

Vanadyl triflate as an efficient and recyclable catalyst for trimethylsilyl cyanide addition to carbonyl compounds

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Abstract

Vanadyl triflate is found to catalyze trimethylsilyl cyanide addition to a variety of ketones and aldehydes in acetonitrile at room temperature under very mild and convenient conditions to afford the corresponding cyanohydrins in excellent yields (79–96%) in a short reaction period (1–7 h). The high yields of products, compatibility of the other functional groups, and reusability of catalyst is the advantages of this method. © 2005 Elsevier B.V. All rights reserved.

Keywords: Vanadyl triflate; Cyanohydrins; Carbonyl compounds; Trimethylsilyl cyanide; Recyclability

1. Introduction

Cyanohydrins are versatile intermediates [1] for the synthesis of α -hydroxyacids, α -hydroxyaldehydes, β -aminoalcohols, α -cyanoketones, anesthetic drugs [2], and many other types of compounds. They are generally prepared by the nucleophilic addition of cyanide to carbonyl compounds. Among various cyanide ion sources, trimethylsilyl cyanide is a safer and easily handled reagent compared to sodium cyanide or potassium cyanide. For the synthesis of cyanohydrins a plethora of procedures has been reported employing ZnI_2 [3], Ti(IV), $\text{Cu}(\text{OTf})_2$ [4] Ce(IV), AlCl_3 [1], In(III) [5], Sm(III) [1], $\text{Yb}(\text{OTf})_3$ [6], and others [7,8]. Some chiral Lewis acids and chiral Lewis bases have been used for the synthesis of non-racemic cyanohydrins [9]. However, many of these methods have some drawbacks such as low yields of products, long reaction times, harsh reaction conditions, the requirement for an inert atmosphere, and the use of excess reagents. Some of the reported methods work well on aldehydes only [8], some of these are limited to simple

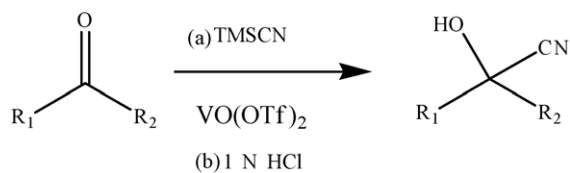
aliphatic ketones [6], and are not applicable to aryl ketones. Moreover, the main disadvantage of almost all existing methods is that the catalysts are destroyed in the work-up procedure and cannot be recovered or reused. Therefore, there is still a need to develop a simple and efficient method for the cyanation of both aldehydes and ketones.

In this communication, we wish to report a mild and efficient method for cyanation of aldehydes and ketones using a catalytic amount of vanadyl triflate in acetonitrile at room temperature.

2. Results and discussion

Recently, there has been considerable interest growing in the use of vanadium(IV) species as Lewis acids in various organic reactions [10]. The catalyst vanadyl triflate is commercially available [11] (or very easily prepared using a reported procedure [12]) and can be used for preparation of cyanohydrins from carbonyl compounds. While most conventional Lewis acids are decomposed or deactivated in the presence of water or protic solvents, vanadyl triflate is stable in water and does not decompose under aqueous work-up conditions. Thus, recycling is often possible. These unique

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Scheme 1.

properties of vanadyl triflate make this method friendly and more environmentally acceptable.

The reaction of benzaldehyde with trimethylsilyl cyanide in the presence of 1 mol% vanadyl triflate at room temperature afforded the desired compound in 1 h. Similarly, several aliphatic and aromatic aldehydes underwent the cyanation reactions in excellent yields (Scheme 1). Ketones are less reactive toward cyanation reactions and underwent cyanation smoothly. The results have been summarized in Table 1, which clearly indicates the scope and generality of the reaction with respect to aliphatic, aromatic, and unsaturated carbonyl compounds. The method is compatible with a variety of other functional groups such as methoxy, benzyloxy, and ester. It should be mentioned that for most of the substrates, the reaction time is reduced drastically even at room temperature conditions in contrast to some reported methods. Although recently several metal triflates have been reported as Lewis acids for cyanation reactions, the catalytic vanadyl triflate method is more effective than others. Acetophenone underwent the cyanation reaction in the presence of 1 mol% of vanadyl triflate in 4 h; the same reaction required 20 h in the presence of 5 mol% $\text{Cu}(\text{OTf})_2$, and $\text{Yb}(\text{OTf})_3$ failed to produce any cyanation product with aromatic ketones. Thus, α -tetralone was cyanated by vanadyl triflate in 6 h; the same reaction required 50 h in the presence of $\text{Cu}(\text{OTf})_2$.

Table 1
Vanadyl triflate catalyzed cyanation of aldehydes and ketones with trimethylsilyl cyanide at room temperature

Entry	Substrate	Time (h)	Yield ^a (%)
1	Benzaldehyde	1	91/87 ^b
2	2,4-Dimethoxybenzaldehyde	1	93/86 ^b
3	Cinnamaldehyde	1	81
4	4-Chlorobenzaldehyde	1	88
5	4-Carbomethoxybenzaldehyde	2	79
6	Hexaldehyde	2	83
7	Decylaldehyde	2	82
8	Acetophenone	4	92
9	Benzophenone	7	82
10	4- <i>tert</i> -Butyl-cyclohexanone	2	96
11	Cyclopentanone	6	80
12	Furfural	1	89
13	Thiophene 2-carboxaldehyde	1	82
14	4-Benzyloxybenzaldehyde	3	83
15	α -Tetralone	6	89
16	4-Methoxyacetophenone	2	91

^a Yields refer to pure isolated products, characterized by ¹H NMR and MS.

^b Isolated yields with reused catalyst.

3. Conclusion

In conclusion, a very simple and efficient method has been developed for the synthesis of cyanohydrins using a catalytic amount of vanadyl triflate. The catalyst can be readily recovered and reused thus making this method friendly and more environmentally acceptable. In most cases, the reaction requires low catalyst loadings, short reaction times, and proceeds under non-inert atmosphere conditions. The high yield of products, mildness of the reaction conditions, ease of operation, and compatibility with other functional groups should make a valuable tool for the synthesis of cyanohydrins.

4. Experimental

All products are known and were identified by comparison of their spectral data and physical properties with those of authentic samples [13–16]. The progress of reaction was monitored by thin layer chromatography on silica gel. All yields refer to isolated products.

4.1. Typical procedure

To a mixture of benzaldehyde (1 mmol) and trimethylsilyl cyanide (1.2 mmol) in acetonitrile (2 mL) was added vanadyl triflate (1 mol%) at room temperature. After completion of reaction (TLC), the reaction mixture was diluted with water (20 mL) and extracted with ethyl acetate (2 mL \times 15 mL). The organic layer was washed sequentially with 1N HCl (15 mL), water (10 mL), and brine (10 mL). The organic layer dried over MgSO_4 and concentrated. The residue was chromatographed over silica gel (15% ethyl acetate in hexane) to afford a pure product. Although we could isolate TMS-ether of cyanohydrin by quenching the reaction mixture with water, the isolated yield was low due to partial cleavage of silyl group to cyanohydrin. The aqueous layer containing the catalyst could be evaporated under reduced pressure to give a solid. The IR spectrum of the recovered catalyst was identical with an authentic sample, which could be reused for the next cyanation reaction, without losing any significant activity (Table 1, entries 1 and 2).

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