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ORIGINAL ARTICLE

Melamine trisulfonic acid: A new, efficient and reusable catalyst for the synthesis of some fused pyranopyrrole derivatives

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Abstract Synthesis of a new series of 5-amino-7-aryl-6-cyano-4*H*-pyrano[3,2-*b*]pyrrole derivatives has been reported. The cyclocondensation synthesis proceeded by the one-pot reaction of 3-hydroxypyrrole, malononitrile and various aromatic aldehydes in the presence of melamine trisulfonic acid (MTSA). The process presented here is operationally simple, environmentally benign and has excellent yield. Furthermore, the catalyst can be recovered conveniently and reused efficiently.

1. Introduction

Over the past decades, multi-component reactions (MCRs) have proved to be very powerful and efficient bond-forming tools in organic, combinatorial and medicinal chemistry in the context of green chemistry. The MCRs are very flexible, atom economic in nature, and proceed through a sequence of reaction equilibria, yielding the target product (Zhu and Bienayme, 2005; Domling and Ugi, 2000; Lu and Wang, 2010; Ganem, 2009; Domling, 2006). Along with other reaction parameters, the nature of the catalyst plays a significant role in determining yield, selectivity, and general applicability. Thus, development of an inexpensive, mild, reusable, and general catalyst for MCRs remains an issue of interest.

The 4*H*-pyran derivatives are of the immense interests in the area of synthesizing various drugs due to their pharmacological and biological activities (Shehab and Ghoneim, 2011). 4*H*-Pyran is a constituent of some natural products (Kamaljit and Harjit, 1996; Martin et al., 1993). 4*H*-Pyrans possess potent biological activities like antitumor, antibacterial, antiviral, spasmolytic, and antianaphylactic (Wang et al., 2000; Kumar et al., 2009; Martinez and Marco, 1997; Valizadeha and Azimi, 2011; Thumar and Patel, 2009; Bonsignore et al., 1993). 4*H*-Pyran derivatives are also potential calcium channel antagonists which are structurally similar to biologically active 1,4-dihydropyridines (Suarez et al., 2002). Some of these compounds are widely employed as cosmetics and pigments and as potential biodegradable agrochemicals (Hafez et al., 1987). Therefore, the synthesis of such compounds has attracted strong interest.

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Realizing the importance of 4*H*-pyran derivatives, several synthetic methods have been reported with the aim of obtaining more biologically potent heterocyclic systems using different catalysts like magnesium oxide (Ye et al., 2010), SB-DABCO (Hasaninejad et al., 2011), silica nanoparticles (Banerjee et al., 2011), electro generated base (Fotouhi et al., 2007), Baker's yeast (Pratap et al., 2011) and amino functionalized ionic liquid (Salvi et al., 2011). However, only few reports are available for the synthesis of 5-amino-7-aryl-6-cyano-4*H*-pyrano[3,2-*b*]pyrrole derivatives (Sandaroos and Damavandi, 2012; Sandaroos et al., 2012).

In continuation of our work on the development of simple and environmentally friendly experimental procedures using readily available reagents and catalysts for the synthesis of biologically active molecules, such as 3,4-dihydropyrimidin-2(1*H*)-ones/-thiones/imines (Mansoor et al., 2011), β-amino ketone compounds (Mansoor et al., 2012a), amidoalkyl naphthols (Mansoor et al., 2012b) and 2-amino-4,6-diphenylpyridine-3-carbonitrile derivatives (Mansoor et al., 2012c), we became interested in the possibility of developing a one-pot synthesis of 5-amino-7-aryl-6-cyano-4*H*-pyrano[3,2-*b*]pyrrole derivatives catalyzed by MTSA. We present our results about a MTSA catalyzed multi-component reaction. To the best of our knowledge, 5-amino-7-aryl-6-cyano-4*H*-pyrano[3,2-*b*]pyrrole derivatives catalyzed by MTSA have not been reported.

Recently, the use of MTSA as a catalyst in organic synthesis has increased considerably. MTSA can be easily prepared. It is effectively used as a catalyst in organic reactions, such as acetylation of alcohols, phenols and amines (Shirini et al., 2010a), trimethylsilylation of alcohols and phenols (Wu et al., 2011), solvent free synthesis of coumarins (Shirini et al., 2010b), synthesis of β-acetamido ketones (Zare, 2012), protection of alcohols, phenols, aldehydes and amines (Shirini et al., 2011a), chemoselective oxathioacetalyzation of aldehydes (Shirini and Albadi, 2010), chemoselective methoxymethylation of alcohols (Shirini et al., 2010c), synthesis of chromen-6-ones (Ma et al., 2011) and synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones/thiones (Shirini et al., 2011b).

In view of its inherent properties like environmental compatibility, reusability, greater selectivity, operational simplicity, non corrosiveness, easy preparation and ease of isolation, we wish to describe our results on melamine trisulfonic acid catalyzed one pot synthesis of reactions of 3-hydroxy pyrrole, aromatic aldehydes and malononitrile in a solvent-free condition at 80 °C. The generality of this reaction was examined using several types of aldehydes. In all cases, the reactions gave the corresponding products in good to excellent yield. This methodology offers significant improvements with regard to the scope of this transformation, simplicity in operation, short reaction time and green aspects by avoiding expensive or corrosive solvents.

2. Experimental

Chemicals were purchased from Merck, Fluka and Aldrich Chemical Companies. All yields refer to isolated products unless otherwise stated. ^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) spectra were obtained using Bruker DRX- 500 Advance at ambient temperature, using TMS as an internal standard. FT-IR spectra were obtained as KBr disks on Shimadzu spectrometer. Mass spectra were determined on a Varian–Saturn 2000 GC/MS instrument. Elemental analyses were measured by means of Perkin Elmer 2400 CHN elemental analyzer flowchart.

2.1. Preparation of melamine trisulfonic acid (MTSA)

Melamine trisulfonic acid was prepared from Melamine and chlorosulfonic acid as reported in the literature by (Shirini et al., 2010b) (Scheme 1).

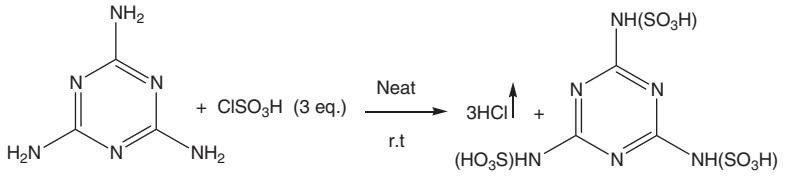
2.2. General procedure for synthesis of pyranopyrrole derivatives (4a–4i)

A mixture of 3-hydroxypyrrole 1 (10 mmol), aldehyde 2 (10 mmol), malononitrile 3 (11 mmol) and MTSA catalyst (5 mol%) was stirred at 80 °C for the appropriate time. The reaction was monitored by TLC and after completion of the reaction; the catalyst was simply recovered by filtration and washed by ethanol. The residue was concentrated in vacuo and the crude product was purified by column chromatography on silica gel (Scheme 2).

2.3. Spectral data for the synthesized pyranopyrrole derivatives

2.3.1. 5-Amino-7-phenyl-6-cyano-4H-pyrano[3,2-b]pyrrole (**4a**)

IR (KBr, cm^{-1}): 3406, 3422, 3266, 2144, and 1264. ^{1}H NMR (500 MHz, DMSO-d_6): δ = 5.44 (s, 1H, pyran H_4), 6.33 (d, 1H, pyrrole H_3), 6.78 (d, 1H, pyrrole H_2), 6.783(s, 2H, NH_2), 7.09–7.15 (m, 5H, Ar–H), 7.44 (s, 1H, pyrrole NH) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 29.9, 55.4, 100.9, 105.9, 117.4, 122.0, 123.2, 127.8, 129.2, 129.8, 130.6, and 173.9 ppm; MS (ESI): m/z 238 $(M + H)^+$. Anal Calcd. for $C_{14}H_{11}N_3O$: C, 70.89; H, 4.64; N, 17.72%. Found: C, 70.66; H, 4.62; N, 17.62%.



Melamine — Melamine trisulfonic acid (MTSA)

Scheme 1 Preparation of melamine trisulfonic acid.

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