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Boric acid as a highly efficient and reusable catalyst for the one-pot synthesis of *1,8*-dioxo-octahydroxanthenes under solvent-free conditions

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ABSTRACT

An efficient and simple procedure for the synthesis of 1,8-dioxo-octahydroxanthenes from the aromatic aldehydes and 5,5-dimethylcyclohexane-1,3-dione (dimedone) in the presence of boric acid [BO_3H_3 or $B(OH)_3$] as an inexpensive and reusable catalyst is described. The salient features of this methodology are: the elimination of corrosive liquid acids, high yields, simple methodology, short reaction times, easy work-up and green heterogeneous catalyst.

***Keywords**: Boric acid, Aromatic aldehyde, Dimedone, Solid acid, One-pot reaction, Xanthenes.*

1. Introduction

Xanthenes especially benzoxanthenes are an important class of organic compounds that attracted the attention of organic chemists because of their wide range of biological and pharmaceutical properties such as: anti inflammatory [1], antiviral activity [2] and agricultural bactericide activity [3]. Furthermore, these compounds are very important in the industry because they are used as a local-dyes [4], in fluorescent material for visualization of biomolecules [5], Photodynamic therapy (PDT) [6] and in laser technologies [7]. Various methods have been reported for the synthesis of benzoxanthenes, including cyclodehydrations [8-12], trapping of benzynes by phenols [13], cyclocondensation between 2-hydroxyaromatic aldehydes and 2-tetralone [14] intra molecular phenyl carbonyl coupling reactions of benzaldehydes and acetophenones [15] and cyclization of polycyclic aryltriflate esters [16]. Various reagents and catalyst have been employed for the synthesis of benzoxanthenes such as heteropolyacid [17-18], $K_5COW_{12}O_{40}.3H_2O$ [19], molecular iodine [20-21], silca sulfuric acid [22-23] dowex-50w_3 [24], Ferric Hydrogen Sulfate [25], Triethylamine-bonded sulfonic acid [26] and montmorillonite K10 [27].

Most of the reported methods for the synthesis of the xanthenes derivatives are associated with one or more of the following drawbacks such as long reaction times, the use of toxic organic solvents, strong acidic conditions, moderate or low yields, the use of large amounts of catalyst, harsh reaction conditions, and excessive use of reagents and catalysts. Recently, boric acid has gained special attention as catalyst in organic synthesis because the excellent solubility in water, uncomplicated handling, inexpensiveness, eco-friendly nature and readily available [28-30].

In this research, boric acid as an efficient and reusable catalyst has been used for the one-pot preparation of *1,8*-dioxo-octahydroxanthene derivatives via condensation between various aromatic aldehydes with dimedone under solvent-free and thermal conditions (Scheme 1).

2. Experimental

2.1. General

All reagents were purchased from Aldrich (USA) or Merck Fine Chemicals and were used without further purification. Products were separated and purified by different chromatographic techniques and were identified by the comparison of their IR and NMR with those reported for the authentic samples. The IR spectra of the compounds were obtained on a Perkin-Elmer spectrometer (USA), version 10.03.06 using a KBr disk. The nuclear magnetic resonance (^{1}H NMR)

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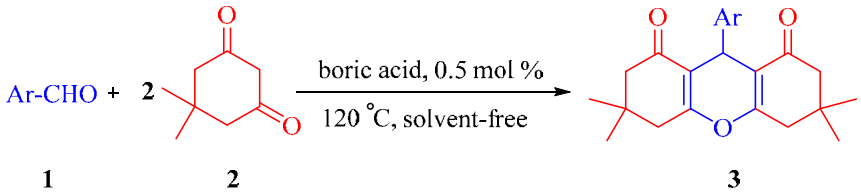


1 2 3

Scheme 1. Condensation of various aromatic aldehydes with dimedone for preparing of *1,8*-dioxo-octahydroxanthene derivatives.

spectra were recorded on a BRUKER DRX-400 AVANCE (Germany) instrument at 300 MHz (in $CDCl_3$ solution). Thin-layer chromatography (TLC) was performed on pre-coated aluminium plates (silica gel 60 F254, Merck, Germany). The chromatographic spots on the plates were visualised under UV light and iodine vapour. Melting points were taken on an electrothermal capillary melting point apparatus (UK) and are uncorrected.

2.2. Typical procedure for the preparation of 1,8-dioxo-octahydroxanthenes

A mixture of the dimedone (4 mmol), aromatic aldehydes (2 mmol) and boric acid (0.5 mol%) was added and the mixture was kept on an oil-bath at 120 °C and The progress of the reaction was monitored by TLC (hexane:ethyl acetate, 8:2). After completion of the reaction, the mixture was cooled to room temperature and the mixture was washed with $CHCl_3$ (10 ml) and filtered to recover the catalyst. The solvent was evaporated and the crude product recrystallized from EtOH to afford pure product.

3. Results and Discussion

In recent years, solid acid catalyst have gained special attention in organic synthesis, because of uncomplicated handling, inexpensiveness, eco-friendly nature and readily available. Recently, several synthetically useful organic transformations using solid acids as catalyst have been reported in the literature [31-36]. As a continuation of our research devoted to the development of green organic chemistry by performing organic transformations under solvent-free conditions [37-39], we observed that Boric acid [BO_3H_3 or $B(OH)_3$] as an efficient, recyclable solid Brønsted acid catalyst is safe, nontoxic, environmentally benign and presents fewer disposal problems. In this research, we wish to describe highly efficient and simple method for the synthesis of *1,8*-dioxo-octahydroxanthenes from various aromatic aldehydes (2 eq) and dimedone (4 eq) using a catalytic amount of boric acid (Scheme 1).

We initially, Investigated the catalytic effect of boric acid as a solid acid in the condensation reaction of dimedone and benzaldehyde as a sample reaction under different reaction conditions. To determine the role of boric acid, the model reaction was carried out in the absence of catalyst at room temperature under solvent-free conditions. The desired product was not obtained after 720 min (Table 1, Entry 1). In the course of optimization of reaction conditions, 0.5 mol% of boric acid as a catalyst was found optimum to catalyze this condensation (Table 1, Entry 3). When the reaction was carried out in the presence of higher amounts of catalyst, there was longer reaction time and lower yield (Table 1, Entry 4-6). The effect of temperature was also studied by carrying out the model reaction in the presence of boric acid (0.5 mol%) (Table 2). As can be seen, the shorter time and excellent yield for *1,8*-dioxo-octahydroxanthenes were achieved at 120 °C (Table 2, Entry 4).

Table 1. Effect of the boric acid in the synthesis of *1,8*-dioxo-octahydroxanthenes.[a]

Entry	Catalyst (mol %)	Time (min)	Yield (%)[b]
1	-	12 h	Trace
2	0.3	120	71
3	0.5	55	90
4	0.7	60	85
5	1	80	81
6	1.5	110	76
7	2	185	66

[a]Reaction conditions: benzaldehyde (1 mmol) with dimedone (2 mmol) in the presence of boric acid under solvent-free conditions at room temperature.

[b]Yield of isolated products.

Table 2. Effect of temperature on the synthesis of *1,8*-dioxo-octahydroxanthenes.[a]

Entry	Temperature (°C)	Time (min)	Yield (%)[b]
1	80	55	81
2	100	50	88
3	110	35	91
4	120	25	98
5	130	45	93

[a]Reaction conditions: benzaldehyde (1 mmol) with dimedone (2 mmol) in the presence of boric acid (0.5 mol%) under solvent-free conditions at different temperature.
[b]Yield of isolated products.

In the next study, the model reaction was performed in different solvents such as acetonitrile, chloroform, water and also solvent-free conditions. The results are shown in Table 3. It was found that the reaction under solvent-free conditions lead to the product in higher yield after shorter reaction time. After optimization of the reaction conditions, various aromatic aldehydes and dimedone were reacted in the presence of boric acid under solvent-free conditions at 120 °C (Table 4, Scheme 1).

As shown in Table 4, many functionalities present in the aryl aldehydes such as alkyl, methoxy, halogen and nitro group were tolerated. In all the cases the corresponding benzoxanthenes were obtained in excellent yield after 10-45 min.

Table 5 compares the efficiency of the boric acid catalyst with some reported catalysts in the synthesis of *1,8*-dioxo-octahydroxanthenes. It is clear that the present work has several advantagies such as: solvent-free conditions, excellent yield and short reaction time in compared to other methods.

The recycling of the catalyst is one of the most advantages of this method. In these experiments the product was isolated by filtration and the catalyst could then be reused together with fresh reagents in further reactions. Thus, for the reaction of benzaldehyde with dimedone good yield was observed when boric acid was reused even after six times recycling (Yield decreased from 98 to 91%).

A plausible mechanism for the formation of *1,8*-dioxo-octahydroxanthenes is shown in Scheme 2. It seems that boric acid as a heterogeneous catalyst might activate the carbonyl group of aromatic aldehyde to promote the reaction.

4. Conclusions

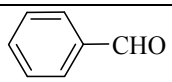
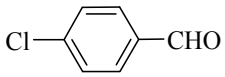
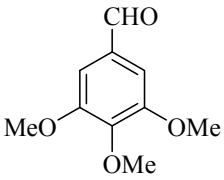
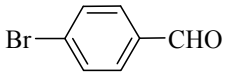
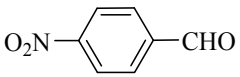
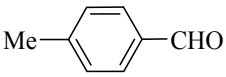
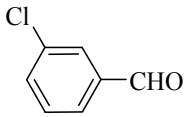
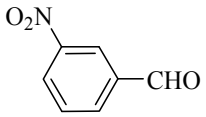
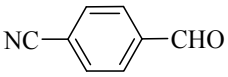
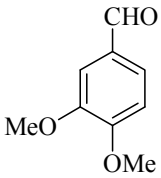
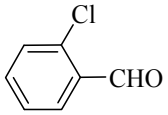
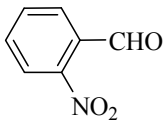
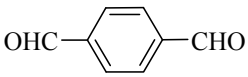
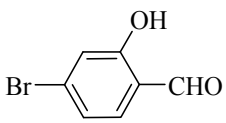
A facile and green procedure for the synthesis of *1,8*-dioxo-octahydroxanthenes using boric acid as an efficient catalyst under solvent-free conditions has been developed. This method is significant from an environmental point and economic considerations. Excellent yields, short reaction times, simple experimental procedure, eco-friendly and reusable of catalyst are the advantages of the present method.

Table 3. Effect of solvents on synthesis of *1,8*-dioxo-octahydroxanthenes.[a]

Entry	Solvent	Time (h)	Yield (%)[b]
1	H_2O	5	85
2	EtOH	24	35
3	$PhCH_3$	24	Trace
4	CH_2Cl_2	24	Trace
5	$CHCl_3$	24	Trace
6	CH_3CN	24	40
7	MeOH	24	45
8	Solvent-Free	20	98

[a]Reaction conditions: benzaldehyde (1 mmol) with dimedone (2 mmol) in the presence of boric acid (0.5 mol%) under solvent-free conditions at room temperature.
[b]Yield of isolated products.

Table 4. Boric acid catalyzed synthesis of *1,8*-dioxo-octahydroxanthenes.

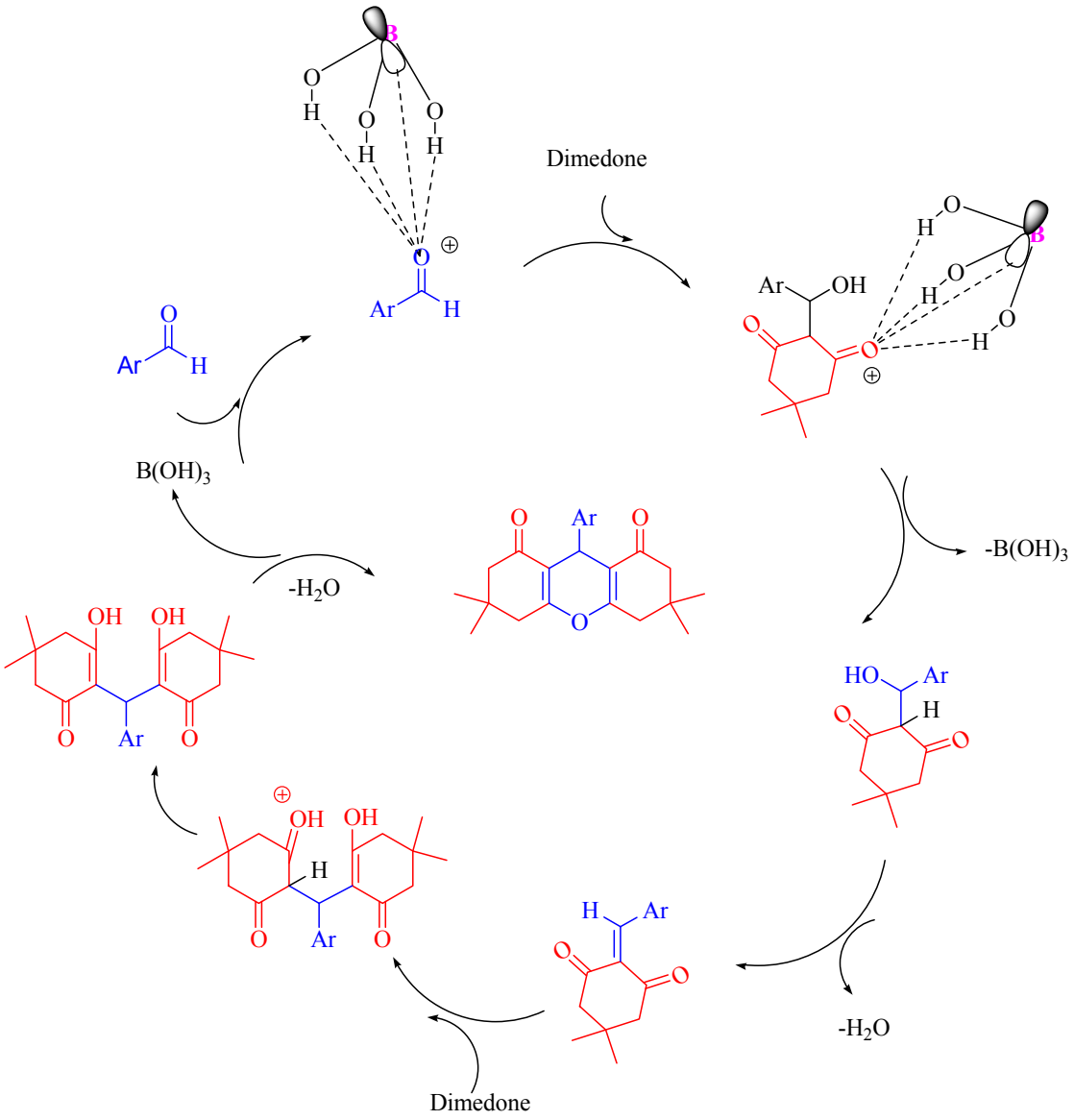
Entry	Aldehydes	Time (min)	Yield (%)[a]	m.p. (°C)		Ref.
				Found	Reported	
1		20	98	199-201	201-202	[37]
2		15	96	229-230	230-232	[40]
3		50	84	204-207	205-208	[40]
4		15	95	238-240	240-242	[40]
5		20	85	238-240	242-243	[41]
6		10	95	220-222	222-224	[41]
7		20	89	212-214	215-216	[41]
8		25	93	181-182	183-185	[41]
9		15	93	162-164	165-166	[41]
10		10	89	216-219	217-218	[41]
11		35	90	173-174	175-176	[41]
12		25	91	223-225	226-227	[41]
13		15	90	250-252	252-254	[42]
14		45	88	>300	>300	[42]
15		15	95	249-250	249-252	[42]

[a]Yield of isolated products.

Table 5. Comparison of efficiency of various catalysts in synthesis of 1,8-dioxo-octahydroxanthenes.

Entry	Catalyst	Condition	Loading catalyst	Time (h)	Yield (%)[a]
1	Dowex-50W	Solvent-free, 100 ˚C	0.1 g	2-5	78-91
2	SiO_2-SO_3H	Solvent-free, 80 ˚C	0.0 g	1-2.5	88-97
3	Amberlyst-15	CH_3CN, reflux	0.2 g	5	90-96
4	TMSCl	H_2O:1,4-dioxan[b], reflux	0.1 mmol	3-3.5	88-94
5	$Fe(HSO_4)_3$	Solvent-free, 120 ˚C	0.14 mmol	5-18 min	81-93
6	$Fe(HSO_4)_3$	Solvent-free, 450 W	0.29 mmol	3-11 min	70-93
7	$Fe(HSO_4)_3$	H_2O, reflux	0.14 mmol	1.5-3	70-94
8	This work	Solvent-free, 120 ˚C	0.05 mol%	10-50 min	84-98

[a]Yield of isolated products.
[b]Ratio 1:4.



Scheme 2. Suggested reaction pathway for the catalytic synthesis of *1,8*-dioxo-octahydroxanthenes.

References

[1] J.M. Jamison, K. Krabill, A. Hatwalkar, Cell. Biol. Int. Rep. 14 (1990) 1075-1084.
[2] R.M. Ion, D. Frackowiak, K. Wiktorowicz, Acta Biochim. Pol. 45 (1998) 833-845.
[3] K. Muharrem, B. Erhan, C. Ferdag, Med. Chem. Res. 20 (2011) 1214-1219.
[4] B.B. Bhowmik, P. Ganguly, Spectrochim. Acta A: Mol. Biomol. Spectrosc. 61 (2005) 1997-2003.
[5] C.G. Knight, T. Stephens, Biochem. J. 258 (1989) 683-689.
[6] J.P. Poupelin, G. Saint-Ruf, O. Foussard-Blanpin, G. Narcisse, G. Uchida Emouf, R. Lacroix, Eur. J. Med. Chem. 13 (1978) 67-71.
[7] M. Ahmad, T.A. King, Do-K. Ko, B.H. Cha, J. Lee. J. Phys. D: Appl. Phys. 35 (2002) 1473-1476.
[8] B. Rajitha, B. Sunil Kumar, Y. Thirupathi Reddy, P. Narsimha Reddy, N. Sreenivasulu, Tetrahedron Lett. 46 (2005) 8691-8693.
[9] A. Saini, S. Kumar, J.S. Sandhu, Synlett (2006) 1928-1932.
[10] S. Ko, C.F. Yao, Tetrahedron Lett. 47 (2006) 8827-8829.
[11] A.R. Khosropour, M.M. Khodaei, H. Moghannian, Synlett (2005) 955-958.
[12] M.A. Bigdeli, M.M. Heravi, G.H. Mahdavinia, J. Mol. Catal. A: Chem. 275 (2007) 25-29.
[13] D.W. Knight, P.B. Little, J. Chem. Soc., Perkin Trans. 1. 14 (2001) 1771-1777.
[14] A. Jha, J. Beal, Tetrahedron Lett. 45 (2004) 8999-9001.
[15] C.W. Kuo, J.M. Fang, Synth. Commun. 31 (2001) 877-892.
[16] J.Q. Wang, R.G. Harvey, Tetrahedron 58 (2002) 5927-5931.
[17] M.M. Amini, M. Seyyedhamzeh, A. Bazgir, Appl. Catal. A: Gen. 323 (2007) 242-245.
[18] M.M. Heravi, K. Bakhtiari, Z. Daroogheha, F.F. Bamoharram, J. Mol. Catal. A: Chem. 273 (2007) 99-101.
[19] L. Nagarapu, S. Kantevari, V.C. Mahankhali, S. Apuri, Catal. Commun. 8 (2007) 1173-1177.
[20] M.A. Pasha, V.P. Jayashankara, Bioorg. Med. Chem. Lett. 17 (2007) 621-623.
[21] F.Q. Ding, L.T. An, J.P. Zou, Chin. J. Chem. 25 (2007) 645-648.
[22] H.R. Shaterian, M. Ghashang, A. Hassankhani, Dyes Pigm. 76 (2008) 564-568.
[23] M. Seyyedhamzeh, P. Mirzaei, A. Bazgir, Dyes Pigm. 76 (2008) 836-839.
[24] I.G. Shakibaei, P. Mirzaei, A. Bazgir, Appl. Catal. A: Gen. 325 (2007) 188-192.
[25] H.R. Shaterian, A. Hosseinian, M. Ghashang, Turk. J. Chem. 33 (2009) 233-240.
[26] A.K. Zare, A.R. Moosavi-Zare, M. Merajoddin, M.A. Zolfigol, T. Hekmat-Zadeh, A.R. Hasaninejad, A. Khazaei, M. Mokhlesi, V. Khakyzadeh, F. Derakhshan-Panah, M.H. Beyzavi, E. Rostami, A. Arghoon, R. Roohandeh, J. Mol. Liq. 167 (2012) 69-77.
[27] M. Dabiri, S.C. Azimi, A. Bazgir, Chem. Pap. 62 (2008) 522-526.
[28] A. Kumar, R.A. Maurya, Tetrahedron Lett. 49 (2008) 5471-5474.
[29] K.F. Shelke, S.B. Sapkal, S.S. Sonar, B.R. Madje, B.B. Shingate, M.S. Shingare, Bull. Korean Chem. Soc. 30 (2009) 1057-1060.
[30] K.F. Shelke, S.B. Sapkal, G.K. Kakade, P.V. Shinde, B.B. Shingate, M.S. Shingare, Chin. Chem. Lett. 20 (2009) 1453-1456.
[31] M. Hosseini-Sarvari, J. Iran. Chem. Soc. 8 (2011) 119-128.
[32] R. Ghorbani-Vaghei, S.M. Malaekehpoor, J. Iran. Chem. Soc. 7 (2010) 957-964.
[33] A.R. Hajipour, Y. Ghayeb, N. Sheikhan, J. Iran. Chem. Soc. 7 (2010) 447-454.
[34] B. Tamami, H. Firouzabadi, F. Ebrahimzadeh, A. Fadavi, J. Iran. Chem. Soc. 6 (2009) 722-728.
[35] A. Sharifi, M.S. Abaee, A. Tavakkoli, M. Mirzaei, J. Iran. Chem. Soc. 5 (2008) 113-117.
[36] R. Hajinasiri, S. Rezayati, Z. Naturforsch. 68b (2013) 818-822.
[37] D. Zareyee, P. Alizadeh, M.S. Ghandali, M.A. Khalilzadeh, Chem. Pap. 67 (2013) 713-721.
[38] S. Sajjadifar, S. Rezayati, Chem. Pap. 68 (2014) 531-539.
[39] B. Karimi, D. Zareyee, Org. Lett. 10 (2008) 3989-3992.
[40] S. Kantevari, R. Bantu, L.J. Nagarapu, J. Mol. Catal. A: Chem. 269 (2007) 53-57.
[41] Z.H. Zhang, Y.H. Liu, Catal. Commun. 9 (2008) 1715-1719.
[42] M. Dabiri, M. Baghbanzadeh, E. Arzroomchilar, Catal. Commun. 9 (2008) 939-942.