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Recent advances in the iron-catalyzed C–C bond formation via polar reactions of alcohols with carbon-centered nucleophiles

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We summarized here the recent developments in the iron-catalyzed C–C bond formation via the polar reactions of alcohols with various carbon-centered nucleophiles. It is composed of three sections according to the categories of the C-centered nucleophiles such as C(sp^3), C(sp^2), and C(sp).

iron-catalysis, C–C bond formation, alcohol activation, polar reaction, carbon-centered nucleophile

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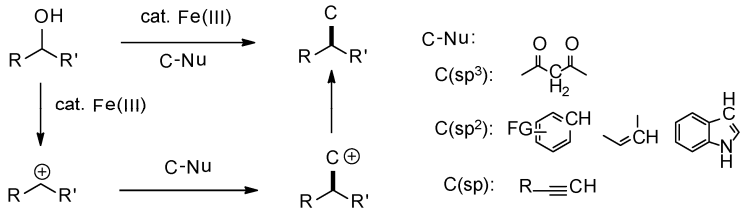
Carbon-carbon bond formation by direct coupling of alcohols with other partners might be very attractive since it would be atom-efficient and environmentally benign since water is the major by-product [1,2]. However, very few successful systems to generate a C–C bond by using alcohols as alternatives to halides as coupling partners have been achieved due to the poor leaving ability of the hydroxyl group [3–16]. Recently, some efficient iron-catalyzed methods to form C–C bonds via polar reactions of alcohols with various carbon-centered nucleophiles have been developed. The possible mechanism for this type of reactions could be depicted in Scheme 1. The recent development of the Fe(III)-catalyzed C–C bond formation reactions of carbon-centered nucleophiles with alcohols via carbocation intermediate will be summarized here.

1 Iron-catalyzed C–C bond formation using alcohols as the electrophiles

1.1 C(sp^3)-centered nucleophiles[1)]

In 2007, several efficient iron-catalyzed C–C bond formation reactions of benzylic alcohols with 1,3-dicarbonyl compounds have been reported by Kischel et al. [17], Yuan et al. [18], and Jana et al. [19] respectively (Scheme 2). Although some examples of alkylations of 1,3-dicarbonyl



Scheme 1

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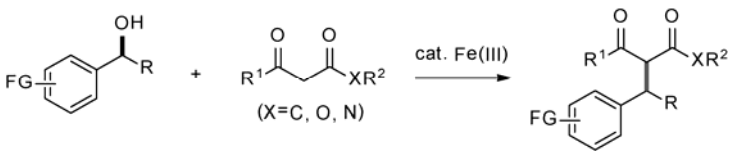
1) In this part, the acidic 2-CH in the 1,3-dicarbonyl compounds described as sp^3 C-centered neucleophiles is only for convenience of classification. It is the enolate (sp^2 C) that acts as the real neucleophile in these reactions.



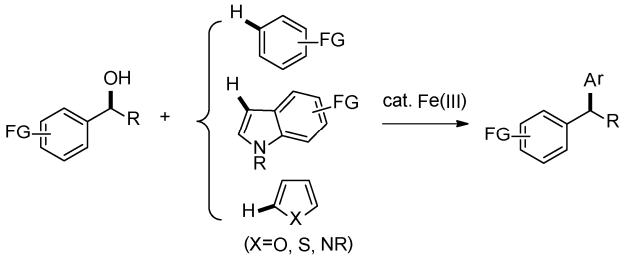
Scheme 2

compounds using alcohols as electrophiles catalyzed by Lewis acids/acids such as $Et_2O \cdot BF_3$ and formic acid have been explored [20,21], it is novel and very interesting to apply simple $FeCl_3$/$FeCl_3 \cdot 6H_2O$ as the effective catalyst.

In 2008, Fan et al. [22] reported a tandem benzylation-cyclization strategy for preparation of 3-quinolinecarboxylic esters by reactions of 2-amino-benzylic alcohols with β-ketoesters catalyzed by $FeCl_3$. One year later, Chan et al. [23] found that a direct nucleophilic α-substitution of Morita-Baylis-Hillman alcohols by 1,3-dicarbonyl compounds to form the corresponding C–C bond could also be realized by $FeCl_3 \cdot 6H_2O$ catalysis. In 2010, an $Fe(ClO_4)_3 \cdot xH_2O$-catalyzed direct C–C bond coupling reactions of 1,3-dicarbonyl compounds with benzylic alcohols has been developed by Thirupathi et al. [24].

1.2 C(sp^2)-centered nucleophiles

In 2005, Iovel et al. [25] reported a general and efficient $FeCl_3$-catalyzed Friedel-Crafts alkylations of arenes and heteroarenes by using benzylic alcohols and benzyl carboxylates. The features of inexpensive-iron-catalysis, easy and practical handling, and water as the only by-product make this system very attractive (Scheme 3).

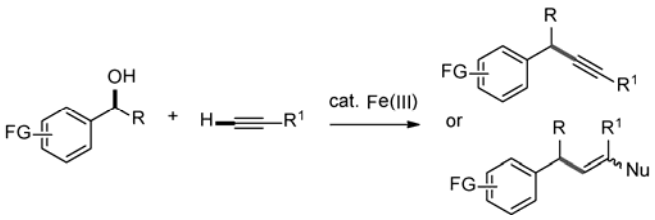


Scheme 3

In 2006, Zhan et al. [26] developed an efficient and general $FeCl_3$-catalyzed nucleophilic substitution of propargylic alcohols by using various nucleophiles including many C(sp^2)-centered nucleophiles. In 2007, Jana et al. [27] reported an $FeCl_3$-catalyzed selective 3-C alkylation of indoles with benzylic alcohols. One year later, Huang et al. [28,29] developed some interesting $FeCl_3 \cdot 6H_2O$-catalyzed intramolecular Friedel-Crafts reactions of propargylic alcohols to prepare substituted hydroisoquinolines and hydronaphthalenes. In 2009, Nishimoto et al. [30] reported an α-alkylation of carbonyl compounds by $FeCl_3$-catalyzed addition of enol acetates to alcohols. In 2011, an efficient Fe(III)-catalyzed direct coupling of alkenes with alcohols and cross-coupling of alcohols with alcohols to give the corresponding substituted (*E*)-alkenes stereospecifically was developed by us [31].

1.3 C(sp)-centered nucleophiles

In 2008, Jana et al. [32] reported a novel iron(III)-catalyzed addition of benzylic alcohols with terminal aryl alkynes to give substituted aryl ketones. One year later, several other efficient Fe(III)-catalyzed additions of alkynes to alcohols have been explored by Xiang et al. [33], Li et al. [34], Biswas [35], and our group [36] (Scheme 4).



Scheme 4

In 2010, Ren et al. [37] also reported an FeX_3-promoted addition of benzylic alcohols to aryl alkynes to generate alkenyl halides. A year later, Bu et al. [38] explored an $FeCl_3 \cdot 6H_2O$-catalyzed tandem mono- and/or dibenzylation/cyclization reactions of benzylic alcohols with alkynes to prepare polysubstituted indenes.

2 Conclusions

The foregoing sections have demonstrated the recently significant progress made in the area of Fe(III)-catalyzed C–C bond formation reactions of alcohols with various carbon-centered nucleophiles. Whereas these strategies could be utilized to prepare a variety of C–C bonds such as C(sp^3)–C(sp^3), C(sp^3)–C(sp^2), C(sp^3)–C(sp) which would be useful in organic synthesis. However, only benzylic alcohols are the effective substrates in most of the systems, which could be a problem for their applications in synthetic chemistry, remains to be achieved in the future.

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