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Tetrabutylammonium Hydrogen Sulfate (TBAHS) Catalyzed Microwave-Assisted Synthesis of 3,4,5,6,7,9-Hexahydro-1*H*-xanthene-1,8-(2*H*)-dione Derivatives and its Biological Study

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In this study, a facile and eco-friendly synthesis of novel 3,4,5,6,7,9-hexahydro-1*H*-xanthene-1,8(2*H*)-dione derivatives using tetrabutylammonium hydrogen sulfate (TBAHS) as a catalyst in the microwave reactor is presented. The reaction involved the condensation of aromatic aldehydes with 1,3-cyclohexanedione in ethanol as solvent, offering significant advantages in terms of reaction rate, yield and purity. The use of TBAHS as catalyst in conjunction with microwave irradiation facilitated the formation of the target xanthene derivatives in remarkably short reaction times. Moreover, Monowave 50 microwave reactor provided precise control over reaction parameters, enabling rapid optimization of reaction conditions. Further these synthesized compounds were systematically evaluated for their antibacterial, antituberculosis and antioxidant activities.

Keywords: Xanthene-1,8(2*H*)-dione, Microwave irradiation, 1,3-Cyclohexanedione, Biological activity, Antitubercular.

INTRODUCTION

The emergence of multidrug-resistant microbial pathogens poses a significant threat to global public health, underscoring the urgent need for the development of novel antimicrobial agents [1]. Heterocyclic compounds, particularly xanthene derivatives, have attracted considerable attention due to their diverse pharmacological properties, xanthene derivatives are a class of organic compounds containing a pyran nucleus. 1,8-Dioxohexahydroxanthene derivatives are chemical compounds based on the hexahydroxanthene structure with two ketone (oxo) functional groups at positions 1 and 8 of the molecule. In recent years, microwave-assisted synthesis has emerged as a powerful tool for the rapid and efficient generation of organic compounds, offering several advantages such as accelerated reaction rates, enhanced yields and reduced environmental impact [2].

1,8-Dioxohexahydroxanthene derivatives are known for their versatility and various applications such as an antiviral [3], anti-inflammatory [4], antibacterial [5], antifungal [6], anti-tumor [7], anticancer [8,9], antimalarial [10], cytotoxic agents [11], antagonists of the paralyzing action of zoxazolamine [12], photodynamic therapy [13], as novel ccr1 receptor antagonists [14], potent non-peptidic inhibitors of recombinant human calpain [15], antioxidant [16], estrogen receptors [17], selective positive allosteric modulators of the opioid receptor [18], bone morphogenetic protein (bmp-2) targeted osteogenic agents [19], leishmanicidal agents [20], antiproliferative activity [21], α-glucosidase inhibitors [22]. Therefore, these derivatives are of interest in medicinal chemistry and organic synthesis.

Several workers have reported 1,8-dioxoxanthene derivatives with different substituent's and functional groups, to the xanthene-1,8-dione structure to tailor their properties for specific applications [11,23]. Moreover, the utilization of green and sustainable synthetic methodologies is paramount for addressing the growing concerns regarding environmental sustainability and resource conservation in drug discovery. Recently numerous protocols and catalysts were used for the synthesis of xanthene derivatives *e.g.* $Zr(HSO_4)_4$ [24], Fe_3O_4@Agar-Ag [25], *p*-toluenesulfonic acid (*p*-TSA) [26], triple superphosphate/titanium

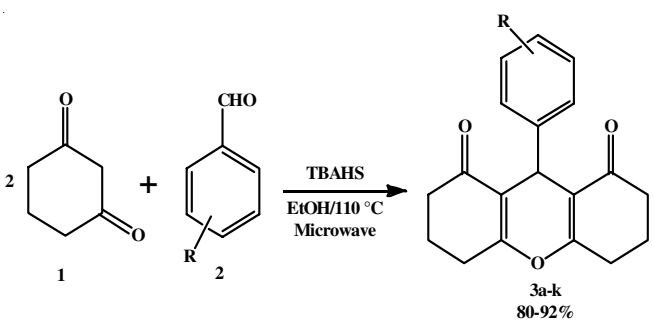
tetrachloride [27], iron oxide nanomaterial [28], activated carbon/MoO_3 [29], copper chromite nanoparticles [30], L-proline [31], $CuCeO_2$ nanoparticle [32], cobalt nanoparticles (CoNP@SBA-15) in water [33], $H_3PW_{12}O_{40}$ [34], SnP_2O_7 [35], functionalized magnetic PAMAM dendrimer [36], ionic liquid [37,38], TiO_2-CNTs nanocomposite [39], nanodiatomite@ melamine-SO_3H [40], Fe_3O_4@SiO_2/PEtOx [41], trifluoroacetic [42], deep eutectic solvents [43], borax [44], DABCO [45], *p*-DBSA [46], poly AMPS-*co*-AA [47], polyaniline *p*-TSA [48], N-sulfonic acid poly(4-vinyl pyridinium) chloride [49], aqueous hydrotrope [50] and Amberlyst-15/DES [51].

While these methods have shown potential in some cases, they are not without their share of drawbacks. Some of these include prolonged reaction time spans, poor yields, highly acidic conditions, rigorous work-up, costly reagents and hazardous catalysts. In this work, the microwave-assisted synthesis of 3,4,5,6,7,9-hexahydro-1*H*-xanthene-1,8-(2*H*)-dione derivatives using tetrabutylammonium hydrogen sulfate (TBAHS) as a catalyst in the monowave 50 microwave reactor. This approach offers significant advantages in terms of reaction efficiency, scalability and environmental compatibility. Subsequently, the synthesized compounds are systematically evaluated for their antibacterial, antituberculosis and antioxidant activities, aiming to identify potent antimicrobial agents with broad-spectrum efficacy.

EXPERIMENTAL

All chemicals were of laboratory grade and used as obtained from Sigma-Aldrich, USA. The melting points were determined in Contech digital melting point apparatus and are uncorrected. The reaction progress and purity of products were determined by TLC silica gel plates (Merck 60 F_{254}). IR spectra were recorded on Shimadzu FT-IR, using KBr pellets. The ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker Avance 400 MHz instrument using $CDCl_3$ as solvent.

General procedure: In a reaction vial, a mixture of 1,3-cyclohexanedione (**1**) (4 mmol) and aromatic aldehyde (**2**) (2 mmol) were taken along with 10 mol% of TBAHS in 5 mL ethanol was heated in 10 mL pressure vial under microwave system operating at 110 ºC for 30-50 min. The progress of the reaction was monitored by TLC (pet. ether: ethyl acetate). After completion of the reaction, the mixture was cooled to room temperature. The solid product was separated by the filtration method and recrystallized to obtain pure compound (**Scheme-I**).



Scheme-I

9-(3-Bromophenyl)-3,4,5,6,7,9-hexahydro-1*H*-xanthene-1,8(2*H*)-dione (3a): m.p.: 274.4 ºC; IR (KBr, ν_{max}, cm^{-1}): 2960, 2951,1663, 1361, 1196, 1163, 1124; ^{1}H NMR: 1.96-2.08 (m, 4H), 2.27-2.41 (m, 4H), 2.59-2.70 (m, 4H), 4.76 (s, 1H), 7.09 (t, 1H), 7.23-7.26 (dd, 1H), 7.32 (d, 2H); ^{13}C NMR: 196.9, 161.3, 146.6, 132.0, 129.6, 127.7, 122.3, 115.3, 36.5, 31.6, 27.8, 21.8 ppm, *m/z*: 373.1 M$^+$.

9-(4-Nitrophenyl)-3,4,5,6,7,9-hexahydro-1*H*-xanthene-1,8(2*H*)-dione (3c): m.p.: 250.1 ºC; IR (KBr, ν_{max}, cm^{-1}): 2954, 2921, 1719, 1607, 1379, 1224, 1064, 965, 786; ^{1}H NMR: 1.93-2.10 (m, 4H), 2.33-2.40 (m, 4H), 2.56-2.72 (m, 4H), 4.87 (s, 1H), 7.46 (d, 2H), 8.07 (d, 2H),^{13}C NMR: 196.3 (2C), 153.8 (2C), 149.8, 145.2, 126.7 (2C), 113.1 (2C), 39.6, 35.8 (2C), 30.3 (2C), 21.4 (2C) *m/z*: 340.7 M+.

9-(2-Chlorophenyl)-3,4,5,6,7,9-hexahydro-1*H*-xanthene-1,8(2*H*)-dione (3f): m.p.: 227.9 ºC; IR (KBr, ν_{max}, cm^{-1}): 2956, 2892, 1670, 1624, 1476, 1357, 1201, 1175, 1127, 848, 684; ^{1}H NMR: 7.26-7.28 (dt, 1H, *J* = 1.8 Hz), 7.13-7.17 (dd,2H, *J* = 1.8 & 8Hz), 7.08-7.10 (d,1H, *J* = 1.8 Hz), 4.78 (s,1H), 2.57-2.70 (m, 4H), 2.27-2.57 (m, 4H), 1.90-2.07 (m, 4H), ^{13}C NMR: 196 (2C), 164.14 (2C), 146.30, 133.87, 129.24, 128.10, 127.15, 126.66, 116.29 (2C), 36.85 (2C), 31.54, 27.11 (2C), 20.21 (2C); *m/z*: 329.7 (M+1) 331.7 (M+3).

9-(4-(Dimethylamino)phenyl)-3,4,5,6,7,9-hexahydro-1*H*-xanthene-1,8(2*H*)-dione (3i): m.p.: 223.5 ºC; IR (KBr, ν_{max}, cm^{-1}): 2960, 2879, 1666, 1620, 1459, 1199; ^{1}H NMR: 7.14 (d, 2H, *J* = 8.7Hz), 6.60 (d, 2H, *J* = 8.5Hz), 4.72 (s, 1H), 2.86 (s, 6H), 2.50-2.66 (m, 4H), 2.27- 2.40 (m, 4H), 1.60-2.05 (m, 4H); *m/z*: 338.5.

9-(2-chloro-4-fluorophenyl)-3,4,5,6,7,9-hexahydro-1*H*-xanthene-1,8(2*H*)-dione (3j): m.p.: 214.5 ºC, IR (KBr, ν_{max}, cm^{-1}): 2957, 2876, 1662, 1617, 1453, 1357,1203; ^{1}H NMR: 7.42-7.46 (dd, 1H, *J* = 2.4 & 6.4Hz), 6.94-6.97 (dd, 1H, *J* = 2.6 & 6.2 Hz), 6.86-6.91 (dt, 1H, *J* = 2.6 & 5.7 Hz), 4.97 (s, 1H), 2.50-2.66 (m, 4H), 2.26-2.39 (m, 4H), 1.91-2.07 (m, 4H); *m/z*: 347.8.

Disk diffusion assay: The antimicrobial activity of the synthesized compounds was evaluated using Kirby-Bauer disk diffusion method [52,53]. Briefly, each sterile disk (Himedia Pvt. Ltd. Mumbai, India) loaded with synthesized compounds 50 µL (1 mg/mL). Each disk was then placed on the surface of the sterile solidified nutrient agar medium which was spreaded with 24 h old inoculums of *E. coli*, *P. aeruginosa*, *S. aureus*, *B. megaterium* and *M. tuberculosis* H_{37}Ra and streptomycin and rifampicin (1 mg/mL) were used as standards. After 1 h of refrigeration for diffusion, the plates were placed in incubator at 37 ºC for 24-48 h. The zones were measured using a zone scale (Himedia Pvt. Ltd. Mumbai) after incubation.

Resazurinmicrotiter assay (REMA): The REMA plate assay was carried out as described elsewhere [53,54]. In brief, 0.1 mL of broth of nutrient medium was dispensed in each well of a sterile flat-bottom 96-well plate and serial two-fold dilutions of each synthesized compounds were prepared directly in the plate. 0.05 mL of respective inoculums was added to each well. Incubation was carried out at 37 ºC for 24 h after the plate was covered and the sterile plastic bag was sealed. Each well was supplemented with 0.03 mL of resazurin solution

(0.01% in sterile deionized water) after 24 h of incubation, and the plate was re-incubated for another 24 h. If the colour changed from blue to pink indicating the growth of bacteria and the MIC was defined as the lowest concentration of drug that prevented this change in colour.

DPPH assay: A 50:50 proportions of each of the synthesized compounds and the DPPH were mixed and incubated the samples for 20 min. Absorbance was measured at 517 nm using Shimadzu UV Vis- Spectrophotometer and ascorbic acid (1 mM) was used as a standard [54]. The percent inhibition was calculated using following formula:

$$\text{Radical scavenging activity (\%)} = 1 - \frac{T}{C} \times 100$$

Hydroxyl radical assay: The hydroxyl radical scavenging activity was conducted with Fenton reaction [54,55]. Briefly, the reaction mixture contained 1,10-phenanthroline (90 µL of 1 mM) and phosphate buffer (2.4 mL of 0.2 M, pH 7.8),$FeCl_2$ (60 µL of 1 mM), H_2O_2 (150 µL of 0.17 M) and of synthesized compound (1.5 mL of 1 mg/mL). Ascorbic acid (1 mM) was used as reference and after 5 min of incubation at room temperature, the absorbance was observed at 560 nm.

$$\text{Radical scavenging activity (\%)} = 1 - \frac{T}{C} \times 100$$

RESULTS AND DISCUSSION

In continuation of our research interest [38,56], herein a novel method for the synthesis of 3,4,5,6,7,9-hexahydro-1*H*-xanthene-1,8(2*H*)-dione derivatives is presented. The synthesis was achieved through the reaction of 1,3-cyclohexanedione (**1**) (4 mmol) and 4-nitrobenzaldehyde (**2**) (2 mmol) in ethanol, employing TBAHS as catalyst. The reaction was conducted under microwave irradiation, providing an efficient and rapid synthetic route to access these important heterocyclic compounds. In order to optimize the reaction, initially the reaction was conducted in various solvents such as acetonitrile, toluene, chloroform and ethanol at different temperatures and the results are shown in Table-1. At room temperature no progress was observed in acetonitrile and toluene even after 6 h. In chloroform, a yield of 20% and in ethanol, a yield of 35% was achieved within the same time frame. Consequently, ethanol was selected as the preferred solvent. On further optimization of reaction temperature, 65% yield is obtained at reflux condition with ethanol in 4 h as confirmed by TLC. To enhance the product yield and reduce reaction time, it was decided to transition from reflux to utilizing the microwave synthesizer using sealed vials under fast conventional heating. Interestingly, transitioning from reflux temperature to 110 ºC not only increased the product yield but also reduced the reaction time. The most favourable results in terms of both time and yield for the model reaction was achieved at 110 ºC using the microwave synthesizer, as shown in Table-1. The catalytic efficiency of TBAHS among other catalysts for the reaction was also evaluated and the comparative data is presented in Table-2.

TABLE-1
REACTION OF 1,3-CYCLOHEXANEDIONE, 4-NITROBENZALDEHYDE UNDER VARIOUS CONDITIONS[a]

Entry	Solvent	Temp. (°C)	Time (min)	Yield[b] (%)
1	Acetonitrile	R.T.	360	–
2	Toluene	R.T.	360	–
3	Chloroform	R.T.	360	20
4	Ethanol	R.T.	360	35
5	Ethanol	Reflux	240	65
6	Ethanol[c]	90	80	80
7	Ethanol[c]	100	50	84
8	Ethanol[c]	110	35	92
9	Ethanol[c]	120	35	90

[a]Reaction conditions: 1,3-cyclohexanedione (4 mmol), 4-nitro benzaldehyde (2 mmol), TBAHS 10 mol%. [b]isolated yields, R.T.-room temperature, [c]in microwave, – no product.

In order to extend the strength and scope of this protocol, a reaction with different substituted aromatic aldehydes was investigated. The results (Table-3) displayed that electronic effect of different substituents on the aromatic ring did not affect more in the product yields. The entire product synthesized was confi-rmed by IR, ^{1}H NMR, ^{13}C NMR and mass spectra.

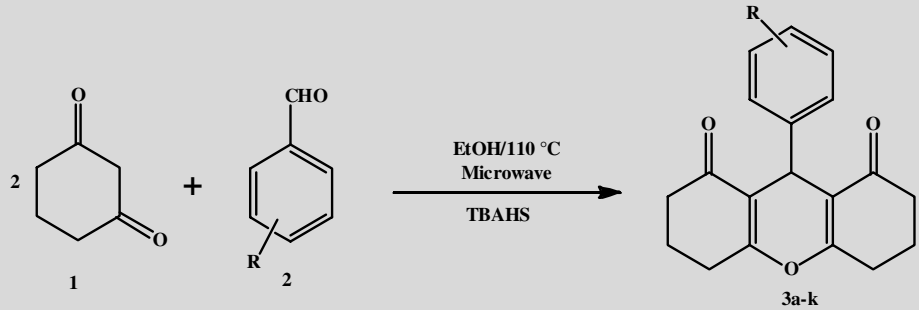
In synthesized xanthene-1,8-(2H)-dione derivatives (**3c**), a medium band obtained at 2954 and 2922 cm^{-1} represents the -CH- stretching of alkanes, a strong band at 1667 cm^{-1} represents the presence of general carbonyl group (C=O *str.*) a medium band at 1379 cm^{-1} for alkanes (C-H *bend.*) a strong band at 1202 cm^{-1} confirms the presence of ether (C-O *str.*). The determination of structure for the product was further confirmed by ^{1}H NMR spectra. A singlet obtained at δ 4.87 ppm (s, 1H, -CH) confirms the formation of product. In ^{13}C NMR peak at δ 196.3 ppm for 2 carbonyl carbon and peak δ 39.6 ppm (-CH carbon) confirms the structure. The mass of the product is confirmed by LC-MS spectra indicating the peak at *m/z* 340.7 ppm (M+1), which authenticates the formation of the product.

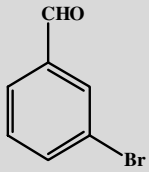
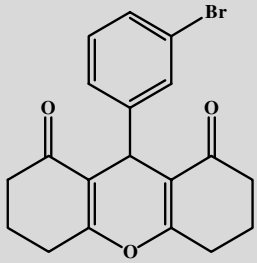
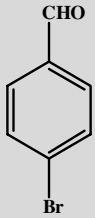
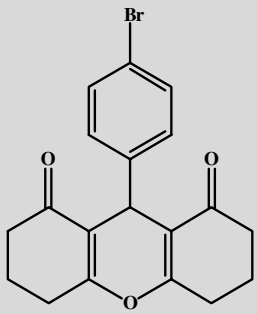
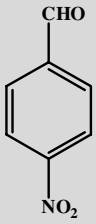
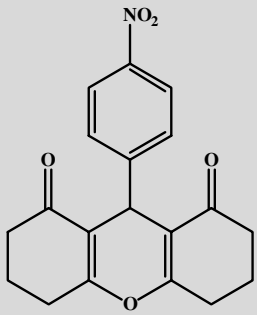
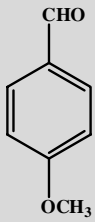
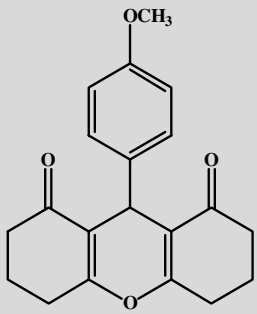
Mechanism: A plausible mechanism for the synthesis of 3,4,5,6,7,9-hexahydro-1*H*-xanthene-1,8(2*H*)-dione catalyzed by TBAHS is shown in **Scheme-II**. It is suggested that in order to obtain intermediate **4**, one molecule of 1,3-cyclohexanedi-

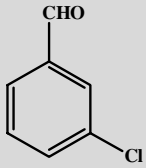
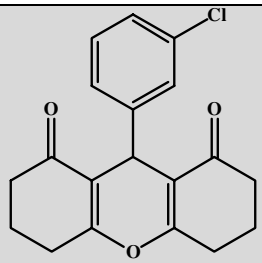
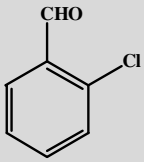
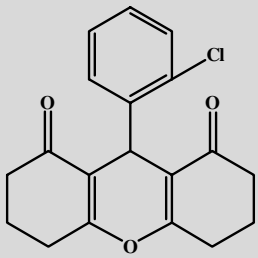
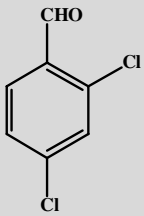
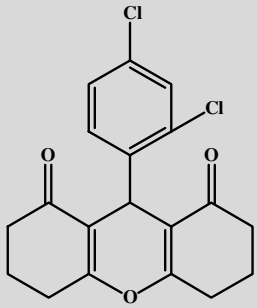
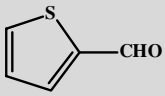
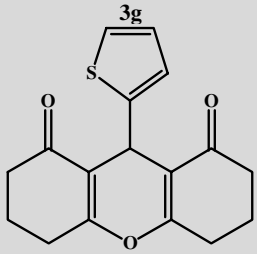
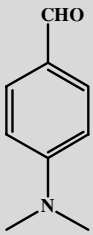
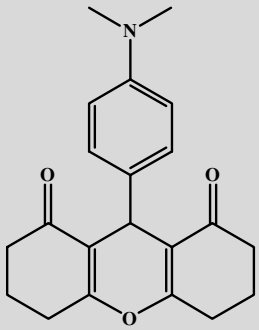
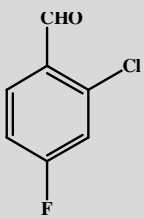
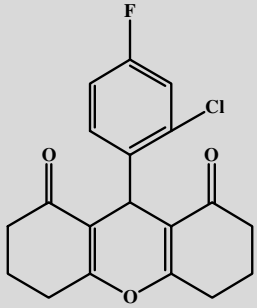
TABLE-2
COMPARISON WITH VARIOUS REPORTED CATALYSTS

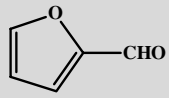
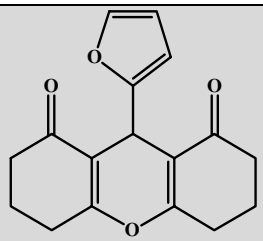
Catalyst	Condition	Time h/(min)	Yield (%)	Ref.
p-DBSA	H_2O/reflux	3	67-91	[46]
Poly AMPS-co-AA	Solvent free	(25)	70-84	[47]
Polyaniline *p*-TSA	H_2O/reflux	6	73-84	[48]
N-Sulfonic acid poly (4-vinyl pyridinium) chloride	Oil bath/100 °C	(1-40)	90-98	[49]
Aq. hydrotrope	80 °C	1.5	82-87	[50]
Amberlyst -15/DES	Electrochemical	1.5	74-99	[51]
TBAHS	Microwave	(30-50)	80-92	This work

TABLE-3
SYNTHESIS OF 3,4,5,6,7,9-HEXAHYDRO-1*H*-XANTHENE-1,8(2*H*)-DIONE DERIVATIVES BY REACTION OF 1,3-CYCLOHEAXANEDIONE AND SUBSTITUTED ALDEHYDE[a]

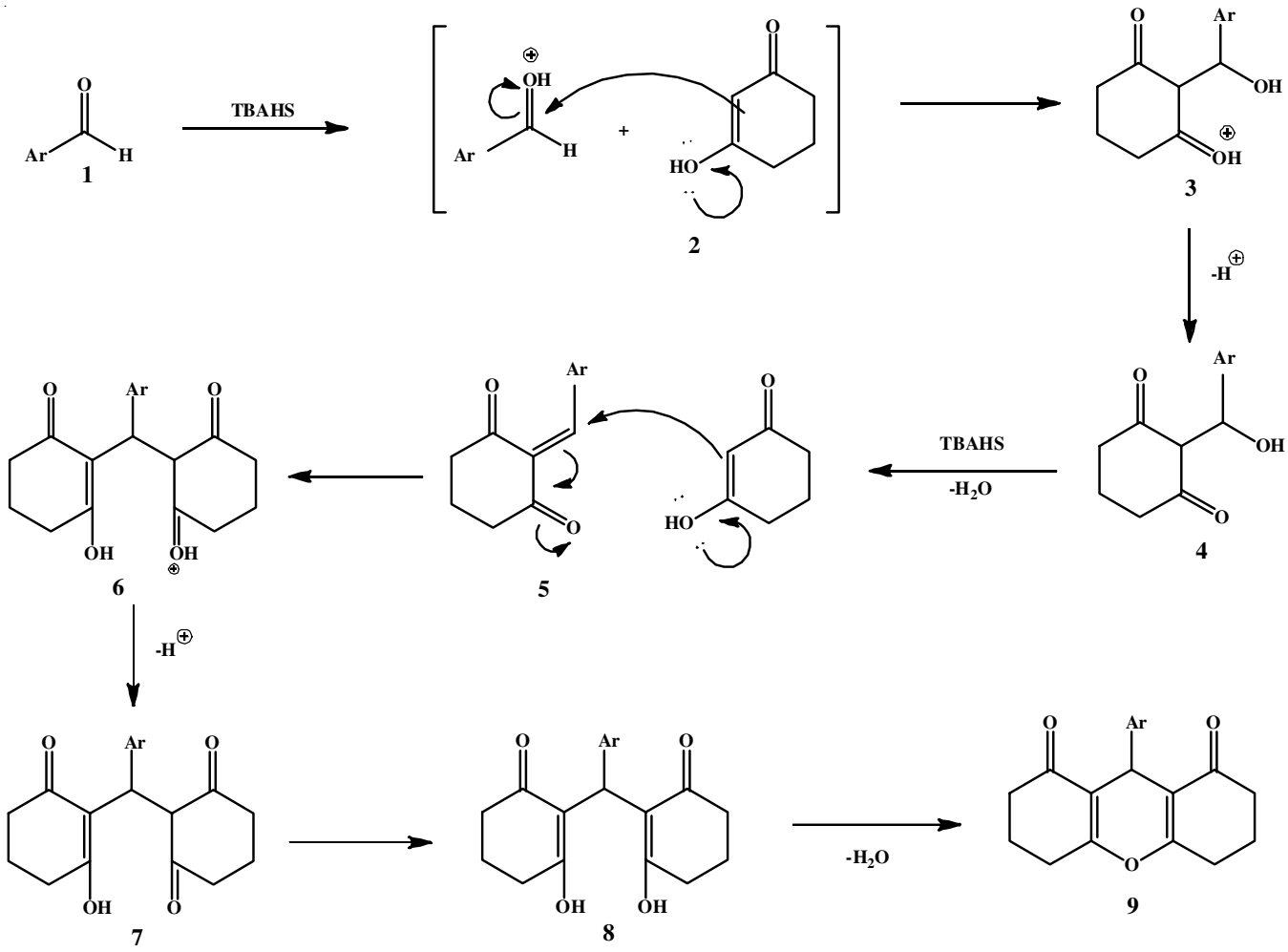


Entry	Aldehyde	Product	Time (min)	Yield[b] (%)
1		 **3a**	40	90
2		 **3b**	35	90
3		 **3c**	35	92
4		 **3d**	45	84

5		 **3e**	40	82
6		 **3f**	40	86
7		 **3g**	30	87
8		 **3h**	50	82
9		 **3i**	40	85
10		 **3j**	35	88

11		 **3k**	50	80

[a]Reaction conditions: 1,3-cyclohexanedione **1** (4 mmol), aromatic aldehyde **2** (2 mmol), TBAHS 10 mol%, ethanol 5 mL, in microwave reactor at 110 °C. [b]isolated yields.



Scheme-II

one was initially reacted with an aldehyde that had been activated by TBAHS (**2**). Intermediate **8** was produced when a second 1,3-cyclohexanedione molecule underwent a Michael addition reaction with intermediate **4**. The desired 3,4,5,6,7,9-hexahydro-1*H*-xanthene-1,8(2*H*)-dione was finally produced by cyclodehydration of intermediate **8**.

Biological studies: Antimicrobial and antituberculosis screening of the synthesized 3,4,5,6,7,9-hexahydro-1*H*-xanthene-1,8(2*H*)-dione derivatives (**3a-k**) against 5 threatened pathogens were performed in persuit of novel heterocyclic molecules with potent antimicrobial and antituberculosis action. Evaluation of biological potential of the synthesized compounds, the antibacterial activity against *E. coli*, *P. aerugenosa*, *S. aureus* and *B. megaterium* and antituberculosis activity on *M. tuberculosis* were assessed. Streptomycin used as a reference for assessing the antibacterial competences of newly synthesized compounds, whereas rifampicin was utilized as a standard for antituberculosis examinations. For antibacterial and antituberculosis studies, Kirby-Bauer disc diffusion method and for MIC the REMA assay was performed. The zone of inhibition was determined using the disc diffusion method and the MIC of the newly synthesized drugs was determined using the REMA assay. Table-4 shows the zone of inhibition of synthesized 3,4,5,6,7,9-hexahydro-1*H*-xanthene-1,8(2*H*)-diones (**3a-k**)

TABLE-4
ZONE OF INHIBITION OF 3,4,5,6,7,9-HEXAHYDRO-1*H*-XANTHENE-1,8(2*H*)-DIONE DERIVATIVES AGAINST BACTERIAL STRAINS (**3a-k**)

Compounds	*E. coli*	*P. aerugenosa*	*B. megaterium*	*S. aureus*	*M. tuberculosis*
3a	++	++	++	++	NZ
3b	NZ	++	++	++	NZ
3c	+	NZ	++	++	++
3d	+	+	++	+	++
3e	++	++	++	++	+
3f	++	+++	+++	+++	+++
3g	+++	+++	+++	+++	+++
3h	+	+	+	+	+
3i	+	NZ	++	++	NZ
3j	NZ	+	++	+++	NZ
3k	NZ	NZ	++	++	NZ
Sterptomycin	+++	+++	+++	+++	NA
Rifampicin	NA	NA	NA	NA	+++

+ = < 5 mm, ++ = >5 &< 10 mm, +++ = >10 &< 14 mm, Results are the average mean of three parallel experiments.

TABLE-5
MIC OF INHIBITION OF 3,4,5,6,7,9-HEXAHYDRO-1*H*-XANTHENE-1,8(2*H*)-DIONE DERIVATIVES AGAINST BACTERIAL STRAINS (**3a-k**)

Compounds	*E. coli*	*P. aerugenosa*	*B. megaterium*	*S. aureus*	*M. tuberculosis*
3a	250	250	250	250	500
3b	500	250	250	250	500
3c	250	500	500	125	125
3d	250	250	250	500	62.5
3e	125	62.5	125	125	62.5
3f	31.25	15.62	31.25	31.25	15.62
3g	7.81	7.81	3.9	3.9	15.62
3h	250	250	250	125	31.25
3i	250	500	500	125	NZ
3j	500	250	125	15.62	NZ
3k	500	500	250	250	NZ
Streptomycin	1.95	1.95	1.95	1.95	NA
Rifampicin	NA	NA	NA	NA	3.9

The results are the mean values of three independent experiments.

against bacterial strains and Table-5 shows the MIC values. Among the synthesized compounds, compounds **3g** and **3f** showed the maximum zone of inhibition and having MIC ranges from 3.9 to 15.62 μg/mL among all the tested pathogens and showed the prominent activity.

Free radical scavenging activity: Neutralization of excessively produced reactive species is an important aspect can be fulfill by antioxidant ability of synthesized compounds. This was done using OH and DPPH radical procedures, the % free radical scavenging activity of 3,4,5,6,7,9-hexahydro-1*H*-xanthene-1,8(2*H*)-dione derivative was determined. Ascorbic acid (vitamin C) and α-tocopherol (vitamin E) were the controls to compare the antioxidant properties of these newly synthesized compounds. Table-6 indicated that these compounds have strong antioxidant properties. In comparison to the $OH^{\bullet}$, the synthesized compounds have a higher DPPH radical scavenging activity. The order of DPPH radical scavenging effects was **3j > 3i > 3d > 3h > 3c** and the order of OH radical scavenging activity was determined as **3h > 3i > 3k > 3g > 3d**. Compounds **3j** and **3i** responded better in the DPPH assay, while compounds **3h** and **3i** functioned better in the OH assay.

TABLE-6
% FREE RADICAL SCAVENGING ACTIVITY OF INHIBITION OF 3,4,5,6,7,9-HEXAHYDRO-1*H*-XANTHENE-1,8(2*H*)-DIONE DERIVATIVES (**3a-k**)

Compound	DPPH	OH
3a	63.5 ± 0.36	65.7 ± 0.05
3b	61.36 ± 1.0	59.14 ± 0.41
3c	68.63 ± 0.05	59.06 ± 0.17
3d	72.64 ± 0.63	68.07 ± 0.08
3e	65.03 ± 0.51	64.12 ± 0.04
3f	63.71 ± 0.37	62.60 ± 0.87
3g	68.74 ± 0.84	70.04 ± 0.05
3h	69.05 ± 0.75	73.09 ± 0.06
3i	72.14 ± 0.70	71.68 ± 0.87
3j	74.65 ± 0.21	58.75 ± 0.47
3k	62.73 ± 0.79	71.68 ± 0.11
Ascorbic acid	82.09 ± 0.01	NA
α-Tochopherol	NA	84.07 ± 0.57

Results are the mean values of three independent experiments ± SD.

Conclusion

An efficient, rapid and simple synthetic protocol for the synthesis of 3,4,5,6,7,9-hexahydro-1*H*-xanthene-1,8(2*H*)-

dione derivatives (**3a-k**) using tetrabutylammonium hydrogen sulfate (TBAHS) as catalyst in microwave irradiation was developed. The synthesized novel compounds were characterized by spectrochemical methods *i.e.* ^{1}H NMR, ^{13}C NMR and mass. The novel compounds was carried out for their *in vitro* antimicrobial, antitubercular, antioxidant activity against bacterial strain. The antibacterial activity of compounds **3g** and **3f** showed excellent activity with MIC of 3.9 µg/mL against selected human pathogens. Compounds **3j** and **3i** showed best DPPH and compounds **3h** and **3i** showed OH radical scavenging potential as compared with the standard ascorbic acid. The key improvements of this protocol are simple experimental process, easy product isolation, good to excellent yields, avoiding hazardous solvents and laborious column chromatography.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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