

## *p*-Toluenesulfonic Acid Catalyzed Synthesis of 14-Aryl-14*H*-dibenzo[*a, i*]xanthene-8, 13-diones

DI LIU\*, DONGMEI XU, JUN GAO and SHIXUE ZHOU

College of Chemical and Environmental Engineering, Shandong University of Science and Technology, Qingdao, Shandong-266590, P. R. China

ld002037132@163.com

Received 28 March 2013 / Accepted 30 April 2013

**Abstract:** A series of 14-aryl-14*H*-dibenzo[*a, i*]xanthene-8,13-diones was synthesized by the one-pot condensation of  $\beta$ -naphthol, aldehydes and 2-hydroxy-1, 4-naphthoquinone under solvent-free conditions in the presence of *p*-toluenesulfonic acid. This method has the advantages of high yield, clean reaction, simple methodology.

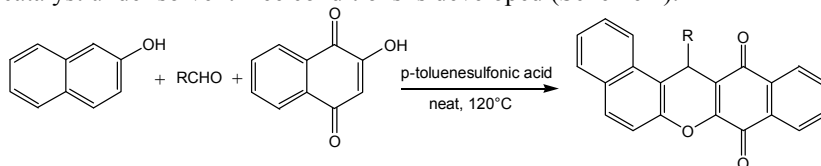
**Keywords:** Dibenzo[*a, i*]xanthenes,  $\beta$ -Naphthol, 2-Hydroxy-1,4-naphthoquinone, Aldehyde, Solvent-free, *p*-Toluenesulfonic acid

### Introduction

Xanthenes and benzoxanthenes are important biologically active heterocycles because of their wide range of biological and pharmaceutical properties, such as agricultural bactericide activity<sup>1</sup>, anti-inflammatory<sup>2</sup> and antiviral activity<sup>3</sup>. They have also been used for photodynamic therapy<sup>4</sup>, used as dyes<sup>5</sup> and in laser technologies<sup>6</sup>.

Many synthetic methods exist for the synthesis of xanthenes and benzoxanthenes, which include the cyclocondensation reaction of 2-hydroxyaromatic aldehydes and 2-tetralone<sup>7</sup>, the reaction of benzaldehydes and acetophenones<sup>8</sup> and the condensation of  $\beta$ -naphthol with alkyl or aryl aldehydes<sup>9</sup>. 2-Hydroxy-1, 4-naphthoquinone has been employed as a synthetic intermediate for the preparation of numerous heterocyclic compounds with interesting biological properties<sup>10-12</sup>. Compounds containing heterocyclic quinone group represent an important class of biologically active molecules<sup>13</sup>. Herein, 2-hydroxy-1, 4-naphthoquinone,  $\beta$ -naphthol and aldehydes were used as raw material to synthesize 14-aryl-14*H*-dibenzo[*a, i*]xanthene-8, 13-dione. According to current report, the reaction has been improved in the presence of a catalyst, such as poly(4-vinylpyridinium) hydrogen sulfate<sup>14</sup>, silica supported perchloric acid<sup>15</sup>, silica chloride<sup>16</sup>, xanthan sulfuric acid<sup>17</sup>, acetic acid<sup>18</sup> and Amberlyst-15<sup>19</sup>. However, these methods show varying degrees of success as well as limitations such as low yields, use of toxic or expensive reagents/catalysts, laborious work-up procedures, the requirement of special apparatus, or harsh reaction conditions. Thus, the development of an

alternate milder and clean procedure is highly demanding for the synthesis of 14-aryl-14*H*-dibenzo[*a, i*]xanthene-8, 13-dione. Considering the above reports, our program aimed at developing selective and simple methodologies for the preparation of 14-aryl-14*H*-dibenzo[*a, i*]xanthene-8, 13-diones. In this paper, a simple and efficient route using *p*-toluenesulfonic acid as catalyst under solvent-free conditions is developed (Scheme 1).



**Scheme 1.** Synthesis of 14-aryl-14*H*-dibenzo[*a, i*]xanthene-8, 13-diones

## Experimental

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 14-aryl-14*H*-dibenzo[*a, i*]xanthene-8, 13-diones

A mixture of  $\beta$ -naphthol (5 mmol), aldehyde (5 mmol), 2-hydroxynaphthalene-1, 4-dione (5 mmol) and *p*-toluenesulfonic acid (0.5 mmol) was finely mixed together and heated at 120 °C. The reaction was monitored by TLC. After completion, the reaction mixture was washed with ethanol and water. Further purification was followed by crystallization from ethanol.

All the products are known compounds. The desired pure products were characterized by spectral (IR,  $^1\text{H}$  and  $^{13}\text{C}$  NMR) and analytical data, and by comparison of their physical and spectral data with those of known benzoxanthenes<sup>13,14</sup>.

14-Phenyl-14*H*-dibenzo[*a, i*]xanthene-8, 13-dione (Table 2, Entry 1). Orange powder, m. p. 317-319 °C; IR (KBr,  $\text{cm}^{-1}$ ): 3024, 1698, 1650, 1593, 1576, 1372, 1288, 1237;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  = 8.19-7.09 (m, 15H, ArH), 5.90 (s, 1H, CH);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz) :  $\delta$  = 178.4, 157.3, 147.3, 143.2, 135.3, 132.0, 131.2, 131.0, 130.1, 129.5, 128.6, 127.6, 126.9, 125.6, 124.4, 123.6, 116.9, 116.6; Anal. Calcd. for  $\text{C}_{27}\text{H}_{16}\text{O}_3$ : C 83.4 9, H 4.15; found: C 83.25, H 4.12.

14-(2-Chlorophenyl)-14*H*-dibenzo[*a, i*]xanthene-8, 13-dione (Table 2, entry 2). Yellow powder, m. p. 281-282 °C; IR (KBr,  $\text{cm}^{-1}$ ) : 3068, 1665, 1636, 1590, 1574, 1360, 1287, 1238;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  = 8.27-7.06 (m, 14H), 6.20 (s, 1H, CH);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  = 178.3, 157.2, 147.2, 135.2, 133.3, 131.8, 131.4, 131.30, 130.8, 130.1, 129.8, 129.3, 128.6, 128.2, 127.6, 127.0, 125.5, 124.6, 124.0, 116.6, 115.7, 33.7; Anal. Calcd. for  $\text{C}_{27}\text{H}_{15}\text{ClO}_3$ : C 76.69, H 3.58; found: C 76.80, H 3.39.

14-(4-Chlorophenyl)-14*H*-dibenzo[*a, i*]xanthene-8, 13-dione (Table 2, entry 3). Yellow powder, m. p. 303-306 °C; IR (KBr,  $\text{cm}^{-1}$ ) : 3039, 1663, 1637, 1590, 1579, 14 87, 1359, 1292;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  = 8.18-7.17 (m, 14H, ArH), 5.85 (s, 1H, CH);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  = 178.2, 157.1, 147.2, 141.4, 135.1, 132.7, 131.9, 131.3, 130.7, 130.0, 129.6, 129.4, 128.7, 127.4, 125.7, 124.5, 123.4, 116.8, 116.1, 116.0, 34.8; Anal. Calcd. for  $\text{C}_{27}\text{H}_{15}\text{ClO}_3$ : C 76.69, H 3.58; found: C 76.84, H 3.46.

14-(4-Methoxyphenyl)-14*H*-dibenzo[*a, i*]xanthene-8, 13-dione (Table 2, entry 4). Yellow powder, m. p. 279-282 °C; IR(KBr,  $\text{cm}^{-1}$ ): 2923, 1669, 1635, 1591, 1577, 1368, 1284, 1251, 1236;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 3.67 (s, 3H,  $\text{OCH}_3$ ), 5.95 (s, 1H, CH), 7.30-8.16 (d, 14H, ArH.);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 178.4, 158.2, 157.0, 147.2, 135.5, 135.0, 131.6, 131.1, 129.8, 129.5, 129.4, 128.4, 127.3, 125.4, 124.5, 123.7, 117.1, 116.6, 113.7, 55.1, 34.4; Anal. Calcd. for  $\text{C}_{28}\text{H}_{18}\text{O}_4$ : C 80.37; H 4.34, found: C 80.48; H 4.26.

14-(4-Methylphenyl)-14*H*-dibenzo[a, i]xanthene-8, 13-dione (Table 2, entry 5). Orange powder, m. p. 255-256 °C; IR(KBr, cm<sup>-1</sup>): 2928, 17031, 1669, 1641, 1590, 1574, 1374, 1280; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 8.22-7.29 (m, 14H, ArH), 5.87 (s, 1H, CH), 2.16 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 178.3, 157.0, 147.2, 136.4, 135.0, 131.9, 131.0, 130.9, 130.0, 129.4, 129.3, 128.4, 127.2, 125.0, 124.6, 123.9, 117.2, 116.7, 34.8, 21.1; Anal. Calcd. for C<sub>28</sub>H<sub>18</sub>O<sub>3</sub>: C 83.57; H 4.51, found: C 80.48; H 4.34.

14-(2,4-Dichlorophenyl)-14*H*-dibenzo[a, i]xanthene-8, 13-dione (Table 2, entry 6). Yellow powder, m. p. 301-302 °C; IR(KBr, cm<sup>-1</sup>): 3050, 1663, 1637, 1593, 1574, 146 1, 1288, 1233; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 8.23-7.07 (m, 13H), 6.11(s, 1H, CH); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 178.1, 157.8, 147.3, 139.4, 135.0, 134.0, 133.2, 132.4, 131.8, 131.2, 130.3, 130.1, 129.9, 129.3, 128.6, 127.6, 125.7, 124.6, 123.8, 117.0, 33.3; Anal. Calcd. for C<sub>27</sub>H<sub>14</sub>Cl<sub>2</sub>O<sub>3</sub>: C 70.91, H 3.09, found: C 79.83; H 3.13.

## Results and Discussion

Initially, in search of an effective catalyst, various sulfonic acids were tested as catalysts for the three-component reaction of β-naphthol, 2-hydroxy-1, 4-naphthoquinone and benzaldehyde (Table 1). When the reaction was performed in the presence of sulfonic acids, it proceeded mildly and rapidly to give the desired product in high yields, *p*-toluenesulfonic acid was found to be the most efficient catalyst compared with other organic sulfonic acids, and aminosulfonic acid exhibited moderate catalytic properties. In addition, it was also found that no conversion to 14-phenyl-14-aryl-14*H*-dibenzo[a, i]xanthene-8, 13-dione occurred without catalyst.

**Table 1.** Effect of catalyst on the formation of 14-phenyl-14-aryl-14*H*-dibenzo[a, i]xanthene-8, 13-dione

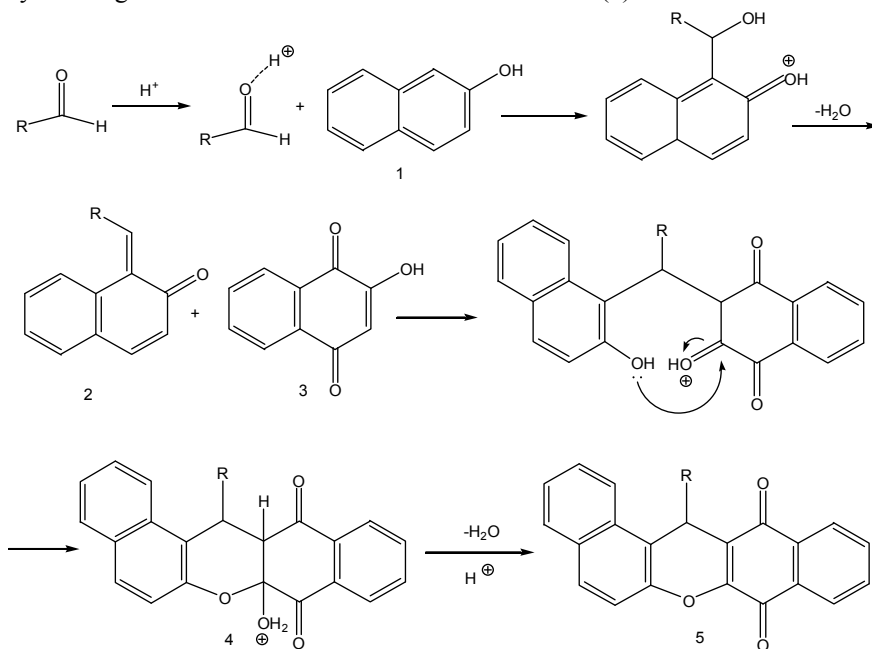
Entry	Catalyst 10 mol%	Time, min	Yield, %
1	<i>p</i> -Toluenesulfonic acid	65	85.5
2	Methanesulfonic acid	70	81.0
3	Aminosulfonic acid	70	62.2
4	Benzenesulfonic acid	70	82.5
5	<i>o</i> -Toluenesulfonic acid	75	80.6
6	-	120	-

With this optimized procedure in hand, a range of 14-aryl-14*H*-dibenzo[a, i]xanthene-8, 13-dione derivatives was synthesized by the one-pot condensation of β-naphthol, aldehydes, and 2-hydroxy-1, 4-naphthoquinone under solvent-free conditions. The reaction proceeded at 120 °C about 1 h in excellent yields (Table 2) after the addition of the catalyst *p*-toluenesulfonic acid (10 m%).

**Table 2.** Preparation of 14-aryl-14*H*-dibenzo[a, i]xanthene-8, 13-diones catalyzed by *p*-toluenesulfonic acid

Entry	Aldehyde	Time, min	Yield, %
1	C <sub>6</sub> H <sub>5</sub> CHO	65	85.5
2	2-ClC <sub>6</sub> H <sub>4</sub> CHO	65	93.0
3	4-ClC <sub>6</sub> H <sub>4</sub> CHO	60	82.8
4	4-(CH <sub>3</sub> O)C <sub>6</sub> H <sub>4</sub> CHO	65	84.8
5	4-(CH <sub>3</sub> )C <sub>6</sub> H <sub>4</sub> CHO	70	85.0
6	2, 4-ClC <sub>6</sub> H <sub>4</sub> CHO	70	83.7

Although the detailed mechanism of the above reaction remains to be fully clarified, a reasonable possibility is shown in Scheme 2. The reaction proceeds via a reaction sequence of condensation, addition, cyclization and dehydration. First, a proton from *p*-toluenesulfonic acid is donated to the oxygen atom of the aldehyde. Next, the carbonyl carbon is attacked by the nucleophilic  $\beta$ -naphthol (1) to form ortho-quinone methide intermediate (2). Subsequent Michael addition to the ortho-quinone methide with nucleophile followed by addition of the phenolic hydroxyl moiety (3) to the carbonyl of ketone provides cyclic hemiketal (4) which on dehydration gives rise to the desired xanthene derivatives (5).



**Scheme 2.** Proposed mechanism of the reaction

## Conclusion

A series of 14-aryl-14*H*-dibenzo[*a, i*]xanthene-8,13-diones was efficiently synthesized by the one-pot condensation of  $\beta$ -naphthol, aldehydes and 2-hydroxy-1, 4-naphthoquinone under solvent-free conditions in the presence of *p*-toluenesulfonic acid. In summary, a simple work-up procedure, short time, and good yields make our methodology a valid contribution to the synthesis of 14-aryl-14*H*-dibenzo[*a, i*]xanthene-8, 13-dione.

## Acknowledgement

The authors are thankful to Shandong University of Science and Technology for the partial support of this research.

## References

1. Hideo T and Teruomi J, Jpn Patent, 1981, 56005480.
2. Jamison J M, Krabill K, Hatwalkar A, Jamison E and Tsai C C, *Cell Biol Int Rep.*, 1990, **14**(12), 1075-1084; [http://dx.doi.org/10.1016/0309-1651\(90\)90015-Q](http://dx.doi.org/10.1016/0309-1651(90)90015-Q)

3. Ion R M, Frackowiak D, Alfons Planner and Wiktorowicz K. *Acta Biochim Pol.*, 1998, **45(3)**, 833-845.
4. Poupelin J P, Saint-Ruf G, Foussard-Blanpin O, Narcisse G, Uchida Emouf G and Lacroix R, *Eur J Med Chem.*, 1978, **13**, 67-71.
5. Bhowmik B B and Ganguly P, *Spectrochim Acta A: Mole Biomole Spectro.*, 2005, **61(9)**, 1997-2003; <http://dx.doi.org/10.1016/j.saa.2004.07.031>
6. Sirkecioglu O, Talinli N and Akar A, *J Chem Res (S)*, 1995, 502.
7. Jha A and Beal J, *Tetrahedron Lett.*, 2004, **45(49)**, 8999-9001; <http://dx.doi.org/10.1016/j.tetlet.2004.10.046>
8. Kuo C W and Fang J M. *Synth Commun.*, 2001, **31(6)**, 877-892; DOI:10.1081/SCC-100103323.
9. Kumar R, Nandi G C, Verma R K and Singh M S, *Tetrahedron Lett.*, 2010, **51(2)**, 442-445; <http://dx.doi.org/10.1016/j.tetlet.2009.11.064>
10. Sartori M F. *Chem Rev.*, 1963, **63(3)**, 279-296; DOI:10.1021/cr60223a005
11. Behforouz M, Haddad J, Cai W and Gu Z, *J Org Chem.*, 1998, **63(2)**, 343-346; DOI:10.1021/jo971823i
12. Hammam A S, Youssef M S K, Radwansh M, Abdel-Rahman M A, *Bull Korean Chem Soc.*, 2004, **25**, 779-785.
13. Patai S and Rappoport Z, *The chemistry of the Quinonoid Compounds*, John Wiley and Sons: London, England, 1988.
14. Khaligh N G, *Catal Sci Technol.*, 2012, **2(11)**, 2211-2215.
15. Wu L Q, Wu Y F, Yang C G, Yang L M and Yang L J, *J Braz Chem Soc.*, 2010, **221(5)**, 941-945.
16. Wu L, Zhang J, Fang L, Yang C and Yan F, *Dye Pigment.*, 2010, **86(1)**, 93-96; DOI:10.1016/j.dyepig.2009.12.008
17. Suresh K B, Crooks P A and Rajitha B, *Adv Appl Sci Res.*, 2012, **3(1)**, 1-5.
18. Srinivas V and Rajeswar R V, *Synth Commun.*, **2012**, **42(3)**, 388-393; DOI:10.1080/00397911.2010.524961
19. Chao S, Lu G and Wu L, *Asian J Chem.*, 2011, **23(9)**, 3865-3869.