
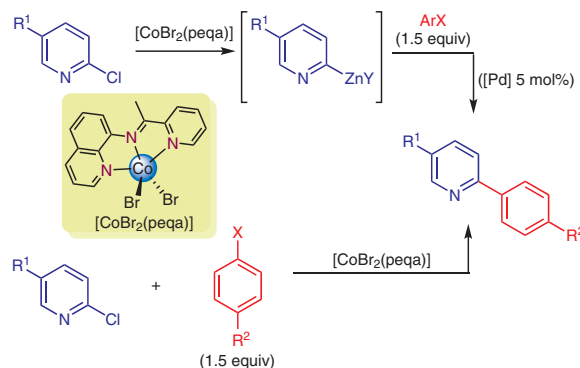


# Cobalt-Catalyzed Formation of 2-Pyridylzinc Reagents and Their Subsequent Coupling

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**Abstract** The preparation of pyridylzinc compounds from the corresponding pyridyl halides using a cobalt catalyst is described. The complex employed features a polydentate N-heterocyclic ligand and allows the reaction to be carried out in the absence of pyridine as co-solvent and also in THF in place of acetonitrile. First cross-coupling attempts are also presented. Satisfactory yields were obtained via a one-pot protocol without the addition of another catalyst.

**Key words** cobalt catalysis, N-heterocyclic ligand, zinc, cross-coupling, pyridines

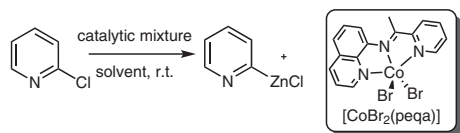
The pyridyl group is an important motif, which can be found in a variety of molecules ranging from pharmaceuticals<sup>1</sup> and natural products<sup>2</sup> to metal-complexing ligands<sup>3</sup> and photoactive materials.<sup>4</sup> Therefore, the synthesis of pyridyl organometallic reagents has been much investigated. However, the preparation of pyridylmetal compounds by direct deprotonative metalation resulted in numerous side reactions that can be circumvented by working at low temperatures with hindered lithium bases.<sup>5</sup> The use of additives, such as aminoalkoxides or metal salts forming bimetallic bases, offers other alternatives.<sup>5b,d</sup> Nevertheless, those pyridylmetal species are rather unstable. Since Suzuki–Miyaura coupling reactions allow an efficient introduction of heteroaryls,<sup>6</sup> the stabilization of pyridylboronates using *N*-methyliminodiacetic acid (MIDA), proposed by Burke and co-workers in 2012, represents an important progress.<sup>7</sup> However, at some point all these protocols involve lithium species, which impose some limitations in terms of functional group tolerance. In that sense, the development of 2-pyridylzinc halides is promising; they can be prepared under Rieke conditions.<sup>8</sup> Most interestingly, Buchwald, Knöchel and co-workers reported the synthesis of solid 2-pyr-

idylzinc reagents which presents moderate air-stability.<sup>9</sup> Some years ago, we developed a convenient cobalt-catalyzed methodology to prepare organozinc reagents that does not require an inert atmosphere and distilled solvents.<sup>10</sup> However, it does not work with pyridyl halides; therefore, we were interested in extending the methodology to such motifs. This is the subject of the current paper which presents an easy preparation of pyridylzinc reagents, thanks to cobalt catalysis, and our first attempts to further couple these reagents with aryl halides. In the course of these investigations, we developed an unprecedented cobalt(II) complex featuring an *N*-(1-(pyridin-2-yl)ethylidene)quinolin-8-amine ligand, which proved very useful.

To prepare 2-pyridylzinc halides from 2-pyridyl halides by a cobalt-catalyzed procedure, we decided to use the catalytic conditions which were effective with aryl and thienyl chlorides to start the optimization study; however, a poor yield was obtained (Table 1, entry 1).<sup>10b</sup> Better results were obtained when associating CoBr<sub>2</sub> salt and zinc dibromide; the 2-pyridylzinc derivative was formed in 61% yield after 24 hours (Table 1, entry 2). Adding more cobalt (20 mol%) during the course of the reaction increased the proportion of side products, leading to a lower yield of the 2-pyridylzinc halide (Table 1, entry 3). Cobalt complexes featuring nitrogen-based ligands were then used; preformed [CoBr<sub>2</sub>(phen)] afforded 66% of zinc compound (Table 1, entry 4) which is quite similar to the yield obtained with only CoBr<sub>2</sub>. Reaction with [CoBr<sub>2</sub>(bipy)(CH<sub>3</sub>CN)<sub>2</sub>] was more efficient, since an 84% yield was obtained (Table 1, entry 5). Finally, two bidentate phosphine ligands were tested; the reactions were conducted by adding cobalt salt and the free ligand. The outcome of these reactions highly depends on the carbon linker between the phosphorus atoms: with 1,3-bis(diphenylphosphino)propane (dppp) the zinc compound was formed in 42% yield (Table 1, entry 6) compared to 86% with 1,2-bis(diphenylphosphino)ethane (dppe) (Table 1, entry

7). As the results of entries 5 and 7 were similar, we compared the cost of the ligands. The phosphorus ligand is approximately five times more expensive than the bipyridine; thus, we decided to continue with the latter, and the use of preformed complex can also be considered as an advantage. With these reaction conditions in hand, we were interested in reducing the amount of pyridine, replacing it or even suppressing it, as we thought that a ligand should be sufficient to stabilize the formed cobalt intermediates. However, no reaction was observed when suppressing pyridine or substituting it by bipyridine, triethylamine, quinoline or isoquinoline. When the quantity of pyridine was decreased from 4, to 1, and 0.5 mL, the GC yield of the zinc derivative after 5 hours was 68%, 74% and 61%, respectively. With 0.25 mL of pyridine, no organozinc compound was detected.

**Table 1** Optimization of the Catalytic System



catalytic mixture: Co cat. (13 mol%), Zn (3.3 equiv), ZnBr<sub>2</sub> (0.13 equiv), allyl chloride (0.3 equiv), CF<sub>3</sub>CO<sub>2</sub>H (traces)

Entry	Cobalt catalyst	Solvent	Yield (%) of ArZnX <sup>a</sup>
1	CoBr <sub>2</sub> <sup>b</sup>	CH <sub>3</sub> CN/py	5
2	CoBr <sub>2</sub>	CH <sub>3</sub> CN/py	61
3	CoBr <sub>2</sub> + CoBr <sub>2</sub>	CH <sub>3</sub> CN/py	40 <sup>c</sup>
4	[CoBr <sub>2</sub> (phen)]	CH <sub>3</sub> CN/py	66
5	[CoBr <sub>2</sub> (bipy)(CH <sub>3</sub> CN) <sub>2</sub> ]	CH <sub>3</sub> CN/py	84
6	CoBr <sub>2</sub> + dppp	CH <sub>3</sub> CN/py	42
7	CoBr <sub>2</sub> + dppe	CH <sub>3</sub> CN/py	86
8	[CoBr <sub>2</sub> (peqa)]	CH <sub>3</sub> CN/py	88 <sup>d</sup>
9	[CoBr <sub>2</sub> (peqa)]	CH <sub>3</sub> CN	88 <sup>e</sup>
10	[CoBr <sub>2</sub> (peqa)] <sup>f</sup>	CH <sub>3</sub> CN	74
11	[CoBr <sub>2</sub> (peqa)] <sup>g</sup>	CH <sub>3</sub> CN	42
12	[CoBr <sub>2</sub> (peqa)] <sup>f,g</sup>	CH <sub>3</sub> CN	76
13	[CoBr <sub>2</sub> (peqa)] <sup>f,g</sup>	THF	74

<sup>a</sup> GC yield (%) determined after iodolysis after 24 h, using *n*-dodecane or decane as internal reference.

<sup>b</sup> Reaction conducted without ZnBr<sub>2</sub>.

<sup>c</sup> Reaction was stopped after 5 h (no more starting material).

<sup>d</sup> Reaction was stopped after 8 h (no more starting material).

<sup>e</sup> Reaction was stopped after 20 h (no more starting material).

<sup>f</sup> At 50 °C.

<sup>g</sup> With 5 mol% catalyst.

As many equivalents of pyridine relative to the cobalt center were necessary to ensure an efficient catalysis, we thought to develop a polydentate ligand incorporating N-heterocyclic donors. To maintain a good balance between activity and stability, we focused on tridentate ligands and were interested in incorporating a quinoline motif which

was demonstrated to have an accelerating effect in cobalt- and iron-catalyzed cross-coupling reactions.<sup>11</sup> Inspired by the work of W.-H. Sun and co-workers with nickel,<sup>12</sup> we synthesized a cobalt(II) complex featuring an *N*-(1-(pyridin-2-yl)ethylidene)quinolin-8-amine ligand (abbreviated as peqa). The synthesis was realized as reported for nickel, by refluxing 8-aminoquinoline, 2-acetylpyridine and CoBr<sub>2</sub> in acetic acid. The highly insoluble complex was isolated in 88% yield. Unfortunately, all our crystallization attempts failed, precluding a structural determination by X-ray analysis. Nevertheless, a satisfying elemental analysis was obtained, and the magnetic moment in solution was measured as 3.9(1) μ<sub>B</sub> by the Evans method,<sup>13</sup> in agreement with a high spin complex (*S* = 3/2) for which we propose the structure depicted in Table 1.

With [CoBr<sub>2</sub>(peqa)] under the previously determined conditions, the 2-pyridylzinc derivative was formed in 88% yield (Table 1, entry 8). When the same reaction was performed in the absence of pyridine, this catalyst was able to generate the zinc compound as efficiently after 20 hours (Table 1, entry 9). Thus, our interest in this tridentate ligand was well-founded. In an attempt to decrease the reaction time, the reaction medium was heated at 50 °C, but the yield was lower (Table 1, entry 10). To further test the ability of [CoBr<sub>2</sub>(peqa)], reactions were conducted at a lower catalyst loading. With 5 mol% cobalt catalyst, the organozinc compound was formed in only 42% yield (Table 1, entry 11), but increasing the temperature to 50 °C resulted in an increased 76% yield (Table 1, entry 12). Finally, reasoning that acetonitrile may not be necessary to stabilize cobalt intermediates with this ligand, we attempted the reaction in THF and were pleased to observe the formation of the organozinc compound in 74% yield at 50 °C (Table 1, entry 13). This nicely illustrates that the use of an appropriate ligand for the cobalt center allows the employment of a less-coordinating solvent such as THF. This is the first time that we have been able to form the organozinc compound in this solvent via a cobalt-catalyzed procedure.

With these conditions in hand, we explored the scope of this cobalt-catalyzed methodology (Table 2). From 2-bromopyridine, the organozinc species formed in 80% yield at 50 °C. At this temperature, the metalation is almost as efficient in THF (73% yield) (Table 2, entry 1). For 3-bromopyridine, the reaction worked well in both solvents (Table 2, entry 2). On the contrary, for 2-fluoropyridine only the metalation in acetonitrile was satisfactory (Table 2, entry 3). The formation of the 2-pyridylzinc species from the corresponding fluoride seems rather unusual, although some cobalt-catalyzed biaryl couplings through C–F cleavage have been described.<sup>14</sup>

For some other halides, surprisingly, the reaction worked better in THF, with the organozinc derivative formed in 84% yield for 2-chloro-3-cyanopyridine (Table 2, entry 6). For 2-chloro-6-cyanopyridine, there was almost no solvent effect (Table 2, entries 7 and 8).

**Table 2** Catalytic Reactions with 5 mol% [CoBr<sub>2</sub>(peqa)]<sup>a</sup>

Entry	Substrate	Yield (%) of ArZnX <sup>b</sup>	
		In CH <sub>3</sub> CN <sup>c</sup>	In THF <sup>c</sup>
1	2-bromopyridine	80	73
2	3-bromopyridine	90	86
3	2-fluoropyridine	81	39
4	2-chloro-5-(trifluoromethyl)pyridine	42 <sup>d</sup>	70 <sup>d</sup>
5	2-chloro-5-nitropyridine	70	65
6	2-chloro-3-cyanopyridine	60	84
7	2-chloro-6-cyanopyridine	80	84

<sup>a</sup> Reaction conducted in the presence of Zn (3.3 equiv), ZnBr<sub>2</sub> (0.13 equiv), allyl chloride (0.3 equiv) and CF<sub>3</sub>CO<sub>2</sub>H (traces).

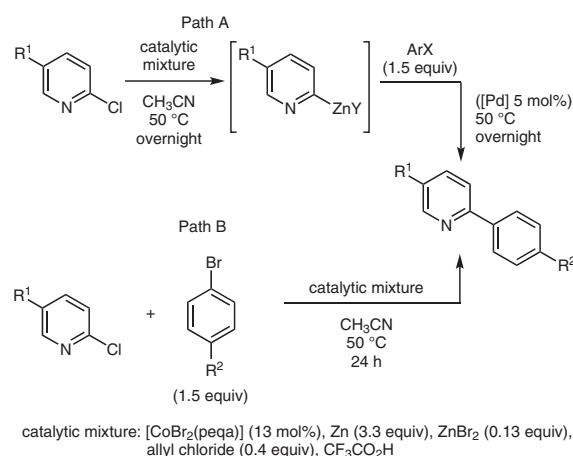
<sup>b</sup> GC yield (%) determined after iodolysis, using *n*-dodecane or decane as internal reference.

<sup>c</sup> Performed at 50 °C.

<sup>d</sup> Performed at 60 °C.

Even though interesting to establish that the organozinc halides can form quite efficiently with 5 mol% catalyst, when examining the possibility of further coupling with another aryl halide, we decided to use 13 mol% cobalt catalyst. Indeed, when the zincation was performed in pure acetonitrile at room temperature, full conversion into the organozinc compound (70–80% GC yield) was observed, starting from 2-chloro-5-(trifluoromethyl)pyridine or 2-chloropyridine. Thus, these were chosen as substrates to evaluate the following coupling reactions, with the results gathered in Table 3.

For the first attempts, the 2-pyridylzinc compound was formed in a first step, then the coupling partner (*p*-bromoanisole) was added without any additional catalyst and the reaction mixture was heated at 50 °C for 8 hours; the corresponding coupling product was isolated in 48% yield (Table 3, entry 1). The introduction of a palladium catalyst (5 mol%) to perform a classical Negishi reaction gave slightly better yields: 58% and 56% using [Pd(dppf)Cl<sub>2</sub>] and [Pd(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub>], respectively (Table 3, entries 2 and 3). The use of a chromium catalyst<sup>15</sup> was disappointing; no product could be detected when adding [Cr(acac)<sub>3</sub>] (5 mol%), whereas CrCl<sub>2</sub> (5 mol%) only led to 4% product. Starting from 2-chloropyridine, via the intermediate formation of the corresponding zinc species, 65% yield was obtained (Table 3, entry 5). Having observed that the filtration of the reaction mixture before the eventual addition of a second catalyst almost inhibits the coupling reaction, we wondered if the zincation and the coupling reaction could be conducted in the same pot without any additional catalyst, as previously reported by us when using a nickel catalyst.<sup>16</sup>

**Table 3** Coupling Reactions

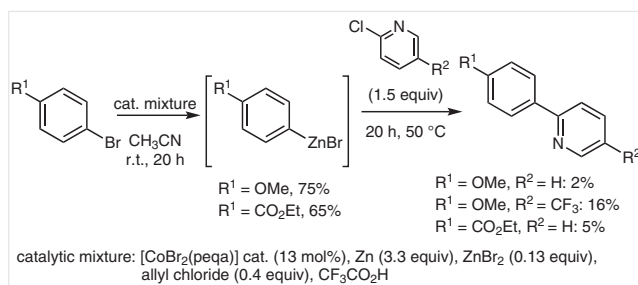
Entry	R <sup>1</sup>	R <sup>2</sup>	Path	Catalyst 2	Yield (%) <sup>a</sup>
1	CF <sub>3</sub>	OMe	A	–	48
2	CF <sub>3</sub>	OMe	A	Pd(dppf)Cl <sub>2</sub> (5 mol%)	58
3	CF <sub>3</sub>	OMe	A	Pd(PPh <sub>3</sub> ) <sub>2</sub> Cl <sub>2</sub> (5 mol%)	56
4	CF <sub>3</sub>	OMe	A	CrCl <sub>2</sub> (5 mol%)	4
5	H	OMe	A	Pd(PPh <sub>3</sub> ) <sub>2</sub> Cl <sub>2</sub> (5 mol%)	65
6	CF <sub>3</sub>	OMe	B	–	66 <sup>b</sup>
7	CF <sub>3</sub>	SMe	B	–	62
8	CF <sub>3</sub>	Me	B	–	46
9	CF <sub>3</sub>	CO <sub>2</sub> Et	B	–	41
10	H	OMe	B	–	31

<sup>a</sup> Isolated yield.

<sup>b</sup> 4% yield (GC yield, using *n*-dodecane or decane as reference) when the reaction was conducted in CH<sub>3</sub>CN/pyridine (6:1).

Thus, heating 2-chloro-5-(trifluoromethyl)pyridine and *p*-bromoanisole in the presence of the cobalt catalytic system at 50 °C in acetonitrile (path B) gave the coupling product in 66% yield after 24 hours (Table 3, entry 6). Adding pyridine (CH<sub>3</sub>CN/pyridine, 6:1) nearly annihilated the catalytic ability, since only 4% product was observed by GC analysis. A comparable coupling yield was obtained with 4-bromothioanisole (Table 3, entry 7). Use of aryl bromides with less electron-rich substituents led to lower yield: the coupling yield decreased to 46% and 41% when using *p*-bromotoluene and ethyl 4-bromobenzoate, respectively (Table 3, entries 8, 9). Starting from 2-chloropyridine, the coupling product with *p*-bromoanisole was isolated in 31% yield (Table 3, entry 10).

To prove that these one-pot reactions do involve the formation of a pyridylzinc compound, we tested the reverse reaction, namely that involving the coupling of arylzinc derivatives formed under cobalt catalysis with chloropyridines (Scheme 1).



**Scheme 1** Coupling of arylzinc compounds with pyridyl chlorides

With  $[\text{CoBr}_2(\text{peqa})]$ , the arylzinc derivatives are formed in a satisfactory yield from *p*-bromoanisole and *p*-bromobenzoate (Scheme 1). These yields are lower than those obtained with  $\text{CoBr}_2$  salt.<sup>10a</sup> Nevertheless, the addition of chloropyridine, followed by heating at 50 °C, only led to traces of coupling product. The best result was obtained with 4-methoxyphenylzinc bromide and 2-chloro-5-(trifluoromethyl)pyridine, yielding 16% of coupling product. Therefore, the observed 66% yield obtained with the one-pot methodology (path B; Table 3, entry 6) previously discussed should involve a pyridylzinc adduct.

In conclusion, we have developed an efficient cobalt methodology for the preparation of pyridylzinc compounds. Interestingly, only  $[\text{CoBr}_2(\text{peqa})]$  allows the reaction to be conducted without pyridine. Quite without precedent, the reaction with this catalyst allowed the zincation in THF with a comparable efficiency. First attempts for subsequent coupling with aryl bromides led to average to good yields (31–66% for 2 steps). Best results with two steps were obtained with an additional palladium catalyst. Nevertheless, in one case, the one-pot cobalt-catalyzed procedure exhibited a similar better performance. This first study shows that cobalt catalysts featuring a polydentate N-heterocyclic ligand may offer an interesting alternative. Ligand tuning would be necessary to improve the coupling efficiency. Developing bidentate ligands may be an option to facilitate the interaction between substrates and catalyst.

#### $[\text{CoBr}_2(\text{peqa})]$

8-Aminoquinoline (1.8 g, 12.5 mmol), 2-acetylpyridine (1.40 mL, 12.5 mmol) and  $\text{CoBr}_2$  (2.72 g, 12.5 mmol) were refluxed at 130 °C in 0.21 M AcOH (60 mL) for 5 h. After cooling to r.t., the suspension was filtered and the obtained black solid was washed with  $\text{Et}_2\text{O}$  ( $3 \times 50$  mL). This solid was dissolved in hot EtOH (100 mL). The solution was concentrated in vacuo (to roughly half-volume) and  $\text{Et}_2\text{O}$  (80 mL) was added to induce precipitation. The obtained solid was washed with  $\text{Et}_2\text{O}$  ( $3 \times 20$  mL) and dried in vacuo to give  $[\text{CoBr}_2(\text{peqa})]$ ; yield: 5.05 g (88%).

Mp 128.9 °C;  $\mu = 3.9(1) \mu_{\text{B}}$ .

Anal. Calcd for  $\text{C}_{16}\text{H}_{13}\text{Br}_2\text{CoN}_3$ : C, 41.24; H, 2.81; N, 9.02. Found: C, 41.35; H, 2.77; N, 8.95.

#### Preparation of the Arylzinc Reagents, Followed by Cross-Coupling with Aryl Halides; General Procedure 1

##### Arylzinc Reagents

An oven-dried flask was equipped with a stirring bar and closed with a septum. Zinc dust (1.08 g, 16.5 mmol, 3.33 equiv),  $\text{ZnBr}_2$  (146 mg, 0.65 mmol, 0.13 equiv) and  $\text{Co(II)}$  catalyst were added and stirred in  $\text{CH}_3\text{CN}$  (4 mL). TFA (0.1 mL, 1.3 mmol, 0.26 equiv) and allyl chloride (0.17 mL, 2.05 mmol, 0.4 equiv) were added subsequently which caused a rise in temperature and gas evolution. Pyridine was added if necessary. Once the mixture again reached r.t., the aryl halide (5.0 mmol) was added and the reaction mixture was stirred at the indicated temperature 50 °C until iodolyzed aliquots showed full conversion of the starting material (GC analysis). The yield was determined by addition of an internal standard (*n*-decane or *n*-dodecane, 100  $\mu\text{L}$ ).

##### Cross-Coupling with Aryl Halides

The crude arylzinc reagent was used unless indicated otherwise (in these cases, the reagent was filtered using a syringe filter and/or additives were added). The corresponding aryl halide 1.5 equiv was added neat and the reaction mixture was stirred at the indicated temperature 50 °C until iodolyzed aliquots showed full conversion of the arylzinc reagent (GC analysis). The reaction was quenched by addition of saturated aqueous  $\text{NH}_4\text{Cl}$  solution (20 mL) which was followed by extraction with DCM ( $3 \times 50$  mL). The combined organic layers were dried over  $\text{MgSO}_4$  and, after filtration, the solvents were evaporated in vacuo. Purification by flash column chromatography furnished the desired biaryls.

##### One-Pot Synthesis of Biaryls; General Procedure 2 (GP2)

An oven-dried flask was equipped with a stirring bar and closed with a septum. Zinc dust (1.08 g, 16.5 mmol, 3.33 equiv),  $\text{ZnBr}_2$  (146 mg, 0.65 mmol, 0.13 equiv) and  $\text{Co(II)}$  catalyst were added and stirred in  $\text{CH}_3\text{CN}$  (4 mL). TFA (0.1 mL, 1.3 mmol, 0.26 equiv) and allyl chloride (0.17 mL, 2.05 mmol, 0.4 equiv) were added subsequently which caused a rise in temperature and gas evolution. Pyridine was added if necessary. Once the mixture again reached r.t., the two aryl halides were added and the reaction mixture was stirred at the indicated temperature 50 °C until iodolyzed aliquots showed full conversion of the starting material (GC analysis). The reaction was quenched by addition of saturated aqueous  $\text{NH}_4\text{Cl}$  solution (20 mL) which was followed by extraction with DCM ( $3 \times 50$  mL). The combined organic layers were dried over  $\text{MgSO}_4$  and, after filtration, the solvents were evaporated in vacuo. Purification by flash column chromatography furnished the desired biaryls.

##### 2-(4-Methoxyphenyl)pyridine (Table 3, Entry 10)<sup>16</sup>

According to GP 2 using 2-chloropyridine (0.47 mL, 5.0 mmol) and 4-bromoanisole (0.94 mL, 7.5 mmol). Flash column chromatography (silica gel; petroleum ether/ $\text{Et}_2\text{O}$ , 4:1) afforded the desired product; yield: 287 mg (1.55 mmol, 31%).

$^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ ):  $\delta = 8.67$  (d,  $J = 4.7$  Hz, 1H), 7.98 (d,  $J = 8.9$  Hz, 2H), 7.74–7.63 (m, 2H), 7.16 (ddd,  $J = 6.7, 4.8, 1.5$  Hz, 1H), 7.01 (d,  $J = 9.0$  Hz, 2H), 3.85 (s, 3H).

$^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ ):  $\delta = 160.60, 157.20, 149.59, 136.80, 132.08, 128.28, 121.51, 119.92, 114.25, 55.46$ .

HRMS:  $m/z$  calcd for  $\text{C}_{12}\text{H}_{11}\text{NO}$ : 185.0841; found: 185.0834.

**2-(4-Methoxyphenyl)-5-(trifluoromethyl)pyridine (Table 3, Entry 6)<sup>16</sup>**

According to GP 2 using 2-chloro-5-(trifluoromethyl)pyridine (0.64 mL, 5.0 mmol) and 4-bromoanisole (0.94 mL, 7.5 mmol). Flash column chromatography (silica gel; petroleum ether/DCM, 2:1) afforded the desired product; yield: 822 mg (3.25 mmol, 66%).

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ = 8.89 (s, 1 H), 8.00 (d, *J* = 8.8 Hz, 2 H), 7.92 (d, *J* = 8.2 Hz, 1 H), 7.76 (d, *J* = 8.4 Hz, 1 H), 7.02 (d, *J* = 8.6 Hz, 2 H), 3.87 (s, 3 H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ = 161.50, 160.38, 146.62 (q, *J* = 4.0 Hz), 133.93 (q, *J* = 3.5 Hz), 130.62, 128.82, 124.18 (q, *J* = 33 Hz), 124.02 (q, *J* = 270 Hz), 119.18, 114.50, 55.55.

HRMS: *m/z* calcd for C<sub>13</sub>H<sub>10</sub>F<sub>3</sub>NO: 253.0714; found: 253.0724.

**2-(4-(Methylthio)phenyl)-5-(trifluoromethyl)pyridine (Table 3, Entry 7)<sup>17</sup>**

According to GP 2 using 2-chloro-5-(trifluoromethyl)pyridine (0.64 mL, 5.0 mmol) and 4-bromothioanisole (1.52 g, 7.5 mmol). Flash column chromatography (silica gel; pentane/DCM, 4:1) afforded the desired product; yield: 874 mg (3.24 mmol, 62%).

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ = 8.91 (s, 1 H), 8.02–7.90 (m, 3 H), 7.80 (d, *J* = 8.4 Hz, 1 H), 7.35 (d, *J* = 8.6 Hz, 2 H), 2.54 (s, 3 H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ = 160.12, 146.72 (q, *J* = 4.0 Hz), 141.74, 134.49, 134.01 (q, *J* = 3.5 Hz), 127.63, 126.34, 124.68 (q, *J* = 33 Hz), 123.91 (q, *J* = 270 Hz), 119.47, 15.43.

HRMS: *m/z* calcd for C<sub>13</sub>H<sub>10</sub>F<sub>3</sub>NS: 269.0486; found: 269.0482.

**2-(*p*-Tolyl)-5-(trifluoromethyl)pyridine (Table 3, Entry 8)<sup>18</sup>**

According to GP 2 using 2-chloro-5-(trifluoromethyl)pyridine (0.64 mL, 5 mmol) and *p*-bromotoluene (0.46 mL, 3.75 mmol). Flash column chromatography (SiO<sub>2</sub>, pentane : Et<sub>2</sub>O = 20:1) afforded the desired product: 255 mg (1.16 mmol; 46%) overall yield.

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ = 8.92 (s, 1 H), 8.01–7.89 (m, 3 H), 7.82 (d, *J* = 8.4 Hz, 1 H), 7.32 (d, *J* = 8.0 Hz, 2 H), 2.43 (s, 3 H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ = 160.80, 146.67 (q, *J* = 4.0 Hz), 140.45, 135.31, 134.45 (q, *J* = 3.5 Hz), 129.83, 127.28, 124.62 (q, *J* = 32 Hz), 123.69 (q, *J* = 270 Hz), 119.69, 21.46.

**Ethyl 4-(5-(Trifluoromethyl)pyridin-2-yl)benzoate (Table 3, Entry 9)<sup>16</sup>**

According to GP 2 using 2-chloro-5-(trifluoromethyl)pyridine (0.64 mL, 5.0 mmol) and ethyl 4-bromobenzoate (1.22 mL, 7.5 mmol). Flash column chromatography (silica gel; pentane/DCM, 4:1) afforded the desired product; yield: 604 mg (2.05 mmol, 41%).

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ = 8.98 (s, 1 H), 8.31–8.07 (m, 4 H), 8.02 (d, *J* = 9.0 Hz, 1 H), 7.90 (d, *J* = 8.2 Hz, 1 H), 4.42 (q, *J* = 7.1 Hz, 2 H), 1.43 (t, *J* = 7.1 Hz, 3 H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ = 166.28, 159.61, 146.91 (q, *J* = 4.0 Hz), 141.92, 134.22 (q, *J* = 3.5 Hz), 131.89, 130.27, 127.31, 125.65 (q, *J* = 33 Hz), 123.74 (q, *J* = 270 Hz), 120.54, 61.35, 14.46.

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