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Synthesis of 9,10-Substituted 3,4,10,10a-Tetrahydro-2*H*,9*H*-1-oxa-4a,9-diazaphenanthrenes by Reductive Cyclization Method

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Commercially available *o*-phenylenediamine (**1**) was treated with methyl α-bromo-α-aryl acetate to obtain 3-aryl-3,4-dihydro-1*H*-quinoxalin-2-one (**2**). The latter was reacted with benzyl bromide to obtain 4-benzyl-3-aryl-3,4-dihydro-1*H*-quinoxalin-2-one (**3**). Treatment of **3** with ethyl 3-bromopropionate resulted in the formation of 3-(4-benzyl-3-aryl-2-oxo-3,4-dihydro-2*H*-quinoxalin-1-yl)propionic acid ethyl ester (**4**), which on reaction with $LiAlH_4$ gave 9-benzyl-10-phenyl-3,4,10,10a-tetrahydro-2*H*,9*H*-1-oxa-4a,9-diazaphenanthrene (**5**) *via* a reductive cyclization. In another sequence of reactions, **2** was treated with benzyl chloroformate to obtain 3-oxo-2-aryl-3,4-dihydro-2*H*-quinoxalin-1-carboxylic acid benzyl esters (**6**). The latter on treatment with ethyl 3-bromopropionate gave 4-(2-ethoxycarbonylethyl)-3-oxo-2-phenyl-3,4-dihydro-2*H*-quinoxaline-1-carboxylic acid benzyl esters (**7**). Then **7** was reductively cyclized with $LiAlH_4$ to obtain 10-phenyl-3,4,10,10a-tetrahydro-2*H*-1-oxa-4a,9-diazaphenanthrene-9-carboxylic acid benzyl esters (**8**). In an yet another sequence of reactions, **2** was treated with catalytic amount of *p*-toluene sulphonic acid in toluene under refluxing conditions to obtain 3-phenyl-1*H*-quinoxaline-2-one (**9**). The latter, on treatment with ethyl 3-bromopropionate gave 3-[3-phenyl-2-oxo-2*H*-quinoxalin-1-yl]propionic acid ethyl esters (**10**), followed by reductive cyclization with $LiAlH_4$ to afford 10-phenyl-3,4-dihydro-2*H*,10aH-1-oxa-4a,9-diazaphenanthrene (**11**). All the new products obtained in the above three sequences of reactions have been adequately characterized by spectral data.

Keywords: Synthesis, Substituted diazaphenanthrenes, Reductive cyclization.

INTRODUCTION

The presence of two functionally active amino groups in *o*-phenylenediamine increases the possibility of various interactions leading to a number of products like benzofused 2-quinoxalinones. Their use in different therapeutic areas have been listed as antidepressant[1], anticancer[2], antidiabetic[3], anti-inflammatory[4,5], antimicrobial[6,7] and antiviral[8,9] activities. Of particular interest are the styryl, N-alkyl[10], arylhydrazino-carbony[l9-12], oxadiazolyl[12-15], and thioalkyl[16,17] quinoxalines which are reported to possess antibacterial[10,13-16], antifungal[11,12,15,17] and antiviral[9] activity, *etc*. Keeping in view the biological activities of various quinoxalines derivatives, it was considered worthwhile to prepare fused derivatives of quinoxalines as potentially biologically active compounds.

EXPERIMENTAL

All experiments were conducted under nitrogen atmosphere unless stated otherwise. All solvents and reagents were of reagent grade and used without further purification. All melting points were determined on Pullman MP-96 melting point apparatus. ^{1}H NMR spectra were recorded using a Bruker 300 MHz spectrometer (300 MHz) with TMS as internal standard in DMSO-d_6 or $CDCl_3$. Mass spectra were recorded on a agilent 6120 single qudrapole LC-MS instrument giving as M^+. Values either on $(M + H)^+$ or $(M - H)^+$ modes. IR spectra were obtained on a Perkin-Elmer 1720 FT-IR spectrometer (KBr Pellets). Analytical TLC was conducted on E-Merck 60F254 aluminum-packed silicagel plates (0.2 mm). Developed plates were visualized under UV light or iodine chamber.

General procedure for the preparation of 2: A mixture of **1** (10 g, 0.092 mol), K_2CO_3 (25.5 g, 0.185 mol) DMF (40 mL) and α-bromo-α-aryl acetate (Ar = Ph or 4-F-phenyl) (0.097 mol) was stirred at 60 °C for 0.5 h. At the end of this period, the reaction mixture was poured into ice-cold water (100 mL). The separated solid was filtered, washed with water (50 mL) and dried to obtain **2**.

2a: yield = 15 g (72.8 %); m.p. = 202-205 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.28 (br s, 1H), 6.59 (s, 1H), 6.75-6.76 (d, 3H), 6.93 (m, 1H), 7.32-7.44 (m, 5H), 8.15 (br s, 1H); LC-MS (ESI) $(M + H)^+$ *m/z* 225.

2b: Yield = 17.3 g (77 %); m.p. = 185-187 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.91 (s, 1H), 5.08 (s, 1H), 6.71-6.80 (d, *J* = 4.2 Hz, 3H), 7.03-7.05 (t, *J* = 8.1 Hz, 1H), 7.36-7.39 (m, 4H), 10.34 (s, 1H); LC-MS (ESI) $(M + H)^+$ *m/z* 243.

General procedure for the preparation of 3: A mixture of **2** (0.022 mol), benzyl bromide (4.38 g, 0.025 mol), Na_2CO_3 (4.73 g, 0.044 mol) and ethanol-water (9:1, 30 mL/3 mL) was stirred at reflux temperature for 5 h, at the end of this period, ethanol was rotary evaporated and the residue diluted with water (30 mL). The separated solid was filtered, washed with water and dried to obtain **3**.

3a: Yield = 6 g (86 %); m.p. = 154-158 °C; IR (KBr, ν_{max}, cm^{-1}) 3064, 1681, 1507, 1381, 739, 693; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.12 (d, *J* = 11.2 Hz, 1H), 4.71(d, *J* = 11.2 Hz, 1H), 4.99 (s, 1H), 6.72-6.82 (m, 3H), 6.99 (m, 1H), 7.16-7.43 (m, 10H), 8.65 (br s, 1H); LC-MS (ESI) $(M + H)^+$ *m/z* 315.

3b: Yield = 6.1 g (88 %); m.p. =174-177 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.03-4.08 (d, *J* = 15 Hz, 1H), 4.65-4.70 (d, *J* = 15 Hz, 1H), 4.94 (s, 1H), 6.74-6.82 (m, 3H), 6.91 (m, 1H), 7.11-7.16 (m, 2H), 7.26-7.36 (m, 5H), 8.45 (s, 1H); LC-MS (ESI) $(M + H)^+$ *m/z* 333.

General procedure for the preparation of 4: A mixture of **3** (0.0127 mol), K_2CO_3 (3.5 g, 0.025 mol), DMF (20 mL) and 3-bromopropionate (2.76 g, 0.015 moL) was stirred at 80 °C for 12 h. At the end of this period, the reaction mixture was diluted with water and ethyl acetate (40/30 mL) .The separated organic layer was washed with water (20 mL), dried over Na_2SO_4 and evaporated to obtain crude **4**. This was purified by column chromatography (6 % EtOAc/hexane) giving pure compound **4**.

4a: Yield = 4 g (76 %); m.p. = 65-66 °C; IR (KBr, ν_{max}, cm^{-1}) 3443, 1730, 1680, 1454, 697; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.21 (t, *J* = 6.6 Hz, 3H), 2.65 (m, 2H), 4.12 (m, 3H), 4.30 (2H), 4.67 (d, *J* = 12.3 Hz, 1H), 5.02 (s, 1H), 6.75-7.12 (m, 5H), 7.23-7.42 (m, 9H); LC-MS (ESI) $(M + H)^+$ *m/z* 414.

4b: Yield = 3.8 g (73 %); m.p. =72-74 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.21 (t, *J* = 6.6 Hz, 3H), 2.83 (t, *J* = 8.7 Hz, 2H), 4.06-4.21 (m, 3H), 4.60-4.67 (m, 3H), 4.96 (s, 1H), 6.91-7.44 (m, 9H), 7.56-7.61 (m, 1H), 7.93-7.96 (d, *J* = 8.1 Hz, 1H), 8.38-8.43 (m, 1H); LC-MS (ESI) $(M + H)^+$ *m/z*: 433.

General procedure for the preparation of 5: To a solution of **4** (0.0024 mol) in THF (10 mL) was added $LiAlH_4$ (0.11 g, 0.0029 mol) in 5 min at 10 °C and the mixture stirred at room temperature for 1 h. At the end of this period, the reaction mixture was quenched with saturated Na_2SO_4 solution (1 mL) at 5 °C and diluted with ethyl acetate (20 mL). The separated cake was filtered and washed with EtOAc (10 mL).The filtrate was dried over Na_2SO_4 and then evaporated to obtain a crude product which was purified by column chromatography (4 % EtOAc/hexane) affording pure **5**.

5a: Yield = 0.65 g (64 %); m.p. = 138-143 °C; IR (KBr, ν_{max}, cm^{-1}) 2949, 1592, 1511, 727; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.22 (d, *J* = 6.3 Hz, 1H), 2.20 (m, 1H), 3.20 (m, 1H), 3.90-(m, 1H), 4.30 (m, 3H), 4.59 (s, 1.6 H), 4.60 (s, 0.4 H), 4.78 (s, 0.8H), 4.82 (s, 0.2H), 6.50 (d, *J* = 7.5 Hz, 1H), 6.66 (m, 2H), 6.82 (d, *J* = 7.5 Hz, 1H), 7.12-7.35 (m,10H); LC-MS (ESI) $(M + H)^+$ *m/z* 357.

5b: Yield = 0.6 g (69 %); m.p. = 153-157 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.43 (d, *J* = 11.7 Hz, 1H), 1.99-2.13 (m, 1H), 3.21 (t, *J* = 9.6 Hz, 1H), 3.94 (t, *J* = 9.3 Hz, 1H), 4.19-4.20 (m, 2H), 5.22 (d, *J* = 7.5 Hz, 1H), 5.34 (d, *J* = 10.8 Hz, 1H), 5.72 (s, 1H), 5.92 (s, 1H), 6.85-6.90 (m, 5H), 7.18 (d, *J* = 10.8 Hz,1H), 7.25-7.33 (m, 7H); LC-MS (ESI) $(M + H)^+$ *m/z*: 375.

General procedure for the preparation of 6: A mixture of **2** (21.4 mmol), benzyl chloroformate (7.3 g, 42.9 mmol), $NaHCO_3$ (3.6 g, 42.8 mmol) and DMF (25 mL) was stirred at 60 °C for 5 h. Then the reaction mixture was poured into ice-cold water (150 mL). The separated solid was filtered, washed with water (50 mL) and dried to obtain **6**.

6a: Yield = 6.2 g (81 %); m.p. = 154-158 °C; IR (KBr, ν_{max}, cm^{-1}) 3074, 2918, 1686, 1504,1383, 1229, 754, 534; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.27 (d, *J* = 12.0 Hz, 1H), 5.34 (d, *J* = 12.0 Hz, 1H), 6.29 (br s, 1H), 6.85 (t, *J* = 6.1 Hz, 1H), 7.06 (m, 2H), 7.23-7.52 (m, 11H), 8.99 (br s, 1H); LC-MS (ESI) $(M + H)^+$ *m/z*: 359.

6b: Yield = 6.0 g (80 %); m.p. = 171-173 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.25-5.29 (d, *J* = 11.1 Hz, 1H), 5.32-5.36 (d, *J* = 12.0 Hz, 1H), 6.29 (br s, 1H), 6.89-7.07 (m, 5H), 7.24-7.36 (m, 9H), 9.36 (br s, 1H); LC-MS (ESI) $(M + H)^+$ *m/z*: 377.

General procedure for the preparation of 7: Same as above general procedure for **4**.

7a: Yield = 4.3 g (67 %); m.p. = 52-54 °C; IR (KBr, ν_{max}, cm^{-1}) 1730, 1678; ^{1}H NMR ($CDCl_3$,300 MHz) δ 1.20 (t, *J* = 6.7 Hz, 3H), 2.60-2.81 (m, 2H), 4.12 (q, *J* = 6.7 Hz, 2H), 4.32 (m, 2H), 5.29 (m, 2H), 6.37 (s, 1H), 7.03-7.37 (m, 14H); LC-MS (ESI) $(M + H)^+$ *m/z* 459.

7b: Yield = 4.1 g (70 %); thick syrup; IR (KBr, ν_{max}, cm^{-1}) 3443, 1715, 1681, 1507, 1393, 1270, 1026, 754; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.24 (t, *J* = 7.2 Hz, 3H), 2.83 (t, *J* = 6.7 Hz,2H), 4.17 (q, *J* = 7.2 Hz, 2H), 4.63 (t, *J* = 6.7 Hz, 2H), 5.26 (m, 2H), 6.33 (s, 1H), 7.15-7.19 (m, 2H), 7.36-7.44 (m, 2H), 7.56-7.61 (m, 1H), 7.93-7.96 (m, 1H), 8.38-8.42 (m, 2H); LC-MS (ESI) $(M + H)^+$ *m/z*: 477.

General procedure for the preparation of 8: Same as above general procedure for **5**.

8a: Yield = 0.56 g (64 %); m.p. = 82-85 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.38-1.40 (m, 1H), 2.13-2.19 (m, 1H), 3.31 (t, *J* = 12.6 Hz, 1H), 3.92 (t, *J* = 9.3 Hz, 1H), 4.15-4.28 (dd, *J* = 8.4, 12 Hz, 2H), 4.96 (br s, 1H), 5.44 (d, *J* = 10.8 Hz, 1H), 5.64 (m, 1H), 5.75 (br s, 1H), 6.82-6.89 (m, 2H), 7.19-7.10 (m, 1H), 7.23-7.320 (m, 11H); LC-MS (ESI) $(M + H)^+$ *m/z* 401.

8b: Yield = 0.6 g (69 %); m.p. = 89-93 °C; IR (KBr, ν_{max}, cm^{-1}) 3442,1693,754; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.43 (d, *J* = 11.7 Hz, 1H), 1.99-2.13 (m, 1H), 3.21 (t, *J* = 9.6 Hz, 1H), 3.94 (t, *J* = 9.3 Hz, 1H), 4.19-4.20 (m, 2H), 4.92 (s, 1H), 5.21 (d, *J* = 7.5 Hz, 1H), 5.34 (d, *J* = 10.8 Hz, 1H), 5.72 (s, 1H), 6.85-6.90 (m, 5H), 7.18-7.19 (d, *J* = 10.8 Hz, 1H), 7.25-7.33 (m, 7H); LC-MS (ESI) $(M + H)^+$ *m/z* 419.

General procedure for the preparation of 9: To a stirred solution of **2** (7.9 mmol) in toluene (20 mL) was added catalytic amount of PTSA (27 mg) at room temperature. Then, the reaction mixture was stirred at reflux temperature for 5-24 h. On completion of the reaction (as shown by disappearance of **2** on TLC), the mixture was cooled to room temperature. The resulting solid was filtered, washed with hexane to obtain **9**.

9a: yield = 1.74 g (89 %); m.p. = 225-228 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.29-7.36 (m, 2H), 7.81-7.84 (d, *J* = 7.8 Hz, 1H), 8.27-8.30 (d, *J* = 6.3 Hz, 1H), 12.63 (br s, 1H); LC-MS (ESI) $(M + H)^+$ *m/z*: 223.

9b: Yield = 1.8 g (91 %); m.p. = > 230 °C; IR (KBr, ν_{max}, cm^{-1}) 2838, 1665, 1590, 1222, 1162, 847; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.31-7.35 (m, 4H), 7.53-7.54 (t, *J* = 6.5 Hz, 2H), 7.83-7.84 (d, *J* = 7.5 Hz,1H), 8.40-8.43 (d, *J* = 7.5 Hz, 2H), 12.59 (br s, 1H); LC-MS (ESI) $(M + H)^+$ *m/z:* 241.

General procedure for the preparation of 10: Same as above general procedure **4**.

10a: Yield = 1.43 g (66 %); m.p. = 61-64 °C; IR (KBr, ν_{max}, cm^{-1}) 1678; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.25 (t, *J* = 6.9 Hz, 3H), 2.83 (t, *J* = 7.8 Hz, 2H), 4.17 (q, *J* = 6.9 Hz, 2H), 4.63 (t, *J* = 7.8 Hz, 2H), 7.35-7.61 (m, 6H), 7.95-7.98 (dd, *J* = 8.1 Hz, 1H), 8.30-8.33 (m, 2H); LC-MS (ESI) $(M + H)^+$ *m/z* 323.

10b: Yield = 1.5 g (70.5 %); m.p.= 69-71 °C; IR (KBr, ν_{max}, cm^{-1}) 2989, 1725, 1644, 1049, 848, 543, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.25 (t, *J* = 6.9 Hz, 3H), 2.82 (t, *J* = 6.3 Hz, 2H), 4.17 (t, *J* = 6.9 Hz, 2H), 4.62 (t, *J* = 6.3 Hz, 2H), 7.17 (t, *J* = 6.6 Hz, 2H), 7.44 (m, 2H), 7.60 (t, *J* = 6.7 Hz, 1H), 7.96 (d, *J* = 7.7 Hz, 1H), 8.39 (m, 2H); LC-MS (ESI) $(M + H)^+$ *m/z*: 341.

General procedure for the preparation of 11: Same as above general procedure **5**.

11a: Yield = 0.56 g (62 %); Low melting solid; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.56-1.58 (m, 1H), 2.23-2.30 (m, 1H), 3.49 (t, *J* = 12.0 Hz, 1H), 4.13 (d, *J* = 7.5 Hz, 2H), 4.30 (d, *J* = 12.9 Hz, 1H), 5.87 (s, 1H), 6.92-7.01 (m, 2H), 7.30 (d, *J* = 1.2 Hz, 1H), 7.44-7.48 (m, 3H), 7.57 (dd, *J* = 7.5 Hz, 1H), 8.03 (dd, *J* = 9.6 Hz, 2H); LC-MS (ESI) $(M + H)^+$ *m/z* 265.

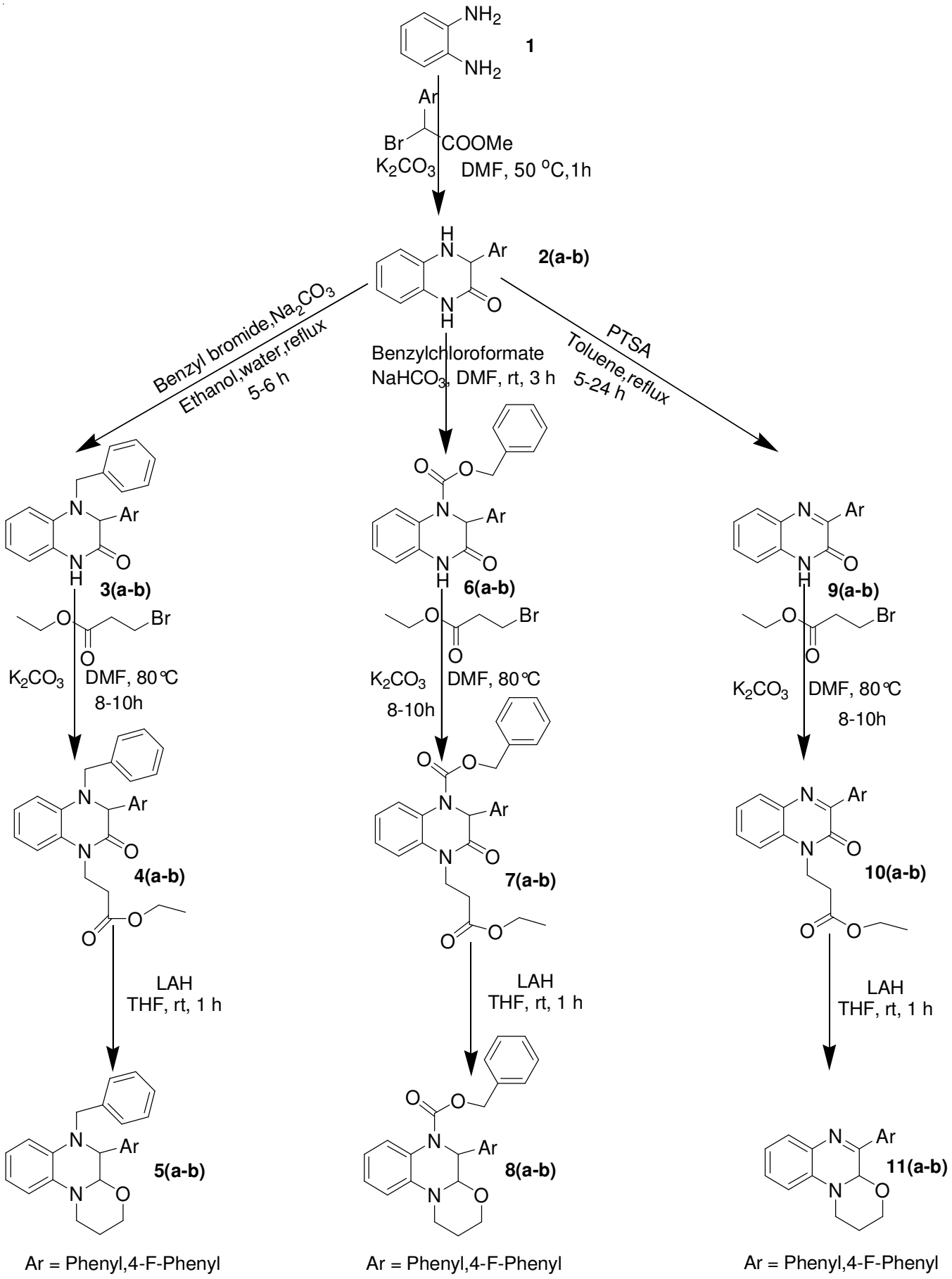
11b: Yield = 0.5 g (60 %); m.p. = 141-143 °C; IR (KBr, ν_{max}, cm^{-1}) 2844, 1611, 1491, 1221, 745; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.50 (d, *J* = 8.7 Hz, 1H), 2.39 (m, 1H), 3.50 (t, *J* = 8.7 Hz, 1H), 4.12 (d, *J* = 5.1 Hz, 2H), 4.29 (d, *J* = 9.3 Hz, 1H), 5.83 (s, 1H), 6.94 (t, *J* = 4.5 Hz, 1H), 6.99 (d, *J* = 11.4 Hz, 1H), 7.13 (t, *J* = 5.1 Hz, 1H), 7.25-7.26 (m, 2H), 7.56 (d, *J* = 4.5 Hz, 1H), 8.02 (m, 2H); LC-MS (ESI) $(M + H)^+$ *m/z* 283.

RESULTS AND DISCUSSION

Commercially available *o*-phenylenediamine (**1**) was treated with methyl α-bromo-phenyl acetate in the presence of K_2CO_3 in DMF to obtain the 3-phenyl-3,4-dihydro-1*H*-quinoxalin-2-one[18] (**2a**) (**Scheme-I**). The latter, on treatment with benzyl bromide in the presence of sodium carbonate in aqueous ethanol (9:1) under reflux for 4-5 h, gave the 4-benzyl-3-phenyl-3,4-dihydro-1*H*-quinoxaline-2-one[19] (**3a**). Then **3a** was treated with ethyl 3-bromopropionate in the presence of K_2CO_3 in DMF at 80 °C for 10 h, to yield a crude product which on purification by column chromatography afforded the pure product **3a**, which has been characterized as 3-(4-benzyl-3-phenyl-2-oxo-3, 4 dihydro 2*H*-quinoxalin-1-yl propionic acid ethyl ester (**4a**). Its IR (KBr) spectrum showed diagnostic peaks at 1749 cm^{-1} (due to ester carbonyl stretching) and at 1678 cm^{-1} (due to amide carbonyl stretching). It's ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.21 (t, *J* = 6.6 Hz, 3H), 2.65 (m, 2H), 4.12 (m, 3H), 4.30 (2H), 4.67 (d, *J* = 12.3 Hz, 1H), 5.02 (s, 1H), 6.75-7.12 (m, 5H), 7.23-7.42 (m, 9H). Its LC-MS showed the molecular ion $(M + H)^+$ peak at *m/z* 415 corresponding to a molecular mass of 414. Finally, **4a** was treated with lithium aluminium hydride in tetrahydrofuran (THF) to yield a product which has been characterized as 9-benzyl-10-phenyl-3,4,10,10a-tetrahydro-2*H*,9*H*-1-oxa-4a,9-diazaphenanthrene (**5a**). Its IR (KBr) spectrum did not show any diagnostic peaks due to -NH- and -CO- group Its ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.22 (d, *J* = 6.3 Hz, 1H), 2.20 (m, 1H), 3.20 (m, 1H), 3.90 (m, 1H), 4.30 (m, 3H), 4.59 (s, 1.6H), 4.60 (s, 0.4H), 4.78 (s, 0.8H), 4.82 (s, 0.2H), 6.50 (d, *J* = 7.5 Hz, 1H), 6.66 (m, 2H), 6.82 (d, *J* = 7.5 Hz, 1H), 7.12-7.35 (m,10H); Its LC-MS showed the molecular ion ($(M + H)^+$ peak at *m/z* 357 corresponding to a molecular mass of 356. (**Scheme -I**). The above reactions were found to be general and were carried out through the sequence **2b** → **3b** → **4b** → **5b** (**Scheme-I**).

In another sequence of reactions, **2a** was treated with benzyl chloroformate in the presence of sodium bicarbonate in DMF at room temperature, to obtain the 3-oxo-2-phenyl-3,4-dihydro-2*H*- quinoxalin-1-carboxylic acid benzyl ester (**6a**), which was treated with ethyl 3-bromopropionate in the presence of K_2CO_3 in DMF at 80 °C for 12 h, to yield a product which has been characterized as 4-(2-ethoxycarbonylethyl)-3-oxo-2-phenyl-3,4-dihydro-2*H*-quinoxaline-1-carboxylic acid benzyl ester (**7a**). Its IR (KBr) spectrum showed diagnostic peaks at 1730 cm^{-1} (due to ester carbonyl stretching) and at 1678 cm^{-1} (due to amide carbonyl stretching). ^{1}H NMR ($CDCl_3$,300 MHz) δ 1.20 (t, *J* = 6.7 Hz, 3H), 2.60-2.81 (m, 2H), 4.12 (q, *J* = 6.7 Hz, 2H), 4.32 (m, 2H), 5.29 (m, 2H), 6.37 (s, 1H), 7.03-7.37 (m, 14H); Its LC-MS showed the molecular ion $(M + H)^+$ peak at *m/z* 459 corresponding to a molecular mass of 458. Then **7a** was treated with lithium aluminium-hydride in tetrahydrofuran to yield a crude product that was purified by column chromatography giving a pure product which has been characterized as 10-phenyl-3,4,10,10a-tetrahydro-2*H*-1-oxa-4a,9-diazaphenanthrene-9- carboxylic acid benzyl ester (**8a**) on the basis of its spectral data. Thus, its IR (KBr) spectrum did not show any diagnostic peaks due to -NH- and -CO- groups. Its ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.38-1.40 (m, 1H), 2.13-2.19 (m, 1H), 3.31 (t, *J* = 12.6 Hz, 1H), 3.92 (t, *J* = 9.3 Hz, 1H), 4.15-4.28 (dd, *J* = 8.4, 12 Hz, 2H), 4.96 (br s, 1H), 5.44 (d, *J* = 10.8 Hz, 1H), 5.64 (m, 1H), 5.75 (br s, 1H), 6.82-6.89 (m, 2H), 7.19-7.10 (m, 1H), 7.23-7.320 (m, 11H); Its LC-MS showed the molecular ion $(M + H)^+$ peak at *m/z* 401 corresponding to a molecular mass of 400 (**Scheme-I**). The above reaction was found to be general and was carried out through the sequence **2b** → **6b** → **7b** → **8b** (**Scheme-I**).

In an yet another sequence of reactions, **2a** was treated with catalytic amount of *p*-toluene sulphonic acid in toluene under reflux for 5 h, resulted 3-phenyl-1*H*-quinoxaline-2-one (**9a**). The latter on treatment with ethyl 3-bromopropionate in the presence of K_2CO_3 in DMF at 80 °C for 8 h, gave a crude product which was purified by column chromatography to obtain a product that has been characterized as 3-[(3- phenyl)-2-oxo-2*H*-quinoxalin-1-yl]-propionic acid ethyl ester (**10a**). Its IR (KBr) spectrum peaks showed diagnostic peaks at 1678 cm^{-1} (due to amide carbonyl stretching). Its ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.25 (t, *J* = 6.9 Hz, 3H), 2.83 (t, *J* = 7.8 Hz, 2H),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NH2
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Ar
Br
COOMe
K2CO3
DMF, 50 °C,1h
H
N
Ar
N
H
O
2(a-b)
Benzyl bromide,Na2CO3
Ethanol,water,reflux
5-6 h
Benzylchloroformate
NaHCO3, DMF, rt, 3 h
PTSA
Toluene,reflux
5-24 h
3(a-b)
6(a-b)
9(a-b)
Br
K2CO3
DMF, 80 °C
8-10h
4(a-b)
7(a-b)
10(a-b)
LAH
THF, rt, 1 h
5(a-b)
8(a-b)
11(a-b)
Ar = Phenyl,4-F-Phenyl
Ar = Phenyl,4-F-Phenyl
Ar = Phenyl,4-F-Phenyl

Scheme-I

4.17 (q, *J* = 6.9 Hz, 2H), 4.63 (t, *J* = 7.8 Hz, 2H), 7.35-7.61 (m, 6H), 7.95-7.98 (dd, *J* = 8.1 Hz, 1H), 8.30-8.33 (m, 2H); Its LC-MS showed the molecular ion $(M + H)^+$ peak at *m/z* 323 corresponding to a molecular mass of 322. Compound **10a** on treatment with lithium aluminium hydride in tetrahydrofuran gave a crude product that on purification by column chromatography afford a product which has been characterized as 10-phenyl-3,4-dihydro-2*H*,10a*H*-1-oxa-4a,9-diazaphenanthrene (**11a**). Its IR (KBr) spectrum did not show any diagnostic peaks due to -NH and -CO groups. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.56-1.58 (m, 1H), 2.23-2.30 (m, 1H), 3.49 (t, *J* = 12.0 Hz, 1H), 4.13 (d, *J* = 7.5 Hz, 2H), 4.30 (d, *J* = 12.9 Hz, 1H), 5.87 (s, 1H), 6.92-7.01 (m, 2H), 7.30 (d, *J* = 1.2 Hz, 1H), 7.44-7.48 (m, 3H), 7.57 (dd, *J* = 7.5 Hz, 1H), 8.03 (dd, *J* = 9.6 Hz, 2H); Its LC-MS showed the molecular ion $(M + H)^+$ peak at *m/z* 265 corresponding to a molecular mass of 264 (**Scheme-I**). The above reactions were found to be general and were carried out through the sequence **2b** → **9b** → **10b** → **11b** (**Scheme-I**).

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REFERENCES

1. R. Sarges, H.R. Howard, R.G. Browne, L.A. Lebel, P.A. Seymour and B.K. Koe, *J. Med. Chem*., **33**, 2240 (1990).
2. H.-W. Yoo, M.-E. Suh and S.W. Park, *J. Med. Chem*., **41**, 4716 (1998).
3. M.Y. Chu-Moyer, W.E. Ballinger, D.A. Beebe, R. Berger, J.B. Coutcher, W.W. Day, J. Li, B.L. Mylari, P.J. Oates and R.M. Weekly, *J. Med. Chem*., **45**, 511 (2002).
4. S.B. Kadin, Ger. Offen., 2,186 (1974); *Chem. Abstr.*, **81**, 37574 (1974).
5. C.V. Reddy Sastry, K.S. Rao, V.S.H. Krishnan, K. Rastogi, M.L. Jain and G.K.A.S.S. Narayan, *Indian J. Chem*., **29B**, 396 (1990).
6. I.M.A. Awad, *Indian J. Chem*., **30B**, 89 (1991).
7. Y. Kurasawa and H.S. Kim, *J. Heterocycl. Chem.*, **35**, 1101 (1998).
8. Z. Zhu, S. Saluja, J.C. Drach and L.B. Townsend, *J. Chin. Chem. Soc,* **45**, 465 (1998).
9. G. Campiani, F. Aiello, M. Fabbrini, E. Morelli, A. Ramunno, S. Armaroli, V. Nacci, A. Garofalo, G. Greco, E. Novellino, G. Maga, S. Spadari, A. Bergamini, L. Ventura, B. Bongiovanni, M. Capozzi, F. Bolacchi, S. Marini, M. Coletta, G. Guiso and S. Caccia, *J. Med. Chem*., **44**, 305 (2001).
10. M.M. Ali, M.M.F. Ismail, M.S.A. El-Gaby, M.A. Zahran and Y.A. Ammar, *Molecules*, **5**, 864 (2000).
11. Y. Kurasawa, M. Muramatsu, K. Yamazaki, S. Tajima, Y. Okamoto and A. Takada, *J. Heterocycl. Chem*., **23**, 1379 (1986).
12. Y. Kurasawa, M. Muramatsu, K. Yamazaki, S. Tajima, Y. Okamoto and A. Takada, *J. Heterocycl. Chem*., **23**, 1391 (1986).
13. Y. Kurasawa, M. Muramatsu, K. Yamazaki, Y. Okamoto and A. Takada, *J. Heterocycl. Chem*., **23**, 1387 (1986).
14. M.Z.A. Badr, S.A. Mahgoub, F.F. Abdel-Latif, A.M. Fahmy and O.S. Moustafa, *J. Indian Chem. Soc*., **67**, 216 (1990).
15. H.M. Refaat, A.A. Moneer and O.M. Khalil, *Arch. Pharm. Res*., **27**, 1093 (2004).
16. J.P. Dirlam, J.E. Presslitz and B.J. Williams, *J. Med. Chem*., **26**, 1122 (1983).
17. M.M. Badran, K.A.M. Abouzid and M.H.M. Hussein, *Arch. Pharm. Res*., **26**, 107 (2003).
18. (a) E.C. Taylor, C.A. Maryanoff and J.S. Skotnicki, *J. Org. Chem.*, **45**, 2512 (1980); (b) E. R. Biehl and S. Kamila, *Heterocycles*, **68**, 1931 (2006).
19. (a) V. Laurinavicius, B. Kurtinaitiene, V. Liauksminas, B. Puodziunaite, R. Janciene, L. Kosychova and R. Meskys, *Monatsh. Chem.*, **130**, 1269 (1999); (b) R.F. Smith, W.J. Rebel and T.N. Beach, *J. Org. Chem*., **24**, 205 (1959).