



Synthesis of Xanthenediones by Silica Supported Orthophosphoric Acid ($\text{H}_3\text{PO}_4\cdot\text{SiO}_2$)

RAHUL S. PATIL^{1*}, SURESH S. SHENDAGE², UDAY P. LAD¹ and UTTAM B. MORE^{3,*}

¹Department of Chemistry, Yashwantrao Chavan College of Science, Karad-415 124, India

²KET'S Vinayak Ganesh Vaze College of Arts, Science and Commerce, Mithagar Road, Mulund (E), Mumbai-400 081, India

³Department of Chemistry, Sadguru Gadage Maharaj College, Karad-415 110, India

*Corresponding authors: Fax: +91 2164 271356; Tel: +91 2164 271356; E-mail: rspatilorg@gmail.com; uttambmore@rediffmail.com

Received: 5 June 2018;

Accepted: 16 July 2018;

Published online: 31 August 2018;

AJC-19071

The novel protocol was developed for the synthesis of xanthenediones by silica supported orthophosphoric acid ($\text{H}_3\text{PO}_4\cdot\text{SiO}_2$) as a heterogeneous catalyst. The reported protocol is simple, scalable, mild and effective for the synthesis of xanthenediones. The ($\text{H}_3\text{PO}_4\cdot\text{SiO}_2$) catalyst demonstrated excellent catalytic activity for various substituted aromatic aldehydes. This catalyst can be reused four times without much loss in catalytic activity.

Keywords: Xanthenediones, Heterogeneous catalysis, $\text{H}_3\text{PO}_4\cdot\text{SiO}_2$, Condensation reaction.

INTRODUCTION

In recent years the xanthene fascinated considerable interest to organic synthesis since it exhibits antibacterial, antiviral, anticoagulant, anticancer, diuretic, spasmolytic and anti-inflammatory properties [1,2]. Besides, these compounds have been explored for agricultural bactericidal activity and photodynamic therapy [3,4]. Xanthenediones are integral part of number of natural products [5]. The presence of pyran ring in xanthenediones makes it as versatile synthons [6]. Moreover, their applications are explored in cosmetics, pigments, laser technologies [7,8] and in fluorescent material for revelation of biomolecules [9,10].

In synthesis of xanthenediones, usually acid or base catalyzed condensation of suitable active methylene group containing carbonyl compounds with aldehydes is carried out [11]. In literature different methods have been reported for synthesis of xanthenediones such as condensation of active methylene compounds with aldehydes catalyzed by sulfuric acid or hydrochloric acid [12], $\text{TiO}_2/\text{SO}_4^{2-}$ [13], polyaniline *p*-toluenesulfonate [14], PPA- SiO_2 [15], Amberlyst-15 [16], Fe^{3+} -montmorillonite [17], $\text{NaHSO}_4\cdot\text{SiO}_2$ or silica chloride [18], cellulose-sulfuric acid [19], InCl_3 /ionic liquid [20], Dowex-50W [21], $\text{ZrOCl}_2\cdot 8\text{H}_2\text{O}_4$, trimethylsilyl chloride (TMSCl) [22], ω -4^o-ammoniumalkyl sulfonate [23], polytungstozincate acid [24]

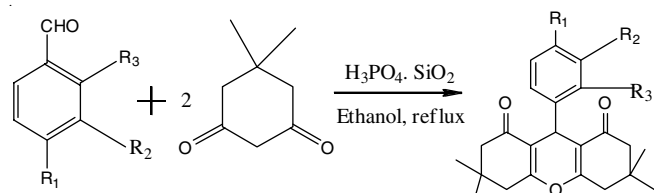
and cyanuric chloride [10]. However these methods require harsh reaction conditions, long reaction time, low yields, use toxic and expensive catalysts. So in preparation of xanthenediones, novel methods are desirable, which overcomes aforementioned drawbacks.

Heterogeneous catalysis has more advantages than homogeneous catalysis because in industrial practice, the removal of the product and recovery of the catalysts are comparatively easier. The development of nonmetallic heterogeneous catalyst is essential due to their advantage of nominal product contamination from metal release during reaction. Recently, silica supported catalysts such as $\text{HClO}_4/\text{SiO}_2$ [25], $\text{H}_3\text{PO}_4\cdot\text{SiO}_2$ [26] and ionic liquid prompted microwave irradiation [27] have been used by various research group for organic transformation.

Herein, we report silica supported orthophosphoric acid as a novel heterogeneous, reusable catalyst for synthesis of xanthenediones. To the best of our knowledge, catalyst ($\text{H}_3\text{PO}_4\cdot\text{SiO}_2$) has not been reported earlier for synthesis of xanthenediones (**Scheme-I**). This catalyst was found to be highly efficient, recyclable and environmentally benign for synthesis of xanthenediones.

EXPERIMENTAL

All commercially available reagents were used as received without further purification. ¹H NMR spectra were recorded



Scheme-I: Synthesis of xanthenediones by silica supported ortho- H_3PO_4

on a Bruker AC-400 (400 MHz) spectrometer with TMS as an internal standard.

Synthesis of silica supported orthophosphoric acid:

Silica supported orthophosphoric acid catalyst was prepared by reported method [26]. In typical procedure suspension of (5 g) SiO_2 in 30 mL chloroform was obtained. Then 3.5 g of orthophosphoric acid was added to above suspension of SiO_2 and stirred at room temperature for 2 h. This reaction mass was concentrated by heating at 100°C to get free-flowing powder. This powder was washed with water and finally with 50 mL of ethanol and dried at 110°C to get a desired catalyst.

General procedure for the synthesis of xanthenediones:

Aldehyde, dimedone (1:2 mmol) and 30 mg catalyst was refluxed at 80°C in ethanol. Completion of reaction was monitored on TLC. After completion of reaction, product was filtered to remove catalyst. Product was purified by column chromatography (ethyl acetate and petroleum ether). Product were characterized by melting points were compared with the literature and proved by spectroscopic data.

RESULTS AND DISCUSSION

Reaction between 4-methoxybenzaldehyde and dimedone was used as model reaction for optimization of reaction conditions (Table-1). As shown in Table-1, the reaction could proceed efficiently in presence of 30 mg silica supported orthophosphoric acid as heterogeneous catalyst (Table-1 entries 1-3). The reaction temperature effects on the yields of the products were studied by performing the condensation reaction at room temperature and reflux, respectively (Table-1 entries 4-6). The

TABLE-1
OPTIMIZATION OF REACTION PARAMETERS
FOR SYNTHESIS OF XANTHENEDIONES^a

S. No.	Solvent	Temp.	Time (min)	Catalyst amount (mg)	Yield ^b (%)
1	Ethanol	Reflux	30	30	94
2	Ethanol	Reflux	30	20	88
3	Ethanol	Reflux	30	10	70
4	Ethanol	Reflux	20	30	81
5	Ethanol	Reflux	10	30	45
6	Ethanol	Room temp.	30	30	16
7	Water	Reflux	30	30	31
8	DMSO	Reflux	10	30	61
9	DMF	Reflux	10	30	73

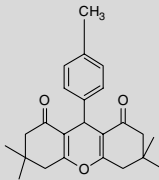
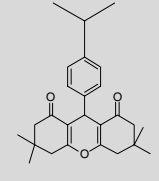
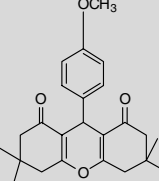
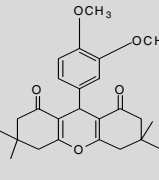
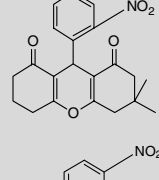
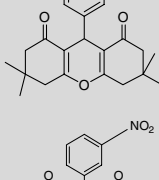
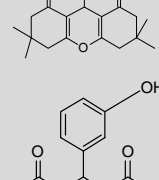
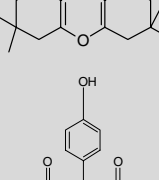
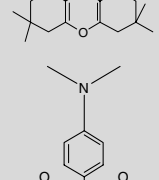
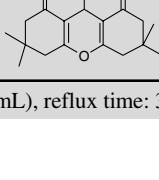
^aReaction condition: *p*-methoxy benzaldehyde (1 mmol), dimedone (2 mmol), Ethanol (5 mL), Catalyst ($\text{H}_3\text{PO}_4\cdot\text{SiO}_2$) and temperature reflux
^bIsolated yield.

results shows that the higher reaction temperature, the more efficiently the reaction could proceed. The various solvents such as water, DMSO, DMF and ethanol have been tried for these reaction Table-1 entries 7-9). The reaction gave high yield of corresponding product in presence of ethanol. The optimized reaction conditions are catalyst: 30 mg ($\text{H}_3\text{PO}_4\cdot\text{SiO}_2$), solvent: ethanol, time 30 min and temperature: reflux.

Then at above optimized conditions, various aldehydes were studied and the results are presented in Table-2. The catalyst ($\text{H}_3\text{PO}_4\cdot\text{SiO}_2$) was found to be worked effectively for substituted and unsubstituted benzaldehyde (Table-2 entries 1-13). Electron-withdrawing substituents bearing aromatic aldehydes reacted smoothly in short time as compared to electron donating substituents (Table-2 entries 3-13). We have also investigated activity of catalyst for cinnamaldehyde which

TABLE-2
SUBSTRATE STUDY

S. No.	R ₁	R ₂	R ₃	Time (min)	Product	Yield ^b (%)
1	H	H	H	30		94
2	H	H	H	30		91
3	Cl	H	H	40		92

4	CH_3	H	H	60		91
5	$\text{CH}(\text{CH}_3)_2$	H	H	80		89
6	OCH_3	H	H	45		93
7	OCH_3	OCH_3	H	60		89
8	H	H	NO_2	30		90
9	H	NO_2	H	60		86
10	NO_2	H	H	45		91
11	H	OH	H	70		85
12	OH	H	H	45		92
13	$\text{N}(\text{CH}_3)_2$	H	H	55		87

^aReaction conditions: Aromatic aldehyde (1 mmol), dimedone (2 mmol) $\text{H}_3\text{PO}_4\cdot\text{SiO}_2$ (30 mg), ethanol (2 mL), reflux time: 30 min. ^bIsolated yield.

TABLE-4
COMPARISON OF RESULTS USING (H₃PO₄:SiO₂) CATALYST WITH RESULTS OBTAINED BY OTHER WORKERS

S. No.	Catalyst	Reaction conditions	Time (min)	Yield (%)	Ref.
1	(H ₃ PO ₄ :SiO ₂)	Ethanol, reflux	30-80	85-94	This work
2	InCl ₃ .4H ₂ O	Ionic liquid/80 °C	240-600	76-95	[28]
3	Fe ³⁺ -montmorillonite	EtOH (reflux)	360	84-96	[29]
4	NaHSO ₄ -SiO ₂	CH ₃ CN (reflux)	360	90-98	[18]
5	Amberlyst-15	CH ₃ CN (reflux)	300	90-96	[16]

afforded 91 % yield of the corresponding product (Table-2 entry 2). All the reactions were monitored by TLC. The synthesized compounds were characterized by ¹H NMR, ¹³C NMR and DEPT-135 spectral techniques. Further structures of compounds were confirmed by FTIR spectroscopy.

In order to check usefulness of the catalyst for commercial applications, reusability of the catalyst was also investigated for model reaction (Table-3). After completion of the reaction, the reaction mixture was isolated with CH₂Cl₂. The catalyst was easily recovered by filtration after washing with ethyl acetate and drying at 80 °C. The recycled catalyst was used for the next. The decrease in product yield after 4th cycle could be due to leaching of the catalyst. Thus catalyst, (H₃PO₄:SiO₂) could be reused four times without any loss of its activity.

TABLE-3
REUSABILITY OF THE CATALYST^a

Run	1 st	2 nd	3 rd	4 th	5 th
Yield ^b	94	92	91	89	84

^aReaction conditions: Aromatic aldehyde (1 mmol), dimedone (2 mmol) H₃PO₄:SiO₂ (30 mg), ethanol (2 mL), reflux time: 30 min.
^bIsolated yield

The catalytic activity of our catalyst is compared with earlier reported catalyst for synthesis of xanthenedione (Table-4). The catalyst reported in this work is simple, more efficient and less time consuming compared with other reported catalysts.

Conclusion

In summary, the reported protocol is simple and effective for the synthesis of various substituted and unsubstituted xanthenediones. In addition to this, low-cost, easy availability, recyclability, low toxicity, stability of the catalyst, excellent yields of products and short reaction time make this protocol a viable contribution to the existing processes.

ACKNOWLEDGEMENTS

The authors are thankful for Instrumentation Department, Solapur University, Solapur, India for ¹H NMR analysis.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

REFERENCES

- Q.-B. Han, N.-Y. Yang, H.-L. Tian, C.-F. Qiao, J.-Z. Song, D.C. Chang, S.-L. Chen, K.Q. Luo and H.-X. Xu, *Phytochemistry*, **69**, 2187 (2008); <https://doi.org/10.1016/j.phytochem.2008.05.019>.
- N. Mulakayala, P.V.N.S. Murthy, D. Rambabu, M. Aeluri, R. Adepu, G.R. Krishna, C.M. Reddy, K.R.S. Prasad, *Bioorg. Med. Chem. Lett.*, **22**, 2186 (2012); <https://doi.org/10.1016/j.bmcl.2012.01.126>.
- A. Ilangovan, S. Muralidharan, P. Sakthivel, S. Malayappasamy, S. Karuppusamy and M.P. Kaushik, *Tetrahedron Lett.*, **54**, 491 (2013); <https://doi.org/10.1016/j.tetlet.2012.11.058>.
- E. Mosaddegh, M.R. Islami and A. Hassankhani, *Arab. J. Chem.*, **5**, 77 (2012); <https://doi.org/10.1016/j.arabjc.2010.07.027>.
- S. Hatakeyama, N. Ochi, H. Numata and S. Takano, *J. Chem. Soc. Chem. Commun.*, **0**, 1202 (1988); <https://doi.org/10.1039/C39880001202>.
- A. Thakur, A. Sharma and A. Sharma, *Synth. Commun.*, **46**, 1766 (2016); <https://doi.org/10.1080/00397911.2016.1226340>.
- O. Sirkecioglu, N. Talinli, A. Akar, M. Ahmad, T.A. King, D.K. Ko, B.H. Cha and J. Lee, *J. Chem. Res. (S)*, **35**, 502 (1995).
- M. Ahmad, T.A. King, D.K. Ko, B.H. Cha and J. Lee, *J. Phys. D Appl. Phys.*, **35**, 1473 (2002); <https://doi.org/10.1088/0022-3727/35/13/303>.
- J.F. Callan, P. De Silva and D.C. Magri, *Tetrahedron*, **61**, 8551 (2005); <https://doi.org/10.1016/j.tet.2005.05.043>.
- Z.-H. Zhang and X.-Y. Tao, *Aust. J. Chem.*, **61**, 77 (2008); <https://doi.org/10.1071/CH07274>.
- A. Pramanik and S. Bhar, *Catal. Commun.*, **20**, 17 (2012); <https://doi.org/10.1016/j.catcom.2011.12.036>.
- E.C. Horning and M.G. Horning, *J. Org. Chem.*, **11**, 95 (1946); <https://doi.org/10.1021/jo01171a014>.
- T.S. Jin, J.S. Zhang, A.Q. Wang and T.S. Li, *Synth. Commun.*, **35**, 2339 (2005); <https://doi.org/10.1080/00397910500187282>.
- A. John, P.J.P. Yadav and S. Palaniappan, *J. Mol. Catal. A*, **248**, 121 (2006); <https://doi.org/10.1016/j.molcata.2005.12.017>.
- S. Kantevari, R. Bantu and L. Nagarapu, *J. Mol. Catal. Chem.*, **269**, 53 (2007); <https://doi.org/10.1016/j.molcata.2006.12.039>.
- B. Das, P. Thirupathi, I. Mahender, V.S. Reddy and Y.K. Rao, *J. Mol. Catal. Chem.*, **247**, 233 (2006); <https://doi.org/10.1016/j.molcata.2005.11.048>.
- G. Song, B. Wang, H. Luo and L. Yang, *Catal. Commun.*, **8**, 673 (2007); <https://doi.org/10.1016/j.catcom.2005.12.018>.
- B. Das, P. Thirupathi, K.R. Reddy, B. Ravikanth and L. Nagarapu, *Catal. Commun.*, **8**, 535 (2007); <https://doi.org/10.1016/j.catcom.2006.02.023>.
- H.A. Oskooie, L. Tahershamsi, M.M. Heravi and B. Baghernejad, *E-J. Chem.*, **7**, 717 (2010); <https://doi.org/10.1155/2010/936107>.
- X. Fan, X. Hu, X. Zhang and J. Wang, *Can. J. Chem.*, **83**, 16 (2005); <https://doi.org/10.1139/v04-155>.
- J. Shakibaei, P. Mirzaei and A. Bazgir, *Appl. Catal. A*, **325**, 188 (2007); <https://doi.org/10.1016/j.apcata.2007.03.008>.
- S. Kantevari, R. Bantu and L. Nagarapu, *ARKIVOC*, 136 (2006); <http://dx.doi.org/10.3998/ark.5550190.0007.g15>.
- D. Fang, K. Gong and Z.-L. Liu, *Catal. Lett.*, **127**, 291 (2009); <https://doi.org/10.1007/s10562-008-9677-0>.
- M.M. Amini, Y. Fazaeh, Z. Yassaee, S. Feizi and A. Bazgir, *Open Catal. J.*, **2**, 40 (2009); <https://doi.org/10.2174/1876214X00902010040>.
- A. Khan, T. Parvin and L. Choudhury, *Synthesis*, 2497 (2006); <https://doi.org/10.1055/s-2006-942465>.
- A.D. Sawant, D.G. Raut, A.R. Deorukhkar, U.V. Desai and M.M. Salunkhe, *Green Chem. Lett. Rev.*, **4**, 235 (2011); <https://doi.org/10.1080/17518253.2010.544682>.
- A.N. Dadhanian, V.K. Patel and D.K. Raval, *J. Saudi Chem. Soc.*, **21**, S163 (2017); <https://doi.org/10.1016/j.jscs.2013.12.003>.
- J.P. Poupelin, G. Saint-Rut, O. Fussard-Blanpin, G. Narcisse, G. Uchida-Ernouf and R. Lacroix, *Eur. J. Med. Chem.*, **13**, 67 (1978).
- A. Sharifi, M.S. Abaee, A. Tavakkoli, M. Mirzaei and A. Zolfaghari, *Synth. Commun.*, **38**, 2958 (2008); <https://doi.org/10.1080/00397910802005299>.