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

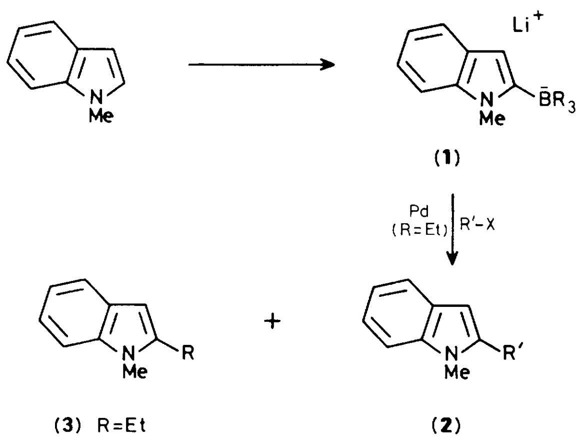
Minoru Ishikura and Masanao Terashima*

Faculty of Pharmaceutical Sciences, Higashi-Nippon-Gakuen University, Ishikari-Tobetsu, Hokkaido 061-02, Japan

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.[1] 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 $Pd(Ph_3P)_4$ as a catalyst resulted in disappointing yields of the products.[2]

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



Scheme 1

The reaction of (**1**; R = Et) (derived from 1-methylindole and Bu^{t}Li, followed by treatment with triethylborane)[3] 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).[a]

R′–X	Procedure[b]	Yield (%)[c] (**2**)	Yield (%)[c] (**3**; 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

[a] 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 ^{1}H n.m.r. analysis. In the absence of Pd catalyst, (**3**; R = Et) was obtained in 81% yield, solely. [b] A: $PdCl_2(Ph_3P)_2$, room temp., overnight; B: $Pd(Ph_3P)_4$, room temp., overnight; C: $PdCl_2(Ph_3P)_2$, reflux, 3 h; D: $Pd(Ph_3P)_4$, reflux, 3 h. [c] Isolated yields based on 1-methylindole. All products gave spectral (^{1}H, ^{13}C n.m.r., i.r., mass) data in agreement with their structures.

Table 2. The formation of (**3**) through intramolecular 1,2-alkyl migration of (**1**).[a]

BR_3 in (**1**)	Yield (%) of (**3**)[b]
BEt_3	80
BBu^s_3	60
BBNB-$(CH_2)_2$-4-cyclohexene[c]	71
BBNB-$(CH_2)_2CH(OEt)_2$[c]	67
BBNB-$(CH_2)_3$-OOCBu^t[c]	62

[a] A solution of (**1**) in THF under argon at room temp. was stirred overnight. [b] Isolated yields based on 1-methylindole. All products were identified by spectral (^1H, ^{13}C n.m.r., i.r., mass) data. [c] 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^0 species.[4]

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

References

1 A. Suzuki, *Acc. Chem. Res.*, 1982, **15**, 178; S. Hyuga, N. Yamashita, S. Hara, and A. Suzuki, *Chem. Lett.*, 1988, 809.

2 N. Miyaura, K. Yamada, H. Suginome, and A. Suzuki, *J. Am. Chem. Soc.*, 1985, **107**, 972; E. Negishi, T. Takahashi, S. Baba, D. E. van Horn, and N. Okukado, *ibid.*, 1987, **109**, 2393; S. Sharma and A. C. Oehlschlager, *Tetrahedron Lett.*, 1988, **29**, 261.

3 M. Ishikura and M. Terashima, *Heterocycles*, 1988, **27**, 203, and references therein.

4 R. F. Heck, 'Palladium Reagents in Organic Synthesis,' Academic Press, London, 1985; H. M. Colquhoun, J. Holton, D. J. Thompson, and M. V. Twigg, 'New Pathways for Organic Synthesis,' Plenum Press, New York, 1984.