

Solvent-free Synthesis of 5H-dibenzo[*b,i*]xanthene-tetraones and Aryl-14H-dibenzo[*a,j*]xanthenes Using Ferric Chloride Hexahydrate as Catalyst

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Abstract. A simple and convenient procedure for the synthesis of 5H-dibenzo[*b,i*]xanthene-tetraones and aryl-14H-dibenzo[*a,j*]xanthenes is described through the condensation of aldehydes with 2-naphthol or 2-hydroxy-1, 4-naphthoquinone under solvent-free conditions in the presence of ferric chloride hexahydrate. This method has the advantages of high yields, cleaner reaction, simple work-up and cost efficiency.

Keywords: xanthenes; aldehydes; 2-hydroxy-1, 4-naphthoquinone; 2-naphthol; solvent-free; ferric chloride hexahydrate.

Resumen. Se describe una metodología simple para la síntesis de 5H-dibenzo[*b,i*]xanteno-tetraonas y aril-14H-dibenzo[*a,j*]xantenos. Los xantenos son obtenidos por condensación de aldehídos con 2-naftol o 2-hidroxi-1,4-naftoquinona en presencia de cloruro férrico hexahidratado. Las reacciones se llevan a cabo en ausencia de disolvente, son limpias, de bajo costo y con alto rendimiento.

Palabras clave: Xantenos; aldehidos; 2-hidroxi-1,4-naftoquinona; 2-naftol; ausencia de disolvente; cloruro férrico hexahidratado.

Introduction

The development of simple method to synthesize worthful organic compounds from readily available compounds is one of the major tasks in organic synthesis [1]. Xanthene's heterocycles and derivatives are interest due to their wide range of biological and pharmaceutical properties, such as agricultural bactericide, [2] anti-inflammatory [3] and antiviral activities [4]. They have also been used for photodynamic therapy, [5] used as dyes [6] and in laser technologies [7]. Thus, the synthesis of xanthenes currently is of continuing interest.

Many synthetic methods exist for the synthesis of xanthenes, such as the cyclocondensation reaction of 2-hydroxyaromatic aldehydes and 2-tetralone[8], the reaction of benzaldehydes and acetophenones [9], etc. Recently, the synthesis reaction of 13-aryl-5H-dibenzo[*b,i*]xanthene-5, 7, 12, 14(13H)-tetraones by the one-pot condensation of 2-hydroxy-1, 4-naphthoquinone and aldehydes has been achieved in the presence of a catalyst, such as *p*-toluenesulfonic acid [10, 11], ionic liquid [12-14]. Also aryl-14H-dibenzo[*a,j*]xanthenes were prepared by the condensation of 2-naphthol with aldehydes, and this reaction could catalyzed by TaCl₅ [15], BiCl₃ [16], others have been summarized by Kumar [17]. However, these methods show varying degrees of success as well as limitations such as prolonged reaction times, laborious work-up procedures, harsh reaction conditions, use of an excess of expensive reagents/catalysts and use of toxic organic solvents. Thus, the development of an alternate milder and clean procedure is highly demanding for the synthesis of benzoxanthenes. Recently, much attention has been paid to iron as an effective, easily available, and promising transition-metal catalyst for different organic reactions-oxidation, hydrogenation, rearrangement, Michael addition [18]. Cao et al [19] effectively synthesized aryl-14H-dibenzo[*a,j*]xanthenes catalyzed by Fe(OTf)₃, but Fe(OTf)₃ suffered from laborious preparation and high cost. So, as part of our research program

directed towards the development of highly expedient methods, we herein introduce a new, convenient and solvent-free synthesis of 13-aryl-5H-dibenzo[*b,i*]xanthene-5, 7, 12, 14(13H)-tetraones and 14-aryl-14H -dibenzo[*a,j*]xanthenes catalyzed by ferric chloride hexahydrate (FeCl₃·6H₂O). To the best of our knowledge in the open literature, one-pot syntheses of benzoxanthenes catalyzed by FeCl₃·6H₂O have not been reported. And solvent-free synthesis has advantages of easy workup, low cost and friendly environment compared to the synthesis with various solvent.

Results and Discussion

Initially, in search of an effective catalyst, various Lewis acids were tested as catalysts using the reaction of 2-hydroxy-1, 4-naphthoquinone and benzaldehyde as model. A summary of the experiment optimization is provided in Table 1. It was found that FeCl₃·6H₂O was the most efficient catalyst compared with other chlorides-SnCl₄, CoCl₂ and NiCl₂ hydrate, which exhibited from moderate to poor catalytic properties. The effect of the amount of catalyst was examined in this reaction. The results showed that a 20% mol amount of FeCl₃·6H₂O was sufficient to promote the reaction and larger amounts of the catalyst did not lead to any significant changes in the reaction yield. Also we studied the model reaction catalyzed by FeCl₃ (20 mol%) at different temperatures. The yields increased as the reaction temperature was raised. When it was carried out at 90 °C, the good yield could be obtained in a short time. The reaction was also carried out at 110 °C, but the yield of the expected product was not further improved at this temperature, and the colour of the product changed from red to dark red. Thus, based on an overall consideration, 90 °C should be reasonable choice. Finally, it should be mentioned that when the reactions were carried out without catalyst, almost no conversion occurred.

With this optimized procedure in hand, a range of 13-aryl-5H-dibenzo[*b,i*]xanthene-5, 7, 12, 14(13H)-tetraones was synthesized by the one-pot condensation of aldehydes and 2-hydroxy-1, 4-naphthoquinone under solvent-free conditions. The reaction proceeded about 2-3 h in excellent yields at 90 °C after the addition of the catalyst FeCl₃·6H₂O (see Table 2). The reaction worked well with electron-withdrawing (Cl, Br) as well as electron-donating (CH₃, CH₃O) groups, giving various xanthene derivatives in 87-95% yields. So, the method is general and includes a variety of functional groups.

Encouraged by these results, we carried out the reaction of 2-naphthol with various aromatic aldehydes under solvent-free conditions at 90 °C, which afforded 14-aryl-14H-dibenzo[*a,j*]xanthenes in good yields within a short period of time (2-3 h) (see Scheme 2, Table 3).

Although the detailed mechanism of the above reaction remains to be fully clarified, a reasonable possibility is shown in Scheme 3.

Experimental

Melting points were determined in X-6 micro melting point apparatus without further correction. IR spectra were recorded on a Perkin Elmer FTIR spectrometer in KBr. ¹H NMR spectra were obtained from solution in DMSO-*d*₆ or CDCl₃ using a Bruker AVANCE 400 spectrometer. Elemental analyses were performed using elemental Vario EL CHNS/O Element analyzer.

All reagents were of analytical grade and purchased from Sinopharm Chemical Reagent Co., Ltd., and were used without further purification.

General procedure for the synthesis of benzoxanthenes: A mixture of aldehyde (5 mmol), 2-hydroxynaphthalene-1, 4-dione or 2-naphthol (10 mmol) and FeCl₃·6H₂O (1 mmol) was finely mixed together and heated at 90 °C. The reaction was monitored by Thin-Layer Chromatography (TLC). After completion, the system was cooled to ambient temperature, the reaction mixture was washed with aqueous EtOH (60 %, v) and filtered to afford the crude product. Further purification was followed by crystallization from ethanol (95%).

All the products are known compounds. The desired pure products were characterized by spectral (IR, ¹H NMR) and analytical data, and by comparison of their physical and spectral data with those of known benzoxanthenes [10, 12, 16, 17, 19].

13-Phenyl-5H-dibenzo[*b,i*]xanthene-5, 7, 12, 14(13H)-tetraone (**4a**). IR (KBr, cm⁻¹): 3042, 1705, 1575, 1280, 745; ¹H NMR (DMSO-*d*₆, 400 MHz): δ 5.14 (s, 1H, CH), 7.20-8.13 (m, 13H, Ar); Anal. Calcd. for C₂₇H₁₄O₅: C 77.51, H 3.37 found: C 77.38, H 3.44.

13-(4-Chlorophenyl)-5 H-dibenzo[*b,i*]xanthene-5, 7, 12, 14(13H)-tetraone (**4b**). IR (KBr, cm⁻¹): 3016, 1662, 1614, 829; ¹H NMR (DMSO-*d*₆, 400 MHz): δ 5.12 (s, 1H, CH), 7.730-8.11 (m, 12H, ArH); Anal. Calcd. for C₂₇H₁₃ClO₅: C 77.61, H 2.89 found: C 77.69, H 2.95.

13-(4-Bromophenyl)-5 H-dibenzo[*b,i*]xanthene-5, 7, 12, 14(13H)-tetraone (**4c**). IR (KBr, cm⁻¹): 3084, 1660, 1606; ¹H

Table 1. Optimization of the reaction conditions for synthesis of 13-phenyl-5 H-dibenzo[*b,i*]xanthene-5, 7, 12, 14(13H)-tetraone.

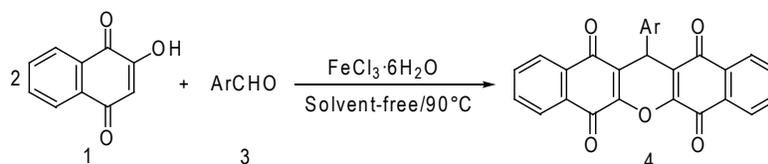
Entry	Catalyst(mol%)	Temperature(°C)	Time (h)	Yield (%)
1	FeCl ₃ (10)	90	3	80.8
2	FeCl ₃ (20)	90	2.5	92.0
3	FeCl ₃ (25)	90	2.5	92.4
4	FeCl ₃ (20)	80	2.5	84.5
5	FeCl ₃ (20)	110	2.5	90.0
6	SnCl ₄ (20)	90	3	77.6
7	CoCl ₂ (20)	90	2.5	<30.0
8	NiCl ₂ (20)	90	2.5	<30.0
9	—	90	3	trace

Table 2. Synthesis of 13-aryl-5H-dibenzo[*b,i*]xanthene-5, 7, 12, 14(13H)-tetraones catalyzed by FeCl₃·6H₂O^a.

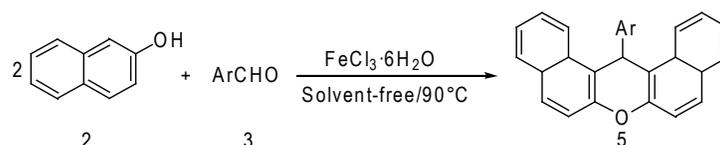
Entry	Aldehyde	Product	Time (h)	Yield (%) ^b	Mp (°C)/(lit.)
1	C ₆ H ₅ CHO	4a	2.5	92.0	305–307(305–307)[10]
2	4-ClC ₆ H ₄ CHO	4b	2.5	95.3	329–330(330–332)[10]
3	4-BrC ₆ H ₄ CHO	4c	2.0	94.0	333–335(333–335)[10]
4	4-(CH ₃)C ₆ H ₄ CHO	4d	3.0	87.2	304–307(304–307)[10]
5	2-CH ₃ OC ₆ H ₄ CHO	4e	3.0	90.2	262–265(264–266)[12]

^aReaction conditions: aldehyde (5 mmol); 2-hydroxy-1, 4-naphthoquinone(10 mmol); FeCl₃·6H₂O (1 mmol); 90°C; neat.

^bIsolated yield.



Scheme 1. Synthesis of 13-aryl-5H-dibenzo[*b,i*]xanthene-5, 7, 12, 14(13H)-tetraones.



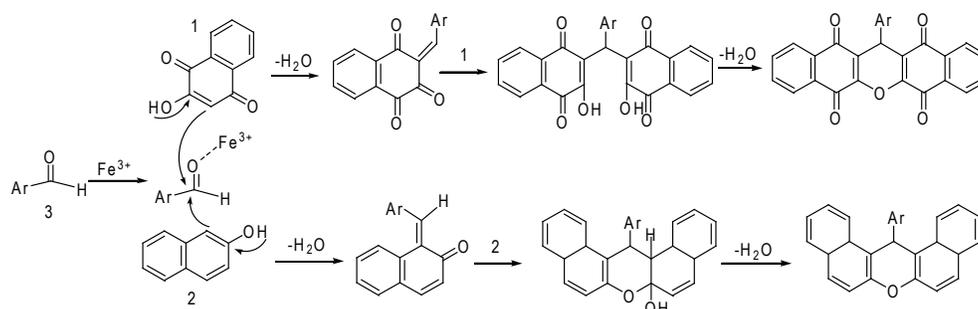
Scheme 2. Synthesis of 14-aryl-14H-dibenzo[*a,j*]xanthenes.

Table 3. Synthesis of 14-aryl-14H-dibenzo[*a,j*]xanthenes catalyzed by $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ ^a.

Entry	Aldehyde	Product	Time (h)	Yield (%) ^b	Mp (°C)/(lit.)
1	$\text{C}_6\text{H}_5\text{CHO}$	5a	2.0	86.6	187-189(188.5–189.8)[19]
2	4-Cl $\text{C}_6\text{H}_4\text{CHO}$	5b	2.0	93.7	289-291(287–288)[17]
3	4-Br $\text{C}_6\text{H}_4\text{CHO}$	5c	2.0	91.6	295–297(295.6–296.9)[19]
4	4-(CH_3) $\text{C}_6\text{H}_4\text{CHO}$	5d	2.5	84.2	230-232(230.6–232.1)[19]
5	2- $\text{CH}_3\text{OC}_6\text{H}_4\text{CHO}$	5e	3.0	83.1	257–260(260)[16]

^aReaction conditions: aldehyde (5 mmol); 2-naphthol (10 mmol); $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ (1 mmol); 90°C; neat.

^bIsolated yield.



Scheme 3. Proposed reaction mechanism for the synthesis of xanthenes catalyzed by FeCl_3 .

NMR (DMSO- d_6 , 400 MHz): δ 5.14 (s, 1H, CH), 7.45–8.18(m, 12H, ArH); Anal. Calcd. for $\text{C}_{27}\text{H}_{13}\text{BrO}_5$: C 65.21, H 2.63 found: C 65.07, H 2.44.

13-(4-Methylphenyl)-5H-dibenzo[*b,i*]xanthene-5, 7, 12, 14(13H)-tetraone (**4d**). IR (KBr, cm^{-1}): 3067, 1658, 1598, 1385; ^1H NMR (DMSO- d_6 , 400 MHz): δ 2.19 (s, 3H, CH_3), 5.09 (s, 1H, CH), 7.07–8.08 (m, 12H, ArH); Anal. Calcd. for $\text{C}_{28}\text{H}_{16}\text{O}_5$: C 77.77, H 3.73 found: C 77.62, H 3.69.

13-(2-Methoxyphenyl)-5H-dibenzo[*b,i*]xanthene-5, 7, 12, 14(13H)-tetraone (**4e**). IR (KBr, cm^{-1}): 1675, 1604, 1591; ^1H NMR (DMSO- d_6 , 400 MHz): δ 3.63 (s, 3H, OCH_3), 5.22(s, H,

CH), 6.85–8.11 (m, 14H, ArH); Anal. Calcd for $\text{C}_{28}\text{H}_{16}\text{O}_6$: C 75.00, H 3.60 found: C 74.89; H 3.63.

14-Phenyl-14H-dibenzo[*a,j*]xanthene (**5a**). IR (KBr, cm^{-1}): 3075, 2998, 1593, 1513, 1458; ^1H NMR (CDCl_3 , 600MHz): δ 6.48 (s, 1H, CH), 8.38–6.96 (m, 17H, ArH); Anal. Calcd. for $\text{C}_{27}\text{H}_{18}\text{O}$: C 90.47, H 5.06 found: C 90.39, H 5.15.

14-(4-Chlorophenyl)-14H-dibenzo[*a,j*]xanthene (**5b**). IR (KBr, cm^{-1}): 3069, 2915, 1622, 1592; ^1H NMR (CDCl_3 , 600MHz): δ 6.46 (s, H, CH), 8.31–7.08 (m, 16H, ArH); Anal. Calcd. for $\text{C}_{27}\text{H}_{17}\text{ClO}$: C 82.54, H 4.36 found: C 82.44, H 4.40.

14-(4-Bromophenyl)-14H-dibenzo[*a,j*]xanthene (**5c**). IR (KBr, cm^{-1}): 3030, 1624, 1586; $^1\text{H NMR}$ (CDCl_3 , 600MHz): δ 6.46(s, 1H, CH), 7.25-8.34 (m, 16H, ArH); Anal. Calcd. for $\text{C}_{27}\text{H}_{17}\text{BrO}$: C 74.15, H 3.92 found: C 74.19, H 3.97.

14-(4-methylphenyl)-14H-dibenzo[*a,j*]xanthene (**5d**). IR (KBr, cm^{-1}): 3073, 2913, 1625, 1595; $^1\text{HNMR}$ (CDCl_3 , 600 MHz): δ 2.13 (s, 3H, CH_3), 6.46 (s, 1H, CH), 8.39-6.95 (m, 16H, ArH); Anal. Calcd. for $\text{C}_{28}\text{H}_{20}\text{O}$: C 90.29, H 5.41; found: C 90.18, H 5.46.

14-(2-Methoxyphenyl)-14H-dibenzo[*a,j*]xanthene (**5e**). IR(KBr, cm^{-1}): 3013, 2951, 2936, 1594, 1487; $^1\text{H NMR}$ (CDCl_3 , 600 MHz): δ 3.61 (s, 3H, CH_3), 6.41 (s, 1H, CH), 8.38-6.53 (m, 16H, ArH); Anal. Calcd. for $\text{C}_{28}\text{H}_{20}\text{O}_2$: C 86.45, H 5.06 found: C 86.55, H 5.11.

Conclusion

A simple and efficient method for the synthesis of xanthenes using $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ under solvent-free conditions has been developed, which affords short reaction times, excellent yields and utilization of an inexpensive catalyst.

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