Available online at www.scholarsresearchlibrary.com

Scholars Research Library

Der Pharmacia Lettre, 2011, 3 (6):193-197
(http://scholarsresearchlibrary.com/archive.html)

Scholars Research Library
ISSN 0974-248X
USA CODEN: DPLEB4

Multi Component Reactions (MCRs) as a Green Approach Towards the Synthesis of Xanthene Derivatives, an Important Heterocyclic Nucleus of various Dyes and Drugs: A mini review

G. M. Nazeruddin*, A.A.Shaikh and Y.I.Shaikh.

Dept. of Chemistry (P.G. Center), Poona College of Arts, Science and Commerce. Camp, PUNE

ABSTRACT

Multi component reactions (MCRs) have been exploited for the synthesis of Xanthene derivatives using various catalysts under different reaction conditions such as Silica sulfuric acid (SSA) or Amberlyst-15 as an efficient and reusable heterogeneous catalyst has been used for the preparation of 12-aryl-8,9,10,12-tetrahydrobenzo[a]xanthene-11-one derivatives from the three-component condensation reaction of β-naphthol, cyclic 1,3 dicarbonyl compounds and aromatic aldehydes under solvent-free conditions in good to excellent yields and short reaction times. Microwave Promoted Perchloric Acid catalyzed One Pot Synthesis of 14-aryl –14H - dibenzo[a,j] xanthene and 12-aryl-8, 9, 10, 12-tetrahydrobenzo[a]-xanthen-11-one derivatives by condensation of various substituted benzaldehydes , β-naphthol and dimedone under solvent free conditions. Similarly condensation of β-naphthol, aromatic aldehydes and cyclic 1,3-dicarbonyl compounds in presence of Chlorosulphonic acid ($ClSO_3H$) as a catalyst to furnish 12-Aryl -8,9,10,12-tetrahydrobenzo [a]xanthen-11-ones derivatives in good to excellent yields under ultrasound and solvent free conditions at ambient temperature . All these methodologies are efficient and environmentally benign and can be developed further for industrial application.

Key words: Xanthenes, Amberlyst-15/ SSA, Ultra sound, Microwave irradiation.

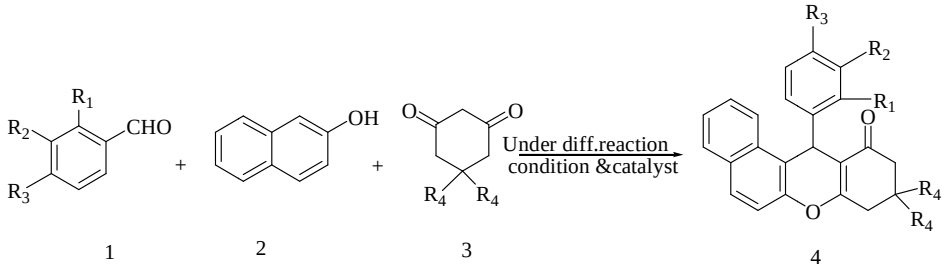
INTRODUCTION

Green chemistry emphasizes the development of environmentally benign chemical processes and technologies[1]. Multi component reactions (MCRs) are processes in which three or more reactants are combined in a single chemical step to produce products that incorporate substantial portions of all the reactants. MCRs comply with the principles of green chemistry in terms of economy of steps as well as many of the stringent criteria of an ideal organic synthesis. These reactions are effective in building highly functionalized small organic molecules from readily

available starting materials in a single step with inherent flexibility for creating molecular complexity and diversity coupled with minimization of time, labor, cost and waste products[2]. Hence, the development of multi-component reaction protocols for the synthesis of heterocyclic compounds has attracted various medicinal chemists.

Xanthenes and benzoxanthenes have attracted considerable interest because they possess various pharmaceutical activities. In addition, these compounds have been employed as dyes,[3]and pH-sensitive fluorescent materials for visualization of biomolecular assemblies[4] and utilized in laser technologies[5]. The well known dyes having xanthene nucleus are Rhodamine B and Rhodamine 6G. Thus a broad utility range has made xanthenes as a prime synthetic candidates there by accentuating the need to develop newer synthetic routes for scaffold manipulation of xanthene derivatives. The synthesis of tetrahydrobenzo[a]xanthen-11-ones has been reported in the presence of strontium triflate[6], indium trichloride, phosphorus pentaoxide[7] $NaHSO_4$-SiO_2 under reflux in halogenated solvents[8] for long hours.Thus, there is a need for development of an alternative route to synthesize the xanthene derivatives. In this context, we decided to investigate the possibility of synthesizing tetrahydrobenzo[a]xanthen-11-one derivatives through one-pot three-component condensation reaction strategy of β-naphthol with aldehydes and cyclic 1, 3-dicarbonyl compounds using various catalyst such as Silica sulfuric acid (SSA)[9] or Amberlyst-15[10] as an efficient and reusable heterogeneous catalyst has been used for the preparation of 12-aryl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one derivatives under solvent-free conditions in good to excellent yields and short reaction times. Similarly under microwave irradiation [11] using perchloric acid as catalyst and under ultrasound [12] irradiation using Chlorosulphonic acid ($ClSO_3H$) as a catalyst the desired product was obtain in excellent yield.

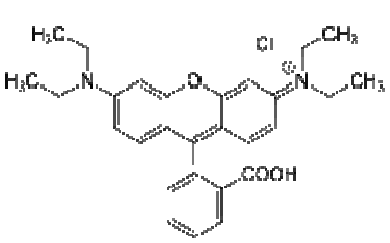
All these methodologies are efficient and environmentally benign and can be developed further for industrial applications. The reaction is depicted in (Scheme 1).



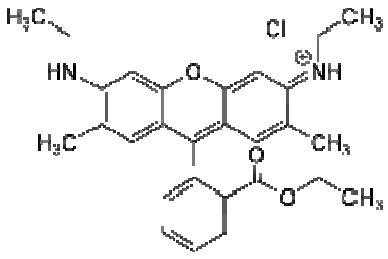
1 2 3 4

R_1,R_2,R_3 = H,Cl,OCH_3,NO_2,OH R_4 = H,CH_3

Scheme 1



RhodamineB



Rhodamine 6G

RESULTS AND DISCUSSION

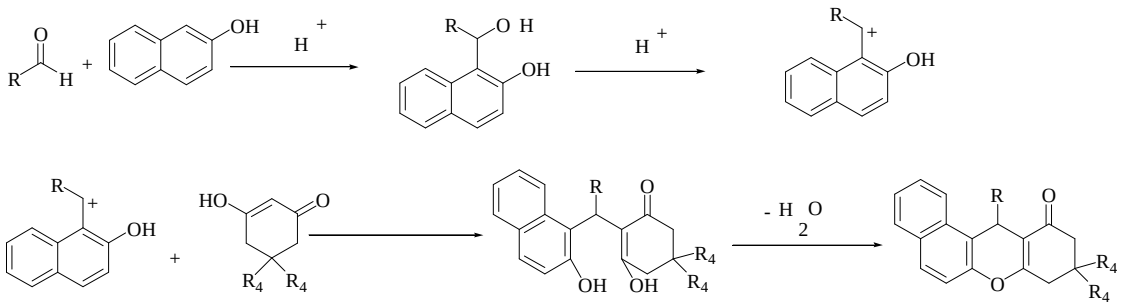
We wish to present here only four simple and efficient methodologies for one pot synthesis of 14-aryl -14H- dibenzo[a,j] xanthene and 12-aryl-8, 9, 10, 12-tetrahydrobenzo[a]-xanthen-11-one derivatives by condensation of various substituted benzaldehydes, β-naphthol and dimedone using various catalyst and under various reaction condition such as under microwave irradiation and solvent free condition. In all cases, aromatic aldehydes substituted with either electron-donating or electron-withdrawing groups underwent the reaction smoothly and gave the products in good to excellent yields. The results are shown in table 1.

Table: 1 synthesis of 12-aryl-8, 9, 10, 12-Tetrahydrobenzo [a] xanthen-11-one derivative (4a–4j) Using various catalyst under different reaction condition

	SSA used as Catalyst						Amberlyst 15 used as Catalyst		Micro-Wave promoted		Ultra sound promoted	
Entry	R1	R2	R3	R4	Time (min)	Yield %	Time (min)	Yield %	Time (min)	Yield %	Time (min)	Yield %
4a	H	H	H	Me	60	83	90	84	90	92	20	98
4b	H	H	NO_2	Me	100	87	60	87	80	91	20	98
4c	NO_2	H	H	Me	80	90	90	79	85	88	15	90
4d	H	H	Cl	Me	130	81	60	85	100	90	20	85
4e	Cl	H	H	Me	180	76	90	81	120	85	35	92
4f	H	H	OMe	Me	70	81	80	84	2.2	86	30	83
4g	OMe	H	H	Me	50	89	90	78	2.0	89	40	88
4h	H	H	OH	Me	210	75	120	78	3.0	88	30	95
4i	OH	H	H	Me	90	82	30	92	2.5	85	40	94
4j	OH	H	H	H	15	91	30	90	2.5	85	40	90

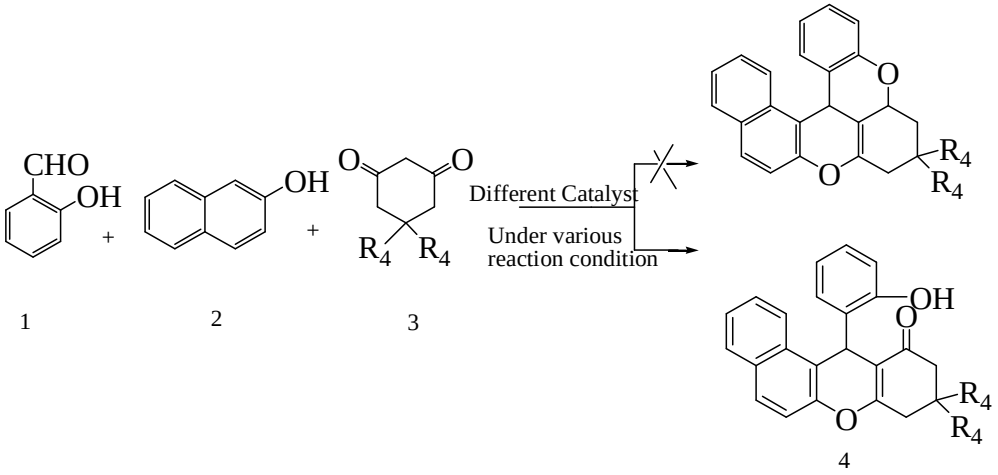
Concerning the reaction mechanism, we proposed that a carbocation is initially formed from aryl aldehydes with β-naphthol, this carbocation is reacted with cyclic 1, 3-dicarbonyl compounds in the second step, which then undergo dehydration to give the final product which is similar to the literature reports[13]. Mechanism of the reaction is depicted in *scheme II*.

Scheme: II Mechanistic pathway of xanthene derivatives



It is interesting to note that in this multi component reaction there is no formation of epoxide with 2-hydroxy bezaldehyde as depicted in *scheme III*. However in literature there are several reports[14] that there is generally epoxide formation in such type of multi component reactions.

Scheme III: Formation of the desired 12-(2-Hydroxyphenyl)-9, 9-dimethyl-8, 9, 10, 12-tetrahydro - benzo[a]xanthen-11-one without formation of the epoxide



1 2 3 4

CONLUSION

In summary we have developed an efficient one pot synthesis of 14-aryl -14H- dibenzo[a,j] xanthene and 12-aryl-8, 9, 10, 12-tetrahydrobenzo[a]-xanthen-11-one derivatives by condensation of various substituted benzaldehydes, β-naphthol and dimedone using different catalyst under various reaction conditions. These methodologies are having several advantages such as inexpensive catalyst and easily available reactants, shorter reaction time and products are obtained in excellent yields. Further this methodology also follows several principles of green chemistry.

Acknowledgement
The authors are thankful to the University Grants Commission, New Delhi, for financial Assistance.

REFERENCES

[1] (a) P. T Anastas,.; J. C. Warner, Green Chemistry: Theory and Practice; Oxford University Press: Oxford, UK, **1998**; (b) Anastas, P. T.; Williamson, T. Green Chemistry, Frontiers in Benign Chemical Synthesis and Process; Oxford University Press: Oxford, UK, **1998**.
[2] J.Zhu,; H.Bienayme, In Multicomponent Reactions; Zhu, J., Bienayme, H., Eds.; WILEY-VCH Verlag GmbH & Co: KGaA, Weinheim, **2005**. References Cited therein;
[3] (a)A.Banerjee,; A.K. Mukherjee, *Stain Technol.*, 56, 83; (**1981**)(b) S. M.Menchen, ; S. C Benson,.; J. Y. L Lam,.; W.-G Zhen,.; D.-Q Sun,.; B. B..Rosenblum,; S. H.Khan,; M. Taing, *U.S. Patent* 6,583,168, (**2003**)
[4] C. G.Knight,; T.Stephens, *Biochem. J.*, 258, 683. (**1989**)
[5] a) O.Sirkencioglu,; N.Talinli,;A.Akar, *J. Chem. Res.*, 502(**1995**,;(b) M Ahmad,.; T. A King,.; D.-K Ko,.; B. H Cha,.; J. J. Lee, Phys. D: *Appl. Phys* 35,1473. (**2002**),
[6] J Li, W Tang., L Lu., W Su. *Tetrahedron Letters* ., 49, 7117. (**2008**)
[7] G. C Nandi, S Samai., K. Ram, M.S. Singh *Tetrahedron.*, 65, 7129(**2009**)
[8] B Das,.; K Laxminarayana,.; M Krishnaiah,.; Y.Srinivas, *Synlet.*, 3107(**2007***)*

[9] G.M.,Nazeruddin , M.S. Pandharpatte, K.B Mulani. *Indian Journal of chemistry Sect*-B (In Press)
[10] G.M., Nazeruddin , A.A. Shaikh & M.S. Pandharpatte *Res. J Chem. Environ.*, 15,. (2) 74-76 (**2011**)
[11] Nazeruddin N. Gulam Mohammed, Mahesh S. Pandharpatte, *Der Pharma Chemica*, **2011**, 3(1): 65-71
[12] Abdulkarim M. A. Al-Kadasi and G. M. Nazeruddin , *R J of Pharmaceutical, Biological and chemical Sciences* 2(1),71-76.(**2011**)
[13] (a) P Rashidi-Ranjbar,.;A Mohajeri,.; A. H. Mahmoudkhani, *J. Phys. Org.* 14, 210(**2001**), ; (b) A. Khoramabadi-zad,.; Z. Kazemi,.; H. A. Rudbari, *J. Korean Chem. Soc*., 46, 541(**2002**)
[14] Tlik J. S., Veizerova L., kettmann V. ,*Tetrahedron Lett.* 49 3520(**2008**).