Supplementary Materials

Microwave- Assisted Multicomponent Ecofriendly Synthesis of 3-Bihetaryl-2-oxindole Derivatives Grafted with Phenothiazine Moiety

A. S. Al-Bogami¹ and A. S. El-Ahl^{1,2*}

¹*Chemistry Department, faculty of Science, University of Jeddah, Jeddah, 21589, Saudi Arabia*

²*Chemistry Department, Faculty of Science, Mansoura University, Mansoura, 35516, Egypt*

* Address correspondence to A. S. El-Ahl, Chemistry Department, Faculty of Science, University of Jeddah, Jeddah 21589, Saudi Arabia, P.O.B. 80327, Mobile: 009660564949970, E-mail: elahl2002@yahoo.com

Table of contents

Content	page
General experimental methods	3
Figure S1. ¹ H NMR of compound 1a	20
Figure S2. ¹³ C of compound 1a	20
Figure S3. ¹ H NMR of compound 1b	21
Figure S4. ¹³ C NMR of compound 1b	21
Figure S5. Mass spectrum of compound 1b	22
Figure S6. ¹ H NMR of compound 1c	22
Figure S7. ¹³ C NMR of compound 1c	23
Figure S8. ¹ H NMR of compound 2a	23
Figure S9. ¹³ C NMR of compound 2a	24
Figure S10. Mass spectrum of compound 2a	25
Figure S11. ¹ H NMR of compound 2b	26
Figure S12. ¹³ C NMR of compound 2b	26
Figure S13. Mass spectrum of compound 2b	27
Figure S14. ¹ H NMR of compound 2c	28
Figure S15. ¹³ C NMR of compound 2c	28
Figure S16. ¹ H NMR of compound 2d	29
Figure S17. ¹³ C NMR of compound 2d	29
Figure S18. ¹ H NMR of compound 2e	29
Figure S19. ¹³ C NMR of compound 2e	30
Figure S20. ¹ H NMR of compound 2f	30
Figure S21. ¹³ C NMR of compound 2f	30
Figure S22. Mass spectrum of compound 2f	31
Figure S23. ¹ H NMR of compound 3a	32
Figure S24. ¹³ C NMR of compound 3a	32

Figure S25. Mass spectrum of compound 3a	33
Figure S26. ^1H NMR of compound 3b	34
Figure S27. ^{13}C NMR of compound 3b	34
Figure S28. ^1H NMR of compound 3c	34
Figure S29. ^{13}C NMR of compound 3c	35
Figure S30. Mass spectrum of compound 3c	36
Figure S31. Mass spectrum of compound 4	37
Figure S32. Mass spectrum of compound 5	38
Figure S33. ^1H NMR of compound 6	39
Figure S34. ^{13}C NMR of compound 6	39
Figure S35. HMBC spectrum of compound 6	39
Figure S36. ^1H NMR of compound 8	40
Figure S37. HMBC spectrum of compound 8	40
Figure S38. ^1H NMR of compound 9	41
Figure S39. ^{13}C NMR of compound 9	41
Figure S40. HMBC spectrum of compound 9	41
Figure S41. ^{15}N HMBC spectrum of compound 9	42
Figure S42. ^1H NMR of compound 10	42
Figure S43. ^{13}C NMR of compound 10	42
Figure S44. Mass spectrum of compound 10	43

4 EXPERIMENTAL

Melting points were determined on a Stuart melting point apparatus and are uncorrected. IR spectra were recorded on Nicolet iS10 FT-IR spectrometer. The NMR spectra were recorded on a Bruker Avance III 400 (9.4 T, 400.13 MHz for ^1H and 100.62 MHz for ^{13}C) spectrometer and on a Varian Mercury VX-300 NMR spectrometer (Varian, Palo Alto, CA, USA). HMBC-gs was acquired and processed using standard Bruker NMR software (Topspin 3.2). Elemental analyses were carried out on a EuroVector instrument C, H, N, S analyzer EA3000 Series. Mass spectra were measured using Shimadzu GCMS-QP 1000 EX mass spectrometer (Shimadzu) at 70 eV. Microwave experiments were performed using CEM Discover and Explorer SP microwave apparatus (300 W), utilizing 35 ml capped glass reaction vessels and automated power control based on temperature feedback. The chemicals and solvents were purchased from Merck, Aldrich or Acros. Thin-layer chromatography (TLC) was performed on precoated Merck 60 GF254 silica gel plates with a fluorescent indicator. Compounds **1a-c** were prepared following standard literature procedures.^{[27]*}

4.1 Synthesis of 3-(2-(phenothiazin-2-yl)-2-oxoethylidene)-2-oxindoles **1a-c**:

The hitherto unknown compounds **1a-c** was synthesized according to the reported procedure.^[27] The structure of the compounds was confirmed by IR, ^1H NMR, and Mass spectroscopy.

General Procedure:

*[27] Popp, F. D. *J. Heterocycl. Chem.* **1982**, 19, 589-592.

A mixture of appropriate isatin (0.01 mol) and 2-acetylphenothiazine (0.01 mol, 2.41 g) was suspended in 50 ml absolute ethanol containing 5 drops of diethylamine. The reaction mixture was refluxed for 30 minutes and left to stand overnight at room temperature. The formed yellow precipitate was collected by filtration and washed several times by ethanol and suspended in 50 ml ethanol containing 0.5 ml of concentrated hydrochloric acid. The reaction mixture was refluxed for 1h, and cooled to room temperature. The formed violet precipitate was collected by filtration, washed with ethanol and recrystallized from acetone to give compounds **1a-c**.

3-(2-Oxo-2-(10H-phenothiazin-2-yl)ethylidene)indolin-2-one 1a:

Yield: 80%, violet solid. Mp 191-192°C, IR (V, thin film, cm^{-1}): 3316, 2972, 1700, 1646, 1619, 1597, 1459, 1433, 1307, 1215, 1127, 1076, 1046, 734. ^1H NMR (DMSO-d_6): δ 6.63-6.65 (dd, $J_1 = 8 \text{ Hz}$, $J_2 = 1 \text{ Hz}$, 1H, ArH), 6.74-6.78 (td, $J_1 = 8 \text{ Hz}$, $J_2 = 1 \text{ Hz}$, 1H, ArH), 6.88-6.91 (m, 2H, ArH), 6.98 (t, $J = 8 \text{ Hz}$, 1H, ArH), 7.03 (t, $J = 8 \text{ Hz}$, 1H, ArH), 7.08 (d, $J = 8 \text{ Hz}$, 1H, ArH), 7.31 (d, $J = 1 \text{ Hz}$, 1H, ArH), 7.35 (t, $J = 8 \text{ Hz}$, 1H, ArH), 7.40-7.43 (dd, $J_1 = 8 \text{ Hz}$, $J_2 = 1.8 \text{ Hz}$, 1H, ArH), 7.62 (s, 1H, ArH), 8.00 (d, $J = 8 \text{ Hz}$, 1H, ArH), 8.86 (s, 1H, NH), 10.80 (s, 1H, NH). ^{13}C NMR (DMSO-d_6): δ 110.84, 113.50, 115.07, 115.46, 120.42, 122.32, 122.66, 122.70, 125.25, 126.34, 126.75, 126.98, 127.13, 128.57, 133.32, 136.57, 136.74, 141.39, 142.72, 145.28, 168.66, 190.44. *Anal.* Calcd. For $\text{C}_{22}\text{H}_{14}\text{N}_2\text{O}_2\text{S}$: C, 71.33; H, 3.81; N, 7.56; S, 8.66. Found: C, 71.15; H, 3.56; N, 7.35; S, 8.48

5-Methyl-3-(2-oxo-2-(10H-phenothiazin-2-yl)ethylidene)indolin-2-one 1b:

Yield: 85%, violet solid. Mp 175-176 °C, IR: 3279, 2987, 1693, 1669, 1617, 1595, 1448, 1328. MS, M/Z (%): 384 (M^+ , 23), 370 (100), 342 (8), 325 (23),

309 (11), 293 (10), 198 (46), 186 (11), 172 (9), 116 (16), 89 (17). ^1H NMR (DMSO- d_6): δ 2.23 (s, 3H, 5-CH₃), 6.64 (d, J = 8 Hz, 1H, ArH), 6.75-6.79 (m, 2H, ArH), 6.91 (d, J = 8 Hz, 1H, ArH), 7.01 (t, J = 8 Hz, 1H, ArH), 7.08 (d, 2H, J = 8 Hz, ArH), 7.16 (d, J = 8 Hz, 1H, ArH), 7.32 (s, 1H, ArH), 7.41 (d, J = 8 Hz, 1H, ArH), 7.58 (s, 1H, =CH), 7.87 (s, 1H, NH), 8.85 (s, 1H, NH). ^{13}C NMR (DMSO- d_6): δ 21.18, 110.57, 113.55, 115.07, 115.49, 120.49, 122.59, 122.70, 125.16, 125.94, 126.75, 126.97, 127.61, 128.57, 130.93, 133.77, 136.97, 136.98, 141.40, 142.71, 143.09, 168.74, 190.33. *Anal.* Calcd. for C₂₃H₁₆N₂O₂S: C, 71.85; H, 4.19; N, 7.29; S, 8.34. Found: C, 71.97; H, 4.32; N, 7.51; S, 8.52.

5-Bromo-3-(2-oxo-2-(10*H*-phenothiazin-2-yl)ethylidene)indolin-2-one 1c:

Yield: 78%, violet Solid. Mp 204-205 °C, IR: 3270, 2980, 1685, 1660, 1620, 1590, 1445, 1320. ^1H NMR(DMSO- d_6): δ 6.63 (d, J = 8 Hz, 1H, ArH), 6.76 (t, J = 8 Hz, 1H, ArH), 6.85 (d, J = 8 Hz, 1H, ArH), 6.90 (d, J = 8 Hz, 1H, ArH), 7.00 (t, J = 8 Hz, 1H, ArH), 7.07 (d, J = 8 Hz, 1H, ArH), 7.31 (s, 1H, ArH), 7.42 (d, J = 8 Hz, 1H, ArH), 7.52-7.54 (dd, J_1 = 8 Hz, J_2 = 1.12, 1H, ArH), 7.68 (s, 1H, ArH), 8.26 (s, 1H, =CH), 8.85 (s, 1H, NH), 10.94 (s, 1H, NH). ^{13}C NMR (DMSO- d_6): δ 112.76, 113.49, 113.69, 115.08, 115.43, 122.37, 122.70, 122.76, 125.52, 126.73, 126.94, 127.33, 128.58, 129.64, 135.62, 135.96, 136.76, 141.31, 142.70, 144.58, 168.28, 189.93. *Anal.* Calcd. for C₂₂H₁₃BrN₂O₂S: C, 58.81; H, 2.92; N, 6.23; S, 7.14. Found: C, 58.97; H, 2.75; N, 6.45; S, 7.42.

4.2 Reaction of 3-(2-(phenothiazin-2-yl)-2-oxoethylidene)-2-oxindole derivatives 1a-c with 1,3-dicarbonyl compounds: General Procedure

4.2.1 Conventional method:

A mixture of 3-(2-(phenothiazin-2-yl)-2-oxoethylidene)-2-oxindole derivatives **1a-c** (3 mmol; **1a**, 1.11g; **1b**, 1.152 g and **1c**, 1.347 g), 1,3-dicarbonyl compound (3 mmol; ethyl acetoacetate, 0.39 g; methyl acetoacetate, 0.348 g; acetylacetone, 0.3 g; 2-hydroxynaphthalene-1,4-dione, 0.522 g and indan-1,3-dione, 0.438 g) and ammonium acetate (9 mmol, 0.693 g) was suspended in glacial acetic acid (20 ml) and the reaction mixture was refluxed until TLC showed disappearance of the starting materials. The formed precipitate was collected by suction filtration and washed several times with cold ethanol. The collected solid materials were recrystallized from ethanol/dimethylformamide (2/1) mixture and oven dried at 120 °C to afford compounds **2a-f**, **3a-c**, **4** and **5** (Table 1).

4.2.2 Microwave method:

A mixture of 3-(2-(phenothiazin-2-yl)-2-oxoethylidene)-2-oxindole derivatives **1a-c** (3 mmol; **1a**, 1.11g; **1b**, 1.152 g and **1c**, 1.347 g), 1,3-dicarbonyl compound (3 mmol; ethyl acetoacetate, 0.39 g; methyl acetoacetate, 0.348 g; acetylacetone, 0.3 g; 2-hydroxynaphthalene-1,4-dione, 0.522 g and indan-1,3-dione, 0.438 g) and ammonium acetate (9 mmol, 0.693 g) was charged into a 35 ml glass reaction vessel (CEM, Discover and Explorer SP Vessels) and glacial acetic acid (5 ml) was added and the vessel was sealed with a control cap. The reaction was subjected to microwave irradiation, stirred and heated at 120 °C and power of 200 W, until completion of the reaction (TLC monitoring, Table 1). The reaction mixture was cooled and the formed precipitate was collected by filtration, washed several times with cold ethanol and recrystallized from ethanol/dimethylformamide (2/1) mixture to give compounds **2a-f**, **3a-c**, **4** and **5**.

Ethyl 4-(2-oxoindolin-3-yl)-2-methyl-5-(10*H*-phenothiazin-2-yl)-1*H*-pyrrole-3-carboxylate 2a:

Colorless solid. Mp > 300 °C, IR (ν , thin layer, cm^{-1}): 3345 (NH), 3315 (NH), 3248 (NH), 1710 (CO_2Et), 1658 ($\text{C}=\text{O}$, 2-oxindol), 1600, 1585, 1462, 1440, 1340, 1318, 1293, 1142, 1130. MS, M/Z (%): 481(M^+ , 35), 435 (100), 407 (70), 391(25), 362 (25), 323 (20), 309 (25), 218 (30), 201 (35), 154 (38), 127(37), 77(27). ^1H -NMR (DMSO-d_6): δ 0.85 (t, $J=7\text{Hz}$, 3H, OCH_2CH_3), 2.41(s, 3H, 2'- CH_3), 3.71-3.75 (dq, 2H, OCH_2CH_3), 4.57 (s, 1H, H-3), 6.69-6.75 (t, $J = 7 \text{ Hz}$, 2H, ArH) 6.78-6.86 (m, 4H, ArH), 6.88-6.90 (m, 2H, ArH), 6.92-6.97 (m, 2H, ArH), 7.09-7.11 (m, 1H, ArH), 8.70 (s, 1H, NH), 10.27 (s, 1H, NH), 11.54 (s, 1H, NH). ^{13}C NMR (DMSO-d_6): δ 13.63, 14.37, 45.12, 58.32, 109.11, 110.07, 114.01, 114.32, 115.04, 116.19, 116.69, 121.33, 121.88, 122.38, 122.99, 126.70, 126.97, 127.40, 128.08, 131.58, 131.63, 132.04, 137.08, 142.22, 142.83, 143.42, 164.37, 178.89. *Anal.* Calcd. for $\text{C}_{28}\text{H}_{23}\text{N}_3\text{O}_3\text{S}$: C, 69.83; H, 4.81; N, 8.73; S, 6.66. Found: C, 69.65; H, 4.93; N, 8.62; S, 6.38.

Ethyl 4-(5-methyl-2-oxoindolin-3-yl)-2-methyl-5-(10*H*-phenothiazin-2-yl)-1*H*-pyrrole-3-carboxylate 2b:

Colorless solid. Mp 298-299 °C, IR (ν , thin layer, cm^{-1}): 3361 (NH), 3270 (NH), 3229 (NH), 2994 (C-H aliphatic), 1708 (CO_2Et), 1652 ($\text{C}=\text{O}$, oxindole), 1625, 1601, 1588, 1487, 1469, 1439, 1391, 1346, 1296, 1271, 1148, 1111, 1096, 1077, 960. MS, M/Z (%): 495 (M^+ , 40), 446 (50), 467(30), 448 (40), 439 (30), 409 (30), 398 (46), 377(42), 345 (50), 290 (45), 269(45), 197(50), 155 (48).128 (40), 64 (100). ^1H NMR (DMSO-d_6): δ 0.87 (t, $J = 7.5 \text{ Hz}$, 3H, OCH_2CH_3), 2.18 (s, 3H, 5- CH_3), 2.43 (s, 3H, 2'- CH_3), 3.7-3.82 (dq, 2H, OCH_2CH_3), 4.56 (s, 1H, H-3), 6.62 (s, 1H, ArH), 6.7-6.73 (m, 2H, ArH), 6.76

(d, $J = 7.5$ Hz, 1H, ArH), 6.81 (s, 1H, ArH), 6.89-6.94 (m, 3H, ArH), 6.98-7.02 (m, 2H, ArH), 8.77 (s, 1H, NH), 10.23 (s, 1H, NH), 11.60 (s, 1H, NH). ^{13}C NMR (DMSO- d_6): δ 13.66, 14.39, 21.16, 45.14, 58.34, 108.85, 110.09, 113.97, 114.47, 115.04, 116.15, 116.70, 121.85, 122.38, 123.66, 126.71, 126.99, 127.58, 128.09, 129.98, 131.55, 131.60, 132.11, 137.07, 140.98, 142.22, 142.85, 164.38, 178.84. *Anal.* Calcd. for $\text{C}_{29}\text{H}_{25}\text{N}_3\text{O}_3\text{S}$: C, 70.28; H, 5.08; N, 8.48; S, 6.47. Found: C, 70.05; H, 4.89; N, 8.57; S, 6.68.

Ethyl 4-(5-bromo-2-oxoindolin-3-yl)-2-methyl-5-(10H-phenothiazin-2-yl)-1H-pyrrole-3-carboxylate 2c:

Colorless solid. Mp 296-297 °C, IR (ν , thin layer, cm^{-1}): 3354 (NH), 3305 (NH), 3241(NH), 1712 (CO_2Et), 1655 ($\text{C}=\text{O}$, 2-oxindol), 1600, 1588, 1467, 1440, 1346, 1313, 1296, 1147, 1133, 1111, 1097, 1078, 920, 887. ^1H NMR (DMSO- d_6): δ 0.92 (t, $J = 7$ Hz, 3H, OCH_2CH_3), 2.43 (s, 3H, 2'- CH_3), 3.73-3.81 (dq, 2H, OCH_2CH_3), 4.65 (s, 1H, H-3), 6.71-6.73 (m, 1H, ArH), 6.74-6.77 (m, 3H, ArH), 6.78 (s, 1H ArH), 6.78-6.87 (m, 2H, ArH), 7.0-7.03 (m, 2H, ArH), 7.30-7.33 (dd, $J_1 = 0.8$ Hz, $J_2 = 4\text{Hz}$, 1H, ArH), 8.76 (s, 1H, NH), 10.49 (s, 1H, NH), 11.65 (s, 1H, NH). ^{13}C NMR (DMSO- d_6): δ 13.72, 14.44, 45.15, 58.48, 109.82, 111.04, 112.95, 113.57, 113.99, 115.05, 116.30, 116.66, 121.96, 122.40, 125.50, 126.71, 127.03, 128.09, 130.13, 131.34, 131.89, 134.68, 137.21, 142.20, 142.84, 142.90, 164.31, 178.41. *Anal.* Calcd. for $\text{C}_{28}\text{H}_{22}\text{BrN}_3\text{O}_3\text{S}$: C, 60.00; H, 3.96; N, 7.50; S, 5.72. Found: C, 60.22; H, 3.85; N, 7.62; S, 5.53.

Methyl 4-(2-oxoindolin-3-yl)-2-methyl-5-(10H-phenothiazin-2-yl)-1H-pyrrole-3-carboxylate 2d:

Colorless solid. Mp > 300 °C, IR (ν , thin layer, cm^{-1}): 3353 (NH), 3301 (NH), 3244 (NH), 2988 (C-H aliphatic), 1710, (CO_2Me), 1666 ($\text{C}=\text{O}$, 2-oxindole),

1626, 1602, 1588, 1536, 1486, 1467, 1444, 1392, 1376, 1315, 1297, 1271, 1193, 1145, 1135, 1104, 1046, 1035, 914, 893. ^1H NMR (DMSO- d_6): δ 2.41 (s, 3H, 2'-CH₃), 3.2 (s, 3H, CO₂CH₃), 4.59 (s, 1H, H-3), 6.71-6.72 (m, 1H, ArH), 6.76-6.80 (m, 2H, ArH), 6.82-6.91 (m, 3H, ArH), 6.93-6.97 (m, 2H, ArH), 6.97-6.99 (m, 2H, ArH), 7.01-7.12 (m, 1H, ArH), 8.73 (s, 1H, NH), 10.33 (s, 1H, NH), 11.60 (s, 1H, NH). ^{13}C NMR (DMSO- d_6): δ 14.13, 45.02, 49.68, 109.06, 109.80, 113.97, 114.53, 115.04, 116.20, 116.96, 121.37, 121.87, 122.38, 122.98, 126.70, 126.98, 127.45, 128.08, 131.53, 131.62, 131.69, 137.00, 142.22, 142.36, 143.42, 164.81, 178.99. *Anal.* Calcd. for: C₂₇H₂₁N₃O₃S. C, 69.36; H, 4.53; N, 8.99; S, 6.86. Found: C, 69.61; H, 4.75; N, 8.71; S, 6.63.

Methyl 4-(5-bromo-2-oxoindolin-3-yl)-2-methyl-5-(10*H*-phenothiazin-2-yl)-1*H*-pyrrole-3-carboxylate 2e:

Colorless solid. Mp > 300 °C, IR (ν , thin layer, cm⁻¹): 3350 (NH), 3304 (NH), 3250 (NH), 2944 (CH), 1714 (C=O, ester), 1663 (C=O, 2-oxindole), 1605, 1588, 1466, 1445, 1313, 1297, 1277, 1265, 1161, 1145, 1133, 1104, 1133, 1105, 1080, 918. ^1H NMR (DMSO- d_6): δ 2.42 (s, 3H, 2'-CH₃), 3.26 (s, 3H, CO₂Me), 4.65 (s, 1H, H-3), 6.71-6.76 (m, 2H, ArH), 6.76-6.81 (m, 2H, ArH), 6.85 (s, 1H, ArH), 6.89-6.93 (t, J = 8 Hz, 2H, ArH), 6.79-7.01 (m, 2H, ArH), 7.30 (d, J = 8 Hz, 1H, H-6, ArH), 8.74 (s, 1H, NH), 10.48 (s, 1H, NH), 11.65 (s, 1H, NH). ^{13}C NMR (DMSO- d_6): δ 13.51, 45.06, 49.83, 109.54, 110.99, 112.98, 113.75, 113.98, 115.05, 116.33, 116.68, 121.96, 122.39, 125.52, 126.70, 127.03, 128.09, 130.19, 131.30, 131.90, 134.63, 137.20, 142.2, 142.84, 142.89, 164.74, 178.49. *Anal.* Calcd. for: C₂₇H₂₀BrN₃O₃S: C, 59.35; H, 3.69; N, 7.69; S, 5.87. Found: C, 59.45; H, 3.51; N, 7.53; S, 5.62.

Methyl 2-methyl-4-(5-methyl-2-oxoindolin-3-yl)-5-(10*H*-phenothiazin-2-yl)-1*H*-pyrrole-3-carboxylate 2f:

Colorless solid. Mp > 300 °C, IR (ν , thin layer, cm^{-1}): 3353 (NH), 3301(NH), 3244 (NH), 2988 (CH_3), 1710 (CO_2Me), 1666 ($\text{C}=\text{O}$, 2-oxindole), 1626, 1602, 1588, 1536, 1486, 1467, 1444, 1392, 1376, 1315, 1297, 1271, 1218, 1193, 1145, 1135, 1104. MS, M/Z (%): 478 ($\text{M}^+ - 3$, 45), 458 (41), 437 (52), 422 (51), 412 (54), 402 (47), 390 (53), 365 (57), 319 (51), 256 (43), 207(48), 158 (53), 134 (49), 96 (59), 80 (100). ^1H NMR (DMSO-d_6) δ 2.18 (s, 3H, 2'- CH_3), 2.42 (s, 3H, 5'- CH_3), 3.22 (s, 3H, CO_2CH_3), 4.57 (s, 1H, H-3), 6.6 (s, 1H, ArH), 6.71-6.78 (m, 3H, ArH), 6.82(d, $J = 1.6$ Hz, 1H, ArH), 6.91-6.97(m, 3H, ArH), 7.0-7.02 (m, 2H, ArH), 8.77(s, 1H, NH), 10.25(s, 1H, NH), 11.61(s, 1H, NH). ^{13}C NMR(DMSO-d_6) δ 13.45, 21.17, 45.04, 49.68, 108.79, 109.8, 113.93, 114.67, 115.05, 116.16, 116.70, 121.84, 122.38, 123.67, 126.71, 127.00, 127.67, 128.09, 130.01, 131.54 (2c), 132.04, 137.02, 140.97, 142.23, 142.8, 164.82, 178.95. *Anal.* Calcd. for $\text{C}_{28}\text{H}_{23}\text{N}_3\text{O}_3\text{S}$: C, 69.83; H, 4.81; N, 8.73; S, 6.66. Found: C, 69.62; H, 4.65; N, 8.94; S, 6.42.

3-(4-Acetyl-5-methyl-2-(10*H*-phenothiazin-2-yl)-1*H*-pyrrol-3-yl)indolin-2-one 3a:

Colorless solid. Mp 244-245 °C, IR (ν , thin layer, cm^{-1}): 3318 (NH), 2988 (C-H, aliphatic), 1705 (COCH_3), 1680 ($\text{C}=\text{O}$, 2-oxindol), 1561, 1464, 1393, 1356, 1330, 1298, 1279, 1253, 1213, 1128, 1074, 1018, 968, 928. MS, M/Z (%): 451(M^+ , 60), 409 (100), 380 (60), 277 (100), 167 (30), 128 (30), 77(25), 64(38). ^1H -NMR (DMSO-d_6): δ 2.09 (s, 3H, CH_3), 2.12 (s, 3H, CH_3), 4.5 (s, 1H, H-3), 6.7-6.77(m, 4H, ArH), 6.79 (d, $J = 8$ Hz, 2H, ArH), 6.89-6.91(m, 2H, ArH), 6.93-7.0 (m, 2H, ArH), 7.00-7.08 (m, 1H, ArH), 8.77 (s, 1H, NH), 10.24

(s, 1H, NH), 11.56 (s, 1H, NH). ^{13}C (DMSO- d_6): δ 15.16, 30.39, 45.05, 108.96, 113.96, 114.81, 115.04, 116.23, 120.51, 120.96, 121.84, 122.39, 122.60, 126.71, 126.99, 127.18, 128.09, 131.43, 131.46, 131.75, 135.94, 139.73, 142.21, 142.85, 143.95, 172.53, 192.10. *Anal.* Calcd. for: $\text{C}_{27}\text{H}_{21}\text{N}_3\text{O}_2\text{S}$. C, 71.82; H, 4.69; N, 9.31; S, 7.10. Found: C, 71.95; H, 4.81; N, 9.52; S, 6.91.

3-(4-Acetyl-5-methyl-2-(10*H*-phenothiazin-2-yl)-1*H*-pyrrol-3-yl)-5-methylindolin-2-one 3b:

Colorless solid. Mp > 300 °C, IR (ν , thin layer, cm^{-1}): 3391, 3277, 1704, 1610, 1536, 1488, 1466, 1445, 1432, 1379, 1343, 1318, 1304, 1257, 1219, 1109, 973, 947, 867. ^1H NMR (DMSO- d_6): δ 2.12 (s, 3H, CH_3), 2.14 (s, 3H, CH_3), 2.16 (s, 3H, CH_3), 4.49 (s, 1H, H-3), 6.54 (s, 1H, ArH), 6.67-6.82 (m, 4H, ArH), 6.87-6.88 (m, 3H, ArH), 7.00-7.02 (m, 2H, ArH) 8.79 (s, 1H, NH), 10.14 (s, 1H, NH), 11.56 (s, 1H, NH). ^{13}C NMR (DMSO- d_6): δ 15.17, 21.18, 30.43, 45.28, 108.71, 113.93, 114.92, 115.04, 116.20, 116.71, 120.52, 121.81, 122.39, 123.31, 126.71, 127.00, 127.42, 128.09, 129.56, 131.45, 131.55, 131.69, 135.94, 141.51, 142.22, 142.86, 172.51, 192.06. *Anal.* Calcd. for $\text{C}_{28}\text{H}_{23}\text{N}_3\text{O}_2\text{S}$: C, 72.23; H, 4.98; N, 9.03; S, 6.89. Found: C, 72.15; H, 4.77; N, 9.31; S, 6.63.

3-(4-Acetyl-5-methyl-2-(10*H*-phenothiazin-2-yl)-1*H*-pyrrol-3-yl)-5-bromoindolin-2-one 3c:

Colorless solid. Mp 280-281 °C, IR (ν , thin layer, cm^{-1}): 3379 (NH), 3287 (NH), 3189 (NH), 1708 (C=O, ketonic), 1612, 1560, 1536, 1466, 1432, 1413, 1344, 1318, 1303, 1205, 1110, 1067, 972. MS, M/Z (%): 489 (M^+ - 41, 75), 473 (97), 454 (60), 432 (75), 324(90), 299 (90), 232 (100) 178 (97), 143 (81), 137 (90), 93 (69) ^1H NMR (DMSO- d_6): δ 2.16 (s, 3H, 5'- CH_3), 2.53 (s, 3H, COCH_3), 4.56

(s, 1H, H-3), 6.7-6.779 (m, 5H, ArH), 6.85-6.90 (m, 1H, ArH), 6.92-6.98 (m, 1H, ArH), 6.99-7.02 (m, 2H, ArH), 7.26 (d, $J = 8$ Hz, 1H, H-6, ArH). 8.76 (s, 1H, NH), 10.37 (s, 1H, NH), 11.59 (s, 1H, NH). ^{13}C NMR (DMSO- d_6): δ 15.19, 30.41, 45.30, 110.85, 112.61, 113.94, 115.05, 116.37, 116.67, 116.95, 120.26, 121.94, 122.39, 125.04, 126.70, 127.04, 128.09, 129.86, 131.19, 132.00, 134.25, 136.24, 142.18, 142.85, 143.44, 172.48, 192.29. *Anal.* Calcd. for $\text{C}_{27}\text{H}_{20}\text{BrN}_3\text{O}_2\text{S}$: C, 61.14; H, 3.80; N, 7.92; S, 6.05. Found: C, 61.32; H, 4.01; N, 7.98; S, 5.82.

3-(2-Oxindolin-3-yl)-2-(10*H*-phenothiazin-2-yl)-1*H*-benzo[*f*]indole-4,9-dione 4:

Violet solid. Mp > 300 °C, IR (ν , thin layer, cm^{-1}): 3328 (NH), 1680 (C=O), 1618, 1583, 1462, 1434, 1303, 1254, 1118, 1081, 1032, 870, 744, 725, 667. MS, M/Z (%): 495 (M^+ , 30, 55), 490 (72), 481(77), 474(63), 368 (90), 300 (71), 261(100), 226 (69), 186 (87), 177(66), 150 (64), 91(67). ^1H NMR (DMSO- d_6): δ 5.4 (s, 1H, H-3), 6.78 (m, 2H, ArH), 6.81-6.92 (m, 3H, ArH), 7.0-7.02 (m, 2H, ArH), 7.2-7.46 (m, 4H, ArH), 8.07(m, 2H, ArH), 8.50-8.52 (m, 2H, ArH), 8.9 (s, 1H, NH), 9.54 (s, 1H, NH), 10.74 (s, 1H, NH). *Anal.* Calcd. for $\text{C}_{32}\text{H}_{19}\text{N}_3\text{O}_3\text{S}$: C, 73.13; H, 3.64; N, 8.00; S, 6.10. Found: C, 73.24; H, 3.51; N, 7.83; S, 5.92.

3-(2-Oxoindolin-3-yl)-2-(10*H*-phenothiazin-2-yl)indeno[1,2-*b*]pyrrol-4(1*H*)-one 5:

Violet solid. Mp 270-272 °C, IR (ν , thin layer, cm^{-1}): 3280 (NH), 1685 (C=O), 1600, 1575, 1537, 1462, 1431, 1377, 1275, 1193, 1155, 1094, 1031, 994. MS, M/Z (%): 497 (M^+ , 51), 469 (51), 450 (57), 438 (65), 421(42), 403 (51), 389 (58), 362 (52), 321 (47), 304 (69), 293 (62), 269 (60), 251 (60), 227 (44), 219

(56), 191(87), 180 (58), 161(57), 144 (73), 134 (71), 120 (58), 109 (71), 97 (71), 57(100). ^1H NMR (DMSO- d_6): δ 5.41, (s, 1H, H-3), 6.64-6.76 (m, 4H, ArH), 6.90-6.98 (m, 5H, ArH), 7.2-7.29 (m, 3H, ArH), 7.5-7.66 (m, 1H, ArH), 8.12 (d, J = 7.5 Hz, 1H, ArH), 8.51(d, J = 7.5 Hz, 1H, ArH), 8.82 (s, 1H, NH), 10.97(s, 1H, NH), 11.85 (s, 1H, NH). *Anal.* Calcd. for $\text{C}_{31}\text{H}_{19}\text{N}_3\text{O}_2\text{S}$: C, 74.83; H, 3.85; N, 8.45; S, 6.44. Found: C, 74.72; H, 3.64; N, 8.62; S, 6.25.

4.3 Synthesis of ethyl 5-(10-(2-chloroacetyl)-10*H*-phenothiazin-2-yl)-4-(1-(2-chloro-acetyl)-2-oxoindolin-3-yl)-2-methyl-1*H*-pyrrole-3-carboxylate 6:

4.3.1 Conventional Method:

A mixture of 3-pyrrolyl-2-oxindole **2a** (3 mmol, 1.449 g) and chloroacetyl chloride (3.1 mmol, 0.350 g, 0.247 ml) was suspended in toluene (25 ml) and the reaction mixture was refluxed for 3 h with extrusion of moisture (TLC monitoring). The solvent and excess reagent was removed under reduced pressure and the formed precipitate was crystallized from toluene to give 1.37 g of compound **6** as colorless crystals.

4.3.2 Microwave method:

A mixture of 3- pyrrolyl-2-oxindole **2a** (3 mmol, 1.449 g) and chloroacetyl chloride (3.1 mmol, 0.350 g, 0.247 ml) was suspended in toluene (15 ml) and the reaction mixture was heated under microwave irradiation at 110 °C and power of 200 W for 1 h (TLC monitoring). The solvent and excess reagent was removed under reduced pressure and the formed precipitate was crystallized from toluene to give 1.62 g of compound **6**.

Colorless solid. Mp 218-219 °C, IR (ν , thin layer, cm^{-1}): 3305, 2960, 1753, 1694, 1672, 1552, 1525, 1464, 1443, 1407, 1351, 1332, 1275, 1252, 1241, 1189, 1169, 1137, 1096, 1086, 1047, 1015, 924, 815. ^1H NMR (DMSO-

δ) 0.85 (t, J = 7.0 Hz, 3H, 2'-CH₃), 2.47(s, 3H, CH₃), 3.70-3.76 (dq, 2H, CO₂CH₂CH₃), 3.79 (br, 2H, COCH₂Cl, diastereotopic CH₂), 4.98 (d, J = 20 Hz, 1H, diastereotopic H), 4.99 (s, 1H, H-3), 5.09 (d, J = 20 Hz, 1H, diastereotopic H) 7.01 (d, J = 7Hz, 1H, ArH), 7.17 (t, 1H, J = 7 Hz, ArH), 7.37-7.45 (m, 2H, ArH), 7.47-7.5 (m, 2H, ArH), 7.62 (d, J = 7.5 Hz, 1H, ArH), 7.70-7.71(m, 2H, ArH), 7.81(s, 1H, ArH), 8.12 (d, J = 8.4 Hz, 1H, ArH) 11.91(s, 1H, NH). ¹³C NMR (DMSO- d_6) 13.82, 14.30, 43.34, 45.01, 46.41, 59.02, 109.57, 114.13, 115.64, 123.16, 125.65, 126.43, 126.80, 127.02, 127.44, 127.98 (2C), 128.17, 128.61, 128.93, 129.37, 131.05, 131.27, 132.59, 137.87, 138.02, 140.20, 164.33, 165.72, 166.71, 166.95, 177.59. *Anal.* Calcd. for C₃₂H₂₅Cl₂N₃O₅S: C, 60.57; H, 3.97; N, 6.62; S, 5.05. Found: C, 60.68; H, 4.11; N, 6.79; S, 4.82.

4.4 Ethyl 5-(10-(2-azidoacetyl)-10*H*-phenothiazin-2-yl)-2-methyl-4-(2-oxindolin-3-yl)-1*H*-pyrrole-3-carboxylate **8:**

4.4.1 Conventional method A:

A suspension of the dichloroacetyl 2-oxindole derivative **6** (3 mmol, 1.902 g) and sodium azide (6.6 mmol, 0.43 g) in acetone (30 ml) was heated under reflux for 4 h (TLC monitoring). The solvent was removed under reduced pressure and the solid residue was crystallized from ethyl acetate to give 1.35 g of compound **8** as colorless solid.

4.4.2 Conventional Method B:

To a solution of dichloroacetyl-2-oxindole **6** (3 mmol, 1.902 g mmol) in chloroform (30 mL) were added sodium azide (6.6 mmol, 0.43 g), water (15 mL), and benzyltriethylammonium bromide (0.026 g, 0.10 mmol). The reaction mixture was stirred at reflux temperature for 48 h and the organic layer was separated. The organic layer was washed with water (3 x 20 mL), dried on

anhydrous Na_2SO_4 and concentrated in vacuum. The residue was recrystallized from ethyl acetate (15 ml) to give 0.338 g of compound **8** (20% yield).

4.4.3 Microwave method:

A suspension of the dichloroacetyl 2-oxindole derivative **6** (1mmole, 0.634 g) and sodium azide (2.2 mmol, 0.143 g) in acetone (5 ml) was irradiated in CEM microwave apparatus at 56 °C and power of (200 W). The completion of the reaction was monitored by TLC. The reaction mixture was processed in the same manner in the conventional method to give 0.49 g of compound **8**.

Colorless solid. Mp 230-231 °C, IR (ν , thin layer, cm^{-1}): 3266 (NH), 2105 (N_3), 1685 (C=O), 1680 (C=O), 1618, 1560, 1524, 1466, 1444, 1330, 1268, 1173, 704, 560. ^1H NMR ($\text{DMSO}-d_6$): δ 0.86 (t, J = 7 Hz, 3H, $-\text{CO}_2\text{CH}_2\text{CH}_3$), 2.45 (s, 3H, $2'\text{-CH}_3$), 3.75 (dq, 2H, $-\text{CO}_2\text{CH}_2\text{CH}_3$) 4.26 (br, 2H, COCH_2N_3 , diastereotopic CH_2), 4.62 (s, 1H, H-3), 6.81-6.83 (m, 2H, ArH) 7.11 -7.15 (m, 1H, ArH), 7.36 (m, 1H, ArH), 7.41-7.7.45 (m, 1H, ArH), 7.49 (d, J = 8 Hz, 1H, ArH), 7.61-7.63 (dd, J_1 = 1.2 Hz, J_2 = 7.5 Hz, 1H, ArH), 7.67 (s, 1H, ArH), 7.69-7.72 (m, 2H, ArH), 7.80 (m, 1H, ArH), 10.35 (s, 1H, NH), 11.71(s, 1H, NH). ^{13}C NMR ($\text{DMSO}-D_6$): 13.58, 14.34, 45.04, 51.16, 58.45, 109.21, 110.55, 115.15, 121.34, 122.89, 126.53, 127.44 (2C), 128.12 (2C), 128.64, 128.89, 130.73, 131.54 (2C), 132.0 (2C), 132.68 (2C), 137.54, 138.12, 143.46, 164.34, 167.19, 178.84. *Anal.* Calcd. for $\text{C}_{30}\text{H}_{24}\text{N}_6\text{O}_4\text{S}$: C, 63.82; H, 4.28; N, 14.88 ; S, 5.68. Found: C, 63.59; H, 4.32; N, 14.95; S, 5.83.

4.5 Diethyl 1-(2-(2-(4-(ethoxycarbonyl)-3-(2-hydroxy-1*H*-indol-3-yl)-5-methyl-1*H*-pyrrol-2-yl)-10*H*-phenothiazin-10-yl)-2-oxoethyl)-1*H*-1,2,3-triazole-4,5-dicarboxylate **9**:

4.5.1 Conventional method:

Ethyl 5-(10-(2-azidoacetyl)-10*H*-phenothiazin-2-yl)-2-methyl-4-(2-oxoindolin-3-yl)-1*H*-pyrrole-3-carboxylate **8** (3 mmol, 1.692 g) and diethyl acetylene dicarboxylate (3.3 mmol, 0.561 g, 0.49 ml) was dissolved in 25 ml acetone and refluxed for 2h until TLC showed the consuming of the starting material. The solvent was removed under reduced pressure and the solid residue was recrystallized from ethanol to give 1.87 g of compound **9**.

4.5.2 Microwave method:

Ethyl 5-(10-(2-azidoacetyl)-10*H*-phenothiazin-2-yl)-2-methyl-4-(2-oxoindolin-3-yl)-1*H*-pyrrole-3-carboxylate **8** (3 mmol, 1.692 g) and diethyl acetylene dicarboxylate (3.3 mmol cap, 0.561 g, 0.49 ml) was dissolved in 10 ml acetone and subjected to microwave irradiation at 56 °C (200 W) for 1h until TLC showed the disappearance of the starting material. The solvent was removed under reduced pressure and the solid residue was recrystallized from ethanol to give 2.02 g of compound **9**.

Colorless solid. Mp 274-276 °C, IR (ν , thin layer, cm^{-1}): 3222 (NH), 2982 (C-H, aliphatic), 1694, 1665, 1619, 1560, 1523, 1465, 1299, 1272, 1248, 1212, 1171, 1143, 1096, 1059, 1017, 932, 818. ^1H NMR (DMSO-d_6) δ 0.83 (t, $J = 7$ Hz, 3H, $-\text{CO}_2\text{CH}_2\text{CH}_3$), 1.17 (t, $J = 7$ Hz, 3H, $-\text{CO}_2\text{CH}_2\text{CH}_3$), 1.25 (t, $J = 7$ Hz, 3H, $-\text{CO}_2\text{CH}_2\text{CH}_3$), 2.41(s, 3H, 2'- CH_3), 4.22-4.32 (m, 6H, $3\times\text{CH}_2$), 4.60 (d, $J = 10$ Hz, 2H, COCH_2N_3), 6.74 (d, $J = 7$ Hz, 1H, ArH), 6.79-6.84 (m, 3H, ArH), 7.11 (t, $J = 7.5$ Hz, 1H, ArH), 7.38-7.5 (m, 3H, ArH), 7.62 (m, 1H, ArH), 7.68 (m, 2H, ArH), 7.79 (brs, 1H, enolic-OH), 10.34 (s, 1H, NH) 11.72 (s, 1H, NH). ^{13}C NMR (DMSO-d_6): δ 13.46, 14.05, 14.26, 14.68, 44.98, 52.95, 58.63, 62.33, 63.11, 109.43, 110.44, 110.51, 114.99, 121.57, 122.82, 126.37,

127.55, 128.68, 128.77 (2C), 128.80, 129.83 (2C), 130.72 (2C), 131.73, 131.78, 137.74 (2C), 140.35 (2C), 143.11, 143.16, 157.63, 160.55, 164.51, 164.93, 179.11. *Anal.* Calcd. for C₃₈H₃₄N₆O₈S: C, 62.11; H, 4.66; N, 11.44; S, 4.36. Found: C, 62.23; H, 4.45; N, 11.61; S, 4.52.

4.6 Ethyl 5-(10-(2-chloroacetyl)-10*H*-phenothiazin-2-yl)-2-methyl-4-(3-oxo-2,3-dihydrooxazolo[3,2-*a*]indol-9-yl)-1*H*-pyrrole-3-carboxylate **10:**

4.6.1. Conventional method:

Dichloroacetyl 2-oxindole derivative **6** (3 mmol, 1.902 g) was added into a suspension of sodium hydride (60% in paraffin oil, 3 mmol, 0.12 g) in toluene (40 ml). The reaction mixture was heated with extrusion of moisture under reflux for 3h (TLC monitoring). The reaction mixture was cooled and the solvent was removed under reduced pressure. The solid residue was crystalized from toluene to give 1.49 g of compound **10**.

4.6.2 Microwave method: Dichloroacetyl 2-oxindole derivative **6** (3 mmol, 1.902 g) was added into a suspension of sodium hydride (60% in paraffin oil, 3 mmol, 0.12 g) in toluene (20 ml). The reaction mixture was subjected to microwave irradiation at 110 °C (200 W) for 1h (TLC monitoring). The reaction mixture was cooled and the solvent was removed under reduced pressure. The solid residue was crystalized from toluene to give 1.61 g of compound **10** as colorless solid.

Colorless solid. Mp 214-216 °C, IR (ν , thin layer, cm⁻¹): 3280 (NH), 2978 (C-H aliphatic), 1756 (C=O, 4-oxazolone), 1667(C=O, 2-oxindole), 1603, 1524, 1458, 1341, 1260, 1236, 1189, 1134, 1098, 1000, 784, 755. MS, M/Z(%): 493 (M⁺ - 105, 40), 485 (60), 470 (50), 420 (50), 378 (80), 353 (60), 274 (60), 229 (60), 198 (65), 123 (70), 92 (70), 80 (100). ¹H NMR (DMSO-d₆): 0.9 (t, *J* = 7.5

Hz, 3H, CH₃), 2.38 (s, 3H, CH₃), 3.86 (brs, 2H, COCH₂Cl), 3.96-4.15 (dq, 2H, OCH₂CH₃), 4.86 (d, $J = 16$ Hz, 1H, H_a), 5.03 (d, $J = 16$ Hz, 1H, H_b). 6.99 (d, $J = 7.5$ Hz, 1H, ArH), 7.19-7.21(m, 3H, ArH), 7.26-7.28 (m, 4H, ArH), 7.3-7.54 (m, 2H, ArH), 7.87(d, $J = 6$ Hz, 1H, ArH), 8.96 (s, 1H, NH). ¹³C NMR (DMSO-d₆): 13.96, 21.46, 41.72, 59.37, 76.28, 110.17, 112.96 (2C), 119.61, 120.01, 121.93, 124.25, 124.70, 125.30 (2C), 127.47, 127.66, 128.23 (2C), 129.04 (2C), 131.12, 136.09, 137.26, 137.88, 138.20, 139.41, 142.02, 144.15, 146.32, 153.23, 164.52; *Anal.* calcd. for C₃₂H₂₄ClN₃O₅S: C, 64.26; H, 4.04; N, 7.03; S, 5.36. Found: C, 64.10; H, 4.19; N, 7.22; S, 5.19.

Table 1. Comparison between conventional and microwave-assisted method of synthesis of compounds **2a-f**, **3a-c**, **4**, **5**, **6**, **8-10** in terms of yield and time.

Number	Reaction conditions	
	Conventional Yield (%) (time, min.)	Microwave Yield (%) (time, min.)
2a	83 (20) ^a	92 (10) ^b
2b	87 (15) ^a	93 (5) ^b
2c	85 (30) ^a	91 (10) ^b
2d	87(20) ^a	92(10) ^b
2e	86 (20) ^a	93(10) ^b
2f	88(15) ^a	95(10) ^b
3a	82(20) ^a	90(10) ^b
3b	81(20) ^a	88(10) ^b
3c	82(30) ^a	87(10) ^b
4	75(30) ^a	85(15) ^b
5	70(40) ^a	85(15) ^b
6	72 (180) ^c	85(60) ^e
8	80 (240) ^d	87(90) ^f
9	85 (120) ^d	92(60) ^f
10	83(180) ^c	90(60) ^e

a. AcOH, reflux; b. AcOH, MW (120 °C, 200 W); c. Toluene, reflux; d. acetone, reflux; e.

Toluene, MW (110 °C, 200 W); f. Acetone, MW (56 °C, 200 W).

Figure S1. ¹H NMR of compound 1a

Figure S2. ¹³C NMR of compound 1a

Figure S3. ¹H NMR of compound 1b

Figure S4. ¹³C NMR of compound 1b

Figure S5. Mass Spectrum of compound 1b

Figure S6. ¹H NMR of compound 1c

Figure S7. ^{13}C NMR of compound 1c

Figure S8. ^1H NMR of compound 2a

Figure S9. ¹³C NMR of compound 2a

Cairo University Micro Analytical Center

DI Analysis Shimadzu Qp-2010 Plus

Sample Information
 Analyzed by : A.GABR
 Analyzed : 21/01/2014 03:06:01 م
 Sample Name : E147
 Sample ID :
 Customer Name : عبد العزيز سيد - طوم المنصوره
 Data File : C:\GCMSolution\Data\Project1\E147.QGD
 Org Data File : C:\GCMSolution\Data\Project1\E147.QGD
 Method File : C:\GCMSolution\Data\Project1\A.GABR.qgm
 Org Method File : C:\GCMSolution\Data\Project1\A.GABR.qgm
 Report File :
 Tuning File : C:\GCMSolution\System1\Tune1_default1.gct
 SEndIfSModified by : A.GABR
 Modified : 21/01/2014 03:13:15 م

Method
 Analytical Line 1
 IonSourceTemp : 250.00 °C
 [MS Table]
 -Group 1 - Event 1-
 Start Time : 0.00min
 End Time : 10.00min
 ACQ Mode : Scan
 Event Time : 0.50sec
 Scan Speed : 1000
 Start m/z : 50.00
 End m/z : 500.00
 Electron Voltage : 70 eV
 Ionization Mode : EI

C:\GCMSolution\Data\Project1\E147.QGD

Line#1 R.Time:6.2(Scan#:742)
 MassPeaks:230
 RawMode:Single 6.2(742) BasePeak:435(476)
 BG Mode:None Group 1 - Event 1

Mass Table
 Line#1 R.Time:6.2(Scan#:742)
 MassPeaks:230
 RawMode:Single 6.2(742) BasePeak:435(476)
 BG Mode:None Group 1 - Event 1

#	m/z	Abs. In	Rel. Int.	#	m/z	Abs. In	Rel. Int.	#	m/z	Abs. In	Rel. Int.
1	50.00	74	15.55	4	54.00	62	13.03	7	59.00	58	12.18
2	51.00	63	13.24	5	55.00	94	19.75	8	60.00	62	13.03
3	53.00	108	22.69	6	57.00	58	12.18	9	62.00	65	13.66

Figure S10. Mass spectra of compound 2a

Figure S11. ¹H NMR spectrum of compound 2b

Figure S12. ¹³C NMR spectrum of compound 2b.

2b

Cairo University Micro Analytical Center

DI Analysis Shimadzu Qp-2010 Plus

Sample Information
 Analyzed by : A.GABR
 Analyzed : 21/01/2014 03:34:43 م
 Sample Name : E84
 Sample ID :
 Customer Name : عبد العزيز سيد - علوم الصيدلة
 Data File : C:\GCMSSolution\Data\Project1\E84.QGD
 Org Data File : C:\GCMSSolution\Data\Project1\E84.QGD
 Method File : C:\GCMSSolution\Data\Project1\A.GABR.eggm
 Org Method File : C:\GCMSSolution\Data\Project1\A.GABR.eggm
 Report File :
 Tuning File : C:\GCMSSolution\System\Tune1_default1.tgt
 \$End!\$Modified by : A.GABR
 Modified : 21/01/2014 03:41:35 م

Method

Analytical Line 1
 IonSource/Temp : 250.00 °C
 [MS Table]
 -Group 1 - Event 1-
 Start Time : 0.00min
 End Time : 10.00min
 ACQ Mode : Scan
 Event Time : 0.50sec
 Scan Speed : 1000
 Start m/z : 50.00
 End m/z : 500.00

Electron Voltage : 70 eV
 Ionization Mode : EI

C:\GCMSSolution\Data\Project1\E84.QGD

Line#1 R.Time:4.1(Scan#:495)
 MassPeaks:169
 RawMode:Single 4.1(495) BasePeak:64(204)
 BG Mode:None Group 1 - Event 1

Mass Table

Line#1 R.Time:4.1(Scan#:495)

MassPeaks:169

RawMode:Single 4.1(495) BasePeak:64(204)

BG Mode:None Group 1 - Event 1

#	m/z	Abs. In	Rel. Int.	#	m/z	Abs. In	Rel. Int.	#	m/z	Abs. In	Rel. Int.
1	50.00	78	38.24	4	56.00	63	30.88	7	59.00	54	26.47
2	54.00	71	34.80	5	57.00	84	41.18	8	60.00	70	34.31
3	55.00	94	46.08	6	58.00	97	47.55	9	64.00	204	100.00

Figure S13. Mass spectrum of compound 2b

Figure S14. ¹H NMR of compound 2c

Figure S15. ¹³C NMR spectrum of compound 2c

Figure S16. ¹H NMR of compound 2d.

Figure S17. ¹³C NMR of compound 2d.

Figure S18. ¹H NMR of compound 2e

Figure S19. ¹³C NMR of compound 2e

Figure S20. ¹H NMR spectrum of 2f

Figure S21. ¹³C NMR spectrum of compound 2f

21-Jan-14 16:24:39

Cairo University Micro Analytical Center

DI Analysis Shimadzu Qp-2010 Plus

Sample Information
Analyzed by : A.GABR
Analyzed : 21/01/2014 04:17:06
Sample Name : E89
Sample ID :
Customer Name : عبد العزيز سيد - علوم المنسوبة
Data File : C:\GCMSSolution\Data\Project1\E89.QGD
Org Data File : C:\GCMSSolution\Data\Project1\E89.QGD
Method File : C:\GCMSSolution\Data\Project1\A.GABR.qgm
Org Method File : C:\GCMSSolution\Data\Project1\A.GABR.qgm
Report File :
Tuning File : C:\GCMSSolution\System1\Tune1\default1.qgt
SEndIfsModified by : A.GABR
Modified : 21/01/2014 04:23:06

Method
Analytical Line 1
IonSourceTemp : 250.00 °C
[MS Table]
-Group 1 - Event 1--
Start Time : 0.00min
End Time : 10.00min
Scan :
ACQ Mode : Scan
Event Time : 0.50sec
Scan Speed : 1000
Start m/z : 50.00
End m/z : 500.00
Electron Voltage : 70 eV
Ionization Mode : EI

C:\GCMSSolution\Data\Project1\E89.QGD

Line# 1 R.Time:3.2(Scan#:387)
MassPeaks:159
RawMode:Single 3.2(387) BasePeak:80(151)
BG Mode:None Group 1 - Event 1

Mass Table
Line# 1 R.Time:3.2(Scan#:387)
MassPeaks:159
RawMode:Single 3.2(387) BasePeak:80(151)
BG Mode:None Group 1 - Event 1

#	m/z	Abs. In	Rel. Int.	#	m/z	Abs. In	Rel. Int.	#	m/z	Abs. In	Rel. Int.
1	50.00	95	62.91	4	55.00	66	43.71	7	62.00	54	35.76
2	53.00	54	35.76	5	57.00	116	76.82	8	63.00	68	45.03
3	54.00	71	47.02	6	61.00	76	50.33	9	64.00	106	70.20

Figure S 22. Mass spectrum of compound 2f

Figure S23. ^1H NMR spectrum of compound 3a

Figure S24. ^{13}C NMR spectrum of compound 3a

Cairo University Micro Analytical Center

DI Analysis Shimadzu Qp-2010 Plus

Sample Information
 Analyzed by : A.GABR
 Analyzed : 21/01/2014 01:58:55 م
 Sample Name : E34
 Sample ID :
 Customer Name : جيد العزيز سيد - علوم فاسموره
 Data File : C:\GCMSolution\Data\Project1\E34.QGD
 Org Data File : C:\GCMSolution\Data\Project1\E34.QGD
 Method File : C:\GCMSolution\Data\Project1\A.GABR.qgm
 Org Method File : C:\GCMSolution\Data\Project1\A.GABR.qgm
 Report File :
 Tuning File : C:\GCMSolution\System\Tune1_default1.qgt
 SEndIfSModified by : A.GABR
 Modified : 21/01/2014 02:05:17 م

Method

Analytical Line 1
 IonSourceTemp : 250.00 °C
 [MS Table]
 -Group 1 - Event 1-
 Start Time : 0.00min
 End Time : 10.00min
 ACQ Mode : Scan
 Event Time : 0.50sec
 Scan Speed : 1000
 Start m/z : 50.00
 End m/z : 500.00

Electron Voltage : 70 eV
 Ionization Mode : EI

C:\GCMSolution\Data\Project1\E34.QGD

Line#:1 R.Time:5.2(Scan#:629)

MassPeaks:207

RawMode:Single 5.2(629) BasePeak:277(594)

BG Mode:None Group 1 - Event 1

Mass Table

Line#:1 R.Time:5.2(Scan#:629)

MassPeaks:207

RawMode:Single 5.2(629) BasePeak:277(594)

BG Mode:None Group 1 - Event 1

#	m/z	Abs. In	Rel. Int.	#	m/z	Abs. In	Rel. Int.	#	m/z	Abs. In	Rel. Int.
1	50.00	62	10.44	4	53.00	63	10.61	7	57.00	79	13.30
2	51.00	84	14.14	5	54.00	57	9.60	8	63.00	95	15.99
3	52.00	87	14.65	6	55.00	68	11.45	9	64.00	145	24.41

Figure S 25. Mass spectrum of compound 3a

Figure S 28. ^1H NMR spectrum of compound 3c

Figure S29. ^{13}C NMR spectrum of compound 3c

Cairo University Micro Analytical Center

DI Analysis Shimadzu Qp-2010 Plus

Sample Information
 Analyzed by : A.GABR
 Analyzed : 21/01/2014 02:13:39
 Sample Name : E85
 Sample ID :
 Customer Name : عبد العزيز سيد - علوم المنسوبة
 Data File : C:\GCMSolution\Data\Project1\VB85.QGD
 Org Data File : C:\GCMSolution\Data\Project1\VB85.QGD
 Method File : C:\GCMSolution\Data\Project1\A.GABR.qgm
 Org Method File : C:\GCMSolution\Data\Project1\A.GABR.qgm
 Report File :
 Tuning File : C:\GCMSolution\System1\Tune1\default1.qgt
 \$Endl\$ Modified by : A.GABR
 Modified : 21/01/2014 02:19:44

Method
 Analytical Line 1
 IonSourceTemp : 250.00 °C
 [MS Table]
 -Group 1 - Event 1-
 Start Time : 0.00min
 End Time : 10.00min
 ACQ Mode : Scan
 Event Time : 0.50sec
 Scan Speed : 1000
 Start m/z : 50.00
 End m/z : 500.00
 Electron Voltage : 70 eV
 Ionization Mode : EI

C:\GCMSolution\Data\Project1\VB85.QGD

Line#:1 R.Time:3.1(Scan#:368)

MassPeaks:69

RawMode:Single 3.1(368) BasePeak:232(86)

BG Mode:Averaged 3.0-3.0(360-360) Group 1 - Event 1

Mass Table

Line#:1 R.Time:3.1(Scan#:368)

MassPeaks:69

RawMode:Single 3.1(368) BasePeak:232(86)

BG Mode:Averaged 3.0-3.0(360-360) Group 1 - Event 1

#	m/z	Abs. In	Rel. Int.	#	m/z	Abs. In	Rel. Int.	#	m/z	Abs. In	Rel. Int.
1	55.00	42	48.84	4	61.00	52	60.47	7	65.00	71	82.56
2	57.00	59	68.60	5	62.00	58	67.44	8	66.00	60	69.77
3	59.00	58	67.44	6	64.00	40	46.51	9	73.00	66	76.74

Figure S30. Mass spectrum of compound 3c

21-Jan-14 12:57:48

**Cairo University
Micro Analytical Center**

**DI Analysis
Shimadzu Qp-2010 Plus**

Sample Information
Analyzed by : A.GABR
Analyzed : 21/01/2014 12:51:27
Sample Name : E50
Sample ID :
Customer Name : عبد العزيز سيد - علوم المنسوبة
Data File : C:\GCMSsolution\Data\Project1\E50.QGD
Org Data File : C:\GCMSsolution\Data\Project1\E50.QGD
Method File : C:\GCMSsolution\Data\Project1\A.GABR.qgm
Org Method File : C:\GCMSsolution\Data\Project1\A.GABR.qgm
Report File :
Tuning File : C:\GCMSsolution\System1\Tune1\default1.gct
SEndfSM Modified by : A.GABR
Modified : 21/01/2014 12:56:43

Method
Analytical Line 1
IonSourceTemp : 250.00 °C
[MS Table]
-Group 1 - Event 1-
Start Time : 0.00min
End Time : 10.00min
ACQ Mode : Scan
Event Time : 0.50sec
Scan Speed : 1000
Start m/z : 50.00
End m/z : 500.00

Electron Voltage : 70 eV
Ionization Mode : EI

C:\GCMSsolution\Data\Project1\E50.QGD

Line#:1 R.Time:2.8(Scan#:336)

MassPeaks:96

RawMode:Single 2.8(336) BasePeak:262(98)

BG Mode:Averaged 2.7-2.7(330-330) Group 1 - Event 1

Mass Table

Line#:1 R.Time:2.8(Scan#:336)

MassPeaks:96

RawMode:Single 2.8(336) BasePeak:262(98)

BG Mode:Averaged 2.7-2.7(330-330) Group 1 - Event 1

#	m/z	Abs. In	Rel. Int.	#	m/z	Abs. In	Rel. Int.	#	m/z	Abs. In	Rel. Int.
1	53.00	16	16.33	4	62.00	79	80.61	7	66.00	58	59.18
2	55.00	57	58.16	5	64.00	5	5.10	8	67.00	79	80.61
3	61.00	3	3.06	6	65.00	74	75.51	9	69.00	66	67.35

Figure S31. Mass spectrum of compound 4

21-Jan-14 15:29:22

**Cairo University
Micro Analytical Center**

**DI Analysis
Shimadzu Qp-2010 Plus**

Sample Information
Analyzed by : A.GABR
Analyzed : 21/01/2014 03:20:44 م
Sample Name : E128
Sample ID :
Customer Name : عبد العزيز سيد - علوم الصيدلة
Data File : C:\GCMSolution\Data\Project\VE128.QGD
Org Data File : C:\GCMSolution\Data\Project\VE128.QGD
Method File : C:\GCMSolution\Data\Project\VA.GABR.qgm
Org Method File : C:\GCMSolution\Data\Project\VA.GABR.qgm
Report File :
Tuning File : C:\GCMSolution\System\Tune\1_default1.qgt
SEnd1\$Modified by : A.GABR
Modified : 21/01/2014 03:26:56 م

Method
Analytical Line 1
IonSource Temp : 250.00 °C
[MS Table]
-Group 1 - Event 1-
Start Time : 0.00min
End Time : 10.00min
ACQ Mode : Scan
Event Time : 0.50sec
Scan Speed : 1000
Start m/z : 50.00
End m/z : 500.00
Electron Voltage : 70 eV
Ionization Mode : EI

C:\GCMSolution\Data\Project\VE128.QGD

Line# : 1 R.Time: 2.3 (Scan#: 277)

MassPeaks: 127
RawMode: Single 2.3 (277) BasePeak: 57 (121)
BG Mode: None Group 1 - Event 1

Mass Table

Line# : 1 R.Time: 2.3 (Scan#: 277)

MassPeaks: 127

RawMode: Single 2.3 (277) BasePeak: 57 (121)

BG Mode: None Group 1 - Event 1

#	m/z	Abs. In	Rel. Int.	#	m/z	Abs. In	Rel. Int.	#	m/z	Abs. In	Rel. Int.
1	51.00	60	49.59	4	56.00	65	53.72	7	60.00	63	52.07
2	54.00	63	52.07	5	57.00	121	100.00	8	67.00	63	52.07
3	55.00	78	64.46	6	59.00	65	53.72	9	68.00	65	53.72

Figure S32. Mass spectrum of compound 5

Figure S33. ¹H NMR of compound 6

Figure S34. ¹³C NMR spectrum of compound 6

Figure S35. HMBC spectrum of compound 6

Figure S36. ¹H NMR spectrum of compound 8

Figure S37. HMBC of compound 8

Figure S38. ¹H NMR spectrum of compound 9

Figure S39. ¹³C NMR spectrum of compound 9

Figure S40. HMBC spectrum of compound 9

Figure S41. ^{15}N HMBC of compound 9

Figure S42. ^1H NMR of compound 10

Figure S43. ^{13}C NMR of compound 10

Cairo University Micro Analytical Center

DI Analysis Shimadzu Qp-2010 Plus

Sample Information

Analyzed by : A.GABR
 Analyzed : 21/01/2014 02:26:36 م
 Sample Name : E79
 Sample ID :
 Customer Name : عبد العزيز محمد - طوم القنطرة
 Data File : C:\GCMSolution\Data\Project\1\E79.QGD
 Org Data File : C:\GCMSolution\Data\Project\1\E79.QGD
 Method File : C:\GCMSolution\Data\Project\1\A.GABR.qgm
 Org Method File : C:\GCMSolution\Data\Project\1\A.GABR.qgm
 Report File :
 Tuning File : C:\GCMSolution\System\Tune\1_default1.tgf
 \$Endf\$ Modified by : A.GABR
 Modified : 21/01/2014 02:32:48 م

Method

Analytical Line 1
 IonSourceTemp : 250.00 °C
 [MS Table]
 --Group 1 - Event 1--
 Start Time : 0.00min
 End Time : 10.00min
 ACQ Mode : Scan
 Event Time : 0.50sec
 Scan Speed : 1000
 Start m/z : 50.00
 End m/z : 500.00
 Electron Voltage : 70 eV
 Ionization Mode : EI

C:\GCMSolution\Data\Project\1\E79.QGD

Chromatogram E79 C:\GCMSolution\Data\Project\1\E79.QGD

Line# 1 R.Time:3.8(Scan#:458)
 MassPeaks:152
 RawMode:Single 3.8(458) BasePeak:80(146)
 BG Mode:None Group 1 - Event 1

Mass Table

Line# 1 R.Time:3.8(Scan#:458)

MassPeaks:152

RawMode:Single 3.8(458) BasePeak:80(146)

BG Mode:None Group 1 - Event 1

#	m/z	Abs. In	Rel. Int.	#	m/z	Abs. In	Rel. Int.	#	m/z	Abs. In	Rel. Int.
1	50.00	76	52.05	4	55.00	84	57.53	7	64.00	110	75.34
2	51.00	82	56.16	5	56.00	81	55.48	8	65.00	87	59.59
3	52.00	63	43.15	6	57.00	52	35.62	9	71.00	58	39.73

Figure S44. Mass spectrum of compound 10