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Short Communication

Bis(perfluorooctanesulfonyl)imide supported on fluorous silica gel: Application to protection of carbonyls

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ABSTRACT

The immobilization of bis(perfluorooctanesulfonyl)imide ($HNPf_2$) on fluorous silica gel (FSG) and its utilization in protection of carbonyls have been investigated. This system is reasonably general and can be applied to converting several carbonyls to the corresponding acetals and ketals in good to excellent yields. There is no need for the use of anhydrous solvents or inert atmosphere. Recycling studies have shown that the FSG-supported $HNPf_2$ catalyst can be readily recovered and reused several times without significant loss of activity.

1. Introduction

Protection of carbonyl groups plays an important role during multistep syntheses in organic, medicinal, carbohydrate, and drug design chemistry. Among carbonyl protecting procedures, acetalization or ketalization is one of the most widely used methods for aldehydes and ketones. The protection of carbonyl groups as acetals is now commonly used as an important synthetic technique in the course of preparation of many organic compounds [1,2]. In addition, the acetals are important reactants for synthesis of enantiomerically pure compounds, which are widely used as steroids, pharmaceuticals, and fragrances [3–7]. Traditional methods [1] for the formation of acetals and ketals involve condensation of an aldehyde or ketone with an alcohol or diol using Brønsted or Lewis acid catalysis with a Dean-Stark trap or a dehydrating agent to remove water. Examples of these include dry HCl in alcoholic solvent [8], $(MeO)_3CH/p\text{-}TsOH$ [9], $(MeO)_3CH/Sc(NTf_2)_3$ [10], $(EtO)_3CH$/Amberlyst-15 [11], $(MeO)_3CH/InCl_3$ in refluxing cyclohexane–MeOH (3:1) [12] and $In(OTf)_3$ [13]. Unfortunately, some of these methods lead to a series of problems, such as product separation, catalyst recovery and corrosion. One way to avoid these problems is to use solid acid as catalyst, which is insoluble in the reaction medium, providing for facile separation by simple filtration. Some solid catalysts such as sulfonic acid-functionalized FSM-16 mesoporous silica [14], MCM-41 [15], ammonium triflate-functionalized silica [16] and imidazolium–styrene copolymer-supported $GaCl_3$ [17] have been reported to be active for acetalization.

In recent decades, the catalytic application of metal bis(perfluorooctanesulfonyl)imides in FBS has undergone rapid growth [18–20]. But perfluorinated solvents are expensive and environmentally persistent. Nishikido et al. have already reported the immobilization of fluorous Lewis acids using β-cyclodextrin epichlorohydrin copolymer as a support to catalyze Diels–Alder and Mukaiyama-aldol reactions in water [21]. They also reported that FSG-supported fluorous Lewis acids act as effective catalysts of Baeyer–Villiger and Diels–Alder reactions in water [22]. FSG has been generally used in solid–liquid extraction to separate fluorous compounds from organic compounds as well as in HPLC [23–27]. Bannwarth et al. originally reported Suzuki-Miyaura and Sonogashira coupling reactions catalyzed by fluorous-tagged palladium complexes immobilized on FSG in 1,2-dimethoxyethane [28]. From both economical and environmental point of views, the use of nontoxic solvents and nonmetallic catalysts is very promising. In this paper, we wish to introduce the immobilization of $HNPf_2$ on FSG and its utilization in protection of carbonyls.

2. Results and discussion

2.1. Characterization of the catalyst

Fig. 1 shows the IR spectra between 4500 and 500 cm^{-1} of FSG, $HNPf_2$ and FSG–$HNPf_2$, respectively. The results reveal that the supported catalyst possesses characteristic peaks of both support and bis(perfluorooctanesulfonyl)imide.

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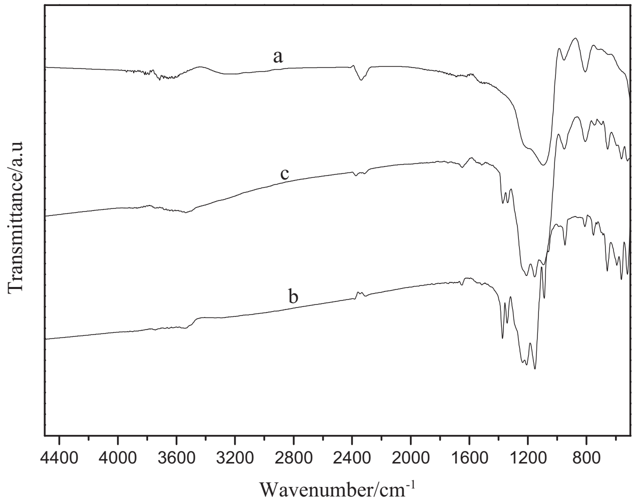


Fig. 1. FTIR spectra of: (a) the pure FSG; (b) $HNPf_2$; (c) FSG–$HNPf_2$.

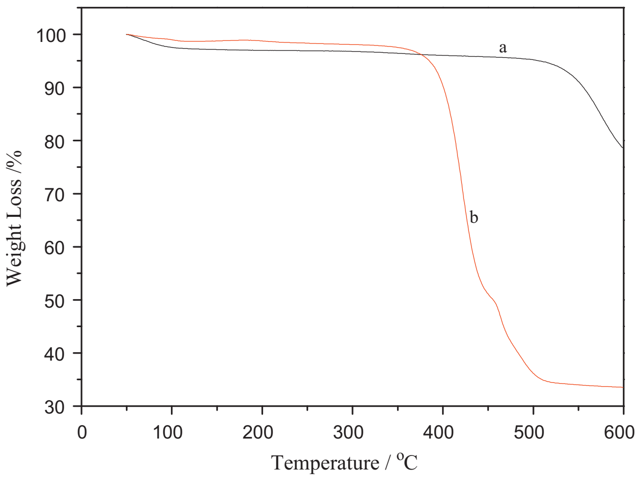


Fig. 3. Thermal analysis of samples: (a) TGA of the pure FSG; (b) TGA of FSG–$HNPf_2$.

From Fig. 2, it can be seen that FSG–$HNPf_2$ presents obvious Lewis acid sites as well as Brønsted acid sites. The intensive band at 1540 cm^{-1} and weaker one at 1450 cm^{-1} are assigned to Brønsted acid sites and Lewis acid sites, respectively. Another intensive band at 1490 cm^{-1} is attributed to a combination signal associated with both Lewis acid and Brønsted acid sites. For fluorous silica gel, no significant signals are observed at 1540 cm^{-1} band indicating that the pure fluorous silica gel offers very weak Brønsted acidity.

The TGA curve of FSG (Fig. 3(a)) shows a fairly flat line, which indicates that the support is highly stable before 500 °C. There is one main stage of weight loss for TGA of FSG–$HNPf_2$ (Fig. 3(b)) between 350 and 500 °C, which corresponds to the decomposition of $HNPf_2$ from the FSG framework. It implies that the supported catalyst cannot be treated above 350 °C.

2.2. Protection of carbonyls

We herein report effective protocols that facilitate the protection of carbonyls as either their cyclic or acyclic acetals and ketals using catalytic amounts of FSG–$HNPf_2$ (Scheme 1). The catalyst is very versatile and works well for the synthesis of dimethyl acetals and ketals, diethyl acetals and ketals as well as 1,3-dioxolanes from a variety of aldehydes and ketones. The reactions are extremely simple and do not generally require chromatographic purification and proceed without the requirement for inert or anhydrous reaction conditions.

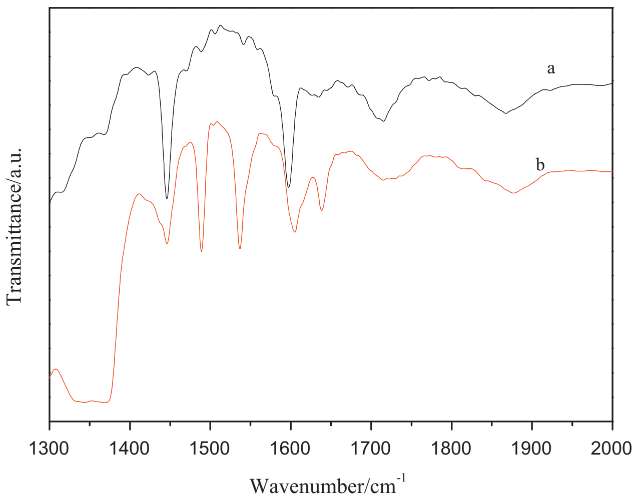


Fig. 2. Pyridine-FTIR spectra of: (a) the pure FSG; (b) FSG–$HNPf_2$.

For the beginning of this study, reactivities of FSG–$HNPf_2$, $HNPf_2$ and metal bis(perfluorooctanesulfonyl)imide complexes were investigated in the acetalization of benzaldehyde with trimethyl orthoformate in methanol. FSG–$HNPf_2$ catalyzed the reaction to give benzaldehyde dimethyl acetal in the highest conversion of >99% (Table 1, entry 5). The reaction catalyzed by $HNPf_2$ without support gave moderate yield (Table 1, entry 6), and the reaction in the presence of FSG without $HNPf_2$ gave low yield (Table 1, entry 7).

We next undertook examination of the conversion of a series of aldehydes and ketones to the corresponding dimethyl acetals and ketals using FSG–$HNPf_2$. Acyclic acetals have frequently been paid to special attention, owing to their liability as compared with cyclic *O*,*O*-acetals. The reaction was carried out by stirring the carbonyl compounds and trimethyl orthofomate (2 equiv.) in methanol with 1 mol% of FSG–$HNPf_2$. While acetal formation was observed in the presence of the catalyst and trialkyl orthoformate alone, the addition of the alcohol accelerated the rate of the reaction. When the reaction was attempted using the catalyst and alcohol alone (no trialkyl orthoformate), significant acetal formation was not observed. A wide variety of aldehydes and ketones underwent smooth reaction to give the corresponding acetals and ketals in good yield (Table 2). Aromatic aldehydes, such as *p*-chlorobenzaldehyde, *p*-bromobenzaldehyde, *p*-nitrobenzaldehyde and *p*-methoxybenzaldehyde could be acetalized to afford the corresponding dimethyl acetals in excellent yields. The electronic nature or position of the substituents on the aromatic ring showed no effect on the conversion. Acid-sensitive substrate such as

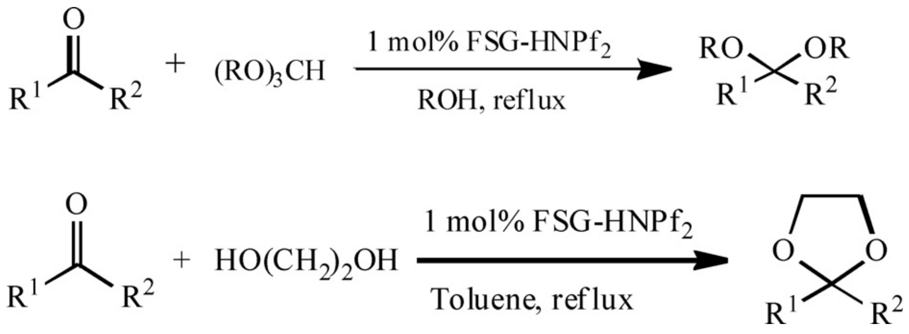
Table 1
Comparison of catalytic activities in the acetalization of benzaldehyde with trimethyl orthoformate.[a]

Entry	Catalyst	Conversion (%)[b]
1	FSG–$Sn(NPf_2)_4$	68
2	FSG–$Hf(NPf_2)_4$	79
3	FSG–$Sc(NPf_2)_3$	89
4	FSG–$Yb(NPf_2)_3$	87
5	FSG–$HNPf_2$	>99
6	$HNPf_2$	83
7	FSG[c]	34
8	None	Trace

[a] Reaction conditions: 1 mmol benzaldehyde, 2 mmol trimethyl orthoformate, 3 mL methanol, 1 mol% catalyst, reflux, 2 h.

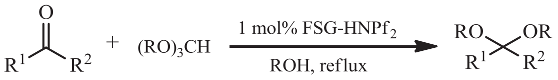
[b] Detected by GC/MS. Conversion based on benzaldehyde.

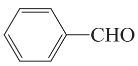
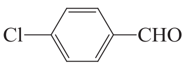
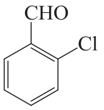
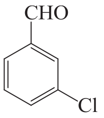
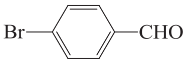
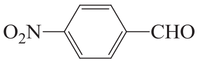
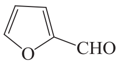
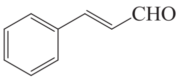
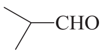
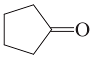
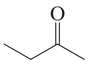
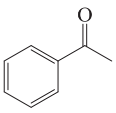
[c] The amount of the catalyst: 0.1 g.



Scheme 1. Acetalization of carbonyl compounds catalyzed by FSG-supported bis(perfluorooctanesulfonyl)imide.

Table 2
Protection of carbonyls as dialkyl acetals (ketals).[a]



Entry	Aldehydes (ketones)	Time (h)	Conversion (%)[b]		Selectivity (%)	
			Dimethyl acetals (ketals)	Diethyl acetals (ketals)	Dimethyl acetals (ketals)	Diethyl acetals (ketals)
1		2	>99	97	100	100
2		2	93	98, 99, 97, 96[c]	100	100
3		2	>99	81	100	100
4		2	>99	79	100	100
5		2	94	80	100	100
6		2	93	>99	100	100
7		3	91	91	100	100
8		2	99	91	100	100
9		2	81	91	100	100
10		2	57	93	100	100
11		4	63	97	100	100
12		4	88	68	100	100
13		4	99	90	100	100

[a] Reaction conditions: 1 mmol aldehyde or ketone, 2 mmol trialkyl orthofomate, 3 mL alcohol, 1 mol% FSG–HNPf$_2$, reflux.
[b] Detected by GC/MS. Conversion based on the carbonyls.
[c] Catalyst was reused in three times. Loss of catalyst (<5%) during handling.

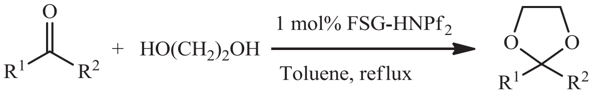
furfural was efficiently protected as dimethyl acetal without any accompanying self-condensation or ring cleavage (Table 2, entry 8). Notably, α,β-unsaturated aldehyde was facilely acetalized without concomitant double-bond isomerization (Table 2, entry 9). Aliphatic aldehyde (Table 2, entry 10) reacted sluggishly, however, the product yield was much lower than those obtained with aromatic aldehydes. The ketalization reaction was also examined over the FSG–HNPf$_2$ system. A moderately hindered ketone, acetophenone which is difficult to protect as its acetal is also converted to the corresponding dimethyl acetal in 99% yield (Table 2, entry 13).

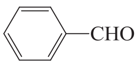
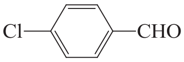
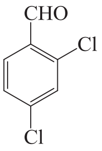
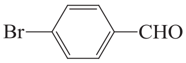
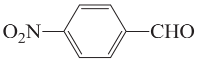
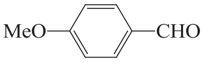
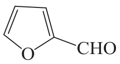
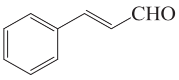
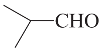
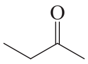
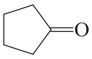
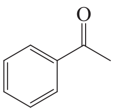
A large number of methods exist for the synthesis of dimethyl acetals, while fewer methods are available for the synthesis of diethyl acetals [29,30]. We also examined the diethyl acetalization of a variety of structurally different aldehydes and ketones (Table 2). Both activated and deactivated aldehydes underwent smooth acetalization without any trace of by-products to give the corresponding acetals in excellent yields. For reactions of some less reactive ketones, such as cyclohexanone and acetophenone, ketalization were also observed in excellent yields.

Cyclic acetals are also important protecting groups for carbonyl compounds. The standard method for synthesis of 1,3-dioxolanes consists of heating a mixture of the carbonyl compound and ethylene glycol in refluxing benzene with the azeotropic removal of water. This method is not particularly suitable for large-scale synthesis and also uses the carcinogenic solvent benzene. We have developed a practical method for the synthesis of 1,3-dioxolanes (Table 3). In the method, toluene is used as a solvent and 1 mol% FSG–HNPf$_2$ serves as the catalyst. Under these conditions, at 110 °C, the reactions reached moderate to excellent conversion.

It is notable that *o*-hydroxybenzaldehyde did not form any trace of dialkyl acetal and 1,3-dioxolane even after 24 h, mostly because

Table 3
Protection of carbonyls as 1,3-dioxolanes.[a]



Entry	Aldehydes (ketones)	Time (h)	Conversion (%)[b]	Selectivity (%)
1		2	97, 98, 97, 97[c]	100
2		2	>99	100
3		2	>99	100
4		2	93	100
5		2	>99	100
6		3	90	100
7		2	>99	100
8		2	71	100
9		2	72	100
10		5	88	100
11		5	>99	100
12		5	97	100

[a] Reaction conditions: 1 mmol aldehyde or ketone, 2 mmol ethylene glycol, 3 mL toluene, 1 mol% FSG–HNPf$_2$, reflux.
[b] Detected by GC/MS. Conversion based on the starting carbonyls.
[c] Catalyst was reused in three times. Loss of catalyst (<5%) during handling.

o-hydroxybenzaldehyde has higher electron density around the carbonyl carbon and it is less susceptible to nucleophilic attack by alcohols.

2.3. Effect of the recovered FSG–HNPf$_2$ on acetalization of carbonyls

The recycling performance of FSG–HNPf$_2$ was also investigated in the reactions of both *p*-chlorobenzaldehyde with triethyl orthoformate in ethanol and benzaldehyde with ethylene glycol in toluene. After the reaction, FSG–HNPf$_2$ was recovered by simple filtration. The data listed in Tables 2 and 3 showed recycling of the catalyst was achieved by FSG–HNPf$_2$ without obvious loss of catalytic activities indicating the non-leaching behavior of acidic contents from the catalyst during the course of reaction. The non-leaching behavior of the acidic contents was also checked by doing several blank experiments [31].

3. Experimental

3.1. General

Mass spectra were recorded on Saturn 2000 GC/MS instrument. ^{1}H NMR and ^{13}C NMR spectra were measured on Bruke Advance RX500. The quantitative analysis of the reaction mixture was determined by HP4890 GC analyzer with HP-5. FTIR and pyridine-FTIR were conducted on a Bruker VERTEX70 spectrophotometer. The thermogravimetric analysis (TGA) was carried out on a Shimadazu TGA-50 with a heating rate of 10 °C/min from 50 to 600 °C under nitrogen atmosphere. Fluorous silica gel was purchased from Fluorous Technologies Inc. All chemicals (AR grade) were commercially available and used without further purification.

3.2. Preparation of catalyst [22]

Into a solution of bis(perfluorooctanesulfonyl)imide (200 mg) in ethanol (10 mL), fluorous silica gel (2 g) was added and the resulting mixture was stirred for 1 h at room temperature. After removal of the solvent under reduced pressure, residual FSG-supported bis(perfluorooctanesulfonyl)imide was dried under vacuum at 80 °C for 6 h.

3.3. Typical procedure for the synthesis of dialkyl acetals

A solution of benzaldehyde (1 mmol) and trimethyl orthoformate (2 mmol) in methanol (3 mL) was stirred as FSG–HNPf$_2$ (1 mol%) was added. The reaction mixture was heated at reflux for 2 h and then cooled to room temperature. Supported catalyst was recovered by filtration and washed with 1,2-dichloroethane (5 mL). FSG–HNPf$_2$ was dried under vacuum for reuse in the next cycle. The reaction mixture was analyzed by GC and GC/MS. The crude residue was purified by column chromatography using silica gel with hexanes/ethyl acetate (20:1 to 5:1 gradient) as the eluent system. Spectroscopic data for selected examples are shown below.

Benzaldehyde diethyl acetal: ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.48 (d, *J* = 7.6 Hz, 2H), 7.41–7.33 (m, 3H), 5.56 (s, 1H), 3.69–3.47 (m, 4H), 1.25 (t, *J* = 7.1 Hz, 6H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 139.5, 129.7, 128.3, 126.7, 101.6, 61.5, 15.1. MS *m*/*z* 180 (M$^+$).

(1,1-Dimethoxyethyl)benzene: ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.51–7.43 (m, 2H), 7.41–7.26 (m, 3H), 3.17 (s, 6H), 1.53 (s, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 142.6, 128.3, 127.5, 126.1, 101.5, 48.9, 26.1. MS *m*/*z* 166 (M$^+$).

3.4. Typical procedure for the synthesis of 1,3-dioxolanes

A mixture of benzaldehyde (1 mmol), ethylene glycol (2 mmol) and toluene (3 mL) was stirred as FSG–HNPf$_2$ (1 mol%) was added. The reaction mixture was heated at reflux for 2 h and then cooled to room temperature. Supported catalyst was recovered by filtration and washed with 1,2-dichloroethane (5 mL). FSG–HNPf$_2$ was dried under vacuum for reuse in the next cycle. The reaction mixture was analyzed by GC and GC/MS. The crude residue was purified by column chromatography using silica gel with hexanes/ethyl acetate (20:1 to 5:1 gradient) as the eluent system. Spectroscopic data for selected examples are shown below.

2-Phenyl-1,3-dioxolane: ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.53–7.45 (m, 2H), 7.41–7.32 (m, 3H), 5.81 (s, 1H), 4.18–4.07 (m, 2H), 4.09–3.97 (m, 2H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 137.8, 129.3, 128.1, 126.3, 103.7, 65.5. MS *m*/*z* 150 (M$^+$).

2-Methyl-2-phenyl-1,3-dioxolane: ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.51–7.45 (m, 2H), 7.38–7.24 (m, 3H), 4.15–3.93 (m, 2H), 3.87–3.73 (m, 2H), 1.67 (s, 3H). ^{13}C NMR (CDCl$_3$) δ 143.1, 128.3, 127.6, 125.3, 108.7, 64.5, 27.6. MS *m*/*z* 164 (M$^+$).

2-(4-Methoxyphenyl)-1,3-dioxolane: ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.43 (d, *J* = 8.5 Hz, 2H), 6.92 (d, *J* = 8.8 Hz, 2H), 5.78 (s, 1H), 4.17–4.09 (m, 2H), 4.07–3.95 (m, 2H), 3.83 (s, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 160.5, 130.1, 127.6, 113.8, 103.9, 65.2, 55.3. MS *m*/*z* 180 (M$^+$).

4. Conclusion

In conclusion, the present procedure using FSG–HNPf$_2$ as a catalyst provides a very simple, efficient and general methodology for the protection of a variety of structurally diverse aldehydes and ketones to the corresponding 1,3-dioxolanes and dialkyl acetals. The significant advantages offered by this method are: (a) general applicability to all types of carbonyl compounds providing 1,3-dioxolanes as well as acetals, (b) high yields, (c) considerably lower catalyst loading, (d) no migration of double bonds during acetalization, (e) ease of handling, and (f) recyclability of the catalyst. Thus, we believe that this procedure will provide a practical and better alternative to the existing procedures for acetalization.

References

[1] T.W. Greene, P.G.M. Wuts, Protective Groups in Organic Synthesis, 3rd ed., John Wiley and Sons, New York, 1999.
[2] P.J. Kocienski, Protecting Groups, 1st ed., Thieme, New York, 1994.
[3] W.S. Johnson, C.A. Harbert, B.E. Ratcliffe, R.D. Stipanovic, Journal of the American Chemical Society 98 (1976) 6188–6193.
[4] P.A. Bartlett, W.S. Johnson, J.D. Elliott, Journal of the American Chemical Society 105 (1983) 2088–2089.
[5] A. Mori, H. Yamamoto, Journal of Organic Chemistry 50 (1985) 5444–5446.
[6] K. Narasaka, M. Inoue, T. Yamada, J. Sugimori, N. Iwasawa, Chemistry Letters (1987) 2409–2412.
[7] D.M. Clode, Chemical Reviews 79 (1979) 491–513.
[8] A.F.B. Cameron, J.S. Hunt, J.F. Oughton, P.A. Wilkinson, B.M. Wilson, Journal of the Chemical Society (1953) 3864–3869.
[9] E. Wenkert, T.E. Goodwin, Synthetic Communications 7 (1977) 409–415.
[10] K. Ishihara, Y. Karumi, M. Kubota, H. Yamamoto, Synlett (1996) 839–841.
[11] S.A. Patwardhan, S. Dev, Synthesis (1974) 348–349.
[12] B.C. Ranu, R. Jana, S. Samanta, Advanced Synthesis and Catalysis 346 (2004) 446–450.
[13] B.T. Gregg, K.C. Golden, J.F. Quinn, Tetrahedron 64 (2008) 3287–3295.
[14] K. Shimizu, E. Hayashi, T. Hatamachi, T. Kodama, T. Higuchi, A. Satsuma, Y. Kitayama, Journal of Catalysis (2005) 131–138.
[15] Y. Tanaka, N. Sawamura, M. Iwamoto, Tetrahedron Letters 39 (1998) 9457–9460.
[16] B. Karimi, M. Ghoreishi-Nezhad, Journal of Molecular Catalysis A: Chemical 277 (2007) 262–265.
[17] Q.X. Bao, K. Qiao, D. Tomida, C. Yokoyama, Catalysis Communications 10 (2009) 1625–1628.
[18] X.H. Hao, O. Yamazaki, A. Yoshida, J. Nishikido, Greem Chemistry 5 (2003) 524–528.
[19] X.H. Hao, A. Yoshida, J. Nishikido, Greem Chemistry 6 (2004) 566–569.
[20] X.H. Hao, A. Yoshida, J. Nishikido, Tetrahedron Letters 46 (2005) 2697–2700.
[21] J. Nishikido, M. Nanbo, A. Yoshida, H. Nakajima, Y. Matsumoto, K. Mikami, Synlett (2002) 1613–1616.
[22] O. Yamazaki, X.H. Hao, A. Yoshida, J. Nishikido, Tetrahedron Letters 44 (2003) 8791–8795.
[23] E. de Wolf, G. van Koten, B.-J. Deelman, Chemical Society Reviews 28 (1999) 37–41.

[24] S. Kainz, Z. Luo, D.P. Curran, W. Leitner, Synthesis (1998) 1425–1427.
[25] D.P. Curran, Synlett (2001) 1488–1496.
[26] Q. Zhang, A. Rivkin, D.P. Curran, Journal of the American Chemical Society 124 (2002) 5774–5781.
[27] W. Zhang, Z. Luo, C.H.T. Chen, D.P. Curran, Journal of the American Chemical Society 124 (2002) 10443–10450.
[28] C.C. Tzschucke, C. Markert, H. Glatz, W. Bannwarth, Angewandte Chemie International Edition 41 (2002) 4500–4503.
[29] H. Firouzabadi, N. Iranpoor, B. Karimi, Synlett (1999) 321–323.
[30] B. Karimi, H. Seradj, G.R. Ebrahimian, Synlett (1999) 1456–1458.
[31] The catalyst (HNPf$_2$–FSG) along with solvent (CH_3OH, C_2H_5OH and $PhCH_3$) was stirred under the experimental conditions for 24 h. The catalyst was filtered and the fresh reactants were added to the filtrate (by assuming if the leaching of acidic contents occur, it may lead to some conversion). However no conversion was observed for the reactions indicating the non-leaching behavior of the acidic contents.