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Calcium Chloride/HCl An Efficient Co-catalytic System For Synthesis Xanthene Under Microwave Condition

By

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Content

Introduction

- Multicomponent reactions are process in which three or more reactants are united in a one-pot to construct products that include substantial portions of all the reactants.
- Multicomponent reactions are effective in construction of highly functionalized small organic molecules from readily available starting materials in a one-pot with inherent flexibility for creating molecular complexity and diversity coupled with minimization of time, labour, cost and waste product

Applications of Xanthene

- Xanthene and its derivatives are an important class of oxygen-containing heterocyclic compounds present in natural product with biological activity.
- The important biological and pharmacological activities of xanthenes are antiviral, anti-inflammatory, anti-bacterials , antimalarial agent, antitumor activity, anti-plasmodial as well as in photodynamic therapy and as antagonists of the paralyzing action of zoxazolamine.

- Furthermore due to their useful spectroscopic properties, they are used as dye, pH sensitive fluorescent materials for the visualization of biomolecular assemblies and in laser technologies.

Reported Methods for Synthesis of Xanthene

- Reaction of cyclodehydration
- Cyclocondensation of 2-tetralone with 2-hydroxyaromaticaldehyde
- Reaction of aryloxymagnesium halides with triethylorthoformate
- Phenyl carbonyl coupling reaction of benzaldehyde and acetophenone
- Trapping of benzynes by phenol

- Carbon monoxide , aldehyde acetal ,
- Formamide
- 2-naphthol-1-methanol
- Cycloacylation of carbamates
- Palladium catalysed cyclization of polycyclic aryltriflate esters
- However, many of these methods suffer from shortcoming such as use of expensive reagents, low yields or mixture of products, long reaction time, strongly acidic condition, the use of an excess of regents and catalysts and use of toxic organic solvent, drastic reaction condition.

- An improvement in reaction procedure is made by reacting 2-naphthol with alkyl/aryl aldehydes employing various catalysts such as
- Bronsted acids
- solid supported reagent
- Metal salt,
- Metal triflate,
- I_2 ,
- Phosphosulfonic acid
- 1, 3, 5 Trichloro-2,4,6-triazinetrion (TCCA) ,
- Vanadatesulfuric acid
- HBF_4-SiO_2

- However, some these methods are suffer from one or more shortcomings like expensive and toxic catalyst, acidic condition, long reaction time, low yield, preparation of catalyst require in some cases, use of heavy and toxic metal.
- Hence, to avoid these shortcomings, the innovation of a new and efficient catalyst with high catalytic activity, short reaction time, inexpensive and easily available, simple work-up procedure for the preparation of xanthenes under neutral, mild and practical conditions is of key interest.

Present Work

- In recent years, there has been considerable interest in developing more economical and environmental – friendly conversion processes. $CaCl_2$ is an inexpensive and commercially available reagent and as it has been shown recently to be a very good catalyst in organic reactions [38-41]. We herein report an efficient, practical environmentally benign and high yielding method for the synthesis of Xanthene using $CaCl_2$ as catalyst.

- The advancement of microwave assisted reaction in organic synthesis has improved the speed, reduced cost, reduced energy used up producing it a sustainable process and is often pictured as “green chemistry” process whose applications are encouraged to minimize the use of non renewable resources as well as polluting solvent, to reduce generation of inferior products which are frequently toxic and to burn down the emission of harmful gases.
- During the last 25 years a noteworthy number of ~ 5000 publications using microwave-assisted organic transformations are published.

Results and Discussions

- Calcium chloride is polar covalent molecules due to high electronegative difference between calcium and chlorine. The binding electron pair in calcium and chlorine is pulled towards chlorine atom, forming a dipole within the molecule. Due to this dipole calcium chloride absorbs microwave energy and converts into heat. This generated heat used to bring reaction between benzaldehyde and β-naphthol .

- In a preliminary study, β-naphthol(2mmol) (1a) and benzaldehyde (1mmol) (2a) in the 2:1 mole ratio was irradiated in presence of calcium chloride (0.1mmole)/one drop of Conc. HCl under microwave condition.
- The function of conc.HCl in this reaction is it increase the acidic character of calcium chloride as well as rate of the reaction. The progress of the reaction was monitored by TLC.
- As the time moves reaction proceed in forward direction and the reaction was found to be complete within 10 minutes affording 14-(2-phenyl)-14H-dibenzo[a,j]xanthene(3a)in 95% yield.

- The structure of the product is confirmed by spectroscopy method. In ^{1}HNMR spectra the aliphatic CH proton of 14-(2-phenyl)-14H-dibenzo[a,j]xanthene (3a) is obtained as singlet at 7.48 ppm and in ^{13}CNMR CH carbon at 32.4ppm which is in closely agreement with the reported values of 14-(2-phenyl)-14H-dibenzo[a,j]xanthene. This proton and carbons are coming from benzaldehyde, the adlehyde proton appears at 9ppm and this peak is disappearing in product which confirms the bond formation between C-1 carbon of β-naphthol and aldehyde carbon. Aliphatic CH proton is obtained as singlet in all the compounds.

- Next we extend the scope of this reaction with substituted benzaldehyde, monosubstituted, disubstituted and trisubstituted benzaldehyde and β-naphthol (Figure 1).
- Substituent on aromatic aldehyde is varied from electron donating as well as electron withdrawing. Electron donating groups are generally more reactive than their corresponding benzaldehydes with electron withdrawing groups and give the desired product in a short reaction time.

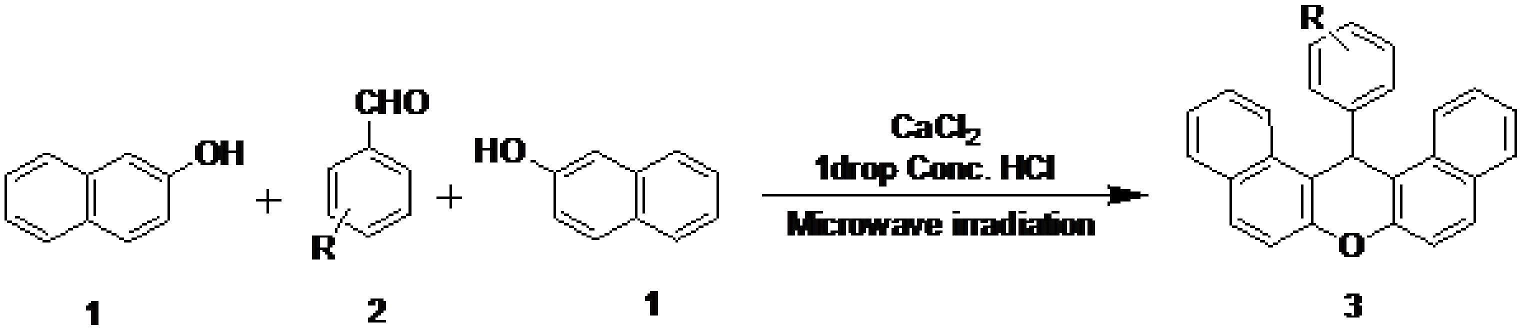

Figure 1 Synthesis of Xanthene via one-pot condensation between 2-naphthol and benzaldehyde catalyzed by calcium chloride/Conc. HCl under microwave condition

20 examples yield in the range 65-97%

Mechanism of Reaction

- The formation of the products was assumed to proceed via formation of a Knoevenagel product followed by Michael addition. One molecule of β-naphthol was firstly condensed with aldehyde which is activated by calcium chloride to afford intermediate Knoevenagel product. Then the active methylene of the second molecule of β-naphthol reacted with the Knoevenagel product via conjugate Michael addition to generate the intermediate which undergoes intramolecular cyclodehydration to give the desired product.

Conclusions

- We have established an efficient, absolutely clean and high yielding eco-friendly methodology, for the synthesis of aryl 14*H*-dibenzo[a,j] xanthenes under microwave condition using calcium chloride as solid support catalyst. The merits of this method are high yield, easy to work out, short reaction time, minimal environmental impact, avoid use of toxic solvent, thus making it one of the attractive and practical protocols for the synthesis of aryl 14*H*-dibenzo[a,j] xanthenes.

Thank You