

A novel one pot synthesis of 14-aryl-14*H*-dibenzo[*a,j*]xanthenes catalyzed by SelectfluorTM under solvent free conditions

P. S. Kumar^a, B. Sunil Kumar^a, B. Rajitha^{a*}, P. Narsimha Reddy^a,
N. Sreenivasulu^a, and Y. Thirupathi Reddy^b

^a*Department of Chemistry, National Institute of Technology, Warangal, India*

^b*College of Pharmacy Kentucky University, Lexington, USA*

E-mail: rajitabhargavi@yahoo.com

Abstract

A novel procedure for the synthesis of aryl-14*H*-dibenzo[*a,j*]xanthenes through one-pot condensation of β -naphthol with aryl aldehydes in the presence of selectfluorTM [1-(chloromethyl)-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate)] as catalyst under solvent free conditions is described.

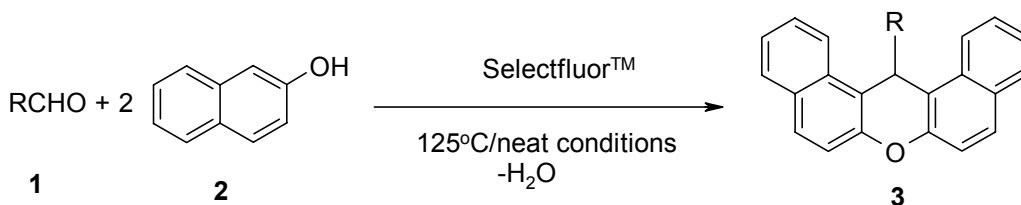
Keywords: Xanthene, one-pot reaction, condensation, aldehyde, β -naphthol, SelectfluorTM, solvent-free conditions

Introduction

Research on xanthenes, especially benzoxanthenes, has emerged in organic synthesis due to their wide range of biological and therapeutic properties like antiviral,¹ antibacterial², and antiinflammatory activities³, as well as in photodynamic therapy⁴ and as antagonists of the paralyzing action of zoxazolamine⁵. Xanthenes are also available from natural sources. Popularly known, Santalin pigments have been isolated from a number of plant species⁶. Furthermore, due to their useful spectroscopic properties they are used as dyes⁷, in laser technologies⁸, and in fluorescent materials for visualization of biomolecules⁹. Many procedures are disclosed to synthesize xanthenes and benzoxanthenes like cyclodehydrations¹⁰, trapping of benzyne by phenols¹¹, alkylations of hetero atoms¹², cyclocondensations between 2-hydroxy aromatic aldehydes and 2-tetralone¹³. Benzaldehydes and acetophenones bearing tethered carbonyl chains underwent the intramolecular phenyl-carbonyl coupling reactions in presence of samarium diiodide and hexamethylphosphoramide to afford xanthenes¹⁴. In addition, 14*H*-dibenzo[*a,j*]xanthenes and related products are prepared by reaction of β -naphthol with formamide¹⁵, 1-hydroxy methyl-naphthalen-2-ol¹⁶ and carbon monoxide¹⁷.

While many procedures have been reported, disadvantages like low yield, prolonged reaction time, use of excess of reagents/catalysts and use of toxic organic solvents prompted us

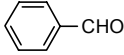
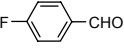
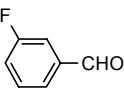
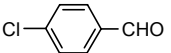
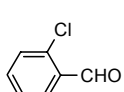
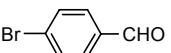
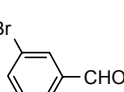
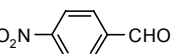
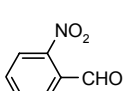
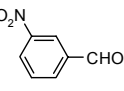
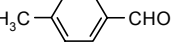
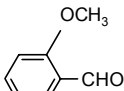
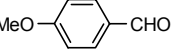
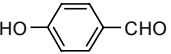
to develop an alternate route for the synthesis of xanthene derivatives in improved yield, short reaction time and safe reaction conditions using SelectfluorTM [1-(chloromethyl)-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetra fluoroborate)] as catalyst. Recently selectfluorTM has been introduced commercially as an electrophilic fluorinating agent. SelectfluorTM is a low-cost readily available acidic material and recently it has been employed as an efficient Lewis acid catalyst for the one-pot allylation of imines, hydrolysis of acetals and dithio acetals as well as tetrahydropyranyl ethers and for the synthesis of β -hydroxy thiocyanates.¹⁸ The traditional route is an efficient, convenient and novel method for condensation of aldehydes with β -naphthol in presence of SelectfluorTM as catalyst (Scheme 1).



Scheme 1

To obtain products **3**, β -naphthol (**2**) is heated with different aromatic aldehydes **1** at 125°C in presence of 10%mol selectfluorTM for an appropriate time (Table1). The Compounds are characterized by IR, ¹H NMR, ¹³C NMR and mass spectral data, the results are closely matching with reported spectral data. Aliphatic CH proton is obtained as singlet in all the compounds. The aliphatic CH proton of 14-(2-nitrophenyl)-14*H*-dibenzo[*a,j*]xanthene **9** is obtained as singlet at δ 7.52 and in ¹³C NMR CH carbon at δ 32.9 which is in closely agreement with the reported values of 14-(2-nitrophenyl)-14*H*-dibenzo[*a,j*]xanthene **10**. The CH proton of 14-(2-nitrophenyl)-14*H*-dibenzo[*a,j*]xanthene **10** is reported as singlet at δ 6.65 (200 MHz, CDCl₃) and ¹³C NMR (50 MHz, CDCl₃) CH carbon at δ 38.1.

Table 1. SelectfluorTM catalyzed efficient synthesis of aryl-14*H*-dibenzo[*a,j*]xanthenes

Entry	Aldehyde	Time (h)	Yield (%) ^a	Mp (°C)
1		8	93	183 ^{10b}
2		6	93	238 ^{10c}
3		7	93	259
4		7	95	287 ^{10c}
5		8	90	215 ^{10c}
6		10	95	296 ^{10b}
7		9	92	190 ^{10c}
8		11	94	312 ^{10b}
9		12	93	293
10		12	91	213 ^{10c}
11		11	92	228 ^{10b}
12		12	93	258 ^{10c}
13		10	92	205 ^{10c}
14		6	90	140

Experimental Section

General Procedure. A mixture of the aldehyde (1 m mol), β -naphthol (2 m mol) and selectfluorTM (0.1 m mol) was stirred at 125 °C for the appropriate time (Table 1). Completion of the reaction was monitored by TLC (thin layer chromatography). The material was cooled to 25 °C, and after addition of water the mixture was stirred for 5 min. The solid so obtained was filtered off and recrystallized from ethyl alcohol.

Selected characterization data

14-(3-Fluorophenyl)-14H-dibenzo[*a,j*]xanthene (Table 1, entry 3). Brown solid: mp. 259 °C. IR (KBr, cm^{-1}): 3154, 1594, 1403, 1240, 1207, 1069, 817, 747; ^1H NMR (300 MHz, CDCl_3): δ = 6.51 (s, 1H) 6.72-8.38(m, 16H). ^{13}C NMR (75 MHz, CDCl_3): δ = 38.1, 113.8 and 90, 114.0 (JC-F 21.5 Hz), 115.6 and 115.9 (JC-F 21.5 Hz), 117.1, 118.2, 122.9, 124.31 and 124.34 (JC-F 2.8 Hz), 124.8, 127.4, 129.3, 129.5, 130.1 and 130.2 (JC-F 8.3 Hz), 131.5, 131.7 (JC-F 19.4 Hz), 147.8, 147.9 (JC-F 6.2 Hz), 149.2, 161.7, 165.0; EIMS, 70 eV, m/z : 376 (M^+), 281, 268; Anal. Calcd for $\text{C}_{27}\text{H}_{17}\text{FO}$: C, 86.15; H, 4.55; F, 5.05. Found: C, 86.11; H, 4.54, F, 5.07.

14-(2-Nitrophenyl)-14H-dibenzo[*a,j*]xanthene (Table 1, entry 9). Yellow solid: mp 293 °C. IR (KBr, cm^{-1}): 3400, 3058, 1593, 1523, 1350, 1240, 1142, 810, 748; ^1H NMR (300 MHz, CDCl_3): δ = 7.52 (s, 1H) 7.10-8.56 (m, 16H). ^{13}C NMR (75 MHz, CDCl_3): δ = 32.9, 118.0, 118.4, 123.0, 124.6, 125.0, 125.3, 127.8, 128.0, 129.4, 129.5, 129.9, 130.8, 132.1, 132.6, 134.5, 141.3, 147.5, 149.8; EIMS, 70eV, m/z : 403 (M^+), 281, 268; Anal. Calcd for $\text{C}_{27}\text{H}_{17}\text{NO}_3$: C, 80.38; H, 4.25; N, 3.47, Found: C, 80.25; H, 4.24, N, 3.57.

14-(4-Hydroxyphenyl)-14H-dibenzo[*a,j*]xanthene (Table 1, entry 14). Pink solid: mp.140 °C IR (KBr, cm^{-1}): 3404,1592, 1511, 1401, 1250, 1242, 816; ^1H NMR (300 MHz, CDCl_3): δ = 4.97 (br s, 1H, OH), 6.42(s, 1H, CH), 6.56-8.36 (m, 16H, Ar-H). ^{13}C NMR (75 MHz, CDCl_3): δ = 37.5, 115.7, 117.9, 118.4, 123.1, 124.6, 127.2, 129.1, 129.2, 129.8, 131.5, 131.8, 137.9, 149.1, 154.2, EIMS, 70 eV, m/z : 374 (M^+), 281, 268; Anal. Calcd for $\text{C}_{27}\text{H}_{18}\text{O}_2$: C, 86.61; H, 4.85; Found: C, 86.63; H, 4.80.

References

1. Lambert, R. W.; Martin, J. A.; Merrett, J. H.; Parkes, K. E. B.; Thomas, G. J. *Chem. Abstr.* **1997**, *126*, 212377y, PCT Int. Appl. WO 9706178. 1997.
2. Hideo, T. Jpn. Tokkyo Koho, *Chem. Abstr.* **1981**, *95*, 80922b, JP 56005480, 1981.
3. Poupelin, J. P.; Saint- Rut, G.; Foussard-Blanpin. O.; Narcisse, G.; Uchida-Ernouf, G.; Lacroix, R. *Eur. J. Med. Chem.* **1978**, *13*, 67.
4. (a) Ion, R. M. *Progr. Catal.* **1997**, *2*, 55. (b) Ion, R. M.; Frackowiak, D.; Planner, A.; Wiktorowicz, K. *Acta Biochim. Pol.* **1998**, *45*, 833.
5. (a) Saint-Ruf, G.; De, A.; Hieu, H. T. *Bull. Chim. Ther.* **1972**, *7*, 83. (b) Saint-Ruf, G.; Hieu, H. T.; Poupelin. J. P. *Naturwissenschaften* **1975**, *62*, 584.

6. (a) Arnone, A.; Merlini, L.; Nasini, G. *Tetrahedron Lett.* **1972**, 3503. (b) Ravindranath, B. ; Sheshadri, T. R. *Phytochemistry* **1973**, *12*, 2781. (c) Kinjo, J.; Uemura, H.; Nohara, T.; Yamashita, M.; Marubayashi, N.; Yoshihira, K. *Tetrahedron Lett.*, **1995**, *36*, 5599.
7. (a) Menchen, S. M.; Benson, S. C.; Lam, J. Y. L.; Zhen, W.; Sun, D.; Rosenblum, B. B.; Khan, S. H.; Taing, M. *Chem. Abstr.* **2003**, *139*, p54287f, U. S. Patent, US6583168, 2003. (b) Banerjee, A.; Mukherjee, A. K. *Stain Technol.* **1981**, *56*, 83. (c) Reynolds, G. A.; Tuccio, S. A.; Peterson, O. G.; Specht, D. P. *Chem. Abstr.* **1971**, *71*, p81334c, Ger. Offen. DE2109040, 1971.
8. (a) Sirkecioglu, O.; Talinli, N.; Akar, A. *J. Chem. Res. Synop.* **1995**, 502. (b) Ahmad, M.; King, T. A.; Ko. Do.-K.; Cha. B. H.; Lee, J.; *J. Phys. D: Appl. Phys.* **2002**, *35*, 1473.
9. Knight, C. G.; Stephens, T. *Biochem. J.* **1989**, *258*, 683.
10. (a) Bekaert, A.; Andrieux, J.; Plat, M.; *Tetrahedron Lett.* **1992**, *33*, 2805. (b) Sarma, R. J.; Baruah, J. B.; *Dyes Pigm.* **2005**, *64*, 91. (c) Khosropour, A. R.; Khodaei, M. M.; Moghannian, H. *Synlett* **2005**, (6) 955. (d) Buehler, C. A.; Cooper, D. E.; Scrudder, E. O. *J. Org. Chem.* **1943**, *8*, 316.
11. (a) Knight, D. W.; Little, P. B. *Synlett* **1998**, 1141. (b) Knight, D. W.; Little, P. B. *J. Chem. Soc., Perkin Trans. I* **2001**, *14*, 1771.
12. (a) Vazquez, R.; de la Fuente, M. C.; Castedo, L.; Domínguez, D. *Synlett* **1994**, 433. (b) Ishibashi, H.; Takagaki, K.; Imada, N.; Ikeda, M. *Synlett* **1994**, 49.
13. Jha, A.; Beal, J.; *Tetrahedron Lett.* **2004**, *45*, 8999.
14. Kuo, C.-W.; Fang, J.-M. *Synth. Commun.* **2001**, *31*, 877.
15. Papini, P.; Cimmarusti, R. *Gazz. Chim. Ital.* **1947**, *77*, 142.
16. Sen, R. N.; Sarkar, N. N.; *J. Am. Chem. Soc.* **1925**, *47*, 1079.
17. Ota, K.; Kito, T.; *Bull. Chem. Soc. Jpn.* **1976**, *49*, 1167.
18. (a) Liu, J.; Wong, C. H.; *Tetrahedron Lett.* **2002**, *43*, 3915. (b) Liu, J.; Wong, C. H.; *Tetrahedron Lett.* **2002**, *43*, 4037. (c) Yadav, J. S.; Reddy, B. V. S.; Srinivas Reddy, C. H. *Tetrahedron Lett.* **2004**, *45*, 1291.