MgO, a Reusable Catalyst For Greener Synthesis of Pyranopyrazole In Water.
4.1 INTRODUCTION AND LITERATURE SURVEY

Functionalized chromene and benzopyrans are important class of heterocyclic compounds due to their broad spectrum of biological activity and imply wide range of applications in medicinal chemistry. The benzopyran moiety is found in variety of natural products. Many of these exhibit interesting biological properties.[1-2]


Some marine invertebrates anti-inflammatory sesquiterpenes containing a pyranofuranones grouped into monoalide (1)[4] and cacospongionolide B3(2). Monoalide inhibit PLA2, it is believed that α,β-unsaturated compound generated by opening of pyranofuranone [4, 5] moiety reacts with lysine residue of PLA2
on other hand, cocospongionolide B(2), which lacks the hemiacetal function in the pyran ring showed potent inhibitory activity on recombinant human synovial PLA2. Margherita and co-workers have synthesized monoalide and cocospongionolide B3 analogues and examined their anti-inflammatory activity of natural sources.

![Chemical Structure 4](image1)

![Chemical Structure 5](image2)


![Chemical Structure 6](image3)

![Chemical Structure 7](image4)

\[ R_1 = -C_2H_5, -CH_3, -C_2H_5; R_2 = -CH_3, -CH_3, -H. \]

Naturally occurring compounds containing fused pyran rings exhibit molluscidial activity. Bergapten [8], ricchiocarpin A [9] and ricchiocrpin B [10], pyranopyrazole [11] are well known for their molluscidial property. Fathy M. Abdelrazek reported few pyran derivatives which are effective against Biomphalaria alexandrina.[6] Mohamed I. Hegab derived some fused polycyclic heterocycles starting with 4-chloro-2,2 disubstituted chromene-3-carboxaldehyde [12]. The synthesized heterocycles showed considerable anti-inflammatory, analgesic, anticonvulsant and antiparkinson activity.[7] By the
use of salicyaldehyde, M. Al Neirabeyeh and his group synthesized 3,4-dihydro-3-(di-n propylamino)-2H-1benzopyrans [13] as new derivatives of benzopyran for dopaminergic activity.[8]

\[ R^1 = OH, H, H, H; R^2 = H, H, H, OH; R^3 = H, H, H, OH; R^4 = H, OH, OH, \]

4.2 METHODS OF SYNTHESIS

Several methods for benzopyran synthesis have been reported by the scientists around the world which involves one step as well as multistep synthesis.

A tandem Wolff rearrangement with t-amino effect found an effective route for synthesis of benzopyran nucleus.[9] The thermal decomposition of 1-diazo-2-oxo-(2-N, N-disubstituted aminomethyl)phenyl ethylphosphonates [14] in toluene extruded 1H-2-benzopyran in good to

![Scheme 4.1](image)

The utility of tetrathiafulvene (TTF) as a catalyst was demonstrated by Nadeem Bashir and co-workers. [10] They synthesized tetrahydropyran [17] by conversion of amine into tetrahydropyran through diazonium salt. This transformation believed to take place via radical mechanism. In this reaction the tetrathiafulvene acts as a weak nucleophile (Scheme 4.2).

![Scheme 4.2](image)
Cordiachromen, chemically named 6-hydroxy-2-methyl-2-(4-methylpent-3-en-1-yl)-2H-chromene \[18\] present in the *cordia alliodora* exhibited anti-inflammatory activity. Samir bouzbouz et al\[11\] have synthesized cordiochromene enantioselectively from chroman in four step involving bromination, dehydrohalogenation, nucleophilic substitution reaction with Grignards reagent and alkaline hydrolysis in aqueous ethanol (Scheme 4.3).

Wide range of organic compounds of pharmaceutical importance found through solid phase synthesis of benzopyrane reported by K. C. Nicolaou et al.\[12\] The synthetic strategy behind this methodology is use of selenium bound 2,2-dimethylbenzopyrans \[19\], synthesized from selenium bound with ortho-prenulated phenols. It undergoes condensation, annulation, glycosidation, aryl coupling reaction to offer various lead compounds \[20, 21, 22\] (Scheme 4.4). Same author employed selenium based solid phase synthesis of medicinally relevant small organic molecules\[13\] from selenium bound 2,2-dimethylbenzopyrans for different derivatives of pyran (Scheme 4.5).
Bjorn C. G. Soderberg et al\textsuperscript{[14]} have prepared isomeric mixture of 5-nitro-1-benzopyrans (Scheme 4.6)\textsuperscript{[24, 25, 26]} starting from 2-bromo-3- hydroxy-1-
nitrobenzene [23] by O-alkylation with 1-bromo-3-butene. Intramolecular Heck reaction extrudes the mixture of isomeric 5-nitro-1-benzopyrans in 60 %, 15 % and 3 % yield respectively. These mixture underwent N-heteroannulation resulting in the formation of 3, 4-fused indoles (Scheme 4.6).

![Scheme 4.6](image)

Biomolecular cyclization reaction between salicyaldehyde with conjugated olefins such as acrylate derivatives or α,β-unsaturated ketene resulting to form different substituted chromene [28] is quite routine, Min Shi [15] demonstrated reaction of salicyaldehyde with allenic ketone [27] and ester under basic condition. A systematic study of this reaction catalyzed by various bases including K$_2$CO$_3$, KOH, PPh$_3$, DABCO and DMAP in a variety of solvents concluded that K$_2$CO$_3$ system gives good yield of the product (Scheme 4.7).

![Scheme 4.7](image)

A series of benzo[c]chromen-6-ones [31] prepared by a Suzuki coupling and lactonisation reported by Geradus J. Kemperman et al. [16] The starting compounds in this reaction were 2-methoxyphenylboronic acids [29] and methyl 2-bromobenzoate [30] derivatives. The ionic liquids [BMI][PF$_6$], [Bmim][Al$_2$Cl$_7$] accelerates the rate of reaction (Scheme 4.8).
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[29] [30]

Scheme 4.8

In recent years resin catalyzed reactions have gained valuable synthetic importance. Various report on Amberlyst, dowex catalyzed reactions were found in the literature. Enrique Alvarez-Manzaneda described an enantiospecific route towards the cationic resin promoted Friedel–Craft alkylation of alkoxyarenes with α,β-unsaturated ketone [32], further reaction of ketone with 3,4-methylenedioxyphenol offers corresponding chromene [33] \(^{17}\) (Scheme 4.9).

[31]

Scheme 4.9

Previous report describe two component coupling between salicyaldehyde and allenic ketones/ester. Yong–Ling Shi et al\(^ {18}\) have reported the chromene synthesis by replacing salicyaldehyde by salicyl N-tosylamines [34], which on reaction with acetylenecarboxylate ester [35] in the presence of DABCO as catalyst (Scheme 4.10). The resultant substituted benzopyran [36] obtained at 80 °C temperature in dichloromethane.
Phenylene linked bis-naphthopyrans were synthesized in good yields via the one pot reaction of bis-propargyl alcohols \([37]\) with naphthols. These synthesized pyrans \([38]\) exhibited temperature dependant photochromism \([19]\) (Scheme 4.11)

Annamaria Deagostiono et al\([20]\) synthesized benzopyrans starting from dienylboronates and 2-iodophenol in the presence of a Pd catalyst. The reaction marches through the cross coupling intermediates which cyclizes to the chromene derivatives, which on hydrolysis offers 2, 2-dimethylchromen-4-one \([39]\), which is known to be an important building block for the synthesis of many important pharmaceuticals. (Scheme 4.12)
An enantioselective Oxa-Michael–Henry reaction of substituted salicyldehyde with nitro olefins [40] that proceeds through an aromatic iminium activation (AIA) has been developed using a chiral secondary amine organocatalyst and salicylic acid as a co-catalyst. The corresponding 3-nitro-2H-chromene [41] were obtained in moderate to good yields under mild conditions, reported by Dan-Quin xu et al. [21] Different amine were screened for their catalytic activity. Amongst them pyrrolidine thioimidazole is the most effective catalyst in terms of stereo control (Scheme 4.13).

An effective enantioselective access to benzopyran [44] was given by Magnus Pueping [22] et al by reaction between cyclic 1,3-diketone [42] and α,β -
unsaturated aldehyde [43] in the presence of organocatalyst, diarylprolinol silyl ether. The reaction offered good enantioselectivity in dichloromethane at 10 °C (Scheme 4.14).

Liang-Yeh chen et al [23] have introduced a novel carbanian-olefin intramolecular cyclization where 2-aryloyl-3, 4-dihydro-2H-benzopyrans [45] obtained from salicyaldehyde. It is based on strategy that salicyaldehyde underwent Wittig reaction with methyltriphenylphosphonium bromide (MTPPB) and potassium tertbutoxide as base and subsequent reaction with 2-bromoacetophenone without isolation, afforded condensation product which again on heating with tert-butoxide yielded benzopyran (Scheme 4.15).
Mechanism

Solvent free and catalyst free organic synthesis is most demanded synthetic approach. One pot synthesis of 3, 3’-(benzylene)-bis (4-hydroxy-2H-chromene-2-one) [46] derivatives have been synthesized by Shaterian Hamid Reza et al [24] through the coupling of aldehydes and 2 mol. equivalent of 4-hydroxycoumarine. The reaction proceeds at 130 °C without use of any externally added catalyst. The product obtained in an excellent yields (Scheme 4.16).

Scheme 4.16

Electrochemically induced multi-component condensation [25] of resorcinol, malononitrile and various aldehydes in propanol in an undivided cell in the presence of NaBr as an electrolyte results in the formation of 2-amino-4H-chromenes reported by S. Makarem et al. [26]
All methods discussed above has its own merit but overed by long reaction time, use of costly reagent and lack of reusability of the catalyst. As far as greener methodology is concern, the solvent is at centre point. Therefore use of nontoxic, nonflammable, non-volatile solvent has prime importance. In recent years ionic liquids, supercritical fluids are some alternatives but water is the best among them because it is cheap, easily available, non-toxic, non-flammable and non-volatile.

4.2 PRESENT WORK

Pyranopyrazole is one of the important pyran derivatives. Which exhibit molluscicidal activity. Very few methods have been reported in the literature for its synthesis. Routine method describe its synthesis involving reaction between pyrazole derivative and cyanoolefins formed by Knoevenagel condensation between aldehydes and malononitrile under basic condition. The limitation of this method is that both reactant coupled in this reaction requires more time for condensation. However, this problem could be solved by one step multicomponent synthesis to some extent. Gnanasambandam Vasuki et al have demonstrated four component one step synthesis of pyranopyrazole by condensation of ethylacetoacetate, hydrazine hydrate, arylaldehyde and malononitrile in water at room temperature, using piperidine as base. Reaction took place at room temperature. In recent years, MgO successfully catalyzed organic reactions altering the use of organic bases like piperidine, morpholine, trimethylamine etc. MgO is non toxic inorganic base required in catalytic amount and can be reused. Taking into account the merits of MgO, we decided to explore catalytic efficiency of MgO for synthesis of pyranopyrazole [51] by condensing hydrazine hydrate [47], ethylacetoacetate [48], arylaldehyde [49] and malononitrile [50] (Scheme 4. 17).
4.4 RESULT AND DISCUSSION

In initial attempts, ethylacetoacetate, hydrazine hydrate was stirred for 5 min. then aldehyde, malononitrile and catalytic amount of MgO were added in water and the reaction mixture stirred at room temperature. It was found that reaction between ethylacetoacetate and hydrazine hydrate occurred under catalyst free condition, forming water soluble pyrazolone. After stirring for one hr. the progress of reaction was examined by running TLC of reaction mixture, which indicated the formation of pyranopyrazole along with unreacted cyanoolefine. After continuous stirring for few hours, desired condensation product, pyranopyrazole wasn’t obtained considerably. Moreover, increased catalytic quantity of MgO over 20 mol % and continuous stirring the reaction mixture was failed to emit a satisfactory yield. Therefore, attempts were made to modify the thermal conditions of reaction which might be a hurdle for progress of reaction towards formation pyranopyrazole. In next experimental trial a mixture of ethylacetoacetate, hydrazine hydrate, benzaldehyde and malononitrile in equivalent amount was stirred in preheated oil bath at 80 °C. We noticed that cyanoolefin and pyrazolone get consumed but some side reaction product was observed along with pyranopyrazole on TLC. In optimization of thermal condition, we tried the reaction at 50 °C with stirring and the progress of the reaction was examined by TLC. After 1 hr it was observed that reaction went on completion without formation of any side reaction. Finally reaction mass was filtered at the pump. The separated catalyst
was recycled three times without losing its catalytic activity. The purified sample matched with the physical constant reported in literature. The IR spectrum exhibited bands at 3540 cm\(^{-1}\) for N-H stretching, 3370, 3210 cm\(^{-1}\) asymmetric and symmetric stretching frequency for primary amino group, medium intensity band at 2199 cm\(^{-1}\) for -CN group. The \(^1\)H NMR showed expected signal at \(\delta\) 5.5 for methine proton and protons of primary amino group as broad singlet at \(\delta\) 4.2. The remaining protons of the structure appeared in the aromatic region in the form of multiplet. This result encouraged us to extend this protocol for variety of aldehydes bearing an electron donating and withdrawing groups in them. (Table 4.1).

The aryl aldehyde with an electron donating group took longer reaction time as compared to electron withdrawing groups on arylaldehydes. In an efforts to minimize the amount of MgO, 20 mol % of MgO was sufficient for completion of reaction. Increasing the amount of MgO over 20 % does not affect on yield and time of the reaction considerably (Table 4.2).

One important aspect of this methodology is the survival of the functional groups like –OH, -CH\(_3\), -NO\(_2\) present on arylaldehyde. All the compounds were obtained in an excellent yields. The recrystalization of the product in ethyl alcohol gives analytically pure pyranopyrazoles. Other basic catalysts like K\(_2\)CO\(_3\), DABCO showed less catalytic activity giving lower yield under identical conditions for this reaction.

The plausible mechanism involving the formation of pyrazolone [52] and cyanoolefin [53] through the reaction between hydrazine hydrate and ethylacetoacetate and aldehyde and malononitrile. The Michael addition of active methylene group of pyrazolone to an electron deficient carbon of cyanoolefin gives an intermediate [54] which rearranges to give targeted pyranpyrazole (Scheme 4.18).
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Scheme 1.18
### Table 4.1 Reaction time and yield of Pyranopyrazoles.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Compound</th>
<th>Time (min)</th>
<th>Yield $^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td><img src="image1" alt="Compound 1" /></td>
<td>55</td>
<td>88</td>
</tr>
<tr>
<td>2.</td>
<td><img src="image2" alt="Compound 2" /></td>
<td>110</td>
<td>85</td>
</tr>
<tr>
<td>3.</td>
<td><img src="image3" alt="Compound 3" /></td>
<td>50</td>
<td>90</td>
</tr>
<tr>
<td>4.</td>
<td><img src="image4" alt="Compound 4" /></td>
<td>30</td>
<td>95</td>
</tr>
<tr>
<td>Entry</td>
<td>Compound</td>
<td>Time (min)</td>
<td>Yield&lt;sup&gt;(a)&lt;/sup&gt; (%)</td>
</tr>
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<td>-------</td>
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</tr>
<tr>
<td>5.</td>
<td><img src="image1" alt="Chemical Structure" /></td>
<td>85</td>
<td>88</td>
</tr>
<tr>
<td>6.</td>
<td><img src="image2" alt="Chemical Structure" /></td>
<td>40</td>
<td>92</td>
</tr>
<tr>
<td>7.</td>
<td><img src="image3" alt="Chemical Structure" /></td>
<td>85</td>
<td>88</td>
</tr>
<tr>
<td>8.</td>
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<td>40</td>
<td>90</td>
</tr>
<tr>
<td>9.</td>
<td><img src="image5" alt="Chemical Structure" /></td>
<td>45</td>
<td>87</td>
</tr>
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<td>10</td>
<td><img src="image6" alt="Chemical Structure" /></td>
<td>150</td>
<td>79</td>
</tr>
</tbody>
</table>
11. 

Table 4.2 Effect of catalyst amount of on MgO the yield of pyranpyrazole.

<table>
<thead>
<tr>
<th>Amount of MgO (mol %)</th>
<th>5</th>
<th>10</th>
<th>15</th>
<th>20</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yield in (%)</td>
<td>55</td>
<td>67</td>
<td>80</td>
<td>91</td>
</tr>
</tbody>
</table>

4.5 SPECTRAL ANALYSIS

The structures of synthesized compounds (Table 4.1, Entry 1-5) were confirmed on the basis of IR, $^1$H and $^{13}$C NMR and mass spectroscopic data. The spectroscopic data were in full agreement with the literature values.

In 6-amino-3-methyl-4-phenyl-2,4dihydropyrapylo[2,3-c]pyrazole-5-carbonitrile, (Table 4.1, entry 1) the IR spectrum shows band at 3373, 3310 cm$^{-1}$ are due to asymmetric and asymmetric stretching of free primary amino group and a band at 2192 cm$^{-1}$ for cyano stretching frequency (Spectrum 4.1). $^1$H NMR spectrum of same compound exhibits a singlet resonate at $\delta$ 1.763 for methyl protons linked to pyrazole ring and a sharp singlet for one methine proton appeared at $\delta$ 4.575 and a broad singlet for amino protons resonate at $\delta$ 6.868 While aromatic protons gave downfield shift in form of multiplet between $\delta$ 7.3-7.1. The NH proton of pyrazole ring is strongly deshielded observed at $\delta$ 12.096 (Spectrum 4.2). In $^{13}$C NMR (Spectrum 4.3) following peaks were observed at $\delta$ 10.17, 36.67, 57.64, 98.09, 121.24, 127.19, 127.91,
128.89, 136.03, 144.89, 155.21, 161.31. The mass spectrum exhibited spectral lines at (m/z) 253 (M⁺), 226, 187, 170, 146, 142, 129, 115 (Spectrum 4.4).

The IR spectrum of 6-amino-3-methyl-4-[4-hydroxyphenyl]-2,4-dihydropyran[2,3-c]pyrazole-5-carbonitrile (Table 4.1, entry 2) exhibit sharp peak at 3500 cm⁻¹ due to for N-H broad stretching band at 3465 cm⁻¹ for -O-H. A sharp doublet encountered at 3390, 3300 cm⁻¹ due to asymmetric and symmetric stretching of primary amino group. Intense peak at 2176 cm⁻¹ is for -CN group (Spectrum 4.5). The ¹H spectrum of the same compound showed singlet at δ 1.766 for methyl protons attached to pyrazole ring whereas the methine protons appeared as singlet at δ 4.454. The four aromatic protons of phenyl ring gave a two sets of doublets encoutetred at δ 6.684 (J =8.4 Hz) and δ 6.949 (J =8.4 Hz). A broad singlet at δ 6.785 is due to two protons of amino group. The two singlet appeared at δ 9.297 and 12.049 for -OH and NH proton (Spectrum 4.6). The ¹³C NMR of same compound exhibited peaks at δ 10.19, 35.91, 58.22, 98.50, 115.55, 121.35, 128.88, 135.20, 135.97, 155.19, 156.45, 161.07 (Spectrum 4.7). The mass spectrum exhibited lines at (m/z) 268 (M⁺), 242, 202, 186, 175, 160.(Spectrum 4.8).

IR spectrum 6-amino-3-methyl-4-[3-nitrophenyl]-2,4dihydropyran[2,3-c]pyrazole-5-carbonitrile (Table 4.1, entry 3) showed a band at 3474 cm⁻¹ for N-H stretching whereas asymmetric and symmetric band for amino group attached to the ring were observed at 3223, 3118 cm⁻¹. A intense peak at 2195 cm⁻¹ is due to the presence of –CN. The band for –NO₂ stretching observed at 1492 cm⁻¹(Spectrum 4.9). The ¹H NMR of same compound showed a single at δ 1.788 for three protons of methyl group attached to pyrazole ring. Singlet at δ 4.862 is due to methine proton, whereas a triplet and multiplet at δ 7.653 and 8.131 for two protons each. A broad singlet observed at δ 7.045 for amino group protons and a sharp singlet at δ 12.209 for N-H proton of pyrazole ring (Spectrum 4.10). ¹³C NMR spectrum showed the signal peaks at δ 10.19, 36.08, 56.59, 97.11, 122.28, 122.44, 130.71, 134.84, 136.37, 147.26, 148.34,
161.59 (Spectrum 4.11). The mass spectrum showed spectral lines at (m/z) 298, 232, 216, 186 (Spectrum 4.12).

IR Spectrum of 6-amino-3-methyl-4-[4-chlorophenyl]-2,4-dihydro-
pyrano[2,3-c]pyrazole-5-carbonitrile (Table 4.1, entry 4) showed a band at
3373, 3311 cm⁻¹ for -NH₂ The sharp peak observed at 2193 cm⁻¹ for –CN
group (Spectrum 4.13). In PMR spectrum, methyl protons attached to pyrazole
ring resonated at δ 1.776 whereas a singlet encountered at δ 4.619 for methine
proton. Two doublets observed at δ 7.194 (J =8.4 Hz) and 7.377 (J=8.4 Hz) for
aromatic protons. Amino protons observed as broad singlet at δ 6.923 as broad
singlet. NH proton of pyrazole ring appeared at δ 12.185 (Spectrum 4.14). ¹³C
NMR spectrum for the said compound showed the signal at δ 10.18, 36.00,
57.21, 97.61, 121.10, 128.90, 129.81, 131.67, 136.15, 143.93, 155.12, 161.35
in good agreement with the literature data(Spectrum 4.15). In mass spectrum of
the compound, spectral lines observed at (m/z) 286 (M⁺), 260, 221,204, 185,
178, 129 (Spectrum 4.16).

The IR spectrum of 6-amino-3-methyl-4-[3-hydroxyphenyl]-2,4-dihydro-
pyrano[2,3-c]pyrazole-5-carbonitrile (Table 4.1, entry 5) showed a peak at
3407 cm⁻¹ for the -O-H stretching. Two sharp peaks at 3362-3332 cm⁻¹ for
amino group and cyano group appeared at 2177 cm⁻¹(Spectrum 4.17). ¹H
NMR spectrum of same compound (Spectrum 4.18) has a sharp singlet at δ
1.805 indicating the presence of methyl group attached on aromatic ring of
pyrazole, singlet at δ 4.472 is due to methine proton. The aromatic protons
appeared at δ 6.523-6.617 and 7.057-7.109. The amino protons appeared as
broad singlet at δ 6.8. The phenolic O-H proton appeared at δ 9.318 while N-H
proton at δ 12.087. The ¹³C NMR of same compound exhibited peak at δ 10.22,
36.61, 57.72, 98.14, 114.29, 114.58, 118.64, 121.28, 129.73, 136.05,146.42,
155.19, 157.87, 161.29 which confirm the structure of desired compound
(Spectrum 4.19).The mass spectrum showed spectral lines observed at (m/z)
268 (M⁺), 252, 242, 203, 187, 175 (Spectrum 4.20).
4.6 EXPERIMENTAL

Materials and Methods.

All aryl aldehydes, ethylacetoacetate, hydrazine hydrate and malononitrile were purchased from S. D. fine and spectrochem Co. and were used without further purification.

Instrumental details and their operational conditions

NMR analysis.

NMR analysis was performed on Brucker–Avance 300 MHz, NMR spectrophotometer. For $^1$H NMR analysis, DMSO was used as solvent and tetramethylsilane as an internal standard, the chemical shifts are reported in ppm. Multiplicities are indicated by ‘s’ (singlet), ‘d’ (doublet), ‘t’ (triplet), ‘q’ (quartet), ‘m’ (multiplet) and ‘bs’ (broad singlet). The coupling constant ($J$) are reported in Hz.

IR Analysis
Infrared spectra were recorded on Perkin Elmer 1310 FT-IR spectrometer with KBr pellets.

LCMS Analysis

LCMS analysis was performed on Mass spectromete –API 5500Qtrap (Applied biosystems, Canada). The column used for analysis were, Atalantis dC18 (100mmx2mmx5um) Waters India Pvt Ltd, Bangalore. The mobile phase used for sample is: 5mM ammonium formate in methanol 5mM ammonium formate in water and flow rate was 0.4mL /min.

General Experimental procedure

A mixture of ethylacetoacetate (1mmol) and hydrazine hydrate (1mmol) were stirred in 10mL of water for 10 min. then arylaldehyde (1mmol), malononitrile (1mmol) and 20 mol % MgO were added and the reaction was mixture stirred at 50 °C for appropriate time on an oil bath. The product formed was isolated by simple filtration and further purified by recrystallization to separate desired pyrano[2,3-C]pyrazole in high yield.
4.7 CONCLUSION

We have reported a simple, ecofriendly and elegant protocol for the synthesis of pyrano[2, 3-c]pyrazole through one step four component coupling using magnesium oxide as a solid reusable and basic catalyst. The reaction proceeds efficiently in water without any use of flammable, volatile organic solvent. As reaction occurs in the water it excludes the cumbersome separation methods and hence it avoids use of the harmful solvents. Therefore the use of MgO as a catalyst renders this method environmentally benign.
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Spectrum 4.1: IR Spectrum of 6-amino-3-methyl-4-phenyl-2,4-dihydropyranol2,3-epoxypyrazole-5-carbonitrile.
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Spectrum 4.2: $^1$H NMR Spectrum of 6-amino-3-methyl-4-phenyl-2,4-dihydropyranzo[2,3-d]pyrazole-5-carbonitrile.
Spectrum 4.3: $^{13}$C NMR Spectrum of 6-amino-3-methyl-4-phenyl-2,4dihydropyrano[2,3-c]pyrazole-5-carbonitrile.
Spectrum 4.4: Mass Spectrum of 6-amino-3-methyl-4-phenyl-2,4dihydropyran- [2,3-c]pyrazole-5-carbonitrile.
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Spectrum 4.5: IR Spectrum 6-amino-3-methyl-1H-[14-hydroxyphenyl]-2,4-dihydropyran-2,3-dipyrazole-5-carbonitrile.
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Spectrum 4.6: $^1$H NMR Spectrum 6-amino-3-methyl-4-[4-hydroxyphenyl]-2,4-dihydropyran-2-oxo-3-carboxylic acid 2,3-c-pyrazole-5-carboxamide.
Spectrum 4.7: $^{13}$C NMR Spectrum 6-amino-3-methyl-4-[4-hydroxyphenyl]-2,4-dihydropyranopyrazole-5-carbonitrile.
Spectrum 4.8: Mass Spectrum 6-amino-3-methyl-4-[4-hydroxyphenyl]-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile.
Spectrum 4.9: IR Spectrum of 6-amino-3-methyl-4-[3-nitrophenyl]-2,4dihydropyrano[2,3-c]pyrazole-5-carbonitrile.
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Spectrum 4.10: $^1$H NMR Spectrum of 6-amino-3-methyl-4-[3-nitrophenyl]-2,2-dihydroxy-
[2,3]-pyrazole-5-carbonitrile.
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Spectrum 4.11: $^1$H NMR Spectrum of 6-amino-3-methyl-4-[3-nitrophenoxy]-2,4-diethylpyranopyrazole [2-H] at room temperature.
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Spectrum 4.13: IR Spectrum of 6-amino-3-methyl-1-[4-(4-chlorophenyl)]-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile.
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Spectrum 4.14: $^1$H NMR Spectrum of 6-amino-3-methyl-4-[4-chlorophenyl]-2,4-dihydropyran-2,3-c]pyrazole-5-carbonitrile.
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Spectrum 4.15: $^{13}$C NMR Spectrum of 6-amino-3-methyl-4-[4-chlorophenyl]-2,4-dihydropyrano-[2,3-c]pyrazole-5-carbonitrile.
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Spectrum 4.16: Mass Spectrum of 6-amino-3-methyl-4-[4-chlorophenyl] -2,4-dihydropyranopyrazole-5-carbonitrile.
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Figure 4.17: IR Spectrum of 6-amino-3-methyl-4-3-hydroxyphenyl-2,4-dihydropyrano
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Spectrum 4.19: $^{13}$C NMR Spectrum of 6-amino-3-methyl-4-[3-hydroxyphenyl]-2,4-dihydropyrazine [2,3-c]pyrazole-3-carbonitrile
Spectrum 4.20: Mass Spectrum of 6-amino-3-methyl-4-[3-hydroxyphenyl]-2,4-dihydropyran-2,3-di(pyrazole-5-carbonitrile.

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4.8 REFERENCES


