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NICKEL OXIDE NANOPARTICLES AS SUSTAINABLE CATALYSTS FOR EFFICIENT SYNTHESIS AND ANTI-MICROBIAL EVALUATION OF 2-AMINO-4*H*-PYRAN DERIVATIVES

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ABSTRACT. In the current paper, nickel oxide nanoparticles (NiO NPs) was successfully applied as a sustainable effective and recoverable catalyst for the preparation of 2-amino-*4H* pyran derivatives **2-11** *via* one-pot, three-component reaction of 4-formylphenyl-4-methyl benzenesulfonate (**1**) with malononitrile and active methylene compounds in green solvent water and ethanol in ratio (3:1) in excellent yield (95-98%) and shorter reaction time (5-8 min). The structures of the pyran derivatives were elucidated by elemental and spectral analyses such as IR, ^{1}H NMR, ^{13}C NMR and DEPT 135 spectra. Moreover, the characterization of the catalyst after and before the reaction were studied using X-ray diffraction (X-RD), scanning electron microscope (SEM), EDX techniques and IR-spectra. It has been indicated that catalyst has the same efficiency. The application of this protocol has many advantages such as eco-friendly, inexpensive, simple protocol and easy recovery of the catalyst. Overall products are designed, synthesized and studied for their anti-microbial evaluation. It has been found that is compounds **2**, **3**, **7** and **10** are the most active against antibacterial compression with the stander drug Ampicillin. On the other hand, Compounds **2**, **3**, **8,** and **11** displayed the most promising antifungal activities with Amphotericin B.

KEY WORDS: Nickel oxide nanoparticles, Pyran derivatives, X-Ray diffraction (X-RD), Antimicrobial evaluation, One-pot, Three-component reaction

INTRODUCTION

It is known that pyran derivatives are an important compound in organic chemistry [1] due to their wide application in the field of medicinal and pharmaceutical chemistry such as antitumor, antiviral, antimicrobial, alzheimer's disease, anti-proliferative, sex pheromone, natural pigments [2-4], in addition to anti-aging agents and antiviral. Moreover, multi-component reaction are useful in organic synthesis [5, 6] due to their higher yields, shorter reaction times, easier procedures, lower cost compared to multistep reactions in addition to an eco-friendly application [7-10]. Recently the use of catalysts has become very important in organic synthesis which plays a crucial role in the creation of fine compounds [11-15]. Today every scientific and technological discipline, including catalysis, has become very interested in transition metal nanoparticles [16-

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18]. Numerous studies on the transition metal nanoparticles demonstrated their extraordinary level of performance as catalysts in terms of selectivity, reactivity, and increased product yields [19, 20]. One of the most important catalyst is NiO NPs due to their eco-friendly, cheap, simplicity and easy recoverable [21]. Furthermore, it has been extensively studied as catalysts in various applications such as catalysis, sensing, batteries, solar cells, and regioselective synthesis of triazole derivatives. Also it applied as p-type semiconductor, which is characterized by stable wide band gap (3.6–4.0 eV) [22]. Additionally, NiO NPs are used as an efficient catalyst for the multicomponent one-pot synthesis in organic synthesis derivatives [21-23].

Our goal in this study is the designing of *4H*-pyran derivatives in the presence of NiO NPs as a green catalyst. Eco-friendly, low cost, and simplicity in synthesis, in addition to investigation their anti-microbial Evaluation.

EXPERIMENTAL

Chemicals and instruments

All of the chemical components were purchased from Aldrich and used without further processing. All reactions were monitored by thin layer chromatography (TLC) using precoated plates of silica gel G/UV-254 of 0.25 mm thickness (Merck 60F254). The X-rays diffracted (Bruker *D8*) are recorded on a scintillation counter detector located behind a set of long Soller slits/parallel foils at a wavelength of 1.5406 Å from a generator operating at 40 kV and 40 mA. An FT-IR ALPHBROKER-Platinum-ATR spectrophotometer with the ATR method was used to gather infrared spectra. The ^{1}H NMR and 13C NMR spectra were captured using the DMSO-*d6* for the Bruker Bio Spin AG spectrometer at 400 MHz, respectively. The chemical shifts for ^{1}H NMR are measured in parts per million (ppm) in relation to tetramethyl silane (TMS), which serves as an internal standard. The Perkin-Elmer model, CHN analyzers, detected elemental analyses. The melting points were recorded with a Kofler melting point and uncorrected.

General procedure for the synthesis of pyran derivatives

A mixture of (0.1 mol) 4-formylphenyl 4-methyl benzenesulfonate with malononitrile (0.1 mol and appropriate carbonyl compounds (0.1 mol namely; 5-methyl-2,4-dihydro-3H-pyrazol-3-one, 5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one, ethyl benzoyl acetate, benzoyl acetone, cyclohexane 1,3-dione, 1,3-dimidone, cyclopentanone, acetylacetone, ethyl acetoacetate in presence of 0.40 g of NiO NPs was refluxed with stirred at 80 °C in a mixture solvent (H_2O/EtOH) in ratio 3:1 until the reaction completed (TLC). The reaction mixture was diluted with water and the product was filtered, washed with water, dried, and recrystallized from ethanol.

*p-Tolyl 4-(6-amino-5-cyano-3-methyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)benzene sulfonate (**2**).* IR; 3336, 3250, 3180 (NH_2 + NH), 2199 (C≡N) cm^{-1}; ^{1}H NMR: δ 12.04 (s, 1H, NH, D_2O disappear),7.72-6.77 (m, 10H, Ar-H+ NH_2, D_2O disappear), 4.62 (s, 1H, CH_{pyran}), 2.42 (s, 3H, CH_3), 1.74 (s, 3H, CH_3); ^{13}C NMR: δ: 161.46, 155.28, 148.34, 146.21, 144.08, 136.20, 132.14, 130.64, 129.67, 128.59, 128.50, 125.43, 122.91, 97.97, 97.79, 57.69, 36.19, 21.68, 10.07; DEPT 135 δ 130.56, 129.86, 128.60, 122,58, 36.07, 23.25, 21.67, 10.06; DEPT-135; anal. calcd. for $C_{21}H_{18}N_4O_4S$ (422.52): C (59.70%), H (4.29%), N (13.26%), S (7.59%); found C (59.41%), H (4.39%), N (13.23%). S (7.80%).

*p-Tolyl4-(6-amino-5-cyano-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)benzene-sulfonate (**3**).* IR; 3314, 3246 (NH_2), 2213 (C≡N), cm^{-1}; ^{1}H NMR: δ 7.80-7.78 (d, 2H, Ar-H), 7.71-7.69(d, 2H, Ar-H), 7.50-7.48(d, 2H, Ar-H), 7.56-7.44 (d, 2H, Ar-H), 7.29-7.27 (d, 2H, Ar-H), 7.18(s, 2H, NH_2, D_2O disappear), 7.03-7.01 (d, 2H, Ar-H), 4.70 (s, 1H, CH_{pyran}), 2.41 (s, 3H, Me), 1.73 (s, 3H, Me); ^{13}C NMR: δ 160.99, 155.81, 147.01, 146.72, 139.68, 138.24, 137.59, 137.09,

131.97, 130.75, 130.09, 129.26, 129.02, 128.51, 128.12, 126.80, 124.98, 123.27, 122.23, 120.35, 97.79, 57.38, 30.20, 21.60, 10.16; anal. calcd. for $C_{27}H_{22}N_4O_4S$ (498.68): C (65.05%), H (4.45%), N (11.24%), S (6.43%); found: C (65.18%), H (4.61%), N (11.32%), S (6.50%).

*Ethyl 6-amino-5-cyano-2-phenyl-4-(4-(tosyloxy)phenyl)-4H-pyran-3-carboxylate (**4**).* IR; 3369, 3268 (NH_2), 2221 (C≡N), 1724 (C=O), cm^{-1}; ^{1}H NMR: δ 7.87 - 7.80-6.93 (m, 5H, Ar-H + 2H, NH_2, D_2O disappear), 4.44 (s, 1H, CH_{pyran}), 4.9 - 4.05 (q, 2H, CH_2), 2.46 (s, 3H, CH_3), 1.10 - 1.05 (t, 3H, CH_3); ^{13}CNMR: δ 164.69, 158.20, 154.14, 147.34, 138.99, 136.90, 133.00, 132.94, 134.01, 130.93, 130.56, 128.90, 127.03, 126.10, 121.69, 119.14, 109.10, 61.26, 58.20, 37.09, 21.05, 14.21; anal. calcd. for $C_{28}H_{24}N_2O_6S$(516.56): C (65.10%), H (4.68%), N (5.42%), S (6.21%); found: C (65.15), H (4.62%), N (5.48%), S (6.32%).

*4-(2-Amino-5-benzoyl-3-cyano-6-methyl-4H-pyran-4-yl)phenyl4-methylbenzene sulfonate (**5**).* IR; 3316, 3276 (NH_2), 2198 (C≡N), 1671 (C=O) cm^{-1}; ^{1}H NMR: δ 7.58-7.53 (m, 5H, Ar-H), 7.48 (d, 2H, *J* = 8.0 Hz, Ar-H), 7.36 (d, 2H, *J* = 8.0 Hz, Ar-H), 7.13-7.06 (m, 4H, Ar-H), 6.93 (s, 2H, NH_2, D_2O disappear), 4.45 (s, 1H, CH_{pyran}), 2.42 (s, 3H, CH_3), 1.75 (s, 3H, CH_3); ^{13}C NMR: δ 191.24 (C=O), 158.06, 156.21, 147.98, 139.08, 138.58, 136.52, 134.15, 132.79, 132.59, 130.78, 130.47, 128.85, 126.43, 121.20, 119.80, 105.11, 58.13, 37.40, 21.90, 18.69; anal. calcd. for $C_{27}H_{22}N_2O_5S$ (486.53): C (66.65%), H (4.56%), N (5.76%), S (6.59%); found: (66.41%), H (4.61%), N (5.68%), S (6.51%).

*4-(2-Amino-3-cyano-5-oxo-5,6,7,8-tetrahydro-4H-chromen-4-yl)phenyl-4-methylbenzenesulfonate (**6**).* IR; 3334, 3258 (NH_2), 2195 (C≡N), 1682 (C=O), 1362, 1155 (SO_2); ^{1}H NMR: δ 7.78-7.76 (d, 2H, *J* = 8.0 Hz, Ar-H), 7.49-7.47 (d, 2H, *J* = 8.0 Hz, Ar-H), 7.19-7.17 (d, 2H, *J* = 8.0 Hz, Ar-H), 7.02 (s, 2H, NH_2, D_2O disappear), 6.97- 6.95 (d, 2H, *J* = 8.0 Hz, Ar-H), 4.22 (s, 1H, CH_{pyran}), 2.61 (s, 2H, CH_2), 2.46 (s, 3H, CH_3): 2.27 (s, 2H, CH_2), 1.95 (s, 2H, CH_2); ^{13}C NMR: δ 196.31, 165.21, 158.95, 148.02, 146.17, 144.38, 132.32, 130.72, 129.14, 128.51, 122.28, 120.01, 113.81, 58.25, 36.74, 35.39, 26.95, 21.64, 20.18: DEPT 135 δ 130.71, 129.14, 128.51, 122.28, 36.73, 26.94, 20.18; anal. calcd. for $C_{23}H_{20}N_2O_5S$ (436.48): C (63.29%), H (4.62%), N (6.42%), S (7.35%); found: C (63.36%), H (4.49%), N (6.56%), S (7.42%).

*4-(2-Amino-3-cyano-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromen-4-yl)phenyl-4-methylbenzenesulfonate (**7**).* IR; 3326, 3265 (NH_2), 2210 (C≡N), 1678 (C=Ocm^{-1}; ^{1}H NMR: δ 7.75-7.73 (d, 2H, Ar-H), 7.46 -6.44(d, 2H, Ar-H), 7.18-7.16 (d, 2H, Ar-H),7.03 (s, 2H, NH_2, D_2O disappear), 6.95-6.93 (d, 2H, Ar-H), 4.19 (s, 1H, CH_{pyran}), 2.41(s, 3H, CH_3), 2.27- 2.10 (d, 4H, $2CH_2$), 1.04 (s, 3H, CH_3), 0.93 (s, 3H, CH_3); ^{13}CNMR: δ 196.06, 163.10, 159.06, 148.03, 146.16, 144.31, 132.18, 130.65, 130.17, 129.53, 128.32, 122.98, 58.17, 50.42, 40.66,35.50, 32.24, 28.76, 27.29, 21.64: DEPT 135 δ 130.71, 129.14, 128.52, 122.29, 40.29, 35.39, 21.64; anal. calcd. for $C_{25}H_{24}N_2O_5S$ (464.48): C (64.64%), H (5.21%), N (6.03%), S (6.90%); found: C (64.66%), H (5.17%), N (6.12%), S (6.78%).

*4-(2-Amino-3-cyano-4,5,6,7-tetrahydrocyclopenta[b]pyran-4-yl)phenyl-4-methylbenzenesulfonate (**8**).* IR; 3315, 3283 (NH_2), 2190 (C≡N) cm^{-1}; ^{1}H NMR: δ 7.76 - 6.90 (10H, Ar-H NH_2, D_2O disappear), 4.40 (s, 1H, CH_{pyran}); 2.43 (s, 3H, CH_3), 1.98 - 1.94 (m, 4H, $2CH_2$) 1.91-1.85 (m, 2H, CH_2); ^{13}C NMR: δ 158.13, 148.14, 147.08, 137.82, 134.14, 132.22, 130.72, 130.34, 126.60, 121.10, 119.16, 107.71, 55.20, 40.52, 31.13, 27.30, 21.20, 18.32; Anal. Calcd. for $C_{22}H_{20}N_2O_4S$ (408.47): C (64.69%), H (4.94%), N (6.86%), S (7.85%) Found: C (64.52%), H (4.91%), N (6.80%), S (7.87%).

*4-(2-Amino-3-cyano-5,6,7,8-tetrahydro-4H-chromen-4-yl)phenyl-4-methylbenze nesulfonate (**9**).* IR; 3346, 3276 (NH_2), 2219 (C≡N) cm^{-1}; ^{1}H NMR: δ 7.69 - 6.94 (10H, Ar-H NH_2, D_2O disappear),

4.25 (s, 1H, CH_{pyran}), 2.50 (s, 3H, CH_3), 2.03-1.99 (m, 4H, $2CH_2$), 1.65-161 (m, 2H, CH_2), 1.58-1.31 (m, 2H, CH_2); ^{13}C NMR: δ 160.14, 146.16, 144.05, 137.95, 134.43, 132.06, 130.58, 130.09, 126.76, 119.99, 119.00, 110.04, 53.82, 37.97, 26.31, 22.38, 22.29, 22.05, 20.93; anal. calcd. for $C_{23}H_{22}N_2O_4S$ (422.49): C (65.38%), H (5.25%), N (6.63%), S (7.59%); found: C (65.34%), H (5.21%), N (6.41%), S (7.46%).

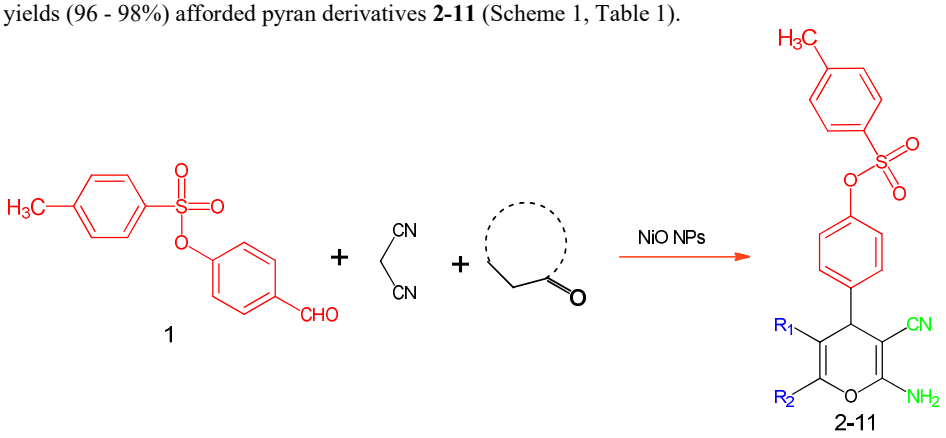
4-(3-Acetyl-6-amino-5-cyano-2-methyl-4H-pyran-4-yl)phenyl-4-methylbenzene sulfonate (***10***). IR; 3354, 3221 (NH_2), 2185 (C≡N), 1665 (C=O)cm^{-1}; ^{1}H NMR: δ 7.73-7.71 (d, 2H, Ar-H), 7.47-7.45(d, 2H, Ar-H), 7.20-7.18(d, 2H, Ar-H), 7.02-7.00(d, 2H, Ar-H), 6.77 (s, 2H, NH_2, D_2O disappear), 4.47 (s, 1H, CH_{pyran}), 2.43 (s, 3H, CH_3), 2.24 (s, 3H, CH_3), 2.04 (s, 3H, CH_3); ^{13}C NMR: δ 194.26, 159.31, 137.12, 136.58, 132.52, 132.17, 130.56, 130.36, 128.63, 128.12, 121.23, 118.04, 112.52, 58.19, 36.61, 27.46, 21.16, 18.21; anal. calcd. for $C_{22}H_{20}N_2O_5S$ (424.48): C (62.25%), H (4.75%), N (6.60%), S (7.55%); found: C (62.21%), H (4.68%), N (6.63%), S (7.51%).

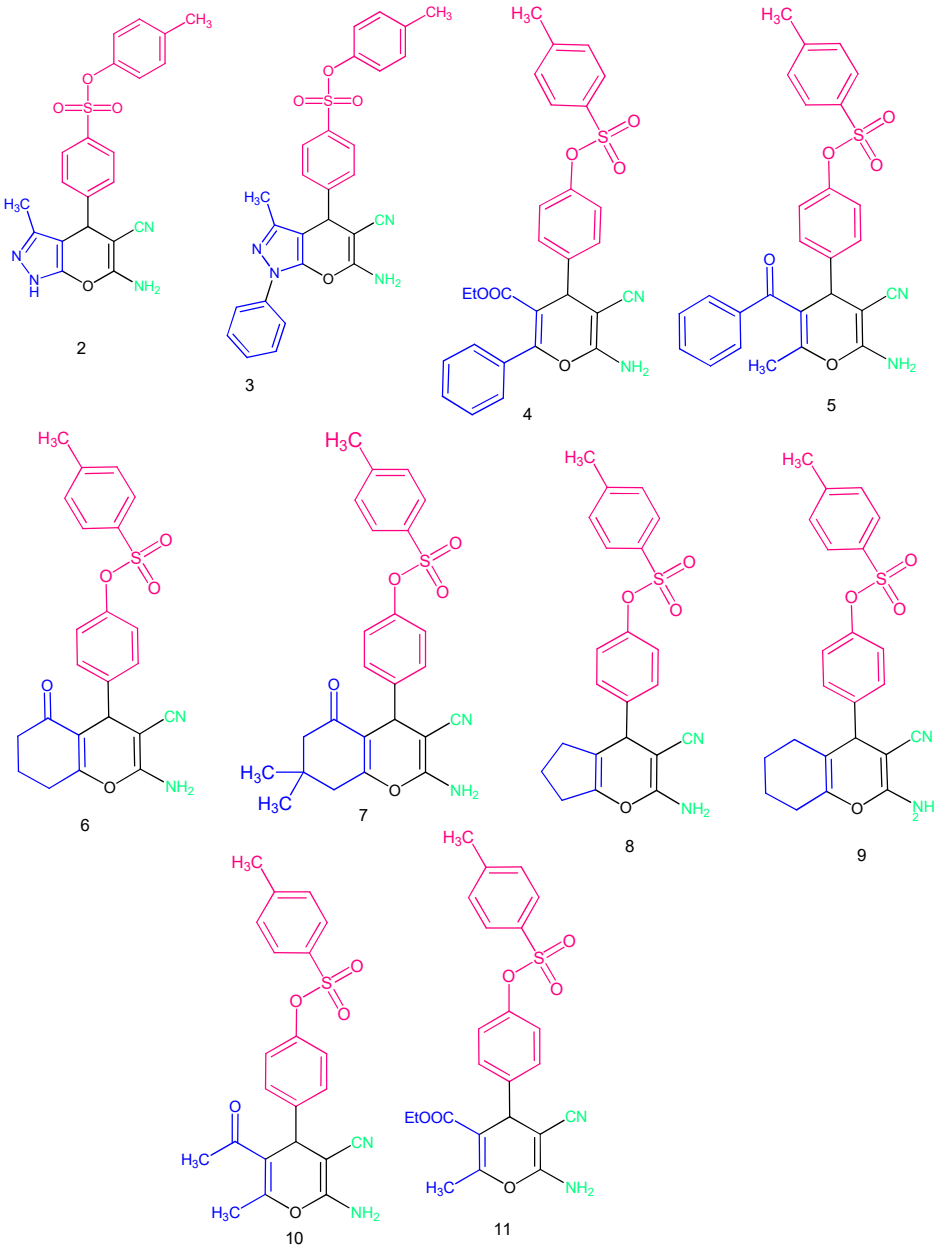
Ethyl 6-amino-5-cyano-2-methyl-4-(4-(tosyloxy)phenyl)-4H-pyran-3-carboxylate (***11***). IR; 3311, 3218 (NH_2), 2197 (C≡N),1734 (C=O) cm^{-1}; ^{1}H NMR: δ 7.73-7.71 (d, 2H, Ar-H), 7.46 (d, 2H, J = 8.0 Hz, Ar-H), 7.15 (d, 2H, Ar-H), 6.99 (d, 2H, J = 8.0 Hz, Ar-H), 6.87 (s, 2H, NH_2, D_2O disappear), 4.30 (s, 1H, CH_{pyran}), 3.98-3.94 (q, 2H, CH_2), 2.43 (s, 3H, CH_3), 2.30 (s, 3H, CH_3), 0.97 - 0.96 (t, 3H, CH_3); ^{13}C NMR: δ 165.70, 158.88, 157.43, 148.23, 146.15, 144.58, 132.12, 130.61, 129.22, 128.55, 122.38, 119.88, 107.24, 60.57, 57.49, 39.48, 21.60, 18.59, 14.10; DEPT 135: δ 130.61, 129.22, 128.38, 122.38, 60.57, 38.80, 21.60, 18.59, 14.10; anal. calcd. for $C_{23}H_{22}N_2O_6S$ (454.49): C (60.78%), H (4.88%), N (6.16%), S (7.06%); found: C (60.59%), H (4.91%), N (6.21%), S (7.11).

RESULTS AND DISSECTION

Chemistry

In this study, we present a one-pot, three-component method for producing highly efficiently of 2-amino-3-cyano-4-pyran derivatives [1] *via* treatment of 4-formylphenyl-4-methylbenzenesulfonate (**1**) with malononitrile and suitable carbonyl compounds namely; 5-methyl-2,4-dihydro-3*H*-pyrazol-3-one, 5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one, ethyl benzoyl acetate, benzoyl acetone, cyclohexane 1,3-dione, 1,3-dimidone, cyclopentanone, acetylacetone, ethyl acetoacetate in presence of 0.40 g of NiO NPs for (5-8) minutes in excellent yields (96 - 98%) afforded pyran derivatives **2-11** (Scheme 1, Table 1).





Scheme 1. Synthesis of 2-amino-3-cyano-4-pyran derivatives.

The NiO NPs are characterized as inexpensive, environmentally friendly, non-toxic, and thermally stable. After the reaction was finished (TLC), the catalyst was simply recovered by boiling the mixture in ethanol, followed by filtration. Infra-red and X-ray examination of the

recoverable catalyst before and after the reaction has the same characterization which shown that the catalyst is stable. The advanced of these applications has many benefits such as environmental friendliness, low cost, simplicity and easy recovery of the catalyst using simple method. The structures of the pyran derivatives **2 -11** were elucidated by elemental and spectral analyses such as IR, ^{1}H NMR, ^{13}C NMR and DEPT 135 spectra.

IR spectra of the synthetic pyrans **2-11** revealed absorption bands for amino groups in the range 3369 – 3218 cm^{-1}; NH in compound **2** at 3179 as well as cyano groups around 2221 - 2185 cm^{-1}. ^{1}H NMR spectra showed singlet signal that related to amino groups in range 7.18-6.87 ppm and singlet at 4.71 - 4.20 ppm due to the -CH groups; methyl signals at 2.46 - 2.41 and NH group in compound **2** appeared as singlet signals at 12.10 ppm beside the aromatic signals. Furthermore, their ^{13}C NMR and spectra revealed the following siginals; 161.46, 155.28, 148.34, 146.21, 144.08, 136.20, 132.14, 130.64, 129.67, 128.59, 128.50, 125.43, 122.91, 97.97, 97.79, 57.69, 36.19, 21.68, 10.07 ppm., Furthermore, their DEPT 135 spectrum disappeared the quaternary carbon and showed signals at δ 130.56, 129.86, 128.60, 122,58, 36.07, 23.25, 21.67, 10.06 ppm.

Table 1. Synthesis of 2-amino-4H-pyran derivatives.

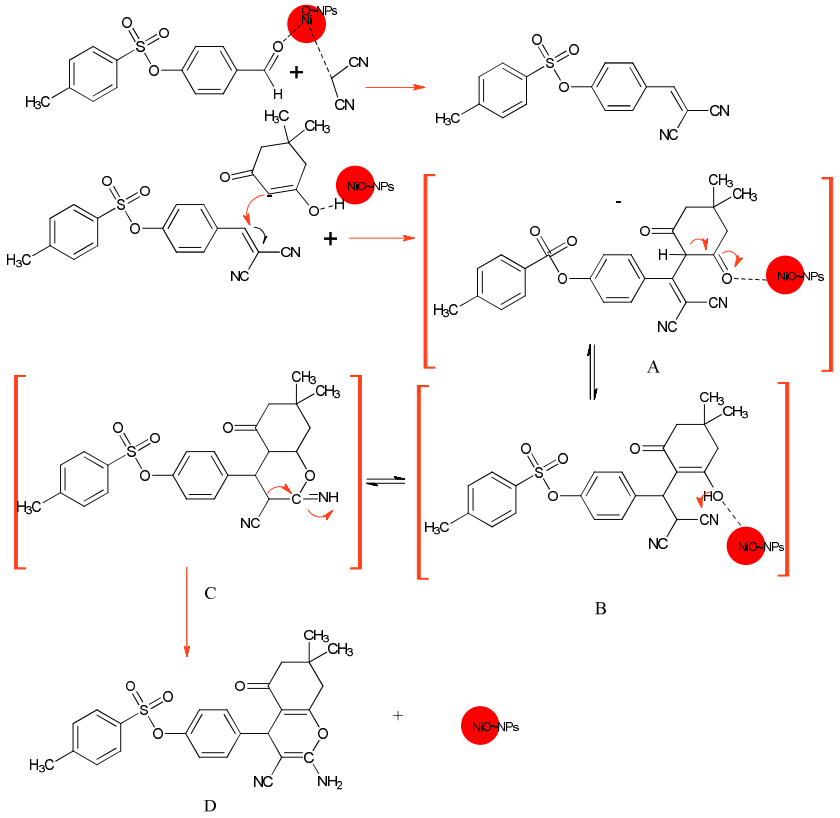
Comp.	Yield	Time (min)	m.p.	Reported [1]
2	98%	5	217	216
3	98%	6	248	247
4	97%	6	180	180
5	97%	6	224	225
6	95%	5	226	226
7	98%	8	239	238
8	97%	6	193	192
9	98%	7	189	188
10	96%	8	194	194
11	98%	6	184	183

We note from Table 1 that the use of NiO NPs for preparation of pyran derivatives is very successful and has many advances including high yield (95%-98%), as well as reducing time from hours to minutes (5-8 min.) in addition to reducing the use of harmful solvents.

The suggested mechanism for the formation of compound **4** can be occurs *via* activation the C=O of aldehyde (**1**) is activated *via* NiO NPs which then react with malononitrile, *via* Knoevenagel condensation to give arylidenemalononitrile with eliminating H_2O molecule which reacts the enolic form of dimedone as Michael acceptor to afford the intermediate (A). Then, nucleophilic attack of enolizedhydroxyl to cyano group to give intermediate (B). After ring closure in intermediate (C) and subsequently cyclizes to afford the pyran derivative (D) (Scheme 2).

Antimicrobial in vitro testing

The tested pyrans were examined for antimicrobial activity using Kirby-Bauer method [22, 23]. Two gram-positive and two gram-negative bacteria namely; *Bacillus subtilis*, *Staphylococcus aureus* and *Pseudomonas aeuroginosa*, *Escherichia coli*, respectively are compared with the standard drug. On the other hand, Amphotericin B used as a reference drug for investigations of antifungal properties. *Aspergillus flavus* and *Candida albicans* have been used to test antifungal properties of the synthesized compounds. The mean inhibition zone diameters were measured in mm/mg sample (Table 2) and Figures 1a-f.



Scheme 2. Suggested mechanism for the synthesis of compound **4**.

Table 2. Antibacterial activity of pyrans.

Comp.	*Bacillus subtilis*	*Staphylococcus aureus*	*Escherichia coli*	*Pseudomonas aeuroginosa*
	The mean inhibition zone (mm)			
2	24	22	18	16
3	26	25	20	17
4	17	14	13	11
5	18	16	14	13
6	14	11	13	11
7	17	19	15	12
8	24	18	16	14
9	15	13	12	10
10	23	21	19	16
11	14	18	16	13
Control (*DMSO*)	0	0	0	0
Ampicillin	28	26	23	25

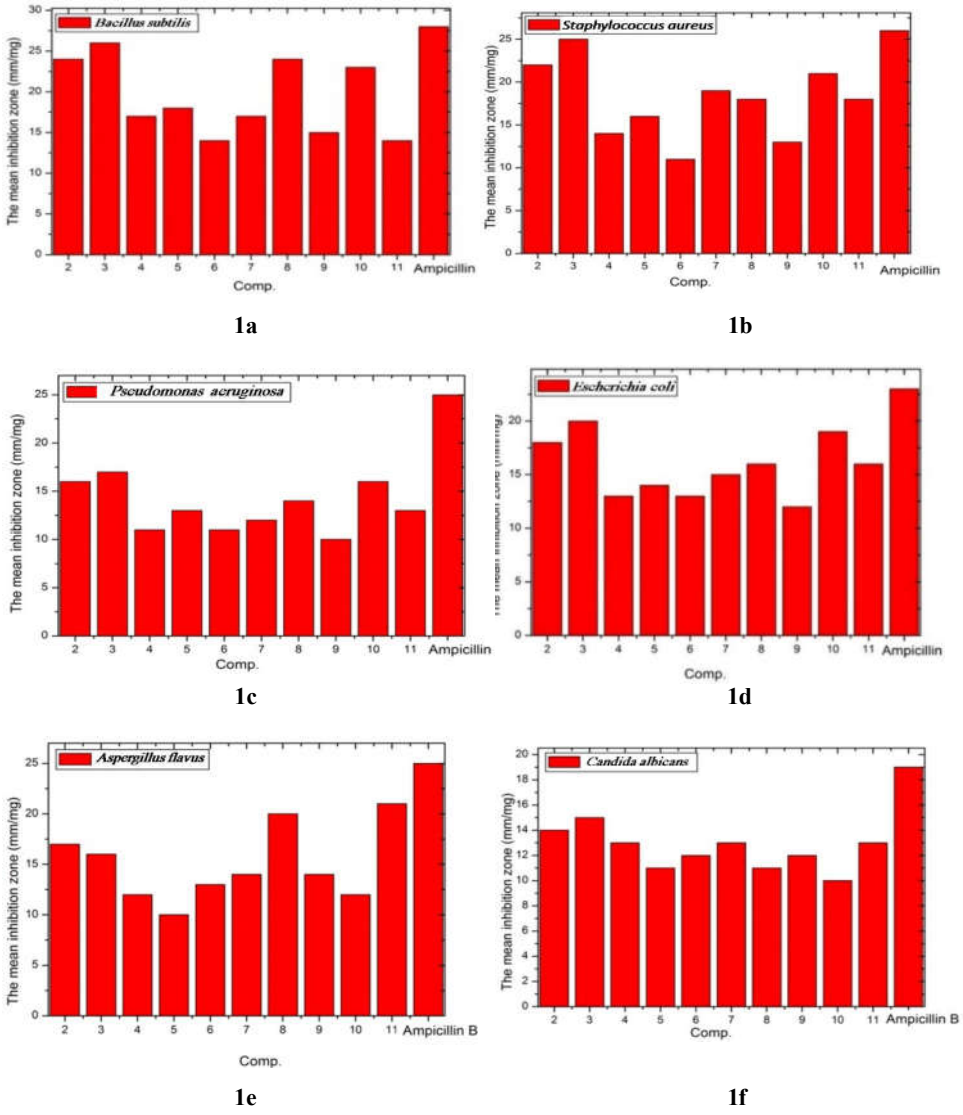


Figure 1. Antibacterial and Antifungal activity of pyran derivatives.

Table 3. Antifungal activities of pyrans.

Comp.	*Aspergillus flavus*	*Candida albicans*
	The mean inhibition zone (mm)	
2	17	14
3	16	15
4	12	13
5	10	11
6	13	12
7	14	13
8	20	11
9	14	12
10	12	10
11	21	13
Control (*DMSO*)	0	0
Ampicillin B	25	19

We note from the results recorded in the Table 3 and Figure 1 that compounds **2, 3, 7** and **10** are the most active against antibacterial compression with the stander drug Ampicillin. On the other hand, compounds **2, 3, 8** and **11** displayed the most promising antifungal activities compression with Amphotericin B.

Amount effect of catalyst

To synthesize pyrans, we investigated the amount of NiO NPs catalyst *via* treatment of 4-formylphenyl 4-methylbenzenesulfonate (**1**); malononitrile and pyrazol derivative at 80 ^{0}C in a mixture solvent (H_2O: EtOH in ratio 3:1) and different weights of NiO NPs (0.1–0.60 g) afforded pyran derivative **2**. It was found that the best yield obtained when the amount of catalyst is 0.4 gm as shown in Table 4.

Table 4. Amount effect of NiO NPs for synthesis of compound **2**.

Entry	Cat.gm	Yield %	Time
1	0	No product	4 h
2	0.1	26	45 min
3	0.2	48	30 min
4	0.3	83	20 min
5	0.4	98	6 min
6	0.5	98	5 min
7	0.6	98	6 min

From Table 4. It has been found that the maximum yield (98%) was obtained from pyran derivative when the amount of NiO NPs is 0.4 g. Moreover, increasing the catalyst amount more than 4.0 gm. afforded the same yield percentage (98%).

Recoverable of NiO NPs

One of the important useful in this article is to reuse the catalyst several times with the same efficiency. Once the reaction finished (TLC) the NiO NPs was recovered simply by filtration and reused successfully without losing any amount of the catalyst or changing its characterization. The catalyst washed with ethanol several times. Then dried at 90 °C for 5hr. Finally, it is examined using IR and X-ray spectra, which show that the catalyst is stable and has the same efficiency after and before the reaction.

Characterization of nickle oxide nanoparticles

Adjusting metal oxides' sizes in nanoscales that represent the sole of their surface activities and catalytic characteristics the one way to increase the use of metal oxides in catalytic reactions is to increase their surface area. NiO NPs have recently been employed in synthetic organic chemistry as heterogeneous catalysts [24, 25].

FT-IR spectrum of NiO NPs after and before the reaction

The IR spectrum of NiO NPs after and before the reaction has the same behaviour as shown in Figure 2.

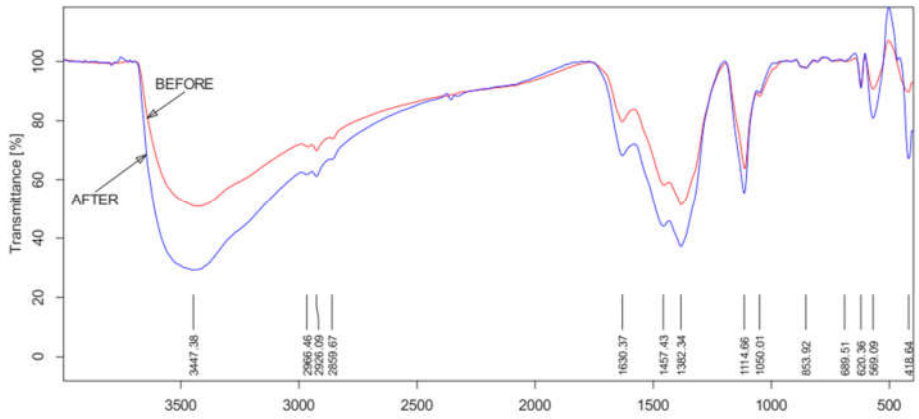


Figure 2. The IR spectrum of NiO NPs after and before the reaction has the same behavior.

X-Ray diffraction (XRD)

The structure of NiO NPs was investigated using X-Ray diffraction, which showed a face centre cubic (FCC), crystalline lattice was confirmed by prominent diffraction peaks and miller indexes (hkl) as shown in Table 5 space group F m -3 m (225), a = 4.19860, and volume [CD] = 74.02, all these parameters do not change after the reaction complicated.

Table 5. X-Ray parameters of NiO NPs.

d	2θ	I fix	h	k	l
2.4241	37.056	765	1	1	1
2.0993	43.053	1000	2	0	0
1.4844	62.521	531	2	0	2
1.2659	74.962	243	3	1	1
1.212	78.923	151	2	2	2
1.0497	94.417	68	4	0	0
0.96320	106.209	104	3	1	3
0.93880	110.273	211	4	0	2
0.85700	128.01	220	4	2	2
0.80800	144.857	179	5	1	1

d is the d-spacing; h, k and l are Miller indices; 2θ is the two theta.

X-Ray patterns of NiO-NPs (Figure 3) have characteristic peaks at 2θ values of 37.056, 43.053, and 62.521. The characteristic peak identical to 2th values of nickel oxide were indexed by the (111), (200) and (202), (JCPDS card no. 14-0481). Applying Debye-Scherrer's formula, the crystal size of NiO NPs based on the strong Bragg peaks at 37.056° (111), 43.053° (200) and 62.521° (202) are 86.0, 74.9, and 98.9 nm, respectively.

$$D = \frac{0.89\lambda}{\beta cos\theta}\ (m)$$

where λ is the wavelength, ß is the Bragg diffraction angle and D is the full width at half maximum. Net area of the nickel oxide before reaction completion was calculated 15.95, 31.03 and 14.72 for the main peaks respectively.

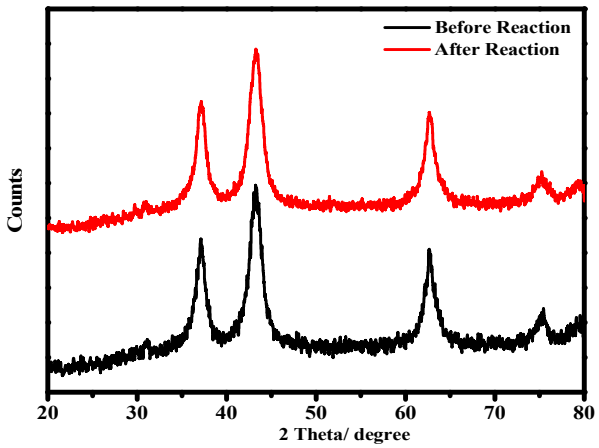
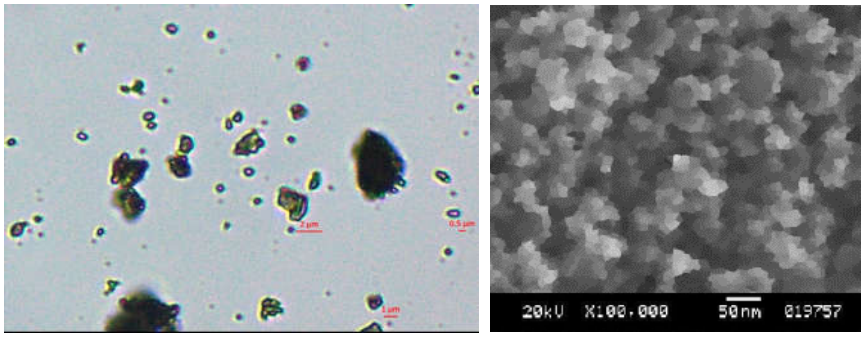


Figure 3. X-Ray pattern of NiO NPs before and after the reaction completion.

Comparing the X-ray pattern of NiO NPs before and after the reaction completion shows that the crystallinity of the catalyst increase the crystallinity% of NiO NPs before the reaction completion equals 49.2% and the amorphous % equals 50.8%. While the crystallinity% of the NiO NPs after the reaction completion equal 51.0% and the amorphous % equal 49.0%. Moreover, the Specific surface area (SSA) of NiO NPs as calculated from Brunauer–Emmett–Teller (BET) equation [26-28], equal 12.01 ($m^2\ g^{-1}$).

SEM and EDAX analysis

Surface morphology of the applied NiO NPs was studied by high resolution transmitted polarized microscope (Figure 4) the photomicrograph image depicts the agglomerated particles with in aggregate irregular shape, micro structure measurement showed that the aggregate of about 0.5µm. Morphology analysis were carried also using Scanning Electron Microscope (SEM) to study the surface texture and particle size of the samples. SEM image (Figure 4) indicate that, the average particle size of nickle oxide were nanoscale range about 55 nm, crystals shape of the catalyst are cubic shape and extremely monodisperse nature.



(A) (B)

Figure 4. A photomicrograph image showing the agglomerated particles of the NiO-NPs; B scanning electron microscope (SEM) image showing morphology of the NiO-NPs.

The elemental composition of applied NiO NPs sample was determined using the EDX technique. The elemental composition of the used nanoparticles are shown in Figure 5.

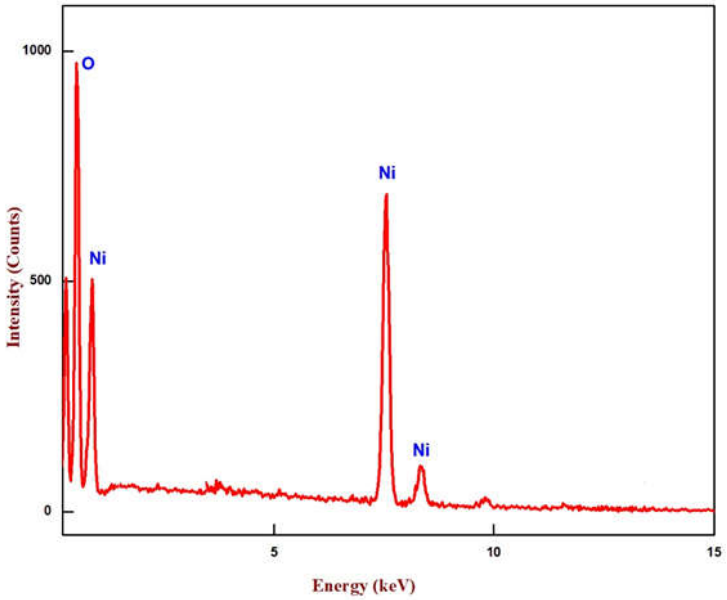


Figure 5. Elemental composition of NiO-NPs using EDX technique.

CONCLUSION

In conclusion, we have successfully developed a convenient, efficient and quick method for the designing of *4H*-pyran derivatives via the reaction of 4-formylphenyl 4-methylbenzenesulfonate with malononitrile and active methylene compounds in the presence of NiO NPs as a green catalyst., eco-friendly, low cost, and simplicity in synthesis, in addition to recovering the catalyst,

are some advances of this application. Overall products were designed, synthesized, and studied for their anti-microbial evaluation. It has been found that is compounds **2**, **3**, **7**and **10** are the most active against antibacterial compression with the stander drug Ampicillin. On the other hand, Compounds **2**, **3**, **8** and **11** displayed the most promising antifungal activities compression with Amphotericin B against *Candida albicans* and *Aspergillus flavus* fungi.

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