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SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF SOME NEW QUINOLINE AND ^{1}H-PYRAZOLO[3,4-b]QUINOLINE DERIVATIVES

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تفاعل فالسماير على الأسيتانيليد (١) ثم معالجة الناتج بالهيدروكسيل أمين أعطى ٢ كلورو كينولين-٣ كربونايتريل **II** الذى تم تكاثفه مع بعض الأمينات ليعطى الأمينوكينولينات المقابلة. معالجة **II** بالثيويوريا أنتج ٢ مركابتوكينولين ٣ كربونايتريل **IV** الذى تم تحويله الى الملح البوتاسيومى ثم تفاعله مع بعض استرات كلوروحمض الخليك ليعطى الثيوكينولينات المقابلة. وبتفاعل الهيدرازين مع **II** و **IV** نتج البيرازولوكينولين أمين **VII**. تكاثف المركب الأخير مع بعض الألدهيدات الأروماتيه أعطى بعض الإمينات الجديدة ، وبتفاعل **VII** مع كلوريد الباراكلورو البنزويل أعطى الأميد المقابل. وقد تم اختبار المركبات الجديدة بيولوجياً كمضادات للبكتريا والفطريات حيث أظهرت بعض المركبات فاعلية مضادة لهذه الميكروبات.

*Vilsmeier formylation of acetanilide **I** followed by treatment with hydroxylamine produced 2-chloroquinoline-3-carbonitrile **II** that was condensed with different amines to give 2-substituted aminoquinolines-3-carbonitriles **III**. Treatment of **II** with thiourea yielded 2-mercaptoquinoline-3-carbonitrile **IV**, which was converted to its potassium salt **V** that was condensed with some chloroacetate esters to produce 2-substituted thioquinoline-3-carbonitriles **VI**. Hydrazinolysis of **II** or **IV** gave 1H-pyrazolo[3,4-b]quinolin-3-ylamine **VII**. Condensation of **VII** with different aryl aldehydes resulted in the corresponding imines **VIII**. Treatment of **VII** with p-chloro-benzoyl chloride afforded the amide **IX**. Some of the synthesized compounds were evaluated for their antibacterial and antifungal activity.*

INTRODUCTION

The quinoline ring system represents the building block of many biologically active compounds that possess antimalarial,[1-4] antiamebic,[5,6] bronchodilator,[7,8] antihypertensive,[9-11], anti-inflammatory,[12] antidepressant,[13] and Scr kinase inhibitory action.[14] In addition many pyrazoloquinolines have been reported to possess antibacterial, antifungal, and antiviral.[15,16] On the other hand, 2-chloroquinoline-3-carbonitrile (**II**) is a good starting material for the preparation of different quinoline derivatives.[17] Accordingly, it was decided to prepare (**II**) as a versatile synthon from which some new 2-substituted quinoline-3-carbonitrile derivatives [(**III**) and (**VI**)] and some new pyrazoloquinolines [(**VIII**) and (**IX**)] could be prepared as shown in Scheme (1) with the aim to evaluate their antimicrobial action.

EXPERIMENTAL

All melting points were carried on a Gallenkamp melting point apparatus and are uncorrected. The infrared spectra were recorded on Brucker-Vector-22-FT-IR Spectrophotometer using the potassium bromide disc technique. The ^{1}HNMR spectra were recorded on Varian-Gemini-200-MHz-Spectrophotometer using $CDCl_3$ or DMSO-d_6 as solvents and TMS as internal reference. The chemical shift values were recorded in δ ppm downfield the TMS signal. The Mass spectra were recorded on AZH-Ph-AR-XO_2 Mass spectrometer. Elemental analyses were

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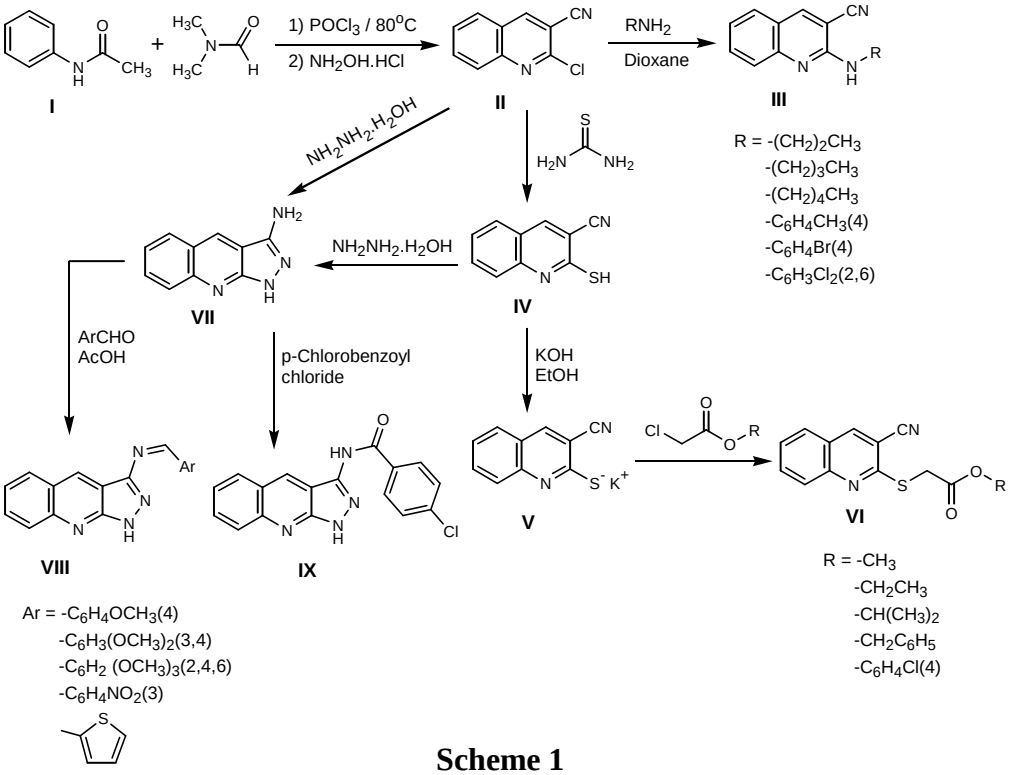


Scheme 1

performed on a CHN analyzer. All analyses were preformed at the Microanalytical Unit of Cairo University, Cairo, Egypt.

Following reported procedures, 2-chloroquinoline-3-carbonitrile (**II**)[16] 2-mercaptoquinoline-3-carbonitrile (**IV**)[21] and 1H-pyrazolo[3,4-b]quinolin-3-ylamine (**VII**)[16] were prepared.

2-Substituted aminoquinoline-3-carbonitriles (IIIa-f)

A mixture of 2-chloroquinoline-3-carbonitrile (**II**) (1.89 g, 0.01mol) and alkyl amine or aryl amine (0.01 mol) in dry dioxane (50 ml) was refluxed overnight then the mixture was allowed to cool. The separated solid was collected, filtered, dried, washed with ethanol and crystallized from absolute ethanol (Table 1).

Potassium salt of 2-mercaptoquinoline-3-carbonitnile (V)

2-Mercaptoquinoline-3-carbonitrile (**IV**) (1.86 g, 0.01 mol) was dissolved in absolute ethanol (50 ml) and then treated with alcoholic potassium hydroxide (0.56 g, 0.01 mol). The reaction mixture was stirred for an hour and the resulting solid was filtered, washed with diethyl ether and dried. m.p, >300°, Yield, 95%.

3-Cyano-2-alkoxy / aryloxycarbonylmethyl-thioquinolines (VIa-e)

A mixture of potassium salt of 2-mercaptoquinoline-3-carbonitrile (**V**) (2.24 g, 0.01 mol) and the appropriate chloroacetate esters (0.01 mol) in dimethylformamide (30 ml) was heated for four hours at 100°. The reaction mixture was poured onto ice-cooled water and the solid produced was filtered, dried and crystallized from ethanol (Table 2).

1H-Pyrazolo[3,4-b]quinolin-3-ylamine (VII) (New Method)

To a stirred suspension of 2-mercapto-quinoline-3-carbonitrile (**IV**) (14.4 g, 0.078 mol) in absolute ethanol (100 ml) was added hydrazine hydrate (20 ml, 80%). The mixture was stirred at reflux for 12 hours and then cooled. The resulting solid was filtered boiled with water and filtered. The crude product was dried and recrystallized from ethanol. m.p, >300°, Yield, 10.7 g, 75%, as the reported.[23]

IR (KBr, cm^{-1}): 3385.2, 3306.6, 3178.3 (NH_2, N-H), 1641.2, 1577.6, 1483.6 (C=C, C=N).

Table 1: Physical data and elemental analysis of 2-substituted aminoquinoline-3-carbonitrile (**IIIa-f**).

Comp. (**III**)	R	m.p.°	Yield %	M. Formula/ M. Weight	Elemental Analysis % Calcd./Found		
					C	H	N
a	$-(CH_2)_2CH_3$	100-101	80	$C_{13}H_{13}N_3$ 211.26	73.91 73.45	6.20 5.80	19.89 20.00
b	$-(CH_2)_3CH_3$	90-91	85	$C_{14}H_{15}N_3$ 225.29	74.64 74.52	6.71 6.76	18.65 18.42
c	$-(CH_2)_4CH_3$	85-86	85	$C_{15}H_{17}N_3$ 239.32	75.28 75.30	7.16 7.15	17.56 17.32
d	$-C_6H_4CH_3(4)$	125-126	40	$C_{17}H_{13}N_3$ 259.31	78.74 78.84	5.05 5.06	16.20 16.22
e	$-C_6H_4Br(4)$[22]	115-116	80	$C_{16}H_{10}BrN_3$ 324.17	59.28 59.57	3.11 3.54	12.96 12.32
f	$-C_6H_3Cl_2(2,6)$	135-137	70	$C_{16}H_9Cl_2N_3$ 314.17	61.17 61.11	2.89 3.17	13.38 13.12

III-a, IR (KBr, cm^{-1}): 3391 (s, N-H), 2218 (s, C≡N), 1620-1541 (s, C=N, C=C, aromatic). ^{1}HNMR ($CDCl_3$, δ ppm): 8.16 (s, 1H, H-4), 7.66-7.63 (m, 3H, H-5, H-8, H-7), 7.27-7.23 (t, 1H, H-6), 5.25 (b.s, 1H, N-H), 3.63-3.53 (t, 2H, NH-C<u>H</u>$_2$), 1.83-1.63 (sex, 2H,CH_2-<u>CH_2</u>CH_3), 1.07-0.99 (t, 3H, CH_2-<u>CH_3</u>). MS (m/z, abund.%): 211 (30.3, M), 196 (28.6, M-CH_3), 182 (100, M-C_2H_5), 169 (91.6, M-CH_2CHCH_3), 153 (62.6, M- NHC_3H_7), 127 (23.9, M-NHC_3H_7/CN)

III-d, IR (KBr, cm^{-1}): 3449.8 (b, -N-H-), 3055.3 (s, C-H aromatic), 2953 (s, CH, aliphatic), 2211.9 (s, C≡N), 1620.5 (s, C=C aromatic). ^{1}HNMR ($CDCl_3$, δ ppm): 8.56 (s, 1H, H-4), 8.00-7.86 (m, 3H, H-5, H-7, H-8), 7.58-7.57(d, 2H, H2-,H-6 of tolyl), 7.55-7.54(t,1H, H-6), 7.53-7.52 (s, 1H, NH), 7.51(d, 2H, H-3, H-5 of tolyl), 3.59 (s, 3H, C-H, aliphatic). MS (m/z, abund.%): 259 (37.3, M^+), 258 (66.7, M-H), 168 (100, M- $C_6H_4CH_3$), 153 (36.7, M-$NHC_6H_4CH_3$), 127 (33.3, M-$NHC_6H_4CH_3$/ CN).

III-e, ^{1}HNMR ($CDCl_3$, δ ppm): 8.36 (s, 1H, H-4), 8.25 (s, 1H, NH), 7.84-7.65 (m, 5H, H-5, H-8, H-7 & $H_{3,5}$ of phenyl), 7.43-7.40 (t,1H, H-6), 7.26-7.23 (d, 2H, $H_{2,6}$ of phenyl). MS (m/z, abund.%): 323/325 (51.3/56.7, M^+), 243 (53.8, M-HBr), 216 (14.1, M-HBr, HCN), 153 (37.3, M-NHC_6H_4Br), 127 (31.3, M-NHC_6H_4Br /CN).

Table 2: The physical data and elemental analysis of (3-Cyano-2-alkoxy/aryloxy carbonylmethylthioquinolines (**VIa-e**).

Comp. **(VI)**	R	M.P.°	Yield %	M. Formula/ M. Weight	Elemental Analysis % Calcd./Found		
					C	H	N
a	$-CH_3$	129-130	80	$C_{13}H_{10}N_2O_2S$ 258.30	60.45 60.31	3.90 3.94	10.85 10.37
b	$-CH_2CH_3$	120-121	85	$C_{14}H_{12}N_2O_2S$ 272.32	61.75 62.74	4.44 4.82	10.29 10.39
c	$-CH(CH_3)_2$	180-182	70	$C_{15}H_{14}N_2O_2S$ 286.35	62.92 62.48	4.93 4.69	9.78 9.89
d	$-CH_2C_6H_5$	188-190	60	$C_{19}H_{14}N_2O_2S$ 334.39	68.24 68.10	4.22 4.30	8.38 8.75
e	$-C_6H_4Cl(4)$	200-202	65	$C_{18}H_{11}ClN_2O_2S$ 354.81	60.93 60.86	3.12 3.06	7.90 8.35

VI-a, IR (KBr, cm^{-1}): 3451.8 (b, C-H, aromatic), 2926 (s, C-H, aliphatic), 2223.2 (s, C≡N), 1736 (s, C=O). ^{1}HNMR ($CDCl_3$, δ ppm): 8.36 (s, 1H, H-4), 7.94-7.76 (m, 3H, H-7, H-5 and H-8) 7.58-7.50 (t, 1H, H-6), 4.15 (s, 2H, -S$\underline{CH_2}$-CO), 3.79 (s, 3H, COO$\underline{CH_3}$).

VI-b, IR (KBr, cm^{-1}): 3445.5 (s, C-H aromatic), 2987 (s, C-H aliphatic), 2223.3 (s, C≡N), 1729.3 (s, C=O). MS (m/z, abund.%): 272 (15.6, M^+), 227 (3.3, M-OC_2H_5), 199 (100, $C_{11}H_7N_2S$), 185 (7.7, M-$CH_2COOC_2H_5$), 153 (62.6, cyanoquinoline cation), 126 (53.3, C_9H_4N), 76 (23.6, C_6H_4).

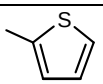
VI-c, IR (KBr, cm^{-1}): 3270.3 (s, C-H aromatic), 2978 (s, C-H aliphatic), 2222.2 (s, C≡N), 1728 (s, C=O). ^{1}HNMR (DMSO, δ ppm): 9.21 (s, 1H, H-4), 8.11-8.04 (d, 1H, H-8), 7.91-7.83 (t, 1H, C-7), 7.68-7.60 (t, 1H, H-6), 7.52 (bs, 1H, H-5), 4.07 (s, 2H, -S$\underline{CH_2}$-CO), 2.0 (septet, 1H, isopropyl), 0.89-0.86 (d, 6H, two $\underline{CH_3}$ of isopropyl).

VI-e, IR (KBr, cm^{-1}): 3282.8 (s, C-H aromatic), 2984.2 (s, C-H aliphatic), 2222.5 (s, C≡N), 1728 (s, C=O). ^{1}HNMR (DMSO, δ ppm): 9.39 (s, 1H, H-4), 8.11-8.09 (m, 1H, H-8), 8.07-7.81 (m, 3H, C-7, H-5, H-6), [7.56-7.51 (d, 2H), 7.38-7.23 (d, 2H) *p*-disubstituted phenyl), 3.38 (s, 2H, -S$\underline{CH_2}$-CO). MS (m/z, abund.%): 354/356 (7.9/2.8, M^+), 227 (100, M-OC_6H_4Cl), 199 (23.5, M-$OCOC_6H_4Cl$), 172 (14.7, M-$OCOC_6H_4Cl$, HCN), 155 (20.3, M-S=CHCOOC_6H_4Cl), 127 (7.1, $C_9H_4N^+$).

Substituted Arylidene-(1H-pyrazolo[3,4-b]quinolin-3-yl)-amines (VIII a-e)

To solution of 1H-pyrazolo[3,4-b]-quinolin-3-ylamine (**VII**) (1.84 g, 0.01 mole) in ethanol (25 ml) containing 0.5 ml of acetic acid, the appropriate aldehyde (0.01 mole) was added and the mixture was heated under reflux for 2 hours. The reaction mixture was concentrated and allowed to cool. The separated solid was filtered and recrystallized from ethanol (Table 3).

Table 3: The physical data and elemental analysis of arylidene-1H-pyrazolo[3,4-b]quinolin-3-yl)amine derivatives (**VIIIa-e**).

Comp. **VIII**	Ar	M.P.°	Yield %	M.Formula M. Weight	Elemental Analysis % (Calcd./Found)		
					C	H	N
a	$C_6H_4OCH_3(4)$	230-232	70	$C_{18}H_{14}N_4O$ 302.33	71.51 71.45	4.67 4.96	18.53 17.55
b	$C_6H_3(OCH_3)_2(3,4)$	240-241	65	$C_{19}H_{16}N_4O_2$ 332.36	68.66 67.88	4.85 5.11	16.86 16.50
c	C_6H_2 $(OCH_3)_3(2,4,6)$	195-196	70	$C_{20}H_{18}N_4O_3$ 362.38	66.29 67.00	5.01 5.00	15.46 15.52
d	$C_6H_4NO_2(3)$	280-282	73	$C_{17}H_{11}N_5O_2$ 317.30	64.35 64.42	3.49 3.51	22.07 21.82
e		223-4	80	$C_{15}H_{10}N_4S$ 378.33	64.73 64.64	3.62 4.35	20.13 19.72

VIII-a, IR (KBr, cm^{-1}): 3420 (broad, N-H), 3180 (s, C-H, aromatic), 2839 (s, C-H, aliphatic), 1610.2 (s, C=C, C=N), 1510 (s, C=C, C=N aromatic). ^{1}H NMR (DMSO, δ ppm): 13.37 (s, 1H, N-H pyrazolo.), 9.29 (s, 1H, -N=CH-), 9.21(s,1H, H-4), 8.23-8.19 (d, 1H, H-8), 8.12-8.07 (d, 2H, $H_{2,6}$ of *p*-phenyl), 8.04-8.00 (d, 1H, H-5) 7.85-7.78 (t, 1H, H-7), 7.56-7.52 (t,1H, H-6), 7.18-7.14 (d,2H, $H_{3,5}$ of *p*-phenyl), 3.89 (s, 3H, O-CH_3). MS (m/z, abund.%): 302 (94.7, M^+), 301 (100, M-1), 271 (9.6, M-OCH_3), 184 (2.6, M+2-$CHC_6H_4OCH_3$) 169 (22.9, M-$NCHC_6H_4OCH_3$), 142 (13.5, aziridinoquinoline cation).

VIII-d, ^{1}H NMR (DMSO, δ ppm): 13.65 (s, 1H, N-H pyrazolo), 9.53 (s, 1H, -N=CH-), 9.33 (s,1H, H-4), 8.92 (s, 1H, H-2 of the phenyl), 8.54-7,78 (3d, m, 6H, H-4, H-5, H-6 of phenyl & H-8, H-5, H-7 of quinoline), 7.57-7.49 (t, 1H, H-6).

VIII-e, MS (m/z, abund.%) 278 (54%) (M^+), 184 (100%) ([M+2]– C_5H_4S), 169 (34.0%) (M-C_4H_4SCN), 142 (28.9%) (aziridinoquinoline cation).

4-Chloro-N-(1H)-pyrazolo[3,4-b]quinolin-3-yl)-benzamide (IX)

1H-Pyrazolo[3,4-b]quinolin-3-ylamine **(VII)** (1.84 g, 0.01 mol) was suspended in dry pyridine; then *p*-chlorobenzoyl chloride (1.75 g, 0.01 mol) was added dropwise with continuous stirring at room temperature. The reaction mixture was stirred for 24 hour and was poured gradually while stirring onto ice-cold water. The separated solid, was filtered, washed with water, dried and crystallized from absolute ethanol.

m.p, 305°, Yield, 70%. $C_{17}H_{11}ClN_4O$ (322.75), Calcd. (Found) C% 63.26 (63.81), H% 3.44 (4.17), N% 17.36 (17.20).

^{1}HNMR ($CDCl_3$, δ ppm): 13.29 (s, 1H, NH-pyrazole), 11.36 (s, 1H, N-H, -NHC=O), 9.05 (s, 1H, H-4), 8.19-8.15 (d, 3H, H-8 & H-$_{2,6}$ of phenyl), 8.02-7.98 (d, 1H, H-5), 7.84-7.7.77 (t, 1H, H-7), 7.69-7.7.65 (d, 2H, H-$_{3,5}$ of phenyl), 7.52-7.45 (t, 1H, H-7). MS *(m/z, abound.%)*:- 322/324 (14.3/4.2 M^+), 141 (35,6, aziridino-quinoline cation), 139 (100, ClC6H4CO$^+$), 111/113 (37.8/11.4, $^+C_6H_4Cl$), 75 (17.8, $^+C_6H_3$).

Antimicrobial Testing

Staphylococcus aureus, *Bacillus subtilis*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Candida albicans* were obtained from stock culture collection of Faculty of Pharmacy (Boys), Al-Azhar University, Cairo. Ofloxacin was used as antibacterial standard and Nystatin as antifungal standard. Suspension of the above mentioned microorganisms were prepared by inoculating fresh stock cultures into separate broth tubes, each containing 7 ml of nutrient broth (peptone, 0.3% and beef extract 0.3%). The inoculated tubes were incubated at 37° for 24 hours before use. 10-25 mg of each compound were dissolved in 2 ml dimethylformamide with or without the aid of heat.

Agar Diffusion Method[19]

Tells of nutrient agar in test tube each containing 15 ml of nutrient agar sterilized by autoclaving at 121° for 30 minutes were prepared and poured each in an empty sterile *Petri*-dish (15x150 mm), the depth of agar was approximately 6 mm. The culture of each organism was spread with dry sterile swab on the surface of the previously prepared plates. Sterile discs (6 mm diameter) were impregnated with pervious solution of each compound, left to dry and were then placed on the surface of inoculated plates. Disc of antimicrobial standard were put in the center of plate agar; these plates were incubated at 37° for 24 hours. After incubation the plates were examined visually and the zones of inhibition were measured.

RESULTS AND DISCUSSION

2-Chloroquinoline-3-carbonitrile **(II)** was prepared by one-pot reaction via *Vilsmeier* formylation of acetanilide **(I)** using ($DMF/POCl_3$)[20] followed by treating with hydroxylamine hydrochloride whereby 44% yield of **(II)** was obtained. 2-Chloro-quinoline-3-carbonitrile **(II)** was condensed with a variety of aliphatic and aromatic amines in dioxane, whereby several new 2-substituted aminoquinoline-3-carbonitriles **(III)** were obtained. The structures of **(III)** were confirmed by elemental analysis and spectral data obtained from IR, NMR and mass spectra. The IR spectra of compounds **(III)** in KBr are characterized by strong absorption band at about 3386 cm^{-1} (due N-H stretching) and a sharp intense band around 2229 cm^{-1} (due to C≡N stretching). The ^{1}HNMR spectra of **(III)** are characterized by the presence of a broad singlet of one proton at about 5.32 ppm (due to the NH in case of aliphatic substitution). This signal appeared around 7.5 ppm in case of aryl substitution. The aromatic protons of the quinoline nucleus displayed a triplet of one proton at 7.30-7.22 (H-6), a multiplet of three protons at 7.75-7.56 ppm (H-7, H-5 and H-8), and a singlet of one proton at 8.18 ppm (H-4). The EI mass spectra of compounds **(III)** show prominent molecular ion peak, which might represent the base peak. Loss of ·H, ·CN, HCN and the 2-substituent from the molecular ion was observed.

In addition, 2-chloroquinoline-3-carbonitrile **(II)** was treated with thiourea in the presence of sodium hydroxide to give 2-thioquinoline-3-carbonitrile **(IV)**[21] which was treated with potassium hydroxide in absolute ethanol to give the corresponding potassium salt **(V)**. Condensation of **(V)** with different alkyl and aryl chloroacetates afforded the desired 3-cyano-2-alkoxy / aryloxycarbonyl-methylthioquinolines **(VI)**. The structures of **(VI)** were also confirmed by elemental and spectral analysis. The IR spectra of **(VI)** in KBr are characterized by sharp intense peak around 1730 cm^{-1} (due to C=O stretching) and another peak at 2223 cm^{-1} (due to C≡N stretching). The ^{1}HNMR spectra of **(VI)** are characterized by the presence of a singlet of two protons at about 4.15 ppm (due to –S-$\underline{CH_2}$-CO). The EI mass spectra of compounds **(VI)** showed prominent molecular ion peaks. The fragmentation patterns of these compounds are characterized by loss of the alkoxy or aryloxy group, which might produce the base peak. Loss of CO, 2-substituent and CN or HCN is also observed.

Moreover, 2-chloroquinoline-3-carbonitrile **(II)** was allowed to react with hydrazine in absolute ethanol at the reflux temperature for 24 hours whereby 1H-pyrazolo[3,4-b]quinolin-3-amine **(VII)** in 60% yield.[16] An alternative method was tried to obtain **(VII)** in a short time with an improved yield. This method involved reaction of hydrazine hydrate with 2-mercaptoquinoline **(IV)** in refluxing ethanol for 12 hours whereupon 1H-Pyrazolo[3,4-b]quinolin-3-ylamine **(VII)** was obtained in 75% yield. The later **(VII)** was allowed to condense with different aromatic aldehydes whereby some new Schiff's bases **(VIII)** were obtained. The structures of compounds **(VIII)** were confirmed by elemental and spectral analysis. The ^{1}HNMR spectra of **(VIII)** revealed a downfield singlet of one proton at about 13.37 ppm, disappeared on equilibration with D_2O (pyrazolo NH), a singlet of one proton at 9.21 ppm (-N=C$\underline{H}$-). The characteristic pattern of quinoline protons appeared in the region of 9.29-7.52 ppm. It is important to indicate that fusion of the pyrazole ring bearing an imine function at position-3 with a quinoline nucleus led to downfield shift of the H-4 signal of quinoline ring by about 1 ppm. The EI spectra of **(VIII)** are characterized by distinct molecular ion peaks. The spectra are characterized by the presence of common peaks at m/z 184(due to cleavage of azomethine double bond and abstraction of two hydrogen atoms), 169 (due to loss of the 3-substituent moiety) and 142 (aziridinoquinoline radical cation).

Furthermore, 1H-pyrazolo[3,4-b]quinolin-3-amine **(VII)** was allowed to react with *p*-chlorobenzoyl chloride to give 4-chloro-N-(1H-pyrazolo-[3,4-b]quinolin-3-yl)-benzamide **(IX)**. Its ^{1}HNMR of **(IX)** in DMSO revealed two downfield singlets each of one proton around 13.00 and 11.00 ppm disappeared on deuteration. These are due to NH of pyrazole ring and the amidic NH respectively.

The data obtained from the preliminary antimicrobial testing of the newly synthesized compounds using the agar diffusion method[19] and presented in (Table (4) reveals that some 2-substituted aminoquinoline-3-carbonitriles **(IIIa-IIIc)** showed a moderate antibacterial activity against *S. aureus* and weak activity against *B. subtilis*. Compounds **(III)** were found to be inactive against *E. coli, P. aeruginosa* and *C. albicans*. The 2-alkoxycarbonylmethylthioquinoline-3-carbonitriles **(VI)** showed a moderate activity against *S. aureus* and *E. coli*. They exhibited a weak to moderate antifungal activity against *C. albicans*. The compounds are ineffective against *P. aeruginosa*. The arylidene-pyrazoloquinolines **(VIII)** were found to possess a weak to moderate antifungal activity against *C. albicans*. Some of such derivatives are only effective *E. coli*.

Table 4: Antimicrobial Testing of the newly synthesized compounds, Ofloxacin and Nystatin.

Comp. No.	Microorganism (Inhibition Zone)				
	Staphylococcus aureus	*Basillus subtilis*	*Escherichia coli*	*Pseudomonas aeruginosa*	*Candida albicans*
IIIa	16 mm	4 mm	--	--	--
IIIb	15 mm	2 mm	--	--	--
IIIc	15 mm	2 mm	--	--	--
IIId	--	2 mm	--	--	--
IIIe	--	--	--	--	--
IIIf	--	--	--	--	--
VIa	15 mm	--	4 mm	--	2 mm
VIb	12 mm	-	6 mm	--	4 mm
VIc	10 mm	-	8 mm	--	4 mm
VId	10 mm	12 mm	9 mm	--	11 mm
VIe	10 mm	10 mm	8 mm	--	10 mm
VIIIa	--	--	--	--	5 mm
VIIIb	--	--	--	--	8 mm
VIIIc	--	--	--	--	10 mm
VIIId	--	--	8 mm	--	12 mm
VIIIe	--	--	6 mm	4 mm	8 mm
IX	10 mm	2 mm	10 mm	--	--
Ofloxacin	20 mm	20 mm	15 mm	30 mm	--
Nystatin	--	--	--	--	20 mm

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