.01
Int-I-Cl-2Ph_s	4.95	5.06	0.11
Int-I-Cl-2Ph_t	1.16	1.23	0.07
Int-I-Cl-2Ph_y	1.38	1.51	0.13
Int-I-Cl-3Ph_r	8.01	8.07	0.06
Int-I-Cl-3Ph_s	6.82	6.88	0.06
Int-II-Cl-2Ph_k	10.77	10.75	0.02
TS-II-Cl-2Ph_e	24.75	24.80	0.05
Int-IV-Cl-2Ph_d	0.47	0.51	0.04
Int-IV-Cl-3Ph_b	4.71	4.74	0.03
Product-2Ph_a + Phosphine-product_b	-6.10	-6.09	0.01
Product-2Ph_b + Phosphine-product_b	-6.28	-6.28	0.00
Product-3Ph_a + Phosphine-product_b	-2.97	-3.00	0.03
Product-3Ph_c + Phosphine-product_b	-0.64	-0.65	0.01
MAE = 0.04 kcal/mol; SD = 0.04 kcal/mol			

The computation times of the two types of single-point corrections were measured. The results strongly suggested that using Def2-QZVPPD requires considerably longer times than Def2-QZVPP while leading to very similar results (Table S8).

Table S8. Comparison of job CPU times required to calculate reaction intermediates and transition states for (i) ω B97X-D/Def2-QZVPP// ω B97X-D/Def2-SVP and (ii) ω B97X-D/Def2-QZVPPD// ω B97X-D/Def2-SVP. MAE = mean absolute error. SD = standard deviation.

System	Time (h) with ω B97X-D/Def2-QZVPP// ω B97X-D/Def2-SVP	Time (h) with ω B97X-D/Def2-QZVPPD// ω B97X-D/Def2-SVP
Int-I-Cl-2Ph_a	141	609
Int-I-Cl-2Ph_b	175	696
Int-I-Cl-2Ph_c	172	697
Int-I-Cl-2Ph_d	178	656
Int-I-Cl-2Ph_e	173	613
Int-I-Cl-2Ph_g	173	594
Int-I-Cl-2Ph_h	175	659
Int-I-Cl-2Ph_s	176	500
Int-I-Cl-2Ph_t	177	500
Int-I-Cl-2Ph_y	176	769
Int-I-Cl-3Ph_r	198	650
Int-I-Cl-3Ph_s	198	429
Int-II-Cl-2Ph_k	168	433
TS-II-Cl-2Ph_e	185	524
Int-IV-Cl-2Ph_d	174	445
Int-IV-Cl-3Ph_b	181	473
MAE = 176 h; SD = 13 h		MAE = 578 h; SD = 107 h

Calculation of the overall reaction activation energy with different DFT methods

Table S9. Calculation of the overall reaction activation energy (ΔG^\ddagger , from most to least favorable energies) using different levels of theory and solvents. For this study, the two most stable conformers found at the ω B97X-D/Def2-QZVPP// ω B97X-D/Def2-SVP were used.

Reaction step	G_{rel} (kcal/mol) ω B97X-D/Def2-QZVPP// ω B97X-D/Def2-SVP (dioxane)	G_{rel} (kcal/mol) ω B97X-D/Def2-QZVPP// ω B97X-D/Def2-SVP (AcOEt)	G_{rel} (kcal/mol) M06-2X-D3/Def2-QZVPP// ω B97X-D/Def2-SVP (dioxane)
For 1a'			
1a' + HCl	0.0	0.0	0.0
Int-I-Cl-3Ph	0.4	1.0	2.3
Int-II-Cl-3Ph	7.3	6.2	5.8
TS-I-Cl-3Ph	16.5	19.3	14.7
TS-II-Cl-3Ph	19.7	23.4	16.4
ΔG^\ddagger (kcal/mol)	19.7	23.4	16.4
For 1b'			
1b' + HCl	0.0	0.0	0.0
Int-I-Cl-2Ph	-0.2	1.8	2.4

Int-II-Cl-2Ph	7.3	4.8	7.4
TS-I-Cl-2Ph	16.7	18.4	16.8
TS-II-Cl-2Ph	22.3	25.2	20.4
ΔG^\ddagger (kcal/mol)	22.5	25.2	20.4

Thermochemical data and absolute energy values

Boltzmann weighted G (G_{av}) were calculated with the *GoodVibes* program (option --pes) as:

$$G_{av} = \sum_i G_i \times p_i \quad (1)$$

where G_i is the relative Gibbs free energy of the corresponding conformers of a certain reaction step and p_i is the probability of each conformer calculated as:

$$p_i = \frac{e^{\frac{-G_i}{RT}}}{\sum_i \left(e^{\frac{-G_i}{RT}} \right)} \quad (2)$$

G values, including the energies of all the conformers of each reaction step, are detailed in a separate file included in the ESI. Also, the commands and options used by *GoodVibes* are represented in the same file.

Molecular coordinates

A separated xyz file containing all the geometries considered in this study is provided along with this ESI.

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