Silicotungstic Acid: An Efficient and Ecofriendly Catalyst for Synthesis of 12-Aryl / Alkyl-8,9,10,12-Tetrahydrobenzo[a]xanthen-11-one derivatives

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Abstract

An efficient, one-pot, condensation of 2-naphthol, aldehydes and dimedone catalyzed by silicotungstic acid has been accomplished for the synthesis of series of 12-aryl / alkyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-ones under solvent free condition at 60°C. The present methodology offers several advantages such as high yields, short reaction time, mild condition, ecofriendly catalyst and easy work up procedure.

Keywords: Heteropolyacid, Silicotungstic acid, Benzoxanthenes, Multicomponent reaction.

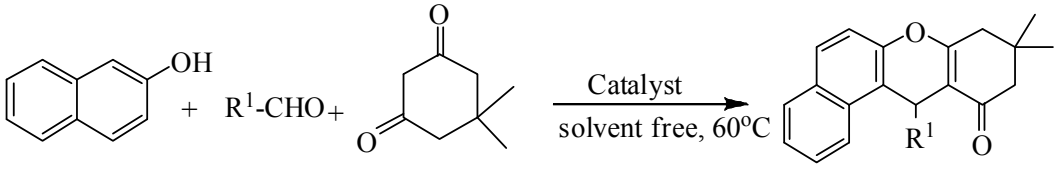
Introduction

Due to super acidic properties of solid heteropolyacids (HPAs), in the last three decades, heteropolyacids have found numerous applications as useful and versatile acid catalyst for some acid catalysed reactions [1]. They are usually solids that are insoluble in non-polar solvents but highly soluble in polar ones. They can be used as in bulk or supported forms in both homogenous and heterogeneous systems. Furthermore, heteropolyacids have several advantages, including high flexibility on modification of the acid strength, ease of handling, environmental compatibility, non toxicity and experimental simplicity [2]. In the recent years, the use of solid acids as heterogeneous catalyst has received considerable attention in different areas of organic synthesis [3]. The use of HPAs as a catalyst makes the process convenient and environmentally benign. Heteropolyacids found to exhibit excellent catalytic properties in the dehydration of diols [4], rearrangements [5], tetrahydropyranylation of alcohols [6], Friedel-Craft alkylation [7], Prins reaction [8], synthesis of dihydroquinolines [9], pyrimidine synthesis [10], Biginelli reaction [11] and Dakin-West reaction [12].

Xanthenes and benzoxanthenes are important biologically active heterocycles. They possess anti-inflammatory [13], antiviral [14] and antibacterial activities [15]. Some of them have been used as antagonists for paralysing the action of zoxazolamine [16] and in photodynamic therapy (PDT) [17], is method of treating tumours by combined use of photosensitizer and light. In this method photosensitizers are injected directly into malignant tissue and by using specific wavelength light excites photosensitizer drug, this causes killing the tumour cells. Furthermore these compounds can be employed as dyes [18], pH sensitive fluorescent materials for visualization of biomolecules [19] and in laser technology [20]. In a view of great importance of benzoxanthenes various methods for synthesis of 12-aryl / alkyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-ones has been reported in presence of $NaHSO_4$-SiO_2 under reflux in halogenated solvent [21], strontium triflate [22], $InCl_3$ and P_2O_5 under solvent free condition [23], PTSA in ionic liquid as well as solvent free condition [24]. Even though various reported methods shows varying degree of success and limitations such as, prolonged reaction time, use of toxic solvents, use of excess catalyst / reagents, expensive catalyst and high temperature. To avoid these limitations, the

discovery of new and efficient catalyst with catalytic activity, short reaction time and simple workup is of prime interest.

As a part of our research programme directed towards development of highly expedient methods [25-31], we herein disclose an efficient, environmentally benign, one pot synthesis of 12-aryl / alkyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one from 2-naphthol, aldehyde and dimedone catalyzed by silicotungstic acid under solvent free condition at 60°C. (**Scheme 1**).



1 **2** **3** **4a-q**

Scheme1. Reaction of 2-naphthol, benzaldehyde and dimedone

Experimental Section

General procedure for synthesis 12-aryl / 8, 9, 10, 12-tetrahydrobenzo[a]xanthen-11-one

Silicotungstic acid (2 mol%) was added to a mixture of 2-naphthol (1.0 mmol), benzaldehyde (1.0 mmol) and dimedone (1.2 mmol) in round bottom flask, heated at 60°C under solvent free condition. After completion of reaction (TLC), flask was cooled to room temperature, methanol was added, stirred for 15 min poured over crushed ice, precipitated product was filtered and recrystallized from methanol.
Spectral data of products given below

9,9-dimethyl-12-phenyl-9,10-dihydro-8H-benzo[a]xanthen-11(12H)-one (4a): White solid**;** mp 151-153 °C; IR (KBr, cm^{-1}): 3055, 2954, 2884, 1651, 1374, 1229, 1178, 1076, 811; ^{1}H NMR (DMSO-d^6, 400 MHz): δ = 8.06 (d, *J* = 8.4 Hz, 1H), 7.76-7.80 (m, 2H), 7.32-7.50 (m, 5H), 7.02-7.20 (m, 3H), 5.71 (s, 1H), 2.61 (s, 2H), 2.34 (d, *J* = 16 Hz, 1H), 2.15 (d, *J* = 16 Hz, 1H), 1.06 (s, 3s), 0.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 197.2, 164.0, 148.1, 142.1, 135.5, 131.3, 131.0, 129.4, 128.5, 128.2, 127.8, 127.0, 125.2, 123.7, 117.6,m 117.2, 114.0, 50.8, 41.3, 34.3, 32.6, 29.0, 27.1, 20.8; Mass: m/z = 355 [M+1].

12-(4-methoxyphenyl)-9,9-dimethyl-9,10-dihydro-8H-benzo[a]xanthen-11(12H)-one (4m): White solid; mp 203-205 °C; IR (KBr, cm^{-1}): 3057, 2949, 1643, 1227, 1172, 1024; ^{1}HNMR (DMSO-d^6, 400 MHz,): δ = 8.10 (d, *J* = 8.4 Hz, 1H), 7.95 (d, *J* = 8.4 Hz, 1H), 7.40-7.52 (m, 4H), 7.18 (d, *J* = 8 Hz, 2H), 6.75 (d, *J* = 8 Hz, 2H), 5.56 (s, 1H), 3.65 (s, 3H), 2.70 (d, *J* = 17.6, 1H), 2.61 (d, *J* = 17.6 Hz, 1H), 2.34 (d, *J* = 16 Hz, 1H), 2.15 (d, *J*= 16 Hz, 1H), 1.07 (s, 3H), 0.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 197.0, 163.3, 160.8, 156.2, 136.4, 135.5, 130.3, 129.5, 129.0, 128.8, 126.5, 124.1, 123.8, 120.5, 118.9, 116.8, 111.6, 60.0, 57.6, 52.0, 29.8, 28.7, 28.5, 18.4; Mass: m/z = 385 [M+1].

12-(2,4-dichlorophenyl)-9,9-dimethyl-9,10-dihydro-8H-benzo[a]xanthen-11(12H)-one (4f): White solid; mp 179-180 °C; IR (KBr, cm^{-1}): 3058, 2952, 2869, 1652, 1396, 1227, 1103,1024, 751; ^{1}H NMR (DMSO-d^6, 400 MHz): δ = 8.09 (d, *J* = 8.4 Hz, 1H), 7.94-7.91 (m, 2H), 7.56-7.40 (m, 4H), 7.33-7.26 (m, 2H), 5.80 (s, 1H), 2.73 (d, *J* = 17.6 Hz, 1H), 2.59 (d, *J* = 17.6 Hz, 1H), 2.34 (d, *J* = 16 Hz, 1H), 2.11 (d, *J* = 16 Hz, 1H),1.07 (s, 3H), 0.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 198.8, 167.4, 155.2, 143.6, 136.0,

133.6, 132.8, 131.2, 130.6, 128.4, 128.2, 127.3, 126.0, 123.5, 122.0, 119.2, 115.5, 110.0, 58.4, 49.7, 27.6, 27.5, 20.8, 17.2; Mass: m/z = 423 [M+1].

12-(3-bromophenyl)-9,9-dimethyl-9,10-dihydro-8H-benzo[a]xanthen-11(12H)-one (4h): White solid; mp 176-178 ^{o}C; IR (KBr, cm^{-1}): 3125, 2954, 2864, 1649, 1228, 1025, 812, 748; ^{1}H NMR (DMSO-d^{6}, 400 MHz): δ = 8.04 (d, *J* = 8.4 Hz, 1H), 7.94 (d, *J* = 8.4 Hz, 1H), 7.89 (s, 1H), 7.53-7.42 (m, 4H), 7.27-7.12 (m, 3H), 5.60 (s, 1H), 2.70 (d, *J* = 17.6 Hz, 1H), 2.55 (d, *J* = 17.6 Hz, 1H), 2.34 (d, *J* = 16 Hz, 1H), 2.15 (d, *J* = 16 Hz, 1H), 1.06 (s, 3H), 0.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 199.1, 165.4, 156.2, 144.8, 136.1, 132.2, 131.6, 130.3, 129.4, 128.8, 127.9, 127.2, 125.5, 124.0, 123.0, 122.6, 120.0, 117.4, 110.5, 57.2, 48.7, 29.9, 27.3, 27.1, 18.5; Mass: m/z = 435 [M+2].

9,10-dihydro-9,9-dimethy-12-p-tolyl-8H-benzo[a]xanthen-11(12H)-one (4l): White solid; mp 176-178 ^{o}C; IR (KBr, cm^{-1}): 3071, 2949, 2865, 1648, 1512, 1375, 1233, 1072, 816; ^{1}H NMR (DMSO-d^{6}, 400 MHz): δ = 8.02 (d, *J* = 8.4 Hz, 1H), 7.90 (d, *J* = 8.4 Hz, 1H), 7.50-7.40 (m, 4H), 7.16 (d, *J* = 8 Hz, 2H), 6.94 (d, *J* = 8 Hz, 2H), 5.52 (s, 1H), 2.73 (d, *J* = 17.6 Hz, 1H), 2.59 (d, *J* = 17.6 Hz, 1H), 2.34 (d, *J* = 16 Hz, 1H), 2.11 (d, 16 Hz, 1H), 2.10 (s, 3H), 1.06 (s, 3H), 0.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 195.2, 167.0, 164.8, 148.1, 144.2, 137.4, 132.5, 129.8, 128.0, 127.6, 127.0, 126.6, 124.4, 123.0, 119.2, 118.4, 116.3, 38.9, 34.8, 28.1, 27.1, 20.8, 20.0; Mass: m/z = 369 [M+1].

Results and Discussion

In this paper, we herein disclose an efficient and environmentally benign process for the synthesis of 12-aryl / alkyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one derivatives by multicomponent one pot condensation of 2-napthol, aldehydes and dimedone catalyzed by silicotungstic acid under solvent free condition at 60^{o}C. The products were obtained in high yield within short reaction time with simple work up.

Table 1. Condensation reaction catalyzed by different catalyst[a]

Entry	Catalyst	Condition	Time (min / h)	Yield[b]
1	H_2SO_4-SiO_2	Reflux	10 h	35
2	$ZnCl_2$	Reflux	8 h	42
3	CAN	Reflux	5 h	35
4	$H_4[SiW_{12}O_{40}]$ (2 mol%)	Reflux	8 h	72
5	$H_4[SiW_{12}O_{40}]$ (2 mol%)	60^{o}C / Solvent free	33	90
6	$H_4[SiW_{12}O_{40}]$ (1 mol%)	60^{o}C / Solvent free	50	75
7	$H_4[SiW_{12}O_{40}]$ (5 mol%)	60^{o}C / Solvent free	30	84
8	--	60^{o}C / Solvent free	48	20
9	$H_4[SiW_{12}O_{40}]$ (2 mol%)	80^{o}C / Solvent free	30	90

[a]Reaction condition: 2-naphthol (1.0 mmol), benzaldehyde (1.0 mmol) and dimedone (1.2 mmol) in acetonitrile. [b]Isolated yield.

Initially, we investigated the reaction of 2-naphthol, benzaldehyde and dimedone using different catalyst at reflux (Table 1). It was found that silicotungstic acid found to be good catalyst (Table 1, entry 4). However very long reaction time prompted us to carry out the reaction under solvent free condition at 60^{o}C the reaction proceeds smoothly, clean reaction with exclusively desired product **4a** (Table 1, entry 5) in short reaction time and excellent yield. Latter on we also studied effect of catalyst loading on

reaction time, we found that 2 mol% catalyst was sufficient to give excellent yield, further increase in amount of catalyst showed no appreciable increase in yield (Table 1, entry 5), we also carried the reaction in the absence of catalyst at 60°C for 48 h (Table 1, entry 8) it was found that only 20% conversion of product. Advantage of catalyst is environmentally benign, all the reactions were clean without any side products, easy to handle and simple work up procedure.

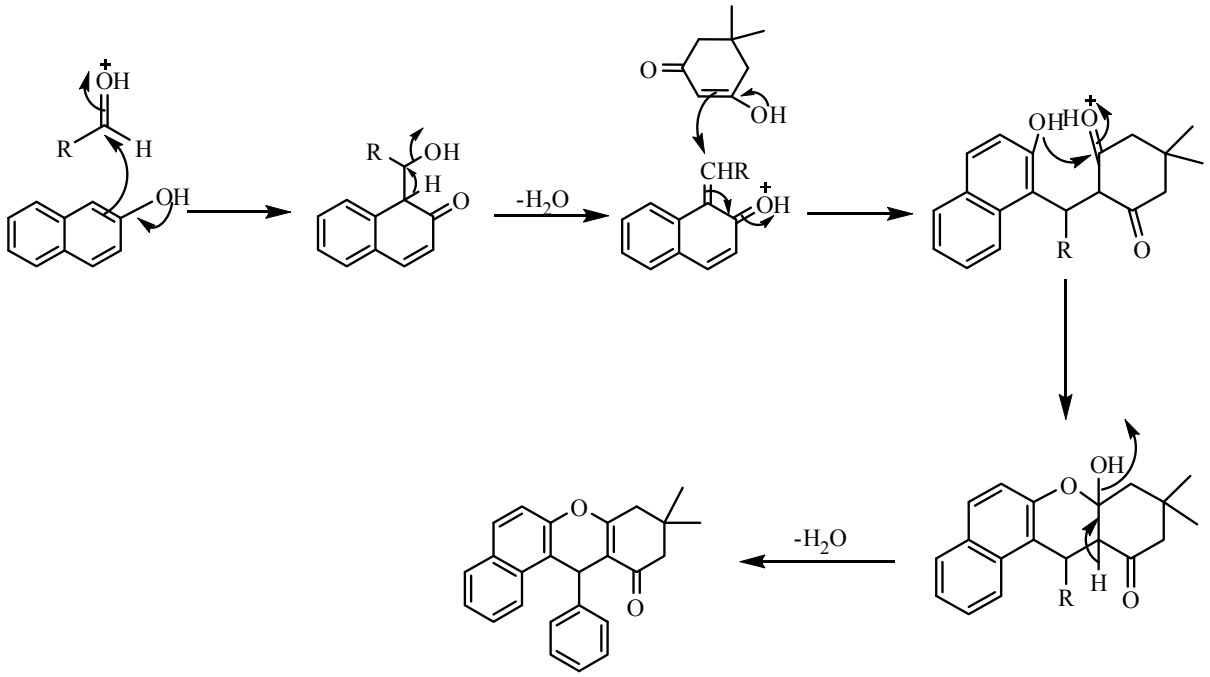
With the optimized conditions to show the generality of the reaction, we extended our study to different aromatic and aliphatic aldehydes to prepare series of 12-aryl / alkyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-ones (**Table 2**).

Table 2. Synthesis of 12-aryl / alkyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one derivatives using silicotungstic acid.

Entry	R^1	Product	Time (min)	Yield (%)[b]
1	C_6H_5	**4a**	33	90
2	o-$NO_2C_6H_4$	**4b**	40	80
3	m-NO_2 C_6H_4	**4c**	35	85
4	p-NO_2 C_6H_4	**4d**	30	89
5	m-Cl C_6H_4	**4e**	30	89
6	2,4-Cl_2 C_6H_3	**4f**	27	92
7	p-Cl C_6H_4	**4g**	32	88
8	m-Br C_6H_4	**4h**	33	90
9	o-Br C_6H_4	**4i**	40	83
10	2,4-F_2 C_6H_3	**4j**	25	93
11	p-FC_6H_4	**4k**	30	88
12	p-$CH_3C_6H_4$	**4l**	42	86
13	p-$OCH_3C_6H_4$	**4m**	40	87
14	o-OHC_6H_4	**4n**	33	90
15	p-OHC_6H_4	**4o**	40	80
16	CH_3CH_2	**4p**	50	71
17	$CH_3(CH_2)_4$	**4q**	55	74

[b] Isolated yields.

In all cases the corresponding benzoxanthenes were obtained in good to excellent yields. However aromatic aldehydes having electron withdrawing groups (Table 2, entries 2-11) require short reaction time than those counterpart electron donating groups (Table 2, entries 12-15), further meta and para substituted aromatic aldehydes gave excellent yield while ortho substituted aldehydes gave good yields with exception of **4f** (Table 2, entry 6) and **4j** (Table 2, entry 10). On the other hand, aliphatic aldehydes (Table 2, entries 16-17) also gave desired product in good yield. The plausible mechanism for formation of 12-aryl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one derivatives in presence of silicotungstic acid is proposed in scheme 2. The advantages of this methodology are mild reaction condition, short reaction time and high yield, very easy work up procedure and ecofriendly catalyst. We feel that this economically viable procedure will find practical utility for synthesis of novel xanthenes.



Scheme 2. Proposed mechanism for the formation of 12-aryl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one derivative

References

[1] Kozhhevnikov, I.V. *Chem. Rev*. **1989**, 98, 171-198.

[2] Kozhhevnikov, I.V. in; E. Derouane (Ed.), *Catalysis for Fine Chemical Synthesis*, *Catalysis by Polyoxometalates 2*, Wiley New York, 2002;

[3] Clark, J.H. *Acc. Chem. Res*. **2002**, 35, 791-797.

[4] Torok, B.; Bucsi, I.; Beregszászi, T.; Kaposci, I.; Molnar, A. *J. Mol. Cat A: Chem.* **1996,** 107, 305-311.

[5] Torok, B.; Bucsi, I.; Beregszászi, T.; Kapocsi, I. Molnar, A. *Catalysis of Organic Reactions,* Marcel Dekker, New York*,* 1996, 393.

[6] Molnar, A.; Beregszászi, T. *Tetrahedron Lett*. **1996**, 37, 8597-8600.

[7] Beregszászi, T.; Torok, B.; Molnar, A. Olah, G.A.; Prakash, G.K.S. *Catalysis Lett*. **1997**, 42, 83-87.

[8] Molnar, A.; Keresszegi, C.S.; Beregszászi, T.; Torok, B.; Bartok, M. *Catalysis of organic reactions*, Marcell Dekker, New York 1998, 507.

[9] Kamakshi, R.; Reddy, B.S.R. *Catalysis Commun*. **2007**, 8, 825-828.

[10] Heravi, M.M.; Sadjadi, S.; Oskooie, H.A.; Shoar, R.H.; Bamoharram, F.F. *Tetrahedron Lett*. **2009**, 50. 662-666.

[11] Rafiee, E.; Shahbhazi, F. *J. Mol. Cat A: Chemical*. **2006**, 250, 57-61.

[12] Rafiee, E.; Shahbhazi, F.; Joshaghani, M.; Tork, F. *J. Mol. Cat A: Chemical*. **2005**, 242, 129-134.

[13] Poupelin, J.P.; Saint-Ruf, G.; Foussard-Blanpin, O.; Marcisse, G.; Uchida-Ernouf, G.; Lacroix, R. *Eur. J. Med. Chem.* **1978**, 13, 67.

[14] Lambert, R.W.; Martin, J.A.; Merrett, J.H.; Parkes, K.E.B.; Thomas, G.J. PCT Intl Appl. W09706178, 1997.

[15] Hideo, T.; Teruomi, J. (Sankyo Co) Jpn. Patents 5, 600, 5480, 1981.
[16] Saint-Rauf, G.; Hieu, H.T.; Poupelin, J.P. *Naturwissenschaften*. **1975,** 62, 584-585.
[17] Ion, R.M.; Frackowaik, D.; Planner, A.; Wiktorowicz, K. *Acta Biochim Pol*. **1998**, 45, 833-846.
[18] Banerjee, A.; Mukherjee, A.K. *Stain Technol***. 1981**, 56, 83-85.
[19] Knight, C.G.; Stephens, T. *Biochem. J*. **1989**, 258, 683-687.
[20] Ahmed, M.; King, T.A.; Ko, D.K.; Cha, B.H.; Lee, J.J. *Phy. D: Appl Phys*. **2002**, 35, 1473.
[21] Das, B.; Laxminarayana, K.; Krishnaiah, M.; Srinivas, Y. *Synlett* **2007**, 20, 3107- 3112.
[22] Li, J.; Tang, W.; Lu, L.; Su, W. *Tetrahedron Lett*. **2008,** 49, 7117-7120.
[23] Nandi, G.C.; Samai, S.S.; Ram, K.; Singh, M.S. *Tetrahedron* **2009**, 65, 7129-7134.
[24] Gao, S.; Tsai, C.H.; Yao, Ching-Fa. *Synlett* **2009**, 6, 949-954.
[25] Bandgar, B.P.; Korbad, B.L.; Patil, S.A.; Bandgar, S.B.; Chavan, H.V.; Hote, B.S. *Aust .J. Chem*. **2008**, 61, 700.
[26] Chavan, H. V.; Babar, S, B.; Hoval, R. U.; Bandgar, B. P. *Bull. Korean Chem. Soc.* **2011**, *32,* 3963;
[27] Chavan, H. V.; Adsul, L. K.; Bandgar, B. P. *J. Chem. Sci.* **2011**, *123*, 477
[28] Bandgar, B. P.; Korbad, B. L.; Patil, S. A.; Bandgar, S. B.; Chavan, H. V.; Hote, B. S. *Aust. J. Chem.* **2008**, *61*, 700.
[29] Chavan H. V.; Bandgar, B. P. *ACS Sustainable Chem. Eng.* **2013**, 1, 929−936
[30] Dhakane, V. D.; Gholap, S. S.; Deshmukh, U. P.; Chavan, H. V.; Bandgar, B. P. *C. R. Chimie* **2014**, 17, 431–436
[31] Jalde, S. S.; Chavan, H. V.; Adsul, L. K.; Dhakane, V. D.; Bandgar, B. P. *Synthesis and Reactivity in Inorganic, Metal-Organic, and Nano-Metal Chemistry*, **2014**, 44, 623-626.