

Palladium-catalysed Tandem Cyclisation–Cross-coupling Reaction with Triethyl-(1-methylindol-2-yl)borate

Minoru Ishikura

Faculty of Pharmaceutical Sciences, Health Sciences University of Hokkaido, Ishikari-Tobetsu, Hokkaido 061-02, Japan

Triethyl(1-methylindol-2-yl)borate **1** is successfully applied for the palladium-catalysed tandem cyclisation–cross-coupling reaction, which is used for a concise access to ellipticine derivatives.

In the connection of continuous interest to utilize indolylborate to advantage in synthetic situations,¹ triethyl(1-methylindol-2-yl)borate **1** ('ate' complex) was found to be effective for the palladium-catalysed cross-coupling reaction² and 2-indolyl ketone synthesis *via* the palladium-catalysed carbonylative cross-coupling reaction as well.³ There are several examples of transition metal-catalysed tandem cyclisation–cross coupling processes,⁴ where reactive organo-zinc and -tin compounds have received wide study as transfer agents. However, attempted reactions with organoboron compounds as transfer agents are less satisfactory in terms of yields, selectivity of the reaction and severe reaction conditions.⁴ This paper describes a further extension of this palladium-catalysed cross-coupling procedure with borate **1** to the palladium-catalysed tandem cyclisation–cross-coupling reaction.

Treatment of borate **1** in excess (*ca.* 2 equiv., derived from 2-lithio-1-methylindole⁵ and triethylborane *in situ*) with alkynes **2** in THF containing Pd catalyst (5 mol%) under reflux

readily afforded coupling products **3**[†] (Scheme 1), as summarized in Table 1, which shows that the presence of triphenylphosphine markedly inhibits the reaction of borate **1** with alkyne **2b**, accompanied by substantial recovery of alkyne **2b**. Similarly, the reaction of alkynes **4** and **5** with borate **1** in the presence of Pd(OAc)₂ in THF afforded coupling products **6** (**6a** based on **4a** in 74%; **6b** based on **4b** in 73%; **6b** based on **4c** in 40%) and **7** (based on **5** in 75% yield), respectively.

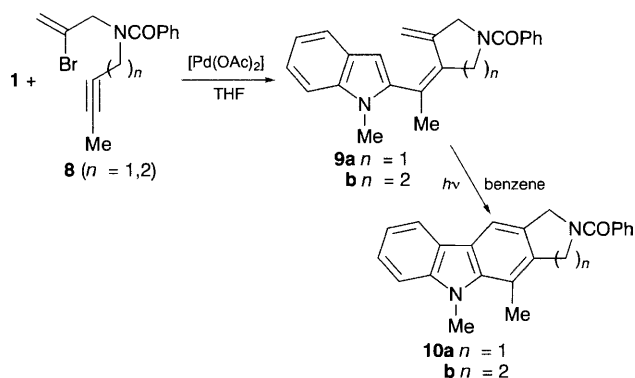
The present tandem procedure can be used for a concise construction of tetracyclic indole systems such as compound **10b**, a basic skeleton of ellipticine. The reaction between borate **1** (*ca.* 2 equiv.) and vinylic bromide **8** with Pd(OAc)₂ (5 mol%) in THF under reflux readily led to triene **9** (**9a** in 45% yield; **9b** in 43% yield). Compound **9** was subsequently irradiated in benzene with a 500 W high-pressure mercury lamp for 5 h, allowing the isolation of tetracyclic indole **10** as an oxidized form (**10a** in 32% yield; **10b** in 35% yield) (Scheme 2).

Furthermore, the present tandem reaction of borate **1** has proven to be also effective even with olefin **11**. Borate **1** (*ca.* 2 equiv.) was allowed to react with olefin **11a** in the presence of Pd(OAc)₂ (5 mol%) in THF at 60 °C, which resulted in the production of coupling product **12** in 10% yield, accompanied

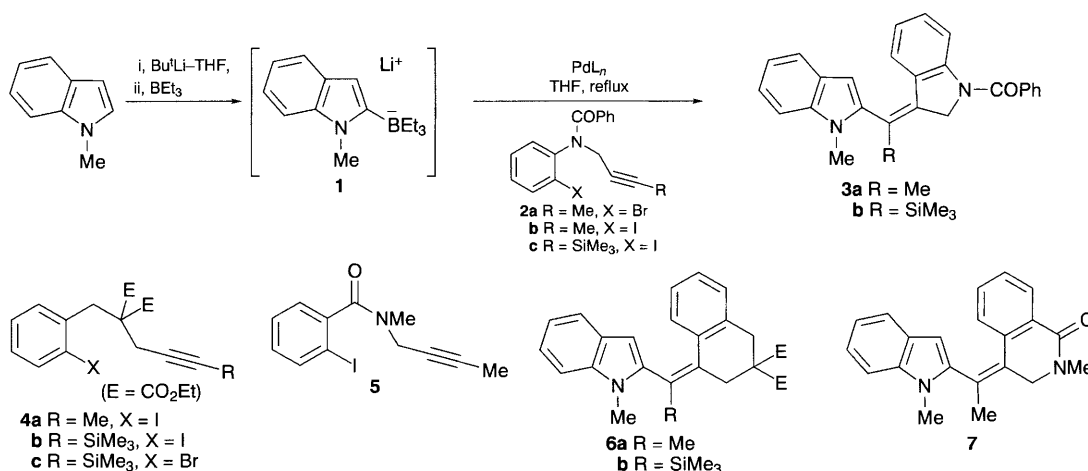
Table 1 Preparation of **3** from **1** and **2**^a

PdL _n	2	Reaction time/h	3 Yield (%) ^b
[PdCl ₂ (MeCN) ₂]	a	0.5	a (53)
	b	0.5	a (76)
	c	0.5	b (70)
[Pd(OAc) ₂]	a	0.5	a (53)
	b	0.5	a (78)
	c	0.5	b (71)
[Pd ₂ (dba) ₃]-CHCl ₃	b	0.5	a (70)
[Pd(PPh ₃) ₄]	b	4.5	a (29) ^c
[PdCl ₂ (MeCN) ₂]-2PPh ₃	b	1	a (10) ^d
[Pd(OAc) ₂]-2PPh ₃	b	4	a (37) ^e

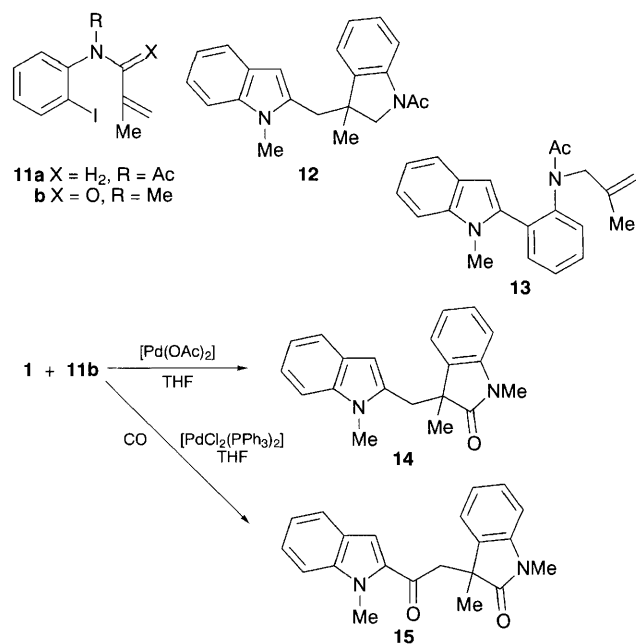
^a A mixture of borate **1** [derived from 1-methylindole (2 mmol) and Bu^tLi (2.2 mmol), followed by treatment with BEt₃ (2.2 mmol) in THF] and alkyne **2** (1 mmol) with Pd catalyst (5 mol%) in THF under an argon atmosphere was heated under reflux. ^b Yields based on **2**. ^c Recovery of **2b** (29%). ^d Recovery of **2b** (50%); longer reaction times did not improve the yield of **3a**. ^e Recovery of **2b** (20%).



Scheme 2



Scheme 1



Scheme 3

by cross-coupling product **13** in 65% yield. Whereas, subjecting of acryloyl amide **11b**, involving appreciably restricted geometry, to the reaction with borate **1** under similar conditions gave coupling product **14** in 75% yield. Moreover, treatment of borate **1** and olefin **11b** with $[\text{PdCl}_2(\text{PPh}_3)_2]$ (5 mol%) in THF at 60 °C under a carbon monoxide atmosphere (15 atm) allowed

the tandem cyclisation–carbonylation–cross-coupling process, providing ketone **15** in 66% yield (Scheme 3).

In summary, the present results show that borate **1** can serve as an effective transfer agent in the palladium-catalysed tandem cyclisation–cross-coupling reaction, which has been applied for a concise formation of ellipticine analogues.

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Footnote

† Treatment of an equimolar mixture of borate **1** and alkyne **2b** produced no cross-coupling product.

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