



RESEARCH ARTICLE

GREEN, RAPID, SIMPLE, AND AN EFFECTIVE ONE-POT MULTICOMPONENT STRATEGY FOR SYNTHESIS OF NOVEL DIHYDROPYRANO[2,3-C]PYRAZOL-6-AMINES IN AQUEOUS MEDIUM

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Abstract

Objectives: A series of new dihydropyrano [2,3-c]pyrazol-6-amines in this investigation study, are synthesized by the strategy of one-pot four component reaction in an aqueous medium.

Methods: After getting optimum conditions the reaction of different substituted aromatic aldehydes, ethyl acetoacetate, hydrazine hydrate, and phenylacetonitrile catalysed by Sodium hydrogen sulphate NaHSO₄ (0.5 m mol) by refluxing in ethanol-water (1:1) (5 ml) and heated at 80°C. The synthesized molecules product was filtered and washed with water to get nearly pure product in excellent yield.

Results: The pure products which were got in a short duration, with excellent yield (80-87%). Those new compounds were identified by using spectroscopic techniques FT-IR, ¹H-NMR and ¹³C-NMR.

Conclusion: In conclusion, the usefulness of this one-pot multicomponents protocol include easily available starting materials, facile, simple and environment-friendly procedure, and easier separation of products by filtration.

Keywords: Araldehydes, ethyl acetoacetate, fluoro phenylacetonitrile, hydrazine hydrate, pyrano[2,3-c]pyrazol-6-amines, water.

INTRODUCTION

In the last two decades, the rising environmental concern in chemistry has redressed spotlight on the multicomponent reactions strategy as new trends in organic synthesis chemistry^{1,2}. Multicomponent reactions (MCRs) are very useful for the construction of huge numbers of heterocyclic compounds³, using this strategy biologically active substances and natural product compounds have been synthesized⁴. The nitrogen containing heterocycles synthesis is one of great interest field in organic synthesis because of they constitute an important class of natural and synthetic products, many of them which exhibit useful biological activity and find application in pharmaceutical preparations⁵⁻¹¹.

The need to develop the concept of green chemistry to help safeguard human life was started after the first chemical revolution, which changed modern life with excellent entertainment and services, but also created the serious issue of environmental pollution. Thus, The essential principle of the green chemistry concept is to protect the environment, not only by cleaning it up, but

by discovery and designing of new chemistry and pharmaceutical industries to concern the effect on human life when new chemicals are introduced into our society¹²⁻¹⁶. Compared to others green solvents water appears to be a better option because of its super abundant and non-inflammable nature non-toxic, non-corrosive. In addition, water can be governed because of its relatively high vapour pressure as compared to organic solvents, that making it a green and sustainable alternative¹⁷⁻²⁰. Water offers several benefits such as control over exothermic reactions, salting in and salting out, as well as variation of pH range²¹. Recently, organic reactions in water without use of hurtful organic solvents have drawn much more attention, because water is cheap, safe and environment friendly solvent^{22,23}.

Dihydropyrano[2,3-c]pyrazole scaffold represents very motivating template in medicinal chemistry, and play an essential role as biological active molecules²⁴. Many of the pyrano[2,3-c]pyrazoles are known for their antimicrobial²⁵, insecticidal²⁶, anti-inflammatory²⁷, anticancer²⁸ and molluscicidal activities²⁹. During the

last few years, synthesis of dihydropyrano[2,3-*c*]pyrazoles has received major interest^{30,31}.

Pyranopyrazoles are also used as pharmaceutical ingredients and biodegradable agrochemicals³². Derivatives of dihydropyrano[2,3-*c*]pyrazole possess useful pharmacological and biological properties³³. Only a few reports are available on the synthesis of dihydropyrano[2,3-*c*]pyrazol-6-amines^{34,35}. A Four-Component Domino Combinatorial Synthesis in presence of DIPEA is reported by Kanchithalaivan *et al.*,³⁶. In continuation of current efforts to find and develop a new routes for the synthesis of biologically active heterocyclic molecules using inexpensive,

readily available, and environmentally benign catalysts³⁷⁻⁴³, thus herein, we wish to report a mild, efficient method for the synthesis of some novel and simple one-pot four-component synthesis of dihydropyrano [2, 3-*c*] pyrazol-6-amines using green chemistry principles. In the present study, a series of novel dihydropyrano [2,3-*c*]pyrazol-6-amines (5) are synthesized by a one-pot four-component reaction of hydrazine hydrate (4), araldehydes, ethyl acetoacetate (2), and 4-fluoro phenylacetonitrile (3) in water using sodium hydrogen sulphate as a catalyst in good yields as shown in the following Figure 1.

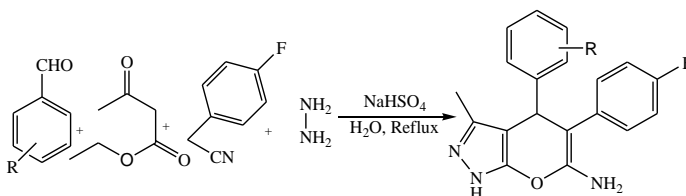


Figure 1: Synthesis of dihydropyrano [2,3-*c*]pyrazol-6-amines.

MATERIALS AND METHODS

Chemicals of analytical grade were arranged locally. The chemicals that has been used were commercial (SD fine Company AR grade) and without further purification. The progress of the reaction was monitored on TLC (Eluent; 2:8 ethyl acetate–petroleum ether). Melting points were measured in open capillary tubes and are uncorrected using Raaga, melting point apparatus, Indian make. FT-IR spectra were recorded on SHIMADZU FT-IR-8400s spectrophotometer (Shimadzu Company). ¹H NMR and ¹³C NMR spectra of the synthesised products were recorded on Bruker AMX 400 MHz (Bruker Company) and 100 MHz respectively in DMSO-*d*₆ as solvent and TMS as internal standard reference.

General procedure for preparation of dihydropyrano [2,3-*c*]pyrazol-6-amines :

The mixture of aromatic aldehyde (1 m mol), malononitrile (1 m mol), ethyl acetoacetate (1 m mol) hydrazine hydrate (1 m mol) and NaHSO₄ (0.5 m mol) were taken in ethanol-water (1:1) (5 ml) and heated at 80°C. The progress of the reaction was monitored using Silica gel-G TLC plates with a mixture of petroleum ether (60–80°C) and ethyl acetate (20:80) as eluent. After the reaction has been completed, the mixture was cooled to room temperature and the precipitated product was filtered, washed with water to get nearly pure product.

RESULTS AND DISCUSSION

At the beginning, to identify the optimum reaction conditions, a representative reaction between 3-methoxy, 4-hydroxy benzaldehyde (vanillin), ethylacetoacetate, 4-fluoro phenylacetonitrile and hydrazine hydrate (1 m mol each) was considered. To begin with, the reaction was carried out without any catalyst in ethanol, at room temperature, ultrasonic and microwave irradiation which didnot afford desired product. This test reaction was then probed using

different catalysts in refluxing ethanol which gave different product yields. In present study, NaHSO₄, the reaction afforded better yield when compared to other catalysts (Table 1).

Table 1: Selection of suitable catalyst and solvent for the synthesis of (5d)^a.

Entry	Catalyst (10 mol%)	Solvent	Time (min)	Yield ^a (%)
1	Imidazole	Ethanol	120	45
2	NaOH	Ethanol	140	50
3	Ba(OH) ₂	Ethanol	130	45
4	NaHSO ₄	Ethanol	120	55
5	NaHSO ₄	Water	120	50
6	NaHSO ₄	Water-ethanol(1:1)	65	87
7	NaHSO ₄	Acetonitrile	120	40

^a isolated yields

Table 2: Effect of the amount of NaHSO₂ on the synthesis of (5e)^a.

Entry	NaHSO ₄ (mol%)	Yield (%)
1	5	50
2	7	65
3	10	89
4	12	89

^aReactions are performed on a 1 mmol scale of the reactants.

After selection of catalyst for the reaction, investigation for an appropriate solvent was performed. The representative reaction was carried out in solvents such as ethanol, water, acetonitrile and water: ethanol (1: 1) mixture (Table 1). As seen from the data in Table 1, Water-ethanol (1:1) was found to be the ideal solvent for this reaction. The explanation of the difference between those solvents is due to their relative polarity which indicates water (1.0) is the most polar solvent among them then ethanol (0.654) less than water and acetonitrile (0.460) the least polar among them, thus the mixture of water and ethanol (1: 1) made the polarity of water ethanol is proper for the reaction and gives the best result as well as easily to

remove them from the product by washing. Acetonitrile is not proper solvent which gives low yield of the product due to its low relative polarity and difficult to remove from product it needs sophisticated means to remove from the product. The reaction

template, with NaHSO₄ as catalyst and Water-ethanol (1:1) as a solvent system, was applied to a different substituted araldehydes to prepare a library of compounds. The template works well for all the araldehydes to give corresponding products (Table 3).

Table 3: Synthesis of novel dihydropyrano [2,3-*c*]pyrazol-6-amines from various aldehydes, hydrazine hydrate, ethyl acetoacetate, and 4-chloro phenylacetonitrile and NaHSO₄ in ethanol-water (1:1) solvent.

Entry	Aldehyde (1)	Product	Time (min)	Yield ^a (%)	MP (°C) found
1.	3-NO ₂ C ₆ H ₄ CHO	5a	120	85	185–187
2.	4-HOC ₆ H ₄ CHO	5b	120	82	236–239
3.	4-ClC ₆ H ₄ CHO	5c	120	80	199–200
4.	3-MeO,4-HOC ₆ H ₃ CHO	5d	80	87	260–263
5.	3-MeOC ₆ H ₄ CHO	5e	80	89	195–197
6.	3,4,5-(MeO) ₃ C ₆ H ₂ CHO	5f	90	80	180–184
7.	4-NO ₂ C ₆ H ₄ CHO	5g	90	82	271–273
8.	2,4-Cl ₂ C ₆ H ₃ CHO	5h	120	80	205–207
9.	3,4-(MeO) ₂ C ₆ H ₃ CHO	5i	120	80	175–178
10.	2-HOC ₆ H ₄ CHO	5j	90	82	200–204
11.	HCHO	5k	240	ND	-
12.	CH ₃ CHO	5l	240	ND	-
13.	C ₆ H ₅ CH=CHCHO	5m	240	ND	-

^aisolated yields. ND: not detected

The reaction template failed for the using of aliphatic aldehydes (Table 3, entries 11-12) and the α,β -unsaturated aldehydes such as cinnamaldehyde (Table 3, entry 13) as well did not give any product even after the reaction was carried out for longer duration. To select a best catalyst and proper solvent, we carried out the reaction between 3-methoxy, 4-hydroxy benzaldehyde (vanillin), ethylacetoacetate, 4-fluoro phenylacetonitrile and hydrazine hydrate (1 m mol each) was considered in the presence of 10 mol% of different basic catalysts such as NaOH, Ba(OH)₂, imidazole, and NaHSO₄ and ethanol as solvent. We found that, imidazole did not afford the product in good yield and reaction time was very long, similar results were obtained with Ba(OH)₂ as basic catalyst. The desired product yield improved to a very less extent when NaOH was used as a basic catalyst and the product was a sticky mass. When the same reaction was carried out in the presence of NaHSO₄, and different solvent such as ethanol, water, water : ethanol in the ratio 1 : 1 and acetonitrile, we found that the desired product improved to a very less extent when ethanol solvent was used but the time still little long then it was not improved when pure water used as solvent, whilst the product yield obtained in very high yield 87% within 65 mins, when ethanol-water in the ratio (1 : 1) used as solvent. In presence of acetonitrile has been used the very poor yield of product has been obtained in long duration time of the reaction because of less polar than water and ethanol and it is aprotic polar solvent. The results of this study are presented in (Table 1). We have also varied the amount of NaHSO₄ from 5, 7, 10 to 12 mol% and the results revealed that, 10 mol% gives excellent yield of the product in a short duration as shown in Table 2. When the optimization of the conditions have been done, the generality of this method was examined by the reaction of different

substituted aromatic aldehydes with ethyl acetoacetate, 4-fluoro phenylacetonitrile and hydrazine hydrate in the presence of 10 mol% NaHSO₄ in ethanol-water (1:1) solvent under reflux; and the results of this study are shown in the Table 3.

Spectral data analysis

The structural elucidation of the desired new compounds have been explained using spectronic techniques such as Infra-Red spectrum FT-IR, which give concise view about the functional groups, isomers, geometry, and substituent present in the molecule like OH group, NH₂, C≡N, C≡C, C=C, NO₂, C=O, C-X, ortho, meta, para isomers, cis, trans, CH₂, CH₃ etc. ¹HNMR (Power 400 MHz, Solvent DMSO-*d*₆) spectrum which identified the number of protons exist in the molecule CH, CH₂, CH₃, aromatic protons, aldehyde, carboxylic proton, cis, trans geometry and equivalency in the molecule. ¹³CNMR (100 MHz, DMSO-*d*₆) spectrum that used to identify the number of carbon atoms either equivalent or non-equivalent carbon atoms exist in the molecule such as CH, CH₂, CH₃, C≡N, C≡C, C=C aliphatic or aromatic, C=O ester, amide, carboxylic acid, aldehyde, ketone respectively etc. Below the spectral data of the synthesised new compounds as they are arranged in Table 3: Yellow crystalline solid (85%, 0.590 g); mp 185-187°C: IR (KBr) ν cm⁻¹: 3387 (br), 3065 (ws) 2968 (s), 1694 (vs), 1622 (s), 1375 (s), 1236 (s), 1173 (vs), 1033 (s); Figure 2a. ¹HNMR (400 MHz, DMSO-*d*₆): δ 2.48 (2H, NH₂), 3.29 (s, 3H, Me), 4.89 (s, 1H, CH), 6.85 – 6.38 (d,d, *J* = 8.4 Hz, 4H, Ph), 7.84 – 8.87 (m, 4H, Ph), 10.74 (s, 1H, NH); Figure 2b. ¹³CNMR (100 MHz, DMSO-*d*₆): δ 160.0 (O-C=N), 157.0, 153.0, 148.1, 135.0, 134.4, 130.0, 122, 115.1 (all ArC), 144.0 (C-C=N pyrazole), 133.5(O-C=C pyrazole), 115.1 (C=C pyrazole), 105.3. (C=C pyrano), 25.1 (CH), 11.1(CH₃) (Figure 2c).

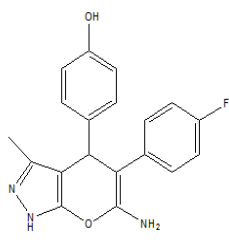


Figure 3

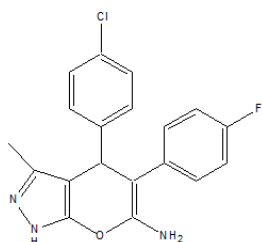


Figure 4

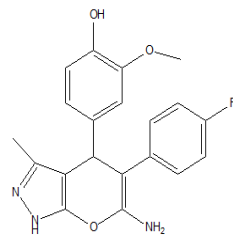


Figure 5

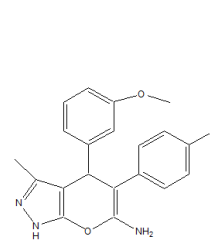


Figure 6

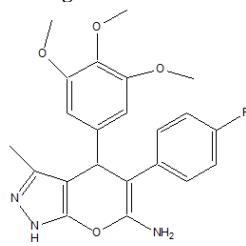


Figure 7

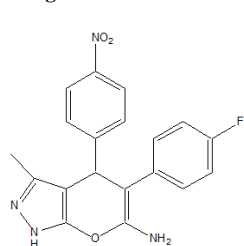


Figure 8

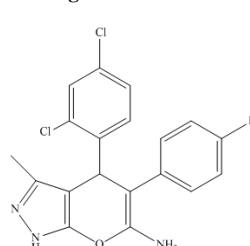


Figure 9

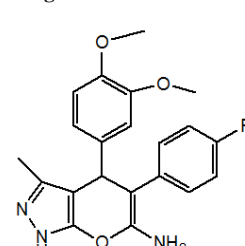


Figure 10

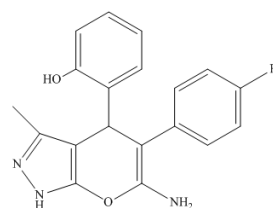
Figure 11
IUPAC Name

Figure No.-

3	4-(6-amino-5-(4-fluorophenyl)-3-methyl-1,4-dihydropyranopyrazol-4-yl)phenol (5b)
4	4-(4-chlorophenyl)-5-(4-fluorophenyl)-3-methyl-1,4-dihydropyranopyrazol-6-amine (5c)
5	4-(6-amino-5-(4-fluorophenyl)-3-methyl-1,4-dihydropyranopyrazol-4-yl)-2-methoxyphenol (5d)
6	5-(4-fluorophenyl)-4-(3-methoxyphenol)-3-methyl-1,4-dihydropyranopyrazol-6-amine (5e)
7	5-(4-fluorophenyl)-4-(3,4,5-trimethoxyphenol)-3-methyl-1,4-dihydropyranopyrazol-6-amine (5f)
8	5-(4-fluorophenyl)-3-methyl-4-(4-nitrophenyl)-1,4-dihydropyranopyrazol-6-amine (5g)
9	4-(2,4-dichlorophenyl)-5-(4-fluorophenyl)-3-methyl-1,4-dihydropyranopyrazol-6-amine (5h)
10	5-(4-fluorophenyl)-4-(3,4-dimethoxyphenol)-3-methyl-1,4-dihydropyranopyrazol-6-amine (5i)
11	2-(6-amino-5-(4-fluorophenyl)-3-methyl-1,4-dihydropyranopyrazol-4-yl)phenol (5j)

White crystalline solid (82%, 0.570 g); mp 236-239 °C: IR (KBr) v: 3534 (br), 3343 (br), 3065 (ws) 2968 (s), 1684 (s), 1598 (s), 1375 (s), 1236 (s), 1173 (vs), 1033 (s), 834 (s) cm⁻¹; ¹HNMR (400 MHz, DMSO-d₆): δ 2.00 (2H, NH₂), 2.48 (s, 3H, Me), 4.09 (s, 1H, OH), 5.0 (s, 1H, CH), 6.85 – 6.38 (d,d, J = 8.4 Hz, 2H, Ph), 6.85 – 6.38 (d,d, J = 8.4 Hz, 4H, Ph), 10.04 (s, 1H, NH). White amorphous solid (80%, 0.560 g); mp 199-200 °C: IR (KBr) v: 3378 (br), 3047 (ws) 2968 (s), 1684 (s), 1623 (s), 1400 (s), 1235(s), 1163 (vs), 1053 (s), 821 (vs), 653(s) cm⁻¹; ¹HNMR (400 MHz, DMSO-d₆): δ 2.00 (2H, NH₂), 2.48 (s, 3H, Me), 5.0 (s, 1H, CH), 6.85 – 6.38 (d,d, J = 8.4 Hz, 2H, Ph), 6.85 – 6.38 (d,d, J = 8.4 Hz, 4H, Ph), 10.04 (s, 1H, NH). ¹³CNMR (100 MHz, DMSO-d₆): δ 160.5 (O-C=N), 154.5, 151.5, 143.9, 132.5, 129.0, 120.9, 116.9, 115.6 (all ArC), 143.0 (C-C=N pyrazole), 135.9 (O-C=C pyrazole), 108.7 (C=C pyrazole), 104.7 (C=C pyrano), 23.1 (CH), 11.1(CH₃). Pale orange crystalline solid (87%, 0.598 g); mp 260-263 °C: IR (KBr) v: 3534 (br), 3452 (s), 3363 (s), 3225 (b), 3065 (ws) 2968 (s), 1680 (s), 1591 (s), 1455 (s), 1423 (s), 1107 (s), 1055 (s), 802 (s), 622 (s) cm⁻¹; ¹HNMR (400 MHz, DMSO-d₆): δ 2.23 (2H, NH₂), 2.49 (s, 3H, Me), 3.82 (s, 3H, OCH₃), 5.10 (s, 1H, OH), 5.65 (s, 1H, CH), 6.85 – 6.87 (d,d, J = 8.4 Hz, 4H, Ph), 7.23 – 7.53 (d,d, J = 8.4 Hz, 2H, Ph), 7.44 (s, 1H, Ph), 8.57 (s, 1H, NH); ¹³CNMR (100

MHz, DMSO-d₆): δ 161.5 (O-C=N), 158.6, 150.8, 148.8, 146.6, 134.9, 126.3, 124.4, 116.4 (all ArC), 140.0 (C-C=N pyrazole), 130.0 (O-C=C pyrazole), 110.9 (C=C pyrazole), 90.4 (C=C pyrano), 56.4 (OCH₃), 23.6 (CH), 12.1(CH₃). Pale yellow amorphous solid (89%, 0.614 g); mp 195-197 °C: IR (KBr) v: 3484 (w), 3354 (w), 3222 (w), 3014 (ws) 2935 (s), 1675 (s), 1604 (s), 1454 (s), 1387 (s), 1150 (s), 1043 (s), 764 (s) cm⁻¹; ¹HNMR (400 MHz, DMSO-d₆): δ 2.48 (2H, NH₂), 3.40 (s, 3H, Me), 3.80 (s, 3H, OCH₃), 4.89 (s, 1H, CH), 7.07 – 7.09 (d,d, J = 8.4 Hz, 4H, Ph), 7.38 – 7.45 (m, 3H, Ph), 8.67 (s, 1H, Ph), 10.03 (s, 1H, NH); ¹³CNMR (100 MHz, DMSO-d₆): δ 161.3 (O-C=N), 159.4, 151.5, 145.9, 138.8, 135.1, 129.9, 125.1, 117.4 (all ArC), 144.4 (C-C=N pyrazole), 134.0 (O-C=C pyrazole), 112.4 (C=C pyrazole), 88.8 (C=C pyrano), 55.1 (OCH₃), 23.1 (CH), 11.1(CH₃).

Pale orange crystalline solid (80%, 0.560 g); mp 180–184 °C: IR (KBr) v: 3484 (w), 3354 (w), 3222 (w), 3014 (ws) 2986 (s), 1675 (s), 1622 (s), 1438 (s), 1413 (s), 1342 (s), 1234 (s), 1130 (s), 1053 (s), 993 (s), 765 (s), 619 (s) cm⁻¹; ¹HNMR (400 MHz, DMSO-d₆): δ 2.48 (2H, NH₂), 3.29 (s, 3H, Me), 3.72 (s, 3H, OCH₃), 3.83 (s, 6H, 2OCH₃), 4.64 (s, 1H, CH), 7.2 (s, 1H, Ph), 8.06 – 8.08 (d,d, J = 8.4 Hz, 4H, Ph), 8.64 (s, 1H, Ph), 10.09 (s, 1H, NH); ¹³CNMR (100 MHz, DMSO-d₆): δ 161.1 (O-C=N), 155.4, 153.2, 144.5, 136.4, 132.1,

129.2, 122.1, 120.1 (all ArC), 144.5 (C=C=N pyrazole), 132.1 (O=C=C pyrazole), 105.5 (C=C pyrazole), 88.9 (C=C pyrano), 60.1(OCH₃), 55.1 (2OCH₃), 23.1 (CH), 11.9(CH₃). Pale orange crystalline solid (82%, 0.570 g); mp 271-273 °C: IR (KBr) v: 3484 (w), 3354 (w), 3222 (w), 3114 (ws) 2925 (s), 1675 (s), 1620 (s), 1596 (s), 1523(vs), 1454 (s), 1346 (vs), 1161 (s), 1014 (s), 844 (s) cm⁻¹; ¹HNMR (400 MHz, DMSO-*d*₆): δ 2.48 (2H, NH₂), 3.29 (s, 3H, Me), 4.84 (s, 1H, CH), 8.14 – 8.16 (d,d, *J* = 8.4 Hz, 4H, Ph), 8.35 – 8.37 (d,d, *J* = 8.4 Hz, 4H, Ph), 10.05 (s, 1H, NH). White crystalline solid (80%, 0.560 g); mp 205-207 °C: IR (KBr) v: 3448 (w), 3354 (w), 3222 (w), 3089 (ws) 2935 (s), 1733 (ws), 1616 (s), 1583 (s), 1319 (s), 1139 (s), 1053 (s), 885 (s), 786 (s) cm⁻¹; ¹HNMR (400 MHz, DMSO-*d*₆): δ 2.48 (2H, NH₂), 3.28 (s, 3H, Me), 4.89 (s, 1H, CH), 7.54 – 7.56 (d,d, *J* = 8.4 Hz, 4H, Ph), 8.14 – 8.16 (d,d, *J* = 8.4 Hz, 2H, Ph), 8.96 (s, 1H, Ph), 11.08 (s, 1H, NH); ¹³CNMR (100 MHz, DMSO-*d*₆): δ 162.2 (O-C=N), 158.1, 143.7, 141.3, 134.6, 133.1, 130.4, 128.1, 127.7 (all ArC), 143.7 (C-C=N pyrazole), 130.1 (O-C=C pyrazole), 114.4 (C=C pyrazole), 88.9 (C=C pyrano), 23.1 (CH), 11.1(CH₃). Orange crystalline solid (80%, 0.560 g); mp 175–178 °C: IR (KBr) v: 3484 (wbr), 3421 (w), 3222 (w), 3002 (ws) 2942 (s),

1675 (s), 1623 (s), 1508 (s), 1421 (s), 1344 (s), 1271 (s), 1157 (s), 1018 (s), 867 (s), 754 (s) cm⁻¹; ¹HNMR (400 MHz, DMSO-*d*₆): δ 2.48 (2H, NH₂), 3.42 (s, 3H, Me), 3.81 (s, 6H, 2OCH₃), 4.82 (s, 1H, CH), 7.05 – 7.07 (d,d, *J* = 8.4 Hz, 4H, Ph), 7.35 – 7.37 (d,d, *J* = 8.4 Hz, 2H, Ph), 8.62 (s, 1H, Ph), 10.09 (s, 1H, NH); ¹³CNMR (100 MHz, DMSO-*d*₆): δ 160.6 (O-C=N), 157.5, 151.5, 148.9, 143.3, 135.3, 131.4, 126.6, 123.3 (all ArC), 140.0 (C-C=N pyrazole), 117.5 (O-C=C pyrazole), 115.4 (C=C pyrazole), 88.8 (C=C pyrano), 55.5 (OCH₃), 55.3 (OCH₃), 23.1 (CH), 11.1 (CH₃). White crystalline solid (82%, 0.570 g); mp 200-204 °C: IR (KBr) v: 3534 (br), 3343 (br), 3065 (ws) 2968 (s), 1684 (s), 1598 (s), 1375 (s), 1236 (s), 1173 (vs), 1033 (s), 834 (s) cm⁻¹; ¹HNMR (400 MHz, DMSO-*d*₆): δ 2.00 (2H, NH₂), 2.48 (s, 3H, Me), 4.09 (s, 1H, OH), 5.0 (s, 1H, CH), 6.94 – 6.96 (d,d, *J* = 8.4 Hz, 2H, Ph), 7.37 – 7.41 (t,d, *J* = 16 Hz, 2H, Ph), 7.67 – 7.69 (d,d, *J* = 8.4 Hz, 2H, Ph), 11.09 (s, 1H, NH). ¹³CNMR (100 MHz, DMSO-*d*₆): δ 163.2 (O-C=N), 159.1, 155.5, 150.3, 149.7, 136.7, 133.7, 131.3, 120.0 (all ArC), 143.3 (C-C=N pyrazole), 118.6 (O-C=C pyrazole), 117.0 (C=C pyrazole), 89.9 (C=C pyrano), 23.0 (CH), 11.1 (CH₃).

CONCLUSION

To conclude, we have reported a new, simple, rapid, and an effective one-pot multi component protocol for the expedient synthesis of dihydro-pyrano [2,3-*c*]pyrazol-6-amines. The noteworthy usefulness of this protocol includes easily available starting materials, simple procedure, and easier separation of products by filtration. The reaction is facile, simple and environment-friendly.

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AUTHOR'S CONTRIBUTION

Saleh Azzam SH: writing original draft, methodology, **Siddekha A:** writing, review, project administration. **Pasha MA:** conceptualization, methodology. The final manuscript was read and approved by all authors.

DATA AVAILABILITY

Data will be made available on request.

CONFLICT OF INTEREST

No conflict of interest associated with this work.

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