Synthesis of 4-Triazolylamino- and 4-Benzo[1]thiazolylamino-3-nitro-2H-[1]-Benzopyran-2-ones and their Antimicrobial Activity

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\textbf{Abstract:} Novel substituted benzopyran-2-one derivatives were synthesized by catalytic condensation reactions under reflux conditions. 4-(1,2,4-Triazolyl-3-amino)-3-nitro-2H-[1]-benzopyran-2-ones \textsuperscript{4(a-b)} were synthesized by condensation of 4-chloro-3-nitro-2H-[1]-benzopyran-2-one \textsuperscript{2} and corresponding 3-aminotriazoles \textsuperscript{3(a-b)}. 4-(4'-methoxy-2-benzothiazolylamino)-3-nitro-2H-[1]-benzopyran-2-one \textsuperscript{4c}, 4-(6'-nitro-2-benzothiazolylamino)-3-nitro-2H-[1]-benzopyran-2-one \textsuperscript{4d} and 4-(6'-fluoro-2-benzothiazolylamino)-3-nitro-2H-[1]-benzopyran-2-one \textsuperscript{4e} were synthesized by condensation of 4-chloro-3-nitro-2H-[1]-benzopyran-2-one \textsuperscript{2} and corresponding 2-aminobenzothiazole \textsuperscript{3(c-e)} under reflux reaction conditions. Further, alkali hydrolysis of \textsuperscript{4(a-e)} afforded the 2-hydroxy-ω-nitroacetophenone \textsuperscript{5}. Antimicrobial activity of products \textsuperscript{4(a-e)} against \textit{S. aureus}, \textit{E. coli} and \textit{Klebsiella} were investigated measuring of inhibition zones around the discs which are marked with DMF, concentration 2 mg/mL, 4 mg/mL and 6 mg/mL solutions. Compounds \textsuperscript{4c}, \textsuperscript{4e} and \textsuperscript{4d} were more active against \textit{S. aureus}. Emphatic activity against \textit{E. coli} exhibited compounds \textsuperscript{4b} and \textsuperscript{4e}, whereas \textsuperscript{4c} and \textsuperscript{4d} were more active against \textit{Klebsiella}.

\textbf{Keywords:} benzopyran-2-one; triazolylamine; benzo[1]thiazolylamine; antibacterial activity

\section{1. INTRODUCTION}

2H-[1]-Benzopyran-2-one derivatives are heterocyclic oxygen compounds which find wide usage in pharmacy \cite{1}. Many of them are plant components and play an important role in various processes of life. A significant number of them show different biological activities \cite{2-3} as antimicrobial \cite{4-6}, antioxidant \cite{7-9}, antifungal \cite{10-11}, antimalarial \cite{12-14} and hepatoprotective activities \cite{15-17}. Many of substituted benzopyran-2-one derivatives showed anticoagulant, HIV protease \cite{18} inhibition, sedative, analgesic and antitubercular \cite{19} activity. Biological activity of these derivatives is conditioned by their structure. The presence of different substituents on benzopyran ring shows impact on the type and potency of biological activity. Despite efforts to find sufficient connection between the structure and biologic activity of these derivatives, until now there was no such general connection. Extraordinary biological importance of such derivatives has generated a great interest in their synthesis. In support of this, these compounds are the subject of study by many researchers. In continuation of our previous studies and our attempts for synthesis of new derivatives \cite{20-21}, in this paper we aimed to synthesize some new derivatives by condensation reaction of condensation reaction of 4-chloro-3-nitrobenzopyran-2-one and heteroarylamines, and through other condensation reactions, which could serve as parapharmaceutical products.

\section{2. MATERIAL AND METHODS}

All experiments were carried out in acetonitrile as an aprotic solvent, under reflux reaction conditions. The reactions were monitored by TLC using Merck Kieselgel-60 (F-254) on benzene:toluene:glac. acetic acid bath (ratio 85:10:5, by volume, and observed by UV-lamp). Purification of products was done by recrystallization from various solvents. Melting points

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were measured on a paraffin oil bath in open capillary tubes and they were not corrected. The IR spectra were recorded in KBr discs on a Shimadzu 8400S FTIR Spectrometer with 4 cm\(^{-1}\) resolution. \(^1\)H-NMR spectra were obtained in DMSO-d\(_6\) on UNITYplus-500 “NMR 1” Spectrometer. Chemical shifts are reported in parts per million (ppm) downfield from tetramethylsilane as an internal standard (60.00). Microanalyses were preformed on a Perkin-Elmer 240 B CHN analyzer.

Antibacterial activity of compounds were screened applying the Kirby-Bayers method (discs d=5.5 mm, max. capacity 10 μg), measuring of inhibition zones around the discs which are marked with DMF, concentration 2 mg/mL and 6 mg/mL solutions) were investigated.

4-Triazolylamino- and 4-benzothiazolylamino-3-nitro-2H-[1]benzopyran-2-ones 4(a-e), (general procedure)

In a typical reaction, 4-chloro-3-nitro-2H-[1]-benzopyran-2-one 2, equimolar amounts of 3-aminotriazole 3(a-b), respectively 2-aminobenzothiazole 3(c-e) and a catalytic amount of triethylamine were refluxed in a water bath for 1–16 h. The product was filtered off under vacuum and the crude product was purified by recrystallization.

4-(5-Carboxy-1,2,4-triazolyl-3-amino)-3-nitro-2H-[1]-benzopyran-2-one (4b)

To 3-amino-5-carboxy-1,2,4-triazole hemihydrate 3b (0.62 g, 4.62 mmol) in 40 mL of acetonitrile solution, triethylamine (0.5 mL) and 4-chloro-3-nitro-2H-[1]-benzopyran-2-one 2 (1 g, 4.6 mmol) was added. The mixture was heated slightly and refluxed for 3 h then cooled on an ice bath. The crude product was filtered off under vacuum, washed with acetonitrile (3 x 0.5 mL) and dried. Recrystallization from methanol gave 0.68 g (47%) of green crystalline product 4b, mp > 270 °C

IR (KBr, cm\(^{-1}\)): 3345, 3283, 3160, 2910, 1735, 1611, 1560, 1545, 1499, 1386, 1335, 1238, 1200, 766. \(^1\)H-NMR (δ): 11.20 (s, 1H), 9.60 (s, 1H), 7.70 (d, J=8.6 Hz, 1H), 7.55 (d, J=7 Hz, 1H), 7.50 (m, 2H), 4.30 (s, 1H), \(^1\)C-NMR (δ) 167.6, 157.6, 154.5, 153.6, 152.4, 150.6, 125.9, 125.6, 125.3, 124.9, 122.9, 104.0. Anal: Calculated for C\(_{15}\)H\(_{12}\)N\(_4\)O\(_7\): (C, 45.42%), (H, 2.23%), (N, 22.08%), (O, 30.27%).

4-(4-Methoxy-2-benzothiazolyl amino)-3-nitro-2H-1-benzopyran-2-one (4c)

A mixture of 4-chloro-3-nitro-2H-1-benzopyran-2-one 2 (0.22 g, 1 mmol) in acetonitrile (5 mL) and 3-amino-5-mercapto-1,2,4-triazole 3c (0.180 g, 1 mmol), containing triethylamine (three drops) in acetonitrile (5 mL) was refluxed on a water bath. A CaCl\(_2\) guard tube was mounted and after 15 min. a yellow crystalline product was formed. The reaction mixture was stirred under reflux for 3 h then cooled on an ice bath. The crude product was filtered off under vacuum, washed with acetonitrile (3 x 0.5 mL) and dried. Recrystallization from methanol gave 0.20 g (68%) of grey crystalline product 4c, mp = 185 °C.

IR (KBr, cm\(^{-1}\)): 3345, 3116, 3077, 2913, 2721, 1688, 1672, 1613, 1352, 1420, 1305, 1204, 750, 705. \(^1\)H-NMR (δ): 9.80 (s, 1H), 7.65 (d, J=8.6 Hz, 1H), 7.25 (d, J=2 Hz, 1H), 7.10 (dd, J=8.5 Hz, J=2 Hz 1H), 4.60 (s, 1H), 2.10 (s, 1H). \(^1\)C-NMR (δ): 164.5, 151.6, 147.2, 145.5, 144.9, 128.1, 125.3, 125.0, 124.9, 119.6, 114.1, 113.4. Anal: Calculated for C\(_{15}\)H\(_{12}\)N\(_4\)O\(_7\): (C, 43.28%), (H, 2.31%), (N, 22.95%), (O, 20.97%), (S, 10.49%). Found: (C, 43.35%), (H, 2.39%), (N, 22.84%), (S, 10.37%).

4-(5-Carboxy-1,2,4-triazolyl-3-amino) -3-nitro-2H-[1]-benzopyran-2-one (4b)

A mixture of 4-chloro-3-nitro-2H-1-benzopyran-2-one 2 (0.22 g, 1 mmol) and 2-amino-4-methoxy-benzothiazole 4-amino-5-carboxy-1,2,4-triazole 3e (0.180 g, 1 mmol), containing triethylamine (three drops) in acetonitrile (5 mL) was refluxed on a water bath. A CaCl\(_2\) guard tube was mounted and after 15 min. a yellow crystalline product was formed. The reaction mixture was stirred under reflux for 2 h, then cooled to room temperature and filtered off under vacuum. The residue was washed with 2 x 1 mL portions of acetonitrile. Recrystallization from methanol gave 0.32g (87%) of yellow crystalline product 4e, mp = 219 °C.

IR (KBr, cm\(^{-1}\)): 3325, 3177, 2940, 1709, 1596, 1481, 1367, 1281, 1041, 764. \(^1\)H-NMR (δ): 7.92 (d, J=6.5 Hz, 1H), 7.84 (d, J=6.8 Hz, 1H), 7.74 (t, J=6.8 Hz, 1H), 7.28 (m, 2H), 7.16 (d, J=8.8 Hz, 1H), 7.03 (d, J=2 Hz, 1H), 4.65 (s, 1H), 3.90 (s, 3H). \(^1\)C-NMR (δ): 162.4, 146.5, 134.6, 132.1, 126.6, 125.7, 125.1.
4-(6-Nitro-2-benzothiazolylamino)-3-nitro-2H-[1]-benzopyran-2-one (4d)

2-Amino-6-nitrobenzothiazole 3d (0.7 g, 3.55 mmol) was added to a 4-chloro-3-nitro-2H-[1]-benzopyran-2-one (2) (0.8 g, 3.55 mmol) in 12 mL of acetonitrile solution, then three drops of triethylamine were added under vigorous stirring. Recrystallization from ethanol gave 0.78 g (56%) of 4-(6-nitro-2-benzothiazolylamino)-3-nitro-2H-[1]-benzopyran-2-one 4d as orange crystalline product.

IR (KBr, cm⁻¹): 3280, 3107, 2740, 1695, 1632, 1580, 1521, 1460, 1355, 1210, 1080, 900, 775. ¹H-NMR (δ): 8.69 (s, 1H), 8.30 (d, J=6.8 Hz 1H), 7.88 (d, J=7.5 Hz, 1H), 7.52 (d, J=8.6 Hz, 1H), 7.44 (m, 2H), 7.19 (d, J=2 Hz, 1H), 4.97 (s, 1H). ¹³C-NMR (δ): 171.8, 167.5, 157.6, 156.4, 132.5, 141.1, 132.7, 130.7, 125.6, 123.0, 122.3, 120.6, 118.1, 116.5, 116.1, 115.8.

3. RESULTS AND DISCUSSION

Our study on physiologically active compounds shows a preparative method for obtaining new substituted benzopyran-2-ones via condensation reactions. We report that 4-chloro-3-nitro-2H-[1]-benzopyran-2 one (2) reacts readily with various substituted aminotriazoles and 2-aminobenzothiazoles to form the corresponding 4-triazolylamino-, respectively 4-benzothiazolylamino-3-nitro-2H-[1]-benzopyran-2-ones 4(a-e).

4-Chloro-3-nitro-2H-[1]-benzopyran-2 one (2) was obtained in 92% yield by reacting equimolar amounts of 4-hydroxy-3-nitro-2H-[1]-benzopyran-2-one (1) with phosphorus oxychloride and N,N-dimethylformamide [24]. Product 2 was subjected to condensation with substituted aminotriazoles 3(a-b) and 2-aminobenzothiazoles 3(c-e) in acetonitrile under reflux to yield the respective 4-triazolylamino-3-nitro-2H-[1]-benzopyran-2-ones 4(a-e) and 4-benzothiazolylamino-3-nitro-2H-[1]-benzopyran-2-ones 4(c-e).

Condensation of 2 with 3-amino-5-mercaptol-1,2,4-triazole (3a) in acetonitrile solution under reflux yielded 4-(5-mercaptol-1,2,4-triazolyl-3-amino)-3-nitro-2H-[1]-benzopyran-2-one (4a). Similarly, treatment of 2 with 3-amino-5-carboxy-1,2,4-triazole (3b) gave 4-(5-carboxy-1,2,4-triazolyl-3-amino)-3-nitro-2H-[1]-benzopyran-2-one (4b). Moreover, compound 2 reacts with 2-amino-4-methoxybenzothiazole (3c), to afford 4-(4-methoxybenzothiazolylamino)-3-nitro-2H-[1]-benzopyran-2-one (4c). When compound 2 reacts with 2-amino-6-nitrobenzothiazole (3d) gives 4-(6-nitro-2-benzothiazolylamino)-3-nitro-2H-[1]-benzopyran-2-one (4d) and when it reacts with 2-amino-6-fluorobenzothiazole (3e) in the presence of...
A catalytic amount of triethylamine gives 4-(6-fluoro-2-benzothiazolylamino)-3-nitro-2H-[1]-benzopyran-2-one (4e). Alkali hydrolysis of the products 4(a-e) affords 2-hydroxy-o-nitroacetophenone (5). By tautomerization of precursors of the product 5 an imine intermediate was formed. Then, reaction is followed by imine hydrolysis and decarboxylation respectively (See Scheme 1).

The structure of the resulting products was analyzed using IR, $^{1}$H-NMR and $^{13}$C-NMR spectra, as well as their elemental analysis.

Formation of 4a was confirmed by using $^{1}$H-NMR (DMSO-d$_6$) spectrum. A proton singlet at δ2.10 ppm corresponds to S-H proton, the proton doublet at δ7.65 ppm, corresponds to H-5 and doublet at δ7.25 ppm resulted from H-8 of benzene ring. The spectrum also displayed a doublet of doublet at δ7.00 ppm resulted from aromatic H-6 and a doublet of doublet at δ7.10 ppm, from H-7. Signals at δ9.80 and δ4.60 ppm assigned for triazole NH and coumarin NH group also are displayed. $^{13}$C-NMR spectrum of 4a showed characteristic absorptions responsible for 11 carbon atoms at δ164.5 ppm for C=O, δ151.6 and δ114.1 ppm for pyrone C, δ147.2 ppm and δ145.5 ppm for triazole C and δ144.9, δ128.1, δ125.3, δ125.0, δ124.9, δ119.6 ppm for aromatic C.

IR spectrum of 4a is characterized with an absorption appearing at 3345 cm$^{-1}$ due to typical νNH stretching of secondary amines. IR spectrum of this product also showed the absorption modes at 3116-3077 and 2721 cm$^{-1}$ corresponding to νCH stretching of aromatic ring and νSH stretching of mercapto group. Typical νCO absorption of unsaturated six-membered lactones is observed at 1722 cm$^{-1}$. Signals which are responsible for aromatic νC=N and νC=C vibrations appears at 1677 and 1613 cm$^{-1}$, respectively. At 1420 and 1305 cm$^{-1}$ we see the absorptions of the stretching νNO$_2$ (as) and νNO$_2$ (sym), and at 750 cm$^{-1}$ absorption of the bending δCH out of plane of the aromatic system were also appeared.

In the $^{1}$H-NMR spectrum of compound 4b, appeared a doublet at δ7.70 ppm (assigned from H-5), a doublet at δ7.55 ppm, from H-8, and a multiplet at δ7.50 ppm responsible for H-6 and H-7. Two singlets at δ11.20 ppm and δ9.60 ppm correspond to OH and triazole NH proton absorptions, whereas a singlet at δ4.30 ppm resulted from coumarin NH.

In the $^{13}$C-NMR spectrum of 4b, 12 characteristic absorptions are displayed at δ167.6 and δ157.6 ppm for COOH and C=O, δ154.5 and δ104.0 ppm for pyrone C, δ153.6 and δ152.4 ppm for triazole C and δ150.6, δ125.9, δ125.6, δ125.3, δ124.9, δ122.9 ppm for aromatic C.

IR spectrum of 4b showed a broad absorption at 3250-3600 cm$^{-1}$ resulted from decoupled νNH (str) and νCOOH (str) vibrations. Signals at 3160 cm$^{-1}$ and at 2980 cm$^{-1}$ present the stretching of aromatic νCH (as) and νCH (sym) vibrations. A sharp peak at 1735 cm$^{-1}$ and the peaks at 1611 cm$^{-1}$ and 1560 cm$^{-1}$ are responsible for νCO str, νC=N and νC=C (ar), respectively. Two absorptions at 1545 cm$^{-1}$ and 1335 cm$^{-1}$ correspond to νNO$_2$ (as) and νNO$_2$ (sym), and the δCH bending (ip) and δCH bending (oop) mode at 1200 cm$^{-1}$ and 766 cm$^{-1}$ also were observed. A sharp peak at 1238 cm$^{-1}$ is responsible for δC-O of sixteen-membered lactonic ring.
Formation of 4c is identified from $^1$H-NMR (dmso-$d_6$) spectrum where the absorption of a singlet at δ3.90 ppm (3H, methoxy protons) appeared. The spectrum also displayed a signal at δ4.65 ppm (s, 1H, assigned for NH), and for aromatic protons: δ7.92 ppm (d, 1H, H’-5), δ7.84 ppm (d, 1H, H’-7), δ7.74 ppm (t, 1H, H’-6), δ7.28 ppm (m, 2H, H-6 and H-7), δ7.16 ppm (d, 1H, H-5) and δ7.03 ppm (d, 1H, H-8) (H- benzopyrane-2-one aromatic protons, H’- benzothiazole aromatic protons).

$^{13}$C-NMR spectrum of 4c showed quality absorption peaks responsible for 17 carbon atoms at δ162.4 ppm for C=O, δ146.5, δ134.6 ppm for benzopyrone C-N and benzothiazole C-N and δ132.1, δ126.6, δ125.7, δ125.1, δ124.5, δ124.3, δ122.9, δ117.2, δ116.1, δ114.6, δ114.5, δ109.4, δ109.3, δ56.2 ppm for aromatic benzothiazole and benzopyrone C.

In the IR spectrum for 4c an absorption peak appeared at 3325 cm$^{-1}$ due to typical νNH stretching of secondary amines. Absorption at 1709 cm$^{-1}$ attributed to a typical νCO of unsaturated six-membered lactones was observed. IR spectrum of this product also showed the absorption modes at 3000–3190 cm$^{-1}$ responsible for νCH stretching absorption of aromatic ring, at 2940 cm$^{-1}$ for νCH stretching of methoxy group and at 1646 cm$^{-1}$ and 1596 cm$^{-1}$ which are responsible for aromatic νC=N and νC=C absorption. At 1481 cm$^{-1}$ and 1367 cm$^{-1}$ for the stretching νNO$_2$ (as) and νNO$_2$ (sym), and at 764 cm$^{-1}$ for the bending δCH (ar) absorption peaks were also appeared.

The IR spectrum of 4d showed a characteristic mode at 3280 cm$^{-1}$ as a result of νNH stretching absorption. The absorption peaks at 3107 cm$^{-1}$ are responsible for aromatic ν CH stretching vibrations. The characteristic band which may have resulted from stretching carbonyl vibration was appeared at 1695 cm$^{-1}$. Absorptions at 1632 cm$^{-1}$ and at 1580 cm$^{-1}$ are responsible for νC=N and νC=C (ar) vibrations. The absorption modes at 1521 cm$^{-1}$ and 1355 cm$^{-1}$ may be assigned to stretching νNO$_2$ (as) and νNO$_2$ (sym). Absorption for νC–O–C of lactonic system appears at 1210 cm$^{-1}$. A sharp peak at 775 cm$^{-1}$ resulted from aromatic δCH absorptions.

In the $^1$H-NMR spectrum of compound 4d two singlets at δ4.97 ppm (1H, assigned from amine proton absorption) and at δ8.69 ppm (1H, responsible for H’-7) were observed. Doublets at δ8.30, δ7.88, δ7.52 ppm, and δ7.19 ppm, correspond to aromatic H’-5, H’-4, H-5 and H-8, whereas a triplet signal at δ7.44 ppm resulted from H-6 and H-7 protons’ absorptions.

IR spectrum of 4e showed the absorption at 3430 cm$^{-1}$ responsible for νNH stretching. The νCH stretching vibrations from aromatic ring appeared at 3082 cm$^{-1}$. A sharp peak at 1719 cm$^{-1}$ and peaks at 1625 cm$^{-1}$ and 1497 cm$^{-1}$ responsible for νCO str., νC=N and νC=C (ar) were observed. Two absorptions at 1476 cm$^{-1}$ and 1360 cm$^{-1}$ attributable to νNO$_2$ (as) and νNO$_2$ (sym), and the δCH (oop) mode at 754 cm$^{-1}$ also were observed. The peak at 1275 cm$^{-1}$ may have resulted from νC-F absorption of aromatic benzothiazole system. The νC-O of lactonic system is assigned at 1350 cm$^{-1}$.

$^1$H-NMR spectrum of 4e showed a singlet at δ4.76 ppm resulting from NH proton. Doublets at δ7.88 and δ7.55 ppm are responsible for H’4 and H’-5 absorptions, whereas a singlet peak at δ8.76 ppm resulted from H’-7 proton. A multiple peak at δ7.41 ppm corresponds to aromatic H-6 and H-7, whereas doublets at δ7.63 and δ7.20 ppm resulted from H-5 and H-8 absorptions. $^{13}$C-NMR spectrum of 4e showed characteristic absorptions at δ168.3, δ167.6, and δ159.3 ppm for C=O, C-2 and C-4. Characteristic peaks at δ156.9, δ152.5, δ140.5 and, δ109.5 ppm results from C'-7, C-O, C-N (benzothiazole) and C-3 whereas signals at δ132.1, δ127.8, δ125.6, δ123.0, δ122.2, δ120.5, δ116.4, δ116.1, δ114.4 are responsible for aromatic carbon atoms.

Hydrolysis of products 4(a-e) in alkaline media resulted in formation of 2-hydroxy-o-nitroacetophenone (5). This argues that derivatives which contain benzopyran-2-one moiety are very sensitive to basic conditions. The characteristic IR absorptions of product 5 appeared at 3080–3400 cm$^{-1}$ (a broad band) and 2950 cm$^{-1}$ which are responsible for νOH stretching, νOH (chelate), aromatic νCH and methylene νCH absorptions. The characteristic peak derived from lactonic carbonyl as a result of intramolecular hydrogen bond appears to have moved down at 1637 cm$^{-1}$. In the IR spectrum of the hydrolysis product 5 also showed bands at 1560 cm$^{-1}$ for νC=C (ar), 1449 cm$^{-1}$ for νNO$_2$ (as), 1369 cm$^{-1}$ for νNO$_2$ (sym) and 754 cm$^{-1}$ aromatic δCH (oop). These values and melting point have been compared to the previous reported analysis [22] and show similar results.

We also have examined the antibacterial activity of the synthetic compounds. Our investigation is directed toward testing their activity against S.
aureus, E. coli and Klebsiella. Applying the Kirby-Bayer method [23] we measured diameters of the inhibition zone around discs which are previously marked with DMF solutions of 2 mg/mL, 4 mg/mL and 6 mg/mL.

These derivatives have shown moderate to high activity against S. aureus, E. coli and Klebsiella. A series of methoxybenzotiazoly- fluorobenzothiazolyl- and nitrobenzothiazolyl-derivatives were more active against S. aureus. Emphatic activity against E. coli exhibited triazolylcarboxylic- fluorobenzothiazolyl-derivatives, whereas methoxybenzothiazoly- and nitrobenzothiazolyl-derivatives are more active against Klebsiella. Product 4c was more active against S. aureus relative to compound 2 (d_4c/d_2=1.4-1.6), whereas the same product was more active against Klebsiella (d_4c/d_2=1.2-1.5). Furthermore, product 4b was more active against E. coli (d_4b/d_2=1.5 -1.9). In general, increasing the concentration causes high activity against these microorganisms (figures 1, 2 and 3).

4. CONCLUSION

By catalytic condensation reaction of 4-chloro-3-nitro-2H-[1]-benzopyran-2-one (2) and substituted aminotriazoles 3(a-b) and 2-aminobenzothiazoles 3(c-e), 4-triazolylamino-3-nitro-2H-[1]-benzopyran-2-ones 4(a-b) and 4-benzothiazolylamino-3-nitro-2H-[1]-benzopyran-2-ones 4(c-e) are synthesized in good yield. We may conclude that these derivatives have shown moderate to high activity against S aureus, E. coli and Klebsiella. Compounds 4c, 4e and 4d are more active against S. aureus. Emphatic activity against E. coli exhibited compounds 4b and 4e, whereas 4c and 4d are more active against Klebsiella. In general, products of series 4 are more active against these microorganisms relative to compound 2. Increasing the concentration causes high activity against these microorganisms.

5. REFERENCE AND NOTES

Osman, H.; Arshad, A.; Lam, C. K.; Bagley, M. C. Chem. Cent. J. 2012, 6, 32. [CrossRef]


