Current Chemistry Letters 4 (2015) 169–180

Contents lists available at Growing Science

Current Chemistry Letters

homepage: www.GrowingScience.com/ccl

An adapted route to efficient synthesis of 1,8-dioxooctahydro-xanthene derivatives using $InCl_3$ and $(HPO_3)_n$ as recyclable catalysts

Bahador Karami[a*] Shahin Nejati[b] and Khalil Eskandari[c*]

[a]*Department of Chemistry, P.O.Box 353, Yasouj University, Yasouj 75918-74831, Iran*
[b]*Department of Chemistry, Gachsaran Branch, Islamic Azad University, Gachsaran, Iran*
[c]*Young Researchers and Elites Club, Shahrekord Branch, Islamic Azad University, Shahrekord, Iran*

C H R O N I C L E

Article history:
Received February 21, 2015
Received in revised form
April 29, 2015
Accepted 23 May 2015
Available online
23 May 2015

Keywords:
Indium trichloride
Metaphosphoric acid
Recyclable catalyst
Cyclic β-diketone
Solvent-free

A B S T R A C T

Indium (III) chloride ($InCl_3$) and metaphosphoric acid ($(HPO_3)_n$) were found to be efficient and recyclable catalysts for the synthesis of 1,8-dioxooctahydroxanthene derivatives as biologically important molecules in high turnover numbers and rates. Several substituted xanthenes can be prepared in high yield and purity by direct reaction of cyclic *β*-diketones and aldehyde derivatives in the presence of a catalytic amount of $InCl_3$ and $(HPO_3)_n$ as Lewis acids and at ambient temperature under solvent-free conditions. This newly reported procedure profit some advantages such as short reaction times, high yields of products, cheap, easy to use, facile practical conditions, and wholesome with green chemistry without using harmful solvents.

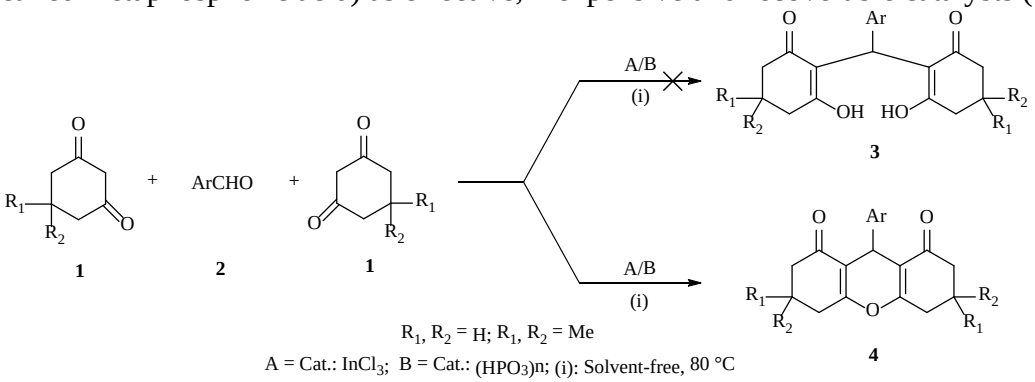
1. Introduction

Solid acids play a significant role in clean and economic technology, especially in chemical manufacturing processes.[1-5] Solid acids as catalyst generally have high turnover numbers and have significant role in the synthesis of heterocyclic compounds.[6-10] Furthermore, they can be easily separated from the organic components.[11] Among organic compounds, xanthenes and its derivatives have received significant attention in recent years due to their wide range of biological and therapeutic properties.[12,13] The importance of xanthene derivatives clearly was realized from their usage as dyes,[14] sensitizers in photodynamic therapy for destroying the tumor cells,[15] pH-sensitive fluorescent materials for visualization of biomolecules,[16] and in laser technologies.[17] Furthermore, some of the xanthene based compounds have found applications as antagonists for paralyzing the action of zoxalamine and in photodynamic therapy.[18] Several polycyclic compounds containing the xanthene skeleton are isolated from natural sources.[19] Xanthenes and its derivatives are prepared by different methods,

* Corresponding author.
E-mail address: karami@mail.yu.ac.ir (B. Karami) khalileskandari@yahoo.com (K. Eskandari)

doi: 10.5267/j.ccl.2015.5.001

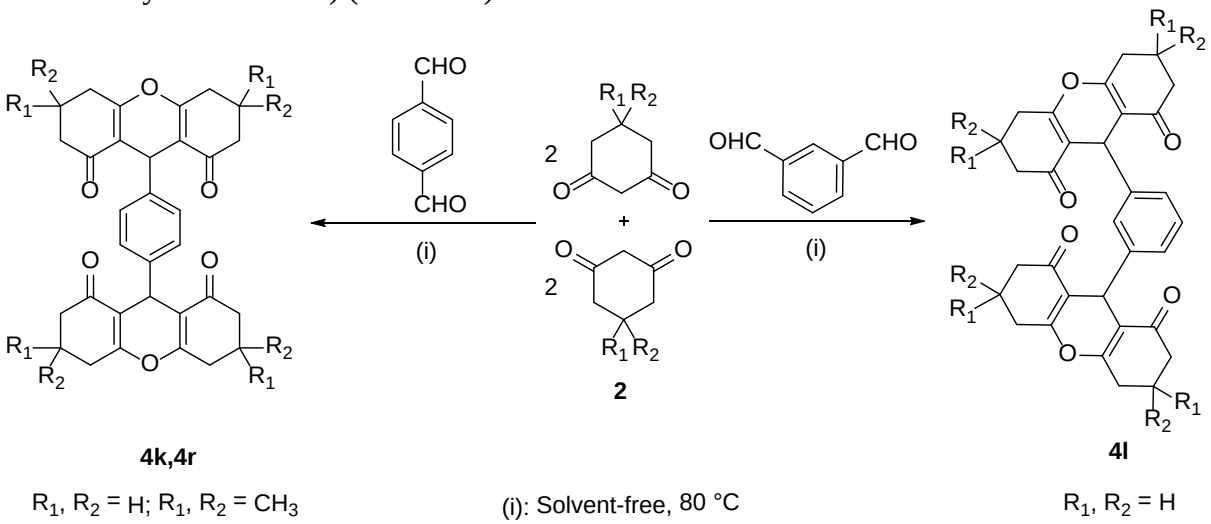
including the reaction of aryloxymagnesium halides with triethylorthoformate,[20] cyclodehydration,[21] trapping of benzynes by phenols,[22] intramolecular phenyl carbonyl coupling reactions of benzaldehydes and acetophenones,[23] and cyclocondensation between 2-hydroxy aromatic aldehydes and 2-tetralone.[24] In view of the importance of xanthene derivatives, many methods for the synthesis of these compounds were reported including condensation of *β*-naphthol and aldehydes or acetals catalyzed by silica sulfuric acid, HCl/CH_3COOH or H_3PO_4.[25] However some of these methods involved long reaction times, harsh reaction conditions and unsatisfactory yields. Therefore improvements in these syntheses have been sought continuously. In scope of our study on the catalytic synthesis of heterocyclic compounds,[26-28] In this work an efficient and adapted route to synthesis of 1,8-dioxooctahydroxanthenes (**4**) was obtained by condensation of 1,3-cyclohexanediones (**1**) and aromatic aldehydes (**2**) using Indium (III) chloride and metaphosphoric acid (when an average of one molecule of water per phosphoric unit has been driven off, the resulting substance is a glassy solid having an empirical formula of $(HPO_3)_n$ and is called metaphosphoric acid) as effective, inexpensive and recoverable catalysts (Scheme 1).



Scheme 1. Catalyzed synthesis of 1,8-dioxooctahydroxanthenes using $InCl_3$ and $(HPO_3)_n$.

2. Results and Discussion

From catalytic condensation reaction of cyclic 1,3-diketones **1** such as dimedone (R_1, R_2 = Me) with several aromatic aldehydes **2**, in first view, synthesis of 2,2'-(arylmethylene)bis(3-hydroxycyclohex-2-enone) (**3)** has expected, but as can be seen from Scheme 1, 2,2'-(arylmethylene)bis(3-hydroxycyclohex-2-enone) **3** was not formed and cyclic 1,3-diketones **1** with aromatic aldehydes **2** were effectively cyclized to obtain 9-aryl-substituted 1,8-dioxooctahydroxanthenes **4**. In another variation, when using aromatic dialdehyde substrate, instead of benzaldehyde derivatives lead to condensation with 1,3-cyclic diketones (1:4 ratio) to afford bisxanthene products. In this case four 1,3-diketones with dialdehyde were effectively cyclized to obtain bis(9-aryl-substituted 1,8-dioxooctahydroxanthenes) (Scheme 2).



Scheme 2. Catalyzed synthesis of bis(1,8-dioxooctahydroxanthenes) by the use of $InCl_3$ and $(HPO_3)_n$.

The structures of the products **4** were deduced from their IR, ^1H, ^{13}CNMR spectroscopic data and their melting points. To find the optimum conditions for synthesis of xanthenes derivatives in the presence of $InCl_3$ and $(HPO_3)_n$ as two efficient catalysts, firstly, synthesis of 3,3,6,6-tetramethyl-9-phenyl-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8 (2H)-dione (**4a**) was chosen as a model reaction. In model reaction, in the presence of $InCl_3$ and $(HPO_3)_n$ as catalyst separately, the reaction carried out in different solvents such as water, ethanol, methanol, chloroform, acetonitrile and solvent-less conditions. From these experiments, found that the reaction was compeleted with short time and high yield under solvent free condition (Table 1). Therefore, the reaction carry out in solvent free condition which has very advantage in chemistry such as reduce pollution, and help to decrease costs due to the simplification of experimental procedure, work up technique and saving in labour.[29]

Table 1. Effect of solvents in synthesis of xanthenes derivatives (model reaction)

Entry	Solvent	A	B
		Time, min/Yield, %	Time, min/Yield, %
1	Water	120/50	180/50
2	Ethanol	120/60	120/50
3	Methanol	180/50	180/55
4	Chloroform	180/45	180/40
5	Acetonitrile	180/30	180/25
6	Dimethylformamide	180/30	180/25
7	Dioxane	60/75	60/80
8	Solvent-free	60/98	60/92

A) Reaction catalyzed by $InCl_3$
B) Reaction catalyzed by $(HPO_3)_n$

Evaluated quantity of required catalysts in synthesis 1,8-dioxooctahydroxanthene derivatives for model reaction (compound **4a**) was shown that maximum yield obtained, when the reaction was loaded with 10 mol% of $InCl_3$ and 8 mol% $(HPO_3)_n$ (Table 2).

Table 2. Optimization of molar ratio of the catalysts in synthesis of 1,8-dioxooctahydroxanthene (model reaction)

$InCl_3$ (mol%)	Time (min)	Yield (%)	$(HPO_3)_n$ (mol%)	Time (min)	Yield (%)
1	120	35	1	120	40
2	120	60	2	120	55
5	60	88	5	60	85
8	60	92	8	60	92
10	60	98	10	60	88

As can be seen from Table 2, the best molar ratios of the catalysts for this reaction were found to be 10 mol% for $InCl_3$ and 8 mol% for $(HPO_3)_n$ for the model reaction whereas the larger amounts of the catalysts did not improve the results.

In the following study on the model reactions, we examined the reactions at various temperatures to find out the effect of temperature on the progress of reaction in the presence of optimized amount of

catalysts. The maximum rate of reaction was obtained at 80 °C in the presence of both $InCl_3$ and $(HPO_3)_n$ (Table 3).

Table 3. Optimization of temperature for model reaction

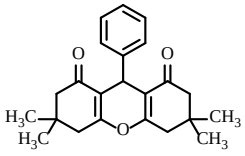
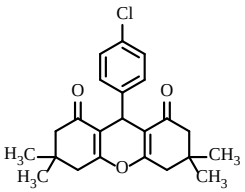
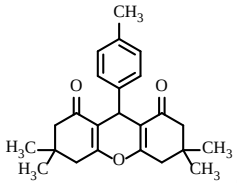
Temp. (°C)[a]	Time (min)[a]	Yield (%)[a]	Temp. (°C)[b]	Time (min)[b]	Yield (%)[b]
r.t.	120	25	r.t.	300	30
40	120	50	40	120	45
50	90	70	50	100	50
60	70	80	60	90	70
70	60	90	70	80	85
80	60	98	80	60	92
90	60	94	90	60	88
100	60	92	100	60	82
110	60	88	110	60	80

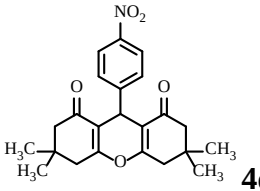
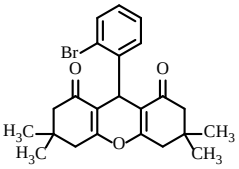
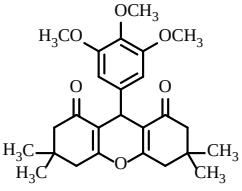
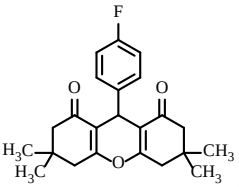
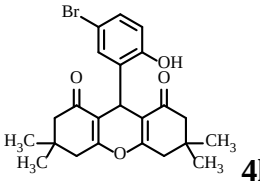
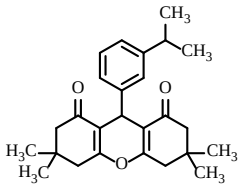
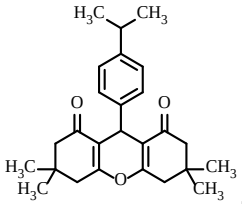
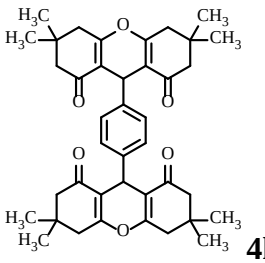
[a] $InCl_3$ as catalyst
[b] $(HPO_3)_n$ as catalyst

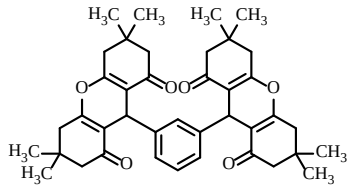
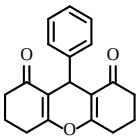
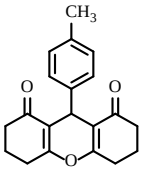
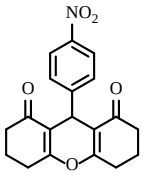
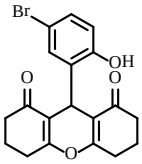
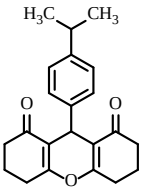
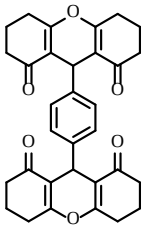
As can be seen from Table 3, at room temperature, reaction was completed slowly. Increasing temperature to 80 °C increased the yield of reaction and decreased the time of reaction. When, the reaction was heated above 80 °C, so high temperatures did not further improved yield and decrease time of reaction. According to the archived optimal condition, we conducted the synthesis of xanthenes derivatives in the presence of $InCl_3$ (10 mol%) and $(HPO_3)_n$ (8 mol%) in solvent-free condition at 80 °C.

Under the obtained conditions several aromatic aldehydes **2** containing electron-donating as well as electron-withdrawing groups with different substitution pattern were effectively condensed to give 9-aryl substituted 1,8-dioxooctahydroxanthene derivatives **4**. In all the cases, corresponding xanthene derivatives were obtained in good to excellent yields (Table 4).[20,30-42]

Table 4. Catalytic synthesis of 9-aryl-substituted 1,8-dioxooctahydroxanthenes by the use of $InCl_3$ and $(HPO_3)_n$.

Compound **4**	$InCl_3$ Time (min)/Yield (%)[a]	$(HPO_3)_n$ Time (min)/Yield (%)[a]	M.p. (°C)/[lit].
 **4a**	60/98	60/92	202-204 (201-202)[30]
 **4b**	70/92	70/90	230-232 (230-232)[30]
 **4c**	70/92	70/88	215-217 (216-217)[31]

 **4d**	40/96	40/90	219-221 (221-223)[31]
 **4e**	65/92	70/88	226-227 (226-228)[32]
 **4f**	60/94	60/90	209-211 (210-212)[33]
 **4g**	60/94	65/90	223-225 (224-226)[32]
 **4h**	60/92	70/85	250-252 (249-252)[34]
 **4i**	60/88	100/85	189-191 (190-191)[35]
 **4j**	70/90	90/85	238-239 (236-239)[36]
 **4k**	60/92	80/88	245-247 (>300)[37]

 **4l**	75/88	100/85	238-240 (236-238)[38]
 **4m**	60/96	70/95	271-273 (272-273)[39]
 **4n**	65/94	65/90	260-262 (262-263)[30]
 **4o**	40/96	45/90	224-227 (224-226)[40]
 **4p**	55/90	70/85	250-252 (249-252)[20]
 **4q**	60/88	80/85	170-172 (169-171)[41]
 **4r**	50/94	60/88	282-285 (280-282)[42]

a) Refers to isolated yield

At the end of the reactions, the catalysts were filtered, washed with diethyl ether, dried at 120 °C for 1 h, and reused in another reaction. We found that both $InCl_3$ and $(HPO_3)_n$ showed high catalytic activity with very short reaction times. Moreover, can be recovered and reused five times without significant loss of activity (Fig. 1). The results of these observations for the model reaction are shown in Table 5.

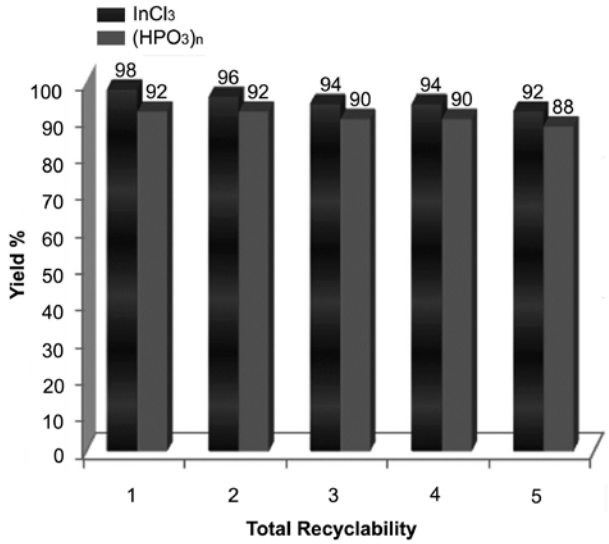
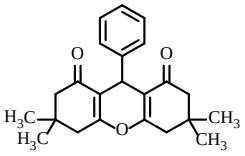


Fig. 1. Reusability of handled catalysts in further cycles

Table 5. Reusability results of catalysts on the reaction process for the model reaction.

product	Total reusability	$InCl_3$	$(HPO_3)_n$
		Yield (%)/Time (min)	Yield (%)/Time (min)
	1	98/60	92/60
	2	96/60	92/60
	3	94/60	90/60
	4	94/60	90/65
	5	92/65	88/75

Comparison of this method with others for the synthesis of 3,3,6,6-tetramethyl-9-phenyl-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione **4a** as a model reaction is shown in Table 6.[30-32,43-46]

Table 6. Comparison of the results for synthesis of 3,3,6,6-tetramethyl-9-phenyl-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8 (2H)-dione (compound **4a**) with other catalysts.

Entry	Catalyst	Mol (%)	Solvent/Temp. (°C)	Time (min)	Yield (%)/Ref.
1	$InCl_3$	10	Solvent free/80	60	98[This work]
2	$(HPO_3)_n$	8	Solvent free/80	60	92[This work]
3	DBSA[a]	10	H_2O-Ultrasonic /30	60	89[43]
4	TMSCl[b]	100	CH_3CN/Reflux	420	95[44]
5	TBAHS[c]	10	Dioxane, H_2O/Reflux	210	88[30]
6	DBSA[a]	20	H_2O/Reflux	180	91[45]
7	Selectfluor™ [d]	10	Solvent free/120	60	95[46]
8	PPA-SiO_2[e]	10	Solvent free/140	30	93[31]
9	$HClO_4$-SiO_2	10	Solvent free/140	180	32[31]
10	$SbCl_3$-SiO_2	10	Solvent free/120	50	93[32]

[a] *p*-dodecylbenzenesulfonic acid.
[b] Trimethylsilyl chloride.
[c] Tetrabutylammonium hydrogen sulfate.
[d] 1-(chloromethyl)-4-fluoro-1,4-diazoniabicyclo[2,2,2]octane bis(tetrafluoroborate).
[e] metaphosphoric acid supported on silica.

These results show that these catalysts prepared good to excellent conditions for the synthesis of xanthene derivatives than other catalysts and methods that were reported. This method not only affords the products with high yields but also avoids the problems associated with handling, pollution and catalysts cost.

3. Conclusions

In conclusion, new application of indium (III) chloride ($InCl_3$) and metaphosphoric acid $(HPO_3)_n$ as two effective and reusable solid acid catalysts in the preparation of 9-aryl substituted 1,8-dioxooctahydro xanthene derivatives are presented. All products in the presence of catalytic amount of $InCl_3$ and $(HPO_3)_n$ were obtained in excellent yields. The presence of $InCl_3$ and $(HPO_3)_n$ in condensation between cyclic 1,3-diketones with aromatic aldehydes is a key factor to progress of reaction. $(HPO_3)_n$ not only prepared cheap and facile procedure but also developed the green chemistry. Other advantages of these methods are simple experimental procedure, utilization of clean and recyclable catalysts, the use of ready available starting materials, and short period of reaction.

Acknowledgements

Financial support from Yasouj University of Iran is gratefully acknowledged.

4. Experimental

4.1. Materials and Methods

Melting points were measured on an elecrtothermal KSB1N apparatus. IR spectra were recorded in the matrix of KBr with JASCO FT-IR-680 plus spectrometer. ^1H NMR and ^{13}C NMR spectra were determined on a FT-NMR Bruker Avance Ultra Shield Spectrometer at 400.13 and 100.62 MHz in $CDCl_3$ as solvent in the presence of tetramethylsilane as internal standard. TLC was performed on TLC-Grade silica gel-G/UV 254 nm plates (*n*-hexane, ethyl acetate 2:1). Chemicals were purchased from Fluka and Merck chemical companies.

4.2. General procedure for the Preparation of 9-Aryl-substituted 1,8-Dioxooctahydroxanthenes

A mixture of cyclic 1,3-diketone (2 mmol), aromatic aldehyde (1 mmol) and $InCl_3$ (0.022 g, 0.1 mmol) or $(HPO_3)_n$ (0.003 g, 0.08 mmol) was heated at 80 °C for the time indicated in Table 4. The progress of the reaction was monitored by TLC on silica gel (SILG/UV 254) plates (*n*-hexane, ethyl acetate 2:1). After completion of the reaction, the reaction mixture was cooled to room temperature and was washed with $CHCl_3$ (10 mL), then was filtered to remove the catalyst and the filtrate was concentrated in vacuum to afford the crude product. Crude product was recrystallized from EtOH to afford the crystalline pure product. The catalyst was washed with ethanol, dried at 120 °C for 1 h, and reused five times in other reactions.

4.3. Preparation of 3,3,6,6-tetramethyl-9-phenyl-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8 (2H)-dione (compound 4a):

The compound **4a** was prepared according to the general procedure using dimedone (**2**, R_1, R_2 = Me) (0.28 g, 2 mmol), benzaldehyde (0.106 g, 1 mmol) and $InCl_3/SiO_2$ (0.117 g, 0.05 mmol) or $In(CF_3SO_3)_3$ (0.011 g, 0.02 mmol). The reaction progress was monitored by TLC. After the completion of the reaction, the solid product was washed with $CHCl_3$ (10 mL), and filtered to remove the catalyst. After evaporation of filtrate by vacuum, the resulting crude product was recrystallized from hot EtOH to give a white crystalline solid.

4.4. Physical and Spectral Data

Compound **4a**: mp 202-204 °C; IR (KBr) ν_{max}: 3060, 2958, 1661, 1624, 1468, 1199, 742, 700 cm^{-1}; ^1H NMR (400 MHZ, $CDCl_3$) δ: 0.79 (6H, s, $2CH_3$), 0.90 (6H, s, $2CH_3$), 2.00 (4H, dd, $2\times CH_2$, ^1J = 16.4 Hz, ^4J = 28.8 Hz), 2.27 (4H, s, $2CH_2$), 4.55 (1H, s, CH), 6.90-7.10 (5H, m, H Ar); ^{13}C NMR (100 MHZ, $CDCl_3$) δ: 28.47, 30.44, 32.97, 33.36, 42.00, 51.88, 116.79, 127.51, 129.19,129.52, 145.25, 163.42, 196.66; Anal. Calcd for $C_{23}H_{26}O_3$: C, 78.83; H, 7.48; Found: C, 78.75; H, 7.55.
Compound **4f**: mp 209-211 °C; IR (KBr) ν_{max}: 3050, 2995, 1660, 1620, 1480, 1375, 1188, 1090, 845 cm^{-1}; ^1H NMR (400 MHZ, $CDCl_3$) δ: 1.04 (6H, s, $2CH_3$), 1.12 (6H, s, $2CH_3$), 2.24 (4H, s, $2CH_2$), 2.47 (4H, s, $2CH_2$), 3.78 (3H, s, OCH_3), 3.81 (6H, s, $2OCH_3$), 4.72 (1H, s, CH), 6.52 (2H, s, H Ar); ^{13}C NMR (100 MHZ, $CDCl_3$) δ: 27.18, 29.36, 31.80, 32.17, 40.90, 50.75, 56.09, 60.68, 105.75, 115.57, 136.60, 139.73, 152.79, 162.34, 196.45; Anal. Calcd for $C_{26}H_{32}O_6$: C, 70.89; H, 7.32; Found: C, 70.91; H, 7.40.

Compound **4g**: mp 223-225 °C; IR (KBr) ν_{max}: 3040, 2990, 2970, 1660, 1620, 1500, 1360, 1200, 1160, 1180 cm^{-1}; ^1H NMR (400 MHZ, $CDCl_3$) δ: 1.00(6H, s, $2CH_3$), 1.11(6H, s, $2CH_3$), 2.21(4H, q, J = 16.4 Hz, $2CH_2$), 2.47 (4H, s, $2CH_2$), 4.73 (1H, s, CH), 6.91 (2H, m, H Ar), 7.27 (2H, m, H Ar); ^{13}C NMR (100 MHZ, $CDCl_3$) δ: 27.28, 29.26, 32.19, 40.84, 50.73, 114.71, 114.93, 115.49, 129.88, 139.99, 160.15, 162.58, 196.34; Anal. Calcd for $C_{23}H_{25}FO_3$: C, 74.98; H, 6.84; Found: C, 74.89; H, 6.88.
Compound **4i**: mp 189-191 °C; IR (KBr) ν_{max}: 3065, 2960, 2880, 1660, 1615, 1450, 1375, 1200, 1160, 1138 cm^{-1}; ^1H NMR (400 MHZ, $CDCl_3$) δ: 1.01 (6H, s, $2CH_3$), 1.10 (6H, s, $2CH_3$), 1.18 (6H, d, J = 5.2 Hz, $2CH_3$), 2.21 (4H, m, $2CH_2$), 2.46 (4H, s, $2CH_2$), 2.79 (1H, bb, CH), 4.73 (1H, s, CH), 7.05 (2H, d, J = 6.8 Hz, H Ar), 7.19 (2H, m, H Ar); ^{13}C NMR (100 MHZ, $CDCl_3$) δ: 23.90, 27.49, 29.21, 31.30, 32.21, 33.60, 40.90, 50.80, 126.12, 128.12, 141.39, 146.51, 162.15, 196.46; Anal. Calcd for $C_{26}H_{32}O_3$: C, 79.56; H, 8.22; Found: C, 79.62; H, 8.16.

Compound **4k**: mp 245-247 °C; IR (KBr) ν_{max}: 3040, 2957, 1666, 1620, 1462, 1425, 1365, 1200, 1162, 1003, 808 cm^{-1}; ^1H NMR (400 MHZ, $CDCl_3$) δ: 0.97 (12H, s, $4CH_3$), 1.07 (12H, s, $4CH_3$), 2.18 (8H, s, $4CH_2$), 2.44 (8H, dd, ^1J = 36.4, ^4J = 17.6, $4CH_2$), 4.71 (2H, s, 2CH), 7.08 (2H, s, H Ar), 7.27 (2H, s, H Ar); ^{13}C NMR (100 MHZ, $CDCl_3$) δ 25.01, 27.66, 28.98, 30.74, 32.24, 40.85, 50.64, 115.70, 127.88, 141.74, 162.42, 196.36; Anal. Calcd for $C_{40}H_{46}O_6$: C, 77.14; H, 7.45; Found: C, 77.20; H, 7.37.
Compound **4l**: mp 238-240 °C; IR (KBr) ν_{max} 3095, 2957, 1659, 1629, 1462, 1203, 1158, 769 cm^{-1}; ^1H NMR (400 MHZ, $CDCl_3$) δ: 1.03 (12H, s, $4CH_3$), 1.08 (12H, s, $4CH_3$), 2.15 (8H, dd, ^2J = 24 Hz, ^4J = 16 Hz, $4CH_2$), 2.48 (8H, dd, ^2J = 45.2 Hz, ^4J = 17.6 Hz, $4CH_2$), 4.72 (2H, s, 2CH), 7.07-7.09 (3H, m, H Ar), 7.15 (1H, s, H Ar); ^{13}C NMR (100 MHZ, $CDCl_3$) δ: 28.02, 29.57, 31.76, 32.56, 41.27, 51.27, 116.01, 126.84, 128.18, 144.04, 162.72, 196.66; Anal. Calcd for $C_{40}H_{46}O_6$: C, 77.14; H, 7.45; Found: C, 77.18; H, 7.41.

Compound **4n**: mp 260-262 °C; IR (KBr) ν_{max}: 3050, 2955, 1658, 1616, 1467, 1175, 1126, 827 cm^{-1}; ^1H NMR (400 MHZ, $CDCl_3$) δ: 2.01 (4H, m, $2CH_2$), 2.26 (3H, s, CH_3), 2.35 (4H, m, $2CH_2$) 2.59 (4H, m, $2CH_2$) 4.78 (1H, s, CH), 7.03 (2H, d, J = 7.2 Hz, H Ar), 7.19 (2H, d, J = 7.2 Hz, H Ar); ^{13}C NMR (100 MHZ, $CDCl_3$) δ: 20.31, 21.07, 27.15, 31.22, 36.99, 117.00, 128.25, 128.83, 135.85, 141.56, 163.84, 196.56; Anal. Calcd for $C_{20}H_{20}O_3$: C, 77.90; H, 6.54; Found: C, 77.93; H, 6.50.

Compound **4o**: mp 224-227 °C; IR (KBr) ν_{max}: 3070, 2950, 1664, 1617, 1467, 1172, 830 cm^{-1}; ^1H NMR (400 MHZ, $CDCl_3$) δ: 2.07 (4H, m, $2CH_2$), 2.35 (4H, m, $2CH_2$) 2.61 (4H, m, $2CH_2$), 4.88 (1H, s, CH), 7.48 (2H, d, J = 8.8 Hz, H Ar), 8.10 (2H, d, J = 8.8 Hz, H Ar); ^{13}C NMR (100 MHZ, $CDCl_3$) δ: 20.22, 27.14, 32.23, 36.81, 115.70, 123.41, 129.42, 145.48, 151.73, 164.60, 196.45; Anal. Calcd for $C_{19}H_{17}NO_5$: C, 67.25; H, 5.05; N, 4.13; Found: C, 67.31; H, 4.98, N, 4.16.

Compound **4p**: mp 250-252 °C; IR (KBr) ν_{max}: 3095, 2960, 1619, 1563, 1463, 1367, 1290, 1215, 1180, 1086, 1033, 1005, 814, 650 cm^{-1}; ^1H NMR (400 MHZ, $CDCl_3$) δ: 1.86 (2H, s, CH_2), 2.05 (3H, t, J =

12.4 Hz, CH_2), 2.15 (1H, d, *J* = 8.4 Hz, CH_2), 2.43 (2H, m, CH_2), 2.57 (3H, t, *J* = 19.21 Hz, CH_2), 2.75 (1H, d, *J* = 8.8 Hz, CH_2), 4.58 (1H, s, CH), 6.91 (1H, d, *J* = 4.4 Hz, H Ar), 7.13 (1H, s, H Ar), 7.26 (1H, d, *J* = 4.4 Hz, H Ar) 10.77 (1H, s, OH); ^{13}C NMR (100 MHZ, $CDCl_3$) δ: 19.54, 19.87, 27.89, 27.97, 29.72, 35.95, 36.95, 112.02, 117.00, 117.26, 119.39, 126.92, 130.46, 130.68, 150.03, 170.73, 173.37, 197.09, 201.31; Anal. Calcd for $C_{19}H_{17}BrO_4$: C, 58.63; H, 4.40; Found: C, 58.68; H, 4.34.

Compound **4q**: mp 170-172 °C; IR (KBr) ν_{max}: 3050, 2990, 1660, 1620, 1450, 1200, 1130, 828 cm^{-1}; ^{1}H NMR (400 MHZ, $CDCl_3$) δ: 1.19 (6H, d, *J* = 6.8 Hz, $2CH_3$), 2.01 (4H, m, $2CH_2$), 2.34 (4H, m, $2CH_2$), 2.61 (4H, m, $2CH_2$), 2.81 (1H, t, *J* = 7.2 Hz, CH), 4.80 (1H, s, CH) 7.06 (2H, d, *J* = 8 Hz, H Ar), 7.19 (2H, d, *J* = 8 Hz, H Ar); ^{13}C NMR (100 MHZ, $CDCl_3$) δ: 20.28, 23.92, 27.15, 31.04, 33.59, 36.99, 117.03, 126.16, 146.52, 163.95, 196.64; Anal. Calcd for $C_{22}H_{24}O_3$: C, 78.54; H, 7.19; Found: C, 78.57; H, 7.15.

References

1. Movassaghi M., and Jacobsen E. N., (2002) A direct method for the conversion of terminal epoxides into γ-butanolides. *J. Am. Chem. Soc*., 124, 2456-2457.
2. Qi X., Rice G. T., Lall M. S., Plummer M. S., and White M. C., (2010) Diversification of a β-lactam pharmacophore via allylic C–H amination: accelerating effect of Lewis acid co-catalyst *Tetrahedron*, 66, 4816-4826.
3. Wedge T. J., and Hawthorne M. F., (2003) Multidentate carborane-containing Lewis acids and their chemistry: mercuracarborands, *Coord. Chem. Rev.*, 240, 111-128.
4. Stone M. T., and Anderson H. L., (2007) A cyclodextrin-insulated anthracene rotaxane with enhanced fluorescence and photostability. *Chem. Commun.*, 126, 2387-2389.
5. (a) Kumar G. G. K. S., and Laali K. K., (2013) Condensation of propargylic alcohols with N-methylcarbazole and carbazole in [bmim] PF 6 ionic liquid; synthesis of novel dipropargylic carbazoles using TfOH or Bi (NO 3) 3· 5H 2 O as catalyst. *Tetrahedron Lett.*, 54, 965-969. (b) Aridoss G., Sarca V. D., Ponder J. F. Jr., Crowe J., and Laali K. K., (2011) Electrophilic chemistry of propargylic alcohols in imidazolium ionic liquids: Propargylation of arenes and synthesis of propargylic ethers catalyzed by metallic triflates [Bi (OTf) 3, Sc (OTf) 3, Yb (OTf) 3], TfOH, or B (C 6 F 5) 3. *Org. Biomol. Chem.* 9, 2518-2529. (c) Kalkhambkar R. G., and Laali K. K., (2011) Highly efficient synthesis of amides via Ritter chemistry with ionic liquids. *Tetrahedron Lett*. 52, 5525-5529.
6. (a) Sartori G., Neto J. S. S., Pesarico A. P., Back D. F., Nogueira C. W., and Zeni G. (2013) Bis-vinyl selenides obtained via iron (III) catalyzed addition of PhSeSePh to alkynes: synthesis and antinociceptive activity. *Org. Biomol. Chem.*, 11, 1199-1208. (b) Speranca A., Godoi B., and Zeni G. (2013) Iron (III) chloride/diorganyl diselenides: a tool for intramolecular cyclization of alkynone O-methyloximes. *J. Org. Chem.* 78, 1630-1637. (c) Stein A. L., Bilheri F. N., Rosario A. R., and Zeni G., (2013) FeCl 3–diorganyl dichalcogenides promoted cyclization of 2-organochalcogen-3-alkynylthiophenes: synthesis of chalcogenophene [2, 3-b] thiophenes. *Org. Biomol. Chem*., 11, 2972-2978.
7. Kitano M., Nakajima K., Kondo J. N., Hayashi S. and Hara M. (2010) Protonated titanate nanotubes as solid acid catalyst. *J. Am. Chem. Soc.*, 132, 6622-6623.
8. Stefani H. A., and Gatti P. M. (2000) 3, 4-Dihydropyrimidin-2 (1H)-ones: fast synthesis under microwave irradiation in solvent free conditions. *Synth. Commun.*, 30, 2165-2173.
9. Maleki A., Javanshir S., and Sharifi S. (2014) Silica-based sulfonic acid (MCM-41-SO3H): a practical and efficient catalyst for the synthesis of highly substituted quinolines under solvent-free conditions at ambient temperature. *Curr. Chem. Lett.*, 3, 125-132.
10. Havaei M., Karami B., and Khodabakhshi S., (2014) Silica supported yttrium trinitrate: preparation, characterization and application in catalytic Biginelli condensation. *Curr. Chem. Lett.*, 3 167-174
11. Clark J. H., *Acc.* (2002) Solid acids for green chemistry. *Chem. Res*., 35, 791-797.

12. El-Brashy A. M., Metwally M. E., and El-Sepai F. A., (2004) Spectrophotometric determination of some fluoroquinolone antibacterials by binary complex formation with xanthene dyes. *Il Farmaco*, 59, 809-817.
13. (a) Chibale K., Visser M., Schalkwyk D. V., Smith P. J., Saravanamuthu A., and Fairlamb A. H. (2003) Exploring the potential of xanthene deriva- tives as trypanothione reductase inhibitors and chloroquine potentiating agents. *Tetrahedron*, 59, 2289-2296. (b) Borah R., Dutta P., and Sarma P. (2013) Investigation of efficient synthesis of 1, 8-dioxo-octahydroxanthene derivatives under solvent-free grinding method. *Curr. Chem. Lett.*, 2, 159-166.
14. Bhowmik B. B., and Ganguly P. (2005) Photophysics of xanthene dyes in surfactant solution. *Spect. Chim. Acta A*, 61, 1997-2003.
15. Ion R. M., Frackowiak D., and Wiktorowicz K. (1998) The incorporation of various porphyrins into blood cells measured via flow cytometry, absorption and emission spectroscopy. *Acta Biochim. Pol.*, 45, 833-845.
16. Knight C. G., and Stephens T. (1989) Xanthene-dye-labelled phosphatidylethanolamines as probes of interfacial pH. *Biochem. J.*, 258, 683-687.
17. Ahmad M. T., King A., Ko D. K., Cha B. H., and Lee J. (2002) Performance and photostability of xanthene and pyrromethene laser dyes in sol-gel phases. *J. Phys. D: Appl. Phys.*, 35, 1473-1476.
18. Saint-Ruf G., Hieu H. T., and Poupelin J. P. (1975) The effect of dibenzoxanthenes on the paralyzing action of zoxazolamine. *Naturwissenschaften*, 62, 584-590.
19. Kinjo J., Uemura H., Nohara T., Yamashita M., Marubayashi N., and Yoshihira K., (1995) Novel yellow pigment from Pterocarpus santalinus: biogenetic hypothesis for santalin analogs. *Tetrahedron Lett.*, 36, 5599-5602.
20. Casiraghi G., Casnati G., and Cornia M. (1973) Regiospecific reactions of phenol salts: reaction-pathways of alkylphenoxy-magnesiumhalides with triethylorthoformate. *Tetrahedron Lett.*, 14, 679-682.
21. Bekaert A., Andrieux J., and Plat M. (1992) New total synthesis of bikaverin. *Tetrahedron Lett.*, 33, 2805-2806.
22. Knight D. W., and Little P. B., (2001) The first efficient method for the intramolecular trapping of benzynes by phenols: a new approach to xanthenes. *J. Chem. Soc. Perkin Trans.1*, 14, 1771-1777.
23. Kuo C. W., and Fang J.-M., (2001) Synthesis of xanthenes, indanes, and tetrahydronaphthalenes via intramolecular phenyl–carbonyl coupling reactions. *Synth. Commun.*, 31, 877-892.
24. Jha A., and Beal J., (2004) Convenient synthesis of 12H-benzo [a] xanthenes from 2-tetralone. *Tetrahedron Lett.*, 45, 8999-9001.
25. Seyyedhamzeh M., Mirzaei P., and Bazgir A., (2008) Solvent-free synthesis of aryl-14H-dibenzo [a, j] xanthenes and 1, 8-dioxo-octahydro-xanthenes using silica sulfuric acid as catalyst. *Dyes Pigm.*, 76, 836-839.
26. Karami B., and Kiani M. (2011) ZrOCl 2. 8H 2 O/SiO 2: An efficient and recyclable catalyst for the preparation of coumarin derivatives by Pechmann condensation reaction. *Catal. Commun.*, 14, 62-67.
27. Eskandari K., Karami B., and Khodabakhshi S., (2014) Titanium dioxide nanowires as green and heterogeneous catalysts for the synthesis of novel pyranocoumarins. *Catal. Commun.* 54, 124-130.
28. Karami, B., Eskandari, K., Farahi, M. and Barmas, A. (2012) An Effective and New Method for the Synthesis of Polysubstituted Imidazoles by the Use of CrCl3. 6H2O as a Green and Reusable Catalyst: Synthasis of Some Novel Imidazole Derivatives. *J. Chin. Chem. Soc.*, 59, 473-479.
29. Karami B., Eskandari K., Gholipour S., and Jamshidi M. (2013) Green synthesis of three substituted methane derivatives by employing ZnO nanoparticles as a powerful and recyclable catalyst. *Org. Prep. Proced. Int.* 45, 220-226.
30. Kantevari S., Bantu R., and Nagarapu L. (2007) HClO 4–SiO 2 and PPA–SiO 2 catalyzed efficient one-pot Knoevenagel condensation, Michael addition and cyclo-dehydration of

dimedone and aldehydes in acetonitrile, aqueous and solvent free conditions: Scope and limitations. *J. Mol. Catal. A: Chem.*, 269, 53-57.

31. Venkatesan K., Pujari S. S., Lahoti R. J., and Srinivasan K. V. (2008) An efficient synthesis of 1, 8-dioxo-octahydro-xanthene derivatives promoted by a room temperature ionic liquid at ambient conditions under ultrasound irradiation. *Ultr. Sonochem. Chem.*, 15, 548-553.
32. Fan X., Hu X., Zhang X., and Wang J. (2005) InCl3⊙ 4H2O-promoted green preparation of xanthenedione derivatives in ionic liquids. *Can. J. Chem.*, 83, 16-20.
33. Zhang Z. H., and Lui Y. (2008) Antimony trichloride/SiO 2 promoted synthesis of 9-ary-3, 4, 5, 6, 7, 9-hexahydroxanthene-1, 8-diones. *Catal. Commun.*, 9, 1715-1719.
34. Kozlov N. G., and Basalaeva L. I. (2005) Vanilline alkanoates in the synthesis of hexahydrobenzacridine and octahydroxanthene derivatives. *Russ. J. Chem.*, 75, 617-621.
35. Horning E. C., and Horing M. G. (1946) Methone derivatives of aldehydes. *J. Org. Chem.*, 11, 95-99.
36. Bekaert A., Andrieux J., and Plat M. (1992) New total synthesis of bikaverin. *Tetrahedron Lett.*, 33, 2805-2806.
37. Niknam K., and Damya M. (2009) 1-Butyl-3-methylimidazolium Hydrogen Sulfate [Bmim] HSO4: An Efficient Reusable Acidic Ionic Liquid for the Synthesis of 1, 8-Dioxo-Octahydroxanthenes. *J. Chin. Chem. Soc.*, 56, 659-665.
38. Karade H. N., Sathe M., and Kaushik M. P. (2007) Synthesis of 4-aryl substituted 3, 4-dihydropyrimidinones using silica-chloride under solvent free conditions. *Arkivoc*, xiii, 252-258.
39. Das B., Thirupathi P., Mahender I., Reddy V. S., and Rao Y. K. (2006) Amberlyst-15: An efficient reusable heterogeneous catalyst for the synthesis of 1, 8-dioxo-octahydroxanthenes and 1, 8-dioxo-decahydroacridines. *J. Mol. Catal. A: Chem.*, 247, 233-239.
40. John A., Yadav P. J. P., and Palaniappan S. (2006) Clean synthesis of 1, 8-dioxo-dodecahydroxanthene derivatives catalyzed by polyaniline-p-toluenesulfonate salt in aqueous media. *J. Mol. Catal. A: Chem.*, 248, 121-125.
41. Tavakoli H. R., Zamani H., Ghorbani M. H., and Etedali-Habibabadi H. (2009) Solvent-free synthesis of 14-aryl (alkyl)-14H-dibenzo [a, j] xanthene, 9-aryl (alkyl)-3, 3, 6, 6-tetramethyl-3, 4, 5, 6, 7, 9-hexahydro-2H-xanthene-1, 8-dione and 2-amino-5, 6, 7, 8-tetrahydro-5-oxo-4-aryl-7, 7-dimethyl-4Hbenzo-[b]-pyran derivatives using InCl 3 as catalyst. *Iran. J. Org.Chem.*, 2, 118-126.
42. Sachar A., Sharma R. L., Kumar S., Kaur D., and Singh J. (2006) Synthesis of novel bis-condensed heterocyclic ring assembly systems. *J. Heterocycl. Chem.*, 43, 1177-1181.
43. Jin T-S., Zhang J-S., Wang A-Q., and Li T-S. (2006) Ultrasound-assisted synthesis of 1, 8-dioxo-octahydroxanthene derivatives catalyzed by p-dodecylbenzenesulfonic acid in aqueous media. *Ultr. Sonochem. Chem.*, 13, 220-224.
44. Kantevari S., Bantu R., and Nagarapu L., (2006) TMSCl mediated highly efficient one-pot synthesis of octahydroquinazolinone and 1, 8-dioxo-octahydroxanthene derivatives. *Arkivoc*, xvi, 136-148.
45. Bin L. L., Shou J. T., Sha H. L., Meng L., Na Q., L. and Shuang T. (2006) The Reaction of Aromatic Aldehydes and 1,3-Cyclohexanedione in Aqueous Media. *E-J. Chem.*, 3, 117-121.
46. Poor-Heravi M. R. (2009) Selectfluor™ promoted synthesis of 9-aryl-1, 8-dioxooctahydroxanthane derivatives under solvent-free conditions. *J. Iran Chem. Soc.*, 6, 483-488.