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Synthesis of Pyrazolopyranopyrimidine and Dihydropyrano[2,3-c]pyrazole Derivatives using Vitamin D as an Efficient Catalyst under Green Condition

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Abstract

An efficient, rapid, and eco-friendly protocol for one-pot, four-component preparation of dihydropyrano[2,3-*c*]pyrazole and pyrazolopyranopyrimidine derivatives has been developed using vitamin D as an efficient catalyst. This method involves several advantages such as low-cost and non-toxic catalysts, high yields of products, simple workup, no hazardous solvent, and no need for column chromatography.

Keywords: Dihydropyrano[2,3-*c*] pyrazoles, Pyrazolopyranopyrimidines, Vitamin D, Green conditions.

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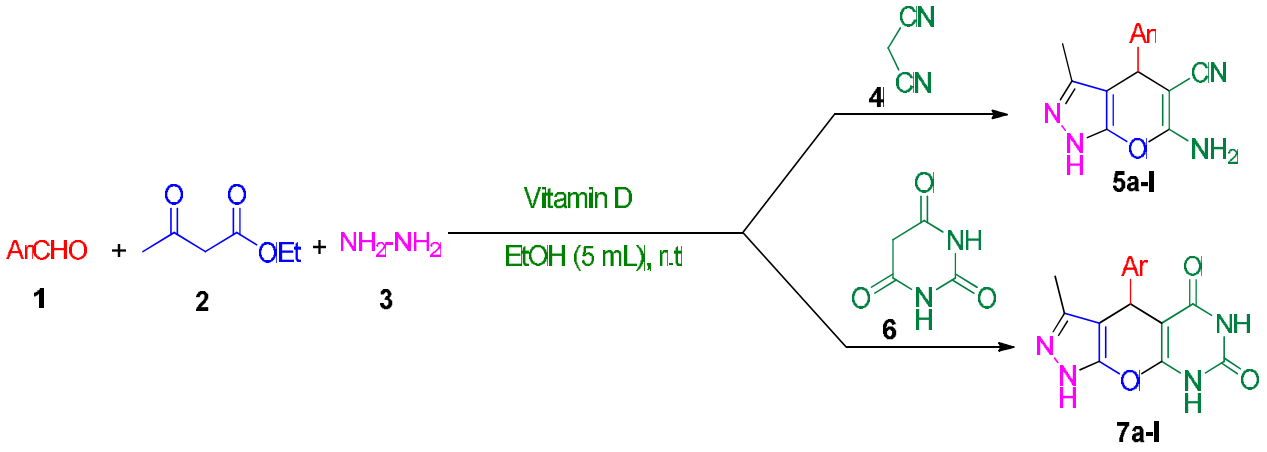
Introduction

Multicomponent reactions (MCRs) are one of the most successful methods that use a simple process for increasing structural diversity and molecular complexity of the desired product, especially in the manufacture of diverse drug-like heterocyclic compounds[1,2]. As an evolving process for the preparation of pharmaceutical material, MCRs have rapidly expanded over the past few decades for a fundamental change in the synthesis of natural products [3-5].

Heterocyclic rings have been considered a privileged architecture that is frequently utilized in the synthesis of bioactive natural products, functional compounds, and marketed pharmaceuticals[6,7]. Amongst the heterocyclic compounds, pyranopyrazole and pyrazolopyranopyrimidinederivatives have attracted increasing attention as valuable structural scaffolds in many biologically and therapeutically active molecules. For example, pyranopyrazole and pyrazolopyranopyrimidine derivatives have been reported to possess anticancer [8], antibacterial [9], anti-inflammatory [10], analgesic [11], antitubercular, antimicrobial [12], antibronchitic [13], and hepatoprotective activities[14].

Metal-free organic molecules as safe organic compounds originating from biological compounds afford an irrefutable benefit considering the viewpoint of both the principles of green chemistry and the economic issue, plus properties including robust, cheap, available, nontoxic, insensitivity to moisture and oxygen, attractive for the preparation of compound that does not tolerate metal contamination (pharmaceutical products), and effective in complex reactions [15,16]. Vitamin D is one of the essential fat-soluble vitamins in our body, which helps the growth and strength of bones by controlling the balance and increasing the absorption of calcium, phosphorus, and magnesium. It is often found to be more related to osteoporosis, parathyroid hormone imbalance, and weakened immune systems, leading to a lack of attention to other very effective aspects of the vitamin [17-19].

In this research work, in continuation of our endeavors toward the development of efficient and eco-friendly methods [20–26], herein, we report rapid and convenient access to the synthesis of dihydropyrano[2,3-c]pyrazole and pyrazolopyranopyrimidine derivatives in the presence of vitamin D as a novel, heterogeneous, and green catalyst. The results indicated that vitamin D can promote the reaction to afford the desired products in high yields. (Scheme 1).



Scheme 1. Synthesis of dihydropyrano[2,3-c]pyrazoles and pyrazolopyranopyrimidines using vitamin D.

Experimental

General

The Melting points of all pure compounds were obtained by an Electrothermal 9100 apparatus. IR spectra were measured by an FT-IR-JASCO-460 plus spectrometer. Known products were identified by a Bruker DRX-300 Avance instrument in DMSO at 300 and 75MHz (^{1}HNMR and ^{13}C NMR spectra). All chemicals were purchased from Merck (Darmstadt, Germany) and Fluka (Buchs, Switzerl) companies and used without further purification.

General procedure for the four-component synthesis of dihydropyrano[2,3-c]pyrazole derivatives

Initially, 3-methyl-2-pyrazoline-5-one was precipitated as a white solid using the reaction between hydrazine hydrate (1.25 mmol) and ethyl acetoacetate (1.0 mmol) at room temperature. Then, aromatic aldehydes (1.0 mmol), malononitrile (1.0 mmol), vitamin D (0.03g), and ethanol (5mL) were added to the reaction mixture and stirred for a suitable time at room temperature, and the progress of the reaction was monitored through TLC (thin layer chromatography). After completion of the reaction, the catalyst was separated with filtration. The reaction mixture was diluted in hot ethanol. Then, the obtained solution was cooled to 25 °C to obtain the pure product.

General procedure for the four-component synthesis of pyrazolopyranopyrimidine derivatives

Initially, 3-methyl-2-pyrazoline-5-one was precipitated as a white solid using the reaction between hydrazine hydrate (1.25 mmol) and ethyl acetoacetate (1.0 mmol) at room temperature. Then, barbituric acid (1.0 mmol), aldehydes (1.0 mmol), vitamin D (0.03 g), and ethanol (5 mL) were added to the reaction mixture and stirred for the appropriate time at room temperature. The progress of the reaction was monitored through TLC (thin-layer chromatography). After completion of the

reaction, the catalyst was separated with filtration. The reaction mixture was diluted in hot ethanol. Then, the obtained solution was cooled to 25 °C to obtain the pure product.

Characterization data of compounds.

6-Amino-2,4-dihydro-3-methyl-4-phenylpyrano[2,3-c]pyrazole-5-carbonitrile **(5a)**

IR (KBr): 3372, 3311, 2193, 1649, 1596, 1489. ^{1}HNMR (300MHz, DMSO-d_6): 1.81 (s, 3H, CH_3), 4.62 (s, 1H, CH), 6.91 (s, 2H, NH_2), 7.19-7.33 (m, 5H, Ar), 12.14 (s, 1H, NH).^{13}C NMR (75MHz, DMSO-d6): 161.3, 155.2, 144.9, 136.1, 128.9, 127.9, 127.2, 121.3, 98.1, 57.7, 36.7, 10.2.

6-Amino-4-(3-hydroxyphenyl)-3-methyl-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile **(5b)**

IR (KBr): 3411, 3360, 3165, 2177, 1648, 1593, 1485, 877. ^{1}HNMR (300MHz, DMSO-d_6): 1.85 (s, 3H, CH_3), 4.51 (s, 1H, CH), 6.57-6.64 (m, 2H, Ar), 6.88 (s, 1H, Ar) 7.09-7.14 (m, 1H, Ar), 9.34 (s, 1H), 12.11 (s, 1H, NH). ^{13}C NMR (75MHz, DMSO-d6): 161.3, 157.9, 155.2, 146.4, 136.0, 129.7, 121.3, 118.6, 114.6, 114.3, 98.1, 57.7, 36.6, 10.2.

6-Amino-4-(4-methylphenyl)-3-methyl-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile **(5c)**

IR (KBr): 3410, 3377, 2193, 1647, 1599, 1487. ^{1}HNMR (300MHz, DMSO-d_6): 1.81 (s, 3H, CH_3), 4.57 (s, 1H, CH), 6.86 (s, 2H, NH_2), 7.07 (d, 2H, Ar), 7.13 (d, 2H, Ar), 12.10 (s, 1H, NH). ^{13}C NMR (75MHz, DMSO-d6): 161.2, 155.2, 141.9, 136.2, 136.0, 129.4, 127.8, 121.2, 98.2, 57.9, 36.3, 21.0, 10.2.

6-Amino-4-(4-chlorophenyl)-3-methyl-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile **(5d)**

IR (KBr): 3409, 3368, 2188, 1645, 1400. ^{1}HNMR (300MHz, DMSO-d_6): 1.82 (s, 3H, CH_3), 4.66 (s, 1H, CH), 6.96 (s, 2H, NH_2), 7.22 (d, 2H, Ar), 7.39 (d, 2H, Ar), 12.17 (s, 1H, NH). ^{13}C NMR (75 MHz, DMSO-d6): 161.4, 155.2, 143.9, 136.1, 131.7, 129.8, 128.9, 121.1, 97.6, 57.3, 36.0, 10.2.

6-Amino-4-(4-methoxyphenyl)-3-methyl-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile **(5e)**

IR (KBr): 3484, 3254, 2192, 1643, 1598, 1492. ^{1}HNMR (300MHz, DMSO-d_6): 1.81 (s, 3H, CH_3), 3.74 (s, 3H, OCH_3), 4.57 (s, 1H, CH), 6.84 (d, 2H, Ar), 6.88 (s, 2H, NH_2), 6. 90 (d, 2H, Ar), 12.10 (s, 1H, NH). ^{13}C NMR (75MHz, DMSO-d6): 161.1, 158.4, 155.2, 136.9, 136.0, 128.9, 121.3, 114.2, 98.3, 58.1, 55.4, 35.9, 10.2

6-Amino-4-(2-chlorophenyl) -3-methyl-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile **(5f)**

IR (KBr): 3390, 3353, 2190, 1654, 1595, 1489. ^{1}HNMR (300MHz, DMSO-d_6): 1.79 (s, 3H, CH_3), 5.11 (s, 1H, CH), 6.99 (s, 2H, NH_2), 7.23-7.28 (m, 2H, Ar), 7.41 (d, 1H, Ar), 12.16 (s, 1H, NH). ^{13}C NMR (75MHz, DMSO-d6): 161.8, 155.4, 141.4, 135.9, 132.5, 131.1, 129.9, 129.0, 128.1, 120.9, 97.3, 56.3, 33.9, 10.0.

6-Amino-4-(4-(dimethylamino)phenyl)-3-methyl-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile **(5g)**

IR (KBr): 3385, 3304, 3172, 2189, 1644, 1598, 1488. ^{1}HNMR (300MHz, DMSO-d_6): 1.82 (s, 3H, CH_3), 2.87 (s, 6H), 4.49 (s, 1H, CH), 6.68 (d, 2H), 6.79 (s, br, 2H), 7.01 (d, 2H), 12.07 (s, 1H, NH). ^{13}C NMR (75MHz, DMSO-d6): 161.0, 155.3, 149.7, 136.0, 132.5, 128.4, 121.4, 112.7, 98.6, 58.5, 35.9, 10.2.

3-Methyl-4-phenyl-1,4-dihydropyrazolo[4',3':5,6]pyrano[2,3-d]pyrimidine-5,7(6H,8H)-dione **(7a)**

IR (KBr): 3420, 2900, 2700, 1679, 1632, 1588, 1542, 1472, 1356, 1308. ^{1}HNMR (300MHz, DMSO-d_6): 2.26 (s, 3H, CH_3), 5.47 (s, 1H, CH), 7.08-7.025 (m, 5H, Ar), 10.25 (s, 1H, NH). ^{13}C NMR (75MHz, DMSO-d6): 164.8, 160.9, 151.1, 144.1, 142.9, 128.3, 127.1, 125.8, 106.3, 91.7, 10.4.

3-Methyl-4-(2-chlorophenyl)-1,4-dihydropyrazolo[4',3':5,6]pyrano[2,3-d]pyrimidine-5,7(6H, 8H)-dione **(7b)**

IR (KBr): 3403, 3066, 2971, 1717, 1604, 1538, 1469, 1397. ^{1}HNMR (300MHz, DMSO-d_6): 2.25 (s, 3H, CH_3), 5.57 (s, 1H, CH), 7.14 (t, 1H, Ar), 7.21(t, 1H, Ar), 7.30 (d, 1H, Ar), 7.51 (d, 1H, Ar), 10.31(s, 1H, NH). ^{13}C NMR (75MHz, DMSO-d6): 165.1, 161.0, 151.2, 143.7, 140.1, 133.0, 130.6, 129.9, 128.0, 126.6, 105.3, 91.0, 10.7.

3-Methyl-4-(4-chlorophenyl)-1,4-dihydropyrazolo[4',3':5,6]pyrano[2,3-d]pyrimidine-5,7(6H, 8H)-dione **(7c)**

IR (KBr): 3436, 3136, 1681, 1625, 1589, 1488, 796. ^{1}HNMR (300MHz, DMSO-d_6): 2.25 (s, 3H, CH_3), 5.43 (s, 1H, CH), 7.08 (d, 2H, Ar), 7.28 (d, 2H, Ar), 10.23 (s, 1H, NH). ^{13}C NMR (75MHz, DMSO-d6): 161.1, 151.1, 144.0, 139.9, 134.6, 128.8, 127.0, 106.5, 91.7, 30.6, 20.9, 10.4

3-Methyl-4-(4-nitrophenyl)-1,4-dihydropyrazolo[4',3':5,6]pyrano[2,3-d]pyrimidine-5,7(6H, 8H)-dione **(7d)**

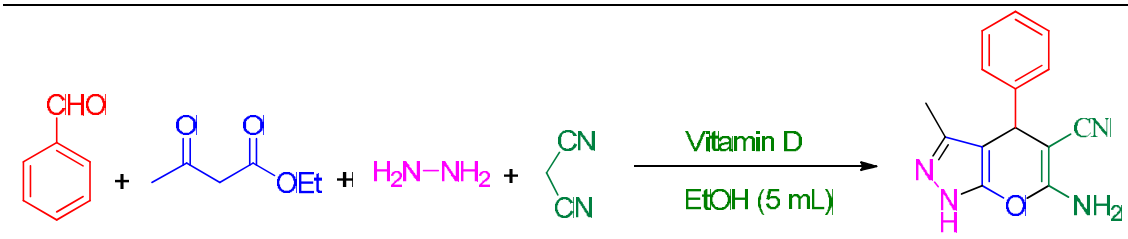
IR (KBr): 3454, 3133, 3038, 2905, 1685, 1625, 1595, 1516, 1488, 1366, 1350, 1275, 841, 549. ^{1}HNMR (300MHz, DMSO-d_6): 2.28 (s, 3H, CH_3), 5.55 (s, 1H, CH), 7.34 (d, 2H, Ar), 8.12 (d, 2H, Ar), 10.29 (s, 1H, NH). ^{13}C NMR (75MHz, DMSO-d6): 165.2, 160.4, 151.7, 151.1, 146.0, 144.1, 128.4, 123.6, 105.3, 91.5, 31.6, 10.4.

Results and discussion

Optimization of the reaction conditions

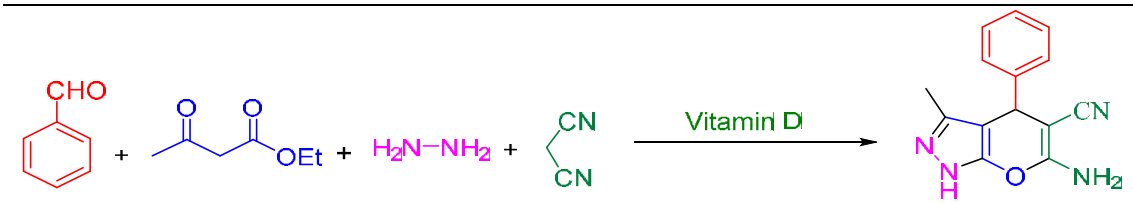
In the study, describe two practical protocols using vitamin D as an efficient catalyst.In the first protocol, the optimization of the reaction conditions in the synthesis of dihydro-pyrano[2,3-c]pyrazole, the reaction of benzaldehyde (1.0mmol), malononitrile (1.0 mmol), ethyl acetoacetate (1.0 mmol) and hydrazine hydrate (1.25 mmol) was chosen as a model. Initially, the effect of the amount of catalyst and different temperatures on the model reaction was evaluated. The results are summarized in Table 1. Observably, when the model reaction was performed in the percent of 0.03 g of catalyst at room temperature, the best yield reaction was achieved. In the absence of any catalyst, even after 24 hours of stirring of the reaction mixture, no product was observed.

Table 1. Optimization of conditions.



Entry	Catalyst (g)	Temperature (°C)	Time (min)	Yield (%)
1	0.01	rt	80	65
2	0.02	rt	60	74
3	**0.03**	**rt**	**45**	**85**
5	0.04	rt	45	85
6	0.05	rt	45	85
7	0.03	40	35	85
8	0.03	50	20	80
9	0.03	60	15	72

Table 2.The effect of solvent for the synthesis of dihydro-pyrano[2,3-c]pyrazoles.

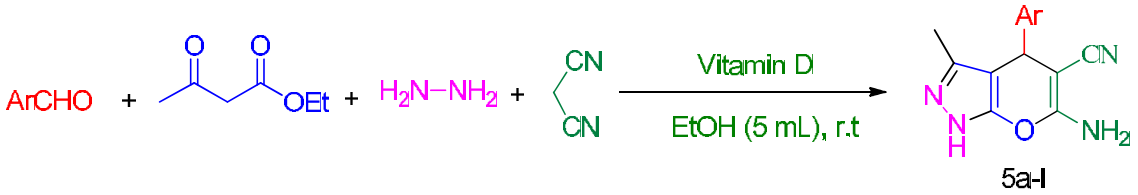


Entry	Solvent	Temperature (°C)	Time (min)	Yield (%)
1	H_2O	rt	65	70
2	**EtOH**	**rt**	**45**	**85**
3	H_2O:EtOH(1:1)	rt	55	77
4	H_2O:EtOH (2:1)	rt	45	74
5	H_2O:EtOH (1:2)	rt	55	82
6	CH_2Cl_2	rt	80	72
7	CH_3CN	rt	75	77

Then, to screen the effect of solvent, the model reaction was performed in H_2O, EtOH, a mixture of H_2O: EtOH, CH_2Cl_2, and CH_3CN. The results are summarized in Table 2. The results suggest that EtOH better solvent for the reaction (Table 2, entry 2). After the evaluation of the optimal condition, the synthesis of dihydropyrano[2,3-c]pyrazole derivatives was investigated using various aromatic aldehydes to evaluate the catalytic activity of vitamin D (Table 3).

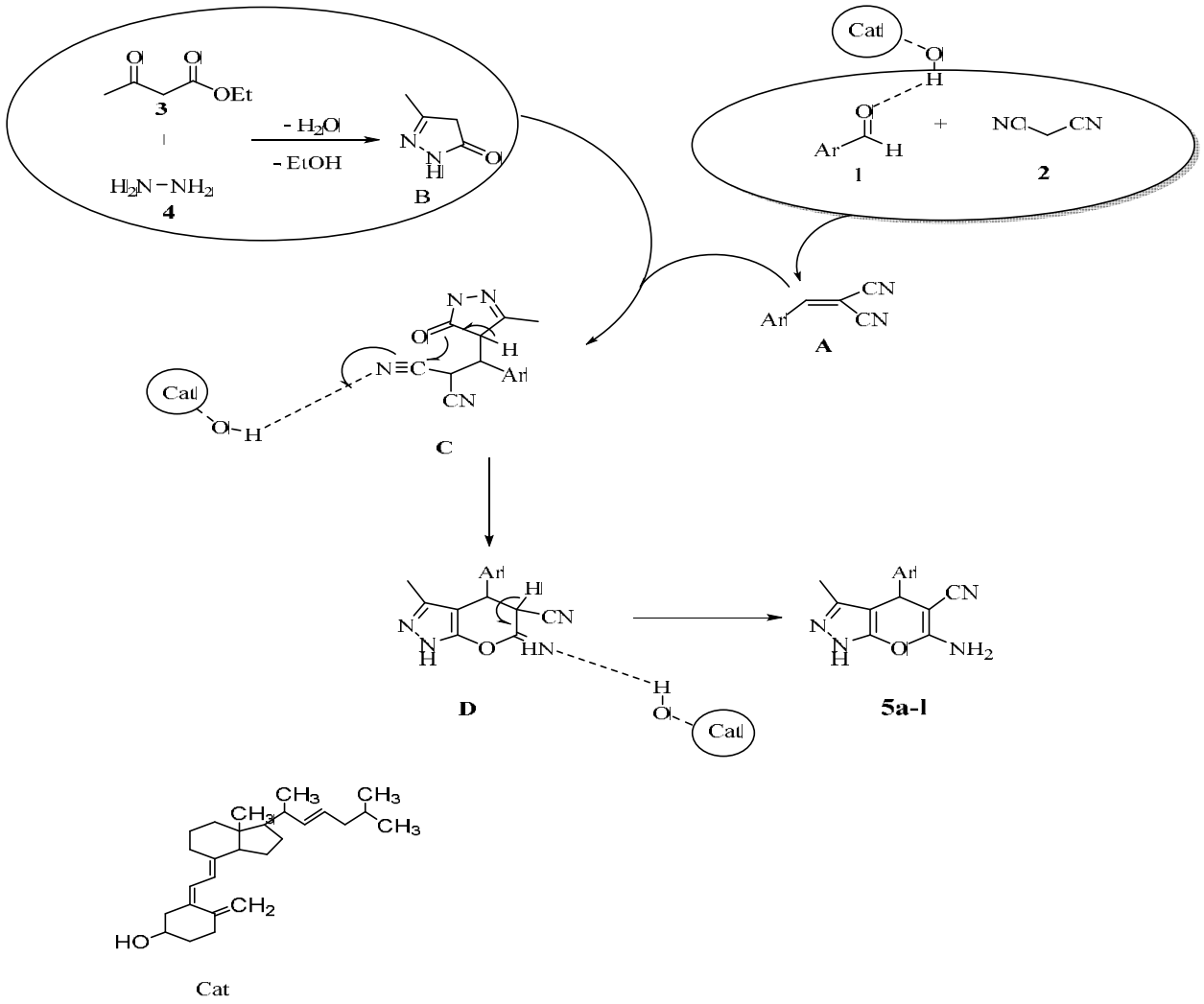
A plausible mechanism for the formation of dihydropyrano[2,3-*c*]pyrazoles catalyzed by vitamin D is shown in Scheme 3. At first, vitamin D deprotonates the carbonyl group of aldehydes (1) to facilitate the Knoevenagel condensation between aldehyde (**1**) and malononitrile (**2**) and generates intermediate (**A**). In the second step, the Michael addition of pyrazolone (**B**) to intermediate (**A**) generates the intermediate (**C**) and subsequent tautomerization produces the corresponding dihydropyrano[2,3-*c*]pyrazoles**(5a-l)**.

Table 3. Synthesis of dihydropyrano[2,3-c]pyrazoles.



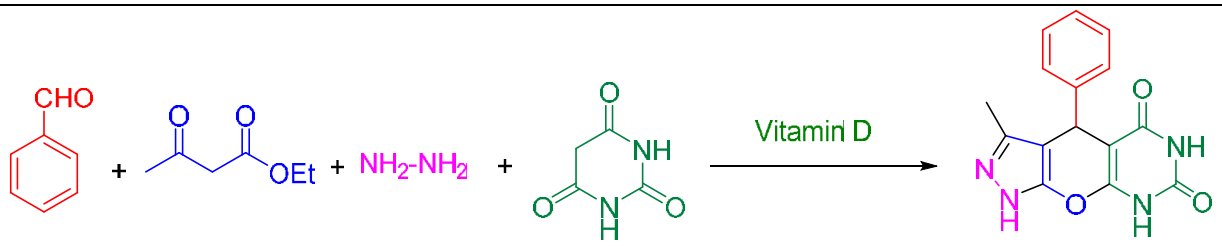
Entry	Ar	Product	Time (min)	Yield (%)	Mp (°C)[Ref]
1	C_6H_5	**5a**	45	85	257-259 (264-266)[30]
2	3-OH C_6H_4	**5b**	55	78	260-262 (262-264)[34]
3	4-Me C_6H_4	**5c**	65	76	204-206 (206-208)[28]
4	4-Cl C_6H_4	**5d**	35	85	235-237(234-236)[34]
5	4-OM C_6H_4e	**5e**	60	75	262-264 (262-264)[33]
6	2-Cl C_6H_4	**5f**	55	81	255-257 (261-263)[34]
7	4-N$(CH_3)_2$ C_6H_4	**5g**	40	88	224-226 (227-229)[34]
8	2-NO_2 C_6H_4	**5h**	50	80	225-227 (227-228)[32]
9	3-NO_2 C_6H_4	**5i**	50	80	210-212 (208-210)[29]
10	4-NO_2 C_6H_4	**5j**	35	90	244-246 (250-252)[28]
11	4-Br C_6H_4	**5k**	40	85	182-184 (185-187)[31]
12	4-F C_6H_4	**5l**	40	83	240-242 (244-245)[27]

To demonstrate the merit of the usage of vitamin D catalyst in organic synthesis, we planned to use it as the catalyst in the synthesis of pyrazolopyranopyrimidines (Table 6). Therefore, for evaluation of the optimum conditions, the reaction of benzaldehyde(1.0 mmol), barbituric acid(1.0 mmol), ethyl acetoacetate(1.0 mmol), and hydrazine hydrate(1.25 mmol) was picked up as a model reaction, and the effect of the involved parameters such as temperature, catalyst amount, and the solvent was checked. Based on the obtained data summarized in Table 4,5. It is clarified that the best condition was found in vitamin D (0.03g) in EtOH(5 mL) at room temperature (Table 4, entry 2).



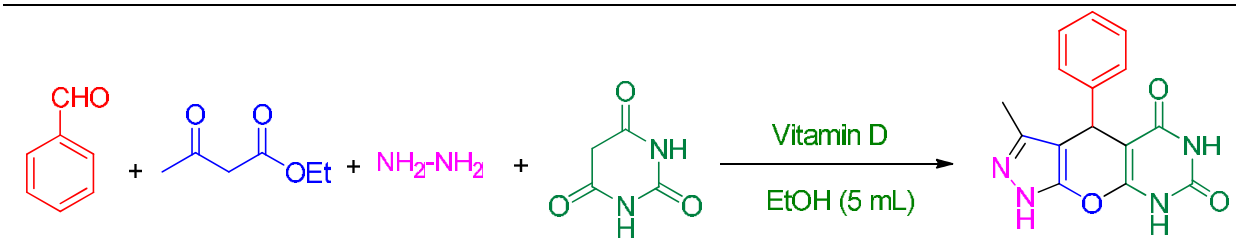
Scheme3. Plausible reaction mechanism for the synthesis of dihydropyrano[2,3-c]pyrazoles catalyzed by vitamin D.

Table 4. Optimization of conditions.



Entry	Solvent	Temperature (°C)	Time (min)	Yield (%)
1	H_2O	rt	80	81
2	**EtOH**	**rt**	**55**	**90**
3	H_2O:EtOH(1:1)	rt	60	85
4	H_2O:EtOH(2:1)	rt	60	**81**
5	H_2O:EtOH(1:2)	rt	55	88
6	CH_2Cl_2	rt	75	74
7	CH_3CN	rt	75	71

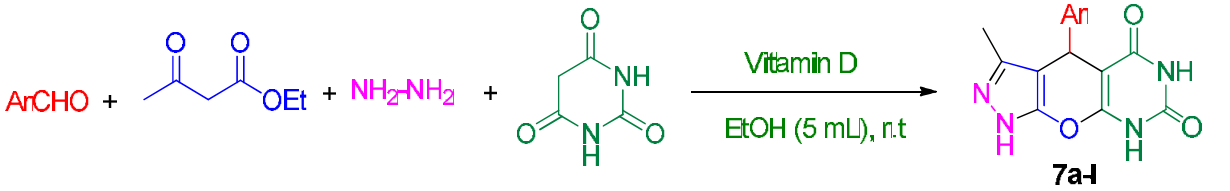
Table 5. Optimization of conditions.



Entry	Catalyst (g)	Temperature (°C)	Time (min)	Yield (%)
1	0.01	rt	85	72
2	0.02	rt	78	82
3	**0.03**	**rt**	**55**	**90**
4	0.04	rt	55	90
5	0.05	rt	55	90
7	0.03	40	40	82
8	0.03	50	30	78
9	0.03	60	20	72

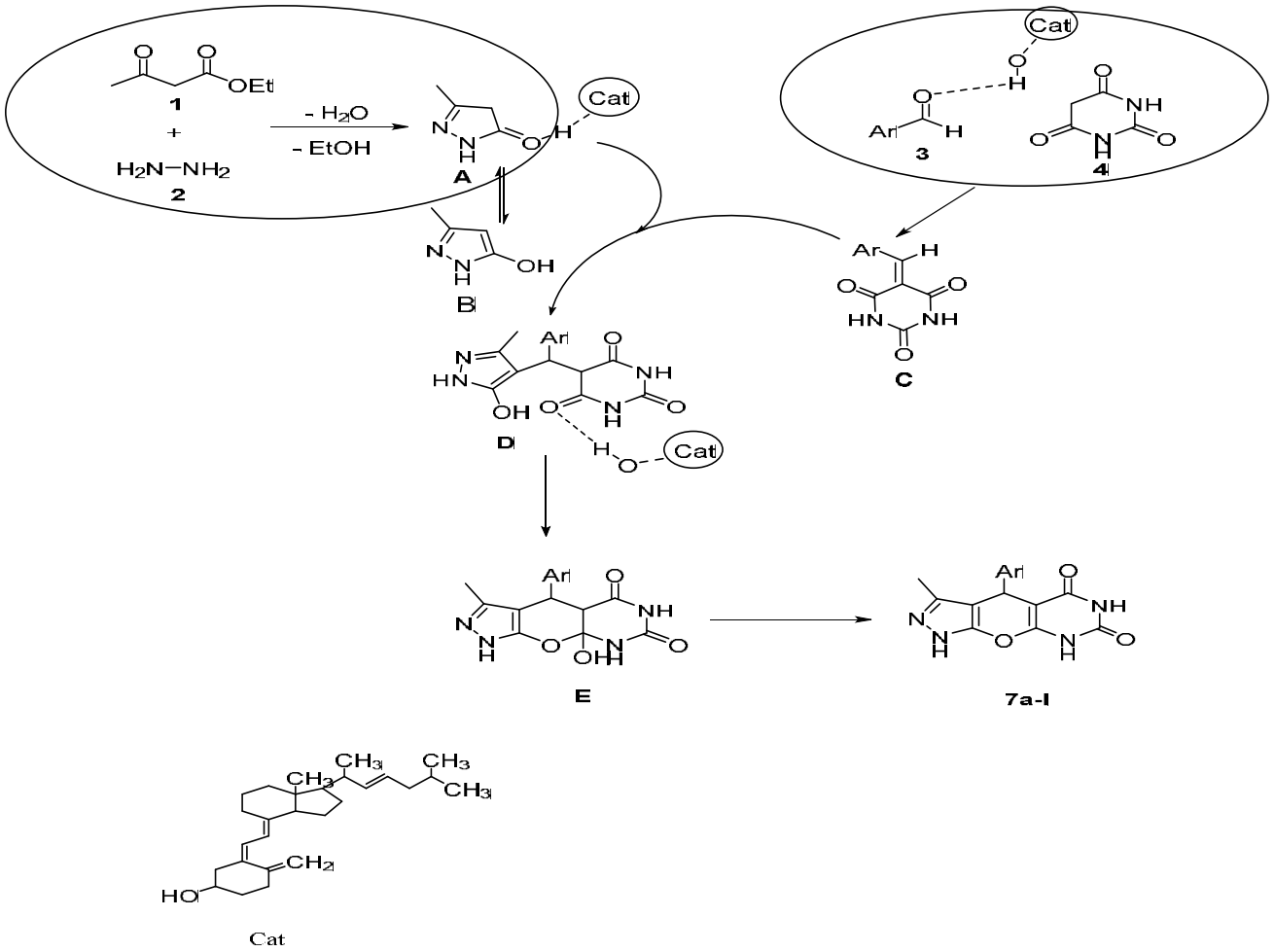
After the evaluation of the optimal condition, the synthesis of pyrazolopyranopyrimidine derivatives was investigated using various aromatic aldehydes to evaluate the catalytic vitamin D (Table 6).

Table 6. Synthesis of pyrazolopyranopyrimidines.



Entry	Ar	Product	Time (min)	Yield (%)	Mp (°C)[Ref]
1	C_6H_5	**7a**	50	90	218-220 (218-219)[36]
2	2-Cl C_6H_4	**7b**	60	88	228-230 (223-225)[36]
3	4-Cl C_6H_4	**7c**	55	92	218-220 (222-223)[36]
4	4-NO_2 C_6H_4	**7d**	45	94	230-232 (233-234)[36]
5	2-NO_2 C_6H_4	**7e**	55	86	208-210 (208-209)[36]
6	3-NO_2 C_6H_4	**7f**	55	88	264-266 (265-267)[36]
7	4-Me C_6H_4	**7g**	70	85	205-206 (200-201)[36]
8	4-OMe C_6H_4	**7h**	70	85	224-226 (225-227)[35]
9	4-Br C_6H_4	**7i**	55	90	210-212 (211-212)[36]
10	4-F C_6H_4	**7j**	50	88	238-240 (237-238)[36]
11	3-OH C_6H_4	**7k**	75	83	272-274 (279-280)[37]
12	4-$N(CH_3)_2$ C_6H_4	**7l**	50	90	270-272 (276-277)[37]

A plausible mechanism for the formation of pyrazolopyranopyrimidines catalyzed by vitamin D is shown in Scheme 4. At first, vitamin D deprotonates the carbonyl group of aldehyde (**1**) to facilitate the Knoevenagel condensation between aldehyde (**1**) and barbituric acid (**4**) and generates intermediate (**C**). In the second step, the Michael addition of pyrazolone (**B**) to intermediate (**C**) results in the intermediate (**D**) and subsequent tautomerization produces the corresponding pyrazolopyranopyrimidines **(7a-l)**.



Scheme 4. plausible reaction mechanism for the synthesis of pyrazolopyranopyrimidines catalyzed by vitamin D.

In Table 7, the merit of our catalytic system for the synthesis of dihydropyrano[2,3-*c*]pyrazoles and pyrazolopyranopyrimidines has been studied in the comparison with some of the selected studies in the literature. As shown in the obtained results, the efficiency of vitamin D is equal or even higher compared to other selected studies.

Table 7. Screening of different catalytic systems for the synthesis of dihydropyrano[2,3-*c*]pyrazoles and pyrazolopyranopyrimidinesunder different conditions.

Entry	Product	Catalyst	Conditions	Time(min)	Yield(%)	Ref.
1	**5a**	MorT (10 mol %)	H_2O/EtOH, reflux	540	92	[41]
2	**5a**	CTACl (20 mol %)	H_2O, 90 °C	240	88	[31]
3	**5a**	$Ba(OH)_2$ (10 mol %)	H_2O, reflux	90	93	[40]
4	**5a**	Vitamin D	EtOH, rt	45	85	This Work
5	**7a**	OMN/CNTs	H_2O/EtOH, reflux	70	94	[43]
6	**7a**	TiO_2 NWs	H_2O/EtOH, reflux	60	95	[39]
7	**7a**	HPA-F-HNTs	H_2O, reflux	35	96	[38]
8	**7a**	Saccharose (20 mol %)	Solvent-Free, 100 °C	10	75	[42]
9	**7a**	Vitamin D	EtOH, rt	50	90	This Work

Conclusion

In summary, in the present work, we have successfully developed a one-pot four-component for the synthesis ofdihydropyrano[2,3-c]pyrazole and pyrazolopyranopyrimidine derivatives via a reaction between aromatic aldehydes, malononitrile or barbituric acid, ethyl acetoacetate, and hydrazine hydrate at room temperature and vitamin D as an eco-friendly and efficient catalyst. These synthetic strategies showed some advantages such as simple purification and workup, mild reaction conditions**,** cheap and available starting materials, green solvents, and excellent yields.

Acknowledgments

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References

[1] H. Bienayme, C. Hulme, G. Oddon, P. Schmitt, *Chem. Eur. J.,*6, 3321(2000).

[2] T. ZarganesTzitzkas, C.G. Neochoritis, A. Domling, *Acs Med. Chem. Let*.,10, 389 (2019).

[3] S. Balalaie, L. Baoosi, F. Tahoori, F. Rominger, H.R. Bijanzadeh, *Tetrahedron.,*69, 738 (2013).

[4] M.N. Elinson, V.M. Merkulova, A.I. Ilovaiskya, F. Barba, B. Batanero, *Electrochim. Acta.,* 56, 8219 (2011).

[5] S. Verma,S.L. Jain, *Terahedron Lett*., 53, 6055 (2012).

[6] I. Yavari, L. Moradi, *Tetrahedron Lett.*,47, 1627 (2006).

[7] D. Azarifar, D. Sheikh, *Synth. Commun*.,43, 2517(2013).

[8] A.B. Atar, J.T. Kim, K.T. Lim, Y.T. Jeong, *Synth. Commun*., 44, 2679 (2014).

[9] M.A. Zolfigol, S. Baghery, A.R. MoosaviZare, S.M. Vahdat*, RSC Adv*., 5, 32933 (2015).

[10]M.E.A. Zaki, H.A. Soliman, O.A. Hiekal, A.E.Z. Rashad, *Naturforsch. C.,*61, 1 (2006).

[11] S.C. Kuo, L.J. Huang, H.Nakamura, *J. Med. Chem*., 27, 539(1984).

[12] N.R. Komdar, D.D. Haveliwala, P.T. Mistry, S.K. Patel, *Eur. J. Med. Chem*., 45, 5056 (2010).

[13] M.C. Bagley, D.D. Hughes, M.C. Lubinu, E.A. Merrit, P.H. Taylor, N.C.O. Tomkinson, *QSAR Comb. Sci*., 23, 859 (2004).

[14]S.B. Guo, S.X. Wang, J.T. Li, *Commun*.,37**,** 2111 (2007).

[15] J. H. Clark, *Pure Appl. Chem.*, 73,103, (2001).

[16] D.W.C. MacMillan, *Nature*., 455, 304 (2008).

[17] P. Lips, *Prog. Biophys. Mol. Biol*., 92, 4, (2006).

[18] A. Hossein-nezhad, M.F. Holick, *Mayo Clin. Proc*.,88, 720 (2013).

[19] D. Bikle, *J. Clin. Endocrinol. Metab*., 94, 26 (2009).

[20] A. Oudi, N. Hazeri, M. Fatahpour, *J. Appl. Chem. Res*., 13, 36 (2019).

[21] M. Narouei, N. Hazeri, E. Molashahi, S. Zhaleh, M. Fatahpour, *J. Appl. Chem. Res.*, 11, 38 (2017).

[22] N. Hazeri, M. Lashkari, M. Fatahpour, M. Sheikhveisi, *Bull. Korean. Chem. Soc*.,41, 786 (2020).

[23]M. Roozifar. N. Hazeri. H. FaroughiNiya. *J. Heterocycl. Chem*.,58, 1117, (2021).

[24] B. Adrom. N. Hazeri. M. T. Maghsoodlou. M. Lashkari, M. Fatahpour, *Maced. J. Chem. Chem. Eng*., 36, 223 (2017).

[25] M. Kangani, M.T. Maghsoodlou, N. Hazeri*, Chin. Chem. Lett*., 27, 66, (2016).

[26] M. Kangani, N. Hazeri, M.T Maghsoodlou,K. Khandan-Barani, M. Kheyrollahi, F. Nezhadshahrokhabadi, *J. Iran. Chem. Soc*.,12, 47 (2015).

[27]A.B. Atar, J.T. Kim, K.T. Lim, Y.T. Jeong.*Synth. Commun*., 44, 2679 (2014).

[28] K. Ablajan, W. Liju, A. Tuoheti, Y. Kelimu, *Lett. Org. Chem*., 9, 639 (2012).

[29] S.B. Guo, S.X. Wang, J.T. Li, *Synth. Commun*., 37, 2111 (2007).

[30] A.R. MoosaviZare, M.A. Zolfigol, E. Noroozizadeh, M. Tavasoli, V. Khakyzadeh, A. Zare, *New J. Chem*.,37, 4089 (2013).

[31] W. Mingshu, F. Qinqin, W. Dehui, M. Jinya,*Synth. Commun*., 43, 1721 (2013).

[32] H. FaroughiNiya, N. Hazeri, M.T. Maghsoodlou, *J. Org. Chem.,* 11, 5472 (2020).

[33] A.R. MoosaviZare, M.A. Zolfigol, E. Noroozizadeh, M. Tavasoli, V. Khakizadeh, A. Zare, *New J. Chem*., 37, 4089(2013).

[34] M.A. Zolfigol, M. Tavasoli, A.R. Moosavi-Zare, P. Moosavi, H.G. Kruger, M. Shiri, V. Khakyzadeh, *RSC Adv.*, 3, 25681(2013).

[35]S. Dastkhoon, Z. Tavakoli, S. Khodabakhshi, *New J. Chem*., 39, 7268 (2015).

[36] X.T.Li, A.D.Zhao, L.P.Mo, Z.H.Zhang, *RSC Adv*.,4, 51580 (2014).

[37] M.R. Tipale, L.D. Khillare, A.R.Deshmukh, M.R. Bhosle,*J.Heterocycl. Chem*.,55, 716 (2018).

[38] S. Sadjadi, M.M. Heravi, M. Daraie, *Res. Chem. Intermed*., 43, 2201 (2017).

[39] S. Dastkhoon, Z. Tavakoli, S. Khodabakhshi, M. Baghernejad, M. Khaleghi Abbasabadi, *New J. Chem.***,** 39, 7268 (2015).

[40] S.H.S.Azzam, M.A. Pasha, *Tetrahedron Lett*.,53, 6834 (2012).

[41] C.F.Zhou, J.J. Li, W.K.Su,*Chin. Chem*. *Lett*., 27, 1686 (2016)**.**

[42] M. Kangani, N. Hazeri, M.T. Maghsoodlou, K. KhandanBarani, M. Kheyrollahi, F. Nezhadshahrokhabadi, *J. Iran. Chem. Soc*., 12, 47 (2015).

[43]S**.** Khodabakhshi, A. Rashidi, Z. Tavakoli, M. Baghernejad, A. Yadegari, *Monatsh. Chem*.,147**,** 791 (2016).