Article

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Piperidine-Promoted Three-Component Condensation: Synthesis of Chromene Heterocycles and Pyrazolotriazoles

Mehrnoush Kangani,* Nourallah Hazeri,* Afshin Yazdani-Elah-Abadi and Malek-Taher Maghsoodlou

Department of Chemistry, Faculty of Science, University of Sistan and Baluchestan, P.O. Box 98135-674, Zahedan, Iran

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Chromenes, the oxygen-containing heterocyclic compounds, have a "special" place in biologically active natural products and in synthetic chemistry and in the fields of medicinal, agrochemical, cosmetic, and pigment industries. In this work, piperidine was used as a base catalyst for the convenient synthesis of 1,4-dihydropyrano[2,3-*c*]pyrazole, 5,10-dihydro-4*H*-benzo[*g*]chromene, and pyrazolo[1,2-*a*] [1,2,4]triazole derivatives at ambient temperature. This methodology has several advantages including the use of easily accessible and inexpensive catalysts, short reaction times, high yields, convenient work-up, and not needing column chromatography.

Keywords: Piperidine; 1,4-dihydropyrano[2,3-*c*]pyrazole; 5,10-dihydro-4*H*- benzo[*g*]chromene; pyrazolo[1,2-*a*] [1,2,4]triazole-1,3-dione, ambient temperature

INTRODUCTION

Multi-component reactions (MCRs) have gained much attention as a broad synthetic strategy for the preparation of drugs and industrial compounds.[1] MCRs provide environmentally friendly processes via reducing waste production, energy consumption, and the number of steps.[2] Oxygen heterocycles occupy a distinct position among heterocyclic compounds because of their wide natural abundance and broad biological and pharmaceutical significance. In the particular classes of O-heterocycles, the "chromene" heterocyclic scaffolds represent a "privileged" structural motif well-distributed in natural products with a broad spectrum of potent biological activities that include antimicrobial,[3] antiviral,[4] antimalarial,[5] antitumor,[6] and anticancer.[7] Chromene heterocycles also find uses in the cosmetic and pigment industries,[8] and also as biodegradable agrochemicals.[9] Recently, a series of synthetic chromene derivatives have been prepared and evaluated for their potential anticancer, antibacterial, antifungal, and anti-rheumatic properties and many more (Figure 1). Some catalysts have been reported to facilitate the synthesis of dihydropyrano-[2,3-c]pyrazole derivatives and 5,10-dihydro-4*H*-benzo[g] chromenes, including γ-alumina,[10] nanosized magnesiumoxide,[11] TEAA (triethylammonium acetate),[12] imidazole,[13] L-proline,[14] KF-alumina,[14] trichloroaceticacid,[15] ceric sulfate,[15] SB-DABCO,[16] Et_3N,[17] and TEBA.[18] However, some of these methods have drawbacks, such as long reaction times, unsatisfactory yields, high catalyst loading, or the use of expensive catalysts. Therefore, it is necessary to further develop a simple synthesis method of these chromene heterocycles without these problems.

Pyrazolourazoles and their fused derivatives with diverse structures have attracted much interest because of their wide range of biological properties such as analgesic, antibacterial, anti-inflammatory, antidiabetic, and psychoanaleptic activities[19–24] (Figure 1). Many methods have been reported for their synthesis in recent years,[25–34] and development of new approaches for their synthesis seems to be an interesting challenge. Piperidine has been used as an organocatalyst in different organic syntheses.[35–37] In continuation of our research on MCRs,[38–46] we report here an efficient synthesis of 1,4-dihydropyrano[2,3-c]pyrazole, 5,10-dihydro-4*H*-benzo [g]chromene, and pyrazolo[1,2-*a*] [1,2,4]triazole derivatives in the presence of piperidine as an efficient catalyst in EtOH at ambient temperature (Scheme 1).

*Corresponding author. Email: mehrnooshkangani@gmail.com; nhazeri@chem.usb.ac.ir

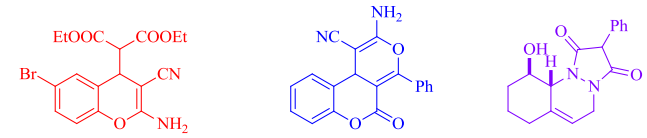
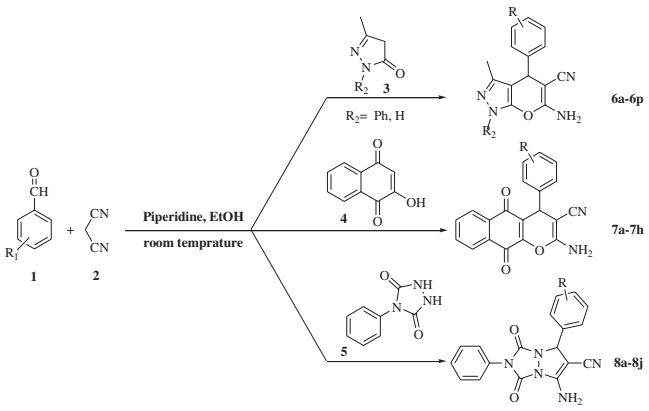


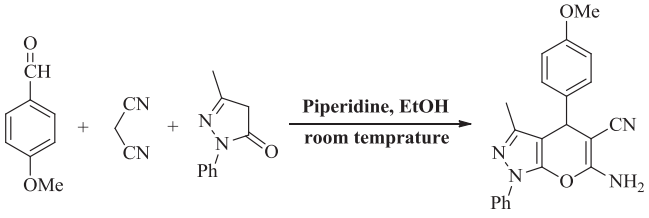
Fig. 1. Synthetically important drug-like chromenea and pyrazolourazoles heterocycles.



Scheme 1. Synthesis of 1,4-dihydropyrano[2,3-*c*]pyrazole, 5,10-dihydro-4*H*-benzo[g]chromene, and pyrazolo[1,2-*a*] [1,2,4]triazole derivatives in the presence of piperidine as catalyst in EtOH at ambient temperature.

RESULTS AND DISCUSSION

The reaction between 4-methoxybenzaldehyde, malononitrile, and 3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one was chosen as a model reaction. The reaction was performed in the presence of different amounts of the catalyst and solvent (Scheme 2) (Table 1), and it was found that 15 mol% of piperidine gave the best result in EtOH (2 mL). In this experiment, no other organic solvent was tested because of the green chemistry concept. Optimization was repeated for the synthesis of 5,10-dihydro-4*H*-benzo[g]chromene and pyrazolo [1,2-*a*] [1,2,4]triazole, and in all cases 15 mol% of piperidine in EtOH (2 mL) gave the best results. Piperazine



Scheme 2. Model reaction for optimizing the amount of catalyst and solvent for the synthesis of 1,4-dihydropyrano[2,3-*c*]pyrazoles.

Table 1. Different catalytic systems evaluated for the synthesis of 1,4-dihydropyrano[2,3-*c*]pyrazole at ambient condition

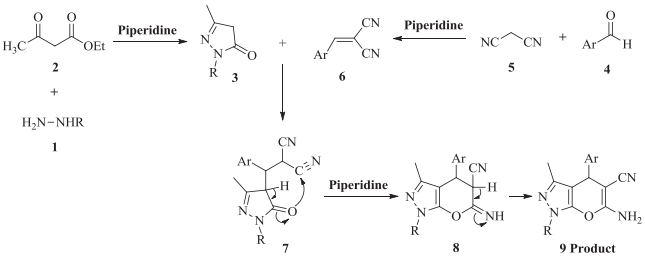
Entry	Catalyst (mol%)	Solvent	Time	Isolated yield (%)
1	—	EtOH (2 mL)	48 h	—
2	Piperazine (15)	EtOH (2 mL)	24 h	Trace
3	Pyridine (15)	EtOH (2 mL)	24 h	—
4	Piperidine (15)	EtOH (2 mL)	5 min	90
5	Piperidine (20)	EtOH (2 mL)	5 min	90
6	Piperidine (10)	EtOH (2 mL)	20 min	75
7	Piperidine (5)	EtOH (2 mL)	30 min	70

and pyridine were used as the catalyst under reaction conditions, and the results are summarized in Table 1.

With these optimized conditions, we tested a variety aromatic aldehydes including electron-withdrawing and electron-donating groups. In all cases, the products were obtained in good to high yields (Table 2). Aliphatic aldehydes such as heptanal and pentanal were also tested under the reaction conditions, but even after 48 h no product was formed (Table 2, Entries 17, 18, 27, 38) .

In order to assess the efficiency and generality of this methodology, the obtained results from the reaction of aromaticaldehyde and malononitrile with substrates **3**, **4**, and **5** by this method were compared with those of the previously reported methods (Table 3). It was found that the present method is convincingly superior to the reported methods with respect to reaction time, yield of the product, and the amount of catalyst. If possible, synthetic methods should be conducted at ambient temperature and pressure to reduce the energy consumption.[49] This methodology has been carried out at ambient conditions for good economic and environmental impacts.

The proposed mechanism for the preparation of 1,4-dihydropyrano[2,3-*c*]pyrazoles is described in



Scheme 3. Proposed mechanism for the synthesis of 1,4-dihydropyrano[2,3-*c*]pyrazoles in the presence of piperidine as base catalyst.

Table 2. Synthesis of 1,4-dihydropyrano[2,3-*c*]pyrazole, 5,10-dihydro-4*H*-benzo[g]chromene and pyrazolo[1,2-*a*] [1,2,4]triazole derivatives in the presence of piperidine as catalyst in EtOH at ambient temperature

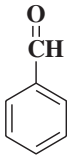
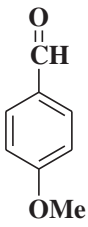
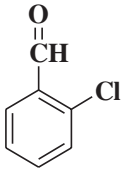
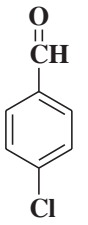
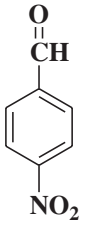
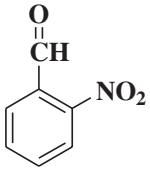
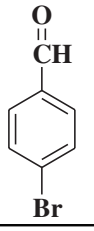
Entry	Aldehyde	Substrate	Product	Time (min)	Isolated yield (%)	Ob. mp (°C)	Lit. mp (°C)
1		3 R_2 = H	**6a**	60	75	166–168	169[10]
2		3 R_2 = H	**6b**	30	90	176–178	174[10]
3		3 R_2 = H	**6c**	40	75	143–145	143–145[10]
4		3 R_2 = H	**6d**	20	80	178–179	175[11]
5		3 R2 = H	**6e**	10	90	202–203	195[11]
6		3 R_2 = H	**6f**	10	90	188–190	191[10]
7		3 R2 = H	**6g**	10	80	175	177[11]

Table 2. Continued

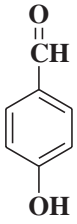
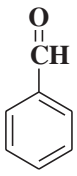
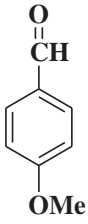
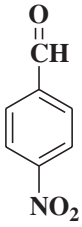
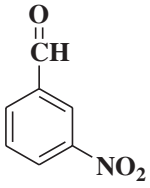
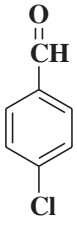
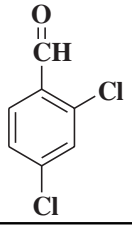
Entry	Aldehyde	Substrate	Product	Time (min)	Isolated yield (%)	Ob. mp (°C)	Lit. mp (°C)
8		3 R_2 = H	**6h**	20	75	222–224	223–226[12]
9		3 R_2 = Ph	**6i**	20	80	165–167	168–170[40]
10		3 R_2 = Ph	**6j**	5	90	213–214	210–212[40]
11		3 R_2 = Ph	**6k**	5	90	170–172	169–171[40]
12		3 R2 = Ph	**6l**	5	90	198–200	195–197[40]
13		3 R_2 = Ph	**6m**	10	85	200–202	190–192[40]
14		3 R_2 = Ph	**6n**	5	80	181–183	181–183[40]

Table 2. Continued

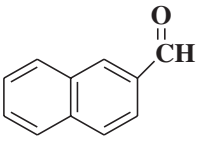
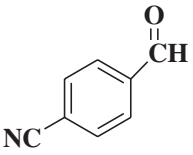
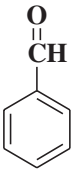
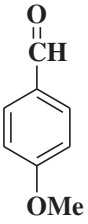
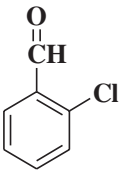
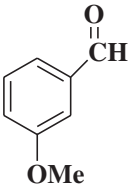
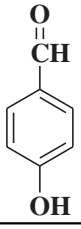
Entry	Aldehyde	Substrate	Product	Time (min)	Isolated yield (%)	Ob. mp (°C)	Lit. mp (°C)
15		3 R_2 = Ph	**6o**	5	90	196–198	198–200[40]
16		3 R_2 = Ph	**6p**	10	86	216–218	217–219[16]
17	*n*-Heptanal	3 R2 = H	—	—	—	—	—
18	*n*-Pentanal	3 R_2 = Ph	—	—	—	—	—
19		4	**7a**	20	80	259–261	260–262[17]
20		4	**7b**	15	85	242–244	242–244[17]
21		4	**7c**	30	75	240–242	236–239[18]
22		4	**7d**	15	80	242–244	242–244[18]
23		4	**7e**	15	80	253–255	254–256[18]

Table 2. Continued

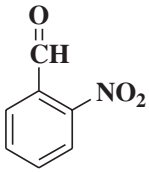
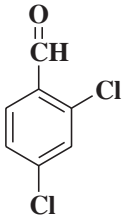
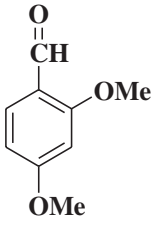
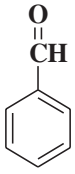
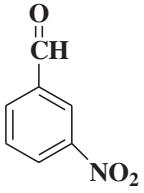
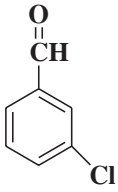
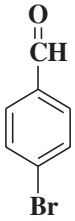
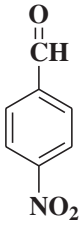
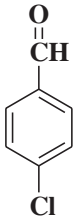
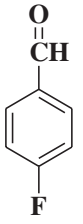
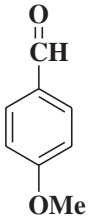
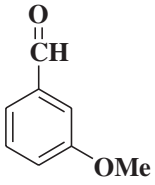
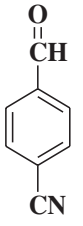
Entry	Aldehyde	Substrate	Product	Time (min)	Isolated yield (%)	Ob. mp (°C)	Lit. mp (°C)
24		4	**7f**	18	85	245–246	242–244[48]
25		4	**7g**	10	90	284	286–288[48]
26		4	**7h**	15	85	245–246	246–249[48]
27	*n*-Pentanal	4	—	—	—	—	—
28		5	**8a**	30	70	>300	>300[32]
29		5	**8b**	15	80	>300	>300[32]
30		5	**8c**	30	70	>300	>300[32]
31		5	**8d**	20	85	>300	>300[32]

Table 2. Continued

Entry	Aldehyde	Substrate	Product	Time (min)	Isolated yield (%)	Ob. mp (°C)	Lit. mp (°C)
32		5	**8e**	20	70	>300	>300[32]
33		5	**8f**	30	85	>300	>300[32]
34		5	**8g**	30	70	>300	>300[32]
35		5	**8h**	30	80	>300	>300[32]
36		5	**8i**	30	80	>300	232–234[47]
37		5	**8j**	15	90	>300	>300[32]
38	*n*-Heptanal	5	—	48	—	—	—

Scheme 2. First, Knoevenogel condensation between aromatic aldehyde and malononitrile took place, then the 2-benzylidenemalononitrile (**3**) was attacked by the (**5**), which led to the intermediate (**6**). Tautomerization and cyclization (**6**) gave the intermediate (**7**). The subsequent tautomerization gave the desired product (**8**).

Table 3. Comparison of the efficiency of piperidine with other reported catalysts in the literature

Entry	Product	Catalyst/condition	Time	Yield (%)	References
1	**6b**	Boiling water	5 h	80	[50]
2	**6b**	Cinchona derivatives/CH_2Cl_2, r.t	20 h	96	[51]
3	**6b**	γ-alumina/H_2O, reflux	60 min	79	[10]
4	**6b**	Piperidine/EtOH,r.t	30 min	90	Present work
5	**6j**	TEAA/r.t	45 min	92	[12]
6	**6j**	$Ce(SO_4)_2.4H_2O$/100°C	10 min	80	[15]
7	**6j**	Electrolysis, 0.62 F mol/ NaBr, EtOH, r.t.	20 min	85	[40]
8	**6j**	Piperidine/EtOH,r.t	5 min	90	Present work
9	**7b**	Et_3N/ CH_3CN, r.t	24 h	86	[17]
10	**7b**	Piperidine/EtOH,r.t	15 min	85	Present work
11	**7c**	TEBA/solvent-free, 85°C	3.5 h	90	[18]
12	**7c**	DBU/H_2O, reflux	90 min	87	[52]
13	**7c**	Piperidine/EtOH,r.t	30 min	75	Present work
14	**8f**	DABCO/ultrasound irradiation, EtOH, 50°C	35 min	95	[32]
15	**8f**	Et_3N, ultrasound irradiation, EtOH, 50°C	30 min	91	[53]
16	**8f**	Nano Zno/solvent-free, 100°C	25	88	[47]
17	**8f**	Piperidine/EtOH,r.t	30	85	Present work

EXPERIMENTAL

Chemicals and apparatus

Melting points were measured on an Electrothermal 9100 apparatus. IR spectra were obtained on a JASCO FT/IR-460 plus spectrometer. ^1H and ^{13}C NMR spectra were recorded on Bruker DRX-400 and DRX-300 Advance instruments with DMSO as solvent and TMS as internal reference at 300, 400, and 75 MHz, respectively. Chemicals were purchased from Merck (Darmastadt,Germany) and Fluka (Buchs, Switzerland), and used without further purification.

General procedure for the synthesis of 3-methyl-1*H*-pyrazol-5(4*H*)-one

In an ice bath, hydrazine monohydrate (1 mmol) was added to ethylacetoacetate (1 mmol) and stirred until 3-methyl-1*H*-pyrazol-5(4*H*)-one precipitated and its formation was complete (5 min).

General procedure for the synthesis of 3-methyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile derivatives

To a magnetically stirred solution of aromatic aldehydes (1 mmol), malononitrile (1 mmol) and 3-methyl-1*H*-pyrazol-5(4*H*)-one (1 mmol) or 3-methyl-1 (phenyl)-pyrazol-5(4*H*)-one (1 mmol) in EtOH (2 mL), piperidine (0.01 g) was added at ambient temperature. The progress of the reaction was monitored by TLC. After completion of the reaction, the crude solid product was filtered for separation of the product and washed with EtOH (3 × 2 mL) to give the pure product.

General procedure for the synthesis of 5,10-dihydro-4*H*-benzo[*g*]chromene derivatives

Piperidine (15 mol%) (0.0127 g) was added to a magnetically stirred solution of aromatic aldehydes (1.0 mmol), malononitrile (1.0 mmol), and 2-hydroxy-1,4-naphtoquinone (1.0 mmol) in EtOH (2 mL) at ambient temperature. The progress of the reaction was monitored by TLC. After completion of the reaction, the crude solid product was filtered for separation of the product and washed with EtOH (3 × 2 mL) to give the pure product.

General procedure for the synthesis of pyrazolo[1,2-*a*][1,2,4]triazole derivatives

To a magnetically stirred solution of aromatic aldehydes (1 mmol), malononitrile (1 mmol), and 4-phenylurazole (1 mmol) in EtOH (2 mL), piperidine (0.01 g) was added at ambient temperature. The progress of the reaction was monitored by TLC. After completion of the reaction, the crude solid product was filtered for the separation of product and washed with EtOH (3 × 2 mL) to give the pure product.

Characterization data of selected compound (Appendix S1)

6-Amino-1,4-dihydro-3-methyl-4-(4-methoxyphenyl) pyrano[2,3-*c*]pyrazole-5-carbonitrile (6b): IR (KBr, cm^{-1}): 3455, 3320, 2190, 1654; ^1H NMR (300 MHz, (DMSO-d_6) δ 1.79 (s, 3H, CH_3), 3.73 (s, 3H, OCH_3), 4.55 (s, 1H, CH), 6.85 (br,2H,NH_2), 6.88 (d, J = 9 Hz, 2H,Ar), 7.07 (d, J = 9 Hz, 2H, Ar), 12.03 (s, 1H, NH) ppm.

6-Amino-1,4-dihydro-3-methyl-4-(2-chlorophenyl)pyrano[2,3-c]pyrazole-5-carbonitrile (6c): IR (KBr, cm^{-1}): 3470, 3240, 2180, 1638; ^1H NMR (300 MHz, (DMSO-d_6) δ 1.77 (s, 3H, CH_3), 5.08 (s, 1H, CH), 6.99 (br, 2H, NH_2), 7.18–7.43 (m, 4H, Ar), 12.16 (s, 1H, NH) ppm.

6-Amino-1,4-dihydro-3-methyl-4-(4-nitrophenyl)pyrano[2,3-*c*]pyrazole-5-carbonitrile (6e): IR (KBr, cm^{-1}): 3414, 3316, 2186, 1748, ^1H NMR (400 MHz, (DMSO-d_6) δ 1.82 (s, 3H, CH_3), 4.84 (s, 1H, CH), 7.06 (s, 2H, NH_2),7.48 (d, J = 8.4 Hz, 2H, Ar), 8.22 (d, J = 8.4 Hz, 2H, Ar), 12.22 (s,1H, NH) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 10, 31, 36, 41, 97, 121, 124, 129 (2C), 136, 147, 153, 155, 162 ppm.

6-Amino-1,4-dihydro-3-methyl-4-(2-nitrophenyl)pyrano[2,3-*c*]pyrazole-5-carbonitrile (6f): IR (KBr, cm^{-1}): 3477, 3228, 2196, 1651. ^1H NMR (400 MHz, (DMSO-d_6) δ 1.78 (s,3H, CH_3), 5.11 (s, 1H, CH), 7.04 (s, 2H, NH_2), 7.34 (d, J = 6.8 Hz, 1H, Ar), 7.50 (t, J = 7.4 Hz 1H, Ar), 7.67 (, t, J = 7.2 Hz, 1H, Ar), 7.86 (d, J = 8.0 Hz, 1H, Ar), 12.22 (s, 1H, NH) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 10, 32, 57, 97, 121, 124, 129, 132, 134, 136, 138, 150, 155, 167 ppm.

6-Amino-1,4-dihydro-3-methyl-4-(4-bromophenyl)pyrano[2,3-*c*]pyrazole-5-carbonitrile (6g): IR (KBr, cm^{-1}): 3400, 3150, 2175,1649; ^1H NMR(300 MHz, (DMSO-d_6) δ 1.80 (s, 3H, CH_3), 4.63 (s, 1H, CH), 6.96 (br, 2H, NH_2), 7.14 (d, J = 8 Hz, 2H, Ar), 7.52 (d, J = 8 Hz, 2H,Ar), 12.16 (s, 1H, NH) ppm.

6-Amino-1,4-dihydro-3-methyl-4-(4-hydroxyphenyl) pyrano[2,3-*c*]pyrazole-5-carbonitrile (6h): IR (KBr, cm^{-1}): 3766, 3214, 3169, 2190, 1489. ^1H NMR (300 MHz, (DMSO-d_6) δ 1.77 (s, 3H, CH_3), 4.45 (s, 1H,CH), 6.62–6.98 (m,6 H, Ar, NH_2), 9.23 (s, 1H, OH), 12.02 (s, 1H, NH) ppm.

6-Amino-1,4-dihydro-4-(4-methoxyphenyl)-3-methyl-1-phenylpyrano[2,3-*c*]pyrazole-5-carbonitrile (6j): IR (KBr, cm^{-1}): 3392, 2933, 2197, 1663; ^1H NMR (400 MHz, (DMSO-d_6) δ 1.80 (s, 3H, CH_3), 3.64 (s, 3H, OCH_3), 4.64 (s, 1H, CH), 6.92 (d, J = 8 Hz, 2H,Ar), 7.19 (br, 2H, NH_2), 7.20 (d, J = 8 Hz, 2H, Ar),7.33 (t, J = 8 Hz,1H, Ar), 7.50 (t, J = 8 Hz, 2H, Ar), 7.80 (d, J = 8 Hz, 2H, Ar) ppm.

6-Amino-1,4-dihydro-3-methyl-4-(naphthalen-2-yl)-1-phenylpyrano[2,3-*c*]pyrazole-5-carbonitrile (6o): IR (KBr, cm^{-1}): 3390, 3200, 2180, 1655; ^1H NMR (400 MHz, (DMSO-d_6) δ 1.77 (s, 3H, CH_3), 4.88 (s, 1H, CH), 7.29 (br, 2H, NH_2), 7.33–7.96 (m,12H, Ar) ppm.

2-Amino-5,10-dihydro-4-(2-chlorophenyl)-5,10-dioxo-4*H*-benzo[*g*]chromene-3-carbonitrile (7c): IR (KBr, cm^{-1}):3365, 3220, 2215, 1652; ^1H NMR (300 MHz, (DMSO-d_6) δ (ppm) 5.16 (s, 1H,CH), 7.29 (t, J = 8 Hz, 2H,Ar), 7.39 (br, 2H, NH_2), 7.41–8.10 (m,6H, Ar) ppm.

2-Amino-5,10-dihydro-4-(3-methoxyphenyl)-5,10-dioxo-4*H*-benzo[*g*]chromene-3-carbonitrile (7d): IR (KBr, cm^{-1}): 3340, 3215, 2215, 1660; ^1H NMR (300 MHz, DMSO- d_6) δ 3.73 (s, 3H, OCH_3), 4.59 (s, 1H, CH), 6.80–6.90 (m, 3H, Ar), 7.24 (t, J = 9 Hz, 1H, Ar), 7.35 (br, 2H, NH_2), 7.82–8.08 (m, 4H, Ar,) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 55.50, 57.84, 112.47, 114.31, 119.76, 120.36, 122.24, 126.29, 126.54, 130.17, 131.16, 131.50, 134.61, 134.98, 145.58, 149.44, 158.75, 158.79, 159.83, 177.32, 183.05 ppm.

2-Amino-5,10-dihydro-4-(4-hydroxyphenyl)-5,10-dioxo-4*H*-benzo[*g*]chromene-3-carbonitrile (7e): IR (KBr, cm^{-1}): 3515, 3415, 3130,2215, 1771; ^1H NMR (400 MHz, (DMSO-d_6) δ 4.52 (s, 1H, CH), 6.69 (d, J = 8 Hz, 2H, Ar), 7.10 (d, J = 8 Hz, 2H, Ar), 7.28 (br, 2H, NH_2), 7.83–8.07 (m, 4H, Ar) ppm.

2-Amino-3-cyano-4-(2-nitrophenyl)-5,10-dioxo-5,10-dihydro-4*H*-benzo[*g*]chromene (7f): IR (KBr, cm^{-1}): 3429, 3338, 2207,1666, 1631; ^1H NMR (400 MHz, DMSO-d_6) δ 5.40 (s,1H, CH), 7.46–8.07(m,10H, Ar and NH_2) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 31.4, 56.2, 105.6, 119.3, 121.6122.4, 124.5, 126.4, 128.0, 130.3, 130.9, 131.4, 134.6, 135.0,149.6, 158.2, 159.3, 177.3, 183.1 (2C = O) ppm.

2-Amino-3-cyano-4-(2,4-dichlorophenyl)-5,10-dioxo-5,10-dihydro-4*H*-benzo[*g*]chromene (7g): IR (KBr, cm^{-1}): 3428, 3344, 2203,1688, 1593.; ^1H NMR (400 MHz, DMSO-d_6) δ 5.65 (s,1H, CH), 7.29–8.06 (m, 9H, Ar and NH_2) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ33.5, 56.3, 105.6, 119.3, 120.6, 124.2, 126.2, 126.4, 126.5, 129.3, 130.6, 130.8, 131.2, 134.8136.1, 150.2, 159.7, 177.1, 182.8 (2C═O) ppm.

2-Amino-3-cyano-4-(2,4-dimethoxyphenyl)-5,10-dioxo-5,10-dihydro-4*H*-benzo[*g*]chromene (7h): (KBr, cm-1): 3450, 3337, 2194,1661, 1590 cm^{-1}.; ^1H NMR (400 MHz, DMSO-d_6) δ 3.72(s, 3H, OMe), 3.77 (s, 3H, OMe), 4.83 (s, 1H, CH), 6.43–7.11(m, 3H, Ar), 7.17–8.06 (m, 6H, Ar and NH_2) ppm; ^{13}CNMR (100 MHz, DMSO-d_6) δ 31.2, 55.6, 56.2, 57.2, 105.6, 119.2, 120.1, 122.4, 124.2, 126.2, 126.5, 130.3, 131.5, 134.5135.0, 149.7, 158.3, 159.7 (2C), 177.5, 183.0 (2C═O) ppm.

7-Amino-5-(4-bromophenyl)-1,2,3,5-tetrahydro-1,3-dioxo-2-phenylpyrazolo[1,2-*a*] [1,2,4]triazole-6-carbonitrile (8d): IR (KBr, cm^{-1}): 3400, 3250, 2255, 1660; ^1H NMR (400 MHz, (DMSO-d_6) δ 5.60 (s, 1H, CH), 7.45 (d, J = 8 Hz, 2H, Ar), 7.46–7.50 (m, 5H, Ar), 7.66 (d, J = 8 Hz, 2H, Ar), 7.89 (br, 2H, NH_2) ppm.

7-Amino-5-(4-nitrophenyl)-1,2,3,5-tetrahydro-1,3-dioxo-2-phenylpyrazolo[1,2-*a*] [1,2,4]triazole-6-carbonitrile (8e): IR (KBr, cm^{-1}): 3427, 317 350, 2209, 1663; ^1H NMR (400 MHz, (DMSO-d_6) δ 6.44 (s, 1H, CH), 7.53 (m, 5H, Ar), 7.79 (m, 4H, Ar), 8.33 (br, 2H, NH_2) ppm; ^{13}C NMR (100 MHz,DMSO-d_6) δ 60.52, 61.42, 111.9, 116.86, 124.63, 127.38 (2CH),128.81 (2CH), 129.25, 129.54(2CH), 131.43, 146.79, 148.09, 150.76, 151.10, 154.45 ppm.

7-Amino-5-(3-methoxyphenyl)-1,2,3,5-tetrahydro-1,3-dioxo-2-phenylpyrazolo[1,2-*a*] [1,2,4]triazole-6-carbonitrile (8i): IR (KBr, cm^{-1}): 3400, 3220, 2210, 1044; ^1H NMR (300 MHz, (DMSO-d_6) δ 3.80 (s, 3H, OCH_3), 5.79 (s, 1H, CH), 6.96–7.57 (m, 9H, Ar), 7.63 (br, 2H, NH_2) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 55.66, 61.90, 64.40, 113.08, 114.40, 117.03, 119.48, 127.33, 129.15, 129.49, 130.50, 131.51, 141.17, 150.30, 150.37, 150.45, 151.06, 154.05,60.02 ppm.

7-Amino-6-cyano-1,2,3,5-tetrahydro-5-(4-cyanophenyl)-1,3-dioxo-2-phenylpyrazolo[1,2-a] [1,2,4]triazole (8j) IR (KBr, cm^{-1}): 3758, 3374, 3193, 2807, 2135, 2190, 1778, 1400,1350, ^1H NMR (400 MHz, DMSO-d_6) δ 5.93 (s, 1H, CH), 7.51 (m, 5H, Ar), 7.73 (t, J = 7.7 Hz, 4H, Ar), 7.94 (d, J = 7.9 Hz, 2H, NH_2) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 61.32, 63.81, 111.90, 116.93, 119.11, 127.42 (2CH),128.53 (2CH), 129.34, 129.52 (2CH), 131.43, 133.41, 144.91150.73, 151.11, 154.20 ppm.

CONCLUSIONS

In summary, piperidine was used as an efficient base catalyst for the synthesis of chromene heterocycles and pyrazolotriazoles with antibacterial properties. All products were obtained just with simple filtration, and there was no need for recrystallization or column chromatography.

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Supporting information

Additional supporting information is available in the online version of this article.

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