Friedel–Crafts acylation using bismuth triflate in [BMI][PF$_6$]

Phuong Hoang Tran [a,b], Fritz Duus [a], Thach Ngoc Le [b,*]

[a] Department of Science, Systems and Models, University of Roskilde, POB 260, Roskilde DK-4000, Denmark
[b] Department of Organic Chemistry, Faculty of Chemistry, University of Science, Vietnam National University-Hochiminh city 70000, Viet Nam

ARTICLE INFO

ABSTRACT

Bismuth trifluoromethanesulfonate was found to be a good catalyst for the Friedel–Crafts acylation. Bismuth triflate immobilized in an ionic liquid was the most efficient catalytic system. Bismuth triflate in [BMI][PF$_6$] catalyzes this reaction under microwave irradiation allowing the rapid synthesis of aryl ketones in excellent yields. The catalyst system was easily recovered and reused several times.

© 2011 Elsevier Ltd. All rights reserved.

Friedel–Crafts acylation is an important reaction for the synthesis of aromatic ketones, which are useful precursors for the synthesis of various valuable pharmaceutical compounds.[1] However, the use of Lewis acids such as AlCl$_3$, BF$_3$, FeCl$_3$, TiCl$_4$, SnCl$_2$, etc., leads to a number of issues: complexation of the Lewis acid with the ketone product; a stoichiometric amount of acid is needed; hydrolysis of excess starting material is always required leading to the generation of a large amount of corrosive and toxic waste.[2] Besides, the reaction is extremely sensitive to moisture because most Lewis acids immediately react with water and then lose their reactivity. The disadvantage of anhydrous conditions is that substrates containing water or aqueous solutions can not be used directly.[3] Usually, Lewis acid catalysts are not recovered or recycled.[2] Consequently, conducting such a reaction on an industrial scale generates considerable amounts of hazardous waste.[4–7]

The use of metal triflates as water-compatible Lewis acids was first reported in 1991. These triflates possess strong Lewis acidity and exhibit high tolerance toward water.[8] Metal triflates act as strong Lewis acids due to their hard character and strong affinity toward carbonyl oxygens. In addition, their hydrolysis was postulated to be slow. Immobilized triflate salts can be recovered after the reaction and reused.[8] Recently, triflates in an ionic liquid[9] and triflates in supercritical carbon dioxide[10] have been successfully employed as environmentally benign Lewis acid catalysts.

Ionic liquids consist of positively and negatively charged ions, whereas water and organic solvents exist as neutral molecules. While common salts do not melt below 800 °C, most ionic liquids remain liquid at room temperature. In general, ionic liquids are

useful for reactions that involve reactive ionic intermediates.[11,12] The use of ionic liquids instead of conventional solvents as reaction media enhances both the selectivity and rates of various reactions. In addition, the catalyst and solvent are easily recycled.[12] Friedel–Crafts acylation in ionic liquids has been studied extensively.[13] Gmouh has shown the acylation of arenes in an ionic liquid.[14] More recently, Alleti applied gadolinium triflate immobilized in imidazolium based ionic liquids for the acetylation of alcohols and amines,[15] and Hardacre reported the Friedel–Crafts benzoylation of anisole in ionic liquids.[16]

Microwave irradiation provides a powerful tool for organic synthesis, with its direct reaction mixture heating, thus time and energy are saved.[17] Many organic reactions proceed much faster with higher yields under microwave irradiation compared to conventional heating.[18] The microwave energy can be transferred to the reaction medium via two mechanisms: dipole rotation and ionic conduction. Therefore, ionic liquids should be highly suitable media for microwave-assisted reactions.

As part of our ongoing research on the application of green chemistry in organic synthesis, we report here the Friedel–Crafts acylation using bismuth triflate in an ionic liquid under microwave irradiation.

The acetylation of anisole using acetic anhydride was selected as a model reaction and Bi(OTf)$_3$ was chosen as the catalyst for the Friedel–Crafts acylation in an ionic liquid because this catalyst is water stable and its catalytic activity is much higher than other metallic triflates [M(OTf)$_3$].[19] In our procedure, 5 mol % of Bi(OTf)$_3$ was used to catalyze the acetylation of anisole in [BMI][PF$_6$] (0.5 g). If the amount of catalyst was increased to 10 mol %, the yield was slightly improved. All attempts to reduce the amount of catalyst loading led to diminished yields. After intensively screening the

* Corresponding author.
  E-mail address: lenthach@yahoo.com (T.N. Le).

reaction conditions we obtained optimized conditions for the acetylation of anisole. Typical procedure: Bi(OTf)$_3$ (0.0328 g, 0.05 mmol), [BMI][PF$_6$] (0.5 g), anisole (0.108 g, 1 mmol), and acetic anhydride (0.102 g, 1 mmol) were stirred at 80 °C for 30 min. After cooling, the reaction mixture was extracted by diethyl ether (2 × 40 mL). The ether layer was decanted, washed with water, aqueous NaHCO$_3$, and brine, and dried over MgSO$_4$. The solvent was then removed on a rotary evaporator. The residue was purified by flash chromatography (n-hexane/ethyl acetate = 9:1) to give 4-methoxyacetophenone (0.120 g, 80% yield). The purity and authenticity of the product were confirmed by GC–MS[20] and ^{1}H NMR spectroscopy.

The optimized conditions were then applied for the acylation of other aromatic compounds to study the scope of our method. The results are summarized in Table 1. The combination of ionic liquid and microwave irradiation was found to significantly shorten the reaction time while affording high conversions and selectivity. The method is applicable for various arenes bearing at least one electron-donating substituent. Besides acetylation, other acylations such as pivaloylation and benzoylation also work well under our conditions to afford the desired product in a good yield. p-Acylated products were obtained as the major products (>95%). Benzoyl chloride was the best acylating reagent under conventional heating. Benzoylation usually provides a better yield compared to other acylations under both conventional

heating and microwave irradiation. Bismuth triflate in [BMI][PF$_6$] was shown to be a very efficient microwave absorber. In the context of our work on the Friedel–Crafts acylation of aromatic compounds, we examined the optimal conditions in a microwave oven (60 W, 5 min). In fact, microwave irradiation efficiently accelerates the acylations with different acylating reagents. Benzoyl chloride was revealed to be the best reagent providing the highest yields in most cases. However, the use of acetic anhydride was not advantageous for the acylation of 1,3-dimethoxybenzene, 1,4-dimethoxybenzene, and 4-methylanisole (Table 1, entries 3,4 and 6).

Recycling of the catalytic system was also studied. Interestingly, the acetylation of anisole using bismuth triflate in [BMI][PF$_6$] under conventional heating was run for five consecutive cycles at 80 °C over 30 min. Isolated yields were slightly decreased after each cycle. Under microwave irradiation, the catalytic system was run for three consecutive cycles at 60 W over 5 min, but in this case, the yield was slightly decreased (from 74 to 64%), strongly in the fourth cycle (35%).

In conclusion, an efficient method for the Friedel–Crafts acylation of aromatic compounds employing bismuth triflate in an ionic liquid has been developed. The catalyst and reaction media are air-stable and easy to handle. Bismuth triflate in [BMI][PF$_6$] shows an excellent catalytic activity. In addition, the catalytic system could be reused up to five times.

Table 1
Bi(OTf)$_3$ catalyzed Friedel–Crafts acylation of aromatic compound in [BMI][PF$_6$]

Entry	Substrate (Ar–H)	R^{1}COX[a]	ArCOR^1	Yield (%)	
				Δ[b]	MW[c]
1		Ac$_2$O	CH$_3$CO-C$_6$H$_4$-OMe	80	74
		(CH$_3$)$_3$CCOCl	(CH$_3$)$_3$CCO-C$_6$H$_4$-OMe	93	69
		PhCOCl	PhCO-C$_6$H$_4$-OMe	95	98
		(PhCO)$_2$O	PhCO-C$_6$H$_4$-OMe	90	68
2		Ac$_2$O	CH$_3$CO-C$_6$H$_3$(OMe)$_2$	86	82
		(CH$_3$)$_3$CCOCl	(CH$_3$)$_3$CCO-C$_6$H$_3$(OMe)$_2$	74	55
		PhCOCl	PhCO-C$_6$H$_3$(OMe)$_2$	95	100
		(PhCO)$_2$O	PhCO-C$_6$H$_3$(OMe)$_2$	77	68
3		Ac$_2$O	CH$_3$CO-C$_6$H$_3$(OMe)$_2$	63	40
		(CH$_3$)$_3$CCOCl	(CH$_3$)$_3$CCO-C$_6$H$_3$(OMe)$_2$	58	74
		PhCOCl	PhCO-C$_6$H$_3$(OMe)$_2$	85	98
		(PhCO)$_2$O	PhCO-C$_6$H$_3$(OMe)$_2$	70	97
4		Ac$_2$O	CH$_3$CO-C$_6$H$_3$(OMe)$_2$	29	18
		(CH$_3$)$_3$CCOCl	(CH$_3$)$_3$CCO-C$_6$H$_3$(OMe)$_2$	31	41
		PhCOCl	PhCO-C$_6$H$_3$(OMe)$_2$	84	85
		(PhCO)$_2$O	PhCO-C$_6$H$_3$(OMe)$_2$	Trace	41
5		Ac$_2$O	CH$_3$CO-C$_6$H$_4$-SMe	50	85
		(CH$_3$)$_3$CCOCl	(CH$_3$)$_3$CCO-C$_6$H$_4$-SMe	42	45
		PhCOCl	PhCO-C$_6$H$_4$-SMe	92	90
		(PhCO)$_2$O	PhCO-C6H4-SMe	86	54
6		Ac$_2$O	CH$_3$CO-C$_6$H$_3$(CH$_3$)-OMe	23	17
		(CH$_3$)$_3$CCOCl	(CH$_3$)$_3$CCO-C$_6$H$_3$(CH$_3$)-OMe	22	39
		PhCOCl	PhCO-C$_6$H$_3$(CH$_3$)-OMe	86	98
		(PhCO)$_2$O	PhCO-C$_6$H$_3$(CH$_3$)OMe	57	95

[a] Low boiling acid chlorides such as CH$_3$COCl and C$_2$H$_5$COCl were not convenient for use.
[b] Conventional heating: 80 °C, 30 min.
[c] Microwave irradiation: 60 W, 5 min (microwave irradiation performed using of a CEM MDS 2000 batch microwave oven).

Acknowledgment

References and notes

1. March, J. Advanced Organic Chemistry; Wiley: New York, 2007.
2. Olah, G. A. Friedel–Crafts Chemistry; John Wiley and Sons: New York, 1973.
3. Kobayashi, S.; Manabe, K. Pure Appl. Chem. 2000, 72, 1373–1380.
4. (a) Veverková, E.; Meciarová, M.; Gotov, B.; Toma, S. Green Chem. 2002, 4, 361–365; (b) Kaur, K.; Griffin, K.; Harrison, B. J. Catal. 2002, 208, 448–455.
5. Smith, K.; El-Hiti, G. A.; Jayne, A. J.; Butters, M. Org. Biomol. Chem. 2003, 1, 1560–1564.
6. Duris, F.; Barbier-Baudry, D.; Dormond, A.; Desmurs, R. J.; Bernard, J. M. J. Mol. Catal. 2002, 188, 97–104.
7. Parvulescu, A. N.; Gagea, B. C.; Poncelet, G.; Pârvulescu, V. I. Appl. Catal. 2006, 301, 133–137.
8. (a) Kobayashi, S.; Sugiura, M.; Kitagawa, H. Chem. Rev. 2002, 102, 2227–2302; (b) Kobayashi, S.; Iwamoto, S. J. Catal. 1998, 39, 4697–4970; (c) Koshima, H.; Kabota, M. Synth. Commun. 2003, 33, 3983–3988.
9. (a) Berardi, S.; Conte, V.; Fiorani, G.; Floris, B.; Galloni, P. Organomet. Chem. 2008, 693, 3015–3020; (b) Goodrich, P.; Hardacre, C.; Mehdi, H.; Nancarrow, P.; Rooney, D. W.; Thompson, J. P. Ind. Eng. Chem. Res. 2006, 45, 6640–6647.
10. Zayed, F.; Greiner, L.; Schulz, P. S.; Lapkin, A.; Leitner, W. Chem. Commun. 2008, 79–81.
11. Hallett, J.; Welton, T. Chem. Rev. 2011, 111, 3508–3576.
12. Keskin, S.; Kayrak-Talay, D.; Akman, U.; Hortacsu, O. J. Supercrit. Fluids 2007, 43, 150–180.
13. Ross, J.; Xiao, J. Green Chem. 2002, 4, 129–133.
14. Gmouh, S.; Yang, H.; Vayltier, M. Org. Lett. 2003, 5, 2219–2222.
15. Alleti, R.; Oh, W. S.; Perambuduru, M.; Afrasiabi, Z.; Sinn, E.; Reddy, V. P. Green Chem. 2005, 7, 203–206.
16. Hardacre, C.; Nancarrow, P.; Rooney, D. V.; Thompson, J. M. Org. Process Res. Dev. 2008, 12, 1156–1163.
17. Loupy, A. Microwaves in Organic Synthesis; Wiley-VCH: Weinheim, 2006.
18. (a) Gopalakrishnan, M.; Sureshkumar, P.; Kanagarajan, V.; Thanusu, J. Catal. Commun. 2005, 6, 753–756; (b) Deng, W.; Xu, Y.; Guo, Q. X. Chin. Chem. Lett. 2005, 16, 327–330.
19. Labrouillere, M.; Roux, C. L.; Gaspard, H.; Laporterie, A.; Dubac, J. Tetrahedron Lett. 1997, 38, 8871–8874.
20. GC–MS analyses were performed on an Agilent GC System 6890 Series, equipped with a mass selective detector Agilent 5973 and a capillary column DB-5MS (60 m × 0.25 mm × 0.3 μm).