ISSN: 0974 - 7516 Volume 11 Issue 8

Trade Science Inc.

Organic CHEMISTRY

An Indian Journal

Full Paper

OCAIJ, 11(8), 2015 [283-287]

Boric acid catalyzed convenient and greener synthesis of tetrahydrobenzo[*a*]xanthene-11-ones

Balasaheb V.Shitole[1], Nana V.Shitole [2], Gopal K.Kakde[3]*
[1]Department of Chemistry, a Vasant College Kaij-431518, (INDIA)
[2]Shri Shivaji College, Parbhani-431401 (M.S), (INDIA)
[3]Arts, Commers and Science College, Dharur(Kille)-431519, (INDIA)
E-mail: kakdeg44 @gmail.com

ABSTRACT

A simple, efficient, mild and environmentally benign route has been developed for cyclocondensation of aromatic aldehydes, β-naphthol and cyclic 1,3-dicarbonyl compounds were carried out in the presence of catalytic amount of Boric acid at reflex temperature. The remarkable advantages of the present method are mild conditions, less reaction time, simple work-up procedure, excellent yields and green aspects by avoiding toxic catalyst and hazardous solvent.

KEYWORDS

Multicomponent reaction;
One-pot synthesis;
Boric acid;
Tetrahydrobenzo[*a*]xanthen-11-ones.

INTRODUCTION

Xanthenes and benzoxanthenes constitute important classes of biodynamic heterocycles and their synthesis has received much attention especially in the field of medicinal/pharmaceutical chemistry due to their wide range of biological/pharmacological activities, e.g., anti-inflammatory[1] antiviral[2] and antibacterial[3]. Some of them have been used as antagonists for paralyzing the action of zoxazolamine[4] and in photodynamic therapy.[5] In addition,their derivatives can be used as dyes[6,7], pH sensitive fluorescent materials for the visualization of biomolecular assemblies[8] and in laser technologies[9],[10].

Among the xanthene based compounds, tetrahydrobenzo[*a*]xanthene-11-ones are of interest and have great potential for further synthetic transformations[11][12]. Some novel methods for the synthesis of tetrahydrobenzo[*a*]xanthene-11- ones via multicomponent condensation reaction have been developed and catalysts such as $Sr(OTf)_2$[13], $H_{14}[NaP_5W_{30}O_{11}]$[14] $InCl_3$ and P_2O_5[15], *p*-toluenesulfonic acid (PTSA)/ionic liquid[16], tetradecyltrimethylammonium bromide (TTAB);[17], iodine[18], $HClO_4/SiO_2$[19], proline triflate[20], ceric ammonium nitrate (CAN)[21], Silica supported boron triuoride nanoparticles (BF_3-SiO_2 NPs)[22] and citric acid[23] have been employed for their synthesis. However, in an era where green methods are desirable many of these methods are unsatisfactory as they involve the use of halogenated solvents, catalyst loadings of up to 30 mol %, low yields, drastic reaction conditions, prolonged reaction times and tedious isolation procedures. All of these disadvantages make further improvements for the synthesis of such molecules essential.

It is evident from the recent literature that boric acid has invoked enormous interest as a green and potential catalyst to construct carbon-carbon and carbon–heteroatom bonds in various organic transformations such as aza-Michael reaction[24], transesterification of ethyl acetoacetate[25], oxidation of sulfides[26], Biginelli reaction[27], and Mannich reaction[28]. It has received considerable attention due to its,commercially availability, environmentally benign, inexpensive and easy to handle.

EXPERIMENTAL

Apparatus and reagents

All aldehydes were obtained from freshly opened container and used without further purification with the exception of benzaldehyde and 2- furaldehyde which were distilled prior to use. Melting points were determined in open capillary tubes in a paraffin bath. The progresses of the reactions were monitored by TLC (Thin Layer Chromatography). IR spectra were recorded on Perkin-Elmer FT spectrophotometer in KBr disc.^{1}H NMR spectra were recorded on an 200 MHz FT NMR spectrometer in $CDCl_3$ as a solvent and chemical shift values are recorded in units δ (ppm) relative to TMS as an internal standard.

General procedure for the synthesis synthesis of tetrahydrobenzo[*a*]xanthene-11-one(4a-4m)

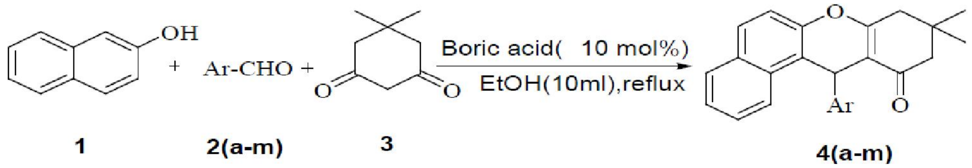
To a mixture of β-naphthol (1 mmol), 4-chlorobenzaldehyde (1mmol) and dimedone (1 mmol) in ethanol (5 mL), was added boric acid (10mol %). This reaction mixture was allowed to stir vigorously at reflex temperature. Progress of the reaction was monitored by TLC (ethyl acetate:*n*-hexane = 2:8). After completion of the reaction (2.0 h) evaporates the solvent the solid product obtain wash this product with water. The crude product was recrystallized from ethanol to afford the pure product which required no further purification

RESULT AND DISCUSSION

In continuation of our research devoted novel synthetic methodologies[30], herein, we report a simple, efficient, and rapid method for the synthesis of 12-aryl-8,9,10,12-tetrahydrobenzo[*a*]xanthen-11-ones derivatives catalyzed by boric acid (Scheme).

The reaction of an 4-chlorobenzaldehyde 2e as a representative aromatic aldehyde, β-naphthol and dimedone in the presence of boric acid has been considered as a standard model reaction for the optimization of reaction condition.

To evaluate the effect of solvent, we have screened different solvents such as water, water: ethanol (1:1), tetrahydrofuran, acetonitrile, dichloromethane, methanol and ethanol at reflux temperature. Ethanol stand out as the solvent of choice



Scheme 1

TABLE 1 : Screening of solvents[a]

Entry	Solvent	Time (hr)	Yield[b] (%)
1	Water	2	30
2	Water:ethanol (1:1)	2	45
3	Tetrahydrofuran	2	48
4	Acetonitrile	2	55
5	Dichloromethane	2	50
6	Methanol	2	70
7	Ethanol	2	91

[a]Reaction conditions: 1 (1 mmol), 2 (1 mmol), 3 (1 mmol), boric acid; [b]Isolated yields

TABLE 2 : Synthesis of tetrahydrobenzo[*a*]xanthene-11-ones catalysed by boric acid [a]

Entry	Ar-	Time(hr)	Yield(%)[b]	M.P.(°C)
4a	C_6H_5	2.5	89	151-153[16]
4b	4-HO-C_6H_4	2	90	223-225[16]
4c	4-MeO-C_6H_4	2	87	2o4-205[16]
4d	4-Me-C_6H_4	3.5	86	176-178[16]
4e	4-Cl-C_6H_4	2	91	180-182[16]
4f	4-F-C_6H_4	2	90	184-187[23]
4g	3-HO-C_6H_4	2	88	242-244[23]
4h	4-NO_2-C_6H_4	3	92	178-180[16]
4i	3-NO_2-C_6H_4	2	88	168-170[16]
4j	4-$(CH_3)_2N$-C_6H_4	2	88	183-185[24]
4k	4-Br-C_6H_4	2.5	89	187-189[18]
4l	2-Thienyl	3.5	80	176-178[18]
4m	2-Furfuryl	4.5	77	170-172[18]

[a] Reaction conditions:- 1 (1 mmol), 2 (1 mmol), 3 (1mmol) catalyst (10 mol%)[b] Isolated yield.

among the solvents tested because of the rapid conversion and excellent yield (91%) of desired product, where as the product formed in lower yields (30-70 %) by using other solvents (TABLE 1, Entry 1-6)

To determine the optimum concentration of catalyst, we have investigated the model reaction at 5, 7.5, 10 and 12.5 mol% of boric acid in ethanol at reflux temperature. The product was obtained in 65, 79, 91 and 91 % yield respectively. This indicates that the use of 10 mol% of boric acid is sufficient to promote the reaction forward

Here we extended this reaction on several substituted β-naphthol, aromatic aldehydes, and dimedone under similar conditions, furnishing the respective tetrahydrobenzo[*a*]xanthene-11-ones in excellent yields (80-95%). In all cases, aromatic aldehydes with substituent carrying either electron-donating or electron withdrawing groups reacted successfully and gave the products in excellent yields. This method is also effective for the heteroaromatic aldehydes which form their corresponding tetrahydrobenzo[*a*]xanthene-11-ones derivatives. All the synthesized compounds were characterized by spectral data and compared (MS and NMR) with authentic sample

To determine the optimum concentration of catalyst, we have investigated the model reaction at 5, 7.5, 10 and 12.5 mol% of boric acid in ethanol at reflux temperature. The product was obtained in 65, 79, 91 and 91 % yield respectively. This indicates that the use of 10 mol% of boric acid is sufficient to promote the reaction forward

Here we extended this reaction on several substituted β-naphthol, aromatic aldehydes, and dimedone under similar conditions, furnishing the respective tetrahydrobenzo[*a*]xanthene-11-ones in excellent yields (80-95%). In all cases, aromatic aldehydes with substituent carrying either electron-donating or electron withdrawing groups reacted successfully and gave the products in excellent yields. This method is also effective for the heteroaromatic aldehydes which form their corresponding tetrahydrobenzo[*a*]xanthene-11-ones derivatives. All the synthesized compounds were characterized by spectral data and compared (MS and NMR) with authentic sample

Spectral data of the the principal products:

9,9-Dimethyl-12-phenyl-8,9,10,12-tetrahydrobenzo[a]-xanthen-11-one (4a) ^1H NMR ($CDCl_3$, 200MHz): δ= 1.01 (s, 3H), 1.09(s, 3H), 2.11 (s, 2H), 2.33 (s, 2H), 5.69 (s, 1H), 7.20–7.51 (m, 6H, Ar-H), 7.81–7.94 (m, 5H, Ar-H); IR (KBr, cm^{-1}): *v* 2977, 1657, 1581, 1361,1231, 1174, 811; ES-MS: 354. 2 [M^+].

12-(4-Methoxyphenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one (4c) ^1H NMR

($CDCl_3$ 200 MHz): δ=1.01(s, 3H), 1.12(s, 3H), 3.61(s, 3H), 2.11 (s, 2H), 2.39 (s, 2H), 5.59 (s, 1H), 7.77–7.72 (m, 2H), 7.44–7.22 (m, 5H), 7.97 (d,2H),6.98(d,2H).IR (KBr, cm^{-1}): *v* 2954, 1671, 1587, 1231, 1174, 833; ES-MS: 384.2 [M$^+$].

12-(4-chlorophenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[*a*]xanthen-11-one (4e) ^{1}H NMR ($CDCl_3$, 200MHz): δ= 1.02 (s, 3H), 1.06 (s, 3H), 2.13 (s, 2H), 2.43 (s, 2H), 5.67 (s, 1H), 7.20–7.51 (m, 6H, Ar-H), 7.81–7.94 (m, 4H, Ar-H); IR (KBr, cm^{-1}): *v* 2944, 1667, 1577, 1371,1221, 1174, 823; ES-MS: 389.14 [M$^+$], 391.13 [M^{++2}].

12-(thiophen-2-yl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[*a*]xanthen-11-one (4l) ^{1}H NMR ($CDCl_3$, 200 MHz): δ=1.04 (s, 3H), 1.09 (s, 3H), 2.21 (s, 2H), 2.47 (s, 2H), 6.12 (s,1H), 6.72–6.75 (m, 3 H), 7.40–7.51 (m,2H), 7.75–7.87 (m, 6H), IR (KBr, cm-1): *v* 2951, 1642, 1573, 1367, 1232, 1041, 724; ES-MS: 361.13 [M$^+$].

12-(furan-2-yl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[*a*]xanthen-11-one (4m) ^{1}H NMR ($CDCl_3$, 200 MHz): δ=1.02 (s, 3H), 1.12 (s, 3H), 2.29 (s, 2H), 2.51 (s, 2H), 5.92 (s,1H), 6.76–6.81 (m, 3 H), 7.46–8.58 (m,6H), IR (KBr, cm-1): *v* 2944, 1641, 1587, 1354, 1231, 1054, 735; ES-MS: 345.09 [M$^+$].

CONCLUSION

In conclusion, we have developed efficient and environmentally benign methodology for the synthesis of tetrahydrobenzo[*a*]xanthene-11-one derivatives by a one-pot, multi-component reaction. The advantages of this method over other existing methods are reduced reaction times, higher yields, mild reaction condition, easy purification and economic viability of the catalyst. We feel that this economically viable procedure will find practical utility for the one pot synthesis of novel xanthenes.

ACKNOWLEDGEMENTS

We are thankful to the University Grants Commission, New Delhi, for financial support which is gratefully acknowledged and the Sophisticated Analytical Instrument Facility, Punjab University, Chandigarh for providing spectroscopic data.

REFRENCES

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

[2] R.W.Lambert, J.A.Martin, J.H.Merrett, K.E.B.Parkes, G.Thomas; J.PCT Int.Appl.WO, **9**, 178 **(1997)**.

[3] T.Hideo, J.Teruomi; Jpn.Patent, **56**, 480 **(1981)**.

[4] N.P.Buu-Hoi, G.Saint-Ruf, A.De, H.T.Hieu; Chim.Ther., **7**, 83 **(1972)**.

[5] R.M.Ion; Prog.Catal., **6**, 55 **(1997)**.

[6] A.Banerjee, A.K.Mukherjee; Stain Technol., **56**, 83 **(1981)**.

[7] S.M.Menchen, S.C.Benson, J.Y.L.Lam, W.Zhen, D.Sun, B.B.Rosenblum, S.H.Khan, M.Taing; Sulfonated Diarylrhodamine Dyes.U.S.Patent, **6**, 583 **(2003)**.

[8] C.G.Knight, T.Stephens; Biochem.J., **258**, 683 **(1989)**.

[9] O.Siirkecioglu, N.Talini, A.Akar; J.Chem.Res., Synop, 502 **(1995)**.

[10] M.Ahmad, T.A.King, D.K.Ko, B.H.Cha, J.Lee; J.Phys.D: Appl.Phys., **35**, 1473 **(2002)**.

[11] B.Lesch, S.Bräse; Angew.Chem., Int.Ed., **43**, 115 **(2004)**.

[12] Y.L.Shi, M.Shi; Synlett, 2623 **(2005)**.

[13] J.Li, W.Tang, L.Lu, W.Su; Tetrahedron Lett., **49**, 7117 **(2008)**.

[14] G.H.Mahdavinia, S.Rostamizadeh, A.M.Amani, Z.Emdadi; Ultrason.Sonochem, **16**, 7 **(2009)**.

[15] G.C.Nandi, S.Samai, R.Kumar, M.S.Singh; Tetrahedron., **65**, 7129 **(2009)**.

[16] J.M.Khurana, D.Magoo; Tetrahedron Lett., **50**, 4777 **(2009)**.

[17] P.V.Shinde, A.H.Kategaonkar, B.B.Shingate, M.S.Shingare; Beilstein J.Org.Chem., **7**, 53 **(2011)**.

[18] R.Z.Wang, L.F.Zhang, Z.S.Cui; Synth.Commun., **39**, 2101 **(2009)**.

[19] L.P.Mo, H.L.Chen; J.Chin.Chem.Soc., **57**, 157 **(2010)**.

[20] J.Li, L, Lu, W.Su; Tetrahedron Lett., **51**, 2434 **(2010)**.

[21] A.Kumar, S.Sharma, R.A.Maurya, J.Sarkar; J.Comb.Chem., **12**, 20 **(2010)**.

[22] B.Sadeghi; Sci.Irani.Tran.C: Chem.Chem.Engi., **21**, 708 **(2014)**.

[23] P.B.Pawar, S.D.Jadhav, M.B.Deshmuka S.Patil; Ind.J Chem., **53B**, 1185 **(2014)**.

[24] M.K.Chaudhuri, S.Hussain, M.L.Kantam, B.Neelima; Tetrahedron Lett., **46**, 8329 **(2005)**.

[25] G.C.M., Kondaiah, L.A.Reddy, K.S.Babu, V.M.Gurav, K.G.Huge, R.Bandichhor, P.P.Reddy; Tetrahedron Lett., **49**, 106 **(2008)**.

[26] A.Rostami, J.Akradi; Tetrahedron Lett., **51**, 3501 **(2010)**.

[27] S.Tu, F.Fang, C.Miao, H.Jiang, Y.Feng, Y.Shi, X.Wang; Tetrahedron Lett., **44**, 6153 **(2003)**.

[28] C.Mukhopadhyay, A.Datta, R.J.Butcher; Tetrahedron Lett., **50**, 4246 **(2009)**.