

INTRODUCING AN EFFECTIVE NANOCATALYTIC FOR THE ONE-POT SYNTHESIS AND INVESTIGATION OF BIOLOGICAL PROPERTIES OF PYRANOPYRIMIDINONE AND XANTHENE DERIVATIVES

A. AMININIA ^a, K. POURSHAMSIAN ^{a*} AND B. SADEGHI ^a

^aDepartment of Chemistry, Tonekabon branch, Islamic azad university, Tonekabon, Iran.

ABSTRACT

In this study, an effective method for the synthesis of pyranopyrimidinone and xanthene derivatives is introduced. In this method, zinc oxide-chitosan nanocomposite has been used as a catalyst and all reactions were performed under irradiated in a microwave oven at a power of 230W. The properties of zinc oxide-chitosan nanocomposite were characterized by X-ray diffraction (XRD), energy dispersive X-ray (EDAX) analysis and scanning electron microscopy (SEM). The results indicated that the size of zinc oxide-chitosan nanocomposite varies between 76–95 nm. The catalyst activity has maintained its activity after four runs. The main advantages of this method are; Eco-friendly procedure, catalytic synthesis of affordable and inexpensive materials, short reaction time, and excellent yields which makes it more economic than the other conventional methods. The antibacterial activity of the products was investigated using Minimum Inhibitory Concentration (MIC) and the Minimum Bactericidal Concentration (MBC) methods. Pyranopyrimidinone derivatives exhibit more antibacterial activity.

Keywords: Zinc oxide-chitosan nanocomposite, microwave, pyranopyrimidinone, xanthene, Biological activity, MIC, MBC.

INTRODUCTION

Pyranopyrimidinone and xanthene derivatives are widely used in pharmaceutical chemistry [1]. This group of organic compounds have various pharmaceutical activities such as antiviral², antibacterial³, antitumor [4], hepatoprotective [5], antifungal activities [6], in the food industry as additives [7] and anti-inflammatory properties [8]. In order to synthesize this class of compounds, several methods have been reported, including the reaction of the palladium-catalysed cyclisation [9-12], different Lewis acids such as NbCl₅ [13-16] and Brønsted acids [17-20].

Many of the reported methods for synthesizing these compounds have limitations, including strong acidic conditions, long reaction times, low yields, N₂ atmosphere, expensive reagents and toxic organic solvents [21-25]. Given the limitations, it seems that the introduction of a more appropriate, new and effective high-activity catalyst for the synthesis of these important drug compounds is necessary.

In almost all organic reactions that require heat to produce the product, traditional heating methods such as an oil bath or a sand bath are used. These methods cause certain problems, such as sudden rise in temperature or temperature constraints, which can lead to product decomposition or the production of side products. While heating up the reaction by microwave, in addition to solving the problems created by heating in the traditional ways can be very rapid and generate a heat system that cannot be easily accessed by other methods [26-30]. The main advantage of using microwave in synthesis of organic compounds is the shorter reaction times.

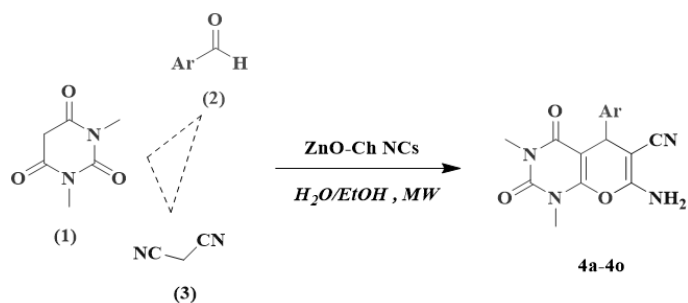
The goal of this study is introduction of efficient method using a new catalyst with high activity, shorten the reaction time, recyclability, and simple reaction working-up for the preparation of pyranopyrimidinone and xanthene derivatives under neutral, mild and practical conditions.

RESULTS AND DISCUSSION

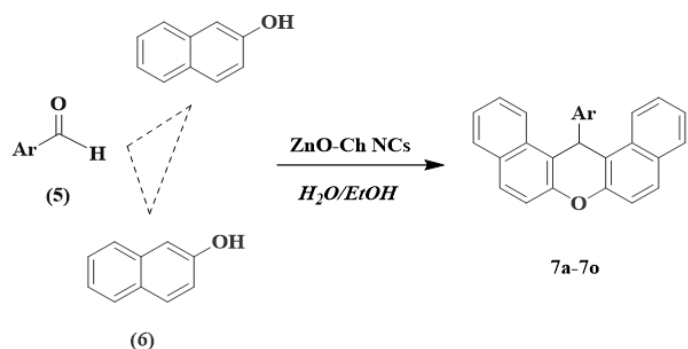
In continuation of our previous studies [31-37], our research team has tried to introduce a simple and effective method for the synthesis of pyrano[2,3-d]pyrimidine and xanthene derivatives.

The results show that the use of the ZnO-Ch NCs as a catalyst with microwave radiation significantly increases the reaction speed. Also, the catalyst produced a good yield on products in neutral conditions and in ecofriendly solvents. In the conditions, the working-up of the reaction is also very easy. (Schemes 1 and 2).

The morphology of the ZnO-Ch NCs was investigated with a scanning electron microscopy (SEM). Figure 1 (left) illustrated that the ZnO-Ch NCs was with an average size of 85 nm. SEM image at higher magnification is also shown in Figure 1 (right).



Scheme 1. Synthesis of pyrano[2,3-d]pyrimidine derivatives.



Scheme 2. Synthesis of xanthene derivatives.

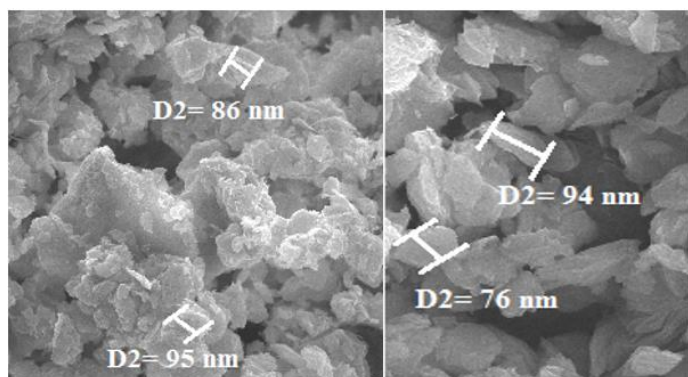


Figure 1. SEM images of a ZnO-Ch NCs. higher magnification; View field: 3.5 μm (right), lower magnification; View field: 8.5 μm (left).

The chemical purity of the samples was tested by EDAX spectra. The EDAX spectra given in Figure 2 shows the presence of zinc, oxygen, carbon and nitrogen as the only elementary components.

The X-ray diffraction patterns (XRD) of the ZnO-Ch NCs is shown in Figure 2. XRD study of ZnO-Ch NCs confirmed presence of ZnO in the ZnO-Ch NCs (Figure 2).

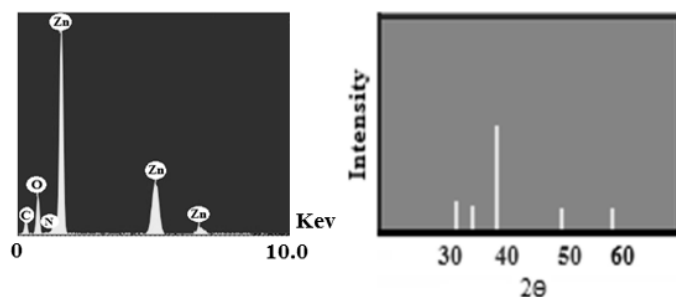


Figure 2. EDAX spectra of ZnO-Ch NCs (left) and XRD patterns of ZnO-starch nanocomposite (right).

Initially, in order to find optimal conditions for the synthesis of pyranopyrimidinone and xanthene derivatives, reactions were designed in different conditions. The results are tabulated in Tables 1 and 2. The optimized reaction conditions are shown with red pen (Table 1 entry 13 and Table 2, entry 11).

In scheme 3, a proposed mechanism for the synthesis of pyranopyrimidinone and xanthene derivatives in the presence of a catalyst was introduced. In synthesis process of pyranopyrimidinone derivatives, initially via a Knoevenagel reaction of activated malononitrile and activated aromatic aldehyde was formed the yellowish arylidenemalononitrile in a quantitative yield. The formation of the pyranopyrimidinone derivatives is shown in scheme 3.

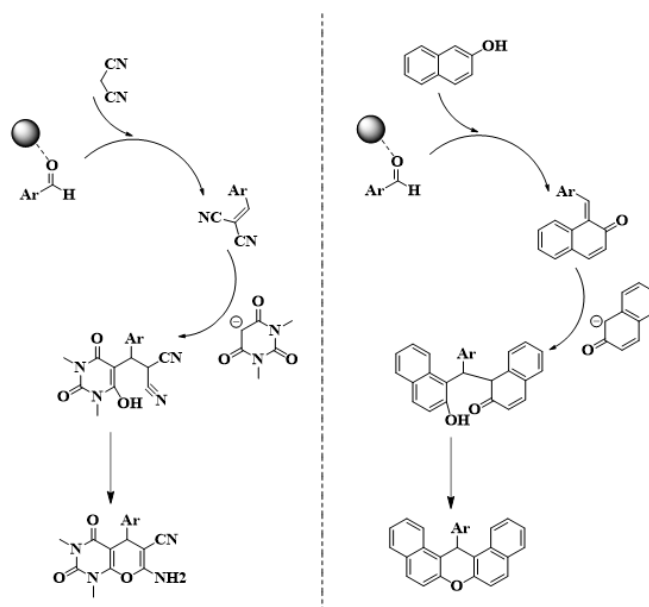
Table 1. Effect of temperature, amount of the catalyst and solvent on the synthesis of 4a in the presence of ZnO-Ch NCs.

Entry	Catalyst amount (mg)	Solvent	Temperature (°C)	Time (min)	Yield (%)
1	5	H ₂ O	MW	10	-
2	10	H ₂ O	MW	10	33
3	15	H ₂ O	MW	10	54
4	20	H ₂ O	MW	10	72
5	25	H ₂ O	MW	10	75
6	27	H ₂ O	MW	10	80
7	28	H ₂ O	MW	10	84
8	30	H ₂ O	MW	10	85
9	35	H ₂ O	MW	10	86
10	28	EtOH	MW	10	80
11	28	DMF	MW	10	61
12	28	CH ₂ Cl ₂	MW	10	70
13	28	EtOH/H ₂ O (1/1)	MW	10	93
14	28	H ₂ O	Reflux	45	79
15	28	EtOH/H ₂ O (1/1)	Reflux	25	77
16	28	EtOH/H ₂ O (1/1)	Reflux	35	81
17	28	EtOH/H ₂ O (1/1)	Reflux	45	87
18	28	EtOH/H ₂ O (1/1)	Reflux	60	92
19	28	Solvent free	MW	60	38

Table 2. Effect of temperature, amount of the catalyst and solvent on the synthesis of 7c in the presence of ZnO-Ch NCs.

Entry	Catalyst amount (mol%)	Solvent	Temperature (°C)	Time (min)	Yield (%)
1	5	H ₂ O	MW	15	38
2	10	H ₂ O	MW	15	57
3	15	H ₂ O	MW	15	60
4	20	H ₂ O	MW	15	69
5	25	H ₂ O	MW	15	72
6	30	H ₂ O	MW	15	81
7	35	H ₂ O	MW	15	83
8	30	EtOH	MW	15	79
9	30	DMF	MW	15	65
10	30	CH ₂ Cl ₂	MW	15	72
11	30	EtOH/H ₂ O (1/1)	MW	15	92
12	30	H ₂ O	Reflux	45	80
13	30	EtOH/H ₂ O (1/1)	Reflux	25	67
14	30	EtOH/H ₂ O (1/1)	Reflux	35	74
15	30	EtOH/H ₂ O (1/1)	Reflux	45	87
16	30	EtOH/H ₂ O (1/1)	Reflux	60	92
17	30	Solvent free	MW	60	38

After obtaining optimal reaction conditions, in order to produce the corresponding products in high yields and in short reaction times, various aromatic aldehydes were reacted with malononitrile and barbituric acid in synthesis of pyranopyrimidinone derivatives and also, with β -naphthol in synthesis of xanthene derivatives. The obtained results are summarized in tables 3 and 4.



Scheme 3. proposed mechanism for the synthesis of pyranopyrimidinone and xanthene derivatives in the presence of ZnO-starch nanocomposite.

Table 3. Preparation of pyranopyrimidinone derivatives using ZnO-starch nanocomposite.

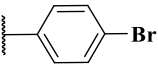
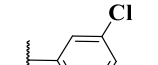
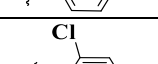
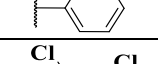
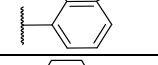
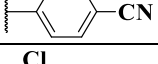
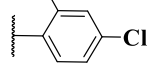
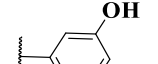
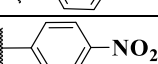
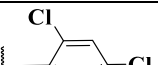
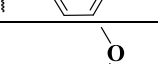
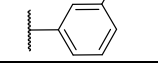
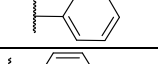
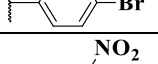
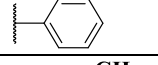
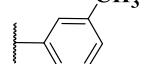
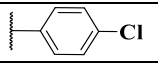
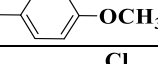
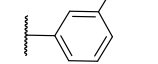
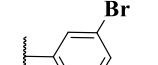
Entry	Structure	Time (min)	Yield (%)	mp		Product
				Found	Reported (Ref)	
1		12	91	230-231	235-237 [38-40]	4a
2		13	92	240-241	245-247 [41]	4b
3		14	85	240-241	247-249 [42]	4c
4		19	81	240-242	250-251 [43]	4d
5		11	95	254-256	265-266 [43]	4e
6		18	85	241-242	238-239 [44]	4f
7		17	90	158-160	165-166 [45]	4g
8		11	91	239-240	241-242 [45]	4h
9		12	93	250-251	260-261 [46]	4i

Table 4. Preparation of xanthene derivatives using ZnO-starch nanocomposite

Entry	Structure	Time (min)	Yield (%)	mp		Product
				Found	Reported (Ref)	
1		14	88	251-252	255-257 [47]	7a
2		15	91	181-183	179-181 [48]	7b
3		12	92	184-185	187-189 [49]	7c
4		17	88	303-305	310-312 [50]	7d
5		17	95	213-215	217-220 [50]	7e
6		11	95	197-200	190-192 [51]	7f
7		14	90	288-290	295-297 [52]	7g
8		13	89	215-217	219-221 [53]	7h
9		14	88	217-220	225-227 [53]	7i
10		12	85	198-200	201-202 [54]	7j
11		15	89	255-258	265-266 [55]	7k

Recycling and Reusing of the nanocatalyst

One of the most important features of a heterogeneous catalyst is its ability to recycle and reuse it. In order to investigate the recyclability of ZnO-Ch NCs, after completion of the reaction, the catalyst was filtered and washed well with plenty of water and acetone. The results showed that the catalyst activity has maintained its activity after four runs (Figure 3).

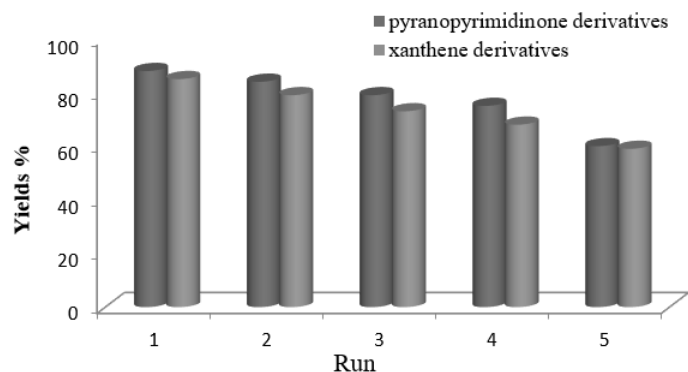


Figure 3. Reusability of nano catalyst in synthesis of pyranopyrimidinone and xanthene derivatives.

Biology

Antibacterial activity of all of the all synthesized products were evaluated *in vitro* against *Staphylococcus aureus* (*S. aureus*) and *Escherichia coli* (*E. coli*), by MIC and MBC method. Tetracycline used as a positive control. All the synthesized products showed good antibacterial activity. According to the results, pyranopyrimidinone derivatives had stronger antibacterial activity against *S. aureus* and *E. coli* than the xanthene derivatives. The MIC and MBC Results are tabulated in Tables 5 and 6.

Table 5. Results of *in vitro* antibacterial activity with MIC method against *S. aureus* of synthesized compounds.

Sample	MIC $\mu\text{g/mL}$						MBC $\mu\text{g/mL}$
	2000	1000	500	250	125	62.5	
4a	Inhibit.	Inhibit.	Inhibit.	Inhibit.	Grow.	Grow.	250
4b	Inhibit.	Inhibit.	Inhibit.	Inhibit.	Grow.	Grow.	250
4c	Inhibit.	Inhibit.	Inhibit.	Inhibit.	Grow.	Grow.	250
4d	Inhibit.	Inhibit.	Inhibit.	Inhibit.	Grow.	Grow.	250
4e	Inhibit.	Inhibit.	Inhibit.	Inhibit.	Grow.	Grow.	250
4f	Inhibit.	Inhibit.	Inhibit.	Inhibit.	Grow.	Grow.	250
4g	Inhibit.	Inhibit.	Inhibit.	Inhibit.	Grow.	Grow.	250
4h	Inhibit.	Inhibit.	Inhibit.	Inhibit.	Grow.	Grow.	250
4i	Inhibit.	Inhibit.	Inhibit.	Inhibit.	Grow.	Grow.	250
7a	Inhibit.	Inhibit.	Inhibit.	Grow.	Grow.	Grow.	500
7b	Inhibit.	Inhibit.	Inhibit.	Grow.	Grow.	Grow.	500
7c	Inhibit.	Inhibit.	Inhibit.	Grow.	Grow.	Grow.	500
7d	Inhibit.	Inhibit.	Inhibit.	Grow.	Grow.	Grow.	500
7e	Inhibit.	Inhibit.	Inhibit.	Grow.	Grow.	Grow.	500
7f	Inhibit.	Inhibit.	Inhibit.	Grow.	Grow.	Grow.	500
7g	Inhibit.	Inhibit.	Inhibit.	Grow.	Grow.	Grow.	500
7h	Inhibit.	Inhibit.	Inhibit.	Grow.	Grow.	Grow.	500
7i	Inhibit.	Inhibit.	Inhibit.	Grow.	Grow.	Grow.	500
7j	Inhibit.	Inhibit.	Inhibit.	Grow.	Grow.	Grow.	500
7k	Inhibit.	Inhibit.	Inhibit.	Grow.	Grow.	Grow.	500
Tetracycline	Inhibit.	Inhibit.	Inhibit.	Inhibit.	Inhibit.	Inhibit.	< 62.5

Table 6. Results of *in vitro* antibacterial activity with MIC method against *E. coli* of synthesized compounds.

Sample	MIC $\mu\text{g/mL}$						MBC $\mu\text{g/mL}$
	2000	1000	500	250	125	62.5	
4a	Inhibit.	Inhibit.	Inhibit.	Grow.	Grow.	Grow.	500
4b	Inhibit.	Inhibit.	Inhibit.	Grow.	Grow.	Grow.	500
4c	Inhibit.	Inhibit.	Inhibit.	Grow.	Grow.	Grow.	500
4d	Inhibit.	Inhibit.	Grow.	Grow.	Grow.	Grow.	1000
4e	Inhibit.	Inhibit.	Grow.	Grow.	Grow.	Grow.	1000
4f	Inhibit.	Inhibit.	Grow.	Grow.	Grow.	Grow.	1000
4g	Inhibit.	Inhibit.	Grow.	Grow.	Grow.	Grow.	1000
4h	Inhibit.	Inhibit.	Grow.	Grow.	Grow.	Grow.	1000
4i	Inhibit.	Inhibit.	Grow.	Grow.	Grow.	Grow.	1000
7a	Inhibit.	Inhibit.	Grow.	Grow.	Grow.	Grow.	1000
7b	Inhibit.	Inhibit.	Grow.	Grow.	Grow.	Grow.	1000
7c	Inhibit.	Inhibit.	Grow.	Grow.	Grow.	Grow.	1000
7d	Inhibit.	Inhibit.	Grow.	Grow.	Grow.	Grow.	1000
7e	Inhibit.	Inhibit.	Grow.	Grow.	Grow.	Grow.	1000
7f	Inhibit.	Inhibit.	Grow.	Grow.	Grow.	Grow.	1000
7g	Inhibit.	Inhibit.	Grow.	Grow.	Grow.	Grow.	1000
7h	Inhibit.	Inhibit.	Grow.	Grow.	Grow.	Grow.	1000
7i	Inhibit.	Inhibit.	Inhibit.	Grow.	Grow.	Grow.	500
7j	Inhibit.	Inhibit.	Inhibit.	Grow.	Grow.	Grow.	500
7k	Inhibit.	Inhibit.	Inhibit.	Grow.	Grow.	Grow.	500
Tetracycline	Inhibit.	Inhibit.	Inhibit.	Inhibit.	Inhibit.	Inhibit.	< 62.5

Figure 6 shows an overview of the steps to perform the MIC test on product 4a against *S. aureus* (positive germ) and *E. coli* (negative germ).

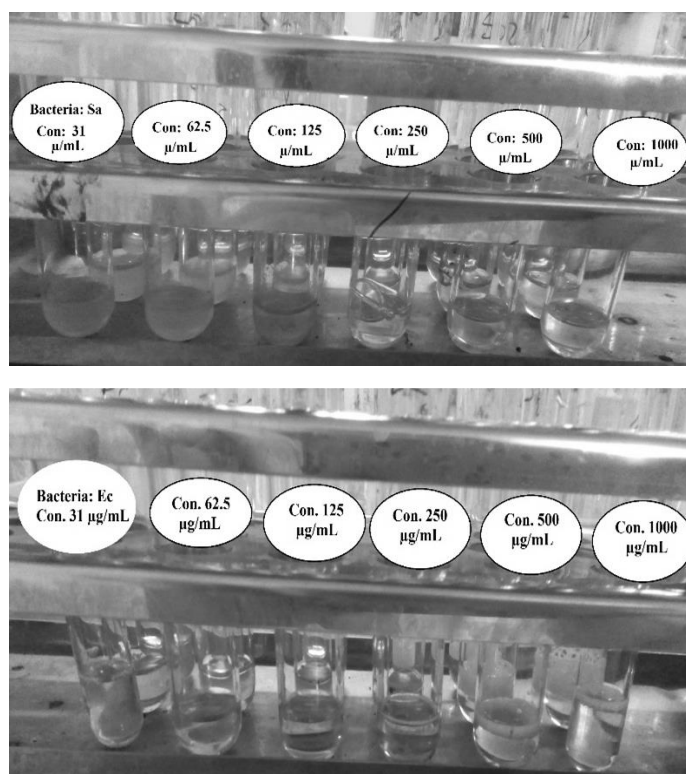


Figure 6. Perform MIC test on product 4a and against *S. aureus* (gram positive) and *E. coli* (gram negative).

EXPERIMENTAL

Material and Instrumentation

The chemicals used in the synthesis of the pyranopyrimidinone and xanthene derivatives were obtained from the Merck and Aldrich Chemical Co. All chemicals and solvents were analytical reagent grade. Reactions were monitored by thin layer chromatography on 0.2 mm silica gel F-252 (Merck) plates. Melting points were determined by open capillary Electrothermal 9100 s and were uncorrected. ^1H (400 MHz) and ^{13}C (100 MHz) spectra were recorded on Bruker 3000 NMR spectrometer in $\text{CDCl}_3/\text{DMSO}-d^6$ (with TMS as internal reference). Ultrasound device Astra 3D (9.5 L, 45 kHz frequency, input power with heating, 305 W, number of transducers, 2) from TECNO-GAZ was used. All the reactions were carried out in a microwave oven.

Preparation of ZnO-Chitosan nanocomposite (ZnO&Ch NCs)

The synthesis of the ZnO&Ch NCs according to the articles was done with some changes [56]. first 0.75 g of ZnO powder (9.2 mmol) was dissolved in 100 mL of 1% acetic acid solution. The solution is sonicated for 10 min. After this time 1 g of chitosan was added to the solution. The mixture was sonicated for 30 min. After this time, added a drop by drop of 1M NaOH solution to the mixture until the solution attained pH 10. The solution was heated in microwave oven for about 10 min. The mixture was then filtered and washed with distilled water several times then dried in an oven at 50°C for 1hr.

General procedure for the preparation of pyrano-pyrimidinones

A mixture of the aromatic aldehyde (1 mmol), malononitrile 1.2 mmol (~ 80 mg), barbituric acid 1 mmol (156 mg) in the presence of 28 mg ZnO-Ch NCs in $\text{H}_2\text{O}:\text{EtOH}$ (2ml:2ml) was irradiated in a microwave oven at a power of 230W. After completion of the reaction, the resulting solid (crude product) was filtered and then recrystallized from EtOH to obtain pure product. The physical data (m.p., NMR, IR) of these known compounds were found to identical with those reported in the literature.

Spectral data of selected compounds are given below;

7-amino-5-(3-chlorophenyl)-2,4-dioxo-1,3,4,5-tetrahydro-2H-pyrano[2,3-d]pyrimidine-6-carbonitrile (4b); Dark yellow powder, m.p. 240–241°C. IR (KBr) ($\nu_{\text{max}}/\text{cm}^{-1}$): 3419, 3300(NH_2), 3186 (NH), 2192 ($\text{C}\equiv\text{N}$), 1689 and 1654 ($\text{C}=\text{O}$). $^1\text{H-NMR}$: $\delta=4.47$ (s, 1H, H-5), 7.28 (broad, 2H, H-Ar, NH_2), 7.61 (t, 1H, $^3J=7.6$ Hz, H-Ar), 7.74 (d, 1H, $^3J=7.6$ Hz, H-Ar), 7.61 (t, 1H, $^3J=7.6$ Hz, H-Ar), 8.06 (broad, 1H, H-Ar), 8.08-8.13 (m, 1H, H-Ar), 11.11 (s, 1H, NH), 12.16 (brs, 1H, NH) ppm.

7-amino-5-(2-chlorophenyl)-2,4-dioxo-1,3,4,5-tetrahydro-2H-pyrano[2,3-d]pyrimidine-6-carbonitrile (4c); Dark yellow powder, m.p. 240–241°C. IR (KBr) ($\nu_{\text{max}}/\text{cm}^{-1}$): 3410, 3370(NH_2), 3158 (NH), 2185 ($\text{C}\equiv\text{N}$), 1689 ($\text{C}=\text{O}$); $^1\text{H-NMR}$: $\delta=4.72$ (s, 1H, H-5), 7.153 (broad, 2H, NH_2), 7.208-7.281 (m, 3H, H-Ar), 7.36 (d, 1H, H-Ar), 11.06 (s, 1H, NH), 12.08 (board, 1H, NH) ppm.

7-amino-5-(2,3-dichlorophenyl)-2,4-dioxo-1,3,4,5-tetrahydro-2H-pyrano[2,3-d]pyrimidine-6-carbonitrile (4d); White color powder, m.p. 240–242°C. IR (KBr) ($\nu_{\text{max}}/\text{cm}^{-1}$): 3401, 3385 (NH_2), 3255 (NH), 2225 ($\text{C}\equiv\text{N}$), 1688, 1642 ($\text{C}=\text{O}$).

7-amino-5-(4-nitrophenyl)-2,4-dioxo-1,3,4,5-tetrahydro-2H-pyrano[2,3-d]pyrimidine-6-carbonitrile (4h); White color powder, m.p. 239– 240°C. IR (KBr) ($\nu_{\text{max}}/\text{cm}^{-1}$): 3477, 3238 (NH_2), 3127 (NH), 2192 ($\text{C}\equiv\text{N}$), 1677, 1645 ($\text{C}=\text{O}$); $^1\text{H-NMR}$: $\delta=4.42$ (s, 1H), 7.21 (broad, 2H, NH_2), 7.52 (d, 2H, $^3J_{\text{HH}}=8.8$ Hz, H-Ar), 8.16 (d, 2H, $^3J_{\text{HH}}=8.8$ Hz, H-Ar), 11.12 (brs, 1H, NH), 12.17.

General procedure for the synthesis of tetrahydrobenzo[a]xanthene

288 mg of β -naphthol (2 mmol), benzaldehyde (1 mmol) and 30 mg ZnO-Ch NCs were added to the reaction vessel containing $\text{H}_2\text{O}:\text{EtOH}$ (2 ml:2 ml). The solution was irradiated in a microwave oven at a power of 230 W. The progress of reactions monitored by TLC. After completion of the reaction, the reaction mixture was cooled to room temperature. Then the catalyst was separated by filtration. Finally, the crude product was recrystallized from EtOH to yield pure xanthene derivatives. All products were characterized by comparison of their melting point and FT-IR spectra with references. Some of them were $^1\text{H-NMR}$ spectral to prove the structure of the compounds.

Spectral data of selected compounds are given below;

14-phenyl-14H-dibenzo[a,j]xanthene (7c); White solid, mp 184-185 °C , IR (KBr, cm^{-1}): $\nu_{\text{max}}= 3069, 3041, 2927, 1614, 1581, 1508, 1474, 1361$; $^1\text{H NMR}$

(400 MHz, CDCl_3): $\delta = 6.53$ (s, 1H, CH), 7.045 (t, J = 7.2 Hz, 1H, ArH), 7.183 (t, J = 7.2 Hz, 2H, ArH), 7.450 (t, J = 7.5 Hz, 2H, ArH), 7.53–7.60 (m, 6H, ArH), 7.621 (t, J = 8 Hz, 4H, ArH), 8.437 (d, J = 8 Hz, 2H, ArH) ppm.

14-(3-methylphenyl)-14H-dibenzo[a,j]xanthene (7f); Yellow solid, mp 197-200 °C. IR (KBr, cm^{-1}): $\nu_{\text{max}}= 3018, 2921, 1623, 1591, 1512, 1457, 1400, 1249, 960, 806, 806, 743$; $^1\text{H NMR}$ (400 MHz, CDCl_3): $\delta = 2.074$ (s, 3H, CH_3), 6.67 (s, 1H, CH), 6.77 (d, J = 7.6 Hz, 1H, ArH), 7.04 (t, J = 7.6 Hz, 1H, ArH), 7.312 (s, 1H, CH), 7.454 (m, 2H, ArH), 7.537 (s, 1H, CH), 7.56 (d, J = 8.8 Hz, 2H, ArH), 7.630 (m, 2H, ArH) ppm, 7.908-7.936 (m, 4H, ArH) ppm, 8.671 (d, J = 8.4 Hz, 2H, ArH) ppm.

14-(4-methoxyphenyl)-14H-dibenzo[a,j]xanthene (7h); White solid, mp 215-217°C. IR (KBr, cm^{-1}): $\nu_{\text{max}}= 3072, 2834, 1622, 1592, 1509, 1458, 1438, 1399, 1249, 1082$. $^1\text{H NMR}$ (400 MHz, CDCl_3): $\delta = 3.377$ (s, 3H, CH_3), 6.68 (s, 1H, CH), 6.69 (d, J = 8.4 Hz, 2H, ArH), 7.456 (t, J = 7.2 Hz, 2H, ArH), 7.53 (t, J = 7.5 Hz, 4H, ArH), 7.621 (t, 2H, ArH), 7.926 (t, J = 8.4 Hz, 4H, ArH), 8.66 (d, J = 8.4 Hz, 2H, ArH) ppm.

14-(3-chlorophenyl)-14H-dibenzo[a,j]xanthene (7i); White solid, mp 217-220°C. IR (KBr, cm^{-1}): $\nu_{\text{max}}= 3467, 3057, 1658, 1622, 1591, 1514, 1473, 1458, 1431, 1400, 1240, 1238$. $^1\text{H NMR}$ (400 MHz, CDCl_3): $\delta = 6.73$ (s, 1H, CH), 7.00 (t, J = 8.4 Hz, 1H, ArH), 7.07 (t, J = 7.2 Hz, 1H, ArH), 7.31 (d, J = 8 Hz, 1H, ArH), 7.43 (s, 1H, ArH), 7.46 (t, 2H, ArH), 7.53 (d, J = 8.4 Hz, 2H, ArH), 7.62 (d, J = 7.2 Hz, 2H, ArH), 7.93 (d, J = 8.4 Hz, 4 H, ArH), 8.59 (d, J = 8.4, 2H, ArH) ppm.

14-(3-bromophenyl)-14H-dibenzo[a,j]xanthene (7j); White solid, mp 198-200°C. IR (KBr, cm^{-1}): $\nu_{\text{max}}= 3065, 2923, 1622, 1590, 1566, 1514, 1472, 1456, 1432, 1392, 1239$. $^1\text{H NMR}$ (400 MHz, CDCl_3): $\delta = 6.76$ (s, 1H, CH), 7.11 (t, J = 7.6 Hz, 1H, ArH), 7.17-7.19 (m, 1H, ArH), 7.47 (t, J = 7.2 Hz, 2H, ArH), 7.57 (d, 2H, J = 8.8 Hz, ArH), 7.63-7.67 (m, 3H, ArH), 7.81 (broad, 1H, ArH), 7.94 (d, J = 8.8 Hz, 4H, ArH), 8.70 (d, J = 8.4, 2H, ArH) ppm.

Recycling and reusing of the nanocatalyst

The catalyst used after the completion of the reaction is filtered and washed with plenty of water and acetone and then dried at 70 °C for 8 h. The reusability of the catalyst was tested by repeating the reaction in its optimal conditions. The results showed that the catalytic activity of the ZnO-Ch NCs did not decrease significantly even after four catalytic cycles.

Biology

MIC assay

To prepare a liquid culture medium, first 0.8 gr of Nutrient Broth was added into 100 ml of distilled water and then 1 ml of it was added into the test tube. The test tubes were autoclaved at 115 °C for 15 minutes.

Six concentrations of each sample were prepared (1000, 500, 250, 125, 62.5, 31.25 $\mu\text{g}/\text{ml}$) in DMSO. 1 ml of samples were added to the autoclaved test tubes. The concentration of the standard bacteria (0.5 McFarland standard) was made. 100 μl of each bacterium was poured into each test tube. The tubes were incubating overnight. Broth tubes that appear turbid are indicative of bacterial growth while tubes that remain clear indicate no growth. The MIC of the antibiotic is the lowest concentration that does not show growth.

MBC assay

The concentration of sample which showed MIC and two higher concentrations were applied to MBC test. The concentration in which the bacterium has not grown is reported as MBC.

CONCLUSION

In conclusion this paper describes a convenient and efficient process for the synthesis of corresponding pyranopyrimidinone and xanthene derivatives in the presence of ZnO-Ch NCs under microwave radiation. The protocol used in this research has many advantages such as reduced time, low cost, the simplicity of using the catalyst, separating the catalyst only by filtering, recycling the catalyst, simple processing. In many cases, the products crystallized directly from the reaction mixture in high purity. In general, in this method, aldehydes bearing electron-donating groups require more time to complete the reaction, but the rate of formation of the product in aldehydes with electron-withdrawing groups will be higher. It was observed that ZnO-Ch NCs catalyzed both types of reactions well under microwave irradiation and green solvent to the formation of the corresponding pyranopyrimidinone and xanthene derivatives.

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