



Microwave Promoted Perchloric Acid catalyzed One Pot Synthesis of Xanthene Derivatives under solvent –free conditions

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ABSTRACT

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 is described .

Keywords: xanthenes, perchloric acid, solvent free conditions, microwave irradiation.

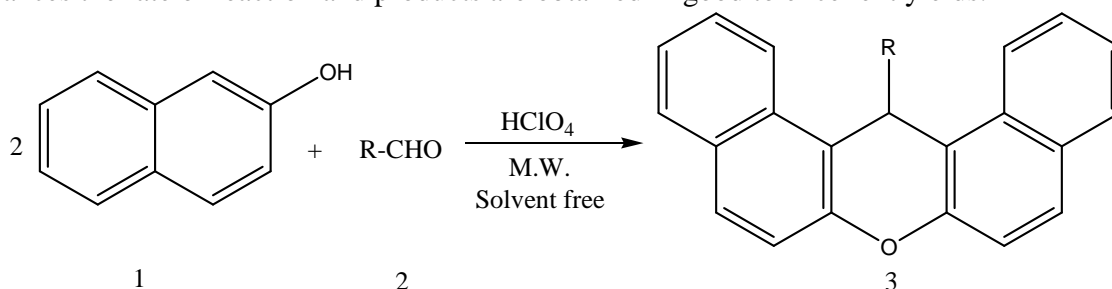
INTRODUCTION

Multi component reactions (MCRs) are continuously increasing their importance in organic and medicinal chemistry [1–3]. In the drug discovery process multi component reaction strategies offer significant advantages over conventional linear type syntheses [4-6]. In such reactions, three or more reactants come together in a single reaction vessel to form new products that contain portions of all the components. The search and discovery for new MCRs on one hand [7] and the full exploitation of the already known multi component reactions on the other hand, is therefore of considerable current interest. One such MCR that belongs to the latter category is synthesis of xanthene derivatives.

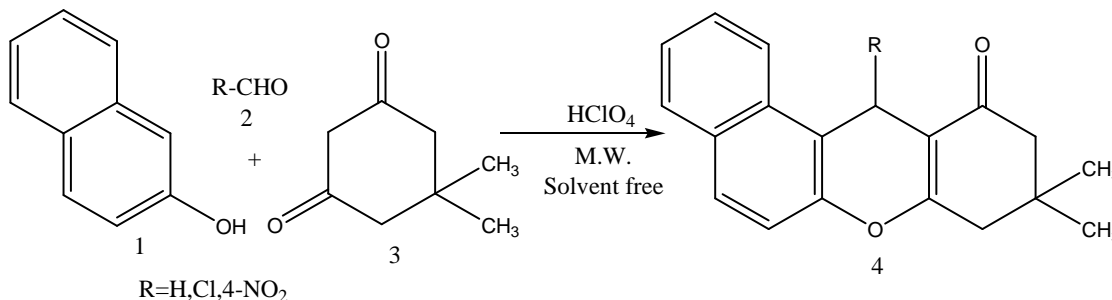
Xanthenes and benzoxanthenes have attracted considerable interest because they possess various pharmaceutical activities such as anti-bacterial [8], anti-inflammatory [9], and anti-viral [10]. These structural motifs have also found a niche as antagonists for paralyzing the action of zoxazolamine[11] and demonstrate efficacy in photodynamic therapy[12]. In addition, these compounds have been employed as dyes [13] and pH-sensitive fluorescent materials for visualization of biomolecular assemblies [14] and utilized in laser technologies [15]. Thus a broad utility range has made xanthenes as a prime synthetic candidate thereby 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[16], indium trichloride, phosphorus pentoxide[17], NaHSO₄-SiO₂ under reflux in halogenated solvents[18] for long hours. However, these methodologies suffer from one or more disadvantages such as low yields, lack of easy availability of the starting materials, prolonged reaction time (16 h), use of toxic organic solvents, requirement of excess of reagent catalyst and special apparatus. 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 Perchloric acid as a catalyst under Microwave irradiation and solvent free conditions. The reaction is depicted in (Scheme 1 & 2).

The application of microwave irradiation [19] to the combinatorial chemistry becomes powerful tool in accelerating the pace of library synthesis. Microwave oven is most popularly used in synthesis because of its low cost and readily availability. Generally microwave irradiation enhances the rate of reaction and products are obtained in good to excellent yields.



Scheme 1



Scheme 2

MATERIALS AND METHODS

All reagents were purchased from Merck and Loba and used without further purification. Melting points were measured in open capillary and are uncorrected. The products were characterized by IR spectra and ¹H NMR. IR spectra were recorded on Perkin-Elmer FT-IR-1710 instrument. ¹H NMR was recorded on BrukerAC-200 MHz and BrukerMSL-300 MHz instrument using TMS as an internal standard. Microwave oven was used LG MOD-MG-1742WE with 230V, 2450MHz and 700 W maximum.

General procedure for the synthesis of 12-aryl-8, 9, 10, 12-tetrahydrobenzo[a]-xanthen-11-one and 14-aryl -14H- dibenzo[a,j] xanthene derivatives : A mixture of aromatic aldehydes(1mmol), and β -naphthol (1mmol), dimedone (1.1mmol) was taken in a borosil beaker (50mL), followed by addition of Perchloric acid (0.3 mmol). The reaction mixture was mixed properly with help of a glass rod and irradiated in a microwave oven at 420W for an appropriate time (Table 1). The reaction was monitored by TLC. After completion of the reaction, the reaction mixture was cooled to room temperature and treated with ice cool water. The product was filtered, dried and recrystallized from ethanol. Identification of the compounds was done by comparing the physical constant and spectral data with those reported in the literature. The same procedure is applied for 14-aryl -14H- dibenzo[a,j] xanthene derivative using aldehydes(1mmol), and β -naphthol (2mmol) and Perchloric acid (0.3mmol).

14-(phenyl)-14H-dibenzo[a,j]xanthene(3a): Yield: 92%.; mp 183°C. IR (KBr, cm^{-1}): 1151(C-O- Str).; $^1\text{H NMR}$ (300MHz, CDCl_3): δ ppm 6.4(s, 1H), 6.89-8.4(m, 17H).

14-(4-chlorophenyl)-14H-dibenzo[a,j]xanthene(3b):Yield: 91%.; mp 286-288°C. IR(KBr, cm^{-1}): 1163(C-O-C Str); $^1\text{H NMR}$ (300MHz, CDCl_3): δ ppm 6.43(s, 1H), 7.051-8.2(m, 16H).

14-(2-chlorophenyl)-14H-dibenzo[a,j]xanthene(3c): Yield: 88%.; mp 213-215°C. IR(KBr, cm^{-1}): 1165(C-O- Str).; $^1\text{H NMR}$ (300 MHz, CDCl_3): δ ppm 6.81(s, 1H), 6.902-8.7(m, 6H).

14-(4-methoxyphenyl)-14H-dibenzo[a,j]xanthene(3d):Yield:90%.; mp 202°C. IR(KBr, cm^{-1}): 1180(C-O- Str). ; $^1\text{H NMR}$ (300MHz, CDCl_3): δ ppm 6.422(s, 1H), 6.634-8.36(m, 16H), 3.59(s, 3H)

14-(4-Nitrophenyl)-14H-dibenzo[a,j]xanthene(3e):Yield:85%.; mp 291-293°C. IR (KBr, cm^{-1}): 1166(C-O- Str); $^1\text{H NMR}$ (300MHz, CDCl_3): δ ppm 6.7(s, 1H), 7.019-8.511(m, 16H).

9, 9-Dimethyl-12-phenyl-8, 9, 10, 12-tetrahydrobenzo[a]-xanthen-11-one: (4a): Yield: 83%.; mp 150–152 °C. IR (KBr, cm^{-1}): 1645(C=O), 1185(C-O Str). $^1\text{H NMR}$ (300 MHz, CDCl_3): δ ppm: 7.99 (d, $J=8.1\text{Hz}$, 1H), 7.78–7.74 (m, 2H, Ar-H), 7.42–7.04 (m, 8H, Ar-H), 5.70(s, 1H, CH), 2.57(s, 2H, CH_2), 2.33(d, $J=16.2\text{Hz}$, 1H), 2.26(d, $J=16.2\text{Hz}$, 1H), 1.11 (s, 3H, CH_3), 0.96 (s, 3H, CH_3).

12-(4-Chlorophenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one(4b): Yield: 89%.: mp 180°C. IR (KBr, cm^{-1}): 1649(C=O), 1185(C-O Str). $^1\text{H NMR}$ (300 MHz, CDCl_3): δ ppm: 7.92 (d, $J=8.1\text{Hz}$, 1H), 7.79–7.75(m, 2H, Ar-H), 7.45–7.11 (m, 7H, Ar-H), 5.67 (s, 1H, CH), 2.34(d, $J=16.2\text{Hz}$, 1H), 2.24(d, $J=16.2\text{Hz}$, 1H), 1.12 (s, 3H, CH_3), 0.96 (s, 3H, CH_3).

12-(4-Methoxyphenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one(4c): Yield :87%.; m.p. 206 °C. IR (KBr, cm^{-1}): 1646(C=O), 1185 (C-O Str). $^1\text{H NMR}$ (300 MHz, CDCl_3): δ ppm: 7.99 (d, $J=8.1\text{Hz}$, 1H), 7.77–7.72 (m, 2H, Ar-H), 7.44–7.22 (m, 5H, Ar-H), 6.70 (d, $J=8.4\text{Hz}$, 1H), 5.65 (s, 1H, CH_2), 3.8 (s, 3H, $-\text{OCH}_3$), 2.55 (s, 2H, CH_2), 2.33(d, $J=16.2\text{Hz}$, 1H), 2.26(d, $J=16.2\text{Hz}$, 1H), 1.11 (s, 3H, CH_3), 0.97 (s, 3H, CH_3).

12-(4-nitrophenyl)-9,9-Dimethyl-8,9,10,12-tetrahydrobenzo-[a]xanthen-11-one (4d): Yield :90%.: mp 174–176°C. IR (KBr, cm⁻¹): 1646(C=O), 1184(C-O Str). ¹H NMR (300 MHz, CDCl₃): δ ppm: 8.04 (d, J=8.5, 1H), 7.82–7.79 (m, 3H, Ar-H), 7.52–7.33 (m, 5H, Ar-H), 5.81 (s, 1H, CH), 2.59 (s, 2H, CH₂), 2.37(d, J=16.4Hz, 1H), 2.3(d, J=16.4Hz, 1H), 1.13 (s, 3H, CH₃), 0.94 (s, 3H, CH₃).

12-(2-Chlorophenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one (4e): Yield :85%.; mp 179–180°C. IR (KBr, cm⁻¹): 1651(C=O), 1184(C-O Str). ¹H NMR (300 MHz, CDCl₃): δ ppm: 8.23 (d, J=8.4Hz, 1H), 7.76–7.72 (m, 2H, Ar-H), 7.49–7.26 (m, 5H, Ar-H), 7.07–6.96 (m, 2H, Ar-H), 5.98 (s, 1H, CH), 2.60 (s, 2H, CH₂), 2.34(d, J=16.2Hz, 1H), 2.24 (d, J=16.2Hz, 1H), 1.13 (s, 3H,CH₃), 0.99 (s, 3H,CH₃).

RESULT AND DISCUSSION

We report here in a simple and efficient one pot synthesis of 14-aryl -14H- dibenzo[a,j] xanthen and 12-aryl-8, 9, 10, 12-tetrahydrobenzo[a]-xanthen-11-one derivatives by condensation of various substituted benzaldehydes, β-naphthol and dimedone using perchloric acid as catalyst 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 14-aryl 14H –dibenzo [a,j] xanthen derivative in presence of perchloric acid as catalyst from β-naphthol and aromatic aldehydes under microwave irradiation and solvent free condition

^a Product	R	Time (min)	Yield (%) Pure and Isolated	M.P.(°C) (Obs / lit)	
3a	H	90	92	183	183[20]
3b	4-Cl	80	91	286-288	287-288[22]
3c	2-Cl	85	88	213-215	215[21]
3d	4-OCH ₃	100	90	202	200[20]
3e	2-NO ₂	120	85	292	293[23]
4a	H	2.2	86	150-152	151-153[17]
4b	4-Cl	2.0	89	180	180-182[17]
4c	4-OMe	3.0	88	206	204-205[17]
4d	4-NO ₂	2.5	85	176-178	178-180[17]
4e	2-Cl	2.5	85	179-180	179-180[17]

CONCLUSION

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

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