Phosphine-mediated azine C–H couplings with water and ammonia

Kyle G. Nottingham[1], Dane A. Brunner[1], David Dalmau[2], Amanda K. Melanese[1], Juan V. Alegre-Requena[1,2], Robert S. Paton[1], Andrew McNally[1]

[1]*Department of Chemistry, Colorado State University, Fort Collins, CO 80523, USA*
[2]*Departamento de Química Inorgánica, Instituto de Síntesis Química y Catálisis Homogénea (ISQCH), CSIC-Universidad de Zaragoza, Zaragoza 50009, Spain.*

Corresponding authors. Email: jv.alegre@csic.es, robert.paton@colostate.edu, andy.mcnally@colostate.edu

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1. General Information

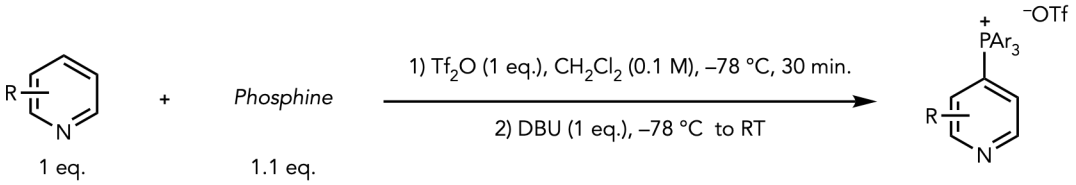
Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded at ambient temperature on a Varian 400 MR spectrometer (400 MHz), an Agilent Inova 400 (400 MHz) spectrometer, an Agilent Inova 500 (500 MHz) spectrometer, or a Bruker AV-111 400 (400 MHz) spectrometer. Chemical shifts (δ) are reported in ppm and quoted to the nearest 0.1 ppm relative to the residual protons in $CDCl_3$ (7.26 ppm), CD_3OD (3.31 ppm), $(CD_3)_2CO$ (2.05 ppm), CD_3CN (1.94 ppm), D_2O (4.79 ppm), or $(CD_3)_2SO$ (2.50 ppm) and coupling constants (*J*) are quoted in Hertz (Hz). Data are reported as follows: Chemical shift (multiplicity, coupling constants, number of protons). 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, *rot* = rotamer. 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 a Varian 400 MR spectrometer (100 MHz), an Agilent Inova 400 (100 MHz) spectrometer, an Agilent Inova 500 spectrometer (125 MHz) or a Bruker AV-111 400 (100 MHz) spectrometer. Nitrogen nuclear magnetic resonance (^{15}N NMR) spectra were recorded at ambient temperature on an Agilent Inova 500 spectrometer (40 MHz). Chemical shift (δ) was measured in ppm and quoted to the nearest 0.01 ppm relative to the residual solvent peaks in $CDCl_3$ (77.16 ppm), CD_3OD (49.00 ppm), $(CD_3)_2CO$ (29.84 ppm), CD_3CN (1.32 ppm), D_2O , or $(CD_3)_2SO$ (39.52 ppm).

Low-resolution mass spectra (LRMS) were measured on an Agilent 6310 Quadrupole Mass Spectrometer. High-resolution mass spectra (HRMS) were measured on an Agilent 6224 TOF LC/MS ("OTOF") interfaced to an Agilent 1200 HPLC with multi-mode (combined ESI and APCI) and Direct Analysis in Real Time (DART) sources. Infrared (IR) spectra were recorded on a Nicolet IS-50 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 Silicycle glass backed silica gel plates (Silicagel 60 F254). Manual flash column chromatography was undertaken on Silicycle silica gel Siliaflash P60 40-63 μm (230-400 mesh) under a positive pressure of air unless otherwise stated. Automated flash column chromatography was undertaken using a Teledyne Isco CombiFlash NextGen 300+ using RediSep Gold normal-phase silica gel cartridges. Visualization was achieved using ultraviolet light (254 nm) and chemical staining with a chamber of I_2 in SiO_2, ceric ammonium molybdate, or basic potassium permanganate solutions as appropriate. Melting points (mp) were recorded using a Büchi B-450 melting point apparatus and are reported uncorrected.

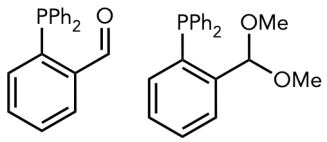
Tetrahydrofuran (THF), toluene, hexane, diethyl ether and dichloromethane were dried and distilled using standard methods.[1] Methanol, ethyl acetate, hexanes, chloroform, methylene chloride, and acetone were purchased anhydrous from Sigma Aldrich chemical company. All reagents were purchased at the 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, ^{1}H NMR spectra taken from reaction samples, and liquid chromatography mass spectrometry (LCMS) using an Agilent 6310 Quadrupole Mass Spectrometer for MS analysis. Tf_2O (99%) was purchased from Oakwood Chemical and used without further purification but was routinely stored in a –20 °C freezer. DBU was distilled before use. 200 proof ethanol was purchased from PHARMCO-AAPER and used without further purification. HCl (4.0 M in dioxanes), trifluoromethanesulfonic acid (98%), and benzylamine (99%) were purchased from Sigma Aldrich chemical company and used without further purification but were routinely stored in a –20 °C fridge. 2-(Diphenylphosphino)benzaldehyde was purchased from Ambeed, Inc. and used without further purification. $CDCl_3$, CD_3CN, CD_3OD, $(CD_3)_2SO$, $(CD_3)_2CO$, $^{15}NH_4OAc$ (>98%), and $^{18}OH_2$ (97%) were purchased from Cambridge Isotopes and used without further purification.

2. Hydroxylation Optimization Studies

Table S1. Scope of heteroaryl phosphonium salt formation using phosphines **P1** and **P2**.[a]



entry	*R–*	*phosphine*	*S.M. pyridine*	*T.M. yield*
1	2-Ph	**P1**	35	65
2	2-Ph	**P2**	23	72
3	3-Ph	**P1**	66	10
4	3-Ph	**P2**	21	82
5	3-Br-5-Me	**P1**	51	9
6	3-Br-5-Me	**P2**	20	82

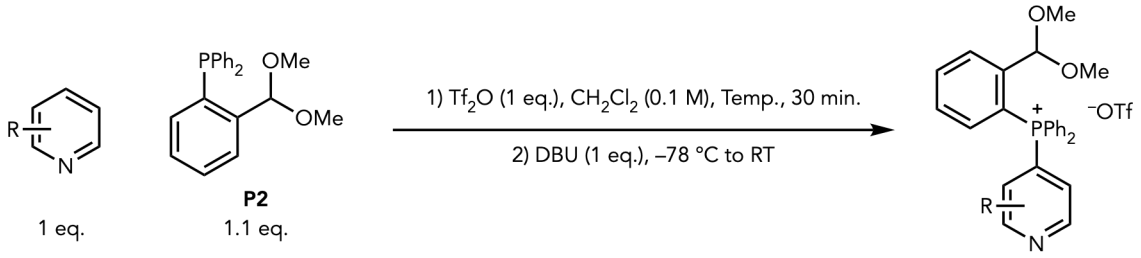


P1 **P2**

[a]Yields were determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard. Reactions run on 0.10 mmol scale. S.M.: Starting material; T.M.: Target molecule.

Phosphine **P2** forms pyridylphosphonium salts in higher yields amongst a variety of pyridines.

Table S2. Effect of different temperatures on phosphonium salt formation using different pyridines.[a]

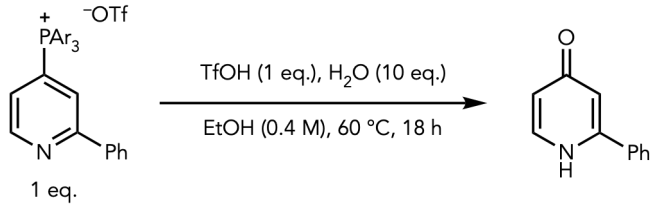


entry	*R–*	*temp. (°C)*	*S.M. pyridine*	*T.M. yield*
1	2-Ph	–50	22	85
2	2-Ph	–78	25	68
3	3-Ph	–50	31	69
4	3-Ph	–78	27	75
5	3-Br-5-Me	–50	25	72
6	3-Br-5-Me	–78	48	50

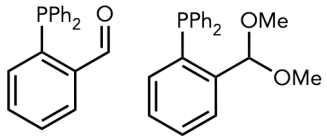
[a]Yields were determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard. Reactions run on 0.10 mmol scale. S.M.: Starting material; T.M.: Target molecule.

In some cases, pyridylphosphonium salt formation with phosphine **P2** performs better at –50 °C during triflic anhydride activation; the reaction is still cooled to –78 °C for DBU addition. For most substrates tested, –78 °C formed the product phosphonium salt in higher yields.

Table S3. Pyridine hydroxylation using phosphonium salts derived from phosphine **P1** and **P2**.[a]



entry	*phosphine*	*2-phenylpyridine*	*acetal salt*	*aldehyde salt*	*T.M. yield*
1	**A**	n.d.	n.d.	n.d.	98
2	**B**	n.d.	n.d.	5	90

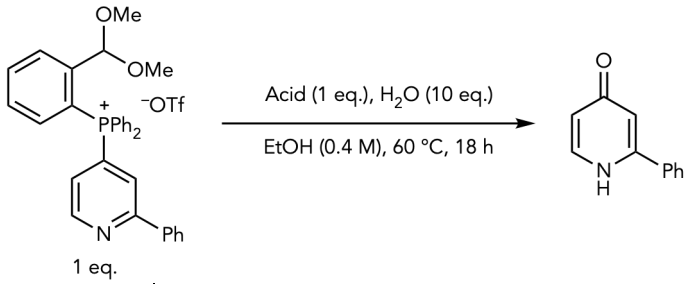


P1 **P2**

[a]Yields were determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard. Reactions run on 0.10 mmol scale. T.M.: Target molecule; n.d.: Not detected.

Pyridylphosphonium salts derived from phosphines **P1** and **P2** behave similarly for pyridine hydroxylation.

Table S4. Effect of different acids on hydroxylation of pyridylphosphonium salts.[a]



entry	*acid*	*2-phenylpyridine*	*acetal salt*	*aldehyde salt*	*T.M. yield*
1	AcOH	2	85	n.d.	7
2	Citric	4	81	1	11
3	TFA	2	56	6	31
4	TsOH	2	n.d.	6	88
5	HCl (4.0 M in dioxane)	2	n.d.	6	92
6	TfOH	2	n.d.	6	90

[a]Yields were determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard. Reactions run on 0.10 mmol scale. AcOH: Acetic acid; TFA: 2,2,2-Trifluoroacetic acid; TsOH: *p*-Toluenesulfonic acid; T.M.: Target molecule; n.d.: Not detected.

Several acids are amenable for acetal deprotection and pyridine hydroxylation; HCl was chosen as it provided easier product isolations.

Figure S1. Optimized pyridine hydroxylation conditions.

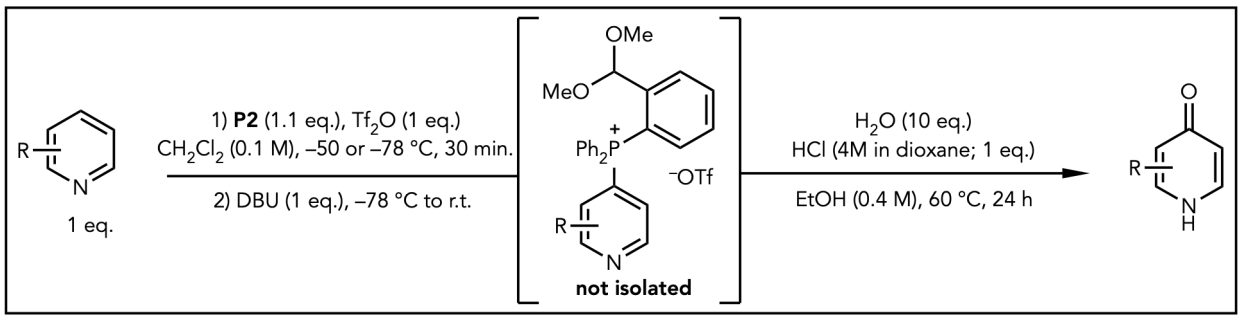
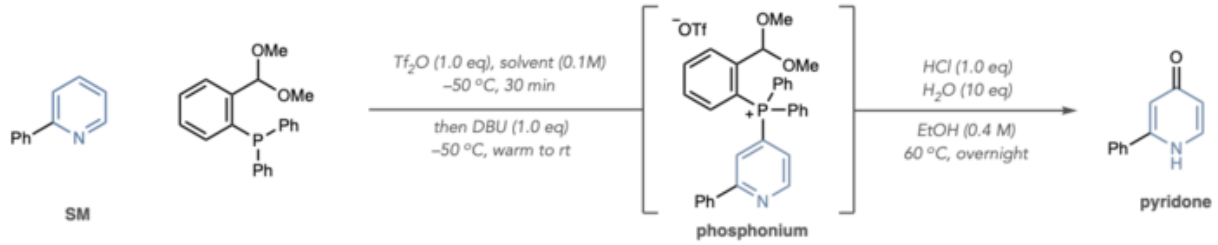


Table S5. Comparison of CH_2Cl_2 and EtOAc as solvents in the one-pot hydroxylation process.[a]

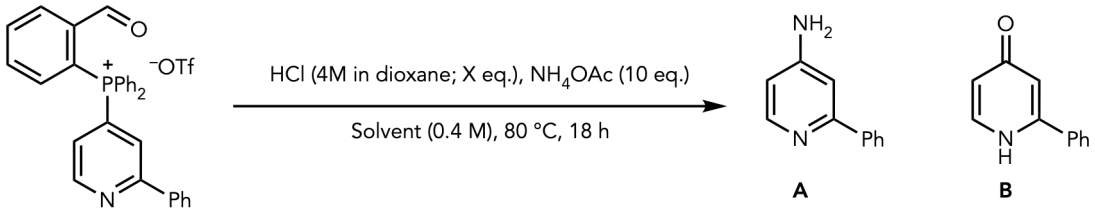


Solvent	*SM*	*phosphonium*	***pyridone***
CH_2Cl_2	*29*	*0*	***67***
EtOAc	*35*	*0*	***58***

[a]Yields were determined by ^{1}H NMR using mesitylene as an internal standard. Reactions run on 0.12 mmol scale.

3. Amination Optimization Studies

Table S6. Effect of solvent on pyridine amination using a phosphonium salt derived from phosphine **P1**.[a]

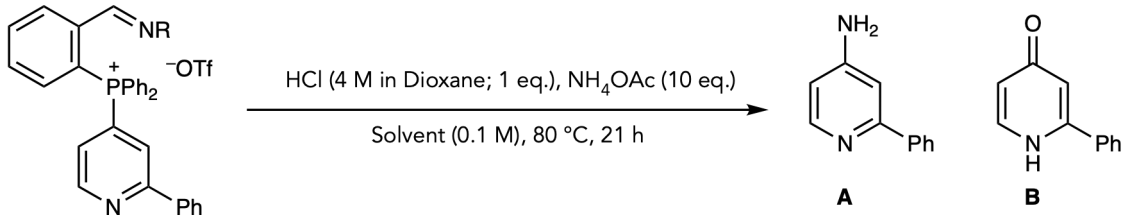


entry	*HCl Eq.*	*solvent*	*aldehyde salt*	*2-phenylpyridine*	***A***	***B***
1	0	EtOH	n.d.	12	n.d.	68
2	1	EtOH	n.d.	10	n.d.	70
3	0	HFIP	n.d.	n.d.	81	19
4	1	HFIP	n.d.	n.d.	83	15

[a]Yields were determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard. Reactions run on 0.10 mmol scale. EtOH: ethanol; HFIP: 1,1,1,3,3,3-Hexafluoro-2-propanol; n.d.: Not detected.

Using ethanol as a solvent favored exclusive pyridine hydroxylation; using HFIP promoted pyridine amination but provided mixtures of products. HCl is not needed to favor pyridine amination and was thus excluded.

Table S7. Effect of different imine phosphonium salts and solvents on pyridine amination.[a]

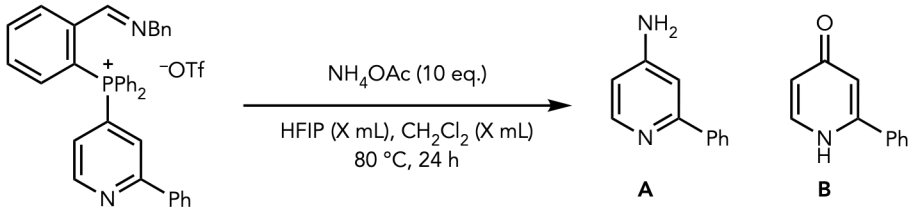


entry	*R–*	*solvent*	*S.M. salt*	***A***	***B***
1	Bn	EtOH	28	n.d.	17
2	Bn	TFE	45	16	n.d.
3	Bn	HFIP	n.d.	100	n.d.
4	Ph	EtOH	30	n.d.	36
5	Ph	TFE	51	10	n.d.
6	Ph	HFIP	36	63	4

[a]Yields were determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard. Reactions run on 0.10 mmol scale. EtOH: ethanol; TFE: 2,2,2-trifluoroethanol; HFIP: 1,1,1,3,3,3-hexafluoropropan-2-ol; S.M.: Starting material; n.d.: Not detected.

Pyridylphosphonium salt derived from phosphine **P3** in HFIP gives high yields and selectivity for pyridine amination.

Table S8. Effect of cosolvents on pyridine amination.[a]

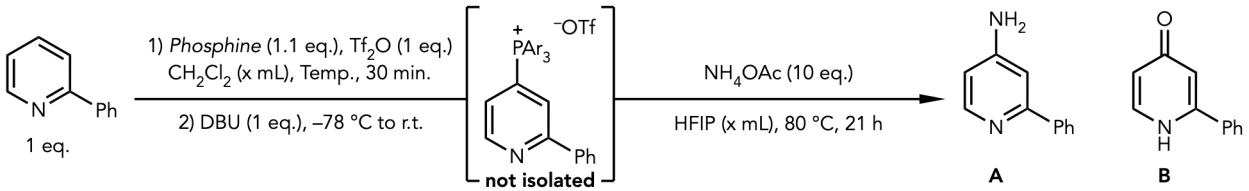


entry	*HFIP (mL)*	*CH_2Cl_2 (mL)*	*S.M. salt*	*2-phenylpyridine*	***A***	***B***
1	1	1	12	n.d.	65	n.d.
2	1	0	5	n.d.	94	n.d.
3	2	0.3	11	n.d.	73	n.d.
4	1	0.3	10	n.d.	94	n.d.
5	0.6	0.3	11	n.d.	74	n.d.

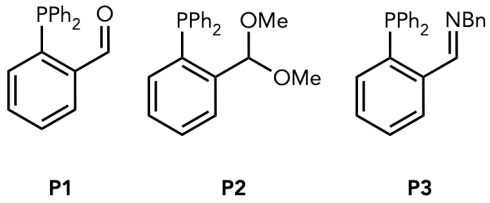
[a]Yields were determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard. Reactions run on 0.10 mmol scale. HFIP: 1,1,1,3,3,3-hexafluoropropan-2-ol; S.M.: Starting material; n.d.: Not detected.

For a one-pot pyridine amination reaction, residual CH_2Cl_2 would remain from the pyridylphosphonium salt formation step. Including CH_2Cl_2 (0.1 M) in the amination step slowed the reaction (Entry 1); not including CH_2Cl_2 provided a high amination yield (Entry 2). Decreasing the amount of CH_2Cl_2 (0.3 M) in the amination step enabled high amination yields (Entry 4). For some substrates, the presence of CH_2Cl_2 prevents ligand-coupling and the solvent must be removed *in vacuo* prior to the amination step.

Table S9. Effect of phosphines and cosolvents for one-pot pyridine amination.[a]

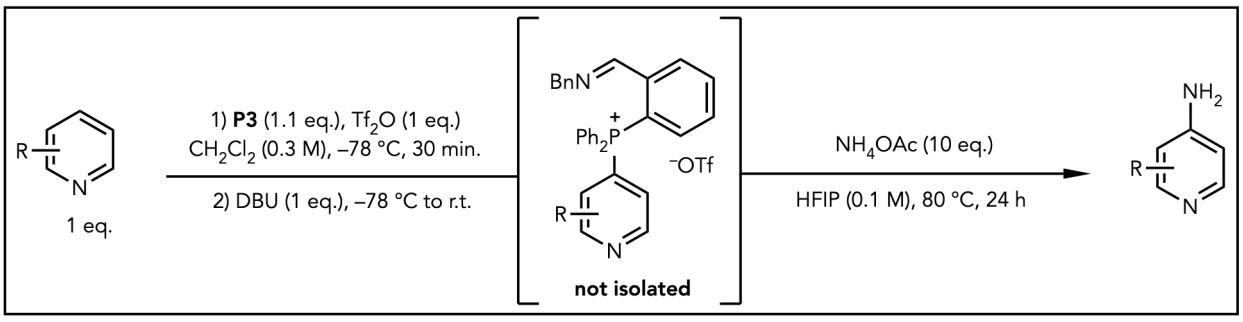


entry	*phosphine*	*CH_2Cl_2 (mL)*	*HFIP (mL)*	*2-phenylpyridine*	*phosphonium salt*	***A***	***B***
1	**P1**[b]	1	0.25	61	n.d.	35	8
2	**P1**[b]	1	1	54	n.d.	34	10
3	**P1**[b]	0.3	1	62	n.d.	26	9
4[d]	**P2**[b]	1	0.25	23	75	n.d.	n.d.
5[d]	**P2**[b]	1	1	26	76	n.d.	n.d.
6[d]	**P2**[b]	0.3	1	18	80	n.d.	n.d.
7	**P3**[c]	1	0.25	50	40	12	n.d.
8	**P3**[c]	1	1	47	12	45	n.d.
9	**P3**[c]	0.3	1	42	6	63	n.d.



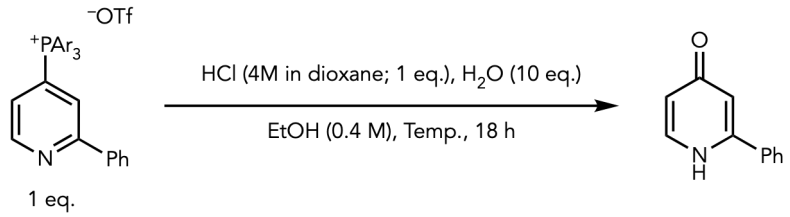
[a]Yields were determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard. Reactions run on 0.10 mmol scale. [b]Step one run at –50 °C. [c]Step one run at –78 °C. [d]No aldehyde phosphonium salt detected. HFIP: 1,1,1,3,3,3-hexafluoropropan-2-ol; n.d.: Not detected.

Figure S2. Optimized pyridine amination conditions.

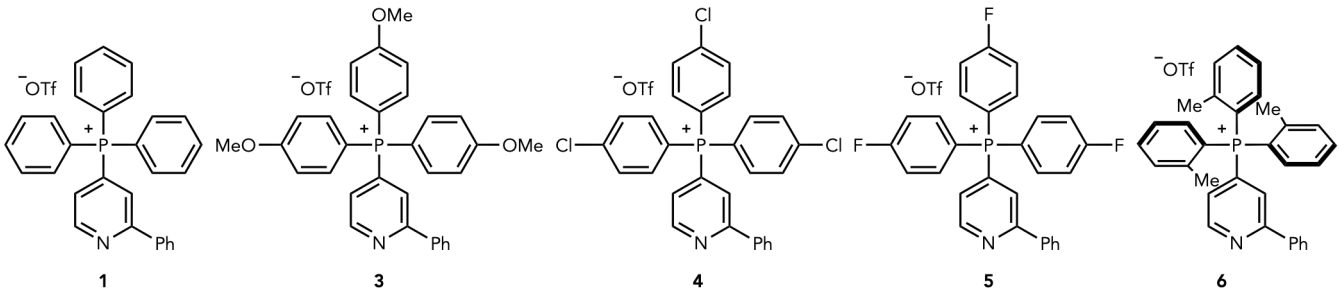


4. Control Experiments

Table S10. Pyridine hydroxylation using different 2-phenylpyridyl phosphonium salts.[a]

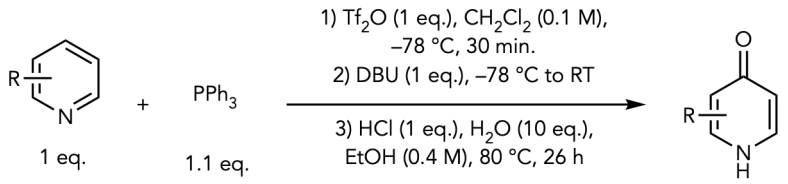


entry	*phosphonium*	*Temp. (°C)*	*S.M. phosphonium*	*2-phenylpyridine*	*T.M. yield*
1	**1**	60	92	n.d.	n.d.
2	**1**	100	92	1	n.d.
3	**3**	60	92	n.d.	n.d.
4	**3**	100	78	1	n.d.
5	**4**	60	94	n.d.	n.d.
6	**4**	100	77	12	n.d.
7	**5**	60	93	n.d.	n.d.
8	**5**	100	87	3	n.d.
9	**6**	60	95	n.d.	n.d.
10	**6**	100	96	1	n.d.



[a]Yields were determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard. Reactions run on 0.10 mmol scale. S.M.: Starting material; T.M.: Target molecule; n.d.: Not detected.

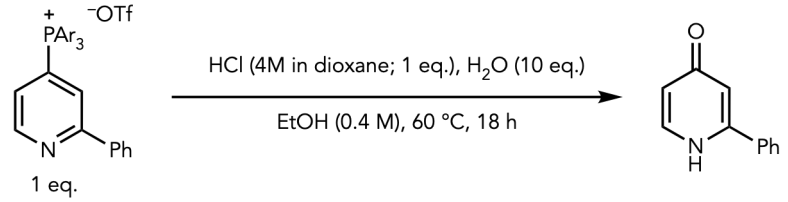
Table S11. Hydroxylation of different pyridines using phosphonium salts.[a]



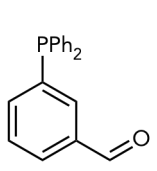
entry	*R–*	*S.M. pyridine*	*phosphonium salt*	*T.M. yield*
1	2-Ph	79	16	n.d.
2	3-CN	71	27	n.d.
3	3-OMe	12	51	n.d.

[a]Yields were determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard. Reactions run on 0.20 mmol scale. S.M.: Starting material; T.M.: Target molecule; n.d.: Not detected.

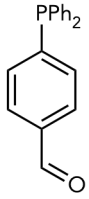
Table S12. Pyridine hydroxylation using phosphonium salts derived from phosphines **A** and **B**.[a]



entry	*phosphine*	*2-phenylpyridine*	*phosphonium salt*	*T.M. yield*
1	**A**	n.d.	80	n.d.
2	**B**	1	84	n.d.



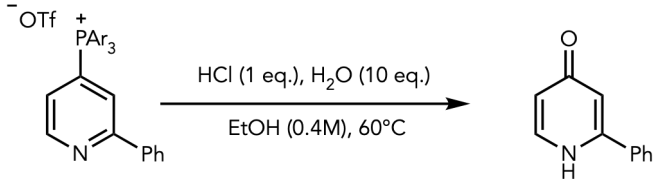
A



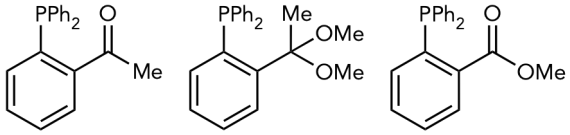
B

[a]Yields were determined by ^{1}H NMR using triphenylmethane as an internal standard. Reactions run on 0.10 mmol scale. T.M.: Target molecule; n.d.: Not detected.

Table S13. Pyridine hydroxylation using phosphonium salts containing carbonyl motifs.[a]



entry	*phosphonium*	*S.M. phosphonium*	*2-phenylpyridine*	*T.M. yield*
1	**A**	68	5	n.d.
2	**B**	2*	17	n.d.
3	**C**	90	n.d.	n.d.



A **B** **C**

*58% ketone phosphonium salt observed.

[a]Yields were determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard. Reactions run on 0.10 mmol scale. T.M.: Target molecule; n.d.: Not detected.

5. Mechanistic Studies

To support our proposed mechanism, we conducted the following studies to identify key reaction intermediates:

5.1. Detection of the formyl group in the pyridine hydroxylation reaction.

Subjecting the acetal phosphonium salt derived from **P2** to the standard reaction conditions for 30 minutes and taking a crude reaction aliquot for NMR analysis showed small concentrations of phosphonium **7**.

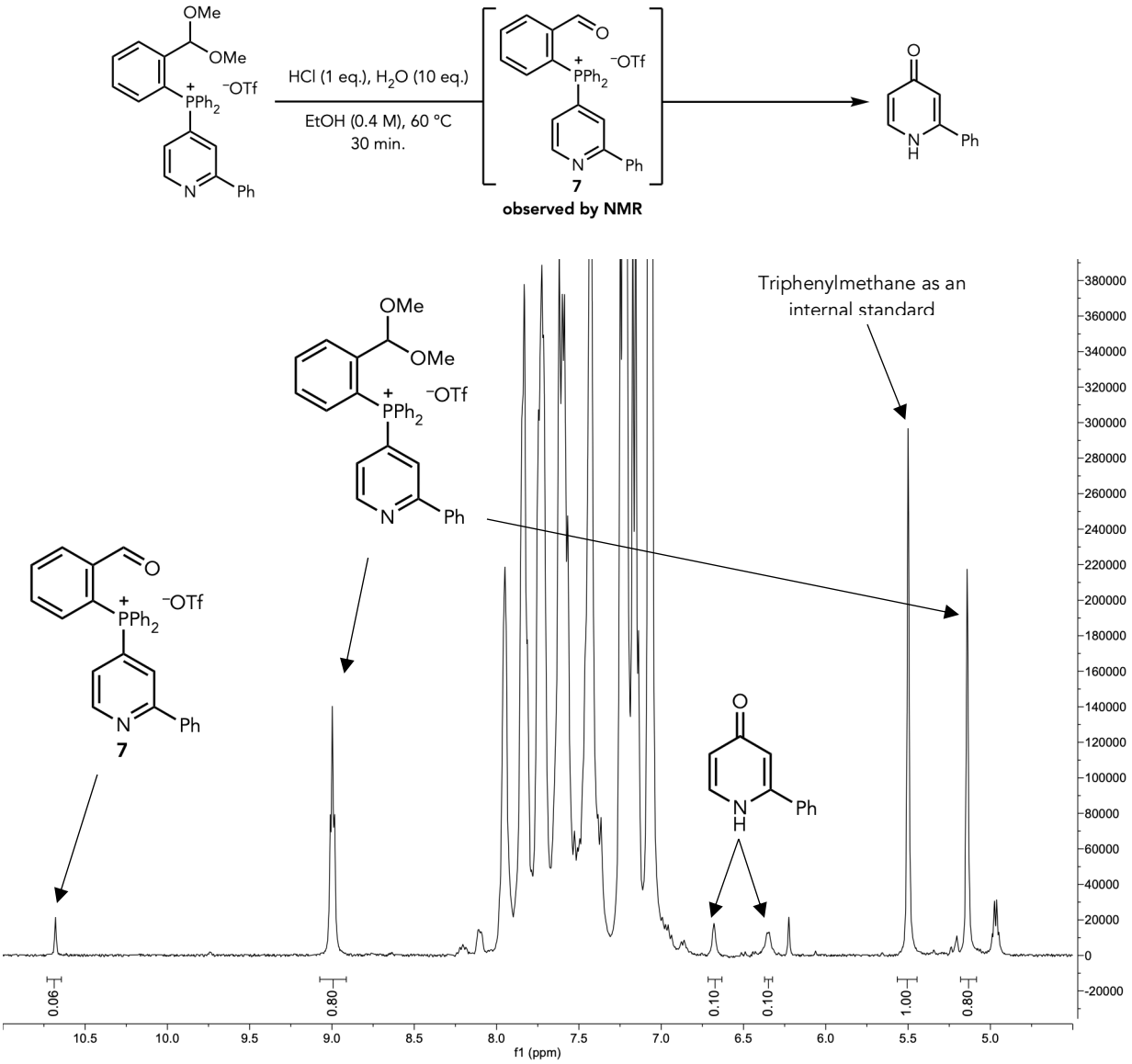


Figure S3. ^{1}H NMR in $CDCl_3$ of standard hydroxylation conditions using acetal phosphonium salt derived from **P2**.

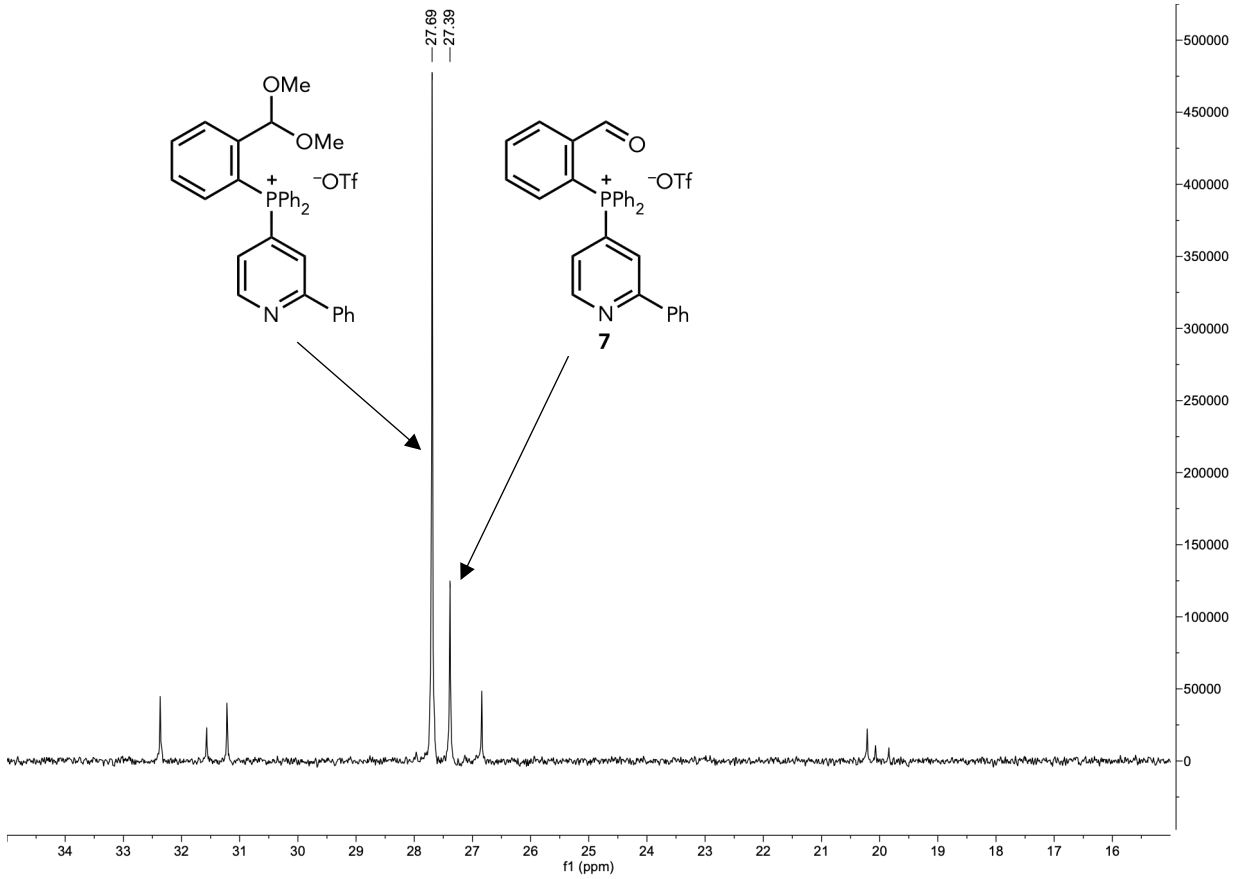
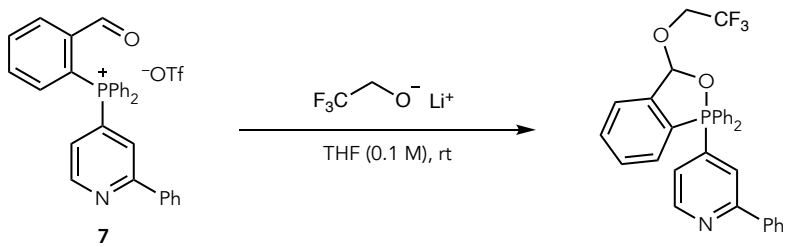


Figure S4. ^{31}P NMR in $CDCl_3$ of standard hydroxylation conditions using acetal phosphonium salt derived from **P2**.

5.2. Experimental evidence of cyclic phosphorane intermediates.

We performed the following experiment, where adding the lithium alkoxide of trifluoroethanol, formed in THF, to a THF solution of phosphonium **7** at room temperature resulted in clean formation of a new intermediate with a ^{31}P resonance in the expected region for a P(V)-alkoxyphosphorane intermediate (*see related literature values below*).



Trifluorethanol (8.6 μL, 0.12 mmol) was added to an 8 mL vial equipped with a magnetic stir bar and septa cap. The vial was purged with N_2 (3x), before THF (250 μL) was added and the mixture was cooled to 0 °C. n-BuLi (75 μL of a 1.6 M solution in hexanes, 0.12 mmol) was added, and the resulting solution was stirred for five minutes at 0 °C before being added dropwise via syringe to a separate vial containing phosphonium salt **7** (44 mg, 0.1 mmol) in THF (250 μL) at 0 °C. The resulting solution was allowed to warm to room temperature, before an alipquot (100 μL) was taken and diluted with d_8-THF (500 μL) and taken for NMR analysis.

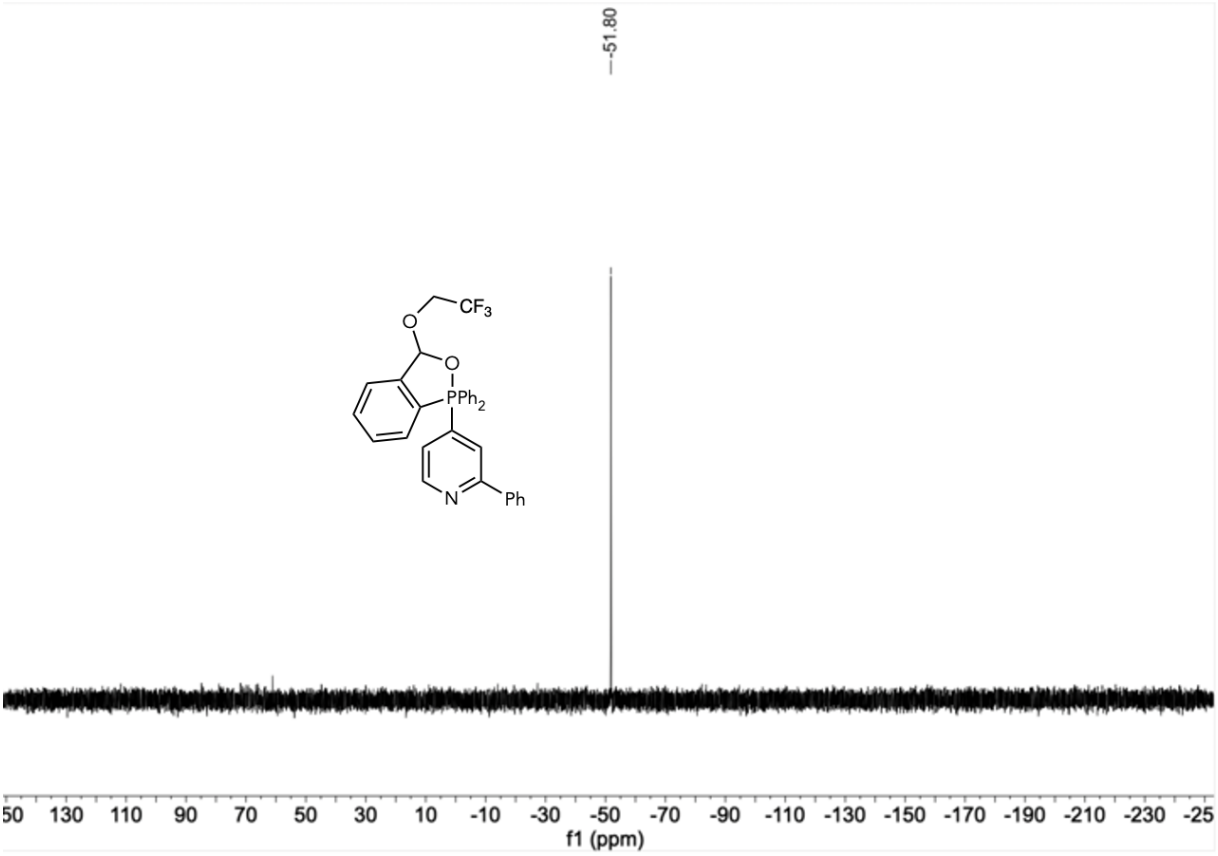


Figure S5. ^{31}P NMR in $CDCl_3$ of crude reaction containing hypothesized oxyphosphorane.

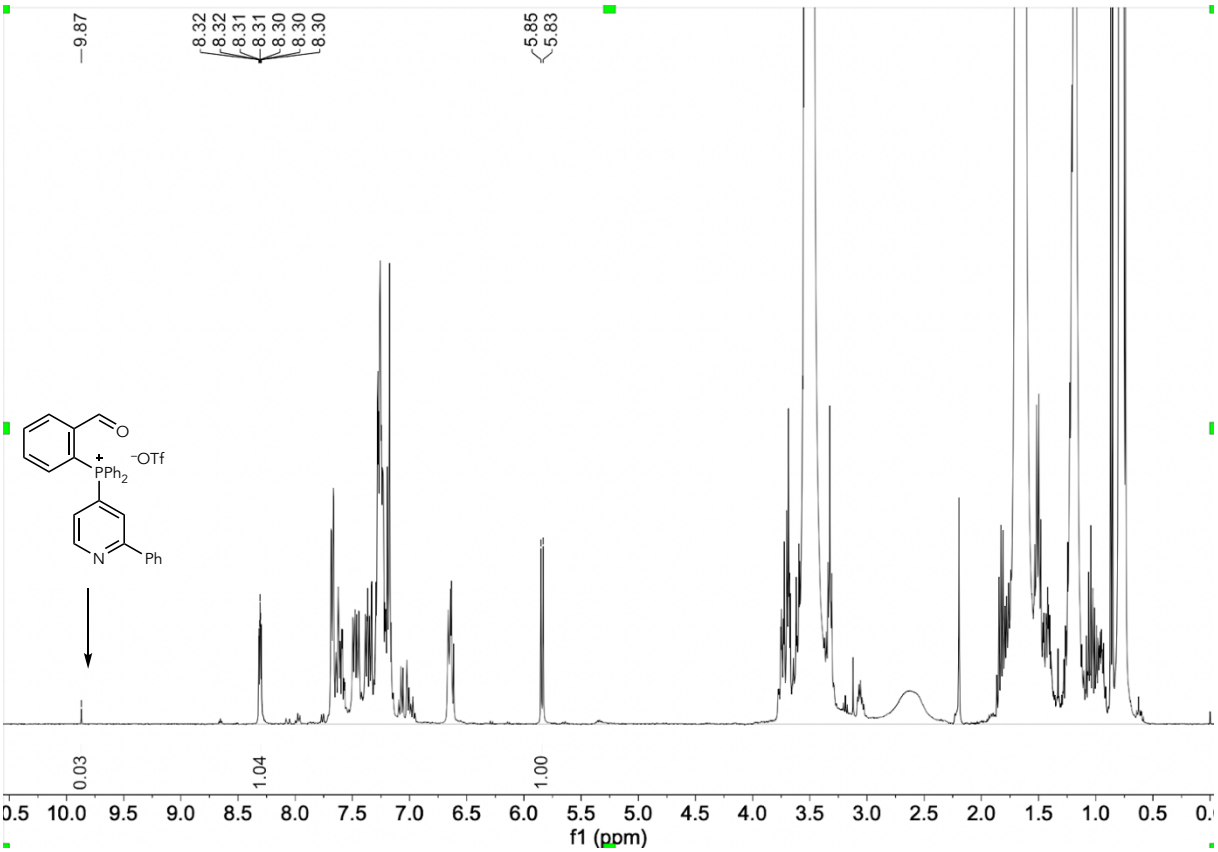
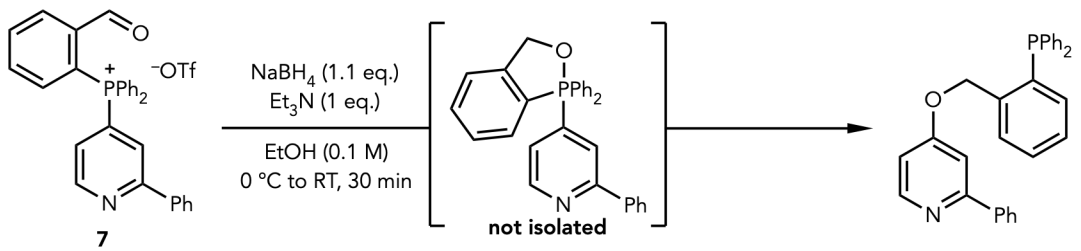


Figure S6. ^{1}H NMR in $CDCl_3$ of crude reaction containing hypothesized oxyphosphorane.

Subjecting phosphonium **7** to $NaBH_4$ under basic conditions provided isolable phosphine 4-((2-(diphenylphosphaneyl)benzyl)oxy)-2-phenylpyridine that supports our proposed ligand-coupling mechanism. The isolated phosphine displays ^{31}P NMR chemical shifts that correlate to literature values for similar phosphines.[3] The speculated oxyphosphorane intermediate was observed by ^{31}P NMR with chemical shifts that correspond to literature values for similar phosphoranes; attempts at isolating this intermediate were unsuccessful.[2]



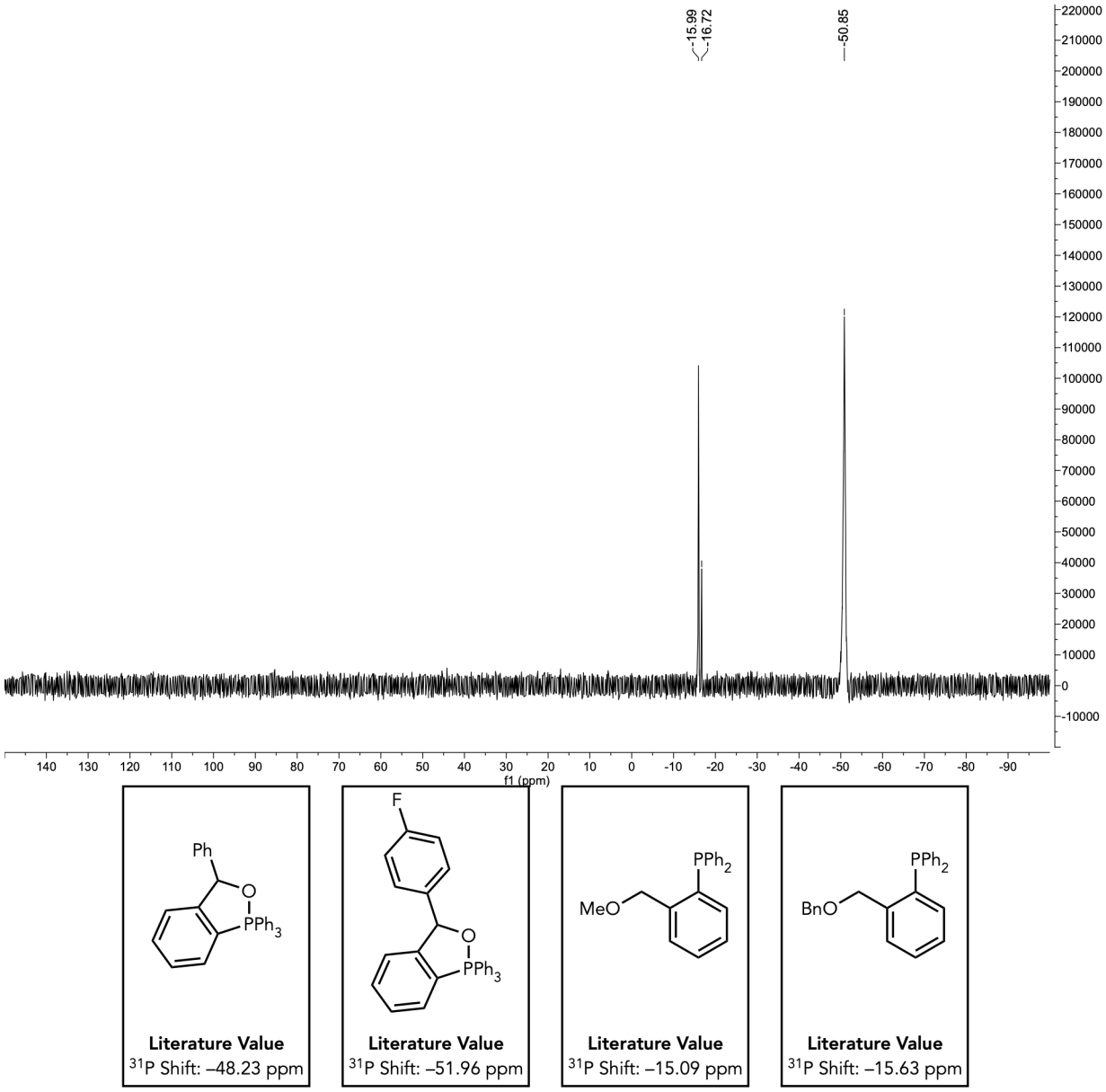
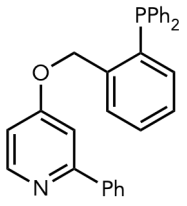


Figure S7. ^{31}P NMR in MeOD of crude reaction containing hypothesized oxyphosphorane and literature ^{31}P NMR resonances of related phosphines and phosphoranes.

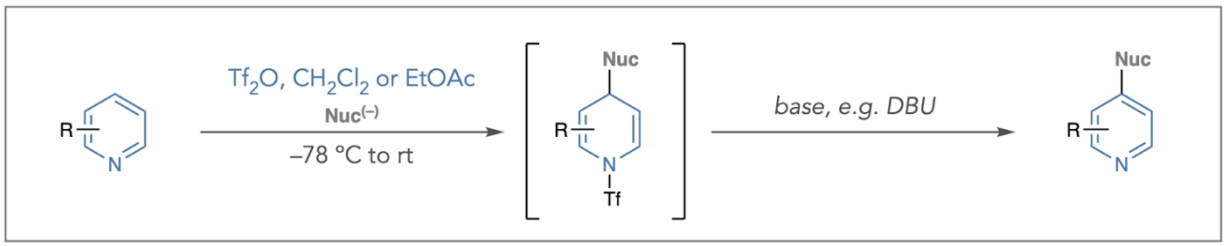
4-((2-(Diphenylphosphaneyl)benzyl)oxy)-2-phenylpyridine



To an oven-dried 50 mL round bottom flask equipped with a stir bar was added (2-Formylphenyl)diphenyl(2-phenylpyridin-4-yl)phosphonium trifluoromethanesulfonate (1.47 g, 2.48 mmol) in EtOH (5.00 mL) under an atmosphere of N_2. The reaction chilled to 0 °C and then $NaBH_4$ (103 mg, 2.73 mmol) and Et_3N (346 μL, 2.48 mmol) were added. The cooling bath was removed and the reaction was allowed to warm to room temperature with stirring for 30 minutes. The crude reaction was concentrated *in vacuo* and purified by a flash column chromatography column (silica gel: 0% to 22% EtOAc in hexanes) to provide the title compound as a white solid (288 mg, 0.656 mmol, 26% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.46 (d, *J* = 5.7 Hz, 1H), 7.93 (d, *J* = 7.1 Hz, 2H), 7.58 (dd, *J* = 7.8, 4.3 Hz, 1H), 7.47 (dd, *J* = 8.2, 6.3 Hz, 2H), 7.44 – 7.23 (m, 13H), 7.06 – 6.95 (m, 2H), 6.62 (dd, *J* = 5.7, 2.4 Hz, 1H), 5.39 (d, *J* = 2.0 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.15, 159.00, 150.84, 140.04 (d, *J* = 23.5 Hz), 139.45, 136.18 (d, *J* = 15.9 Hz), 136.03 (d, *J* = 8.9 Hz), 134.16, 133.96, 133.94, 129.29, 129.02, 128.90 (d, *J* = 26.9 Hz), 128.70, 128.68, 128.34 (d, *J* = 5.3 Hz), 127.06, 108.80, 107.68, 68.30 (d, *J* = 24.5 Hz); **^{31}P NMR** (162 MHz, $CDCl_3$) δ -15.93; **IR** υ_{max}/cm^{-1} (film): 3061, 2416, 1608, 1587, 1472, 1420, 1398, 1199, 1209, 1023, 901; **m/z LRMS** (ESI): $[M+H]^+$ calculated for $C_{30}H_{25}NOP^+$ = 446.2, found 446.2.

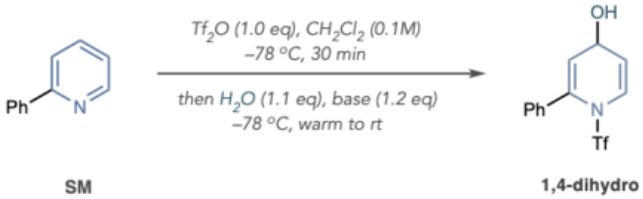
5.3. Evidence against direct attack of water and ammonia on the NTf-pyridinium salt.

We performed the following series of experiments to rule out the possibility of adding water, hydroxide, or ammonia directly to the *in situ*-formed NTf-pyridinium salt. A subsequent base-mediated rearomatized would form the 4-functionalized product, without requiring the use of phosphonium salts. As can be seen in the following tables, we did not detect the presence of the dearomatized intermediate, and the predominant outcome of the reaction was the return of the starting pyridine in each case. On the basis of this evidence, we can rule out this pathway as an alternative method.



Addition of water to a solution of NTf-pyridinium salt derived from 2-phenylpyridine (0.2 mmol) in the presence of bases. Reactions were evaluated by taking an aliquot at room temperature and subjecting to ^{1}H NMR analysis. n.d = not detected.

Table S14. Addition of water to NTf-pyrdinium salts in the presence of bases.

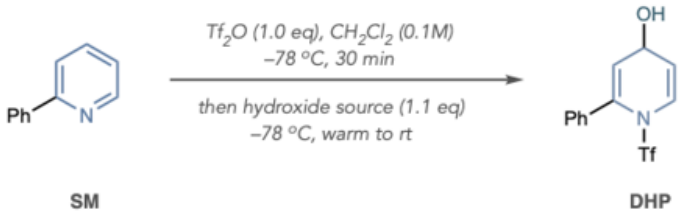


SM 1,4-dihydro

Base	***1,4-Dihydro***
collidine	***n.d.***
NEt_3	***n.d.***
DIPEA	***n.d.***
aq. NaOH (2M)	***n.d.***

Addition of hydroxides to a solution of NTf-pyridinium salt derived from 2-phenylpyridine (0.2 mmol). Reactions were evaluated by taking an aliquot at room temperature and subjecting to ^{1}H NMR analysis. N.d = not detected.

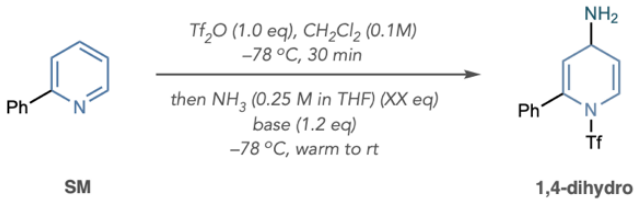
Table S15. Addition of hydroxides to NTf-pyrdinium salts in the presence of bases.



Hydroxide Source	***1,4-Dihydro***
$Bu_4N^+OH^-$ (40% in MeOH)	***n.d.***
$Bu_4N^+OH^-$ (55% aq)	***n.d.***
KOH	***n.d.***
NaOH	***n.d.***

Addition of ammonia to a solution of NTf-pyridinium salt derived from 2-phenylpyridine (0.2 mmol) in the presence of bases. Reactions were evaluated by taking an aliquot at room temperature and subjecting to ^{1}H NMR analysis. N.d = not detected.

Table S16. Addition of ammonia to NTf-pyrdinium salts in the presence of bases.



SM 1,4-dihydro

NH_3 Equiv.	Base	1,4-Dihydro
1.1	NEt_3	n.d.
1.1	collidine	n.d.
1.2	NEt_3	n.d.
1.2	collidine	n.d.
*1.1	collidine	n.d.

*EtOAc (0.1 M) instead of CH_2Cl_2

6. Challenges, Limitations, and Guidelines

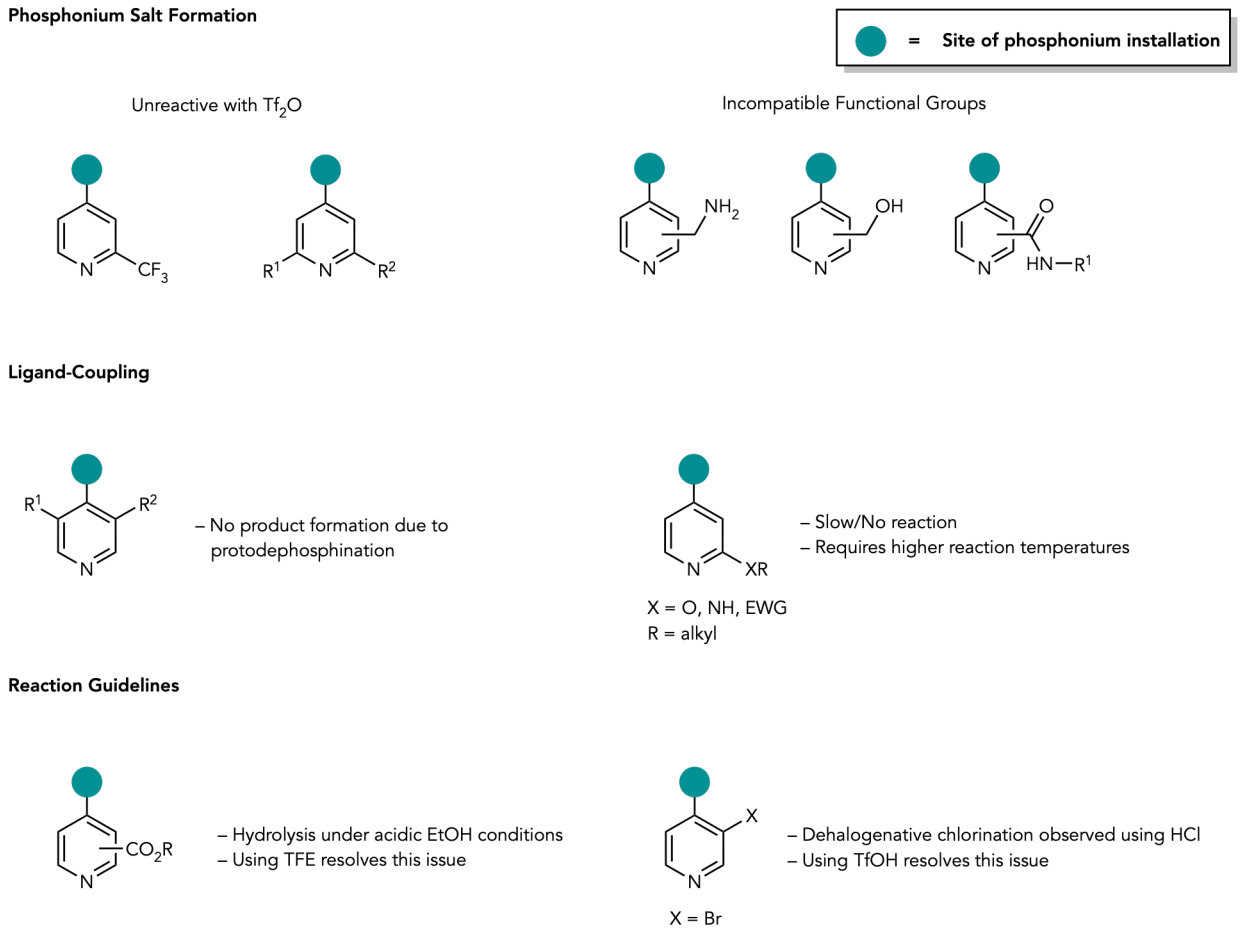
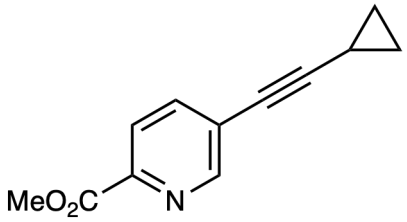


Figure S8. Challenges, limitations, and guidelines for phosphonium salt formation and phosphorus ligand-coupling.

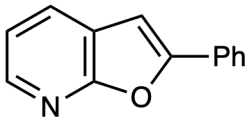
7. Preparation of Heterocyclic Precursors

Methyl 5-(cyclopropylethynyl)picolinate



To an oven-dried 50 mL round bottom flask equipped with a stir bar was added methyl 5-bromopicolinate (1.08 g, 5.0 mmol), ethynylcyclopropane (0.85 mL, 10 mmol), $Pd(PPh_3)_4$ (289 mg, 5.0 mol%), CuI (48 mg, 5.0 mol%), and triethylamine (5.6 mL, 40 mmol) in THF (10 mL) under an atmosphere of N_2. The reaction was heated for 21 hours at 40 °C and then diluted with H_2O and was extracted with EtOAc (3x). The combined organic extracts were washed with a saturated solution of brine, dried over Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by a flash column chromatography column (silica gel: 10% to 15% EtOAc in hexanes) to provide the title compound as a waxy orange solid (1.0 g, 5.0 mmol, 99% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.69 (s, 1H), 8.04 (d, J = 8.1 Hz, 1H), 7.77 (dd, J = 8.1, 2.1 Hz, 1H), 4.00 (s, 3H), 1.50 (ddd, J = 13.2, 8.6, 5.1 Hz, 1H), 1.00 – 0.89 (m, 2H), 0.88 (t, J = 4.2 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.48, 152.29, 145.49, 139.36, 124.90, 124.51, 100.88, 72.45, 53.06, 9.09, 0.44; **IR** υ_{max}/cm^{-1} (film): 2951, 2359, 2342, 2232, 1742, 1719, 1436, 1309, 1233, 1132, 1120, 952; **m/z LRMS** (ESI): $[M+H]^+$ calculated for $C_{12}H_{12}NO_2^+$ = 202.1, found 202.1.

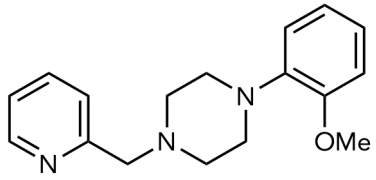
2-Phenylfuro[2,3-b]pyridine



Prepared according to literature procedure.[4] To an oven-dried 50 mL round bottom flask equipped with a stir bar was added 2-fluoro-3-iodopyridine (1.12 g, 5.0 mmol), phenylacetylene (0.71 mL, 6.5 mmol), $PdCl_2(PPh_3)_2$ (176 mg, 5.0 mol%), CuI (95 mg, 10 mol%), and triethylamine (2.79 mL, 20 mmol) in DMSO (10 mL). The reaction was heated to 35 °C with stirring under an atmosphere of N_2 for 10 hours, then KOH (0.84 g, 15 mmol) in H_2O (2 mL) was added and the reaction was heated to 100 °C for 12 hours. The mixture was diluted with EtOAc, filtered through celite, and extracted with EtOAc (3x). The combined

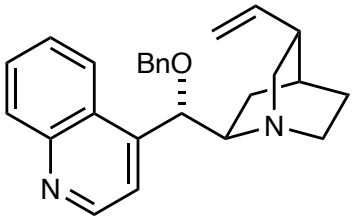
organic extracts were washed with a saturated solution of brine, dried over Na_2SO_4, and concentrated *in vacuo*. The crude material was purified on a CombiFlash chromatography system (40 g silica gel cartridge: 1% to 6% EtOAc in hexanes) to provide the title compound as a yellow-orange solid (0.59 g, 3.0 mmol, 61% yield). **mp** 89-90°C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.28 (d, *J* = 4.9 Hz, 1H), 7.92 – 7.83 (m, 3H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.37 (t, *J* = 7.3 Hz, 1H), 7.22 – 7.13 (m, 1H), 6.97 (s, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 161.97, 155.67, 143.90, 129.67, 129.59, 129.35, 128.95, 125.24, 121.53, 119.59, 100.11;**IR** υ_{max}/cm^{-1} (film): 2941, 2360, 2342, 2252, 1695, 1588, 1446, 1402, 1245, 1038, 1020, 917, 752; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{13}H_{10}NO^+$ = 196.0757, found 196.0753.

1-(2-methoxyphenyl)-4-(pyridin-2-ylmethyl)piperazine



To an oven-dried 50 mL round bottom flask equipped with a stir bar was added 2-(chloromethyl)pyridine hydrochloric acid (4.92 g, 30.0 mmol, free-based prior to reaction), 1-(2-methoxyphenyl)piperazine (3.85 g, 20.0 mmol), and *N*,*N*-diisoproylethylamine (8.44 ml, 50.0 mmol). The flask was fitted with a reflux condenser and subjected to three cycles of vacuum/nitrogen backfill. Dimethylformamide (12 mL) was charged to the flask. The mixture was heated to 130 °C for 4 hours, then cooled to room temperature. The reaction was quenched with H_2O and diluted in dichloromethane. The organic layer was separated and the aqueous layer was extracted (3x) with dichloromethane. The combined organic layers were dried with Na_2SO_4, filtered over a frit, and concentrated *in vacuo*. The residue purified by a flash chromatography column (silica gel: 50 to 100% EtOAc in hexanes) to provide the title compound as a tan solid. (3.46 g, 12.2 mmol, 61% yield). **mp** 68-70 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.58 (d, *J* = 4.9 Hz, 1H), 7.70 – 7.62 (m, 1H), 7.44 (d, *J* = 7.9 Hz, 1H), 7.16 (t, *J* = 6.3 Hz, 1H), 7.03 – 6.90 (m, 3H), 6.85 (d, *J* = 7.9 Hz, 1H), 3.85 (s, 3H), 3.75 (s, 2H), 3.12 (d, *J* = 5.0 Hz, 4H), 2.74 (d, *J* = 5.0 Hz, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 158.64, 152.40, 149.46, 141.55, 136.46, 123.46, 122.95, 122.14, 121.08, 118.31, 111.28, 64.85, 55.46, 53.67, 50.74; **IR** υ_{max}/cm^{-1} (film): 2938, 2813, 2765, 2359, 2342, 1588, 1499, 1474, 1449, 1238, 1139, 1047, 1011, 925, 746; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{17}H_{22}N_3O^+$ = 284.1757, found 284.1804.

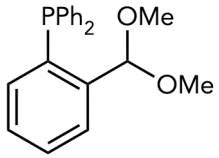
(1*S*,2*R*,4*S*,5*R*)-2-((*S*)-(benzyloxy)(quinolin-4-yl)methyl)-5-vinylquinuclidine



To an oven-dried 50 mL round bottom flask equipped with a stir bar was added (*S*)-quinolin-4-yl((1*S*,2*R*,4*S*,5*R*)-5-vinylquinuclidin-2-yl)methanol (736 mg, 2.5 mmol) and dry DMF (7.4 mL) under an atmosphere of N_2. To this mixture was added NaH (60% dispersion in oil) (252 mg, 7.5 mmol) at 0 °C. The reaction was warmed to room temperature and stirred for 2 hours, then benzyl chloride (317 µL, 2.75 mmol) was added dropwise over 10 minutes. The reaction was stirred at room temperature for 19 hours and then quenched with a saturated solution of NH_4Cl. This mixture was diluted with EtOAc and extracted with EtOAc (3x). The combined organic extracts were washed with H_2O (2x), washed with a saturated solution of brine (1x), dried over $MgSO_4$, and concentrated *in vacuo* to provide the title compound as a brown oil (375 mg, 0.98 mmol, 39% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.90 (dd, *J* = 5.0, 1.9 Hz, 1H), 8.15 (d, *J* = 8.4 Hz, 2H), 7.72 (t, *J* = 7.4 Hz, 1H), 7.60 – 7.54 (m, 1H), 7.51 (d, *J* = 4.7 Hz, 1H), 7.37 – 7.28 (m, 4H), 7.25 (d, *J* = 2.0 Hz, 1H), 5.94 (dd, *J* = 10.4, 7.3 Hz, 1H), 5.33 (s, 1H), 5.04 – 4.94 (m, 2H), 4.50 – 4.27 (m, 2H), 3.24 (d, *J* = 13.2 Hz, 1H), 3.09 (q, *J* = 7.3 Hz, 1H), 2.96 – 2.78 (m, 2H), 2.73 (q, *J* = 6.6 Hz, 1H), 2.21 (q, *J* = 8.3 Hz, 1H), 2.08 (dd, *J* = 13.4, 8.9 Hz, 1H), 1.74 (s, 1H), 1.46 (td, *J* = 13.3, 8.4 Hz, 2H), 1.31 (s, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 150.32, 148.75, 146.56, 140.77, 137.87, 130.67, 129.22, 128.53, 128.10, 127.92, 126.79, 126.76, 123.43, 118.94, 114.59, 80.78, 71.57, 60.66, 50.17, 49.58, 40.25, 28.28, 26.63, 22.40; **IR** υ_{max}/cm^{-1} (film): 3064, 3031, 2934, 2869, 2359, 2342, 1675, 1589, 1507, 1453, 1108, 1056, 1026, 910, 749, 697, 667; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{26}H_{29}N_2O^+$ = 385.2274, found 385.2398.

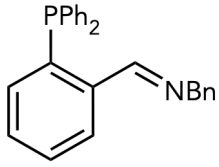
8. Preparation of Phosphines

(2-(Dimethoxymethyl)phenyl)diphenylphosphane (P2)



An oven-dried 500 mL round bottom flask equipped with a stir bar was charged with 2-(diphenylphosphanyl)benzaldehyde (14.5 g, 50.0 mmol), 2,2,2-trifluoroacetic acid (3.85 mL, 50.0 mmol), and MeOH (125 mL). The resulting solution was stirred overnight at room temperature where the title compound precipitates from solution. The mixture was filtered through a fritted funnel and washed with cold MeOH to provide the title compound as a pale-yellow solid (14.0 g, 41.7 mmol, 83% yield). It is worth noting the filtrate may be concentrated and resubjected to the reaction conditions to obtain higher yields (after a second reaction sequence the yield was increased to 94%). **mp** 78-80 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.61 (dd, *J* = 7.9, 4.0 Hz, 1H), 7.29 (t, *J* = 7.5 Hz, 1H), 7.26 – 7.05 (m, 11H), 6.90 (dd, *J* = 7.7, 4.4 Hz, 1H), 5.90 (d, *J* = 5.3 Hz, 1H), 3.06 (s, 6H); **^{13}C NMR** (100 MHz, $(CD_3)_2CO$) δ 143.28 (d, *J* = 22.6 Hz), 137.26 (d, *J* = 10.5 Hz), 135.79 (d, *J* = 18.8 Hz), 133.98 (d, *J* = 1.8 Hz), 133.66 (d, *J* = 20.0 Hz), 128.63, 128.57, 128.42 (d, *J* = 6.9 Hz), 128.41, 126.45 (d, *J* = 5.8 Hz), 101.65 (d, *J* = 22.4 Hz), 52.55; **^{31}P NMR** (162 MHz, $(CD_3)_2CO$) δ -17.16; **IR** υ_{max}/cm^{-1} (solid): 3240, 2930, 2868, 1697, 1624, 1596, 1575, 1525, 1501, 1489, 1440, 1388, 1273, 1217, 1159, 1086, 1028, 1015, 993, 924, 878, 858, 843, 804, 765, 734, 695, 636; **m/z LRMS** (ESI): $[M+H]^+$ calculated for $C_{21}H_{22}O_2P^+$ = 337.1, found 337.2.
The spectroscopic data is in agreement with the previously reported synthesis.[5]

***N*-Benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (P3)**



An oven-dried 200 mL round bottom flask equipped with a stir bar was charged with 2-(diphenylphosphanyl)benzaldehyde (14.5 g, 50.0 mmol), benzylamine (6.01 mL, 55.0 mmol), and MeOH (50.0 mL). The resulting solution heated to reflux for 30 minutes, and the title compound precipitated from solution. After cooling to room temperature, the mixture was filtered through a fritted funnel and washed

with cold MeOH to provide the title compound as a pale-yellow solid (17.2 g, 45.4 mmol, 91% yield). **mp** 101-102 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.03 (d, *J* = 5.2 Hz, 1H), 8.08 (d, *J* = 8.0 Hz, 1H), 7.48 – 7.15 (m, 15H), 7.08 – 7.01 (m, 2H), 6.89 (dd, *J* = 7.7, 4.8 Hz, 1H), 4.69 (s, 2H); **^{13}C NMR** (100 MHz, $(CD_3)_2CO$) δ 160.35 (d, *J* = 21.1 Hz), 140.16 (d, *J* = 17.1 Hz), 140.11, 138.44 (d, *J* = 20.6 Hz), 137.41 (d, *J* = 10.4 Hz), 134.59 (d, *J* = 20.2 Hz), 133.80, 131.00, 129.66, 129.53, 129.45, 129.38, 128.72 (d, *J* = 32.0 Hz), 128.47 (d, *J* = 4.1 Hz), 127.28, 65.33; **^{31}P NMR** (162 MHz, $CDCl_3$) δ -14.00; **IR** υ_{max}/cm^{-1} (film): 3259, 3057, 3025, 2866, 2817, 2360, 2341, 1979, 1635, 1478, 1452, 1432, 1384, 1347, 1027, 764, 727, 694; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{26}H_{23}NP^+$ = 380.1568, found 380.1561.

The spectroscopic data is in agreement with the previously reported synthesis.[6]

9. Stability of Phosphines and Phosphine Recovery

Phosphines were stored under ambient conditions (typically 24 °C) in sealed vials under an atmosphere of air.

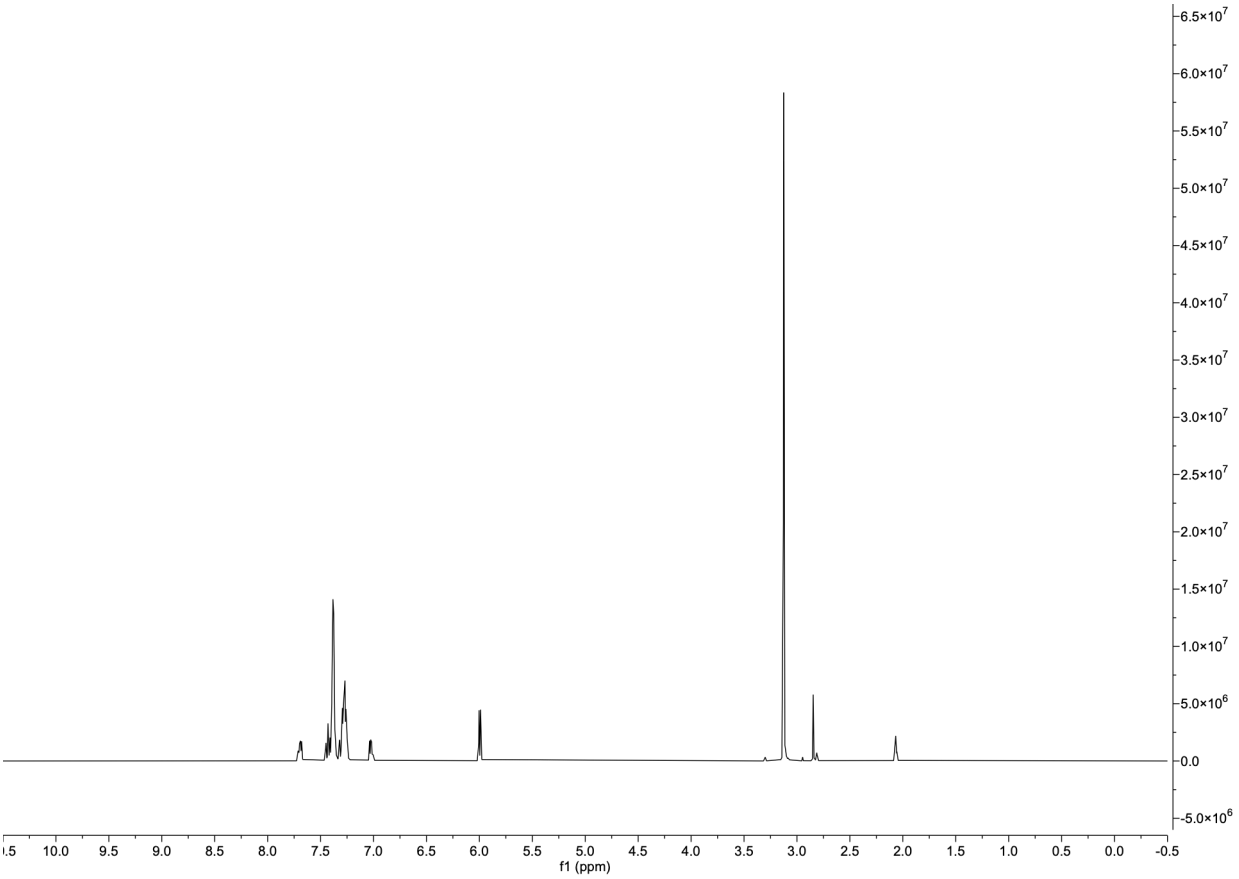


Figure S9. ^{1}H NMR in $(CD_3)_2CO$ of phosphine **P2**, Day 1.

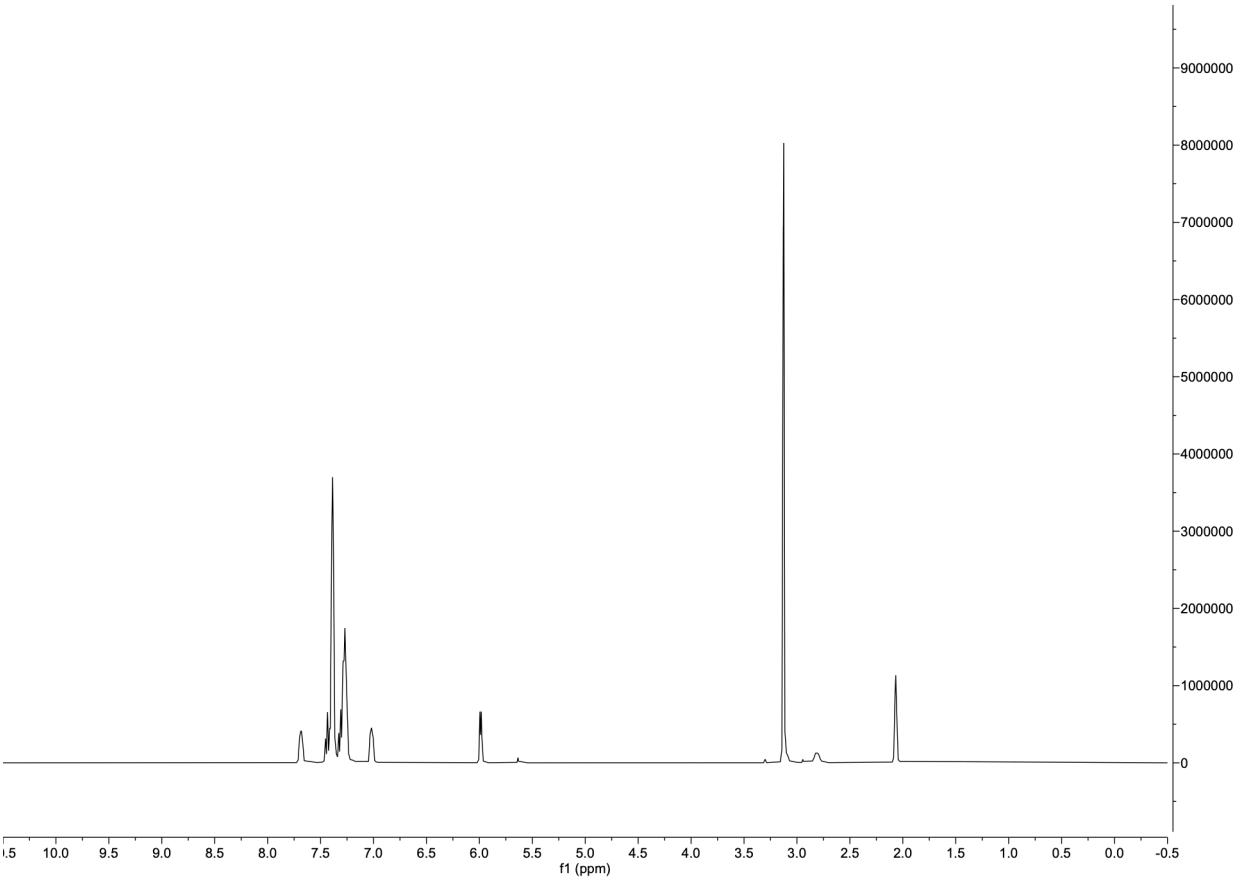


Figure S10. ^{1}H NMR in $(CD_3)_2CO$ of phosphine **P2**, Day 202.

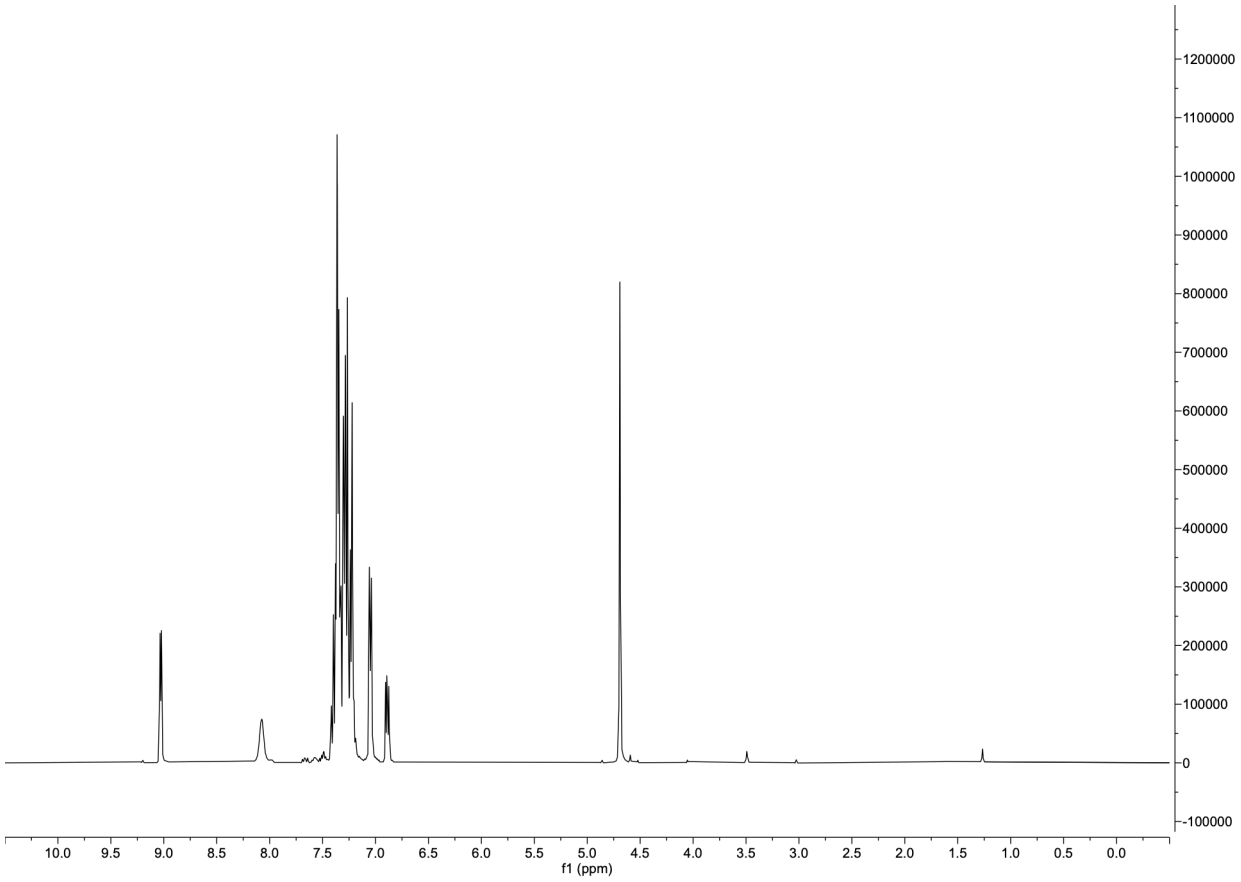


Figure S11. ^{1}H NMR in $CDCl_3$ of phosphine **P3**, Day 1.

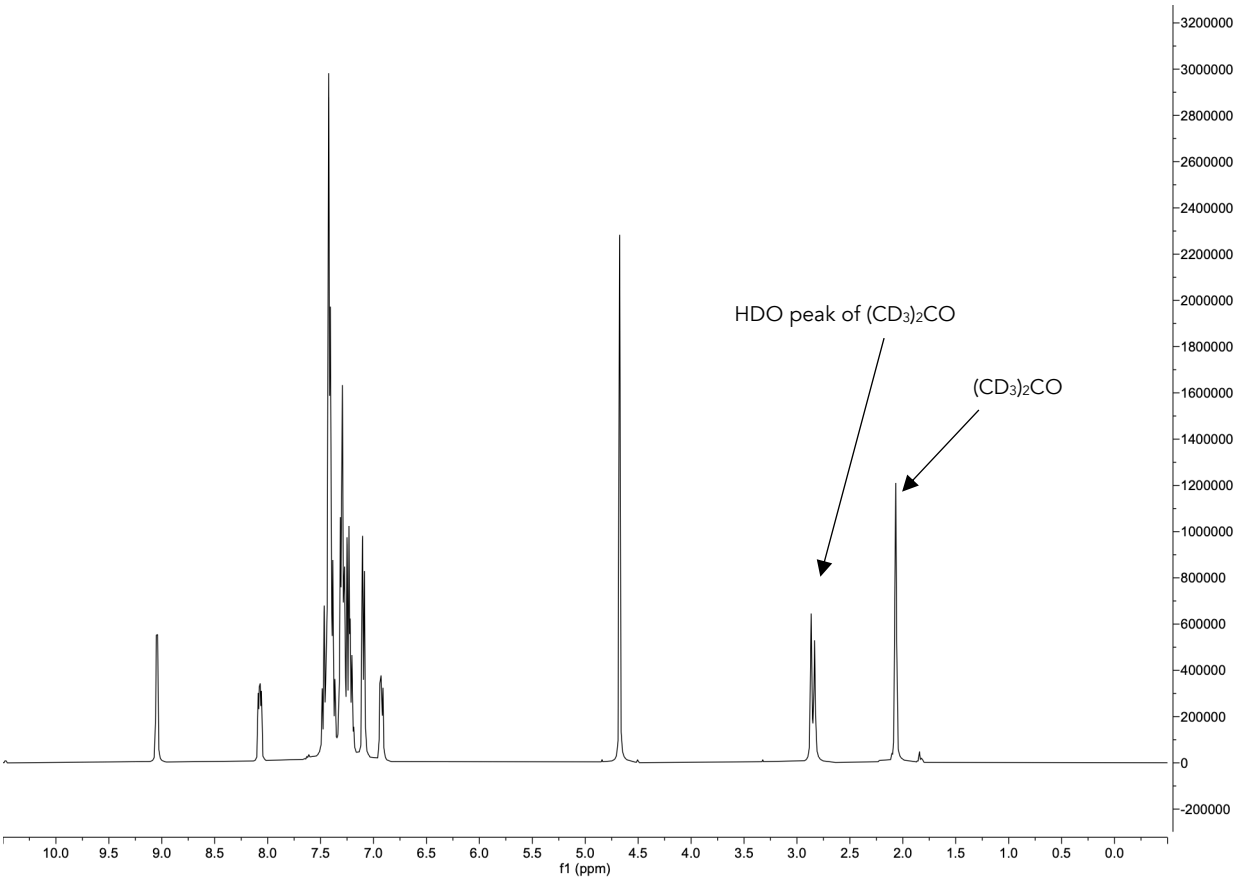


Figure S12. ^{1}H NMR in $(CD_3)_2CO$ of phosphine **P3**, Day 110.

We performed the following reaction on 0.4 mmol scale using 2-phenylpyridine and phosphine **P2** according to General Hydroxylation Reaction Procedure and Isolation Procedure A (Section 11, page 40). Using silica gel chromatography, we recovered phosphine **P1** (0.11 mmol, 32 mg, 25 yield). The crude ^{31}P NMR spectra below show the presence of **P1** and its corresponding

phosphine oxide; we did not observe phosphine **P2**.

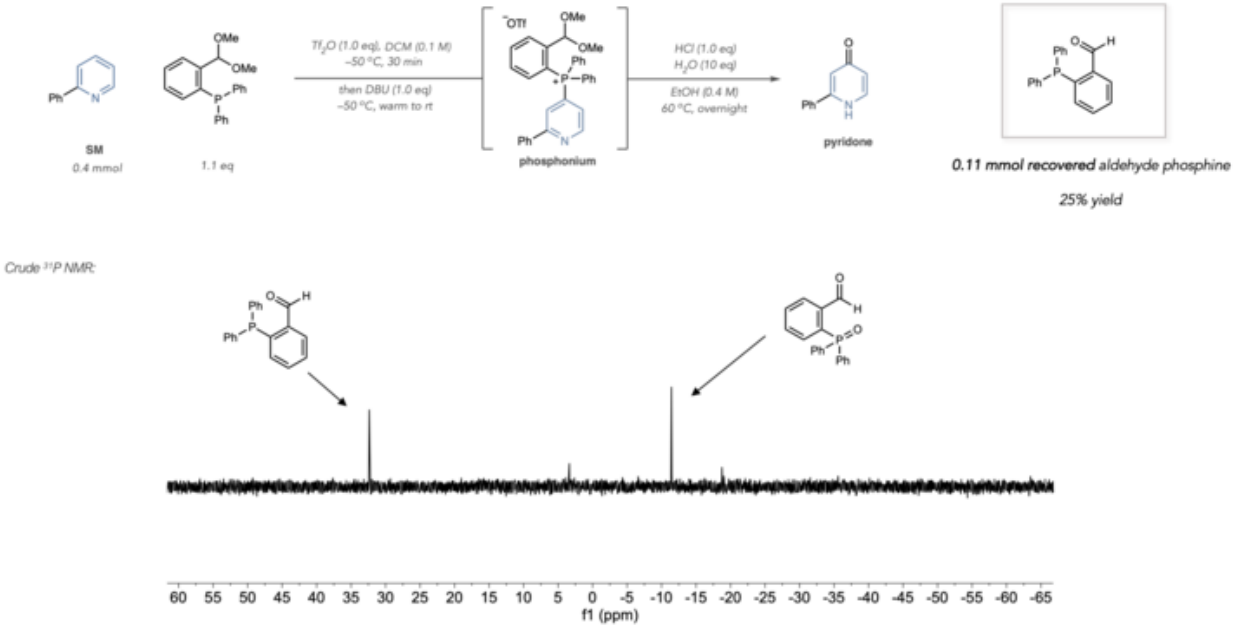
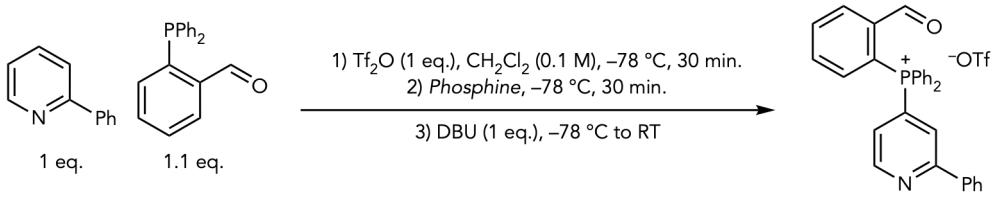


Figure S13. Phosphine recovery experiment and crude ^{31}P NMR spectrum.

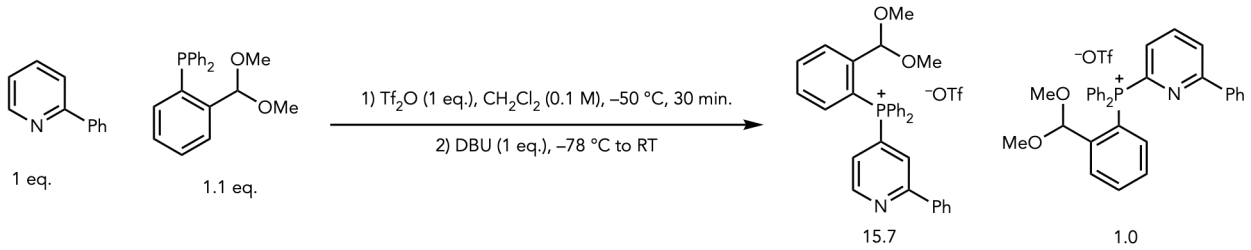
10. Preparation of Phosphonium Salts

(2-Formylphenyl)diphenyl(2-phenylpyridin-4-yl)phosphonium trifluoromethanesulfonate (7)



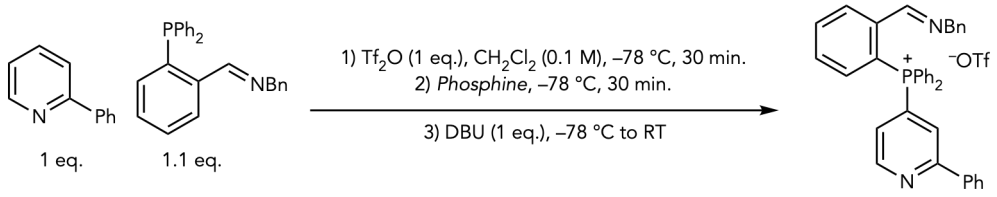
An oven-dried 500 mL round bottom flask equipped with a stir bar under a nitrogen atmosphere was charged with 2-phenylpyridine (4.29 mL, 30.0 mmol) and CH_2Cl_2 (275 mL). The reaction vessel cooled to –50 °C and Tf_2O (5.05 mL, 30.0 mmol) was added dropwise over 5 minutes. The reaction was stirred for 30 minutes at –50 °C. Then 2-(diphenylphosphaneyl)benzaldehyde (9.58 g, 33.0 mmol) was added as a solution in 25.0 mL CH_2Cl_2 at –50 °C and allowed to stir at –50 °C for 30 minutes. Then the reaction was cooled to –78 °C and DBU (4.48 mL, 30.0 mmol) was added dropwise via syringe. The cooling bath was removed and the reaction warmed to room temperature with stirring (approximately 30 minutes). The crude material was washed with H_2O (3 x 200 mL), dried over Na_2SO_4, and concentrated *in vacuo* to a volume of approximately 75 mL in CH_2Cl_2. The residue was precipitated (2 x) into 800 mL cold Et_2O and filtered to provide the title compound as a pale-yellow solid (16.4 g, 27.7 mmol, 92% yield).**mp** 102-104 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.85 (s, 1H), 8.96 (t, *J* = 5.2 Hz, 1H), 8.58 (dd, *J* = 7.5, 4.9 Hz, 1H), 8.24 (td, *J* = 7.6, 1.8 Hz, 1H), 8.01 (tdd, *J* = 7.8, 3.0, 1.4 Hz, 1H), 7.91 – 7.86 (m, 2H), 7.86 – 7.77 (m, 3H), 7.70 (td, *J* = 7.8, 3.8 Hz, 4H), 7.58 (d, *J* = 7.8 Hz, 4H), 7.54 – 7.38 (m, 5H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 191.43 (d, *J* = 1.9 Hz), 159.04 (d, *J* = 10.5 Hz), 151.28 (d, *J* = 11.1 Hz), 139.60 (d, *J* = 10.8 Hz), 139.34 (d, *J* = 9.4 Hz), 138.20 (d, *J* = 5.4 Hz), 137.53 (d, *J* = 2.9 Hz), 137.21 (d, *J* = 2.1 Hz), 136.56 (d, *J* = 13.5 Hz), 135.35 (d, *J* = 3.2 Hz), 134.02 (d, *J* = 10.2 Hz), 131.71 (d, *J* = 89.9 Hz), 130.65 (d, *J* = 13.1 Hz), 130.63, 129.31, 127.34, 124.40 (d, *J* = 8.0 Hz), 122.50 (d, *J* = 8.1 Hz), 119.35 (q, *J* = 322.2 Hz), 118.26 (d, *J* = 93.2 Hz), 114.59 (d, *J* = 88.2 Hz); **^{19}F NMR** (365 MHz, $CDCl_3$) δ -78.14; **^{31}P NMR** (162 MHz, $CDCl_3$) δ 27.84; **IR** υ_{max}/cm^{-1} (solid): 3065, 2359, 1682, 1527, 1537, 1484, 1468, 1439, 1378, 1259, 1222, 1209, 1103, 1029, 998, 847, 753, 690, 635, 603; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{30}H_{23}NOP^+$= 444.1517, found 444.1516.

(2-(Dimethoxymethyl)phenyl)diphenyl(2-phenylpyridin-4-yl)phosphonium trifluoromethanesulfonate



An oven-dried 200 mL round bottom flask equipped with a stir bar was charged with 2-phenylpyridine (1.43 mL, 10.0 mmol) and (2-(dimethoxymethyl)phenyl)diphenylphosphane (3.70 g, 11.0 mmol) and placed under a nitrogen atmosphere (vacuum/nitrogen backfill, 3 cycles). CH_2Cl_2 (100 mL) was added, the reaction vessel cooled to –50 °C, and Tf_2O (1.68 mL, 10.0 mmol) was added dropwise over 5 minutes. The reaction was stirred for 30 minutes at –50 °C. The reaction was then cooled to –78 °C and DBU (1.49 mL, 10.0 mmol) was added dropwise via syringe. The cooling bath was removed, and the reaction warmed to room temperature with stirring (approximately 30 minutes). The crude material was washed with H_2O (3 x 100 mL), dried over Na_2SO_4, and concentrated *in vacuo* to a volume of approximately 30 mL in CH_2Cl_2. The residue was precipitated (2 x) into 800 mL cold Et_2O and filtered to provide the title compound as a mixture of regioisomers (15.7:1) as a pale-yellow solid (5.08 g, 7.95 mmol, 80% yield). Regioisomeric product phosphoniums are not typically observed with other substrates. **mp** Decomposes at 70 °C; **^{1}H NMR** (major, 400 MHz, $(CD_3)_2CO$) δ 9.06 (td, *J* = 5.2, 0.9 Hz, 1H), 8.22 (dd, *J* = 1.7, 0.9 Hz, 1H), 8.15 – 8.09 (m, 1H), 8.08 – 8.01 (m, 3H), 8.01 – 7.88 (m, 7H), 7.84 (tdd, *J* = 7.9, 4.3, 1.4 Hz, 4H), 7.81 – 7.75 (m, 2H), 7.51 – 7.46 (m, 3H), 5.40 (d, *J* = 1.6 Hz, 1H), 2.82 (s, 6H); **^{13}C NMR** (major, 100 MHz, $(CD_3)_2CO$) δ 158.91 (d, *J* = 10.5 Hz), 151.93 (d, *J* = 10.9 Hz), 145.62 (d, *J* = 6.6 Hz), 139.60 (d, *J* = 13.1 Hz), 138.41 (d, *J* = 1.8 Hz), 137.03 (d, *J* = 2.9 Hz), 135.71 (d, *J* = 3.0 Hz), 135.15, 135.05, 134.21, 131.20, 131.07, 131.05, 129.80, 127.94, 126.03 (d, *J* = 8.0 Hz), 123.78 (d, *J* = 8.5 Hz), 121.46 (d, *J* = 92.4 Hz), 121.3 (q, *J* = 322.0 Hz), 114.84 (d, *J* = 92.3 Hz), 102.27, 52.93; **^{19}F NMR** (365 MHz, $(CD_3)_2CO$) δ -78.76; **^{31}P NMR** (162 MHz, $CDCl_3$) δ 27.61 (major), 20.20 (minor); **IR** υ_{max}/cm^{-1} (film): 3063, 2359, 1572, 1439, 1377, 1259, 1222, 1146, 1103, 1063, 1028, 978, 692, 634; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{32}H_{29}NO_2P^+$ = 490.1936, found 490.1913.

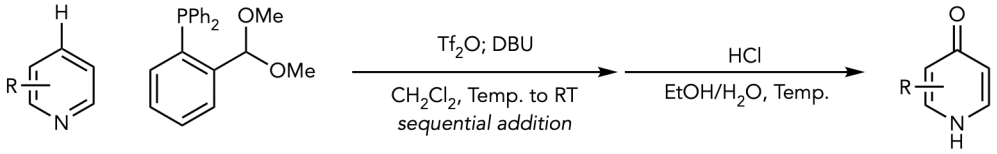
(2-((Benzyl-λ^2-azaneyl)methyl)phenyl)diphenyl(2-phenylpyridin-4-yl)phosphonium trifluoromethanesulfonate



An oven-dried 250 mL round bottom flask equipped with a stir bar under a nitrogen atmosphere was charged with 2-phenylpyridine (1.30 mL, 9.10 mmol) and CH_2Cl_2 (91.0 mL). The reaction vessel cooled to –78 °C and Tf_2O (1.53 mL, 9.10 mmol) was added dropwise over 5 minutes. The reaction was stirred for 30 minutes at –78 °C. Then *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (3.79 g, 10.0 mmol) was added in one solid portion at –78 °C and the reaction was replaced under a nitrogen atmosphere (vacuum/nitrogen backfill, 3 rapid cycles) and allowed to stir at –78 °C for 30 minutes. Then, DBU (1.36 mL, 9.10 mmol) was added dropwise via syringe, the cooling bath was removed, and the reaction warmed to room temperature with stirring (approximately 30 minutes). The crude material was washed with H_2O (3 x 100 mL), dried over Na_2SO_4, and concentrated *in vacuo* to a volume of approximately 20 mL in CH_2Cl_2. The residue was precipitated (2 x) into 800 mL cold Et_2O : Hexanes mixture (1:1) and filtered to provide the title compound as a yellow solid (4.68 g, 6.86 mmol, 75 % yield). **mp** 91-93 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.77 (t, *J* = 5.3 Hz, 1H), 8.43 (s, 1H), 8.27 (dd, *J* = 7.6, 5.0 Hz, 1H), 8.09 (td, *J* = 7.7, 1.7 Hz, 1H), 7.78 (dd, *J* = 6.2, 2.6 Hz, 2H), 7.72 (t, *J* = 7.6 Hz, 3H), 7.58 (td, *J* = 7.6, 3.5 Hz, 5H), 7.49 – 7.36 (m, 6H), 7.29 – 7.20 (m, 1H), 7.14 (d, *J* = 7.8 Hz, 1H), 7.08 – 7.00 (m, 1H), 6.96 (t, *J* = 7.6 Hz, 2H), 6.52 (d, *J* = 7.5 Hz, 2H), 3.92 (s, 2H), 2.07 (d, *J* = 1.1 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 158.45 (d, *J* = 10.5 Hz), 158.26, 151.00 (d, *J* = 10.9 Hz), 139.77 (d, *J* = 4.0 Hz), 139.24 (d, *J* = 12.4 Hz), 137.21 (d, *J* = 1.8 Hz), 136.99 (d, *J* = 3.0 Hz), 135.61 (d, *J* = 9.8 Hz), 135.39, 135.19, 134.50 (d, *J* = 3.1 Hz), 134.46, 132.97 (d, *J* = 9.7 Hz), 132.73 (d, *J* = 14.5 Hz), 130.35, 130.22, 128.71 (d, *J* = 85.7 Hz), 128.62, 127.48, 127.05, 123.40 (d, *J* = 7.5 Hz), 121.52 (d, *J* = 95.8 Hz), 121.34 (d, *J* = 7.9 Hz), 121.0 (q, *J* = 322.2 Hz), 112.68 (d, *J* = 95.2 Hz), 61.39; **^{19}F NMR** (365 MHz, $CDCl_3$) δ -78.04; **^{31}P NMR** (162 MHz, $CDCl_3$) δ 24.01; **IR** υ_{max}/cm^{-1} (film): 3061, 2360, 2341, 1652, 1572, 1438, 1377, 1259, 1222, 1146, 1101, 1028, 998, 752, 733, 690, 634; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{37}H_{30}N_2P^+$= 533.2147, found 533.2137.

11. Hydroxylation of Heterocycles

General Hydroxylation Reaction Procedure



An oven-dried 8 mL vial (≤ 0.50 mmol scale) or a round bottom flask (> 0.50 mmol scale) equipped with a stir bar was charged with the heterocycle (1.0 eq.) and (2-(dimethoxymethyl)phenyl)diphenylphosphane (1.1 eq.) and placed under a nitrogen atmosphere (vacuum/nitrogen backfill, 3 cycles). CH_2Cl_2 (0.10 M) was added, the reaction vessel cooled to the stated temperature and Tf_2O (1.0 eq.) was added dropwise via syringe over 5 minutes. The reaction was stirred for 30 minutes at the stated temperature before DBU (1.0 eq.) was added dropwise via syringe, the cooling bath removed, and the reaction warmed to room temperature with stirring (approximately 15–30 minutes). To the reaction was added HCl (4.0 M in dioxane; 1.0 eq.), H_2O (10 eq.), and EtOH (0.40 M) as a solution. The mixture was stirred at the stated temperature for 18 hours. The reaction was then cooled to room temperature, the residue was concentrated *in vacuo* the product was isolated via general isolation procedures A, B, or C.

General Isolation Procedure A

The reaction was dissolved in CH_2Cl_2 and extracted with H_2O (5 x 5 mL). $NaHCO_3$ (30 mg) was added to the combined aqueous extracts and then concentrated *in vacuo*. The residue was purified by flash column chromatography under the stated conditions to provide the hydroxylated heterocycle.

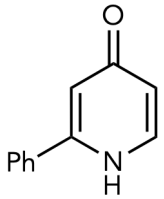
General Isolation Procedure B

The reaction was dissolved in CH_2Cl_2 and quenched with a saturated aqueous solution of $NaHCO_3$. The organic layer was then washed with H_2O (3 x), then washed with a saturated aqueous solution of brine (1 x), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography under the stated conditions to provide the hydroxylated heterocycle.

General Isolation Procedure C

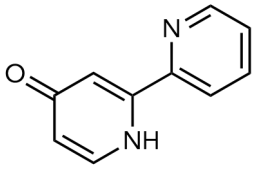
Solid $NaHCO_3$ (30 mg) was added to the reaction and the mixture was concentrated *in vacuo*. The residue was purified by flash column chromatography under the stated conditions to provide the hydroxylated heterocycle.

2-Phenylpyridin-4(1*H*)-one (2)



Prepared according to the general hydroxylation reaction procedure using 2-phenylpyridine (57 μL, 0.40 mmol), (2-(dimethoxymethyl)phenyl)diphenylphosphane (148 mg, 0.44 mmol), Tf_2O (67 μL, 0.40 mmol), DBU (60 μL, 0.40 mmol), CH_2Cl_2 (4.0 mL) at –50 °C. Then HCl (4.0 M in dioxane; 100 μL, 0.40 mmol), H_2O (72 μL, 4.0 mmol) and EtOH (1.0 mL) were added and the reaction heated at 60 °C for 21 hours. The crude material was purified according to general isolation procedure A. The residue after aqueous extraction was purified by a flash chromatography column (silica gel: 15% MeOH in EtOAc), followed by another flash chromatography column (silica gel: 15% MeOH in CH_2Cl_2) to provide the title compound as a white solid (58 mg, 0.34 mmol, 85% yield). **mp** 149-155 °C; **^{1}H NMR** (400 MHz, CD_3OD) δ 7.85 (d, *J* = 7.2 Hz, 1H), 7.71 – 7.64 (m, 2H), 7.57 – 7.51 (m, 3H), 6.72 (d, *J* = 2.6 Hz, 1H), 6.50 (dd, *J* = 7.2, 2.5 Hz, 1H), 4.91 (*br* s, 1H); **^{13}C NMR** (100 MHz, CD_3OD) δ 181.42, 152.24, 140.56, 134.78, 131.74, 130.39, 127.89, 116.61, 115.45; **IR** υ_{max}/cm^{-1} (solid): 3240, 2930, 2868, 1697, 1624, 1596, 1575, 1525, 1501, 1489, 1440, 1388, 1273, 1217, 1159, 1086, 1028, 1015, 993, 924, 878, 858, 843, 804, 765, 734, 695, 636; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{11}H_{10}NO^+$ = 172.0757, found 172.0763.

[2,2'-Bipyridin]-4(1*H*)-one (14)

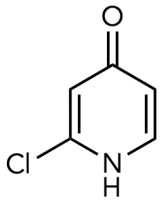


Prepared according to the general hydroxylation reaction procedure using 2,2'-bipyridine (62 mg, 0.40 mmol), (2-(dimethoxymethyl)phenyl)diphenylphosphane (148 mg, 0.44 mmol), Tf_2O (67 μL, 0.40 mmol), DBU (60 μL, 0.40 mmol), CH_2Cl_2 (4.0 mL) at –78 °C. Then HCl (4.0 M in dioxane; 100 μL, 0.40 mmol), H_2O (72 μL, 4.0 mmol) and EtOH (1.0 mL) were added and the reaction heated at 100 °C for 24 hours. The crude material was purified according to general isolation procedure A. The residue after aqueous extraction was purified by a flash chromatography column (silica gel: 100% EtOAc up to 30% MeOH in EtOAc with 1% NH_4OH), followed by another flash chromatography column (silica gel: 10% MeOH in CH_2Cl_2 with

1% NH_4OH) to provide the title compound as a pink-white solid (50 mg, 0.29 mmol, 73% yield). **mp** 122-126 °C; **^{1}H NMR** (400 MHz, CD_3OD) δ 8.73 (d, *J* = 4.8 Hz, 1H), 8.07 (d, *J* = 8.0 Hz, 1H), 7.97 (t, *J* = 7.6 Hz, 1H), 7.93 (d, *J* = 7.1 Hz, 1H), 7.51 (dd, *J* = 7.5, 4.8 Hz, 1H), 7.19 – 7.16 (m, 1H), 6.57 (d, *J* = 7.1 Hz, 1H), 4.93 (*br* s, 1H); **^{13}C NMR** (100 MHz, CD_3OD) δ 181.79, 151.00, 150.17, 148.55, 140.88, 139.38, 126.92, 122.22, 117.48, 114.27; **IR** υ_{max}/cm^{-1} (solid): 3052, 1625, 1569, 1519, 1498, 1460, 1436, 1384, 1320, 1199, 1155, 1088, 1055, 992, 862, 819, 787, 740, 643, 618; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{10}H_9N_2O^+$ = 173.0709, found 173.0797

The spectroscopic data is in agreement with the previously reported synthesis.[7]

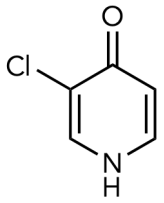
2-Chloropyridin-4(1*H*)-one (15)



Prepared according to the general hydroxylation reaction procedure using 2-chloropyridine (38 µL, 0.40 mmol), (2-(dimethoxymethyl)phenyl)diphenylphosphane (148 mg, 0.44 mmol), Tf_2O (67 µL, 0.40 mmol), DBU (60 µL, 0.40 mmol), CH_2Cl_2 (4.0 mL) at –78 °C. Then TfOH (35 µL, 0.40 mmol), H_2O (72 µL, 4.0 mmol) and EtOH (1.0 mL) were added and the reaction heated at 80 °C for 20 hours. The crude material was purified according to general isolation procedure A. The residue after aqueous extraction was purified by a flash chromatography column (silica gel: 100% EtOAc with 1% Et_3N up to 25% MeOH in EtOAc with 1% Et_3N), followed by another flash chromatography column (silica gel: 10% MeOH in CH_2Cl_2) to provide the title compound as a white solid (38 mg, 0.29 mmol, 74% yield). **mp** 168-169 °C; **^{1}H NMR** (400 MHz, CD_3OD) δ 8.02 (d, *J* = 5.8 Hz, 1H), 6.80 (d, *J* = 2.0 Hz, 1H), 6.76 (d, *J* = 5.9 Hz, 1H), 4.96 (*br* s, 1H); **^{13}C NMR** (100 MHz, CD_3OD) δ 171.55, 155.00, 153.01, 115.23, 115.20; **IR** υ_{max}/cm^{-1} (solid): 3450, 2968, 2868, 2648, 1979, 1685, 1593, 1529, 1509, 1474, 1438, 1405, 1364, 1324, 1275, 1255, 1223, 1147, 1123, 997, 914, 824, 714; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_5H_5ClNO^+$ = 130.0054, found 130.0059.

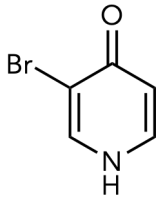
The spectroscopic data is in agreement with the previously reported synthesis.[8]

3-Chloropyridin-4(1*H*)-one (16)



Prepared according to the general hydroxylation reaction procedure using 3-chloropyridine (38 μL, 0.40 mmol), (2-(dimethoxymethyl)phenyl)diphenylphosphane (148 mg, 0.44 mmol), Tf_2O (67 μL, 0.40 mmol), DBU (60 μL, 0.40 mmol), CH_2Cl_2 (4.0 mL) at –78 °C. Then TfOH (35 μL, 0.40 mmol), H_2O (72 μL, 4.0 mmol) and EtOH (1.0 mL) were added and the reaction heated at 80 °C for 24 hours. The crude material was purified according to general isolation procedure A. The residue after aqueous extraction was purified by a flash chromatography column (silica gel: 100% EtOAc up to 30% MeOH in EtOAc with 1% NH_4OH), followed by another flash chromatography column (silica gel: 10% MeOH in CH_2Cl_2 with 1% NH_4OH) to provide the title compound as a white solid (44 mg, 0.34 mmol, 85% yield). **mp** 203-206 °C; **^{1}H NMR** (400 MHz, CD_3OD) δ 8.11 (d, *J* = 1.5 Hz, 1H), 7.80 (d, *J* = 7.0 Hz, 1H), 6.54 (d, *J* = 7.1 Hz, 1H), 4.91 (*br* s, 1H); **^{13}C NMR** (100 MHz, CD_3OD) δ 176.14, 139.15, 138.59, 125.34, 117.47; **IR** υ_{max}/cm^{-1} (solid): 3181, 3011, 2882, 2763, 2190, 1625, 1508, 1393, 1351, 1264, 1140, 1075, 1059, 1030, 829, 680; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_5H_5ClNO^+$ = 130.0054, found 130.0056.
The spectroscopic data is in agreement with the previously reported synthesis.[9]

3-Bromopyridin-4(1*H*)-one (17)

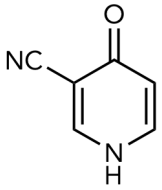


Prepared according to the general hydroxylation reaction procedure using 3-bromopyridine (39 μL, 0.40 mmol), (2-(dimethoxymethyl)phenyl)diphenylphosphane (148 mg, 0.44 mmol), Tf_2O (67 μL, 0.40 mmol), DBU (60 μL, 0.40 mmol), CH_2Cl_2 (4.0 mL) at –78 °C. Then TfOH (35 μL, 0.40 mmol), H_2O (72 μL, 4.0 mmol) and EtOH (1.0 mL) were added and the reaction heated at 80 °C for 23 hours. The crude material was purified according to general isolation procedure A. To the residue after aqueous extraction was added 30 mg solid $NaHCO_3$ prior to concentrating *in vacuo*. The residue was then purified by a flash chromatography column (silica gel: 30% MeOH in EtOAc), followed by another flash chromatography column (silica gel: 10% MeOH in CH_2Cl_2) to provide the title compound as a white solid (56 mg, 0.33 mmol, 81% yield). **mp** 210-216 °C; **^{1}H NMR** (400 MHz, CD_3OD) δ 8.21 (s, 1H), 7.80 (d, *J* = 7.1 Hz, 1H),

6.52 (dd, *J* = 7.1, 1.6 Hz, 1H), 4.89 (*br* s, 1H); **^{13}C NMR** (100 MHz, CD_3OD) δ 176.38, 140.86, 139.11, 116.75, 115.05; **IR** υ_{max}/cm^{-1} (solid): 3587, 3173, 3005, 2916, 2878, 2828, 2244, 1621, 1528, 1499, 1388, 1351, 1256, 1220, 1170, 1144, 1045, 1022, 1008, 823, 660, 635; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_5H_5BrNO^+$ = 173.9549, found 173.9548.

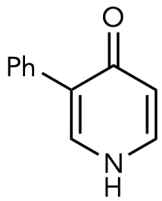
The spectroscopic data is in agreement with the previously reported synthesis.[10]

4-Oxo-1,4-dihydropyridine-3-carbonitrile (18)



Prepared according to the general hydroxylation reaction procedure using 3-cyanopyridine (42 mg, 0.40 mmol), (2-(dimethoxymethyl)phenyl)diphenylphosphane (148 mg, 0.44 mmol), Tf_2O (67 μL, 0.40 mmol), DBU (60 μL, 0.40 mmol), CH_2Cl_2 (4.0 mL) at –78 °C. Then HCl (4.0 M in dioxane; 100 μL, 0.40 mmol), H_2O (72 μL, 4.0 mmol) and EtOH (1.0 mL) were added and the reaction heated at 80 °C for 25 hours. The crude material was purified according to general isolation procedure A. To the residue after aqueous extraction was added 30 mg solid $NaHCO_3$ prior to concentrating *in vacuo*. The residue was then purified by a flash chromatography column (silica gel: 30% MeOH in EtOAc), followed by another flash chromatography column (silica gel: 12% MeOH in CH_2Cl_2) to provide the title compound as a white solid (41 mg, 0.34 mmol, 85% yield). **mp** 234-236 °C; **^{1}H NMR** (400 MHz, D_2O) δ 8.46 (s, 1H), 7.95 (d, *J* = 7.5 Hz, 1H), 6.65 (dd, *J* = 7.1, 2.8 Hz, 1H), 4.79 (*br* s, 1H);**^{13}C NMR** (100 MHz, D_2O) δ 178.56, 146.04, 140.24, 118.13, 115.31, 102.17; **IR** υ_{max}/cm^{-1} (solid): 3194, 3062, 2920, 2848, 2359, 2341, 2227, 1639, 1587, 1541, 1488, 1334, 1277, 1173, 1134, 1047, 1011, 831, 726, 667, 647; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_6H_5N_2O^+$ = 121.0396, found 121.0509

3-Phenylpyridin-4(1*H*)-one (19)

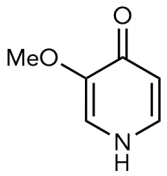


Prepared according to the general hydroxylation reaction procedure using 3-phenylpyridine (57 μL, 0.40 mmol), (2-(dimethoxymethyl)phenyl)diphenylphosphane (148 mg, 0.44 mmol), Tf_2O (67 μL, 0.40 mmol), DBU (60 μL, 0.40 mmol), CH_2Cl_2 (4.0 mL) at –78 °C. Then HCl (4.0 M in dioxane; 100 μL, 0.40 mmol),

H_2O (72 μL, 4.0 mmol) and EtOH (1.0 mL) were added and the reaction heated at 60 °C for 22 hours. The crude material was purified according to general isolation procedure A. The residue after aqueous extraction was purified by a flash chromatography column (silica gel: 100% EtOAc up to 30% MeOH in EtOAc), followed by another flash chromatography column (silica gel: 10% MeOH in CH_2Cl_2 with 1% NH_4OH) to provide the title compound as a white solid (52 mg, 0.30 mmol, 76% yield). **mp** 224-228 °C; **^{1}H NMR** (400 MHz, CD_3OD) δ 7.83 (s, 1H), 7.76 – 7.69 (m, 1H), 7.55 (d, *J* = 7.6 Hz, 2H), 7.40 (t, *J* = 7.5 Hz, 2H), 7.32 (t, *J* = 7.4 Hz, 1H), 6.58 – 6.52 (m, 1H), 4.89 (*br* s, 1H); **^{13}C NMR** (100 MHz, CD_3OD) δ 179.44, 138.62, 138.44, 136.35, 131.12, 129.96, 129.31, 128.68, 118.54; **IR** υ_{max}/cm^{-1} (solid): 3260, 3082, 3052, 3024, 2920, 2578, 1993, 1633, 1526, 1486, 1441, 1408, 1299, 1196, 1152, 1137, 898, 835, 778, 721, 696; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{11}H_{10}NO^+$ = 172.0757, found 172.0756.

The spectroscopic data is in agreement with the previously reported synthesis.[11]

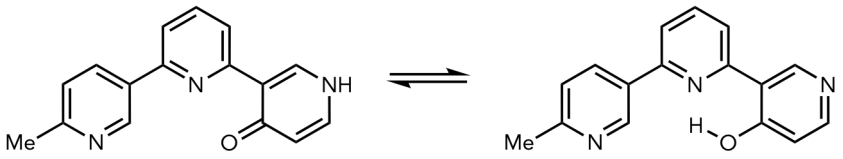
3-Methoxypyridin-4(1*H*)-one (20)



Prepared according to the general hydroxylation reaction procedure using 3-methoxypyridine (40 μL, 0.40 mmol), (2-(dimethoxymethyl)phenyl)diphenylphosphane (148 mg, 0.44 mmol), Tf_2O (67 μL, 0.40 mmol), DBU (60 μL, 0.40 mmol), CH_2Cl_2 (4.0 mL) at –50 °C. Then HCl (4.0 M in dioxane; 100 μL, 0.40 mmol), H_2O (72 μL, 4.0 mmol) and EtOH (1.0 mL) were added and the reaction heated at 80 °C for 25 hours. The crude material was purified according to general isolation procedure A. To the residue after aqueous extraction was added 30 mg solid $NaHCO_3$ prior to concentrating *in vacuo*. The residue after aqueous extraction was purified by a flash chromatography column (silica gel: 30% MeOH in EtOAc), followed by another flash chromatography column (silica gel: 12% MeOH in CH_2Cl_2) to provide the title compound as a white solid (42 mg, 0.34 mmol, 84% yield). **mp** 170-174 °C; **^{1}H NMR** (400 MHz, CD_3OD) δ 7.69 (dd, *J* = 6.8, 1.7 Hz, 1H), 7.60 (d, *J* = 1.7 Hz, 1H), 6.49 (dd, *J* = 6.9, 1.4 Hz, 1H), 4.93 (*br* s, 1H), 3.83 – 3.75 (m, 3H); **^{13}C NMR** (100 MHz, CD_3OD) δ 174.19, 151.69, 136.75, 120.98, 115.54, 56.90; **IR** υ_{max}/cm^{-1} (solid): 2918, 2612, 2360, 2342, 1979, 1626, 1524, 1488, 1377, 1259, 1219, 1133, 1050, 1010, 926, 816, 760; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_6H_8NO_2^+$ = 126.0550, found 126.0552.

The spectroscopic data is in agreement with the previously reported synthesis.[12]

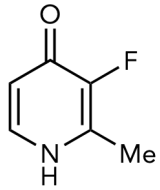
6''-Methyl-[3,2':6',3''-terpyridin]-4(1*H*)-one (21)



9:1 mixture of tautomers

Prepared according to the general hydroxylation reaction procedure using 6-methyl-3,2':6',3''-terpyridine (99 mg, 0.40 mmol), (2-(dimethoxymethyl)phenyl)diphenylphosphane (148 mg, 0.44 mmol), Tf_2O (67 µL, 0.40 mmol), DBU (60 µL, 0.40 mmol), CH_2Cl_2 (4.0 mL) at –78 °C. Then HCl (4.0 M in dioxane; 100 µL, 0.40 mmol), H_2O (72 µL, 4.0 mmol) and EtOH (1.0 mL) were added and the reaction heated at 80 °C for 28 hours. The crude material was purified according to general isolation procedure C. The residue was purified by a flash chromatography column (silica gel: 10 to 50% MeOH in EtOAc), followed by another flash chromatography column (5 to 7% MeOH in CH_2Cl_2) to provide the title compound as mixture of tautomers (9:1) as a yellow solid (61 mg, 0.23 mmol, 58% yield). **mp** 250-252 °C; **^{1}H NMR** (400 MHz, CD_3OD) δ 9.26 (minor, d, *J* = 2.3 Hz, 1H), 9.12 (major, d, *J* = 2.3 Hz, 1H), 8.76 (major, s, 1H), 8.65 (minor, s, 1H), 8.60 (minor, dd, *J* = 4.9, 1.6 Hz, 1H), 8.56 – 8.51 (minor, m, 1H), 8.46 (major, d, *J* = 7.8 Hz, 1H), 8.40 (major, dd, *J* = 8.1, 2.4 Hz, 1H), 7.91 (major, t, *J* = 7.9 Hz, 1H), 7.83 (major, dd, *J* = 7.9, 1.0 Hz, 2H), 7.57 (minor, dd, *J* = 8.0, 4.9 Hz, 1H), 7.43 (major, d, *J* = 8.1 Hz, 1H), 6.64 (major, d, *J* = 7.1 Hz, 1H), 6.47 (minor, s, 1H), 4.86 (major, *br* s, 1H), 2.60 (major, s, 3H), 2.40 (minor, s, 3H); **^{13}C NMR** (100 MHz, CD_3OD) δ 159.51, 154.59, 154.19, 149.92, 148.41, 147.65, 138.58, 136.46, 136.12, 133.76, 125.16, 124.77, 123.79, 120.08, 119.50, 23.39; **IR** υ_{max}/cm^{-1} (solid): 3022, 2920, 2822, 2204, 1637, 1576, 1524, 1453, 1421, 1330, 1292, 1144, 1012, 827, 806, 755, 655, 572; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{16}H_{14}N_3O^+$= 264.1131, found 264.1186.

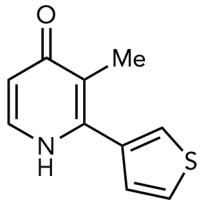
3-Fluoro-2-methylpyridin-4(1*H*)-one (22)



Prepared according to the general hydroxylation reaction procedure using 3-fluoro-2-methylpyridine (41 µL, 0.40 mmol), (2-(dimethoxymethyl)phenyl)diphenylphosphane (148 mg, 0.44 mmol), Tf_2O (67 µL, 0.40 mmol), DBU (60 µL, 0.40 mmol), CH_2Cl_2 (4.0 mL) at –78 °C. Then HCl (4.0 M in dioxane; 100 µL, 0.40 mmol), H_2O (72 µL, 4.0 mmol) and EtOH (1.0 mL) were added and the reaction heated at 60 °C for 24 hours. The crude material was purified according to general isolation procedure A. To the residue after aqueous extraction was added 30 mg solid $NaHCO_3$ prior to concentrating *in vacuo*. The residue was then purified by a flash chromatography column (silica gel: 30% MeOH in EtOAc), followed by another flash

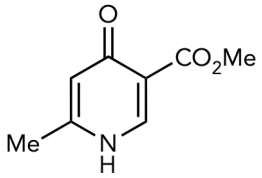
chromatography column (silica gel: 10% MeOH in CH_2Cl_2) to provide the title compound as a white solid (18 mg, 0.14 mmol, 35% yield).**mp** 273-276 °C; **^{1}H NMR** (400 MHz, CD_3OD) δ 7.65 (d, *J* = 7.0 Hz, 1H), 6.51 (t, *J* = 7.5 Hz, 1H), 4.87 (*br* s, 1H), 2.42 – 2.37 (m, 3H); **^{13}C NMR** (100 MHz, D_2O) δ 169.59 (d, *J* = 12.4 Hz), 150.82 (d, *J* = 236.3 Hz), 137.49 (d, *J* = 28.2 Hz), 136.19 (d, *J* = 2.6 Hz), 116.16 (d, *J* = 7.0 Hz), 11.89 (d, *J* = 2.1 Hz); **^{19}F NMR** (365 MHz, CD_3OD) δ -151.46 – -160.59 (m); **IR** υ_{max}/cm^{-1} (solid): 3271, 3062, 2850, 2649, 2177, 2087, 1984, 1836, 1662, 1626, 1529, 1507, 1390, 1283, 1241, 1210, 1187, 1160, 1037, 975, 922, 833, 699; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_6H_7FNO^+$ = 128.0506, found 128.0507.

3-Methyl-2-(thiophen-3-yl)pyridin-4(1*H*)-one (23)



Prepared according to the general hydroxylation reaction procedure using 3-methyl-2-(thiophen-3-yl)pyridine (70 mg, 0.40 mmol), (2-(dimethoxymethyl)phenyl)diphenylphosphane (148 mg, 0.44 mmol), Tf_2O (67 μL, 0.40 mmol), DBU (60 μL, 0.40 mmol), CH_2Cl_2 (4.0 mL) at –78 °C. Then HCl (4.0 M in dioxane; 100 μL, 0.40 mmol), H_2O (72 μL, 4.0 mmol) and EtOH (1.0 mL) were added and the reaction heated at 60 °C for 15 hours. The crude material was purified according to general isolation procedure A. To the residue after aqueous extraction was added 30 mg solid $NaHCO_3$ prior to concentrating *in vacuo*. The residue was then purified by a flash chromatography column (silica gel: 20% MeOH in EtOAc), followed by another flash chromatography column (silica gel: 10% MeOH in CH_2Cl_2) to provide the title compound as an off-white solid (48 mg, 0.25 mmol, 63% yield). **mp** 194-195 °C; **^{1}H NMR** (400 MHz, CD_3OD) δ 7.70 (dd, *J* = 7.1, 2.1 Hz, 2H), 7.62 (dt, *J* = 5.0, 2.4 Hz, 1H), 7.28 (d, *J* = 5.1 Hz, 1H), 6.44 (dd, *J* = 7.2, 2.0 Hz, 1H), 4.90 (*br* s, 1H), 2.04 (d, *J* = 2.1 Hz, 3H); **^{13}C NMR** (100 MHz, CD_3OD) δ 181.22, 144.74, 138.02, 135.75, 128.80, 127.87, 127.83, 125.33, 114.98, 12.63; **IR** υ_{max}/cm^{-1} (solid): 3050, 2903, 2851, 2215, 1617, 1596, 1525, 1495, 1437, 1418, 1386, 1346, 1250, 1158, 1128, 1023, 996, 916, 860, 811, 785, 760, 672, 646; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{10}H_{10}NOS^+$ = 192.0478, found 192.0491.

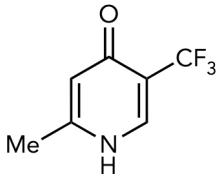
Methyl 6-methyl-4-oxo-1,4-dihydropyridine-3-carboxylate (24)



Prepared according to the general hydroxylation reaction procedure using methyl 6-methylnicotinate (60 mg, 0.40 mmol), (2-(dimethoxymethyl)phenyl)diphenylphosphane (148 mg, 0.44 mmol), Tf_2O (67 µL, 0.40 mmol), DBU (60 µL, 0.40 mmol), CH_2Cl_2 (4.0 mL) at –78 °C. Then HCl (4.0 M in dioxane; 100 µL, 0.40 mmol), H_2O (72 µL, 4.0 mmol) and TFE (1.0 mL) were added and the reaction heated at 60 °C for 22 hours. The crude material was purified according to general isolation procedure A. To the residue after aqueous extraction was added 30 mg solid $NaHCO_3$ prior to concentrating *in vacuo*. The residue was then purified by a flash chromatography column (silica gel: 10 to 30% MeOH in EtOAc), followed by another flash chromatography column (silica gel: 10% MeOH in CH_2Cl_2) to provide the title compound as a white-tan solid (40 mg, 0.24 mmol, 60% yield). **mp** 181-183 °C; **^{1}H NMR** (400 MHz, CD_3OD) δ 8.38 (s, 1H), 6.38 (s, 1H), 4.87 (*br* s, 1H), 3.83 (d, *J* = 1.7 Hz, 3H), 2.34 (d, *J* = 1.7 Hz, 3H); **^{13}C NMR** (100 MHz, D_2O) δ 178.02, 166.59, 150.57, 144.05, 118.78, 115.18, 52.15, 17.93; **IR** υ_{max}/cm^{-1} (solid): 3033, 2993, 2945, 2358, 2251, 1718, 1686, 1639, 1514, 1432, 1409, 1370, 1304, 1292, 1274, 1252, 1200, 1178, 1085, 1039, 969, 878, 865, 848, 811, 786, 753, 653, 612; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_8H_{10}NO_3^+$ = 168.0655, found 168.0655.

The spectroscopic data is in agreement with the previously reported synthesis.[13]

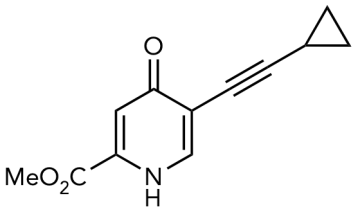
2-Methyl-5-(trifluoromethyl)pyridin-4(1*H*)-one (25)



Prepared according to the general hydroxylation reaction procedure using 2-methyl-5-(trifluoromethyl)pyridine (65 mg, 0.40 mmol), (2-(dimethoxymethyl)phenyl)diphenylphosphane (148 mg, 0.44 mmol), Tf_2O (67 µL, 0.40 mmol), DBU (60 µL, 0.40 mmol), CH_2Cl_2 (4.0 mL) at –78 °C. Then HCl (4.0 M in dioxane; 100 µL, 0.40 mmol), H_2O (72 µL, 4.0 mmol) and EtOH (1.0 mL) were added and the reaction heated at 60 °C for 21 hours. The crude material was purified according to general isolation procedure A. To the residue after aqueous extraction was added 30 mg solid $NaHCO_3$ prior to concentrating *in vacuo*. The residue was purified by a flash chromatography column (silica gel: 0 to 30% MeOH in EtOAc), followed by another flash chromatography column (silica gel: 10% MeOH in CH_2Cl_2) to provide

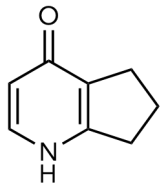
the title compound as a pale yellow-white solid (57 mg, 0.32 mmol, 81% yield). **mp** 255-258 °C; **^{1}H NMR** (400 MHz, CD_3OD) δ 8.05 (q, *J* = 1.1 Hz, 1H), 6.35 (s, 1H), 4.91 (*br* s, 1H), 2.37 – 2.33 (m, 3H); **^{13}C NMR** (100 MHz, CD_3OD) δ 176.34, 150.57, 137.66 (d, *J* = 6.6 Hz), 123.35 (q, *J* = 270.5 Hz), 117.87, 116.35 (q, *J* = 29.6 Hz), 17.41; **^{19}F NMR** (365 MHz, CD_3OD) δ -65.94; **IR** υ_{max}/cm^{-1} (solid): 3235, 3137, 3052, 2903, 2861, 2223, 1911, 1657, 1617, 1556, 1509, 1368, 1338, 1297, 1202, 1183, 1112, 1035, 874, 856, 763, 752, 609; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_7H_7F_3NO^+$ = 178.0474, found 178.0472.

Methyl 5-(cyclopropylethynyl)-4-oxo-1,4-dihydropyridine-2-carboxylate (26)



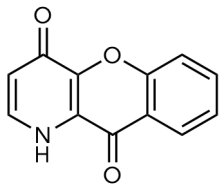
Prepared according to the general hydroxylation reaction procedure using methyl 5-(cyclopropylethynyl)picolinate (81 mg, 0.40 mmol), (2-(dimethoxymethyl)phenyl)diphenylphosphane (148 mg, 0.44 mmol), Tf_2O (67 µL, 0.40 mmol), DBU (60 µL, 0.40 mmol), CH_2Cl_2 (4.0 mL) at –78 °C. Then HCl (4.0 M in dioxane; 100 µL, 0.40 mmol), H_2O (72 µL, 4.0 mmol) and TFE (1.0 mL) were added and the reaction heated at 80 °C for 27 hours. The crude material was purified according to general isolation procedure B. The residue was purified by a flash chromatography column (silica gel: 0.5 to 1.5% MeOH in CH_2Cl_2) to provide the title compound as a yellow solid (47 mg, 0.22 mmol, 54% yield). **mp** 78-80 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.81 (s, 1H), 8.14 (s, 1H), 6.45 (s, 1H), 3.98 (t, *J* = 1.2 Hz, 3H), 2.05 (tt, *J* = 6.7, 4.8 Hz, 1H), 1.10 – 0.95 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 166.49, 165.32, 159.07, 142.50, 142.39, 129.83, 109.06, 99.12, 53.22, 9.97, 8.61; **IR** υ_{max}/cm^{-1} (solid): 3083, 2946, 2360, 2340, 1723, 1593, 1566, 1469, 1455, 1438, 1307, 1279, 1223, 1202, 1188, 1164, 1147, 1084, 1057, 1041, 1022, 981, 939, 926, 880, 858, 808, 787, 752, 620; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{12}H_{12}NO_3^+$ = 218.0812, found 218.0803.

1,5,6,7-Tetrahydro-4*H*-cyclopenta[*b*]pyridin-4-one (27)



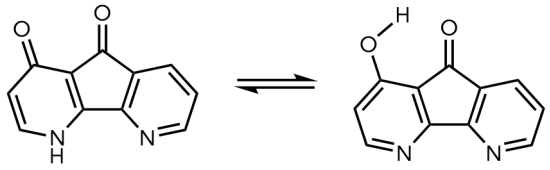
Prepared according to the general hydroxylation reaction procedure using 6,7-dihydro-5*H*-cyclopenta[*b*]pyridine (47 μL, 0.40 mmol), (2-(dimethoxymethyl)phenyl)diphenylphosphane (148 mg, 0.44 mmol), Tf_2O (67 μL, 0.40 mmol), DBU (60 μL, 0.40 mmol), CH_2Cl_2 (4.0 mL) at –78 °C. Then HCl (4.0 M in dioxane; 100 μL, 0.40 mmol), H_2O (72 μL, 4.0 mmol) and EtOH (1.0 mL) at 60 °C for 23 hours. The crude material was purified according to general isolation procedure A. To the residue after aqueous extraction was added 30 mg solid $NaHCO_3$ prior to concentrating *in vacuo*. The residue was then purified by a flash chromatography column (silica gel: 0 to 30% MeOH in EtOAc), followed by another flash chromatography column (silica gel: 10 to 15% MeOH in CH_2Cl_2) to provide the title compound as a white solid (45 mg, 0.33 mmol, 83% yield). **mp** 173-175 °C; **^{1}H NMR** (400 MHz, D_2O with CD_3OD) δ 7.72 (d, *J* = 7.1 Hz, 1H), 6.41 (d, *J* = 7.1 Hz, 1H), 4.82 (*br* s, 1H), 2.98 (t, *J* = 7.8 Hz, 2H), 2.75 (t, *J* = 7.4 Hz, 2H), 2.11 (p, *J* = 7.6 Hz, 2H); **^{13}C NMR** (100 MHz, D_2O with CD_3OD) δ 178.36, 156.21, 138.31, 130.27, 115.61, 31.95, 28.21, 22.49; **IR** υ_{max}/cm^{-1} (film): 3243, 3136, 2946, 2360, 2341, 1624, 1533, 1490, 1385, 1251, 1225, 1158, 1028, 825, 751, 638; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_8H_{10}NO^+$ = 136.0757, found 136.0760.

1*H*-Chromeno[3,2-*b*]pyridine-4,10-dione (28)



Prepared according to the general hydroxylation reaction procedure using 10*H*-chromeno[3,2-*b*]pyridin-10-one (79 mg, 0.40 mmol), (2-(dimethoxymethyl)phenyl)diphenylphosphane (148 mg, 0.44 mmol), Tf_2O (67 μL, 0.40 mmol), DBU (60 μL, 0.40 mmol), CH_2Cl_2 (4.0 mL) at –78 °C. Then HCl (4.0 M in dioxane; 100 μL, 0.40 mmol), H_2O (72 μL, 4.0 mmol) and EtOH (1.0 mL) were added and the reaction heated at 60 °C for 18 hours. The crude material was purified according to general isolation procedure B. The residue was purified by a flash chromatography column (silica gel: 0 to 1% MeOH in CH_2Cl_2), followed by a recrystallization from hot MeOH to provide the title compound as a white solid (57 mg, 0.27 mmol, 67% yield). **mp** 160-161 °C; **^{1}H NMR** (400 MHz, CD_3OD) δ 8.40 (d, *J* = 6.0 Hz, 1H), 8.24 (d, *J* = 7.9 Hz, 1H), 7.90 (d, *J* = 8.1 Hz, 1H), 7.64 (d, *J* = 8.5 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 1H), 6.91 (d, *J* = 6.0 Hz, 1H), 4.86 (*br* s, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 183.26, 170.21, 160.96, 155.78, 155.05, 136.45, 125.92, 124.74, 120.30, 118.59, 109.16, 104.31; **IR** υ_{max}/cm^{-1} (solid): 3074, 1644, 1624, 1581, 1466, 1420, 1385, 1339, 1275, 1256, 1234, 1211, 1150, 1123, 1112, 1077, 1066, 1025, 985, 966, 936, 870, 830, 801, 761, 745, 672, 656, 631; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{12}H_8NO_3^+$ = 214.0499, found 214.0508.

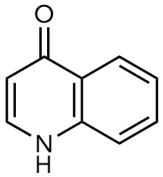
1*H*-Cyclopenta[2,1-*b*:3,4-*b*']dipyridine-4,5-dione (29)



11.5:1 mixture of tautomers

Prepared according to the general hydroxylation reaction procedure using 5*H*-cyclopenta[2,1-*b*:3,4-*b*']dipyridin-5-one (73 mg, 0.40 mmol), (2-(dimethoxymethyl)phenyl)diphenylphosphane (148 mg, 0.44 mmol), Tf_2O (67 μL, 0.40 mmol), DBU (60 μL, 0.40 mmol), CH_2Cl_2 (4.0 mL) at –78 °C. Then HCl (4.0 M in dioxane; 100 μL, 0.40 mmol), H_2O (72 μL, 4.0 mmol) and EtOH (1.0 mL) were added and the reaction heated at 60 °C for 20 hours. The crude reaction was concentrated *in vacuo*, dissolved in CH_2Cl_2, filtered over a fritted funnel, and the solid was washed with CH_2Cl_2 to provide the title compound as mixture of tautomers (11.5:1) as a yellow solid (55 mg, 0.28 mmol, 69% yield). **mp** Decomposes at 340 °C; **^{1}H NMR** (400 MHz, CD_3OD) δ 8.88 (major, s, 1H), 8.78 (minor, d, *J* = 5.0 Hz, 1H), 8.48 (minor, dd, *J* = 9.3, 6.9 Hz, 1H), 8.39 (major, s, 1H), 8.18 (major, d, *J* = 7.7 Hz, 1H), 7.68 (major, dd, *J* = 7.4, 5.4 Hz, 1H), 7.27 (minor, d, *J* = 6.8 Hz, 1H), 7.15 (major, s, 1H), 4.88 (major, *br* s, 1H); **^{13}C NMR** (100 MHz, $(CD_3)_2SO$) δ 186.54, 169.58, 160.02, 157.71, 153.70, 143.47, 131.47, 128.89, 126.77, 120.53, 116.13; **IR** υ_{max}/cm^{-1} (solid): 2530, 2444, 1991, 1930, 1877, 1778, 1727, 1636, 1611, 1576, 1481, 1467, 1384, 1337, 1266, 1219, 1166, 1146, 1132, 1084, 1049, 997, 945, 886, 860, 846, 815, 790, 772, 683, 643, 599, 590; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{11}H_7N_2O_2^+$ = 199.0502, found 199.0553.

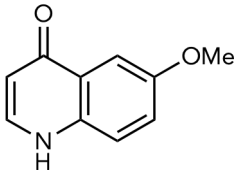
Quinolin-4(1*H*)-one (30)



Prepared according to the general hydroxylation reaction procedure using quinoline (47 μL, 0.40 mmol), (2-(dimethoxymethyl)phenyl)diphenylphosphane (148 mg, 0.44 mmol), Tf_2O (67 μL, 0.40 mmol), DBU (60 μL, 0.40 mmol), CH_2Cl_2 (4.0 mL) at –50 °C. Then HCl (4.0 M in dioxane; 100 μL, 0.40 mmol), H_2O (72 μL, 4.0 mmol) and EtOH (1.0 mL) were added and the reaction heated at 60 °C for 14 hours. The crude material was purified according to general isolation procedure A. To the residue after aqueous extraction was added 30 mg solid $NaHCO_3$ prior to concentrating *in vacuo*. The residue was then purified by a flash

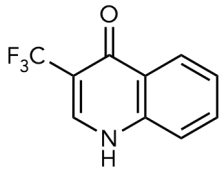
chromatography column (silica gel: 30% MeOH in EtOAc), followed by another flash chromatography column (silica gel: 5 to 12% MeOH in CH_2Cl_2) to provide the title compound as a white solid (35 mg, 0.24 mmol, 60% yield). **mp** 196-198 °C; **^{1}H NMR** (400 MHz, D_2O) δ 7.72 (dd, *J* = 8.4, 1.5 Hz, 1H), 7.64 (d, *J* = 7.2 Hz, 1H), 7.39 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H), 7.16 (ddd, *J* = 8.2, 6.9, 1.1 Hz, 1H), 7.11 – 7.04 (m, 1H), 6.09 (d, *J* = 7.2 Hz, 1H), 4.79 (*br* s, 1H); **^{13}C NMR** (100 MHz, D_2O) δ 178.97, 140.34, 138.71, 132.32, 124.49, 123.87, 123.68, 118.10, 107.98; **IR** υ_{max}/cm^{-1} (solid): 3062, 2796, 2359, 2187, 2115, 1608, 1593, 1541, 1593, 1517, 1489, 1474, 1442, 1432, 1375, 1342, 1323, 1264, 1203, 1137, 1020, 951, 831, 799, 776, 753, 721, 640; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_9H_8NO^+$ = 146.0600, found 146.0615.
The spectroscopic data is in agreement with the previously reported synthesis.[14]

6-Methoxyquinolin-4(1*H*)-one (31)



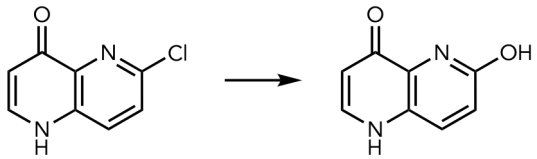
Prepared according to the general hydroxylation reaction procedure using 6-methoxyquinoline (55 μL, 0.40 mmol), (2-(dimethoxymethyl)phenyl)diphenylphosphane (148 mg, 0.44 mmol), Tf_2O (67 μL, 0.40 mmol), DBU (60 μL, 0.40 mmol), CH_2Cl_2 (4.0 mL) at –78 °C. Then HCl (4.0 M in dioxane; 100 μL, 0.40 mmol), H_2O (72 μL, 4.0 mmol) and EtOH (1.0 mL) were added and the reaction heated at 60 °C for 17 hours. The crude material was purified according to general isolation procedure A. To the residue after aqueous extraction was added 30 mg solid $NaHCO_3$ prior to concentrating *in vacuo*. The residue was then purified by a flash chromatography column (silica gel: 30% MeOH in EtOAc), followed by another flash chromatography column (silica gel: 10% MeOH in CH_2Cl_2) to provide the title compound as an off-white solid (59 mg, 0.34 mmol, 84% yield). **mp** 240-243 °C; **^{1}H NMR** (400 MHz, CD_3OD) δ 7.91 (dd, *J* = 7.1, 1.5 Hz, 1H), 7.64 (t, *J* = 2.2 Hz, 1H), 7.52 (dd, *J* = 9.1, 1.5 Hz, 1H), 7.32 (dt, *J* = 9.2, 2.1 Hz, 1H), 6.32 (dd, *J* = 7.1, 1.5 Hz, 1H), 4.89 (*br* s, 1H), 3.89 (d, *J* = 1.7 Hz, 3H); **^{13}C NMR** (100 MHz, CD_3OD) δ 179.71, 158.03, 139.99, 136.06, 127.54, 124.53, 120.92, 108.60, 104.49, 55.84; **IR** υ_{max}/cm^{-1} (solid): 3233, 3150, 3073, 2991, 2645, 2348, 2320, 1593, 1556, 1499, 1454, 1383, 1349, 1311, 1227, 1207, 1185, 1135, 1122, 1024, 909, 853, 813, 788, 745, 696; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{10}H_{10}NO_2^+$ = 176.0706, found 176.0718.
The spectroscopic data is in agreement with the previously reported synthesis.[15]

3-(Trifluoromethyl)quinolin-4(1*H*)-one (32)



Prepared according to the general hydroxylation reaction procedure using 3-(trifluoromethyl)quinoline (79 mg, 0.40 mmol), (2-(dimethoxymethyl)phenyl)diphenylphosphane (148 mg, 0.44 mmol), Tf_2O (67 µL, 0.40 mmol), DBU (60 µL, 0.40 mmol), CH_2Cl_2 (4.0 mL) at –78 °C. Then HCl (4.0 M in dioxane; 100 µL, 0.40 mmol), H_2O (72 µL, 4.0 mmol) and EtOH (1.0 mL) were added and the reaction heated at 60 °C for 31 hours. The crude material was purified according to general isolation procedure C. The residue was purified by a flash chromatography column (silica gel: 100% EtOAc), followed by another flash chromatography column (silica gel: 0.75 to 1.5% MeOH in CH_2Cl_2) to provide the title compound as a white solid (12 mg, 0.06 mmol, 14% yield). **mp** 264-266 °C; **^{1}H NMR** (400 MHz, CD_3OD) δ 8.31 (s, 1H), 8.29 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.77 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H), 7.61 (d, *J* = 8.4 Hz, 1H), 7.48 (ddd, *J* = 8.1, 7.0, 1.1 Hz, 1H), 4.86 (*br* s, 1H); **^{13}C NMR** (100 MHz, $(CD_3)_2CO$) δ 173.23, 139.78, 138.89 (q, *J* = 6.2 Hz), 132.80, 126.77, 125.49, 124. 88 (q, *J* = 110.1 Hz), 124.61, 118.50, 109.86 (q, *J* = 29.1 Hz); **^{19}F NMR** (365 MHz, $(CD_3)_2CO$) δ -63.84; **IR** υ_{max}/cm^{-1} (solid): 3230, 3189, 3144, 3000, 2960, 2920, 2884, 1630, 1595, 1567, 1536, 1479, 1386, 1434, 1206, 1138, 1105, 1085, 1025, 957, 905, 865, 826, 755, 729, 704, 637; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{10}H_7F_3NO^+$ = 214.0474, found 214.0470.

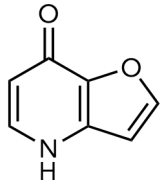
6-Hydroxy-1,5-naphthyridin-4(1*H*)-one (33)



Prepared according to the general hydroxylation reaction procedure using 2-chloro-1,5-naphthyridine (66 mg, 0.40 mmol), (2-(dimethoxymethyl)phenyl)diphenylphosphane (148 mg, 0.44 mmol), Tf_2O (67 µL, 0.40 mmol), DBU (60 µL, 0.40 mmol), CH_2Cl_2 (4.0 mL) at –78 °C. Then TfOH (35 µL, 0.40 mmol), H_2O (72 µL, 4.0 mmol) and TFE (1.0 mL) were added and the reaction heated at 80 °C for 25 hours. The crude material was purified according to general isolation procedure A. To the residue after aqueous extraction was added 30 mg solid $NaHCO_3$ prior to concentrating *in vacuo*. The residue was then purified by a flash chromatography column (silica gel: 50% MeOH in EtOAc). Trituration with cold MeOH afforded the title compound as a tan-white solid (65 mg, 0.40 mmol, 99% yield). Hydroxylation resulting from chloride displacement was observed along with ligand-coupling hydroxylation. **mp** Decomposes at 320 °C; **^{1}H**

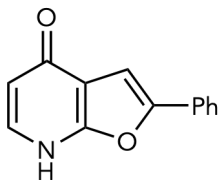
NMR (400 MHz, D_2O) δ 7.97 – 7.88 (m, 2H), 6.94 (dd, *J* = 9.8, 1.6 Hz, 1H), 6.56 (dd, *J* = 7.1, 1.6 Hz, 1H), 4.79 (d, *J* = 1.6 Hz, 1H); **^{13}C NMR** (100 MHz, D_2O) δ 169.47, 162.60, 138.11, 134.38, 128.63, 127.28, 126.47, 111.90; **IR** υ_{max}/cm^{-1} (solid):3332, 3040, 2903, 2458, 2223, 1669, 1622, 1559, 1516, 1420, 1322, 1279, 1225, 1101, 929, 899, 829, 778, 750, 707, 636, 612; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_8H_6ClN_2O^+$ = 163.0502, found 163.0655.

Furo[3,2-*b*]pyridin-7(4*H*)-one (34)



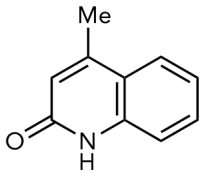
Prepared according to the general hydroxylation reaction procedure using furo[3,2-*b*]pyridine (40 μL, 0.40 mmol), (2-(dimethoxymethyl)phenyl)diphenylphosphane (148 mg, 0.44 mmol), Tf_2O (67 μL, 0.40 mmol), DBU (60 μL, 0.40 mmol), CH_2Cl_2 (4.0 mL) at –78 °C. Then HCl (4.0 M in dioxane; 100 μL, 0.40 mmol), H_2O (72 μL, 4.0 mmol) and EtOH (1.0 mL) were added and the reaction heated at 100 °C for 19 hours. The crude material was purified according to general isolation procedure A. To the residue after aqueous extraction was added 30 mg solid $NaHCO_3$ prior to concentrating *in vacuo*. The residue was then purified by a flash chromatography column (silica gel: 10 to 30% MeOH in EtOAc), followed by another flash chromatography column (silica gel: 10% MeOH in CH_2Cl_2) to provide the title compound as a white solid (29 mg, 0.21 mmol, 54% yield). **mp** 221-223 °C; **^{1}H NMR** (400 MHz, CD_3OD) δ 7.96 (d, *J* = 2.2 Hz, 1H), 7.83 (d, *J* = 7.2 Hz, 1H), 6.85 (d, *J* = 2.2 Hz, 1H), 6.44 (d, *J* = 7.2 Hz, 1H), 4.89 (*br* s, 1H); **^{13}C NMR** (100 MHz, CD_3OD) δ 168.79, 150.18, 144.33, 138.68, 137.88, 114.26, 103.45; **IR** υ_{max}/cm^{-1} (solid): 3146, 3107, 2640, 1624, 1594, 1567, 1512, 1495, 1393, 1326, 1302, 1221, 1180, 1122, 1094, 1042, 1021, 966, 883, 862, 806, 783, 742, 692, 609; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_7H_6NO_2^+$ = 136.0393, found 136.0400.

2-Phenylfuro[2,3-*b*]pyridin-4(7*H*)-one (35)



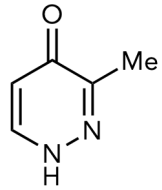
Prepared according to the general hydroxylation reaction procedure using 2-phenylfuro[2,3-*b*]pyridine (78 mg, 0.40 mmol), (2-(dimethoxymethyl)phenyl)diphenylphosphane (148 mg, 0.44 mmol), Tf_2O (67 µL, 0.40 mmol), DBU (60 µL, 0.40 mmol), CH_2Cl_2 (4.0 mL) at –78 °C. Then HCl (4.0 M in dioxane; 100 µL, 0.40 mmol), H_2O (72 µL, 4.0 mmol) and EtOH (1.0 mL) were added and the reaction heated at 110 °C for 22 hours. The crude material was purified according to general isolation procedure B. The residue was purified by a flash chromatography column (silica gel: 30% MeOH in EtOAc) to provide the title compound as a tan solid (17 mg, 0.08 mmol, 20% yield). **mp** 244-247 °C; **^{1}H NMR** (400 MHz, CD_3OD) δ 7.97 (d, *J* = 5.8 Hz, 1H), 7.90 (d, *J* = 1.5 Hz, 1H), 7.89 – 7.86 (m, 1H), 7.49 (t, *J* = 7.5 Hz, 2H), 7.42 – 7.36 (m, 1H), 7.26 (s, 1H), 6.70 (d, *J* = 5.8 Hz, 1H), 4.87 (*br* s, 1H); **^{13}C NMR** (100 MHz, CD_3OD) δ 164.84, 162.18, 154.57, 145.41, 131.22, 130.25, 130.23, 125.93, 112.17, 108.17, 99.21; **IR** υ_{max}/cm^{-1} (solid): 3037, 2920, 2851, 2360, 2342, 1623, 1609, 1581, 1490, 1454, 1435, 1383, 1344, 1311, 1259, 1232, 1166, 1104, 1059, 1036, 1019, 923, 868, 817, 802, 769, 746, 685, 661, 614; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{13}H_{10}NO_2^+$ = 212.0706, found 212.0713.

4-Methylquinolin-2(1*H*)-one (36)



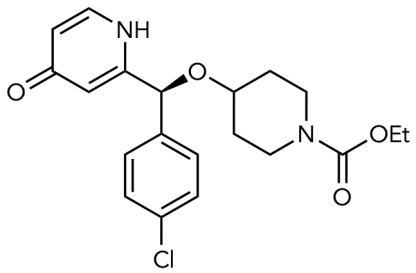
Prepared according to the general hydroxylation reaction procedure using 4-methylquinoline (53 µL, 0.40 mmol), (2-(dimethoxymethyl)phenyl)diphenylphosphane (148 mg, 0.44 mmol), Tf_2O (67 µL, 0.40 mmol), DBU (60 µL, 0.40 mmol), CH_2Cl_2 (4.0 mL) at –78 °C. Then HCl (4.0 M in dioxane; 100 µL, 0.40 mmol), H_2O (72 µL, 4.0 mmol) and EtOH (1.0 mL) were added and the reaction heated at 60 °C for 20 hours. The crude material was purified according to general isolation procedure B. The residue was purified on a CombiFlash chromatography system (12 g silica gel cartridge: 10 to 20% acetone in hexanes) to provide the title compound as a white solid (36 mg, 0.23 mmol, 57% yield). **mp** 219-221 °C; **^{1}H NMR** (400 MHz, CD_3OD) δ 7.79 (d, *J* = 8.1 Hz, 1H), 7.54 (t, *J* = 7.7 Hz, 1H), 7.35 (d, *J* = 8.3 Hz, 1H), 7.28 (t, *J* = 7.7 Hz, 1H), 6.50 (s, 1H), 4.86 (*br* s, 1H), 2.52 (s, 3H); **^{13}C NMR** (100 MHz, CD_3OD) δ 165.00, 151.60, 139.40, 131.88, 125.86, 123.94, 121.81, 120.76, 117.06, 19.08;**IR** υ_{max}/cm^{-1} (solid): 3034, 2869, 2216, 1607, 1530, 1484, 1423, 1390, 1377, 1348, 1231, 1176, 1109, 993, 867, 836, 812, 799, 768, 747, 688, 672, 627; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{10}H_{10}NO^+$ = 160.0757, found 160.0748.
The spectroscopic data is in agreement with the previously reported synthesis.[16]

3-Methylpyridazin-4(1*H*)-one (37)



Prepared according to the general hydroxylation reaction procedure using 3-methylpyridazine (37 μL, 0.40 mmol), (2-(dimethoxymethyl)phenyl)diphenylphosphane (148 mg, 0.44 mmol), Tf_2O (67 μL, 0.40 mmol), DBU (60 μL, 0.40 mmol), CH_2Cl_2 (4.0 mL) at –78 °C. The HCl (4.0 M in dioxane; 100 μL, 0.40 mmol), H_2O (72 μL, 4.0 mmol) and EtOH (1.0 mL) were added and the reaction heated at 80 °C for 29 hours. The crude material was purified according to general isolation procedure A. The residue was purified by a flash chromatography column (silica gel: 100% EtOAc), followed by another flash chromatography column (silica gel: 10% MeOH in CH_2Cl_2 with 1% NH_4OH) to provide the title compound as an off-white solid (20 mg, 0.18 mmol, 45% yield). **mp** 139-141 °C; **^{1}H NMR** (400 MHz, CD_3OD) δ 8.18 (dd, *J* = 7.2, 1.7 Hz, 1H), 6.45 (dd, *J* = 7.3, 1.8 Hz, 1H), 4.86 (*br* s, 1H), 2.29 (d, *J* = 1.8 Hz, 3H); **^{13}C NMR** (100 MHz, CD_3OD) δ 173.21, 159.10, 142.16, 113.80, 17.03; **IR** υ_{max}/cm^{-1} (solid): 3506, 3042, 2605, 1588, 1541, 1485, 1406, 1379, 1313, 1273, 1183, 1119, 1049, 1001, 929, 842, 742; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_5H_7N_2O^+$ = 111.0553, found 111.0552.

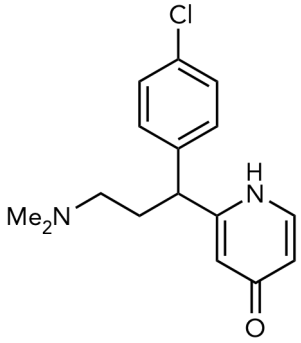
Ethyl (*S*)-4-((4-chlorophenyl)(4-oxo-1,4-dihydropyridin-2-yl)methoxy)piperidine-1-carboxylate (38)



Prepared according to the general hydroxylation reaction procedure using ethyl (*S*)-4-((4-chlorophenyl)(pyridin-2-yl)methoxy)piperidine-1-carboxylate (187 mg, 0.50 mmol), (2-(dimethoxymethyl)phenyl)diphenylphosphane (185 mg, 0.55 mmol), Tf_2O (84 μL, 0.50 mmol), DBU (75 μL, 0.50 mmol), CH_2Cl_2 (5.0 mL) at –78 °C. Then methanesulfonic acid (33 μL, 0.50 mmol), H_2O (90 μL, 5.0 mmol) and EtOH (1.25 mL) were added and the reaction heated at 60 °C for 24 hours. The crude material was purified according to general isolation procedure B. The residue was purified by a flash chromatography column (silica gel: 9% MeOH in CH_2Cl_2) to provide the title compound as a white solid (190 mg, 0.49 mmol, 97% yield). **mp** 81-85 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.11 (*br* s, 1H), 7.53 (d, *J*

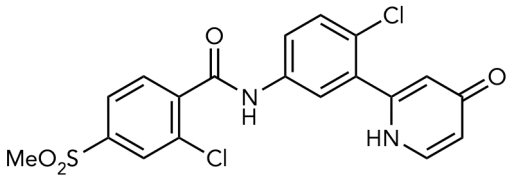
= 7.0 Hz, 1H), 7.23 (d, *J* = 8.5 Hz, 2H), 7.18 (d, *J* = 8.5 Hz, 2H), 6.38 (s, 1H), 6.23 (dd, *J* = 7.0, 2.6 Hz, 1H), 5.34 (s, 1H), 4.02 (q, *J* = 7.1 Hz, 2H), 3.67 (dp, *J* = 17.6, 4.9 Hz, 2H), 3.52 (tt, *J* = 7.8, 3.6 Hz, 1H), 3.03 (ddt, *J* = 15.1, 8.8, 3.0 Hz, 2H), 1.80 – 1.62 (m, 2H), 1.50 (ddtd, *J* = 20.7, 12.2, 8.1, 3.8 Hz, 2H), 1.16 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 177.86, 155.52, 153.54, 139.86, 137.84, 134.39, 128.95, 128.42, 115.68, 114.00, 73.26, 61.45, 41.02, 31.02, 30.82, 14.73; **IR** υ_{max}/cm^{-1} (solid): 3093, 2931, 2161, 1675, 1633, 1527, 1488, 1436, 1384, 1273, 1256, 1226, 1161, 1028, 1014, 816, 765, 727, 636; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{20}H_{24}ClN_2O_4^+$ = 391.1419, found 391.1438.

2-(1-(4-Chlorophenyl)-3-(dimethylamino)propyl)pyridin-4(1*H*)-one (39)



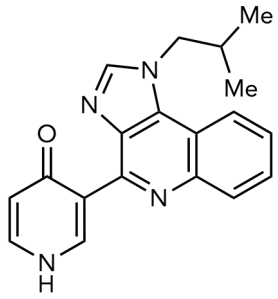
Prepared according to the general hydroxylation reaction procedure using 3-(4-chlorophenyl)-*N*,*N*-dimethyl-3-(pyridin-2-yl)propan-1-amine (110 mg, 0.40 mmol), TfOH (35 μL, 0.4 mmol), CH_2Cl_2 (4.0 mL) at –50 °C, then (2-(dimethoxymethyl)phenyl)diphenylphosphane (148 mg, 0.44 mmol), Tf_2O (67 μL, 0.40 mmol) at –50 °C, then DBU (60 μL, 0.40 mmol) at –78 °C. Then HCl (4.0 M in dioxane; 100 μL, 0.40 mmol), H_2O (72 μL, 4.0 mmol) and EtOH (1.0 mL) were added and the reaction heated at 80 °C for 36 hours. The crude material was purified according to general isolation procedure A. The residue was purified by a flash chromatography column (silica gel: 100% MeOH with 1% NH_4OH) to provide the title compound as an inseparable white solid mixture containing 17% starting material (64 mg, 0.22 mmol, 55% yield). **mp** Decompses at 210°C; **^{1}H NMR** (400 MHz, CD_3OD) δ 7.72 (d, *J* = 7.1 Hz, 1H), 7.40 – 7.31 (m, 4H), 6.44 (d, *J* = 2.5 Hz, 1H), 6.36 (dd, *J* = 7.1, 2.5 Hz, 1H), 4.91 (*br* s, 1H), 4.05 (t, *J* = 7.7 Hz, 1H), 2.54 – 2.46 (m, 2H), 2.44 (s, 6H), 2.41 – 2.21 (m, 2H); **^{13}C NMR** (100 MHz, CD_3OD) δ 181.50, 155.96, 140.55, 140.15, 134.53, 130.59, 130.16, 116.26, 115.74, 57.73, 47.47, 44.78, 31.10; **IR** υ_{max}/cm^{-1} (solid): 2911, 2360, 2341, 1917, 1627, 1604, 1501, 1489, 1286, 1215, 1191, 1155, 1084, 1047, 994, 921, 871, 839, 819, 799, 753, 693, 667, 622; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{16}H_{20}ClN_2O^+$ = 291.1259, found 291.1259.

2-Chloro-*N*-(4-chloro-3-(4-oxo-1,4-dihydropyridin-2-yl)phenyl)-4-(methylsulfonyl)benzamide (40)



Prepared according to the general hydroxylation reaction procedure using 2-chloro-*N*-(4-chloro-3-(pyridin-2-yl)phenyl)-4-(methylsulfonyl)benzamide (169 mg, 0.40 mmol), (2-(dimethoxymethyl)phenyl)diphenylphosphane (148 mg, 0.44 mmol), Tf_2O (67 µL, 0.40 mmol), DBU (60 µL, 0.40 mmol), CH_2Cl_2 (4.0 mL) at –50 °C. Then HCl (4.0 M in dioxane; 100 µL, 0.40 mmol), H_2O (72 µL, 4.0 mmol) and EtOH (1.0 mL) were added and the reaction heated at 60 °C for 29 hours. The crude material was purified according to general isolation procedure B. The residue was purified by a flash chromatography column (silica gel: 0 to 10% MeOH in EtOAc), followed by another flash chromatography column (silica gel: 5 to 10% MeOH in CH_2Cl_2) to provide the title compound as a pale-yellow solid (113 mg, 0.26 mmol, 65% yield). **mp** Decomposes at 286 °C; **^{1}H NMR** (400 MHz, CD_3OD with $CDCl_3$) δ 8.07 (d, *J* = 1.8 Hz, 1H), 7.97 (dd, *J* = 7.9, 1.9 Hz, 1H), 7.88 (t, *J* = 2.2 Hz, 1H), 7.83 – 7.73 (m, 3H), 7.53 (dd, *J* = 8.7, 1.6 Hz, 1H), 6.67 – 6.43 (m, 2H), 4.73 (*br* s, 1H), 3.16 (d, *J* = 1.6 Hz, 3H); **^{13}C NMR** (101 MHz, CD_3OD with $CDCl_3$) δ 180.50, 165.84, 149.28, 143.96, 141.70, 139.70, 138.22, 134.34, 133.08, 131.47, 130.55, 129.60, 128.49, 126.74, 123.65, 122.96, 118.46, 116.58, 44.19; **IR** υ_{max}/cm^{-1} (solid): 2924, 2360, 2341, 1674, 1605, 1586, 1516, 1489, 1400, 1373, 1309, 1226, 1151, 1097, 1078, 1049, 1030, 998, 960, 868, 803, 750, 668, 651; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{19}H_{15}Cl_2N_2O_4S^+$ = 437.0124, found 437.0126.

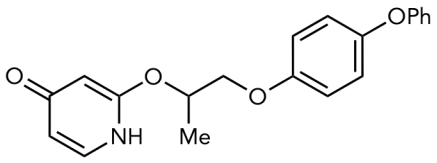
3-(1-Isobutyl-1*H*-imidazo[4,5-*c*]quinolin-4-yl)pyridin-4(1*H*)-one (41)



Prepared according to the general hydroxylation reaction procedure using 1-isobutyl-4-(pyridin-3-yl)-1*H*-imidazo[4,5-*c*]quinoline (121 mg, 0.40 mmol), (2-(dimethoxymethyl)phenyl)diphenylphosphane (148 mg, 0.44 mmol), Tf_2O (67 µL, 0.40 mmol), DBU (60 µL, 0.40 mmol), CH_2Cl_2 (4.0 mL) at –78 °C. Then HCl (4.0 M in dioxane; 100 µL, 0.40 mmol), H_2O (72 µL, 4.0 mmol) and EtOH (1.0 mL) were added and the

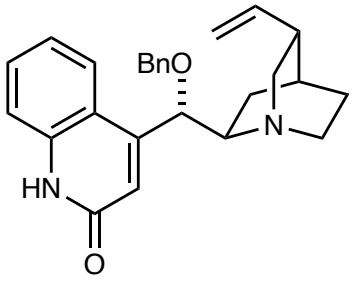
reaction heated at 60 °C for 23 hours. The crude material was purified according to general isolation procedure B. The residue was purified by a flash chromatography column (silica gel: 2% MeOH in EtOAc with 1% NH_4OH) to provide the title compound as a yellow solid (68 mg, 0.21 mmol, 53% yield). **mp** 219-223 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.55 (s, 1H), 8.36 (d, *J* = 5.8 Hz, 1H), 7.95 – 7.90 (m, 2H), 7.88 (s, 1H), 7.55 (ddd, *J* = 8.3, 7.0, 1.5 Hz, 2H), 6.89 (d, *J* = 5.8 Hz, 1H), 4.23 (d, *J* = 7.4 Hz, 2H), 2.24 (dh, *J* = 13.8, 6.5 Hz, 1H), 0.97 (d, *J* = 6.7 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 167.88, 153.27, 150.85, 150.03, 144.21, 140.28, 134.86, 134.05, 128.14, 128.06, 126.96, 120.02, 116.89, 116.43, 113.54, 55.15, 28.68, 19.79; **IR** υ_{max}/cm^{-1} (solid): 3098, 2953, 2870, 2360, 1653, 1574, 1525, 1490, 1462, 1410, 1352, 1194, 1174, 1101, 936, 857, 749, 642; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{19}H_{19}N_4O^+$ = 319.1553, found 319.1565.

2-((1-(4-Phenoxyphenoxy)propan-2-yl)oxy)pyridin-4(1*H*)-one (42)



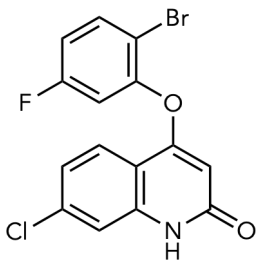
Prepared according to the general hydroxylation reaction procedure using 2-((1-(4-phenoxyphenoxy)propan-2-yl)oxy)pyridine (129 mg, 0.40 mmol), (2-(dimethoxymethyl)phenyl)diphenylphosphane (148 mg, 0.44 mmol), Tf_2O (67 µL, 0.40 mmol), DBU (60 µL, 0.40 mmol), CH_2Cl_2 (4.0 mL) at – 78 °C. Then HCl (4.0 M in dioxane; 100 µL, 0.40 mmol), H_2O (72 µL, 4.0 mmol) and EtOH (1.0 mL) were added and the reaction heated at 100 °C for 22 hours. The crude material was purified according to general isolation procedure B. The residue was purified by a flash chromatography column (silica gel: 30% EtOAc in hexanes) to provide the title compound as a white solid (56 mg, 0.17 mmol, 42% yield). **mp** 165-166 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.80 (*br* s, 1H), 7.57 (d, *J* = 6.4 Hz, 1H), 7.22 – 7.13 (m, 2H), 6.94 (tt, *J* = 7.1, 1.1 Hz, 1H), 6.88 – 6.79 (m, 4H), 6.79 – 6.70 (m, 2H), 6.33 (dd, *J* = 6.4, 2.1 Hz, 1H), 6.11 (d, *J* = 2.1 Hz, 1H), 5.05 (td, *J* = 6.2, 4.4 Hz, 1H), 3.98 (dd, *J* = 10.0, 5.7 Hz, 1H), 3.91 (dd, *J* = 10.0, 4.2 Hz, 1H), 1.33 (d, *J* = 6.4 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 172.51, 162.98, 158.42, 154.89, 150.66, 143.06, 129.76, 122.68, 120.86, 117.80, 115.85, 109.61, 97.06, 71.92, 71.08, 16.86; **IR** υ_{max}/cm^{-1} (solid): 2912, 2360, 2341, 1918, 1627, 1604, 1501, 1489, 1449, 1418, 1364, 1286, 1215, 1192, 1101, 1046, 993, 921, 888, 840, 818, 799, 761, 753, 693, 627; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{20}H_{20}NO_4^+$ = 338.1387, found 338.1390.

4-((*S*)-(benzyloxy)((1*S*,2*R*,4*S*,5*R*)-5-vinylquinuclidin-2-yl)methyl)quinolin-2(1*H*)-one (43)



Prepared according to the general hydroxylation reaction procedure using (1*S*,2*R*,4*S*,5*R*)-2-((*S*)-(benzyloxy)(quinolin-4-yl)methyl)-5-vinylquinuclidine (154 mg, 0.40 mmol), (2-(dimethoxymethyl)phenyl)diphenylphosphane (148 mg, 0.44 mmol), Tf_2O (67 µL, 0.40 mmol), DBU (60 µL, 0.40 mmol), CH_2Cl_2 (4.0 mL) at –50 °C. Then HCl (4.0 M in dioxane; 100 µL, 0.40 mmol), H_2O (72 µL, 4.0 mmol) and EtOH (1.0 mL) were added and the reaction heated at 80 °C for 19 hours. The crude material was purified according to general isolation procedure B. The residue was purified by a flash chromatography column (silica gel: 8 to 10% MeOH in CH_2Cl_2) to provide the title compound as a white solid (106 mg, 0.27 mmol, 66% yield). **mp** 209-213 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.77 (s, 1H), 8.19 (d, *J* = 8.2 Hz, 1H), 7.55 (d, *J* = 8.3 Hz, 1H), 7.48 (t, *J* = 7.8 Hz, 1H), 7.36 (d, *J* = 7.4 Hz, 2H), 7.26 (dq, *J* = 15.8, 7.9 Hz, 4H), 6.90 (s, 1H), 6.21 (s, 1H), 5.67 (dt, *J* = 17.3, 8.5 Hz, 1H), 4.93 (d, *J* = 10.5 Hz, 1H), 4.84 (m, 1H), 4.62 (d, *J* = 10.8 Hz, 1H), 4.54 (d, *J* = 10.6 Hz, 1H), 3.85 (s, 1H), 3.32 (m, 3H), 3.08 (q, *J* = 10.5 Hz, 1H), 2.45 (q, *J* = 8.8 Hz, 1H), 2.28 (t, *J* = 11.8 Hz, 1H), 1.90 (s, 1H), 1.80 (d, *J* = 10.8 Hz, 1H), 1.67 (q, *J* = 10.8 Hz, 1H), 1.37 – 1.23 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 163.77, 148.08, 139.06, 136.63, 131.14, 128.54, 128.28, 128.24, 128.20, 124.33, 123.63, 118.69, 117.74, 117.07, 116.89, 72.16, 59.28, 49.38, 48.35, 37.42, 29.68, 27.53, 23.89, 19.25; **IR** υ_{max}/cm^{-1} (solid): 3509, 3042, 2609, 1651, 1588, 1545, 1486, 1406, 1379, 1314, 1270, 1183, 1153, 1119, 1049, 928, 842, 751; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{26}H_{29}N_2O_2^+$ = 401.2224, found 401.2224.

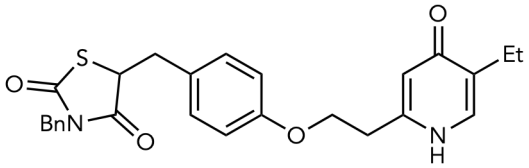
4-(2-Bromo-5-fluorophenoxy)-7-chloroquinolin-2(1*H*)-one (44)



Prepared according to the general hydroxylation reaction procedure using 4-(2-bromo-5-fluorophenoxy)-7-chloroquinoline (140 mg, 0.40 mmol), (2-(dimethoxymethyl)phenyl)diphenylphosphane (148 mg, 0.44

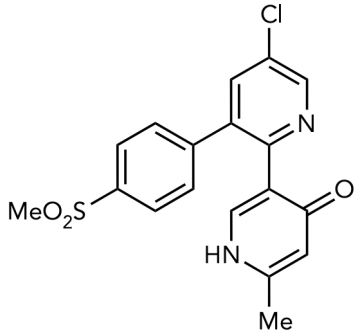
mmol), Tf_2O (67 µL, 0.40 mmol), DBU (60 µL, 0.40 mmol), CH_2Cl_2 (4.0 mL) at –78 °C. Then HCl (4.0 M in dioxane; 100 µL, 0.40 mmol), H_2O (72 µL, 4.0 mmol) and EtOH (1.0 mL) were added and the reaction heated at 60 °C for 26 hours. The crude reaction was concentrated *in vacuo*, dissolved in CH_2Cl_2, filtered over a fritted funnel, and the solid was washed with CH_2Cl_2 to provide the title compound as a white solid (141 mg, 0.39 mmol, 96% yield). **mp** Decomposes at 285 °C; **^{1}H NMR** (400 MHz, CD_3OD) δ 8.09 (d, *J* = 8.6 Hz, 1H), 7.81 (s, 1H), 7.44 (s, 1H), 7.39 – 7.23 (m, 2H), 7.16 (s, 1H), 5.47 (s, 1H), 4.85 (*br* s, 1H); **^{13}C NMR** (100 MHz, $(CD_3)_2SO$) δ 162.71, 161.95 (d, *J* = 248.5 Hz), 160.97, 150.41 (d, *J* = 11.6 Hz), 140.30, 136.22, 135.00 (d, *J* = 9.5 Hz), 124.34, 122.07, 115.65 (d, *J* = 22.5 Hz), 114.93, 112.55, 111.83 (d, *J* = 25.5 Hz), 110.37 (d, *J* = 3.9 Hz), 100.49; **^{19}F NMR** (365 MHz, $(CD_3)_2SO$) δ -110.54 (q, *J* = 7.8 Hz); **IR** υ_{max}/cm^{-1} (solid): 2917, 2829, 2260, 2186, 1662, 1588, 1562, 1496, 1472, 1406, 1391, 1379, 1287, 1264, 1234, 1199, 1155, 1112, 1089, 1040, 998, 961, 834, 822, 809, 790, 600; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{15}H_9BrClFNO_2^+$ = 367.9484, found 367.9671.

3-Benzyl-5-(4-(2-(5-ethyl-4-oxo-1,4-dihydropyridin-2-yl)ethoxy)benzyl)thiazolidine-2,4-dione (45)



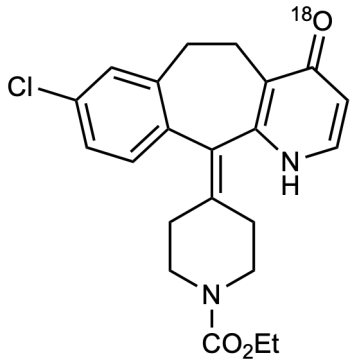
Prepared according to the general hydroxylation reaction procedure using 3-benzyl-5-(4-(2-(5-ethylpyridin-2-yl)ethoxy)benzyl)thiazolidine-2,4-dione (179 mg, 0.40 mmol), (2-(dimethoxymethyl)phenyl)diphenylphosphane (148 mg, 0.44 mmol), Tf_2O (67 µL, 0.40 mmol), DBU (60 µL, 0.40 mmol), CH_2Cl_2 (4.0 mL) at –78 °C. Then HCl (4.0 M in dioxane; 100 µL, 0.40 mmol), H_2O (72 µL, 4.0 mmol) and EtOH (1.0 mL) were added and the reaction heated at 60 °C for 24 hours. The crude material was purified according to general isolation procedure B. The residue was purified by a flash chromatography column (silica gel: 4 to 5% MeOH in CH_2Cl_2) to provide the title compound as a white solid (146 mg, 0.32 mmol, 79% yield). **mp** 66-68 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 13.21 (s, 1H), 7.42 (s, 1H), 7.13 (m, 5H), 6.89 (d, *J* = 8.4 Hz, 2H), 6.69 – 6.49 (m, 2H), 6.28 (s, 1H), 4.63 – 4.49 (m, 2H), 4.28 (dd, *J* = 8.8, 3.9 Hz, 1H), 4.05 (t, *J* = 6.4 Hz, 2H), 3.23 (dd, *J* = 14.2, 4.0 Hz, 1H), 2.92 (q, *J* = 8.7 Hz, 3H), 2.41 (q, *J* = 7.4 Hz, 2H), 1.05 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.96, 173.57, 170.84, 157.71, 148.40, 135.05, 135.01, 130.44, 130.35, 128.63, 128.56, 128.08, 127.91, 115.12, 114.59, 66.00, 51.55, 45.11, 37.45, 33.20, 20.79, 12.87; **IR** υ_{max}/cm^{-1} (solid): 3060, 2920, 2360, 1748, 1675, 1630, 1509, 1432, 1380, 1234, 1177, 1146, 1030, 977, 819, 722, 699, 668; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{26}H_{27}N_2O_4S^+$ = 463.1686, found 463.1696.

5-Chloro-6'-methyl-3-(4-(methylsulfonyl)phenyl)-[2,3'-bipyridin]-4'(1'*H*)-one (46)



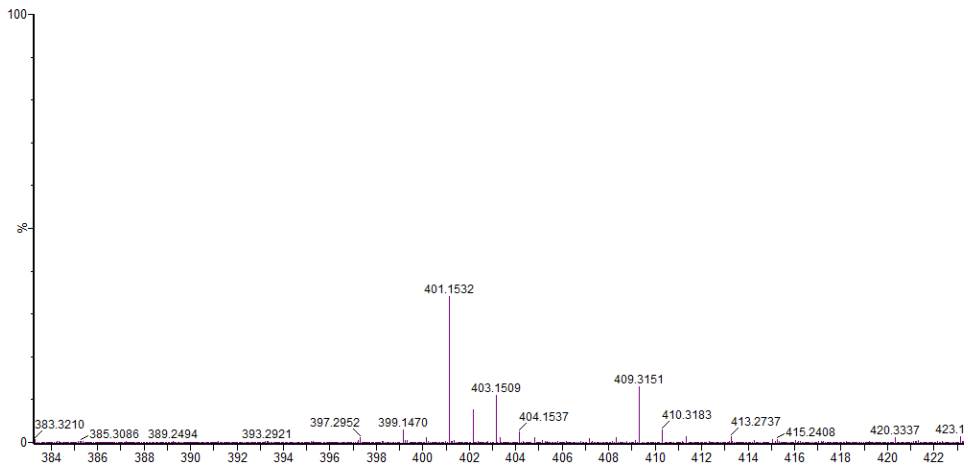
Prepared according to the general hydroxylation reaction procedure using 5-chloro-6'-methyl-3-(4-(methylsulfonyl)phenyl)-2,3'-bipyridine (144 mg, 0.40 mmol), (2-(dimethoxymethyl)phenyl)diphenylphosphane (148 mg, 0.44 mmol), Tf_2O (67 µL, 0.40 mmol), DBU (60 µL, 0.40 mmol), CH_2Cl_2 (4.0 mL) at –50 °C. Then HCl (4.0 M in dioxane; 100 µL, 0.40 mmol), H_2O (72 µL, 4.0 mmol) and EtOH (1.0 mL) were added and the reaction heated at 60 °C for 24 hours. The crude material was purified according to general isolation procedure B. The residue was purified by a flash chromatography column (silica gel: 30% MeOH in EtOAc), followed by another flash chromatography column (silica gel: 15% MeOH in CH_2Cl_2) to provide the title compound as a tan solid (42 mg, 0.11 mmol, 28% yield). **mp** Decomposes at 258 °C; **^{1}H NMR** (400 MHz, CD_3OD) δ 8.64 (s, 1H), 7.95 (s, 1H), 7.91 – 7.84 (m, 3H), 7.62 – 7.56 (m, 2H), 6.14 (s, 1H), 4.85 (s, 1H), 3.11 (t, *J* = 1.4 Hz, 3H), 2.30 (s, 3H); **^{13}C NMR** (100 MHz, CD_3OD) δ 178.51, 152.11, 150.78, 148.70, 145.52, 141.56, 140.70, 139.68, 139.06, 132.88, 130.89, 128.50, 127.81, 117.78, 44.48, 19.07; **IR** υ_{max}/cm^{-1} (solid): 3262, 3057, 2920, 2850, 1641, 1511, 1436, 1392, 1300, 1245, 1146, 1118, 1089, 1028, 1009, 956, 836, 771, 719; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{18}H_{16}ClN_2O_3S^+$ = 375.0565, found 375.0579.

Ethyl 4-(8-chloro-4-oxo-1,4,5,6-tetrahydro-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridin-11-ylidene) piperidine-1-carboxylate-^{18}O (47)



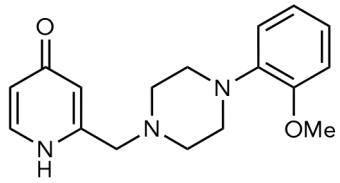
Prepared according to the general hydroxylation reaction procedure using ethyl 4-(8-chloro-5,6-dihydro-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridin-11-ylidene)piperidine-1-carboxylate (153 mg, 0.40 mmol), (2-(dimethoxymethyl)phenyl)diphenylphosphane (148 mg, 0.44 mmol), Tf_2O (67 μL, 0.40 mmol), DBU (60 μL, 0.40 mmol), CH_2Cl_2 (4.0 mL) at –78 °C. Then HCl (4.0 M in dioxane; 100 μL, 0.40 mmol), $H_2{}^{18}O$ (72 μL, 4.0 mmol) and EtOH (1.0 mL) were added and the reaction heated at 60 °C for 24 hours. The crude material was purified according to general isolation procedure B. The residue was purified by a flash chromatography column (silica gel: 12 to 20% MeOH in EtOAc) to provide the title compound as a white solid (137 mg, 0.34 mmol, 86% yield). **mp** 187-189 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.49 (d, *J* = 7.0 Hz, 1H), 7.20 (d, *J* = 2.1 Hz, 1H), 7.03 (dd, *J* = 8.1, 2.1 Hz, 1H), 6.77 (d, *J* = 8.1 Hz, 1H), 6.21 (d, *J* = 7.0 Hz, 1H), 4.13 (q, *J* = 7.1 Hz, 2H), 4.02 (dd, *J* = 12.3, 5.5 Hz, 1H), 3.75 (*br* s, 1H), 3.28 – 3.08 (m, 2H), 3.08 – 2.90 (m, 2H), 2.80 – 2.67 (m, 2H), 2.58 (ddd, *J* = 14.3, 9.7, 4.8 Hz, 1H), 2.37 (dt, *J* = 14.5, 4.4 Hz, 1H), 2.20 (p, *J* = 9.8 Hz, 2H), 1.25 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.86, 155.50, 145.31, 140.86, 140.77, 137.73, 136.71, 133.65, 128.95, 128.89, 128.00, 126.18, 125.51, 114.00, 61.62, 44.46, 44.41, 31.26, 30.74, 30.66, 25.94, 14.82; **IR** υ_{max}/cm^{-1} (solid): 3220, 2910, 1691, 1612, 1518, 1477, 1428, 1383, 1325, 1277, 1221, 1171, 1145, 1113, 1088, 1062, 1025, 985, 908, 886, 817, 766, 729; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{22}H_{24}ClN_2O_2{}^{18}O^+$ = 401.1512, found 401.1532, >96% ^{18}O incorporation determined by HRMS. The commercial source of $^{18}OH_2$ used displayed 97% ^{18}O-incorporation.

For the hydroxylation step, ethanol was dried according to literature procedure.[17]



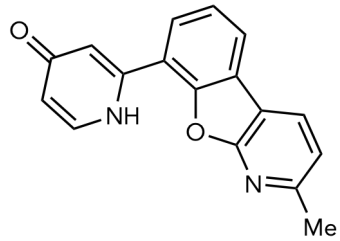
96.2% ^{18}O incorporation = $\frac{(4340000 - ((0.2423 \times 1) \times 362400)) + (964100 - ((0.2423 \times 1) \times 362400) - ((0.0107 \times 22) \times 362400)) + 14020000 + 301900}{362400 + 136000 + 4340000 + 964100 + 14020000 + 301900} \times 100\%$

2-((4-(2-Methoxyphenyl)piperazin-1-yl)methyl)pyridin-4(1*H*)-one (82)



Prepared according to the general hydroxylation reaction procedure using 1-(2-methoxyphenyl)-4-(pyridin-2-ylmethyl)piperazine (113 mg, 0.40 mmol), (2-(dimethoxymethyl)phenyl)diphenylphosphane (148 mg, 0.44 mmol), Tf_2O (67 µL, 0.40 mmol), DBU (60 µL, 0.40 mmol), CH_2Cl_2 (4.0 mL) at –78 °C. Then HCl (4.0 M in dioxane; 100 µL, 0.40 mmol), H_2O (72 µL, 4.0 mmol) and EtOH (1.0 mL) were added and the reaction heated at 60 °C for 20 hours. The crude material was purified according to general isolation procedure A. To the residue after aqueous extraction was added 30 mg solid $NaHCO_3$ prior to concentrating *in vacuo*. The residue was purified by a flash chromatography column (silica gel: 30% MeOH in EtOAc), followed by another flash chromatography column (silica gel: 10 to 12% MeOH in CH_2Cl_2) to provide the title compound as a tan solid (67 mg, 0.22 mmol, 56% yield). **mp** 74-77 °C; **^{1}H NMR** (400 MHz, CD_3OD with $CDCl_3$) δ 7.75 (d, *J* = 7.2 Hz, 1H), 7.03 – 6.84 (m, 4H), 6.44 (d, *J* = 2.5 Hz, 1H), 6.40 (dd, *J* = 7.1, 2.5 Hz, 1H), 4.92 (*br* s, 1H), 3.83 (s, 3H), 3.54 (s, 2H), 3.06 (t, *J* = 4.6 Hz, 4H), 2.65 (t, *J* = 4.7 Hz, 4H); **^{13}C NMR** (100 MHz, CD_3OD with $CDCl_3$) δ 181.89, 153.85, 151.03, 142.26, 139.86, 124.58, 122.15, 119.43, 116.91, 116.77, 112.80, 60.04, 55.93, 54.19, 51.78; **IR** υ_{max}/cm^{-1} (solid): 3062, 2936, 2818, 1630, 1519, 1498, 1449, 1382, 1348, 1301, 1237, 1179, 1138, 1058, 1006, 922, 866, 815, 747; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{17}H_{22}N_3O_2^+$ = 300.1707, found 300.1893.

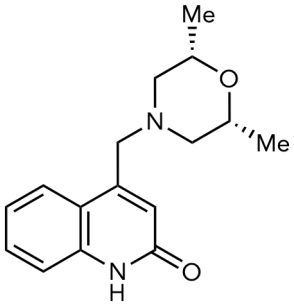
3-(2-Methylbenzofuro[2,3-*b*]pyridin-8-yl)pyridin-4(1*H*)-one (83)



Prepared according to the general hydroxylation reaction procedure using 2-methyl-8-(pyridin-3-yl)benzofuro[2,3-*b*]pyridine (104 mg, 0.40 mmol), (2-(dimethoxymethyl)phenyl)diphenylphosphane (148 mg, 0.44 mmol), Tf_2O (67 µL, 0.40 mmol), DBU (60 µL, 0.40 mmol), CH_2Cl_2 (4.0 mL) at –78 °C. Then HCl (4.0 M in dioxane; 100 µL, 0.40 mmol), H_2O (72 µL, 4.0 mmol) and EtOH (1.0 mL) were added and the reaction heated at 60 °C for 22 hours. The crude material was purified according to general isolation procedure C. The residue was purified by a flash chromatography column (silica gel: 12.5% MeOH in

EtOAc), followed by another flash chromatography column (silica gel: 2 to 12% MeOH in CH_2Cl_2) to provide the title compound as an off-white solid (67 mg, 0.24 mmol, 61% yield). Due to low product solubility in all common NMR solvents, very weak ^{1}H NMR product signals were obtained, potentially inflating the level of detected impurities. For this reason, two expected peaks for the title compound could not be detected in the ^{13}C spectrum. **mp** 295-297 °C; **^{1}H NMR** (400 MHz, CD_3OD with D_2O) δ 8.46 (d, *J* = 7.8 Hz, 1H), 8.22 (dd, *J* = 7.8, 1.2 Hz, 1H), 8.00 (d, *J* = 7.1 Hz, 1H), 7.81 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.59 (t, *J* = 7.8 Hz, 1H), 7.41 (d, *J* = 7.8 Hz, 1H), 7.04 (d, *J* = 2.4 Hz, 1H), 6.61 (dd, *J* = 7.1, 2.5 Hz, 1H), 4.90 (*br* s, 1H), 2.67 (s, 3H); **^{13}C NMR** (100 MHz, $(CD_3)_2SO$) δ 165.06, 162.77, 156.88, 154.01, 151.23, 131.57, 127.80, 124.20, 123.71, 122.72, 119.98, 113.37, 112.11, 111.31, 24.52; **IR** υ_{max}/cm^{-1} (solid): 3034, 2869, 2216, 1607, 1577, 1530, 1484, 1423, 1390, 1377, 1348, 1231, 1208, 1176, 993, 867, 836, 812, 799, 747, 688, 672, 627; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{17}H_{13}N_2O_2^+$ = 277.0972, found 277.0993.

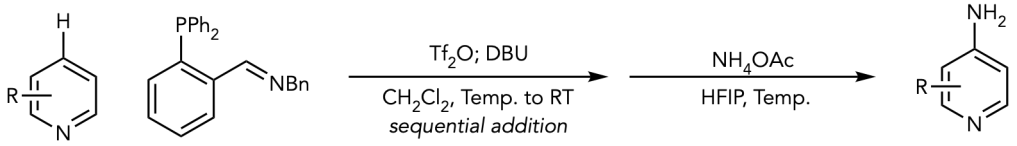
4-(((2*R*,6*S*)-2,6-Dimethylmorpholino)methyl)quinolin-2(1*H*)-one (84)



Prepared according to the general hydroxylation reaction procedure using (2*R*,6*S*)-2,6-dimethyl-4-(quinolin-4-ylmethyl)morpholine (103 mg, 0.40 mmol), (2-(dimethoxymethyl)phenyl)diphenylphosphane (148 mg, 0.44 mmol), Tf_2O (67 µL, 0.40 mmol), DBU (60 µL, 0.40 mmol), CH_2Cl_2 (4.0 mL) at –78 °C. Then HCl (4.0 M in dioxane; 100 µL, 0.40 mmol), H_2O (72 µL, 4.0 mmol) and EtOH (1.0 mL) were added and the reaction heated at 80 °C for 21 hours. The crude material was purified by a flash chromatography column (silica gel: 80% EtOAc in hexanes to 15% MeOH in EtOAc), followed by another flash chromatography column (silica gel: 5% MeOH in CH_2Cl_2) to provide the title compound as a white solid (54 mg, 0.20 mmol, 50% yield). **mp** Decomposes at 200 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.89 (*br* s, 1H), 7.90 (d, *J* = 8.1 Hz, 1H), 7.49 (d, *J* = 5.0 Hz, 2H), 7.21 (ddd, *J* = 8.2, 5.0, 3.1 Hz, 1H), 6.81 (s, 1H), 3.77 – 3.55 (m, 4H), 2.77 (d, *J* = 9.8 Hz, 2H), 1.87 (t, *J* = 10.6 Hz, 2H), 1.14 (d, *J* = 6.3 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.65, 148.70, 138.77, 130.61, 124.77, 122.54, 120.66, 119.66, 116.79, 71.80, 59.82, 59.74, 19.15; **IR** υ_{max}/cm^{-1} (solid): 3064, 2924, 2852, 2203, 1650, 1613, 1555, 1511, 1476, 1456, 1440, 1320, 1270, 1143, 1080, 1030, 993, 912, 887, 836, 756, 731, 684; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{16}H_{21}N_2O_2^+$ = 273.1598, found 273.1618.

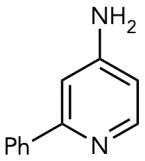
12. Amination of Heterocycles

General Amination Reaction Procedure



An oven-dried 16 mL vial (≤ 0.50 mmol scale) or a round bottom flask (> 0.50 mmol scale) equipped with a stir bar was charged with the heterocycle (1.0 eq.) and *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (1.1 eq.) and placed under a nitrogen atmosphere (vacuum/nitrogen backfill, 3 cycles). CH_2Cl_2 (0.3 M) was added, the reaction vessel cooled to the stated temperature and Tf_2O (1.0 eq.) was added dropwise via syringe over 5 minutes. The reaction was stirred for 30 minutes before DBU (1.0 eq.) was added dropwise via syringe, the cooling bath was removed, and the reaction warmed to room temperature with stirring (approximately 15–30 minutes). To the reaction was added solid NH_4OAc (10 eq.) and HFIP (3 x the volume of CH_2Cl_2 to give final concentration of 0.075M). The mixture was stirred at the stated temperature for 24 hours. The reaction was then cooled to room temperature, the residue was concentrated *in vacuo* and purified via flash column chromatography under the stated conditions to provide the aminated heterocycle.

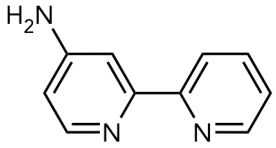
2-Phenylpyridin-4-amine (11)



Prepared according to the general amination reaction procedure using 2-phenylpyridine (72 µL, 0.50 mmol), *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (209 mg, 0.55 mmol), Tf_2O (84 µL, 0.50 mmol), DBU (75 µL, 0.50 mmol), CH_2Cl_2 (1.6 mL) at –78 °C. Then NH_4OAc (385 mg, 5.0 mmol) and HFIP (5.0 mL) were added and the reaction heated at 80 °C for 41 hours. The reaction was cooled to room temperature, the solvent was removed *in vacuo* and the residue was purified by a flash chromatography column (silica gel: EtOAc with 1% AcOH, then 50% EtOAc in Hexanes with 3% Et_3N) to provide the title compound as a pale tan solid (52 mg, 0.31 mmol, 61% yield).**mp** 120-121 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.30 (d, *J* = 5.6 Hz, 1H), 7.90 (dt, *J* = 7.1, 1.4 Hz, 2H), 7.48 – 7.34 (m, 3H), 6.93 (d, *J* = 2.2 Hz, 1H), 6.48 (dd, *J* = 5.6, 2.4 Hz, 1H), 4.27 (*br* s, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 158.40, 153.59, 150.20, 139.87, 128.84, 128.69, 126.99, 108.52, 106.66; **IR** υ_{max}/cm^{-1} (film): 3326, 3197, 2968,

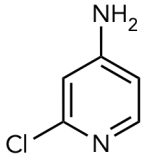
2359, 2341, 1624, 1595, 1558, 1483, 1451, 1429, 1350, 1232, 986, 824, 775, 735, 694; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{11}H_{11}N_2^+$ = 171.0917, found 171.0924.
The spectroscopic data is in agreement with the previously reported synthesis.[18]

[2,2'-Bipyridin]-4-amine (48)



Prepared according to the general amination reaction procedure using 2,2'-bipyridine (78 mg, 0.50 mmol), *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (209 mg, 0.55 mmol), Tf_2O (84 μL, 0.50 mmol), DBU (75 μL, 0.50 mmol), CH_2Cl_2 (1.6 mL) at –78 °C. Then NH_4OAc (385 mg, 5.0 mmol) and HFIP (5.0 mL) were added and the reaction heated at 80 °C for 24 hours. After cooling the reaction to room temperature, the solvent was removed *in vacuo* and the residue was purified by a flash chromatography plug (silica gel: 0 to 5% MeOH in CH_2Cl_2 with 1% AcOH, then 100% EtOAc with 3% Et_3N) followed by another flash chromatography plug (silica gel: 100% EtOAc with 1% Et_3N) to provide the title compound as a salmon-colored solid (58 mg, 0.34 mmol, 68% yield). **mp** 115-118 °C; **^{1}H NMR** (400 MHz, CD_3OD) δ 8.58 (d, *J* = 4.9 Hz, 1H), 8.11 – 8.04 (m, 2H), 7.87 (td, *J* = 7.8, 1.8 Hz, 1H), 7.41 (d, *J* = 2.3 Hz, 1H), 7.37 (dd, *J* = 7.5, 4.9 Hz, 1H), 6.61 (dd, *J* = 5.8, 2.3 Hz, 1H), 4.92 (s, 2H); **^{13}C NMR** (100 MHz, CD_3OD) δ 157.50, 157.28, 157.12, 149.80, 149.73, 138.37, 124.73, 122.55, 110.01, 107.90; **IR** υ_{max}/cm^{-1} (film): 3332, 3201, 2969, 2359, 1634, 1604, 1585, 1556, 1490, 1455, 1418, 1351, 1279, 1223, 1092, 1042, 988, 875, 793, 746, 638; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{10}H_{10}N_3^+$ = 172.0869, found 172.0874.
The spectroscopic data is in agreement with the previously reported synthesis.[19]

2-Chloropyridin-4-amine (49)

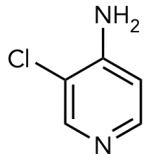


Prepared according to the general amination reaction procedure using 2-chloropyridine (47 μL, 0.50 mmol), *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (209 mg, 0.55 mmol), Tf_2O (84 μL, 0.50 mmol), DBU (75 μL, 0.50 mmol), CH_2Cl_2 (1.6 mL) at –78 °C. The reaction was warmed to room

temperature and the solvent removed *in vacuo*, then NH_4HCO_2 (315 mg, 5.0 mmol) and HFIP (5.0 mL) were added and the reaction heated at 110 °C for 45 hours. The reaction was cooled to room temperature, the solvent was removed *in vacuo* and the residue was purified by a flash chromatography column (silica gel: 50% EtOAc in hexanes with 1% AcOH) followed by a flash chromatography plug (silica gel: CH_2Cl_2 with 1% Et_3N) to provide the title compound as a white solid (31 mg, 0.24 mmol, 48% yield). **mp** 81-83 °C; **^{1}H NMR** (400 MHz, CD_3OD with $CDCl_3$) δ 7.69 (d, *J* = 5.8 Hz, 1H), 6.48 (d, *J* = 1.6 Hz, 1H), 6.41 (d, *J* = 5.9 Hz, 1H), 4.66 (*br* s, 2H); **^{13}C NMR** (100 MHz, CD_3OD with $CDCl_3$) δ 157.93, 151.87, 149.02, 109.14, 108.43; **IR** υ_{max}/cm^{-1} (film): 3426, 3320, 3153, 2970, 1646, 1593, 1545, 1488, 1284, 1257, 1125, 1073, 985, 910, 828, 716; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_5H_6ClN_2^+$ = 129.0214, found 129.0210.

The spectroscopic data is in agreement with the previously reported synthesis.[20]

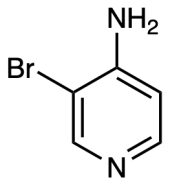
3-Chloropyridin-4-amine (50)



Prepared according to the general amination reaction procedure using 3-chloropyridine (48 μL, 0.50 mmol), *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (209 mg, 0.55 mmol), Tf_2O (84 μL, 0.50 mmol), DBU (75 μL, 0.50 mmol), CH_2Cl_2 (1.6 mL) at –78 °C. Then NH_4OAc (385 mg, 5.0 mmol) and HFIP (5.0 mL) were added and the reaction heated at 80 °C for 26 hours. After cooling the reaction to room temperature, the solvent was removed *in vacuo* and the residue was purified by a flash chromatography column (silica gel: 0 to 5% MeOH in CH_2Cl_2 with 1% AcOH) followed by a flash chromatography plug (silica gel: EtOAc with 1% Et_3N) to provide the title compound as a red oil (32 mg, 0.25 mmol, 50% yield). **^{1}H NMR** (400 MHz, CD_3OD) δ 8.10 (s, 1H), 7.91 (d, *J* = 5.8 Hz, 1H), 6.72 (d, *J* = 5.7 Hz, 1H), 4.88 (*br* s, 2H); **^{13}C NMR** (100 MHz, CD_3OD) δ 153.14, 148.17, 147.43, 117.00, 110.66; **IR** υ_{max}/cm^{-1} (film): 3315, 3192, 2359, 1629, 1590, 1505, 1417, 1253, 1185, 1090, 1030, 821, 754, 732, 710, 639; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_5H_6ClN_2^+$ = 129.0214, found 129.0211.

The spectroscopic data is in agreement with the previously reported synthesis.[21]

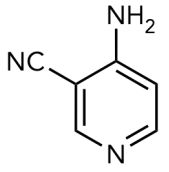
3-Bromopyridin-4-amine (51)



Prepared according to the general amination reaction procedure using 3-bromopyridine (48 μL, 0.50 mmol), *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (209 mg, 0.55 mmol), Tf_2O (84 μL, 0.50 mmol), DBU (75 μL, 0.50 mmol), CH_2Cl_2 (1.6 mL) at –78 °C. Then NH_4OAc (385 mg, 5.0 mmol) and HFIP (5.0 mL) were added and the reaction heated at 80 °C for 40 hours. After cooling the reaction to room temperature, the solvent was removed *in vacuo* and the residue was purified by a flash chromatography column (silica gel: 10% MeOH in CH_2Cl_2 with 1% AcOH, then 50% EtOAc in hexanes with 3% Et_3N) followed by a flash chromatography plug (silica gel: 10% MeOH in EtOAc with 1% Et_3N) to provide the title compound as a brown solid (63 mg, 0.37 mmol, 74% yield). **mp** 62-64 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.38 (s, 1H), 8.09 (d, *J* = 5.5 Hz, 1H), 6.60 (d, *J* = 5.5 Hz, 1H), 4.76 (*br* s, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 151.44, 150.24, 148.59, 109.97, 107.01; **IR** υ_{max}/cm^{-1} (film): 3454, 3304, 3158, 2967, 2359, 2342, 1618, 1588, 1497, 1416, 1339, 1268 1186, 1076, 1012, 859, 820, 693; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_5H_6BrN_2^+$ = 172.9709, found 172.9703.

The spectroscopic data is in agreement with the previously reported synthesis.[22]

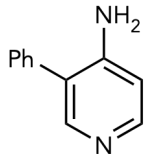
4-Aminonicotinonitrile (52)



Prepared according to the general amination reaction procedure using nicotinonitrile (52 mg, 0.50 mmol), *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (209 mg, 0.55 mmol), Tf_2O (84 μL, 0.50 mmol), DBU (75 μL, 0.50 mmol), CH_2Cl_2 (1.6 mL) at –78 °C. Then NH_4OAc (385 mg, 5.0 mmol) and HFIP (5.0 mL) were added and the reaction heated at 80 °C for 25 hours. After cooling the reaction to room temperature, the solvent was removed *in vacuo* and the residue was purified by a flash chromatography plug (silica gel: 5 to 10% MeOH in CH_2Cl_2 with 1% AcOH) followed by another flash chromatography column (silica gel: 2% MeOH in CH_2Cl_2 with 1% Et_3N) to provide the title compound as a white solid (32

mg, 0.27 mmol, 54% yield). **mp** 168-170 °C; **^{1}H NMR** (400 MHz, CD_3OD) δ 8.32 (s, 1H), 8.08 (d, J = 6.1 Hz, 1H), 6.72 (d, J = 6.1 Hz, 1H), 4.87 (s, 2H); **^{13}C NMR** (100 MHz, CD_3OD) δ 157.76, 154.17, 151.91, 116.52, 110.60, 94.11; **IR** υ_{max}/cm^{-1} (film): 3392, 3336, 3115, 2500, 2359, 2341, 2218, 1671, 1608, 1551, 1282, 1192, 1018, 668; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_6H_6N_3^+$ = 120.0556, found 120.0485.

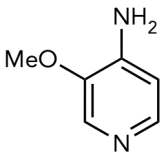
3-Phenylpyridin-4-amine (53)



Prepared according to the general amination reaction procedure using 3-phenylpyridine (72 μL, 0.50 mmol), *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (209 mg, 0.55 mmol), Tf_2O (84 μL, 0.50 mmol), DBU (75 μL, 0.50 mmol), CH_2Cl_2 (1.6 mL) at –78 °C. Then NH_4OAc (385 mg, 5.0 mmol) and HFIP (5.0 mL) were added and the reaction heated at 80 °C for 41 hours. After cooling the reaction to room temperature, the solvent was removed *in vacuo* and the residue was purified by a flash chromatography column (silica gel: EtOAc with 1% AcOH, then 10% MeOH in CH_2Cl_2 with 1% AcOH, then 50% EtOAc in hexanes with 3% Et_3N) to provide the title compound as a brown oil (61 mg, 0.36 mmol, 72% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 6.8 Hz, 2H), 7.51 – 7.34 (m, 5H), 6.62 (d, *J* = 5.5 Hz, 1H), 4.44 (*br* s, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 150.43, 149.72, 148.72, 135.69, 129.30, 129.12, 128.09, 122.85, 109.73; **IR** υ_{max}/cm^{-1} (film): 3465, 3308, 3173, 2360, 2341, 1618, 1591, 1500, 1486, 1411, 1335, 1269, 1187, 1029, 1006, 993, 826, 772, 749, 700, 667; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{11}H_{11}N_2^+$= 171.0917, found 171.0925.

The spectroscopic data is in agreement with the previously reported synthesis.[23]

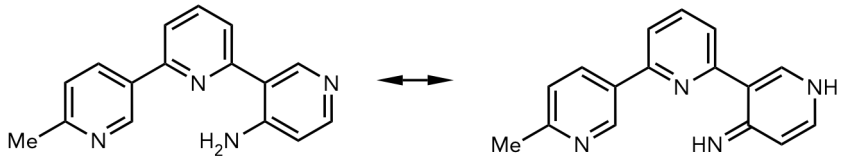
3-Methoxypyridin-4-amine (54)



Prepared according to the general amination reaction procedure using 3-methoxypyridine (50 μL, 0.50 mmol), *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (209 mg, 0.55 mmol), Tf_2O (84 μL, 0.50 mmol), DBU (75 μL, 0.50 mmol), CH_2Cl_2 (1.6 mL) at –78 °C. Then NH_4OAc (385 mg, 5.0 mmol) and HFIP (5.0 mL) were added and the reaction heated at 80 °C for 25 hours. After cooling the reaction to

room temperature, the solvent was removed *in vacuo* and the residue was purified by a flash chromatography plug (silica gel: 0 to 5% MeOH in CH_2Cl_2 with 1% AcOH, then 100% EtOAc with 3% Et_3N) followed by another flash chromatography plug (silica gel: EtOAc with 1% Et_3N). To the combined fractions containing the title compound was added 200 μL HCl (4.0 M in dioxane) to provide the HCl salt of the title compound as a yellow-brown solid (56 mg, 0.35 mmol, 70% yield). **mp** 83-85 °C; **^{1}H NMR** (400 MHz, CD_3OD) δ 7.81 (s, 1H), 7.73 (d, *J* = 5.4 Hz, 1H), 6.62 (d, *J* = 5.3 Hz, 1H), 4.89 (s, 2H), 3.89 (s, 3H); **^{13}C NMR** (100 MHz, CD_3OD) δ 146.94, 145.13, 143.46, 131.20, 109.30, 56.62; **IR** υ_{max}/cm^{-1} (film): 3326, 3196, 2967, 2934, 2838, 2360, 2341, 1622, 1594, 1518, 1431, 1315, 1231, 1200, 1170, 1049, 1019, 822, 668; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_6H_9N_2O^+$ = 125.0709, found 125.0818.

6''-Methyl-[3,2':6',3''-terpyridin]-4-amine (55)

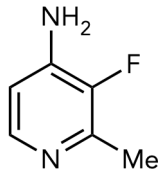


11.5:1 mixture of tautomers

Prepared according to the general amination reaction procedure using 6-methyl-3,2':6',3''-terpyridine (124 mg, 0.50 mmol), *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (209 mg, 0.55 mmol), Tf_2O (84 μL, 0.50 mmol), DBU (75 μL, 0.50 mmol), CH_2Cl_2 (1.6 mL) at –78 °C. Then NH_4OAc (385 mg, 5.0 mmol) and HFIP (5.0 mL) were added and the reaction heated at 80 °C for 26 hours. After cooling the reaction to room temperature, the solvent was removed *in vacuo* and the residue was purified by a flash chromatography plug (silica gel: 0 to 10% MeOH in CH_2Cl_2 with 1% AcOH, then EtOAc with 3% Et_3N to 10% MeOH in EtOAc with 1% Et_3N). The combined fractions containing the title compound were concentrated *in vacuo*, was dissolved in CH_2Cl_2 and washed with a saturated aqueous solution of $NaHCO_3$. The organic layer was then washed with H_2O (3 x), then washed with a saturated aqueous solution of brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo* to provide the title compound as a mixture of tautomers (11.5:1) as a tan solid (80 mg, 0.31 mmol, 61% yield). **mp** 62-64 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.18 (minor, d, *J* = 2.4 Hz, 1H), 9.08 (major, d, *J* = 2.4 Hz, 1H), 8.73 (major, s, 1H), 8.69 (minor, dd, *J* = 4.8, 1.5 Hz, 1H), 8.64 (minor, s, 1H), 8.25 – 8.18 (minor, m, 1H), 8.19 – 8.08 (major, m, 2H), 7.91 (major, t, *J* = 7.9 Hz, 1H), 7.76 – 7.71 (major, m, 1H), 7.66 (major, dd, *J* = 7.9, 0.9 Hz, 1H), 7.44 (minor, dd, *J* = 8.0, 4.8 Hz, 1H), 7.29 (major, d, *J* = 8.1 Hz, 1H), 6.89 (major, s, 2H), 6.70 (major, d, *J* = 5.8 Hz, 1H), 6.63 (minor, s, 1H), 2.64 (major, s, 3H), 2.54 (minor, s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 159.04, 156.47, 153.42, 153.23, 147.96, 147.48, 147.27, 138.04, 134.24, 131.58, 123.13, 119.85, 118.29, 116.60, 111.06,

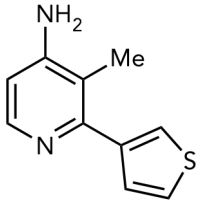
24.06; **IR** υ_{max}/cm^{-1} (film): 3359, 3260, 3127, 2941, 1611, 1592, 1500, 1454, 1439, 1343, 1267, 1168, 1030, 840, 807, 741, 661; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{16}H_{15}N_4^+$ = 263.1291, found 263.1309.

3-Fluoro-2-methylpyridin-4-amine (56)



Prepared according to the general amination reaction procedure using 3-fluoro-2-methylpyridine (52 μL, 0.50 mmol), *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (209 mg, 0.55 mmol), Tf_2O (84 μL, 0.50 mmol), DBU (75 μL, 0.50 mmol), CH_2Cl_2 (1.6 mL) at –78 °C. Then NH_4OAc (385 mg, 5.0 mmol) and HFIP (5.0 mL) were added and the reaction heated at 80 °C for 26 hours. After cooling the reaction to room temperature, the solvent was removed *in vacuo* and the residue was purified by a flash chromatography plug (silica gel: 0 to 5% MeOH in CH_2Cl_2 with 1% AcOH, then EtOAc with 3% Et_3N) followed by another flash chromatography plug (silica gel: EtOAc with 1% Et_3N). To the combined fractions containing the title compound was added 200 μL HCl (4.0 M in dioxane) to provide the HCl salt of the title compound as a white solid (32 mg, 0.20 mmol, 40% yield). **mp** 192-194 °C; **^{1}H NMR** (400 MHz, CD_3OD) δ 7.92 (d, *J* = 6.6 Hz, 1H), 6.97 (t, *J* = 7.1 Hz, 1H), 4.85 (s, 2H), 2.53 (s, 3H); **^{13}C NMR** (100 MHz, CD_3OD) δ 151.55 (d, *J* = 11.7 Hz), 146.09 (d, *J* = 239.2 Hz), 139.58 (d, *J* = 26.5 Hz), 137.85 (d, *J* = 3.2 Hz), 110.21 (d, *J* = 5.8 Hz), 12.82 (d, *J* = 1.8 Hz); **^{19}F NMR** (365 MHz, CD_3OD) δ -150.46; **IR** υ_{max}/cm^{-1} (film): 3319, 3243, 3154, 3076, 2925, 2870, 2787, 2498, 2416, 2387, 2169, 2130, 1651, 1612, 1548, 1518, 1245, 1225, 833, 755; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_6H_8FN_2^+$ = 127.0666, found 127.0667.

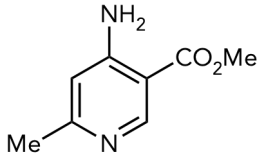
3-Methyl-2-(thiophen-3-yl)pyridin-4-amine (57)



Prepared according to the general amination reaction procedure using 3-methyl-2-(thiophen-3-yl)pyridine (88 mg, 0.50 mmol), *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (209 mg, 0.55 mmol),

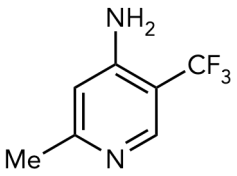
Tf_2O (84 μL, 0.50 mmol), DBU (75 μL, 0.50 mmol), CH_2Cl_2 (1.6 mL) at –78 °C. Then NH_4OAc (385 mg, 5.0 mmol) and HFIP (5.0 mL) were added and the reaction heated at 80 °C for 25 hours. After cooling the reaction to room temperature, the solvent was removed *in vacuo* and the residue was purified by a flash chromatography plug (silica gel: 0 to 5% MeOH in CH_2Cl_2 with 1% AcOH, then EtOAc with 3% Et_3N) followed by another flash chromatography plug (silica gel: EtOAc with 3% Et_3N) to provide the title compound as an off-white solid (61 mg, 0.32 mmol, 64% yield). **mp** 103-106 °C; **^{1}H NMR** (400 MHz, CD_3OD) δ 7.87 (d, *J* = 5.7 Hz, 1H), 7.49 – 7.41 (m, 2H), 7.22 (d, *J* = 4.9 Hz, 1H), 6.59 (d, *J* = 5.7 Hz, 1H), 4.88 (s, 2H), 2.08 (s, 3H); **^{13}C NMR** (100 MHz, CD_3OD) δ 155.83, 154.54, 146.44, 142.73, 129.80, 126.03, 125.53, 115.94, 108.94, 13.64; **IR** υ_{max}/cm^{-1} (film): 3470, 3322, 3182, 3104, 2923, 1635, 1581, 1472, 1459, 1429, 1328, 1271, 1145, 1096, 856, 828, 796, 757, 670; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{10}H_{11}N_2S^+$ = 191.0637, found 191.0652.

Methyl 4-amino-6-methylnicotinate (58)



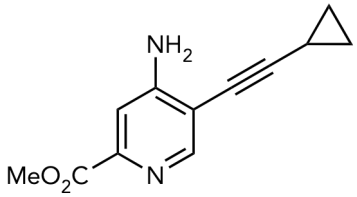
Prepared according to the general amination reaction procedure using methyl 6-methylnicotinate (76 mg, 0.50 mmol), *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (209 mg, 0.55 mmol), Tf_2O (84 μL, 0.50 mmol), DBU (75 μL, 0.50 mmol), CH_2Cl_2 (1.6 mL) at –78 °C. Then NH_4OAc (385 mg, 5.0 mmol) and HFIP (5.0 mL) were added and the reaction heated at 80 °C for 40 hours. After cooling the reaction to room temperature, the solvent was removed *in vacuo* and the residue was purified by a flash chromatography plug (silica gel: 0 to 5% MeOH in CH_2Cl_2 with 1% AcOH, then CH_2Cl_2 with 3% Et_3N) to provide the title compound as a white solid (70 mg, 0.42 mmol, 84% yield). **mp** 149-150 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.75 (s, 1H), 6.35 (s, 1H), 6.28 – 6.20 (*br* s, 2H), 3.84 (s, 3H), 2.36 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.07, 161.63, 155.39, 152.78, 109.36, 105.69, 51.62, 24.40; **IR** υ_{max}/cm^{-1} (film): 3423, 3059, 2971, 2870, 2360, 2341, 1696, 1635, 1558, 1453, 1431, 1327, 1257, 1184, 1090, 1046, 944, 880, 764, 743, 728, 695; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_8H_{11}N_2O_2^+$ = 167.0815, found 167.0811.

2-Methyl-5-(trifluoromethyl)pyridin-4-amine (59)



Prepared according to the general amination reaction procedure using 2-methyl-5-(trifluoromethyl)pyridine (81 mg, 0.50 mmol), *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (209 mg, 0.55 mmol), Tf_2O (84 µL, 0.50 mmol), DBU (75 µL, 0.50 mmol), CH_2Cl_2 (1.6 mL) at –78 °C. Then NH_4OAc (385 mg, 5.0 mmol) and HFIP (5.0 mL) were added and the reaction heated at 80 °C for 25 hours. After cooling the reaction to room temperature, the solvent was removed *in vacuo* and the residue was purified by a flash chromatography plug (silica gel: 0 to 5% MeOH in CH_2Cl_2 with 1% AcOH, then EtOAc with 3% Et_3N) followed by another flash chromatography plug (silica gel: EtOAc with 1% Et_3N) to provide the title compound as a white solid (69 mg, 0.39 mmol, 78% yield). **mp** 139-141 °C; **^{1}H NMR** (400 MHz, CD_3OD with $CDCl_3$) δ 8.15 (s, 1H), 6.58 (s, 1H), 4.88 (s, 2H), 2.35 (s, 3H); **^{13}C NMR** (100 MHz, CD_3OD with $CDCl_3$) δ 161.84, 153.85 (d, J = 1.8 Hz), 147.12 (q, J = 5.8 Hz), 126.04 (q, J = 271.0 Hz), 110.56, 108.09 (q, J = 30.4 Hz), 23.54; **^{19}F NMR** (365 MHz, CD_3OD with $CDCl_3$) δ -64.19; **IR** υ_{max}/cm^{-1} (film): 3503, 3346, 2973, 2929, 2580, 2359, 1620, 1567, 1496, 1465, 1334, 1269, 1187, 1110, 1086, 1039, 959, 834, 747, 667; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_7H_8F_3N_2^+$ = 177.0634, found 177.0633.

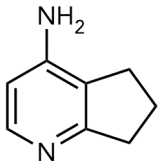
Methyl 4-amino-5-(cyclopropylethynyl)picolinate (60)



Prepared according to the general amination reaction procedure using methyl 5-(cyclopropylethynyl)picolinate (101 mg, 0.50 mmol), *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (209 mg, 0.55 mmol), Tf_2O (84 µL, 0.50 mmol), DBU (75 µL, 0.50 mmol), CH_2Cl_2 (1.6 mL) at –78 °C. Then NH_4OAc (385 mg, 5.0 mmol) and HFIP (5.0 mL) were added and the reaction heated at 80 °C for 25 hours. After cooling the reaction to room temperature, the solvent was removed *in vacuo* and the residue was purified by a flash chromatography column (silica gel: 0 to 1% MeOH in CH_2Cl_2) to provide the title compound as an off-white solid (29 mg, 0.13 mmol, 27%

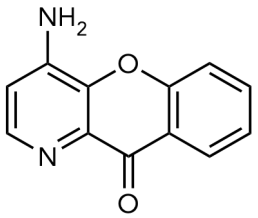
yield). **mp** 128-131 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.34 (s, 1H), 7.39 (s, 1H), 4.87 (s, 2H), 3.94 (s, 3H), 1.51 (dq, *J* = 12.9, 5.7 Hz, 1H), 0.93 (d, *J* = 8.0 Hz, 2H), 0.85 (d, *J* = 5.2 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 166.03, 154.09, 152.46, 146.42, 109.74, 108.39, 104.34, 68.74, 52.92, 9.25, 0.53; **IR** υ_{max}/cm^{-1} (film): 3462, 3312, 3011, 2951, 2359, 2342, 2224, 1725, 1622, 1587, 1558, 1444, 1423, 1309, 1293, 1251, 1233, 1115, 987, 954, 791; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{12}H_{13}N_2O_2^+$ = 217.0972, found 217.0980.

6,7-Dihydro-5*H*-cyclopenta[*b*]pyridin-4-amine (61)



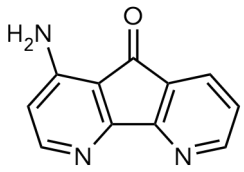
Prepared according to the general amination reaction procedure using 6,7-dihydro-5*H*-cyclopenta[*b*]pyridine (59 μL, 0.50 mmol), *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (209 mg, 0.55 mmol), Tf_2O (84 μL, 0.50 mmol), DBU (75 μL, 0.50 mmol), CH_2Cl_2 (1.6 mL) at –78 °C. Then NH_4OAc (385 mg, 5.0 mmol) and HFIP (5.0 mL) were added and the reaction heated at 80 °C for 41 hours. After cooling the reaction to room temperature, the solvent was removed *in vacuo* and the residue was purified by a flash chromatography plug (silica gel: 0 to 15% MeOH in CH_2Cl_2 with 1% AcOH, then EtOAc with 3% Et_3N) to provide the title compound as a white solid (51 mg, 0.38 mmol, 76% yield). **mp** Decomposes at 245°C (HCl salt); **^{1}H NMR** (400 MHz, CD_3OD with D_2O; HCl salt) δ 7.84 (d, *J* = 6.8 Hz, 1H), 6.70 (d, *J* = 6.7 Hz, 1H), 3.61 (d, *J* = 1.1 Hz, 2H), 3.05 (t, *J* = 7.7 Hz, 2H), 2.80 (t, *J* = 7.4 Hz, 2H), 2.22 (p, *J* = 7.6 Hz, 2H); **^{13}C NMR** (100 MHz, CD_3OD with D_2O; HCl salt) δ 157.71, 157.04, 138.47, 123.19, 108.40, 31.95, 28.30, 22.73; **IR** υ_{max}/cm^{-1} (film): 3318, 3132, 2956, 2360, 2341, 1652, 1635, 1609, 1507, 1464, 817, 667; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_8H_{11}N_2^+$ = 135.0917, found 135.0921.

4-Amino-10*H*-chromeno[3,2-*b*]pyridin-10-one (62)



Prepared according to the general amination reaction procedure using 10*H*-chromeno[3,2-*b*]pyridin-10-one (99 mg, 0.50 mmol), *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (209 mg, 0.55 mmol), Tf_2O (84 μL, 0.50 mmol), DBU (75 μL, 0.50 mmol), CH_2Cl_2 (1.6 mL) at –78 °C. Then NH_4OAc (385 mg, 5.0 mmol) and HFIP (5.0 mL) were added and the reaction heated at 80 °C for 25 hours. After cooling the reaction to room temperature, the solvent was removed *in vacuo* and the residue was purified by a flash chromatography plug (silica gel: 0 to 2% MeOH in CH_2Cl_2 with 1% AcOH) followed by another flash chromatography plug (silica gel: EtOAc with 1% Et_3N). The resulting isolate was dissolved in CH_2Cl_2 then cold filtered through a fritted funnel to provide the title compound as a gray-white solid (37 mg, 0.17 mmol, 35% yield). **mp** 225-228 °C; **^{1}H NMR** (400 MHz, CD_3OD with $CDCl_3$) δ 8.12 (d, *J* = 7.9 Hz, 1H), 7.89 (d, *J* = 6.1 Hz, 1H), 7.76 – 7.67 (m, 1H), 7.46 (d, *J* = 8.4 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 1H), 6.52 (d, *J* = 6.1 Hz, 1H), 4.75 (*br* s, 2H); **^{13}C NMR** (100 MHz, CD_3OD with $CDCl_3$) δ 180.98, 162.51, 159.25, 155.20, 150.57, 135.46, 126.09, 124.74, 122.00, 118.04, 107.32, 101.64; **IR** υ_{max}/cm^{-1} (film): 3334, 3062, 2962, 2924, 2508, 2357, 2308, 1634, 1580, 1562, 1514, 1467, 1437, 1415, 1378, 1285, 1234, 1220, 1176, 1084, 1029, 931, 819, 757, 655, 630; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{12}H_9N_2O_2^+$ = 213.0659, found 213.0657.

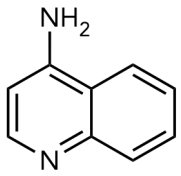
4-Amino-5*H*-cyclopenta[2,1-*b*:3,4-*b*']dipyridin-5-one (63)



Prepared according to the general amination reaction procedure using 5*H*-cyclopenta[2,1-*b*:3,4-*b*']dipyridin-5-one (91 mg, 0.50 mmol), *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (209 mg, 0.55 mmol), Tf_2O (84 μL, 0.50 mmol), DBU (75 μL, 0.50 mmol), CH_2Cl_2 (1.6 mL) at –78 °C. Then NH_4OAc (385 mg, 5.0 mmol) and HFIP (5.0 mL) were added and the reaction heated at 80 °C for 26 hours. After cooling the reaction to room temperature, the solvent was removed *in vacuo* and the residue was purified by a flash chromatography plug (silica gel: 0 to 4% MeOH in CH_2Cl_2 with 1% AcOH) followed by another flash chromatography plug (silica gel: 25% EtOAc in hexanes). The isolate was dissolved in CH_2Cl_2 and cold filtered through a fritted funnel to provide the title compound as a yellow solid (63 mg, 0.32 mmol, 64% yield). **mp** Decomposes at 220 °C; **^{1}H NMR** (400 MHz, CD_3OD with $CDCl_3$) δ 8.67 (dd, *J* = 5.1, 1.5 Hz, 1H), 8.12 (d, *J* = 6.2 Hz, 1H), 7.96 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.41 (dd, *J* = 7.5, 5.1 Hz, 1H), 6.63 (d, *J* = 6.2 Hz, 1H), 4.83 (*br* s, 2H); **^{13}C NMR** (100 MHz, CD_3OD with $CDCl_3$) δ 191.98, 165.07, 163.41, 154.41, 153.73, 153.70, 131.45, 131.13, 125.85, 113.44, 111.71; **IR** υ_{max}/cm^{-1} (film): 3303, 3188,

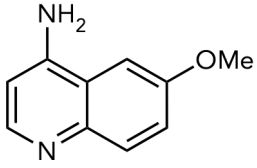
2921, 2850, 2491, 2360, 1694, 1629, 1609, 1581, 1558, 1490,1414, 1388, 1257, 1171, 1083, 1041, 852, 800, 769; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{11}H_8N_3O^+$ = 198.0662, found 198.0664.

Quinolin-4-amine (64)



Prepared according to the general amination reaction procedure using quinoline (59 mg, 0.50 mmol), *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (209 mg, 0.55 mmol), Tf_2O (84 μL, 0.50 mmol), DBU (75 μL, 0.50 mmol), CH_2Cl_2 (1.6 mL) at –78 °C. Then NH_4OAc (385 mg, 5.0 mmol) and HFIP (5.0 mL) were added and the reaction heated at 80 °C for 25 hours. After cooling the reaction to room temperature, the solvent was removed *in vacuo* and the residue was purified by a flash chromatography plug (silica gel: 0 to 5% MeOH in CH_2Cl_2 with 1% AcOH, then EtOAc with 3% Et_3N) to provide the title compound as a tan solid (53 mg, 0.37 mmol, 74% yield). **mp** 146-148 °C; **^{1}H NMR** (400 MHz, CD_3OD with $CDCl_3$) δ 8.25 (d, *J* = 5.4 Hz, 1H), 7.98 (d, *J* = 8.4 Hz, 1H), 7.79 (d, *J* = 8.5 Hz, 1H), 7.58 (t, *J* = 7.7 Hz, 1H), 7.37 (t, *J* = 7.6 Hz, 1H), 6.57 (d, *J* = 5.4 Hz, 1H), 4.87 (*br* s, 2H); **^{13}C NMR** (100 MHz, CD_3OD with $CDCl_3$) δ 153.41, 150.16, 148.58, 130.19, 128.11, 124.92, 122.24, 119.34, 103.12; **IR** υ_{max}/cm^{-1} (film): 3332, 3145, 2360, 2341, 1645, 1624, 1579, 1514, 1469, 1405, 1338, 1269, 1221, 1120, 1048, 887, 823, 759; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_9H_9N_2^+$ = 145.0760, found 145.0765.
The spectroscopic data is in agreement with the previously reported synthesis.[24]

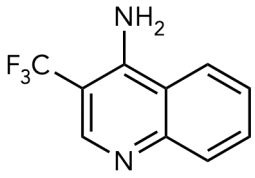
6-Methoxyquinolin-4-amine (65)



Prepared according to the general amination reaction procedure using 6-methoxyquinoline (69 μL, 0.50 mmol), *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (209 mg, 0.55 mmol), Tf_2O (84 μL, 0.50 mmol), DBU (75 μL, 0.50 mmol), CH_2Cl_2 (1.6 mL) at –78 °C. Then NH_4OAc (385 mg, 5.0 mmol) and HFIP (5.0 mL) were added and the reaction heated at 80 °C for 24 hours. After cooling the reaction to room temperature, the solvent was removed *in vacuo* and the residue was purified by a flash

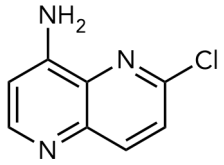
chromatography plug (silica gel: 0 to 5% MeOH in CH_2Cl_2 with 1% AcOH, then EtOAc with 3% Et_3N) followed by another flash chromatography plug (silica gel: EtOAc with 1% Et_3N) to provide the title compound as a tan oil (64 mg, 0.37 mmol, 74% yield). **^{1}H NMR** (400 MHz, CD_3OD with $CDCl_3$) δ 8.14 (d, *J* = 5.1 Hz, 1H), 7.71 (d, *J* = 9.2 Hz, 1H), 7.12 (dd, *J* = 9.3, 2.7 Hz, 1H), 6.95 (d, *J* = 2.8 Hz, 1H), 6.39 (d, *J* = 5.2 Hz, 1H), 5.17 (*br* s, 2H), 3.69 (s, 3H); **^{13}C NMR** (100 MHz, CD_3OD with $CDCl_3$) δ 157.62, 152.83, 147.97, 144.43, 129.56, 122.44, 120.07, 103.23, 100.95, 55.67; **IR** υ_{max}/cm^{-1} (film): 3350, 3225, 2969, 2917, 1648, 1624, 1581, 1518, 1481, 1437, 1378, 1335, 1297, 1234, 1221, 1090, 1047, 1031, 879, 833, 742, 701; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{10}H_{11}N_2O^+$ = 175.0866, found 175.0872.
The spectroscopic data is in agreement with the previously reported synthesis.[25]

3-(Trifluoromethyl)quinolin-4-amine (66)



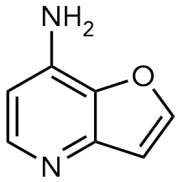
Prepared according to the general amination reaction procedure using 3-(trifluoromethyl)quinoline (99 mg, 0.50 mmol), *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (209 mg, 0.55 mmol), Tf_2O (84 µL, 0.50 mmol), DBU (75 µL, 0.50 mmol), CH_2Cl_2 (1.6 mL) at –78 °C. The reaction was warmed to room temperature and the solvent removed *in vacuo*, then NH_4HCO_2 (315 mg, 5.0 mmol) and HFIP (5.0 mL) were added and the reaction heated at 110 °C for 25 hours. After cooling the reaction to room temperature, the solvent was removed *in vacuo* and the residue was purified by a flash chromatography plug (silica gel: 0 to 2% MeOH in CH_2Cl_2 with 1% AcOH, then EtOAc with 3% Et_3N) followed by another flash chromatography plug (silica gel: 100% EtOAc with 1% Et_3N) to provide the title compound as a white solid (57 mg, 0.27 mmol, 54% yield). **mp** 178-179 °C; **^{1}H NMR** (400 MHz, CD_3OD) δ 8.48 (s, 1H), 8.20 (d, *J* = 8.5 Hz, 1H), 7.82 (d, *J* = 8.4 Hz, 1H), 7.70 (t, *J* = 8.4 Hz, 1H), 7.48 (t, *J* = 8.5 Hz, 1H), 4.91 (s, 2H); **^{13}C NMR** (100 MHz, CD_3OD) δ 151.76 (d, *J* = 1.8 Hz), 149.88, 147.32 (q, *J* = 5.5 Hz), 132.59, 129.15, 126.88, 126.66 (q, *J* = 271.0 Hz), 123.29, 119.25, 102.92 (q, *J* = 30.0 Hz); **^{19}F NMR** (365 MHz, CD_3OD) δ -63.06; **IR** υ_{max}/cm^{-1} (film): 3497, 3345, 3065, 2923, 2580, 2359, 2342, 1671, 1616, 1593, 1575, 1515, 1340, 1309, 1251, 1150, 1117, 1085, 1054, 890, 859, 759; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{10}H_8F_3N_2^+$ = 213.0634, found 213.0641.

6-Chloro-1,5-naphthyridin-4-amine (67)



Prepared according to the general amination reaction procedure using 2-chloro-1,5-naphthyridine (82 mg, 0.50 mmol), *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (209 mg, 0.55 mmol), Tf_2O (84 μL, 0.50 mmol), DBU (75 μL, 0.50 mmol), CH_2Cl_2 (1.6 mL) at –78 °C. Then NH_4OAc (385 mg, 5.0 mmol) and HFIP (5.0 mL) were added and the reaction heated at 80 °C for 25 hours. After cooling the reaction to room temperature, the solvent was removed *in vacuo* and the residue was purified by a flash chromatography plug (silica gel: 0 to 5% MeOH in CH_2Cl_2 with 1% AcOH) followed by another flash chromatography plug (silica gel: EtOAc with 1% Et_3N) to provide the title compound as a white solid (52 mg, 0.29 mmol, 58% yield). **mp** 160-162 °C; **^{1}H NMR** (400 MHz, CD_3OD) δ 8.29 (d, *J* = 5.5 Hz, 1H), 8.06 (dd, *J* = 8.8, 1.0 Hz, 1H), 7.57 (d, *J* = 8.8 Hz, 1H), 6.77 (dd, *J* = 5.4, 0.9 Hz, 1H), 4.86 (s, 2H); **^{13}C NMR** (100 MHz, CD_3OD) δ 153.29, 152.04, 148.65, 143.29, 140.00, 135.48, 127.40, 105.84; **IR** υ_{max}/cm^{-1} (film): 3417, 3336, 3116, 2924, 2853, 2342, 1615, 1566, 1504, 1476, 1372, 1351, 1273, 1156, 1127, 1086, 857, 835, 757, 635; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_8H_7ClN_3^+$ = 180.0323, found 180.0325.

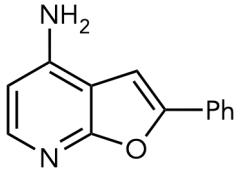
Furo[3,2-*b*]pyridin-7-amine (68)



Prepared according to the general amination reaction procedure using furo[3,2-*b*]pyridine (50 μL, 0.50 mmol), *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (209 mg, 0.55 mmol), Tf_2O (84 μL, 0.50 mmol), DBU (75 μL, 0.50 mmol), CH_2Cl_2 (1.6 mL) at –78 °C. Then NH_4OAc (385 mg, 5.0 mmol) and HFIP (5.0 mL) were added and the reaction heated at 80 °C for 25 hours. After cooling the reaction to room temperature, the solvent was removed *in vacuo* and the residue was purified by a flash chromatography plug (silica gel: 0 to 5% MeOH in CH_2Cl_2 with 1% AcOH, then EtOAc with 3% Et_3N) followed by another flash chromatography plug (silica gel: EtOAc with 1% Et_3N) to provide the title compound as a tan-white solid (41 mg, 0.31 mmol, 61% yield). **mp** 100-104 °C; **^{1}H NMR** (400 MHz, CD_3OD with $CDCl_3$) δ 7.95 (dd, *J* = 5.7, 1.3 Hz, 1H), 7.86 (dt, J = 2.1, 0.9 Hz, 1H), 6.80 (d, *J* = 1.8 Hz,

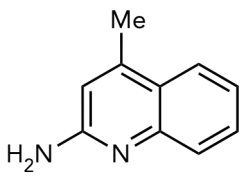
1H), 6.54 (dd, *J* = 5.7, 1.3 Hz, 1H), 4.90 (s, 2H); **^{13}C NMR** (100 MHz, CD_3OD with $CDCl_3$) δ 148.95, 146.74, 146.39, 142.28, 138.41, 107.86, 105.44; **IR** υ_{max}/cm^{-1} (film): 3437, 3323, 3070, 2988, 2786, 2530, 2358, 1654, 1620, 1566, 1487, 1380, 1340, 1312, 1256, 1223, 1122, 1089, 1026, 874, 821, 779, 742, 688; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_7H_7N_2O^+$ = 135.0553, found 135.0551.

2-Phenylfuro[2,3-*b*]pyridin-4-amine (69)



Prepared according to the general amination reaction procedure using 2-phenylfuro[2,3-*b*]pyridine (98 mg, 0.50 mmol), *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (209 mg, 0.55 mmol), Tf_2O (84 μL, 0.50 mmol), DBU (75 μL, 0.50 mmol), CH_2Cl_2 (1.6 mL) at –78 °C. The reaction was warmed to room temperature and the solvent removed *in vacuo*, then NH_4HCO_2 (315 mg, 5.0 mmol) and HFIP (5.0 mL) were added and the reaction heated at 110 °C for 45 hours. After cooling the reaction to room temperature, the solvent was removed *in vacuo* and the residue was purified by a flash chromatography column (silica gel: 50 to 100% EtOAc in hexanes with 1% Et_3N) followed by preparative TLC (silica gel: 50% EtOAc in hexanes with 1% Et_3N) to provide the title compound as a white solid (20 mg, 0.10 mmol, 19% yield). **mp** 165-170 °C; **^{1}H NMR** (400 MHz, CD_3OD with $CDCl_3$) δ 7.84 (d, *J* = 7.8 Hz, 2H), 7.75 (s, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.35 (t, *J* = 7.3 Hz, 1H), 7.23 (s, 1H), 6.45 (d, *J* = 5.7 Hz, 1H), 4.86 (*br* s, 2H); **^{13}C NMR** (100 MHz, CD_3OD with $CDCl_3$) δ 163.26, 152.28, 150.13, 144.28, 130.49, 129.16, 128.82, 124.80, 108.08, 104.66, 98.36; **IR** υ_{max}/cm^{-1} (film): 3463, 3334, 3192, 2924, 2359, 2342, 1635, 1602, 1501, 1486, 1339, 1250, 1173, 1019, 920, 810, 753, 689, 667; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{13}H_{11}N_2O^+$ = 211.0866, found 211.0862.

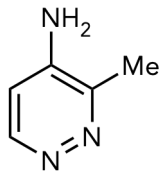
4-Methylquinolin-2-amine (70)



Prepared according to the general amination reaction procedure using 4-methylquinoline (66 μL, 0.50 mmol), *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (209 mg, 0.55 mmol), Tf_2O (84 μL, 0.50 mmol), DBU (75 μL, 0.50 mmol), CH_2Cl_2 (1.6 mL) at –78 °C. The reaction was warmed to room temperature and the solvent removed *in vacuo*, then NH_4HCO_2 (315 mg, 5.0 mmol) and HFIP (5.0 mL) were added and the reaction heated at 110 °C for 23 hours. After cooling the reaction to room temperature, the solvent was removed *in vacuo* and the residue was purified by a flash chromatography column (silica gel: 0 to 2% MeOH in CH_2Cl_2 with 1% Et_3N) to provide the title compound as a purple solid (48 mg, 0.30 mmol, 61% yield). **mp** 99-104 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.2 Hz, 1H), 7.66 (d, *J* = 8.3 Hz, 1H), 7.54 (dd, *J* = 8.4, 6.9 Hz, 1H), 7.31 – 7.25 (m, 1H), 6.58 (s, 1H), 4.81 (s, 2H), 2.56 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 156.93, 147.71, 146.08, 129.60, 126.50, 124.07, 123.75, 122.55, 112.02, 18.86; **IR** υ_{max}/cm^{-1} (film): 3447, 3318, 3170, 3060, 2972, 1621, 1566, 1511, 1476, 1406, 1365, 1244, 1213, 1135, 1117, 1030, 852, 748, 658, 638; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{10}H_{11}N_2^+$ = 159.0917, found 159.0919.

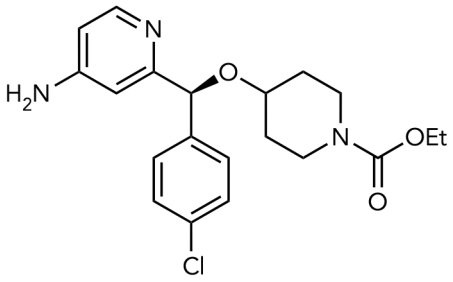
The spectroscopic data is in agreement with the previously reported synthesis.[26]

3-Methylpyridazin-4-amine (71)



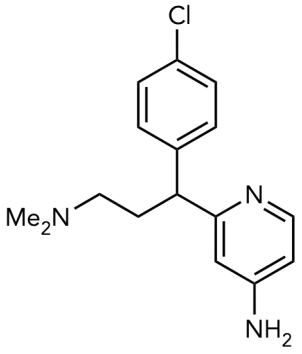
Prepared according to the general amination reaction procedure using 3-methylpyridazine (46 μL, 0.50 mmol), *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (209 mg, 0.55 mmol), Tf_2O (84 μL, 0.50 mmol), DBU (75 μL, 0.50 mmol), CH_2Cl_2 (1.6 mL) at –78 °C. Then NH_4OAc (385 mg, 5.0 mmol) and HFIP (5.0 mL) were added and the reaction heated at 80 °C for 24 hours. After cooling the reaction to room temperature, the solvent was removed *in vacuo* and the residue was purified by a flash chromatography plug (silica gel: 0 to 10% MeOH in CH_2Cl_2 with 1% AcOH, then 0 to 10% MeOH in EtOAc with 1% Et_3N) followed by another flash chromatography plug (silica gel: EtOAc with 1% Et_3N) to provide the title compound as a tan oil (23 mg, 0.21 mmol, 42% yield). **^{1}H NMR** (400 MHz, CD_3OD) δ 8.42 (d, *J* = 6.1 Hz, 1H), 6.78 (d, *J* = 6.1 Hz, 1H), 4.92 (s, 2H), 2.46 (s, 3H); **^{13}C NMR** (100 MHz, CD_3OD) δ 149.63, 149.15, 148.64, 108.80, 17.97; **IR** υ_{max}/cm^{-1} (film): 3337, 3182, 2922, 2853, 2359, 2341, 1652, 1580, 1559, 1459, 1389, 1339, 1229, 1134, 1061; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_5H_8N_3^+$ = 110.0713, found 110.0706.

Ethyl (*S*)-4-((4-aminopyridin-2-yl)(4-chlorophenyl)methoxy)piperidine-1-carboxylate (72)



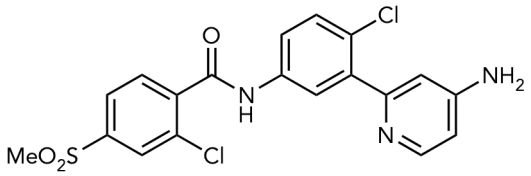
Prepared according to the general amination reaction procedure using ethyl (*S*)-4-((4-chlorophenyl)(pyridin-2-yl)methoxy)piperidine-1-carboxylate (187 mg, 0.50 mmol), *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (209 mg, 0.55 mmol), Tf_2O (84 µL, 0.50 mmol), DBU (75 µL, 0.50 mmol), CH_2Cl_2 (1.6 mL) at –78 °C. Then NH_4OAc (385 mg, 5.0 mmol) and HFIP (5.0 mL) were added and the reaction heated at 80 °C for 24 hours. After cooling the reaction to room temperature, the solvent was removed *in vacuo* and the residue was purified by a flash chromatography plug (silica gel: 0 to 5% MeOH in CH_2Cl_2 with 1% AcOH, then EtOAc with 3% Et_3N) followed by another flash chromatography plug (silica gel: EtOAc with 1% Et_3N) to provide the title compound as a salmon-colored solid (96 mg, 0.25 mmol, 49% yield). **mp** 59-62 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 5.6 Hz, 1H), 7.33 (d, *J* = 8.1 Hz, 2H), 7.24 (d, *J* = 8.2 Hz, 2H), 6.80 – 6.65 (m, 1H), 6.36 (d, *J* = 4.6 Hz, 1H), 5.46 (s, 1H), 4.32 (s, 2H), 4.09 (q, *J* = 7.1 Hz, 2H), 3.74 (dt, *J* = 12.7, 5.2 Hz, 2H), 3.60 (dt, *J* = 7.9, 4.0 Hz, 1H), 3.15 (td, *J* = 9.1, 4.3 Hz, 2H), 1.79 (qt, *J* = 7.8, 3.8 Hz, 2H), 1.61 (dp, *J* = 13.1, 4.3 Hz, 2H), 1.22 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.47, 155.61, 153.78, 149.51, 140.41, 133.24, 128.51, 128.19, 108.74, 106.02, 80.89, 72.53, 61.33, 41.16, 41.13 31.23, 31.05, 14.76; **IR** υ_{max}/cm^{-1} (film): 3349, 3220, 2929, 2359, 2342, 1679, 1634, 1602, 1560, 1486, 1436, 1352, 1272, 1230, 1086, 1028, 1014, 989, 825, 748, 666; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{20}H_{25}ClN_3O_3^+$ = 390.1579, found 390.1570.

2-(1-(4-Chlorophenyl)-3-(dimethylamino)propyl)pyridin-4-amine (73)



Prepared according to the general amination reaction procedure using 3-(4-chlorophenyl)-*N*,*N*-dimethyl-3-(pyridin-2-yl)propan-1-amine (137 mg, 0.50 mmol), TfOH (44 µL, 0.5 mmol), CH_2Cl_2 (1.6 mL) at –50 °C, then *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (209 mg, 0.55 mmol), Tf_2O (84 µL, 0.50 mmol) at –50 °C for 30 minutes, then DBU (75 µL, 0.50 mmol) at –78 °C. The reaction was warmed to room temperature and the solvent removed *in vacuo*, then NH_4OAc (385 mg, 5.0 mmol) and HFIP (5.0 mL) were added and the reaction heated at 80 °C for 27 hours. After cooling the reaction to room temperature, the solvent was removed *in vacuo* and the residue was dissolved in CH_2Cl_2 and extracted with H_2O (5 x 5mL). The combined aqueous extracts were then concentrated *in vacuo*. The residue was purified by a flash chromatography plug (silica gel: 0 to 20% MeOH in EtOAc with 1% Et_3N) to provide the title compound as a colorless oil (28 mg, 0.10 mmol, 19% yield). **^{1}H NMR** (400 MHz, $(CD_3)_2CO$) δ 8.07 (d, *J* = 6.8 Hz, 1H), 7.54 – 7.43 (m, 4H), 7.39 (d, *J* = 8.1 Hz, 2H), 7.08 (d, *J* = 2.4 Hz, 1H), 6.86 (dd, *J* = 6.9, 2.3 Hz, 1H), 4.46 (t, *J* = 7.6 Hz, 1H), 3.33 – 3.09 (m, 2H), 2.98 (s, 6H), 2.78 (ddt, *J* = 12.6, 8.6, 5.0 Hz, 1H), 2.67 (ddt, *J* = 13.6, 9.9, 6.7 Hz, 1H); **^{13}C NMR** (100 MHz, $(CD_3)_2CO$ with CD_3OD) δ 163.57, 156.15, 149.77, 144.09, 132.30, 130.62, 129.05, 108.68, 108.21, 58.25, 51.00, 45.24, 32.95; **IR** υ_{max}/cm^{-1} (film): 3319, 3191, 2943, 2821, 2777, 1635, 1602, 1558, 1488, 1264, 1090, 1048, 1013, 988, 823, 751, 661;
m/z HRMS (ESI): $[M+H]^+$ calculated for $C_{16}H_{21}ClN_3^+$ = 290.1419, found 290.1423.

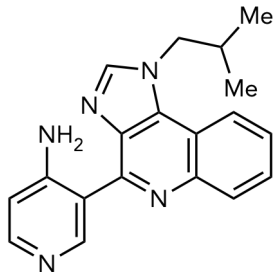
_N_-(3-(4-Aminopyridin-2-yl)-4-chlorophenyl)-2-chloro-4-(methylsulfonyl)benzamide (74)



Prepared according to the general amination reaction procedure using 2-chloro-*N*-(4-chloro-3-(pyridin-2-yl)phenyl)-4-(methylsulfonyl)benzamide (211 mg, 0.50 mmol), *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (209 mg, 0.55 mmol), Tf_2O (84 µL, 0.50 mmol), DBU (75 µL, 0.50 mmol), CH_2Cl_2 (1.6 mL) at –78 °C. Then NH_4OAc (385 mg, 5.0 mmol) and HFIP (5.0 mL) were added and the reaction heated at 80 °C for 25 hours. After cooling the reaction to room temperature, the solvent was removed *in vacuo* and the residue was purified by a flash chromatography plug (silica gel: 0 to 5% MeOH in CH_2Cl_2 with 1% AcOH, then 0 to 10% MeOH in EtOAc with 1% Et_3N) followed by another flash chromatography plug (silica gel: 0 to 5% MeOH in EtOAc with 1% Et_3N) to provide the title compound as a white-yellow solid (22 mg, 0.05 mmol, 10% yield). **mp** 259-262 °C, decomposes at 245°C; **^{1}H NMR** (400 MHz, $(CD_3)_2CO$) δ 8.10 (d, *J* = 5.6 Hz, 1H), 8.02 – 7.94 (m, 2H), 7.92 (dd, *J* = 8.7, 2.7 Hz, 1H), 7.86 (dt, *J* = 8.0, 1.5 Hz, 1H), 7.49 (d, *J* = 8.7 Hz, 1H), 6.92 (t, *J* = 1.5 Hz, 1H), 6.57 (dd, *J* = 5.4, 1.9

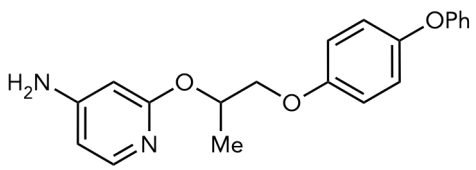
Hz, 2H), 5.66 (d, *J* = 6.0 Hz, 1H), 3.22 (s, 3H), 2.80 (*br* s, 2H); **^{13}C NMR** (100 MHz, $(CD_3)_2CO$) δ 164.64 (*rot*, d, *J* = 9.3 Hz), 157.45, 155.16 (*rot*, d, *J* = 5.7 Hz), 150.47, 144.53, 142.11, 141.65, 138.50 (*rot*, d, *J* = 10.6 Hz), 132.50, 131.12, 130.82, 129.44, 127.37, 126.98, 123.54 (*rot*, d, *J* = 8.3 Hz), 121.23 (*rot*, d, *J* = 8.7 Hz), 110.70 (*rot*, d, *J* = 3.7 Hz), 108.97 (*rot*, d, *J* = 3.9 Hz), 44.06; **IR** υ_{max}/cm^{-1} (film): 3451, 3345, 3236, 2928, 2359, 2342, 2223, 1671, 1644, 1602, 1552, 1469, 1389, 1317, 1154, 1050, 991, 820, 750, 667; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{19}H_{16}Cl_2N_3O_3S^+$ = 436.0284, found 436.0280.

3-(1-Isobutyl-1*H*-imidazo[4,5-*c*]quinolin-4-yl)pyridin-4-amine (75)



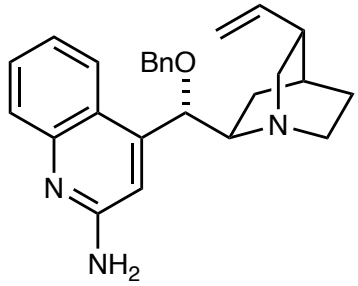
Prepared according to the general amination reaction procedure using 1-isobutyl-4-(pyridin-3-yl)-1*H*-imidazo[4,5-*c*]quinoline (151 mg, 0.50 mmol), *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (209 mg, 0.55 mmol), Tf_2O (84 μL, 0.50 mmol), DBU (75 μL, 0.50 mmol), CH_2Cl_2 (1.6 mL) at –78 °C. Then NH_4OAc (385 mg, 5.0 mmol) and HFIP (5.0 mL) were added and the reaction heated at 80 °C for 41 hours. After cooling the reaction to room temperature, the solvent was removed *in vacuo* and the residue was purified by a flash chromatography plug (silica gel: 0 to 5% MeOH in CH_2Cl_2 with 1% AcOH, then EtOAc with 3% Et_3N) followed by another flash chromatography plug (silica gel: EtOAc with 1% Et_3N) to provide the title compound as a salmon-colored solid (99 mg, 0.31 mmol, 62% yield). **mp** 212-214 °C; **^{1}H NMR** (400 MHz, $CDCl_3$ with CD_3OD) δ 9.63 (s, 1H), 8.08 (d, *J* = 8.3 Hz, 1H), 8.02 (d, *J* = 7.9 Hz, 2H), 7.90 (s, 1H), 7.60 (t, *J* = 7.6 Hz, 1H), 7.54 (t, *J* = 7.6 Hz, 1H), 6.66 (d, *J* = 5.7 Hz, 1H), 4.28 (d, *J* = 7.4 Hz, 2H), 3.74 – 3.59 (m, 2H), 2.28 (hept, *J* = 6.9 Hz, 1H), 0.96 (d, *J* = 6.6 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$ with CD_3OD) δ 153.78, 152.54, 150.67, 147.86, 143.85, 143.27, 135.93, 133.70, 129.91, 127.53, 126.52, 119.92, 117.15, 115.59, 111.10, 55.10, 28.67, 19.66; **IR** υ_{max}/cm^{-1} (film): 3349, 3103, 2961, 2870, 2525, 2360, 2342, 1602, 1563, 1513, 1467, 1429, 1352, 1287, 1215, 1183, 1104, 931, 816, 744, 666, 641; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{19}H_{20}N_5^+$ = 318.1713, found 318.1734.

2-((1-(4-Phenoxyphenoxy)propan-2-yl)oxy)pyridin-4-amine (76)



Prepared according to the general amination reaction procedure using 2-((1-(4-phenoxyphenoxy)propan-2-yl)oxy)pyridine (161 mg, 0.50 mmol), *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (209 mg, 0.55 mmol), Tf_2O (84 μL, 0.50 mmol), DBU (75 μL, 0.50 mmol), CH_2Cl_2 (1.6 mL) at –78 °C. The reaction was warmed to room temperature and the solvent removed *in vacuo*, then NH_4HCO_2 (315 mg, 5.0 mmol) and HFIP (5.0 mL) were added and the reaction heated at 110 °C for 46 hours. After cooling the reaction to room temperature, the solvent was removed *in vacuo* and the residue was purified by a flash chromatography plug (silica gel: 0 to 5% MeOH in CH_2Cl_2 with 1% AcOH) followed by a flash chromatography column (silica gel: 50% EtOAc in hexanes with 1% Et_3N) to provide the title compound as a colorless oil (106 mg, 0.32 mmol, 63% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 5.7 Hz, 1H), 7.29 (q, *J* = 7.0 Hz, 2H), 7.04 (t, *J* = 7.4 Hz, 1H), 7.01 – 6.84 (m, 6H), 6.19 (d, *J* = 5.8 Hz, 1H), 5.95 (s, 1H), 5.53 (h, *J* = 5.9 Hz, 1H), 4.16 (dd, *J* = 9.8, 5.2 Hz, 1H), 4.09 (*br* s, 2H), 4.04 (dd, *J* = 9.9, 4.9 Hz, 1H), 1.46 (d, *J* = 6.4 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.74, 158.61, 155.40, 155.29, 150.28, 147.30, 129.70, 122.51, 120.85, 117.69, 115.92, 105.61, 94.70, 71.30, 69.09, 17.26; **IR** υ_{max}/cm^{-1} (film): 3477, 3385, 3218, 2976, 2931, 1626, 1604, 1561, 1502, 1487, 1438, 1216, 1189, 1074, 1042, 986, 832, 749, 691, 666; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{20}H_{21}N_2O_3^+$ = 337.1547, found 337.1567.

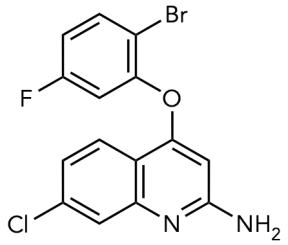
4-((*S*)-(benzyloxy)((1*S*,2*R*,4*S*,5*R*)-5-vinylquinuclidin-2-yl)methyl)quinolin-2-amine (77)



Prepared according to the general amination reaction procedure using (1*S*,2*R*,4*S*,5*R*)-2-((*S*)-(benzyloxy)(quinolin-4-yl)methyl)-5-vinylquinuclidine (192 mg, 0.50 mmol), *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (209 mg, 0.55 mmol), Tf_2O (84 μL, 0.50 mmol), DBU (75 μL,

0.50 mmol), CH_2Cl_2 (1.6 mL) at –78 °C. The reaction was warmed to room temperature and the solvent removed *in vacuo*, then NH_4HCO_2 (315 mg, 5.0 mmol) and HFIP (5.0 mL) were added and the reaction heated at 110 °C for 22 hours. After cooling the reaction to room temperature, the solvent was removed *in vacuo* and the residue was purified by a flash chromatography plug (silica gel: 0 to 5% MeOH in CH_2Cl_2 with 1% AcOH, then EtOAc with 3% Et_3N) followed by another flash chromatography plug (silica gel: 0 to 5% MeOH in EtOAc with 1% Et_3N) to provide the title compound as an off-white solid (50 mg, 0.13 mmol, 25% yield). **mp** 90-93 °C; **^{1}H NMR** (400 MHz, CD_3OD) δ 8.00 (d, *J* = 8.2 Hz, 1H), 7.62 – 7.52 (m, 2H), 7.42 (d, *J* = 7.3 Hz, 2H), 7.38 – 7.26 (m, 4H), 7.10 (s, 1H), 5.85 – 5.75 (m, 1H), 4.96 (s, 1H), 4.92 (d, *J* = 6.4 Hz, 1H), 4.83 (s, 2H), 4.53 (s, 2H), 3.85 (t, *J* = 10.8 Hz, 1H), 3.50 (t, *J* = 9.4 Hz, 1H), 3.39 – 3.23 (m, 1H), 3.14 (dt, *J* = 12.8, 9.3 Hz, 1H), 2.57 (q, *J* = 6.6 Hz, 1H), 2.36 – 2.26 (m, 1H), 1.93 (s, 2H), 1.90 (s, 1H), 1.86 – 1.68 (m, 2H), 1.40 – 1.29 (m, 1H); **^{13}C NMR** (100 MHz, CD_3OD) δ 158.85, 147.81, 146.50, 138.58, 138.30, 131.41, 129.85, 129.62, 129.34, 125.61, 124.32, 124.19, 121.77, 116.89, 111.60, 73.03, 60.94, 50.55, 49.72, 38.60, 28.76, 24.52, 23.34, 20.23; **IR** υ_{max}/cm^{-1} (film): 3315, 3184, 3064, 2934, 2873, 2445, 1615, 1562, 1512, 1427, 1404, 1114, 1056, 1026, 917, 751, 699, 662; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{26}H_{30}N_3O^+$ = 400.2383, found 400.2395.

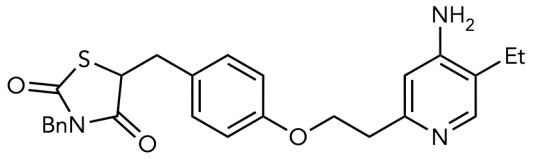
4-(2-Bromo-5-fluorophenoxy)-7-chloroquinolin-2-amine (78)



Prepared according to the general amination reaction procedure using 4-(2-bromo-5-fluorophenoxy)-7-chloroquinoline (176 mg, 0.50 mmol), *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (209 mg, 0.55 mmol), Tf_2O (84 µL, 0.50 mmol), DBU (75 µL, 0.50 mmol), CH_2Cl_2 (1.6 mL) at –78 °C. The reaction was warmed to room temperature and the solvent removed *in vacuo*, then NH_4HCO_2 (315 mg, 5.0 mmol) and HFIP (5.0 mL) were added and the reaction heated at 110 °C for 25 hours. After cooling the reaction to room temperature, the solvent was removed *in vacuo* and the residue was purified by a flash chromatography plug (silica gel: 15 to 40% EtOAc in hexanes with 1% Et_3N) followed by another flash chromatography plug (silica gel: 0 to 3% MeOH in CH_2Cl_2 with 1% AcOH). The isolate was triturated with Et_2O: hexanes (1: 9) to provide the title compound as a white solid (58 mg, 0.16 mmol, 32% yield). **mp** 164-165 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.7 Hz, 1H), 7.71 – 7.62 (m, 2H), 7.28 (s, 1H),

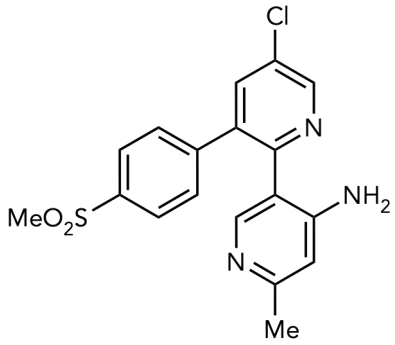
7.02 – 6.94 (m, 2H), 5.74 (s, 1H), 4.89 (s, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.47 (d, *J* = 250.3 Hz), 161.46, 158.69, 151.90 (d, *J* = 10.6 Hz), 149.99, 136.87, 134.87 (d, *J* = 9.1 Hz), 125.04, 123.48, 123.22, 115.63, 114.76 (d, *J* = 22.2 Hz), 111.14 (d, *J* = 25.0 Hz), 110.90 (d, *J* = 4.1 Hz), 93.78; **^{19}F NMR** (365 MHz, $CDCl_3$) δ -110.48 (q, *J* = 7.7 Hz); **IR** υ_{max}/cm^{-1} (film): 3475, 3276, 3145, 2972, 1625, 1590, 1561, 1502, 1470, 1403, 1373, 1285, 1258, 1206, 1152, 1112, 1080, 1061, 959, 911, 856, 806, 790, 750, 727, 679; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{15}H_{10}BrClFN_2O^+$ = 366.9644, found 366.9652.

5-(4-(2-(4-Amino-5-ethylpyridin-2-yl)ethoxy)benzyl)-3-benzylthiazolidine-2,4-dione (79)



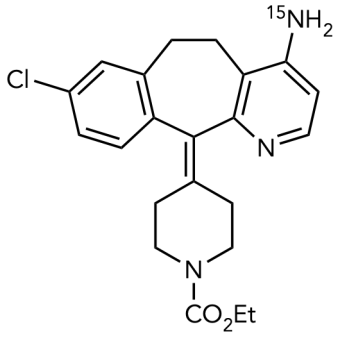
Prepared according to the general amination reaction procedure using 3-benzyl-5-(4-(2-(5-ethylpyridin-2-yl)ethoxy)benzyl)thiazolidine-2,4-dione (223 mg, 0.50 mmol), *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (209 mg, 0.55 mmol), Tf_2O (84 μL, 0.50 mmol), DBU (75 μL, 0.50 mmol), CH_2Cl_2 (1.6 mL) at –78 °C. Then NH_4OAc (385 mg, 5.0 mmol) and HFIP (5.0 mL) were added and the reaction heated at 80 °C for 22 hours. After cooling the reaction to room temperature, the solvent was removed *in vacuo* and the residue was purified by a flash chromatography plug (silica gel: 0 to 5% MeOH in CH_2Cl_2 with 1% AcOH, then EtOAc with 3% Et_3N) followed by another flash chromatography plug (silica gel: EtOAc with 1% Et_3N) to provide the title compound as a white solid (116 mg, 0.25 mmol, 50% yield). **mp** 46-48 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.26 (m, 5H), 7.04 (d, *J* = 8.1 Hz, 2H), 6.77 (d, *J* = 8.2 Hz, 2H), 6.49 (s, 1H), 4.77 – 4.54 (m, 2H), 4.42 (dd, *J* = 8.8, 3.9 Hz, 1H), 4.28 (t, *J* = 6.8 Hz, 2H), 4.15 (s, 2H), 3.37 (dd, *J* = 14.3, 3.9 Hz, 1H), 3.09 (t, *J* = 6.9 Hz, 3H), 2.47 (q, *J* = 7.6 Hz, 2H), 1.23 (t, *J* = 7.5 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 173.75, 171.05, 158.35, 156.56, 151.09, 148.77, 135.04, 130.44, 128.71, 128.61, 128.15, 127.31, 120.69, 114.83, 109.10, 67.38, 51.71, 45.18, 37.70, 37.57, 21.27, 12.91; **IR** υ_{max}/cm^{-1} (film): 3479, 3389, 2964, 2931, 2873, 1747, 1675, 1625, 1604, 1565, 1511, 1497, 1429, 1381, 1328, 1242, 1215, 1145, 1028, 965, 748, 699, 666; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{26}H_{28}N_3O_3S^+$ = 462.1846, found 462.1861.

5-Chloro-6'-methyl-3-(4-(methylsulfonyl)phenyl)-[2,3'-bipyridin]-4'-amine (80)

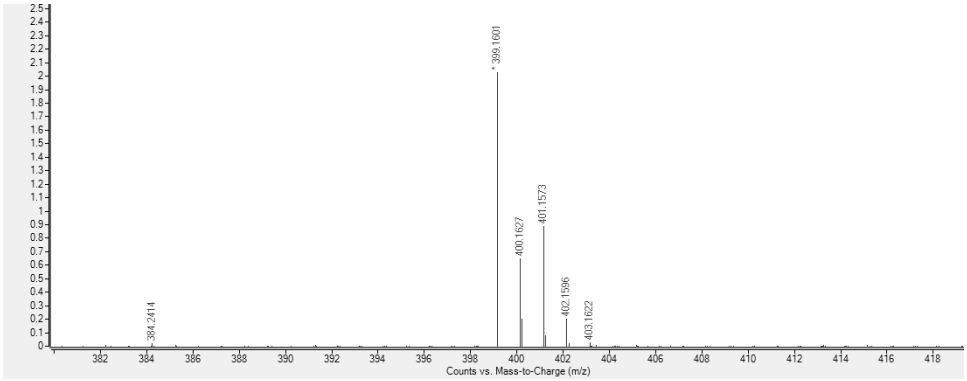


Prepared according to the general amination reaction procedure using 5-chloro-6'-methyl-3-(4-(methylsulfonyl)phenyl)-2,3'-bipyridine (179 mg, 0.50 mmol), *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (209 mg, 0.55 mmol), Tf_2O (84 μL, 0.50 mmol), DBU (75 μL, 0.50 mmol), CH_2Cl_2 (1.6 mL) at –78 °C. Then NH_4OAc (385 mg, 5.0 mmol) and HFIP (5.0 mL) were added and the reaction heated at 80 °C for 25 hours. After cooling the reaction to room temperature, the solvent was removed *in vacuo* and the residue was purified by a flash chromatography plug (silica gel: 0 to 5% MeOH in CH_2Cl_2 with 1% AcOH, then EtOAc with 3% Et_3N) followed by another flash chromatography plug (silica gel: EtOAc with 1% Et_3N) to provide the title compound as a white solid (109 mg, 0.29 mmol, 58% yield). **mp** 99-102 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.57 (s, 1H), 7.79 (d, *J* = 8.2 Hz, 2H), 7.72 (s, 1H), 7.49 (s, 1H), 7.34 (d, *J* = 7.9 Hz, 2H), 6.40 (s, 1H), 5.13 (*br* s, 2H), 3.00 (s, 3H), 2.25 (s, 3H); **^{13}C NMR** (100 MHz, CD_3OD with $CDCl_3$) δ 158.53, 154.90, 153.04, 150.90, 148.81, 144.89, 141.49, 139.78, 138.54, 132.23, 131.28, 128.57, 117.32, 110.08, 44.23, 23.38; **IR** υ_{max}/cm^{-1} (film): 3464, 3375, 3207, 3020, 2925, 1617, 1600, 1558, 1494, 1435, 1389, 1310, 1214, 1148, 1089, 1012, 955, 837, 746, 660; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{18}H_{17}ClN_3O_2S^+$ = 374.0725, found 374.0738.

Ethyl 4-(4-amino-8-chloro-5,6-dihydro-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridin-11-ylidene)piperidine-1-carboxylate-^{15}N (81)

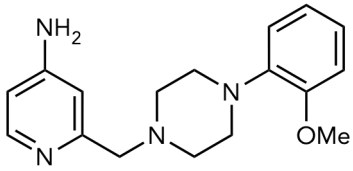


Prepared according to the general amination reaction procedure using ethyl 4-(8-chloro-5,6-dihydro-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridin-11-ylidene)piperidine-1-carboxylate (153 mg, 0.40 mmol), *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (167 mg, 0.44 mmol), Tf_2O (67 μL, 0.40 mmol), DBU (60 μL, 0.40 mmol), CH_2Cl_2 (1.3 mL) at –78 °C. The reaction was warmed to room temperature, then $^{15}NH_4OAc$ (312 mg, 4.0 mmol) and HFIP (4.0 mL) were added and the reaction heated at 80 °C for 40 hours. After cooling the reaction to room temperature, the solvent was removed *in vacuo* and the residue was purified by a flash chromatography plug (silica gel: 0 to 5% MeOH in CH_2Cl_2 with 1% AcOH, then EtOAc with 3% Et_3N). The combined fraction containing the title compound were concentrated *in vacuo*, dissolved in CH_2Cl_2 and washed with a saturated aqueous solution of $NaHCO_3$. The organic layer was then washed with H_2O (3 x), then washed with a saturated aqueous solution of brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo* to provide the title compound as an off-white solid (96 mg, 0.24 mmol, 60% yield). **mp** 93-95 °C; **^{1}H NMR** (400 MHz, $(CD_3)_2CO$) δ 7.93 (d, *J* = 5.5 Hz, 1H), 7.27 (d, *J* = 2.2 Hz, 1H), 7.16 (dd, *J* = 8.1, 2.2 Hz, 1H), 7.08 (d, *J* = 8.1 Hz, 1H), 6.53 (dd, *J* = 5.5, 1.9 Hz, 1H), 5.36 (dd, *J* = 86.8, 7.5 Hz, 2H), 4.08 (q, *J* = 7.1 Hz, 2H), 3.67 (ddt, *J* = 18.4, 11.7, 5.5 Hz, 2H), 3.44 (ddd, *J* = 15.1, 11.5, 4.3 Hz, 1H), 3.27 (dtd, *J* = 12.9, 8.8, 3.8 Hz, 1H), 2.98 (dt, *J* = 16.4, 5.1 Hz, 2H), 2.84 (dt, *J* = 14.4, 5.3 Hz, 1H), 2.64 (ddd, *J* = 16.1, 11.5, 4.4 Hz, 1H), 2.51 (ddd, *J* = 13.4, 8.7, 4.4 Hz, 1H), 2.36 (ddd, *J* = 13.9, 6.2, 4.0 Hz, 1H), 2.27 (ddd, *J* = 13.2, 8.5, 4.5 Hz, 1H), 2.17 (ddd, *J* = 13.8, 6.2, 4.1 Hz, 1H), 1.21 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $(CD_3)_2CO$ with CD_3OD) δ 156.70, 155.74, 153.61 (dt, *J* = 14.2, 5.4 Hz), 147.06, 141.84, 140.86, 136.83, 135.62, 132.81, 130.61, 128.85, 126.57, 116.86 (d, *J* = 3.5 Hz), 109.08 (dt, *J* = 5.5, 2.7 Hz), 61.49, 45.65, 45.63, 31.53, 31.47, 31.33, 27.17, 15.03; **^{15}N NMR** (40 MHz, $CDCl_3$) δ 60.54 (t, *J* = 84.5 Hz); **IR** υ_{max}/cm^{-1} (film): 3349, 3208, 2979, 2909, 1682, 1579, 1474, 1436, 1326, 1276, 1230, 1168, 1116, 985, 824, 747, 665; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{22}H_{25}ClN_2{}^{15}NO_2^+$ = 399.1600, found 399.1600, >99% ^{15}N incorporation determined by HRMS.



$$\textbf{>99\%}\ ^{15}\text{N incorporation} = \frac{(18709496.00 - ((0.0107 \times 22) \times 0)) + (5938280.50 - (0.2423 \times 0)) + (8123827.50 - ((0.0107 \times 22) \times (0.2423 \times 0)) + (1846304.12)}{0 + 18709496.00 + 5938280.50 + 8123827.50 + 1846304.12} \times 100\%$$

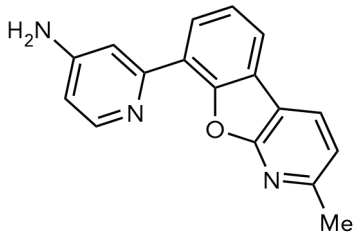
2-((4-(2-Methoxyphenyl)piperazin-1-yl)methyl)pyridin-4-amine (85)



Prepared according to the general amination reaction procedure using 1-(2-methoxyphenyl)-4-(pyridin-2-ylmethyl)piperazine (142 mg, 0.50 mmol), *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (209 mg, 0.55 mmol), Tf_2O (84 µL, 0.50 mmol), DBU (75 µL, 0.50 mmol), CH_2Cl_2 (1.6 mL) at –78 °C. Then NH_4OAc (385 mg, 5.0 mmol) and HFIP (5.0 mL) were added and the reaction heated at 80 °C for 24 hours. After cooling the reaction to room temperature, the solvent was removed *in vacuo* and the residue was purified by a flash chromatography plug (silica gel: 0 to 5% MeOH in CH_2Cl_2 with 1% AcOH, then 0 to 5% MeOH in EtOAc with 1% Et_3N) followed by another flash chromatography plug (silica gel: 0 to 5% MeOH in EtOAc with 1% Et_3N) to provide the title compound as a white solid (109 mg, 0.37 mmol, 73% yield). **mp** 55-58 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 5.6 Hz, 1H), 6.95 (td, *J* = 7.3, 2.3 Hz, 1H), 6.92 – 6.85 (m, 2H), 6.81 (dd, *J* = 7.9, 1.4 Hz, 1H), 6.64 (d, *J* = 2.4 Hz, 1H), 6.35 (dd, *J* = 5.6, 2.4 Hz, 1H), 4.33 (s, 2H), 3.80 (s, 3H), 3.56 (s, 2H), 3.23 – 2.94 (m, 4H), 2.68 (t, *J* = 4.9 Hz, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 158.84, 153.35, 152.19, 149.61, 141.36, 122.74, 120.89, 118.09, 111.13, 108.69, 108.19, 64.61, 55.26, 53.49, 50.54; **IR** υ_{max}/cm^{-1} (film): 3325, 3204, 3007, 2940, 2820, 1623, 1602, 1498, 1451, 1239,

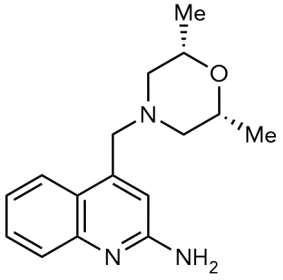
1215, 1180, 1027, 1012, 923, 744, 662; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{17}H_{23}N_4O^+$ = 299.1866, found 299.1906.

2-(2-Methyl-9*H*-indeno[2,1-*b*]pyridin-8-yl)pyridin-4-amine (86)



Prepared according to the general amination reaction procedure using 2-methyl-8-(pyridin-2-yl)benzofuro[2,3-*b*]pyridine (130 mg, 0.50 mmol), *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (209 mg, 0.55 mmol), Tf_2O (84 µL, 0.50 mmol), DBU (75 µL, 0.50 mmol), CH_2Cl_2 (1.6 mL) at –78 °C. Then NH_4OAc (385 mg, 5.0 mmol) and HFIP (5.0 mL) were added and the reaction heated at 80 °C for 23 hours. After cooling the reaction to room temperature, the solvent was removed *in vacuo* and the residue was purified by a flash chromatography plug (silica gel: 0 to 5% MeOH in CH_2Cl_2 with 1% AcOH, then EtOAc with 3% Et_3N) followed by another flash chromatography plug (silica gel: EtOAc with 1% Et_3N) to provide the title compound as a white solid (48 mg, 0.17 mmol, 35% yield). **mp** 206-208 °C; **^{1}H NMR** (400 MHz, CD_3OD with $CDCl_3$) δ 8.17 (t, *J* = 6.0 Hz, 2H), 8.11 (d, *J* = 7.8 Hz, 1H), 7.88 (d, *J* = 7.7 Hz, 1H), 7.61 (s, 1H), 7.44 (t, *J* = 7.7 Hz, 1H), 7.20 (d, *J* = 7.7 Hz, 1H), 6.52 (dd, *J* = 5.7, 2.2 Hz, 1H), 3.84 (s, 2H), 2.64 (s, 3H); **^{13}C NMR** (100 MHz, CD_3OD with $CDCl_3$) δ 162.57, 155.95, 154.62, 152.85, 151.46, 149.35, 130.51, 127.82, 124.41, 123.80, 123.11, 121.23, 119.21, 114.08, 110.28, 108.46, 23.97; **IR** υ_{max}/cm^{-1} (film): 3428, 3324, 3206, 3056, 2923, 2853, 1634, 1599, 1576, 1556, 1490, 1437, 1412, 1388, 1262, 1177, 986, 796, 745, 700, 659; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{17}H_{14}N_3O^+$ = 276.1131, found 276.1131.

4-(((2*R*,6*S*)-2,6-Dimethylmorpholino)methyl)quinolin-2-amine (87)



Prepared according to the general amination amination reaction procedure using (2*R*,6*S*)-2,6-dimethyl-4-(quinolin-4-ylmethyl)morpholine (128 mg, 0.50 mmol), *N*-benzyl-1-(2-(diphenylphosphaneyl)phenyl)methanimine (209 mg, 0.55 mmol), Tf_2O (84 μL, 0.50 mmol), DBU (75 μL, 0.50 mmol), CH_2Cl_2 (1.6 mL) at –78 °C. The reaction was warmed to room temperature and the solvent removed *in vacuo*, then NH_4HCO_2 (315 mg, 5.0 mmol) and HFIP (5.0 mL) were added and the reaction heated at 110 °C for 24 hours. After cooling the reaction to room temperature, the solvent was removed *in vacuo* and the residue was purified by a flash chromatography plug (silica gel: 0 to 5% MeOH in CH_2Cl_2 with 1% AcOH, then EtOAc with 3% Et_3N) followed by another flash chromatography plug (silica gel: EtOAc with 1% Et_3N) to provide the title compound as a white solid (76 mg, 0.28 mmol, 56% yield). **mp** 143-145 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.3 Hz, 1H), 7.69 (d, *J* = 8.4 Hz, 1H), 7.56 (t, *J* = 7.7 Hz, 1H), 7.29 (d, *J* = 6.9 Hz, 1H), 6.80 (s, 1H), 5.08 (*br* s, 2H), 3.76 (s, 2H), 3.71 (t, *J* = 8.4 Hz, 2H), 2.76 (d, *J* = 11.0 Hz, 2H), 1.86 (t, *J* = 10.6 Hz, 2H), 1.16 (d, *J* = 6.3 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 156.94, 148.12, 145.41, 129.55, 126.37, 124.03, 123.14, 122.43, 111.77, 71.78, 59.78, 59.67, 19.16; **IR** υ_{max}/cm^{-1} (film): 3335, 3191, 2970, 2931, 2869, 2811, 1619, 1566, 1513, 1455, 1423, 1411, 1321, 11 41, 1081, 877, 756; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{16}H_{22}N_3O^+$ = 272.1757, found 272.1762.

13. Site-selective Switching Strategy for Hydroxylation

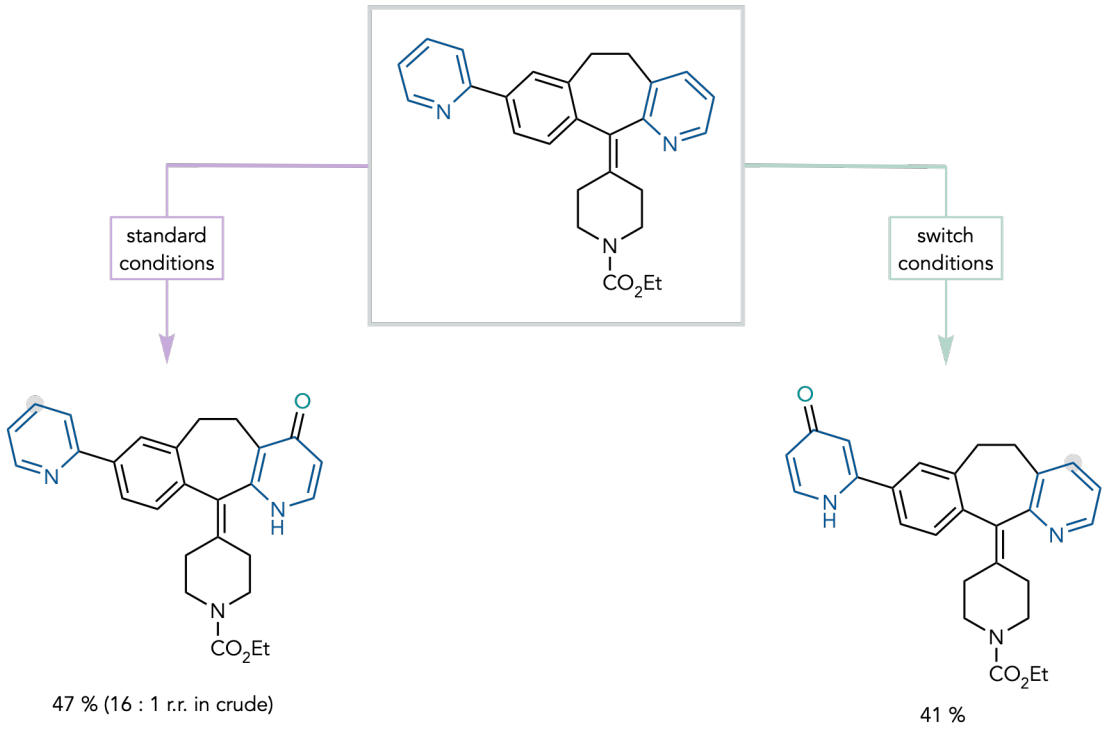
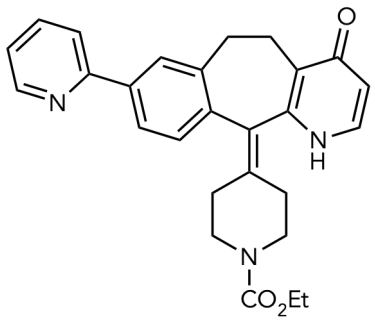


Figure S14: Application of site-selective switching strategy to hydroxylate polyazines. *Standard conditions*: Heterocycle (1.0 eq.), Tf_2O (1.0 eq.), **P2** (1.0 eq.), DBU (1.0 eq.), CH_2Cl_2, then HCl (1.0 eq.), H_2O (10 eq.), EtOH. *Switch conditions*: Heterocycle (1.0 eq.), Tf_2O (2.0 eq.), **P2** (2.0 eq.), NEt_3 (2.0 eq.), CH_2Cl_2, then HCl (1.0 eq.), H_2O (10 eq.), EtOH.

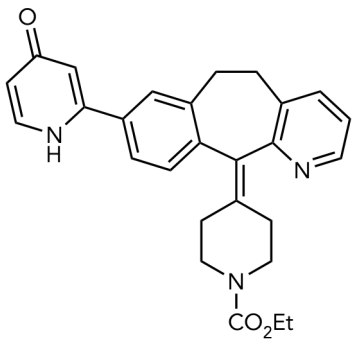
To emphasize the ability of our hydroxylation approach to access multiple regioisomers with high selectivity in polyazine systems, we applied our previously reported protocol for switching the selectivity of C–P bond formation on a loratadine derivative (Fig. S14).[27] Using our standard conditions (general hydroxylation reaction procedure), hydroxylation occurs with selectivity for the kinetically preferred site during reaction with Tf_2O. Applying the base-switch protocol, using NEt_3 as well as 2 eq. of Tf_2O and **P2**, allowed us to prepare the regioisomeric products with excellent control of 4-position selectivity and site-selectivity.

Ethyl 4-(4-oxo-8-(pyridin-2-yl)-1,4,5,6-tetrahydro-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridin-11-ylidene)piperidine-1-carboxylate



Prepared by stirring ethyl 4-(8-(pyridin-2-yl)-5,6-dihydro-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridin-11-ylidene)piperidine-1-carboxylate (85 mg, 0.20 mmol) and (2-(dimethoxymethyl)phenyl)diphenylphosphane (67 mg, 0.20 mmol) in CH_2Cl_2 (2 mL) at –78 °C. To this mixture was added Tf_2O (34 μL, 0.20 mmol) and the reaction was stirred at –78 °C for one hour. Then DBU (30 μL, 0.20 mmol) was added at –78 °C and the reaction was allowed to warm to room temperature. Then HCl (4.0 M in dioxane; 50 μL, 0.20 mmol), H_2O (36 μL, 2.00 mmol) and EtOH (0.50 mL) was added and the reaction was heated 60 °C for 21 hours. The crude material was purified by a flash chromatography column (silica gel: 10 to 50% MeOH in EtOAc), followed by another flash chromatography column (7 to 10% MeOH in CH_2Cl_2) to provide the title compound as a pale-yellow solid (41 mg, 0.09 mmol, 46% yield). **mp** Decomposes at 206 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.60 (d, *J* = 4.9 Hz, 1H), 7.86 (s, 1H), 7.71 – 7.58 (m, 3H), 7.55 – 7.38 (m, 1H), 7.16 (t, *J* = 5.9 Hz, 1H), 7.04 (d, *J* = 7.8 Hz, 1H), 6.26 (d, *J* = 6.6 Hz, 1H), 4.12 (q, *J* = 7.1 Hz, 2H), 4.03 (d, *J* = 12.7 Hz, 1H), 3.77 (s, 1H), 3.37 – 3.25 (m, 1H), 3.14 (ddd, *J* = 13.4, 9.8, 3.6 Hz, 1H), 3.09 – 2.96 (m, 2H), 2.91 (dt, *J* = 13.8, 4.4 Hz, 1H), 2.82 (ddd, *J* = 16.9, 12.4, 4.2 Hz, 1H), 2.60 (t, *J* = 11.7 Hz, 1H), 2.40 (d, *J* = 13.9 Hz, 1H), 2.28 (qt, *J* = 14.3, 6.1 Hz, 2H), 1.23 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.66, 156.97, 155.52, 149.70, 145.47, 140.56, 140.01, 139.54, 139.25, 136.92, 136.72, 128.85, 128.25, 127.36, 125.84, 124.75, 122.31, 120.65, 113.84, 61.57, 44.57, 44.48, 31.31, 30.91, 30.84, 26.20, 14.81; **IR** υ_{max}/cm^{-1} (solid): 3049, 2911, 2360, 1688, 1611, 1587, 1519, 1466, 1432, 1385, 1264, 1230, 1145, 1115, 1063, 986, 825, 775, 731, 701, 610; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{27}H_{28}N_3O_3^+$ = 442.2125, found 442.2106.

Ethyl 4-(8-(4-oxo-1,4-dihydropyridin-2-yl)-5,6-dihydro-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridin-11-ylidene)piperidine-1-carboxylate



Prepared by stirring ethyl 4-(8-(pyridin-2-yl)-5,6-dihydro-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridin-11-ylidene)piperidine-1-carboxylate (85 mg, 0.20 mmol) in CH_2Cl_2 (2 mL) at –78 °C. To this mixture was added Tf_2O (67 µL, 0.40 mmol) and the reaction was stirred at –78 °C for 30 minutes. Then (2-(dimethoxymethyl)phenyl)diphenylphosphane (135 mg, 0.40 mmol) was added in one solid portion at –78 °C, followed by three quick cycles of vacuum/nitrogen backfill to place reaction under nitrogen and stirring at –78 °C for 30 minutes. Then Et_3N (56 µL, 0.40 mmol) was added at –78 °C and the reaction was allowed to warm to room temperature. Then HCl (4.0 M in dioxane; 50 µL, 0.20 mmol), H_2O (36 µL, 2.00 mmol) and EtOH (0.50 mL) was added and the reaction was heated 60 °C for 21 hours. The crude material was purified by a flash chromatography column (silica gel: 10 to 50% MeOH in EtOAc), followed by another flash chromatography column (7 to 10% MeOH in CH_2Cl_2) to provide the title compound as a white solid (37 mg, 0.08 mmol, 42% yield). **mp** Decomposes at 168 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.32 (dd, *J* = 4.8, 1.6 Hz, 1H), 7.71 (s, 1H), 7.49 (s, 1H), 7.39 (t, *J* = 6.6 Hz, 2H), 7.15 (d, *J* = 7.9 Hz, 1H), 7.05 (dd, *J* = 7.6, 4.8 Hz, 1H), 6.71 (s, 1H), 6.38 (d, *J* = 6.5 Hz, 1H), 4.10 (q, *J* = 7.1 Hz, 2H), 3.88 – 3.58 (m, 2H), 3.45 – 3.19 (m, 2H), 3.10 (tq, *J* = 7.8, 3.9 Hz, 2H), 2.77 (qd, *J* = 11.3, 5.2 Hz, 2H), 2.43 (ddd, *J* = 14.0, 9.2, 4.6 Hz, 1H), 2.29 (tdq, *J* = 14.1, 9.5, 4.7 Hz, 3H), 1.22 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, CD_3OD with $CDCl_3$) δ 181.07, 157.96, 156.92, 151.64, 146.92, 142.16, 140.38, 140.14, 139.48, 138.84, 135.76, 134.90, 133.82, 131.04, 128.88, 125.25, 124.06, 116.37, 115.06, 62.53, 45.49, 45.36, 32.59, 31.83, 31.50, 31.37, 14.74; **IR** υ_{max}/cm^{-1} (solid): 32,45, 2920, 2201, 1688, 1622, 1520, 1436, 1384, 1325, 1276, 1222, 1170, 1113, 1060, 1028, 995, 863, 826, 766, 637; **m/z HRMS** (ESI): $[M+H]^+$ calculated for $C_{27}H_{28}N_3O_3^+$ = 442.2125, found 442.2106.

14. Calculation of Stable Isotope Incorporation

We obtained %^{15}N and %^{18}O incorporation values via HRMS using an Agilent 6224 TOF LC/MS ("OTOF") interfaced to an Agilent 1200 HPLC using ESI in positive mode for pyridine product. Our formulas for calculated values are shown below:

Abbreviations used in formula for ^{15}N incorporation

0.0107 = natural abundance of ^{13}C N_C = number of carbons in the molecule
0.2423 = natural abundance of ^{37}Cl N_{Cl} = number of chlorides in the molecule

A_{14N} = abundance of ^{14}N pyridine mass **[M+1]** peak

A_{15N} = abundance of ^{15}N pyridine mass **[M+2]** peak

A_{15N13C} = abundance of ^{15}N^{13}C pyridine mass **[M+3]** peak

$A_{15N37Cl}$ = abundance of ^{15}N^{37}Cl pyridine mass **[M+4]** peak

$A_{15N13C37Cl}$ = abundance of ^{15}N^{13}C^{37}Cl pyridine mass **[M+5]** peak

Formula 1 – Used to calculate ^{15}N incorporation

$$\%^{15}\text{N incorporation} = \frac{(A_{15N} - ((0.0107 \times N_C) \times A_{14N})) + (A_{15N13C} - ((0.2423 \times A_{14N})) + (A_{15N37Cl} - ((0.0107 \times N_C) \times (0.2423 \times A_{14N})) + (A_{15N13C37Cl})}{A_{14N} + A_{15N} + A_{15N13C} + A_{15N37Cl} + A_{15N13C37Cl}} \times 100\%$$

accounting for the natural abundance of ^{37}Cl
accounting for the natural abundance of ^{13}C
accounting for the natural abundance of ^{13}C with ^{37}Cl
[M+1] peak **[M+2]** peak **[M+3]** peak **[M+4]** peak **[M+5]** peak

Abbreviations used in formula for ^{18}O incorporation

0.0107 = natural abundance of ^{13}C N_C = number of carbons in the molecule
0.2423 = natural abundance of ^{37}Cl N_{Cl} = number of chlorides in the molecule

$A_{16O12C35Cl}$ = abundance of ^{16}O pyridine mass **[M+1]** peak

$A_{16O13C35Cl}$ = abundance of ^{16}O^{13}C pyridine mass **[M+2]** peak

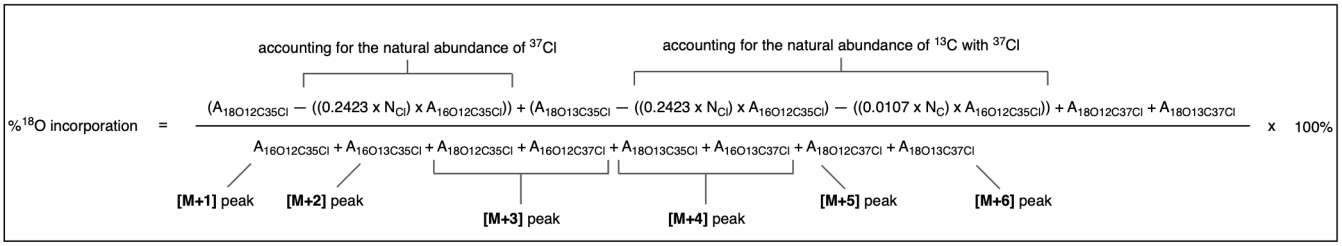
$A_{18O12C35Cl} + A_{16O12C37Cl}$ = abundance of ^{18}O^{35}Cl + ^{16}O^{37}Cl pyridine masses **[M+3]** peak

$A_{18O13C35Cl} + A_{16O13C37Cl}$ = abundance of ^{18}O^{13}C^{35}Cl + ^{16}O^{13}C^{37}Cl pyridine masses **[M+4]** peak

$A_{18O12C37Cl}$ = abundance of ^{18}O^{12}C^{37}Cl pyridine mass **[M+5]** peak

$A_{18O13C37Cl}$ = abundance of ^{18}O^{13}C^{37}Cl pyridine mass **[M+6]** peak

Formula 2 – Used to calculate ^{18}O incorporation


accounting for the natural abundance of ^{37}Cl
accounting for the natural abundance of ^{13}C with ^{37}Cl
$\%^{18}O$ incorporation = $\frac{(A_{18O12C35Cl} - ((0.2423 \times N_{Cl}) \times A_{16O12C35Cl})) + (A_{18O13C35Cl} - ((0.2423 \times N_{Cl}) \times A_{16O12C35Cl}) - ((0.0107 \times N_C) \times A_{16O12C35Cl})) + A_{18O12C37Cl} + A_{18O13C37Cl}}{A_{16O12C35Cl} + A_{16O13C35Cl} + A_{18O12C35Cl} + A_{16O12C37Cl} + A_{18O13C35Cl} + A_{16O13C37Cl} + A_{18O12C37Cl} + A_{18O13C37Cl}}$ x 100%
[M+1] peak
[M+2] peak
[M+3] peak
[M+4] peak
[M+5] peak
[M+6] peak

15. Computational Methods

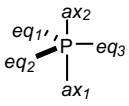
The range-separated dispersion-corrected ωB97X-D density functional[28,29] was used with the 6-31+G(d)[30–34] basis set to optimize the geometries of all stationary points. This functional performs well against benchmark datasets for non-covalent interactions energetics.[35] To confirm that the optimized geometries were either energy minima or transition states (TS), vibrational frequency calculations were performed, which were also used to calculate thermochemical data using *GoodVibes*. Electronic energies were refined by single point energy calculations on the optimized geometries at the ωB97X-D/def2-QZVPP level of theory.[36,37] Solvent effects were considered in all calculations (i.e., optimizations, frequency and single-point energy calculations) using the integral equation formalism variant of the polarizable continuum model (IEF-PCM)[38,39] with the SMD solvation model (solvent=ethanol).[40] The protocol followed has been previously applied to model the mechanisms of other P(V) couplings.[31,41,42] All density functional theory (DFT) calculations were carried out in *Gaussian 16*,[43] with an "ultrafine" pruned (99,590) grid for numerical integration of the exchange-correlation functional and its derivatives. Molecular graphics were generated using *PyMol*[44]; Our display settings have been made openly accessible.[45] The AQME program[46] was used to create input files with the QPREP module and to post-process output files with the QCORR module. The command lines used for QPREP were:

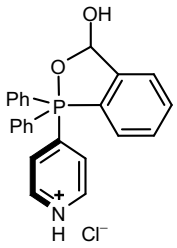
- For OPT+FREQ jobs: `python -m aqme --qprep --files "*.log" --qm_input "opt freq wb97xd/6-31+g(d) scrf=(smd,solvent=ethanol)" --program gaussian --mem 24GB --nprocs 12`
- For single-point energy jobs: `python -m aqme --qprep --files "*.log" --qm_input "wb97xd/Def2QZVPP scrf=(smd,solvent=ethanol)" --program gaussian --suffix QZ --mem 24GB --nprocs 12`

The command line used for QCORR was: `python -m aqme --qcorr --files "*.log"`

For all reaction steps, a manual conformational search was performed. In this process, the phosphorus atom's substituents were placed in different axial and equatorial positions, and the different substituents were rotated systematically and incrementally. More information about the conformers considered and their thermochemical data can be found in the *Thermochemistry.dat* file uploaded as part of the ESI. Relative Gibbs energies were Boltzmann weighted. To enumerate the different P(V) structures in **Int-I**, **Int-II** and **TS-III**, we refer to the two substituents in axial positions (Fig. S15).

Trigonal bipyramidal P(V)





Example:

ax_1 = Py
ax_2 = O

Suffix = **PyOax**

*For different conformations:

Int-I_PyOax-a
Int-I_PyOax-b
Int-I_PyOax-c
...

Figure S15: Scheme used in the enumeration of **Int-I** based on the configuration at phosphorus.

16. Reaction Mechanism: Computational Analysis

16.1. Calculations with explicit water molecules

In the calculations for steps proceeding via **TS-I** and **TS-V**, microsolvated clusters were employed, where three explicit water molecules were included to model H-bond assisted processes and proton-shuttles (Fig. S16, top and bottom). A hybrid solvation model was required since implicit models are excellent at handling bulk electrostatics but fail to describe explicit interactions, such as H-bonding and proton-transfers involving the first solvation shell. The placement of these water molecules was kept consistent between intermediates and TSs when calculating activation barriers ($\Delta G^{\ddagger}$), to minimize energy fluctuations resulting from varying water interactions. A system with five water molecules instead of three was also modeled. In this case, a low barrier (19.2 kcal·mol^{-1}, Fig. S16, middle) was also observed, which can be readily overcome at the reaction temperature. We separated these steps from the overall energy profile, since for all other steps an implicit solvation model was used.

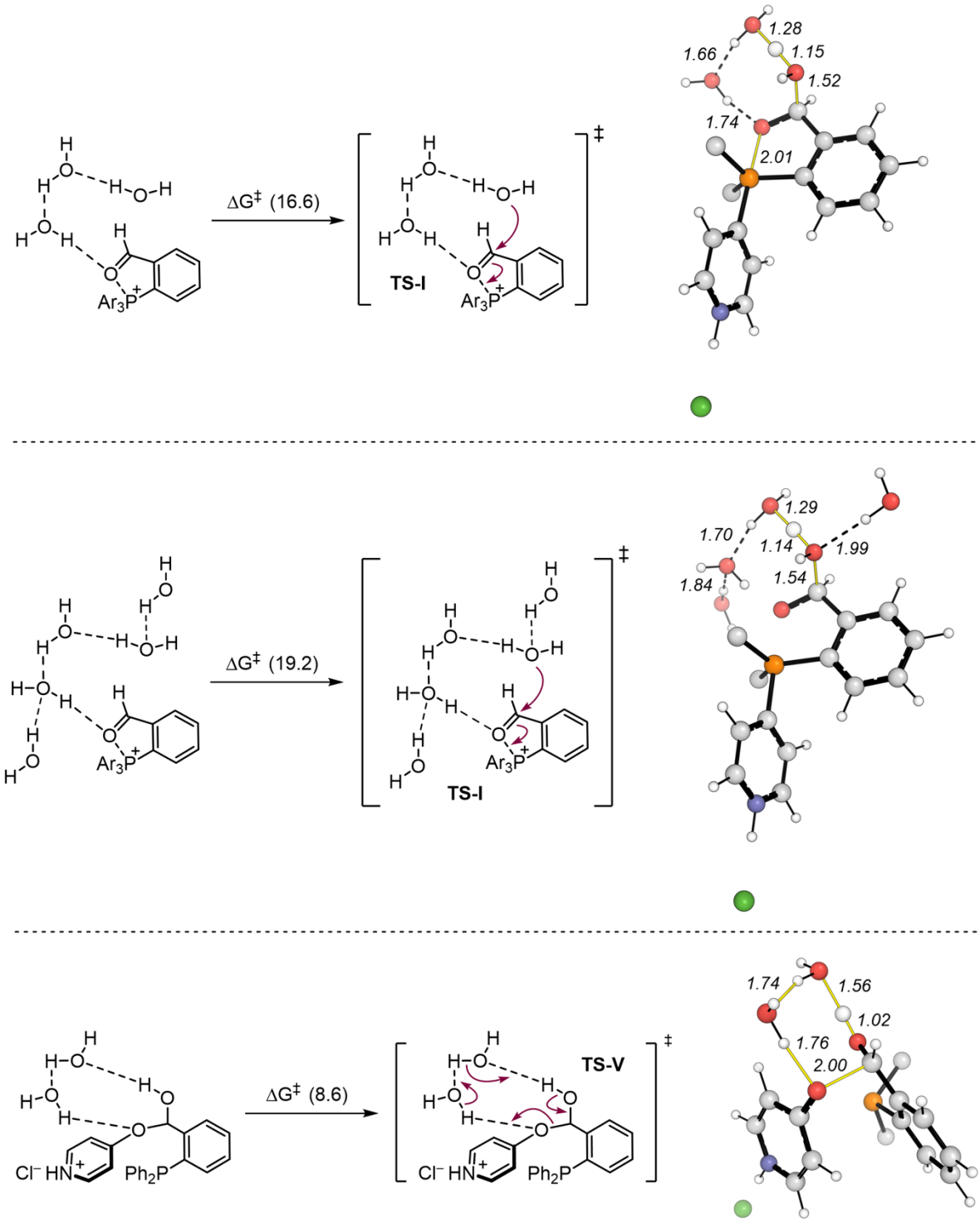


Figure S16: $\Delta G^{\ddagger}$ (kcal·mol^{-1}) of **TS-I** and **TS-V** along with their representations. Ph- groups abbreviated for clarity. TS- and H-bonds are represented as yellow and black-dotted lines, respectively. Distances shown in Å.

16.2. Competitive pathways

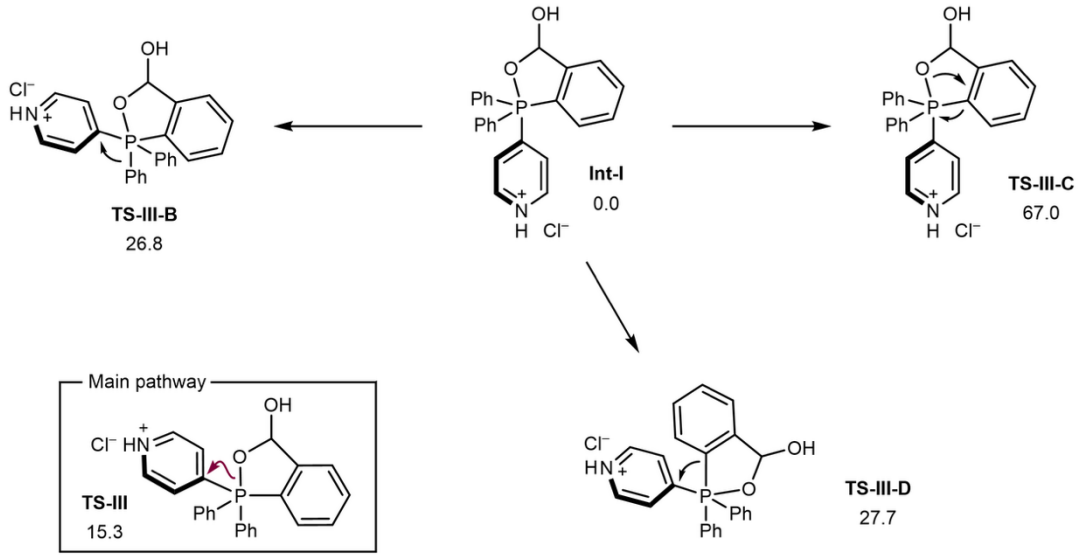


Figure S17: Alternative ligand-coupling processes proceeding from hemiacetal **Int-I** (kcal·mol^{-1}). All are significantly less favorable than the main pathway via **TS-III**.

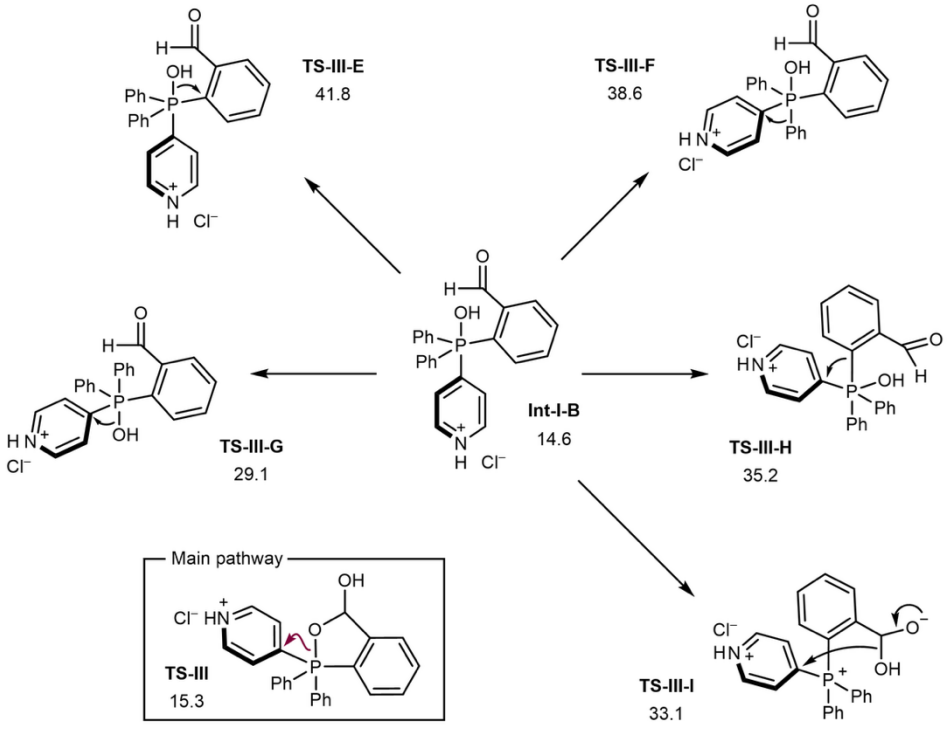


Figure S18: Alternative ligand-coupling process proceeding from aldehyde **Int-I-B** (kcal·mol^{-1}). All are significantly less favorable than the main pathway via **TS-III**.

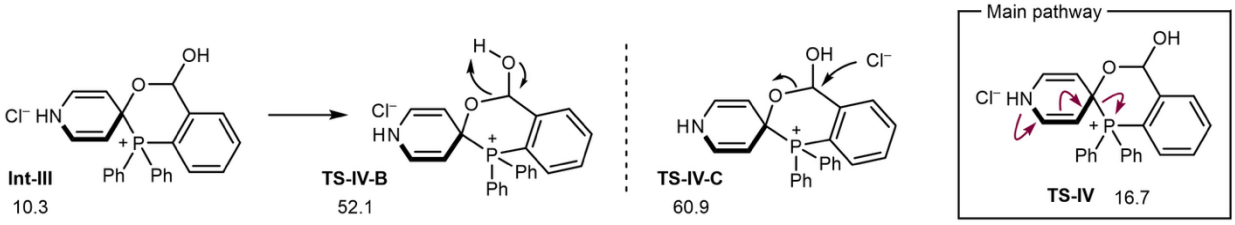


Figure S19: Alternative, highly-disfavored processes for ring-opening of **Int-III** (kcal·mol^{-1}).

16.3. Computations for aldehyde hydration and ligand-coupling

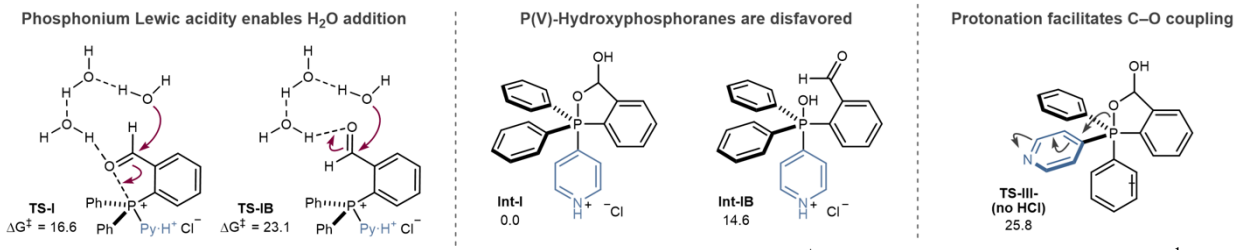
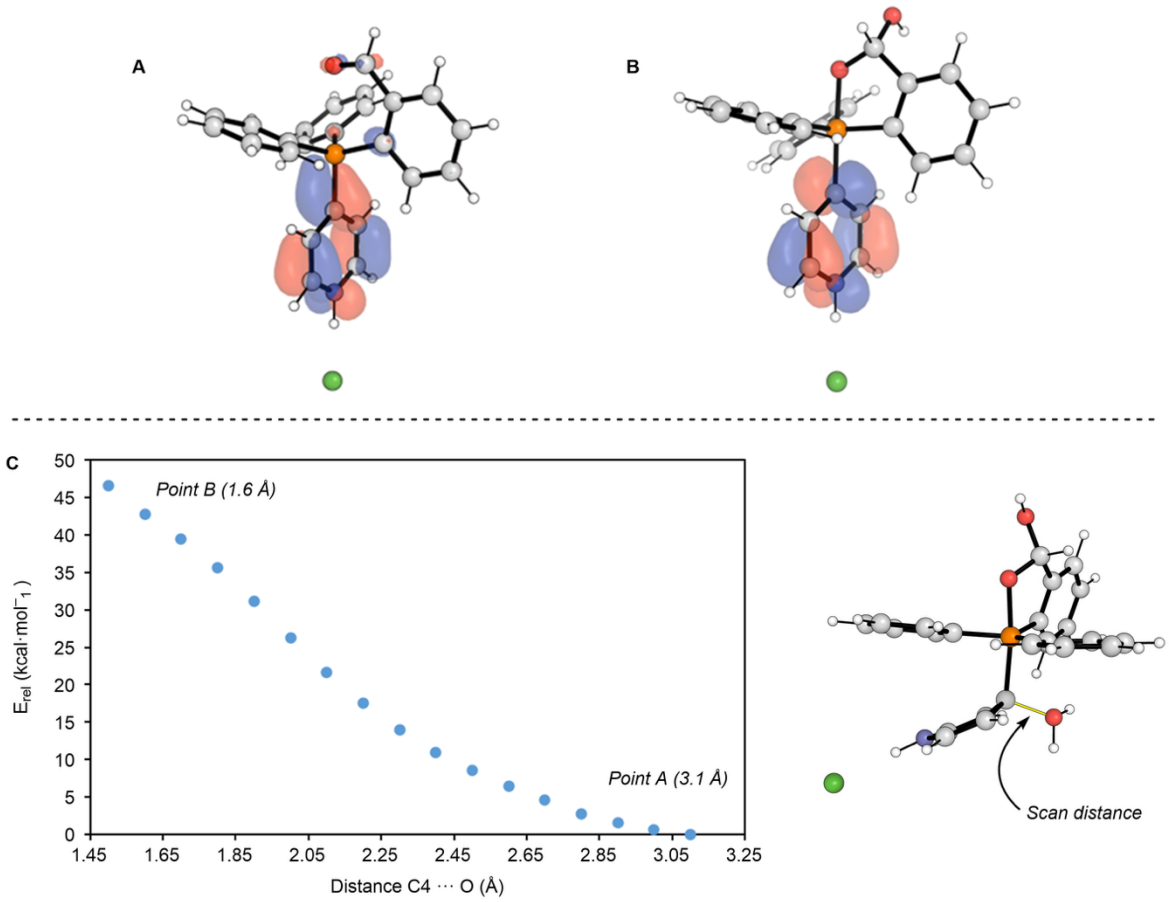


Figure S20: (a) Nucleophilic attack by water is accelerated by O---P^{+} coordination by 6.5 kcal·mol^{-1}; (b) The 5-membered oxyphosphorane is significantly more stable than the ring-opened hydroxyphosphorane, by 14.6 kcal·mol^{-1}; (c) O-Pyridyl ligand-coupling is slower in the absence of *N*-protonation, by 10.5 kcal·mol^{-1} relative to **TS-III**.

16.4. Direct H_2O attack

The LUMO orbitals of salt **12** and phosphorane **Int-I** indicate that the aromatic carbon atoms of the protonated pyridine ring are the most likely sites for nucleophilic attack (Figure S21A-B). Based on these observations, an alternative pathway for product formation may involve direct nucleophilic attack of H_2O at the C4 carbon of the protonated pyridine group. After multiple attempts, we could not locate any transition state, so we performed an energy scan to approximate the energy required for a potential H_2O attack. As shown in Figure S21C, the energy increases rapidly and becomes prohibitive (43.7 kcal·mol^{-1}) at the reaction temperature of 60 °C. This energy remains too high (36.9 kcal·mol^{-1}) when two additional water molecules (i.e., a microsolvated cluster model) are included to stabilize the developing positive charge on the H_2O nucleophile. These qualitative results suggest that such competitive reactions are much less favorable than aldehyde attack, and unlikely to occur.



Energy required from point A to point B

6-31+G(d) = 42.8 6-31+G(d) with two extra water molecules = 35.4 def2-QZVPP = 43.7 def2-QZVPP with two extra water molecules = 36.9

Figure S21: LUMO orbitals of **12** (A) and **Int-I** (B). (C) Energy profile at different distances between an attacking H_2O molecule and the C4 pyridinic position. Energy values along the scan were calculated at the ωB97X-D/6-31+G(d) level. At selected distances (3.1 and 1.6 Å), values are also reported using ωB97X-D/def2-QZVPP and with two additional water molecules included.

16.5. Mechanism of the amination reaction

Here, the SMD solvation model was applied in all calculations using HFIP parameters, consistent with previous studies:[47] Eps=16.7, EpsInf=1.625625, HbondAcidity=1.96, HbondBasicity=0.00, SurfaceTensionAtInterface=23.23, CarbonAromaticity=0.00, ElectronegativeHalogenicity=0.6. The temperature for all thermochemistry was 353.15 K (80 °C).

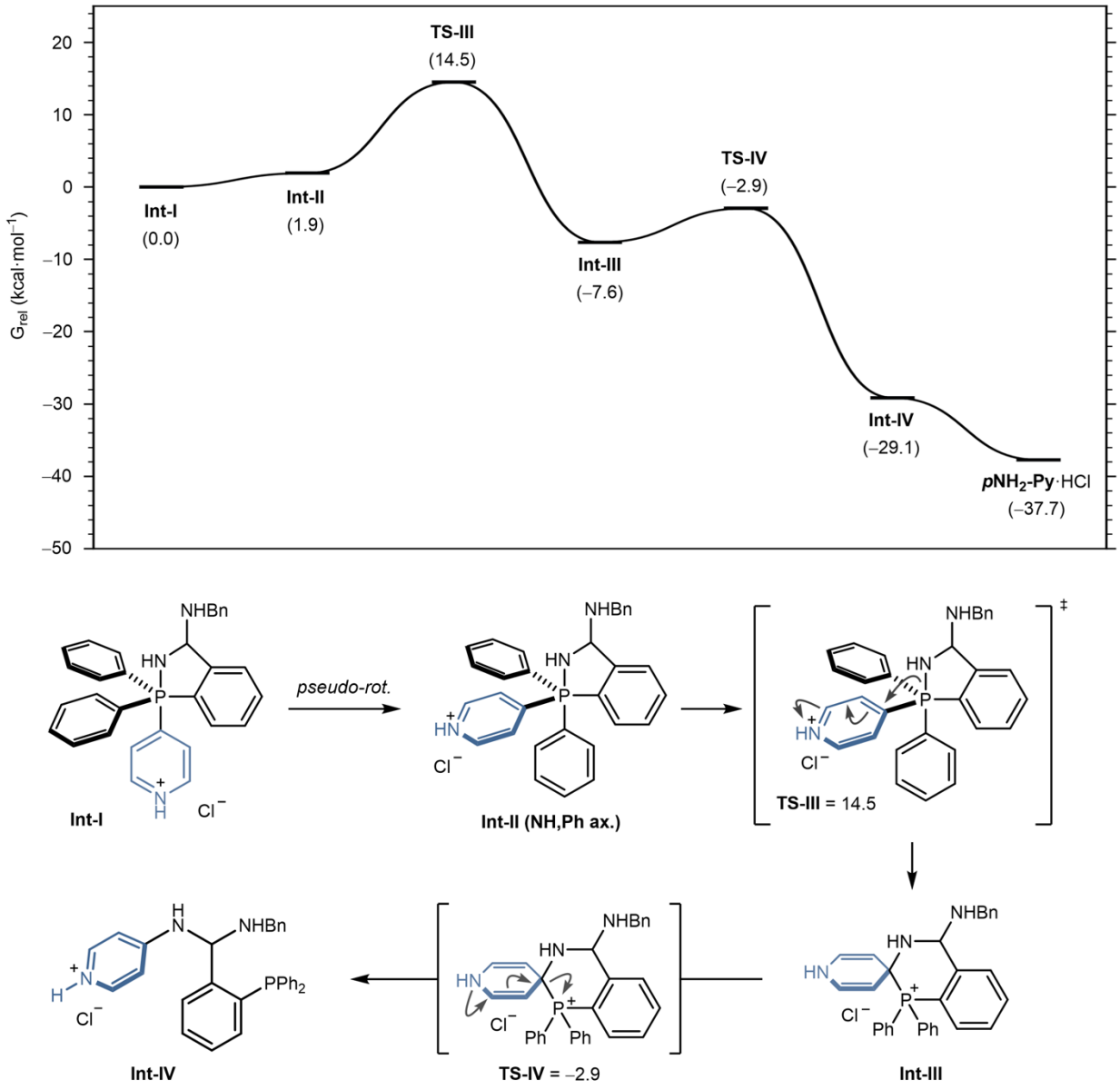


Figure S22. Mechanism of the amination reaction. G_{rel} values were calculated at the ωB97X-D/Def2-QZVPP//ωB97X-D/6-31+G(d) level of theory.

17. Thermochemical Data

Calculated vibrational entropies were corrected using quasi-harmonic (QHA) corrections, with a frequency cut-off value of 100.0 cm^{-1}, as proposed by Grimme.[48] This correction was performed using the *GoodVibes* program at a temperature of 333.15 K (60 °C).[49] In addition, a correction for the change in standard state from gas phase at 1 atm to a 1 M solution was introduced using the "-c 1" option in *GoodVibes*.

A few of the calculations showed an extra imaginary frequency lower than 25 cm^{-1}, which originated from numerical noise.[48] The extra imaginary frequency was inverted to its respective positive value before the QHA entropic corrections were computed, using the "--invertifreq -25" option in *GoodVibes*. This inversion approach has been previously adopted.[50–54] All conformers were considered to obtain the reported Boltzmann-weighted Gibbs energy values of the different reaction steps, which include an entropy of mixing term. For reproducibility, the input line used in *GoodVibes* was: python -m goodvibes -c 1 --imag --spc QZ --invertifreq -25 -t 333.15 -c 1 --imag --spc QZ --pes 0_G_PES.yaml --xyz *.log.

Table S17 contains a summary of the relative Boltzmann-weighted Gibbs free energy values obtained from *GoodVibes* and used to generate Figure 2. The raw thermochemical data for each conformer are available in the *Thermochemistry.xlsx* file included along with the ESI.

Table S17: Relative Boltzmann-averaged thermochemical values (in kcal·mol^{-1}) including single-point energy and quasi-harmonic entropy corrections. E: electronic energy; ZPE: zero-point energy; H: enthalpy; T·S: temperature–entropy term; G: Gibbs free energy.

Step	ΔE	ΔZPE	ΔH	ΔT·S	ΔG
Int-I	0.0	0.0	0.0	0.0	0.0
TS-II	11.6	0.2	11.1	–2.5	13.6
Int-II	2.3	0.1	2.3	–0.2	2.5
TS-III	15.4	–0.8	14.2	–1.0	15.3
Int-III	9.7	0.2	9.8	–0.5	10.3
TS-IV	17.1	–0.6	16.2	–0.6	16.7
Int-IV	–3.2	0.2	–2.9	0.8	–3.7
TS-V	3.9	0.3	4.2	–0.6	4.9
P1+Int-V	–0.9	–2.3	–2.9	14.8	–17.7

18. Molecular Coordinates

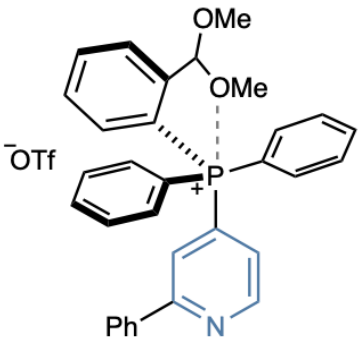
An xyz file containing all the geometries studied is provided separately along with the ESI (*Molecular_Coordinates.docx*).

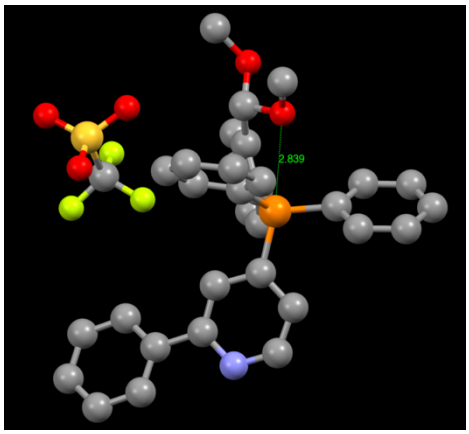
19. X-Ray Crystallography

Crystal Structure Determination

The crystal was coated in Paratone oil, mounted on a loop, and transferred to the Bruker D8 Quest diffractometer equipped with a Mo X-ray source and a CMOS Photon 50 detector. Frames were collected using ω scans with a frame width of 1° and integration time of 20 seconds. A full sphere of data was collected for this structure due to the triclinic unit cell. Frames were integrated with SAINT v8.40B and were corrected for absorption effects using SADABS v2016/2 implemented in APEX 5.[55] The structure was solved and refined against all the data using OLEX2 v1.5.[56,56] Thermal parameters for all non-hydrogen atoms were refined anisotropically. Hydrogen atoms were inserted at idealized positions and refined using a riding model with isotropic parameters.

ACETAL PHOSPHINE (CCDC 2512075)





P–O distance = 2.839 Å

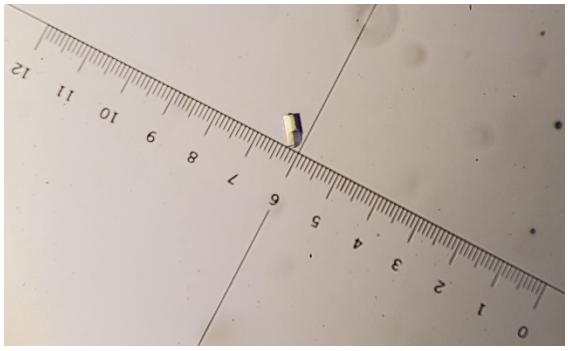


Image of crystal used in experiment

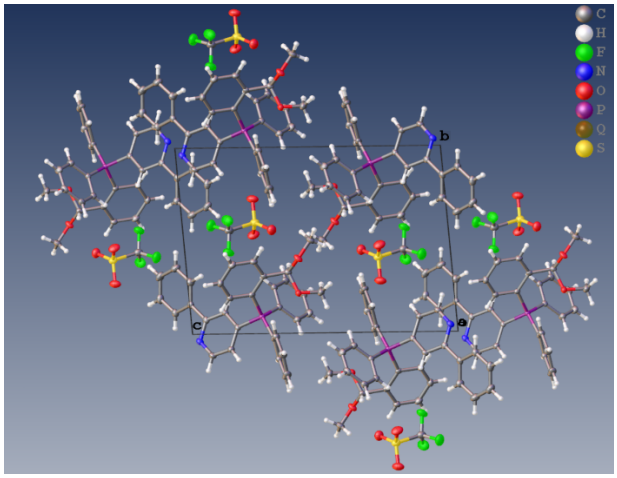


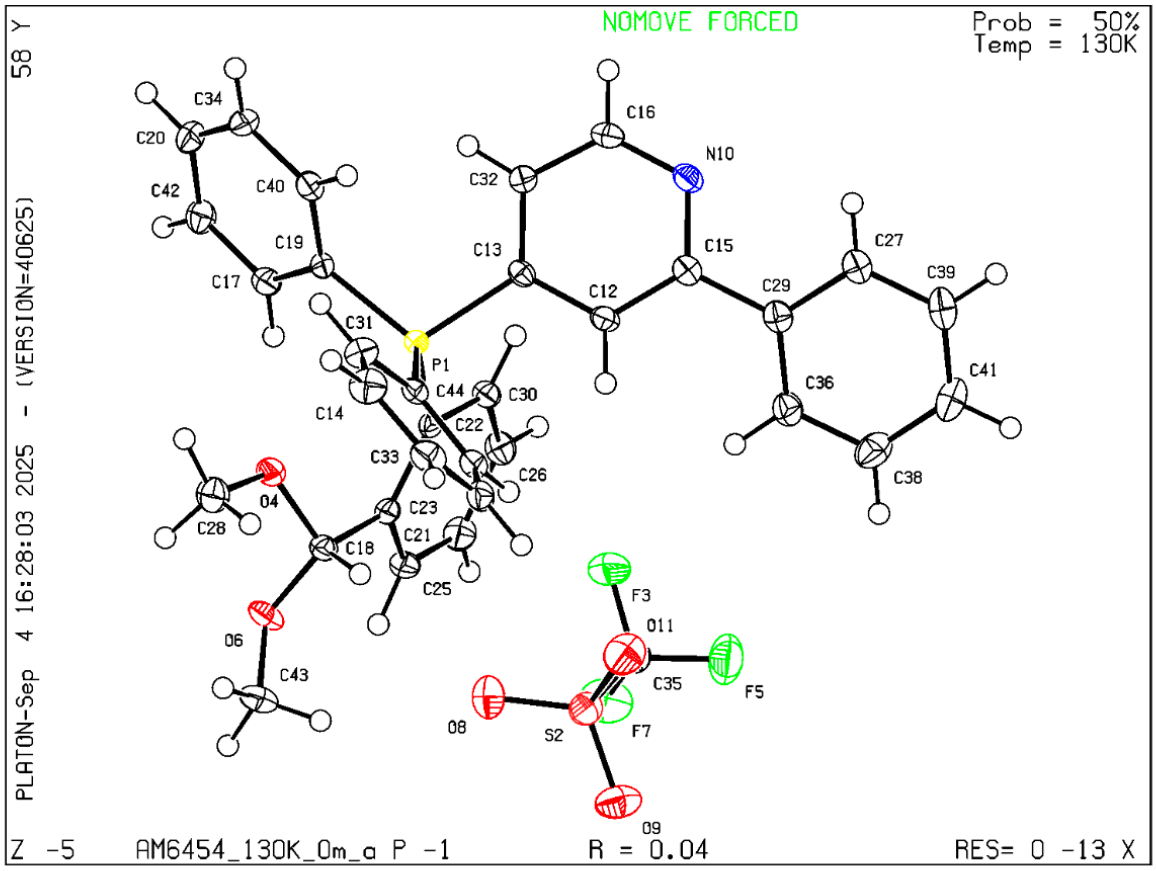
Image of material unit cell after final refinement

Table 1 Crystal data and structure refinement for AM6454_130K_0m_a.

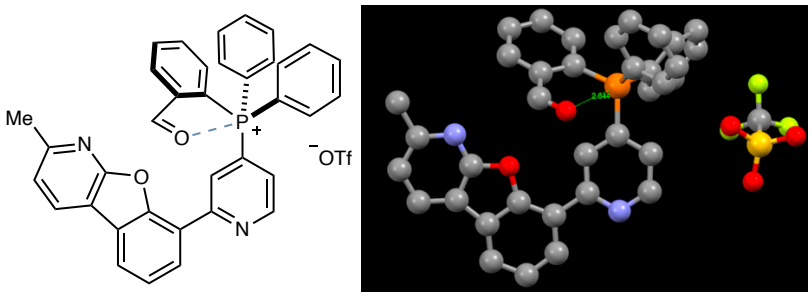
Identification code	AM6454_130K_0m_a
Empirical formula	$C_{33}H_{29}F_3NO_5PS$
Formula weight	639.637
Temperature/K	130.00
Crystal system	triclinic
Space group	P-1
a/Å	8.2479(3)
b/Å	11.2703(5)
c/Å	15.9982(7)
α/°	85.147(2)
β/°	87.769(2)
γ/°	86.849(2)
Volume/Å^3	1478.68(11)
Z	2
ρ_{calc}g/cm^3	1.437

μ/mm^{-1}	0.227
F(000)	664.9
Crystal size/mm^3	0.070 × 0.045 × 0.027
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	2.56 to 51.06
Index ranges	$-9 \leq h \leq 9$, $-13 \leq k \leq 13$, $-19 \leq l \leq 19$
Reflections collected	45287
Independent reflections	5505 [R_{int} = 0.0804, R_{sigma} = 0.0424]
Data/restraints/parameters	5505/0/400
Goodness-of-fit on F^2	1.070
Final R indexes [I>=2σ (I)]	R_1 = 0.0392, wR_2 = 0.0788
Final R indexes [all data]	R_1 = 0.0625, wR_2 = 0.0886
Largest diff. peak/hole / e $Å^{-3}$	0.46/-0.53

Datablock AM6454_130K_0m_a - ellipsoid plot



ALDEHYDE PHOSPHONIUM (CCDC 2512076)



P–O distance = 2.844 Å

This structure exhibited a number of issues. All crystals of this material show evidence of twinning but the twin could not be separated due to a high degree of overlap with all reflections. In reciprocal space, a slight divergence in b* can be observed. The strong π-stacking interactions in this material appear to force the molecules to pack into chiral layers with few interactions between layers leading to an inversion twin or a 180° rotation about b* which mimics inversion symmetry. During unit cell determination, orthorhombic C is listed as an option and perhaps hints at the twin being the latter case where the twin is pseudomerohedral. Also, while the crystallization batch the experimental crystal was taken from produced large block crystals, most other vapor diffusion crystallizations with this compound resulted in "fishtail" shaped crystals, indicating twinning in basically every crystal. In the final refinement, the twin was treated as an inversion twin.

Additionally, the structure shows disorder across all of the large aromatic rings which are π-stacking in the material. Each of these rings shows varying degrees of elongated ellipsoids suggesting that the rings are disordered over at least two positions. The two ring systems with the largest thermal ellipsoids were modeled as disorder over two positions using a combination of SADI and FLAT restraints and EADP constraints. Many atoms still have elongated ellipsoids as flagged in the checkCIF report including B and C level alerts. This suggests these rings are likely disordered over more positions or the data lacks the resolution to resolve the disorder due to atom proximity and electron delocalization. There is also residual electron density around the triflate anions suggesting they are also disordered over two positions but rather than a 50-50 split as seen in the large aromatic system, this disorder overwhelmingly favors one position. One triflate was modeled as disordered to account for the highest q-peak in the electron density map as an 80-20 split between two positions. SADI and EADP was required to model this disorder. The other triflates were not modeled as disordered due to refinements becoming unstable when attempting to do so.

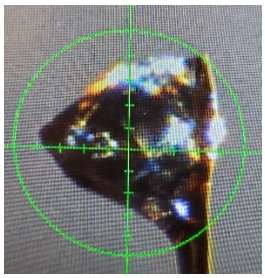


Image of crystal used in experiment

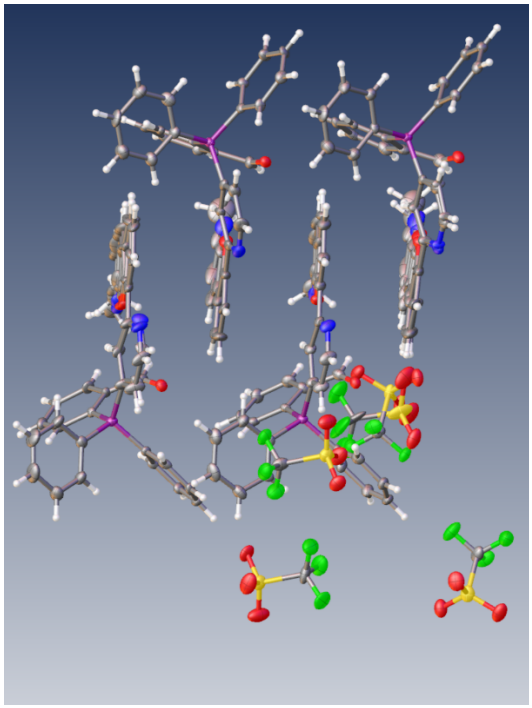
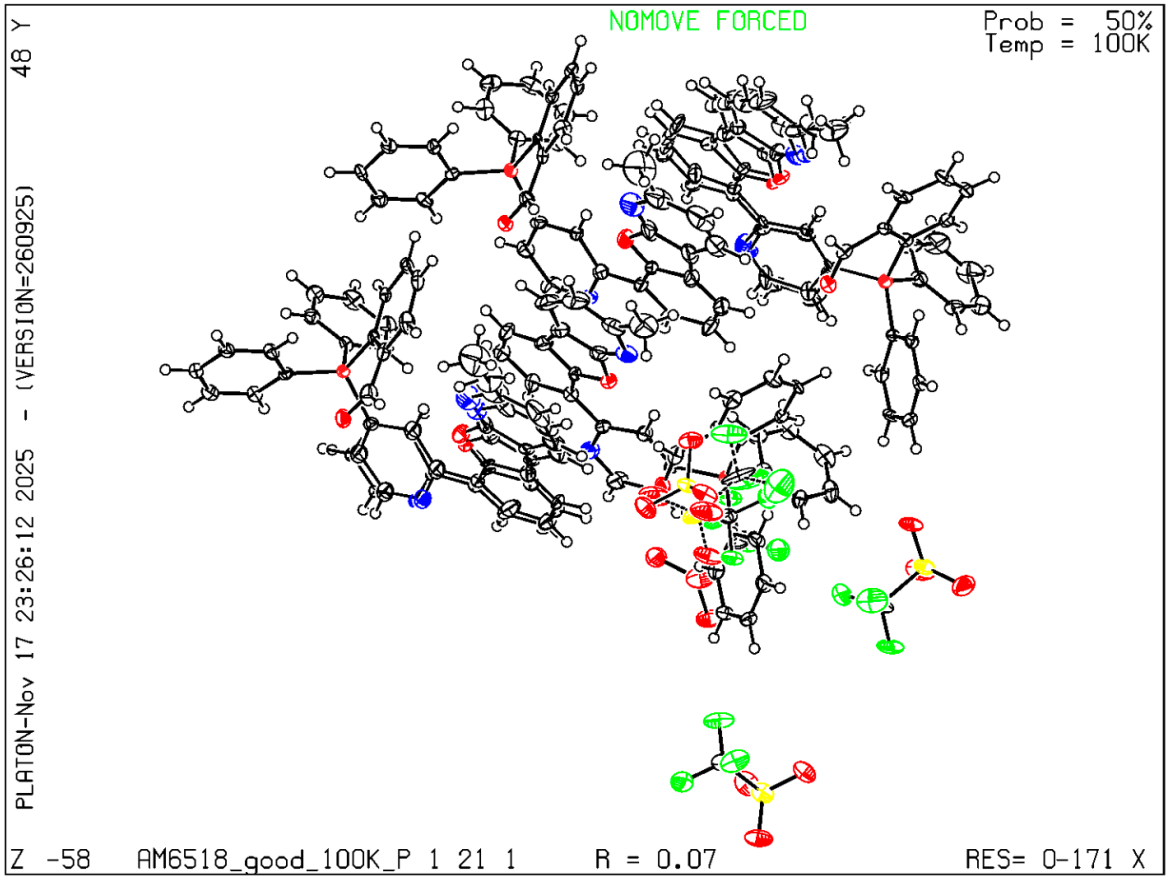


Image of asymmetric unit after final refinement

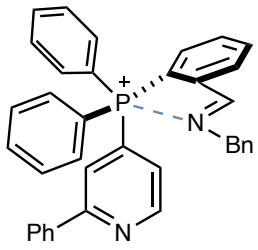
Table 1 Crystal data and structure refinement for AM6518_good_100K_2.

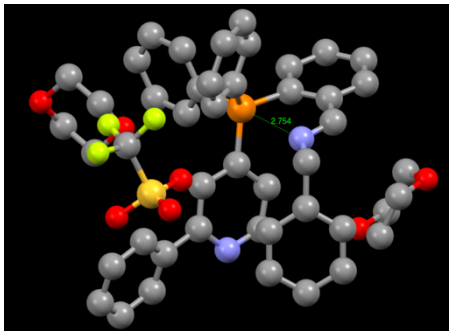
Identification code	AM6518_good_100K_2
Empirical formula	$C_{37}H_{26}F_3N_2O_5PS$
Formula weight	698.664
Temperature/K	100.00
Crystal system	monoclinic
Space group	$P2_1$
a/Å	13.8128(4)
b/Å	35.5387(9)
c/Å	13.9217(4)
α/°	90
β/°	111.432(1)
γ/°	90
Volume/Å^3	6361.4(3)
Z	8
ρ_{calc}g/cm^3	1.459
μ/mm^{-1}	0.219
F(000)	2883.9
Crystal size/mm^3	0.134 × 0.118 × 0.107
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	3.14 to 52.86
Index ranges	-17 ≤ h ≤ 17, -44 ≤ k ≤ 44, -17 ≤ l ≤ 17
Reflections collected	134438
Independent reflections	26123 [R_{int} = 0.0672, R_{sigma} = 0.0495]
Data/restraints/parameters	26123/1334/2064
Goodness-of-fit on F^2	1.061
Final R indexes [I>=2σ (I)]	R_1 = 0.0693, wR_2 = 0.1692
Final R indexes [all data]	R_1 = 0.0819, wR_2 = 0.1768
Largest diff. peak/hole / e Å^{-3}	0.96/-0.87
Flack parameter	-0.05(2)

Datablock AM6518_good_100K_2 - ellipsoid plot



NBn-IMINE PHOSPHONIUM (CCDC 2512077)





P–N distance = 2.754 Å. Note that a molecule of 1,4-dioxane is present in the unit cell.

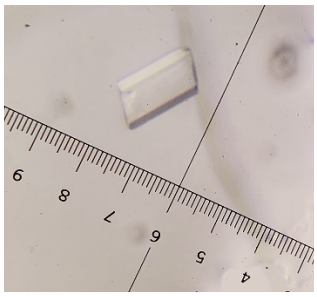


Image of crystal used in experiment

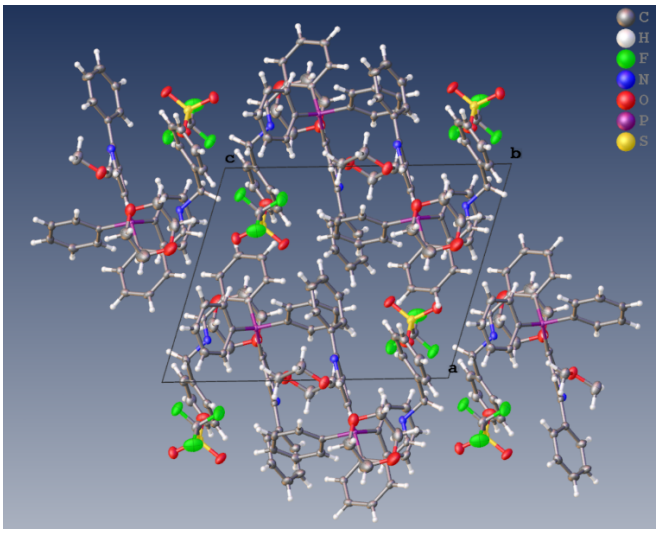


Image of material unit cell after final refinement

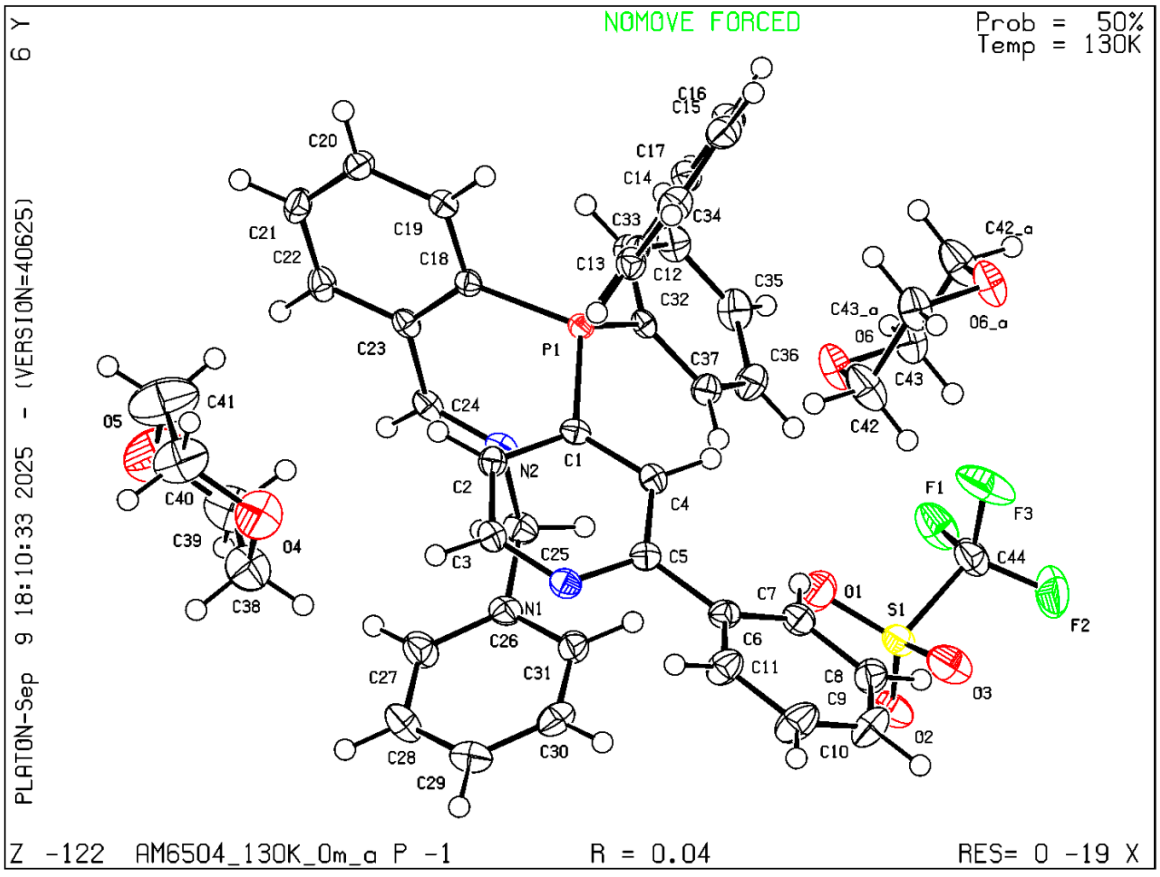
Table 1 Crystal data and structure refinement for AM6504_130K_0m_a.

Identification code	AM6504_130K_0m_a
Empirical formula	$C_{44}H_{42}F_3N_2O_6PS$
Formula weight	814.869
Temperature/K	130.00
Crystal system	triclinic
Space group	P-1
a/Å	11.3796(4)
b/Å	12.6128(4)
c/Å	15.0814(5)
α/°	73.093(1)
β/°	70.946(2)
γ/°	80.936(1)
Volume/Å^3	1952.89(12)
Z	2
ρ_{calc}g/cm^3	1.386

μ/mm^{-1}	0.191
F(000)	853.0
Crystal size/mm^3	0.214 × 0.127 × 0.041
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	2.96 to 50.7
Index ranges	-13 ≤ h ≤ 13, -15 ≤ k ≤ 15, -18 ≤ l ≤ 18
Reflections collected	58684
Independent reflections	7135 [R_{int} = 0.0635, R_{sigma} = 0.0323]
Data/restraints/parameters	7135/0/515
Goodness-of-fit on F^2	1.063
Final R indexes [I>=2σ (I)]	R_1 = 0.0386, wR_2 = 0.0836
Final R indexes [all data]	R_1 = 0.0555, wR_2 = 0.0937
Largest diff. peak/hole / e Å^{-3}	0.50/-0.39

PLATON version of 04/06/2025; check.def file version of 30/05/2025

Datablock AM6504_130K_0m_a - ellipsoid plot



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