Tetrahedron Letters 50 (2009) 446–447

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

A novel Brønsted acid catalyst for Friedel–Crafts acylation

Anna G. Posternak, Romute Yu. Garlyauskayte *, Lev M. Yagupolskii

Institute of Organic Chemistry, National Academy of Sciences of Ukraine, 02094, Murmanskaya str. 5, Kiev, Ukraine

ARTICLE INFO

Article history:
Received 22 August 2008
Revised 3 November 2008
Accepted 11 November 2008
Available online 17 November 2008

ABSTRACT

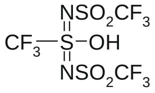
Bis(trifluoroalkylsulfonylimino)trifluoromethanesulfonic acid has demonstrated remarkable catalytic ability in the electrophilic acylation of aromatic substrates. Various perfluoroalkyl substituted aroyl chlorides are employed in Friedel–Crafts acylation typically using 1 mol % of catalyst.

The scope of Friedel–Crafts reactions is extremely wide, and forms a large part of the more general field of electrophilic reactions. Friedel–Crafts acylation is the fundamental method for the preparation of arylketones.[1] Traditionally, Lewis acids such as $AlCl_3$,[2,3] BF_3,[4] $TiCl_4$,[5] $ZnCl_2$,[6] $SbCl_5$[7] and $Fe_2(SO_4)_3$[8] have been employed in these reactions. However, more than stoichiometric amounts of the Lewis acids are needed in many cases due to complex formation with the oxygen atom of the aroyl products.[2] Moreover, these Lewis acids are moisture sensitive and cannot be recovered and reused after the reactions are complete. Although $AlCl_3$ as well as ACF ($AlCl_xF_y$) has been employed in the chemistry of highly fluorinated carbocations,[9] in the case of perfluoroalkyl-substituted aromatic compounds, replacement of fluorine atoms with chlorine takes place on reaction with $AlCl_3$.[10]

More reactive Lewis acids can be obtained with more electronegative ligands. For example, the shift from $(ArO)_2Al–Me$ to $(ArO)_2Al–Cl$ to $(ArO)_2Al–OTf$ and then to $(ArO)_2Al–NTf_2$[11] gave a much more reactive catalyst for a variety of reactions. The Friedel–Crafts acylation of substituted benzenes proceeded smoothly in the presence of a catalytic amount (5–20%) of lanthanide triflates.[12] Aluminium, titanium and ytterbium bis(triflate)imides were found to be highly effective in acylation reactions of anisole and diphenyl ether.[13]

Aromatic ketones can also be prepared by the reaction of carboxylic acids with aromatic compounds catalyzed by Brønsted acids such as methanesulfonic acid,[14] polyphosphoric acid,[15] Nafion-H,[16] trifluoromethanesulfonic acid[17–19] and combinations of Lewis acids–Brønsted acids.[1,20]

The synthesis of bis(trifluoromethylsulfonylimino)trifluoromethanesulfonic acid **1** via condensation of (trifluoromethylsulfonyl)trifluoromethanesulfonimidoyl fluoride with trifluoromethanesulfonamide has been reported.[21] In accordance with calculations of deprotonation enthalpies (DPE = 266 kcal/mol), the gas-phase acidity of acid **1** is in excess of that of TfOH by 30 kcal/mol (i.e., more than 21 pK_a units) and is approximately equal to HF–SbF_5, which is known as 'magic acid'.[22]



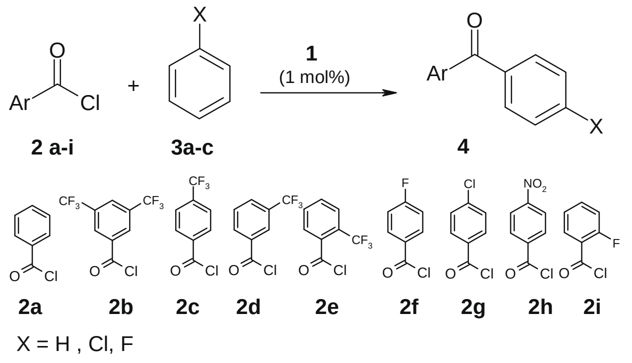
$$CF_3-\overset{\overset{NSO_2CF_3}{\|}}{\underset{\underset{NSO_2CF_3}{\|}}{S}}-OH$$

1

It was of interest to ascertain the potential of this acid as a catalytic agent for Friedel–Crafts reactions and to compare it with TfOH.[17–19,23] We report here the acylation of various aromatic compounds using the new superacid catalytic agent **1**. During the course of our work, we studied aroyl chlorides **2a–i** with various substituents on the aryl ring including CF_3-groups, for the acylation of non-activated aromatic nucleophiles (Scheme 1). Reactions were performed on substrates **2** and **3** (1:3 ratio) in the presence of 1 mol % of bis(trifluoromethylsulfonylimino)trifluoromethanesulfonic acid **1**.[24] The temperatures, reaction times and yields of product benzophenones **4** are listed in Table 1.

Literature data on Friedel–Crafts reactions with analogous substrates but with other catalysts are listed in Table 1 for comparison.

In the case of reactions of CF_3-substituted aroyl chlorides **2c** (entries 22 and 23) and **2d** (entries 16 and 17) and TfOH as



Scheme 1.

---

* Corresponding author. Tel.: +380 44 559 0349; fax: +380 44 573 2643.
E-mail address: roma@ioch.kiev.ua (R. Yu. Garlyauskayte).

0040-4039/$ - see front matter Crown Copyright © 2008 Published by Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2008.11.038

Table 1

Entry	X	Ratio **3**/**2**	**2**	T (°C)	Acid (mol %)	Time	**4**	Isolated yield (%)	Lit.
1	Cl	3:1	**2i**	130	**1** (1%)	24	**4a**	69 (*o*:*p* = 1:8)	
2	Cl	3:1	**2i**	130	**1** (2%)	16	**4a**	96 (*para*)	
3	Cl	3:1	**2f**	130	**1** (1%)	16	**4b**	94 (*para*)	
4	Cl	3:1	**2b**	130	**1** (1%)	17	**4c**	58	
5	Cl	3:1	**2a**	132	TfOH (1%)	5	**4d**	13 (*o*:*p* = 1:3)	17
6	Cl	4:1	**2a**	135	$Fe_2(SO_4)_3$ (1–5%)	24	**4d**	34–55[a]	8
7	H	3:1	**2i**	80	**1** (1%)	22	**4e**	76	
8	H	3:1	**2i**	80	**1** (1%)	3	**4e**	41[b]	
9	H	3:1	**2d**	80	**1** (1%)	16	**4f**	88	
10	H	3:1	**2h**	80	TfOH (1%)	4	**4g**	82	17
11	H	3:1	**2a**	80	TfOH (1%)	8.5	**4h**	14	17
12	F	12:1	**2a**	100	TfOH (50%)	144	**4i**	79[c]	19
13	F	4:1	**2a**	90	$Fe_2(SO_4)_3$ (5%)	43	**4i**	61[a]	8
14	F	3:1	**2i**	85	**1** (1%)	19	**4j**	76	
15	F	2:1	**2i**	—	$AlCl_3$ (117%)	—	**4j**	53	3
16	F	3:1	**2d**	85	**1** (1%)	17	**4k**	76	
17	F	12:1	**2d**	100	TfOH (50%)	144	**4k**	76	19
18	F	3:1	**2b**	85	**1** (1%)	18	**4l**	82	
19	F	12:1	**2b**	100	TfOH (50%)	144	**4l**	85	19
20	F	3:1	**2b**	85	**1** (5%)	15	**4l**	40	
21	F	3:1	**2h**	85	**1** (1%)	20	**4m**	87	
22	F	3:1	**2c**	85	**1** (1%)	21	**4n**	95	
23	F	12:1	**2c**	100	TfOH (50%)	144	**4n**	98	19
24	F	3:1	**2e**	85	**1** (1%)	18	**4o**	99	

[a] Yield includes a small amount of unreacted aroyl chloride **2**.
[b] Yield calculated from the ^{19}F NMR spectrum.
[c] Yield calculated from the ^{1}H NMR spectrum.

catalyst,[19] the yields of the corresponding benzophenones **4** are comparable. However, the amount of TfOH required is 0.5 M equiv (i.e., 50 times greater than acid **1**) and the reactions take a long time.

If activated aromatic nucleophiles (*p*-xylene, toluene) or a strong electrophile such as **2h** is used in the reaction, the acylation proceeds well when 1 mol % of TfOH is used as the catalyst;[17] however, the yield of 4-chlorobenzophenone was very small (entry 5).

It should be stressed that acylation of chlorobenzene in the presence of acid **1** occurs in moderate to excellent yields and preferably at the *para*-position (entries 1–4). This atypical effect is most likely due to steric issues in the transition complex (aroyl chloride:acid **1**) hindering reaction at the *ortho*-position of chlorobenzene.

Thus, the selectivity and small amounts of acid **1** required are advantages over other catalysts for Friedel–Crafts acylation. Acid **1** is very soluble in various organic solvents including methylene chloride. It can be recycled from large-scale synthesis and its catalytic activity in other organic reactions is currently under study.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2008.11.038.

References and notes

1. Olah, G. A. *Friedel–Crafts and Related Reactions*; Wiley-Interscience: New York, 1963.
2. (a) Kranzlein, G. *Aluminium Chloride in der Organischen Chemie*, 3rd ed.; Verlag Chemie: Berlin, 1939; (b) Thomas, C. A. *Anhydrous Aluminium Chloride in Organic Chemistry*; Rainhold: New York, 1961.
3. Bradlow, L. H.; VanderWerf, C. A. *J. Am. Chem. Soc.* **1947**, *69*, 662–663.
4. (a) Hyatt, J. A.; Raynolds, P. W. *J. Org. Chem.* **1984**, *49*, 384; (b) Fodor, G.; Kiss, J.; Szekerke, M. *J. Org. Chem.* **1950**, *15*, 227; (c) Kindler, K.; Oelschlager, H. *Chem. Ber.* **1954**, *87*, 194; (d) Schiemenz, G. P.; Schmidt, U. *Liebigs Ann. Chem.* **1976**, 1514; (e) Walker, H. G.; Sanderson, J. J.; Hauser, C. R. *J. Am. Chem. Soc.* **1953**, *75*, 4109.
5. (a) Bensari, A.; Zaveri, N. T. *Synthesis* **2003**, 267–271; (b) Chiba, K.; Arakawa, T.; Tada, M. *Chem. Commun.* **1996**, 1763–1764; (c) Lin, G.-Q.; Zhong, M. *Tetrahedron Lett.* **1996**, *37*, 3015–3018; (d) Fujisawa, T.; Ito, T.; Fujimoto, K.; Shimizu, M.; Winberg, H.; Staring, E. G. J. *Tetrahedron Lett.* **1997**, *38*, 1593–1596.
6. Paul, S.; Nanda, P.; Gupta, R.; Loupy, A. *Synthesis* **2003**, 2877–2881.
7. (a) Dermer, O. C.; Billmeier, R. A. *J. Am. Chem. Soc.* **1942**, *64*, 464; (b) Murakami, Y.; Tani, M.; Aryuasu, T.; Nischiyama, C.; Watanabe, T.; Yokoyama, Y. *Heterocycles* **1988**, *27*, 1855; (c) Tolkunov, S. V.; Voshchula, V. N.; Zemskaya, E. A.; Dulenko, V. I. *Khim. Geterotsikl. Soedin.* **1990**, 1569; (d) Mukaiyama, T.; Nagaoka, H.; Ohshima, M.; Murakami, M. *Chem. Lett.* **1986**, *165* and references cited therein.
8. Morley, J. O. *Synthesis* **1977**, 54–55.
9. Krespan, C. G.; Petrov, V. A. *Chem. Rev.* **1996**, *96*, 3269.
10. (a) Henne, A. L.; Newman, M. S. *J. Am. Chem. Soc.* **1938**, *60*, 1697–1698; (b) Yagupolskii, L. M.; Kondratenko, N. V. *Zh. Obsch. Khem.* **1967**, *37*, 1770–1775.
11. Marx, A.; Yamamoto, H. *Angew. Chem., Int. Ed.* **2000**, *39*, 178.
12. Kawada, A.; Mitamura, S.; Kobayashi, S. *J. Chem. Soc., Chem. Commun.* **1993**, 1157.
13. Mikami, K.; Kotera, O.; Motoyama, Yu.; Sakaguchi, H.; Maruta, M. *Synlett* **1996**, 171–172.
14. Cho, H.; Matsuki, S.; Mizuno, A.; Annoura, H.; Tatsuoka, T. *J. Heterocycl. Chem.* **1997**, *34*, 87.
15. (a) Mizuno, A.; Miya, M.; Kamei, T.; Shibata, M.; Tatsuoka, T.; Nakanishi, K.; Takiguchi, C.; Hadaka, T.; Yamaki, A.; Inomata, N. *Chem. Pharm. Bull.* **2000**, *48*, 1129; (b) Eaton, P. E.; Yeusaf, T. I. *J. Org. Chem.* **1973**, *38*, 4071–4073.
16. Yamoto, T.; Hideshama, C.; Prakash, G. K. S.; Olah, G. A. *J. Org. Chem.* **1991**, *36*, 3955.
17. Effenberger, F.; Eppel, G. *Angew. Chem.* **1972**, *84*, 295–296.
18. Anderson, K. W.; Tepe, J. J. *Tetrahedron* **2002**, *58*, 8475–8481.
19. Akiko, O.; Katsuya, M.; Hideaki, O.; Noriyuki, Y. *Synth. Commun.* **2007**, *37*, 2701–2715.
20. (a) Yoneda, N.; Fukuhara, T.; Takahashi, Y.; Suzuki, A. *Chem. Lett.* **1979**, 1003; (b) Olah, G. A.; White, A. M.; O'Brien, D. H. *Chem. Rev.* **1970**, *70*, 561; (c) Repinskaya, I. B.; Barkhutova, D. D.; Makarova, Z. S.; Alekseeva, A. V.; Koptyug, V. A. *J. Org. Chem. USSR (Engl. Transl.)* **1985**, *21*, 759.
21. Garlyauskayte, R. Yu.; Chernega, A. N.; Michot, Ch.; Armand, M.; Yagupolskii, Yu. L.; Yagupolskii, L. M. *Org. Biomol. Chem.* **2005**, *3*, 2239–2243.
22. Burk, P.; Koppel, I. A.; Koppel, I.; Yagupolskii, L. M.; Taft, R. W. *J. Comput. Chem.* **1996**, *17*, 30–41 and references cited therein.
23. Prakash, G. K. S.; Yan, P.; Torok, B.; Olah, G. A. *Synlett* **2003**, 527–531 and references cited therein.
24. *Typical procedure for the synthesis of benzophenones* **4**: Benzoyl chloride **2** (1 mmol) was dissolved in aromatic substrate **3** (3 mmol), and acid **1** as 20% solution in CH_2Cl_2 (0.01 mmol) was added at room temperature under a dry Ar-current. The reaction mixture was refluxed with stirring and protection from moisture. On completion, the mixture was diluted with CH_2Cl_2 (10 ml) and carefully neutralized with saturated aqueous $NaHCO_3$ solution, the organic layer was washed with water and dried over anhydrous $MgSO_4$. The solvent and excess of **3** were removed in vacuo. The residue was distilled in vacuo or recrystallized from hexane.