

# An improved synthesis of cyanohydrins in the presence of solid $\text{LiClO}_4$ under solvent-free conditions

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## Abstract

Several cyanohydrins were synthesized by the reaction of trimethylsilyl cyanide with carbonyl compounds in the presence of solid lithium perchlorate in high yields under solvent-free conditions.

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*Keywords:* Cyanohydrin; Lithium perchlorate; Solvent-free, Trimethylsilyl cyanide

## 1. Introduction

The cyanation reaction of carbonyl compounds is one of the most powerful procedures for the synthesis of poly-functional molecules [1]. Cyanohydrins or cyanohydrin trimethylsilyl ethers, can easily be converted to  $\alpha$ -hydroxycarboxylic acids [2],  $\alpha$ -hydroxyaldehydes [3],  $\beta$ -aminoalcohols [4],  $\alpha$ -amino acid derivatives [5]. In addition, they also have been used for the synthesis of insecticides [6], ferroelectrics, and liquid crystals [7,8]. Several useful cyanating reagents have been reported in the literature [9]. Among them, trimethylsilylcyanide (TMSCN) seems to be one of the most effective and safe cyanating sources for nucleophilic addition to carbonyl compounds. Generally TMSCN reacts with a carbonyl compound in the presence of a catalyst. Many different catalysts have been developed for this reaction [9]. Lewis acids and some other additives, both in stoichiometric and catalytic amounts have been used as promoting agents for cyanating of carbonyl compounds [10]. In recent years, several optically active catalysts for asymmetric synthesis of cyanohydrins have also been reported in the literature [11–14].

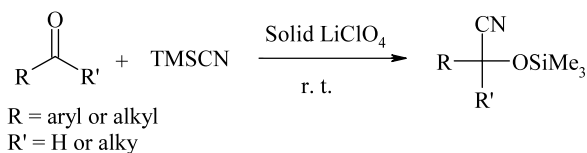
Unfortunately, many of these procedures often require drastic reaction conditions with a tedious work up

procedure and a need for relatively expensive reagents such as titanium complexes and Schiff bases. All of the reactions have been carried out in solvents such as  $\text{CH}_2\text{Cl}_2$ ,  $\text{CH}_3\text{CN}$ , THF, etc. On the other hand, due to the current challenges for developing solvent-free and environmentally benign synthetic systems [15] and in continuation with our interests on the applications of lithium perchlorate for various organic transformations [16], we would like to report a novel method for the cyanation of carbonyl compounds with TMSCN in the presence of solid  $\text{LiClO}_4$  under solvent-free conditions. When an aldehyde or a ketone was allowed to react with TMSCN in the presence of catalytic amounts of solid lithium perchlorate, the cyanation of the carbonyl compounds proceed effectively to give the corresponding cyanohydrins in good yields, *Scheme 1*.

The structures of the cyanohydrins are shown in *Tables 1 and 2*. Benzaldehyde was chosen to optimize the reaction conditions, such as temperature, time, and molar ratio of solid  $\text{LiClO}_4$  to substrate. We found that one equivalent of solid  $\text{LiClO}_4$  was sufficient to obtain the desired cyanohydrins in excellent yield and after short reaction times. The reaction with both aldehydes and ketones afforded the corresponding cyanohydrins in excellent yields. *Tables 1 and 2* clearly show that aliphatic and aromatic aldehydes with electron-donating and withdrawing groups gave excellent yields of cyanohydrins. The nature of the substituent on the aromatic ring seems to have no major effect on the reaction rate.

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Scheme 1.

Table 1  
Addition of TMSCN to aldehydes mediated by LiClO<sub>4</sub> under solvent-free conditions

Entry	Aldehyde	Cyanohydrin	Time (min)	Yield (%) <sup>a</sup>
1	PhCHO		30	100
2	2,4-Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub> CHO		40	94
3	2-MeC <sub>6</sub> H <sub>4</sub> CHO		40	100
4	4-ClC <sub>6</sub> H <sub>4</sub> CHO		40	96
5			40	94
6			30	90
7	Ph-CH=CH-CHO		50	100
8			30	98
9			50	98
10			30	90
11	Ph-CH <sub>2</sub> -CH <sub>2</sub> -CHO		30	100
12	Ph-CH <sub>2</sub> -CHO		30	98

<sup>a</sup>Conversion yields

Furthermore, acid sensitive aldehydes such as furfuraldehyde and cinnamaldehyde worked well without any decomposition or polymerization under the reaction conditions. In the case of aliphatic aldehydes, one also observes quantitative yield after short reaction times. Aliphatic and aromatic ketones, such as acetone, acetophenone, cyclohexanone, cyclopentanone and benzophenone, also gave the corresponding cyanohydrins in good yields, although addition of TMSCN to ketones are slower in comparison with aldehydes, Table 2. All

Table 2  
Addition of TMSCN to ketones mediated by LiClO<sub>4</sub> under solvent-free conditions

Entry	Ketone	Cyanohydrin	Time (min)	Yield (%) <sup>a</sup>
1			90	96
2			90	96
3			180	86
4			120	98
5			120	98
6			180	85

<sup>a</sup>Conversion yields

products were characterized by comparison of their spectral data (GC, IR, NMR) with authentic sample or with those reported in the literature.

## 2. Conclusion

In conclusion solid lithium perchlorate is found to be a mild and efficient Lewis acid for promoting cyanosilylation of carbonyl compounds under neutral conditions. The availability of inexpensive starting materials together with simplicity of the reaction, and green methodology provide a convenient method for the preparation of cyanohydrins in high yields and after short reaction times.

## 3. Experimental

### 3.1. General procedure

A mixture of a carbonyl compound (2 mmol), solid LiClO<sub>4</sub> (2 mmol) and TMSCN (2.4 mmol) was stirred at room temperature (r.t.) for the time indicated in Tables 1 and 2. Then CH<sub>2</sub>Cl<sub>2</sub> was added to the reaction mixture and the lithium perchlorate was filtered off. The organic layer was washed with water, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. Solvent was removed by a rotary evaporator and almost pure crude product was obtained. Further purification was done by flash chromatography (petroleum ether, diethyl ether) to afford the pure cyanohydrins.

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