Iron-catalysed green synthesis of carboxylic esters by the intermolecular addition of carboxylic acids to alkenes†‡

Jun-Chul Choi,* Kazufumi Kohno, Daisuke Masuda, Hiroyuki Yasuda and Toshiyasu Sakakura*

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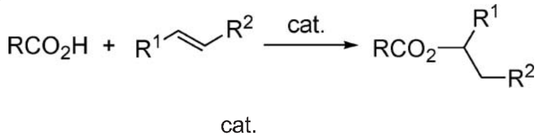
Iron triflate, *in situ*-formed from $FeCl_3$ and triflic acid, or $FeCl_3$ and silver triflate efficiently catalyse the intermolecular addition of carboxylic acids to various alkenes to yield carboxylic esters; the reaction is applicable to the synthesis of unstable esters, such as acrylates.

Transition metal catalysts are powerful tools in organic synthesis. For example, most C–C bond formations *via* cross-coupling,[2] asymmetric hydrogenation,[3,4] asymmetric epoxidation and hydroxylation,[5] stereo-controlled polyolefin synthesis,[6] and C=C bond metathesis[7] are all conducted in the presence of transition metal catalysts. However, disadvantages of transition metal catalysts include high toxicity, high cost and uneven distribution of the transition metal. In order to circumvent these problems, the development of iron-based catalysts has been strongly desired.[8]

On the other hand, ester formation is a key reaction in organic synthesis.[9,10] The addition of carboxylic acids to alkenes is an especially attractive green procedure because the reaction is coproduct-free and energy saving (eqn. (1)), unlike common esterifications, which generally need the coproducts, typically water or HCl, to be removed (eqn. (2)). The conventional procedure of eqn. (1) uses a relatively large amount of sulfuric acid as a catalyst and requires its neutralization before purification of the ester.[11] Meanwhile, high catalytic activities of coinage metals (copper,[12] silver[12] and gold[13,14]) for eqn. (1), especially gold, have recently attracted great attention. Complexes of precious metals like ruthenium are also very effective as catalysts for eqn. (1).[15,16] An intramolecular version of eqn. (1) has also been catalysed by precious metal complexes such as platinum[17] and silver.[18] Herein, we report the efficient catalysis of eqn. (1) by using iron-based catalysts.

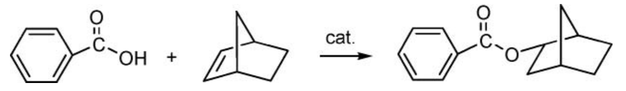


$$RCO_2H + R^1\text{CH=CH}R^2 \xrightarrow{\text{cat.}} RCO_2\text{CH}(R^1)\text{CH}_2R^2 \quad (1)$$

$$\text{RCOX} + \text{R'OH} \xrightarrow{\text{cat.}} \text{RCO}_2\text{R'} + \text{HX} \quad (2)$$
$$(\text{X = OH or halogen})$$

First, the effect of catalyst structure was investigated on the reaction of benzoic acid and norbornene (Table 1). Recently, $FeCl_3$ has been reported as an active catalyst for the intramolecular cyclization of amino-alkenes.[19] However, $FeCl_3$ poorly catalysed the intermolecular addition of carboxylic acids to alkenes (Table 1, entry 1). Interestingly, we found that the addition of a catalytic amount of silver triflate dramatically accelerated the reaction (Table 1, entry 2). The active species is presumably *in situ*-formed $Fe(OTf)_3$. A similar enhancement has been reported for the ruthenium-catalysed reaction using AgOTf.[15] Separately, $Fe(OTf)_3$ was synthesized from $FeCl_3$ and TfOH according to a literature procedure.[20] The isolated $Fe(OTf)_3$ exhibited nearly the same catalytic activity as the $Fe(OTf)_3$ *in situ*-formed from $FeCl_3$ and AgOTf (Table 1, entries 2 and 3). The catalyst formed *in situ* from $FeCl_3$ and TfOH also gave nearly the same high ester yields (Table 1, entry 4). On the other hand, using solely AgOTf or TfOH resulted in a poor catalyst (Table 1, entries 5 and 6).[12] Other metal triflates were much less active than iron triflate (Table 1, entries 7 to 9), as reported previously.[12]

Table 1 The effect of catalyst on ester formation *via* the addition of benzoic acid to norbornene[a]



Entry	Catalyst	Yield (%)[b]
1	$FeCl_3$	5
2	$FeCl_3$ + 3 AgOTf	99
3	$Fe(OTf)_3$	99
4	$FeCl_3$ + 3 TfOH	99
5	AgOTf	2
6	TfOH[c]	3
7	$CoCl_2$ + 2 AgOTf	24
8	$NiCl_2$ + 2 AgOTf	12
9	$Sc(OTf)_3$	20[d]

[a] Reaction conditions: benzoic acid (10 mmol), norbornene (10 mmol), catalyst (0.2 mmol), Bu_2O (20 ml), 80 °C, 18 h. [b] GC yield. [c] TfOH (0.6 mmol). [d] Many unknown products.

The present reaction is applicable to a wide range of carboxylic acids and alkenes, as summarized in Table 2 and Table 3. The compatibility of the $Fe(OTf)_3$ system is shown in Table 2. Various functional groups are tolerant to the presence of catalytic $Fe(OTf)_3$. The $Fe(OTf)_3$-catalysed reaction of reactive norbornene with acetic acid proceeded smoothly in slightly polar solvents like Bu_2O and chloroform (Table 3, entry 1). This is remarkable because the ruthenium catalyst failed to catalyse the reaction of norbornene with aliphatic carboxylic acids.[15] For less-strained alkenes, higher yields are generally obtained under solventless conditions. For example, cyclohexyl acetate was obtained from neat acetic acid and neat cyclohexene in moderate to good yields

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National Institute of Advanced Industrial Science and Technology (AIST), Tsukuba, Ibaraki 305-8565, Japan.
E-mail: junchul.choi@aist.go.jp; t-sakakura@aist.go.jp;
Fax: +81 29-861-4719; Tel: +81 29-861-4719

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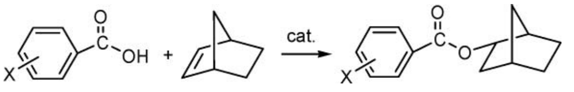
‡ Electronic supplementary information (ESI) available: Representative experimental procedure and characterization of the reaction products. See DOI: 10.1039/b713951a

Table 2 Functional group compatibility of $Fe(OTf)_3$-catalysed ester synthesis[a]

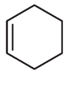
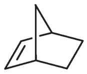
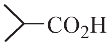
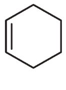
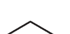
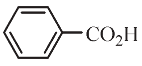
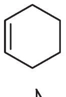
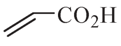
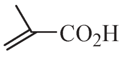
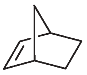


Entry	X	Yield (%)[b]
1	4-NO_2	95
2	4-Br	93
3	3-Cl	99[c]
4	H	99
5	4-OMe	98
6	4-COH	95
7	4-CO_2Me	93

[a] Reaction conditions: aromatic acid (10 mmol), norbornene (10 mmol), $Fe(OTf)_3$ (0.2 mmol), 1,4-dioxane (20 ml), 80 °C, 18 h. [b] GC yield. [c] Bu_2O instead of 1,4-dioxane.

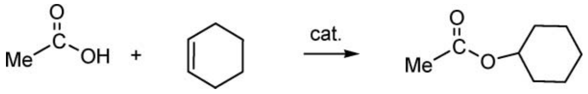
(Table 3, entry 2). It is noteworthy that copper and silver triflates unsuccessfully promoted the esterification of alkenes, except for norbornene.[12] Because the reverse reaction existed under the reaction conditions in Table 3 (eqn. (3)), using an excess amount of carboxylic acid or alkene improved ester yields (Table 3, entry 2). Similarly, bulkier isobutyric acid gave the corresponding norbornyl and cyclohexyl esters in good yields (Table 3, entries 3 and 4). The reaction of such bulky acids was not very successful for the gold-catalysed system.[13] In addition, linear alkenes like 1-octene produced the corresponding esters in good yields (Table 3, entry 5), but the regioisomers were also simultaneously produced. The $Fe(OTf)_3$-catalysed reaction was also applicable to the reaction of aromatic and vinylic acids with strained and unstrained alkenes.

Table 3 Ester formation *via* the addition of acids to alkenes[a]

Entry	Carboxylic acid	Alkene	Yield (%)
1	CH_3CO_2H		98[b]
2	CH_3CO_2H		61 70[c] 69[d]
3			99[b]
4			88[e]
5	CH_3CO_2H		78[f]
6			73[d]
7			99[b]
8			99[b]

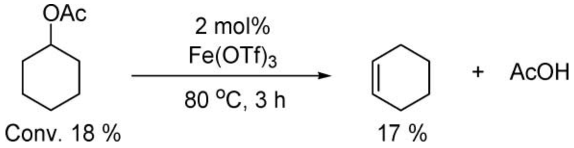
[a] Reaction conditions: carboxylic acid (10 mmol), alkene (10 mmol), $Fe(OTf)_3$ (0.2 mmol), no solvent, 80 °C, 3 h. [b] Bu_2O (20 ml), 18 h. [c] Carboxylic acid (20 mmol). [d] Alkene (20 mmol). [e] Carboxylic acid (40 mmol), 24 h. [f] Carboxylic acid (40 mmol), 12 h. Total yield of isomeric mixture of acetoxyoctane (2- : 3- : 4- = 74 : 21 : 5).

Table 4 The effect of catalyst on ester formation *via* the addition of acetic acid to cyclohexene[a]



Entry	Catalyst	Solvent	T/°C	Time/h	Yield (%)
1	$Fe(OTf)_3$ (2 mol%)	None	80	6	89
2	TfOH (1 mol%)	Toluene	80	18	52
3	TfOH (1 mol%)	Toluene	50	18	22
4	TfOH (2 mol%)	1,4-Dioxane	80	18	4

[a] *Reaction conditions:* Acetic acid : cyclohexene = 1 : 4. Entry 1: see Table 3. Entries 2 and 3: carried out under the recommended conditions of ref. 22. Entry 4: conducted under the recommended conditions of ref. 21.

 (3)

Recently, Hartwig *et al.*[21] and He *et al.*[22] reported that a catalytic amount of triflic acid (*e.g.* 1 mol%) promoted ester formation from alkenes and carboxylic acids, resulting in better yields compared to the reactions catalysed by gold triflate. The catalytic reactivities of $Fe(OTf)_3$ and TfOH were compared under their recommended reaction conditions (Table 4). Iron(III) triflate in solvent-free conditions gave the highest yield for the reaction of acetic acid and cyclohexene.

In summary, we have demonstrated that iron triflate is as effective as, or superior to, the triflates of precious metals, such as gold and ruthenium, or triflic acid alone, for the addition of carboxylic acids to alkenes. Compared to the gold triflate system,[13] less metal catalyst is needed to afford a higher yield, even for bulky isobutyric acid. In addition, the iron catalyst does not necessarily require excess alkene. If toxicity and resource availability are considered, then iron is the best central metal. Although iron compounds have been reported as water-stable Lewis acids,[23] little is known about the catalytic applications of $Fe(OTf)_3$ in organic synthesis, *i.e.* Friedel–Crafts reactions[24] and cyanation of carbonyl compounds.[25] This Communication clearly shows the promising abilities of iron compounds as suitable substitutes for precious metals in a variety of metal-catalysed reactions.

Notes and references

1 A relevant patent has already been applied: (*a*) J.-C. Choi, K. Kohno, H. Yasuda and T. Sakakura, AIST, *Jpn. Pat.*, JP-2006-036999 (February 17, 2006); (*b*) Part of this work was also presented at the 87th Annual Meeting of the Chemical Society of Japan, Osaka, Japan, March 25–28, 2007, abstracts 1D8-13 and 1D8-14.
2 N. Miyaura and A. Suzuki, *Chem. Rev.*, 1995, **95**, 2457–2483.
3 T. Ohkuma and R. Noyori, *J. Synth. Org. Chem., Jpn.*, 1996, **54**, 553–563.
4 S. Hashiguchi, N. Uematsu and R. Noyori, *J. Synth. Org. Chem., Jpn.*, 1997, **55**, 99–109.
5 H. C. Kolb, M. S. Vannieuwenhze and K. B. Sharpless, *Chem. Rev.*, 1994, **94**, 2483–2547.
6 A. L. McKnight and R. M. Waymouth, *Chem. Rev.*, 1998, **98**, 2587–2598.

7 M. R. Buchmeiser, *Chem. Rev.*, 2000, **100**, 1565–1604.
8 C. Bolm, J. Legros, J. Le Paih and L. Zani, *Chem. Rev.*, 2004, **104**, 6217–6254.
9 K. Ishihara, M. Nakayama, S. Ohara and H. Yamamoto, *Tetrahedron*, 2002, **58**, 8179–8188.
10 Y. Nakamura, T. Maki, X. W. Wang, K. Ishihara and H. Yamamoto, *Adv. Synth. Catal.*, 2006, **348**, 1505–1510.
11 *Organic Syntheses, Collective Volume 4*, ed. N. Rabjohn, John Wiley & Sons, New York, 1963, pp. 261.
12 J. G. Taylor, N. Whittall and K. K. M. Hii, *Chem. Commun.*, 2005, 5103–5105.
13 C. G. Yang and C. He, *J. Am. Chem. Soc.*, 2005, **127**, 6966–6967.
14 P. Roembke, H. Schmidbaur, S. Cronje and H. Raubenheimer, *J. Mol. Catal. A: Chem.*, 2004, **212**, 35–42.
15 Y. Oe, T. Ohta and Y. Ito, *Chem. Commun.*, 2004, 1620–1621.
16 Y. Oe, T. Ohta and Y. Ito, *Synlett*, 2005, 179–181.
17 H. Qian, X. Q. Han and R. A. Widenhoefer, *J. Am. Chem. Soc.*, 2004, **126**, 9536–9537.
18 C. G. Yang, N. W. Reich, Z. J. Shi and C. He, *Org. Lett.*, 2005, **7**, 4553–4556.
19 K. Komeyama, T. Morimoto and K. Takaki, *Angew. Chem., Int. Ed.*, 2006, **45**, 2938–2941.
20 J. S. Haynes, J. R. Sams and R. C. Thompson, *Can. J. Chem.*, 1981, **59**, 669–678.
21 D. C. Rosenfeld, S. Shekhar, A. Takemiya, M. Utsunomiya and J. F. Hartwig, *Org. Lett.*, 2006, **8**, 4179–4182.
22 Z. G. Li, J. L. Zhang, C. Brouwer, C. G. Yang, N. W. Reich and C. He, *Org. Lett.*, 2006, **8**, 4175–4178.
23 S. Kobayashi, S. Nagayama and T. Busujima, *J. Am. Chem. Soc.*, 1998, **120**, 8287–8288.
24 S. Kobayashi and I. Komoto, *Tetrahedron*, 2000, **56**, 6463–6465.
25 K. Iwanami, M. Aoyagi and T. Oriyama, *Tetrahedron Lett.*, 2006, **47**, 4741–4744.