Original Article

Ag-CP Mofs Nano Material Catalysed Synthesis Of Xanthene Derivatives: A Valuable Heterogeneous Catalysis Approach Towards Sustainability

Amol Rangrao Suryawanshi[1], **Santosh A.Anantwad**[2], **Prof. Sayyad Hussain**[3*]

1, 2, 3* P.G.Dept of Chemistry, Sir Sayyed College, Roshangate, Aurangabad. (M.S)India University: Dr Baba saheb Ambedkar marathwada University Aurangabad Maharashtra M.S. India 431004

***Corresponding Author**: - Prof. Sayyad Hussain Sajjansab

*P.G.Dept of Chemistry, Sir Sayyed College, Roshangate, Aurangabad. (M.S) India University: Dr Baba saheb Ambedkar marathwada University Aurangabad Maharashtra M.S. India 431004, E-Mail id:drhussainsyyd@yahoo.com

DOI:10.47750/pnr.2023.14.S01.129

Abstract

An efficient one pot multicomponant approach for the synthesis of 1, 8-dioxo-octahydroxanthene derivatives. We have developed a novel method for the synthesis of series of bioactive heterocyclic compounds. **Ag-CP MOFs as** heterogeneous catalyst and use of Ethanol as a green solvent makes the protocol attractive from sustainability point of view. A highlight of our approach is easy separation of catalyst from the reaction medium and so on recyclability of the catalyst. This is simple method is applicable to access wide range of aromatic aldehydes for the synthesis of 1, 8-dioxo-octahydroxanthenes derivatives. The as synthesized derivatives were well characterized by ^{1}HNMR spectroscopy. The results show that the novel **Ag-CP MOFs as** heterogeneous catalyst was very efficient for the traditional reactions with good to excellent yields in short time.

Keywords: Heterogeneous catalyst, Ag-cp MOFs, 1, 8-dioxo-octahydroxanthene derivatives.

INTRODUCTION

Design and synthesis of series of polyfunctionalized heterocyclic moieties is of forthcoming interest, due to most of the application oriented materials, agrochemicals or cosmetics and dyes, catalysis, material science, medicinal field, are either marketed or under clinical trials are synthesized from bioactive natural and synthetic polycyclic heterocyclic lead molecules. [1-4]. Xanthenes and their derivatives are important among all polycyclic heterocyclic compounds containing oxygen atom, quite a lot of methodologies have been reported in the literature for the synthesis of 1,8-dioxooctahydro xanthenes using an array of catalysts and reagents [5]. Xanthenes contains pyran framework and it found that these are important core of natural products and also used as material in fluorescent dyes [6]. They are related with several biological functions such as antimalarial [7], anti-inflammatory [8], analgesic [9], antimicrobial [10], antioxidant [11], anticancer [12], antiviral [13] and also found to have therapeutic importance and can be used as an honored skeleton. They have been used as a P^H sensitive substance for visualization of biomolecules, laser technology and photodynamic therapy [14]. Besides this, they also find their application in dyes due to having high quantum yield and molecular extinction coefficient [15]. Due to their wide range of applications, the development of environmentally sustainable process which follows the principles of green chemistry is very necessary for the synthesis of 1, 8-dioxooctahydro xanthene derivatives. Synthesis of complex multifunctionalised organic compounds in outstanding yield and at more rapid reaction rate in only one step is possible by multicomponent reaction method. It is a powerful tool with simple reaction course and good atom frugality to make the process greener and hamper the waste by the use of safer reagents and green solvents as reaction media. [16, 17, 18].Thus, avoiding difficult purification processes without the formation of significant side products [19, 20].Taking into consideration environmental protection it necessary to design catalysts and catalysis processes. Many transition metals along with their good catalytic activities, they are limited in abundance, toxicity and high cost it is necessary to find alternate catalysts systems from first and second row transition metals. Recently silver based heterogeneous catalyst. Silver is a group IB transition metal with different morphology (nanobar, nanocubic, nanosphere etc) have been a popular functional material applied in many fields specially for heterogeneous catalysis due to its specific physical and chemical structure [21-32].

In continuation of our study towards the synthesis of bioactive heterocyclic compounds, a novel Ag-CP MOFs, has been prepared and applied as an efficient, novel, and heterogeneous magnetic nanocatalyst to synthesize 1, 8-dioxooctahydro xanthene derivatives **(Scheme 1)**. In addition, the experimental results displayed that Ag-CP MOFs could be recycled five times without significant loss of catalytic activity.

EXPERIMENTAL

Instruments and chemicals

Ag-CP MOFs, was prepared according to the procedure given in our previous paper [34]. All reactions were run in dried glassware. Reagents were purchased from Loba, Merck, SRL, Sigma Aldrich and Spectrochem and used without further purification. Melting points were recorded by open capillary method and uncorrected. The structure of synthesized 1, 8-dioxooctahydro xanthenes derivatives was characterized by ^{1}H NMR (400 MHz) spectra was recorded on a FT- NMR Brucker Advance II, 400 MHz spectrometer using either $CDCl_3$ or DMSO-d_6 as the solvent. Data are reported as follows: chemical shifts, multiplicity (s=singlet, d = doublet, t = triplet, m = multiplet), coupling constant (Hz). Thin-layer chromatography (TLC) was performed on GF-25U (Anal. Tech) plates and silica gel glass backed plates.

Present work:

We have explored the use of **Ag-CP MOFs** for the synthesis of 1, 8-dioxo-octahydroxanthenes the reaction proceeds in very superficial fashion to yield the product in a very good to excellent yield **Scheme 1.**

RESULTS AND DISCUSSIONS.

To study the scope and limitations of the method, several substituted monosubstituted, disubstituted and trisubstituted benzaldehydes, cinnamaldehyde, and, Dimedone a, were subjected to the reaction conditions and the results are presented in **Table 1**. Substituent on aromatic aldehyde was varied from electron donating to electron withdrawing and the impact of functional group was observed with respect to yield, reaction time and product purity. As is obvious from the **Table1** reaction with cinnamaldehyde or benzaldehydes proceed faster than with benzaldehyde and electronic factors have little or no effect on reaction and provide the corresponding product in high yield

To improve the yields and for the homogeneity of the reaction mixture, under solvent free conditions, it was found that in reaction at room temperature and 70°**C (Table 1 entry 1, 2)**. When checked the reaction with 5% of catalyst trace amount of product formation take place **(Table 1 entry 3)**, this is the effectiveness of catalyst. In order to study the effect of catalyst amount and effectives of solvent we started to use different solvents like methanol and ethanol, it was found that increased amount of catalyst and ethanol was the excellent solvent **(Table 1 entry 4, 5)**. In presence of solvents like acetonitrile, water, IPA, and dichloromethane there was only trace amount of product was formed or no product was formed **(Table 1 entry 6-9).** In presence of toluene as a solvent there was good amount of product formation take place **(Table 1 entry 10)**. It was found that use of 20 % of catalyst under reflux condition was the proved to be effective for good transformation to desired product **(Table 1 entry 11)**.

Table 1. Screening of reaction conditions for the synthesis of 1, 8-dioxo-octahydroxanthene derivatives

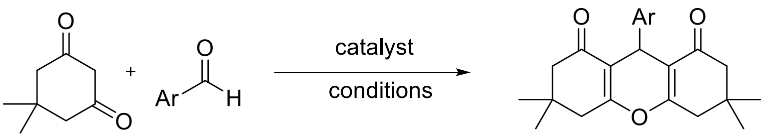
Entry	Catalyst (mol%)	Solvent	Temp (°C)	Time (min)	Yield^b (%)
1	0	Solvent-free	Room Temp.	200	0
2	0	Solvent-free	70	200	Trace
3	5	Solvent-free	70	15	60
4	10	CH_3OH	Reflux	30	60
5	10	C_2H_5OH	Reflux	30	95
6	10	CH_3CN	Reflux	40	Trace
7	10	H_2O	Reflux	120	0
8	10	IPA	Reflux	10	Trace
9	10	CH_2Cl_2	Reflux	15	Trace
10	10	Toluene	Reflux	15	65
11	20	Ethanol	Reflux	30	98

^{a}**Reaction conditions:** Dimedone (100 mg), benzaldehyde (1 equivalent), Ag-CP MOFs, EtOH as a solvent system with continuous stirring at reflux conditions.

Having established the ideal reaction conditions, the methodology was studied with a variety of substituted aromatic aldehydes and cinnamaldehyde the results are presented in **(Table 2).** This protocol tolerates well with electronically divergent aldehydes and cinnamaldehyde containing both electron donating and electron-withdrawing substituents such as –OMe and –NO_2 using Dimedone **(Table 2, entries 1-10).**

Ag-CP MOFs Catalysts reusability

Recycling of catalyst was examined using the condensation reaction of benzaldehyde, cinnamaldehyde and Dimedone using ethanol as a green solvent under reflux conditions. After the reaction was complete, the mixture was filtered and the residue was washed with DCM, and the catalyst was dried in air, and reused in the next reaction. The recycled catalyst could be reused several times without any appreciable loss in the catalytic activity of Ag-CP MOFs **(Table 1, entry 11).** Thus, various aromatic benzaldehyde, cinnamaldehyde and Dimedone under the optimized reaction condition for the preparation of 1, 8-dioxo-octahydroxanthenes derivatives **(Scheme 1).** The results are summarized in **Table 2**, which isolated yields using the appropriate reaction times. The products synthesized thus were obtained in high isolated yields and characterized by ^{1}H NMR, and melting point. Physical and spectral data of known compounds are in agreement with those reported in the literature. The possible mechanism indicates the formation of desired products in high of this conversion is shown in supporting information Scheme 1.



Scheme 1. Synthesis of Xanthene derivatives catalyzed by Ag-CP MOFs nano material

Table 2. Expansion of substrate scope for synthesis of 1, 8-dioxo-octahydroxanthene using Ag-CP MOFs as a catalyst.

Entry	Aldehyde	Product	Time (min)	Yield^b (%)	MP (obsd) (℃)	MP (lit) (℃)
1	2,4 Di-Cl- C_6H_3	3a	120	90	251-252	249-251[33]
2	4-Cl- C_6H_5	3b	35	95	229-230	231-232[33]
3	4-Br- C_6H_5	3c	90	90	240-242	240-241[33]
4	3-NO_2- C_6H_5	3d	120	80	167-168	166-167[33]
5	4-Me- C_6H_5	3f	35	95	215-216	214-215[33]
6	2,3,4-Tri-Ome- C_6H_2	3g	120	80	187-188	189-200[33]
7	4-OH- C_6H_5	3h	40	93	247-248	248-249[33]
8	-CH=CH-2-NO_2-C_6H_4	3i	120	85	198-199	200-201[33]
9	3,4-Di-Ome- C_6H_3	3j	125	83	179-180	177-178[33]

[a] **Reaction conditions:** benzaldehyde (1 equivalent), Dimedone (2 equivalent) Ag-CP MOFs (20 mol %), EtOH solvent system with continuous stirring at Reflux conditions.

General procedure for Preparation of 1, 8-Dioxo-Octahydroxanthene Derivatives:

General procedure for the heterogeneous Ag-CP MOFs **catalyst for synthesis of xanthene**

In a dry round bottom flask, Ag-CP MOFs (20 mol%), Dimedone (1mmol), aromatic aldehyde (1mmol) was mixed and stirred at reflux condition for specified time **(Table 2).** The progress of the reaction was monitored by TLC. After the completion of reaction, the reaction mixture was dissolved in ethanol and boiled. The undissolved Ag-CP MOFs was separated by simple filtration method. The filtrate was cooled down to 0-5℃ to precipitate the desired product which was separated again by simple filtration method. The obtained product was washed 2-3 times by ethanol to afford corresponding pure xanthene derivatives.

CONCLUSION

In summary, we have used inexpensive, non-toxic and readily available reagents, Ag-CP MOFs nanoparticles metal free heterogeneous catalyst for a mild and green synthesis of xanthenes derivatives compounds. These reaction conditions are contributing to the development of sustainable techniques in organic synthesis and to the straightforwardness of reactions with metal free heterogeneous catalyst. This nanocatalyst was found as an efficient catalyst for the synthesis of different industry important xanthenes and its derivatives under greener solvent conditions with excellent yields. Loading of Ag-CP MOFs nanoparticles which are far greater than already known metal-based heterogeneous catalysts which help in attaining this outstanding catalytic performance. Besides, the recyclability test confirmed that it can be reused for five repeated runs without substantial loss in catalytic usefulness. The additional reimbursement of the present catalyst includes cleanness, reaction time, yield, cost, and selectivity as compared to other catalysts available in literature for the same organic transformation. Furthermore, green solvent condition, ambient reaction conditions, faster synthesis, reasonably priced reactants, easy catalyst recovery, and recyclability make this methodology a impending candidate for sustainable synthesis

^{1}HNMR Spectral Data of synthesized Xanthene derivatives

^{1}HNMR of 9-(2,4-dichlorophenyl)-3,3,6,6-tetramethyl-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione (3a)

^{1}H-NMR (**$CDCl_3$**, 400 MHz): **δH** (ppm) = 1.00 (s, 6H), 1.11 (S, 6H), 2.47 (s, 4H), 4.69 (s, 1H), 2.16-2.27 (q, 4H, J = 24.8Hz), 7.18-7.32 (m,3H).

^{1}HNMR of 9-(4-dichlorophenyl)-3,3,6,6-tetramethyl-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione (3b)

^{1}H-NMR (**$CDCl_3$**, 400 MHz): **δH** (ppm) = 0.98(s, 6H), 1.10 (S, 6H), 2.14-2.25 (q, 4H, J = 28Hz), 2.46 (s, 4H), 4.71 (s, 1H), 7.17-7.26 (m, 3H).

^{1}HNMR of 9-(4-bromophenyl)-3,3,6,6-tetramethyl-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione(3c)

^{1}HNMR (**$CDCl_3$**, 400 MHz): **δH** (ppm) = 0.99 (s, 6H), 1.09 (S, 6H), 2.16-2.26 (q, 4H, J = 24.8Hz), 2.46(s, 4H), 4.66 (s, 1H), 6.53-6.55 (d, 2H, J = 8Hz), 7.05-7.07 (d, 2H, J = 8Hz)

^{1}HNMR of 2-amino-7,7-dimethyl-4-(3-nitrophenyl)-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (3d)

^{1}HNMR (**$CDCl_3$**, 400 MHz): **δH** (ppm) = 1.00 (s, 6H), 1.11 (s, 6H), 2.15-2.27 (q, 4H, J = 32 Hz), 2.51 (s, 4H), 4.84 (s, 1H), 7.39-7.43(t, 1H, J = 8Hz), 7.81-7.83 (d, 2H, J = 8Hz), 7.98-8.01 (t, 2H, J = 7.2 Hz)

^{1}HNMR of 3, 3, 6, 6-tetramethyl-9-(2, 3, 4-trimethoxyphenyl)-3,4,5,6,7,9-hexahydro-1H-xanthene-1, 8(2H)-dione (3g)

^{1}**HNMR** (**CDCl$_3$**, 400 MHz): δ**H** (ppm) = 1.03 (s, 6H), 1.11 (S, 6H), 2.19-2.28 (q, 4H, J = 20 Hz), 2.42-2.51 (q, 4H, J = 20 Hz), 3.77 (s, 3H), 3.80(s, 3H), 4.871 (S, 1H), 6.51 (s, 2H).

^{1}HNMR of 9-(4-hydroxyphenyl)-3,3,6,6-tetramethyl-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione (3h)
^{1}**HNMR** (**CDCl$_3$**, 400 MHz): δ**H** (ppm) = 0.98 (s, 6H), 1.10 (S, 6H), 2.14-2.25 (q, 4H, J = 28 Hz), 2.46 (s, 4H), 4.69 (s, 1H), 7.16-7.18(d, 2H, J = 8Hz), 7.32-7.34(d, 2H, J = 8Hz).

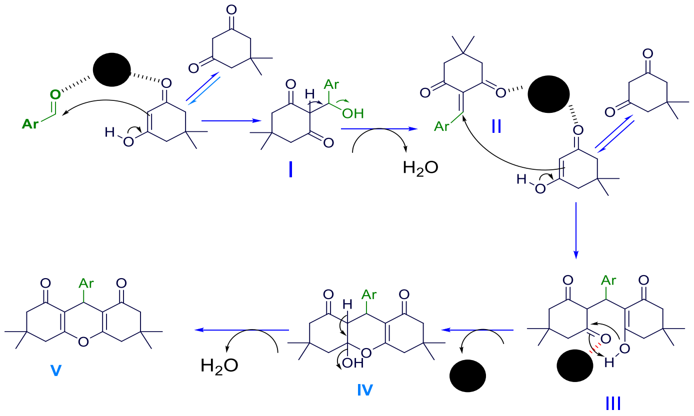
(E)-3,3,6,6-tetramethyl-9-(2-nitrostyryl)-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione 5f
^{1}**H-NMR** (**CDCl$_3$**, 400 MHz): δ**H** (ppm) = 1.12 (s, 12H), 2.27-2.36 (q, 4H, J = 20Hz), 2.40-2.52 (q, 4H, J = 28.8Hz), 4.38 (s,1H), 6.65-6.65 (d, 2H, J = 0.4Hz), 7.29-7.33 (t, 1H, J = 7.2Hz), 7.46-7.55 (m, 2H), 7.85-7.87 (d, 1H, J = 8Hz)

Ag-CP MOFs Nano Material Catalysed Synthesis of Xanthenes Derivatives: A Valuable Heterogeneous Catalysis Approach towards Sustainability

Table of contents

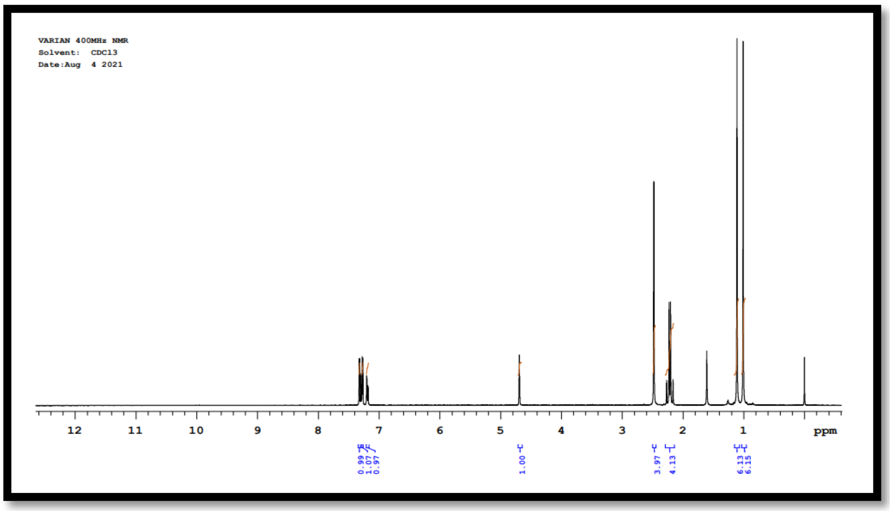
1.1Plausible mechanism for the formation of 1, 8-di-oxo-octahydroxanthenes derivatives

The plausible mechanism for the formation of 1, 8-di-oxo-octahydroxanthenes derivatives is given in scheme **S1** Ag-CP MOFs catalyze synthesis of xanthenes derivatives by activating the carbonyl group of aldehydes making it more susceptible to nucleophilic attack by 5,5-dimethyl-1,3-cyclohexanedione to form intermediate (I), followed by Michael addition of another molecule of 5,5-dimethyl-1,3-cyclohexanedione to form the intermediate (II), which reacts with 5,5-dimethyl-1,3-cyclohexanedione to form intermediate III. Intermediate III on intramolecular cyclization gives IV. IV with the successive elimination of water molecule results in the desired product V.

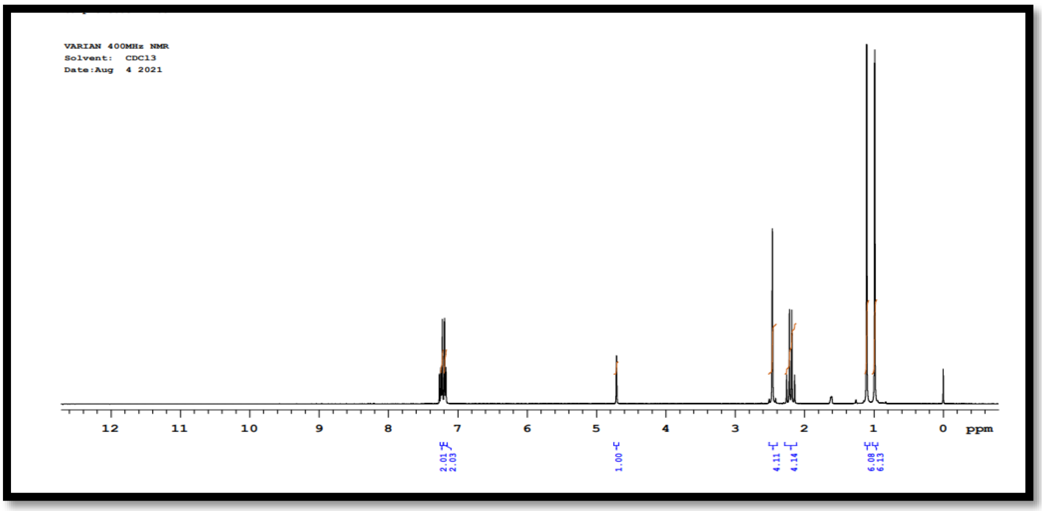


Scheme S1. Mechanism for Ag-CP MOFs catalysed synthesis of Xanthene derivatives.

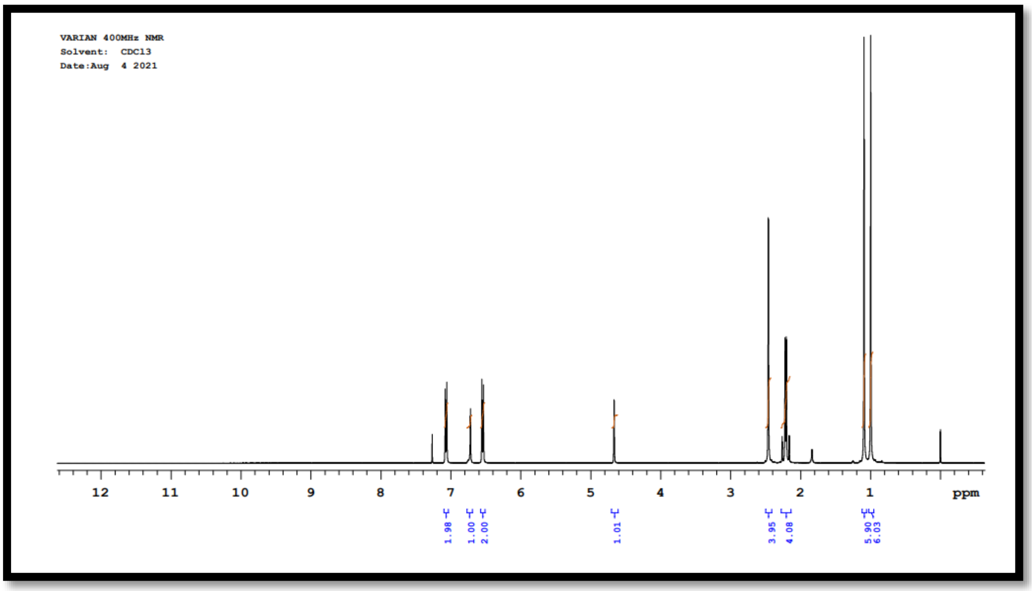
^{1}HNMR spectra of Xanthene Derivatives
^{1}HNMR of 9-(2,4-dichlorophenyl)-3,3,6,6-tetramethyl-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione (3a)



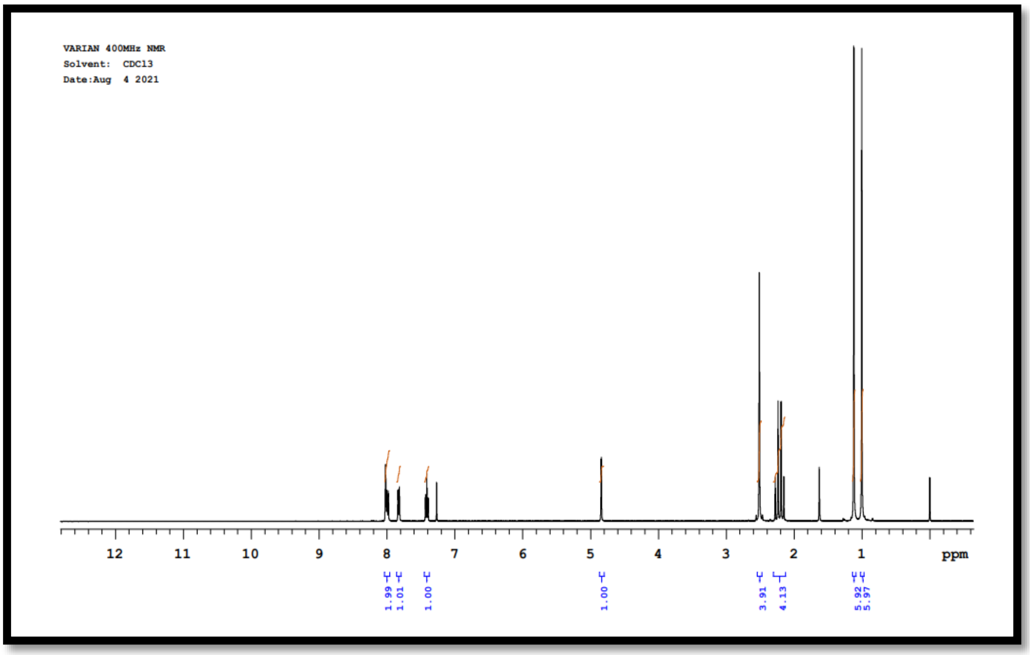
^{1}HNMR of 9-(4-dichlorophenyl)-3,3,6,6-tetramethyl-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione (3b)



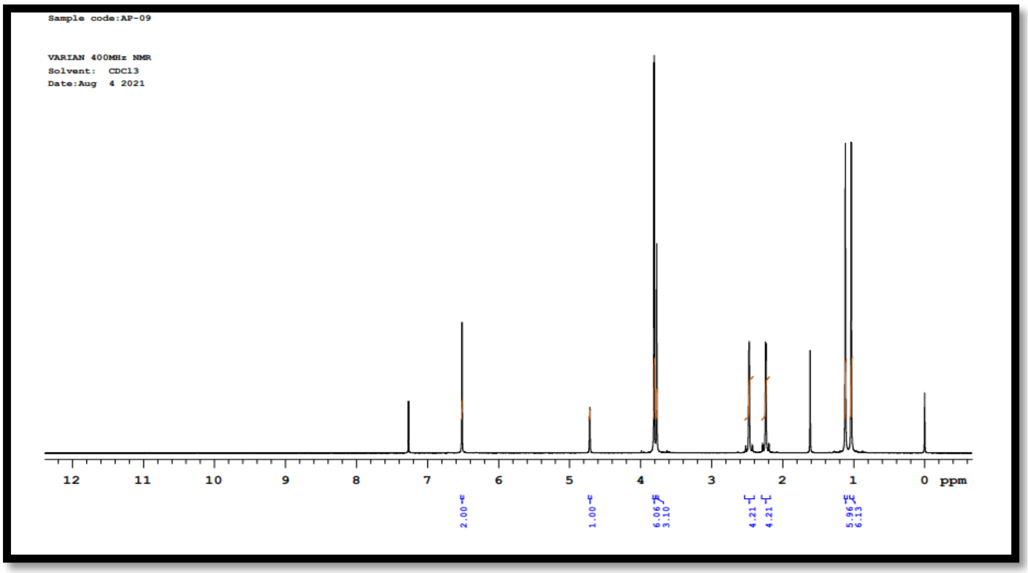
^{1}HNMR of 9-(4-bromophenyl)-3,3,6,6-tetramethyl-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione(3c)



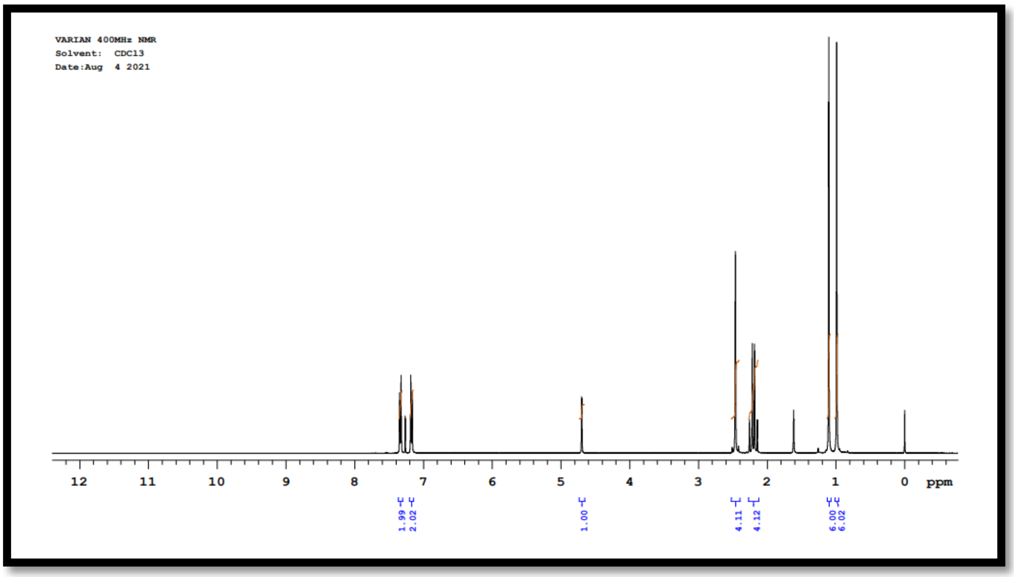
^{1}HNMR of 2-amino-7,7-dimethyl-4-(3-nitrophenyl)-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (3d)



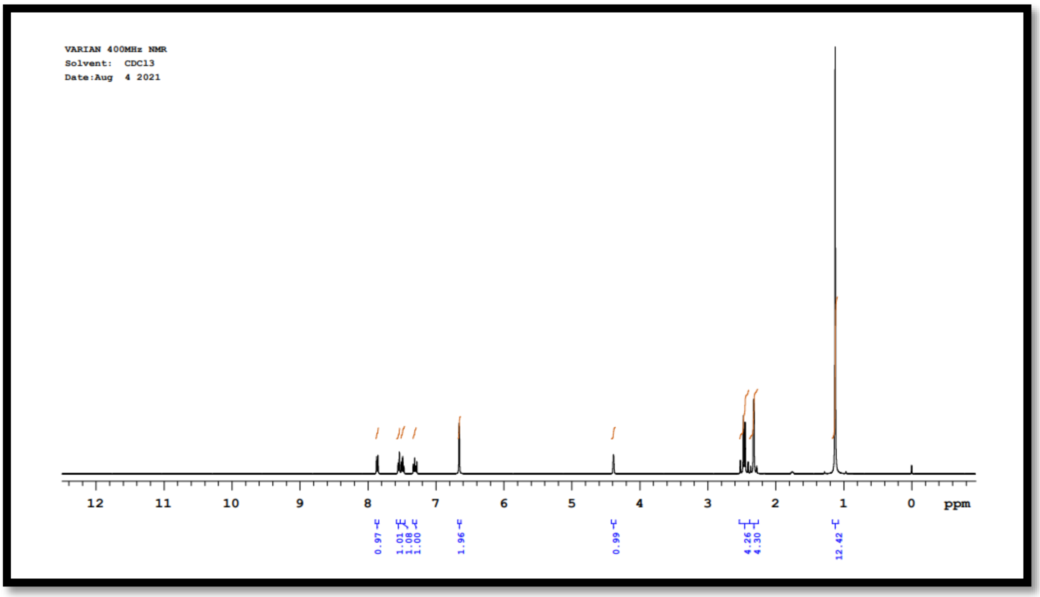
^{1}HNMR of 3, 3, 6, 6-tetramethyl-9-(2, 3, 4-trimethoxyphenyl)-3,4,5,6,7,9-hexahydro-1H-xanthene-1, 8(2H)-dione (3g)



^{1}HNMR of 9-(4-hydroxyphenyl)-3,3,6,6-tetramethyl-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione (3h)



(E)-3,3,6,6-tetramethyl-9-(2-nitrostyryl)-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione (3i)



REFERENCES

1. Martins, P.; Jesus, J.; Santos, S.; Raposo, L. R.; Roma-Rodrigues, C.; Baptista, P. V.;Fernandes, A. R. Heterocyclic anticancer compounds: Recent advances and theparadigm shift towards the use of nanomedicine's tool box. Molecules 2015, 20,16852-16891. (DOI: 10.3390/molecules 200916852)
2. Brahmachari, G. Green Synthetic Approaches for Biologically Relevant Heterocycles, Elsevier, Amsterdam, The Netherlands, 2015.
3. Vitaku, E.; Smith, D. T.; Njardarson, J. T. Analysis of the structural diversity, substitution patterns, and frequency of nitrogen heterocycles among U.S. FDAapproved pharmaceuticals. J. Med. Chem. 2014, 57, 10257-10274. (DOI:10.1021/jm501100b)
4. Brahmachari, G. Handbook of Pharmaceutical Natural Products, Wiley-VCH VerlagGmbH & Co. KGaA, Weinheim, Germany, Vol. 1 and 2, 2010.
5. Anand S. Burange1 · Komal G. Gadam1 · Prajyot S. Tugaonkar1 · Seema D. Thakur1 · Ravish K. Soni1 Rubej R. Khan1 · Mubashira S. Tai1 · Chinnakonda S. Gopinath2., Environmental Chemistry Letters (2021) 19:3283–3314.
6. Barmak, K. Niknam, G. Mohebbi, H. Pournabi, MicrobPathog2019, 130, 95.
7. K. Chibale, M. Visser, D. Van Schalkwyk, P. J. Smith, A. Saravanamuthu, A. H. Fairlamb, Tetrahedron 2003, 59, 2289.
8. T. S. Jin, L. B. Liu, Y. Zhao, T. S. Li, Synth Commun2005, 35, 2379.
9. Kumar, L. Rout, L. S. K. Achary, R. S. Dhaka, P. Dash, Sci Rep 2017, 7, 42975.
10. M. Kaya, E. Demir, H. Bekci, J EnzInhi Med Chem2013, 28, 885.
11. Ilangovan, K. Anandhan, K. M. Prasad, P. Vijayakumar, R. Renganathan, D. A. Ananth, T. Sivasudha, Med Chem Res 2015, 24, 344.
12. K. V. Sashidhara, A. Kumar, R. P. Dodda, B. A. Kumar, Tetrahedron Lett2012, 53, 3281.
13. H. N. Hafez, M. I. Hegab, I. S. Ahmed-Farag, A. B. A. El-Gazzar, Bioorg Med ChemLett2008, 18, 4538.
14. B. Das, P. Thirupathi, K. R. Reddy, B. Ravikanth, and L. Nagarapu, "An Efficient Synthesis of 1, 8-DioxooctahydroxanthenesUsing Heterogeneous Catalysts," Catalysis Communications 8, no. 3 (2007):535–38.
15. B. B. Bhowmik, P. Ganguly, SpectrochimActa Part A: MolBiomolSpect2005, 61, 1997.
16. R. Rahnamafar, L. Moradi, M. Khoobi, J Heterocyclic Chem2020, 57, 1825.
17. Shaabani, A. Rahmati, E. Farhangi, Tetrahedron Lett2007, 48, 7291.
18. T. A. Shah, Z. Ahmad, N. P. Rath, M. Muneer, Tetrahedron Lett2016, 57, 2368.
19. X. Xin, Y. Wang, S. Kumar, X. Liu, Y. Lin and D. Dong, Org. Biomol. Chem., 2010, 8, 3078.
20. W. Xiang-Shan, J. Zhou, K. Yang, and Z. Mei-Mei, Synth Commun., 2010, 40, 3332.
21. X.E. Verykios, F.P. Stein, R.W. Coughlin, Catal. Rev. Sci. Eng. 22 (1980) 197–234.
22. W. Grünert, A. Brückner, H. Hofmeister, P. Claus, J. Phys. Chem. B 108 (2004) 5709–5717
23. P. Claus, H. Hofmeister, J. Phys. Chem. B 103 (1999) 2766–2775.
24. M. Bron, D. Teschner, A. Knop-Gericke, F.C. Jentoft, J. Kröhnert, J. Hohmeyer, C. Volckmar, B. Steinhauer, R. Schlögl, P. Claus, Phys. Chem. Chem. Phys. 9 (2007) 3559–3569.
25. M. Steffan, A. Jakob, P. Claus, H. Lang, Catal. Commun. 10 (2009) 437–441.
26. Y. Chen, C. Wang, H. Liu, J. Qiu, X. Bao, Chem. Commun. (2005) 5298–5300.
27. H. Zhang, Q. Fu, Y. Yao, Z. Zhang, T. Ma, D. Tan, X. Bao, Langmuir 24 (2008) 10874–10878.
28. M. Kreich, P. Claus, Angew. Chem. Int. Ed. 44 (2005) 7800–7804.
29. K. Shimizu, K. Ohshima, A. Satsuma, Chem. Eur. J 15 (2009) 9977–9980.
30. T. Mitsudome, S. Arita, H. Mori, T. Mizugaki, K. Jitsukawa, K. Kaneda, Angew. Chem. 120 (2008) 8056–8058.
31. T. Mitsudome, A. Noujima, Y. Mikami, T. Mizugaki, K. Jitsukawa, K. Kaneda, Angew. Chem. 122 (2010) 5677–5680
32. M.J. Beier, T.W. Hansen, J.-D. Grunwaldt, J. Catal. 266 (2009) 320–330.
33. Kirsten Schuh, Wolfgang Kleist, Martin Høj, Vanessa Trouillet, Pablo Beato, Anker Degn Jensen and Jan-Dierk Grunwaldt., Catalysts 2015, 5, 1554-1573; doi:10.3390/catal5031554
34. Amol Rangrao Suryawanshi1 , Santosh A. Anantwad2 , Prof. Sayyad Hussain Sajjansab, Journal of Positive School Psychology, 2022, Vol. 6, No. 7, 2379-2387