



NaCN/DOWEX(R)50WX4: A Convenient System for Synthesis of Cyanohydrins from Aldehydes

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DOI: <http://dx.doi.org/10.13005/ojc/290340>

(Received: June 25, 2013; Accepted: August 25, 2013)

ABSTRACT

A variety of cyanohydrins were prepared from Aldehydes with sodium cyanide and DOWEX(R)50WX4 in a convenient procedure.

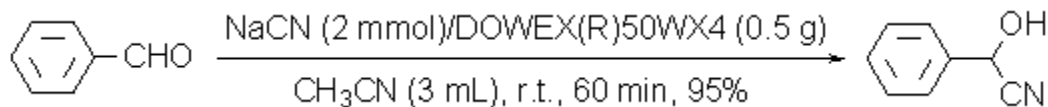
Key words: Aldehyde, Cyanohydrin, NaCN, DOWEX(R)50WX4.

INTRODUCTION

Cyanohydrins are well-known as important synthetic intermediates¹⁻⁴. Recently, we have reported that the DOWEX(R)50WX4 (low price cation exchange resin, strong acid) can be used as recyclable catalyst for the regioselective synthesis of Oximes by $\text{NH}_2\text{OH}\cdot\text{HCl}/\text{DOWEX(R)50WX4}$ system⁵ and reduction of a variety of carbonyl compounds such as aldehydes, ketones, α -diketones, acylolins and α , β -unsaturated carbonyl compounds to their corresponding alcohols by $\text{NaBH}_4/\text{DOWEX(R)50WX4}$ system⁶. In this context, we now wish to report an efficient, facile preparation of cyanohydrins using aldehydes by $\text{NaCN}/\text{DOWEX(R)50WX4}$ system in CH_3CN at room temperature.

RESULTS AND DISCUSSIONS

The model reaction has been selected by cyanation of benzaldehyde. This reaction was carried out in different solvents, different amounts of the NaCN and DOWEX(R)50WX4 for the selection of appropriate conditions at room temperature. Among the tested different solvents, the reaction was most facile and proceeded to give the highest yield in CH_3CN . The optimization reaction conditions showed that using 2 molar equivalents of NaCN and 0.5 g of DOWEX(R)50WX4 in CH_3CN were the best conditions to complete the cyanation of benzaldehyde (1 mmol) to 2-hydroxy-2-phenylacetonitrile (Table 1, Entry 1). Our observation reveals that cyanation completes within 60 min with 95% yields of product as shown in scheme 1.

**Scheme 1:**

The efficiency of this protocol was further examined by using various structurally different aldehydes. In this approach, the corresponding cyanohydrins were obtained in excellent yields (85-95%) within 60-120 min as shown in Table 1.

The reaction takes place under heterogeneous conditions. The mechanism for the influence of DOWEX(R)50WX4 is not clear, but as shown in scheme 2, we think that with the addition of DOWEX(R)50WX4 (as cation exchange resin, strong acid) to the reaction mixture (substrate & NaCN in CH_3CN), Na^+ with H^+ slowly being changed and hydrogen ion concentration increase.

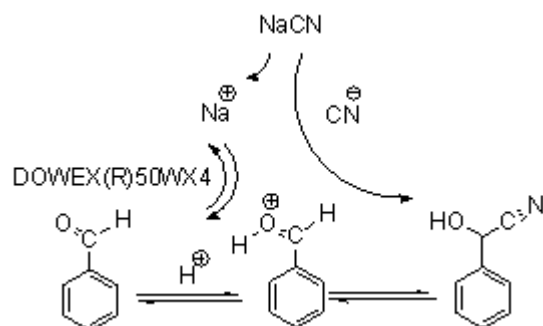
**Scheme 2:**

Table 1: Cyanation of Aldehydes (1 mmol) by NaCN (2mmol) in the presence of DOWEX(R)50WX4 (0.5 g) in CH_3CN (3 mL) at Room Temperature

Entry	Substrate	Products	Time (min)	Yields ^a (%)
1	benzaldehyde	2-hydroxy-2-phenylacetonitrile	60	95
2	2-methoxybenzaldehyde	2-hydroxy-2-(2-methoxyphenyl)acetonitrile	120	90
3	4-methoxybenzaldehyde	2-hydroxy-2-(4-methoxyphenyl)acetonitrile	120	90
4	4-bromobenzaldehyde	2-hydroxy-2-(4-bromophenyl)acetonitrile	90	88
5	4-nitrobenzaldehyde	2-hydroxy-2-(4-nitrophenyl)acetonitrile	60	94
6	4-chlorobenzaldehyde	2-hydroxy-2-(4-chlorophenyl)acetonitrile	60	95
7	4-methylbenzaldehyde	2-hydroxy-2-(4-methylphenyl)acetonitrile	90	95
8	2-methylbenzaldehyde	2-hydroxy-2-(2-methylphenyl)acetonitrile	90	90
9	3-methoxybenzaldehyde	2-hydroxy-2-(3-methoxyphenyl)acetonitrile	90	91
10	2,4-dichloroenzaldehyde	2-hydroxy-2-(2,4-dichlorophenyl)acetonitrile	60	85

^aYields refer to isolated pure products.

Therefore, carbonyl group can be protonated, thus it is more readily to attack with the cyanide anion for the cyanohydrin formation.

EXPERIMENTAL

IR and ^1H NMR spectra were recorded on PerkinElmer FT-IR RXI and 400 MHz Bruker spectrometers, respectively. The products were

characterized by their ^1H NMR or IR spectra and comparison with authentic samples (melting or boiling points). TLC was applied for the purity determination of substrates, products and reaction monitoring over silica gel 60 F_{254} aluminum sheet.

Cyanation of benzaldehyde with NaCN/DOWEX(R) 50WX4, A typical procedure

In a round-bottomed flask (10 mL)

equipped with a magnetic stirrer, a mixture of benzaldehyde (0.106 g, 1 mmol) and DOWEX(R) 50WX4(0.5, g) in CH₃CN (3 mL) was prepared. The resulting mixture was stirred for 5 min at room temperature. Then the NaCN (0.1 g, 2mmol) was added to the reaction mixture and stirred at room temperature. TLC monitored the progress of the reaction (eluent; CCl₄/Ether: 5/2). The reaction was filtered after completion within 60 min. Evaporation of the solvent afforded the 2-hydroxy-2-phenylacetone nitrile (0.126 g, 95% yield, Table 1, entry 1).

CONCLUSION

We have shown that the NaCN/DOWEX(R)50WX4 is suitable for the cyanation of a variety of aldehydes to their corresponding cyanohydrins in high to excellent yields. Cyanation reactions were carried out with 2 molar equivalents of NaCN in the presence of 0.5 g DOWEX(R) 50WX4 in CH₃CN at room temperature.

ACKNOWLEDGMENTS

The authors gratefully appreciated the financial support of this work by the research council of Islamic Azad University branch of Mahabad.

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