Synthesis and Reactivity in Inorganic, Metal-Organic, and Nano-Metal Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsrt20

Ammonium oxalate as an efficient catalyst for one-pot synthesis of tetrahydrobenzo [a]xanthen-11-one derivatives under solvent-free conditions

Hamid R. M. Esfahani [a] , Naser Foroughifar [a] , Akbar Mobinikhaledi [b] & Hassan Moghanian [c]

[a] Department of Chemistry, Tehran North Branch, Islamic Azad University, Tehran, Iran

[b] Department of Chemistry, Faculty of Science, Arak University, Arak, 38156-8-8349, Iran

[c] Young Researchers Club, Dezful Branch, Islamic Azad University, Dezful, Iran

Accepted author version posted online: 19 Feb 2013.

To cite this article: Hamid R. M. Esfahani , Naser Foroughifar , Akbar Mobinikhaledi & Hassan Moghanian (2013): Ammonium oxalate as an efficient catalyst for one-pot synthesis of tetrahydrobenzo [a]xanthen-11-one derivatives under solvent-free conditions, Synthesis and Reactivity in Inorganic, Metal-Organic, and Nano-Metal Chemistry, DOI:10.1080/15533174.2012.754767

To link to this article: http://dx.doi.org/10.1080/15533174.2012.754767

Ammonium oxalate as an efficient catalyst for one-pot synthesis of tetrahydrobenzo [a]xanthen-11-one derivatives under solvent-free conditions

Hamid R. M. Esfahani,[1] Naser Foroughifar,[*1] Akbar Mobinikhaledi[2] and Hassan Moghanian[3]

[1]*Department of Chemistry, Tehran North Branch, Islamic Azad University, Tehran, Iran*

[2]*Department of Chemistry, Faculty of Science, Arak University, Arak 38156-8-8349,Iran*

[3]*Young Researchers Club, Dezful Branch, Islamic Azad University, Dezful, Iran*

E-mail: N_foroughifar@yahoo.com; Tel.: +98-861-4173402; Fax: +98-861-4173406;

Abstract:

A simple and efficient procedure for the synthesis of 12-aryl- or 12-alkyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one derivatives has been developed via one-pot three-component reaction of 2-naphthol, aldehydes and dimedone in the presence of ammonium oxalate as a mild and inexpensive catalyst under solvent-free conditions. The present method is operationally simple and offers several advantages such as high yields, short reaction time, economic availability of the catalyst and simple workup.

***Keywords*:** Xanthene, ammonium oxalate, multi-component, one-pot, solvent-free

Introduction

The synthesis of xanthenes, especially benzoxanthenes has gained considerable attention in organic synthesis due to their wide range of biological and pharmaceutical properties such as antibacterial [1], antiviral [2], anti-inflammatory activities [3] and sensitizers in photodynamic therapy for destroying the tumor cells [4]. Further, these compounds have found wide usage such as leuco-dyes, in laser technologies, and as pH-sensitive fluorescent materials for visualization of biomolecules [5, 6].

Xanthenes and benzoxanthenes are prepared by different methods involving trapping of benzynes by phenols [7], cyclocondensation reaction between 2-hydroxyaromatic aldehydes and 2-tetralone [8], the reaction of aldehydes with 2-naphthol [9], intramolecular phenyl carbonyl coupling reactions of benzaldehydes and acetophenones [10] and reaction of 2-naphthol with 2-naphthol-1-methanol [11]. Recently, the synthesis of benzoxanthenes has been achieved by the condensation of aldehydes, 2-naphthol and cyclic 1,3-dicarbonyl compounds by cyclodehydration in the presence of various catalysts such as $NaHSO_4$-SiO_2 [12], $Sr(OTf)_2$ [13], para-toluenesulfonic acid (*p*-TSA) [14], ceric ammonium nitrate (CAN) [15], $InCl_3$ [16], $H_3PW_{12}O_{40}$ [17], NH_4Cl [18] and sulfamic acid [19]. However, these methods show varying degrees of success as well as limitations such as prolonged reaction times, low yields, use of toxic solvents, requirement of excess of reagents/catalysts, laborious work-up procedures, the requirement of special apparatus, or harsh reaction conditions. Thus, the development of milder and clean procedures is highly demanding for the synthesis of benzoxanthenes.

Results and Discussion

As a continuation of our recent studies, devoted to the development of practical, safe and environmentally friendly procedures for some important transformations [18, 20, 21], we wish to report an efficient, convenient and facile procedure for the condensation of aldehydes, dimedone, and 2-naphthols to the corresponding benzoxanthenes in the presence of inexpensively available ammonium oxalate under solvent-free conditions in good to excellent yields without any by-products (Scheme 1).

Scheme 1.

First, to evaluate the synthetic potential of the proposed procedure and to optimize the reaction conditions, the reaction of 3-nitrobenzaldehyde, dimedone and 2-naphthol in the presence of ammonium oxalate was examined in different solvent and solvent-free conditions. As can be seen from Table 1, the best result was obtained under solvent-free conditions at 110 °C. Next, to evaluate the effect of catalyst concentration, the model reaction was carried out in the presence of different amounts of catalyst at 110 °C. The result showed that for the model reaction 10 mol% of catalyst was sufficient to achieve a fairly high yield (Table 1). A slight excess of the dimedone was found to be advantageous, and hence the molar ratio of 2-naphthol to dimedone was kept as 1:1.1.

Table 1.

With the optimized conditions in hand, to explore the generality of the reaction, we extended our study using ammonium oxalate as catalyst under solvent-free conditions with different aromatic aldehydes bearing electron withdrawing groups and electron-releasing groups to prepare a series

of tetrahydrobenzo [a]xanthen-11-one derivatives in good to excellent yields (Table 2). On the basis of the results listed in Table 2, this reaction is affected by electronic and steric factors. However, with aromatic aldehydes with electron-withdrawing groups as substrates, the reaction time is shorter than those with electrondonating groups. Ortho-substituted aromatic aldehydes (such as 2-chlorobenzadehyde) gave lower yields because of the steric effects.

Table 2.

On the other hand, aliphatic aldehydes such as propionaldehyde and heterocyclic aldehydes such as indol-3-carbaldehyde were also examined under the same conditions, and the corresponding products were obtained successfully. The reactions with aliphatic and heterocyclic aldehydes provided somewhat lower yields than those with aromatic aldehydes (Table 2), probably due to less stability of *o*-quinonemethide intermediate (*o*-QMs).

The results obtained from the condensation reaction of benzaldehyde, 2-naphthol and dimedone under optimized conditions were compared to the best ones published so far for this reaction using different catalysts, the data listed in Table 3. In this study it was found that ammonium oxalate is a more efficient and superior catalyst (Entry 1) over other catalysts with respect to reaction time and yield of the desired xanthene.

Table 3.

Experimental

All products were characterized by a comparison of their spectral data or by comparison of their physical and spectroscopic data with those reported in the literature. IR spectra were recorded as KBr disc on a galaxy series FT-IR 5000 spectrometer. NMR spectra were recorded on a brucker spectrometer (300 MHz) in $CDCl_3$ with TMS as an internal standard.

General procedure for tetrahydrobenzo[a]xanthen-11-one derivatives

A mixture of aldehyde (1 mmol), 2-naphthol (1 mmol), dimedone (1.1 mmol), and ammonium oxalate (0.1 mmol) was stirred magnetically at 110 °C for the appropriate time as shown in Table 2. The reaction progress was followed by TLC. When the reaction was completed, the mixture was cooled to room temperature and a mixture of EtOH-H_2O (10 mL, 1:1) was added, and the mixture was stirred for 15 min. The obtained solid product was filtered and recrystallized from ethanol to yield pure xanthene derivatives.

Representative Spectral Data

Table 2, Entry 6

IR (KBr): ν_{max} = 3530, 3182, 1661, 1595, 1512, 1372, 1228, 1175, 837, 820 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ= 9.30 (s, 1H), 7.81 (d, *J* = 9.0 Hz, 2H), 7.71 (d, *J* = 8.1 Hz, 1H), 7.44-7-36 (m, 3H), 7.05 (t, *J* = 6.1 Hz, 2H), 6.66 (t, *J* = 7.5 Hz, 2H), 5.81 (s, 1H), 2.64 (s, 2H), 2.45 and 2.38 (AB system, *J* = 16.0 Hz, 2H), 1.18 (s, 3H), 1.02 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 201.0, 167.3, 153.3, 148.3, 133.2, 132.0, 131.6, 129.6, 129.2, 128.7, 128.3, 127.9, 125.7, 123.9, 122.0, 119.3, 117.9, 117.0, 114.4, 50.7, 42.0, 32.8, 29.5, 28.5, 27.7.

Table 2, Entry 9

IR (KBr): ν_{max} = 3210, 3059, 2960, 1643, 1595, 1516, 1377, 1226, 1175, 1095, 815, 739 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ= 8.03 (d, *J* = 8.5 Hz, 1H), 7.80 (t, *J* = 9.2 Hz, 2H), 7.46-7.35 (m, 3H), 7.01 (s, 1H), 6.79 (d, *J* = 7.3 Hz, 1H), 6.68 (d, *J* = 7.1 Hz, 1H), 5.71 (s, 1H), 3.84 (s, 3H), 3.78 (s, 3H), 2.59 (s, 2H), 2.35 and 2.29 (AB system, *J* = 15.4 Hz, 2H), 1.15 (s, 3H), 1.01 (s,

3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 197.4, 164.2, 149.0, 148.2, 147.7, 138.0, 131.9, 129.2, 128.8, 127.4, 125.3, 124.1, 120.9, 118.2, 117.4, 114.8, 112.4, 111.3, 56.3, 56.1, 41.9, 34.5, 32.7, 29.8, 27.5.

Table 2, Entry 10

IR (KBr): ν_{max} = 3007, 2953, 1653, 1591, 1502, 1375, 1323, 1222, 1122, 1008, 817, 760 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ= 8.04 (d, *J* = 8.6 Hz, 1H), 7.81 (t, *J* = 8.9 Hz, 2H), 7.51-730 (m, 3H), 6.58 (s, 2H), 5.70 (s, 1H), 3.77 (s, 6H), 3.76 (s, 3H), 2.60 (s, 2H), 2.33 (s, 2H), 1.15 (s, 3H), 1.04 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 197.4, 164.4, 153.3, 148.2, 140.9, 136.8, 131.9, 129.3, 128.8, 124.4, 125.4, 124.1, 118.0, 117.4, 114.7, 106.2, 61.1, 56.5, 51.3, 41.9, 35.1, 32.7, 29.7, 27.6.

Table 2, Entry 13

IR (KBr): ν_{max} = 3045, 2973, 1649, 1593, 1512, 1372, 1229, 1132, 814 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ= 8.08 (d, *J* = 8.8 Hz, 1H), 7.79 (t, *J* = 8.6 Hz, 2H), 7.48-7.21 (m, 5H), 6.58 (d, *J* = 9.1 Hz, 2H), 5.66 (s, 1H), 2.86 (s, 6H), 2.60 (s, 2H), 2.34 and 2.28 (AB system, *J* = 14.7 Hz, 2H), 1.15 (s, 3H), 1.03 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 197.4, 163.8, 149.3, 148.1, 133.7, 132.0, 129.4, 128.9, 128.7, 127.3, 125.2, 124.3, 118.8, 117.5, 115.1, 112.8, 51.4, 41.9, 41.0, 43.0, 32.7, 29.7, 27.9.

Table 2, Entry 14

IR (KBr): ν_{max} = 3047, 2980, 2935, 1653, 1597, 1518, 1373, 1222, 1170, 1018, 797 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ= 8.25 (d, *J* = 8.5 Hz, 1H), 7.83 (d, *J* = 8.4 Hz, 1H), 7.78 (d, *J* = 8.6 Hz, 1H), 7.55 (t, *J* = 9.2 Hz, 1H), 7.46 (t, *J* = 9.0 Hz, 1H), 7.30 (t, *J* = 8.9 Hz, 1H), 5.96 (d, J= 1.8 Hz, 1H), 5.82 (s, 1H), 5.76 (d, J= 1.6 Hz, 1H), 2.63 (s, 2H), 2.39 (s, 2H), 2.13 (s, 3H),), 1.19

(s, 3H), 1.16 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 197.1, 165.6, 154.6, 151.0, 148.2, 132.0, 131.8, 129.2, 128.8, 127.3, 125.4, 124.0, 117.6, 116.1, 111.6, 107.2, 106.6, 51.3, 41.9, 32.7, 29.9, 28.7, 27.5.

Table 2, Entry 15

IR (KBr): ν_{max} = 3055, 2953, 2928, 1647, 1593, 1514, 1377, 1223, 1143, 1028, 810 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ= 8.16 (d, *J* = 8.3 Hz, 1H), 7.77 (d, *J* = 6.0 Hz, 2H), 7.58 (d, *J* = 8.5 Hz, 1H), 7.40-7.23 (m, 5H), 7.20 (s, 1H), 7.07 (s, 1H), 6.06 (s, 1H), 2.66 and 2.60 (AB system, *J* = 16.7 Hz, 2H), 2.33 and 2.24 (AB system, *J* = 18.8 Hz, 2H) 1.14 (s, 3H), 0.94 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 197.9, 164.3, 147.9, 136.8, 132.2, 131.9, 129.0, 128.7, 127.1, 125.1, 124.1, 123.9, 121.9, 119.8, 119.6, 119.7, 117.8, 117.4, 113.8, 111.6, 100.4, 51.4, 41.8, 32.7, 29.5, 27.9, 27.0

Conclusion

In conclusion, we have developed a simple and efficient methodology for the synthesis of tetrahydrobenzo[a]xanthene-11-one derivatives in the presence of ammonium oxalate under solvent-free conditions. 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.

Acknowledgment

We gratefully acknowledge the financial support from the Research Council of Islamic Azad University, Tehran North Branch.

References

[1] El-Brashy, A. M.; Metwally, M. E.; El-Sepai, F. A. Spectrophotometric determination of some fluoroquinolone antibacterials by binary complex formation with xanthene dyes. *II Farmaco* **2004**, *59*, 809-817.

[2] Jamison, J. M.; Krabill, K.; Hatwalkar, A. Potentiation of the antiviral activity of poly r(A-U) by xanthene dyes. *Cell Biology International Reports* **1990**, *14*, 1075-1084.

[3] Chibale, K.; Visser, M.; Schalkwyk. D. V.; Smith, P. J.; Saravanamuthu, A.; Fairlamb, A. H. Exploring the potential of xanthene derivatives as trypanothione reductase inhibitors and chloroquine potentiating agents. *Tetrahedron* **2003**, *59*, 2289-2296.

[4] Ion, R. M.; Frackowiak, D.; Wiktorowicz, K. The incorporation of various porphyrins into blood cells measured via flow cytometry, absorption and emission spectroscopy. *Acta Biochimica Polonica* **1998**, *45*, 833-845.

[5] Bhowmik, B. B.; Ganguly, P. Photophysics of xanthene dyes in surfactant solution. *Spectrochim. Acta, Part A* **2005**, *61*, 1997-2003.

[6] Foroughifar, N.; Mobinikhaledi, A.; Moghanian, H. A Catalytic and Green Procedure for Synthesis of 12-Aryl or 12-Alkyl-8,9,10,12-Tetrahydrobenzo[a]xanthen-11-one derivatives under Solvent-Free Conditions. *International Journal of Green Nanotechnology: Physics and Chemistry* **2009**, *1*, 57-63.

[7] Knight, D. W.; Little, P. B. The first high-yielding benzyne cyclisation using a phenolic

nucleophile: A new route to xanthenes. *Synlett* **1998**, 1141–1143.

[8] Jha, A.; Beal, J. Convenient synthesis of 12H-benzo[a]xanthenes from 2-tetralone. *Tetrahedron Lett*. **2004**, *45*, 8999-9001.

[9] Van Allan, J. A.; Giannini, D. D.; Whitesides, T. H. Dibenzoxanthene derivatives and related products from b-naphthol and aldehydes or acetals. *J. Org. Chem.* **1982**, *47*, 820-823.

[10] Kuo, C. W.; Fang, J. M. Synthesis of xanthenes, indanes, and tetrahydronaphthalenes via intramolecular phenyl–carbonyl coupling reactions. *Synth. Commun.* **2001**, *31*, 877-892.

[11] Sen, R. N.; Sarkar, N. The condensation of primary alcohols with re- sorcinol and other hydroxy aromatic compounds. J. Am. Chem. Soc. **1925**, *47*, 1079-1091.

[12] Das, D.; Laxminarayana, K.; Krishnaiah, M.; Srinivas, Y. An efficient and convenient protocol for the synthesis of novel 12-aryl- or 12-alkyl-8,9,10,12-tetrahydrobenzo[a]-xanthen-11-one derivatives. *Synlett* **2007**, 3107-3112.

[13] Li, J.; Tang, W.; Lu, L.; Su, W. Strontium triflate-catalyzed one-pot condensation of 2-naphthol, aldehydes, and cyclic 1,3-dicarbonyl compounds. *Tetrahedron Lett*. **2008**, *49*, 7117-7120.

[14] Khurana, J. M.; Magoo, D. *p*-TSA-catalyzed one-pot synthesis of 12-aryl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-ones in ionic liquid and neat conditions. *Tetrahedron Lett.* **2009**, *50*, 4777-4780.

[15] Kumar, A.; Sharma, S.; Maurya, R. A.; Sarkar, J. Diversity-oriented synthesis of benzoxanthene and benzochromene libraries via one-pot, three-component reactions and their anti-proliferative activity. *J. Comb. Chem.* **2010**, *12*, 20-24.

[16] Nandi, G. C.; Samai, S.; Kumar, R.; Singh, M. S. An efficient one-pot synthesis of tetrahydrobenzo[a]xanthene-11-one and diazabenzo[a]anthracene-9,11-dione derivatives under solvent-free condition. *Tetrahedron* **2009**, *65*, 7129-7134.

[17] Wang, H.-J.; Ren, X.-Q.; Zhang, Y.-Y.; Zhang, Z.-H. Synthesis 12-aryl or 12-alkyl-8, 9,10,12-tetrahydrobenzo[a]xanthen-11-one derivatives catalyzed by dodecatungstophosphoric acid. *J. Braz. Chem. Soc.* **2009**, *20,* 1939-1943.

[18] Foroughifar, N.; Mobinikhaledi, A.; Moghanian, H.; Mozafari, R.; Esfahani, H. R. M. Ammonium chloride catalyzed one-pot synthesis of tetrahydrobenzo [α]xanthen-11-one derivatives under solvent-free conditions. *Synth. Commun.* **2011**, *41*, 2663-2673.

[19] Heravi, M. M.; Alinejad, H.; Bakhtiari, K.; Oskooie, H. A. Sulfamic acid–catalyzed solvent-free synthesis of 10-aryl-7,7-dimethyl-6,7,8,10-tetrahydro-9H-[1,3]-dioxolo[4,5-b]- xanthen-9-ones and 12-aryl-9,9-dimethyl-8,9,10,12-tetrahydro-11H-benzo[a]xanthen-11-ones. *Mol. Divers.* **2010**, *14*, 621-626.

[20] Foroughifar, N., Mobinikhaledi, A., Moghanian, H. Simple and efficient method for synthesis of novel 4-substituted 1-acylthiosemicarbazides via one-pot multicomponent reactions. *Synth. Commun.* **2009**, *39,* 3668-3676.

[21] Foroughifar, N., Mobinikhaledi, A., Moghanian, H. A straightforward and efficient catalyst-free one-pot synthesis of N-Acyl-1,3-diaryl-2-azaphenalene derivatives via multicomponent reactions. *Chem. Lett.* **2010**, *39,* 180-181.

Table 1. Optimization of reaction conditions

Entry	Solvent	Catalyst (mol%)	Conditions	Time (min)	Yield (%)[a]
1	n-hexane	10	Reflux	150	41
2	CH_2Cl_2	10	Reflux	150	55
3	THF	10	Reflux	150	63
4	EtOH	10	Reflux	150	60
5	CH_3CN	10	Reflux	150	35
6	Solvent-free	10	RT	150	0
7	Solvent-free	10	80 °C	90	67
8	Solvent-free	10	110 °C	15	85
9	Solvent-free	5	110 °C	30	71
10	Solvent-free	20	110 °C	15	85

[a] Isolated yields

Table 2. Synthesis of tetrahydrobenzo[*a*]xanthene-11-one derivatives

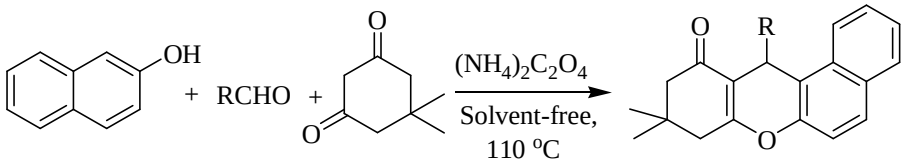
Entry	R	Time/min	Yield/%[a]	Mp (°C)	
				Found	Reported [lit.]
1	C_6H_5	18	88	149-150	151-153 [19]
2	2-ClC_6H_4	20	70	180-181	179-180 [19]
3	4-ClC_6H_4	15	90	187-188	180-182 [19]
4	3-$NO_2C_6H_4$	15	85	170-171	168-170 [19]
5	4-$NO_2C_6H_4$	12	91	173-174	180-181 [19]
6	2-OHC_6H_4	25	66	226-227	-
7	3-OHC_6H_4	20	74	241-242	240-241 [19]
8	4-$MeOC_6H_4$	20	75	206-207	204-205 [19]
9	3,4-di$MeOC_6H_3$	20	70	157-158	-
10	3,4,5-tri$MeOC_6H_2$	20	76	197-198	-
11	4-Me C_6H_4	15	78	191-193	196-198 [19]
12	4-FC_6H_4	12	80	183-185	185-186 [20]
13	4-$N(Me)_2C_6H_4$	20	85	196-197	-
14	5-Mefurfural	30	50	175-176	-
15	Indol-3-carbaldehyde	30	45	141-143	-
16	Propanal	25	58	Liquid	Liquid [16, 18]

[a] Isolated yields

Table 3. Comparison of different catalysts for reaction of benzaldehyde, dimedone and 2-naphthol

Entry	Catalyst	Conditions	Time/min	Yield/ %[a]
1	$(NH_4)_2C_2O_4$	Solvent-free /110 °C	18	88
2	$Sr(OTf)_2$	$ClCH_2CH_2Cl$ / 60 °C	300	85 [16]
3	*p*-TSA	Solvent-free /120 °C	45	88[17]
4	CAN	Solvent-free /120 °C	30	94 [18]
5	$InCl_3$	Solvent-free /120 °C	30	84 [19]
6	NH_4Cl	Solvent-free /120 °C	15	86 [21]
7	$H_3PW_{12}O_{40}$	Solvent-free / 60 °C	70	86 [20]

[a] Isolated yields.



Scheme 1. Synthetic pathway for synthesis of tetrahydrobenzo [α]xanthen-11-one derivatives

