Scientific Research Publishing

International Journal of Organic Chemistry, 2026, 16(1), 1-6
https://www.scirp.org/journal/ijoc
ISSN Online: 2161-4695
ISSN Print: 2161-4687

A Remarkable Regioselective C3-Allylation of Indoles Using Potassium Allyltrifluoroborate under Palladium Catalysis

Mohammad Al-Masum*, Milton Kumar Kundu, Md Shahin Reza

Department of Chemistry, Tennessee State University, Nashville, USA
Email: malmasum@tnstate.edu

How to cite this paper: Al-Masum, M., Kundu, M.K. and Reza, M.S. (2026) A Remarkable Regioselective C3-Allylation of Indoles Using Potassium Allyltrifluoroborate under Palladium Catalysis. *International Journal of Organic Chemistry*, **16**, 1-6.
https://doi.org/10.4236/ijoc.2026.161001

Received: March 10, 2026
Accepted: March 24, 2026
Published: March 27, 2026

Abstract

We report a new and efficient regioselective C3 allylation of indoles using potassium allyltrifluoroborate under $PdCl_2$(dtbpf) catalysis and microwave assisted conditions. The method offers operational simplicity, high regioselectivity, good to excellent yields, and broad substrate compatibility. This study establishes potassium allyltrifluoroborate as a practical allylating reagent for indole functionalization and expands its applicability in synthetic organic chemistry.

Keywords

Indole C3-Allylation, Regioselective Functionalization Potassium Allyltrifluoroborate, Palladium Catalysis, $PdCl_2$(dtbpf) Catalyst

1. Introduction

Indole is a privileged heterocyclic motif widely recognized for its presence in numerous bioactive natural products, pharmaceutical agents, and synthetic drug candidates. Among the many approaches used to functionalize the indole core, allylation—the introduction of an allyl group ($-CH_2CH=CH_2$)—stands out for its synthetic versatility and biological relevance. Allylated indole derivatives often serve as key intermediates in organic synthesis and have been associated with enhanced physicochemical and pharmacological properties [1]-[5].

Allylation can occur at the **N1**, **C2**, or **C3** positions of the indole, and the resulting regioisomers differ significantly in reactivity, lipophilicity, and receptor-binding affinity. Allyl substituted indole frameworks appear in compounds that target key neurotransmitter systems, including serotonin, dopamine, and opioid receptors. Additionally, incorporation of an ally moiety can improve membrane

permeability, metabolic stability, and other pharmacokinetic characteristics.

From a synthetic standpoint, allylated indoles serve as versatile intermediates for downstream transformations such as cross-coupling, oxidation, cycloaddition, and rearrangement reactions. Transition-metal catalysis—especially involving palladium, copper, or iridium—has produced highly regio- and enantioselective allylation methods under mild and environmentally benign conditions [6]-[9].

Compared to highly reactive boronic acid or boronic ester counterpart, potassium allyltrifluoroborate is an air- and moisture-stable organoboron reagent. Its utility in organic transformations has grown rapidly due to its bench stability and predictable reactivity [10] [11]. To date, however, no cross-coupling reaction between indoles and potassium allyltrifluoroborate has been reported.

The present work introduces a new, regioselective **C3**-allylation of indoles using potassium allyltrifluoroborate under palladium catalysis and microwave assisted conditions [12]. This transformation expands the synthetic utility of organotrifluoroborates in heterocyclic chemistry and provides a practical route to structurally diverse 3-allylindole derivatives with potential medicine relevance.

2. Results and Discussion

The primary objective of this study was to evaluate the feasibility of synthesizing 3-allylindoles through a palladium-catalyzed cross-coupling reaction between indoles and potassium allyltrifluoroborate. To obtain an efficient catalyst for allylation reactions using indole and potassium allyltrifluoroborate, we introduced various palladium salts as catalysts, bases and solvents were investigated using both microwave heating and conventional heating. Optimal conditions leading to the formation of 3-allylindoles **3** from the Pd-catalyzed cross-coupling reactions of indoles **1** and potassium allyltrifluoroborate **2** are summarized in Table 1. The formation of 3-allylindole **3a** from the cross-coupling of indole **1** and potassium allyltrifluoroborate **2** was shown as a representative procedure.

Table 1. Regioselective C3-allylation of indoles using potassium allyltrifluoroborate.

Entry	Catalyst, mole %	Base (Equiv)	Solvent (mL)	Temp	Time	Observation
1	$PdCl_2(d^tbpf)$ (5)	K_2CO_3, (1)	1,4-dioxane	140˚C	30 min	Cross-coupling, low yield
2	$PdCl_2(d^tbpf)$ (5)	No base	1,4 dioxane (5)	140˚C	30 min	No reaction
3	$PdCl_2(d^tbpf)$ (5)	K_2CO_3 (2)	IPA/H_2O (5)	100˚C	30 min	No reaction
4	$PdCl_2(d^tbpf)$ (5)	K_2CO_3 (2)	Et_3N (1)	100˚C	30 min	No reaction
5	$Pd(dba)_2$	K_2CO_3 (2)	1,4 dioxane (5)	140˚C	30 min	No reaction
6	$Pd(dba)_2$ (5)	K_2CO_3 (2)	IPA/H_2O (5)	100˚C	30 min	No reaction
7	$Pd_2(dba)_3CH_2Cl_2$ (5)	K_2CO_3 (2)	1,4 dioxane (5)	140˚C	30 min	No reaction
8	$Pd(PPh_3)_4$ (5)	K_2CO_3 (2)	1,4 dioxane (5)	140˚C	30 min	homocoupling
9	$Pd(PPh_3)_4$ (5)	K_2CO_3 (2)	IPA/H_2O (5)	100˚C	30 min	No reaction
10	Pd $(PPh_3)_4$ (5)	K_2CO_3 (2)	IPA/H_2O (5)	100˚C	48 hours	No reaction

Continued

11	$Pd(OAc)_2$ (5)	K_2CO_3 (2)	1,4 dioxane (5)	140˚C	30 min	No reaction
12	$PdCl_2(dppf)CH_2Cl_2$ (5)	K_2CO_3 (2)	1,4 dioxane (5)	140˚C	30 min	poor yield
13	$PdCl_2(dppf)CH_2Cl_2$ (5)	K_2CO_3 (2)	1,4 dioxane (2.5)	120˚C	60 min	poor yield
14	$PdCl_2(dppf)CH_2Cl_2$ (10)	K_2CO_3 (2)	1,4 dioxane (2.5)	120˚C	60 min	high yield
15	$PdCl_2(dppf)CH_2Cl_2$ (5)	K_2CO_3 (2)	DMI (2)	85˚C	30 min	high yield
16	$PdCl_2(d^tbpf)$ (5)	K_2CO_3 (2)	DMI (2)	85˚C	30 min	high yield
17	$PdCl_2(d^tbpf)$ (3)	K_2CO_3 (1)	DMI (1)	80˚C	20 min	high yield

The reaction employs $PdCl_2(d^tbpf)$ as the catalyst under microwave-assisted irradiation to promote rapid and efficient bond formation. A panel of substituted indoles was examined to explore the reaction's scope, regioselectivity, and synthetic efficiency (**Results 1**, **Results 2**).

General Procedure

An argon-flushed Pyrex dry tube was charged with (37.0 mg, 0.25 mmol) of Potassium allyltrifluoroborate, (29.30 mg, 0.25 mmol) of indole **1a**, (69.10 mg, 0.5 mmol) of K_2CO_3, (3.25 mg, 2 mol %) of $PdCl_2(d^tbpf)$ and a magnetic stir bar in a microwave tube. The reaction tube was sealed and flushed with argon for 1 - 2 minutes to avoid Pd catalyst decomposition. 1.0 mL DMI (1,3-Dimethyl-2-imidazolidinone) was added, and the resulting reaction mixture was irradiated at 80˚C for 20 minutes in a 300-W microwave reactor. After cooling, the crude mixture was partitioned between water (25 mL) and ethyl acetate (25 mL). The organic layer was dried over sodium sulfate and filtered through Celite using ethyl acetate as the eluent. Thin-layer chromatography (TLC) analysis of the filtrate revealed the appearance of a new spot when developed with a hexane/ethyl acetate (25:1) showed formation of a new product spot consistent with the desired allylated derivative. Purification was performed using preparative TLC or column chromatography to afford **3a** in 84% isolated yield. The structure was confirmed by GC–MS and NMR spectroscopy, and the product was dried under vacuum.

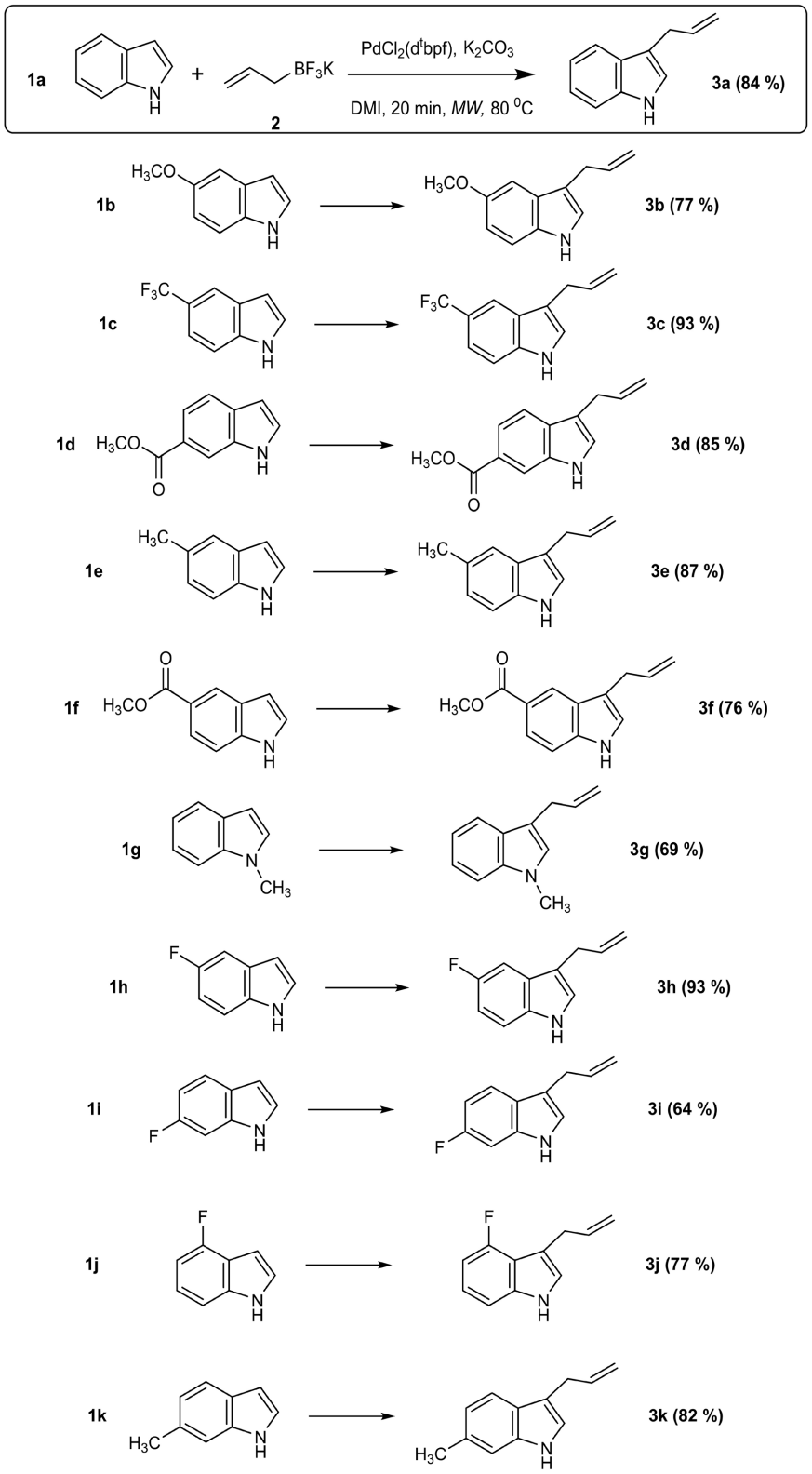
Condition 1, Ratio of Indole : $AllylBF_3K$ (1:1)

Indole	$AllylBF_3K$	$PdCl_2(d^tbpf)$	K_2CO_3	DMI 1 mL	*MW,* 80 ^{0}C 20 min

Condition 2, Ratio of Indole : $AllylBF_3K$ (1:1)

Indole	$AllylBF_3K$	$PdCl_2(dppf)CH_2Cl_2$	K_2CO_3	1, 4- dioxane 2.5 mL or DMI 2 mL	*MW,* 120 ^{0}C 1 h

Results 1. Best two conditions for C3-allylation of indoles.

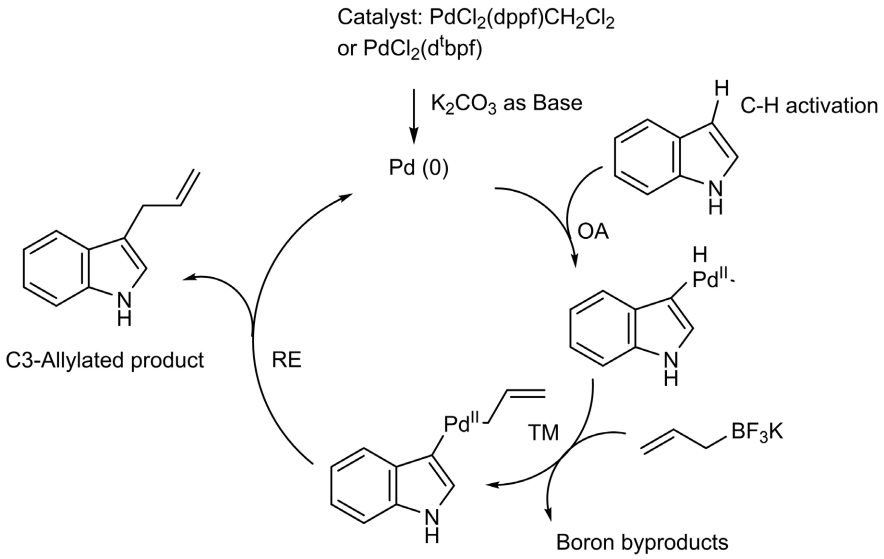


Results 2. Pd-catalyzed C3-allylation of indoles by potassium allyltrifluoroborate[a].

Proposed Mechanism

A plausible mechanism for the **C3**-selective allylation is depicted in **Scheme 1**.

The Pd(II) complex is first reduced to Pd(0) by K_2CO_3. The Pd(0) species then undergoes oxidative addition into the C−H bond. The allylBF_3K reagent delivers the allyl moiety to the palladium center via transmetallation. Finally, reductive elimination affords the desired product and regenerates the Pd catalyst. The method provides a practical, high-yielding synthetic route to 3-allylindoles and contributes to the broader field of palladium-catalyzed heterocyclic functionalization. The findings may hold value for medicinal chemistry and drug discovery by enabling rapid access to bioactive indole derivatives.



Scheme 1. The probable mechanism for the C3 allylation of indoles.

3. Conclusion

We report a new and efficient regioselective **C3**-allylation of indoles using potassium allyltrifluoroborate under $PdCl_2(d^tbpf)$ catalysis and microwave-assisted conditions. The method offers operational simplicity, high regioselectivity, good to excellent yields, and broad substrate compatibility. This study establishes potassium allyltrifluoroborate as a practical allylating reagent for indole functionalization and expands its applicability in synthetic organic chemistry.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Zhang, M., Chen, Q. and Yang, G. (2015) A Review on Recent Developments of Indole-Containing Antiviral Agents. *European Journal of Medicinal Chemistry*, **89**, 421-441. https://doi.org/10.1016/j.ejmech.2014.10.065

[2] Chadha, N. and Silakari, O. (2017) Indoles as Therapeutics of Interest in Medicinal Chemistry: Bird's Eye View. *European Journal of Medicinal Chemistry*, **134**, 159-184. https://doi.org/10.1016/j.ejmech.2017.04.003

[3] Berger, M., Gray, J.A. and Roth, B.L. (2009) The Expanded Biology of Serotonin. *An-*

nual Review of Medicine, **60**, 355-366.
https://doi.org/10.1146/annurev.med.60.042307.110802

[4] Millan, M., Marin, P., Bockaert, J. and Mannourylacour, C. (2008) Signaling at G-Protein-Coupled Serotonin Receptors: Recent Advances and Future Research Directions. *Trends in Pharmacological Sciences*, **29**, 454-464.
https://doi.org/10.1016/j.tips.2008.06.007

[5] Nichols, D.E. (2016) Psychedelics. *Pharmacological Reviews*, **68**, 264-355.
https://doi.org/10.1124/pr.115.011478

[6] Bandini, M. (2013) Recent Advances in the Transition Metal-Catalyzed Functionalization of Indoles at the C3 Position. *Organic & Biomolecular Chemistry*, **11**, Article 5206.

[7] Trost, B.M. and Quancard, J. (2006) Palladium-Catalyzed Enantioselective C-3 Allylation of 3-Substituted-1*H*-Indoles Using Trialkylboranes. *Journal of the American Chemical Society*, **128**, 6314-6315. https://doi.org/10.1021/ja0608139

[8] Kimura, M., Futamata, M., Mukai, R. and Tamaru, Y. (2005) Pd-Catalyzed C3-Selective Allylation of Indoles with Allyl Alcohols Promoted by Triethylborane. *Journal of the American Chemical Society*, **127**, 4592-4593. https://doi.org/10.1021/ja0501161

[9] Cacchi, S. and Fabrizi, G. (2005) Synthesis and Functionalization of Indoles through Palladium-Catalyzed Reactions. *Chemical Reviews*, **105**, 2873-2920.
https://doi.org/10.1021/cr040639b

[10] Al-Masum, M. and Liu, K. (2011) A New Organic Transformation by Introducing Crotyl/Allyltrifluoroborates in Cross-Coupling Reaction with Aroyl Chlorides. *Tetrahedron Letters*, **52**, 5090-5093. https://doi.org/10.1016/j.tetlet.2011.07.107

[11] Al-Masum, M. and Alam, S. (2009) Remarkable Regioselectivity in Microwave-Enhanced Palladium-Catalyzed Allylation Reaction Involving Allyltrifluoroborates and Aryl Halides. *Tetrahedron Letters*, **50**, 5201-5204.
https://doi.org/10.1016/j.tetlet.2009.06.134

[12] Kundu, M.K. (2025) Regioselective C-Allylation of Indole with Potassium Allyltrfluorobo-Rate in the Presence of Pd-Catalyst. Master's Thesis, Tennessee State University.