**Facile and rapid synthesis of divers xanthene derivatives using Lanthanum(III) chloride/chloroacetic acid as an efficient and reusable catalytic system under solvent-free conditions**

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*Abstract:* LaCl3/ClCH2COOH was used as an efficient, recyclable, and inexpensive catalytic system for synthesis of 8H-benzo[a]xanthe, hexahydro-1H-xanthene and pyran-10,12(11H)-dione derivatives via a one-pot three-component reaction of aldehydes, 2-naphthol, and cyclic 1,3-dicarbonyl compounds. The reactions proceeded rapidly at 70 oC under solvent-free conditions and the desired products were obtained in good to excellent yields.

***Keywords:*** Multi-component reactions (MCRs), 8H-benzo[a]xanthe, *Hexahydro-1H-xanthene,* 1,3-Dicarbonyl compounds, Solvent-free conditions*,* Green chemistry

RUNNING TITLE: SYNTHESIS OF XANTHENE DERIVATIVES UNDER SOLVENT-FREE CONDITIONS

INTRODUCTION

Since the past few decades, heterocyclic chemistry has been one of the most important disciplines in organic synthesis and pharmaceutical chemistry.1 A large numbers of these compounds have emerged as active pharmaceutical ingredients in several drugs for their potential anti-inflammatory,2,3 anti-tumor,4 anti-hyperlipidemic,5 anti-hypertensive,6 anti-HIV infections,7 and several other biological properties.8,9

Xanthenes are an important class of heterocyclic compounds with remarkable biological and medicinal properties, for example antiviral, antibacterial and anti-inflammatory activity. 10-13 Furthermore, they are used as leuco-dyes, pH sensitive fluorescent materials, and in laser technologies.14-16 Among this class of molecules, xanthone is a prominent structural motif found in numerous natural products and synthetic compounds with important biological activity.17-21

Multi-component reactions (MCRs) have emerged as efficient and powerful tools in organic and medicinal chemistry due to their ability to synthesize of organic molecules with higher efficiency and atom economy in a single step from three or more reactants. Moreover, MCRs offer the advantage of simplicity and synthetic efficiency over conventional chemical reactions. 22 Therefore, developing new MCRs and improving known MCRs for the synthesis of diverse groups of compounds, especially the ones that are biologically active, have gained great attention in current organic synthesis.23-25 In addition, solvent-free conditions make synthesis simpler, save energy, and prevent solvent waste, hazards, and toxicity.26-28 It therefore remains a challenge to develop multi-component reactions with a suitable heterogeneous catalysts and the use of solvent-free conditions.

One example of the MCRs is the synthesis of xanthene derivatives which can be carried out by condensation of aldehydes with b-naphthol, cyclic 1,3-dicarbonyl compounds and/or mixture of b-naphthol and cyclic 1,3-dicarbonyl compounds in the presence of different catalysts such KAl(SO4)2, 12H2O,29 MeSO3H,30 Nano-ZnO,31 iodine,32 silica sulfuric acid,33 [Et3NSO3H]Cl 34 and have been used for the preparation of 14-aryl-14H-dibenzo[a,j]xanthenes; SbCl3/SiO2,35 SiO2-ReSO3H,36 p-dodecylbenzenesulfonic acid,37 triethylbenzylammonium chloride38 and diammonium hydrogen phosphate,39 and have been used for the preparation of 1,8-dioxo octahydroxanthenes and sulfamic acid,40 dodecatungstophosphoric acid,41 InCl3/P2O5 42and poly(AMPS-co-AA) 43 have been used for preparation of tetrahydrobenzo[a]xanthene-11-ones. However, some of these methods involve long reaction times, harsh reaction conditions, or unsatisfactory yields. Therefore, improvement of these synthesis methods has been continuously sought for.

In continuation of our research on green catalytic systems and their applications in organic synthesis and their applications as catalysts in organic synthesis,44-46 we decided to investigate Lanthanum(III) chloride/chloroacetic acid (LaCl3 /ClCH2COOH) as a high efficient, and reusable catalytic system for the practical, one-pot and three-component synthesis of 8H-benzo[a]xanthen-11(12H)-one, hexahydro-1H-xanthene-1,8(2H)-dione and 11-aryl-10H-diindeno[1,2-b:2',1'-e]pyran-10,12(11H)-diones under solvent-free conditions (Scheme 1).



**Scheme 1.** One-pot synthesis of xanthene derivatives using LaCl3/ClCH2COOH as an efficient and reusable catalytic system.

**EXPERIMENTAL**

**Chemicals**

Chemicals were either prepared in our laboratory or purchased from Merck or Fluka chemical companies, and were used without any further purification.

**Apparatus**

IR spectra were recorded in KBr, using a BRUKER FT-IR spectrophotometer. 1H NMR and 13C NMR were recorded in CDCl3 and DMSO (d6) solvents on a Bruker DRX-500 spectrometer with tetramethylsilane as internal reference. Melting points were determined with a hot-plate microscope apparatus. The purity determination of the substrates and reaction monitoring were accomplished by TLC (petroleum-ethyl acetate 3:1) on silica-gel polygram SILG/UV 254 plates (from Merck Company).

**General procedure for synthesis of 12-aryl-8,9,10,12-tetrahydrobenzo[a]xanthene-11-ones (5):**

A mixture of aldehyde (1, 1 mmol), β-naphthol (3, 1 mmol), cyclic dimedone or 1,3-cyclohexandione (2, 1.2 mmol), and LaCl3/ClCH2COOH (10mol%) was stirred in an oil-bath 70 oC) for the reasonable time. After completion of the reaction, as monitored with TLC, the reaction mixture was cooled, diluted with Et2O (5 mL) and filtered to remove catalyst. The crude product was recrystallized from ethanol to afford the pure product.

The spectral data of the selected compounds are as follow:

**9,10-dihydro-9,9-dimethyl-12-phenyl-8H-benzo[a]xanthene-11(12H)-one (5a):** IR (KBr): ν= 3072, 2960, 1664 (C=O), 1624, 1424, 1359cm-1. 1H NMR (400 MHz, CDCl3) δ= 0.98 (3H, s, CH3), 1.14 (3H, s, CH3), 2.21-2.36 (2H, m, CH2), 2.59 (2H,s, CH2), 5.73 (1H, s, CH), 7.05-7.21 (3H, m, arom), 7.34-7.47 (5H, m, arom), 7.75-8.03 (3H, m, arom)., 13C NMR (CDCl3, 100 MHz): δ= 27.18, 29.30, 34.71, 41.42, 50.89, 109.46, 114.27, 117.05, 117.70, 123.69, 124.91, 126.25, 127.01, 128.07, 128.24, 128.43, 128.84, 129.77, 131.40, 131.49, 144.74, 147.73, 197.02.

**9,10-dihydro-12-(4-hydroxyphenyl)-9,9-dimethyl-8H-benzo[a]xanthene-11(12H)-one (5b):** IR (KBr): ν= 3354 (OH), 3059, 3022, 2954, 2869, 1651(C=O), 1594, 1466, 1373 cm-1. 1H NMR (400 MHz, CDCl3) δ= 0.99 (3H, s, CH3), 1.13 (3H, s, CH3), 2.22-2.36 (2H, m, CH2), 2.59 (2H, s, CH2 ), 4.83 (1H, s, OH), 5.66 (1H, s, CH), 6.61-6.67 (2H, m, arom), 7.14-7.21 (2H, m, arom), 7.32-7.47 (3H, m, arom), 7.69-8.00 (3H, m, arom). 13C NMR (CDCl3, 100 MHz): δ= 27.17, 29.26, 33.87, 41.41, 50.90, 109.47, 114.43, 115.19, 117.02, 117.62, 123.73, 124.91, 126.98, 128.39, 128.77, 129.57, 131.51, 137.00, 147.62, 154.01, 162.32, 197.67**.**

**12-phenyl-9,10-dihydro-8H-benzo[a]xanthen-11(12H)-one (5c):** IR (KBr): ν= 3063, 2967, 2895, 1652(C=O), 1595, 1369 cm-1. 1H NMR (400 MHz, CDCl3) δ= 1.98-2.10 (2H, m, CH2), 2.30-2.52 (2H, m, CH2), 2.64 -2.80 (2H, m, CH2), 5.76 (1H, s, CH), 7.07-7.09 (1H, t, J=7 Hz, arom), 7.11-7.18 (2H, t, J=8Hz, arom), 7.35-7.42 (3H, m, arom), 7.43-7.46 (2H, m, arom), 7.78-7.81 (2H, m, arom), 7.98-8.00 (1H, d, J=8 Hz, arom). 13C NMR (CDCl3, 100 MHz): δ= 27.28, 27.75, 34.64, 37.06, 115.56, 116.98, 117.71, 123.71, 124.89, 126.56, 127.00, 128.28, 128.38, 128.50, 128.64, 131.39, 131.49, 150.09, 145.04, 147.78, 147.78, 165.63, 197.11.

**9,10 -dihydro-12-(3-nitro phenyl)-8H-benzo[a]xanthene-11 (12H)-one (5d):** IR (KBr): ν= 3064, 2954, 2891, 1647(C=O), 1595, 1375 cm-1. 1H NMR (400 MHz, CDCl3) δ= 1.95-2.13 (2H, m, CH2), 2.35-2.47 (2H, m, CH2), 2.69 -2.85 (2H, m, CH2), 5.86 (1H, s, CH), 7.37-7.48 (4H, m, arom), 7.81-7.86 (4H, m, arom), 7.95-8.11 (2H, m, arom). 13C NMR (CDCl3, 100 MHz): δ= 20.25, 27.75, 34.72, 36.91, 114.40, 116.01, 117.16, 121.61, 122.52, 123.16, 123.33, 125.20, 127.36, 128.69, 129.08, 131.61, 134.95, 135.99, 146.99, 147.83, 197.10.

**9,10 -dihydro-12-(4-nitro phenyl)-8H-benzo[a]xanthene-11 (12H)-one (5e):** IR (KBr): ν= 3106, 3068, 2946, 2887, 1651 (C=O), 1593, 1455 cm-1. 1H NMR (400 MHz, CDCl3) δ= 1.93-2.15 (2H, m, CH2), 2.35-2.52 (2H, m, CH2), 2.68-2.83 (2H, m, CH2), 5.86 (1H, s, CH), 7.38-7.54 (5H, m, arom), 7.82-7.85 (3H, m, arom), 8.05-8.12 (2H, m, arom). 13C NMR (CDCl3, 100 MHz): δ= 20.23, 27.78, 34.83, 36.95, 114.25, 116.05, 117.04, 123.15, 123.46, 123.68, 125.25, 127.40, 128.67, 129.44, 129.65, 131.01, 131.57, 143.35, 147.77, 152.13, 196.99.

**9,10 -dihydro-12-(4-hydroxyphenyl)-8H-benzo[a]xanthene-11(12H)-one (5f):** IR (KBr): ν= 3324 (OH), 3022, 2931, 2895, 1632 (C=O), 1591, 1444 cm-1. 1H NMR (400 MHz, CDCl3) δ= 1.95-2.10 (2H, m, CH2), 2.30-2.51 (2H, m, CH2), 2.57 -2.80 (2H, m, CH2), 4.76 (1H, s, -OH), 5.69 (1H, s, CH), 6.62-6.69 (2H, m, arom),7.15-7.20 (2H, m, arom), 7.33-7.47(3H, m, arom), 7.69-7.98 (3H, m, arom). 13C NMR (CDCl3, 100 MHz): δ= 20.30, 27.73, 33.82, 37.05, 115.19, 115.74, 116.96, 117.83, 123.76, 124.90, 126.97, 128.38, 128.77, 129.53, 129.65, 131.36, 131.50, 137.30, 147.65, 154.04, 197.74.

***Synthesis of hexahydro-1H-xanthene (6, 7):***

To a mixture of aromatic aldehyde (1, 1 mmol) and cyclic 1,3-dicarbonyl compounds (2 or 4, 2 mmol), LaCl3/ClCH2COOH (10 mol%) was added and the mixture was heated on an oil bath at 70 oC for the reasonable time. After completion of the reaction, hot ethanol was added to the mixture and then filtered. The residue was recrystallized from ethanol. The results obtained are showed in Table 3.

**3,4,7-tetrahydro-9-phenyl-2H-xanthene-1,8(5H,9H)-dione (6a):** IR (KBr): ν= 3050, 2953, 2885, 1673 (C=O), 1621, 1429 cm-1. 1H NMR (400 MHz, CDCl3) δ= 1.96-2.05 (4H, m, CH2), 2.29-2.41 (4H, m, CH2), 2.54-2.70 (4H, m, CH2), 4.83 (1H, s, CH), 7.12-7.33 (5H, m, arom). 13C NMR (CDCl3, 100 MHz): δ= 20.30, 27.16, 31.62, 36.96, 116.91, 126.42, 128.38, 144.37, 163.91, 196.55.

**9-(4-chiorophenyl)-3,4,6,7-tetrahydro-2H-xanthene-1,8(5H,9H)-dione (6b):** IR (KBr): ν= 3086, 3052, 2958, 2893, 1667(C=O), 1616, 1459 cm-1. 1H NMR (400 MHz, CDCl3) δ= 1.92-2.10 (4H, m, CH2), 2.29-2.42 (4H, m, CH2), 2.54-2.70 (4H, m, CH2), 4.78 (1H, s, CH), 7.18-7.28 (4H, m, arom) 13C NMR (CDCl3, 100 MHz): δ= 20.28, 27.13, 31.29, 36.91, 116.49, 128.24, 129.81, 132.09, 142.94, 164.10, 196.56.

**3,4,7-tetrahydro-9-(4-hydroxyphenyl)-2H-xanthene-1,8(5H,9H)-dione (6c):** IR (KBr): ν= 3378 (OH), 3022, 2949, 2920, 2867, 1661 (C=O), 1609, 1446 cm-1. 1H NMR (400 MHz, CDCl3) δ= 1.98-2.08 (4H, m, CH2), 2.29 -2.44 (4H, m, CH2), 2.53-2.70 (4H, m, CH2), 4.26(1H, s, -OH), 4.76 (1H, s, CH), 6.66 (2H, d, J=8.4 Hz, arom), 7.15 (2H, d, J=8.4 Hz, arom). 13C NMR (CDCl3, 100 MHz): δ= 20.31, 27.14, 30.79, 36.98, 115.08, 117.07, 129.52, 136.58, 154.23, 163.86, 196.94.

**9-(p-tolyl)-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione (6d):** IR (KBr): ν= 3012, 2949, 2919, 2867, 1661 (C=O), 1609, 1446 cm-1. 1H NMR (400 MHz, CDCl3) δ= 1.44-1.47 (4H, m, CH2), 2.11(3H, s, CH3), 2.14-2.22 (4H, m, CH2), 2.63-2. 80 (4H, m, CH2), 4.88 (1H, s, CH), 7.40-7.43 (2H, d, J=7 Hz, arom), 7.47-7.50 (2H, d, J=7 Hz, arom). 13C NMR (CDCl3, 100 MHz): δ= 20.61, 26.40, 27.62, 30.92, 36.14, 118.71, 129.35, 129.65, 129.98, 130.32, 130.78, 130.88, 130.98, 197.04.

**3,4,6,7-tetrahydro-9-(4-nitrophenyl)-2H-xanthene-1,8(5H,9H)-dione** **(6e):** IR (KBr): ν= 3022, 2949, 2920, 2867, 1661 (C=O), 1609, 1446 cm-1. 1H NMR (400 MHz, CDCl3) δ= 1.98-2.10 (4H, m, CH2), 2.35 -2.52 (4H, m, CH2), 2.64-2.80 (4H, m, CH2), 4.76 (1H, s, CH), 7.41-7.44 (2H, d, J=8 Hz, arom), 7.48-7.70 (2H, d, J=8 Hz, arom). 13C NMR (CDCl3, 100 MHz): δ= 20.62, 27.62, 30.63, 36.17, 116.16, 127.96, 129.22, 129.98, 130.98, 145.69, 157.76, 195.41.

**9-(3-nitrophenyl)-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione (6f):** IR (KBr): ν= 3031, 2922, 1664 (CO), 1595. 1H NMR (400 MHz, DMSO, d6) δ= 1.61-1.78 (4H, m, CH2), 2.06-2.19 (m, 4H, 2CH2), 4.72 (s, 1H, CH), 7.52-7.57 (1H, t, J= 7 Hz, 1H, arom), 7.72-7.75 (m, 1H, arom), 7.97-8.16 (2H, m, arom). 13C NMR (DMSO, d6, 100 MHz): δ= 21.10, 26.18, 32.36, 36.54, 113.54, 121.47, 129.35, 148.02, 153.32, 167.37, 196.04.

**3,3,6,6-tetramethyl-9-phenyl-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione (6g):** IR (KBr): ν= 3029, 2988, 1669 (CO), 1596. 1H NMR (400 MHz, DMSO, d6) δ= 0.68 (6H, s, CH3), 0.85 (6H, s, CH3), 1.73 (2H, d, J = 17.4 Hz), 1.97 (2H, d, J = 16.0 Hz), 2.15 (4H, dd, J1 = 15.9 Hz, J2 = 3.6 Hz ), 5.01 (1H,s), 7.20-7.30 (4H, m, arom), 7.47 (1H, d, J = 6.9 Hz, arom). 13C NMR (DMSO, d6, 100 MHz): δ= 26.40, 29.63, 32.47, 41.37, 50.00, 113.55, 126.26, 128.00, 128.42, 135.33, 141.31, 146.68, 150.5, 167.41, 195.6.

**9-(4-chlorophenyl)-3,3,6,6-tetramethyl-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione (6h):** IR (KBr): ν= 3031, 2989, 1670 (CO), 1596. 1H NMR (400 MHz, DMSO, d6) δ= 0.67 (6H, s, CH3), 0.85 (6H, s, CH3), 1.76 (2H, d, J = 17.4 Hz), 1.99 (2H, d, J = 16.0 Hz), 2.17 (4H, dd, J1 = 15.9 Hz, J2 = 3.6 Hz ), 5.11 (1H,s), 7.54-7.56 (2H, d, J=7 Hz, arom), 8.05-8.07 (2H, d, J = 6.9 Hz, arom). 13C NMR (DMSO, d6, 100 MHz): δ= 26.45, 29.59, 32.55, 41.34, 49.80, 112.66, 122.57, 130.26, 134.77, 136.51, 147.86, 148.61, 151.30, 167.34, 195.59.

**11-phenyl-10H-diindeno[1,2-b:2',1'-e]pyran-10,12(11H)-dione (7a):** IR (KBr): ν= 3066, 2945, 2841, 1699 (C=O), 1608cm-1. 1H NMR (400 MHz, CDCl3) δ= 4.66 (1H, s, CH), 7.03-7.05 (1H, m, arom), 7.10-7.18 (2H, m, arom), 7.47-7.60 (3H, m, arom), 7.84-7.94 (3H, m, arom), 8.03-8.07 (2H, m, arom), 8.49 (2H, d, J=6.8 Hz, arom). 13C NMR (CDCl3, 100 MHz): δ= 47.01, 122.08, 123.37, 124.30, 125.68, 128.82, 130.93, 133.23, 134.18, 135.26, 136.65, 147.04, 196.78.

**11-(4-chlorophenyl)-10H-diindeno[1,2-b:2',1'-e]pyran-10,12(11H)-dione (7b):** IR (KBr): ν= 3062, 2950, 29021, 1689 (C=O), 1608cm-1. 1H NMR (400 MHz, DMSO-d6)δ=5.13 (1H, s, CH), 6.63-6.95 (4H, t, J = 8.0 Hz, arom), 6.95-6.97(1H, d, J= 8 Hz, arom), 7.14-7.16 (1H, d, J = 6.8 Hz, arom), 7.58-7.60 (2H, t, J = 7.6 Hz, arom), 7.74-7.76 (1H, d, J = 8.0 Hz, arom), 8.00-8.16 (2H, d, J = 8 Hz, arom), 8.11-8.12 (1H, d, J = 7.0 Hz, arom). 13C NMR (DMSO-d6, 100 MHz): δ= 40.8, 111.9, 116.1, 120.9, 121.9, 129.1, 129.6, 131.0, 134.2, 147.3, 148.3, 151.8, 157.8, 195.1.

RESULTS AND DISCUSSION

To achieve suitable reaction conditions, we initially investigated the one-pot, three-component reaction of β-naphthol, benzaldehyde, dimedone and LaCl3/ClCH2COOH as model reaction and subsequently efforts were focused on optimization of various reaction parameters such as amount of LaCl3/ClCH2COOH and temperature in terms of yield and time period. This observation revealed that use of 10 mol% LaCl3/ClCH2COOH at 70 oC under solvent-free conditions produced 9,9-dimethyl-12-phenyl-9,10-dihydro-8H-benzo[a]xanthene-11(12H)-one (5a), after 10 min, in 96% yield. Notably, the desired product could not be obtained under similar reaction conditions, even after a long time (1 h) in the absence of the catalyst (table I).

Table I. Screening of the reaction conditions for the synthesis of 9,9-dimethyl-

12-phenyl-9,10-dihydro-8H-benzo[a]xanthene-11(12H)-one (5a)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Yielda (%)** | **Time (min)** | | **Temperature (oC)** | **Amount LaCl3/ClCH2COOH (mol%)** | **Entry** |
| 0 | 60 | 70 | | No catalyst | 1 |
| 20 | 35 | 50 | | LaCl3 (10 mol%) | 2 |
| 25 | 30 | 60 | | LaCl3 (15 mol%) | 3 |
| 35 | 50 | 70 | | ClCH2COOH (10 mol%) | 4 |
| 40 | 55 | 80 | | ClCH2COOH (20 mol%) | 5 |
| 70 | 25 | 70 | | LaCl3/ClCH2COOH (5 mol%) | 6 |
| 85 | 20 | 60 | | LaCl3/ClCH2COOH (10 mol%) | 7 |
| 96 | 10 | 70 | | LaCl3/ClCH2COOH (10 mol%) | 8 |
| 96 | 10 | 80 | | LaCl3/ClCH2COOH (10 mol%) | 9 |

a Isolated yields.

In order to study the generality of the procedure, three series of various xanthine derivatives having different steric and electronic properties were synthesized using the optimized conditions. In all cases, the corresponding products were obtained in good to excellent yields. The results are presented in table II and table III. The products obtained were characterized by IR, 1H NMR and 13C NMR spectroscopy and making a comparison between its physical data and that known xanthenes.

Table II.One-pot preparation 12-aryl-8,9,10,12-tetrahydrobenzo[a]xanthene-11-ones



|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| M.P | | Yield | Time | Product | R | X | Entry |
| Reported | Found |
| 153[47]-151 | 152-150 | 96 | 10 |  | CH3 | H | 5a |
| 209-211[47] | 211-209 | 90 | 11 |  | CH3 | OH | 5b |
| 189-190[48] | 191- 189 | 92 | 10 |  | H | H | 5c |
| 236[48]-235 | 238-233 | 97 | 10 |  | H | NO2 | 5d |
| 235[48]-234 | 236-234 | 92 | 10 |  | H | NO2 | 5e |
|  | 269-270[48] | 267-270 | 93 | 10 |  | H | OH | 5f |

a Isolated yields.

Table III.One-pot preparation *hexahydro-1H-xanthene* and diindeno[1,2-b:2',1'-e]pyran-diones



|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| M.P | | Yield | Time | Product | R1 | X | Entry |
| Reported | Found |
| 201-203[49] | 204-202 | 86 | 10 |  | H | H | 6a |
| 231-233[49] | 232- 230 | 92 | 10 |  | H | Cl | 6b |
| 245-247[49] | 246-243 | 97 | 10 |  | H | OH | 6c |
| 216-218[49] | 217-219 | 92 | 10 |  | H | CH3 | 6d |
|  | 246-248[50] | 245-248 | 93 | 8 |  | H | NO2 | 6e |
|  | 277-279[50] | 236-240 | 96 | 7 |  | H | NO2 | 6f |
|  | 203-204[51] | 202-204 | 90 | 8 |  | CH3 | H | 6g |
|  | 230-232[51] | 230-233 | 93 | 9 |  | CH3 | H | 6h |
|  | 290-291[52] | 288-290 | 80 | 10 |  | - | H | 7a |
|  | ----- | 310-312 | 85 | 9 |  | - | Cl | 7b |

a Isolated yields.

In continue, the reusability of the catalyst was checked by the reaction of benzaldehyde and β-naphthol and dimedone in the presence of LaCl3/ClCH2COOH under solvent-free condition. After completion of the reaction, the reaction mixture was dissolved in ethyl acetate and the catalyst was recovered after filtration. The recovered catalyst was reused again for the synthesis of 4m. The reaction was found to proceed smoothly and afforded comparable yields of 93, 92, 92, and 90%, confirming the recyclability and reusability of the catalyst in this reaction.

In order to show the merit of the present work, we compared our results with the results reported by other groups in the synthesis of 9,9-dimethyl-12-phenyl-9,10-dihydro-8H-benzo[a]xanthene-11(12H)-one (5a). It is important to note that, LaCl3/ClCH2COOH acts as an effective catalytic system with respect to reaction time and yield (table IIII).

**Table IIII.** *Comparison of the results for synthesis of xanthene 5a with different catalysts*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Catalyst | Catalyst  Load (mol%) | Solvent | Temp. (°C) | Time  (min) | Yielda  (%) |
| DBSA\* | 10 | H2O, ultrasound | 30 | 60 | 89[53] |
| TMSCl | 100 | MeCN | reflux | 420 | 95[54] |
| HClO4–SiO2 | 10 | Solvent-free | 140 | 180 | 32[55] |
| SbCl3–SiO2 | 10 | Solvent-free | 120 | 50 | 93[56] |
| PPA–SiO2 | 10 | Solvent-free | 140 | 30 | 93[55] |
| TBAHS\*2 | 10 | Dioxane, H2O | reflux | 210 | 88[57] |
| LaCl3 |  |  |  |  |  |
| ClCH2COOH |  |  |  |  |  |
| LaCl3/ClCH2COOH | 10 | Solvent-free | 70 | 10 | 96 |

\*p-Dodecylbenzenesulfonic acid.

\*2Tetrabutylammonium hydrogen sulfate

.aExperimental conditions: benzaldehyde (1 mmol), β-naphthol (1 mmol), dimedone(1 mmol) and LaCl3/ClCH2COOH (10mol%).

In a plausible mechanism, at first, carbonyl group of the aromatic aldehyde is activated through coordination with acidic LaCl3/ClCH2COOHto give **1**. Next, the carbonyl carbon is attacked by the nucleophilic 1,3-dion derivatives to form the Knoevenagel products. The subsequent addition of these fragments to **2**, **3** or **4** gives the acyclic adduct intermediate, which undergoes intramolecular cyclization with participation of two hydroxyl groups to afford the xanthene derivatives (Scheme 2).

**Scheme 2.** The proposed mechanism for the synthesis of xanthene derivatives using LaCl3/ClCH2COOH.

Finally, we investigated the possibility of recycling of LaCl3/ClCH2COOH using the model reaction forming **5a** in the presence of LaCl3/ClCH2COOH. After reaction completion, ice cold water was added to the reaction mixture and the product was extracted with Et2O. The aqueous layer consisting the catalyst was recovered after removal of water under reduced pressure and was reused for subsequent reactions. It showed the same activity as that of the fresh catalyst without any loss of activity in terms of yield and purity. The catalyst was recycled and reused in the same reaction for at least four times with remarkable retention in its activity (Table V).

**Table V.** Recycling yieldsa.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| No of Cyclesa | Fresh | Run 1 | Run 2 | Run 3 | Run 4 |
| Yieldb | 96 | 96 | 96 | 96 | 96 |
| Time (min) | 10 | 10 | 10 | 10 | 10 |

a Reaction condition: benzaldehyde (1 mmol), β-naphthol (1 mmol), dimedone(1 mmol) and

LaCl3/ClCH2COOH (10mol%).

b Yields refer to pure isolated yields.

CONCLUSIONS

In conclusion, we have developed an efficient catalytic system for the synthesis of various xanthene derivatives via one-pot three-component reaction of aldehydes, 2-naphthol, and cyclic 1,3-dicarbonyl compounds. Advantages of our procedure include simplicity of operation, high yields of products, short reaction time, solvent-free conditions, and the use of an inexpensive and readily available catalyst.

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REFERENCES

1. M. Sayyafi, M. Seyyedhamzeh, H. R. Khavasi, A. Bazgir, *Tetrahedron*, **64** (2008) 2375.

2. S. Miwatashi, A. Yasuyoshi, K. Etsuo, M. Maki, N. Ken-ichi, K. Hiroyuki, T. Toshimasa,

A. Satoru, O. Shigenori, *J. Med. Chem.* **48** (2005) 5966.

3. C. Papadopoulou, G. Athina, H. Dimitra, *Il Farmaco*. **60** (2005) 969.

4. Y. Kumar, R. Green, K. Z. Borysko, D. S. Wise, L. L. Wotring, L. B. Townsend, *J. Med.*

*Chem.* **36** (1993) 3843.

5. R. Pereira, C. Gaudon, B. Iglesias, P. Germain, H. Gronemeyer, A. R. De Lera, *Bioorg.*

*Med. Chem. Lett.* **16** (2006) 49.

6. Y. Tsurumi, H. Ueda, K. Hayashi, S. Takase, M. Nishikawa, S. Kiyoto, M. Okuhara, *J.*

*Anti-biot.* **48** (1995) 1066.

7. F. W. Bell, S. C. Amanda, S. Marita Hoegberg, J. Richard, G. Nils, C. L. Johansson, M.

D. Jordan, P. L. Kinnick, M. John, J. Morin*, J. Med. Chem*. **38** (1995) 4929.

8. D. S. Millan, R. H. Prager, C. Brand, P. H. Hart, *Tetrahedron*, **56** (2000) 811.

9. W. L. Wang, D. Y. Yao, M. Gu, M. Z. Fan, J. Y. Li, Y. C. Xing, F. Nan, *J, Bioorg. Med.*

*Chem*. *Lett.* **15** (2005) 5284.

10. Z. Karimi-Jaberi, M. M. Hashemi, *Monatsh. Chem.* **139** (2008), 605.

11. J. J. Li, X. Y. Tao, Z. H. Zhang, *Phosphorus. Sulfur. Silicon. Relat. Elem.* **183** (2008)

1672.

12. A. Kesel, *J. Curr. Med. Chem.* **12** (2005) 2095.

13. Z. H. Zhang, X. Y. Tao, *Aust. J. Chem.* **61** (2008) 77.

14. J. Griffiths, W. J. Lee, *Dyes. Pigm.* **57** (2003) 107.

15. M. Ahmad, T. A. King, D. K. Ko, B. H. Cha, J. Lee, *J. Phys. D Appl. Phys.* **35** (2002)

1473.

16. C. G. Knight, T. Stephens, *Biochem. J.* **258** (1989) 683.

17. N. Sato, M. Jitsuoka, T. Shibata, T. Hirohashi, K. Nonoshita, M. Moriya, Y. Haga, A.

Sakuraba, M. Ando, T. Ohe, H. Iwaasa, A. Gomori, A. Ishihara, A. Kanatani, T. Fukami,

*J. Med. Chem.* **51** (2008) 4765.

18. Z. Y. Lu, Z. J. Lin, W. L. Wang, L. Du, T. J. Zhu, Y. C. Fang, Q. Q. Gu, W. M. Zhu, *J. Nat.*

*Prod.* **71** (2008) 543.

19. A. R. Carroll, J. Lamb, R. Moni, G. P. Guymer, P. I. Forster, R. J. Quinn, *J. Nat. Prod.* **71**

(2008) 1564.

20. F. Shaheen, M. Ahmad, S. N. Khan, S. S. Hussain, S. Anjum, B. Tashkhodjaev, K.

Turgunov, M. N. Sultankhodzhaev, M. I. Choudhary, Atta-ur-Rahman, *Eur. J. Org. Chem.*

**2006** (2006) 2371.

21. M. Makino, Y. Fujimoto, *Phytochemistry*, **50** (1999) 273.

22. H. Bienaymé, C. Hulme, G. Oddon, P. Schmitt, *Chem. Eur. J.* **6** (2000), 3321.

23. A. Nefzi, J. M. Ostresh, R. A. Houghten, *Chem. Rev.* **97** (1997) 449.

24. L. A. Thompson, *Curr. Opin. Chem. Biol.* **4** (2000) 324.

25. A. Dömling, *Curr. Opin. Chem. Biol.* **6** (2002) 306.

26. Y. M. Ren, C. Cai, *Monatsh. Chem.* **140** (2009) 49

27. S. Bondock, H. El-Azap, E. E. M. Kandeel, M. A. Metwally, *Monatsh. Chem.* **139** (2008)

1329.

28. L. Liu, L. Y. Ji, Y. Y. Wei, *Monatsh. Chem.* **139** (2008) 901.

29. M. Dabiri, M. Baghbanzadeh, M. S. Nikcheh, E. Arzroomchilar, *Bioorg. Med. Chem. Lett.*

**18** (2008) 436.

30. B. F. Mirjalili, A. Bamoniri, M. A. Mirhoseini, *Chem. Heterocycl. Compd.* **1**(2012).

31. J. Safaei-Ghomi, M. A. Ghasemzadeh, *Chin. Chem. Lett.* **23** (2012) 1225.

32. (a) B. Das, B. Ravikanth, R. Ramu, K. Laxminarayana, B. V. Rao, *J. Mol. Catal. A Chem.*

**255** (2006), 74. (b) M. A. Pasha, V. P. Jayashankara, *Bioorg. Med. Chem. Lett.* **17** (2007)

621.

33. (a) H. R. Shaterian, M. Ghashang, HA. Assankhani, *Dye. Pigment*. **76** (2008) 564.

(b) M. Seyyedhamzeh, P. Mirzaei, A. Bazgir. Dye. Pigment. **76** (2008) 836.

34. A. Zare, A. R. Moosavi-Zare, M. Merajoddin, M. A. Zolfigol, T. Hekmat-Zadeh, A.

Hasaninejad, *J. Mol. Liq*. **167** (2012) 69.

35. Z. H. Zhang, Y. H. Liu. *Catal. Commun*. **9** (2008) 1715.

36. G. H. Mahdavinia, M.A. Bigdeli, Y. S. Hayeniaz *Chin. Chem. Lett.* **20** (2009) 539.

37. T. S. Jin, J. S. Zhang, J. C. Xiao, A. Q. Wang, T. S. Li, *Synlett*, **5** (2004) 866.

38. X. S.Wang, D. Q. Shi, Y. L. Li, H. Chen, X. Y. Wei, Z. M. Zong. *Synth. Commun*. **35** (2005)

97.

39. F. Darvish, S. Balalaei, F. Chadegani, P. Salehi, *Synth. Commun*. **37** (2007) 1059.

40. M. M. Heravi, H. Alinejhad, K. Bakhtiari, H. A. Oskooie, *Mol. Divers.* **14** (2010) 621.

41. H. J. Wang, X. Q. Ren, Y. Y. Zhang, Z. H. Zhang, *J. Braz. Chem. Soc.* **20** (2009) 1939.

42. G. C. Nandi, S. Samai, R. Kumar, M. S. Singh, *Tetrahedron*, **65** (2009) 7129.

43. B. Maleki, S. Barzegar, Z. Sepehr, M. Kermanian, R. Tayebee, *J. Iran. Chem. Soc*. **9**

(2012) 757.

44. B. Pouramiri, E. Tavakolinejad Kermani, *J. Iran. Chem. Soc.,* **2016***, 1-7.*

45. B. Pouramiri, E. Tavakolinejad Kermani E, *Arab. J. Chem.*, **2012**.

46. B. Pouramiri, E. Tavakolinejad Kermani, *Scientia Iranica C*, 21(2014) 703.

47. G. C. Nandi, S. Samai, R. Kumar, M. S. Singh, *Tetrahedron*, **65** (2009) 7129.

48. Z. H. Zhang, H. J. Wang, X. Q. Ren, Y. Y. Zhang, *Monatsh. Chem.* **140** (2009), 1481.

49. A. John, P. J. P. Yadav, S. Palaniappan, *J. Mol. Catal. A: Chem.* **248** (2006) 121.

50. B. Maleki, S. Barzegar, Z. Sepehr, M. Kermanian, R. Tayebee, *J. Iran. Chem. Soc.* 9

(2012) 757.

51. K. Niknam, M. Damya, *J. Chin. Chem. Soc.* **56** (2009) 659.

52. W. Geita, *Zhu. Obsh. Khim.,* 27 (1975) 3109.

53. T. S. Jin, J. S. Zhang, A. Q. Wang, T. S. Li, *Ultrason. Sonochem.* **13** (2006) 220.

54. S. Kantevari, R. Bantu, L. Nagarapu, *ARKIVOC*, **16** (2006) 136.

55. S. Kantevari, R. Bantu, L. Nagarapu, *J. Mol. Catal. A: Chem.* **269** (2007) 53.

56. Z. H. Zhang, Y. H. Liu, Catal. Commun. **9** (2008) 1715.

57. H. N. Karade, M. Sathe, M. P. Kaushik, *ARKIVOC*, **13** (2007) 252.

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