Mansoura Journal of Chemistry, Vol. 32 (2), December, 2005.

SYNTHESIS OF SOME NEW 8-HETEROLYL QUINOLINES

Hassan, K. Ibrahim*; Adel, S. Orabi; El-Sayed, H. El-Tamany and Ahmed, S. Radwan
Chemistry Department, Faculty of Science, Suez Canal University, Ismailia Egypt. * e-mail: hkhibrahim@yahoo.com

ABSTRACT

2-(Quinolin-8-yloxymethyl)-3,1-benzoxazin-4-one (**2**) is prepared by condensation of ethyl quinolin-8-yl-oxyacetate (**1**) with anthranilic acid. Treatment of **2** with hydrazine hydrate, 4-aminobenzoic acid and ethyl acetate yields the corresponding 2-quinolin-8-yloxymethyl)-3-substituted quinazolin-4-ones (**3,5**) and ethyl 2[(quinolin-8-yloxymethyl) arbonylaminobenzoyl] acetate (**6**). Reaction of the hydrazide **7** with ammonium thoicyanate, phenyl isothiocyanate and carbon disulphide gives the corresponding 1,4-disubstituted thiosemicarbazide (**8,10**) and **12**. Cyclization of **8** and **10** with base gives 4,5-disbstituted 1,2,4-triazol-3-thiones (**9,11**), while compound **12** is cyclized with hydrochloric acid or hydrazine hydrate to give 1,3,4-oxadiazole and 1,2,4-triazole derivatives (**13** and **14**), respectively. Compound **11** reacts with ethyl chloroacetate, acrylonitrile and acryloamide affording the corresponding 2,3-disubstituted-4-phenyl-5-(quinolin-8-yloxymethyl)-1,2,4-triazoles (**17** and **18 a,b**).

INTRODUCTION

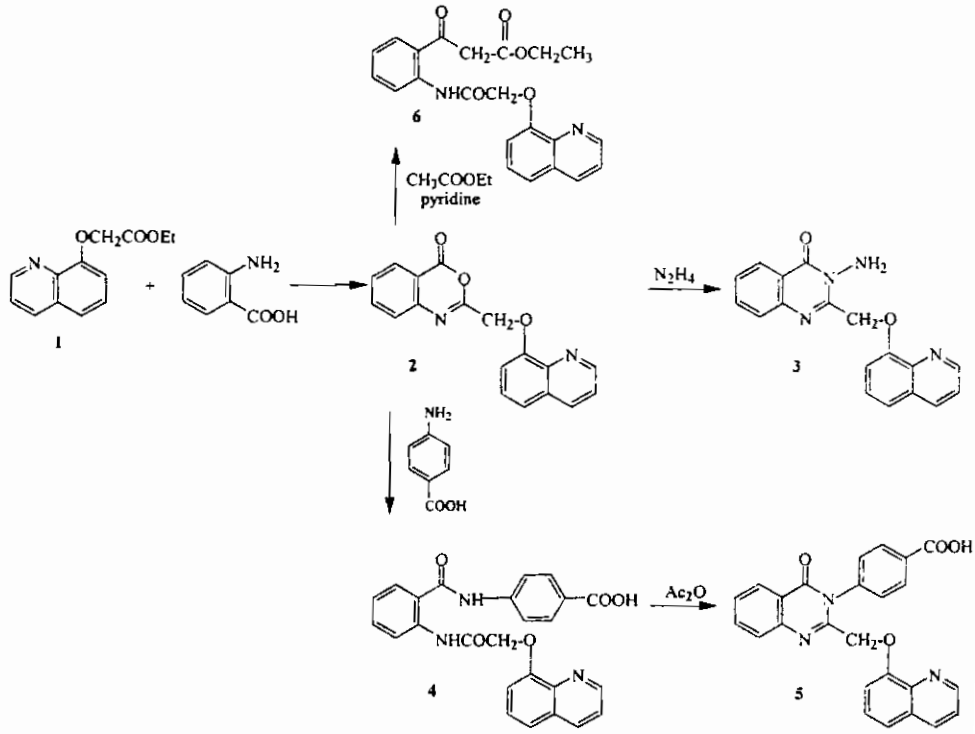
Quinoline derivatives are drugs of therapeutic importance showing wide spectrum of biological activities **[Katritzky, (1984); Latour & Reeves (1965) and Lee, et al., (2001)]**. In the present study ethyl quinolin-8-yl-oxyacetate (**1**) **[Raafat & Nibal (1980)]** reacted with anthranilic acid and hydrazine hydrate to give 2-(quinolin-8-yl-oxymethyl)-3,1-benzoxazinone (**2**) and quinolin-8-yl-oxyacetic acid hydrazide (**7**) as a key starting materials for the preparation of heterocyclic compounds containing quinoline moiety .

Presented at the 8 th ICCRD''2005.

RESULTS AND DISCUSSION

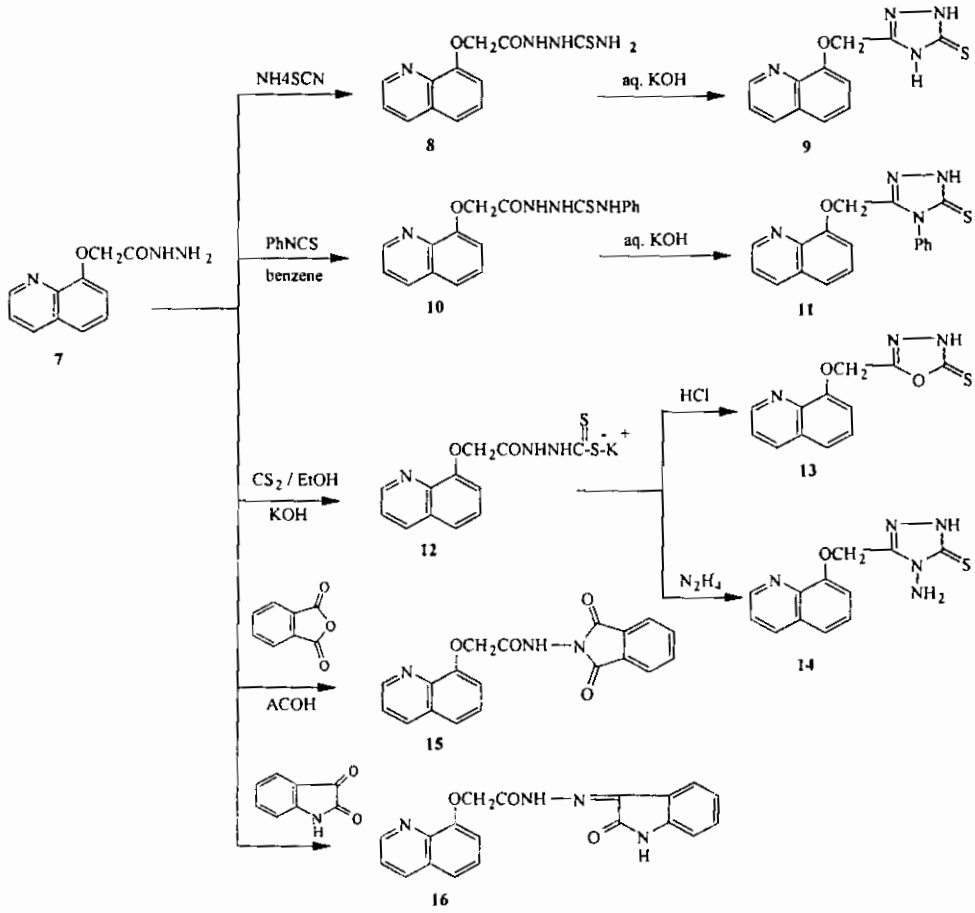
Ethyl quinoline-8-yloxyacetate (**1**) is prepared via alkylation of 8-hydroxy-quinoline with ethyl chloroacetate according to a literature method **[Raafat & Nibal (1980)]**. Condensation **[Soliman, et al., (1990)]** of **1** with anthranilic acid by fussion at 100 °C, gave the corresponding 2-(quinolin-8-yloxymethyl)-3,1-benzoxazin-4-one (**2**), Scheme 1.

The reaction of 2-quinolin-8-yl-oxymethyl)-3,1-benzoxazin-4-one (**2**) with each hydrazine hydrate and 4-aminobenzoic acid in boiling ethanol produced 2-(quinolin-8-yloxymethyl)-3-aminoquinazolin-4-one (**3**) and 4-[2-(quinolin-8-yloxy-methylcarbonylamino)benzoylamino]-benzoic acid (**4**), respectively. Cyclization of compound **4** in boiling acetic anhydride yielded the corresponding 2-(quinolin-8-yloxymethyl)-4-(hydroxycarbonylphenyl)-quinazolin-4-one (**5**).



Scheme 1

Subsequently, (**2**) was transformed to ethyl 2-[(quinolin-8-yloxymethyl)-carbonylaminobenzoyl]-acetate (**6**) via condensation with ethyl acetate in dry pyridine under reflux. In addition, teartment of **1** with hydrazine hydrate in refluxing ethanol **[Raafat & Nibal (1980)]** led to the formation of quinolin-8-yloxyacetic acid hydrazide (**7**).



Scheme 2

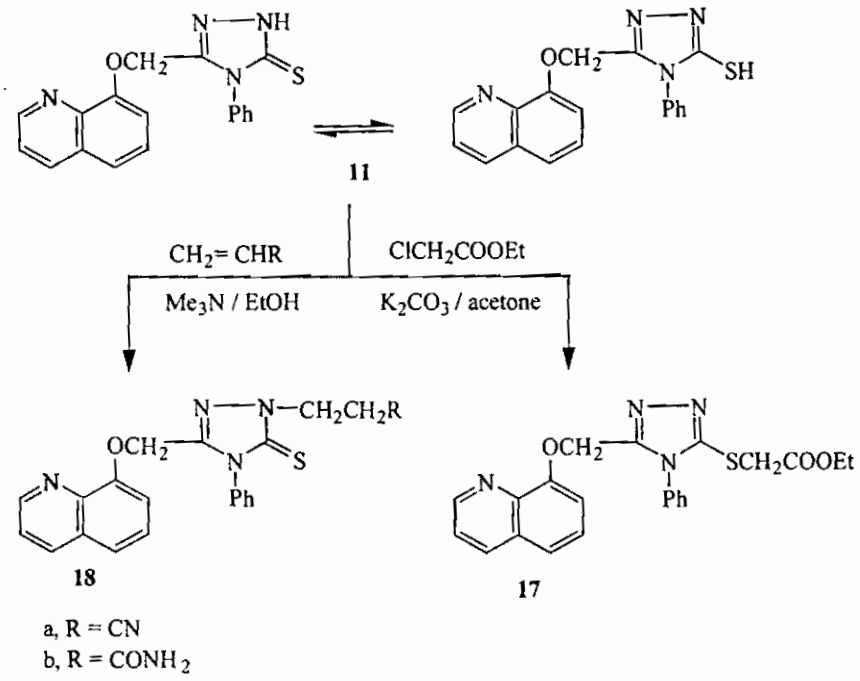
The hydrazide **7** is transformed to 5-(quinolin-8-yloxymethyl)-4-substituted-1,2,4-triazol-3-thiones (**9** and **11**, Scheme 2) via condensation with ammonium thiocyanate or phenyl isothiocyanate to give 1-(quinolin-8-yloxyacetyl)-4-substituted thiosemicarbazide (**8** and **10**), respectively. Cyclization of **8** and **10** with pot. hydroxide (4 %)

[Mohamed, et al., (1992,1993) and El-Deen, et al., (1993,1994)] afforded **9** and **11**.. The reaction of hydrazide **7** with carbon disulfide in ethanolic potassium hydroxide **[Reid & Heindel (1976,1977)]** under reflux to form the non isolable potassium salt **12** in quantitative yield. Subsequently, 5-(quinolin-8-yloxymethyl)-3H-1,3,4-oxadizol-2-thione (**13**) is prepared by cyclization of **12** with hydrochloric acid at room temperature, while compound **12** is cyclized with hydrazine hydrate in refluxing ethanol to give the corresponding 4-(amino-5-(quinolin-8-yloxymethyl)-1,2,4-triazol-3-thione (**14**) Scheme 2.

On the other hand, the reaction of hydrazide **7** with phthalic anhydride in glacial acetic acid gave the corresponding N-(1,3-dioxo-1,3-dihydroisoindol-2-yl)-2-(quinolin-8-yloxy)-acetamide (**15**), while its with isatin in ethanol under reflux led to the formation of 1-(quinolin-8-yloxyacetyl)-2-(2-oxo-1H-2,3-dihydroindol-3-yl)-hydrazine (**16**) Scheme 2.

This tautomeric equilibrium in compound **11** was further established by chemical reaction. Thus, compound **11** reacts as a thiol with ethyl chloroacetate in presence of anhydrous potassium carbonate in acetone under reflux to give the corresponding 3-(ethoxycarbonylmethylthio)-4-phenyl-5-(quinolin-8-yloxymethyl)- 1,2,4-triazole (**17**).

In the detailed work the reaction of compound **11** with activated olefinic compounds (namely, acrylonitrile and acryloamide) in presence of triethyl amine in ethanol led to the formation of 2-(2-substituted) ethyl-4-phenyl-5-(quinolin-8-yloxymethyl)-1,2,4-triazol-3-thiones **18** a,b; Scheme 3.



Scheme 3

EXPERIMENTAL

Melting points were determined on a MEL. TEMP11 melting point apparatus and uncorrected. NMR spectra were recorded on a Varian Gemini-200 (^{1}H NMR-200.0 MHz or 300.13 MHz) instrument and chemical shifts were given with respect to TMS. IR spectra were recorded on a Perkin-Elmer 1430 spectrometer and a Biorad FTS7 (KBr). Mass spectra were obtained on GC-MSQP 1000 EX Shimaduz instrument (70 eV) EI ionzation, source temperature 200 °C. Microanalyses were conducted using a elemental analyzer 1106. The spectra was tested in Cairo University – Egypt and in Zurich University – Zurich .

2-(Quinolin-8-yloxymethyl)-3,1-benzoxain-4-one (2)

A mixture of **1** (2.31gm, 0.01 mol) and anthranilic acid (1.37gm, 0.01 mol) was fused in an oil-bath at 100 °C for 2h. The reaction mixture is cooled and the solid obtained was crystallized from ethanol to give **2** as

yellow powder, yield 73%, mp 210 °C.; IR (KBr) 1740 (C=O), 1625 (C=N), 1309, 1117, 1014 (C-O) cm^{-1}; MS: m/z = 304 (M^+, 4.2), 186 (37.0), 160 (1.6), 159 (17.2), 158 (100), 146 (11.9), 145 (10.0), 129 (56.7), 128 (25.3), 119 (26.1), 102 (13.3), 90 (22.1), 76 (16.7); Found: C, 71.30; H, 3.80; N, 8.90. $C_{18}H_{12}N_2O_3$ requires: C, 71.05; H, 3.97; N, 9.21.

2-(Quinolin-8-yloxymethyl)-3-aminoquinazolin-4-one (3) and 4- [2-(quinolin-8-yloxy-methylcarbmylamino)benzoylamino]-benzoic acid (4)

A mixture of **2** (3.04 gm, 0.01 mol) and the appropriate of hydazine hydrate or 4-aminobenzoic acid (0.01 mol) in ethanol (40 mL) was heated under reflux for 6h, then cooled. The resulting product was filtered off, and recrystallized from ethanol to give **3** and **4**.

Compound **3** as pale yellow crystals, yield 42%, mp 140 °C IR (KBr): 3342, 3125 (NH_2), 1689 (CO), 1620 (C=N), 1216, 1118, 1015 (C-O) cm^{-1}; MS: m/z = 318 (M^+, 1.7), 304 (9.9), 247 (1.7), 186 (31.4), 158 (100), 145 (13.9), 137 (14.2). 129 (85.5), 119 (22.4), 90 (30.8). Found: C, 67.77; H, 4.03; N, 17.38. $C_{18}H_{14}N_4O_2$ requires: C, 67.92; H, 4.43; N, 17.6.

Compound **4** as light brown powder, yield 60%, mp 195 °C, IR (KBr): 3450 – 2750 (br, OH), 3205 (NH), 1710 – 1685 (br, CO), 1620 (C=N), 1205, 1117, 1013 (C-O) cm^{-1}; MS: m/z = 441 (M^+, 1.2), 388 (1.2), 304 (2.2), 263 (1.4), 231 (1.4), 186 (7.8), 185 (51.5), 164 (3.0), 158 (100), 146 (15.5), 145 (21.3), 137 (4.2), 129 (87.0), 121 (5.0), 120 (12.9), 117 (28.9), 77 (22.7), 63 (47.2). Found: C, 67.70; H, 4.00; N, 9.30. $C_{25}H_{19}N_3O_5$ requires: C, 68.02; H, 4.34; N, 9.52.

2-(Quinolin-8-yloxymethyl)-4-(hydroxycarbonylphenyl)-quinazolin-4-one (5)

A solution of **4** (4.41 gm, 0.01 mol) in acetic anhydride (15 mL) was heated under reflux for 4h. The solid formed after cooling was filtered off and recrystallized from ethanol to give **5** as red powder, yield 42%, mp 150 °C, IR (KBr): 3390 – 2850 (br. OH), 1705 – 1680 (br. CO), 1623 (C=N), 1259, 1182, 1090 (C-O) cm^{-1}; MS: m/z = 423 (M^+, 7.5), 188 (25.2), 159 (17.1), 158 (30.8), 145 (22.2), 131 (13.0), 129 (18.8), 118 (12.0), 117 (49.4), 104 (4.1), 102 (34.3), 90 (100), 76 (27.7). Found: C, 70.75; H, 3.85; N, 9.61. $C_{25}H_{17}N_3O_4$ requires: C, 70.91; H, 4.05; N, 9.92.

Ethyl 2-[(quinolin-8-yloxymethyl)carbinylaminobenzoyl]-acetate (6)

A mixture of **2** (3.04 gm, 0.01 mol) and ethyl acetate (0.88 gm, 0.01 mol) in pyridine (40 mL) was heated under reflux for 15h, then cooled and poured onto ice-diluted HCl (100 mL). The resulting product was filtered, washed with water, dried and purified by recrystallization with ethanol to give **6** as pale yellow powder, yield 40%, mp 245 °C IR (KBr): 3391 (NH), 1723, 1698 (C=O), 1621 (C=N), 1239, 117, 1013 (C-O) cm^{-1}; MS: m/z = 392 (M^+, 0.13), 391 (M^+-1, 2.1), 304 (7.9), 247 (2.0), 186 (3.8), 185 (28.8), 158 (100), 145 (11.8), 137 (14.4), 129 (87.2), 128 (25.1), 118 (18.0), 90 (28.9), 77 (21.0), 63 (25.4). Found: C, 67.00; H, 5.30; N, 7.40. $C_{22}H_{20}N_2O_5$ requires: C, 67.34; H, 5.14; N 7.14

Quinolin-8-yloxyacetic acid hydrazide (7)

A mixture of **1** (2.31 gm, 0.01 mol) and hydrazine hydrate (0.5 gm, 0.01 mol) in ethanol (25 mL) was heated under reflux for 4h, then evaporated the solvent of reaction mixture. The solid residue was crystallized from toluene to give 7 as white crystals, yield 69%, mp 115 °C; IR (KBr): 3305, 3256, 3120 (NH_2, NH), 1695 (C=O), 1613 (C=N), 1256, 1118, 1037 (C-O) cm^{-1}. ^1H NMR (DMSO-d_6) δ: 4.76 (s, 2H, OCH_2), 5.21-5.32(br. s, 3H, $NHNH_2$), 7.12-8.83 (m, 6H, Ar H) pmm. Found: 60.60; H, 5.20; N, 19.40. $C_{11}H_{11}N_3O_2$ requires: C, 60.82; H, 5.10; N, 19.43.

1-(Quinolin-8-yloxyacetyl)-thiosemicarbazide (8)

A mixture of 7 (2.17 gm, 0.01 mol), ammonium thiocyanate (0.02 mol) and hydrochloric acid (10 mL) in water (100 mL) was heated under reflux for 3h. The solid obtained after cooling was filtered, washed with water, dried and purified by recrystallization with ethanol to give as green crystals, yield 61%, mp 230 °C. IR (KBr): 3325, 3215, 3152 (NH_2, NH), 1689 (CO), 1613 (C=N), 1320 (C=S), 1215, 1018 (C-O) cm^{-1}; MS: m/z = 276 (M^+, 2.2), 245 (2.0), 201 (2.5), 188 (2.4), 184 (1.8), 158 (45.7), 146 (5.5), 129 (68.8), 128 (58.7), 117 (21.2), 116 (35.7), 103 (23.2), 102 (65.1), 101 (23.6), 90 (22.1), 84 (56.8), 75 (51.1), 74 (52.7). Found: C, 51.96; H, 4.08; N, 20.13, S, 11.43. $C_{12}H_{12}N_4O_2S$ requires: C, 52.16; H, 4.38; N, 20.28, S, 11.60.

1-(Quinolin-8-yloxy acetyl)-4-phenylthiosemicarbazide (10)

A mixture of 7 (2.17 gm, 0.01 mol) and phenyl isothiocyanate (1.62 gm, 0.012 mol) in dry benzene (30 mL) was heated under reflux for

5h. The solid obtained after cooling was filtered off and purified with recrystillzation from methanol to give **10** as white crystals, yield 65%, mp 80 °C; IR (KBr): 3202 (NH), 1691 (C=O), 1621 (C=N), 1317 (C=S), 1225, 1117, 1013 (C-O) cm^{-1}. ^1H NMR (DMSO-d_6) δ: 4.80 (s, 2H, OCH_2), 7.10-8.90 (m, 11H, Ar H), 9.80 (s, 2H, 2NH), 10.5 (s, 1H, CSNHPh) ppm. ^{13}C-NMR (DMSD – d_6) δ: 180.95(C=S), 167.35 (C=O), 153.79(C-O), 149,12(C=N), 139.69, 138.95, 135.89, 129.01, 127.99, 126.58, 125.01, 121.83, 120.85, 111.72(C-aromatic and C-hetroaryl), 67.829 (OCH_2) ppm. MS: m/z = 352 (M^+, 0.5), 351 (M^+-1, 70.5), 229 (64.7), 228 (47.0), 219 (58.8), 217 (64.7), 199 (52.9), 185 (70.5), 173 (58.8), 113 (64.7), 112 (76.4), 96 (70.5), 95 (76.4), 76 (82.3), 75 (100). Found: C, 16.00; H, 4.10; N, 15.60; S, 8.92. $C_{18}H_{16}N_4O_2S$ requires: C, 61.35; H, 4.58; N, 15.90; S, 9.08.

5-(Quinolin-8-yloxymethyl)-4-substituted-1,2,4-triazol-3-thiones (9and 11)

A solution of **8** or **10** (0.014 mol) in aqeous potassium hydroxide or sodium hydroxide (25 mL, 2N) was heated under reflux for 3h. The reaction mixture was cooled and acidified with diluted hydrochloric acid (2N). The deposited solid was filtered off, washed with water, dried and purified by recrystallization with ethanol to give **9** and **11**.

Compound **9** as pale yellow powder, yield 38%, mp 210 °C, IR (KBr): 3394, 3247 (NH), 1625 (C=N), 1342 (C=S), 1035 (C-O) cm^{-1}; MS: m/z = 258 (M^+, 2.2), 257 (M^+-1, 0.1), 204 (0.3), 158 (100), 156 (13.0), 145 (2.2), 130 (19.4), 129 (53.2), 128 (22.1), 117 (5.7), 102 (65.1), 89 (15.4), 75 (8.8), Found: C, 55.71; H, 3.70; N, 21.38; S, 12.03. $C_{12}H_{10}N_4OS$ requires: C, 55.80; H, 3.90; N, 21.69, S, 12.41.

Compound **11** as gray powder, yield 80% mp 250 °C, IR (KBr): 3325 (NH), 1625 (C=N), 1317 (C=S), 117(C-O) cm^{-1}; ^1H NMR DMSO-d_6) δ: 5.20 (s, 2H, OCH_2), 7.1-8.85(m, 11H, Ar-H), 14.10(s, 1H, NH) ppm. ^{13}C-NMR (DMSO-d_6) δ: 168.55 (C=S), 152.79 (C-O), 149.23, 148.01 (C=N), 139.76, 135.78, 133.10, 129.26, 128.87, 128.10, 126.35, 121.80, 121.36, 112.02 (C-aromatic and C-heteroaryl), 61.34 (OCH_2) ppm. MS: m/z = 334 (M^+, 26.1), 302 (0.2), 257 (0.5), 185 (0.4), 184 (1.8), 158 (4.8), 146 (10.4), 145 (87.7), 129 (6.1), 128 (3.4), 117 (100), 116 (17.8), 90 (16.0), 89 (23.7), 77 (14.1), 76 (12.1), 63 (20.4). Found: C, 64.43; H, 4.10; N, 16.52; S, 9.33. $C_{18}H_{14}N_4OS$ requires: C, 64.65; H, 4.22; N, 16.75; S, 9.59.

5-(Quinolin-8-yloxymethyl)-3H-1,3,4-Oxadiazol-2-thione(13)

A mixture of **7** (2.17 gm, 0.01 mol), carbon disulphide (1.14 gm, 0.015 mol) and potassium hydroxide (0.015 mol, 4 %) in ethanol (25 mL) was heated under reflux for 1h. The solvent of reaction mixture was removed by evaporation. The resulting solid was dissolved in water (10 mL) and acidified by diluted hydrochloric acid. The precipitate formed was filtered off, washed with water, dried and purified by recrystallization with ethanol to give **13** as greenish white crystals, yield 30%, mp 210 °C, IR (KBr): 3344 (NH), 1623 (C=N), 1331 (C=S), 1215, 1118, 1030, (C-O) cm^{-1}. MS: m/z = 260 (M^++1, 19.7), 259 (M^+, 51.0), 216 (20.8), 198 (36.4), 186 (38.0), 170 (29.1), 158 (90.1), 145 (87.5), 131 (6.2), 130 (25.5), 129 (72.4), 128 (52.0), 117 (100), 116 (58.3), 102 (25.0), 101 (28.1), 77 (59.3), 75 (37.5). Found: C, 55.10; H, 3.60; N, 15.80; S, 12.01. $C_{12}H_9N_3O_2S$ requires: C, 55.59; H, 3.50; N, 16.21; S, 12.37.

4-Amino-5-(Quinolin-8-yloxymethyl)-1,2,4-triazol-3-thione (14)

A mixture of **7** (2.17 gm, 0.01 mol), carbon disulphide (1.14 gm, 0.015 mol) and potassium hydroxide (0.015 mol, 4 %) in ethanol (30 mL) was heated under reflux on a water-bath for 1h. The solvent of reaction mixture was removed and the residual was dissolved in water (5 mL).The reaction mixture solution was added hydrazine hydrate (0.02 mol) and heated under reflux for 4h, then cooled and acidified with diluted hydrochloric acid. The precipitate formed was filtered off, washed with water, dried and purified by recrystallization with dimethyl formamide to give **14** as gray powder, yield 41%, mp 240 °C, IR (KBr): 3438, 3260 (NH_2), 3133 (NH), 1631 (C=N), 1317 (C=S), 1253, 1171, 1030 (C-O) cm^{-1}, ^1H NMR (DMSO-d_6) δ: 5.10 (s, 2H, OCH_2), 5.70 (s, 2H, NH_2), 7.30 – 8.80 (m, 6H, Ar-H), 14.01 (s, 1H, NH) ppm. ^{13}C-NMR (DMSO – d_6) δ: 166.39 (C=S), 153.28(C-O), 149.15, 147.87 (C=N), 139.76, 135.85, 128.99, 126.53, 121.83, 121.07, 111.67 (C-aromatic and C-heteroaryl), 60.45(OCH_2) ppm. MS: m/z = 273 (M^+, 56.2), 225 (75.0), 201 (50.0), 199 (50.0), 183 (56.2), 174 (75.0), 171 (62.5), 168 (75.0), 158 (62.5), 128 (68.7), 112 (50.0), 107 (100), 74 (33.0). Found: C, 53.03; H, 3.86; N, 25.41; S, 11.50. $C_{12}H_{11}N_5OS$ requires: C, 52.73; H, 4.06; N, 25.62; S, 11.73.

N-(1,3-dioxo-1,3-dihydroisoindol-2-yl)-2-(quinolin-8-yloxy)-acetamide (15)

A mixture of 7 (2.17 gm, 0.01 mol) and phthalic anhydride (1.48 gm, 0.01 mol) in glacial acetic acid (25 mL) was heated under reflux for 4h. The solid obtained after cooling was filtered off, dried and purified by recrystallization with methanol to give **15** as colorless crystals, yield 70%, mp 300 °C, IR (KBr): 3165 (NH), 1747 (C=O), 1661 (C=O of amide), 1621 (C=N), 1120, 1031 (C-O) cm^{-1}, MS: m/z = 347 (M^+, 1.5), 293 (8.0), 292 (34.4), 162 (47.9), 132 (7.4), 130 (2.4), 105 (16.0), 104 (97.9), 88 (1.1), 87 (22.5), 76 (100), 74 (30.3). Found: C, 65.50; H, 3.40; N, 11.70. $C_{19}H_{13}N_3O_4$ requires: C, 65.70; H, 3.77; N, 12.10.

1-(Quinolin-8-yloxacetyl)-2-(2-oxo-1H-2,3-dihydroindol-3-yl)-hydrazine (16)

A mixture of 7 (2.17 gm, 0.01 mol) and isatin (1.47 gm, 0.01 mol) in ethanol 25 (mL) was heated under reflux for 6h. The solid formed after cooling was filtered off, dried and purified by recrystallization with ethanol to give **16** as yellow cystals, yield 70%, mp 245 °C, IR (KBr): 3358, 3155 (NH), 1684–1660(C=O), 1619(C=N), 1035, 1017(C-O) cm^{-1}. MS: m/z = 364 (M^+, 0.7), 236 (1.3), 161 (100), 158 (3.4), 144 (4.8), 133 (11.4), 117 (9.7), 104 (85.5), 77 (18.8). Found: C, 65.62; H, 3.90; N, 16.45. $C_{19}H_{14}N_4O_3$ requires: C, 65.89; H, 4.07; N, 16.18.

3-(Ethoxycarbonylmethylthio)-4-phenyl-5-(Quinolin-8-yloxymethyl)-1,2,4-triazole (17)

A mixture of **11** (3.34 gm, 0.01 mol), ethyl chloroacetate (1.22 gm, 0.01 mol) and anhydrous potassium carbonate (4.14 gm, 0.03 mol) in dry acetone (30 mL) was heated under reflux for 6h. The reaction mixture was cooled and poured into water. The deposited solid was filtered off, washed with water, dried and purified by recrystallization with ethanol to give **17** as colorless crystals, yield 87%, mp 135 °C, IR (KBr): 1733(C=O),1624 (C=N), 1235, 1037, 1021(C-O) cm^{-1}; ^1H NMR (DMSO-d_6) δ: 1.10–1.20 (t, 3H, CH_3, J= 1.4 Hz), 4.10 – 4.20(q, 2H, OCH_2, J= 1.2 Hz; 3.90(s, 2H, SCH_2), 5.20(s, 2H, OCH_2-), 7.10 – 8.80(m, 11H, Ar-H) ppm. MS: m/z = 420 (M^+, 27.0), 392 (26.8), 391 (26.7), 376 (11.1), 375 (13.3), 277 (12.0), 276 (77.8), 265 (15.8), 264 (100), 231 (5.3), 230 (27.5), 203 (7.7), 202 (42.5), 189 (11.3), 158 (19.5), 157 (12.0), 148 (13.4), 145 (20.3), 135 (11.2), 130 (13.7), 129 (33.1), 128 (17.1), 116 (24.2), 89 (30.9), 77 (64.9), 63 (20.1). Found: C, 62.60; H,

5.00; N, 13.10; S, 7.42. $C_{22}H_{20}N_4O_3S$ requires: C, 62.84; H, 4.79; N, 13.32; S, 7.63.

2-(2-Substituted)ethyl-4-phenyl-5-(quinolin-8-yloxymethyl)-1,2,4-traizaol-3-thiones (18a,b).

A mixture of **11** (3.34 gm 0.01 mol), the appropriate acrylonitrile or acryloamide (0.01 mol) and triethyl amine (0.03 mol) in ethanol (30 mL) was heated under reflux for 6h, then cooled. The solid formed was filtered off, washed with water, dried and purified by recrystallization with ethanol to give **18**.

Compound **18a** as gray powder, yield 61%, mp 140 °C, IR (KBr): 2250 (C≡N), 1618 (C=N), 1343 (C=S), 1217, 1030 (C-O) cm^{-1}. ^1H NMR (DMSO – d_6) δ: 3.08 – 3.15(t, 2H, NCH_2, J= 1.4 Hz), 4.45-4.50(t, 2H, CH_2CN, J= 1.4 Hz), 5.20(s, 2H, OCH_2), 7.10-8.80 (m, 11H, Ar-H) ppm. ^{13}C-NMR (DMDSO-d_6) δ: 167.99(C=S), 152.76(C-O), 149.26, 147.18(C=N), 139.76, 135.78, 133.32, 129.52, 128.96, 127.99, 126.36, 121.80, 121.54, 112.28 (C-aromatic and C-heteroaryl), 118.05(C≡N), 15.94(NCH_2), 44.26 (CH_2CN), 61.27(OCH_2) ppm. MS: m/z = 387 (M^+, 100), 333 (3.6), 310 (7.6), 309 (10.1), 230 (3.1), 229 (1.0), 227 (7.7), 190 (72.5), 158 (17.7), 157 (10.8), 132 (26.3), 131 (21.1), 129 (84.5), 128 (10.3), 91 (5.4), 90 (12.1), 77 (45.0). Found: C, 64.84; H, 4.10; N, 18.31; S, 8.02. $C_{21}H_{17}N_5OS$ requires: C, 65.10; H, 4.42; N, 18.07; S, 8.28.

Compound **18b** as red powder, yield 34%, mp 215 °C, IR (KBr): 1670 (C=O), 1617 (C=N), 1314 (C=S), 1035, 1021 (C-O) cm^{-1}. MS: m/z = 406(M^+ +1, 2.8), 405 (M^+, 4.3), 383(2.6), 362(2.3), 334(1.8), 329(2.0), 290(2.0), 273(8.3), 269(3.2), 175(3.7), 174(4.0), 157(14.7), 144(46.7), 135(16.1), 130(12.7), 129(42.6), 128(13.9), 117(62.8), 116(58.9), 101(13.9), 90(35.1), 89(100), 77(73.8), 72(36.5), 63(76.8). Found: C, 62.14, H, 4.40, N, 17.50; S, 7.69. $C_{21}H_{19}N_5O_2S$ requires: C, 62.21; H, 4.72; N, 17.27; S, 7.9.

REFERENCES

El-Deen, I.M.; Mohamed, S.M.; Ismail, M.M.; Abdel-Megid, M.; *Anales de Quimica*, **1993**, *89*, 621; Chem. Abstr., **1994**, *120*, 323471.

Katritzky, A.R., *Comprehensive Heterocyclic Chemistry*, Pergamon, **1984**, Vol. *1*. 143.

Latour, N. G.; Reeves, R.E.; *Exp. Parasitol*, **1965**, *17*, 203; Chem. Abstr., **1967**, 63, 16835.

Lee, Y.H.; Seo, J.; Yoon, I.; Park, K.M.; Lee, S. S.; *Anal. Sci.*, **2001**, *17*, 805. Chem. Abstr., **2001**, 135, 173159.

Mohamed, E.A.; El-Deen, I.M.; lsmail, M.M.; *Pakistan J. Scientific and Ind. Res.*, **1992**, *35*, 226, Chem. Abstr., **1993**, *119*, 8778.

Raafat, S.; Nibal, A. Hammouda; *J. Pharamacentical Sciences*, **1979**, *11*,1377. Chem. Abstr., **1980**, 92, 191183 .

Reid, J.R.; Heindel, N.D.; *J. Heterocycel. Chem.*, **1976**, *13*, 925; Chem. Abstr., **1977**, 86, 5374.

Soliman, A.Y.; El-Assy, N.B.; El-Shahed, F.; El-Kady, M,; El-Deen, I.M.; *Indian J. Chem.*, **1990**, *29*, 326; Chem. Abstr., **1990**, *113*, 78293.

تحضير بعض الكينولات المحولقة فى الوضع ٨ الجديدة

حسن كامل ابراهيم * ، عادل سيد عرابى ، السيد حسين الطمنى و أحمد سيد رضوان
قسم الكيماء ، كلية العلوم ، جامعة قناة السويس ، الإسماعيلية – مصر

٢-(كينولين-٨-يل أوكسى ميثيل) -١،٣-بنزواوكزازين-٤-أون (٢) تم تحضيرة بتكاثف الايثيل كينولين-٨-يل أوكسى اسيتات ١مع حمض الانثرانيليك . معالجة ٢ مع الهيدرازين هيدرات ، ٤- أمينوحمض البنزويك و اسيتات الايثيل أعطى ٢-(كينولين-٨-يل أوكسى مينيل) -٣- مستبدل كينوأوكزالين-٤-أونات (٣ ، ٥) .

وايثيل ٢[(كينولين-٨-يل أوكسى ميثيل) كربونيل أمينوبنزويل] اسيتات (٦) . تفاعل الهيدرازيد ٧ مع ثيوسيانات الامونيوم ، فينيل أيزوثيوسينات و ثانى كبريتيد الكربون أعطى ٤،١-ثنائى مستبدل ثيوسيمىكارابازيد (٨ ، ١٠ و ١٢) . حولقه ٨ و ١٠ مع قاعدة أعطى ٥،٤- ثنائى مستبدل ٤،٢،١- ترايازول-٣- ثيونات (٩، ١١) . بينما حولقة المركب ١٢ مع حمض الهيدروكلوريك أو الهيدرازين هيدرات أعطى مشتقات ٤،٣،١-اوكسادايازول و ٤،٢،١- ترايازول (١٣ و ١٤) على التوالى .

المركب ١١ يتفاعل مع الايثيل كلوروأسيتات ، أكريلونيتريل و أكريلواميد ليعطى ٣،٢- ثنائىمستبدل-٤-فينيل-٥-(كينولين-٨-يل أوكسى ميثيل)-٤،٢،١-ترايازولات (١٧ و ١٨ أ ، ب) .