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# Ionic liquid [omim][$PF_6$] as an efficient and recyclable reaction media for the cyanosilylation of aldehydes without Lewis acid or any special activation

Zhi-Liang Shen,[b] Shun-Jun Ji[b,*] and Teck-Peng Loh[a,b,*]

[a] *Division of Chemistry and Biological Chemistry, Nanyang Technological University, Singapore 637616, Singapore*
[b] *Key Lab. of Organic Synthesis of Jiangsu Province, College of Chemistry and Chemical Engineering of Suzhou University, Suzhou 215006, China*

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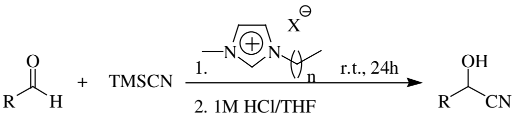
**Abstract**—Ionic liquid [omim][$PF_6$] has been demonstrated as an efficient and environmentally friendly reaction media as well as a promoter for the cyanosilylation of aldehydes under mild conditions. In addition, the recovered ionic liquid could be reused for subsequent runs with only a gradual decrease in activity.

Cyanohydrins are versatile compounds, which can be easily converted into a wide variety of important building blocks such as α-hydroxy carbonyl compounds, β-hydroxy amines and α-amino acid derivatives.[1] Therefore, much effort has been directed towards the development of novel, versatile and practical methods for the synthesis of cyanohydrins. Among them, the addition of trimethylsilyl cyanide (TMSCN) to aldehydes promoted by Lewis acids[2] or Lewis bases[3] is the most widely used procedure for the preparation of cyanohydrins. Although the cyanation reaction of aldehydes has been extensively studied, the cyanation reaction at ambient temperature in the absence of Lewis acid (or Lewis base) or any special activation continues to pose a great challenge to organic chemists. In view of the emerging importance of imidazolium based ionic liquids[4,5] as novel reaction media, we wish to explore the use of ionic liquids as promoters and recyclable solvent systems for the synthesis of cyanohydrins under mild conditions. We envisage that the polar nature of the ionic liquid containing a stable anion will effect the addition of TMSCN to aldehydes without Lewis acid catalyst or any special activation. In this paper, we would like to report cyanosilylation of aldehydes in ionic liquids, which proceeded smoothly with various aldehydes at ambient temperature without Lewis acid (or base) or any special activation to afford the corresponding products in good yields (Scheme 1).

An initial experiment on the reaction of benzaldehyde and TMSCN was carried out in different ionic liquids at room temperature. As shown in Table 1, in all cases, the reaction proceeded smoothly to afford the product in moderate to excellent yield without Lewis acid (or base) or any special activation. It is interesting to note that ionic liquids with longer cation carbon chain length afforded the products in higher yield (Table 1, entries 1 and 2; entries 5 and 6). Especially noteworthy, ionic liquid [omim][$PF_6$] was found to afford the product in highest yield (99% yield; Table 1, entry 6).

It has been reported that HF might be present in [omim][$PF_6$] due to the relatively facile decomposition of $PF_6$ anion in the presence of a trace amount of water.[6] Therefore, HF generated from the ionic liquid might have promoted the reaction. However, in our



**Scheme 1.**

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*Keywords*: Ionic liquid; [omim][$PF_6$]; TMSCN; Cyanosilylation; Cyanohydrins; Recycle.

* Corresponding authors. Tel.: +65 874 1781; fax: +65 779 1691; e-mail: teckpeng@ntu.edu.sg

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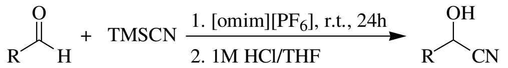
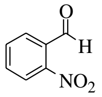
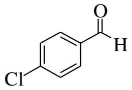
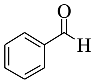
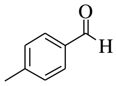
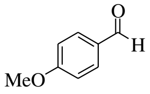
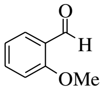
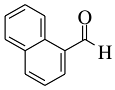
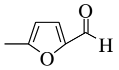
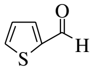
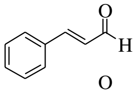
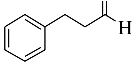
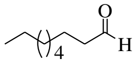
**Table 1.** Investigation of cyanosilylation of benzaldehyde employing various ionic liquids

| Entry | Ionic liquid | Yield[a] (%) |
|---|---|---|
| 1 | [hmim][Cl] ($n = 5$) | 75 |
| 2 | [omim][Cl] ($n = 7$) | 80 |
| 3 | [bmim][BF$_4$] ($n = 3$) | 84 |
| 4 | [omim][BF$_4$] ($n = 7$) | 84 |
| 5 | [bmim][PF$_6$] ($n = 3$) | 86 |
| 6 | [omim][PF$_6$] ($n = 7$) | 99 |

[a] Isolated yield.

**Table 2.** The cyanosilylation of various aldehydes in ionic liquid [omim][PF$_6$][7,a]



| Entry | Aldehyde | Yield[b] (%) |
|---|---|---|
| 1 |  | 83 |
| 2 |  | 82 |
| 3 |  | 99 |
| 4 |  | 92 |
| 5 |  | 87 |
| 6 |  | 95 |
| 7 |  | 96 |
| 8 |  | 65 |
| 9 |  | 74 |
| 10 |  | 94 |
| 11 |  | 99 |
| 12 |  | 80 |

[a] All the reactions have been carried out at room temperature for 24 h using aldehyde (1 mmol), TMSCN (2 mmol) and ionic liquid [omim][PF$_6$] (0.5 mL). All the ionic liquids used were pretreated by drying under reduced pressure before use.

[b] Isolated yield.

experiment utilizing [omim][PF$_6$] as a reaction media, after the completion of the reaction only OTMS protected product was observed according to crude $^1$H NMR analysis. Furthermore, the fact that the reaction also proceeded smoothly in [omim][Cl] (Table 1, entry 2) showed that HF (derived from PF$_6^-$) is not crucial for the success of this reaction. When we carried out the reaction of benzaldehyde (1 mmol) with TMSCN (2 mmol) in the presence of ionic liquid [omim][PF$_6$] (0.5 mL) and water (0.25 mL) at room temperature for 24 h, after the completion of the reaction, only the corresponding desilylated product (cyanohydrin) was obtained and isolated in 81% yield (the HF generated from ionic liquid and water caused desilylation of OTMS protected product, which was derived from the reaction of benzaldehyde and TMSCN). Therefore, in all cases, the reactions must have proceeded through a totally different pathway.

Next, we investigated the cyanation reaction of TMSCN with various aldehydes employing ionic liquid [omim][PF$_6$]. The results are summarized in Table 2. In all cases, the products were obtained in good to excellent yields. It is important to note that even unreactive aldehydes such as aliphatic aldehydes (Table 2, entries 11 and 12) could react with TMSCN to afford the cyanohydrins in good yields. In addition, the reaction of TMSCN with α,β-unsaturated aldehyde (Table 2, entry 10) afforded only the 1,2-addition product in 94% yield. No 1,4-adduct was observed. For acetophenone, no desired product was obtained under the same condition.

With the success of the above reactions, we continued our study by exploring the recyclability of the ionic liquid. The remaining ionic liquid [omim][PF$_6$] was recovered and recycled in subsequent reactions with only a gradual decrease in activity being observed (Table 3). For instance, the recycling procedure using benzaldehyde was found to afford the product in 99% (1st run), 88% (2nd run), 92% (3rd run), 84% (4th run) and 79% (5th run).

In summary, we have developed an efficient and environmentally friendly method for cyanosilylation reaction of aldehydes using recyclable ionic liquid [omim][PF$_6$] as reaction media. Furthermore, this reaction works at room temperature in the absence of Lewis acid (or Lewis base) or any special activation. This method is quite general and it works with a wide variety of aldehydes. The mild reaction conditions, good yields, the simplicity of the reaction procedure, and ease of recovery and reuse of this reaction medium makes this method attractive for scale-up purposes.

**Table 3.** Recycling of [omim][PF$_6$] in the cyanosilylation reaction of benzaldehyde with TMSCN

| Run | Yield[a] (%) |
|---|---|
| 1 | 99 |
| 2 | 88 |
| 3 | 92 |
| 4 | 84 |
| 5 | 79 |

[a] Isolated yield.

## Acknowledgements

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7. *Representative experimental procedure*: To a dried 10 mL round-bottomed flask charged with [omim][$PF_6$] (0.5 mL) was added benzaldehyde (1 mmol) followed by TMSCN (1 mmol) at room temperature. After stirring for 12 h, another 1 mmol TMSCN was added subsequently and stirred for another 12 h before extracting with ether (3 × 15 mL). The combined ether layers were concentrated in vacuo, then desilylated using 2 mL THF and 2 mL 1 M aqueous HCl. Further extraction with ether and passage through a column of silica gel gave the desired product. The residual ionic liquid should be dried at 60 °C under reduced pressure before reusing in further reactions. *Benzaldehyde cyanohydrin*: $R_f = 0.6$ (hexane–ethyl acetate 2:1); FTIR (NaCl, neat): $\nu$ 3416, 2250 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): 3.74 (br s, 1H, O*H*), 5.50 (s, 1H, C*H*(OH)), 7.41–7.52 (m, 5H, $C_6H_5$); $^{13}C$ NMR (75.4 MHz, $CDCl_3$): 63.4, 118.8, 126.6, 129.1, 129.7, 135.2; HRMS (EI, *m/z*): $[M]^+$, calcd for $C_8H_7NO$ 133.0528, found 133.0554.