

## Novel Aspects on the Reaction of Trialkyl-(1-methylindol-2-yl)borates

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A new use of trialkyl-(1-methylindol-2-yl)borates for the synthesis of 2-substituted indoles involving the palladium catalysed cross-coupling with vinylic and aromatic halides, or a facile alkyl migration from boron to carbon without an additional electrophile is described.

The palladium catalysed cross-coupling between trivalent organoboron compounds and organic halides in the presence of a base is an effective method for C–C bond formation.<sup>1</sup> However, the use of tetravalent organoboron compounds ('ate' complexes) in such reactions has not been satisfactory, and the coupling reaction of alkenyltrialkylborates with vinylic halides in the presence of Pd(Ph<sub>3</sub>P)<sub>4</sub> as a catalyst resulted in disappointing yields of the products.<sup>2</sup>

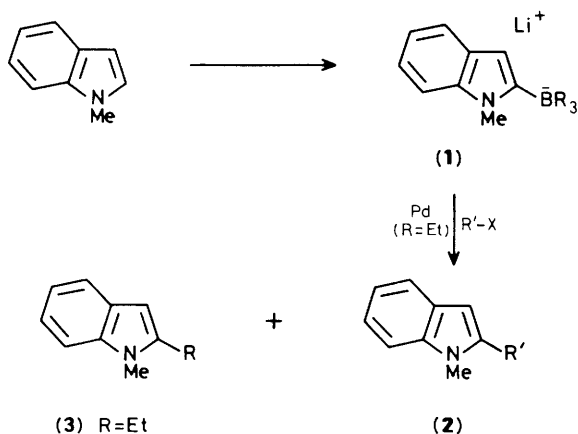
During our studies on heteroarylboron compounds,<sup>3</sup> we investigated the palladium catalysed reaction of the borate (**1**; R = Et) with several organic halides.

The reaction of (**1**; R = Et) (derived from 1-methylindole and Bu<sup>t</sup>Li, followed by treatment with triethylborane)<sup>3</sup> with iodobenzene in the presence of a palladium catalyst (5 mol %) in tetrahydrofuran (THF) under argon, led to 2-phenylindole (**2**; R' = Ph) and 2-ethylindole (**3**; R = Et) as shown in Scheme 1.

**Table 1.** The palladium catalysed coupling of (**1**; R = Et) with organic halides (R'–X).<sup>a</sup>

R'–X	Procedure <sup>b</sup>	Yield (%) <sup>c</sup>	
		( <b>2</b> )	( <b>3</b> ; R = Et)
Ph–I	A	29	56
Ph–I	B	31	57
Ph–I	C	80	7
Ph–I	D	56	28
Ph–Br	C	80	6
β-Bromostyrene	A	16	63
	C	76	8
2-Bromopyridine	C	60	20
3-Bromopyridine	C	70	10
3-Bromothiophene	C	75	9

<sup>a</sup> The reaction was carried out with Pd catalyst (5 mol %), (**1**) (1 equiv.), and R'–X (1.5 equiv.) in THF under argon. Ratio of (**2**; R' = Ph) : (**3**; R = Et) was determined by <sup>1</sup>H n.m.r. analysis. In the absence of Pd catalyst, (**3**; R = Et) was obtained in 81% yield, solely. <sup>b</sup> A: PdCl<sub>2</sub>(Ph<sub>3</sub>P)<sub>2</sub>, room temp., overnight; B: Pd(Ph<sub>3</sub>P)<sub>4</sub>, room temp., overnight; C: PdCl<sub>2</sub>(Ph<sub>3</sub>P)<sub>2</sub>, reflux, 3 h; D: Pd(Ph<sub>3</sub>P)<sub>4</sub>, reflux, 3 h. <sup>c</sup> Isolated yields based on 1-methylindole. All products gave spectral (<sup>1</sup>H, <sup>13</sup>C n.m.r., i.r., mass) data in agreement with their structures.



**Scheme 1**

**Table 2.** The formation of (3) through intramolecular 1,2-alkyl migration of (1).<sup>a</sup>

BR <sub>3</sub> in (1)	Yield (%) of (3) <sup>b</sup>
BEt <sub>3</sub>	80
BBu <sup>s</sup> <sub>3</sub>	60
BBNB-(CH <sub>2</sub> ) <sub>2</sub> -4-cyclohexene <sup>c</sup>	71
BBNB-(CH <sub>2</sub> ) <sub>2</sub> CH(OEt) <sub>2</sub> <sup>c</sup>	67
BBNB-(CH <sub>2</sub> ) <sub>3</sub> -OOCBu <sup>t</sup> <sup>c</sup>	62

<sup>a</sup> A solution of (1) in THF under argon at room temp. was stirred overnight. <sup>b</sup> Isolated yields based on 1-methylindole. All products were identified by spectral (<sup>1</sup>H, <sup>13</sup>C n.m.r., i.r., mass) data. <sup>c</sup> BBNB = 9-Borabicyclo[3.3.1]nonanyl.

The competitive formation of (2; R' = Ph) and (3; R = Et) was markedly affected by reaction temperature. Thus, the 1 : 2 ratio of (2; R' = Ph) and (3; R = Et) from the reaction at room temperature changed to a ratio of 11 : 1 (yields 80 and 7% respectively) when the reaction mixture was heated under reflux. The mechanism of the coupling reaction leading to (2) could be related to the usual cross-coupling reaction catalysed by Pd<sup>0</sup> species.<sup>4</sup>

The palladium catalysed coupling of (1; R = Et) with vinylic and aromatic halides at higher temperatures was found to be

general, and this could provide a new and promising method for introducing a 2-substituent to the indole ring (Table 1).

The formation of (3; R = Et) from (1; R = Et) can be tentatively interpreted in terms of an intramolecular 1,2-alkyl shift from boron to carbon, followed by deboronation. Compound (3) can be readily obtained by formation of (1) in THF under argon at room temperature, suggesting that the formation of (3) does not require the palladium catalyst (Table 2).

Therefore, the reactions of trialkyl-(1-methylindol-2-yl)borates (1) provide new approaches to the synthesis of 2-substituted indole derivatives.

Received, 20th June 1988; Com. 8/02446D

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