Synthesis and Antifungal Activity of Some New Substituted5, 7- Diiodo-8-Hydroxy Quinoline Derivatives

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Abstract: A series of new quinoline derivatives incorporating chalcone, pyrazoleand pyridine moieties using 5, 7-diiodo-8-hydroxy quinolineas starting material have been synthesized and tested for their in vitro antimicrobial activities against Gram-positive *Bacillus subtilis*, Gram-negative *Escherichia coli* and fungi *Candida albicans* and *Aspergillusniger*. Some of the tested compounds showed significant antimicrobial activity and the results suggest that [Ethyl 3-(5,7-diiodoquinolin-8-yloxy) propanoate]would be potent antifungal activity aganist*A. niger*, havinginhibitionzonestwo times more thanthe standard drug (Nystatin)and might thus provide a new class of lead structures in the search for novel antifungal agents.

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Keywords: Diiodo-8-hydroxyquinoline derivatives; Antimicrobial agents; Antifungal activities.

1. Introduction

In the last years, fungi have emerged as major cause of human infections especially among immunocompromised hosts having an enormous impact on morbidity and mortality[Mathew et al., 2009]. Although there are diverse available drugs for the treatment of systemic and superficial mycoses, they are not completely effective for their eradication [Brown et al., 2005; Chen et al., 2010]. In addition, they all possess a certain degree of toxicity and quickly develop resistance due to the large-scale use [Mukherjee et al., 2003]. There is, therefore, an urgent need for new antifungal chemical structures alternatives to the existing ones[Vicente et al., 2003]. Compounds with a quinoline skeleton are considered attractive scaffolds to develop new antifungal agents. So, 8-hydroxyquinolines, 2-aryl- or styryl- quinolines showed potent antifungal activity[Musiol et al., 2006; Meléndez et al., 2008; Vargas et al., 2003; Musiol et al., 2007]. Quinolines are generally recognized as privileged structures in medicinal chemistry and reside in molecules with various biological activities, such as antimalarial, antibacterial, antiprotozoic, anti-HIV, anticancer and antifungal agents[Musiol et al., 1960; Kaur et al., 2010; Krishnakumar et al., 2012; Bongarzone et al., 2011; Luo et al., 2009; Solomon et al., 2011].

Consequently, a lot of research is being performed in order to discover novel and potent antifungal agents[Petrikkos et al., 2007; Kathiravan et al., 2012; Talaviya et al., 2012].Polyenes, azoles, cyclic lipopeptides, allylamines and thiocarbamates are the most frequently encountered structural units within antifungal drug research, but also quinoline-based systems have emerged as an important class of antifungal agents[Musiol et al., 1960]. Herein, we report the synthesis of a series of new analogues containing the 8-hydroxyquinoline core and evaluation of their antifungal and antibacterial properties.

2. Experimental:

Melting points were measured in open capillary tubes using Griffin apparatus and were uncorrected. Elemental analyses were performed at the Microanalytical Center, Cairo University and the results were within ±0.3 from the theoretical values. The infrared (IR) spectra were recorded using potassium bromide disc technique on Schimadzu 435 IR Spectrophotometer, National Research Center, Cairo, egypt. (^{1}HNMR) spectra were performed on varian JEOL 270 MHz (JEOL, Japan) Spectrophotometer using tetramethylsilane (TMS) as internal standard, National Research Center, Cairo, egypt. Mass Spectra were recorded on JEOL-JMS-AX500 70e Spectrometer, National Research Center, Cairo, egypt. Reactions were monitored using thin layer chromatography (TLC), performed on 0.255 mm silica gel plates, with visualization under UV. light (254 nm). Chemical naming, calculation of molecular weight (M.wt.) and microanalyses of new compounds were performed by ChemDraw Program.

Ethyl 2- and 3-(5,7-diiodoquinolin-8-yloxy) propanoate (2a,b).

A mixture of 5, 7-diiodohydroxyquinoline (0.01 mol), ethyl 2- and 3- bromopropionate (0.01 mol) and potassium carbonate (0.012 mol) in absolute ethanol (100 mL) were refluxed for 6 hr. The reaction mixture was filtered off, and the filtrate was concentrated and allowed to cool. The crude ester precipitated was collected by filtration, washed with water and crystallized from 95% ethanol to give the titled compounds.

Ethyl 2-(5,7-diiodoquinolin-8-yloxy) propanoate (2a).

Yield 79%; m.p. 119-121° C; IR (KBr, cm^{-1}) ν_{max}: 1738 (CO), 1586 (C=C); ^{1}HNMR (DMSO-d_6) δ: 1.11 (t, 3H, CH_2-$\underline{CH_3}$), 1.59 (d, 3H, CH-$\underline{CH_3}$), 4.07 (q, 2H, CH_2), 5.55 (q, 1H, CH), 7.65-8.80 (m, 4H, Ar-H); MS: m/z 497 ($M^{+\cdot}$, 40.1), 498 ($M^{+\cdot}$+1, 21.3), 254 (100), consistent with the molecular formula ($C_{14}H_{13}I_2NO_3$).

Ethyl 3-(5,7-diiodoquinolin-8-yloxy) propanoate (2b).

Yield 81%; m.p. 179-181° C; IR (KBr, cm^{-1}) ν_{max}: 1724 (CO), 1551 (C=C); ^{1}HNMR (DMSO-d_6) δ: 1.11 (t, 3H, CH_2-$\underline{CH_3}$), 2.03 (t, 2H, O-CH_2-$\underline{CH_2}$), 4.10 (q, 2H, $\underline{CH_2}$-CH_3), 5.01 (t, 2H, O-$\underline{CH_2}$-CH_2), 7.66-8.82 (m, 4H, Ar-H); MS: m/z 497 ($M^{+\cdot}$, 0.5), 78(100), consistent with the molecular formula ($C_{14}H_{13}I_2NO_3$).

2- and 3-(5,7-diiodoquinolin-8-yloxy) propanoic acid (3a,b)

Compounds **2a** and **2b** (0.01 mol) was dissolved in alcoholic potassium hydroxide solution (50 ml, 5%), the reaction mixture was stirred at room temperature for 30 min then cooled at refrigerator for 1 hr and neutralized with 2N hydrochloric acid. The separated solid product was filtered off, washed with water, then crystallized from ethanol.

2-(5,7-diiodoquinolin-8-yloxy) propanoic acid (3a).

Yield 90%; m.p. 149-151° C; IR (KBr, cm^{-1}) ν_{max}: 3442 (OH), 1739 (C=O), 1557 (C=C); ^{1}HNMR (DMSO-d_6) δ: 1.50 (d, 3H, CH_3), 5.61 (q, 1H, CH), 7.63-8.79 (m, 4H, Ar-H), 13.00 (s, 1H, OH exchangeable with D_2O); MS: m/z 469 ($M^{+\cdot}$, 15.41); 127 (100), consistent with the molecular formula ($C_{12}H_9I_2NO_3$).

3-(5,7-diiodoquinolin-8-yloxy) propanoic acid (3b).

Yield 95%; m.p. 179-181° C; IR (KBr, cm^{-1}) ν_{max}: 3433 (OH), 1730 (C=O), 1552 (C=C); ^{1}HNMR (DMSO-d_6) δ: 2.71(t, 2H, CH_2-CO), 4.49 (t, 2H, O-CH_2), 7.63-9.10 (m, 4H, Ar-H), 11.50 (s, 1H, OH exchangeable with D_2O); MS: m/z 424 (2.26), 410 (100), 398 (20.16), 57 (56.09), consistent with the molecular formula ($C_{12}H_9I_2NO_3$).

2-(5,7-Diiodoquinolin-8-yloxy)propanehydrazide (4)

A mixture of compound **2a** (4.97 g, 0.01 mol) and hydrazine hydrate 99% (3.50 mL, 0.11 mol) in absolute ethanol (50 mL) was refluxed for 4 hr. The crude hydrazide separated on cooling, was filtered off and crystalized from absolute ethanol to give **4** in 95% yield; M.p. 179-181° C; IR (KBr, cm^{-1}) ν_{max}: 3419, 3317, 3221 (NH_2 and NH), 1683 (C=O), 1546 (C=C); ^{1}HNMR (DMSO-d_6) δ: 1.44 (d, 3H, CH-$\underline{CH_3}$); 4.28 (s, 2H, NH_2 exchangeable with D_2O); 5.38 (q, 1H, $\underline{CH}$-CH_3), 7.71-8.87 (m, 4H, Ar-H), 9.41(s, 1H, NH, exchangeable with D_2O); MS: m/z 483 ($M^{+\cdot}$, 3.37), 78 (100), consistent with the molecular formula ($C_{12}H_{11}I_2N_3O_2$).

2-(5,7- Diiodoquinolin -8- yloxy) -1- (3,5-dimethyl-1H-pyrazol -1-yl) propan -1-one (5)

A mixture of compound **4** (1.35 g, 0.0028 mol) and acetylacetone (0.28 g, 0.0028 mol) in 50 mL absolute ethanol was refluxed for 7 hr. The reaction mixture was cooled and the formed precipitate was filtered and crystallized from aqeous DMF. Yield 78%; m.p. 249-251° C; IR (KBr, cm^{-1}) ν_{max}: 1640 (C=O), 1555 (C=C); MS: m/z 397 (17.94), 254 (100), 152 (11.01), 123 (2.88), 97 (33.28), 83 (26.47), 81 (15.01), consistent with the molecular formula ($C_{17}H_{15}I_2N_3O_2$).

1-(2-(5,7-Diiodoquinolin-8-yloxy)propanoyl)-3-methyl-1H-pyrazol-5(4H)-one (6)

A mixture of compound **4** (1.35 g, 0.0028 mol) and ethylacetoacetate (0.36 g, 0.0028 mol) in 50 ml absolute ethanol was heated at reflux temp. for 7 hr. The reaction mixture was cooled and the formed precipitate was filtered and crystallized from aqueous DMF. Yield 85%; m.p. 229-231° C; IR (KBr, cm^{-1}) ν_{max}: 1747 (C=O of pyrazolone), 1640 (C=O), 1555 (C=C); MS: m/z 518 (25.07), 422 (4.68), 412 (26.44), 153 (25.62), 98 (34.94), 69 (22.81), 43 (100), consistent with the molecular formula ($C_{16}H_{13}I_2N_3O_3$).

2-(5,7-Diiodoquinolin-8-yloxy)-N-(1,3-dioxoisoindolin-2-yl) propan- amide (7)

A mixture of compound **4** (2.41 g, 0.005 mol) and phthalic anhydride (0.74 g, 0.005 mol) in 20 mL glacial acetic acid was refluxd for 8 hr. The reaction mixture was cooled then poured onto crushed ice. The separated solid product was filtered off and crystalized from aqueous DMF. Yield 82%; m.p. 219-221° C; IR (KBr, cm^{-1}) ν_{max}: 3429 (NH), 1738 (2C=O of cyclic amide), 1643 (CONH), 1559(C=C); MS: m/z 538 (0.24); 410 (33.43); 189 (5.76); 146 (5.89); 127 (75.91); 114 (100); 78 (29.19), consistent with the molecular formula ($C_{20}H_{13}I_2N_3O_4$).

2-(5,7-Diiodoquinolin-8-yloxy)-N-(2,5-dioxopyrrolidin-1-yl) propan-amide (8)

A mixture of compound **4** (2.41 g, 0.005 mol) and sucsinic anhydride (0.05 g, 0.005 mol) in glacial acetic acid (20 mL) was refluxed for 8 hr. The

reaction mixture was cooled then poured onto crushed ice. The separated solid product was filtered off and crystallized from aqueous DMF. Yield 86%; m.p. 229-231° C; IR (KBr, cm^{-1}) ν_{max}: 3342 (NH), 1732 (2 C=O of cyclic amide), 1642 (CONH), 1558 (C=C); MS: m/z 567 (M^{+}+2, 1.02); 63 (100), consistent with the molecular formula ($C_{16}H_{13}I_2N_3O_4$).

6-((5,7-Diiodoquinolin-8-yloxy)methyl)-4-(4-subistitutedphenyl)-1,2-dihydro-2 oxopyridine-3-carbonitrile (10a,b)

A mixture of compound **9** (0.01 mol), ethyl cyanoacetate (0.01 mol), the appropriate aromatic aldehydes (0.01 mol) namely p-fluorobenzaldehyde or p- methoxybenzaldehyde) and ammonium acetate (6.166 g, 0.08 mol) in absolute ethanol (40 mL) was refluxed for 6 hr. The reaction mixture was concentrated, cooled and the formed precipitate was filtered off, washed with water and crystallized from ethanol to give compounds **10a,b**, respectively.

6-((5,7-Diiodoquinolin-8-yloxy)methyl)-4-(4-fluorophenyl)-1,2-dihydro-2-oxopyr- idine-3-carbonitrile (10a).

Yield 70%; m.p. 119-121° C; IR (KBr, cm^{-1}) ν_{max}: 3423 (NH), 2217 (C≡N), 1732 (C=O), 1561 (C=C); ^{1}HNMR (DMSO-d_6) δ: 4.90 (s, 2H, O-CH_2), 7.05-8.98 (m, 9H, 8Ar-H and 1H of pyridone ring); MS: m/z 412 (0.33), 398 (0.7), 228 (2.4), 219 (7.84), 174 (12.56), 123 (8.59), 95 (8.50), 77 (100), consistent with the molecular formula ($C_{22}H_{12}FI_2N_3O_2$).

6-((5,7-Diiodoquinolin-8-yloxy)methyl)-4-(4-methoxyphenyl)-1,2-dihydro-2-oxo- pyridine-3-carbonitrile (10b).

Yield 74%; m.p. 149-151° C; IR (KBr, cm^{-1}) ν_{max}: 3345 (NH); 2201 (C≡N), 1730 (C=O), 1608 (C=C); ^{1}HNMR (DMSO-d_6) δ: 3.94 (s, 3H, OCH_3), 4.70 (s, 2H, O-CH_2), 6.90-8.95 (m, 9H, 8Ar-H and 1H of pyridone ring); MS: m/z 634 (M^{+}-1, 0.21), 45 (100), consistent with the molecular formula ($C_{23}H_{15}I_2N_3O_3$).

6-((5,7-Diiodoquinolin-8-yloxy)methyl)-1,2-dihydro-2-imino-4-(3,4,5-trimethoxy phenyl)pyridine-3-carbonitrile (11)

A mixture of compound **9** (4.532 g, 0.01 mol), malononitrile (0.66 g, 0.01 mol), trimethoxybezaldhyde (1.96 g, 0.01 mol) and ammonium acetate (6.166 g, 0.08 mol) in absolute ethanol (40 mL) was refluxed for 6 hr. The reaction mixture was concentrated, cooled and the formed precipitate was filtered off, washed with water and crystallized from aqeous DMF to give compound **11** in 91% yield; M.p. 119-121° C; IR (KBr, cm^{-1}) ν_{max}: 3350, 3232 (2 NH), 2211 (C≡N), 1629 (C=N), 1585 (C=C); ^{1}HNMR (DMSO-d_6) δ: 3.72 (s, 3H, p-OCH_3), 3.82 (s, 6H, 2m-OCH_3), 5.28 (s, 2H, O-CH_2), 7.55-8.83 (m, 7H, 6Ar-H and 1H of iminopyridine proton); MS: m/z 694 (M^{+}, 7.25), 127 (100), consistent with the molecular formula ($C_{25}H_{20}I_2N_4O_4$).

(*E*)-1-(5,7-Diiodoquinolin-8-yloxy)-4-substituted but-3-en-2-one (12a-c)

To a solution of compound **9** (4.532 g, 0.01 mol) in ethanol (50 mL), the appropriate aromatic aldehydes (0.01 mol) namely benzaldehyde, p-fluorobenzaldehyde or p-anisaldehyde was added in the presence of 10 % alcoholic potassium hydroxide (5 mL). The reaction mixture was stirred for 10-12 hr at room temperature, then left overnight at the same temperature. The obtained solids were filtered, washed with water, dried and crystallized from ethanol to give the title compounds **12a-c**, respectively.

(*E*)-1-(5,7-diiodoquinolin-8-yloxy)-4-phenylbut-3-en-2-one (12a).

Yield 88%; m.p. 139-141° C; IR (KBr, cm^{-1}) ν_{max}: 3055 (CH-Ar), 2926 (CH-Aliph), 1664 (C=O), 1594 (C=C); ^{1}HNMR (DMSO-d_6) δ: 4.51 (s, 2H, O-CH_2), 7.1-8.9 (m, 11H, 9Ar-H and CH=CH); MS: m/z 540 (M^{+}-1, 10); 78 (100), consistent with the molecular formula ($C_{19}H_{13}I_2N_3O_3$).

(*E*)-1-(5,7-diiodoquinolin-8-yloxy)-4-(4-fluorophenyl)but-3-en-2-one (12b).

Yield 80%; m.p. 129-131° C; IR (KBr, cm^{-1}) ν_{max}: 3073 (CH-Ar), 2975 (CH-Aliph), 1687 (C=O), 1599 (C=C); ^{1}HNMR (DMSO-d_6) δ: 4.02 (s, 2H, O-CH_2), 6.7-8.8 (m, 10H, 8Ar-H and CH=CH); MS: m/z 561 (M^{+}+2, 10); 78 (100), consistent with the molecular formula ($C_{19}H_{12}FI_2NO_2$).

(*E*)-1-(5,7-diiodoquinolin-8-yloxy)-4-(4-methoxyphenyl)but-3-en-2-one (12c).

Yield 78%; m.p. 124-126° C; IR (KBr, cm^{-1}) ν_{max}: 3046 (CH-Ar), 2921 (CH-Aliph), 1686 (C=O), 1609 (C=C); ^{1}HNMR (DMSO-d_6) δ: 2.22 (s, 3H, CH_3); 4.46 (s, 2H, OCH_3); 6.98-8.90 (m, 10 H, 8 ArH and CH=CH); MS: m/z 397 (11.53); 304 (6.53); 288 (2.18); 147 (10.87); 159 (5.33); 91 (100), consistent with the molecular formula ($C_{20}H_{15}I_2NO_2$).

8-((4,5-Dihydro-5-phenyl-1H-pyrazol-3-yl) methoxy) - 5,7-diiodo- quinoline (13)

A mixture of compound **12a** (5.41g, 0.01 mol) and hydrazine hydrate 99% (1 ml, 0.03 mol) in 20 mL absolute ethanol was refluxed for 6 hr. The product, which separated upon cooling, was filtered off and crystallized to give compound **13** in 62% yield; M.p. 119-221° C; IR (KBr, cm^{-1}) ν_{max}: 3176 (NH), 3022 (CH-Ar), 2971 (CH-Alph), 1678 (C=N); MS: m/z 554 (M^{+}-1, 2.55); 43 (100), consistent with the molecular formula ($C_{19}H_{15}I_2N_3O$).

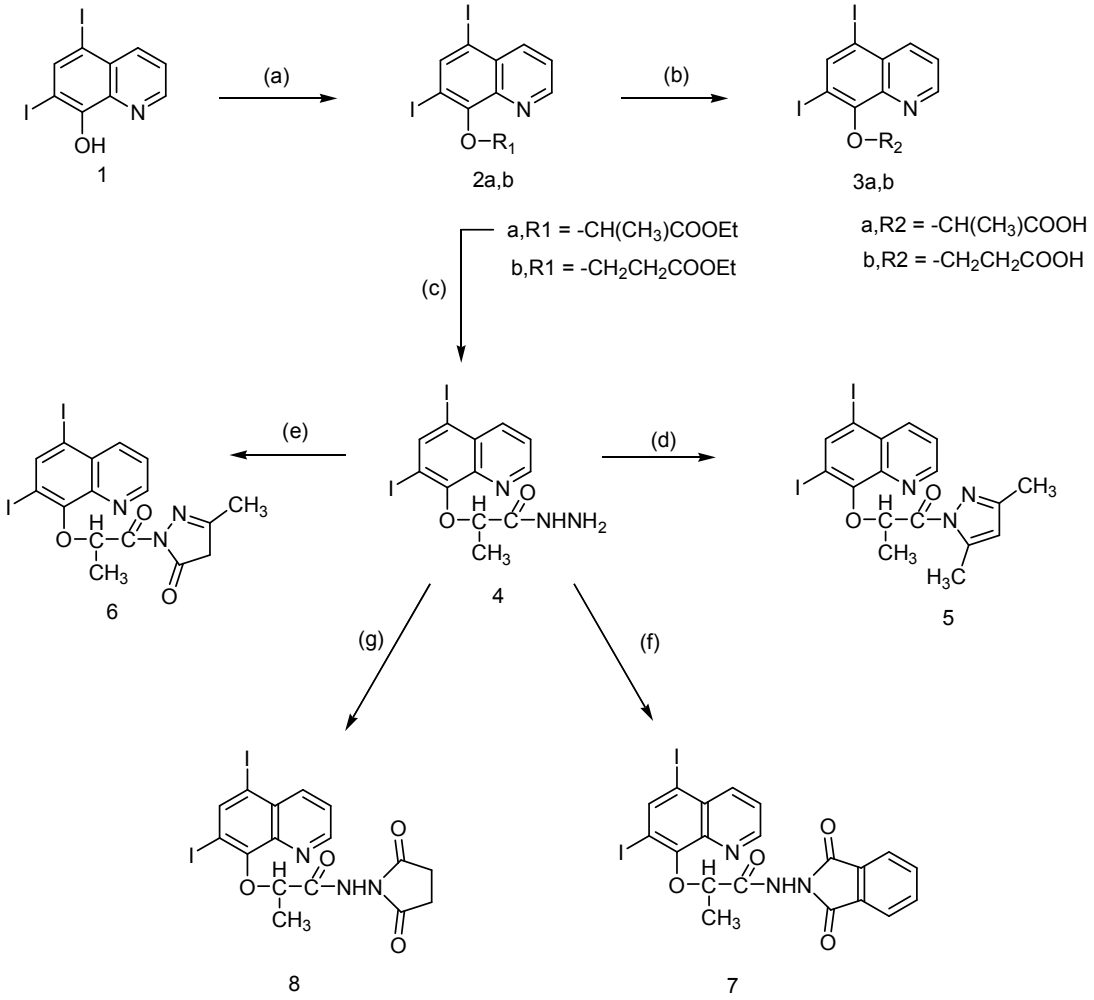
8-((4,5-Dihydro-1,5-diphenyl-1H-pyrazol-3-yl)methoxy)-5,7-diiodoquinoline (14)

A mixture of compound **12a** (5.41g, 0.01mol) and phenylhydrazine (1.97 mL, 0.02 mol) in absolute

ethanol (25 mL) and five drops of acetic acid was refluxed for 5hr then allowed to cool and poured into ice-cold water, the solid formed was filtered off, washed with ethanol–water mixture, and dried. Then, crystallized from chloroform to give compound **14** in 55% yield; M.p. 199-201^{o} C; IR (KBr, cm^{-1}) ν_{max}: 3058 (CH-Ar), 2971 (CH-Alph), 1693 (C=N); ^{1}HNMR (DMSO-d_6) δ: 3.26 (dd, 1H, H_a); 4.02 (m, 1H, H_b); 5.06 (s, 2H, O-CH_2); 5.65 (dd, 1H, H_c); 7.10-8.84 (m, 14H, Ar-H); MS: m/z 630 ($M^{+\cdot}$-1, 1.74); 91 (100), consistent with the molecular formula ($C_{25}H_{19}I_2N_3O$)

3. Results and Discussion

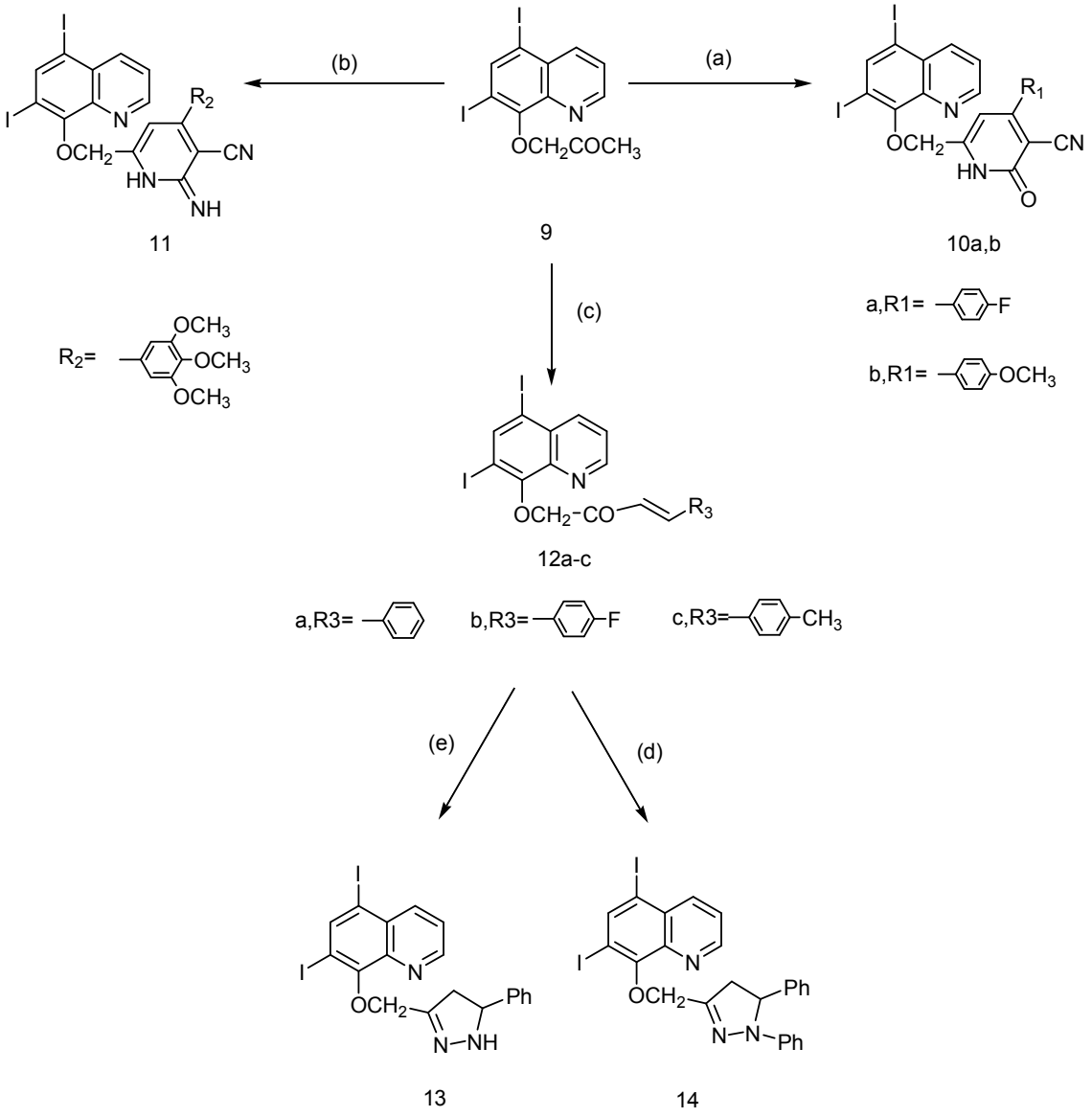
The starting materials **2a,b** were prepared by reaction of 5, 7- diiodo-8-hydroxy quinolinewith 2- and 3-ethyl bromopropionic acid ethyl ester in the presence of anhydrous potassium carbonate in dry acetone, followed by hydrolysis in 5% alcoholic potassium hydroxide at room temperature to afford compounds **3a,b**. compound **2a** was allowed to react with 99% hydrazine hydrate in ethanol to give the corresponding carbohydrazide **4** which can react with acetylacetone and ethyl acetoacetate to give the corresponding dimethylpyrazole **5** and methylpyrazolone **6** derivatives, respectively. Condensation of the carbohydrazide **4** with phthalic anhydride and succinic anhydride in glacial acetic acid gave the corresponding N-(1,3-dioxoisoindolin-2-yl) propan- amide**7** andN-(2,5-dioxopyrrolidin-1-yl) propan-amide **8** derivatives, respectively (Scheme 1).



Scheme 1

Synthesis of compounds **2-8:** Reagents and conditions: (a) Br-$CH(CH_3)$COOEt/Br-CH_2CH_2COOEt, abs.ethanol, reflux; (b) KOH, r.t.; (c) NH_2NH_2, ethanol, reflux; (d) acetylacetone, abs.ethanol, reflux; (e) ethylacetoacetate, abs.ethanol, reflux; (f) phthalic anhydride, acetic acid, reflux; (g) sucssinic anhydride, acetic acid, reflux.

On the other hand,cyclocondensation of the key intermediate **9** with ethyl cyanoacetate or malononitrile and the appropriate aromatic aldehydes in the presence of excess ammonium acetate in absolute ethanol yielded 6-((5,7-diiodoquinolin - 8-yloxy) methyl)-4-(4-subistituted phenyl)-1,2-dihydro-2-oxopyridine-3-carbonitrile **10a,b** and 6-((5,7-diiodoquinolin-8-yloxy)methyl)-1,2-dihydro-2-imino-4-(3,4,5-trimethoxy phenyl)pyridine-3-carbonitrile **11** (Scheme 2). Compound **9** can undergo a one-step Claisene Schmidt condensation, by the reaction with the appropriate aromatic aldehydes in the presence of 10 % KOH to form the α, β-unsaturated ketones (*E*)-1-(5,7-diiodoquinolin-8-yloxy)-4-substituted but-3-en-2-one **(12a-c)**. The synthesis of 5-phenyl pyrazoline and 1, 5 diphenylpyrazoline**1 3** and **14** derivatives were occurred through the reaction of 3- phenyl α, ß unsaturated ketone with either hydrazine hydrate or phenyl hydrazine in absolute ethanol.



Scheme 2

Synthesis of compounds **9-14:** Reagents and conditions: (a) R_1CHO, ethylcyanoacetate, ammonium acetate, abs.ethanol, reflux; (b) R_2CHO, malononitrile, ammonium acetate, abs.ethanol, reflux; (c) R_3CHO, 10%KOH, ethanol, stirring, r.t; (d) phenylhydrazine, drops of acetic acid, ethanol, reflux; (e) hydrazine hydrate, ethanol, reflux

Microbiological Evaluation:

Thirteen synthesized compounds were screened for their antibacterial and antifungal activities using agar-diffusion method [Fahmy et al., 2001].All microbial strains used were local isolates and obtained from National Research Center, Cairo, Egypt. Antibacterial activity was tested against *Escherichia coli* (Gram negative short rods) and *Bacillus subtilis*(Gram positive spore forming bacilli). Antifungal activity was tested against *Aspergillusniger* (mould) and *Candida albicans* (yeast). Inocula of 24 hrs age from each strain (except in case of Aspergillusniger, 27 hrs age inoculum has been used) were prepared and used in seeding bioassay media. Antimicrobial activity was assayed in agar plates of medium 1 (for testing antibacterial activity) or medium 2 (for testing antifungal activity). Molten sterile 80 mL of medium were allowed to cool to 45 ºC before seeding with the test strain and poured in Petri dish of 20 cm diameter.

Medium 1: peptone 5g, glucose 5g, beef extract 3g, Yeast extract 1g, Agar 11g and PH 7.

Medium 2: peptone 2g, glucose 5g,Agar 11g, distilled water 1 L and PH 7.

One mg of each studied compound was loaded on a filter paper disc (Whatman No.3) of 6.5 mm diameter and allowed to dry in air. Discs loaded with tested compounds were gently overlaid on the surface of the agar media under sterile conditions. Then, the agar plates with discs were maintained in refrigerator at 4ºC for 30 min before incubation.

The results have been represented by inhibition zone (mm), <6.5 mm indicates no activity.

Table 1: Antibacterial and antifungal activities of some new synthesized compounds

Compound No.	Test organism Inhibition zone (mm)			
	E.coli	***B.subtilis***	***C.albicans***	***A.niger***
2a	<6.5	<6.5	<6.5	<6.5
2b	13	12	<6.5	15.5
3a	9	9	<6.5	<6.5
3b	10.5	8	<6.5	7.5
4	<6.5	<6.5	<6.5	<6.5
10a	<6.5	<6.5	<6.5	<6.5
10b	<6.5	<6.5	<6.5	<6.5
11	<6.5	<6.5	<6.5	13
12a	<6.5	12.5	<6.5	<6.5
12b	<6.5	<6.5	<6.5	<6.5
12c	<6.5	9	<6.5	<6.5
13	<6.5	<6.5	<6.5	<6.5
14	14	10	<6.5	<6.5
Ciprofloxacin	22	30	-	-
Nystatin	-	-	10	7.6

Based on the microbiological results **(Table 1)**, the antifungal activity against *Aspergillusniger* of compound **3b** showed significant activity having inhibition zone equal to that of the reference compound while compounds **2b** and **11** have potent inhibitory effect as their inhibition zones are as twice as that of the Nystatin (the reference standard). On the other hand none of the compounds have any effect against *Candida albicans*.

Regarding the antibacterial activity, it is inferred that compounds **2b** and **14** have moderate inhibitory effect on the growth of *E.coli* while compounds **3a** and **3b** have slight inhibitory effect.Furthermore, Compounds **2b** and **12a** showed moderate inhibitory effect against *Bacillus subtilis* while compounds**3a**, **3b**, **12c** and **14** have slight inhibitory effect.

4. Conclusion

This investigation, involved the synthesis and *in-vitro* antifungal and antibacterial activities of some 5,7 diiodo-8-hydroxy quinoline derivatives. One compound, 3-(5,7-diiodoquinolin-8-yloxy) propanoic acid (**3b**) showedgoodantifungalactivityaganist*A. niger*, whiletwocompounds, Ethyl 3-(5,7-diiodoquinolin-8-yloxy) propanoate (**2b**) and 6-((5,7-diiodoquinolin-8-yloxy) methyl) -1,2-dihydro -2- imino -4 (3,4,5-trimethoxyphenyl)pyridine-3-carbonitrile (**11**)showedpotentantifungalactivityaganist*A. niger*havinginhibitionzones as twice as that of Nystatin (standarddrug).

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