Chinese Chemical Letters Vol. 16, No. 3, pp 299-302, 2005
http://www.imm.ac.cn/journal/ccl.html

The Synthesis of 2, 4, 6-Triisopropyl-1, 3, 5-trioxane Catalyzed by Ionic Liquids

Jian Guo YANG*, Xin Yu YU, Hai Hong WU, Zhi Lin CHENG,
Yue Ming LIU, Ming Yuan HE

Shanghai Key Laboratory of Green Chemistry and Chemical Processes,
East China Normal University, Shanghai 200062

Abstract: The synthesis of 2, 4, 6-triisopropyl-1, 3, 5-trioxane with high yield and desirable selectivity from solvent-free cyclotrimerization of isobutyraldehyde catalyzed by ionic liquids was reported in this work.

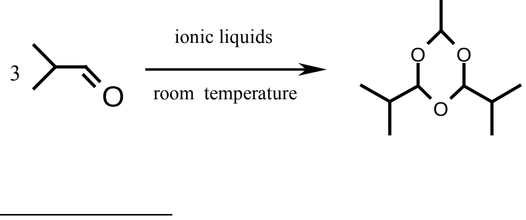
Keywords: Isobutyraldehyde, cyclotrimerization, 2, 4, 6-triisopropyl-1, 3, 5-trioxane, ionic liquids.

2, 4, 6-Triisopropyl-1, 3, 5-trioxane, which is sublimable, nontoxic, odourless and tasteless, was of great interest for the practical application. The conventional approach for snynthesizing 2, 4, 6-triisopropyl-1, 3, 5-trioxane was through the cyclotrimerization of isobutyraldehyde catalyzed by protonic acid such as H_2SO_4, H_3PO_4[1], Lewis acid such as $ZnCl_2$[1], solid acid such as ZrO_2, $Zr(OH)_2$, TiO_2, SnO_2[2], bentonitic earth[3], $Ph_3P^+CH_2CO$-$MeBr^-$[4], Me_3SiCl[5], $Cp_2Zr(OTf)_2$[6], Keggin-type heteropolyacids such as $H_3PMo_{12}O_{40}$, $H_3PW_{12}O_{40}$ and $H_4SiW_{14}O_{40}$[7].

More recently, ionic liquids as an environmentally benign media for organic synthesis and catalytic reaction have attracted extensive attention[8-12]. To the best of our knowledge, the cyclotrimerization of aldehydes using ionic liquids as catalyst has not been reported.

In this work, we report a novel method for the synthesis of 2, 4, 6-triisopropyl-1, 3, 5-trioxane from the cyclotrimerization of isobutyraldehyde catalyzed by ionic liquids. The reaction was illustrated in **Scheme 1**.

Scheme 1



---

[*] E-mail: jgyangsh64@126.com

Experimental

The ionic liquids, BMIC/$AlCl_3$, BMIC/$FeCl_3$ (where BMIC is 1-butyl-3-methylimidazolium chloride), EMIC/ $FeCl_3$(where EMIC is 1-ethyl-3-methylimidazolium chloride), $[Et_3NH]Cl/AlCl_3$, $[Et_3NH]Cl/FeCl_3$, $[BuNH_3]Cl/FeCl_3$, $[NEt_2H_2]Cl/FeCl_3$, $[Hmim]BF_4$ (where $[Hmim]^+$ is N-methylimidazolium cation), BMIC /$ZnCl_2$ and BMIC /CuCl, were synthesized according to the literatures[13-19] respectively. A typical procedure for the synthesis of 2, 4, 6-triisopropyl-1, 3, 5-trioxane was as follows: In a 100 mL three necked flask equipped with a thermometer, a reflux condenser and a N_2-inlet valve, 25 g isobutyraldehyde(Merck, ⩾99%) and 1 g ionic liquid($[Et_3NH]Cl/FeCl_3$) were added. The reaction mixture was stirred at room temperature for 1 h and the crystals formed. After reaction, *n*-hexane(30 mL) was added to the flask to dissolve the crystals, the solvent phase was decanted and monitored by GC-MS(Agilent 6890 Series/5973N). The ionic liquid was reused after rotary distillation in vacuum. 2, 4, 6-Triisopropyl-1, 3, 5-trioxane(22.7 g, yield 91.1%) was obtained after removal of *n*-hexane and isobutyraldehyde. MS(70eV) *m/z*: 215(M^+), 173 (3), 145(23), 73(100), 55(15). ^{1}HNMR (Brucker DX S300, $CDCl_3$，δ_{ppm}) 0.95 (d , 18H, J=6.8Hz, CH_3), 1.75(q, 3H, CH), 4.5(d, 3H, J=5Hz, CH). IR(Nicolet NEXUS-670 FT-IR, KBr), ν(cm^{-1}): 2964 (CH), 1379(CH_3), 1102(C-O-C). Elemental analysis(%): Calcd. for $C_{10}H_{21}O_3$ C, 66.67; H, 11.11; Found: C, 66.60; H, 11.26.

Results and Discussion

The results of the cyclotrimerization of isobutyraldehyde catalyzed by different ionic liquid without solvent were shown in **Table 1**. It was found that both aluminum chloride based ionic liquids and the ferric chloride based ones have excellent catalytic performance for the cyclotrimerization of isobutyraldehyde (Entries 1~7 in **Table 1**), however, the Lewis acidic ionic liquids of $FeCl_3$ immobilized with 1-butyl-3-methylimidazolium chloride, 1-ethyl-3-methylimidazolium chloride and alkylammonium hydrochloride salts were more favorable to the cyclotrimerization of isobutyraldehyde than that of $AlCl_3$. BMIC /$ZnCl_2$ or BMIC /CuCl, which afforded lower conversion and yield (Entry 8~ 9), in addition the Brønsted acidic ionic liquid $[Hmim]BF_4$ gave a low reaction activity (Entry 10 in **Table 1**) possibly due to weak Brønsted acidity. It is notable that ferric chloride based ionic liquids catalyst could obtain better yield and selectivity than those of the aluminum chloride based ionic liquids, probably due to the aluminum chloride based ionic liquids were sensitive to minimal water. The ionic liquids would be destroyed by moisture. In the aluminum chloride based ionic liquids and the ferric chloride based ionic liquids systems existed the following equations[20,21]. $[AlCl_4]^- + AlCl_3 \rightleftharpoons [Al_2Cl_7]^-$, $[FeCl_4]^- + FeCl_3 \rightleftharpoons [Fe_2Cl_7]^-$. $[Al_2Cl_7]^-$ and $[Fe_2Cl_7]^-$ might be the catalytic active species for the cyclotrimerization of isobutyraldehyde. The similar equations existed in BMIC /$ZnCl_2$[14] and BMIC /CuCl[22], respectively. $[ZnCl_3]^- + ZnCl_2 \rightleftharpoons [Zn_2Cl_5]^-$, $[CuCl_2]^- + CuCl \rightleftharpoons [Cu_2Cl_3]^-$. $[Zn_2Cl_5]^-$ and $[Cu_2Cl_3]^-$ possess weaker acidity than $[Fe_2Cl_7]^-$ and $[Al_2Cl_7]^-$, so BMIC /$ZnCl_2$ and BMIC /CuCl give lower yield and selectivity for this reaction.

Table 2 showed the efficiency of the recycled catalyst in the ionic liquid [Et_3NH]Cl/$FeCl_3$ system. The ionic liquid [Et_3NH]Cl/$FeCl_3$ was separated by decantation of solvent phase and distillation in vacuum. The recovered catalyst system kept activity well even after 5 times reuse.

In summary, we have developed a new method for preparation 2, 4, 6-triisopropyl- 1, 3, 5-trioxane with high conversion and yield, using acidic ionic liquids as an environmentally benign catalyst.

Table 1 The results of cyclotrimerization of isobutyraldehyde catalyzed by $FeCl_3$ and different ionic liquids[a]

Entry	Catalyst	Conversion %	Yield %	Selectivity [d] %
1	[Et_3NH]Cl/$FeCl_3$ [b]	91.1	91.0	99.8
2	[NEt_2H_2]Cl/$FeCl_3$ [b]	89.3	88.3	98.9
3	[$BuNH_3$]Cl/$FeCl_3$ [b]	90.9	88.9	97.8
4	EMIC/ $FeCl_3$ [b]	91.8	91.4	99.5
5	BMIC/ $FeCl_3$ [b]	92.0	90.8	98.7
6	[Et_3NH]Cl/$AlCl_3$ [b]	91.9	82.8	90.0
7	BMIC/$AlCl_3$ [b]	87.6	82.5	94.2
8	BMIC /$ZnCl_2$ [b]	43.2	41.5	96.0
9	BMIC /CuCl [b]	35.4	34.8	98.3
10	[Hmim]BF_4 [c]	<15.1	<15.1	—
11	$FeCl_3$	88.4	60.0	67.9

[a] Reaction conditions: isobutyraldehyde(Merch, ≥99%) 25 g, ionic liquids 1g, 25 °C for 1 h.

[b] The molar ratio between alkylammonium hydrochloride salts, 1-butyl-3-methylimidazolium chloride or 1-ethyl-3-methylimidazolium chloride and corresponding Lewis acids is 1:1.6.

[c] The molar ratio between N-methylimidazolium and HBF_4 is 1:1.

[d] Selectivity to 2, 4, 6-triisopropyl-1, 3, 5-trioxane.

Table 2 The efficiency of recycled catalyst of [Et_3NH]Cl/$FeCl_3$[a]

Recycling times	Conversion %	Selectivity [b] %
1	91.2	99.7
2	91.1	99.6
3	91.1	99.7
4	90.6	99.6
5	90.5	99.6

[a] Reaction conditions: isobutyraldehyde 12 g, ionic liquids 3.0 g, 25 °C for 1 h. The molar ratio between [Et_3NH]Cl and $FeCl_3$ is 1:1.6.

[b] Selectivity to 2, 4, 6-triisopropyl-1, 3, 5-trioxane.

Acknowledgments

We gratefully appreciate the financial support from the National Natural Science Foundation of China (G2000048).

References

1. M. F. Amagasaki, T. A. Nagaokakyo, Y. S. Suita, *et al.*, US3,981,889, September 21, **1976**.
2. T. Ogawa, JP 53,101,386, September 4, **1978**.
3. R. Camarena, A. C. Cano, F. Delgado, *et al.*, *Tetrahedron Lett.*, **1993**, *34*, 6857.
4. Y. S. Hon, C. F. Lee, *Tetrahedron*, **2001**, *57*, 6181.
5. J. Auge, R. Gil, *Tetrahedron Lett.*, **2002**, *43*, 7919.
6. Y. Ishii, T. Nakano, JP 2002145877, May 22, **2002**.
7. S. Sato, C. Sakurai, H. Furuta, *et al.*, *J. Chem. Soc.Chem.Commun.*, **1991**, 1327.
8. P. Wasserscheid, W. Keim, *Angew. Chem. Int. Ed.*, **2000**, *39*, 3773.
9. C. J. Adams, M. J. Earle, G. Roberts, *et al.*, *Chem. Commun.*, **1998**, 2097.
10. P. J. Dyson, M. C. Grossel, N. Srinivasan, *et al., J. Chem. Soc, Dalton Trans.*, **1997**, 3465.
11. M. H. Valkenberg, M.Valkenberg, W. F.Holderich, *Appl. Catal. A General.*, **2001**, *215*, 185.
12. M. J. Earle, P. B. McCormac, K. R. Seddon, *Chem. Commun.*, **1998**, 2245.
13. M. S. Sitze, E. R. Schreiter, E. V. Patterson, *et al.*, *Inorg. Chem.*, **2001**, *40*, 2298.
14. S. I. Hsiu, J. F. Huang, I. W. Sun, *et al.*, *Electrochimica Acta*, **2002**, *47*, 4367.
15. S. A. Bolkan, J. T. Yoke, *J. Chem. Eng. Data*, **1986**, *31*, 194.
16. A. Boon, J. A. Levisky, J. L. Pflug, *et al.*, *J. Org. Chem.*, **1986**, *51*, 480.
17. T. Welton, *Chem. Rev.*, **1999**, *99*(8), 2071.
18. F. G. Sherif, L. J. Shyu, C. C. Greco, US5,824,832, October 20, **1998**.
19. J. D. Holbrey, K. R. Seddon, *J. Chem. Soc. Dalton Trans.*, **1999**, 2133.
20. J. S. Wilkes, J. S. Frye, G. F. Reynolds, *Inorg. Chem.*, **1983**, *22*, 3870.
21. A. A. K. Abdul-Sada, A. M. Greenway, K. R. Seddon, *Org. Mass Spectrom.* ,**1993**, *28*,759.
22. J. R. Siikey, J. T. Yoke, J. *Electrochem. Soc.*, **1980**, *127*, 1091.

Received 16 January, 2004