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Friedel–Crafts reactions catalyzed by samarium diiodide

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Abstract—Samarium diiodide is an efficient precatalyst for the Friedel–Crafts reaction involving various aromatic substrates and chelating electrophiles. Alkyl 3,3,3-trifluoropyruvates are transformed into α-hydroxyesters in good yields with total regioselectivity. In reactions involving an ethyl glyoxylate or a glyoxylic imine, α-hydroxyesters or α-aminoesters are obtained with variable amounts of products resulting from a double Friedel–Crafts reaction.

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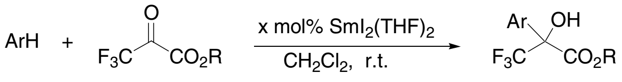
Friedel–Crafts reaction[1] is one of the oldest carbon–carbon bond forming processes, and is still an attractive method to introduce substituents on aromatic rings. Initial works concerned Friedel–Crafts acylation from acyl chlorides or alkylation from alkyl halides. To perform acylations, Lewis acids are needed. More than stoichiometric amounts of $AlCl_3$ or BF_3 are required whereas catalytic amounts of rare-earth triflates,[2] more specially scandium triflate,[3] perfluorinated rare earth metals,[4] gallium triflate[5] or bismuth triflate,[6] allow the formation of the expected products. However, it is sometimes necessary to add $LiClO_4$ and to carry out reactions in nitromethane to improve the activity of $Sc(OTf)_3$ or $Yb(OTf)_3$.[7] Lanthanide chlorides (30 mol %) catalyze the alkylation of benzene with benzyl halides.[8] Catalyzed Friedel–Crafts reactions, involving electron-rich aromatic compounds and electrophiles such as aldehydes, ketones, imines, or benzyl alcohols[9] have been recently described. Reactions with benzyl alcohol can be improved using rare-earth triflates supported in mesoporous silica.[10] Electrophiles such as trifluoropyruvates and activated alkenes were tested in asymmetric Friedel–Crafts reactions using chiral copper[11] or scandium catalysts.[12]

We have previously shown that $SmI_2(THF)_2$ in methylene chloride is an efficient Lewis acid precatalyst for different reactions such as tandem Michael–aldol reactions,[13] tandem Michael–iminoaldol reactions,[14] ring opening of epoxides by amines[15] or aza-Michael reactions.[16] We now wish to report our first results concerning the use of samarium diiodide as a precatalyst for Friedel–Crafts reactions.



Scheme 1.

The catalytic activity of samarium diiodide was first investigated in the reaction of ethyl and methyl pyruvates with indole **1**, which is usually employed as a strong nucleophile in alkylation reactions leading to interesting molecules[17] (Scheme 1). A solution of indole in dichloromethane was added to a suspension of 10 mol % $SmI_2(THF)_2$ in CH_2Cl_2, followed by addition of alkyl trifluoropyruvate. Then, the reaction mixture changed from a blue suspension to a yellow solution, indicating the trivalent state of samarium.[18] The expected α-hydroxy-esters were obtained in good yields after 18 h reaction time at room temperature (Table 1, entries 1 and 3). Reactions of electron-rich aromatic compounds such as *N*,*N*-dimethylaniline **2**, *N*,*N*-dimethyl-*m*-anisidine **3** or 1,3-dimethoxybenzene **4** with ethyl and methyl trifluoropyruvates have been also examined.

In all reactions, a complete conversion was observed and only one product was isolated. No trace of other isomers was detected, indicating a total regioselectivity. Substrates **1**, **2** and **3** react faster than 1,3-dimethoxybenzene **4** and no reaction was observed with 1,4-dimethoxybenzene in the same conditions. The strongly electron

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Keywords: Friedel–Crafts reaction; Samarium diiodide; Catalysis; Carbon–carbon bond formation.

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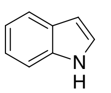
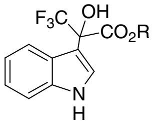
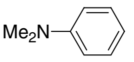
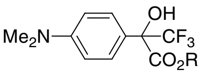
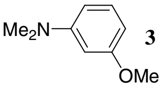
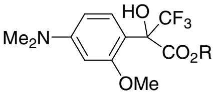
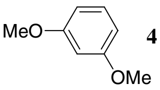
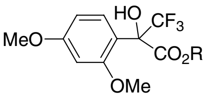
Table 1. Alkylation of trifluoropyruvates catalyzed by samarium diiodide

Entry	ArH	R	x (mol %)	Time (h)	Product		Yield[a,b] (%)
1	 **1**	Et	10	18		**5a**	81
2		Et	1	0.5		**5a**	79
3		Me	10	18		**5b**	91
4	 **2**	Et	10	5		**6a**	90
5		Me	5	1		**6b**	99
6	 **3**	Et	10	18		**7a**	70
7	 **4**	Et	10	63		**8a**	63[c]
8		Me	10	114		**8b**	75

[a] See Ref. 14a for a typical procedure.

[b] Isolated yield. 100% conversion. All products were fully characterized by spectroscopic data and compared to literature.

[c] 75% conversion.

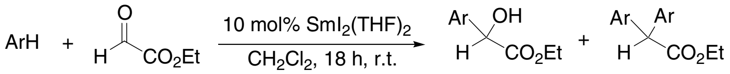
withdrawing trifluoromethyl group increases the electrophilic property of the carbonyl. No reaction was indeed observed between ethyl pyruvate and *N*,*N*-dimethylaniline in the presence of 10 mol % samarium diiodide. For the optimization of the experimental conditions, the reaction between *N*,*N*-dimethylaniline **2** and methyl 3,3,3-trifluoropyruvate was performed using 5 mol % $SmI_2(THF)_2$. Product **6b** was obtained in high yield and a complete conversion was observed in 1 h (entry 5). For this reaction, samarium diiodide appears as a more active catalyst than copper, scandium or indium triflates.[19]

Furthermore, the use of only 1 mol % $SmI_2(THF)_2$ for the reaction of indole **1** with ethyl 3,3,3-trifluoropyruvate allowed a complete conversion into product **5a** within 30 min (entry 2), whereas 10 mol % $Ga(OTf)_3$ had been needed.[20] Under the same conditions, *N*,*N*-dimethylaniline **2** led to 53% conversion, confirming the stronger nucleophilicity of indole.

Friedel–Crafts alkylations with other chelating substrates, such as ethyl glyoxylate and glyoxylic imines, which can lead to interesting α-hydroxy- and α-amino-esters, were also investigated. We first studied the reaction of ethyl glyoxylate with aromatic compounds **1**, **2** and **3** in the presence of 10 mol % samarium diiodide (Scheme 2 and Table 2). Two products are formed, the desired α-hydroxy-esters **9a**–**11a** and products **9b**–**11b** identified as arising from a double Friedel–Crafts reaction with dehydration. This double Friedel–Crafts reaction had already been reported for reactions catalyzed by ytterbium and scandium triflates,[3] and the hydrolysis of the ester group was observed. Surprisingly, in the reactions catalyzed by samarium diiodide, the presence of a small amount of water does not inhibit the activity of the catalyst since the conversion is complete. Moreover, the hydrolysis of the ester function was never observed. We unsuccessfully tested a slow addition of aromatic compounds to reduce the formation of the double Friedel–Crafts product.

The reaction of aromatic compounds with glyoxylic imine **12** has been studied in the same conditions as described above, and afforded the Friedel–Crafts and the double Friedel–Crafts products (Scheme 3 and Table 3).

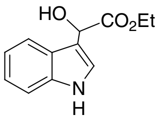
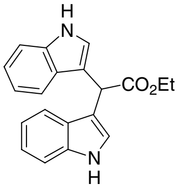
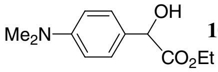
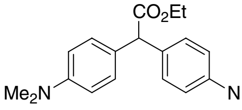
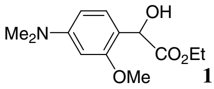
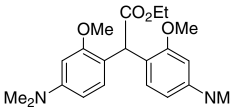
With indole **1**, the reaction gave a mixture of the expected aminoester **13a** and of **9b** arising from a double Friedel–Crafts reaction. These two products could not be separated by chromatography and a 51:49 ratio was evaluated by ^1H NMR analysis of the crude product. Elimination of amine had already been reported in reaction of indole with *N*-benzylidene aniline catalyzed by lanthanide triflates.[21] By the use of 1 mol % samarium diiodide, a complete conversion was observed after 30 min with a 68:32 ratio for compounds **13a** and **9b**, respectively (entry 2).[22] Similarly, for the reaction involving *N*,*N*-dimethyl-*m*-anisidine **3** catalyzed by 10 mol % samarium diiodide, the ratio of products **15a** and **11b** depends on the reaction time. Interestingly, Friedel–Crafts reaction of imine **12** with *N*,*N*-dimethylaniline **2** was highly selective since only aminoester **14a** was isolated in 75% yield (entry 3).



1-3 **9a-11a** **9b-11b**

Scheme 2.

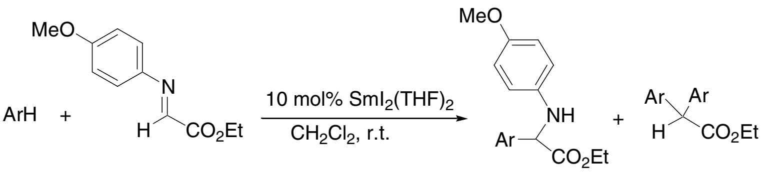
Table 2. Alkylation of ethyl glyoxylate catalyzed by samarium diiodide

Entry	ArH	Product **a**	Product **b**	Yield **a**[a,b] (%)	Yield **b**[a,b] (%)	**a/b**[c]
1	**1**	 **9a**	 **9b**	38	22	75/25
2	**2**	 **10a**	 **10b**	14	50	22/78
3	**3**	 **11a**	 **11b**	32	16	81/19

[a] Isolated yield. Compounds **a** and **b** have been separated by chromatography.

[b] All products were fully characterized by spectroscopic data and compared to literature except **11b** which is a new compound.

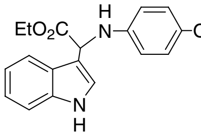
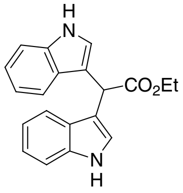
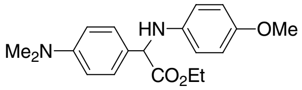
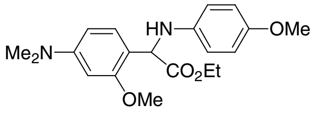
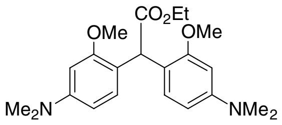
[c] Ratio determined by ^{1}H NMR spectroscopy on the crude product.



1-3 **12** **13a-15a** **9b-11b**

Scheme 3.

Table 3. Alkylation of ethyl glyoxylic imine **12** catalyzed by samarium diiodide

Entry	ArH	Product **a**	Product **b**	Time (h)	**a/b**[a]	Yield (%)
1	**1**		 **9b**	18	51/49	46[b]
2	**1**	**13a**		0.5[d]	68/32	44[b]
3	**2**	 **14a**	—	18	100/0	75[c]
4	**3**			0.5	31/69	69[b]
5	**3**	**15a**	**11b**	18	0/100	35[c]

[a] Ratio determined by ^{1}H NMR spectroscopy on the crude product.

[b] Yield given for the mixture of products.

[c] Isolated yield.

[d] 1 mol % $SmI_2(THF)_2$ was used.

In conclusion, samarium diiodide is an efficient precatalyst for a variety of Friedel–Crafts reactions and compares well to other catalysts in terms of activity. Several selective preparations of aromatic α-hydroxyesters or α-amino-esters have been described. Recently, we have reported that samarium iodo binaphtholate is an enantioselective catalyst for the aminolysis of epoxides[23] and aza-Michael reactions.[24] Studies of enantioselective Friedel–Crafts reactions are currently in progress.

Acknowledgements

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