One-Pot Synthesis of Benzoxanthenes in Solvent Free Condition using Chloroaluminate Ionic Liquids as Catalyst

Sugat kirti,\textsuperscript{a} Dhanraj T. Masram,\textsuperscript{a}*

\textsuperscript{a}Department of Chemistry, University of Delhi, Delhi-110007, India.
skirtidu08@gmail.com
\textsuperscript{a}Department of Chemistry, University of Delhi, Delhi-110007, India.
dhanraj_masram27@rediffmail.com

ABSTRACT

A mild and efficient method has been developed for the preparation of 14-aryl-14H dibenzo[a,j]xanthenes from one-pot condensation of aldehydes with \( \beta \)-naphthol using catalytic amount of Chloroaluminate ionic liquid (imidazolium chloride-3AlCl\(_3\) or pyridinium chloride-3AlCl\(_3\)) under thermal solvent-free conditions. Excellent yields, short reaction times, easy workup and reusability of the catalyst as well as solvent free conditions are advantages of this procedure.

Keywords

Ionic Liquids; Xanthenes; Aldehydes; Naphthol; Solvent free.
INTRODUCTION
Xanthenes related to specific class of oxygen heterocyclic compounds which possess various biological and pharmacological activities such as antibacterial [1-2], anti-proliferative [3], anti-inflammatory [4], and antiviral activities [5]. Xanthenes especially benzoxanthenes are of interest as functional materials in many disciplines due to their useful spectroscopic properties. They are used as dyes [6-7], in laser technologies [8], as pH-sensitive fluorescent materials for visualization of biomolecules [9], as photoactive dyes, polymerizable light emitting dyes [10-11], and white organic light emitting dyes [12]. Natural xanthenes dyes may also be extracted from soil and plants such as Indigo feralongeracemosa [13]. Recently different methods have been reported for the synthesis of benzoxanthenes, including the reaction of β-naphthol with aldehydes in the presence of a catalyst, such as amberlyst-15 [14], sulfamic acid [15], molecular iodine [16], AcOH-H2SO4 in acidic medium [17], heteropoly acids (HPAs) [18], and HClO4-SiO2 [19]. However, some of these methods suffer from one or more disadvantages such as low yields, long reaction times, special apparatus, excess reagents, and the use of toxic catalyst and solvents. Thus, the development of an improved procedure for the synthesis of benzoxanthen derivatives would be highly desirable. In recent years, ionic liquids have attracted extensive interest as benign reaction media in organic synthesis because of their unique properties of non-volatility, non-flammability, recyclability, and ability to dissolve a wide range of materials [20]. As a result of their green credentials and potential to enhance reaction rates and selectivity, ionic liquids have been found increasing applications to organic synthesis. Previously reactions of xanthenes synthesis have been reported in ionic liquid in presence of catalyst, Bronsted acid, and metal salts. Herein, we report one-pot synthesis of 14-aryl-14H-dibenzo[a,j]xanthenes in Lewis acidic ionic liquids such as 1-butylpyridinium chloride and imidazolium chloride · 3AlCl3.

EXPERIMENTAL

Instrumentation:
The 13C NMR and 1H NMR spectrum were recorded on JEOL using TMS as internal standard. FT-IR of all synthesized xanthenes was recorded on a spectrometer Perkin Elmer Spectrum BX II from range 4000-400 cm⁻¹ by making sample pallets with KBr. The melting points of synthesized compounds were determined on a Thomas Hoover Unimelt capillary melting point apparatus.

Reagent and Solutions:
All the Aldehydes used were purchased from Merck and β-naphthol from Fisher Scientific Chemicals. All ionic liquids synthesized in lab according to modified procedure.

RESULTS AND DISCUSSION
The 14-aryl-14H-dibenzo[a,j]xanthenes (3) have been prepared in good to high yields by condensing β-naphthol (2) with aromatic aldehydes (1) in Lewis acid ILs imidazolium (4a and 4b) and pyridinium (4c and 4d) at 100 °C (scheme 1).

![Scheme 1](image-url)
The reaction mixture of β-naphthol (2) and 4-methyl benzaldehyde (1a) in 4a IL was heated at 100 °C for 15 minutes to give 14-(4-methylphenyl)-14-H-dibenzo[a,j]xanthene (3a) in 92% yield (table 2). The structure of 3a was characterized by different spectroscopic techniques. The melting point of 3a (230°C) closely corresponded to the literature value (table 2). The condensation reaction of β-naphthol with 4-methylbenzaldehyde (1a) was compared in 4a, 4b, 4c and 4d Lewis acid ILs at 100 °C, and the best yield of 14-(4-methylphenyl)-14-H-dibenzo[a,j]xanthene (3a) was obtained in 4a IL (table 1).

The poor yield of 3a in 4b and 4d as compared to 4a IL could be attributed to the lower Lewis acidic nature of ZnCl₂, which leads to lower yield of corresponding product. Further, the condensation reaction of (1a) in pyridinium ionic liquid 4c with same counter anion(AlCl₄⁻) found to be less efficient in comparison to imidazolium ionic liquid.

Table 1: Synthesis of 14-(4-methylphenyl)-14-H-dibenzo[a,j]xanthenes (3a) by condensation of β-naphthol with 4-methylbenzaldehyde (1a) in the presence of different ionic liquid (4a-4d) at 100 °C

| Entry | Ionic liquids | Time (min) | Yield (%)<sup>b</sup> |
|-------|---------------|------------|-----------------------|
| 4a    |               | 15         | 92                    |
| 4b    |               | 15         | 2                     |
| 4c    |               | 15         | 83                    |
| 4d    |               | 15         | 41                    |
|       |               | 60         | 53                    |

<sup>a</sup>2-Naphthol 2 mmol; aldehyde 1 mmol, ionic liquid 0.2 equivalent.  
<sup>b</sup>Isolated yields.

The UV-visible spectrum of 3a showed an intense absorption band at 320 nm and 334 nm, inferring extended conjugation in 3a heterocycle (figure 2). The appearance of a strong band at 1248 cm⁻¹ in the IR spectrum of 3a was assigned to C-O stretching. In the ¹H NMR spectrum of 3a, aliphatic CH proton of 3a appeared as a singlet at 6.43 ppm and aromatic protons resonances were observed in 6.93–8.37 ppm region. The appearance of a peak at m/z 372 corresponding to [M]⁺ in the electron impact-mass spectroscopy (EI-MS) spectrum further confirmed the formation of 3a in the reaction.
To check the feasibility of the optimized reaction condition, we carried out this reaction using different aromatic aldehydes (table 2). It has been found that the nature of the functional group on the aromatic ring of the aldehyde affects the reaction time and yield. The presence of electron withdrawing group at para position in comparison to the unsubstituted aromatic aldehyde shows increase of the yield while the presence of an electron donating group decreases the yield. Though meta and para-substituted aromatic aldehydes gave good results, ortho-substituted aromatic aldehydes (such as 2-nitro benzaldehyde) gave lower yields because of the steric effects [21]. Based on the results, a possible explanation for the reaction can be proposed.

The IL 4a was recovered from the reaction mixture by extracting the crude product with dichloromethane and reused for the synthesis of 3a. In the second run, 3a was obtained in 81% yield by condensation of β-naphthol with 1a in the presence of recovered 4a IL. Slight decrease in the yield of 3a was observed in third run, as 3a was isolated in 79% yield.

Table 2: Synthesis of 14-alkyl- or aryl-14-H-dibenzo[a,j]xanthenes by condensation of β-naphthol with aldehydes in the presence of ionic liquid (4a) at 100 °C

| Aromatic Aldehydes | Time (min) | Yield (%) of 3b | M.P. (°C) | Lit. M.P. (°C) |
|--------------------|------------|-----------------|-----------|---------------|
| 1a                 | 15         | 92              | 230       | 22922         |
| 1b                 | 15         | 85              | 150       | 15216         |
| 1c                 | 10         | 94              | 298       | 29722         |
| 1d                 | 10         | 92              | 188       | 19022         |
| 1e                 | 10         | 93              | 261       | 25922         |
| 1f                 | 10         | 95              | 238       | 23922         |
| 1g                 | 10         | 93              | 290       | 28922         |
| 1h                 | 10         | 89              | 213       | 21522         |
| 1i                 | 10         | 93              | 312       | 31022         |
| 1j                 | 10         | 87              | 292       | 29323         |
| 1k                 | 10         | 90              | 210       | 21122         |
| 1l                 | 15         | 89              | 186       | 18522         |

β-Naphthol 2 mmol; aldehyde 1 mmol, ionic liquid 0.2 equivalent.

Isolated yields
REFERENCES

[1] Wang, H.; Lu, L.; Zhu, S.; Li, Y.; Cai, W. The phototoxicity of xanthene derivatives against Escherichia coli, Staphylococcus aureus, and Saccharomyces cerevisiae. Curr. Microbiol. 2006, 52, 1.

[2] Limsuwan, S.; Trip, E. N.; Kouwen, T. R. H. M.; Piersma, S.; Hiranrat, A.; Mahabusaram, W.; Voravuthikunchai, S. P.; Kayser, J. M. V. D. O. Rhodomyrtone: A new candidate as natural antibacterial drug from Rhodomyrtus tomentosa Phytotherapy 2009, 16, 645.

[3] Kumar, A.; Sharma, S.; Maurya, R. A.; Sarkar, J. Diversity Oriented Synthesis of Benzoxanthene and Benzochromene Libraries via One-Pot, Three-Component Reactions and Their Anti-proliferative Activity J. Comb. Chem. 2010, 12, 20.

[4] Hafez, H. N.; Hegab, M. I.; Ahmed-Farag, I. S.; El-Gazzar, A. B. A. A facile regioselective synthesis of novel spiro-thioxanthene and spiro-xanthene-90,2-[1,3,4] thiadiazole derivatives as potential analgesic and anti-inflammatory agents Bioorg. Med. Chem. Lett. 2008, 18, 4538.

[5] Jamison, J. M.; Krabill, K.; Hatwalker, A.; Jamison, E.; Tsai, C. Potentiation of the antiviral activity of poly r(a-u) by xanthene dyes Cell Biol. Int. Rep. 1990, 14, 1075.

[6] Poupelin, J. P.; Saint-Ruf, G.; Foussard-Blanpin, O.; Narisse, G.; Uchida-Ernouf, G.; Lacroix, R. Eur. J. Med. Chem. 1978, 13, 67.

[7] Ion, R. M.; Frackowiak, D.; Planner, A.; Wiktorowicz, K. The Incorporation of various Porphyrians into blood cells measured via flow cytometry, absorption, and emission spectroscopy. Acta Biochim. Pol. 1998, 45, 833.

[8] Kumar, R.; Nandi, G. C.; Verma, R. K.; Singh, M. S. A facile approach for the synthesis of 14-aryl- or alkyl-14H-dibenzo[a,j]xanthenes under solvent-free condition Tetrahedron Lett. 2010, 51, 442.

[9] Prasad, D.; Preetam, A.; Nath, M. C.; Microwave-assisted green synthesis of dibenzo[a,j]xanthenes using p-dodecylbenzenesulfonic acid as an efficient Bronsted acid catalyst under solvent-free conditions. R. Chimie 2012, 15, 675.

[10] Bojinov, V. B.; Panova, I. P.; Simeonov, D. B. The synthesis of novel photostable fluorescein-based dyes containing an s-triazine UV absorber and a HALS unit and their acrylonitrile copolymers Dyes Pigm. 2009, 83, 135.

[11] Bojinov, V. B.; Panova, I. P.; Grabchev, I. K. Novel polymerizable light emitting dyes e combination of a hindered amine with a 9-phenylxanthene fluorophore. Synthesis and photophysical investigations Dyes Pigm. 2007, 74, 187.

[12] Sibrian-Vazquez, M.; Strongin, R. Optimising the synthesis and red–green–blue emission of a simple organic dye Supramol. Chem. 2009, 21, 107.

[13] Alcantara-Licudine, P. J.; Kawate, M. K.; Li, O. X. Method for the Analysis of Phloxine B, Uranine, and Related Xanthen Dyes in Soil Using Supercritical Fluid Extraction and High-Performance Liquid Chromatography J. Agric. Food Chem. 1997, 45, 766.

[14] Shaterian, H. R.; Ghashang, M.; Hassankhani, A. One-pot synthesis of aryl 14H-dibenzo[a,j]xanthenes leuco-dye derivatives Dyes and Pigments 2008, 76, 564.

[15] Rajitha, B.; Kumar, B. S.; Reddy, Y. T.; Reddy, P. N.; Sreenivasulu, N. Sulfamic acid: a novel and efficient catalyst for the synthesis of aryl-14H-dibenzo[a,j]xanthenes under conventional heating and microwave irradiation Tetrahedron Lett. 2005, 46, 8691.

[16] Heravi, M. M.; Bahktiari, K.; Daroochega, Z.; Bamoharram, F. F. Facile heteropolyacid-promoted synthesis of 14-substituted-14H-dibenzo[a,j] xanthenes derivatives under solvent-free conditions J. Mol. Catalysis A: Chemical 2007, 273, 99-101.

[17] Luo, G.; Liu, D.; Liu, C. An Efficient Solvent-FreeSynthesis of Benzoxanthenes Catalyzed by BSA or O-TSA. Biochim. Biophys. Biotechnol. 2008, 38, 265.

[18] Ziarani, G. M.; Badiel, A. R.; Azizi, M. The one-pot synthesis of 14-aryl-14H-dibenzo[a,j]xanthenes derivatives using sulfonic acid functionalized silica (SiO₂-Pr-SO₂H) under solvent free conditions Sciencia Iranica C 2011, 18 (3), 453.

[19] Bigdeli, M. A.; Heravi, M. M.; Mahdavnia, G. H. Silica supported perchloric acid (HClO₄-SiO₂): A mild, reusable and highly efficient heterogeneous catalyst for the synthesis of 14-aryl or alkyl-14H-dibenzo[a,j]xanthenes J. Mol. Catal. A: Chem. 2007, 275, 25.
[20] Ahmad, S.; Yadav, K. K.; Chauhan, S. M. S. Role of Hydroxyl Functionalized Ionic Liquids in Oxygenation and Oxidation of Phenols with H₂O₂ Catalysed by Iron(III) Porphyrins Curr. Org. Chem. 2012, 16, 2989.

[21] Gong, K.; Fang, D.; Wang, H. L.; Zhou, X. L.; Liu, Z. L. The one-pot synthesis of 14-alkyl- or aryl-14H-dibenzo[a,j]xanthenes catalyzed by task-specific ionic liquid Dyes and Pigm. 2009, 80, 30.

[22] Saint Ruf, G.; Hieu, H. T.; Poupelin, P.; The Effect of Dibenzoanthenes on the Paralyzing Action of Zoxazolamine Naturwissenschaften, 1975, 62, 584.

[23] Banerjee, A.; Mukherjee, A. K. Chemical aspects of as a histological satain Stain Technol. 1981, 56, 83.

[24] Kirti, S.; Singh, R.; Masram, D. T.; One pot synthesis of Benzoxanthene in solvent free condition using SbCl₃ as Catalyst. Organic Chemistry An Indian Journal (In Press).