Journal of Saudi Chemical Society (2016) 20, S202–S210

King Saud University

Journal of Saudi Chemical Society

www.ksu.edu.sa
www.sciencedirect.com

ORIGINAL ARTICLE

An efficient one-pot three-component synthesis of α-amino nitriles *via* Strecker reaction catalysed by bismuth(III) nitrate

S. Sheik Mansoor *, **K. Aswin, K. Logaiya, S.P.N. Sudhan**

Research Department of Chemistry, C. Abdul Hakeem College, Melvisharam 632 509, Tamil Nadu, India

Received 23 July 2012; accepted 9 October 2012
Available online 7 November 2012

KEYWORDS

Bismuth nitrate;
Amino nitriles;
One-pot synthesis;
Strecker reaction

Abstract A convenient and efficient one-pot method for the synthesis of a variety of α-amino nitriles from aldehydes, amines and trimethylsilyl cyanide (TMSCN) in the presence of a catalytic amount of $Bi(NO_3)_3$ at room temperature in acetonitrile (MeCN) is described. The significant features of this method are simple work-up procedure, inexpensive and non-toxic catalyst, shorter reaction times and excellent product yields. The catalyst $Bi(NO_3)_3$ can be reused. The reusability of the catalyst has been studied for the synthesis of various amino nitriles.

1. Introduction

One-pot multi-component condensation reactions are important and attractive due to the formation of multi-bonds in one pot, high atom economy, mild and simplified conditions and environmentally benign friendliness. Strecker reaction as the first multi-component reaction (MCR), which was discovered in 1850, represented one of the most important reactions, especially from the life science viewpoint (Strecker, 1850). In this reaction three components including a carbonyl compound (generally an aldehyde), an amine and either alkaline metal cyanide or hydrogen cyanide couple together and produce α-amino nitriles. The Strecker reaction is one of the most straightforward and efficient methods for the synthesis of α-amino nitriles as one of the very useful synthones for the preparation of α-amino acids (Shafran et al., 1989) and heterocyclic compounds such as imidazoles and other biologically important molecules (Matier et al., 1973; Duthaler, 1994). α-Amino acids have the great biological and economical significance because of their widespread use in chemistry and biology. For example, they are the key precursors for the synthesis of proteins and have several applications as the chiral building blocks in the pharmaceutical industry (Enders and Shilvock, 2000; Dyker, 1997). Recently, synthesis of hepatitis C virus NS3 serine protease inhibitors (Arasappan et al., 2007) (±)-phthalascidin 622 (Razafindrabe et al., 2010) and novel boron-containing retinoids (Das et al., 2009) has been reported following this strategy.

Recently Drabina and Sedlák reported recent developments and trends in the application of 2-amino-2-alkyl(aryl)propanenitriles as precursors for the syntheses of heterocyclic systems such as imidazole derivatives, oxazoles, isothiazoles and 1,3,2-diazaphospholidines (Drabina and Sedlák, 2012). Their

---

* Corresponding author. Tel.: +91 9944093020; fax: +91 4172 266487.
E-mail address: smansoors2000@yahoo.co.in (S. Sheik Mansoor).

Peer review under responsibility of King Saud University.

Production and hosting by Elsevier

http://dx.doi.org/10.1016/j.jscs.2012.10.009

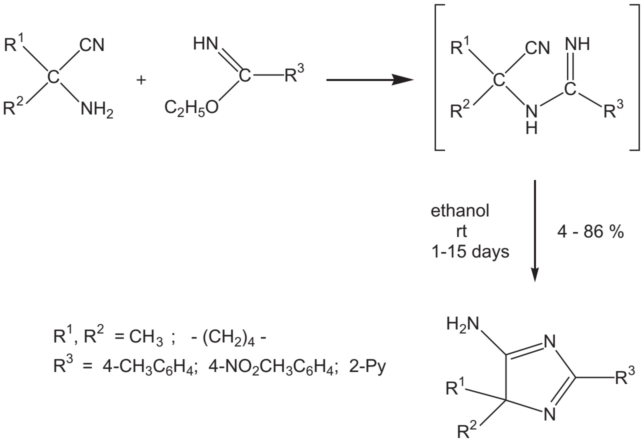
chemical and/or biological properties and potential applications are discussed, along with those of the derived heterocycles. Bifunctional 2-amino-2-alkyl(aryl)propanenitriles contain in their molecules both a nucleophilic centre at amino group and an electrophilic centre at cyano group, which is advantageous from the standpoint of their applications as basic synthetic building blocks used for syntheses of a large number of organic compounds (Schrimsher et al., 1986; Estramareix and David, 1986).

Reactions of substituted α-aminonitriles with imidoesters lead to substituted 5-amino-4*H*-imidazoles, which represent key components in many bioactive compounds, both natural and synthetic (Avendano et al., 1985; Gómez et al., 1986; Soh et al., 2006). The oldest papers describing the syntheses of 5-amino-4*H*-imidazoles from α-aminonitriles were published in the 1980s (Avendano et al., 1985) (Scheme 1).

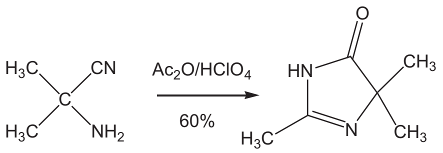
2,4,4-Trimethyl-4,5-dihydro-1*H*-imidazol-5-one was prepared by the reaction of 2-amino-2-propanenitrile with acetic acid anhydride catalysed with perchloric acid. The first reaction step is acylation at the amino group of the aminonitrile which is followed by ring closure reaction (Oniciu et al., 1992) (Scheme 2).

Generally, α-amino nitriles are prepared by the nucleophilic addition of cyanide ion to the imines (*in situ* generated from condensation of aldehydes with amines) in the presence of Lewis acid or Lewis base catalysts. Many cyanide sources such as HCN (Enders and Shilvock, 2000), KCN (Kobayashi and Ishitani, 1999), Bu_3SnCN (Vachal and Jacobsen, 2002), Et_2AlCN (Nakamura et al., 2004), $(Et_2O)P(O)CN$ (Harusawa et al., 1979) and TMSCN (Bhanu Prasad et al., 2004) have been used for Strecker reaction. Among the aforementioned reagents, TMSCN is the safer and more efficient cyanide anion source (Groutas and Felker (1980).

Various Lewis acids such as $Yb(OTf)_3$ (Kobayashi et al., 1997), $Pr(OTf)_3$ (De and Gibbs, 2005), $Cu(OTf)_2$ (Paraskar and Sudalai, 2006), $ZrCl_4$ (Raghu and Reddy, 2009), $BiCl_3$ (De and Gibbs, 2004), $CeCl_3$ (Pasha et al., 2007), $RuCl_3$ (De, 2005), $Sc(OTf)_3$ (Kobayashi et al., 1998), InI_3 (Shen et al., 2008), RhI_3 (Majhi et al., 2008), $La(NO_3)_3{\cdot}6H_2O$ or $GdCl_3{\cdot}6H_2O$ (Narasimhulu et al., 2007), iodine (Royer et al., 2005), and (bromodimethyl)sulphonium bromide (Das et al., 2006), homogeneously catalyse the Strecker-type reaction. On the other hand, several heterogeneous catalysts, which are more advantageous in terms of catalyst/product separation and continuous production, have been proposed for the reaction. The examples include polymer-supported scandium triflate (Kobayashi et al., 1996), montmorillonite (Yadav et al., 2004), MCM-41 anchored sulphonic acid (Dekamin and Mokhtari, 2012), nano powder TiO_2 P 25 (Baghbanian et al., 2011), sulphamic acid-functionalized magnetic Fe_3O_4 nanoparticles (Kassaee et al., 2011), K_2PdCl_4 (Karmakar and Banerji, 2010), heteropoly acid (Rafiee et al.,2008), Al-MCM-41 (Iwanami et al., 2010), xanthan sulphuric acid (Shaabani et al., 2009), and poly(4-vinyl pyridine)-SO_2 complex (Olah et al., 2007). In contrast, many of these reported methods involve the use of expensive reagents, hazardous solvents, longer reaction times and tedious workup procedure. Therefore, it is desirable to develop an efficient and practical method for the Strecker reaction under eco-friendly conditions.

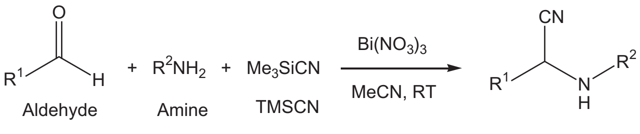


Scheme 1 Synthesis of 5-amino-4*H*-imidazoles from α-aminonitriles.



Scheme 2 Preparation of 2,4,4-trimethyl-4,5-dihydro-1*H*-imidazol-5-one from 2-amino-2-propanenitrile.

Recently, the use of bismuth compounds has attracted much attention due to non-toxicity, low cost, commercial availability, ease handling and resistant to air/moisture. Bismuth(III) compounds are termed as ‘‘green’’ reagents in organic synthesis (Leonard et al., 2002; Hua, 2008; Bothwell et al., 2011). Bismuth has an electron configuration of $[Xe]4f^{14}5d^{10}6s^26p^3$, and due to weak shielding of the 4*f* electrons, bismuth compounds exhibit Lewis acidity. Bismuth(III) nitrate has been used as a catalyst in many organic synthesis (Banik and Cardona, 2006; Mukhopadhyay and Datta, 2008; Alexander et al., 2005; Thirupathi and Kim, 2009; Wang et al., 2012). During the course of our studies towards the development of green catalytic processes to synthesis β-amino carbonyl compounds, we found bismuth nitrate ($Bi(NO_3)_3$) as an inexpensive and commercially available catalyst. It can efficiently catalyse through one-pot condensation of aromatic aldehydes, amines and trimethylsilyl cyanide in short reaction time (Scheme 3). After the reaction, bismuth nitrate could be easily recovered by simple phase separation and could be reused many times without loss of its catalytic activity. Application of such catalyst will lead to minimal pollution and waste material. Moreover, to the best of our knowledge no report has been made so far about the synthesis of α-amino nitriles catalysed by $Bi(NO_3)_3$.



1 **2** **3** **4a - 4l**

Scheme 3 Strecker synthesis of α-aminonitriles.