

PdCl₂(Ph₃P)₂, an Effective Catalyst for Cross-Coupling of Acyl Halides and ArBF₃K

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Abstract

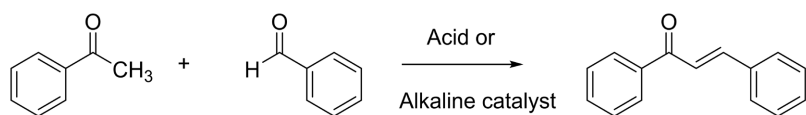
The direct arylation reactions from aryltrifluoroborates and aryl chlorides, crotyl- and allyltrifluoroborate and aryl halides have recently been reported. The scope of the same kind of cross-coupling reactions with acyl halides (sp³- α -Carbon) and potassium organotrifluoroborates is limited. In this project, we have seen the active catalyst effect of PdCl₂(Ph₃P)₂ for direct acylation reaction of organotrifluoroborates in good to high yields.

Keywords

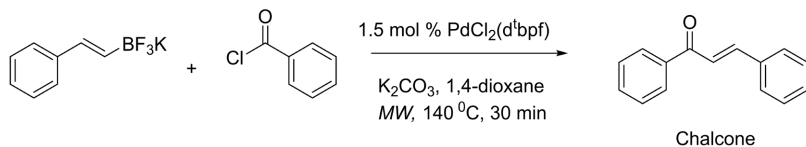
Acyl Chloride, Organotrifluoroborates, Cross-Coupling, Microwave

1. Introduction

Benzoylation is an important organic transformation and has many applications for developing cyclooxygenases (COX) inhibitors like non-steroidal anti-inflammatory drugs (NSAID). In recent years, potassium organotrifluoroborates are successfully applied with aryl chlorides for synthesizing direct aryolated products in one step under microwave heating in minutes [1]-[7]. As for example, Chalcone derivatives continue to captivate medicinal chemists due to their simple chemistry, simplicity of hydrogen atom manipulation, facile synthesis, and a wide range of intriguing biological activities (**Equation 1**). The new literature about green chemistry focused direct arylation reactions in minutes fascinate researchers in the twenty-first century. The Claisen-Schmidt condensation of benzaldehydes with acetophenones is the classical method to synthesize chalcones and it is time consuming comparing to the direct cross-coupling chalcone product from ArCOPdCl and styryltrifluoroborates under microwave heating (**Equation 2**) [7].



Equation 1. The Claisen-Schmidt condensation.



Equation 2. Modern Synthesis of Chalcones by direct arylation reaction.

Stille's pioneer works on palladium catalyzed cross-coupling reaction of benzoyl chloride and aryl-tin [4] [5] encourages us to explore this direct arylation reactions from aryltrifluoroborates and aryl chlorides, crotyl- and allyltrifluoroborate and aryl halides as well (Figure 1) [6]-[8].



Figure 1. Direct arylation reaction of Organotrifluoroborates.

Among all Pd-dppf complexes, the most recent PdCl₂(d^tbpf) complex exhibits the highest P-Pd-P dihedral angle of 104.93 Å⁰ [9] and was effective for these transformations. One of the important questions of these findings was the scope of acylation. The process didn't work for acylation. Later on, we found the good effect of PdCl₂(Ph₃P)₂. We have seen homo-coupling products and in very few cases observed beta-elimination. Finally, overcome those barriers and complete the acylation of organotrifluoroborates. In this communication, we demonstrate the PdCl₂(Ph₃P)₂, an effective catalyst for cross-coupling of acyl halides and ArBF₃K for the direct acylation reaction of organotrifluoroborates (Figure 2).

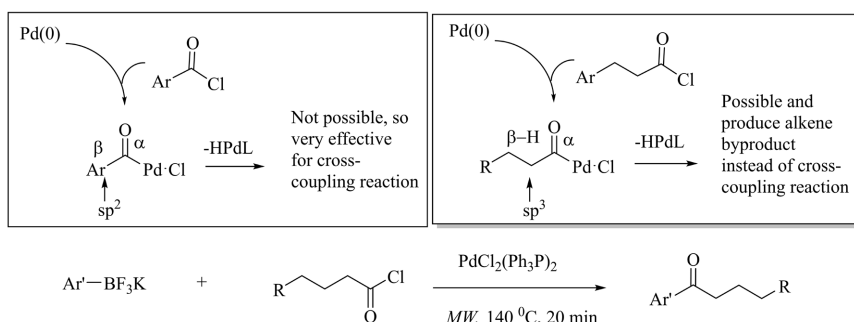


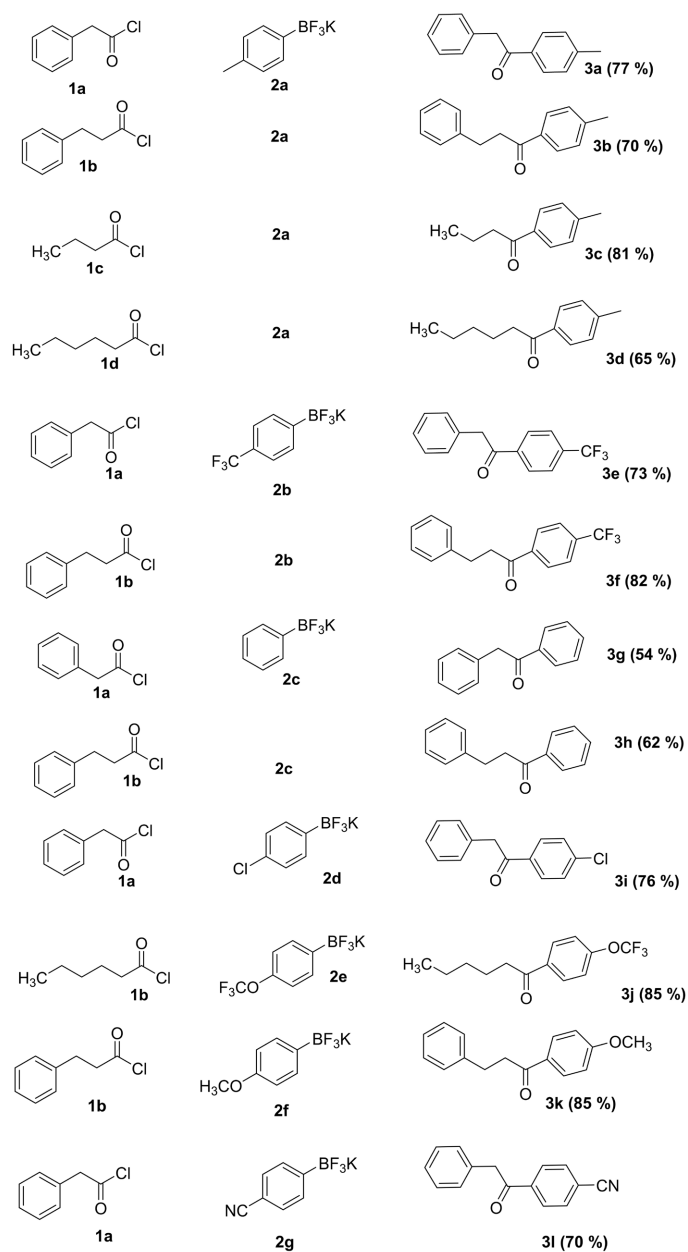
Figure 2. PdCl₂(Ph₃P)₂ catalyzed direct acylation reaction of ArBF₃K in one step.

After a series of experiments with various ratios of starting materials, reaction periods, temperature levels, and other palladium complexes, optimal reactions

conditions were established for this new cross-coupling reaction.

2. Results and Discussion

The catalytic effect of $\text{PdCl}_2(\text{Ph}_3\text{P})_2$ complex has been detected and successfully synthesized a series of acylated cross-coupling products in high yields with this palladium complex under microwave irradiation. The results are summarized in **Figure 3**. The procedure used for the acylated coupling product **3a** from the cross-coupling of phenyl acetyl chloride **1a** and potassium (4-methylphenyl) trifluoroborate **2a** is a representative one.



^aAll products are isolated pure products by chromatography

Figure 3. Pd-catalyzed cross-coupling of acyl chlorides and aryltrifluoroborates^a.

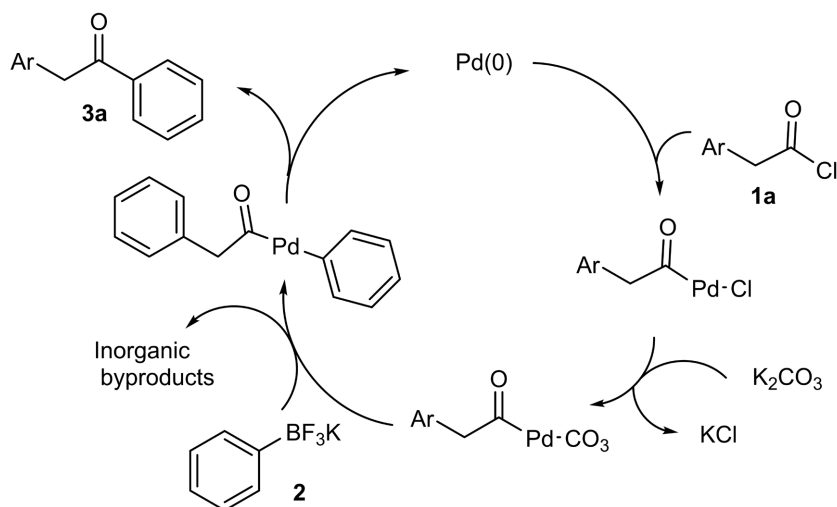
3. Materials and Methods

A dry clean microwave vial was loaded with potassium 4-methylphenyltrifluoroborate (0.100 g, 0.5 mmol), potassium carbonate (0.276 g, 2.0 mmol), $\text{PdCl}_2(\text{Ph}_3\text{P})_2$ (0.011 g, 0.015 mmol), then capped the vial with septum and flushed with argon. After adding phenylacetyl chloride (135 μL , 1.0 mmol) via micro syringe, and 1,4-dioxane (5.0 mL) by syringe in the microwave reaction vial, the resulting mixture was irradiated at 140°C for 20 minutes. The crude reaction product filtered through sintered funnel and concentrated in rotary evaporator. Adding (1.0 mL) of ethyl acetate into the crude reaction, then chromatographed through 7-inch X 7-inch preparative TLC plate with 50:1 hexane: ethyl acetate as eluent. Then put the TLC plate in a big glass TLC jar with 100 mL eluent in the bottom. The eluent soaks into silica gel and reaches at the top of the TLC plate after an hour. The resulting spots shown in UV lamp were collected separately with ethyl acetate and tested collected fractions in GC-MS. We found only fraction 3 (number started from up) has the desired product. The collected fraction 3 in ethyl acetate, then filtered through the sintered funnel and concentrated in rotary evaporator followed by drying the product under vacuo with a trap of liquid nitrogen. The purified product **3a** (77% by weight) was confirmed by NMR study.

^1H NMR (CDCl_3 , δ ppm, 400 MHz): 7.34 - 7.15 (m, 9 H, aromatic), 3.73 (s, 3 H, CH_3), 2.05 (s, 2 H).

All the other reactions followed the same conditions and got good to high yields. The cross-coupling process appears to have been accomplished using 1,4-dioxane as the solvent solution. The formation of a homo-coupling product instead of a cross-coupling product was the most difficult aspect of this research. GC-MS often detects biphenyl as a homo coupling product when ArBF_3K interacts with itself. Using 3 mole% $\text{PdCl}_2(\text{Ph}_3\text{P})_2$ as a catalyst, this problem is usually solved.

In **Scheme 1**, the mechanism for the direct cross-coupling reaction of potassium organotrifluoroborates and acyl chlorides is proposed. Palladium is inserted



Scheme 1. Probable reaction path.

by oxidative addition, followed by ligand exchange with K_2CO_3 . Transmetallation of organoboron species to organopalladium occurs next, followed by reductive elimination to provide the required acylated cross coupling product.

4. Conclusion

In conclusion, the study developed a novel catalytic system for direct acylation from acyl halides and aryl trifluoroborates in the presence of $PdCl_2(Ph_3P)_2$ under microwave irradiation [10]. The green chemistry focusses microwave minute reaction system had advantage over conventional refluxing 12 - 24 hours reaction system in good yields and selectivity. Other than chloride, the research continues to investigate other acyl moieties such as acyl acetate, acyl triflate, acyl nonaflate etc. Because this project was successful and based on prior projects, it is hoped that it will push the boundaries of aromatic ketones synthesis using various acyl moieties. Aromatic ketones are an essential bioactive source that scientists want to learn more about and to improve human health, illness prevention, and pain relief.

Conflicts of Interest

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

References

- [1] Darses, S. and Genet, J.P. (2022) Potassium Organotrifluoroborates: New Perspectives in Organic Synthesis. *Chemical Reviews Journal*, **108**, 288-325. <https://pubs.acs.org/doi/10.1021/cr0509758>
- [2] Frohn, H.J., Franke, H., Fritzen, P. and Bardin, V.V. (2000) (Fluoroorgano)fluoroboranes and -Fluoroborates I: Synthesis and Spectroscopic Characterization of Potassium Fluoroaryltrifluoroborates and Fluoroaryldifluoroboranes. *Journal of Organometallic Chemistry*, **598**, 127-135. [https://doi.org/10.1016/s0022-328x\(99\)00690-7](https://doi.org/10.1016/s0022-328x(99)00690-7)
- [3] Sylvain, S. (2014). Potassium Organotrifluoroborates: New Perspectives in Organic Synthesis. https://www.academia.edu/3162825/Potassium_organotrifluoroborates_new_perspectives_in_organic_synthesis
- [4] Labadie, J.W. and Stille, J.K. (1983) Mechanisms of the Palladium-Catalyzed Couplings of Acid Chlorides with Organotin Reagents. *Journal of the American Chemical Society*, **105**, 6129-6137. <https://doi.org/10.1021/ja00357a026>
- [5] Milstein, D. and Stille, J.K. (1978) A General, Selective, and Facile Method for Ketone Synthesis from Acid Chlorides and Organotin Compounds Catalyzed by Palladium. *Journal of the American Chemical Society*, **100**, 3636-3638. <https://doi.org/10.1021/ja00479a077>
- [6] Al-Masum, M. and Liu, K. (2011) A New Organic Transformation by Introducing Crotyl/Allyltrifluoroborates in Cross-Coupling Reaction with Aryl Chlorides. *Tetrahedron Letters*, **52**, 5090-5093. <https://doi.org/10.1016/j.tetlet.2011.07.107>
- [7] Al-Masum, M., Ng, E. and Wai, M.C. (2011) Palladium-catalyzed Direct Cross-Coupling of Potassium Styryltrifluoroborates and Benzoyl Chlorides—A One Step Method for Chalcone Synthesis. *Tetrahedron Letters*, **52**, 1008-1010. <https://doi.org/10.1016/j.tetlet.2010.12.085>

- [8] Al-Masum, M., Islam, T. and Clopton, G. (2019) Efficient Cross-Coupling Reaction of Aryltrifluoroborates and Aryl Chlorides for the Synthesis of Fluorine Substituted Aromatic Ketones. *International Journal of Organic Chemistry*, **9**, 67-72. <https://doi.org/10.4236/ijoc.2019.91006>
- [9] Mann, G., Shelby, Q., Roy, A.H. and Hartwig, J.F. (2003) Electronic and Steric Effects on the Reductive Elimination of Diaryl Ethers from Palladium(II). *Organometallics*, **22**, 2775-2789. <https://doi.org/10.1021/om030230x>
- [10] Alsafwani, M. (2022) A Novel Process of Pd-Catalyzed Cross-Coupling of Acyl Halides and Aryltrifluoroborates. Ph.D. Thesis, Tennessee State University.