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β-Cyclodextrin mediated synthesis of 1,8-dioxooctahydroxanthenes in water

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ABSTRACT

An experimentally simple, efficient Michael addition reaction was developed for the synthesis of various 1,8-dioxooctahydroxanthene derivatives with 1,3-cyclohexanedione/5,5-dimethyl 1,3-cyclohexane dione and different aldehydes by using β-cyclodextrin as a catalyst in water. A biomimetic approach was employed and the corresponding products were obtained in good to excellent yields. β-cyclodextrin can be recovered and reused upto four cycles without loss of catalytic activity.

1. Introduction

Xanthenes and benzoxanthenes are important class of compounds that are found in numerous biologically active molecules. This structural motif has also been investigated for a wide range of activities such as bactericidal [1], anti-inflammatory [2], antiviral [3], as well as photodynamic therapy [4], In particular, the xanthenedione structure is present in a number of natural products [5], and has been a component of dyes [6], fluorescent materials for visualization of biomolecules and in laser technologies due to their spectroscopic properties [7-9]. Consequently, several methods have been developed for the synthesis of xanthene derivatives, which in general can be obtained by the condensation of appropriate active methylene derivatives with aldehydes catalyzed by mineral acids [10]. Xanthenes were also prepared by the cyclization of polycyclic aryltriflate esters [11], catalyzed by palladium or the reaction of aryl magnesium halides with triethylorthoformate [12,13]. Li *et al.* reported solid state condensation reaction between 5,5-dimethyl-1,3-cyclohaxane-dione and aldehyde by grinding at room temperature [14]. Hua *et al*. and Jin *et al.* described the synthesis of xanthenes catalyzed by *p*-dodecylbenzenesulfonic acid in aqueous media [15,16]. Jin *et al.* and Khosropour *et al.* reported the synthesis of xanthene and benzoxanthene in presence of *p*-toluene-sulfonic acid as a catalyst in organic solvent [17,18]. Other methods developed for the synthesis of 1,8-dioxooctahydro-xanthenes include the use of $NaHSO_4$-SiO_2 (or) silica chloride [19], Amberlyst-15 [20], Dowex50w [21], Montmorillonite [22], cyanuric chloride [23], $BiCl_3$ [24], Fe^{+3}-montmorillonite [25], polyaniline-*p*-toluenesulfonate [26], PMA-SiO_2 [27], $HClO_4$-SiO_2 & PPA-SiO_2 [28], $ZrOCl_2$ [29], $H_3PW_{12}O_{40}$ [30], LiBr [31], and proline triflate [32], as catalysts. Literature survey also indicates the role of ionic liquids [33,34], and acidic ionic liquids in aqueous media [35], in the synthesis of xanthenes. However, these existing methodologies suffer from many drawbacks such as use of toxic organic solvents, drastic reaction conditions, and expensive reagents/catalysts as well as low yields.

Aqueous phase organic synthesis has attracted the attention of chemists as it overcomes the harmful effects associated with the organic solvents and is environmentally benign. These reactions become more sophisticated if they can be performed under supramolecular catalysis. In view of the above, the development of a generally applicable and environmentally benign methodology for the synthesis of xanthenes derivatives is highly desirable. While developing practically simple biomimetic approaches through the supramolecular catalysis for a number of heterocyclic derivatives, to overcome some of the limitations in the existing methodologies, we report herein an aqueous phase synthesis of 1,8-dioxooctahydroxanthenes from 1,3-cyclohexanedione and aromatic aldehydes in the presence of β-cyclodextrin (β-CD).

2. Experimental

2.1. Instrumentation

All reactions were carried out without any special precautions in an atmosphere of air. Chemicals were purchased from Fluka and S. D. Fine Chemicals and directly used for the synthesis. Thin-layer chromatography (TLC): precoated silica gel plates (60 F_{254}, 0.2 mm layer; E. Merck). ^1H NMR and ^{13}C NMR (Avance 300, Innova 400 MHz and Brucker Gemini 200 MHz) spectra were recorded in $CDCl_3$ using TMS as internal standard. Chemical shifts (δ) are reported in ppm, and spin-spin coupling constants (J) are in Hz. Melting points (M.p.) were determined on a Fischer-Johns melting point apparatus. IR and MS were recorded on a Thermo Nicolet Nexus 670 FT-IR spectrometer and Finnegan MAT 1020 mass spectrometer operating at 70 eV.

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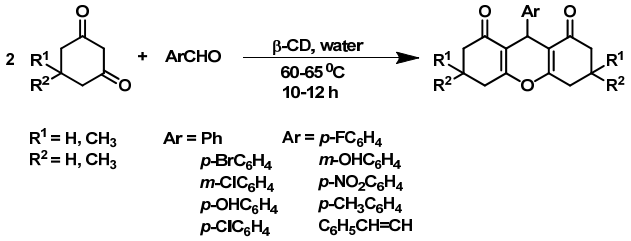
2.2. Synthesis

General procedure for the synthesis of 3,3,6,6,-tetramethyl-9-phenyl-3,4,6,7-tetrahydro-2H-xanthene-1,8(5H,9H)dione derivatives in water: β-cyclodextrin (1.135 g, 1 mmol) was dissolved in water (10 mL) by warming to 60 °C until a clear solution was formed. To this clear solution aldehyde (1.0 mmol) was added and the mixture stirred for 10 min, and then followed by the addition of 1,3-diketone (2.0 mmol). Then, the mixture was heated at 60-65 °C until completion of the reaction as indicated by TLC. The mixture was cooled to room temperature and β-CD was filtered, the aqueous phase was extracted with ethyl acetate (3x10 mL). The organic layers were washed with water, brine solution and dried with anhydrous Na_2SO_4. The combined organic layers were evaporated under reduced pressure and the resulting crude product was purified by column chromatography, using ethyl acetate:hexane (2:8) as eluents to give the corresponding xanthenes in good to excellent yields (Scheme 1, Table 1).



Scheme 1

9-Phenyl-3,4,6,7-tetrahydro-2H-xanthene-1,8(5H,9H)-dione (**3a**) (Table 1, Entry 1): White Solid. Yield: 95%. M.p.: 269-270 °C. FT-IR (KBr, cm^{-1}): 2960, 2928, 1592, 1650, 1372, 1159, 1060, 842, 774, 690. ^1H NMR (300 MHz, $CDCl_3$): 7.10-7.24 (m, 5H, ArH), 5.45 (s, 1H, CH), 2.60-2.67 (m, 4H, 2xCH_2), 2.25-2.30 (m, 4H, 2xCH_2), 1.91-1.99 (m, 2H, CH_2), 1.83-1.90 (m, 2H, CH_2). MS (ESI, m/z): 312 $[M+NH_4]^+$.

9-(4-Bromophenyl)-3,4,6,7-tetrahydro-2H-xanthene-1,8(5H, 9H)-dione (**3b**) (Table 1, Entry 2): White Solid. Yield: 91%. M.p.: 284-285 °C. FT-IR (KBr, cm^{-1}): 3100, 2980, 2878, 1589, 1490, 1303, 1158, 890, 709, 660. ^1H NMR (300 MHz, $CDCl_3$): 7.21-7.27 (m, 4H, ArH), 5.46 (s, 1H, CH), 2.60-2.68 (m, 4H, 2xCH_2), 2.26-2.31 (m, 4H, 2xCH_2), 1.92-1.98 (m, 2H, CH_2), 1.82-1.90 (m, 2H, CH_2). MS (ESI, m/z): 391 $[M+NH_4]^+$.

9-(3-Hydroxyphenyl)-3,4,6,7-tetrahydro-2H-xanthene-1,8 (5H,9H)-dione (**3c**) (Table 1, Entry 3): White Solid. Yield: 87%. M.p.: 255-256 °C. FT-IR (KBr, cm^{-1}): 3250, 3017, 2930, 1655, 1590, 935, 829, 730, 560. ^1H NMR (300 MHz, $CDCl_3$): 7.10-7.14 (m, 4H, ArH), 5.47 (s, 1H, CH), 2.60-2.65 (m, 4H, 2×CH_2), 2.28-2.30 (m, 4H, 2×CH_2), 1.91-1.94 (m, 2H, CH_2), 1.83-1.88 (m, 2H, CH_2). MS (ESI, m/z): 328 $[M+NH_4]^+$.

9-(3-Chlorophenyl)-3,4,6,7-tetrahydro-2H-xanthene-1,8(5H, 9H)-dione (**3d**) (Table 1, Entry 4): White Solid. Yield: 85%. M.p.: 275-276 °C. FT-IR (KBr, cm^{-1}): 2960, 2868, 1593, 1462, 1374, 1155, 1051, 870, 790, 675. ^1H NMR (300 MHz, $CDCl_3$): 7.09-7.14 (m, 4H, ArH), 5.48 (s, 1H, CH), 2.61-2.64 (m, 4H, 2xCH_2), 2.28-2.30 (m, 4H, 2xCH_2), 1.91-1.94 (m, 2H, CH_2), 1.83-1.88 (m, 2H, CH_2). MS (ESI, m/z): 346 $[M+NH_4]^+$.

*9-p-Tolyl-3,4,6,7-tetrahydro-2H-xanthene-1,8(5H,9H)-*dione (**3e**) (Table 1, Entry 5): White Solid. Yield: 90%. M.p.: 262-264 °C. FT-IR (KBr, cm^{-1}): 2960, 2930, 1592, 1372, 1159, 1041, 842, 770, 690. ^1H NMR (300 MHz, $CDCl_3$): 7.01-7.08 (m, 4H, ArH), 5.45 (s, 1H, CH), 2.60-2.63 (m, 4H, 2xCH_2), 2.24-2.27 (m, 4H, 2xCH_2), 1.91-1.95 (m, 2H, CH_2), 1.82-1.85 (m, 2H, CH_2). MS (ESI, m/z): 326 $[M+NH_4]^+$.

9-(4-Chlorophenyl)-3,4,6,7-tetrahydro-2H-xanthene-1,8(5H, 9H)-dione (**3f**) (Table 1, Entry 6): White Solid. Yield: 90%. M.p.: 288-289 °C. FT-IR (KBr, cm^{-1}): 3200, 2960, 2930, 1589, 1305, 1093, 887, 830, 720, 660. ^1H NMR (300 MHz, $CDCl_3$): 7.20 (d, *J* = 8.5 Hz, 2H, ArH), 7.25 (d, *J* = 8.5 Hz, 2H, ArH), 5.45 (s, 1H, CH), 2.61-2.69 (m, 4H, 2xCH_2), 2.26-2.32 (m, 4H, 2xCH_2), 1.93-1.98 (m, 2H, CH_2), 1.83-1.90 (m, 2H, CH_2). MS (ESI, m/z): 346 $[M+NH_4]^+$.

9-(4-Hydroxyphenyl)-3,4,6,7-tetrahydro-2H-xanthene-1,8 (5H,9H)-dione (**3g**) (Table 1, Entry 7): White Solid. Yield: 90%. M.p.: 245-246 °C. FT-IR (KBr, cm^{-1}): 3295, 3017, 2929, 1655, 1590, 930, 835, 750, 585. ^1H NMR (300 MHz, $CDCl_3$): 7.10 (d, *J* = 8.3 Hz, 2H, ArH), 6.78 (d, *J* = 8.3 Hz, 2H, ArH), 5.46 (s, 1H, CH), 2.61-2.65 (m, 4H, 2xCH_2), 2.25-2.30 (m, 4H, 2xCH_2), 1.92-1.96 (m, 2H, CH_2), 1.83-1.89 (m, 2H, CH_2). MS (ESI, m/z): 328 $[M+NH_4]^+$.

9-(4-Fluorophenyl)-3,4,6,7-tetrahydro-2H-xanthene-1,8(5H, 9H)-dione (**3h**) (Table 1, Entry 8): White Solid. Yield: 88%. M.p.: 275-276 °C. FT-IR (KBr, cm^{-1}): 3200 2970, 2935, 1593, 1372, 1228, 1068, 870, 835, 750, 669. ^1H NMR (300 MHz, $CDCl_3$): 7.20-7.28 (m, 4H, ArH), 5.45 (s, 1H, CH), 2.60-2.66 (m, 4H, 2xCH_2), 2.26-2.30 (m, 4H, 2xCH_2), 1.92-1.96 (m, 2H, CH_2), 1.84-1.90 (m, 2H, CH_2). MS (ESI, m/z): 330 $[M+NH_4]^+$.

9-(4-Nitrophenyl)-3,4,6,7-tetrahydro-2H-xanthene-1,8(5H, 9H)-dione (**3i**) (Table 1, Entry 9): White Solid. Yield: 80%. M.p.: 265-266 °C. FT-IR (KBr, cm^{-1}): 3200, 2960, 2928, 1592, 1390, 1550, 1159, 1040, 842, 774, 690. ^1H NMR (300 MHz, $CDCl_3$): 7.99 (d, *J* = 8.2 Hz, 2H, ArH), 7.45 (d, *J* = 8.5 Hz, 2H, ArH), 5.46 (s, 1H, CH), 2.59-2.69 (m, 4H, 2xCH_2), 2.24-2.32 (m, 4H, 2xCH_2), 1.93-1.99 (m, 2H, CH_2), 1.82-1.90 (m, 2H, CH_2). MS (ESI, m/z): 357 $[M+NH_4]^+$.

3,3,6,6-Tetramethyl-9-phenyl-3,4,6,7-tetrahydro-2H-xanthene-1,8(5H, 9H)dione (**3j**) (Table 1, Entry 10): White Solid. Yield: 96%. M.p.: 203-205 °C. FT-IR (KBr, cm^{-1}): 2962, 2928, 1592, 1372, 1159, 1041, 842, 774, 692. ^1H NMR (300 MHz, $CDCl_3$): 7.24-7.19 (m, 2H, ArH), 7.14-7.09 (m, 1H, ArH), 7.04-7.01 (d, *J* = 7.93 Hz, 2H, ArH), 5.47 (s, 1H, CH), 2.47-2.25 (m, 8H, 4xCH_2), 1.25 (s, 6H, 2xCH_3), 1.11 (s, 6H, 2xCH_3). ^{13}C NMR (75 MHz, $CDCl_3$): 190.3, 189.3, 137.9, 128.1, 126.7, 125.7, 115.4, 46.9, 46.4, 32.6, 31.3, 29.6, 27.3. MS (ESI, m/z): 369 $[M+NH_4]^+$.

9-(3-Hydroxyphenyl)-3,3,6,6-tetramethyl-3,4,6,7-tetrahydro-2H-xanthene-1,8(5H, 9H)dione (**3k**) (Table 1, Entry 11): White Solid. Yield: 86%. M.p.: 215-216 °C. FT-IR (KBr, cm^{-1}): 3296, 3017, 2929, 1655, 1592, 930, 829, 755, 590. ^1H NMR (300 MHz, $CDCl_3$): 7.25-7.10 (m, 2H, ArH), 7.01 (s, 1H, ArH), 6.92-6.90 (d, *J* = 7.17 Hz, 1H, ArH), 5.41 (s, 1H, CH), 2.47-2.26 (m, 8H, 4xCH_2), 1.25 (s, 6H, 2xCH_3), 1.11 (s, 6H, 2xCH_3). ^{13}C NMR (75 MHz, $CDCl_3$): 190.6, 189.6, 155.7, 139.9, 129.1, 118.8, 115.4, 114.1, 112.9, 46.9, 46.2, 32.5, 31.3, 29.6, 27.3. MS (ESI, m/z): 385 $[M+NH_4]^+$.

9-(3-Chlorophenyl)-3,3,6,6-tetramethyl-3,4,6,7-tetrahydro-2H-xanthene-1,8(5H, 9H)dione (**3l**) (Table 1, Entry 12): White Solid. Yield: 88%. M.p.: 183-184 °C. FT-IR (KBr, cm^{-1}): 2958, 2868, 1593, 1462, 1374, 1155, 870, 788, 674. ^1H NMR (300 MHz, $CDCl_3$): 7.28-7.12 (m, 2H, ArH), 7.01 (s, 1H, ArH), 6.92-6.91 (d, *J* = 7.17 Hz, 1H, ArH), 5.40 (s, 1H, CH), 2.47-2.26 (m, 8H, 4xCH_2), 1.25 (s, 6H, 2xCH_3), 1.11 (s, 6H, 2xCH_3). ^{13}C NMR (75 MHz, $CDCl_3$): 190.5, 189.3, 140.3, 134.1, 129.3, 127.1, 125.9, 124.8, 115.0, 46.9, 46.3, 32.5, 31.4, 29.5, 27.3. MS (ESI, m/z): 403 $[M+NH_4]^+$.

9-(4-Bromophenyl)-3,3,6,6-tetramethyl-3,4,6,7-tetrahydro-2H-xanthene-1,8(5H, 9H)dione (**3m**) (Table 1, Entry 13): White Solid. Yield: 89%. M.p.: 240-241 °C. FT-IR (KBr, cm^{-1}): 2959, 2878, 1589, 1484, 1303, 1158, 888, 709, 664. ^1H NMR (300 MHz, $CDCl_3$): 7.36-7.33 (d, *J* = 7.58 Hz, 2H, ArH), 6.92-6.89 (d, *J* = 7.58 Hz, 2H, ArH), 5.39 (s, 1H, CH), 2.46-2.25 (m, 8H, 4xCH_2), 1.22 (s, 6H, 2xCH_3), 1.11 (s, 6H, 2xCH_3). ^{13}C NMR (75 MHz, $CDCl_3$): 190.5, 189.3, 137.2, 131.2, 128.5, 119.5, 115.1, 46.9, 46.3, 32.4, 31.3, 29.5, 27.3. MS (ESI, m/z): 447 $[M+NH_4]^+$.

Table 1. Synthesis of 1,8-dioxooctahydroxanthene derivatives catalyzed by *β*-cyclodextrin[a].

Entry	Aldehyde	1,3 dicarbonyl compound	Product	Yield[b] (%)		M.p. (°C)		Reference
				Found	Reported	Found	Reported	
1	Benzaldehyde	1,3-Cyclohexanedione	3a	95	82	269-270	270-271	[33]
2	*p*-Bromo benzaldehyde	1,3-Cyclohexanedione	3b	91	93	284-285	284-285	[33]
3	*m*-Hydroxy benzaldehyde	1,3-Cyclohexanedione	3c	87	89	255-256	255-257	[33]
4	*m*-Chloro benzaldehyde	1,3-Cyclohexanedione	3d	85	86	275-276	276-277	[16]
5	*p*-Methyl benzaldehyde	1,3-Cyclohexanedione	3e	90	87	262-264	262-263	[16]
6	*p*-Chloro benzaldehyde	1,3-Cyclohexanedione	3f	90	92	288-289	289-290	[33]
7	*p*-Hydroxy benzaldehyde	1,3-Cyclohexanedione	3g	90	75	245-246	245-247	[26]
8	*p*-Fluoro benzaldehyde	1,3-Cyclohexanedione	3h	88	90	275-276	275-277	[35]
9	*p*-Nitro benzaldehyde	1,3-Cyclohexanedione	3i	80	93	265-266	265-267	[33]
10	Benzaldehyde	5,5-Dimethyl 1,3-Cyclohexanedione	3j	96	89	203-205	204-205	[17]
11	*m*-Hydroxy benzaldehyde	5,5-Dimethyl 1,3-Cyclohexanedione	3k	86	70.5	215-216	215-218	[28]
12	*m*-Chloro benzaldehyde	5,5-Dimethyl 1,3-Cyclohexanedione	3l	88	94	183-184	184-186	[17]
13	*p*-Bromo benzaldehyde	5,5-Dimethyl 1,3-Cyclohexanedione	3m	89	84.5	240-241	240-242	[28]
14	*p*-Fluoro benzaldehyde	5,5-Dimethyl 1,3-Cyclohexanedione	3n	89	92	223-224	223-225	[35]
15	*p*-Chloro benzaldehyde	5,5-Dimethyl 1,3-Cyclohexanedione	3o	90	92	230-232	230-232	[17]
16	Cinnamaldehyde	5,5-Dimethyl 1,3-Cyclohexanedione	3p	85	90	175-177	175-177	[17]

[a] Reaction conditions: 1,3- diketone (2.0 mmol), aromatic aldehyde (1.0 mmol), *β*-CD (1.0 mmol), water (10 mL), 60-65 °C, 10-12 h.
[b] Yields of the isolated product.

9-(4-Fluorophenyl)-3,3,6,6-tetramethyl-3,4,6,7-tetrahydro-2H-xanthene-1,8(5H, 9H)dione (**3n**) (Table 1, Entry 14): White Solid. Yield: 89%. M.p.: 223-224 °C. FT-IR (KBr, cm^{-1}): 2962, 2930, 1593, 1372, 1228, 1065, 869, 833, 753, 660. ^{1}H NMR (300 MHz, $CDCl_3$): 7.01-6.88 (m, 4H, ArH), 5.41 (s, 1H, CH), 2.46- 2.25 (m, 8H, 4xCH_2), 1.23 (s, 6H, 2xCH_3), 1.11 (s, 6H, 2xCH_3). ^{13}C NMR (75 MHz, $CDCl_3$): 190.4, 189.3, 162.5, 159.3, 133.5, 128.2, 128.1, 115.4, 115.0, 114.7, 46.9, 46.3, 32.1, 31.3, 29.5, 27.3. MS (ESI, m/z): 387 $[M+NH_4]^+$.

9-(4-Chlorophenyl)-3,3,6,6-tetramethyl-3,4,6,7-tetrahydro-2H-xanthene-1,8(5H, 9H)dione (**3o**) (Table 1, Entry 15): White Solid. Yield: 90%. M.p.: 230-232 °C. FT-IR (KBr, cm^{-1}): 2960, 2929, 1589, 1305, 1093, 887, 833, 720, 658. ^{1}H NMR (300 MHz, $CDCl_3$): 7.25-7.18 (m, 2H, ArH), 6.97-6.95 (d, J = 8.12 Hz, 2H, ArH), 5.40 (s, 1H, CH), 2.46-2.25 (m, 8H, 4xCH_2), 1.22 (s, 6H, 2xCH_3), 1.11 (s, 6H, 2xCH_3). ^{13}C NMR (75 MHz, $CDCl_3$): 190.5, 189.3, 136.6, 131.4, 115.2, 46.9, 46.3, 32.3, 31.3, 29.5, 27.3. MS (ESI, m/z): 403 $[M+NH_4]^+$.

(E)-3,3,6,6-Tetramethyl-9-styryl-3,4,6,7-tetrahydro-2H-xanthene-1,8(5H,9H)-dione (**3p**) (Table 1, Entry 16): White Solid. Yield: 85%. M.p.: 175-177 °C. FT-IR (KBr, cm^{-1}): 2962, 2928, 1665, 1610, 1592, 1372, 1159, 1041, 842, 774, 700. ^{1}H NMR (300 MHz, $CDCl_3$): 7.28-7.19 (m, 5H, ArH), 6.24 – 6.34 (m, 2H, -CH=CH), 5.42 (s, 1H, CH), 2.46-2.26 (m, 8H, 4xCH_2), 1.25 (s, 6H, 2xCH_3), 1.11 (s, 6H, 2xCH_3). ^{13}C NMR (75 MHz, $CDCl_3$): 190.9, 163.2, 137.4, 131.2, 128.9, 127.6, 125.9, 115.2, 48.9, 42.9, 32.6, 31.0, 28.3, 27.9. MS (ESI, m/z): 394 $[M+NH_4]^+$.

3. Results and discussion

Cyclodextrins are cyclic oligosaccharides which have generated interest as enzyme models, due to their ability to bind substrates selectively and catalyze chemical reactions, by supramolecular catalysis [36-46], involving the reversible formation of host-guest complexes with a broad range of substrates by non covalent bonding, as seen in enzyme complexation processes. We describe, here in the remarkable catalytic activity of *β*-CD in the reaction of aromatic aldehydes and 1,3-cyclohexanedione to give exclusively substituted 1,8-dioxooctahydroxanthenes (Scheme 1). In general, the reaction was carried out by the addition of benzaldehyde to *β*-CD, dissolved in water. To this aqueous solution of the *β*-CD-benzaldehyde complex, 1,3-cyclohexanedione was added by stirring the mixture at 60-65 °C to give the corresponding xanthene in high yield. To study the scope of this reaction, various aromatic aldehydes were subjected to this protocol. All the reactions have proceeded efficiently and produced high yields without formation of any side products. This can be concluded that the activation of aldehyde by the hydrogen bonding interactions of *β*-CD contribute for the process of the reaction to prove the role of cyclodextrin, NMR studies were carried out on *β*-CD and the *β*-CD-benzaldehyde inclusion complex. It was observed from spectral studies, there is an up field shift of H-C (3) (0.017 ppm) and H-C (5) (0.07 ppm) protons of CD in the *β*-CD-benzaldehyde complex as compared to *β*-cyclodextrin, indicating that the reaction was proceeding through a host-guest complexation phenomenon. The hydrogen bonding interactions activate aldehyde molecule, involved in host-guest complexation in *β*-CD cavity, which in turn facilitates the bonding with tautomeric form of 1,3-cyclohexanedione moiety, stabilised by the primary and secondary -OH groups of *β*-CD, which further reacts with another molecule of 1,3-cyclohexanedione, ultimately leading to 1,8-dioxooctahydroxanthene as a cyclised product in the process of this reaction. No product formation was observed in the absence of cyclodextrin. All products were characterized by their m.p., ^{1}H-NMR, ^{13}C-NMR, IR, and MS and compared with the known compounds. After completion of the reaction, the aqueous layer was cooled to room temperature and *β*-CD was filtered and washed with ice-cooled water and dried. The recovered *β*-cyclodextrin was further used with the same substrates as a catalyst and checked for the yields and catalytic activity of recovered catalyst (*β*-CD). As shown in Table 2, the yields of 1,8-dioxooctahydroxanthene after two (or) three cycles were almost the same.

Table 2. Synthesis of 1,8-dioxooctahydroxanthene derivatives catalyzed by *β*-cyclodextrin[a].

Recycles	Yield[b] (%)	β-CD recovery (%)
1	95	95
2	92	94
3	89	90
4	88	89

[a] Reaction conditions: 1,3- diketone (2.0 mmol), aromatic aldehyde (1.0 mmol), *β*-CD (1.0 mmol), water (10 mL), 60-65 °C, 10-12 h.
[b] Yields of the isolated product.

4. Conclusion

In conclusion, we have developed a simple and efficient aqueous phase synthesis of various 1,8-dioxooctahydro xanthenes by the reaction of the corresponding 1,3-cyclohexanedione with aromatic aldehydes under environmentally benign conditions in the presence of *β*-cyclodextrin. These cyclodextrin mediated aqueous phase organic reactions are useful both from economical and environmental points of view. This methodology also overcomes the formation of unwanted by-products, low yields, and use of hazardous solvents and high temperatures.

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