https://doi.org/10.48047/AFJBS.6.15.2024.8012-8025

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

NOVEL ONE POT MULTICOMPONENT SYNTHESIS OF 7-HYDROXY 4H-CHROMENE CATALYZED BY P-TOLUENE SULFONIC ACID

P. Monisha[a], K. Murugaiah[a], T. Sugumaran[b], K. Gunasundari[c] , M. Pramesh[a,*]

[a]* Post Graduate and Research Department of Chemistry, A.V.V.M. Sri Pushpam College (Affiliated to Bharathidasan University, Tiruchirappalli) Poondi, Thanjavur - 613 503, India.
b, Department of Chemistry, Ayya Nadar Janaki Ammal College (Affiliated to Madurai Kamaraj University, Madurai) Sivakasi - 626 124
c, Post Graduate Department of chemistry, Jawahar Science College (Affiliated to Annamalai University), Neyveli - 607803.
Corresponding Author: mprameshchemistry@gmail.com

Volume 6, Issue 15, Sep 2024

Received: 15 July 2024

Accepted: 25 Aug 2024

Published: 05 Sep 2024

doi: 10.48047/AFJBS.6.15.2024.8012-8025

Abstract:-
An efficient and straightforward reaction of 7-hydroxy-4H-chromenes promoted by p-Toluene sulfonic acid has been studied. The deivatives of novel 7hydroxy-4H-chromenes were prepared with pyrazole aldehyde, malononitrile and resorcinol in ethanol. The outcomes of products were good yields under milder conditions and charecterized by NMR, FT-infrared spectrum and high resolution mass spectrum.

KeyWords:- 7-hydroxy-4H-chromene; p-Toluene sulfonic acid; Chemical synthesis, multicomponent; pyrazole aldehyde.

Introduction:-

Economic factors were recently used in multi-component reactions (MCRs) for synthesising significant economical and medicinal molecules. Modern organic chemistry has benefited from the use of these reactions by eliminating stages in the method of purification, increasing specificity, cutting down on duration, lowering expenses on energy and inputs.[1]. Actually, the emergence of MCRs might lead the way

for an entirely novel and varied synthetic strategy when it comes to innovative organic, bio-organic, and therapeutic chemistry that will enable the synthesis of numerous tiny organic compounds. As a result, MCRs are currently regarded as an essential method in the formation of several significant heterocyclic compounds, including derivatives of chromene[2].

The biologically active features of the intriguing class of chemicals known as chromenes, including their anti-HIV, anticancer, anticoagulant, cytotoxic, diuretic, and spasmolytic action, have garnered considerable curiosity.[3]. Many synthesised and natural compounds containing intriguing pharmacological activities and photochromic qualities include the chromene framework. Similar to cyclopenta[c]chromene derivatives, polycyclic structures illustrating the chromene nucleous occur in the basis of a broad range of biological agents and alkaloids,hematoxylin, which including the β-agonist of the estrogen SERBA receptor, aflatoxine and sesquiterpeneoid (-)herbertenoliede.[4] Implemented an important group of heterocyclic compounds possessing oxygen, 4H-chromenes have demonstrated a wide range of biological and pharmacological characteristics, including anticoagulant, diuretic, cancer-preventing, and anti-anaphylactic effects. They comprise a benzene ring fused towards a 4Hchromene ring, making them bicyclic oxygen heterocycles. These frameworks are frequently employed as antibacterial, antiviral, mutagenic, and in colourants, agricultural chemical products, cosmetics, anti-tumor and antiproliferative drugs. Numerous approaches are currently devised to synthesised a wide range of their derivatives because of their intriguing biological features.[5] Sections of chromene are exceptionally important chemical compounds that are commonly encountered in natural environments. These compounds diverse biological and pharmacological properties have drawn a great deal of interest. Chromenes have been linked to an array of biological characteristics, including antihyperglycemic and antidyslipidemic, antitumor, the cytotoxicity, molluscicidal, antiinflammatory and antifungal actions. It may also be utilized as renewable agricultural chemical products and colourants. In contemporary eternity, exceeding of research camr to be done towards enzymatic inhibitory action as concerns chromene derivatives. A few of these substances have been identified as competitors of monoamine oxidases, α-glucosidase, and acetyl cholinesterase. Furthermore, derivatives of chromène have found extensive application

as useful intermediates in chemical processes and biologically active compounds production .[6]

In most of the organic transformations multicomponent reactions motivate the researchers to elaborate this research using various catalysts like L-proline[7], Ag@KF/NT NPs[8], $BF_3.OET_2$[9], basic alumina[10], NaOAc[11], sodium p-Toluene sulphonate[NaPTS][12], $[Vo_2(L)](NHET_3)$[13], $Fe3O4@SiO_2$-gunanidine-poly acrylic acid[14], potassium titanium oxide oxalate dihydrate[15], TrzDBTH[16], AcONa[17], aminografted CUBTC[18], bovine serum albumin[19] and nano-particles have also been reported.

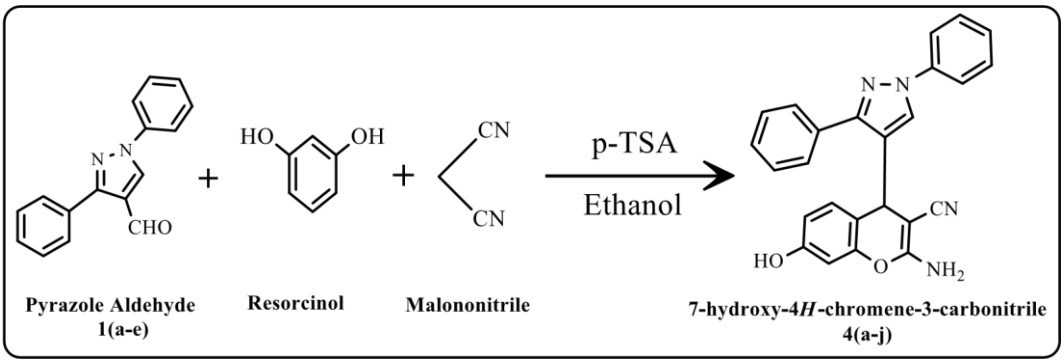
In overall, fresh techniques for synthesis are introduced for improving yielding, precision, unique primary compounds are synthesised, identified and used in the development along with discovery of drugs procedures. In the majority of circumstances, in order to separate the molecules with the crucial activity, the synthesised compounds undergo investigation across multiple pharmacological targets.[20]

Materials and Analytical instruments

The used chemicals and solvents were acquired from Sigma-Aldrich U.S.A. Using the FTIR spectrum analyzer made by Perkin-Elmer(USA), infrared [IR] spectra were taken. In DMSO-D6 , NMR results were acquired at the frequencies of 500 MHz along with 125 MHz accordingly, via a Bruker Avance Neo500 equipment.
Mass spectra have been recorded using a Q-TOF ESI spectrum equipment.

General proceeding for the synthesis of 7-hydroxy-4H-chromene -derivatives [4aj]

To a mixture of pyrazole aldehyde(1m.mol), resorcinol(1m.mol), malononitrile (1 mmol) was stirred with (5m.mol) of pTSA in ethanol. This reaction mixture was agitated beside ambient temperature during 4 hours. After that complete conversion, the solid product was drained and immersed with ethanol to obtain 7hydroxy 4H-chromene 4a. The synthesised compounds were authenticated by abundant spectral ttactics like FT-IR, ^{1}H,and ^{13}C-NMR, HR-MS and& elemental analysis.



Scheme:1 Synthesis of 7-hydroxy-4H-chromene

Results and Discussion:-

The proton NMR spectrum of compound-4a reveals two protons singlets at 8.18,8.20ppm was attributed to -NH_2 protons. 1 proton singlet in 5.97ppm was accredited to -OH proton. The 14 protons multiplet at 6.20–7.94ppm was imputed towards aromatic protons. That singlet 4.46ppm was prescribed to proton of methine.

In the ^{13}C NMR spectra, the peaks arrays between 102.9–171.9ppm were as a consequence of aromatic ring carbons. Peak in 21.2ppm was imputed for methine carbon. Carbon on bearing 3', 4' and 5' of pyrazole ring are emerged at 123.9, 120.9 and 144.9ppm individually. The peak on 118.7ppm manifested towards Carbon of nitrile group.[M]+ of HR-MS spectrum exhibited molecular ion peak at m/z 406.1399. The FT-IR spectra revealed that 3435 cm^{-1} stipulating the endurance of NH in the design. The absorption at 2589 cm^{-1} were correlated in the stretching prior to O-H, and the peak in 1311 cm^{-1} persistent the corporality until C-N. 2996, 2912 and 1407 cm^{-1} were imputed towards the stretching about C-H group. 2223 and 1657 cm^{-1} were demonstrated the stretching until alkyne and alkene on the structure.

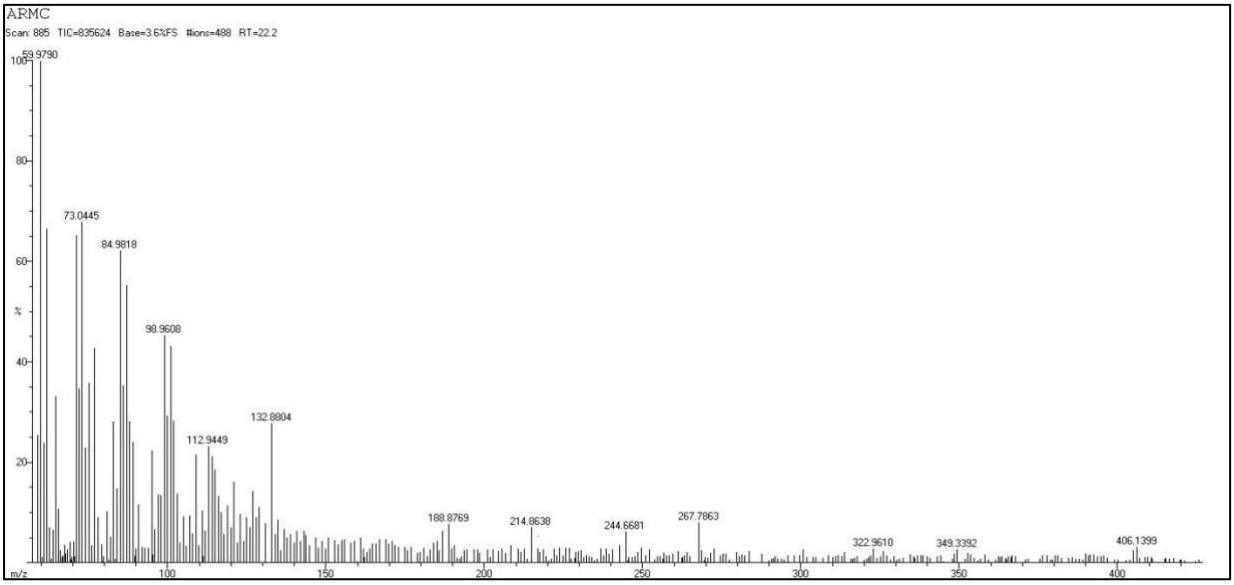


Fig.1 HR-MS spectrum of compound[4a]

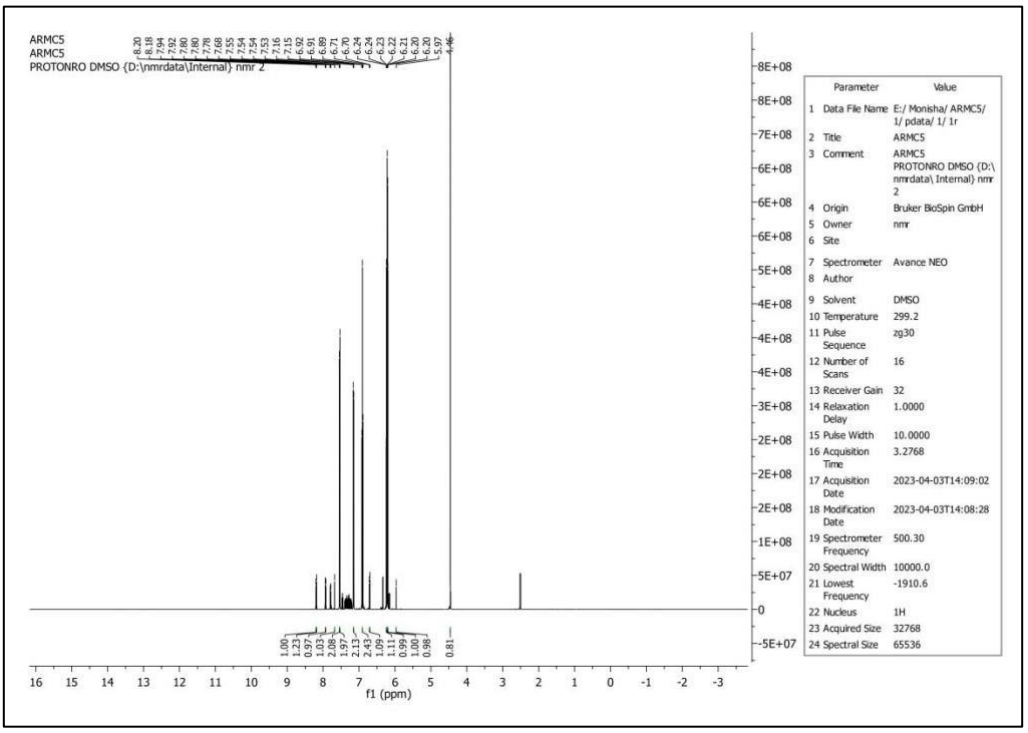


Fig. 2 .Proton NMR spectrum of compound[4a]

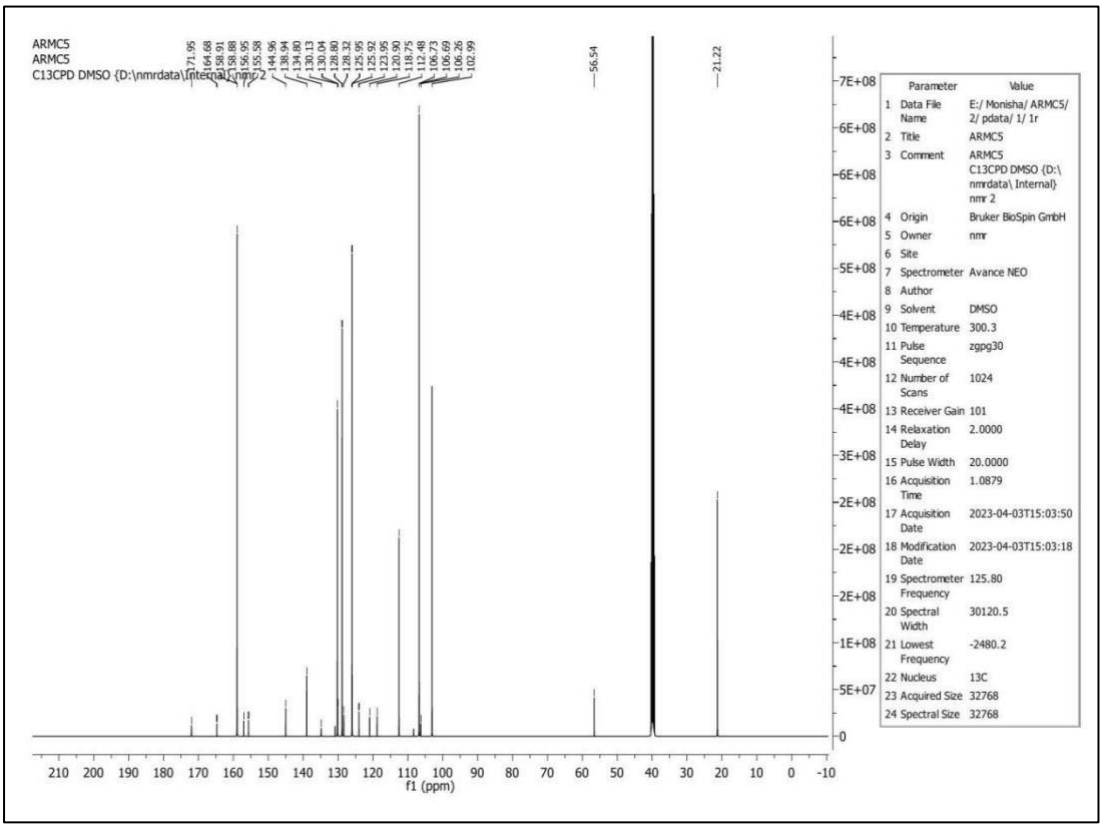


Fig. 3 . ^{13}C NMR spectrum of compound [4a]

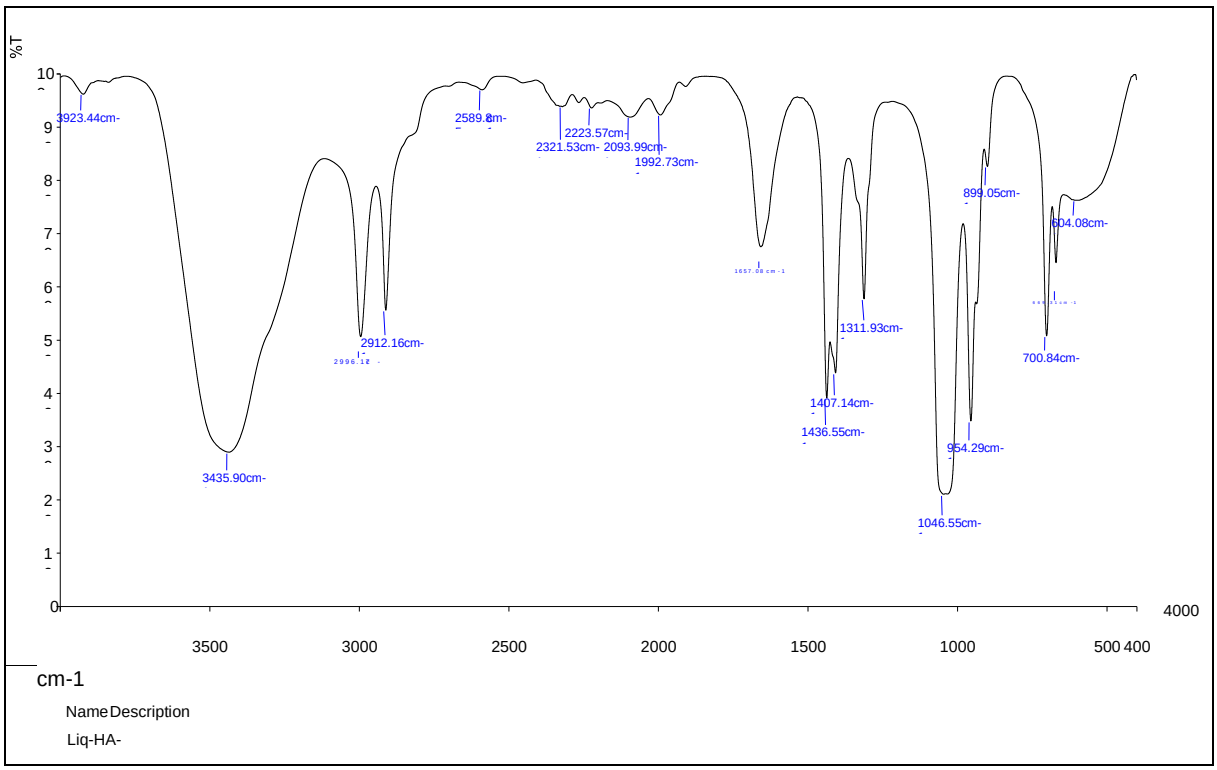
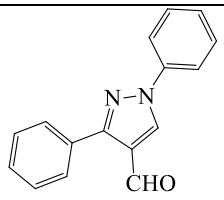
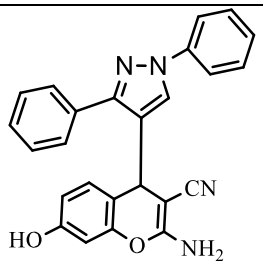
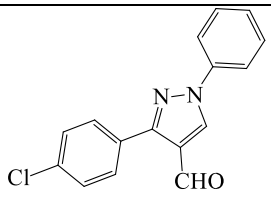
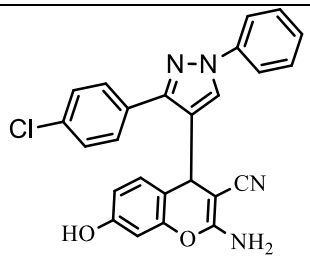
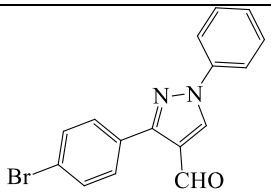
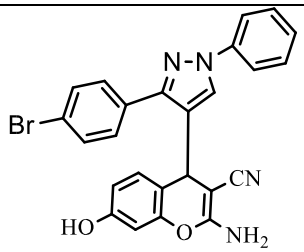
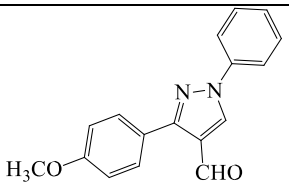
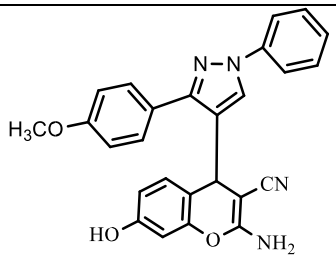
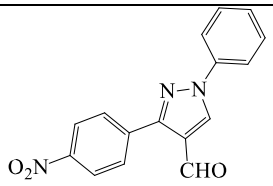
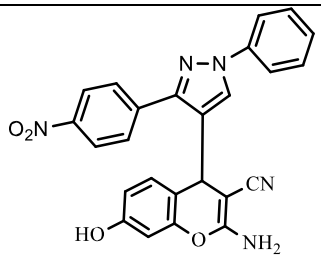
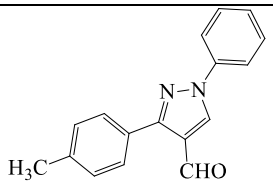
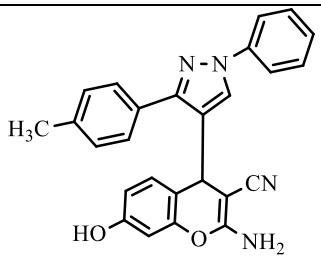
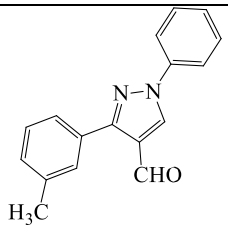
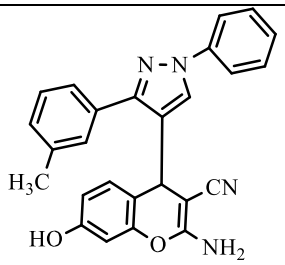
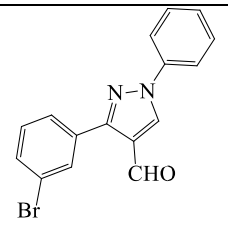
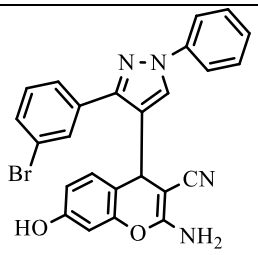
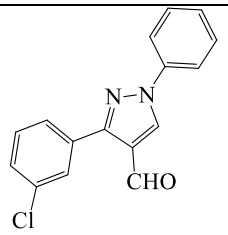
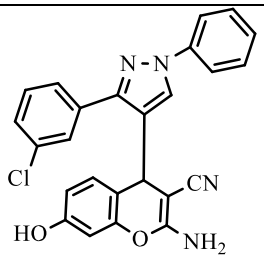
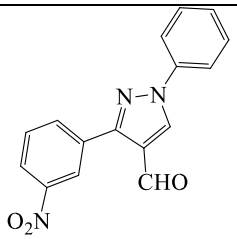
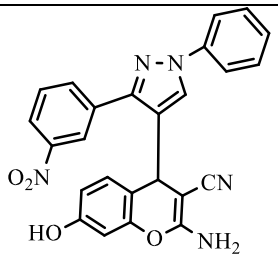


Fig.4 . FT-IR spectrum of compound[4a]

Table 2: Preparation of 7-hydroxy-4H-Chromenes [4a-4j]

CPD ID	Pyrazolealdehyde (1a-j)	Product [4a-j]	Time[hrs]
4-a			4.0
4-b			4.0
4-c			4.0
4-d			4.1

4-e			4.3
4-f			4.0
4-g			4.0
4-h			4.3
4-i			4.1
4-j			4.1

CPD ID:-compound ID

Table 3: Physical properties and Molecular mass of newly synthesized compounds 4a-4j

CPD ID	Nature	Colour	Molecular mass (m/z)	
			Calculated	Found
4a	Solid	Brown	406.14	406.1399
4b	Solid	Yellow	440.10	440.0999
4c	Semi Solid	Beige	484.05	484.0499
4d	Solid	Yellow	436.15	436.1499
4e	Solid	Cream	451.13	451.1299
4f	Solid	Orange	420.16	420.1599
4g	Solid	Pale yellow	420.16	420.1599
4h	Solid	Greyish white	484.05	484.0499
4i	Solid	Brown	440.10	440.0999
4j	Solid	Gray	451.13	451.1299

Table 4: -Elemental analysis data for synthesised compounds [4a-4j]

CPD ID	Molecular Formula		Elemental analysis					
			C	H	N	O	Cl	Br
4a	$C_{25}H_{18}N_4O_2$	Calcd	73.88	4.46	13.78	7.87		
		Found	73.81	4.40	13.69	7.81		
4b	$C_{25}H_{17}ClN_4O_2$	Calcd	68.11	3.89	12.71	7.26	8.04	
		Found	68.04	3.81	12.65	7.21	8.00	
4c	$C_{25}H_{17}BrN_4O_2$	Calcd	61.87	3.53	11.54	6.59		16.46
		Found	61.81	3.47	11.47	6.52		16.40
4d	$C_{26}H_{20}N_4O_3$	Calcd	71.55	4.62	12.84	11.00		
		Found	71.48	4.56	12.76	11.05		

4e	$C_{25}H_{17}N_5O_4$	Calcd Found	66.51 66.42	3.80 3.72	15.51 15.43	14.18 14.10		
4f	$C_{26}H_{20}N_4O_2$	Calcd Found	74.27 74.20	4.79 4.72	13.33 13.26	7.61 7.56		
4g	$C_{26}H_{20}N_4O_2$	Calcd Found	74.27 74.21	4.79 4.72	13.33 13.26	7.61 7.54		
4h	$C_{25}H_{17}BrN_4O_2$	Calcd Found	61.87 61.81	3.53 3.44	12.71 12.65	6.59 6.52		16.46 16.38
4i	$C_{25}H_{17}ClN_4O_2$	Calcd Found	68.11 68.07	3.89 3.82	12.71 12.63	7.26 7.20	8.04 8.00	
4j	$C_{25}H_{17}N_5O_4$	Calcd Found	66.51 66.45	3.80 3.73	15.51 15.44	14.18 14.11		

Table 5: -NMR-Spectral data for innovative synthesised compounds [4a-4j]

CPD ID	**Name of synthesised Compound**	**^{1}H NMR**	**^{13}C NMR**	**FT-IR**
4a	2-amino-4- (1,3-diphenyl- 1Hyl)-pyrazol- 7- 4- 4H-hydroxy- -3-chromene carbonitrile	4.46(s-1H),5.97(s1H), 6.20-6.24 (m-3H), 6.70-7.94 (m11), 8.18-8.20 (s,2HNH$_2$)	21.22,56.54,102.99,106.26,106.69,106.73 ,112.48,118.75,120.90,123.95,125.92,125 .95,128.32,128.80,130.04,130.13,134.80, 138.94,144.96,155.58,156.95,158.88,158. 91,164.68,171.95	3923,3435,2996,2912,2589,23 21,2223,2093,1992,1657,1436 ,1407,1311,1046,954,899
4b	2-amino-4-(3-(4chlorophenyl)-1phenyl-1H -pyrazol4-yl)-7-hydroxy-4Hchromene -3-carbonitrile	4.39(s-1H),5.47(s1H), 6.23-6.29 (m-3H), 6.89-7.89 (m10), 8.15-8.27 (s,2HNH$_2$)	21.09,56.34,102.45,106.12,106.45,106.69 ,112.55,118.37,120.43,123.66,125.51,125 .65,128.44,128.87,130.34,130.58,134.62, 138.99,144.35,155.75,156.33,158.79,158. 87,164.66,171.34	3925,3430,2992,2917,2583,23 25,2229,2097,1995,1650,1431 ,1411,1316,1041,946,886
4c	2-amino-4-(3 -(4bromophenyl)-1phenyl- 1H-pyrazol4-yl)- 7-	4.76(s-1H),5.37(s1H), 6.16-6.21 (m-3H), 6.89-7.87 (m10), 8.12 (s-2H-NH$_2$)	21.62,55.94,102.03,106.24,106.52,106.65 ,112.75,118.32,120.23,123.15,125.53,125 .59,128.45,128.75,130.93,130.98,134.43,	3920,3437,2989,2903,2582,23 26,2228,2099,1997,1655,1439 ,1400,1317,1041,959,891

	hydroxy4H-chromene-3-carbonitrile		138.51,144.07,155.30,156.58,158.00,158.64,164.53,171.66	
4d	2-amino- 7hydroxy-4-(3-(4methoxyphenyl)-1phenyl -1H-pyrazol4-yl)-4H-chromene3-carbonitrile	3.87(s-3H),4.66(s1H),5.49(s-1H), 6.15-6.22 (m-3H), 6.787.74 (m-10), 8.28 (s2H-NH_2)	20.98,55.83,59.25,102.45,106.77,106.71,106.83,112.55,118.37,120.20,123.31,125.43,125.68,128.70,128.78,130.57,130.68,134.42,138.54,144.75,155.21,156.44,158.23,158.59,164.89,171.45	3913,3425,2986,2911,2588,2301,2215,2084,1999,1645,1425,1402,1305,1041,957,893
4e	2-amino- 7hydroxy-4-(3- (4nitrophenyl)-1phenyl- 1H-pyrazol4-yl)- 4H-chromene3-carbonitrile	4.65(s-1H),5.39(s1H), 6.31-6.38 (m-3H), 6.87-7.98 (m10), 8.21-8.23 (s-2HNH_2)	21.53,56.03,102.56,106.34,106.59,106.77,112.23,118.46,120.22,123.44,125.53,125.64,128.59,128.71,130.56,130.43,134.68,138.55,144.42,155.66,156.13,158.09,158.56,164.52,171.50	3912,3423,2987,2910,2576,2301,2213,2073,1972,1647,1426,1417,1308,1039,959,893
4f	2-amino- 7hydroxy-4-(1phenyl-3- (p-tolyl)-	2.43(s-3H),4.33(s1H),5.13(s-1H), 6.32-6.38 (m-3H), 6.69-	21.37,21.64,56.31,102.57,106.11,106.35,106.57,112.20,118.65,120.50,123.65,125.22,125.31,128.47,128.61,130.73,130.85,1	3924,3432,2993,2917,2581,2323,2226,2097,1998,1651,1434,1409,1319,1042,955,890
	1H-pyrazol -4-yl)4H- chromene- 3-carbonitrile	7.84 (m-10), 8.11 (s-2H-NH_2)	34.42,138.57,144.37,155.10,156.93,158.36,158.69,164.75,171.33	
4g	2-amino- 7-hydroxy-4-(1- phenyl-3-(m-tolyl)1H-pyrazol-4-yl)-4H-chromene-3-carbonitrile	2.38(s-3H),4.85(s1H),5.57(s-1H), 6.16-6.22 (m-3H), 6.837.89 (m-10), 8.35 (s2H-NH_2)	21.63,21.78,56.53,102.42,106.31,106.53,106.86,112.55,118.36,120.39,123.43,125.44,125.63,128.10,128.49,130.00,130.58,134.91,138.06,144.38,155.40,156.18,158.37,158.68,164.41,171.49	3926,3436,2994,2914,2580,2323,2225,2096,1993,1654,1437,1402,1316,1049,953,895
4h	2-amino-4-(3-(3bromophenyl)-1phenyl- 1H-pyrazol-4-yl)-7-hydroxy-4H- chromene-3-carbonitrile	4.21(s-1H),5.59(s1H), 6.10-6.18 (m-3H), 6.85-7.96 (m10), 8.15-8.18 (s-2HNH_2)	21.24,56.56,102.90,106.22,106.43,106.64,112.34,118.57,120.34,123.39,125.41,125.57,128.20,128.54,130.75,130.96,134.30,138.55,144.93,155.24,156.63,158.44,158.68,164.93,171.64	3921,3430,2990,2915,2585,2326,2229,2091,1995,1651,1439,1405,1319,1041,955,895

4i	2-amino-4 -(3-(3chlorophenyl)-1phenyl- 1H-pyrazol-4-yl)-7 -hydroxy-4H- chromene- 3-carbonitrile	4.66(s-1H),5.37(s1H), 6.14-6.19 (m-3H), 6.80-7.98 (m10), 8.22 (s-2H-NH_2)	21.08,56.14,102.39,106.46,106.59,106.63,112.18,118.35,120.40,123.55,125.62,125.75,128.82,128.90,130.14,130.33,134.50, 138.64,144.76,155.88,156.25,158.48,158.61,164.38,171.75	3922,3433,2991,2915,2583,2325,2229,2095,1990,1655,1439,1415,1320,1035,965,885
4j	2-amino- 7hydroxy-4-(3-(3nitrophenyl)-1phenyl- 1H-pyrazol-4-yl)-4H- chromene- 3-carbonitrile	4.21(s-1H),5.43(s1H), 6.07-6.14 (m3H), 6.890-7.84 (m10), 8.19 (s-2H-NH_2)	21.13,55.54,103.90,106.21,106.89,106.93,112.88,118.55,120.60,123.65,125.62,125.75,128.02,128.50,130.44,130.53,134.60, 138.74,144.86,155.98,156.05,158.18,158.31,164.58,171.45	3927,3434,2993,2916,2587,2327,2225,2085,1995,1652,1434,1414,1307,1029,949,885

CONCLUSION

To summarise, we have demonstrated a novel three-component reaction that is catalysed by p-TSA. This reaction offers a straightforward approach to synthesise derivatives of 7-hydroxy-4H-chromene by employing pyrazole aldehydes, malononitrile, and resorcinol in a variety of solvents. It was discovered that ethanol was the greatest appropriate solvent. Because of its swifter and less aggressive reaction process, a high concentration of target compounds, eco-friendliness, ease of experimentation, and straightforward purification process, the current technique is an effective synthetic route for 7-hydroxy-4H-chromene. We want to do single-crystal XRD and assess different pharmacological actions related to derivatives of 7hydroxy-4H-chromene in future studies.

REFERENCE:-

1. Nasirmahale. L. N, Jolodar. O. G, Shirini.F, Tajik.H. *Polycycl Aromat Compd.*, 2021, 41, 199-210. https://doi.org/10.1080/10406638.2019.1576748
2. Sabouri. S, Abaszadeh. M. *Polycycl Aromat Compd.*, 2021, 41, 467-477. https://doi.org/10.1080/10406638.2019.1597381
3. Gupta.V, sahu.D, Jain.S, Vanka.K, Singh.R. P. *Org. Biomol. Chem.*, 2019, 17, 8853-8857. https://doi.org/ 10.1039/C9OB01345H.

4. Soares.M. I. L, Gomes.C. S. B, Nunes.S. C. C, Pais.A. A. C. C, Pinho e Melo.T. M. V. D. *Eur. J. Org. Chem.*, 2019, 2019, 5441-5451. DOI:10.1002/ejoc.201900564

5. Shabalala.N. G, Kerru.N, Maddila.S, vanzyl.W. E, Jonnalagadda.S. B. *Chem. Data Collect.*, 2020, 26, 100365.https://doi.org/10.1016/j.cdc.2020.100365

6. Dinparast.L, Valizadeh.H, Vessally.E, Bahadori.M.B. *J. Mol. Struct.*, 2016, 1105, 118127.https://doi.org/10.1016/j.molstruc.2015.10.044

7. Daloee.S, Behbahani.F. K. *Polycycl Aromat Compd.*, 2020, 42, 681689.https://doi.org/10.1080/10406638.2020.1749090

8. Najar.A. H, Hossaini.Z, Abdolmohammadi.S, Zareyee.D. *Polycycl Aromat Compd.*, 2022, 42, 5104-5122.https://doi.org/10.1080/10406638.2021.1926295

9. Satbhaiya.S, Khonde.N. S, Rathod.J, Gonnade.R, Kumar.P. *Eur. J. Org. Chem.*, 2019, 2019, 3127-3133.https://doi.org/10.1002/ejoc.201900370

10. Santhosh Kumar.K, Mohanty. S, Siddaiah.V, Lilakar.J. D, Ganesh.A. *Chem. Data Collect.*, 2020, 29, 100488.https://doi.org/10.1016/j.cdc.2020.100488

11. Vereshchagin.A. N, Elinson.M. N, Ryzhkov.F. V, Nasybullin.R. F, Bobrovsky.S. I, Goloveshkin.A. S, Egorov.M. P. *C. R. Chim.*, 2015, 18, 1344-1349.http://dx.doi.org/10.1016/j.crci.2015.02.005

12. Gaikwad.P, Kamble.S. *Curr. Res. Green Sustain. Chem.*, 2020, 3, 100014.https://doi.org/10.1016/j.crgsc.2020.100014

13. Khosravan.M, Abdolahi.L, Ebrahimipour.S. Y. *Inorg. Chem. Commun.*, 2021, 128, 108561.https://doi.org/10.1016/j.inoche.2021.108561

14. Mohammadi.P, Sheibani.H. *Mater. Chem. Phys.*, 2019, 228, 140-146. https://doi.org/10.1016/j.matchemphys.2018.11.058

15. Manake.A .P., Patil.S.R, Patil.V. *Mater. Today: Proc.*, 2020, 26, 34873491.https://doi.org/10.1016/j.matpr.2020.03.144

16. Kanti Das.S, Chatterjee.S, Mondal.S, Bhaumik.A. *Mol. Catal.*, 2019, 475, 110483.https://doi.org/10.1016/j.mcat.2019.110483 17. Elinson.M. N, Ryzhkov.F. V, Vereshchagin.A. N, Korshunov.A. D, Novikov.R. A, Egorov. M. P. *Mendeleev Commun.*, 2017, 27, 559–561.https://doi.org/10.1016/j.mencom.2017.11.006

18. Gonz´alez-Rodal.D, Turnes Palomino.G, Palomino Cabello.C, P´erez-Mayoral.E.

Microporous Mesoporous Mater., 2021, 323, 111232.https://doi.org/10.1016/j.micromeso.2021.111232

19. Li.L, Zeng.Q, Yang.Y, Hu.H.-F, Xu.M, Guan.Z, He.Y.-H. *J. Mol. Catal. B Enzym.*, 2015, 122, 1-7.http://dx.doi.org/10.1016/j.molcatb.2015.08.005
20. Dinparast.L, Hemmati.S, Akbar Alizadeh.A, Zengin.G, Samadi Kafil.H, Bahadori.M B, S.Dastmalchi. *J. Mol. Struct.*, 2020, 1203, 127426.https://doi.org/10.1016/j.molstruc.2019.127426