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One-pot multicomponent synthetic route for new pyranothiazole derivatives

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Abstract

A rapid, energy efficient and economically viable protocol for the synthesis of pyrano[3,2-*c*]pyridine-2-one derivatives have been developed. A series of aromatic aldehyde and active methylene compounds have been used to obtain Knoevenagel condensed products. The reaction carried out in ethanol as a solvent using DABCO as catalyst giving excellent yields of knoevenagel products.

Keywords: Multicomponent, pyrano[3,2-*c*]pyridine derivatives, DABCO. Knoevenagel Condensation, Excellent yield.

Introduction

Pyranopyridines constitute an important class of heterocyclic compounds having diverse biological activities such as anti-allergic, anti-inflammatory, and estrogenic.[1,2]Among the different substitution patterns that are known, benzopyrano[2,3-b]pyridines exhibit anti proliferative,[3] cancer chemopreventive, [4] anti-bacterial (including anti-tubercular),[5]antimyopic, [6]anti-histamic, [7] hypotensive, [8]anti-rheumatic,[9]
and antiasthmatic activities.[10] Chromenes are important oxygenated heterocyclic compounds endowed with activities such as antidepressant,
antihypertensive, anti-tubulin, antiviral, antioxidative, activator of potassium channels and inhibition of phosphodiesterase IVor dihydrofolate reductase, etc[11-21]As a result, a number of methodologies have been developed to synthesize chromene compounds. [22-27]Pyranopyridines have becomethe object of current synthetic developments and many strategies for their synthesis have been adopted.[28] Previous investigations [29,30]on condensation of these derivatives required prolonged reaction times, use of hazardous reagents and low yields. In view of the above, the development of an efficient and convenient protocol forthe synthesis of pyranopyridinesis of considerable interest. Multicomponent reactions (MCRs) have recently emerged as valuable tool in the preparation of structurally diverse chemical libraries of drug-like heterocyclic compounds.[31]There is great current interest in microwave assisted organic synthesis (MAOS),[32]because such environmentally benign chemical methodologies are strongly required in light of the paradigm shift to “Green Chemistry”.

The heterocyclic compounds and especially those containing sulphur and nitrogen atoms possess a wide variety of biological activities [33,34]. Therapeutic effect of 1,2,4-triazole(**1**) and 1,2,4-triazole-3-one(**2**) containing compounds

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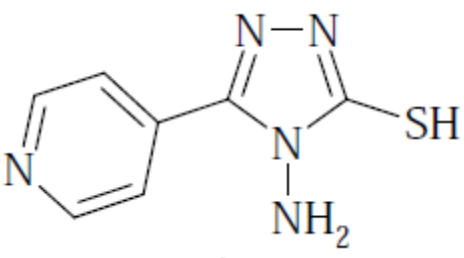
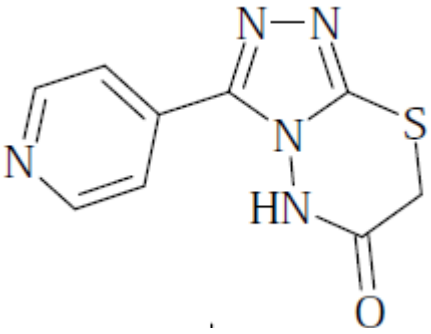
have been well studied for a number of pathological conditions including inflammation, cancer, pain, tuberculosis and hypertension [35,36]. 1,2,4-Triazoles fused with 1,3,4-thiadiazines are found to possess diverse applications in the field of medicine [37,38]. Triazolo-thiadiazines are reported to show a broad spectrum of pharmacologicallly important properties like antifungal [39], antibacterial [40], antiviral [41], anthelmentic [42], antitumor [43], anti-inflammatory [44], antituberculor [45], diuretics [46], anticancer [47] and hypoglycaemic [48]. These two fused systems are reported to possess significant CNS depressant, herbicidal, anthelmintic activities and have been widely used in pharmaceutical and agrochemical industry [49]. In view of these findings about the utility of fused heterocyclic compounds in various fields and as a part of wider programme to provide alternative routes for the synthesis of 5 and 6 membered heterocyclic compounds, we herein report the synthesis of some Pyran[3,2-*c*]pyridine-2-one derivatines using Knoevenegel Condensation.





The Knoevenagel Condensation reaction has been widely used for the synthesis of intermediate such as Pyrano[3,2-*c*]pyridine-2-one derivatives which are useful in many flavoring agents and bioactive compounds. In addition there has been considerable interest in Knoevenagel Condensation products because of their widespread application including inhibition of anti phosphorylation of EGF- receptor and antiproliferative activity [50]. As a result of their importance from pharmacological, industrial, and synthetic point of view several reactions of pyrano fused compounds have been reported.

Material and Method

Material:

All the solvents used were dried and purified before use. Anhydrous calcium oxide, calcium carbonate and calcium chloride were used as drying agents.

All reagents used were of LR grade. The purity of compound were tested and confirmed by TLC examination; silica gel G was used as adsorbent. The chromatogram was developed in iodine chamber. M.P. were taken by open capillary method and are uncorrected. ^{1}H is recorded on 400MHZ spectrometer, in DMSO-d6 using TMS as internal standard. Which are recorded at CDRI Lucknow.IR spectra were recorded on spectrum BX series. Which are recorded at CDRI Lucknow.

Method:

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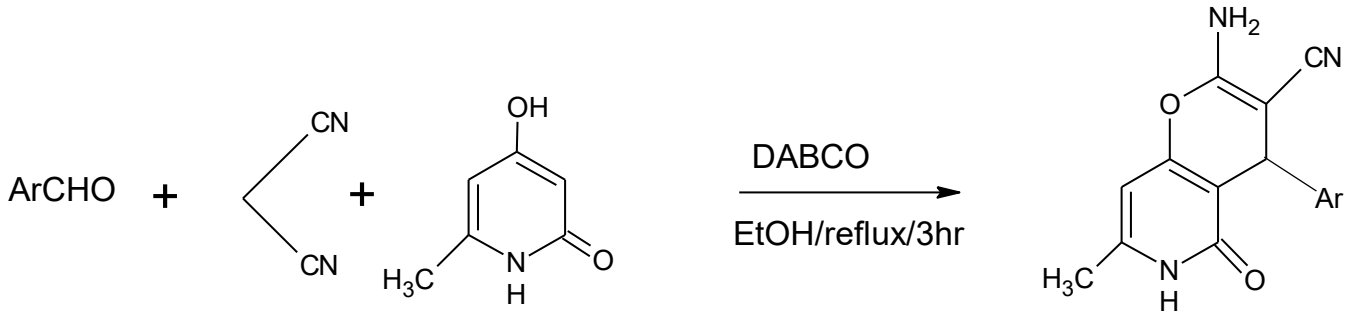
In present work equimolar concentration of aromatic aldehyde **(1)**, malononitrile **(2)** and 4-hydroxy-6-methylpyridin-2(1*H*)-one **(3)** were taken in R.B. and were dissolved in ethanol (10 ml). DABCO was added as catalyst further this mixture was stirred and refluxed for 3 hr at 90°C. The product **(4a-e)** obtained was extracted with ice cold water via vigorous shaking and was filtered with the help of filter paper. It was dried at room temperature and was recrystallized from ethanol.



(1) **(2)** **(3)** **(4a-e)**

Table No:- 1

Compounds	**Ar**
4a	C_6H_5
4b	4-$O_2NC_6H_4$
4c	4-$MeOC_6H_4$
4d	2-Furanyl
4e	2-Thienyl

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Result and Discussion

The 4-hydroxy-6-methylpyridine derivatives obtained are as follows:

2-amino-7-methyl-5-oxo-4-phenyl-5,6-dihydro-4*H*-pyrano[3,2-*c*]pyridine-3-carbonitrile(4a): colorless solid, mp 294°C, IR (KBr) cm^{-1}- 3268, 2944, 2213, 1573, 1698, 1491

2,3,7-trimethyl-4-(4-nitrophenyl)-4,6-dihydro-5*H*-pyrano[3,2-*c*]pyridin-5-one (4b): Pale yellow solid**,** mp 293°C, IR (KBr) cm^{-1} – 3470, 3064, 2160, 1715 1625, 1464, 1366

2-amino-4-(4-methoxyphenyl)-7-methyl-5-oxo-5,6-dihydro-4*H*-pyrano[3,2-*c*]pyridine-3-carbonitrile (4c): colorless solid, mp 249°C, IR (KBr) cm^{-1} -3460, 3140, 2223, 1716, 1621, 1464, 1212.

2-amino-4-(furan-2-yl)-7-methyl-5-oxo-5,6-dihydro-4*H*-pyrano[3,2-*c*]pyridine-3-carbonitrile (4d): off white solid, mp 231°C, IR (KBr) cm^{-1} -2843, 2198, 1696, 1605. ^{1}H NMR Spectrum (400MHz, DMSO-d_6) - δ 6.9 (s), δ 7.3 (d), δ 6.3 (dd), δ 6.2 (d), δ 6.1 (s), δ 4.1 (s), δ 4.4 (s).

2-amino-7-methyl-5-oxo-4-(thiophen-2-yl)-5,6-dihydro-4*H*-pyrano[3,2-*c*]pyridine-3-carbonitrile (4e): brownish color solid, mp 257°C, IR (KBr) cm^{-1} 3435, 3115, 2214, 1678, 1609. ^{1}H NMR Spectrum (400MHz, DMSO-d_6) - δ 7.1 (s) δ 6.97 (d), δ 6.92 (dd), δ 6.1 (d), δ 4.6 (s), δ 2.3 (s).

Conclusion:

Products which are synthesized i.e. 4a-e, from it first three were previously synthesized by using pyridine as catalyst here DABCO is used as a result of it yield of product has been increased which is an energy efficient process.

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