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# A general, mild and efficient palladium-catalyzed 2,2,2-trifluoroethoxylation of activated aryl bromides and bromo-chalcones: bromo-chalcones a new coupling partner in cross-coupling reaction

T. M. Rangarajan [a,*,†], Kavita Devi [b], Ayushee [c], Ashok K. Prasad [d], Rishi Pal Singh [a,*]

[a] Department of Chemistry, Sri Venkateswara College, University of Delhi, New Delhi, India
[b] Fluoroorganic Laboratory, Centre for Fire, Explosive and Environment Safety, DRDO, Delhi, India
[c] Department of Chemistry, Sri Guru Teg Bahadur Khalsa College, University of Delhi, India
[d] Department of Chemistry, University of Delhi, Delhi, India

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ABSTRACT

An efficient protocol for Pd-catalyzed 2,2,2-trifluoroethoxylation of activated aryl bromides and bromo-chalcones has been developed. We unveil a fascinating insight into the Pd-catalyzed C–O cross-coupling reaction. Pd/*t*BuXPhos (**L1**) ligand system facilitates the C–O cross-coupling reaction between 2,2,2-trifluoroethanol and activated aryl bromides at both higher (115 °C) and lower temperatures (40 °C). Unprecedentedly, this catalyst system facilitates the C–O cross-coupling reaction in short span of reaction times, generally 5–25 min (at 115 °C). The structurally simple analogue of *t*BuXPhos ligand so called JohnPhos (**L2**) ligand is also facilitated the C–O bond formation with activated aryl bromides and bromo-chalcones. Interestingly, under the optimal conditions (**L1**), methanol is also coupled rapidly with activated aryl bromides. These catalyst systems (**L1** and **L2**) fail to couple electron rich aryl bromides with 2,2,2-trifluoroethanol, thus these catalyst systems allow the reductive elimination through an electronic pathway of reductive elimination. The unusual reactivity of 2,2,2-trifluoroethanol in Pd-catalyzed C–O cross-coupling reaction makes that the chemistry of fluorinated molecules is unique than that of non-fluorinated analogues. The bromo-chalcones can be used as a new coupling partner in the cross-coupling reaction.



## 1. Introduction

In the past two decades, organic chemists have often been buoyed by unimaginable reactions catalyzed by 'heroic nature' of transition-metals that translated the classical way of thinking organic chemistry into more advanced level in all aspects of organic synthesis.[1] Transition-metal catalysts have now become an indispensable 'toolkit' for organic chemists to do a startling chemistries, especially, Pd and Cu catalyzed cross-coupling reactions play a vital role in the modern organic synthesis.[1n,2] The transition-metal chemistries have become more popular and successful for even difficult substrates or nucleophiles after the advent of various structural derivatives of phosphours, and nitrogen based ligands.[3]

Dialkylbiaryl phosphine ligands, one of the important class of phosphine ligands, developed by Buchwald group,[3a–e] are excellent supporting or auxiliary ligands in Pd-catalyzed cross-coupling reactions for not only to couple C–C, C–N, C–O bonds etc.,[3e,4] but also to couple C–F, C–$CF_3$, C–$SCF_3$ bonds etc.[5] Recently, it has been demonstrated that the dialkylbiaryl phosphine ligand (BrettPhos) has the property of altering the mechanistic pathway of reductive elimination from nucleophile to nucleophile.[6]

It is important to note that the influence of fluorine on Pd-catalyzed C–O bond formation has also been observed in our recent studies. The catalytic activity of Pd/BrettPhos catalyst system was entirely different for fluorinated and non-fluorinated alcohols. This catalyst system could be coupled the fluorinated alcohols, 1*H*,1*H*-perfluoroalcohols, even up to C-9 carbon chain length[6a] albeit fluoroalcohols are week nucleophiles, whereas the catalytic activity of Pd/BrettPhos system has dramatically dropped and finally become inactive when the chain length of the simple alkyl alcohols (non-fluorinated alcohols) increases.[6b] Thus, the fluorinated molecules behave uniquely or differently with the non-

* Corresponding authors. E-mail addresses: rangarajan93150@gmail.com (T.M. Rangarajan), rpsingh54@gmail.com (R. Pal Singh).
† Present address: Center for Process Research and Innovations (CPRI), Dr. Reddy's Institute of Life Sciences, University of Hyderabad Campus, Gachibowli, Hyderabad 500 046, Telangana, India.

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