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Synthesis of 1, 8-dioxo-octahydroxanthenes derivatives using Rochelle salt catalyst under microwave irradiations

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Abstract: Herein, we reports synthesis of 1, 8-dioxo-octahydroxanthenes derivatives by the one-pot-multicomponent reaction of different substituted aromatic aldehyde/heterocyclic aldehydes and dimedone in the presence of Rochelle salt (10 mol %) as a catalyst in water under microwave irradiations at 450 Watt for specified period of time. We found that this is a green, facile and efficient method for the synthesis of 1, 8-dioxo-octahydroxanthenes derivatives. The prominent features of this method are the inexpensive reagents, simple and safe experimental procedure, easy and clean workup, short reaction times (2-5 min), excellent yield (80-96 %), no toxic waste and environmentally benign method.

Keywords: Dimedone, 1, 8-dioxo-octahydroxanthenes, Rochelle salt.

I. INTRODUCTION

Rochelle salt is potassium sodium tartrate tetrahydrate (a double salt of tartaric acid) having molecular formula $KNaC_4H_4O_6 \cdot 4H_2O$. Study of literature indicates that it is efficient catalyst used for the synthesis of used for the synthesis of substituted chromenes and benzochromenes, [1] 2, 4, 5-trisubstitutedimidazoles.[2]

Xanthenes derivatives are essential heterocyclic because of their agricultural bactericide and pharmacological activities.[3] 1,8-Dioxo-octahydroxanthenes are derivatives of xanthenes, in which substituted 4-aryl pyran ring is present in the middle and two fused cyclohexen-2-one rings (dimedone) on the left and right sides. These xanthenediones received attention due to their different biological activities, like antimicrobial,[4-5] antioxidant,[6-9] leishmanicidal,[10] anti-tubercular,[11] agents and photosensitizer in photodynamic therapy.[12]

In literature several strategies have been reported for the synthesis of 1, 8-dioxo-octahydroxanthene derivatives such as $Cu(NO_3)_2 \cdot 3H_2O$ in acetonitrile/reflux,[13] $InCl_3$ and $(HPO_3)_n$,[14] W-doped ZnO nanocomposite,[15] Silicotungstic acid ($H_4SiW_{12}O_{40}$)/reflux,[16] Fe_3O_4@SiO_2-$SnCl_4$ /in ethanol under ultrasonic irradiation,[17] Ionic liquid [cmmim][BF_4] under microwave irradiation,[18] Cu(II)-Fur-APTES/GO,[19] FeNP@SBA-15,[20] Succinic acid,[21] Choline chloride-oxalic acid,[22] and Sulfacetamide.[23] However, most of the methods possesses some disadvantages like tedious work up, drastic reaction conditions, toxic solvents, sluggish and poor yields of the products, and so forth, which demands for further development of a novel catalyst for synthesis of xanthenes with an easy, cost-effective, simple, efficient, and greener method.

Herein, we have carried out the synthesis of 1, 8-dioxo-octahydroxanthene derivatives from dimedone and different substituted benzaldehydes and hetroaldehyde using Rochelle salt catalyst in water solvent under microwave irradiation.

II. EXPERIMENTAL

a) Material and Methods

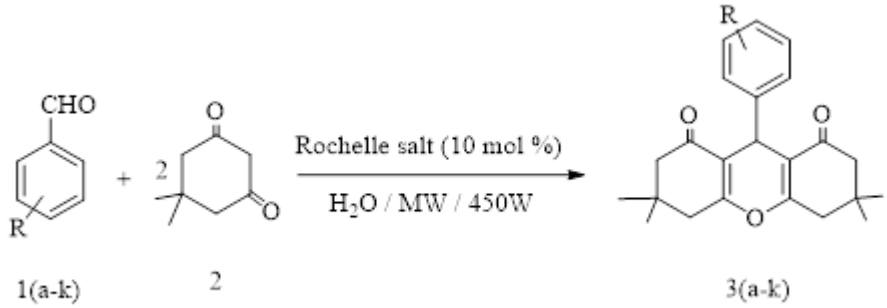
The chemicals were obtained from Fisher Scientific, Loba Chemie Pvt. Ltd., Sigma-Aldrich and used without further purification. All yields refer to isolated products unless otherwise stated. Melting points were determined by an open capillary using heavy paraffin oil in Thieles tube and are uncorrected. Pre-coated silica gel TLC (thin-layer chromatography) plates were used for investigation of rates of reactions under UV lamp. NMR spectrum recorded at 500 MHz with tetramethylsilane as internal standard and $CDCl_3$ as solvent on Bruker Avance Neo 500 MHz NMR spectrometer; Fourier transform infrared (IR) spectra were obtained as KBr discs on a Perkin Elmer spectrum 400 FT-IR/FT-FIR spectrometer and mass spectra on LCMS Water's Synapt-XS Maldi TOF HDMS spectrometer.

b) General procedure for the synthesis of 1, 8-dioxo-octahydroxanthene derivatives:

A mixture of aromatic aldehyde (1 mmol), dimedone (2 mmol), and Rochelle salt (10 mol %) as catalyst were taken in a 50 mL round bottom flask containing 5 mL water. The contents of the beaker were irradiated under microwave at 450 W for appropriate time as shown in Table 1. The progress of the reaction was monitored by thin layer chromatography. After completion of the reaction, the reaction mixture was cooled to room temperature, cold water was added and solid product obtained. It was filtered off and was purified by recrystallization from ethanol. Melting points were determined by open capillary tube using heavy paraffin oil in Thiele tube. Melting points are uncorrected and are compared with the reported literature values.

III. RESULTS AND DISCUSSION

In the this section, we have carried out the Rochelle salt (10 mol %) catalysed synthesis of 1, 8-dioxo-octahydroxanthene derivatives from substituted aromatic aldehydes, dimedone (active methylene compound) in water under microwave irradiated at power 450 Watt.



Scheme: 1: Synthesis of 1, 8-dioxo-octahydroxanthene derivatives using Rochelle salt catalyst under microwave irradiation

To investigate the influence of microwave irradiation on rate of reaction and yield of the product, we carried out a series of experiments at different power levels of the microwave. The obtained results at different power levels are summarized in Table-1. The observed results, indicates that the titled compounds (3a–k) can be synthesized with high purity and yield at power level 450 Watt (Entry 4, Table 1).

Table 1: *Optimization of reaction condition for the synthesis of 1, 8-dioxo-octahydroxanthene (3a) under microwave set up*

Entry	Power (Watt)	Time (min)	Yield (%)
1	200	25	40
2	350	10	60
3	400	6	85
4	450	2	96
5	600	2	96
6	700	2	96

To determine the adequate amount of catalyst for the faster conversion of reactants into product with better yield, we have carried out the model reaction (4-nitrobenzaldehyde and dimedone) with different concentration of catalyst Rochelle salt at 2.5, 5, 7.5, 10 and 12.5 mol % gives the yield of desired product 45, 60, 86, 96 and 96 % respectively (Entry 1-5, in Table-2). The result obtained proved that 10 mol % amount of Rochelle salt catalyst is sufficient to accelerate the reaction.

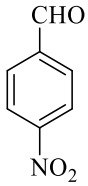
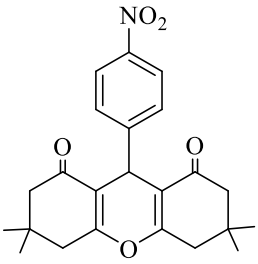
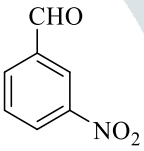
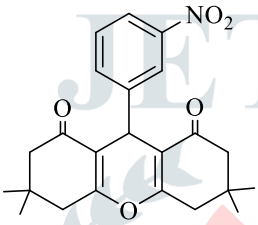
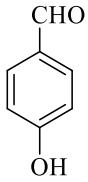
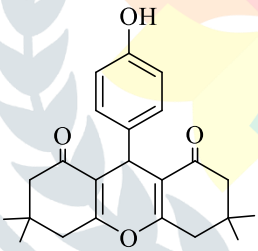
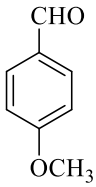
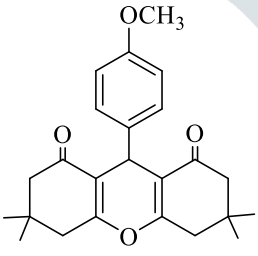
Table 2: *Optimization of amount of catalyst Rochelle salt for the synthesis of 1, 8-dioxo-octahydroxanthene (3a) under microwave irradiation conditions (450 Watt)*

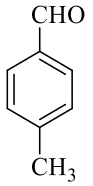
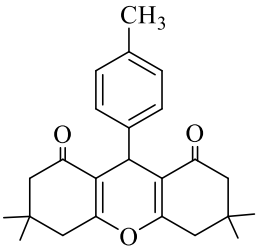
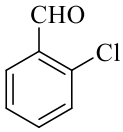
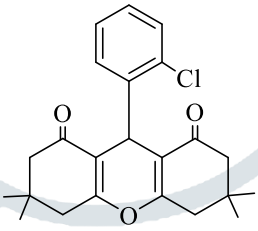
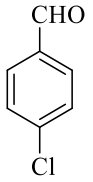
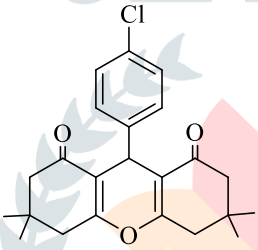
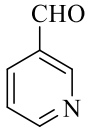
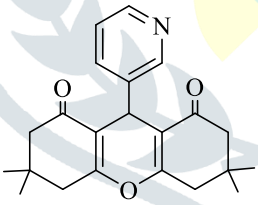
Entry	Concentration (mol %)	Yield (%)
1	2.5	45
2	5	60
3	7.5	86
4	10	96
5	12.5	96

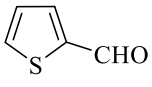
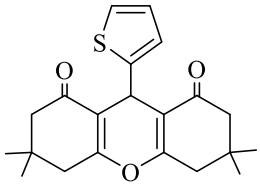
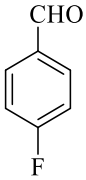
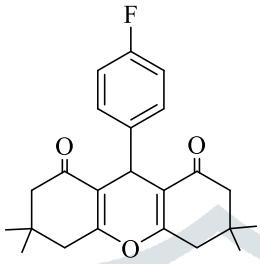
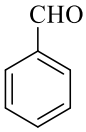
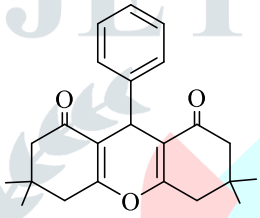
Scope and general applicability of the this methodology were studied by subjecting a broad range of structurally diverse aromatic aldehydes, having electron withdrawing (nitro) and electron donating groups (methyl, methoxy, hydroxy, chloro) as well as hetero aromatic aldehydes (pyridine-3-carbaldehyde, thiophene-2-carbaldehyde and furan-2-carbaldehyde), with dimedone under the found optimized conditions power level at 450W in the presence of 10 mol% Rochelle salt catalyst (Entry1-11, Table-3).

It is observed that all the reactions are taking place within shorter reaction time from 2 to 5 minutes with good to excellent (80-96 %) yield of the product. The obtained results indicate that the aldehydes having electron donating groups were reacts slowly as compared to aldehydes having electron withdrawing groups.

Table 3: *Rochelle salt catalyzed synthesis of 1, 8-dioxo-octahydroxanthene (3a-k) derivatives under the optimized reaction conditions*

Entry	**Aldehydes**	**Product**	**Time (min)**	**Yield (%)**	**MP (°C)** Found	**MP (°C)** Reported
1		 3a	2	96	222-224	223-225[17]
2		 3b	2	95	166-168	169-172[20]
3		 3c	4	80	246-248	244-247[20]
4		 3d	5	90	240-242	241-243[17]

5		 3e	5	81	216-218	216-218[20]
6		 3f	3	93	224-226	227-230[20]
7		 3g	3	94	226-228	230-232[23]
8		 3h	3	83	206-208	204-206[18]

9		 3i	2	85	166-168	162-164[23]
10		 3j	2	92	226-228	230-231[20]
11		 3k	2	90	202-204	201-203[17]

Spectroscopic analysis data of the principal compounds:

3,3,6,6-tetramethyl-9-(4-nitrophenyl)-3,4,5,6,7,9- hexahydro-1H-xanthene-1,8(2H)-dione (3a):

IR (KBr, cm^{-1}): 2961, 2870, 2589, 1636, 1620, 1512, 1464, 1411, 1380, 1117-1016; ^{1}H-NMR (500 MHz, $CDCl_3$, δ ppm): 8.13-8.11(d, 2H, Ar-H), 7.25-7.23 (d, 2H, Ar-H), 5.53 (s, 1H, CH), 2.50-2.23 (m, 8H, $4CH_2$), 1.23 (s, 6H, $2CH_3$), 1.11 (s, 6H, $2CH_3$); ^{13}C-NMR (500 MHz, $CDCl_3$, δ ppm): 197.61, 190.95, 189, 160.55, 146.58, 146.11, 127.66, 123.50, 119.65, 114.69, 52.88, 46.98, 46.39, 41.37, 33.25, 31.47, 29.49, 28.03, 27.46, 25.92; LC-MS (m/z): 396.224 (M+1); (M. F. & M. Wt. $C_{23}H_{25}NO_5$ and 395.2).

3,3,6,6-tetramethyl-9-(pyridine)-3,4,5,6,7,9- hexahydro-1H-xanthene-1,8(2H)-dione (3h):

IR (KBr, cm^{-1}): 3095, 3046, 2932, 2821, 1637, 1623, 1500, 1468, 1411, 1146; ^{1}H-NMR (500 MHz, $CDCl_3$, δ ppm): 8.40-8.36 (m, 2H, Ar-H), 7.39-7.19 (m, 2H, Ar-H), 5.54 (s, 1H, CH), 2.39-2.22 (s, 8H, $4CH_2$), 1.16 (s, 6H, $2CH_3$), 1.06 (s, 6H, $2CH_3$); ^{13}C-NMR (500 MHz, $CDCl_3$, δ ppm): 197.53, 190.28, 160.48, 140.53, 146.88, 134.59, 133.96, 123.01, 119.64, 114.61, 52.87, 46.71, 41.36, 31.47, 31.39, 31.01, 29.52, 28.02, 27.48, 25.91; LC-MS (m/z): 352.18 (M+1); (M.F. & M. Wt. $C_{22}H_{25}NO_3$ & 351.2).

IV. CONCLUSION

We have developed a new green, simple and efficient methodology for the synthesis of 1, 8-dioxo-octahydroxanthene derivatives from substituted aromatic aldehydes, dimedone (active methylene compound) in the presence of Rochelle salt (10 mol %) catalyst in water medium under microwave irradiated at power 450 Watt.

V. ACKNOWLEDGEMENTS

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