

Organocatalytic synthesis of cyanohydrin trimethylsilyl ethers by potassium 4-benzylpiperidinedithiocarbamate under solvent-free conditions

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Potassium 4-benzylpiperidinedithiocarbamate was found to be an efficient organocatalyst for facile addition of trimethylsilyl cyanide to a wide variety of aldehydes and ketones to afford corresponding cyanohydrin trimethylsilyl ethers in high to quantitative yields. The reaction proceeded smoothly by employing 2.0 mol% PBPDC loading under mild conditions at room temperature within a very short reaction time. Copyright © 2009 John Wiley & Sons, Ltd.

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Introduction

The addition of cyanide to carbonyl compounds is one of the most powerful strategies for the synthesis of cyanohydrins as poly-functionalized organic molecules. Cyanohydrins are highly versatile synthetic blocks in organic synthesis as they may be easily converted into other functional groups such as α -hydroxy acids, α -hydroxy aldehydes or ketones, α -amino acids, β -amino alcohols, 1,2-diols, etc. Because of their importance in the pharmaceutical, agrochemical and other industrial applications, a large body of work has been devoted to the development of cyanohydrin synthesis.^[1–5] Various cyanide sources, such as HCN, NaCN, KCN and different trialkylsilyl cyanides have been reported for the nucleophilic addition of cyanide to carbonyl compounds. In particular, the use of trimethylsilyl cyanide (TMSCN) in organic synthesis has proven valuable from the standpoints of improving of the reaction yield, safety and simplicity in the hydrolysis of the products under mild conditions. However, this compound is only effective in the transfer of the CN group to the carbonyl group of aldehydes or ketones under the action of activators.^[6–12]

Many different catalytic systems including Lewis acids^[8–22] and inorganic Lewis bases^[23–26] have been developed for the addition of TMSCN to carbonyl compounds. Furthermore, double activating^[3,27–35] or bifunctional^[36–41] catalytic systems have been described for asymmetric synthesis of cyanohydrin trimethylsilyl ethers. However, many of these procedures suffer from many disadvantages, such as the requirement for relatively expensive heavy metal catalysts, anhydrous toxic solvents, inert atmosphere and drastic reaction conditions with tedious work-up procedures. On the other hand, organocatalytic protocols for organic synthesis have received considerable attention in recent years because they provide a platform for catalyzing reactions in the absence of precious or toxic transition metals. Many organocatalysts are simple molecules that show excellent selectivity and afford good yield. Organocatalysts have several advantages. They are usually robust, inexpensive, readily available and non-toxic. Many

organocatalysts are inert towards moisture and oxygen. Because of these unique features, demanding reaction conditions like inert atmosphere, low temperature, absolute solvents, etc., are in many instances not required. Because of the absence of transition metals, organocatalytic methods seem to be especially attractive for the preparation of compounds that do not tolerate metal contamination, e.g. pharmaceuticals. Therefore, they have a high industrial and also ecological potential to be applied in many branches of chemical science and industry.^[42–46] Although some organocatalytic protocols have been described for cyanosilylation of carbonyl compounds,^[47–71] development of new methods which are catalytic in nature, cost-effective and simple to use is a very active research effort. The bidentate dithiocarbamate ligand has proved to be an extremely versatile and robust motif in coordination chemistry. Its ease of formation and wide ranging coordination chemistry have received a great deal of attention from both academia and industry. Examples are metal-directed self-assembly,^[72,73] speciation of trace elements using non-chromatographic methods,^[74–77] biological studies^[78,79] and catalysis by transition metals.^[80–83] However, there are very few reports available in the literature regarding the use of pure dithiocarbamate (DTC) anions as nucleophilic catalysts in organic transformations. We have previously reported sodium or potassium piperidinedithiocarbamate as effective catalysts for the efficient cyclotrimerization of aryl and alkyl isocyanates under

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