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Gallium(III) trifluormethanesulfonate: a water-tolerant, reusable Lewis acid catalyst for Friedel–Crafts reactions

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The application of gallium(III) trifluoromethanesulfonate (triflate, OTf) in Friedel–Crafts alkylation and acylation reactions is described. Gallium triflate was found to be an excellent catalyst for the adamantylation of toluene with 1-bromoadamantane, where its activity was compared to that of well-known rare earth metal triflates. As $Ga(OTf)_3$ does not decompose in the presence of water the isopropylation of aromatics can be carried out with isopropyl alcohol in moderate to excellent yields. While acetylation provides moderate yields in selective reactions, benzoylation of aromatics takes place in good yields in a catalytic and non-stoichiometric reaction. The catalyst can easily be recovered from the reaction mixture and can be reused without loss of activity, demonstrating its effective and environmentally friendly recyclable character.

KEY WORDS: gallium triflate; regioselective adamantylation; alkylation with isopropyl alcohol; acylation; environmentally benign catalysis.

1. Introduction

Although the first steps in Friedel–Crafts chemistry were carried out more than a century ago [1–3], the topic still receives much attention and is a frequently studied area of catalytic organic chemistry. In recent years, due to the high demand for environmentally benign ("green") processes, the use of conventional, effective but harmful and corrosive catalysts and promoters ($AlCl_3$, BF_3, H_2SO_4, etc.) for large-scale industrial applications is being discouraged. Although $AlCl_3$ can be recycled in some alkylation reactions [4], its use in catalytic amounts in acylation reactions does not work, since the Lewis acid is complexed by the carbonyl product [5]. Powerful Brønsted acids, such as trifluoromethanesulfonic acid [6], etc., were also found to be effective in promoting Friedel–Crafts chemistry. However, since these acid systems are also sensitive to moisture their recovery to an anhydrous state is not practical. As a result, the interest in Lewis acids that can promote Friedel–Crafts chemistry, including acylation, in catalytic amounts has increased. Metal trifluoromethanesulfonates (triflates) are one of the most important candidates in this group. Since the first preparation of trifluoromethanesulfonic acid (triflic acid, HOTf) [7] numerous metal triflates have been synthesized and applied in various organic reactions. Among these applications the rare earth metal triflates have played a dominant role [8,9]. The majority of reports are concerned with Friedel–Crafts alkylation [10] and acylation [11]. However, they are also capable of catalyzing a wide range of organic transformations such as cross aldol chemistry [12]. The triflates of group IIIA metals (B, Al, Ga) are much less studied; however, their synthesis and characterization were described [13,14].

In continuation of our studies on catalytic Friedel–Crafts reactions, herein we report the application of gallium(III) triflate as an effective water-tolerant Lewis acid catalyst in alkylation and acylation of aromatics. The activity of gallium triflate is compared with that of the most well-known rare earth metal triflates. The environmentally friendly character is demonstrated by the catalyst recovery and reuse in benzoylation reaction.

2. Experimental

2.1. Materials

Ga metal (99.9999%) was purchased from Aldrich, while trifluoromethanesulfonic acid (99.5%) was available from 3M. All the other lanthanide triflates used for comparison ($La(OTf)_3$, $Y(OTf)_3$, $Sm(OTf)_3$, $Sc(OTf)_3$ and $Yb(OTf)_3$) were Aldrich products. 1-Bromoadamantane and most of the aromatic solvents were also purchased from Aldrich, while benzene and toluene (99.9%) were J.T. Baker products. Acetyl chloride, benzoyl chloride and 2-propanol were purchased from Aldrich, and used as received.

2.2. Preparation of $Ga(OTf)_3$

$Ga(OTf)_3$ was prepared according to the following procedure [15]: 2.45 g of gallium metal (35 mmol) and

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30 g of trifluoromethanesulfonic acid (200 mmol) were placed into a 100 ml round-bottomed flask and the mixture was stirred at 150 °C for 1 day. After cooling (0 °C) the mixture was poured into 200 g of ice. The solution obtained was filtered to remove the unreacted Ga and other insoluble material. The water and excess triflic acid were removed first by evaporation and then the residue was heated to 200 °C for 5 h under vacuum; 12.2 g of $Ga(OTf)_3$ was obtained as a white powder.

2.3. *General method for adamantylation of toluene with 1-bromoadamantane catalyzed by metal triflates*

The reactions were carried out in a 10 ml round-bottomed flask equipped with a reflux condenser and a magnetic stirrer. A mixture of 200 mg (0.46 mmol) of 1-bromoadamantane and 100 mg of catalyst (0.19 mmol for $Ga(OTf)_3$) were introduced into the flask, and then 2.0 ml of toluene was added. The reaction mixture was heated to the desired temperature and stirred for 15–30 min then poured onto 5 g of ice. The products were extracted with CH_2Cl_2. Removal of the solvent in a rotary evaporator provided the product. Gallium triflate can be simply recovered from the aqueous solution by evaporation of water and extensive drying.

2.4. *General method for $Ga(OTf)_3$-catalyzed alkylation of aromatics with 2-propanol*

A total of 26 mg of $Ga(OTf)_3$ (0.05 mmol) was suspended in 2 ml of ethylene dichloride in a glass pressure tube, then 1 mmol of aromatic substrate and 0.3 ml (4 mmol) of isopropyl alcohol were introduced. The reaction mixture was stirred at 120 °C for 18–24 h. The catalyst was then removed by filtration, and the solution was treated with 3 ml of water, and extracted by CH_2Cl_2. After drying with $MgSO_4$ and evaporation of the solvent, the product was isolated as a colorless liquid.

2.5. *General method for $Ga(OTf)_3$-catalyzed benzoylation of aromatics with benzoyl chloride*

A total of 100 mg of dry $Ga(OTf)_3$ (0.19 mmol) was placed into a 25 ml round-bottomed flask equipped with a rubber septum, and then 0.5 ml of benzoyl chloride (3.7 mmol) and 10 ml of aromatic compound were introduced through the septum. The reaction time and temperature were optimized to achieve maximum yield (see table 3). The reaction mixture was poured into 20 ml of water, the product was extracted by CH_2Cl_2 and isolated, while the gallium triflate was recovered from the aqueous solution.

2.6. *General method for $Ga(OTf)_3$-catalyzed acetylation of aromatics with acetyl chloride*

A total of 100 mg of dry $Ga(OTf)_3$ (0.19 mmol) was placed in a 25 ml round-bottomed flask equipped with a rubber septum, and then 0.32 ml of acetyl chloride (3.7 mmol) and 10 ml of aromatic compound were introduced through the septum. The reaction mixture was stirred at room temperature for 3 h and then poured into 20 ml of water. The product was extracted by CH_2Cl_2 and isolated.

2.7. *Analysis*

The products were identified on the basis of their ^1H and ^{13}C NMR (Varian Unity 300 and Bruker AMX500) and mass spectra (HP-5890 GC coupled with an HP-5970 mass spectrometer). The isomeric distribution of the products was determined by ^1H NMR and gas chromatographic analyses with a Varian 3400 GC coupled with flame ionization detector on a 30 m long DB-5 capillary column, with helium as the carrier gas.

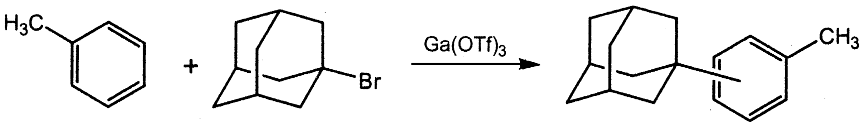
3. Results and discussion

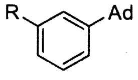
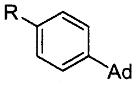
Although rare earth metal triflates are frequently used as Lewis acid catalysts in catalytic organic reactions, the use of gallium triflate, despite its powerful acidic character, is only sporadic. Since gallium(III) triflate is a strong and water-resistant Lewis acid, its use could be useful even in practical/industrial applications. We decided to test the activity and selectivity of gallium triflate and compare the parameters to those of other well-known, mostly lanthadide triflates. The test reaction chosen was the Friedel–Crafts adamantylation of toluene, which theoretically can produce three isomeric products [16].

It was pointed out that in solid acid-catalyzed adamantylation reactions only *m*- and *p*-products were formed and the isomeric ratio of the tolyl adamantanes formed were highly dependent on the acid strength of the catalyst. Kinetic measurements have revealed that the product ratio is the result of a secondary isomerization reaction: the *p*-product can rearrange to the *m*-isomer. Depending on the acid strength the isomerization rates varied; however, no isomerization was observed below the Hammett values of $H_0 \sim -12$ [17]. These features, such as rate and stereoselectivity of the reaction, make this reaction a valuable test reaction for studying acid catalysts. Although with Lewis acids one cannot give exact numerical values such as H_0 to characterize acidity [18], one can still compare the activity and selectivity of the catalysts. The reactions were carried out using different triflates at different temperatures; both the reaction rates and selectivity data were determined. The results are collected in table 1.

As shown, each catalyst is capable of catalyzing the reaction. However, the activity ranges of the various triflates vary widely. While some triflates are effective catalysts only at higher temperature (120 °C), gallium triflate is still active at ambient temperature. This feature

Table 1
Adamantylation of toluene with 1-bromoadamantane catalyzed by metal triflates



Catalyst	Temp. (°C)	Time (min)	Yield (%)	r (mmol g^{-1} min^{-1})	 (%)	 (%)	Di-tolyl adamantane (%)
La(OTf)$_3$	120	15	100	0.54	5	95	–
	80	30	–	–	–	–	–
Sm(OTf)$_3$	120	15	86	0.26	6	94	–
	80	30	–	–	–	–	–
Sc(OTf)$_3$	80	15	21	0.06	0	100	–
Yb(OTf)$_3$	120	30	100	0.82	5	95	–
	80	15	9	0.03	5	95	–
	50	15	0.5	0.001	0	100	–
Y(OTf)$_3$	120	30	100	0.43	42	50	8
	80	15	–	–	–	–	–
Ga(OTf)$_3$	120	5	100	–	45	25	30
	80	5	100	–	47	32	21
	50	5	100	–	60	29	11
	35	5	100	–	53	41	6
	22	5	54	0.49	47	53	1

is also related to the selectivity obtained. While the least reactive triflates produced *p*-tolyl adamantane selectively, using Ga(OTf)$_3$ the selectivity shifted, as a result of the extensive isomerization reaction to the *m*-product. According to the data, gallium triflate was found to be a very effective and strong Lewis acid catalyst, its activity exceeding that of well-known lanthanide triflates.

Having realized the efficacy of Ga(OTf)$_3$ in adamantylation it was used as a catalyst in two important Friedel–Crafts reactions: alkylation reactions with isopropyl alcohol and acylation of aromatics with benzoyl chloride and acetyl chloride.

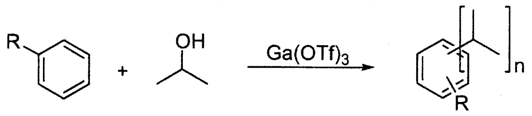
In general, Friedel–Crafts alkylation reactions are carried out using alkyl halides. However, since Ga(OTf)$_3$ does not decompose in the presence of water, alcohols can be used as alkylating agents [19]. As a representative example, the alkylation reaction was carried out using excess isopropyl alcohol as the alkylating agent to demonstrate the catalyst's activity and stability. The results are shown in table 2.

As shown, the alkylation reaction took place in moderate to excellent yields in the case of benzene and activated derivatives. However, using halobenzenes, such as fluoro- and chlorobenzene, the reaction is sluggish, and even after an extended reaction time the yields are low. In most cases, the formation of monoalkylated derivative is preferred; however, dialkylated derivatives were also formed. The high activity of gallium triflate is demonstrated with the formation of tri- and tetraalkylated products, especially with less crowded substrates (benzene, toluene, anisole).

The benzoylation reaction was also studied with a wide range of aromatics, including hydrocarbons and halogenated aromatics. The results are summarized in table 3.

Since Lewis acids are usually used in stoichiometric amount in Friedel–Crafts acylation reactions, it is important to note that gallium triflate was used only in catalytic amount, 8.9 mol% with respect to benzoyl chloride. In contrast, stronger Lewis acids such as

Table 2
Alkylation of aromatics with isopropyl alcohol catalyzed by Ga(OTf)$_3$ at 120 °C (24 h reaction time)

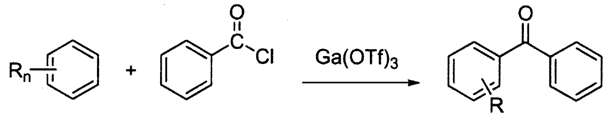


R = H, Me, Et, di-Me (*o*, *m*, *p*), OMe, F, Cl, $n = 1$–4

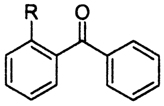
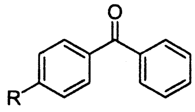
R	Yield (%)	Selectivity [a]			
		Mono (%)	Di (%)	Tri (%)	Tetra (%)
H	56	76	15	5	4
CH$_3$	38	55	29	16	–
o-diMe	70	93	7	–	–
m-diMe	96	23	69	8	–
p-diMe	82	62	38	–	–
1,3,5-triMe	97	45	55	–	–
OCH$_3$	96	22	34	42	2
Cl	2	100	–	–	–
F	16	53	35	12	–

[a] Distribution of mono-, di-, tri- and tetraalkylated products.

Table 3
Benzoylation of aromatics with benzoyl chloride catalyzed by Ga(OTf)$_3$



R = H, Me, Et, *sec*-butyl, *tert*-butyl, di-Me (*o*, *m*, *p*), Tri-Me (1, 3, 5), F, Cl, CF$_3$

Aromatic	Temp. (°C)	Time (h)	Yield (%)	 (%)	 (%)
Benzene	80	20	68	–	–
Toluene	110	8	94	7	93
Ethylbenzene	100	20	71	8	92
Bu^s-benzene	100	24	68	13	87
Bu^t-benzene	100	24	76	15	85
o-Xylene	80	14	73	a	a
m-Xylene	80	14	97	b	b
p-Xylene	80	14	64	c	c
Mesitylene	100	24	76	–	–
F-benzene	90	20	49	0	100
Cl-benzene	100	24	67	5	95
CF$_3$-benzene	100	24	10	1	99

[a] Product selectivity: 3′,4′-dimethylbenzophenone (98%); 2′,3′-dimethylbenzophenone (2%).
[b] Product selectivity: 2′,4′-dimethylbenzophenone (100%).
[c] Product selectivity: 2′,5′-dimethylbenzophenone (100%).

AlCl$_3$ are complexed by the product ketones, and thus they are used in stoichiometric amount [1,2]. Ga(OTf)$_3$ does not form such a strong complex and is able to act as a catalyst in the reaction. The results show that the corresponding ketones were formed in good to excellent yields except in the case of trifluoromethylbenzene, for which only 10% product yield was obtained. The selective formation of *p*-product was observed in each case. Although in the case of deactivated substrates (fluoro-, chlorobenzenes) the yields are only moderate, the *p*-selectivities are, however, excellent (up to 100% selectivity), which make the reaction practical. During the reaction the HCl produced may also catalyze Friedel–Crafts acylation. The product accumulation vs. time plot in the benzoylation of benzene (figure 1), however, shows no induction period, indicating that Ga(OTf)$_3$ is the only catalytic species in the reaction.

Besides benzoylation, acetylation is also a very important reaction in Friedel–Crafts chemistry. However, the acetylation does not occur readily, and to find a proper recyclable solid catalyst for this reaction is still a challenge [11]. The success with gallium triflate-catalyzed benzoylations prompted us to pursue acetylations using acetyl chloride as the acylating agent. The results are shown in table 4.

The reaction took place with high (close to 100%) chemo- and regioselectivity at room temperature. However, the yields are moderate. The application of more

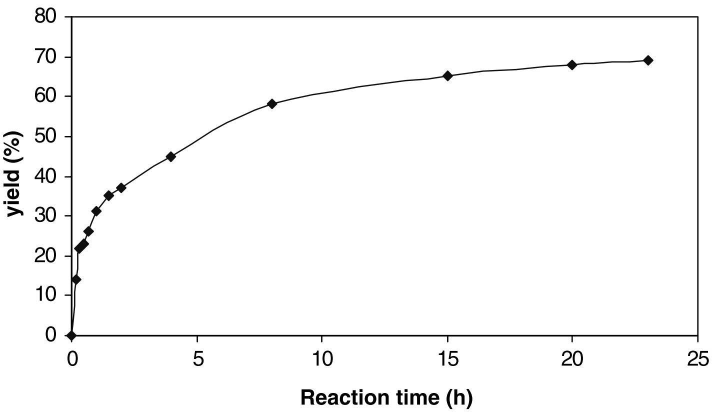
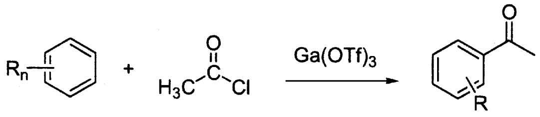
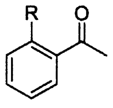
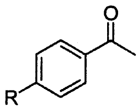


Figure 1. Product accumulation as a function of reaction time in the Ga(OTf)$_3$-catalyzed benzoylation of benzene at 80 °C.

Table 4
Acetylation of aromatics with acetyl chloride catalyzed by $Ga(OTf)_3$ at room temperature (reaction time 3 h)



R = H, Me, Et, *sec*-butyl, *tert*-butyl, di-Me (*o*, *m*, *p*), Tri-Me (1, 3, 5)

Aromatic	Yield (%)	 (%)	 (%)
Benzene	12	–	–
Toluene	23	5	95
$\mathrm{Bu^s}$-benzene	32	1	99
o-Xylene	31	a	a
m-Xylene	37	b	b
p-Xylene	30	c	c
Mesitylene	48	–	–

[a] Product selectivity: 3′,4′-dimethylacetophenone (94%); 2′,3′-dimethylacetophenone (6%).

[b] Product selectivity: 2′,4′-dimethylacetophenone (100%).

[c] Product selectivity: 2′,5′-dimethylacetophenone (100%).

severe reaction conditions, e.g. higher temperatures or increase in reaction time, however, does not result in higher yields, due to the extensive byproduct formation (secondary acylation, self-condensation, etc.).

To represent the environmentally benign “green” character of $Ga(OTf)_3$, the recyclable character of the catalyst was also investigated. $Ga(OTf)_3$ was recovered after the reaction by evaporating the aqueous solution and subsequent drying in vacuum. The dry catalyst was used again in the next reaction without further regeneration and was recovered after each reaction accordingly. The results obtained in the series of reactions are illustrated in figure 2. As the data show no significant deactivation, even after the fourth use, the gallium triflate appears to be a highly stable and easily recoverable catalyst.

4. Conclusion

The application of gallium triflate as an effective Lewis acid catalyst has been illustrated by its use in several Friedel–Crafts reactions. Our comparative study on adamantylation of toluene showed that the activity of gallium(III) triflate clearly exceeds that of traditional rare earth triflates. It should also be pointed out that due to its lower sensitivity to water, alcohols can be used as alkylating agents. Acetylation and benzoylation of aromatics also took place in moderate to good yields with high selectivity in a catalytic, non-stoichiometric reaction. One of the significant features of gallium triflate is that it can be recovered and recycled, even in acylation reactions, increasing its potential as a useful, strong Lewis acid catalyst for other applications.

Acknowledgment

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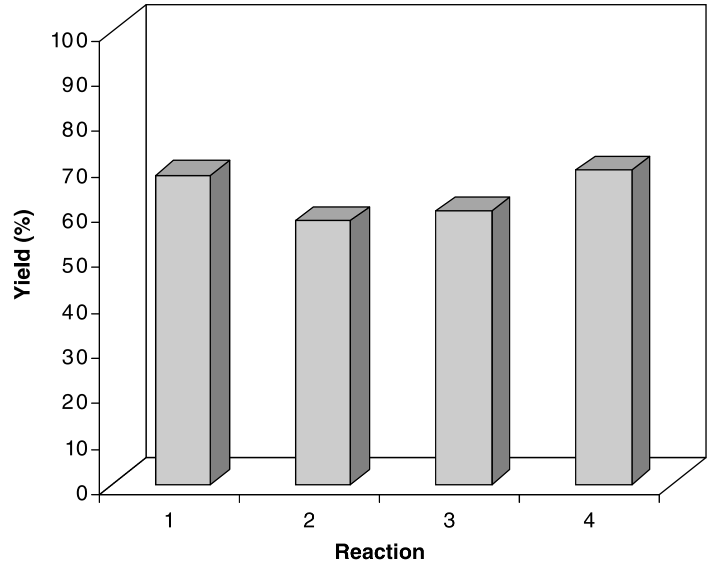

Figure 2. Effect of catalyst reuse on the product yield in the $Ga(OTf)_3$-catalyzed benzoylation of benzene at 80 °C.

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