Chemistry and Materials Research
ISSN 2224- 3224 (Print) ISSN 2225- 0956 (Online)
Vol.3 No.9, 2013

Synthesis of New 2*H*-Pyrano[3,2-*h*]quinolines With Potential Biological Activity

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Abstract

5-Halo-8-hydroxyquinoline-7-carboxaldehyde **1a,b** reacted with diethyl malonate to afford ethyl 6-halo-2-oxo-2*H*-pyrano[3,2-*h*]quinoline-3-carboxylates **2a,b**. Michael addition followed by cyclisation of acetyl acetone with **2a,b** gave 1-acetyl-11-halo-2-methyl-4*H*,5*H*,4,5-dioxo-dipyrano[3,4-*c*,3`,2`-*h*]quinoline derivatives **3a,b**. Compounds **2a,b** were converted into their acid hydrazide **4a,b**. Reaction of **4a,b** with acetyl acetone produced 6-halo-3-(3`,5`-dimethyl-1*H*-pyrazole-1-carbonyl)-2*H*-pyrano[3,2-*h*]quinolin-2-ones **5a,b**. Treatment of acid hydrazides **4a,b** with isatin yielded 1*H*,2*H*-3-(2*H*-6-halo-2-oxo-pyrano[3,2-*h*]quinolin-3-carboxyhydrazono)-2-indolinones **6a,b** which on cyclisation with Conc. H_2SO_4 afforded 3-[1,3,4-oxadiazino(5,6-*b*)indol-2-yl]-6-halo-2*H*-pyrano[3,2-*h*]quinolin-2-ones **7a,b**. The biological screening was showed that pyrano[3,2-*h*] quinoline derivatives which containing pyrazole and indoline moieties have excellent antibacterial and antifungal activities.

Keywords: Quinoline, 2*H*-pyrano[3,2-*h*]quinoline, 8-hydroxyquinoline,microbial activity.

Introduction

Quinolines were reported to show a broad spectrum of pharmacological properties like antimicrobial (Jumade *et al.* 2009, Hussein *et al.* 2009, Mohana *et al.* 2011, Thumar *et al.* 2011, Madhu *et al.* 2012), antimalarial (Kaur *et al.* 2010), anti-inflammatory (Savini *et al.* 1993, Abadi *et al.* 2005), antitumor (Abu-Hashem *et al.* 2012, Lee *et al.* 2000), antioxidant (Korrichi *et al.* 2009) and antiplatelet (Chen *et al.* 2010) activity. In addition, the pyranoquinoline moiety is present in many alkaloids which occur in the plant family Rutaceae. These alkaloids have been reported to be associated with interesting pharmacological properties like antitumor (El-Agrody *et al.* 2013] , antimicrobial (Hassanin *et al.* 2012, Dhanabal *et al.* 2006, Kumar *et al.* 2004, Abdel Hafez 1992), anti-inflammatory (Chen *et al.* 2007) , antiallergic (Cairns *et al.* 1985) and antimalarial (Isaka *et al.* 2001)

properties as well as inhibition of calcium signaling (Koizumi *et al.* 2007) and platelet aggregation (Chen *et al.* 1997). In light of these facts, the present work describes the synthesis of pyrano[3,2-*h*]quinoline derivatives containing pyrane, pyrazole, indole and oxadiazino[5,6-*b*]indole moieties and assesses their antimicrobial activity.

Experimental

Melting points were estimated with a Stuart apparatus in open capillaries and are uncorrected. Purity of compounds was checked by TLC. IR spectra were recorded as KBr pellets on a Jasco FTIR 460 plus spectrophotometer. ^{1}H-NMR (300 MHz) and ^{13}C-NMR (75 MHz) spectra were recorded on a Varion instrument. Chemical shifts are reported as δ,ppm values relative to tetramethylsilane (TMS) as internal reference. Elemental analyses were performed on a Perkin-Elmer 240 microanalyser in the Faculty of Science, Cairo University.

Ethyl 6- halogeno -2-oxo-2H-pyrano[3,2-h]quinoline-3-carboxylate 2a,b :

A mixture of 5-halogeno-8-hydroxyquinoline-7-carboxaldehyde (**1a,b**) (0.01 mole), diethyl malonate (0.01 mole) and piperidine (0.5 ml) in ethanol (20 ml) was heated under reflux for 2h. After cooling, the product was collected by filtration and recrystallized from ethanol to give **2a,b**.

Ethyl 6-bromo-2-oxo-2H-pyrano[3,2-h]quinoline-3-carboxylate 2a:

Yield: 87%; m.p. 260-262 ^{o}C, IR (KBr) υ (cm^{-1}): 1725 (C=O ester), 1703 (C=O). ^{1}H-NMR (DMSO-d_6, δ ppm): 1.25(t, 3H, CH_3), 3.90(q, 2H, CH_2 ethyl), 7.10(s,1H, C_4-H), 7.68(t,1H,C_8-H), 8.06(s,1H, C_5-H), 8.51(d,1H,C_7-H), 8.93(d,1H,C_9-H). ^{13}C-NMR (DMSO-d_6, δ ppm): 166.6, 158.5, 150.4,139.5,133,125.7,122.3,117.1,112.3,60.2,13.9. Anal. calcd. for $C_{15}H_{10}BrNO_4$ (348.152): C,51.74; H, 2.89; N, 4.02; found: C, 51.75; H, 2.90; N, 4.03.

Ethyl 6-chloro-2-oxo-2H-pyrano[3,2-h]quinoline-3-carboxylate 2b:

Yield: 79%; m.p. 232-234 ^{o}C, IR (KBr), υ (cm^{-1}): 1730 (C=O ester), 1709 (C=O). ^{1}H-NMR

(DMSO-d_6, δ ppm): 1.30(t, 3H, CH_3), 3.98(q, 2H, CH_2 ethyl), 7.19(s,1H, C_4-H), 7.77(t,1H,C_8-H), 8.14(s,1H, C_5-H), 8.58(d,1H,C_7-H), 8.70(d,1H,C_9-H). ^{13}C-NMR(DMSO-d_6, δ ppm): 165.1,159.4 ,152.9, 138.5,132.6,123.1,120.4,126.6,112.5,61.2,14. Anal. calcd. for $C_{15}H_{10}ClNO_4$ (303.69): C,59.32; H, 3.31; N, 4.61; found: C, 59.34; H, 3.32; N, 4.60.

1-Acetyl-11-halo-2-methyl-4*H*,5*H*,4,5-dioxo-dipyrano[3,4-*c*,3`,2`-*h*]quinoline derivatives 3a,b:

Compound **2a,b** (0.01mole) was added to ethanol(50 ml) containing sodium ethoxide. The reaction mixture was heated for 6h, then left overnight at room temperature. The solvent was evaporated and the residue acidified with dilute HCl to get the solid product. The solid was collected by filtration, washed with water, dried and crystallized from methanol to yielded **3a,b**.

1-Acetyl-11-bromo-2-methyl-4H,5H,4,5-dioxo-dipyrano[3,4-c,3`,2`-h]quinoline derivatives 3a:

Yield: 53%; m.p. 266-268 ^{o}C, IR (KBr), υ (cm^{-1}): 1682 ($COCH_3$), 1658 and 1650 (C=O). ^{1}H-NMR (DMSO-d_6 , δ ppm): 2.02(s, 3H, CH_3), 2.13(s, 1H, CH_3), 7.21(t,1H, C_9-H), 7.93(s,1H,C_{12}-H), 8.31(d,1H, C_{10}-H), 8.74(d,1H,C_8-H). ^{13}C-NMR(DMSO-d_6, δ ppm): 183.4, 162.7, 159.2,153.8, 148.3,130.8,121.2,117.4,115.2,25.3,12.8. Anal. calcd. for $C_{18}H_{10}BrNO_5$ (400.19):C,54.02; H, 2.52; N, 3.50; found: C, 54.00; H, 2.53; N, 3.53.

1-Acetyl-11-chloro-2-methyl-4H,5H,4,5-dioxo-dipyrano[3,4-c,3`,2`-h]quinoline derivatives 3b:

Yield: 46%; m.p. 248-250 ^{o}C, IR (KBr), υ (cm^{-1}): 1674 ($COCH_3$), 1659 and 1651 (C=O). ^{1}H-NMR (DMSO-d_6 , δ ppm): 2.05(s, 3H, CH_3), 2.15(s, 1H, CH_3), 7.26(t,1H, C_9-H), 7.98(s,1H,C_{12}-H), 8.21(d,1H, C_{10}-H), 8.79(d,1H,C_8-H). ^{13}C-NMR(DMSO-d_6, δ ppm): 182.7,160.9, 162.5,157.5, 150.1,132.3,125.8,121.6,120,27.2,14.3. Anal. calcd. for $C_{18}H_{10}ClNO_5$ (355.74): C,60.78; H, 2.83; N, 3.94; found: C, 60.75; H, 2.81; N, 3.91.

6-Halo-2-oxo-2H- pyrano[3,2-h]quinoline -3-carbohydrazide (4a,b) :

A mixture of **2a,b** (0.01mole), hydrazine hydrazine (0.01 mole), ethanol (15 ml) and acetic acid
(0.5 ml) was refluxed for 5h. The solution was concentrated, cooled and poured into water. The solid product thus obtained was filtered and dried. The product was recrystallized from ethanol to give **4a,b**.

6-Bromo-2-oxo-2H- pyrano[3,2-h]quinoline-3-carbohydrazide 4a :

Yield: 85%; m.p. 210-212 ^{o}C, IR (KBr) υ (cm^{-1}): 3421-3415 (NH_2), 3219 (NH), 1702 (C=O), 1672 (CO amidic). ^{1}H-NMR (DMSO-d_6, δ ppm): 4.15(s, 2H, NH_2, D_2O exchangeable)), 5.75(s,1H, C_4-H), 7.48(t,1H,C_8-H), 7.70(s,1H, C_5-H),), 8.50(d,1H,C_7-H), 8.90(d,1H,C_9-H), 10.81(s,1H,NH, D_2O exchangeable). ^{13}C-NMR(DMSO-d_6, δ ppm): 162.4,154.1, 147.2,135.1,131.1 ,124.6, 120.8,115.2, 111.9. Anal. calcd. % for $C_{13}H_8BrN_3O_3$ (334.13): C,46.73; H, 2.41; N, 12.57; found: C, 46.77; H, 2.42; N, 12.55.

6-Chloro-2-oxo-2H- pyrano[3,2-h]quinoline-3-carbohydrazide 4b :

Yield: 89%; m.p. 198-200 ^{o}C, IR (KBr) υ (cm^{-1}): 3428-3419 (NH_2), 3219 (NH), 1687 (C=O), 1666 (CO amidic). ^{1}H-NMR (DMSO-d_6, δ ppm): 3.88(s, 2H, NH_2, D_2O exchangeable)), 5.11(s,1H, C_4-H), 7.39(t,1H,C_8-H), 7.75(s,1H, C_5-H), 8.50(d,1H,C_7-H), 8.80.(s,1H,NH, D_2O exchangeable), 8.93(d,1H,C_9-H). ^{13}C-NMR(DMSO-d_6, δ ppm): 160.9,152.4,148.7,133.6,130.1,126.1, 122.5,118.5, 112.2. Anal. calcd. % for $C_{13}H_8ClN_3O_3$ (289.67): C,53.90; H, 2.78; N, 14.50; found: C, 53.91; H, 2.80; N,14.52.

6-Halo-3-(3`,5`-dimethyl-1H-pyrazole-1-carbonyl)-2H-pyrano[3,2-h]quinolin-2-one (5 a,b):

To a solution of **4a,b** (0.01 mole for each) in acetic acid (50 ml), acetyl acetone (0.01mole) was added. The reaction mixture was heated under reflux for 6h. The solvent was concentrated and allowed to stand overnight. The product was treatment with ether to solidify and then the solid product was filtered and recrystallized from ethanol to produce **5a,b**.

6-Bromo-3-(3`,5`-dimethyl-1H-pyrazole-1-carbonyl)-2H-pyrano[3,2-h]quinolin-2-one 5a:

Yield: 52%; m.p. 242-244 ^{o}C, IR (KBr) υ (cm^{-1}): 1687 (C=O), 1666 (C=O amidic). ^{1}H-NMR (DMSO-d_6, δ ppm): 2.15(s,6H,2CH_3), 5.24(s,1H, CH-pyrazole), 7.39(t,1H,C_8-H), 7.67(s,1H, C_5-H), 8.52(d,1H,C_7-H), 8.59.(s,1H,C_4-H), 8.93(d,1H,C_9-H). ^{13}C-NMR(DMSO-d_6, δ ppm): 182.4, 157.2, 148.1,146.3,144.3,143.2,132.3,132.1,124.7,122.8,116.8,116.1,103.2,16.7,11.4. Anal. calcd. % for $C_{18}H_{12}BrN_3O_3$ (398.22): C,54.29; H, 3.04; N, 10.55; found: C, 54.26; H, 3.05; N,10.53.

6-Chloro-3-(3`,5`-dimethyl-1H-pyrazole-1-carbonyl)-2H-pyrano[3,2-h]quinolin-2-one 5b:

Yield: 48%; m.p. 228-230 ^{o}C, IR (KBr) υ (cm^{-1}): 1678 (C=O), 1669 (C=O amidic). ^{1}H-NMR (DMSO-d_6, δ ppm): 2.07(s,6H,2CH_3), 5.18(s,1H, CH-pyrazole), 7.14(t,1H,C_8-H),

7.59(s,1H, C_5-H), 8.47(d,1H,C_7-H), 8.61.(s,1H,C_4-H), 8.98(d,1H,C_9-H). ^{13}C-NMR(DMSO-d_6, δ ppm): 181.5, 159.0, 149.4,145.8,144.6,143.1,132.9,132.4,125.3,122.2,113.9,116.7,104.6,17.7,11.2. Anal. calcd. % for $C_{18}H_{12}ClN_3O_3$ (353.77): C,61.11; H, 3.42; N, 11.88; found: C, 61.09; H, 3.42; N,11.84.

1*H*,2*H*-3-(2*H*-6-Halo-2-oxo-pyrano[3,2-*h*]quinolin-3-carboxyhydrazono)-2-indolinones (6a,b):

A mixture of **4a,b** (0.01 mole for each) and isatin (0.01 mole) in ethanol (20 ml) containing drops of acetic acid was heated under reflux for 2 h. The product which precipitated after cooling was filtered off and recrystallized from ethanol to give **6a,b**.

1H,2H-3-(2H-6-Bromo-2-oxo-pyrano[3,2-h]quinolin-3-carboxyhydrazono)-2-indolinones 6a:

Yield: 63%; m.p. 293-295 ^{o}C, IR (KBr) υ (cm^{-1}): 3299 (NH), 1677 (C=O), 1642 (CO amidic).

^{1}H-NMR (DMSO-d_6,δ ppm): 7.30(s,1H,C_5-H), 7.50(t,1H,C_8-H), 8.0(s,1H,NH-indole,D_2O exchangeable),8.12(s,1H,C_4-H), 8.18(d,1H, C_7-H), 8.98(d,1H,C_9-H),10.12 (s,1H,NH, D_2O exchangeable). ^{13}C-NMR(DMSO-d_6, δ ppm): 165.8, 161.5, 155.5, 150.8, 138.6, 132.8, 134.3, 126.2, 122.3,118.3,114.2. Anal. calcd. % for $C_{21}H_{11}BrN_4O_4$ (463.25): C,54.45; H, 2.39; N, 12.09; found: C, 54.41; H, 2.36; N,12.08.

1H,2H-3-(2H-6-Chloro-2-oxo-pyrano[3,2-h]quinolin-3-carboxyhydrazono)-2-indolinones 6b:

Yield: 63%; m.p. 284-286 ^{o}C, IR (KBr) υ (cm^{-1}): 3275 (NH), 1671 (C=O), 1652 (C=O amidic). ^{1}H- NMR (DMSO-d_6, δ ppm): 7.36(s,1H,C_5-H), 7.47(t,1H,C_8-H), 8..04 (s,1H,NH-indole, D_2O exchang-eable),8.11(s,1H,C_4-H),8.19(d,1H,C_7-H),8.87(d,1H,C_9-H),10.16(s,1H,NH,D_2O exchangeable). ^{13}C- NMR(DMSO-d_6, δ ppm): 165.2, 160.8, 153.7, 148.8, 137.5, 133.8, 132.3, 127.1, 123.5,116.2, 111.7. Anal. calcd. % for $C_{21}H_{11}ClN_4O_4$ (418.80): C,60.23; H, 2.65; N, 13.38; found: C, 60.21; H, 2.66; N,13.35.

3-[1,3,4-Oxadiazino(5,6-b)indol-2-yl]-2H-6-halo-2-oxo-pyrano[3,2-h]quinoline (7a,b):

Compound **6a,b** (0.01 mole for each) was dissolved in conc. H_2SO_4 (15 ml) at 0-5 ^{o}C. The reaction mixture was stirred for 30 min and further kept for 4 h at room temperature. The

mixture was poured into crushed ice and then neutralized with saturated sodium carbonate solution. The solid product was filtered, washed with water and recrystallized from DMF to give **7a,b**.

3-[1,3,4-Oxadiazino(5,6-b)indol-2-yl]-2H-6-bromo-2-oxo-pyrano[3,2-h]quinoline 7a:

Yield: 46%, m.p. 283-285 ^{o}C, IR, υ (cm^{-1}): 1682 (C=O), 1545 (C=N). ^{1}H-NMR (DMSO-d_6, δ ppm): 6.44(s,1H, C_4-H), 6.90(d,1H,$C_{5`}$-H), 7.25(t,2H,$C_{6`}$ and $C_{7`}$-H),7.34(t,1H, C_8-H), 7.52 (s,1H,C_5-H), 8.52(d,1H,C_7-H), 8.84(d,1H,C_9-H). ^{13}C-NMR(DMSO-d_6, δppm): 159.2, 155.5, 148.9, 134.3, 132.7, 131.3,129.5,127.4,126.9,122.7, 120.3,117.2. Anal. calcd. % for $C_{21}H_9BrN_4O_3$ (445.23): C,56.65; H, 2.04; N, 12.58; found: C, 56.64; H, 2.01; N,12.55.

3-[1,3,4-Oxadiazino(5,6-b)indol-2-yl]-2H-6-chloro-2-oxo-pyrano[3,2-h]quinoline 7b:

Yield: 42% ,m.p 270-272 ^{o}C, IR, υ (cm^{-1}): 1687 (C=O), 1555 (C=N). ^{1}H NMR (DMSO-d_6, δ ppm): 6.41(s,1H, C_4-H), 6.88(d,1H,$C_{5`}$-H), 7.21(t,2H,$C_{6`}$ and $C_{7`}$-H),7.30(t,1H, C_8-H), 7.48 (s,1H,C_5-H), 8.52(d,1H,C_7-H), 8.81(d,1H,C_9-H). ^{13}C-NMR(DMSO-d_6, δ ppm): 160.4, 152.2, 144.6, 134.5, 133.1, 131.9, 129.1, 126.4, 124.6, 122.2, 118.9,114.2, Anal. calcd. % for $C_{21}H_9ClN_4O_3$ (400.78): C,62.94; H, 2.26; N, 13.98; found: C, 62.92; H, 2.23; N,13.99.

Results and Discussion

Knoevengeal condensation of 5-halo-8-hydroxyquinoline-7-carboxaldehyde (**1a,b)** (Voloshin *et al.* 2004) with diethylmalonate in the presence of piperidine furnished ethyl 6-halo-2-oxo-2*H*-pyrano[3,2-*h*]quinoline-3-carboxylates (**2a,b)** (scheme1). The ^{1}H-NMR spectrum (DMSO-d_6) of compounds **2a**, as an example, showed signals at δ 1.25(t, 3H, CH_3) and 3.90 ppm (q, 2H, CH_2 ethyl) as well as singlet at δ 7.1 ppm for pyrane C4-H. The IR spectra of **2a,b** exhibited carbonyl absorptions bands at 1725 (C=O ester) and 1703 cm^{-1} (C=O) .

Michael addition followed by cyclisation of acetyl acetone with **2a,b** in the presence of sodium methoxide gave 1-acetyl-11-halo-2-methyl-4*H*,5*H*,4,5-dioxo-dipyrano[3,4-*c*,3`,2`-*h*]quinoline derivatives (**3a,b)**(scheme1). The ^{1}H-NMR spectrum (DMSO-d_6) of **3a** revealed the presence of signals at δ 2.12 (s,3H,$COCH_3$), 2.2(s,3H,CH_3) and 8.17 ppm (s,1H,C12-H).

Compounds **2a,b** were converted into its acid hydrazide (**4a,b)** by its reaction with hydrazine hydrate . The later compounds showed the presence of absorption band at 3401-3394, 3219 cm^{-1} for NH_2 and NH, respectively, in its IR spectrum. ^{1}H-NMR of **4a**, as an example, revealed presence of two singlet signals at δ 4.15 and 8.80 ppm for two NH_2 protons and one NH proton ,respectively.

Treatment of **4a,b** with acetyl acetone afforded 6-halo-3-(3`,5`-dimethyl-1*H*-pyrazole-1-carbonyl)-2*H*-pyrano[3,2-*h*]quinolin-2-ones (**5a,b**) (scheme1). The ^{1}H-NMR of **5a** showed signals at δ 2.32 and 2.48 for two methyl groups and 5.9 ppm for pyrazole C4-H. The acid hydrazides **4a,b** on treatment with isatin gave 1*H*,2*H*-3-(2*H*-6-halo-2-oxo-pyrano[3,2-*h*]quinolin-3-carboxyhydrazono)-2-indolinones (**6a,b**). ^{1}H-NMR of **6b** ,as an example, exhibited signals at δ 8.30 for NH of indole, 7.13
(NH hydrazide) and 6.75 ppm(pyrane C_4-H). Compounds **6a,b** undergo to cyclization by action of conc. H_2SO_4 to afford 3-[1,3,4-oxadiazino(5,6-*b*)indol-3yl]-6-halo-2*H*-pyrano[3,2-*h*]quinolin-2-ones (**7a,b**) (scheme1). The IR spectrum of **7a,b** showed the absence of an absorption bands at NH region.

Antimicrobial Activity

The *in vitro* antimicrobial activity of the synthesized compounds was performed by disc diffusion method against Gram-positive bacteria, (*Staphylococcus aureus*, *Bacillus subtilis*, *Bacillus cereus*), Gram-negative bacteria (*Pseudomonas aurignosa*, *Echerichia coli*, *Salmonella typhi*), in addition to pathogenic fungi (*Aspergillus niger*, *Candida albicans* and *Penicillium sp*). Ampicillin and streptomycin were used as standard drugs for the study. The fresh bacterial culture was obtained by inoculating bacteria into peptone water liquid media and incubating at 37± 2 °C for 18-24 hours. This culture was mixed with nutrient agar media and poured into Petri dishes. After culture media solidification four wells were made at equal distance by using a sterile steel cork borer (8mm diameter). Into these wells different concentrations of standard drug and synthesized compounds were introduced. Dimethyl formamide (DMF) was used as a control. The standard drugs and synthesized compounds were dissolved in a minimum quantity of DMF and adjusted, to made up the volume with distilled water to get 50µg/ml. After introduction of standard drug and synthesized

compounds, the plates were placed in a refrigerator at 8-10 °C for proper diffusion of drugs into the media. After two hours of cold incubation, the Petri plates were transferred to incubator and maintained at 37±2 °C for 18-24 hours. Results are recorded as average diameter of inhibition zone in mm and are presented in table 1 and 2. In general, the inhibitory activity against the Gram-negative bacteria was higher than that of the Gram-positive bacteria. Compounds **5a**, **5b**, **6a** and **6b** showed excellent activity against Gram-negative bacteria and good activity against Gram-positive bacteria. On the other hand, compounds **3a** and **7a** showed moderate activity against Gram-negative bacteria. All compounds exhibited moderate activity against fungi except compounds **5a**,**5b**,**6a** and **6b** showed excellent activity.

Conclusion

Ethyl 6-halo-2-oxo-2*H*-pyrano[3,2-*h*]quinoline-3-carboxylates are used as key intermediate to synthesis 4,5-dioxo-dipyrano[3,4-*c*,3`,2`-*h*]quinoline, 3-(3`,5`-dimethyl-1*H*-pyrazole-1-carbonyl)-2*H*-pyrano[3,2-*h*]quinolin-2-ones,3-(2*H*-6-halo-2-oxo-pyrano[3,2-*h*]quinolin-3-carboxyhydrazono)-2-indolinones and 3-[1,3,4-oxadiazino(5,6-*b*)indol-2-yl]-6-halo-2*H*-pyrano[3,2-*h*]quinolin-2-ones derivatives. The biological screening showed that 3-(3`,5`-dimethyl-1*H*-pyrazole-1-carbonyl)-2*H*-pyrano[3,2-*h*]quinolin-2-ones and (3-(2*H*-6-halo-2-oxo-pyrano[3,2-*h*]quinolin-3-carboxyhydrazono)-2-indolinones derivatives exhibited excellent antimicrobial activity.

Acknowledgment

Special thanks to Dr. Hend A. Hamedo, Faculty of Science, King Khaled University, Abha, Saudi Arabia, for her cooperation in determining the antimicrobial activity of the synthesized compounds.

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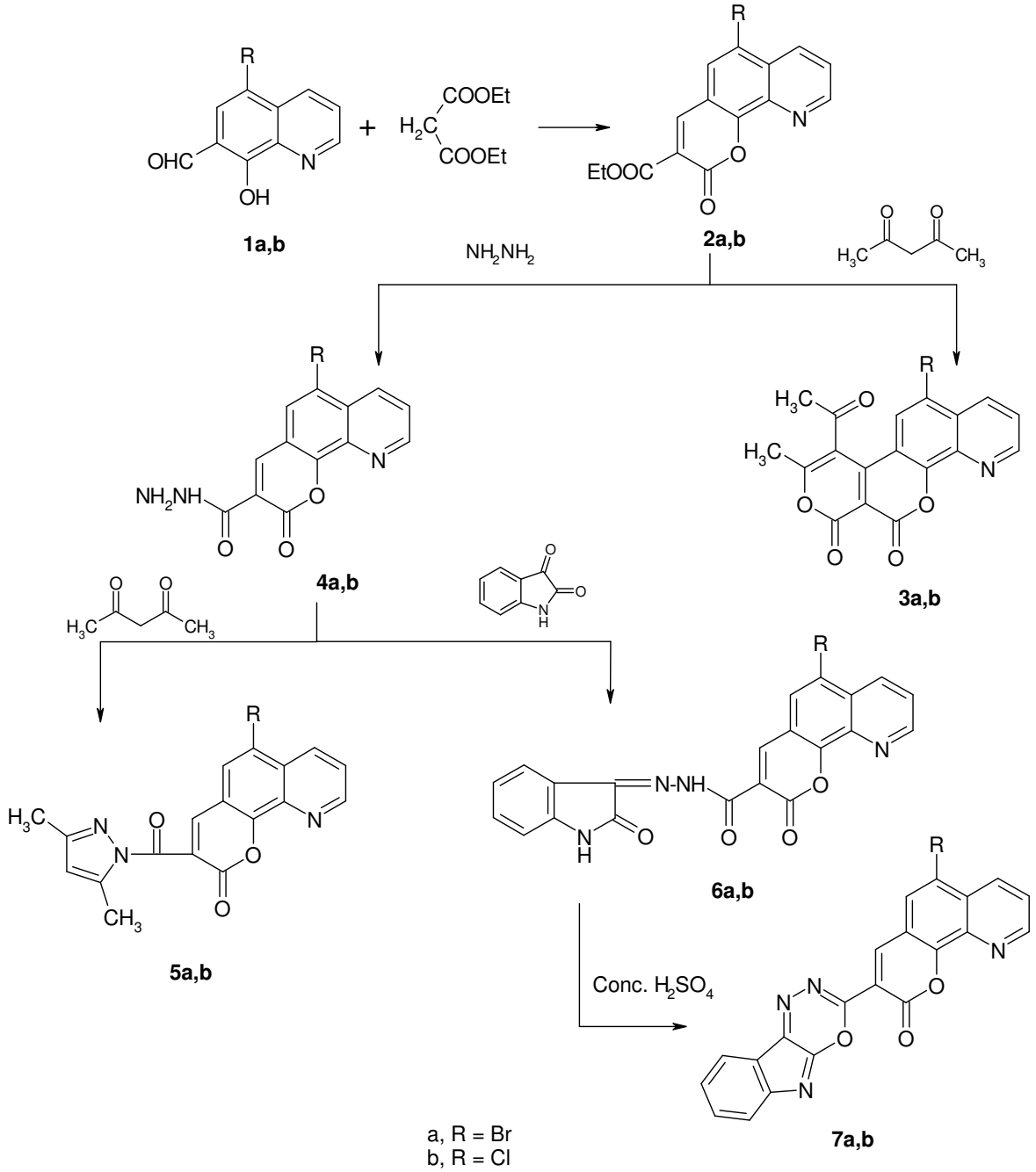
R
OHC
N
OH
1a,b
+
COOEt
H2C
COOEt
R
N
EtOOC
O
O
2a,b
NH2NH2
H3C
CH3
R
NH2NH
N
O
O
4a,b
R
H3C
H3C
N
O
O
O
O
3a,b
H3C
CH3
O
N
H
R
H3C
N
N
O
N
O
CH3
5a,b
R
N-NH
N
H
O
N
O
O
6a,b
Conc. H2SO4
R
N
N
N
O
O
N
7a,b
a, R = Br
b, R = Cl

Scheme 1

Table 1 : Antibacterial activity of the synthesized compounds:

Compd.	Inhibition zones (mm)					
	Gram +ve Bacteria			Gram –ve bacteria		
	S. aureus	*B. subtilis*	*B. cereus*	*P. aurignosa*	*E. coli*	*S. typhi*
2a	17	15	18	10	18	9
2b	15	17	15	13	12	11
3a	11	14	16	15	19	12
3b	13	17	16	10	15	10
4a	11	17	12	14	16	10
4b	8	15	11	10	16	11
5a	20	22	20	19	23	17
5b	19	25	23	17	23	14
6a	21	27	22	19	21	16
6b	20	22	20	17	23	14
7a	15	13	14	16	18	13
7b	13	14	10	12	14	11
Ampicillin	**21**	**24**	**22**	**17**	**21**	**14**

Table 2 : Antifungal activity of the synthesized compounds:

Compd.	Inhibition zones (mm)		
	A. niger	*C. albicans*	*Penicillium sp*
2a	13	11	15
2b	11	9	13
3a	16	13	17
3b	17	9	15
4a	16	13	14
4b	18	14	20
5a	20	17	22
5b	21	16	23
6a	23	18	19
6b	24	19	16
7a	11	10	15
7b	10	11	17
Streptomycin	**20**	**15**	**24**