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(sp³), C(sp²), 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(sp³)-centered nucleophiles¹⁾

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 sp³ C-centered nucleophiles is only for convenience of classification. It is the enolate (sp² C) that acts as the real nucleophile in these reactions.

Scheme 2

compounds using alcohols as electrophiles catalyzed by Lewis acids/acids such as $\text{Et}_2\text{O} \cdot \text{BF}_3$ and formic acid have been explored [20,21], it is novel and very interesting to apply simple $\text{FeCl}_3/\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ 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 $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ catalysis. In 2010, an $\text{Fe}(\text{ClO}_4)_3 \cdot x\text{H}_2\text{O}$ -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(sp²)-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(sp²)-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 $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ -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

$\text{Fe}(\text{III})$ -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 $\text{Fe}(\text{III})$ -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 $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ -catalyzed tandem mono- and/or dibenylation/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 $\text{Fe}(\text{III})$ -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(sp³)-C(sp³), C(sp³)-C(sp²), C(sp³)-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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- 1 Trost B M. The atom economy—A search for synthetic efficiency. *Science*, 1991, 254: 1471–1477
- 2 Trost B M. On inventing reactions for atom economy. *Acc Chem Res*, 2002, 35: 695–705
- 3 Muzart J. Palladium-catalysed reactions of alcohols. Part B: Formation of C–C and C–N bonds from unsaturated alcohols. *Tetrahedron*, 2005, 61: 4179–4212
- 4 Tamaru Y. Activation of allyl alcohols as allyl cations, allyl anions, and amphiphilic allylic species by palladium. *Eur J Org Chem*, 2005, 2647–2656
- 5 Muzart J. Procedures for and possible mechanisms of Pd-catalyzed allylations of primary and secondary amines with allylic alcohols. *Eur J Org Chem*, 2007, 3077–3089
- 6 Muzart J. Gold-catalysed reactions of alcohols: Isomerisation, inter- and intramolecular reactions leading to C–C and C-heteroatom bonds. *Tetrahedron*, 2008, 64: 5815–5849
- 7 Bandini M, Tragni M. π -Activated alcohols: An emerging class of alkylating agents for catalytic Friedel-Crafts reactions. *Org Biomol Chem*, 2009, 7: 1501–1507
- 8 Emer E, Sinisi R, Capdevila M G, et al. Direct nucleophilic S_N1 -type reactions of alcohols. *Eur J Org Chem*, 2011, 647–666
- 9 Bolm C, Legros J, Le Pailh J, et al. Iron-catalyzed reactions in organic synthesis. *Chem Rev*, 2004, 104: 6217–6254
- 10 Shinokubo H, Oshima K. Transition metal-catalyzed carbon-carbon bond formation with Grignard reagents—novel reactions with a classic reagent. *Eur J Org Chem*, 2004, 2081–2091
- 11 Fürstner A, Martin R. Advances in iron catalyzed cross coupling reactions. *Chem Lett*, 2005, 34: 624–629
- 12 Enthaler S, Junge K, Beller M. Sustainable metal catalysis with iron: From rust to a rising star. *Angew Chem Int Ed*, 2008, 47: 3317–3321
- 13 Sherry B D, Fürstner A. The promise and challenge of iron-catalyzed cross coupling. *Acc Chem Res*, 2008, 41: 1500–1511
- 14 Correa A, Mancheño O G, Bolm C. Iron-catalysed carbon-heteroatom and heteroatom-heteroatom bond forming processes. *Chem Soc Rev*, 2008, 37: 1108–1117
- 15 Sarhan A A O, Bolm C. Iron(III) chloride in oxidative C–C coupling reactions. *Chem Soc Rev*, 2009, 38: 2730–2744
- 16 Sun C L, Li B J, Shi Z J. Direct C–H transformation via iron catalysis. *Chem Rev*, 2011, 111: 1293–1314
- 17 Kischel J, Mertins K, Michalik D, et al. A general and efficient iron-catalyzed benzylation of 1,3-dicarbonyl compounds. *Adv Synth Catal*, 2007, 349: 865–870
- 18 Yuan Y, Shi Z, Feng X, et al. Solvent-free reactions of alcohols with β -dicarbonyl compounds catalyzed by iron(III) chloride. *Appl Organometal Chem*, 2007, 21: 958–964
- 19 Jana U, Biswas S, Maiti S. A simple and efficient $FeCl_3$ -catalyzed direct alkylation of active methylene compounds with benzylic and allylic alcohols under mild conditions. *Tetrahedron Lett*, 2007, 48: 4065–4069
- 20 Bisara F, Prestat G, Vitale M, et al. Alkylation of active methylenes via benzhydryl cations. *Synlett*, 2002, 1823–1826
- 21 Gullickson G C, Lewis D E. Compounds with benzhydryl. During solvolysis in formic acid. *Aust J Chem*, 2003, 56: 385–388
- 22 Fan J, Wan C, Sun G, et al. Cascade synthesis of 3-quinolinecarboxylic ester via benzylation/ propargylation-cyclization. *J Org Chem*, 2008, 73: 8608–8611
- 23 Zhang X, Rao W, Chan P W H. Iron(III) chloride-catalyzed direct nucleophilic α -substitution of Morita-Baylis-Hillman alcohols with alcohols, arenes, 1,3-dicarbonyl compounds, and thiols. *Org Biomol Chem*, 2009, 7: 4186–4193
- 24 Thirupathi P, Kim S S. $Fe(ClO_4)_3 \cdot xH_2O$ -catalyzed direct C–C bond forming reactions between secondary benzylic alcohols with different types of nucleophiles. *Tetrahedron*, 2010, 66: 2995–3003
- 25 Iovel I, Mertins K, Kischel J, et al. An efficient and general iron-catalyzed arylation of benzyl alcohols and benzyl carboxylates. *Angew Chem Int Ed*, 2005, 44: 3913–3917
- 26 Zhan Z, Yu J, Liu H, et al. A general and efficient $FeCl_3$ -catalyzed nucleophilic substitution of propargylic alcohols. *J Org Chem*, 2006, 71: 8298–8301
- 27 Jana U, Maiti S, Biswas S. An $FeCl_3$ -catalyzed highly C3-selective Friedel-Crafts alkylation of indoles with alcohols. *Tetrahedron Lett*, 2007, 48: 7160–7163
- 28 Huang W, Shen Q, Wang J, et al. One-step synthesis of substituted dihydro- and tetrahydroisoquinolines by $FeCl_3 \cdot 6H_2O$ catalyzed intramolecular Friedel-Crafts reaction of benzylamino-substituted propargylic alcohols. *J Org Chem*, 2008, 73: 1586–1589
- 29 Huang W, Zheng P, Zhang Z, et al. Controllable one-step synthesis of spirocycles, polycycles, and di- and tetrahydronaphthalenes from aryl-substituted propargylic alcohols. *J Org Chem*, 2008, 73: 6845–6848
- 30 Nishimoto Y, Onishi Y, Yasuda M, et al. α -Alkylation of carbonyl compounds by direct addition of alcohols to enol acetates. *Angew Chem Int Ed*, 2009, 48: 9131–9134
- 31 Liu Z Q, Zhang Y, Zhao L, et al. Iron-catalyzed stereospecific olefin synthesis by direct coupling of alcohols and alkenes with alcohols. *Org Lett*, 2011, 13: 2208–2211
- 32 Jana U, Biswas S, Maiti S. Iron(III)-catalyzed addition of benzylic alcohols to aryl alkynes—A new synthesis of substituted aryl ketones. *Eur J Org Chem*, 2008, 5798–5804
- 33 Xiang S K, Zhang L H, Jiao N. $Sp-sp^3$ C–C bond formation via $Fe(OTf)_3/TfOH$ cocatalyzed coupling reaction of terminal alkynes with benzylic alcohols. *Chem Commun*, 2009, 6487–6489
- 34 Li H H, Jin Y H, Wang J Q, et al. Controllable stereoselective synthesis of trisubstituted alkenes by a catalytic three-component reaction of terminal alkynes, benzylic alcohols, and simple arenes. *Org Biomol Chem*, 2009, 7: 3219–3221
- 35 Biswas S, Maiti S, Jana U. New and efficient iron halide mediated synthesis of alkenyl halides through coupling of alkynes and alcohols. *Eur J Org Chem*, 2009, 2354–2359
- 36 Liu Z Q, Wang J, Han J, et al. An efficient and mild iron-mediated synthesis of alkenyl halides via direct C–C bond formation of benzyl alcohols and aryl alkynes. *Tetrahedron Lett*, 2009, 50: 1240–1242
- 37 Ren K, Wang M, Wang L. FeX_3 -promoted intermolecular addition of benzylic alcohols to aromatic alkynes: A mild and efficient strategy for the synthesis of alkenyl halides. *Eur J Org Chem*, 2010, 565–571
- 38 Bu X, Hong J, Zhou X. Synthesis of substituted indenenes through iron-catalyzed annulations of benzylic alcohols with alkynes. *Adv Synth Catal*, 2011, 353: 2111–2118