Cationic Iron-catalyzed Addition of Carboxylic Acids to Olefins

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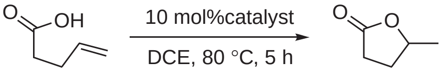
Cationic iron salts were found to be good catalysts for intra- and intermolecular addition of carboxylic acids to olefins, which afforded the corresponding esters in good yields.

The importance of heterofunctionalization of unactivated carbon–carbon multiple bonds has been widely recognized in the field of carbon–heteroatom bond construction, and much effort has been made towards exploitation of this methodology.[1] Of the recently developed processes, late transition metal-catalyzed reaction is a grateful tool in this area; for instance, expensive or toxic Pt, Ir, Ag, Au, Ru, and Hg, which efficiently coordinate carbon–carbon multiple bonds to lead to the corresponding adducts.[2] However, their reactivity for the olefin moiety is low, that is, high temperature and long reaction time are necessary to proceed the reaction. In 2005, Hill et al. reported the addition of carboxylic acids with $Cu(OTf)_2$, which allowed participation of less bulky carboxylic acid in the reaction.[3]

In our previous works, simple and environmentally benign iron salts were found to be highly active catalyst for intramolecular hydroamination[4] and hydroalkoxylation[5] of unactivated olefins, giving rise to a diverse set of heterocyclic compounds in excellent yields under mild conditions. Moreover, the catalyst activity could be improved by addition of silver salts like AgOTf, affording cationic catalyst, $Fe(OTf)_3$,[6] which led to a dramatically improvement of the catalytic activity.[5] During the investigation, we also found that intra- and intermolecular addition of carboxylic acid to olefins took place effectively in the presence of the iron catalyst. In this paper, we would like to disclose these results.

Treatment of 4-pentenoic acid (**1a**) with 10 mol % of $FeCl_3$ in dichloroethane (DCE) for 5 h at 80 °C afforded γ-valerolactone (**2a**) in 45% NMR yield (Entry 1, Table 1).[7] Cationic iron species $Fe(OTf)_3$, generated in situ, completed the reaction under the similar conditions, providing **2a** in high yield (Entry 2). Then, effect of counter ion on the iron was tested. OTf and ClO_4 anions were effective for the transformation (Entries 2 and 3), whereas BF_4 and OAc anions afforded the product in negligible yields (Entries 4 and 5). Other late transition-metal catalysts like $Cu(OTf)_2$, $Zn(OTf)_2$, and AgOTf provided the product in lower yields than the current catalyst (Entries 6–8).

Table 1. Screening of catalyst[a]

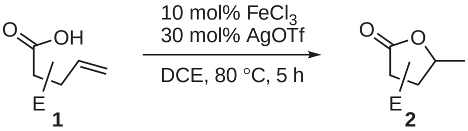


1a **2a**

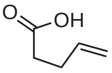
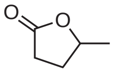
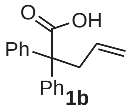
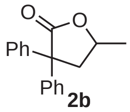
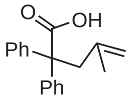
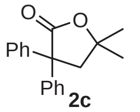
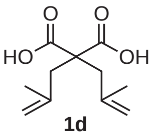
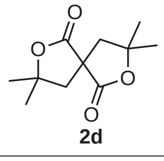
Entry	Catalyst	Yield/%[b]
1	$FeCl_3$	45
2	$FeCl_3$ / 3AgOTf	94
3	$FeCl_3$ / $3AgClO_4$	90
4	$FeCl_3$ / $3AgBF_4$	2
5	$FeCl_3$ / 3AgOAc	0
6	AgOTf	14
7	$Zn(OTf)_2$	0
8	$Cu(OTf)_2$	15

[a]Conditions: **1a** (0.5 mmol), DCE (5 L). [b]NMR yield.

Table 2. Intramolecular addition of carboxylic acids to olefins



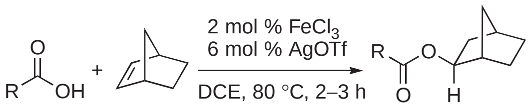
1 **2**

Entry	Substrate	Product	Yield[a]/%
1	 **1a**	 **2a**	93
2	 **1b**	 **2b**	96
3	 **1c**	 **2c**	97
4	 **1d**	 **2d**	99

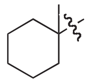
[a]Isolated yield.

Next, we tried out an expansion of the catalytic system for the synthesis of multi-substituted γ-lactones (Table 2). Generally, the cyclization rate depends on a distance between the donor (acid) and the acceptor (olefin) caused by the introduction of substituent(s) in the tether. However, under the present conditions, reaction time of **1a** was not so different from that of 2,2-diphenyl-4-pentenoic acid (**1b**) to give the lactones **1b** and **2b** in 93 and 96% isolated yield, respectively (Entries 1 and 2). The same result was obtained in the cyclization of **1c** to **2c** in 97% yield (Entry 3). The system was also applicable to the synthesis of spirobicyclic ester **2d** in excellent yield (Entry 4). In addition, the heterofunctionalization of internal olefin such as (*E*)-2,2-diphenyl-4-hexenoic acid was permitted

Table 3. Intermolecular addition of carboxylic acids to norbornene[a]



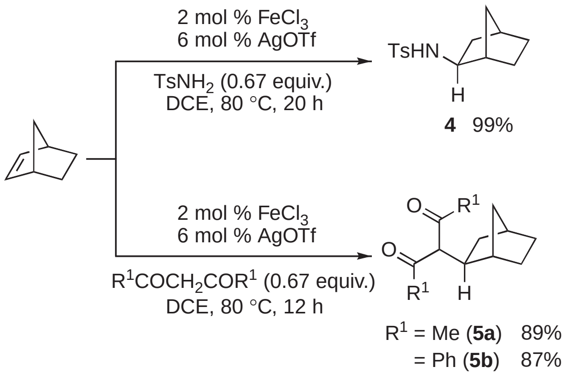
3

Entry	Carboxylic acid	Product	Yield/%[b]
1	Ph	**3a**	95
2	2-MeC_6H_4	**3b**	95
3	2-PhC_6H_4	**3c**	99
4	3-MeC_6H_4	**3d**	95
5	3,5-$Me_2C_6H_3$	**3e**	99
6	2,6-$Me_2C_6H_3$	**3f**	99
7	4-ClC_6H_4	**3g**	99
8	3-BrC_6H_4	**3h**	95
9	PhCH=CH	**3i**	97
10	(furan-2-yl)CH=CH	**3j**	94
11	Me	**3k**	94
12	$PhCH_2CH_2$	**3l**	97
13	$BrCH_2$	**3m**	97
14	cyclohexyl	**3n**	94
15	cycloheptyl	**3o**	98
16		**3p**	99

[a]Conditions: RCO_2H (0.5 mmol), norbornene (0.75 mmol), DCE (1 mL). [b]Isolated yield.

similarly, yielding exo-cyclized product in 71% yield along with endo-product (28%).

The cationic iron catalyst was also greatly effective for intermolecular addition of carboxylic acid to norbornene (Table 3). When benzoic acid and 1.5 equiv. of norbornene were treated with 2 mol % of $Fe(OTf)_3$, ester **3a** was obtained in high yield within 2 h (Entry 1). Stereochemistry of the product was determined by NMR measurements, in which the product was only exo-adduct.[8] Bulky substituents such as 2-Me, 2-Ph, 3-Me, 3,5-Me_2, and 2,6-Me_2 did not inhibit the reaction, leading to the corresponding products in satisfactory yields (Entries 2–6). Halogen-substituted benzoic acids at 4- and 3-position were permitted similarly (Entries 7 and 8). The addition of α,β-unsaturated carboxylic acids was also accomplished, providing the corresponding esters in good yields (Entries 9 and 10). Surprisingly, the present system has a wide range of synthetic scope; similar coupling products could be given from an attack of every type of aliphatic acid to norbornene. Thus, primary, secondary, and tertiary carboxylic acids were easily converted to the corresponding esters in excellent yields (Entries 11–16). In addition, other nucleophiles such as amine and diketone could easily react to norbornene, leading to formations of C–N and C–C bond with exo-selectivity though they required long reaction time (Scheme 1).



Scheme 1.

In conclusion, the cationic iron complex, $Fe(OTf)_3$, has been found to be a highly active catalyst for the intra- and intermolecular addition of carboxylic acid to olefins under mild conditions. Compared to previously described methods, the present catalyst is commercially available and readily preparable material in easy operation. Moreover, in the intermolecular addition of acids, both aromatic and aliphatic carboxylic acids can be employed without exception. Studies on scope and limitation of the system and on details of the reaction path are in progress.

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References and Notes

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7 In similar conditions, when $FeCl_3{\cdot}6H_2O$ as a catalyst was used, 36% yield of **2a** was formed.
8 By Brønsted acid catalyst like TfOH the product was provided in low yield and stereoselectivity.