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## Synthesis and antimicrobial activity of 2-alkylsulfanyl-3-quinoline carboxylic acid derivatives

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### ABSTRACT

2-Alkylsulfanyl-4-oxo-1,4-dihydroquinoline-3-carboxylic acid-amide derivatives (**4-11**) have been synthesized by reactions of 2-alkylsulfonyl-4-hydroxyquinolinecarboxylic acid (**3**), which can be prepared from commercially available aniline in five steps, with aromatic amines in good yields. Condensation of 4-chloro-2-methylsulfanyl-quinoline-3-carboxylic acid ethyl ester (**12**) with some nucleophilic reagents afford 4-substituted quinoline derivatives (**13-16**). The antimicrobial activities of the synthesized compounds are tested towards bacteria.

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### KEYWORDS

Quinoline;  
Alkylsulfanyl;  
Anilides;  
Anthranlic acid;  
Quinoline-3-carboxylic acid.

### INTRODUCTION

Functionalized quinolines analogues represent an important class of organic molecules that have attracted a great deal of attention from synthetic as well as medicinal chemists because of their presence in numerous natural products along with the wide spectrum of physiological activities displayed by these class of compounds<sup>[1]</sup>. Thus, substituted quinolines have found attractive applications as pharmaceuticals (antimalarials, antibacterials, protein kinase inhibitors), NADH models, and agrochemicals as well as being general synthetic blocks<sup>[2]</sup>. Although numerous elegant syntheses have been developed for quinolines<sup>[3-27]</sup> because of their great importance, it is still challenging to explore new and efficient synthetic routes for this class of compounds, particularly those with wide general applicability to achieve more flexible substitution pattern<sup>[28-30]</sup>.

### EXPERIMENTAL

All melting points (m.p.) reported for the compounds prepared are uncorrected and measured on a MELTEMP II melting point apparatus. IR spectra were recorded with a *Perking Elmer 1430* ratio recording infrared spectrophotometer with CDS data station using KBr Wafer technique,  $\nu$  in  $\text{cm}^{-1}$ . Microanalyses were conducted using an elemental analyzer 1106. <sup>1</sup>H-NMR and <sup>13</sup>C-NMR measurements were carried out on a *Bruker ARX* (<sup>1</sup>H-NMR: 300.13 MHz; <sup>13</sup>C-NMR: 75.47 MHz). The solvents are indicated in brackets and the chemical shifts ( $\delta$ ) are given downfield relative to tetramethylsilane (TMS) as internal standard. Mass spectra data given in  $m/z$  (relative %) were obtained on a *A.zonni* model Ms-5888, ionization are initiate by electron impact (EI) with 70 ev of energy. Reaction were monitored by thin-layer chromatography (TLC) on *E.Merck* silica gel 60 F<sub>254</sub> (0.2 mm) precoated alumi-

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num foils, developed with UV light or I<sub>2</sub> vapour. The atmospheric pressure column chromatography (CC) was preformed on silica gel Florisil (100-200 mesh).

### 2-Ethylsulfanyl-4-hydroxy-quinoline-3-carboxylic acid ethyl ester (3a)

Ethyl bromide (11.23 ml, 0.15 mole) in 675.7 ml of acetone was added drop wise to a stirred suspension of potassium salt (50g, 0.15 mole) with ice cooling. After stirring at room temperature for 5h, the reaction mixture was stirred at 50°C for 30min. and concentrated to dryness under reduced pressure. The residue was taken up in water and extracted with CHCl<sub>3</sub> (200 ml), then the organic layer washed with water, dried with Na<sub>2</sub>SO<sub>4</sub> and concentrated to dryness to give the ethyl derivatives (38 g, 78.3%) as an oil. Without purification, the resulting oil was dissolved in 150 ml of xylene and heated under reflux for 6 hrs after cooling, the reaction mixture was diluted with n-hexane and the resulting precipitate collected by filtration, and recrystallized from ethanol to give (3a) (16.6 g, 39.9%) as white crystals, m.p 110-112°C. IR: 2960, 2920, 1596, 1590, 1570, 1550, 1520, 1500, 1490, 1420, 1390, 1350, 1320, 1300, 1260, 1250, 1200, 1180, 1100, 1210, 1180, 1100, 1070, 1050, 1040, 950, 920. <sup>1</sup>H-NMR in (CDCl<sub>3</sub>, 300 MHz): δ 1.42 (t, 3H, CH<sub>2</sub>), 1.52 (t, 3H, CH<sub>3</sub>); 3.2 (q, 2H, SCH<sub>2</sub>), 4.5 (q, 2H, OCH<sub>2</sub>); 7.32 (dd, 1H, H-6); 7.38 (dd, 1H, H-7); 7.76 (d, 1H, H-8); 8.21 (d, 1H, H-5); 13.15 (s, 1H, NH) ppm. <sup>13</sup>C-NMR in (CDCl<sub>3</sub>, 75.45 MHz): δ 13.93 (q); 14.10 (q); 25.04 (t); 62.44 (t); 102.59 (s); 117.90 (s); 123.50 (d); 124.58 (d); 127.46 (d); 132.56 (d); 148.61 (s); 159.71 (s); 168.42 (s); 170.85 (s) ppm. Anal. C<sub>14</sub>H<sub>15</sub>NO<sub>3</sub>S (277.34) Calc. C 60.63, H 5.45, N 5.05; Found: C 60.60, H 4.48, N 5.02.

### 2-Methylsulfanyl-quinoline-3-carboxylic acid ethyl ester (3b)

Diethyl Sulphate (2.83ml, 0.03 mole) in 135 ml of ethyl alcohol was added drop wise to a stirred suspension of potassium salt (10 g, 0.03 mole) with ice cooling. After stirring at room temperature for 5h., the reaction mixture stirred at 50°C for 30 min. and concentrated to dryness under reduced pressure. The residue was taken up in water, extracted with CHCl<sub>3</sub> (200ml) and the organic layer washed with water, dried with Na<sub>2</sub>SO<sub>4</sub> and concentrated to dryness to give methylsulfanyl

compound (6.1 g, 66.1%) as an oil. Without purification the oil was dissolved in 30 ml of xylene and heated under reflux for 6 hr after cooling the reaction mixture was diluted with n-hexane and the resulting precipitate collected by filtration, and recrystallized from ethanol to give (3b) (1.76 g, 22.2%) as yellow crystals, m.p 98-100°C. IR: 3575, 3428, 3065, 2991, 2917, 2712, 2531, 2340, 2300, 1970, 1855, 1728, 1645, 1621, 1582, 1555, 1483, 1446, 1375, 1316, 1240, 1270, 1240, 1168, 1103.9, 1020, 988. <sup>1</sup>H-NMR in (DMSO-d<sub>6</sub>, 300 MHz): δ 1.34 (t, 3H, CH<sub>3</sub>); 2.68 (s, 3H, CH<sub>3</sub>); 4.39 (q, 2H, CH<sub>2</sub>); 7.46 (s, 1H, H-Ar); 7.70 (s, 2H, H-Ar); 8.13 (d, 1H, H-Ar); 11.60 (s, 1H, NH) ppm. Anal. C<sub>13</sub>H<sub>13</sub>NO<sub>3</sub>S (263.32) Calc: C 59.30, H 4.98, N 5.32; Found: C 59.5, H 4.94, N 5.11.

### 2-Ethylsulfanyl-4-oxo-1,4-dihydro-quinoline-3-carboxylic acid phenylamide derivatives (4a-11a)

A mixture of 2-ethylsulfanyl-4-hydroxy-quinoline-3-carboxylic acid ethyl ester (3a) (0.0035 mole), the corresponding aniline derivative (0.0052 mole) and DMF (0.5 ml) is carefully stirred and held on an oil bath at 180-190°C for (30 min). The mixture is cooled prior to the addition of C<sub>2</sub>H<sub>5</sub>OH (20 ml). The residue was filtered off, washed with alcohol and recrystallized TABLE 1.

### 2-Ethylsulfanyl-4-oxo-1,4-dihydro-quinoline-3-carboxylic acid phenylamide (4a):

IR: 3566, 3467, 3327, 3146, 3066, 3022, 2971, 2930, 2870, 2423, 2264, 1961, 1937, 1849, 1499, 1641, 1592, 1523, 1460, 1334, 1270, 1191, 1141, 1106, 1076, 987, 956. <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>, 300 MHz): δ 1.17 (t, 2H, CH<sub>2</sub>); 3.17 (t, 3H, CH<sub>3</sub>); 6.95 (t, 1H, H-4'); 7.22 (t, 2H, H-3', 5'); 7.31 (t, 1H, H-6); 7.60 (d, 3H, H-2', 6', 7); 7.75 (d, 1H, H-8); 8.08 (d, 1H, H-5) ppm. <sup>13</sup>C-NMR (DMSO-d<sub>6</sub>, 75.45 MHz): δ 13.09 (q); 25.77 (t); 114.01 (s); 118.11 (d); 119.30 (d); 122.98 (d); 123.87 (s); 124.39 (d); 125.09 (s); 128.66 (d); 132.44 (d); 139.05 (d); 139.21 (s); 155.45 (s); 163.65 (s); 174 (s) ppm.

### 2-Ethylsulfanyl-4-oxo-1,4-dihydro-quinoline-3-carboxylic acid (4-chloro-phenyl)-amide (5a)

Ms: 358 (M<sup>+</sup>, 5); 359 (M<sup>+</sup>+1, 1.2); (M<sup>+</sup>+2, 2.2); 297 (3); 262 (0.7); 232 (57); 231 (45); 204 (12); 129 (33); 127 (100); 120 (16); 115 (21); 111 (18); 102 (30); 89

(50). IR: 3424, 3335, 3259, 3217, 3139, 3070, 3023, 2965, 2926, 2868, 2364, 2338, 1655, 1618, 1593, 1525, 1459, 1432, 1400, 1336, 1269, 1192, 1104, 1088, 991, 913. <sup>1</sup>H-NMR in (DMSO-d<sub>6</sub>, 300MHz): δ 1.29 (t, 3H, CH<sub>3</sub>); 3.26 (q, 2H, CH<sub>2</sub>); 7.35-7.46 (m, 3H, H-Ar); 7.71-7.76 (m, 3H, H-Ar); 7.86 (d, 1H, H-Ar); 8.20 (d, 1H, H-Ar) ppm.

**2-Ethylsulfanyl-4-oxo-1,4-dihydro-quinoline-3-carboxylic acid (4-bromo-phenyl)-amide (6a)**

**Ms:** 402 (M<sup>+</sup>, 6); 403 (M<sup>+</sup>+1, 15); 404 (M<sup>+</sup>+2, 7); 341 (2.5); 294 (2.6); 232 (100); 204 (19); 171 (91); 146 (12); 120 (10); 114 (14); 91 (19). IR: 3424, 3368, 3280, 3217, 3136, 3069, 3023, 2965, 2927, 2870, 2364, 2338, 2269, 1655, 1620, 1591, 1523, 1460, 1433, 1396, 1335, 1272, 1191, 1109, 1071, 1028, 992, 914. <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>, 300MHz): δ 1.28 (t, 3H, CH<sub>3</sub>); 3.35 (q, 2H, CH<sub>2</sub>); 7.41-7.62 (m, 3H, H-Ar); 7.66-7.77 (m, 3H, H-Ar); 7.86 (d, 1H, H-Ar); 8.18 (d, 1H, H-Ar) ppm.

**2-Ethylsulfanyl-4-oxo-1,4-dihydro-quinoline-3-carboxylic acid (4-methoxy-phenyl)-amide (7a)**

**Ms:** 354 (M<sup>+</sup>, 25); 325 (4); 293 (1); 250 (0.7); 232 (17); 204 (5); 146 (4); 129 (0.68); 123 (100); 115 (3); 80 (4). IR: 3310, 3136, 2992, 2849, 2927, 2829, 2370, 2341, 2065, 1757, 1639, 1602, 1527, 1459, 1433, 1336, 1301, 1244, 1178, 1141, 1107, 1034, 989,

**2-Ethylsulfanyl-4-oxo-1,4-dihydro-quinoline-3-carboxylic acid (4-nitro-phenyl)-amide (8a)**

**IR:** 3366, 3130, 3077, 2960, 2927, 2872, 2364, 2338, 1663, 1599, 1524, 1492, 1456, 1324, 1233, 1176, 1109, 1025, 988, 914. <sup>1</sup>H-NMR in (DMSO-d<sub>6</sub>, 300MHz): δ 1.28 (t, 2H, CH<sub>3</sub>); 3.26 (q, 2H, CH<sub>2</sub>); 7.45 (t, 1H, H-6); 7.74 (t, 1H, H-7); 7.78-7.96 (m, 3H, H-Ar); 8.18-8.28 (m, 3H, H-Ar) ppm.

**2-Ethylsulfanyl-4-oxo-1,4-dihydro-quinoline-3-carboxylic acid (2-chloro-phenyl)-amide (9a)**

**IR:** 3348, 3065, 2926, 2863, 2370, 2341, 1640, 1622, 1585, 1524, 1459, 1436, 1331, 1263, 1236, 1187, 1147, 1053, 1030, 988, 911.

**2-Ethylsulfanyl-4-oxo-1,4-dihydro-quinoline-3-carboxylic acid m-tolylamide (10a)**

**IR:** 3311, 3139, 3030, 2957, 2923, 2868, 2341, 1921, 1851, 1622, 1589, 1530, 1461, 1430, 1335, 1255,

1196, 1179, 1133, 1087, 1052, 1023, 989, 941, 906. <sup>1</sup>H-NMR (DMSO d<sub>6</sub>, 300MHz): δ 1.29 (t, 3H, CH<sub>3</sub>); 2.34 (s, 3H, CH<sub>3</sub>); 3.27 (q, 2H, CH<sub>2</sub>); 6.88 (d, 1H, H-Ar); 7.21 (t, 1H, H-Ar); 7.41 (t, 2H, H-Ar); 7.54 (s, 1H, H-Ar); 7.73 (t, 1H, H-Ar); 7.86 (d, 1H, H-Ar); 8.21 (d, 1H, H-Ar) ppm. <sup>13</sup>C-NMR (DMSO-d<sub>6</sub>, 75.45 MHz): δ 13.05 (q); 21.01 (q); 25.72 (t); 113.82 (s); 116.44 (d); 118.11 (s); 119.80 (d); 123.69 (d); 123.85 (s); 124.4 (d); 125.10 (s); 128.49 (d); 132.46 (d); 137.88 (d); 138.97 (d); 139.17 (s); 155.58 (s); 163.56 (s); 174.36 (s, C=O) ppm.

**2-Ethylsulfanyl-4-oxo-1,4-dihydro-quinoline-3-carboxylic acid o-tolylamide (11a)**

**Ms:** 338 (M<sup>+</sup>, 1.5); 309 (7); 277 (11); 249 (1.7); 231 (47); 204 (11); 172 (7); 146 (7); 107 (100); 77 (18). IR: 3423, 3335, 3144, 3024, 2925, 2868, 2365, 2339, 1644, 1620, 1583., 1528, 1458, 1433, 1334, 1304, 1264, 1191, 1149, 1104, 1044, 991, 913. <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>, 300MHz): δ 1.56 (t, J=, 3H, CH<sub>3</sub>); 2.63 (s, 3H, CH<sub>3</sub>); 3.53 (q, 2H, CH<sub>2</sub>); 7.23 (t, 1H, H-4'); 7.41-7.50 (m, 2H, H-3', 5'); 7.68 (t, 1H, H-6); 7.99 (t, 1H, H-7); 8.20 (t, 1H, H-6'); 8.43 (d, 1H, H-8); 8.50 (d, 1H, H-5) ppm.

**2-Methylsulfanyl-4-oxo-1,4-dihydro-quinoline-3-carboxylic acid phenylamide (4b-11b)**

A mixture of 2-ethylsulfanyl-4-hydroxy-quinoline-3-carboxylic acid ethyl ester (**3b**) (0.0035 mole), the corresponding aniline (0.0052 mole) and DMF (0.5 ml) is carefully stirred and held on an oil bath at 180-190°C for (30min). The mixture is cooled prior to the addition of C<sub>2</sub>H<sub>5</sub>OH (20 ml). The residue was filtered off, washed on the funnel with alcohol TABLE 1.

**2-Methylsulfanyl-4-oxo-1,4-dihydro-quinoline-3-carboxylic acid phenylamide (4b)**

**IR:** 3552, 3485, 3288, 3134, 3023, 2926, 2369, 2340, 1623, 1594, 1524, 1464, 1436, 1341, 1316, 1274, 1240, 1197, 1147, 1111, 1078, 1027, 984, 915. <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>, 300MHz): δ 2.71 (s, 3H, CH<sub>3</sub>); 7.05 (t, 1H, H-4'); 7.33 (t, 2H, H-3', 5'); 7.44 (t, 1H, H-6); 7.68 (d, 2H, H-2', 6'); 7.73 (t, 1H, H-7); 7.93 (d, 1H, H-8); 8.21 (d, 1H, H-5); 10.84 (s, 1H, NH) ppm. <sup>13</sup>C-NMR (DMSO-d<sub>6</sub>, 75.45 MHz): 15.00 (q), 110.66 (s), 118.31 (d), 119.39 (d), 122.98 (d), 123.60 (s), 124.61 (d), 125.12 (d), 128.72 (d), 132.45 (d),

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138.94 (s), 159.30 (s), 163.79 (s), 174(s).

### 2-Methylsulfanyl-4-oxo-1,4-dihydroquinoline-3-carboxylic acid (4-chloro-phenyl)-amide (5b)

**IR:** 3412, 3276, 3140, 3068, 3027, 2923, 2370, 2340, 2274, 1644, 1621, 1592, 1525, 1461, 1432, 1400, 1338, 1314, 1275, 1237, 1106, 1085, 968, 913. <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>, 300 MHz): δ 2.97 (s, 3H, CH<sub>3</sub>); 3.43 (s, 1H, OH); 7.61 (d, 2H, H-3', 5'); 7.68 (t, 1H, H-6); 7.95-8.17 (m, 3H, H-2', 6', 7); 8.17 (d, 1H, H-8); 8.47 (d, 1H, H-5) ppm. <sup>13</sup>C-NMR (DMSO-d<sub>6</sub>, 75.45 MHz): δ 15.00 (q); 110.66 (s); 118.32 (s); 120.93 (d); 123.56 (s); 124.66 (d); 125.10 (s); 126.48 (d); 128.58 (d); 132.51 (s); 137.86 (d); 138.89 (d); 159.36 (s), 163.89 (d); 174.44 (s, C=O) ppm

### 2-Methylsulfanyl-4-oxo-1,4-dihydroquinoline-3-carboxylic acid (4-bromo-phenyl)-amide (6b)

**IR:** 3381, 3273, 3138, 3066, 3027, 2933, 2829, 2371, 2341, 1643, 1620, 1523, 1460, 1429, 1394, 1339, 1312, 1274, 1234, 1195., 1107, 1066, 1026, 997, 963, 912. <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>, 300 MHz): δ 2.98 (s, 3H, CH<sub>3</sub>); 3.4 (s, 1H, OH); 7.71-7.80 (m, 3H, H-3', 5', 6); 7.91 (d, 2H, H-2', 6'); 8.02 (t, 1H, H-7); 8.19 (d, 1H, H-8); 8.47 (d, 1H, H-5) ppm. <sup>13</sup>C-NMR (DMSO-d<sub>6</sub>, 75.45 MHz): δ 15.00 (q); 110.61 (s); 114.45 (d); 118.31 (s); 121.32 (d); 123.56 (s); 124.67 (d); 125.11 (s); 131.48 (d); 132.52 (s), 138.26 (d); 138.88 (s); 159.42 (s); 163.90 (d); 174.45 (s) ppm.

### 2-Methylsulfanyl-4-oxo-1,4-dihydroquinoline-3-carboxylic acid (4-methoxy-phenyl)-amide (7b)

**IR:** 3420, 3257, 3210, 3126, 3033, 2991, 2836, 2370, 2341, 1825, 1639, 1595, 1546, 1511, 1464, 1430, 1343, 1267, 1226, 1177, 1111, 1031, 994, 970, 915.

### 2-Methylsulfanyl-4-oxo-1,4-dihydroquinoline-3-carboxylic acid (4-nitro-phenyl)-amide (8b)

**Ms:** 340 (M<sup>+</sup>-CH<sub>3</sub>, 5); 294 (0.7); 262 (2); 218 (100); 189 (35); 146 (11); 114 (16); 63 (12). **IR:** 3369, 2982, 2856, 2418, 2370, 2340, 1674, 1616, 1598, 1515, 1484, 1455, 1430, 1321, 1295, 1253, 1174, 1128, 1106, 1028, 988, 908.

### 2-Methylsulfanyl-4-oxo-1,4-dihydroquinoline-3-carboxylic acid (2-chlorophenyl)amide (9b)

**IR:** 3412.7, 3069, 2985, 2371, 2341, 1720, 1656,

1618, 1587, 1516, 1434, 1338, 1314, 1288, 1234, 1191, 1136, 1115, 1031, 999, 913. <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>, 300 MHz): δ 2.93 (s, 3H, CH<sub>3</sub>); 7.28 (t, 1H, H-4'); 7.51 (t, 1H, H-5'); 7.64-7.73 (m, 2H, H-3', 6); 8.00 (t, 1H, H-7); 8.17 (d, 1H, H-6'); 8.45 (d, 1H, H-8); 8.72 (d, 1H, H-5); 10.9 (s, 1H, NH) ppm. <sup>13</sup>C-NMR (DMSO-d<sub>6</sub>, 75.45 MHz): δ 14.86 (q); 108.56 (s); 118.39 (s); 121.76 (d); 122.31 (d); 123.41 (s); 123.87 (d); 124.84 (d); 125.26 (d); 127.38 (d); 129.12 (d); 132.60 (s); 136.01 (d); 138.68 (s); 161.92 (s); 164.20 (s); 174.81(s) ppm.

### 2-Methylsulfanyl-4-oxo-1,4-dihydroquinoline-3-carboxylic acid m-tolylamide(10b)

**IR:** 3423, 3314, 3129, 3032, 2370, 2341, 1661, 1604, 1547, 1515, 1462, 1433, 1338, 1312, 1269, 1174, 1116, 1031, 966, 913. <sup>1</sup>H-NMR (DMSO d<sub>6</sub>, 300MHz): δ 2.31 (s, 3H, CH<sub>3</sub>); 2.70 (s, 3H, CH<sub>3</sub>); 3.30 (s, 1H, OH); 6.89 (d, 1H, H-4'); 7.23 (t, J= 1H, H5'); 7.43-7.52 (m, 3H, H-2', 6', 6); 7.74 (t, 1H, H-7); 7.9 (d, 1H, H-8); 8.22 (d, 1H, H-5); 10.82 (s, 1H, NH) ppm. <sup>13</sup>C-NMR (DMSO-d<sub>6</sub>, 75.45 MHz): δ 15.00 (q); 21.04 (); 110.66 (s); 116.52 (d); 118.30 (d); 119.90 (d); 123.69 (s); 124.62 (d); 125.12 (d); 128.55 (d); 132.46 (d); 137.94 (s); 138.86 (d); 159.42 (s); 163.71 (s); 174.36 (s) ppm.

### 2-Methylsulfanyl-4-oxo-1,4-dihydroquinoline-3-carboxylic acid o-tolylamide(11b)

**IR:** 3329, 3022, 2919, 2371, 2341, 1643, 1621, 1584, 1523, 1459, 1434, 1336, 1315, 1271, 1245, 1191, 1148, 1104, 999, 913. <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>, 300 MHz): δ 2.38 (s, 3H, CH<sub>3</sub>); 2.71 (s, 3H, SCH<sub>3</sub>); 3.17 (s, 1H, OH); 7.02 (t, 1H, H-Ar); 7.16-7.25 (m, 2H, H-Ar); 7.45 (t, 1H, H-Ar); 7.75 (t, 1H, H-Ar); 7.97 (d, 1H, H-Ar); 8.20-8.27 (m, 2H, H-Ar); 10.72 (s, 1H, NH) ppm. <sup>13</sup>C-NMR (DMSO-d<sub>6</sub>, 75.45 MHz): δ 14.91 (q); 18.09 (q); 109.53 (s); 118.34 (d); 120.76 (d); 123.02 (d); 123.48 (s); 124.72 (d); 125.23 (s); 126.03 (d); 127.16 (d); 130.03 (d); 132.50 (s); 137.36 (d); 138.71 (s); 161.07 (s); 163.79 (s); 174.81 (s) ppm.

### 4-Chloro-2-ethylsulfanyl-quinoline-3-carboxylic acid ethyl ester (12a)

A mixture of (3a) (1 g, 3.3 mmole) and phosphorus oxychloride (10 ml) was refluxed for 3hr. The reaction mixture was added very slowly with stirring to a

mixture of ice-ammonia hydroxide solution to give (0.8g) 75% yield of (**12a**) as oil. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 300 MHz): δ 1.43 (t, 3H, CH<sub>3</sub>); 1.46 (t, 3H, CH<sub>3</sub>); 3.4 (q, 2H, SCH<sub>2</sub>); 4.5 (q, 2H, OCH<sub>2</sub>); 7.5 (t, 1H, H-6); 7.7 (t, 1H, H-7); 7.9 (d, 1H, H-5); 8.1(d,1H, H-8) ppm. <sup>13</sup>C-NMR (CDCl<sub>3</sub>, 75.45 MHz): δ 13.97 (q); 14.16 (q); 24.95 (t); 62.35 (t); 62.35 (t); 123.01(s); 124.41 (d); 126.38 (d); 126.48 (s); 128.19 (d); 131.15 (d); 138.89 (s); 147.99 (s); 156.02 (s); 164.89 (s) ppm. Anal. C<sub>14</sub>H<sub>14</sub>ClNO<sub>2</sub>S Calc: C 56.85, H 4.77, N 4.74; Found: C 56.81, H 4.91, N 4.69.

#### 4-Chloro-2-methylsulfanyl-quinoline-3-carboxylic acid ethyl ester (**12b**)

To (1 gm, 0.0033 mole) of (**3b**) was added (10ml) of phosphorus oxychloride. The reaction mixture was refluxed for 3h, then it was added very slowly with stirring to a mixture of ice-ammonia hydroxide solution to give (**12b**) (0.9g, 84% yield) as oil. <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>, 300 MHz): δ 1.34 (t, 3H, CH<sub>3</sub>); 2.69 (s, 3H, CH<sub>3</sub>), 4.47 (q, 2H, CH<sub>2</sub>); 7.71 (t,1H, H-6); 7.91 (t, 1H, H-7); 8.04 (d,1H, H-8); 8.15 (d,1H, H-5) ppm. Anal. C<sub>13</sub>H<sub>12</sub>ClNO<sub>2</sub>S Calc: C 55.42, H 4.29, N 4.97; Found: C 55.67, H 4.30, N 4.86.

#### 2-Ethylsulfanyl-4-(2-hydroxyethylamino)-quinoline-3-carboxylic acid ethyl ester (**16a**)

To a solution of 4-chloro-2-ethylsulfanyl-quinoline-3-carboxylic acid ethyl ester (**12a**) (1gm, 3.3 mmole) in 10 ml ethanol was added (0.39 ml, 6.6 mmole) of ethanol amine. The reaction mixture was refluxed for 3hr and then poured into ice-water mixture. The resulting precipitate was filtered off, recrystallized from a mixture of ethanol and water to give (**16a**) (0.5 g, 46% yield) as white crystals m.p 65°C. IR: 3497, 3371, 3068, 2974, 2932, 2910, 2869, 2735, 2685, 2373, 2341, 1944, 1695, 1614, 1560, 1525, 1468, 1448, 1423, 1348, 1298, 1298, 1248, 1226, 1171, 1127, 1080, 1011, 968, 923. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 300 MHz): δ 1.47 (t, 3H, CH<sub>3</sub>); 1.37 (t, 3H,CH<sub>3</sub>); 2.18 (s, 1H, OH); 3.25 (q, 2H, OCH<sub>2</sub>); 3.65 (t, 2H, CH<sub>2</sub>); 3.82 (t, 2H, CH<sub>2</sub>); 4.5 (q,2H, SCH<sub>2</sub>); 6.99 (s, 1H, NH); 7.27 (, 1H, H-6); 7.59 (t, 1H, H-7); 7.80 (d, 1H, H-5); 8.0 (d, 1H, H-8) ppm. <sup>13</sup>C-NMR (CDCl<sub>3</sub>, 75.45 MHz): δ 14.04 (q); 14.21 (q); 25.19 (t); 50.19 (t); 61.60 (t); 61.88 (t); 107.6 (S); 118.27(S); 123.54 (d); 123.73 (d); 128.51 (S) 130.61 (d); 153.60 (S); 158.62 (S);

168.55 (S, C=O) ppm. Anal. C<sub>16</sub>H<sub>20</sub>N<sub>2</sub>O<sub>3</sub>S Calc: C 59.98, H 6.29, N 8.74; Found: C 60.09, H 6.10, N 8.79.

#### 2-Ethylsulfanyl-4-(2-hydroxyethylamino)-quinoline-3-carboxylic acid ethyl ester (**16b**)

To a solution of 4-chloro-2-methylsulfanyl-quinoline-3-carboxylic acid ethyl ester (**12b**) (0.5gm, 0.0017 mole) in 10 ml ethanol was added (0.2 ml, 0.0035 mole) of ethanol amine. The reaction mixture was refluxed for 6h. and then poured into ice-water mixture. The resulting precipitate was filtered off, recrystallized from a mixture of benzene and hexane to give (0.25g) 43% yield (**16b**) as white crystals m.p 38-42°C. IR: 3575, 3260, 2984, 2927, 2872, 2342, 2279, 1856, 1814, 1760, 1666, 1611, 1574, 1501, 1443, 1412, 1370, 1333, 1301, 1233, 1167, 1126, 1077, 1019, 976, 928. <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>, 300MHz): δ 1.2 (t, 2H, CH<sub>3</sub>); 2.5 (s, 3H, CH<sub>3</sub>); 3.3(t, 2H, CH<sub>2</sub>); 3.6 (t, 2H, CH<sub>2</sub>); 4.3 (q, 2H, CH<sub>2</sub>); 4.84 (t, 1H, OH); 6.98 (s, 1H, NH); 7.38 (t,1H, H-Ar); 7.67 (m, 2H, H-Ar); 8.25 (d, 1H, H-Ar) ppm. Anal.C<sub>15</sub>H<sub>18</sub>N<sub>2</sub>O<sub>3</sub>S Calc: C 58.80, H 5.92, N 9.14; Found: C 59.01, H 6.10, N 8.98.

#### 6-Ethylsulfanyl-1,2,3,4-tetrahydro-[1,4]diazepino [6,5-c] quinoline-5-one (**13a**, **14a**)

To a solution (**12a**) (1gm, 0.0033 mole) in 10 ml ethanol was added (0.44ml, 0.0066 mole) of diaminoethane. The reaction mixture was refluxed for 24h., during the reaction a precipitate is formed which was separated by filtration to give (**14a**), when TLC indicated that (**13a**) had completely disappeared the reaction mixture was concentrated, diluted with 5 ml CH<sub>2</sub>Cl<sub>2</sub>, and the resulting precipitate was filtered off, recrystallized from benzene to give 0.5g (54.34%) yield of (**14a**) m.p. 118-120°C. IR for (**14a**): 3600, 3380, 3280, 3180, 3020, 1690, 1630, 1570, 1550, 1480, 1470, 1450, 1410, 1370, 1350, 1290, 1250, 1210, 1140, 940, 900. <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>, 300MHz) for compound (**14a**): δ1.3 (t, 3H, CH<sub>3</sub>); 3.01 (q, 2H, CH<sub>2</sub>); 3.3 (CH<sub>2</sub>); 3.6 (CH<sub>2</sub>) ; 7.3 (2H, CH-Ar); 7.6 (CH-Ar) ; 8.2 (CH-Ar) ppm. Anal. for (**13a**) C<sub>16</sub>H<sub>21</sub>N<sub>3</sub>O<sub>2</sub>S Calc: C 60.16, H 6.63, N 13.15; Found: C 60.06, H 6.70, N 13.21. Anal. for (**14a**) C<sub>14</sub>H<sub>15</sub>N<sub>3</sub>OS ( ) Calc: C 61.51, H 5.53, N 15.37; Found : C 61.40, H 5.62, N 15.31.

## Full Paper

### 6-Methylsulfanyl-1,2,3,4-tetrahydro-[1,4] diazepino[6,5-c] quinoline-5-one (13b-14b)

To a solution of (12b) (0.3 g, 1.1 mmol) in 10ml ethanol was added 1.5 ml of 1, 2 diaminoethane. The reaction mixture was refluxed for 24 hr during the reaction a precipitate is formed which was separated by filtration to give (12b). When TLC indicated that (19b) had completely disappeared the reaction mixture was concentrated, diluted with 5ml CH<sub>2</sub>Cl<sub>2</sub>, and the resulting precipitate was filtered off recrystallized from a mixture of (ethanol-water) to give 0.15g (55.55%) yield of (14b) m.p. 112-115°C. <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>, 300MHz) for compound (13b): δ 1.2 (t, 3H, CH<sub>3</sub>); 2.5 (s, 3H, CH<sub>3</sub>); 3.3 (2H, CH<sub>2</sub>); 3.5 (2H, CH<sub>2</sub>); 4.3 (, 2H, CH<sub>2</sub>); 7.0 (s, 1H, NH); 7.3 (dd, 1H, CH); 7.6 (dd, 1H, CH); 7.7 (d, 1H, CH); 8.2 (d, 1H, CH) ppm. Ms for compound (14b): 259 (M<sup>+</sup>, 22); 244 (21); 226 (100); 212 (18); 185 (5); 184 (15); 156 (12); 129 (19); 127 (10); 102 (16); 75 (10); 63 (6). IR in KBr cm<sup>-1</sup> for compound (14b): 3550, 3442, 3375, 3261, 3181, 3035, 2924, 23.68, 2340, 1637, 1569, 1538, 1452, 1419, 1376, 1359, 1329, 1279, 1248, 1224, 1143, 1118, 1037, 1014, 946, 900, 862, 812, 760. <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>, 300MHz) for compound (14b): δ 2.3 (s, 3H, CH<sub>3</sub>); 3.3 (t, 2H, CH<sub>2</sub>); 3.6 (t, 2H, CH<sub>2</sub>); 7.35 (1H, CH-Ar); 7.40 (s, 1H, NH); 7.61 (2H, 2CH-Ar); 8.21 (2H, 1H, CH-Ar, NH) ppm. Anal. for (13b) C<sub>15</sub>H<sub>19</sub>N<sub>3</sub>O<sub>2</sub>S () Calc: C 58.99, H 6.27, N 13.76; Found: C 59.06, H 6.31, N 13.81. Anal. for (14b) C<sub>13</sub>H<sub>13</sub>N<sub>3</sub>OS () Calc: C 60.21, H 5.05, N 16.20; Found: C 60.30, H 5.10, N 15.99.

### 4-(2-carboxy-phenylamino)-2-ethylsulfanyl-quinoline-3-carboxylic acid ethyl ester (15a)

A mixture of (12a) (0.5g, 0.0016 mole) and anthranilic acid (0.22g, 0.0016 mole) was heated to fusion for one hour at 120°C, then it was cooled and the product obtained was filtered off, dried, and recrystallized from a mixture of (chloroform—hexane) to give 0.35g (47.3%) yield of (15a) as yellow crystals, m.p. 280-285°C. IR in KBr cm<sup>-1</sup>: 3681, 3367, 3181, 3064, 2972, 2928, 1951, 1838, 1720, 1691, 1614, 1543, 1514, 1450, 1410, 1300, 1229, 1157, 1019, 860. <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>, 300MHz): δ 1.15 (t, 3H, CH<sub>3</sub>); 1.31 (t, 3H, CH<sub>3</sub>); 3.28 (q, 2H, CH<sub>2</sub>); 4.03 (q, 2H, CH<sub>2</sub>); 6.58 (d, 1H, CH-Ar); 6.91 (t, 1H, CH-

Ar); 7.43 (t, 1H, CH-Ar); 7.55 (t, 1H, CH-Ar); 7.78-7.92 (m, 4H, CH-Ar); 8.31 (s, 1H, NH); 10.1 (s, 1H, OH) ppm. Anal. C<sub>21</sub>H<sub>20</sub>N<sub>2</sub>O<sub>4</sub>S () Calc: C 63.62, H 5.08, N 7.07; Found: C 63.48, H 5.13, N 7.21.

### Syntjesis of 4-(2-carboxy-phenylamino)-2-methylsulfanyl-quinoline-3-carboxylic acid ethyl ester (15b)

A mixture of (12b) (0.3gm, 0.00114 mole) and anthranilic acid (0.15g, 0.00114 mole) was heated to fusion for one hour at 120°C, then it was cooled, diluted with 5ml ethanol and the product obtained was filtered off, dried and recrystallized from a mixture of (chloroform-hexane) to give 0.17g (42.5%) yield of (15b) as yellow crystals m.p. 171-174°C. Ms: 382 (M<sup>+</sup>, 100); 338 (M<sup>+</sup>-COO, 11); 309 (65); 291 (83); 245 (69); 217 (41); 189 (48); 190 (12); 146 (18); 120 (10); 114 (22); 102 (20); 90 (12); 77 (27); 65 (28); 64 (11). IR in KBr cm<sup>-1</sup>: 3423, 3329, 3215, 3068, 2987, 2932, 2898, 2585, 2463, 2371, 2341, 2291, 1720, 1687, 1626, 1603, 1578, 1545, 1490, 1449, 1386, 1306, 1238, 1155, 1087, 988, 895, 842. Anal. C<sub>20</sub>H<sub>18</sub>N<sub>2</sub>O<sub>4</sub>S () Calc: C 62.81, H 4.74, N 7.32; Found: C 62.90, H 4.82, N 7.40.

## RESULTS AND DISCUSSION

The starting materials 2-alkylsulfanyl-4-hydrox-quinoline-3-carboxylic acid ethyl esters (3) were prepared through the formation of diethyl(phenylamino) (alkylthio)-methylenemalonate (2) in four steps. Cyclization of (2) was performed in refluxing xylene to give (3) as shown in SCHEME 1, Structures of the synthesized compounds were confirmed from the cor-

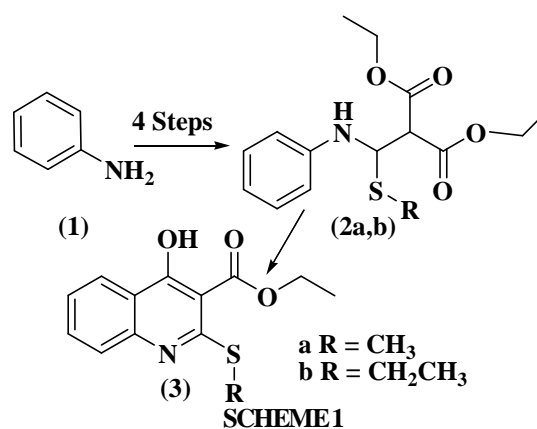


TABLE 1 : The data of some synthetic compound

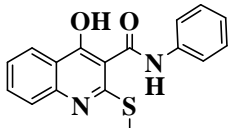
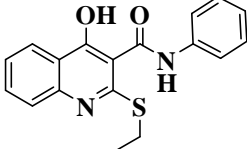
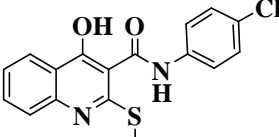
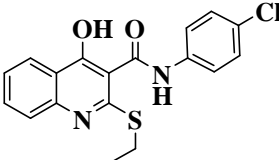
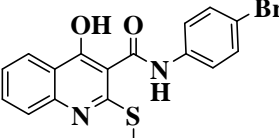
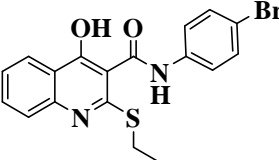
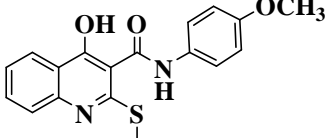
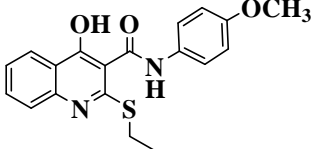
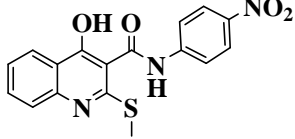
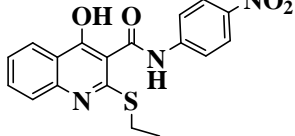
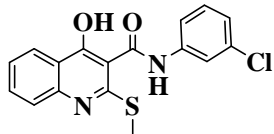
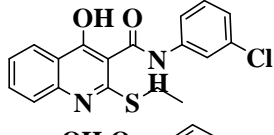
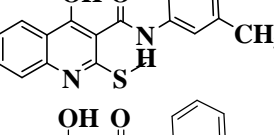
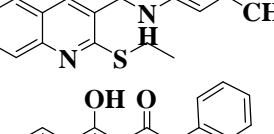
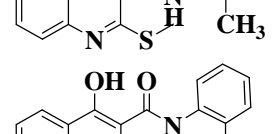
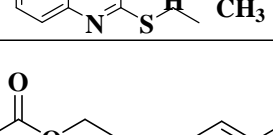
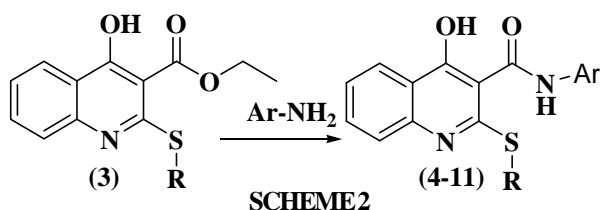
Comp no.	Structural of the products	Yield %	m.p. °C solvent	Mol. formula mol. Wt	% Analysis calcd.(Found)		
					C	H	N
(4a)		63	202-3 MeOH	C <sub>17</sub> H <sub>14</sub> N <sub>2</sub> O <sub>2</sub> S 310.37	66.79 (66.90)	4.55 (4.30)	9.03 (9.20)
(4b)		71	215-7 MeOH	C <sub>18</sub> H <sub>16</sub> N <sub>2</sub> O <sub>2</sub> S 324.35	66.64 (66.50)	4.97 5.11	8.64 (8.52)
(5a)		78	155 EtOH	C <sub>18</sub> H <sub>15</sub> ClN <sub>2</sub> O <sub>2</sub> S 344.82	59.21 (59.43)	3.80 (3.065)	8.12 (8.30)
(5b)		81	166 EtOH	C <sub>18</sub> H <sub>15</sub> ClN <sub>2</sub> O <sub>2</sub> S 358.84	60.25 (60.40)	4.21 (4.43)	7.81 (7.70)
(6a)		75	215-1 EtOH	C <sub>17</sub> H <sub>13</sub> BrN <sub>2</sub> O <sub>2</sub> S 389.27	52.45 (52.70)	3.37 (3.90)	7.20 (7.50)
(6b)		79	220-1 EtOH	C <sub>18</sub> H <sub>13</sub> BrN <sub>2</sub> O <sub>2</sub> S 403.25	53.61 (53.50)	3.75 (3.59)	6.95 (6.76)
(7a)		75	215-216 EtOH	C <sub>18</sub> H <sub>16</sub> N <sub>2</sub> O <sub>2</sub> S 340.39	63.51 (63.70)	4.74 (4.90)	8.23 (8.50)
(7b)		79	220 - 1 EtOH	C <sub>19</sub> H <sub>18</sub> N <sub>2</sub> O <sub>2</sub> S 354.42	64.39 (64.50)	5.12 (5.30)	7.90 (7.74)
(8a)		62	310 AcOH	C <sub>17</sub> H <sub>13</sub> N <sub>3</sub> O <sub>4</sub> S 355.37	57.46 (57.60)	3.69 (3.82)	11.82 (11.60)
(8b)		73	225-6 EtOH	C <sub>18</sub> H <sub>15</sub> N <sub>3</sub> O <sub>4</sub> S 369.39	58.53 (58.41)	4.09 (4.20)	11.38 (11.51)

table 1 continue

TABLE 1 : The data of some synthetic compound

Comp no.	Structural of the products	Yield %	m.p. °C solvent	Mol. formula mol. Wt	% Analysis calcd.(Found)		
					C	H	N
(9a)		76	231-2 EtOH	C <sub>17</sub> H <sub>13</sub> ClN <sub>2</sub> O <sub>2</sub> S 344.82	59.21 (63.80)	3.80 (4.30)	8.12 (15.10)
(9b)		78	284 - 5 D.M.F.	C <sub>18</sub> H <sub>15</sub> ClN <sub>2</sub> O <sub>2</sub> S 358.84	60.25 (60.44)	4.21 (4.30)	7.81 (7.73)
(10a)		83	270 - 1 1,3 Dioxane	C <sub>18</sub> H <sub>16</sub> N <sub>2</sub> O <sub>2</sub> S 324.39	66.64 (66.56)	4.97 (4.80)	8.64 (8.80)
(10b)		79	251 - 2 Chloroform	C <sub>19</sub> H <sub>18</sub> N <sub>2</sub> O <sub>2</sub> S 338.42	67.43 (67.60)	5.36 (5.51)	8.28 (8.39)
(11a)		81	265 - 6 1,3 Dioxane	C <sub>18</sub> H <sub>16</sub> N <sub>2</sub> O <sub>2</sub> S 324.39	66.64 (66.43)	4.97 (4.76)	8.64 (8.71)
(11b)		69	230 - 1 Benzene	C <sub>19</sub> H <sub>18</sub> N <sub>2</sub> O <sub>2</sub> S 338.42	67.43 (67.32)	5.36 (5.21)	8.28 (8.02)



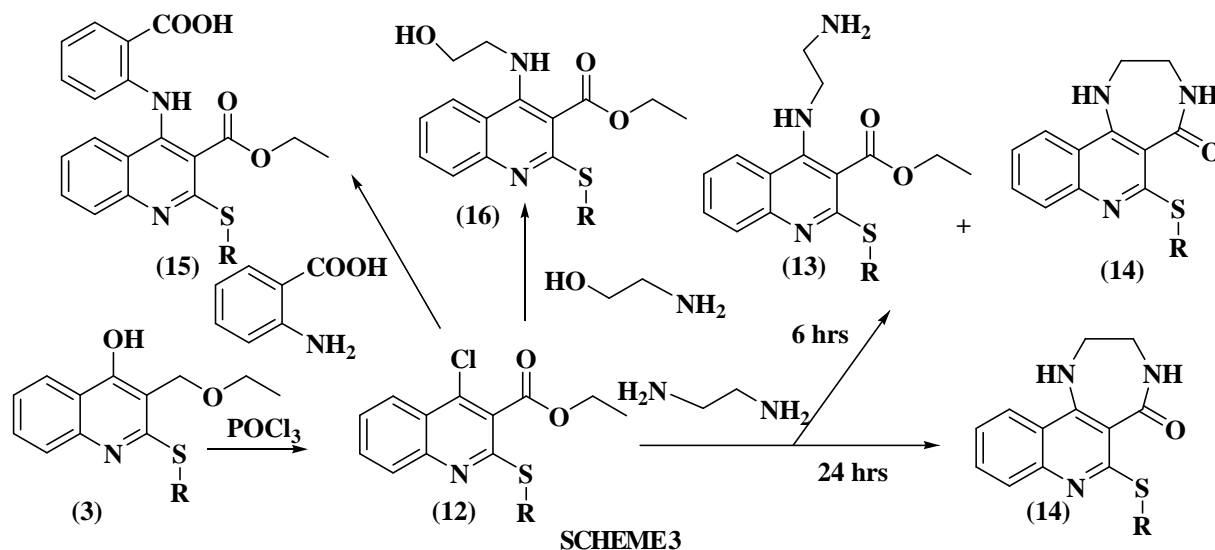
rect analytical and spectroscopic measurements (<sup>1</sup>H-NMR, <sup>13</sup>C-NMR and IR).

The reaction of (3) with different aromatic amines in the presence of a small amount of DMF to guarantee the best mixing of the reagents, and to prevent local overheating of the reaction mixture gave the corresponding anilide (4-11) SCHEME 2.

<sup>1</sup>H-NMR spectrum of (4a) showed nine aromatic protons were detected at δ 7.05-8.21 ppm and the NH proton appeared as singlet at δ10.84 ppm. <sup>13</sup>C-NMR of compound (4a) gave extra confirmation to the suggested structure as it showed signals at δ 15.00, 174.45 ppm related to the CH<sub>3</sub>, C=O groups respectively, and all the expected signals related to the suggested structure have been detected. <sup>1</sup>H-NMR spectrum of (4b) showed the appearance of the character-

istic signals of the SCH<sub>2</sub>CH<sub>3</sub> protons and disappearance of the OCH<sub>2</sub>CH<sub>3</sub> signals instead new 5 aromatic protons appeared together with the 4 quinoline protons at 6.95- 8.08 ppm, the NH proton appeared as singlet at δ10.84 ppm. <sup>13</sup>C-NMR spectrum of (4b) showed signals at δ 13.09, 25.77 ppm corresponding to the CH<sub>3</sub>, CH<sub>2</sub> together with all the other expected signals. <sup>13</sup>C-NMR of compound (5a) gave extra confirmation to the suggested structure as it showed signals at δ 15.00 and 174.45 ppm related to the CH<sub>3</sub> and C=O groups respectively, and all the expected signals related to the suggested structure have been detected. <sup>1</sup>H-NMR spectrum of (5a) showed the expected signals of the CH<sub>3</sub> protons at δ 2.7 ppm, a singlet for the OH proton at δ 3.43, and the 8 aromatic protons gave signals at δ 7.33- 8.20 ppm. <sup>13</sup>C-NMR of (5a) gave signals at δ 15.00 and 174.45 ppm corresponding to the CH<sub>3</sub> and C=O carbons respectively, with all the expected signals. <sup>1</sup>H-NMR spectrum of compound (5b) showed the expected 8 aromatic protons appeared at δ 7.35 8.20 ppm and the NH proton as singlet at δ10.84 ppm. Mass spectrum of (5b) gave more confirmation to the suggested structure where the molecular ion peak





( $M^+$ ) appeared at  $m/z=358$  and the ( $M+2$ )<sup>+</sup> peak appeared at  $m/z=360$  with an intensity equal to one-third the intensity of the molecular ion peak ( $M^+$ ) which proves the presence of ( $Cl^{37}$ ) isotope. <sup>1</sup>H-NMR of compound (6a) showed the characteristic signal of the methyl protons at  $\delta$  2.71 ppm, the (OH) proton as singlet at  $\delta$  3.18 ppm, the 8 aromatic protons at  $\delta$  7.44- 8.20 ppm and the NH proton as singlet at  $\delta$  10.84 ppm. <sup>13</sup>C-NMR of compound (6a) added more assurance to the suggested structure as all the expected signals were detected. <sup>1</sup>H-NMR of compound (6b) showed the 8 aromatic protons that appeared at  $\delta$  7.41- 8.2 ppm and the NH proton as singlet at  $\delta$  10.84 ppm. Mass spectrum of (6b) gave more confirmation for the proposed structure by giving a molecular ion peak at  $m/z=403$  and the expected ( $M+2$ )<sup>+</sup> peak at  $m/z=405$  with an intensity equal to that of the molecular ion peak ( $M^+$ ) which proves the presence of the (Br). Mass spectrum of compound (7a) gave the molecular ion peak ( $M^+$ ) at  $m/z=354$ . Mass spectrum of compound (8a) showed loss of ( $CH_3$ ) fragment to give ( $M^+-CH_3$ ) peak at  $m/z=340$ . <sup>1</sup>H-NMR of (8b) gave the characteristic signals of the  $SC_2H_5$  group, the 8 aromatic protons, and the singlet of the NH proton. <sup>1</sup>H-NMR for compound (9a) showed all the expected signals for the suggested structure. <sup>13</sup>C-NMR for compound (9a), which showed all the expected signals, adds more assurance to the proposed structure. <sup>1</sup>H-NMR of compound (10a) showed two singlet at  $\delta$  2.31 and 2.7 ppm related to the  $CH_3$  at C-3' and the  $CH_3$  of the  $SCH_2CH_3$  respectively, the

OH proton appeared as singlet at  $\delta$  3.3 ppm, the eight aromatic protons appeared at 6.89- 8.22 ppm and the NH proton appeared as singlet at  $\delta$  10.84 ppm. <sup>13</sup>C-NMR of compound (10a) showed signals for the two methyl groups and the C=O carbons at  $\delta$  15.55, 21.04, and 174.36 ppm respectively in addition to all the signals corresponding to the suggested structure. <sup>1</sup>H-NMR of compound (10b) showed the  $CH_3$  at C-3' appeared as singlet at 2.34 ppm, the aromatic signals appeared at  $\delta$  6.88- 8.21 ppm and the NH proton appeared as singlet at 10.84. <sup>13</sup>C-NMR for compound (10b) showed signals at  $\delta$  13.05, 21.01, 25.72 and 174.36 ppm attributed to the  $CH_3$ ,  $CH_3$ ,  $CH_2$ , and C=O carbons respectively, moreover all the expected signals have been detected. <sup>1</sup>H-NMR of compound (11a) showed signals for the two-methyl protons, the OH proton, the aromatic protons of the quinoline ring and the NH proton. <sup>13</sup>C-NMR of compound (11a) showed all the expected signals for the structure proposed. <sup>1</sup>H-NMR for compound (11b) showed the eight aromatic protons and the NH proton. Mass spectrum of compound (11b) gave a molecular ion peak at  $m/z=338$ .

4-Chloro-2-alkylsulfanyl-quinoline-3-carboxylic acid ethyl esters (12) could be obtained by treatment of (3) with phosphorus oxy chloride. Reaction of (12) with 1,2-diaminoethane in ethanol for 6 hrs gave a mixture of the expected compound (13) and (14). Compounds (14) were precipitated through the reaction as very fine crystals, which were separated by filtration. By repetition of the reaction with increasing the reac-

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TABLE 2 : Microbial strains used for investigating the antimicrobial activities

Microbial strain	NRRL strain <sup>a</sup>	Classification	Culture medium
<b>Air-born bacteria</b>			
1- <i>Bacillus subtilis</i>	NRS-744	Gram-positive	Nutrient agar medium
<b>Human-pathogenic bacteria</b>			
2- <i>Staphylococcus aureus</i>	B-767	Gram-positive	Nutrient agar medium
3- <i>Klebsiella pneumoniae</i>	B-17232	Gram-negative	
4- <i>Escherichia coli</i>	B-3704	Gram-negative	
5- <i>Pseudomonas aeruginosa</i>	B-23	Gram-negative	
6- <i>Proteus vulgaris</i>	B-123	Gram-negative	
<b>Human-pathogenic yeasts</b>			
7- <i>Candida albicans</i>	Y-477	Yeast	Sabaroud dextrose agar
8- <i>Candida tropicalis</i>		Yeast	

<sup>a</sup>NRRL= Northern Regional Research Laboratory, U.S. Department of Agriculture, Peoria, Illinois, USA

TABLE 3: Antimicrobial activity of the synthesized compounds

No.	Gram positive		Gram negative				Yeast	
	<i>Bacillus subtilis</i>	<i>Staphylococcus aureus</i>	<i>Klebsiella pneumoniae</i>	<i>Escherichia coli</i>	<i>Pseudomonas aeruginosa</i>	<i>Proteus vulgaris</i>	<i>Candida albicans</i>	<i>Candida tropicalis</i>
(3a,b)	-	-	-	-	-	-	-	-
(4a, b)	-	-	-	-	-	-	-	-
(5a)	-	-	-	-	-	-	-	-
(5b)	+++	+++	-	-	-	-	+++	+++
(6a)	+++	+++	-	-	-	-	+++	+++
(6b)	-	-	-	-	-	-	-	-
(7a, b)	-	-	-	-	-	-	-	-
(8a, b)	-	-	-	-	-	-	-	-
(10a, b)	-	-	-	-	-	-	-	-
(11a, b)	-	-	-	-	-	-	-	-
(12a, b)	-	-	-	-	-	-	-	-
(13a, b)	-	-	-	-	-	-	-	-
(14a, b)	-	-	-	-	-	-	-	-
(15a)	+++	+++	-	-	-	-	+++	+++
(15b)	+++	+++	-	-	-	-	+++	+++
(16a, b)	-	-	-	-	-	-	-	-

tion time for 24 hrs only compounds (**14**) were formed. Condensation of the chloro-derivatives (**12**) with anthranilic acid and ethanol amine afforded (**15**) and (**16**), respectively, SCHEME 3.

The structure of (**13a**) was confirmed by the <sup>1</sup>H-NMR spectrum which showed the characteristic signals for the OCH<sub>2</sub>CH<sub>3</sub> and SCH<sub>3</sub> protons, two signals at δ 3.3, 3.5 ppm corresponding to the two methylene, singlets at δ 7.00 ppm corresponding to the NH proton, and signals for the quinoline protons at δ 7.3- 8.2 ppm. While the <sup>1</sup>H-NMR of (**13b**) showed the SCH<sub>3</sub> signals and the disappearance of the OCH<sub>2</sub>CH<sub>3</sub> signals it also showed the two methylene protons at δ 3.3, 3.6 ppm and aromatic protons with integration equal to 6 protons at δ 7.35- 8.29 ppm. Mass spectrum of (**13b**) added good confirmation to the proposed structure

which showed the molecular ion peak at m/z = 259. <sup>1</sup>H-NMR of compound (**16a**) showed the appearance of the expected signals of the SCH<sub>2</sub>CH<sub>3</sub>, OCH<sub>2</sub>CH<sub>3</sub> protons and a new signal attributed to the OH proton which appeared as singlet at δ 2.18 ppm. The two methylene groups appeared as two triplets at δ 3.65, 3.82 ppm (J= 5.03, 5.18) respectively and the NH proton as singlet at δ 6.99 ppm, the aromatic protons appeared at δ 7.27- 7.97 ppm. <sup>13</sup>C-NMR of compound (**16a**) showed two signals at δ 50.193, 61.61 ppm corresponding to two methylene groups, which indicate the introducing of the hydroxy ethyl to the quinoline ring at the 4-position in addition to all the required signals. <sup>1</sup>H-NMR of compound (**16b**) showed in addition to the SC<sub>2</sub>H<sub>5</sub> and the OC<sub>2</sub>H<sub>5</sub> signals a new two triplets characteristic to the two new methylene groups at δ 3.3,

3.6 ppm, the OH signal at  $\delta$  4.84 ppm as triplet, the NH signal at  $\delta$  6.96 ppm as triplet and the aromatic signals at  $\delta$  7.38-8.25 ppm.

### Antimicrobial activity

The antimicrobial screening procedure of the synthesized compounds as 0.1% solution in DMF was investigated by the disk diffusion method, the antibiotic assay methods as well as the microbial strains used for the bioassay were illustrated TABLE 2. From the data shown in TABLE 3, it is clear that; the synthesized compounds were generally devoid of activity towards the tested gram negative bacteria (*Klebsiella pneumoniae*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Proteus vulgaris*). Compounds (**5b**), (**6a**), (**15a**) and (**15b**) are very active towards the tested gram-positive bacteria (*Bacillus subtilis*, *Staphylococcus aureus*) Yeast (*Candida albicans*, *Candida tropicalis*).

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