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L-Pyrrolidine-2-Carboxylic Acid Sulfate (LPCAS): A New Ionic Liquid for the Synthesis of 14-Aryl-14H-Dibenzo[a,j] Xanthenes under Solvent Free Condition

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Abstract

A new Bronsted acidic ionic liquid, L-Pyrrolidine-2-carboxylic acid sulfate (LPCAS) was employed to promote one-pot synthesis of 14-aryl-14H-dibenzo [a,j] xanthenes via condensation reaction of aldehydes and 2-naphthol under solvent free condition. Distinguishing features of the methodology are excellent yield of products in shorter reaction time, cleaner reaction profile, eco-friendly nature and the use of inexpensive catalyst.

Keywords

Ionic Liquid, 14-Aryl-14H-Dibenzo[a,j] Xanthenes, Solvent-Free

1. Introduction

Organic synthesis commonly includes the use of variety of solvents, which may be lethal, dangerous, corrosive and inflammable. These solvents are mostly hazardous to the environment and human being. Furthermore, multistep reactions for the synthesis of various organic compounds also consumed different solvents and reagents. Hence, there is always a need to search, design and develop environmentally benign multi-component and solvent-free green organic transformations for the synthesis of bioactive heterocyclic compounds. Multicomponent reactions (MCRs) are the process in which number of reactants is combined in one pot to produce the products. The synthesis of organic compounds using a greener process under solvent free conditions has been explored worldwide due to harsh environmental and economic regulations [1].

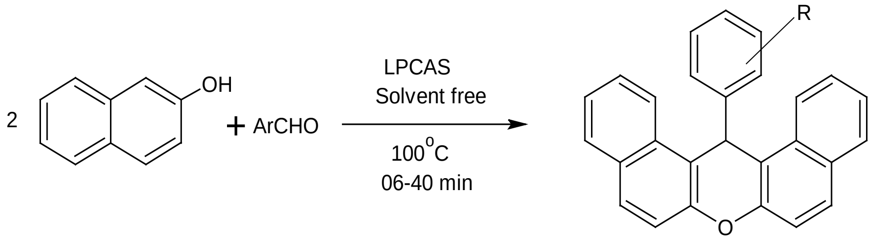
These days, significant attempts from both academic and industrial researchers have been made particularly on designing and developing of multi-component reactions (MCRs), for biologically and pharmaceutically active compounds.

Xanthene derivatives have been attracted to researchers due to their significant value in pharmaceutical aspect. 14-aryl-14H-dibenzo[a, j] xanthene derivatives possesses biological potential such antibacterial [2], antiviral [3] and anti-inflammatory [4] etc. These compounds are also used as precursors in the synthesis of various organic compounds and dyes [5]. 14-aryl-14H-dibenzo[a,j] xanthenes derivatives have medicinal significance. Basic scaffolds of these heterocycles are used as new and potential anticancer agents [6]. Literature survey also shows that such derivatives have activities concern with antimalarial [7], pH-sensitive fluorescent materials [8], laser technologies [9] etc.

Numerous methods have been reported for efficient and facile synthesis of 14-aryl-14H-dibenzo[a, j] xanthenes scaffolds using different catalyst, including Dowex-50 W [10], Molecular iodine [11], Heteropolyacid [12], Fe_3O_4@SiO_2-Imid-PMA^n [13], Montmorillonite K-10 [14], $Et_3N–SO_3H]Cl$ [15], [H-NMP] [HSO_4] [16], SiO_2–Pr–SO_3H [17], HBF_4-SiO_2 [18], NSPV PHS [19], [BMIm] [BF_4] [20] etc.

An ionic liquid (ILs) acts as environmental friendly reaction media or catalysts and attracted the attention of scientists. ILs has many excellent advantages such as negligible volatility, super thermal stability, prominent solubility and variety of available structures. Among the abundant ILs developed, unfortunately most of the ILs showed a degree of solubility in commonly used organic solvents and causes many difficulties in product separation.

In continuation of work in ionic liquid [21] [22], in present work, new bronsted acidic ionic liquid, L-Pyrrolidine-2-carboxylic acid sulfate (LPCAS) [23] catalyst has been used for the first time in the synthesis of bioactive 14-aryl-14Hdiben- zo[a,j]xanthene derivatives. We have developed a mild, efficient and environmentally benign method for the synthesis of bioactive 14-aryl-14H-dibenzo[a,j] xanthene derivatives via multi component reaction of aldehydes and 2-naphthol under solvent free conditions using novel acidic ionic liquid, L-Pyrrolidine-2-carboxylic acid sulfate (LPCAS) as a catalyst. (Scheme 1). The distinguishing features of this method are excellent yield of products in shorter reaction time, cleaner reaction profile, environmental friendly nature, easy separation of inexpensive catalyst.



Scheme 1. Synthesis of 14-aryl-14H-dibenzo[a, j]xanthene derivatives.

2. Result and Discussions

In a model reaction, a mixture of benzaldehyde (1 mmol) and 2-naphthol (2 mmol) and LPCAS (1 mmol) was added to 25 ml round bottom flask. The mixture was refluxed at 100˚C under solvent free conditions. The progress of reaction was monitored by TLC. After completion of reaction the reaction mixture was cooled to room temperature and 10 ml water was added. The separated solid was filtered off. The crude was washed with water twicely, dried and recrystallized in ethanol.

The efficiency of IL catalyst has been determined and compared with those of reported acid catalysts in the synthesis of 14-phenyl-14H-dibenzo[a,j]xanthenes (3a).

In presence of molecular iodine, the reaction proceeds at 90˚C within 20 minutes offering 90% yield of the product under solvent free condition (entry 2, Table 1). In presence of [H-NMP][HSO_4], under solvent free condition the reaction mixture on heating for 12 minutes afforded 94% of product (entry 7, Table 1). Also by using sonication method in presence of catalyst NSPV PHS, reaction completes within 05 minutes offering 95% yield of the product under solvent free condition (entry 10, Table 1).

But surprisingly when the reaction is carried out using ionic liquid L-pyrollidine-2-carboxylic acid sulfate at 100˚C under solvent free condition, it proceeds within 06 minutes and offering the product in 95% (entry 12, Table 1).

All the results have showed that, the catalyst proved its efficiency in terms of yield and reaction times. All the known synthesized compounds were confirmed by comparing their melting points with standards and novel compounds were

Table 1. Comparison of the present catalytic system with some reported protocols in the model reaction.

Entry	Catalyst	Conditions	Time (mins)	Yield (%)	Ref.
1	Dowex-50 W	Solvent free/100˚C	90	78	[10]
2	Molecular iodine	Solvent free/90˚C	20	90	[11]
3	Heteropolyacid	Solvent free/100˚C	30	89	[12]
4	Fe_3O_4@SiO_2-Imid-PMA^n	Solvent free/110˚C	90	95	[13]
5	Montmorillonite K-10	Solvent free/MW	04	92	[14]
6	[Et_3N–SO_3H]Cl	Solvent free/120˚C	30	96	[15]
7	[H-NMP][HSO_4]	Solvent free/110˚C	12	94	[16]
8	SiO_2–Pr–SO_3H	Solvent free/125˚C	20	98	[17]
9	HBF_4-SiO_2	Solvent free/120˚C	90	92	[18]
10	NSPV PHS	Ultrasound irradiation	05	95	[19]
11	[BMIm][BF_4]	Solvent free/80˚C	300	98	[20]
12	**L-Pyrrolidine-2-carboxylic acid sulfate(LPCAS)**	**Solvent free/100˚C**	**06**	95	**This work**

confirmed by spectroscopic data (IR, ^{1}H NMR).

An advantage of the novel ionic liquid catalyst (L-Pyrrolidine-2-carboxylic acid sulfate) is; it is cost effective and more efficient as compare to other reported ionic liquids.

3. Experimental Procedure

All the reagents were purchased from Aldrich/Merck and used without further purification. Melting points were taken using digital melting point apparatus EQ730 (Equiptronics) and uncorrected. Progress of reactions were monitored on thin layer chromatography using silica gel as a stationary phase and hexane:ethyl acetate (8:2) as eluent. The products were characterized by comparing melting points and spectral data with authentic samples melting point and spectroscopic data (IR, ^{1}H NMR). IR spectra were recorded on Schimadzu IR Solution 150SUI spectrophotometer using KBr pellet. NMR spectra were recorded on Bruker 400 MHz spectrometer using appropriate solvent and TMS as an internal standard. Mass spectra were scanned on a Jeol JMSD-300 spectrometer.

General Procedure for Synthesis of 14-Aryl-14H-Dibenzo [a, j]xanthenes Derivatives

To a mixture of benzaldehyde (0.106 Gram) and 2-naphthol (0.144 Gram) L-Pyrrolidine-2-carboxylic acid sulfate (LPCAS) (0.213 Gram) was added and the mixture was refluxed at 100˚C for appropriate time (**Scheme 1**). The progress of reaction was monitored on TLC. After completion of reaction, the reaction mixture was cooled to room temperature and 10 ml water was added. Separated solid was filtered and recrystallized from ethanol to offer the pure product. Similarly the other derivatives were prepared using same procedure as reported in (**Table 2**).

Table 2. Synthesis of 14-aryl-14H-dibenzo[a,j]xanthene derivatives (3a-j).

Sr. No.	Aldehyde	Time (min)	Yield (%)	Melting Point (˚C)		References
				Observed	Reported	
3a	Benzaldehyde	06	95	180 - 182	184 - 185	[15]
3b	2-hydroxy benzaldehyde	20	93	124 - 126	127 - 128	[1]
3c	4-hydroxy benzaldehyde	15	90	134 - 136	135 - 136	[13]
3d	4-nitro benzaldehyde	31	85	310 - 314	311 - 312	[15]
3e	4-chloro benzaldehyde	15	95	288 - 290	289 - 290	[15]
3f	4-methoxy benzaldhyde	06	88	200 - 202	203 - 205	[15]
3g	1-naphthaldehyde	30	86	240 - 242	238 - 240	[25]
3h	3-hydroxy benzaldehyde	40	90	238 - 240	242 - 243	[1]
3i	2-chloro benzaldehyde	20	85	210 - 212	214 - 216	[15]
3j	4-hydroxy-3-methoxy benzaldehyde	10	90	204 - 206	208 - 210	[24]

4. Spectral Data of Selected Compound

Compound 3e: $C_{27}H_{17}ClO$

FTIR (KBr) (cm ^{1}):3068, 3041, 2914, 2312, 1892, 1691, 1593, 1485, 1240, 1063, 960, 833, 711.

^{1}H NMR (400 MHz, DMSO): δ ppm 6.74 (s 1H), 7.21 (m 2H, due to ortho and meta coupling), 7.46 (d 2H, due to ortho coupling), 7.56 (m 2H, due to ortho and meta coupling), 7.65 (d 2H, due to ortho coupling), 7.75 (d 2H, due to ortho coupling), 7.94 (d 2H), 2.51-2.63 (d 2H), 8.67 (d 2H, due to ortho coupling), 9.66 (t 2H, due to ortho and meta coupling). ^{13}C NMR (400 MHz, DMSO): 147.91, 144.40, 130.89, 130.75, 130.60, 129.16, 128.60, 128.31, 126.78, 124.56, 123.25, 117.64, 116.89, 36.08. *m/z*: 392.09.

5. Conclusion

In summary, we have developed a new eco-friendly procedure for the synthesis of 14-aryl-14H-dibenzo[a,j]xanthene via one pot condensation of aromatic aldehydes and 2-naphthol using LPCAS as a ionic liquid catalyst under solvent free conditions. The presented methodology includes an advantage such as simple procedure, short reaction time, excellent yields and easy separation of catalyst and its reusable behavior. This approach therefore represents a precious addition to the existing processes for the synthesis of 14-aryl-14H-dibenzo[a,j] xanthenes.

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