



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

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ABSTRACT

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

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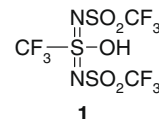
The scope of Friedel–Crafts reactions is extremely wide, and forms a large part of the more general field of electrophilic reactions. Friedel–Crafts acylation is the fundamental method for the preparation of arylketones.¹ Traditionally, Lewis acids such as AlCl_3 ,^{2,3} BF_3 ,⁴ TiCl_4 ,⁵ ZnCl_2 ,⁶ SbCl_5 ⁷ and $\text{Fe}_2(\text{SO}_4)_3$ 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 aryl 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 $\text{ACF} (\text{AlCl}_x\text{F}_y)$ 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 electro-negative ligands. For example, the shift from $(\text{ArO})_2\text{Al}-\text{Me}$ to $(\text{ArO})_2\text{Al}-\text{Cl}$ to $(\text{ArO})_2\text{Al}-\text{OTf}$ and then to $(\text{ArO})_2\text{Al}-\text{NTf}_2$ 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

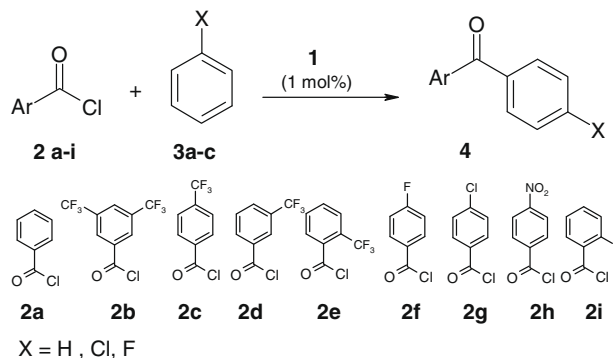
30 kcal/mol (i.e., more than 21 pK_a units) and is approximately equal to $\text{HF}-\text{SbF}_5$, which is known as ‘magic acid’.²²



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 aryl 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 aryl 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).

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 (<i>o:p</i> = 1:8)	
2	Cl	3:1	2i	130	1 (2%)	16	4a	96 (<i>para</i>)	
3	Cl	3:1	2f	130	1 (1%)	16	4b	94 (<i>para</i>)	
4	Cl	3:1	2b	130	1 (1%)	17	4c	58	
5	Cl	3:1	2a	132	TfOH (1%)	5	4d	13 (<i>o:p</i> = 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 aryl chloride **2**.

^b Yield calculated from the ¹⁹F NMR spectrum.

^c Yield calculated from the ¹H 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 (aryl 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.

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- 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 CH₂Cl₂ (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 CH₂Cl₂ (10 ml) and carefully neutralized with saturated aqueous NaHCO₃ solution, the organic layer was washed with water and dried over anhydrous MgSO₄. The solvent and excess of **3** were removed in vacuo. The residue was distilled in vacuo or recrystallized from hexane.