Current Chemistry Letters 5 (2016) 137–144

Contents lists available at GrowingScience

Current Chemistry Letters

homepage: www.GrowingScience.com

An efficient one pot three-component synthesis of dihydropyrano[3,2-c] chromenes using ammonium metavanadate as catalyst

Balasaheb V. Shitole[a], Nana V. Shitole[b], Murlidhar S. Shingare[c] and Gopal K. Kakde[d*]

[a]*Vasant College,Kaij-431519 (M.S), India*
[b]*Shri Shivaji College, Parbhani-431401 (M.S), India*
[c]*Dr. Babasaheb Ambedkar Marathwada University, Aurangabad -431 004, India*
[d]*Arts,Commers and Science College, Dharur(Kille)-431519 (M.S), India*

C H R O N I C L E

Article history:
Received January 21, 2016
Received in revised form
July 10, 2016
Accepted 8 Septemver 2016
Available online
8 September 2016

Keywords:
Chromenes
Multi-component reaction
Ammonium metavanidate

A B S T R A C T

We report ammonium metavanadate catalyzed one-pot synthesis of 3,4-dihydropyrano[3,2-c]chromenes, from aldehydes, active methylene compounds malononitrile and 4-hydroxycoumarin in water:ethanol(1:1) under reflux. The attractive features of this process are mild reaction conditions, short reaction times, easy isolation of products, and excellent yields.

1. Introduction

The development of multi-component reactions (MCRs) designed to produce elaborate biologically active compounds has become an important area of research in organic, combinatorial and medicinal chemistry.[1] One-pot multi-component reaction strategies offer significant advantages over conventional linear-type syntheses by virtue of their convergence, productivity, facile execution and high yields.[2] 2-amino-tetrahydro-4*H*-chromene derivatives represent an important class of bioactive molecules. They are often used in cosmetics, pigments[3] and utilized as potential agrochemicals[4]. Some derivatives of chromenes constitute a core skeleton of many naturalproducts[5] and bioactive molecules which seize various pharmacological actions, such asdiuretic[6], anti-coagulant, anti-cancer[7], anti-HIV[8] antitumor[9] anti-malarial activities[10,] anti-alzheimer[11] anti-leukemic[12-13] antibacterial[14] and anti-anaphylacticactivities[15].

A number of methods have been reported for the synthesis of 3,4-dihydropyrano[*c*]chromenes with the catalysts diammonium hydrogen phosphate[16], $H_6P_2W_{18}O_{62}\cdot 18H_2O$[17]. tetrabutylammonium

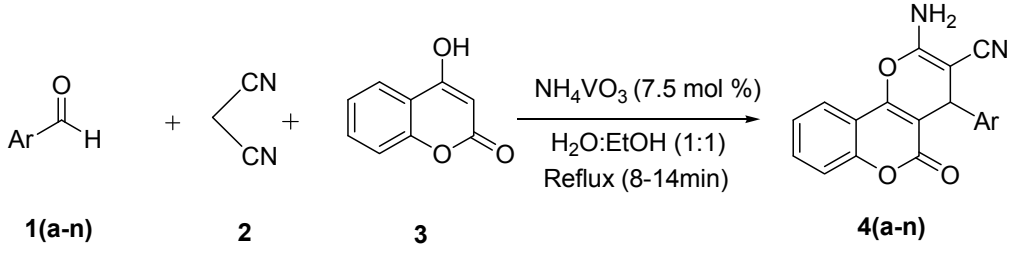
* Corresponding author. Tel.: +91-2445-274129, Fax: +91-2445-274129
E-mail address: kakdeg44@gmail.com (G. K. Kakde)

doi: 10.5267/j.ccl.2016.9.001

bromide[18], hexamethylenetetramine[19],1,8-diazabicyclo[5.4.0]undec-7-ene[20], sodium dodecylsulfate[21], triethylenetetra ammonium trifluoroacetate[22] α-Fe_2O_3nanoparticles[23], 4-(dimethylamino) pyridine[24],CuO nanoparticles[25], silica-bonded *N*-propylpiperazine sodium *n*-propionate[26], silica-grafted ionic liquid[27], potassium phthalimide in aqueous media[28], piperidine-functionalized poly(ethylene glycol) bridged dicationicionic liquid[29], polymer supported sulfanilic acid[30], basic ionic liquid[31], ammonium acetate[32], cellulose-SO_3H[33] electrolysis in an undivided cell in the presence of sodium bromide as an electrolyte[34], piperi-dine/triethyl amine in aqueous media[35] and many of these procedures have merit; however, most require refluxing for hours in organic solvents, complex steps, use of expensive catalysts and tedious work-up. We decided to investigate ammonium metavanadate for use as catalyst for the synthesis of dihydropyrano[3,2-*c*]chromene derivatives in aqueous ethanol. Hence the search continues for a better catalyst in the synthesis of dihydropyrano[3,2-c] chromenes in terms of operational simplicity and economic viability. Herein we report the use of ammonium metavanadate (NH_4VO_3) as a water soluble, inorganic acid[36] that meets the demand for a economic catalyst. It is employed similar to vanadium pentoxide[37] and as a catalyst in oxidation reactions with other cocatalysts.[38] It is a reagent used in analytical chemistry, the photographic industry, and the textile industry.[37]This is the first report of utilizing ammonium metavanadate as a catalyst for the synthesis of dihydropyrano[3,2-c] chromenes.

2. Results and Discussion

As a contribution of our research work devoted to the development of useful synthetic methodologie. We herein report an eco-friendly, facile and efficient methodology for the synthesis of dihydropyrano[3,2-c] chromene. This method involves the efficient synthesis of substituted dihydropyrano[3,2-c] chromenes by treatment of 4-chlorobenzaldehyde (1mmol), malononitrile (1mmol), 4-hydroxycoumarine (1mmol) and ammonium metavanadate (7.5mol%) as catalyst dissolved in 5 ml of ethanol:water(1:1) at reflux temperature for 8 - 14 min (**Scheme 1**).



Scheme 1. An eco-friendly, facile and efficient methodology for the synthesis of dihydropyrano[3,2-c] chromene

To evaluate the effect of solvent, various solvents such as water, ethanol:water (1:3,v:v), ethanol:water (1:2,v:v), ethanol:water (1:1,v:v) and ethanol were used for the model reaction. The desired product was obtained in 39, 47, 65, 94 and 94% yields respectively after 10 min at reflux condition. Water:ethanol (1:1) stand out as the solvent of choice among the solvents tested. Because of the rapid conversion and excellent yield (93%) of desired product obtained (**Table 1, entry 4**), where as the product formed in lower yields (39-65%) by using other solvents **(Table 1, entries 1-3**).

Table1. Screening of solvents

Entry	Solvent	Yield (%)
1	water	39
2	ethanol, water (1:3)	47
3	ethanol, water (1:2)	65
4	**ethanol, water (1:1)**	**93**
5	ethanol	93

To determine the appropriate concentration of the catalyst ammonium metavanadate, it has been investigated the model reaction first without catalyst and very less product is obtained (i.e. trace) at different concentrations of catalyst like 2.5, 5, 7.5and 10 mol% the product formed in 57, 72, 93 and 93% yields, respectively (**Table 2**). This indicates that 7.5mol% of ammonium metavanadate is sufficient for the best result by considering the reaction time and yield of product. A role of ammonium metavanadate has been proposed to activate the carbonyl compound by binding of ammonium metavanadate with the carbonyl oxygen which ultimately enhances the electrophilicity of the carbonyl carbon leads to increase in the reaction rate.

Table2. Optimization of the amount of Ammonium metavanadate[a]

Entry	Ammonium metavanadate (mol %)	Yield[b] (%)
1	2.5	57
2	5	72
3	7.5	93
4	10	93

[a]*Reaction conditions:* 1 (1 mmol), 2 (1 mmol), 3 (1mmol) ammonium metavanadate in water ethanol (1:1) at reflux temperature.;
[b]Isolated yields

In order to show the merit of NH_4VO_3 in comparison with the other catalyst used for the similar reaction, a side by side comparison was run with some of the more common catalysts used for this chemistry. The results are presented in **Table -3**. It is evident from the results that NH_4VO_3 was an effective catalyst for the synthesis of dihydropyrano[3,2-c] chromenes.

Table 3. Effect of different catalysts for the synthesis of 3,4-dihydropyrano[*c*]chromenes from the condensation of on the reaction of benzaldehyde, 4-hydroxycoumarin and malononitrile

Entry	Catalyst	Catalyst Conc.	Solvent/ Medium	Temp (ºC)	Time (min)	Yield (%)	Reference
1	DAHP	(10 mol%)	Ethanol–water	25	240	85	16
2	$H_6P_2W_{18}O_{62}\cdot 18H_2O$	(10 mol%)	Ethanol	Reflux	30-85	80	17
3	TBAB	(10 mol%)	Water	Reflux	45-60	93	18
4	$(CH_2)_6N_4$	(10 mol%)	Ethanol	Reflux	40	95	19
5	SDS	(20 mol%)	Water	60	150	88	21
6	[TETA]TFA	(10mol%)	Ethanol–water	Reflux	30	95	22
7	α-Fe_2O_3	(10 wt%)	Ethanol	Reflux	30	93	23
8	DMAP	(20 mol%)	Ethanol	Reflux	4	94	24
9	CuO nanoparticles	(15 mol%)	Water	100	6	93	25
10	ammonium metavanidate	(7.5 mol%)	Ethanol–water	Reflux	9	94	Present method

To study the generality of this process, variety of examples were illustrated for the synthesis of dihydropyrano[3,2-c] chromenes and the results are summarized in **Table 4**. The reaction is compatible for various substituents such as -CH_3, -OCH_3, -OH, -$N(CH_3)_2$, and –Cl. The formation of desired product has been confirmed by ^{1}H NMR and IR spectroscopic analysis techniques and compared with the corresponding literature data.

Table 4. Synthesis of dihydropyrano[3,2-c] chromenes using Ammonium metavanadate

Sr.No.	Ar-CHO	Product	Time (min)	Yield[a](%)	M. P°C	
					Found	Reported
1	C_6H_5	4a	10	94	257-259	256-258[16]
2	4-ClC_6H_4	4b	09	93	260-262	263-265[16]
3	4-OHC_6H_4	4c	14	92	262-264	266-268[27]
4	4-$CH_3C_6H_4$	4d	12	93	259-261	253-255[27]
5	2-ClC_6H_4	4e	11	90	243-245	245-246[31]
6	3-ClC_6H_4	4f	10	91	244-246	241-243[27]
7	4-$NO_2C_6H_4$	4g	08	95	255-257	258-260[16]
8	4-$OCH_3C_6H_4$	4h	12	90	242-244	240-242[16]
9	3-$NO_2C_6H_4$	4i	09	92	260-262	262-264[16]
10	2-$NO_2C_6H_4$	4j	10	89	261-263	258-260[27]
11	2,4 - Cl_2-C_6H_3	4k	12	91	260-262	257-259[16]
12	3,4,5-$(OCH_3)_3C_6H_2$	4l	13	90	238-240	236-238[27]
13	4-F C_6H_4	4m	09	94	256-258	258-259[31]
14	4-$(CH_3)_2NC_6H_4$	4n	14	92	262-263	265-267[31]

3. Conclusions

In conclusion, this paper has described a simple and proficient approach for the synthesis of dihydropyrano[3,2-c] chromenescatalyzed by ammonium metavanadate in aqueous alcoholic media. Present methodology offers very attractive features such as simple experimental procedure, higher yields and economic viability, when compared with other method as well as with other catalysts, and will have wide scope in organic synthesis.

Acknowledgements

We are thankful to the University Grants Commission, New Delhi, for financial support which is gratefully acknowledged and the Sophisticated Analytical Instrument Facility, Punjab University, Chandigarh for providing spectroscopic data.

4. Experimental

4.1. Materials and Methods

Chemicals were purchased from Merck, Fluka and Aldrich chemical companies. All yields refer to isolated products unless otherwise stated. Melting points were determined in an open capillary. ^{1}H nuclear magnetic resonance (NMR) (500 MHz) with tetramethylsilane as internal standard and dimethylsulfoxide DMSO-d6 as solvent. Fourier transform infrared (IR) spectra were obtained as KBr discs on a Shimadzu spectrometer. Mass spectra (MS) were determined on a Varion-Saturn 2000 GC/MS instrument.

4.2. General procedure for the synthesis of substituted of 3,4-dihydropyrano[*c*]chromenes.

A mixture of subsutited aromatic aldehyde (1mmol), malononitrile (1mmol) and 4-hydroxycoumarine (1mmol) in the presence of ammonium metavanadate (7.5mol %) as a catalyst was stirred at reflux temperature in ethanol:water (1:1) (7 ml) for 8-14 minutes. After the appropriate time, the mixture was cool than poor on ice cold water solidified the product filtered its. The crude solid material was purified by recrystallization from ethanol.

4.3 Spectral data for selected compounds

2-amino-4,5-dihydro-5-oxo-4-phenylpyrano[3,2-c]chromene-3-carbonitrile (4a)

IR (KBr) : 3376 (NH_2), 2195 (CN), 1703 (C=O) cm^{-1}; ^{1}H NMR (d6-DMSO, 400 MHz) δ : 4.46 (s, 1H, CH), 7.23–7.91(m, 11H, Ar, NH_2) ppm; ^{13}C NMR (d6-DMSO, 100 MHz), δ : 37.4, 58.5, 104.5, 113.4,117.0, 119.6, 122.9, 125.1, 127.6, 128.1,128.9, 133.4, 143.8, 152.6, 153.9, 158.4, 159.9 ppm.

2-amino-4-(4-chlorophenyl)-4,5-dihydro-5-oxopyrano[3,2-c]chromene-3-carbonitrile(4b)
IR (KBr): 3281 (NH_2), 2185 (CN), 1701 (C=O) cm^{-1};^{1}HNMR (d6-DMSO 400 MHz) δ : 4.68 (s, 1H, CH), 7.47–8.19 (m, 10H, Ar, NH_2) ppm. ^{13}C NMR (d6-DMSO, 100 MHz), δ : 57.2, 103.2, 113.3, 117.0, 119.3, 123.0, 124.1, 124.7, 125.1, 129.6, 129.7, 133.6, 147.0, 151.2, 152.7, 154.4, 158.5, 160.0 ppm.

2-amino-4,5-dihydro-4-(4-hydroxyphenyl)-5-oxopyrano[3,2-c]chromene-3-carbonitrile(4c)
IR (KBr) : 3353 (NH_2), 2157 (CN), 1712(C=O) cm^{-1}; ^{1}HNMR (d6-DMSO 400 MHz) δ : 4.51 (s, 1H, CH), 7.47–8.05 (m, 10H, Ar, NH_2) 9.03 (s, OH) ppm. ^{13}C NMR (d6-DMSO, 100 MHz), δ : 58.8, 104.5, 112.8, 115.6, 115.9, 119.8, 122.5, 125.0, 128.9, 133.2, 133.8, 152.4, 154.1, 156.8, 158.3, 160.2 ppm.

2-amino-4,5-dihydro-5-oxo-4-p-tolylpyrano[3,2-c]chromene-3-carbonitrile(4d)
IR (KBr) : 3333 (NH_2), 2878 (CH_3),2166 (CN), 1708(C=O) cm^{-1}; ^{1}HNMR (d6-DMSO 400 MHz) δ : 2.26 (s, 3H), 4.42 (s, 1H, CH), 7.32–8.61 (m, 10H, Ar, NH_2) ppm. ^{13}C NMR (d6-DMSO, 100 MHz), δ : 21.4, 58.3, 103.9, 113.2, 116.8, 119.2, 123.2, 125.2,127.9, 128.7, 133.7, 135.9, 139.8, 152.9, 152.9, 159.1, 160.2 ppm

2-amino-4-(2-chlorophenyl)-4,5-dihydro-5-oxopyrano[3,2-c]chromene-3-carbonitrile (4e)
IR (KBr) : 3342 (NH_2), 2159 (CN), 1707(C=O) cm^{-1}; ^{1}HNMR (d6-DMSO 400 MHz) δ : 4.46 (s, 1H, CH), 7.52–8.91 (m, 10H, Ar, NH_2) ppm. ^{13}C NMR (d6-DMSO, 100 MHz), δ : 57.7, 103.9, 112.8, 115.6, 116.1, 119.4, 122.7, 125.3, 128.5, 132.9, 134.4, 152.4, 154.3, 157.9, 158.1, 159.9 ppm.

2-amino-4-(3-chlorophenyl)-4,5-dihydro-5-oxopyrano[3,2-c]chromene-3-carbonitrile (4f)
IR (KBr) : 3376 (NH_2), 2195 (CN), 1703 (C=O) cm^{-1}; ^{1}H NMR (d6-DMSO, 400 MHz) δ : 4.42 (s, 1H, CH), 7.21–8.71(m, 10H, Ar, NH_2) ppm; ^{13}C NMR (d6-DMSO, 100 MHz), δ : 57.81, 104.3, 114.3, 116.2, 119.2, 122.9, 125.1, 127.0, 127.6, 127.8, 130.3, 133.8, 132.9, 146.2, 152.6, 155.4, 158.3, 158.4, 160.3 ppm.

2-amino-4,5-dihydro-4-(4-nitrophenyl)-5-oxopyrano[3,2-c]chromene-3-carbonitrile (4g)
IR (KBr) : 3367 (NH_2), 2171 (CN), 1709 (C=O) cm^{-1}; ^{1}H NMR (d6-DMSO, 400 MHz) δ : 4.43 (s, 1H, CH), 7.23–8.51(m, 10H, Ar, NH_2) ppm; ^{13}C NMR (d6-DMSO, 100 MHz), δ : 57.2, 103.2, 113.3, 117.3, 119.4, 123.2, 124.2, 125.3, 129.7, 133.3, 147.3, 151.4, 152.4, 154.4, 158.5, 158.7, 160.1 ppm

2-amino-4,5-dihydro-4-(4-methoxyphenyl)-5-oxopyrano[3,2-c]chromene-3-carbonitrile (4h)
IR (KBr) : 3367 (NH_2), 2887 (CH_3), 2162 (CN), 1707 (C=O) cm^{-1}; ^{1}H NMR (d6-DMSO, 400 MHz) δ : 3.75 (s CH_3) 4.42 (s, 1H, CH), 7.33–8.22(m, 10H, Ar, NH_2) ppm; ^{13}C NMR (d6-DMSO, 100 MHz), δ : 52.9, 57.6, 104.1, 113.1, 115.7, 116.9, 119.2, 122.9, 124.2, 124.2, 125.2, 126.7, 134.1, 138.1, 152.1, 152.5, 158.2, 159.5 ppm

2-amino-4,5-dihydro-4-(3-nitrophenyl)-5-oxopyrano[3,2-c]chromene-3-carbonitrile (4i)
IR (KBr) : 3361 (NH_2), 2152 (CN), 1705 (C=O) cm^{-1}; ^{1}H NMR (d6-DMSO, 400 MHz) δ : 4.44 (s, 1H, CH), 7.11–8.71(m, 10H, Ar, NH_2) ppm; ^{13}C NMR (d6-DMSO, 100 MHz), δ : 58.6, 104.3, 112.9, 118.0, 119.2, 122.3, 122.3, 122.9, 125.1, 129.8, 133.6, 135.2, 145.6, 148.3, 152.3, 153.9, 158.5, 158.7, 160.1ppm.

2-amino-4,5-dihydro-4-(2-nitrophenyl)-5-oxopyrano[3,2-c]chromene-3-carbonitrile (4j)
IR (KBr) : 3352 (NH_2), 2171 (CN), 1709 (C=O) cm^{-1}; ^{1}H NMR (d6-DMSO, 400 MHz) δ : 4.41 (s, 1H, CH), 7.21–8.52(m, 10H, Ar, NH_2) ppm; ^{13}C NMR (d6-DMSO, 100 MHz), δ : 57.3, 103.24, 119.3, 117.5, 118.9, 123.8, 124.6, 125.8, 129.7, 133.3, 147.3, 151.4, 152.4, 154.4, 158.5, 158.7, 161.2 ppm

2-amino-4-(2,4-dichlorophenyl)-4,5-dihydro-5-oxopyrano[3,2-c]chromene-3-carbonitrile (4k)
IR (KBr) : 3321 (NH_2), 2157 (CN), 1702 (C=O) cm^{-1}; ^1H NMR (d6-DMSO, 400 MHz) δ : 4.44 (s, 1H, CH), 7.29–8.87(m, 09H, Ar, NH_2) ppm; ^{13}C NMR (d6-DMSO, 100 MHz), δ : 34.4, 57.7, 102.9, 113.9, 117.2, 119.4, 123.2, 124.9, 128.6, 129.4, 133.1, 132.2, 133.6, 134.1, 139.1, 153.7, 154.6, 158.5, 160.4 ppm.

2-amino-4,5-dihydro-4-(3,4,5-trimethoxyphenyl)-5-oxopyrano[3,2-c]chromene-3-carbonitrile (4l)
IR (KBr) : 3331 (NH_2), 2177 (CN), 1701(C=O) cm^{-1}; ^1H NMR (d6-DMSO, 400 MHz) δ : 3.64 (s, 3 H), 3.72 (s, 6 H) 4.43 (s, 1H, CH), 7.29–8.87(m, 08H, Ar, NH_2) ppm; ^{13}C NMR (d6-DMSO, 100 MHz), δ : 56.36, 58.32, 60.39, 104.11, 105.38, 113.54, 117.05, 119.71, 123.04, 125.11, 133.39, 137.03, 139.46, 152.64, 153.30, 153.98, 158.38, 160.14.

2-amino-4-(4-fluorophenyl)-4,5-dihydro-5-oxopyrano[3,2-c]chromene-3-carbonitrile (4m)
IR (KBr) : 3366 (NH_2), 2887 (CH_3), 2151 (CN), 1705 (C=O) cm^{-1}; ^1H NMR (d6-DMSO, 400 MHz) δ : 4.42 (s, 1H, CH), 7.41–8.22(m, 10H, Ar, NH_2) ppm; ^{13}C NMR (d6-DMSO, 100 MHz), δ : 52.9, 57.6, 104.1, 113.1, 115.7, 116.9, 119.2, 122.9, 124.2, 124.2, 125.2, 126.7, 134.1, 138.1, 152.1, 152.5, 158.2, 160.5 ppm

2-amino-4-(4-(dimethylamino)phenyl)-4,5-dihydro-5-oxopyrano[3,2-c]chromene-3-carbonitrile (4n)
IR (KBr) : 3234 (NH_2), 2187 (CN), 1702 (C=O) cm^{-1}; ^{1}HNMR (d6-DMSO 400 MHz) δ : 231 (s CH_3) 4.68 (s, 1H, CH), 7.37–8.11 (m, 10H, Ar, NH_2) ppm. ^{13}C NMR (d6-DMSO, 100 MHz), δ : 34.6, 56.2, 103.2, 113.4 117.3, 119.3, 122.9, 124.2, 124.9, 125.2, 129.2, 128.9, 132.3, 146.7, 151.2, 152.7, 154.4, 158.5, 160.1 ppm.

References

1. (a) Orru R. V. A., de Greef, M. **(2003)** Recent Advances in Solution-Phase Multicomponent Methodology for the Synthesis of Heterocyclic Compounds. *Synthesis*, 10, 1471-1499; (b) Balme G., Bossharth E., Monteiro N. **(2003)** Pd-Assisted Multicomponent Synthesis of Heterocycles. *Eur. J. Org. Chem.*, 21 4101-4111; (c) Brase S., Gil, C., Knepper K. **(2002)** The recent impact of solid-phase synthesis on medicinally relevant benzoannelated nitrogen heterocycles. *Bioorg. Med. Chem.* 10(8), 2415-2437.
2. (a) Weber L. **(2002)** Multi-component reactions and evolutionary chemistry. *Drug Discovery. Today,* 7(2), 143-147. (b) Domling A. **(2002)** Recent advances in isocyanide-based multicomponent chemistry. *Curr. Opin. Chem. Biol.,* 6(3), 306-313.
3. Boumoud A., Yahiaoui A., Boumoud T.,Debache A. A. **(2012)** Novel Catalyst for One-pot Synthesis of Tetrahydrobenzo[b]pyran derivatives. *J. Chem. Pharm. Res.,* 4(1), 795-799.
4. Bhargavaand D. and Garg G. **(2011)** Design, synthesis and insilico pharmacokinetic studies of some coumarinan alogues. *J. Chem. Pharm. Res.,* 3(2), 50-57.
5. Faidallah H., Khan K., and Asiri A. **(2011)** Synthesis and characterization of anovel series of benzene sulfonylurea and thiourea derivatives of 2H-pyran and 2H-pyridine-2-ones as antibacterial, antimycobacterial and antifungalagents. *Eur. J. Chem.,* 2(2), 243-250.
6. Hafez E. A. A., Elnagdi M. H., Elagamey A. G. A., and E. L-Taweel F. M. A. A. **(1987)** Nitriles in Heterocyclic Synthesis: Novel Synthesis of Benzo[c]-Coumarinand of Benzo[c]Pyrano[3,2-c]Quinoline Derivatives. *Heterocycles*. 26(4), 903-907.
7. Foye W. O. **(1991)** *Principi di Chimica Farmaceutica*, Piccin: Padova, Italy.
8. Tanabe A., Nakashima H., Yoshida O., Yamamoto N., Tenmyo O., and Oki T. **(1988)** Inhibitory Effect of New Antibiotic, Pradimicin A on Infectivity, Cytopathic Effect and Replication of Human Immunodeficiency Virus in Vitro. *J. Antibiot*., 41(11), 1708-1710.

9. Shijay G., Cheng H. T., Chi T., and Ching-Fa Y. **(2008)** FluorideIon Catalyzed Multicomponet Reactions for Efficient Synthesis of 4H-Chromene and N-Arylquinoline Derivates in Aqueous Media, *Tetrahedron*, 64(38), 9143-9149.
10. Bolognese A., Correale G., Manfra M., Lavecchia A., Mazzoni O., Novellino E., La colla P., Sanna G., and Loddo R. **(2004)** Antitumor Agents, Design, Synthesis, and Biological Evaluation of New Pyridoisoquinolindione and Dihydrothieno quinolindione Derivatives with Potent Cytotoxic Activity. *J. Med. Chem.* 47(4), 849-858.
11. Bayer T. A., Schafer S., Breyh H., Breyhan O., Wirths C., and Treiber G. A. **(2006)** A Vicious Circle: Role of Oxidative Stress, Intraneuronal Aβ and Cu in Alzheimer's Disease Multhaup. *Clin Neuropathol.,* 25(4), 163-171.
12. Fokialakis N., Magiatis P., Chinou L., Mitaka S., and Tillequin F. **(2002)** Megistoquinones I II, Two Quinoline Alkaloids with Antibacterial Activity from the Bark of Sarcomelicope megistophylla. *Chem. Pharm. Bull.,* 50(3), 413-414.
13. Beagley P., Blackie M. A. L., Chibale K., Clarkson C., Meijboom R., Moss J. R., Smith P., and Su, H. **(2003)** Synthesis and Antiplasmodial Activity in Vitro of New Ferrocene-Chloroquine Analogues, *Dalton Trans*, 3046-3051.
14. Morgan L. R., Jursic B. S., Hooper C. L., NeumannD. M., Thangaraj K., and Leblance B. **(2002)** Anticancer Activity for 4,4_-Dihydroxybenzophenone-2,4-Dinitrophenylhydrazone (A-007) Analogues and Their Abilities to Iinteract with Lymphoendothelial Cell Surface Markers. *Bioorg. Med. Chem. Lett.*, 12(23), 3407-3411.
15. Biot C., Glorian G., Maciejewski L. A., BrocardJ. S., Domarle O., Blampain G., Blampain G., Blampain P., Georges A. J., Abessolo H., Dive D., and Lebibi J. **(1997)** Synthesis and Antimalarial Activity in Vitro and in Vivo of a New Ferrocene-Chloroquine Analogue. *J. Med. Chem.,* 40(23) , 3715-3718.
16. Abdolmohammadi S., and Balalaie S. **(2007**) Novel and efficient catalysts for the one-pot synthesis of 3,4-dihydropyrano[*c*]chromene derivatives in aqueous media. *Tetrahedron Lett.* 48(18) 3299–3303.
17. Heravi M. M., Jani B. A. Derikvand F., Bamohar-ram F. F., and OskooieH. A., (**2008**) Three component, one-pot synthesis of dihydropyrano[3,2-*c*]chromene derivatives in the presence of $H_6P_2W_{18}O_{62}\cdot 18H_2O$ as a green and recyclable catalyst. *Catal. Commun.* 10(3), 272–275.
18. Khurana, J. M., and Kumar, S. **(2009)** Tetrabutylammonium bromide (TBAB): a neutral and efficient catalyst for the synthesis of biscoumarin and 3,4-dihydropyrano[*c*]chromene derivatives in water and solvent-free conditions. *Tetrahedron Lett.* 50(28), 4125–4127.
19. Wang H. J., Lu, J., and Zhang Z. H. **(2010)** Highly efficient three component, one-pot synthesis of dihydropyrano[3,2-*c*]chromene derivatives. *Monatsh. Chem.* 141(10), 1107–1112.
20. Khurana J. M., Nand, B., and Saluja, P. **(2010)** DBU: a highly efficient catalyst for one-pot synthesis of substituted 3,4-dihydropyrano[3,2-*c*]chromenes, dihydropyrano[4,3-*b*]pyranes, 2-amino-4*H*-benzo[*h*]chromenes and 2-amino-4*H*-benzo[*g*]chromenes inaqueous medium. *Tetrahedron,* 66(30), 5637–5641.
21. Mehrabi H., and Abusaidi H. **(2010**) Synthesis of biscoumarin and 3,4-dihydropyrano[*c*]chromene derivatives catalysed by sodiumdodecyl sulfate (SDS) in neat water. *J. Iran. Chem. Soc.,* 7(4), 890–894.
22. Zheng, J., and Li, Y. (**2011**) Basic ionic liquid-catalyzed multicomponentsynthesis of tetrahydrobenzo[*b*]pyrans and pyrano[*c*]chromenes, *Mendeleev Commun.* 21(5), 280–281.
23. Nagabhushana H., Saundalkar S. S., Muralidhar L., Nagab-hushana B. M., Girija C.R., Nagaraja D., Pasha M. A., and Jayashankara V. P. **(2011**) α-Fe2O3nanoparticles: an efficient, inexpensive catalyst for theone-pot preparation of 3,4-dihydropyrano[*c*]chromenes. *Chin. Chem. Lett.,* 22(2), 143–146.
24. Khan A. T., Lal M., Ali S., and Khan M. M. **(2011)** One-pot three-component reaction for the synthesis of pyran annulated heterocyclic com-pounds using DMAP as a catalyst, *Tetrahedron Lett.* 52(41)**,** 5327–5332.

25. Mehrabi H., and Kazemi-Mireki M. **(2011**) CuO nanoparticles: an efficient and recyclable nanocatalyst for the rapid and green synthesisof 3,4-dihydropyrano[*c*]chromenes, *Chin. Chem. Lett.* 22(12), 1419–1422.
26. Niknam K., and Jamali, A. **(2012)** Silica-bonded *N*-propylpiperazine sodiumn-propionate as recyclable basic catalyst for synthesis of 3,4-dihydropyrano[c]chromene derivatives and biscoumarins, *Chin. J. Catal.* 33(11), 1840–1849.
27. Niknam, K., and Piran, A. **(2013**) Silica-grafted ionic liquids as recyclable catalysts for the synthesis of 3,4-dihydropyrano[*c*]chromenes and pyrano[2,3-*c*]pyrazoles, *Green Sustain. Chem.* 3, 1–8.
28. Kiyani H., and Ghorbani F. **(2015)**Potassium phthalimide: an effi-cient and simple organocatalyst for the one-pot synthesis of dihydropyrano[3,2-c]chromenes in aqueous media, *Res. Chem. Intermed* 41(6), 4031-4046
29. Wang Y., Luo, J., Xing, T., and Liu, Z. (**2013)** Synthesis of a novel piperidine-functionalized poly(ethylene glycol) bridged dicationic ionicliquid and its application in one-pot synthesis of substituted 2-amino-2-chromenes and 3,4-dihydropyrano[3,2-*c*]chromenes inaqueous media, *Monatsh. Chem.,* 144(12), 1871–1876.
30. Patel J. P., Avalani J. R., and Raval D. K. **(2013**) Polymer supported sulphanilic acid: a highly efficient and recyclable green heteroge-neous catalyst for the construction of 4,5-dihydropyrano[3,2-c]chromenes under solvent-free conditions, *J. Chem. Sci.* 125(3), 531–536.
31. Patel D. S., Avalani J. R., and Raval D. K. (**2013)** One-pot solvent-free rapid and green synthesis of 3,4-dihydropyrano[*c*]chromenesusing grindstone chemistry. *J. Saudi Chem. Soc.* http://dx.doi.org/10.1016/j.jscs.2012.12.008
32. Kanakaraju S., Prasanna B., Basavoju S., and Chandramouli G. V. P. (**2013**) Ammonium acetate catalyzed an efficient one-pot three com-ponent synthesis of pyrano[3,2-*c*]chromene derivatives. *Arab. J. Chem*. http://dx.doi.org/10.1016/j.arabjc.2013.10.014
33. Shaterian H. R., and Rigi F. (**2014**) New applications of cellulose-SO_3H as a bio-supported and biodegradable catalyst for the one-pot synthesis of some three-component reactions, Res. Chem. Intermed. 40(8), 2983–2999
34. Vafajoo Z., Veisi H., Maghsoodlou M. T., and Ahmadian H. **(2014)** Electrocatalytic multicomponent assembling of aldehydes,4-hydroxycoumarin and malononitrile: an efficient approach to 2-amino-5-oxo-4,5-dihydropyrano [3,2-c]chromene-3-carbonitrilederivatives, *C. R. Chim.* 17(4), 301–304.
35. Brahmachari G., and Banerjee B. **(2014**) Facile and one-pot access to diverse and densely functionalized 2-amino-3-cyano-4*H*-pyransand pyran-annulated heterocyclic scaffolds via an eco-friendly multi component reaction at room temperature using urea as anovel organo-catalyst. *Sustain. Chem. Eng.,* 2(3), 411–422.
36. Synecek V., and Hanic F. (1954) *J. Phys.*, 4, 120-130.
37. Stellman, J. M. **(1998)** In Encyclopaedia of Occupational Health and Safety, Fourth Edition, Geneva. vol III, 63.43
38. (a) Garcia T., Solsona B., Murphy D. M., Antcliff K. L., and Taylor S. H. **(2005)** Deep oxidation of light alkanes over titania-supported palladium/vanadium catalysts. *J. of Catalysis*, 229(1), 1-11. (b) Reddy, B. M., Ratnam, K. J., Saikia, P. **(2006)** Characterization of CaO–TiO_2 and V_2O_5/CaO–TiO_2 catalysts and their activity for cyclohexanol conversion. *J. Mol. Catal. A: Chemical,* 252(1), 238-244. (c) Reddy B. M., Rao K. N., Reddy G. K,. Bharali, P. (**2006**) Characterization and catalytic activity of V_2O_5/Al_2O_3-TiO_2 for selective oxidation of 4-methylanisole. *J. Mol. Catal. A: Chemical*, 253(1), 44-51.