

# A Simple Route to $\beta$ -Ferrocenylpyridine Derivatives†

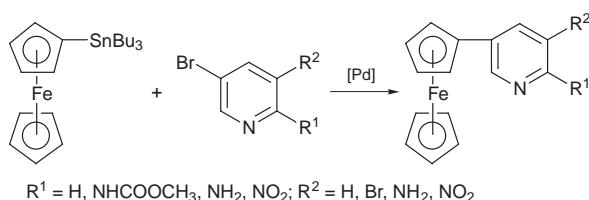
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A convenient method for the synthesis of  $\beta$ -ferrocenylpyridine derivatives, using [Pd]-catalyzed Stille cross-coupling reaction, is described.

Although many pyridine or polypyridine compounds containing the ferrocene nucleus have been synthesized,<sup>1</sup> examples of ferrocenyl directly bonded to the  $\beta$ -position of a pyridine ring are still scarce. Only Schlog and co-workers,<sup>2</sup> in 1963, have reported a synthesis of  $\beta$ -ferrocenylpyridine, via the Gomberg–Bachmann–Hey reaction of ferrocene with [3-NC<sub>5</sub>H<sub>4</sub>-N<sub>2</sub>]Cl in glacial acetic acid, but the yield was only 27%.

As an extension of our previous work,<sup>3</sup> we performed the Stille cross-coupling of tri-*n*-butylstannylderrocene (Fc-SnBu<sub>3</sub>) and a variety of  $\beta$ -bromosubstituted pyridine compounds under Pd-catalysis in DMF at 120–130 °C, and synthesized a series of  $\beta$ -ferrocenylpyridine compounds in satisfactory yield, as indicated in Scheme 1.



Scheme 1

Fc-SnBu<sub>3</sub>, and various  $\beta$ -bromopyridine compounds were prepared according to literature procedures.<sup>4,5</sup> The results were summarized in the Table 1.

tributylstannylderrocene (0.5 mmol) was added in one portion at 100 °C, the resultant mixture was heated and kept at 120–130 °C for 2 h. When the Fc-SnBu<sub>3</sub> had been consumed (according to a TLC test) the mixture was cooled to room temperature, 8 ml water was added, extracted with diethyl ether, washed with saturated KF solution and finally dried over anhydrous MgSO<sub>4</sub>. After the solvent was removed, the residue was chromatographed on silica gel (eluent: light petroleum/acetone) to give products. Spectroscopic data of **3a**:  $\delta_{\text{H}}$  4.07 (s, 5H), 4.38 (m, 2H), 4.68 (m, 2H), 7.18 (m, 1H), 7.73 (m, 1H), 8.44 (m, 1H), 8.75 (d, 1H);  $\nu/\text{cm}^{-1}$ , 3060, 1591, 1496, 1100, 1000, 496; MS  $m/z$  263 (M<sup>+</sup>, 100%). **3c**:  $\delta_{\text{H}}$  2.23 (s, 3H), 4.07 (s, 5H), 4.37 (m, 2H), 4.64 (m, 2H), 7.79 (m, 1H), 8.17 (d, 1H), 8.38 (d, 1H), 8.92 (NH);  $\nu/\text{cm}^{-1}$  3238, 3088, 1663, 1579, 1442, 1102, 999, 489;  $m/z$  320 (M<sup>+</sup>, 100%). **3d**:  $\delta_{\text{H}}$  4.22 (s, 5H), 4.46 (m, 2H), 4.57 (m, 2H), 5.32 (NH<sub>2</sub>), 7.61 (d, 1H), 8.03 (d, 1H);  $\nu/\text{cm}^{-1}$  3446, 3288, 1619, 1560, 1448, 1105, 1000, 493;  $m/z$  356 (M<sup>+</sup>, 99.43%).

**General Procedure Preparing 3b, 3e, 3f, and 3g.**—A mixture of the appropriate  $\beta$ -bromopyridine compound (0.5 mmol), PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> (0.025 mmol) and Fc-SnBu<sub>3</sub> (0.5 mmol) in 4 ml dry DMF was stirred at 120–130 °C for the time given in Table 1. Then the mixture was worked up in the above-mentioned manner and afforded the corresponding products. Spectroscopic data of **3b**:  $\delta_{\text{H}}$  4.11 (s, 5H), 4.56 (m, 2H), 4.81 (m, 2H), 7.98 (m, 1H), 8.19 (d, 1H), 8.68 (d, 1H);  $\nu/\text{cm}^{-1}$  3049, 1576, 1523, 1494, 1107, 1021, 501;  $m/z$  308 (M<sup>+</sup>, 100%). **3e**:  $\delta_{\text{H}}$  4.10 (s, 5H), 4.38 (m, 2H), 4.63 (m, 2H), 8.40 (d, 1H), 8.53 (d, 1H);  $\nu/\text{cm}^{-1}$  3467, 3280, 3055, 1641, 1564, 1522, 1440, 1107, 1000, 471;  $m/z$  323 (M<sup>+</sup>, 100%). **3g**:  $\delta_{\text{H}}$  4.09 (s, 5H), 4.43 (m, 2H), 4.68 (m, 2H), 8.04 (m, 1H), 8.77 (m, 2H);  $\nu/\text{cm}^{-1}$  3037, 1588, 1496, 1102, 1009, 485;  $m/z$  341 (M<sup>+</sup>, 50%), 343 (M<sup>+</sup>, 48.61%).

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Table 1 Results of coupling between Fc-SnBu<sub>3</sub> and various  $\beta$ -bromopyridine compounds

Compound	R <sup>1</sup>	R <sup>2</sup>	Catalyst	Time (t/h)	Yield (%)	m.p. (T/C) <sup>a</sup>
<b>3a</b>	H	H	[Pd <sup>0</sup> ] <sup>b</sup>	1.5	85	52–54 <sup>c</sup>
<b>3b</b>	NO <sub>2</sub>	H	[Pd] <sup>d</sup>	1.0	96	236–238
<b>3c</b>	NHCOOMe	H	[Pd <sup>0</sup> ] <sup>b</sup>	1.3	97	171–173
<b>3d</b>	NH <sub>2</sub>	Br	[Pd <sup>0</sup> ] <sup>b</sup>	3	48	123–124
<b>3e</b>	NH <sub>2</sub>	NO <sub>2</sub>	[Pd] <sup>d</sup>	1.5	90	198–200
<b>3f</b>	NH <sub>2</sub>	NH <sub>2</sub>	[Pd] <sup>d</sup>	3	Trace	
<b>3g</b>	H	Br	[Pd] <sup>d</sup>	10	58	46–48
<b>3h</b>	NH <sub>2</sub>	H	[Pd <sup>0</sup> ] <sup>b</sup>	2.5	Trace	

<sup>a</sup> Uncorrected. <sup>b</sup> Pd(PPh<sub>3</sub>)<sub>4</sub>. <sup>c</sup> Lit.<sup>2</sup> mp 57–59 °C. <sup>d</sup> PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub>.

## Experimental

IR spectra were recorded in KBr on a Nicolet 1795X FT-IR spectrophotometer. <sup>1</sup>H NMR spectra were performed on a FC-80A spectrometer using CDCl<sub>3</sub> as a solvent. Mass spectra were obtained on a HP5989A mass spectrometer by electron impact.

**General Procedure Preparing 3a, 3c, 3d and 3h.**—A mixture of the appropriate  $\beta$ -bromopyridine compound (0.5 mmol), Pd(PPh<sub>3</sub>)<sub>4</sub> (0.025 mmol) and the co-reagent CuO (0.5 mmol) in 4 ml dry DMF was heated to 130 °C under argon. After 30 min, pure

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† This is a **Short Paper** as defined in the Instructions for Authors, Section 5.0 [see *J. Chem. Research (S)*, 1999, Issue 1]; there is therefore no corresponding material in *J. Chem. Research (M)*.

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