Journal of Chemistry and Biochemistry
December 2016, Vol. 4, No. 2, pp. 45-59
ISSN 2374-2712 (Print) 2374-2720 (Online)

Published by American Research Institute for Policy Development
DOI: 10.15640/jcb.v4n2a5
URL: https://doi.org/10.15640/jcb.v4n2a5

Synthesis of Some Novel Derivatives of Substituted 2H-[1]-Benzopyran-2-Ones and Their Antimicrobial Activity

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Abstract

Novel derivatives of substituted bezopyran-2-ones are synthesized by catalytic reactions under refluxing conditions. 4-Hydrazinyl-3-nitrobenzopyran-2-one **4** is synthesized from 4-hydroxybenzopyran-2-one **1** via three steps reaction. By condensation reaction of 4-hydrazinyl-3-nitrobenzopyran-2-one **4** and aromatic aldehydes, corresponding 4-(N-benzylidene-hydrazino)-3-nitrobenzopyran-2-ones **5(a-c)** are obtained. Cyclization reaction of 4-hydroxybenzopyran-2-one **1** with aromatic aldehydes and malononitrile, in the presence of SDS, resulted by formation of 2-amino-5-oxo-4-phenyl-(4H, 5H) pyrano-[3,2-c]-chromen-3-carbonitrile derivatives **6(a-c)**, whereas by reacting of 4-hydroxybenzopyran-2-one **1** and aromatic aldehydes, in presence of SDS, corresponding 3,3'-(benzylidene)-bis-4-hydroxyibenzopyran-2-ones **7(a-c)** are synthesized. The synthesized products are characterized on the basis of spectrometric data. Antimicrobial activity of products **5(a-c), 6(a-c)** and **7(a-c)** against *S. aurous*, *E. coli* and *Klebsiella* are investigated measuring of inhibition zones around the discs which are marked with their N, N-DMF solutions. Compounds of series **5** and **6** showed considerable antimicrobial activity against these microorganisms, whereas compounds of series **7** showed moderate activity. Impact of the substituents in antimicrobial activity also is investigated.

Keywords: Benzopyran-2-one; benzaldehyde condensation; cyclization; antibacterial activity

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1. Introduction

2H [1]-Benzopyran-2-one derivatives are heterocyclic compounds with oxygen, which find wide usage as pharmaceutics agents [1] . Many of them are found in plant and play an important role in various processes of life. These compounds have shown broad spectra of biological activities [2-3]. Some of these compounds show very active as antimicrobial [4-6], antioxidant [7-9], antifungal [10-11], ant malarial [12-13], as veil as hepato protective activity [14-17]. Also some of substituted benzopyran-2-ones showed anticoagulant, HIV protease inhibition [18], analgesic, and sedative and ant tubercular activity [19]. Biological activity of these derivatives is conditioned by their structure.

The presence of different substituent's on the benzopyrone ring has important impact on the type and potency of biological activity. Despite efforts to find sufficient connection between the structure and biological activity of these derivatives, in general until now there is not made much progress. Extraordinary biological importance of these derivatives has generated a great interest in their synthesis. In support of this, these compounds are the subject of study by many researchers. In order to contribute to the development of new biological active compounds, based on our previous studies [20, 21], in the present communication we have designed a series of new derivatives by condensation reaction of 4-hydrazinyl-3-nitrobenzopyran-2 one and aromatic aldehydes, and other condensation reactions, who could serve as pharmaceutical agents.

2. Methods and materials

All reagents are purchased from Aldrich and used without further purification. The reactions were carried out under reflux conditions and monitored using TLC plates (Merck Kieselgel-60 (F-254) on a benzene: toluene: glac. acetic acid bath (ratio 80:10:10 by volume, visualization by UV-lamp).

Purification of products was done by crystallization from ethanol. Melting points were determined on a paraffin oil bath in open capillary tubes. IR spectra were recorded in KBr discs on a Shimadzu 8400S FTIR Spectrometer with 4 cm^{-1} resolution. NMR spectra were recorded in DMSO-d_6 on a UNITYplus-500 "NMR 1" Spectrometer. Chemical shifts are reported in ppm relative to TMS as an internal standard. Antibacterial activity of compounds are investigated applying the Kirby-Bayer's method (discs d=10.0 mm, maximum capacity 10 µg). The discs are impregnated with solutions of the respective compounds in N, N-DMF concentrations 2mg/mL, 4mg/mL and 6mg/mL.

2.1. 4-(N-Benzylidene-hydrazino)-3-nitrobenzopyran-2-ones 5(a-c); general procedure

4-Hydrazinyl-3-nitrobenzopyran-2-one **4** (1.8 mmol) in absolute ethanol (5 mL) was treated with equimolar amount of aromatic aldehydes (benzaldehyde, salicylic aldehyde and 3-nitrobenzaldehyde) and catalytic amount of piperidine (2 drops) was added. The reaction mixture was stirred under reflux for 10-12 h. After cooling, the residue was poured into a baker with ice lump and then filtered under vacuum and dried in air. Crystallization of products is made from N,N-Dimethylforamide, yielding the corresponding 4-(N-benzylidene-hydrazino)-3-nitrobenzopyran-2-ones 5(a-c).

2.2. 2-Amino-5-oxo-4-phenyl-(4H,5H)pyrano[3,2-c]chromen-3-carbonitriles, 6(a-c); general procedure

To a solution of 4-hydroxy-2H [1]-benzopyran-2-one **1** (10 mmol) in 30 mL of distilled water, equimolar amount of aromatic aldehydes (benzaldehyde salycilaldehyde and 3-nitrobenzaldehyde), malononitrile (10 mmol), and sodium dodecylsulfate (SDS) (0,5 mL) was added.

The reaction mixture was stirred and heated in a water bath (90 ^{0}C) for 6 h. After cooling, the residue is filtered off under vacuum and dried in air. Crystallization is made from ethanol yielding the corresponding 2-Amino-5-oxo-4-phenyl-(4H,5H)pyrano-[3,2-c]chromen-3-carbonitrile derivatives **6(a-c).**

2.3. 3, 3'-{Benzylidene)-bis-4-hydroxy-benzopyran-2-ones, 7(a-c); general procedure

To a solution of 4-hydroxy-2H[1]-benzopyran-2-one **1** (10 mmol) in distilled water (40 mL), aromatic aldehydes (benzaldehyde salycilaldehyde and 3-nitrobenzaldehyde) (5 mmol) and SDS (0,3 mL) was added and the reaction mixture was heated in a water bath for 7 h. After cooling, the crude product is filtered off under vacuum, dried in air, and crystallized from ethanol, yielding the corresponding crystalline product of 3,3'-{benzylidene)-bis-4-hydroxy-benzopyran-2-ones **7(a-c)**.

2.4. 4-(N-benzylidene-hydrazino)-3-nitrobenzopyran-2-one, 5a

White crystalline product, reflux for 12h, R=48%, mp.=205^{o}C. **IR** (KBr disc, cm^{-1}): 3446.7, 3098.86, 2924, 1679.79, 1604.40, 1537.39, 1327.83, 1066.87, 754.50. ^{1}**H-NMR**; (300 MHz, δ-ppm) 2,50 (s, 1H, NH), 7,48 (m, 3H, Ar; H-3, H-4, H-5), 7,51 (d, 1H, Bp; H-8), 7,54 (dd, 1H, Bp: H-6), 7,64 (dd, 1H, Bp; H-7), 7,78 (d, 2H, Ar; H-6), ^{13}**C-NMR**; (300 MHz, δ-ppm) 117,748 (Bp; C-3), 124,268 (Bp; C-8), 124,712 (Ar; C-6), 127,463 (Bp; C-5), 128,951 (Bp; C-10), 129,091 (Ar; C-3, C-5), 1130,883 (Ar; C-2, C-6), 133,428 (Ar; C-4), 133,858 (Ar; C-1), 140,755 (Bp; C-9), 149,810 (C-allyl), 151,149 (C=O), 158,656 (Bp; C-4). (S-singlet, d-doublet, t-triplet, m-multiplet, Ar-benzene ring, Bp-benzopyron ring).

2.5. 4-[N-(2-Hydroxy-benzylidene)-hydrazino]-3-nitro-chromen-2-one, 5b

White-yellow crystalline product, reflux for 12h, R=58%, m.p.=150°C. **IR** (KBr disc, cm^{-1}): 3579.19, 3422 2924.94, 1719.37, 1612.51, 1541, 1375.37, 1035.23, 754.50. **^{1}H-NMR**; (300 MHz, δ-ppm) 2.53 (s, 1H, NH), 4,2 (s, 1H, OH), 7.22 (d, 1H, Bp; H-8), 7.24 (dd, 1H, Bp; H-6), 7.46 (dd, 1H, Bp: H-7), 7.64 (dd, 1H, Ar; H-5), 8.1 (d, 1H, Ar; H-6), 8.3 (s, 1H, H-allyl), 8.24 (dd, 1H, Ar, H-4), 8.60 (d, 1H, Ar, H-3).

2.6. 4-[N-(3-Nitro-benzylidene)-hydrazino]-3-nitro-chromen-2-one, 5c

Yellow crystalline product, reflux for 12h, R=50%, mp.=115°C. **IR** (KBr disc, cm^{-1}): 3650,02 3005,07, 2924.94, 1687.64, 1616.47, 1541.34, 1355.51, 1035.28, 758.46.. **^{1}H-NMR**; (300 MHz, δ-ppm) 2.50 (s, 1H, NH), 7.20 (d, 1H, Bp; H-8), 7.22 (dd, 1H, Bp; H-6), 7.45 (dd, 1H, Bp: H-7), 7.60 (dd, 1H, Ar; H-5), 8.0 (d, 1H, Ar; H-6), 8.1 (s, 1H, H-allyl), 8.20 (d, 1H, Ar, H-4), 8.60 (1H, Ar, H-2).

2.7. 2-Amino-5-oxo-4-phenyl-(4H,5H)pyrano[3,2-c]chromen-3-carbonitrile, 6a

White crystalline product, reflux for 6h, R=95,2%, mp.=230°C. **IR** (KBr disc, cm^{-1}): 3415.08 3288.59, 2205.54, 1711.36, 1675.78, 1058.96, 754.50. **^{1}H-NMR**; (300 MHz, δ-ppm) 2.50 (s, 2H, NH_2), 4.45 (s, 1H, pyran), 7.21-7.26 (m, 3H, Bp; H-6), 7.45 (dd, 1H, Bp: H-7), 7.60 (dd, 1H, Ar; H-2, H-6, H-4), 7.27-7.34 (m, 2H, Ar; H-3, H-5), 7.42-7.50 (m, 2H, Bp; H-6, H-8), 7.67-7.92 (m, 2H, Bp, H-5, H-7), **^{13}C-NMR**; (300 MHz, δ-ppm) 36.94 (pyran C-4), 58.005 (pyran C-3), 113.745 (Ar; C-4), 119.197 (Bp; C-8), 122.425 (Ar; C-2), 123.928 (Bp; C-6), 124.611 (Bp; C-5), 126.649 (Bp; C-10), 127.566 (Bp; C-7), 127.889 (Ar; C-5), 128.459 (Ar; C-6), 132.865 (Ar; C-3), 139.522 (Ar; C-1), 152.264 (Bp; C-9), 159.471 (C=O), 165.950 (Bp; C-4).

2.8. 2-Amino-4-(2-hydroxy-phenyl)-5-oxo-(4H,5H)pyrano[3,2-c]chromen-3-carbonitrile, 6b

White-beige crystalline product, reflux for 6h, R=11.78%, m.p.=140°C. **IR** (KBr disc, cm^{-1}): 3610.05, 3407.18, 3170.01, 2225.02, 1719.27, 1604.60, 1165.71, 766.36.

2.9.2-Amino-4-(3-nitro-phenyl)-5-oxo-4H,5H-pyrano[3,2-c]chromen-3-carbonitrile, 6c

White crystalline product, reflux for 7h, R=75.55%, mp.=238°C. **IR** (KBr disc, cm^{-1}): 3612.02, 3201.63, 2197.64, 1747.41, 1675.78, 1533.43, 1383.18, 1058.96, 766.33. **^{1}H-NMR**; (300 MHz, δ-ppm) 2.50 (s, 2H, NH_2), 4.73 (s, 1H, pyran), 7.44-7.47 (d, 1H, Bp; H-8), 7.50-7.53 (d, 1H, Bp: H-6), 7.62-7.63 (t, 1H, Ar; H-3), 7.79-7.82 (m, 2H, Ar; H-2, Bp; H-7), 7.90-7.93 (d, 1H, Bp; H-5), 8.10-8.12 (d, 1H, Ar, H-6), 8.13 (d, 1H, Ar, H-4).

2.10. 3,3'-{Benzylidene)-bis-4-hydroxy-benzopyran-2-one, 7a

White crystalline product, reflux for 7h, R=84.95%, mp.=125°C. **IR** (KBr disc, cm^{-1}): 3200-3050, 3030, 1659.96, 1624.37, 1098.05, 754.50. **^{1}H-NMR**; (300 MHz, δ-ppm) 2.49 (s, 1H, H-methylene), 6.36 (s, 1H, OH), 7.12 (s, 2H, Ar; H-2, H-6), 7.15 (t, 1H, Ar; H-4), 7.21-7.36 (m, 4H, Bp; H-6, H-8), 7.57-7.60 (m, 4H, Bp; H-5, H-7), 7.89-7.91 (d, 2H, Ar; H-3). **^{13}C-NMR**; (300 MHz, δ-ppm) 35.93 (C-methylene), 103.971 (Bp; C-3), 115.786 (Bp; C-8), 118.119 (Bp; C-6), 123.517 (Ar; C-4), 123.844 (Bp; C-5), 123.859 (Bp; C-10), 126.615 (Bp; C-7), 127.905 (Ar; C-3, C-5), 131.653 (Ar; C-2, C-6), 140.171 (Ar; C-1), 152.181 (Bp; C-9), 164.697 (C=O), 165.496 (Bp; C-4).

2.11. 3,3'-{2-Hydroxy-benzylidene)-bis-4-hydroxy-benzopyran-2-one, 7b

White-yellow crystalline product, reflux for 8h, R=85.04%, mp.=175°C. **IR** (KBr disc, cm^{-1}): 3500-3300, 3020, 1723.22, 1616.47, 748.45.

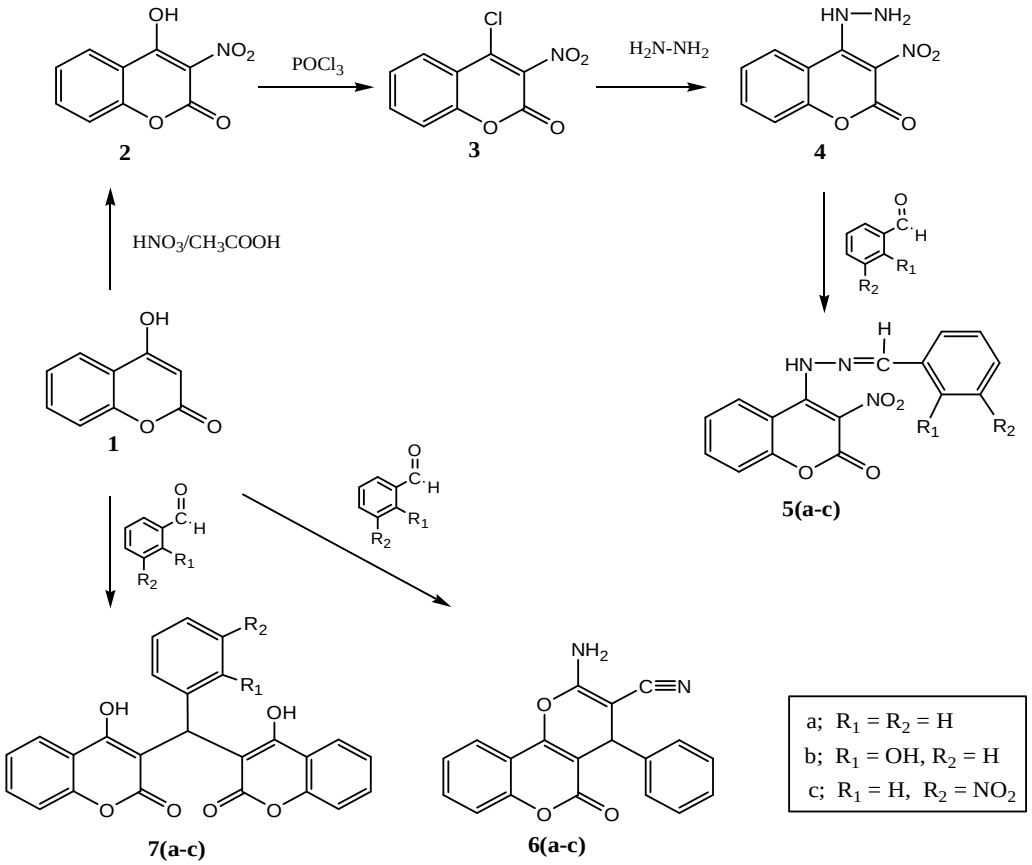
2.12. 3,3'-{3-Nitro-benzylidene)-bis-4-hydroxy-benzopyran-2-one, 7c

White crystalline product, reflux for 6h, R=85.08%, mp.=215°C. **IR** (KBr disc, cm^{-1}): 3500-3400, 3090.96, 1652.05, 1616.47, 1521.57, 1351.55, 1098.05, 762.41. **^{1}H-NMR**; (300 MHz, δ-ppm) 3.177 (s, 1H, H-methylene), 6.932 (s, 1H, OH), 7.333-7.335 (d, 2H, Bp; H-8), 7.475-7.697 (m, 4H, Bp; H-6, H-7), 7.858-7.873 (dd, 1H, Ar; H-5), 8.094-8.096 (s, 1H, Ar; H-6), 8.109 (s, 1H, Ar; H-2), 8.323 (d, 1H, Ar; H-4). **^{13}C-NMR**; (300 MHz, δ-ppm) 26.630 (C-methylene), 113.748 (Bp; C-3), 116.146 (Ar; C-4), 123.353 (Bp; C-8), 124.448 (Ar; C-2), 125.267 (Bp; C-6), 128.272 (Bp; C-5), 128.541 (Bp; C-10), 128.742 (Bp; C-7), 130.901 (Ar; C-5), 132.388 (Ar; C-6), 142.754 (Ar; C-1), 151.323 (Ar; C-3), 153.761 (Bp; C-10), 157.98 (C=O), 158.695 (Bp; C-4).

3. Results and discussion

Based on our previous researches [20, 21], 4-hydrazynil-3-nitrobenzopyran-2-one **4** was synthesized from 4-hydroxybenzopyran-2-one **1** by a three-step reaction. Condensation of 4-hydrazinyl-3-nitrobenzopyran-2-one **4** and benzaldehyde, salicylaldehyde and 3-nitrobenzaldehyde resulted in the synthesis of corresponding 4-(N-benzylidene-hydrazino)-3-nitrobenzopyran-2-ones **5(a-c)**. On the other hand, by cyclization of 4-hydroxybenzopyran-2-one **1** with aromatic aldehydes and malononitrile, 2-amino-5-oxo-4-phenyl (4H, 5H) pyrano[3,2-c]-chromen-3-carbonitrile derivatives **6(a-c)** are synthesized.

Also by reaction of 4-hydroxybenzopyran-2-one **1** and aromatic aldehydes, in presence of sodium dodecylsulphate (SDS), corresponding dimmer products of 3,3'-(benzylidene)-bis-4-hydroxybenzopiran-2-one **7(a-c)** are synthesized**.** Structural characterization of the synthesized products is based on spectrometric data.



Scheme 1

3.1. In the IR spectrum of product **5a** appeared absorptions at 3446.71 cm^{-1} belong to stretching ν(NH) vibrations, whereas at 3098.86 cm^{-1} appeared the absorption signal of ν(CH) stretching aromatic vibrations. A sharp peak at 1679.79 cm^{-1} reflects the ν(C=O) stretching vibrations and the signal at 1604.40 cm^{-1} appeared from ν(C=C) stretching vibrations.

The characteristic absorptions at 1537.39 cm^{-1} and 1327.83 cm^{-1} resulted from asymmetric stretching ν(NO_2) and symmetric ν(NO_2) vibrations of nitro group. The absorption mode at 1066.87 cm^{-1} is derived from the lactonic vibrations ν(COC) stretching vibrations. In the IR spectrum a characteristic absorption at 754.50 cm^{-1} appeared due to δ (CH)oop bending vibrations of aromatic ring. On the other hand, signals of ^{1}H-NMR spectrum correspond to absorptions resulting from the corresponding proton resonance. In addition, signals of ^{13}C-NMR spectrum reflect the carbon absorption of the respective compound.

3.2. IR spectrum of compound **5b** appeared the characteristic absorption peak at 3579 cm^{-1} which corresponds to responsive ν(NH) vibrations, while the peak at 3422 cm^{-1} belongs to ν(OH) stretching vibrations. At 3080 cm^{-1}, the absorption signal of aromatic stretching ν(CH) is observed. The intensive sharp peak at 1719.37 cm^{-1} corresponds to the ν(C=O) stretching vibrations, whereas the absorption signal at 1612.51 cm^{-1} appeared due to aromatic ν(C=C) stretching mode. The characteristic signals of nitro group appeared at 1541 cm^{-1} due to asymmetric, whereas at 1375.37 cm^{-1} for symmetric ν(NO_2) stretching vibrations. The absorption peak appeared at 1035.23 cm^{-1} responds to the lactonic ν(COC) vibrations, whereas the signal at 758.20 cm^{-1} resulted from δ(CH)oop bending vibrations of aromatic ring. The characteristic signals appeared in the ^{1}H-NMR spectrum of this compound also corresponds from absorption of respective proton resonance.

3.3. In the IR spectrum of product **5c** appeared an absorption signal at 3650.02 cm^{-1} resulted from ν(NH)vibrations, while the peak at 3005.07 cm^{-1} is responsible for aromatic ν(CH) stretching vibrations. The sharp peak at 1687.64 cm^{-1} resulted from ν(C=O) stretching vibrations, whereas the signal at 1616.47 cm^{-1} resulted from ν(C=C) stretching vibrations.

The absorption peaks of $\nu(NO_2)$ stretching asymmetric and symmetric are appeared at 1541.34 cm^{-1} and 1355.51 cm^{-1}. The characteristic signal at 1030.65 cm^{-1} is responsible for lactonic ν(COC) vibrations. At 758.46 cm^{-1} displayed absorptions of δ(CH) oop vibrations of aromatic ring. Appeared signals in the ^{1}H-NMR also correspond to characteristic absorptions of protons of compound 5c.

3.4. The IR spectrum of compound **6a**, appeared an absorption signal at 3415 cm^{-1} resulted from ν(NH) vibrations, while the peak at 3228.59 cm^{-1} is responsible for aromatic ν(CH) stretching vibrations fragrant. A sharp peak at 2205.54 cm^{-1} resulted from ν(CN) stretching vibrations whereas signals at 1711.34 cm^{-1} and 1675.68 cm^{-1} resulted from respective ν(C=O) and ν(C=C) stretching vibrations. The absorption peak at 1058.97 cm^{-1} correspond to lactonic ν(COC) stretching vibrations, while at 754.50 cm^{-1} appeared tha absorption signal resulted from aromatic δ(CH) oop vibrations.

3.5. The IR spectrum of compound **6b**, besides other characteristic modes, appeared the absorption signal at 3407 cm^{-1} which resulted from ν(OH) stretching vibrations. Also in the IR spectrum of compound **6c** are displayed characteristic signals at 1533.48 cm^{-1} and 1383.18 cm^{-1}, as a result of $\nu(NO_2)$ asymmetric and symmetric stretching vibrations. Structure of carbonitriles **6(a-c)** is confirmed by the NMR spectra, where the displayed signals are characteristic for proton and carbon absorptions of the respective compounds.

3.6. In the IR spectrum of product **7a** the absorption signal appeared at 3200-3050 cm^{-1} resulted from ν(OH) vibrations, while the peak at 3030 cm^{-1} is responsible for aromatic ν(CH) stretching vibrations. The intensive peak at 1659.96 cm^{-1} and the one at 1624.37 cm^{-1} resulted from respective ν(C=O) and ν(C=C) stretching vibrations. The characteristic peak at 1098.05 cm^{-1} corresponds to lactonic ν(COC) stretching vibrations, while at 754.50 cm^{-1} appeared the peak resulted from aromatic δ(CH) oop vibrations.

3.7. In the IR spectrum of product **7b**, the absorption signal at 3500-3300 cm^{-1} reflects ν(OH) vibrations, while the peak at 3020 cm^{-1} is characteristic for ν(CH) aromatic vibrations. Signals 1616.47cm^{-1} and 1725.22cm^{-1} resulted from stretching ν(C=O) and ν(C=C)vibrations, while the signal at 748.45 cm^{-1} appeared absorptions of δ(CH)oop vibrations of aromatic ring.

3.8. According to the IR spectrum of compound **7c,** the absorption signal appeared at 3500-3400 cm^{-1} resulted from ν(OH) stretching vibrations, while the peak at 3090.96 cm^{-1} is responsible for aromatic ν(CH) modes. The intensive signal at 1652.05 cm^{-1} and the one at 1616.47 cm^{-1} are responsible for corresponding ν(C=O) and ν(C=C) stretching vibrations. Signals at 1551.57 cm^{-1} and 1351.55 cm^{-1} are displayed the characteristic ν(NO_2) asymmetric and symmetric vibrations. The peak at 1098.05 cm^{-1} is responsible for lactonic νC-O-C) vibrations, while at 762.41 cm^{-1} appeared absorptions of δ(CH) oop vibrations of aromatic ring. Appeared signals in the ^{1}H-NMR and ^{13}C-NMR spectra resulted from proton and carbon resonance of the respective compounds **7a**, **7b** and **7c.**

Table 1: Chemical data of the compounds 5(a-c), 6(a-c) and 7(a-c)

Nr.	R_1 & R_2	Formula	m.p. (°C)	Yield (%)	Elemental analysis Found (calcd) (%)
5a	R_1=R_2=H	$C_{16}H_{11}N_3O_4$	205-206	48.0	C:62.13; H:3.56; N:13.59; O:20.69 (C:62.11; H:3.51; N:13.63)
5b	R_1=OH, R_2=H	$C_{16}H_{11}N_3O_5$	148-150	58.2	C:59.08; H:3.41; N:12.92; O:24.59 (C:59.07; H:3.42; N:12.90)
5c	R_1=H, R_2=NO_2	$C_{16}H_{10}N_4O_6$	113-115	51.0	C:54.24; H:2.84; N:15.82; O:27.10 (C:54.26; H:2.81; N:15.79)
6a	R_1=R_2=H	$C_{19}H_{12}N_2O_3$	229-230	95.2	C:72.14; H:3.83; N:8.86; O:15.18 (C:72.16; H:3.79; N:8.83)
6b	R_1=OH, R_2=H	$C_{19}H_{12}N_2O_4$	140-142	11.8	C:68.67; H:3.64; N:8.43; O:19.26 (C:68.64; H:3.66; N:8.46)
6c	R_1=H, R_2=NO_2	$C_{19}H_{11}N_3O_5$	238-239	75.5	C:63.15; H:3.07; N:11.63; O:22.14 (C:63.17; H:3.75; N:8.80)
7a	R_1=R_2=H	$C_{25}H_{16}O_6$	124-125	84.9	C:72.81; H:3.91; O:23.28 (C:72.78; H:3.90)
7b	R_1=OH, R_2=H	$C_{25}H_{16}O_7$	175-177	85.0	C:70.09; H:3.77; O:26.15 (C:70.12; H:3.75)
7c	R_1=H, R_2=NO_2	$C_{25}H_{15}NO_8$	214-215	83.5	C:65.65; H:3.31; O:27.99 (C:65.68; H:3.33)

4. Antimicrobial activity

As part of this report, the aim of the study also was testing the antibacterial activity of the synthesized compounds. Our surveys are oriented to test their activity against bacterium *S. aureus* , *E. coli* and *Klebsiella*, based on the Kirby-Bayers method[21]. Antibacterial activity of the compounds **5(a-c)**, **6(a-c**) and **7(a-c)** against these microorganisms are investigated measuring the diameter of inhibition zones around the disks who are previously marked with the 2mg/mL, 4mg/mL and 6mg/mL solutions of respective compounds in N,N-DMF. Compounds of series **7** and **5** showed significant antimicrobial activity against *S. Aureus*, compounds of series **5** and **6** were more active against *E. Coli*, while those of series **6** and **7** are more active against *Klebsiella*. Results are shown in Fig . 1, 2 and 3.

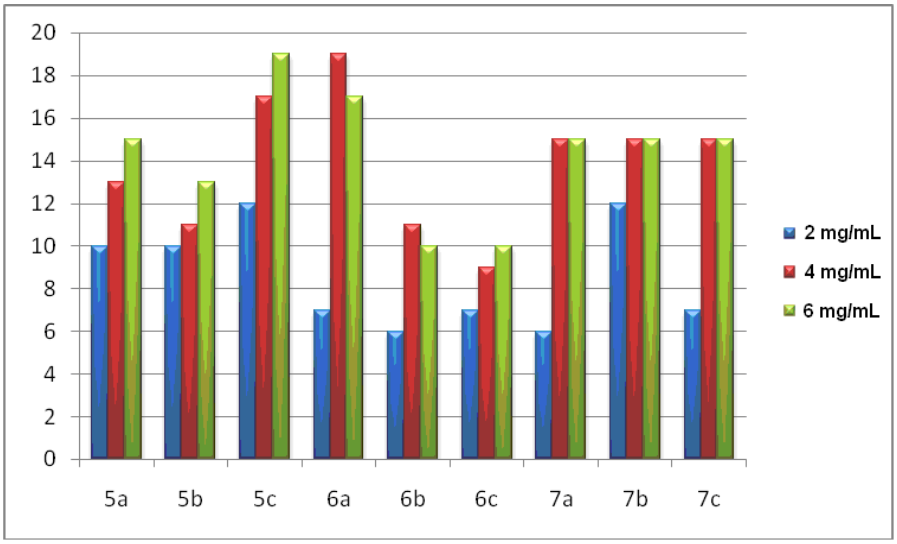


Fig. 1: Graphical presentation of inhibition zone diameter (mm) against *S. aureus*

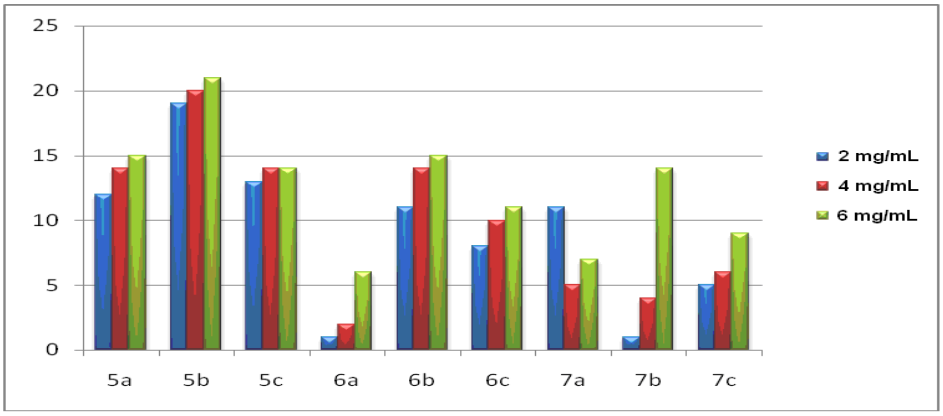


Fig. 2: Graphical presentation of inhibition zone diameter (mm) against *E. coli*

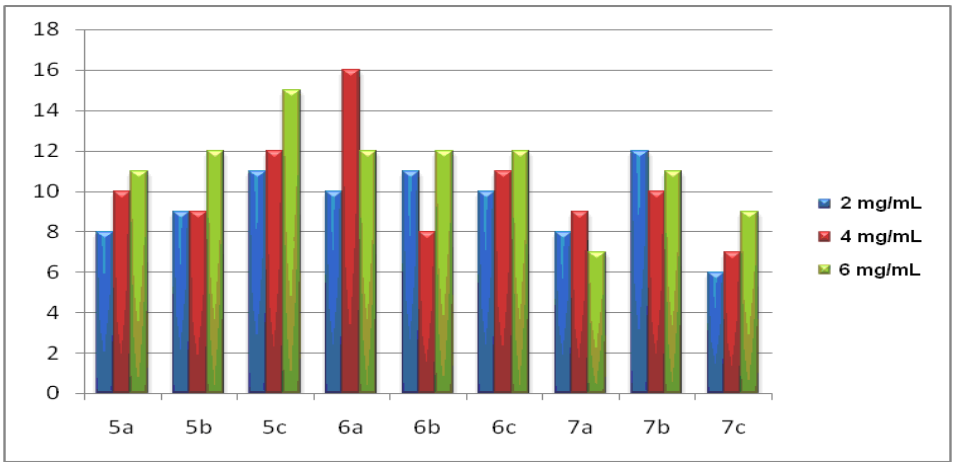


Fig. 3: Graphical presentation of inhibition zone diameter (mm) against *Klebsiella*

5. Conclusions

The derivates of 4-(N-benzylidene-hydrazino)-3-nitrobenzopiran-2-one **5(a-c)**, derivatives of 2-amino-5-oxo-4-phenyl(4H,5H)pyrano[3,2-c]-chromen-3-carbonitrile **6(a-c)** and those of 3,3 '-(benzylidene)-bis-4-hydroxybenzopyran-2-one **7(a-c)** are synthesized in the moderate and high yield.

The tested compounds showed considerable activity against *S. aureus*, *E. coli* and *Klebsiella*. The compounds **7b** and **5c** express more emphatic activity against *S. Aureus*. Compounds **5b** and **6b** have indicated more antibacterial activity against *E. Coli*, while compounds **6a** and **7b** were more active against *Klebsiella*. In general, increasing the concentration of solutions, their antibacterial activity has increased.

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