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# $FeCl_3$-catalyzed propargylation of aromatic compounds with propargylic acetates

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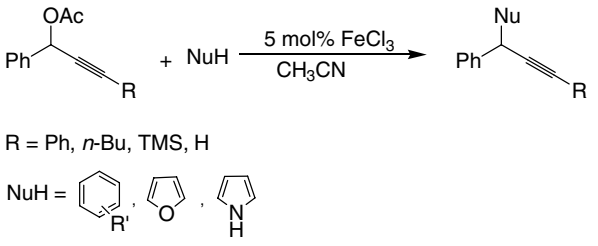
**Abstract**—A new method for the synthesis of propargylated aromatic compounds is developed. The reaction was carried out at room temperature in the presence of a catalytic amount of $FeCl_3$ in acetonitrile, high product yields were obtained with excellent regioselectivity and the reaction proceeded smoothly without exclusion of moisture or air.


Friedel–Crafts alkylation is one of the most important C–C bond forming reactions, which provides an efficient synthetic route to numerous functionalized aromatic compounds possessing special properties. Thus, the research of this reaction has got much attention, a series of aromatic substances with various electrophilic substrates such as active carbonyl compounds, epoxides, and electron-deficient olefins have been extensively studied.[1] However, little attention has been paid to the reaction of propargylic alcohol derivatives with aromatic compounds, despite such reactions playing an important role in the synthesis of some natural products such as *O*-methyldetrol, mimosifoliol, and β-apopicropodophyllin and so on.[2,4] The Nicholas reaction has been known to be effective for propargylation of aromatic compounds by using a stoichiometric amount of $Co_2(CO)_8$, where several steps are necessary to obtain propargylated products from propargylic alcohols via cationic propargyl complexes $[Co_2(CO)_6(propargyl)]^+$.[3] Recently, Toste and co-workers[4] and Uemura and co-workers[5] have described efficient rhenium [(dppm) $ReOCl_3$] and diruthenium [$[Cp^*RuCl(SR)]_2$] catalyzed propargylation of aromatic compounds with propargylic alcohols, respectively. In addition, Campagne and co-workers[6] and Dyker and co-workers[7] introduced the gold [$NaAuCl_4{\cdot}2H_2O$; $AuCl_3$] as an alternative catalyst for the propargylation. However, the peculiarity and high cost of such catalysts are a barrier to their large-scale use. Therefore, development of a general, efficient, cheap, and readily available catalyst for propargylation of aromatic compounds is highly desirable.

Herein, we wish to report an efficient $FeCl_3$-catalyzed propargylation of aromatic compounds with propargylic acetates bearing not only a terminal alkyne group but also internal alkyne group, $sp^3$-C–C bonds were formed after the propargylation event (Scheme 1). To the best of our knowledge, there was no report in the literature on the reaction of propargylic esters with aromatic compounds. The reaction was carried out at room temperature in the presence of a catalytic amount of $FeCl_3$ in acetonitrile. High product yields were obtained with excellent reaction regioselectivity and the reaction proceeded smoothly without exclusion of moisture or air from the reaction mixture.[8]




**Scheme 1.**

*Keywords*: Propargylation of aromatic compounds; Propargylic acetates; Iron(III) chloride.
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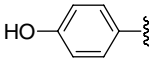
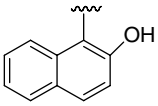
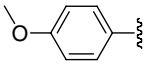
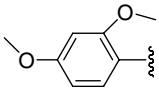
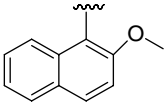
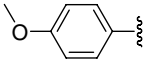
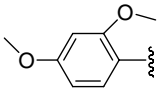
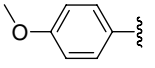
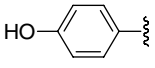
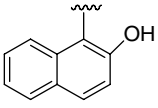
In order to determine the scope and limitation of this reaction, a series of propargylic acetates with various aromatic compounds were investigated. First, reactions of 1,3-diphenylprop-2-ynyl acetate (**1a**) with various aromatic compounds were carried out. Typical results were shown in Table 1. The corresponding propargyl adducts were obtained in high yields with a complete regioselectivity (Table 1, entries 1–7). In the cases of electron-rich arenes such as phenol, β-naphthol, methoxybenzene, 1,3-dimethoxybenzene, and β-methoxy-

**Table 1.** Propargylation of aromatic compounds with propargylic acetates via Scheme 1[a]

| Entry | R | Nu | Time (h) | Product | Yields of **2**[c] (%) |
|---|---|---|---|---|---|
| 1 | **1a**, Ph |  | 0.5 | **2a** | 91 |
| 2 | **1a**, Ph |  | 0.5 | **2b** | 93 |
| 3 | **1a**, Ph |  | 0.5 | **2c** | 83 |
| 4 | **1a**, Ph |  | 3.0 | **2d** | 80 |
| 5 | **1a**, Ph |  | 0.5 | **2e** | 92 |
| 6 | **1a**, Ph |  | 0.5 | **2f** | 81 |
| 7 | **1a**, Ph |  | 4.0 | **2g** | 60[b] |
| 8 | **1b**, TMS |  | 2.0 | **2h** | 80 |
| 9 | **1b**, TMS |  | 3.0 | **2i** | 78 |
| 10 | **1b**, TMS |  | 5.0 | **2j** | 80 |
| 11 | **1c**, *n*-Bu |  | 0.5 | **2k** | 85 |
| 12 | **1c**, *n*-Bu |  | 0.5 | **2l** | 93 |
| 13 | **1c**, *n*-Bu |  | 1.0 | **2m** | 86 |
| 14 | **1d**, H |  | 3.0 | **2n** | 68 |
| 15 | **1d**, H |  | 6.0 | **2o** | 55 |

[a] The reactions of **1** (1 mmol) with NuH (3 mmol) were carried out in the presence of $FeCl_3$ (0.05 mmol) in $CH_3CN$ (2 mL) at room temperature.
[b] The reaction was carried out at 60 °C.
[c] Isolated yields.