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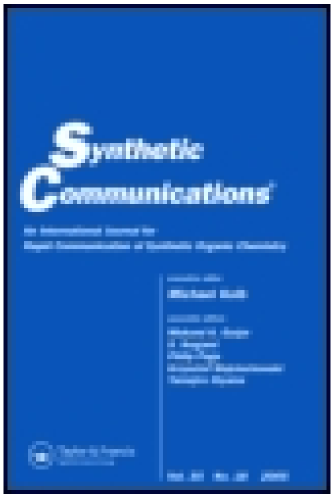

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Microwave-Assisted Facile and Rapid Friedel-Crafts Benzoylation of Arenes Catalysed by Bismuth Trifluoromethanesulfonate

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Microwave-assisted facile and rapid Friedel-Crafts benzoylation of arenes catalysed by bismuth trifluoromethanesulfonate

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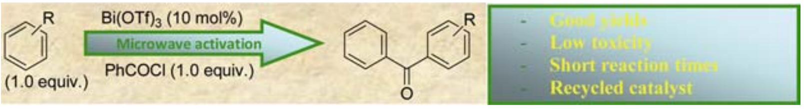
Abstract

Metal triflates were investigated the catalytic activity for Friedel-Crafts benzoylation under microwave irradiation. Among these, bismuth triflate was found to be the most effective. Friedel-Crafts benzoylation of a variety of arenes containing electron-rich and electron-poor rings with benzoyl chloride using bismuth triflate under microwave irradiation is described. This method allows the preparation of aryl ketones under solventless condition in good to excellent yields and short reaction time. Bismuth triflate was easily recovered and reused five times without significant loss of the catalytic activity.



KEYWORDS: Friedel-Crafts benzoylation, bismuth triflate, microwave irradiation, aryl ketone

INTRODUCTION

The Friedel-Crafts benzoylation of arenes is a fundamental and useful reaction to synthesize aryl ketones, which are important precursors in the pharmaceutical and agrochemical industries.[1] Characteristic for Friedel-Crafts reactions is the use of moisture sensitive strong Lewis acids in greater than stoichiometric amounts and the decomposition of the catalysts during work-up.[1] Therefore, the development of moisture-stable and recyclable catalysts is the most interesting challenge in the Friedel-Crafts acylation.[2]

Metal triflates were found to be efficient and green catalysts for the Friedel-Crafts acylation.[3–6] These catalysts are water-tolerant Lewis acids, the metal triflates are used only catalytic amounts and still active in the coexistence of Lewis bases.[7] The metal triflates are also easily recovered and reused without significant loss of the catalytic activity. However, under conventional heating, metal triflates-catalyzed Friedel-Crafts acylations involve long reaction time[8–11] and a large excess of hazardous solvent.[12–15]

From the viewpoint of the green chemistry, safer solvents (or solventless) and energy efficiency are required for environmental and economic processes.[16] Microwave irradiation has been achieved great success in organic synthesis.[17] Microwave irradiation promotes the organic reactions only a few minutes with minimum energy because the energy is transferred directly to the reaction mixture.[18] The Friedel-Crafts acylation under microwave irradiation has been studied intensively in the presence of various catalysts such as EPZG,[19] aluminum metal powder,[20] amberlite XAD-4™ resin,[21] zeolite,[22–24] ZnO,[25] metal chloride,[26]... However, metal triflates-catalyzed the Friedel-

Crafts acylation of arenes under microwave irradiation appeared only in a few reports. In 1999, Dubac and co-workers investigated the acylation of aromatic ethers using $Bi(OTf)_3$, $Sn(OTf)_2$, $Sc(OTf)_3$, $Yb(OTf)_3$ and $Ce(OTf)_3$ under monomode microwave irradiation.[27] In 2003, Koshima and Kubota reported the synthesis of alkylbenzophenones with indium triflate in the absence of solvents using multimode microwave irradiation.[28] In 2005, Gronnow and co-workers reported the Friedel-Crafts acetylation of methyl salicylate with copper triflate on silica and other solid acid catalysts under monomode microwave irradiation.[29] Three years later, in 2008, Berardi and co-workers investigated the acylation of ferrocene using scandium triflate under both conventional and monomode microwave heating.[30] More recently, Jie Li and co-workers reported $Yb(OTf)_3$/TfOH co-catalyzed synthesis of xanthones and thioxanthones by intramolecular Friedel-Crafts reaction under domestic microwave irradiation.[31]

In our previous work,[32] we examined the Friedel-Crafts acylation of electron rich aromatic compounds in ionic liquids using bismuth triflate as the catalyst. The aim of the present paper is to examine the catalytic activity of metal triflates under solventless conditions. Moreover, microwave-assisted Friedel-Crafts benzoylation allowed the synthesis of aryl ketones in good to excellent yields with short reaction time and widened the substrate scope of the reaction.

RESULTS AND DISCUSSION

Initially, anisole was used as the model substrate for the Friedel-Crafts benzoylation with benzoyl chloride as benzoylating agent (Scheme 1). Microwave irradiation was found ineffective in the absence of catalyst. Consequently, bismuth triflate known to be a good catalyst for Friedel-Crafts acylation was suggested. As shown in Table 1, no product was obtained without bismuth triflate, but the reaction could afford 39% conversion when only 1 mol% bismuth triflate catalyst relative to anisole was used. Interestingly, a conversion of over 99% was achieved using 10 mol% bismuth triflate at 100 °C in 10 min without the need for an inert atmosphere. It is found that lower catalyst loading gave incomplete conversion. In addition, the decrease of reaction temperature or reaction time led to diminished conversion (Table 1, entries 6-10). In general, the reaction proceeded smoothly with major selectivity to *p*-benzoylanisole (>95%) in short reaction time using bismuth triflate under monomode CEM microwave irradiation.

The Friedel-Crafts benzoylation of anisole was tested to compare the catalytic activity of each metal triflate. Fourteen commercially available metal triflates were investigated using microwave irradiation at 100 °C (Table 2). The best conversion was observed when bismuth triflate was used as Lewis acid catalyst. Similar conversions were obtained when $La(OTf)_3$, $Pr(OTf)_3$, $Nd(OTf)_3$, $Gd(OTf)_3$, $Dy(OTf)_3$ and $Er(OTf)_3$ were used as catalysts. Anisole can be benzoylated in 92% conversion with copper triflate. Surprisingly, some of the rare-earth metal triflates such as $Eu(OTf)_3$, $Tm(OTf)_3$ and $Yb(OTf)_3$ are not efficient catalysts under these reaction conditions although these rare-earth metal triflates possess a strong Lewis acidity to give a better conversion in many cases. Consequently, bismuth triflate was a chosen for study of Friedel-Crafts acylation reactions. Although bismuth triflate catalyzed Friedel-Crafts acylation has been investigated extensively under conventional heating, the combination of bismuth triflate and microwave irradiation was only carried out in the Friedel-Crafts benzoylation of anisole.[27] To the best of our knowledge, this is the first time that MW irradiation is applied to the Friedel-Crafts benzoylation of various substrates containing both electron-rich and electron-poor substituents using bismuth triflate as catalyst.

The results with respect to arenes (Scheme 2) are presented in Table 3. The benzoylation of arenes shows that both electron-poor (entries 8-11) and most of the electron-rich aromatic compounds are reactive. The benzoylation of unsubstituted aromatics was observed in benzene, naphthalene and anthracene with 85%, 86% and 64% yield. The benzoylation product of anthracene was found to decompose under the high temperature using microwave irradiation, so all attempts to improve yield further were unsuccessful. Naphthalene is benzoylated in both the α-position and β-position (α/β=60/40). The benzoylation of arenes with one electron-donating substituent can be achieved in excellent yields (entries 1-7). Interestingly, electron-deficient halobenzenes were benzoylated in good yields although higher temperature and longer reaction time were required. The reactivity of halobenzenes was shown to decrease in the sequence fluorobenzene > chlorobenzene > bromobenzene > iodobenzene (Table 3). Fluorobenzene was benzoylated in 85% yield, but iodobenzene gave only 65% yield in comparison. In the latter case it was previously shown that iodobenzene could disproportionate in the presence of $AlCl_3$.[33] Good yields have been reported but in nitrobenzene as solvent.[34] Something similar is also found in the present study in which benzophenone and 1,4-diiodobenzene could be identified. We observe the same selectivity as described[8,10,35] under conventional heating. In conventional heating, a surplus of the starting material (starting material/acylating reagent = 2/1)[36] was added whereas the ratio of starting material/benzoyl chloride = 1/1 was used in our method. In addition, the benzoylated products were obtained in high yields with solid starting materials under solventless condition (Table 3, entries 12, 15, 21–23).

1,3-Dimethoxybenzene, 1,4-dimethoxybenzene, *p*-cymene and *p*-bromotoluene were benzoylated in moderate yields (entries 14, 15, 16, 18). The yield was slightly increased in the benzoylation of *m*-xylene, mesitylene (entries 17, 19). Biphenyl was benzoylated in 75% yield. Fluorene was benzoylated in 72% yield with 99% regioselectivity in the 2-position. This result can be compared to the more complicated synthesis using 2-benzyloxypyridine in trifluoroacetic acid.[37] Recycling of bismuth triflate was also carried out in the benzoylation of anisole under microwave irradiation. Interestingly, after running for five consecutive cycles at 100 °C in 10 min, yields were only slightly decreased after each cycle (Table 4).

CONCLUSION

In conclusion, a facile and efficient method for the Friedel-Crafts benzoylation reactions using bismuth triflate under microwave irradiation has been developed. A variety of electron-rich and electron-poor aromatic compounds can be benzoylated. If the substrate is less reactive, a longer reaction time and higher temperature are required. Additionally, bismuth triflate could be easily recovered and reused up to five times without loss of the catalytic activity. The further investigation to focus on carboxylic acids as acylating agent under microwave irradiation is now in progress.

EXPERIMENTAL

General Procedure For Benzoylation

A 10 mL pressurized glass tube with Teflon-coated septum equipped with a magnetic stirrer was charged substrate (1 mmol), benzoyl chloride (1 mmol) and metal triflate (0.1 equiv). The tube was sealed and placed into CEM microwave at the temperature for the appropriate time. The reaction mixture was allowed to cool to the room temperature in MW oven. After cooling, water (15 mL) was added to the mixture and the product was extracted by ethyl acetate or dichloromethane given similar results (3 x 15 mL). The organic layer was decanted, washed with water, aqueous $NaHCO_3$, and brine, and dried with $MgSO_4$. The solvent was then removed on a rotary evaporator and subjected to flash chromatography on silica gel (mixture of hexane and ethyl acetate solvent to elute the product). The fractions containing product were concentrated and dried under vacuum to yield pure product. All products are known compounds, the purity and identity of all products were confirmed by GC-MS, ^1H and ^{13}C NMR spectroscopy.

Supplemental data for this article can be accessed on the publisher's website.

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Table 1. Effects of reaction conditions on benzoylation of anisole[a]

Entry	Amount of catalyst (mol%)	Reaction time (min)	Temperature (°C)	Conversion (%)[b]
1	0	10	100	0
2	1	10	100	39
3	5	10	100	55
4	7	10	100	78
5	10	10	100	>99
6	10	10	70	67
7	10	10	90	80
8	10	1	100	45
9	10	5	100	72
10	10	8	100	83

[a] The mixture of anisole (1 mmol) and benzoyl chloride (1 mmol) with bismuth triflate was activated under monomode CEM microwave oven.

[b] Conversion based on anisole was determined by GC-FID using naphthalene as internal standard.

Table 2. Benzoylation of anisole catalyzed by metal triflates under microwave irradiation at 100 °C[a]

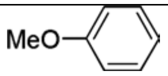
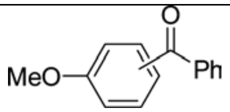
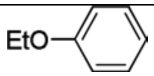
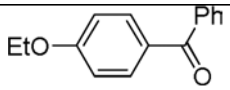
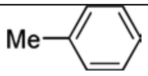
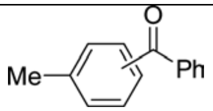
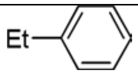
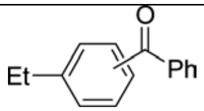
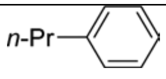
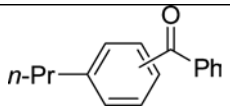
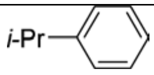
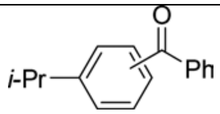
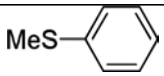
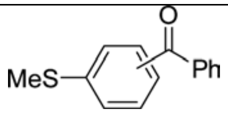
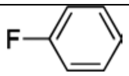
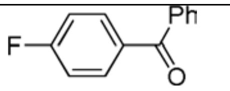
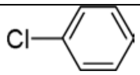
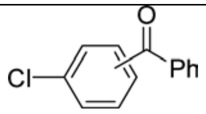
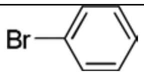
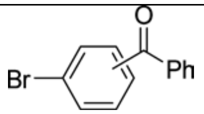
Entry	Metal triflate	Time (min)	Conversion (%)[b]
1	LiOTf	20	80
2	$Cu(OTf)_2$	10	92
3	$La(OTf)_3$	10	95
4	$Ce(OTf)_3$	10	86
5	$Pr(OTf)_3$	10	91
6	$Nd(OTf)_3$	10	94
7	$Eu(OTf)_3$	20	78
8	$Gd(OTf)_3$	10	93
9	$Tb(OTf)_3$	10	84
10	$Dy(OTf)_3$	10	92
11	$Er(OTf)_3$	10	91
12	$Tm(OTf)_3$	20	72
13	$Yb(OTf)_3$	20	68
14	$Bi(OTf)_3$	10	>99 (94)[c]

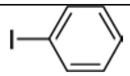
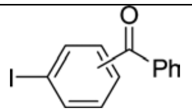
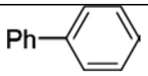
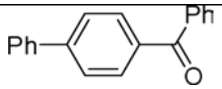
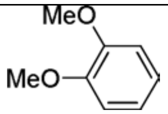
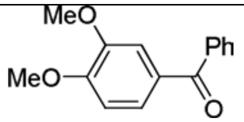
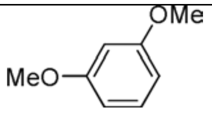
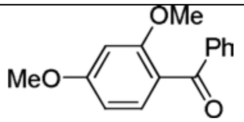
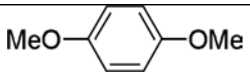
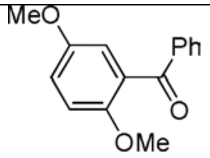
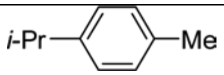
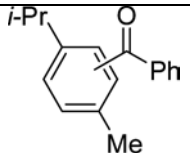
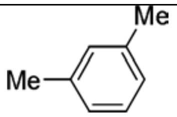
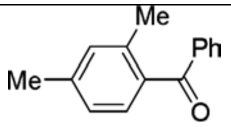
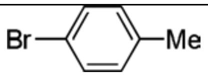
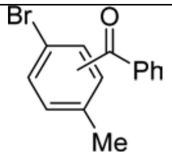
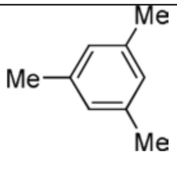
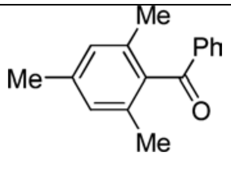
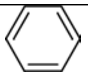
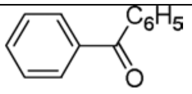
[a] Reaction conditions: anisole (1 mmol), benzoyl chloride (1 mmol), metal triflate (0.1 mmol).

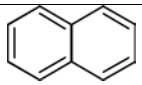
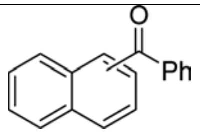
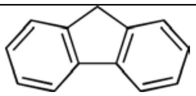
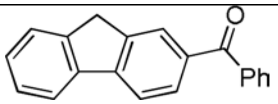
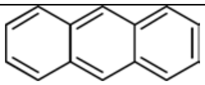
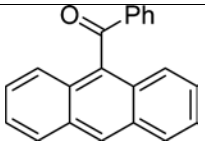
[b] Conversion based on anisole was determined by GC using naphthalene as internal standard.

[c] Yield in parenthesis is isolated yield.

Table 3. Benzoylation of various aromatic compounds catalyzed by bismuth triflate under microwave irradiation^a

Entry	Arene^b	Temperature (°C)	Time (min)	Product	Yield^c (%)	Isomer ratio^d
1		100	10		94	*o-/p-*=2/98
2		100	10		92	*o-/p-*=0/100
3		120	40		90	*o-/m-/p-*=19/4/77
4		140	40		92	*o-/m-/p-*=10/6/84
5		100	20		86	*o-/p-*=7/93
6		100	20		78	*o-/m-/p-*=8/6/86
7		100	10		88	*o-/p-*=6/94
8		140	40		86	>99
9		140	40		81	*o-/m-/p-*=14/2/84
10		140	40		76	*o-/m-/p-*=14/6/80

11		140	40		65	*o*-/*m*-/*p*- =17/5/78
12		100	20		75	>99
13		100	10		82	>99
14		100	10		75	100
15		100	10		70	100
16		100	20		60	79/21
17		100	10		86	>95
18		100	40		58	62/38
19		100	10		82	100
20		80	40		85	100

21		100	20		86	α/β=60:40
22		100	10		72	>99
23		60	5		64	>95

[a] Reaction conditions: arene (1 mmol), benzoyl chloride (1 mmol), bismuth triflate (0.1 mmol).

[b] Low boiling substrates such as: benzene, toluene and fluorobenzene were performed under high pressure (100 psi) and substrates with electron withdrawing substituents such as acetophenone and nitrobenzene were not suitable for this method.

[c] Isolated yield.

[d] Isomer ratio was determined by GC-FID.

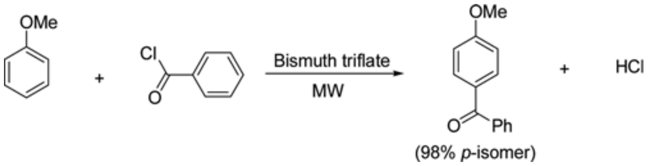
Table 4. Recycling of bismuth triflate on benzoylation of anisole[a]

Cycle	Temperature (°C)	Reaction time (min)	Yield (%)[b]
1	100	10	94
2	100	10	93
3	100	10	92
4	100	10	92
5	100	10	90

[a] After the reaction, bismuth triflate was recovered from aqueous layer by removal of water under vacuum.

[b] Isolated yield

Scheme 1. Benzoylation of anisole.



Scheme 2. Benzoylation of aromatic compounds.