Benzylation of Aromatic Compounds Catalyzed by 3-Methyl-1-sulfonic Acid Imidazolium Tetrachloroaluminate and Silica Sulfuric Acid under Mild Conditions

Mohammad Ali Zolfigol,*[a] Hooshang Vahedi,[b] Saeid Azimi,[b] Ahmad Reza Moosavi-Zare[c]

[a] Faculty of Chemistry, Bu-Ali Sina University, Hamedan 6517838683, Iran
Fax +98(811)8257407; E-mail: mzolfigol@yahoo.com

[b] Department of Chemistry, Payame Noor University, PO Box 19395-4697, Teheran, Iran

[c] Department of Chemistry, University of Sayyed Jamaleddin Asadabadi, Asadabad 6541835583, Iran

Received: 01.02.2013; Accepted after revision: 24.03.2013

Abstract: In this work, efficient procedures for benzylation of a range of aromatic compounds by benzyl acetate in the presence of catalytic amounts of 3-methyl-1-sulfonic acid imidazolium tetrachloroaluminate ([Msim]$AlCl_4$) or silica sulfuric acid (SSA) under mild conditions are described. Simple methodology, easy workup procedure, clean reaction and reusability of the catalyst are some advantages of this work.

Key words: benzylation, benzyl acetate, 3-ethyl-1-sulfonic acid imidazolium tetrachloroaluminate, silica sulfuric acid

Diarylmethanes are an interesting group of bioactive compounds, and are also very important and useful in organic synthesis.[1–3] Catalytic systems used for the benzylation of aromatic compounds include HfO_2–$HfCl_4$,[3] aliquat 336,[4] phosphomolybdic acid supported silica gel,[5] TMSOTf,[6] organozinc and organoboron derivatives, HCl, H_2SO_4, $MeSO_3H$, HOTf and $HNTf_2$.[7] However, some of these procedures suffer from various drawbacks, such as complex workup and purification, production of significant amounts of waste materials, use of strongly acidic conditions, and occurrence of side reactions with poor yields.

In recent years, silica sulfuric acid (SSA), as one of the more important solid acid catalysts,[8–12] and 3-methyl-1-sulfonic acid imidazolium tetrachloroaluminate ([Msim]$AlCl_4$), as a new sulfonic acid functionalized imidazolium salts (SAFIS) with interesting applications, have been reported (Figure 1).[13–15]

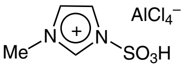


Figure 1

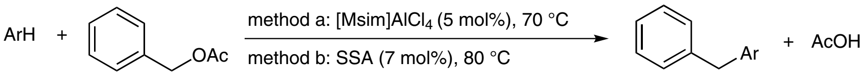
Herein, we describe the use of SSA and [Msim]$AlCl_4$ as catalysts for benzylation of a range of aromatic compounds under mild conditions to give diarylmethanes, and compare their catalytic activity in this reaction (Scheme 1). The promising aspects of this methodology are its efficiency, high yield, cleaner reaction profile, and simplicity, rendering it an attractive process for the preparation of diarylmethanes.

To optimize the reaction conditions, we selected the reaction of anisole and benzyl acetate as a model reaction (Scheme 2).

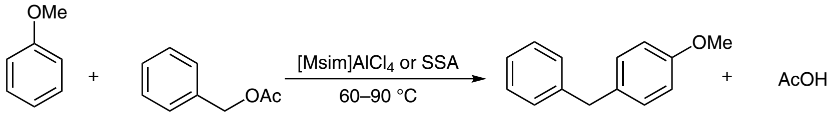
We observed that the best results were obtained using 5 mol% of [Msim]$AlCl_4$ at 70 °C or 7 mol% of SSA at 80 °C (Table 1).

In a further study, the model reaction was tested with [Msim]AlCl in several solvents; the corresponding results are displayed in Table 2, indicating that the best result was obtained under solvent-free conditions.

Subsequently we examined various aromatic substrates with benzyl acetate as electrophile under solvent-free conditions and with solvent using SSA or [Msim]$AlCl_4$ as catalyst (Table 3). In certain instances, reaction occurred



Scheme 1 The preparation of diarylmethanes catalyzed by [Msim]$AlCl_4$ (method a) and SSA (method b)



Scheme 2 Benzylation of anisole as model reaction

SYNLETT 2013, 24, 1113–1116
Advanced online publication: 16.04.2013
DOI: 10.1055/s-0033-1338386; Art ID: ST-2013-D0110-L

Table 1 Effect of Different Amounts of the Catalyst and Temperature on the Reaction of Anisole with Benzyl Acetate under Solvent-Free Conditions

Catalyst	Catalyst (mol%)	Temp (°C)	Time (min)	Yield[a] (%)
[Msim]AlCl$_4$	1	70	90	48
[Msim]AlCl$_4$	3	70	90	60
[Msim]AlCl$_4$	**5**	**70**	**60**	**85**
[Msim]AlCl$_4$	7	70	60	85
[Msim]AlCl$_4$	10	70	60	85
[Msim]AlCl$_4$	5	60	120	40
[Msim]AlCl$_4$	5	80	60	85
SSA	1	80	120	51
SSA	3	80	120	60
SSA	5	80	90	74
SSA	**7**	**80**	**60**	**83**
SSA	10	80	60	83
SSA	7	70	90	69
SSA	7	90	60	83

[a] Isolated yield.

Table 2 Reaction of Anisole with Benzyl Acetate Using [Msim]AlCl$_4$ (5 mol%) in Different Solvents at Reflux

Entry	Solvent	Time (min)	Yield[a] (%)
1	EtOH	120	46
2	MeOH	120	34
3	MeCN	90	15
4	CH_2Cl_2	60	75
5	MeCOOEt	100	15
6[b]	–	60	85

[a] Isolated yield.
[b] Reaction was carried out at 70 °C.

in the absence of solvent (Table 3 entries 1–3, 7 and 8) and in others, CH_2Cl_2 was the reaction solvent. Substrates with electron-donating substituents gave high yields of benzylated products under mild conditions.

Mendoza et. al have reported benzylation of certain aromatic substrates using HOTf as a Brønsted acidic catalyst but indole was found to react poorly with the acid catalyst, leading to decomposition products and unreacted indole.[7] However, with our protocol, 3-benzyl indole was obtained in good yield using [Msim]AlCl$_4$ or SSA as catalyst (Table 3, entry 6). Generally, our protocol is more efficient than previous methods;[16] with substrates possessing additional electron-donating groups, the yield increased and reaction time decreased (Table 3, entries 1 and 2) and, with phenol as substrate, the *p*-benzylphenol was produced rather than the *o*-benzylphenol. Furthermore, with indole, trimerization was not observed.[17]

Table 3 Synthesis of Diarylmethanes Using SSA and [Msim]AlCl$_4$ as Catalyst

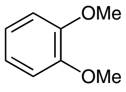
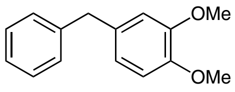
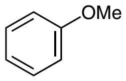
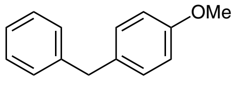
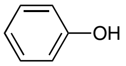
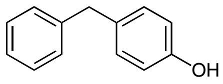
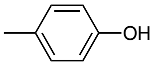
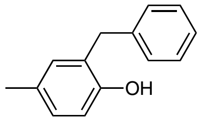
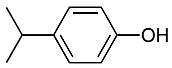
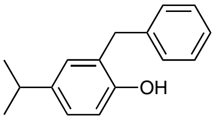
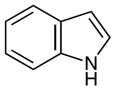
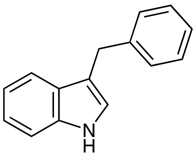
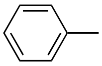
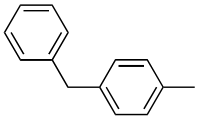
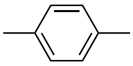
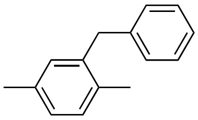
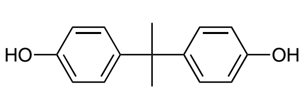
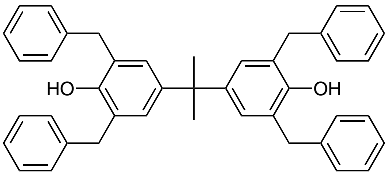
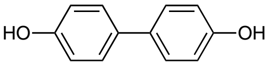
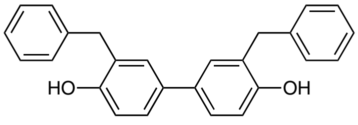
Entry	Nucleophile	Main product	Time (h)/ Yield[a] (%) {[Msim]AlCl$_4$}	Time (h)/ Yield[a] (%) (SSA)	Time (h)/ Yield[a,b] (%)
1			1/93	1/89	1/86[7]
2			1/85	1/83	1/23[21] 5/80.3[18]
3			1.5/86	1.5/82	0.5/23[21]
4[c]			2/95	2/89	0.58/32[20] 6/65[19]
5[c]			2/89	2/80	–

Table 3 Synthesis of Diarylmethanes Using SSA and [Msim]AlCl$_4$ as Catalyst (continued)

Entry	Nucleophile	Main product	Time (h)/ Yield[a] (%) {[Msim]AlCl$_4$}	Time (h)/ Yield[a] (%) (SSA)	Time (h)/ Yield[a,b] (%)
6[c]			3/87	3/80	18/69[16]
7			2/86	2/81	40/63[3]
8			2.5/92	3/87	40/87[3]
9[c,d]			3/95	4/90	–
10[c,e]			3.5/90	4.5/86	–

[a] Isolated yield.

[b] Literature results compared with the presented results.

[c] These reactions were carried out in CH_2Cl_2 under reflux.

[d] Ratio of benzyl acetate to nucleophile was 4:1.

[e] Ratio of benzyl acetate to nucleophile was 2:1.

The recyclability of the catalyst was also investigated with the reaction of anisole and benzyl acetate as a model reaction. The reaction mixture was extracted with CH_2Cl_2 to separate products form the [Msim]AlCl$_4$ or with ethanol to separate from the SSA. Subsequently, the catalyst was employed for a second cycle reaction. We observed that the catalytic activity of [Msim]AlCl$_4$ (Table 4) and SSA (Table 5) was retained, within the limits of experimental error, for five and four successive runs, respectively.

Table 4 Reaction of Anisole and Benzyl Acetate in the Presence of Recycled [Msim]AlCl$_4$ under Solvent-Free Conditions at 70 °C

Entry	Cycle	Time (min)	Yield[a] (%)
1	1st run	60	85
2	2nd run	80	80
3	3rd run	90	73
4	4th run	115	67
5	5th run	120	61

[a] Isolated yield.

Table 5 Reaction of Anisole and Benzyl Acetate in the Presence of Recycled SSA under Solvent-Free Conditions at 80 °C

Entry	Cycle	Time (min)	Yield[a] (%)
1	1st run	60	83
2	2nd run	85	75
3	3rd run	100	68
4	4th run	130	60

[a] Isolated yield.

In summary, we have reported two new procedures[22] for the preparation of diarylmethanes by the benzylation of a range of aromatic compounds using 3-methyl-1-sulfonic acid imidazolium tetrachloroaluminate {[Msim]AlCl$_4$} or silica sulfuric acid (SSA) as heterogeneous catalysts with high yields under mild conditions.

Acknowledgement

The authors gratefully acknowledge partial support of this work by the Research Affairs Office of Bu-Ali Sina University (Grant number 32-1716: Development of Chemical Methods, Reagents and molecules), and the Center of Excellence in Development of Chemical Method (CEDCM), Hamedan, I. R. Iran.

References and Notes

(1) Choudary, B. M.; Mulukutla, R. S.; Klabunde, K. J. *J. Am. Chem. Soc.* **2003**, *125*, 2020.

(2) Martínez, A. G.; Barcina, J. O.; Heras, M. d. R. C.; Cerezo, Á. D. F. *Org. Lett.* **2000**, *2*, 1377.

(3) Zhang, C. Y.; Gao, X. Q.; Zhang, J. H.; Peng, X. J. *Chin. Chem. Lett.* **2009**, *20*, 913.

(4) Yang, H.-M.; Lin, C.-L. *J. Mol. Catal. A: Chem.* **2003**, *206*, 67.

(5) Yadav, J. S.; Reddy, B. V. S.; Reddy, A. S. *J. Mol. Catal. A: Chem.* **2008**, *280*, 219.

(6) Theerthagiri, P.; Lalitha, A. *Tetrahedron Lett.* **2010**, *51*, 5454.

(7) Mendoza, O.; Rossey, G.; Ghosez, L. *Tetrahedron Lett.* **2011**, *52*, 2235.

(8) Mohammadpoor-Baltork, I.; Moghadam, M.; Tangestaninejad, S.; Mirkhani, V.; Mohammadiannejad-Abbasabadi, K.; Zolfigol, M. A. *Compt. Rend. Chim.* **2011**, *14*, 934.

(9) Veisi, H. *Tetrahedron Lett.* **2010**, *51*, 2109.

(10) Shirini, F.; Sadeghzadeh, P.; Abedini, M. *Chin. Chem. Lett.* **2009**, *20*, 1457.

(11) Zolfigol, M. A. *Tetrahedron* **2001**, *57*, 9509.

(12) Khalafi-Nezhad, A.; Parhami, A.; Soltani Rad, M. N.; Zolfigol, M. A.; Zare, A. *Tetrahedron Lett.* **2007**, *48*, 5219.

(13) Zolfigol, M. A.; Kazaei, A.; Moosavi-Zare, A. R. *J. Org. Chem.* **2012**, *77*, 3640.

(14) Zolfigol, M. A.; Khazaei, A.; Moosavi-Zare, A. R.; Zare, A.; Khakyzadeh, V. *Appl. Catal. A: Gen.* **2011**, *400*, 70.

(15) Zolfigol, M. A.; Khazaei, A.; Moosavi-Zare, A. R.; Zare, A. *Org. Prep. Proced. Int.* **2012**, *42*, 95.

(16) Zhu, Y.; Rawal, V. H. *J. Am. Chem. Soc.* **2011**, *134*, 111.

(17) Valentine, R. A.; Whyte, A.; Awaga, K.; Robertson, N. *Tetrahedron Lett.* **2012**, *53*, 657.

(18) Silva, M.; Costa, C.; Pinto, M.; Lachter, E. *Reactive Polymers* **1995**, *25*, 55.

(19) Podder, S.; Roy, S. *Tetrahedron* **2007**, *63*, 9146.

(20) Guo, Q.; Li, L.; Chen, L.; Wang, Y.; Ren, S.; Shen, B. *Energy Fuels* **2009**, *23*, 51.

(21) Keglevich, G.; Balint, E.; Karsai, E.; Grün, A.; Balint, M.; Greiner, S. *Tetrahedron Lett.* **2008**, *49*, 5039.

(22) **General Procedure for the Synthesis of Diarylmethanes Using [Msim]AlCl$_4$**: To a mixture of aromatic substrate (1 mmol) and benzyl acetate (1 mmol) was added [Msim]AlCl$_4$ (0.017 g, 5 mol%) and the mixture was heated to 70 °C for the appropriate time (Table 3). After completion of the reaction, as monitored by TLC, the reaction mixture was cooled to r.t. and CH_2Cl_2 (2–5 mL) was added to separate the catalyst. After filtration, the pure product was obtained using plate chromatography on silica gel with *n*-hexane–EtOAc (10:2) as eluent. Note: In some cases, the reaction was carried out in CH_2Cl_2 (5 mL) at reflux (Table 3, entries 4–6, 9 and 10).

General Procedure for the Synthesis of Diarylmethanes Using SSA: To a mixture of aromatic substrate (1 mmol), and benzyl acetate (1 mmol), silica sulfuric acid (0.054 g, 7 mol%) was added and the mixture was heated to 80 °C for the appropriate time (Table 3). After completion of the reaction, as monitored by TLC, the reaction mixture was cooled to r.t. Absolute EtOH (2–5 mL) was added and the mixture was filtered to separate the catalyst. The pure product was obtained using plate chromatography on silica gel with *n*-hexane–EtOAc (10:2) as eluent. Note: In some cases, the reaction was carried out in CH_2Cl_2 (5 mL) at reflux (Table 3, entries 4–6, 9 and 10).