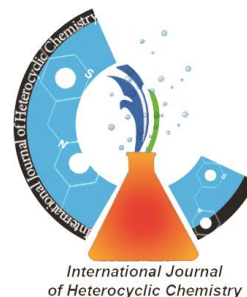

Research article

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Light promoted synthesis of 1,8-dioxooctahydroxanthenes using sulphated tin oxide as solid support catalyst

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Abstract

In the past few years multi component reactions have captured the attention of synthetic chemists as they provide easy access to diverse complex organic molecules through carbon - carbon and carbon - heteroatom bond formations in tandem manner with simple easy to carry out reaction conditions in short time. 1,8-dioxo-octahydroxanthene is a significant class of oxygen containing heterocycle in which a phenyl substituted pyran ring is fused on either side with two cyclohexanone rings and this unit constitutes in a number of natural products with wide range of therapeutic and pharmacological properties. The present paper describes house hold 100 watt bulb promoted multicomponent reaction between dimedone and various substituted cinnamaldehydes/ substituted benzaldehydes to afford the corresponding 1,8-dioxo-octahydroxanthene derivatives using sulphated tin oxide as solid supported catalyst. This green procedure using heterogenous

catalyst and light as source of energy provides facile access to a variety of 1,8-dioxo-octahydroxanthene derivatives in good to excellent yield.

Keywords: Light, solid acid, multicomponent reaction, 1,8-dioxo-octahydroxanthene, dimedone, substituted cinnamaldehyde

Introduction

Synthesis of novel heterocyclic moieties continues to occupy prominent position in organic chemistry owing to their important application in different fields. As a consequence multi component reaction strategies that provide facile access to complex/ diverse heterocycles continue to attract synthetic chemists with vast number of publications in this area [1]. Particularly, in the last four decades a number of three and four-component reactions have developed and their importance in synthesis of heterocycles have been well documented in reviews [2, 3].

Xanthene core and its derivatives serve as an important class of compounds as it is present in several bioactive natural products [4]. Among them 1,8-dioxo-octahydroxanthene is a significant class of oxygen containing heterocycle in which a phenyl substituted pyran ring is fused on either side with two cyclohexanone rings and this unit constitutes in a number of natural products[5]. Also Xanthenedione moiety has been endowed with a wide range of therapeutic and pharmacological properties [6]. Several functionalized 1, 8-dioxo-octahydroxanthene derivatives have been reported to possess several significant medicinal properties like anticancer [7], antimicrobial [8], anti-tubercular and anti-inflammatory [9], antiviral[10], and antiplasmodial [11]. Besides these, heterocyclic molecules have been widely used as agricultural bactericides [12], luminescent dyes[13], sensitizers in photodynamic therapy[14], constituents of cosmetics and pigments[15], in laser technology [16], pH sensitive fluorescent materials [17], potential drug candidates for the treatment of type 2 diabetes mellitus [18] and leishmanicidal agents[36]. There are several reported methods for the synthesis of 1,8-dioxo-octahydroxanthene derivatives employing aromatic aldehydes and 5,5-dimethyl-1,3-cyclohexanedione, in the presence of catalysts such as sulphuric acid or hydrochloric acid [19], silica /sulphuric acid [20], $\text{HClO}_4\text{-SiO}_2$ and PPA-SiO_2 [21], silica chloride and $\text{NaHSO}_4\text{-SiO}_2$ [22], ferric hydrogen sulfate [23], $\text{BiVO}_4\text{-NPs}$ [24], $\text{ZrOCl}_2\cdot 8\text{H}_2\text{O}$ [25], pentafluorophenyl ammonium triflate [26], ionic liquid[4, 27], phosphosulfonic acid[28], SmCl_3 [29], $[\text{Fe(III)(Salen)Cl}]$ [30], TiO_2 [31], tetrabutylammonium hydrogen sulphate

[32], DABCO[33], molecular iodine[7], citric fruit juices[9], trimethylsilyl chloride[34], *p*-toluene sulphonic acid[35], amberlite IR-120H[36], and diammonium hydrogen phosphate[37]. However, most of the reported methods have their own merits and demerits like strong acidic condition [19,20], long reaction times[22, 32,36,27], low yields[21], the use of excess reagents/catalysts [34], and harsh reaction condition [37]. Due to their wide applications, further refinement in the existing methods would of added advantage in terms of cost, availability of reagents and applicability to sensitive systems. In recent years visible light as source of energy to effect reactions under mild conditions has gained importance as green protocol and several reactions have been reported using visible light [38]. This type of photo-activation of substrate very often minimizes formation of by products and requires much less time in comparison to thermal methods. This aspect has been well explored by synthetic chemists in development of several photochemical reactions of synthetic significance [39-44].

Sulfated metal oxides with both Brønsted and Lewis acid sites are extensively used as solid supered catalyst [45-46] which are stable to moisture, air, and heat. Their preparation is simple and environmentally benign. It has the strongest acidity on the surface and being heterogenous catalyst, It can be easily recovered from the reaction mixture by simple filtration for re-use after activation. Thus the sulphated tin oxide is superior than other known acids. Sulfated tin oxide has a higher surface area as compare to aluminosilicates or Zeolites [47] and was found to be an efficient catalyst for several synthetic transformations [47, 48, 49, 50]. To, the best of our knowledge synthesis of 1,8-dioxo-octahydroxanthenes under photochemical reaction is not known. Here in we report synthesis of 1,8-dioxo-octahydroxanthenes with the effect of visible house hold 100watt bulb in the presence of sulphated tin oxide as catalyst.

Experimental

General: Sulfated tin oxide was prepared according to the literature report [51]. All reactions were run in dried glassware. Reagents were purchased from Loba, Merck, SRL, Signa Aldrich and Spectrochem and used without further purification. Melting points recorded by open capillary method and uncorrected. Reactions were irradiated by a 100W tungsten lamp (Philips India Ltd.). ¹HNMR and ¹³CNMR spectra were obtained in CDCl₃ on Bruker AV-300(300MHZ) spectrometers using TMS as an internal standard. IR spectra were recorded on Nicolet Fourier Transform spectrometer. Thin-layer

chromatography (TLC) was performed on GF-25U (Anal. Tech) plates and silica gel glass –backed plates.

Preparation of Sulfated Tin Oxide: 22.56gm of stannous chloride was dissolved in 200ml deionised water to get a clear solution. 25ml of aqueous ammonium hydroxide was added to this solution with stirring until pH 8. The yellowish precipitate thus obtained was washed well with deionised water, dried at 110°C for 12hours to get stannous hydroxide (18gms). 5gm of the dry hydroxide powder was then equilibrated with 25ml of 2N H₂SO₄ for 2hour and then it was evaporated to dryness and calcinated at 500 °C for 4hour to get the sulphated tin oxide.

General procedure for Preparation of 1,8-Dioxo-Octahydroxanthene Derivatives: A mixture of 1,3-cyclohexanedione, dimedone or 5-phenyl-1,3-cyclohexanedione(2mmol) and substituted cinnamaldehyde or substituted benzaldehyde (1mmol), sulphated tin oxide (0.05mmol) were taken in a round bottomed flask and irradiated with a 100W tungsten lamp (Philips India Ltd.). The reaction mixture was irradiated for specified time (see Table 1). The progress of the reaction was monitored by TLC. Upon completion of reaction, the mixture was dissolved in a suitable solvent, filtered to recover the catalyst and removal of solvent followed by chromatography afforded the product.

Results and Discussion

In a preliminary study, the mixture of cinnamaldehyde (1a) and 1,3- cyclohexanedione (2a) in 1:2 mole ratio and sulphated tin oxide (0.05mmole) was subjected to visible light. The progress of the reaction was monitored by TLC. The reaction was found to be complete in 10 minutes to afford 9-styryldecahydro-1H-Xanthene-1,8(2H)-dione (3a) in 95% yield. The structure of the product was confirmed by spectroscopy method. In ¹HNMR spectra the proton at the bridge between the two cyclohexanone rings appears as doublet in the region of 3.84-3.89 ppm and the bridge carbon appears around 39.43. This proton and carbon come from cinnamaldehyde, while absence of aldehyde proton at 9ppm confirms the bond formation between C-2 carbon of cyclohexanedione and aldehyde carbon. In ¹³CNMR the carbonyl group appear in the expected region around 195.3-197.2.

General scheme

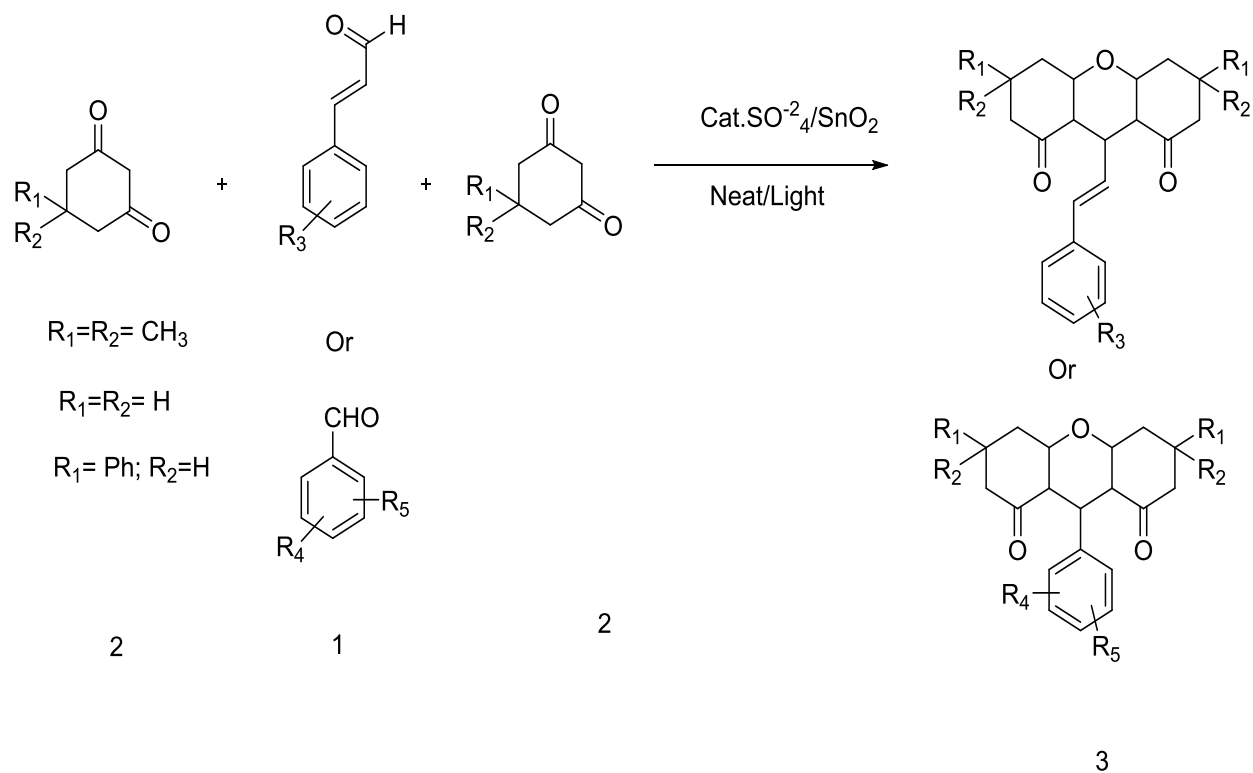
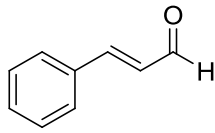
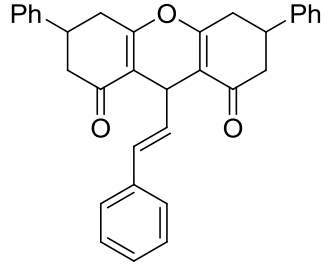
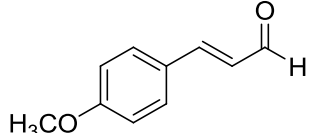
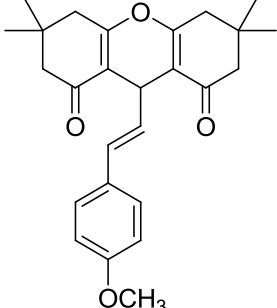
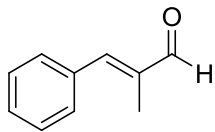
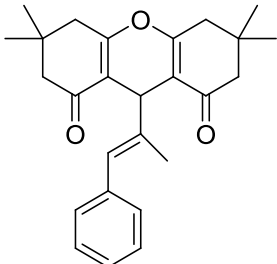
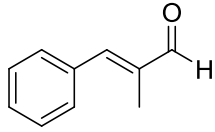
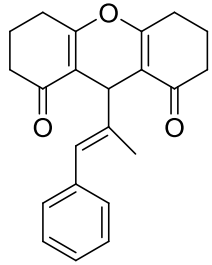
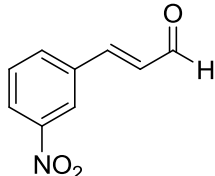
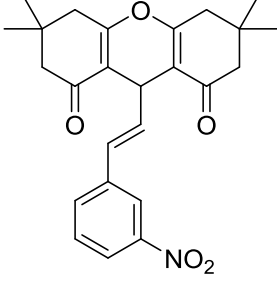
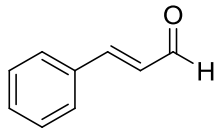
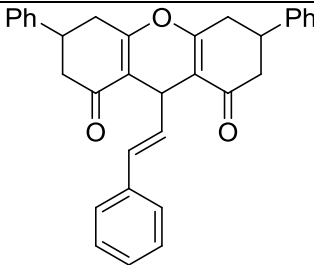
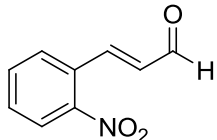
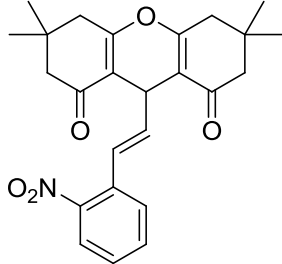
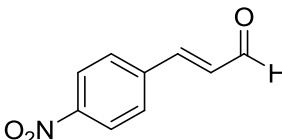
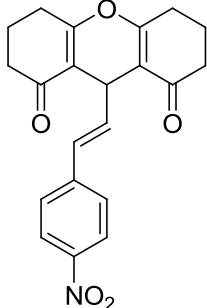
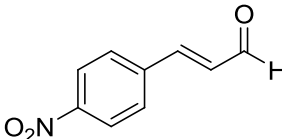
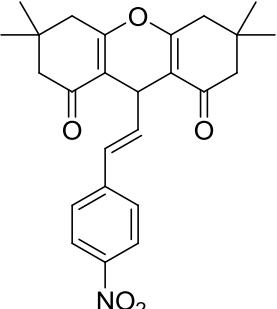
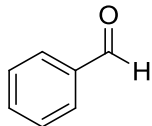
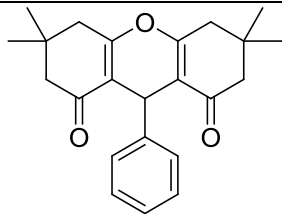
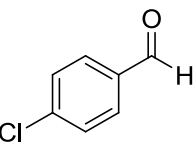
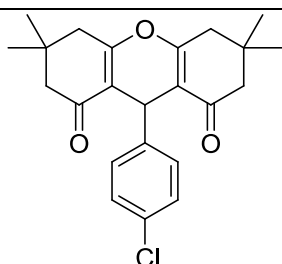


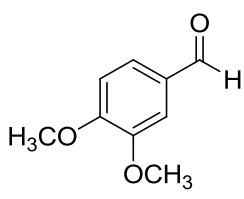
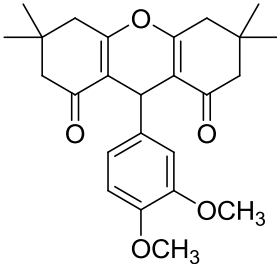
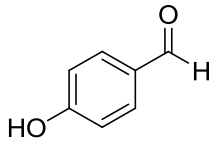
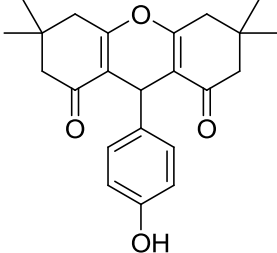
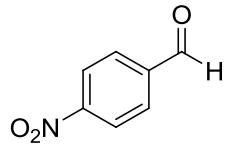
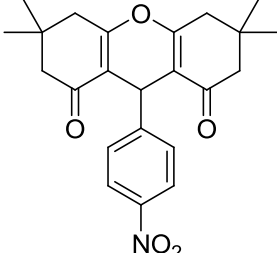
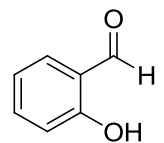
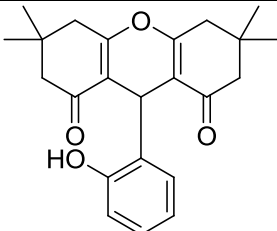
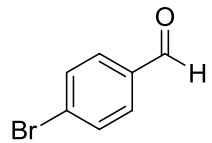
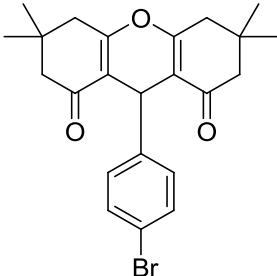
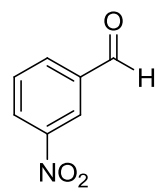
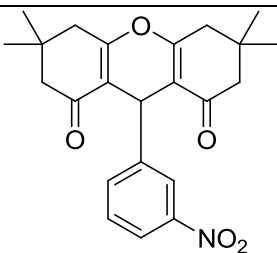
Figure 1. Synthesis of 1,8-dioxooctahydroxanthene derivatives under visible light using sulphated tin oxide as photocatalyst

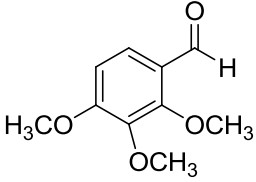
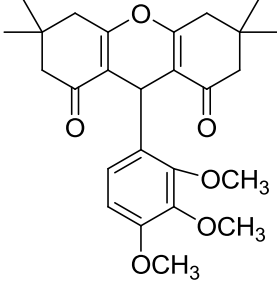
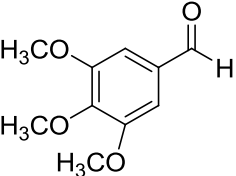
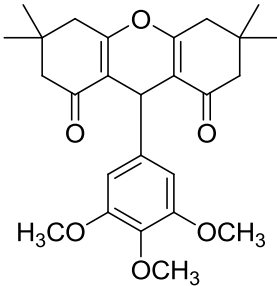
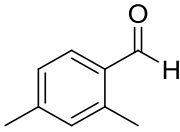
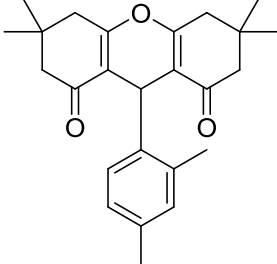
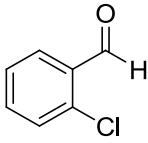
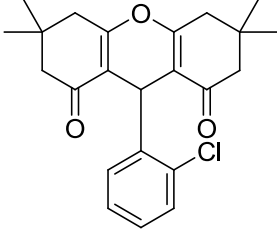
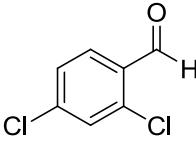
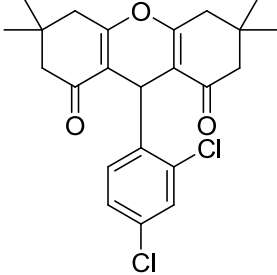
Table 1. Synthesis of 1,8-dioxooctahydroxanthene under visible light using sulfated tin oxide as photocatalyst^a

Entry	Reactant	Product	Time	% Yield ^b
1.			10 Min	95
2.			10 Min	95

3.			10 Min	93
4.			15 Min	90
5.			3 Hrs.	30
6.			3 Hrs	35
7.			25 Min	92

8.			15 Min.	80
9.			30 Min	85
10.			15 Min	92
11.			15 Min.	93
12.			1.5 Hrs.	95
13.			1 Hrs.	90

14.	 <chem>COc1cc(OC)c(C=O)cc1</chem>	 <chem>CC1(C)C(=O)C2=C(C1)OC(=C2)C3=CC(OC)C(OC)=C3C=O</chem>	2 Hrs.	75
15.	 <chem>Oc1ccc(C=O)cc1</chem>	 <chem>CC1(C)C(=O)C2=C(C1)OC(=C2)C3=CC(O)=CC=C3C=O</chem>	1.5 Hrs.	70
16.	 <chem>O=[N+]([O-])c1ccc(C=O)cc1</chem>	 <chem>CC1(C)C(=O)C2=C(C1)OC(=C2)C3=CC(=CC=C3)[N+](=O)[O-]C=O</chem>	2.5Hrs.	80
17.	 <chem>Oc1ccccc1C=O</chem>	 <chem>CC1(C)C(=O)C2=C(C1)OC(=C2)C3=CC(O)=CC=C3C=O</chem>	10 Min	95
18.	 <chem>Brc1ccc(C=O)cc1</chem>	 <chem>CC1(C)C(=O)C2=C(C1)OC(=C2)C3=CC(Br)=CC=C3C=O</chem>	30 Min	85
19.	 <chem>O=[N+]([O-])c1ccc(C=O)cc1</chem>	 <chem>CC1(C)C(=O)C2=C(C1)OC(=C2)C3=CC(=CC=C3)[N+](=O)[O-]C=O</chem>	2 Hrs.	70

20.			3 Hrs.	80
21.			2.5 Hrs.	75
22.			3 Hrs.	70
23.			2 Hrs.	75
24.			2 Hrs.	75

a: Reaction Conditions: 2mmole of 1,3-cyclohexanedione, 1mmole substituted cinnamaldehyde or substituted benzaldehyde, sulphated tin oxide (---mmol) irradiated with a 200W tungsten lamp; b: isolated yield after purification

Next to extend the scope of this reaction, the present method was studied with substituted cinnamaldehydes, monosubstituted, disubstituted and trisubstituted benzaldehydes and 1,3-cyclohexanedione, 5,5-dimethyl-1,3-cyclohexanedione and 5-phenyl-1,3-cyclohexanedione. Substituent on aromatic aldehyde was varied from electron donating to electron withdrawing groups. Cinnamaldehyde and substituted cinnamaldehydes react faster than benzaldehyde or substituted benzaldehydes. Nature of substituent does not seem to have any effect on reaction yield and the reaction proceeds well with all the substrates to afford the corresponding product in high yield.

It is presumed that the reaction proceeds through Knoevenagel condensation between diketone and aldehyde followed by Michael addition of enone to the adduct to afford the intermediate which undergoes intramolecular dehydrative cyclisation to afford the product. The role of catalyst sulphated tin oxide is being to promote enone formation and dehydration and hence accelerate the reaction in terms of time and yield. The light source provides the energy required to bring about the transformation,

Conclusion

We have established an efficient, absolutely clean and high yielding eco-friendly methodology, for the synthesis of 1,8-dioxo-octahydroxanthene under household lamp irradiation in the presence of sulphated tin oxide as solid supported catalyst. The merits of this method are high yield, easy to work out, short reaction time, minimal environmental impact, avoid use of toxic solvent, thus making it one of the attractive and practical protocols for the synthesis of xanthenediones.

References

- [1] A. Domling and I. Ugi, *Angew. Chem. Int. Ed.*, **39**, 3168, (2000).
- [2] A. Domling, W. Wang and K. Wang, *Chem. Rev.*, **112**, 3083, (2012).
- [3] B. Rotstein, S. Zaretsky, V. Rai and A. Yudin, *Chem. Rev.*, **114** (2014) 8323-8359.
- [4] A. Dadhania, V. Patel and D. Raval, *Journal of Saudi Chemical Society* (2014) <http://dx.doi.org/10.1016/j.jscs.2013.12.003>.
- [5] J. Negi, V. Bisht, P. Singh, M. S. M. Rawat and G. Joshi, *Journal of Applied Chemistry* vol. 2013, (2013) Article ID 621459 <http://dx.doi.org/10.1155/2013/621459>.
- [6] J. Fotie and D. Bohle, *Anti-Infective Agents in Medicinal Chemistry*, **5**, 15, (2006).
- [7] N. Mulakayala, P. V. N. S. Murthy, D. Rambabu, M. Aeluri, R. Adepu, G. Krishna, C. Reddy, K. R. S. Prasad, M. Chaitanya, C. Kumar, M. V. Basaveswara Rao and M. Pal, *Bioorganic and Medicinal Chemistry Letters*, **22**, 2186, (2012).
- [8] M. Kaya, E. Basar and F. Colak, *Med Chem Res*, **20**, 1214, (2011).
- [9] A. Napoleon and F. Khan, *Med Chem Res*, **23**, 4749, (2014).
- [10] J. Jamison, K. Krabill, A. Hatwalkar, E. Jamison and C. Tsai, *Biol Int Rep*, **14**, 1075, (1990).
- [11] W. Mahabusarakam, K. Kuaha, P. Wilairat and W. Taylor, *Planta Med*, **72**, 912, (2006).
- [12] A. Bhattachary and K. Rana, *Mendeleev Commun.*, **17**, 247, (2007).
- [13] O. Berndt, F. Bandt, I. Eichwurz and H. Stiel, *Acta Physica Polonica A*, **95**, 207, (1999).
- [14] D. Pellosi, V. Batistela, V. deSouza, I. Scarminio, W. Caetano and N. Hioka, *An.Acad. Bras.Ciênc*, **85**, 1267, (2013).
- [15] a) N. Uesugi, K. Furumiya and T. Mizutani, *Journal of Health science*, **52**, 549, (2006); b) T. Mizutani, *Journal of Environmental and Public Health*, **2009** (2009) Article ID 953952, <http://dx.doi.org/10.1155/2009/953952>.
- [16] E. Klimtchuk, M. A. J. Rodgers and D. Neckers, *J. Phys. Chem.*, **96**, 9817, (1992).
- [17] a) C. Knight and T. Stephens, *Biochem J.*, **258**, 683, (1989); b) J. Liu, Z. Diwu and W. Leung, *Bioorganic and Medicinal Chemistry Letters*, **11**, 2903, (2001).
- [18] Y. Kwon, P. Song, J. Yoon, J. Ghim, D. Kim, B. Kang, T. Lee, J. Kim, J. Choi, I. Youn, H. Lee and S. Ryu, *PLoS ONE*, **9**, (2014) e108771 <http://dx.doi.org/10.1371/journal.pone.0108771>.
- [19] E. Horing and M. Horing, *J. Org. Chem*, **11**, 95, (1946).
- [20] M. Seyyedhamzeh, P. Mirzaei and A. Bazgir, *Dyes Pigment*, **76**, 836, (2008).
- [21] R. Kantevari, R. Bantu and L. Nagarapu, *J. Mol. Catal. A: Chem.*, **269**, 53, ((2007).

- [22] B. Das, P. Thirupathi, K. Reddy, B. Ravikanth and L. Nagarapu, *Catal. Commun.*, **8**, 535, (2007).
- [23] H. Shaterian, A. Hosseinian and M. Ghashang, *Turk J Chem*, **33**, 233, (2009).
- [24] A. Shoja, F. Shirini, M. Abedini and M. Zanjanchi, *J Nanostruct Chem*, **4**, 110, (2014) <http://dx.doi.org/10.1007/s40097-014-0110-5>.
- [25] H. Lü, J. Li and Z. Zhang, *Appl. Organometal. Chem.*, **23**, 165, (2009).
- [26] S. Khaksar and N. Behzadi, *Chinese Journal of Catalysis*, **33**, 982, (2012).
- [27] a) X. Fan, X. Hu, X. Zhang and J. Wang, *Canadian Journal of Chemistry*, **83**, 16, (2005); b) X. Fan, Y. Li, X. Zhang, X. Hu and J. Wang, *Chin. Chem. Lett.*, **16**, 897, (2005); c) J. Ma, C. Wang, Q. Wu, R. Tang, H. Liu and Q. Li, *Heteroatom Chem.*, **19**, 609, (2008).
- [28] A. Kiasat, A. Mouradzadegan and S. Saghanezhad, *J. Serb. Chem. Soc.*, **78**, 1291, (2013).
- [29] A. Ilangovan, S. Malayappasamy, S. Muralidharan and S. Maruthamuthu, *Chemistry Central Journal*, **5**, 81, (2011) <http://dx.doi.org/10.1186/1752-153X-5-81>.
- [30] H. Khabazzadeh, I. Sheikshoaie and N. Sotudeh, *Journal of Sciences, Islamic Republic of Iran*, **24**, 123, (2013).
- [31] S. Kumari, A. Shekhar and D. Pathak, *Chemical Science Transactions*, **3**, 652, (2014).
- [32] H. N. Karade, M. Sathe and M. Kaushik, *Arkivoc*, **xiii**, 252, (2007).
- [33] P. Paliwal, S. Jetti, A. Bhatewara, T. Kadre and S. Jain, *ISRN Organic Chemistry* **2013** (2013) Article ID 526173, <http://dx.doi.org/10.1155/2013/526173>.
- [34] S. Kantevari, R. Bantu and L. Nagarapu, *Arkivoc*, 136, (2006).
- [35] M. Bayat, H. Imanieh and S. Hossieni, *Chin. J. Chem.*, **27**, 2203, (2009).
- [36] M. Nisar, I. Ali, M. Shah, A. Badshah, M. Qayum, H. Khan, I. Khan and S. Ali, *RSC Adv.*, **3**, 21753, (2013).
- [37] F. Darviche, S. Balaie, F. Chadegani and P. Salehi, *Synth. Commun.*, **37**, 1059, (2007).
- [38] R. Pal, *International Journal of Advanced Chemistry*, **2**, 27, (2014).
- [39] N. Hoffmann, *Chemical Reviews*, **108**, 1052, (2008).
- [40] M. Fagnon, D. Dond, D. Ravell and A. Albin, *Chemical Reviews*, **107**, 2725, (2007).
- [41] J. Lalevée, F. Morlet-Savary, C. Dietlin, B. Graff and J.-P. Fouassier, *Molecules*, **19**, 15026, (2014).
- [42] M. Majek, A. Jacobi and von Wangelin, *Angew. Chem. Int. Ed.*, **52**, 5919, (2013).
- [43] W. Fu, F. Xu, Y. Fu, M. Zhu, J. Yu, C. Xu and D. Zou, *J. Org. Chem.*, **78**, 12202, (2013).

- [44] T. McCallum, E. Slavko, M. Morin and L. Barriault, *Eur. J. Org. Chem.*, **1**, 81, (2015).
- [45] K. Arata, *Green Chemistry*, **11**, 1719, (2009).
- [46] J. Deutsch, H. Prescott, D. Müller, E. Kemnitz and H. Lieske, *Journal of Catalysis* **231**, 269, (2005).
- [47] S. Sarda, V. Puri, A. Rode, T. Dalawe, W. Jadhav and R. Pawar, *Arkivoc*, **xvi**, 246, (2007).
- [48] V. Narayana, P. Zubaidha and R. Varala, *Org. Communication*, **6**, 110, (2013).
- [49] S. Dake, M. Khedkar, G. Irmale, S. Ukalgaonkar, V. Thorat, S. Shintre and R. Pawar, *Synthetic Communications*, **42**, 1509, (2012).
- [50] R. Magar, P. Thorat, V. Thorat, B. Patil and R. Pawar, *Chinese Chemical Letters*, **24**, 1070, (2013).
- [51] S. P. Chavan, P. K. Zubaidha, S. D. Dantle, A. Keshavaraja, A. V. Ramaswamy and T. Ravindranathan, *Tetrahedron Letters*, **37**, 233, (1996).