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$FeCl_3$ catalyzed addition of activated methylenes to styrene derivatives under air

Zheng Duan,* Xuejie Xuan and Yangjie Wu*

Chemistry Department, The Key Lab of Chemical Biology and Organic Chemistry of Henan Province, The Key and Open Lab of Applied Chemistry of Henan Universities, Zhengzhou University, Zhengzhou 450052, PR China

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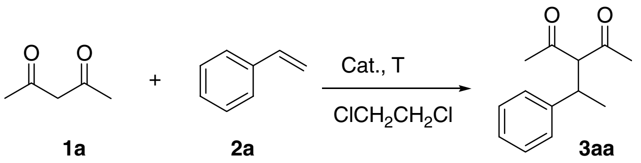
Abstract—An efficient addition of activated methylene to styrene derivatives catalyzed by cheap and environment-friendly $FeCl_3$ was developed. The reaction can be carried out under 'open-flask' conditions in which no precautions were taken to exclude moisture and air.

Transition metal catalyzed addition of 1,3-dicarbonyl compounds to alkene represents one of the efficient atom-economical organic processes and have attracted much attention in recent years. Very recently, Pd,[1] Au/Ag,[2] Ag[3] and Pt[4] catalyzed intra- or intermolecular addition of 1,3-dicarbonyl compounds to alkene[5] has been reported. Although these procedures are highly efficient, expensive catalysts have been used. It would be interesting to develop less expensive and environment-friendly catalyst for this type of reaction.

On the other hand, $FeCl_3$ is a green and efficient Lewis acid catalyst in modern organic synthesis.[6] It has become the focus of attention in several environmentally friendly and atom-economical organic transformations. Recent reports have highlighted the applications of $FeCl_3$ in organic synthesis.[7] Notably, $FeCl_3$ catalyzed hydroarylation of styrenes and arylation of benzyl alcohols.[7a,b] Christoffers reported ferric chloride hexahydrate catalyzed the Michael reaction of 1,3-dicarbonyl compounds with α,β-unsaturated ketones under mild and non-basic conditions with extraordinary efficiency.[8] These results encouraged us to attempt the addition of 1,3-dicarbonyl compounds to styrene catalyzed by cheaper and environment-friendly $FeCl_3$.

For the initial screening of catalyst performance, the addition of 2,4-pentanedione to styrene was selected as a model. After the reaction conditions were optimized, 1,2-dichloroethane (DCE) was chosen as the solvent. The effects of catalyst and reaction temperature were summarized in Table 1.

Table 1. Addition of 2,4–pentanedione to styrene catalyzed by iron(III) compounds



Entry	Catalyst (mol %)		T (°C)	**1**:**2**[a] (mol:mol)	Yield[b] (%)
1	$FeCl_3$	(20)	25	1:2.4	Trace
2	$FeCl_3$	(20)	60	1:2.4	63
3	$FeCl_3$	(20)	80	1:2.4	69
4	$FeCl_3$	(20)	85	1:2.4	17
5	$FeCl_3$	(20)	80	1:1.2	38
6	$FeCl_3$	(20)	80	1:6	77
7	$FeCl_3$	(20)	80	1:4.8	77
8	$FeCl_3$	(10)	80	1:4.8	Trace
9	$FeCl_3$	(30)	80	1:4.8	86
10	$FeCl_3$	(40)	80	1:4.8	82
11	$FeCl_3·6H_2O$	(20)	80	1:2.4	64
12	$Fe(acac)_3$	(20)	80	1:2.4	—
13	Fe_2O_3	(10)	80	1:2.4	—

[a] 0.5 mmol styrene was dissolved in 2 mL DCE. The solution was added by a syringe to the mixture of catalyst and 2,4-pentanedione in DCE (3 mL) in 5 h.

[b] Isolated yield.

Keywords: $FeCl_3$; Catalyzed; Hydroalkylation.

* Corresponding authors. Tel.: +86 371 67767993; fax: +86 371 67979408 (Z.D.); e-mail addresses: duanzheng@zzu.edu.cn; wyj@zzu.edu.cn

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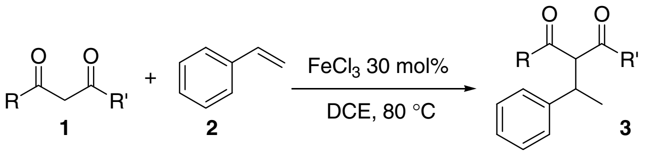
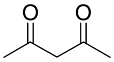
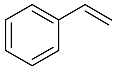
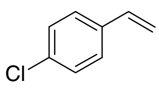
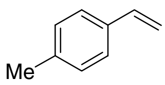
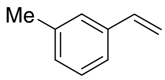
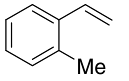
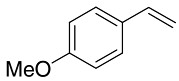
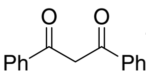
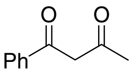
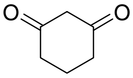
As shown in Table 1, $FeCl_3$ exhibited good catalytic activity. The best result was obtained in the presence of 30 mol % $FeCl_3$ (Table 1, entry 9). Only trace amount of product was obtained, when 10 mol % $FeCl_3$ was used (entry 8). This $FeCl_3$ catalyzed addition reaction is moisture and air stable. The solvent and chemicals were used as they were received commercially. Small amount of water did not affect the reaction and the experimental result using $FeCl_3$ (69%, entry 3) and $FeCl_3{\cdot}6H_2O$ (64%, entry 11). All the reactions were carried out under air. The use of other common Fe(III) species such as $Fe(acac)_3$ and Fe_2O_3 showed no catalytic activity. The reaction temperature is crucial. Low or high temperature decreased the catalytic activity of the reaction considerably (entries 1, 4). The best result was obtained when the reaction was carried out at 80 °C.

Subsequently, we explored the generality of the $FeCl_3$-catalyzed addition. In most cases, the reactions between the activated methylenes and the styrene derivatives proceeded very well and moderate to good yields were obtained (Table 2). In some cases, the reaction must be carried out under room temperature in order to prevent the polymerization of the styrenes (Table 2, entries 6, 7, 9, 10). When highly activated styrene **2f** was used, the product was isolated only in 52% yield. No desired product was obtained when cyclic 1,3-diketones **1d** was used.

In conclusion, we have developed an efficient addition of activated methylenes to styrene derivatives by using cheap and environment-friendly iron catalyst. This catalytic addition can be operated under 'open-flask' conditions. No precautions were taken to exclude moisture

Table 2. The typical results of $FeCl_3$ catalyzed addition



Entry	β-Diketone	Alkene	Product	Isolated yield (%)
1	 **1a**	 **2a**	**3aa**	86
2	**1a**	 **2b**	**3ab**	72
3	**1a**	 **2c**	**3ac**	92
4	**1a**	 **2d**	**3ad**	82
5	**1a**	 **2e**	**3ae**	79
6	**1a**	 **2f**	**3af**	23(52)[a]
7	 **1b**	**2a**	**3ba**	90(92)[a]
8	**1b**	**2b**	**3bb**	66
9	**1b**	**2d**	**3bd**	45(81)[a]
10	**1b**	**2e**	**3be**	32(90)[a]
11	 **1c**	**2a**	**3ca**	89
12	**1c**	**2b**	**3cb**	51
13	**1c**	**2d**	**3cd**	96
14	**1c**	**2e**	**3ce**	84
15	 **1d**	**2a**	—	—

[a] The results of the reactions carried out at room temperature are given in parantheses.

and air from the reaction system. Our efforts are currently directed to the reaction mechanism and the application scope of this $FeCl_3$ catalyzed reaction.

Acknowledgements

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