New Synthesis of Diazepino[3,2,1-*ij*]quinoline and Pyrido[1,2,3-*de*] quinoxalines via Addition–Elimination Followed by Cycloacylation

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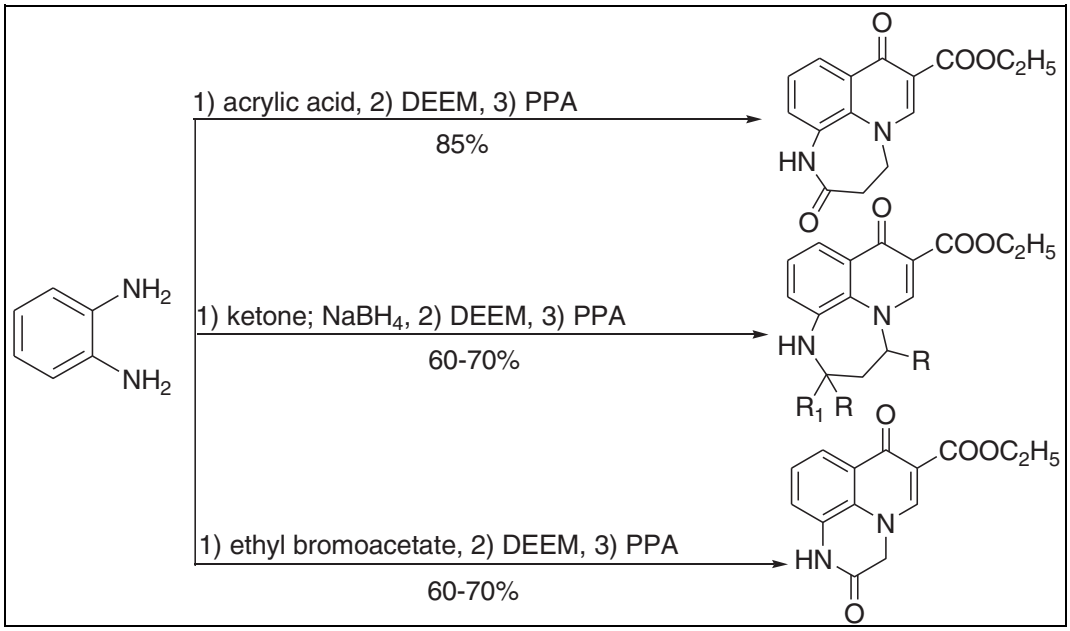


This paper describes a convenient and efficient synthesis of new fused tricyclic diazepino[3,2,1-*ij*] quinolines and substituted pyrido[1,2,3-*de*]quinoxalines. *o*-Phenylenediamines are transformed in the tricycle nucleus in only a few-step synthetic sequence to produce ethyl 2,8-dioxo-1,2,3,4-tetrahydro-8*H* [1,4]diazepino[3,2,1-*ij*]quinoline-7-carboxylate, ethyl 8-oxo-1,2,3,4-tetrahydro-8*H*-[1,4]diazepino[3,2,1-*ij*] quinoline-7-carboxylate and ethyl 2,7-dioxo-2,3-dihydro-1*H*,7*H*-pyrido[1,2,3-*de*]quinoxaline-6-carboxylate. The method is economical and simple to perform.

INTRODUCTION

Bicyclic and tricyclic quinolone derivatives potentially useful as antibacterial agents in medicinal chemistry represent an attractive starting point for the design of pharmacological targets. Many publications have reported the importance role of 4-quinolones (Fig. 1) in various biological areas, as demonstrated by compounds **1** (A-65282, antitumor agent) [1], **2** (ofloxacin, chemotherapeutic agent) [2], and pyridoquinoxalines **3** (inhibitors of human cytomegalovirus polymerase) [3].

In this paper, we describe the synthesis of a number of fused tricyclic quinolones and pyridoquinoxalines (analogues **4–6**, Fig. 2) of pharmacological interest in this chemical series. This simple method for the preparation of compounds **4–6**, as illustrated in Schemes 1, 3, and 4, could be synthetically accessible with a good number of rapid functionalization and increase hit rates at biological targets. The choice of the starting material was based on the cost and readily availability of *o*-phenylenediamines variously substituted.

RESULTS AND DISCUSSION

The 2,8-dioxo-1,2,3,4-tetrahydro-8*H*[1,4]diazepino[3,2,1-*ij*]quinoline-7-carboxylate **4** was prepared as outlined in Scheme 1 by a three-step synthetic sequence. Condensation of *o*-phenylenediamine with acrylic acid yielded lactam **7** [4] in 68% yield. Subsequent reaction with diethyl ethoxymethylene malonate (DEEM) at 140°C furnished the methylenemalonate **8** in 90% yields. A thermally induced cyclization of **8** in polyphosphoric acid (PPA) for 30 min resulted in target diazepinoquinolone **4** in 95% yields.

Our initial route to prepare the targets **5a–c** is shown in Scheme 2. The formation of 2,3-dihydro-1*H*-benzo[*b*] [1,4]diazepines **9a–c** proceeded in 80–95% yield, from

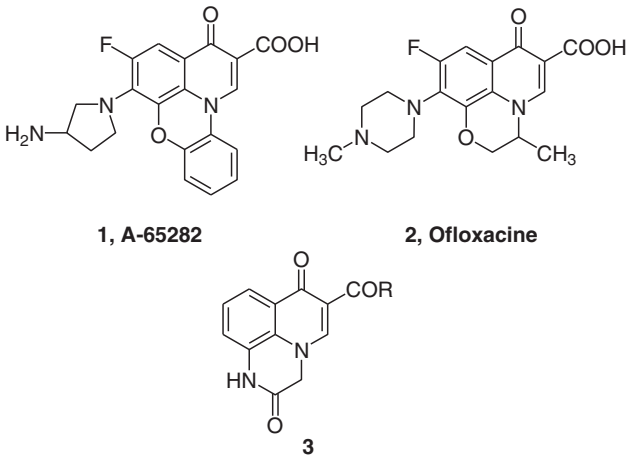


Figure 1. Structures of 4-quinolones endowed with pharmacological activity.

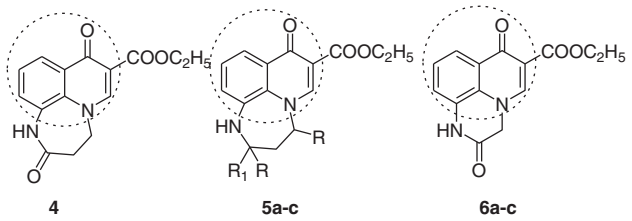
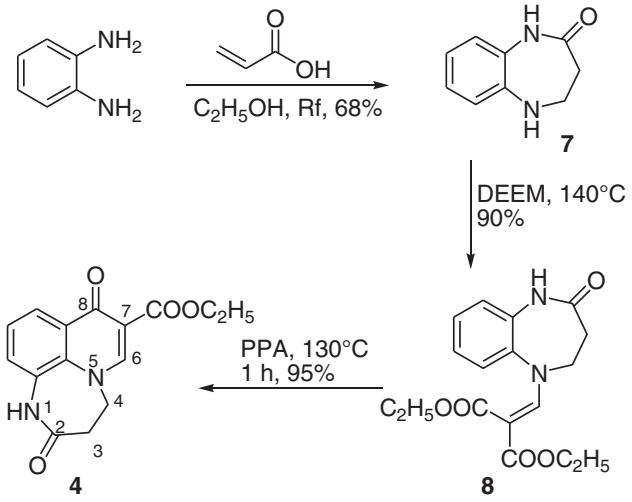


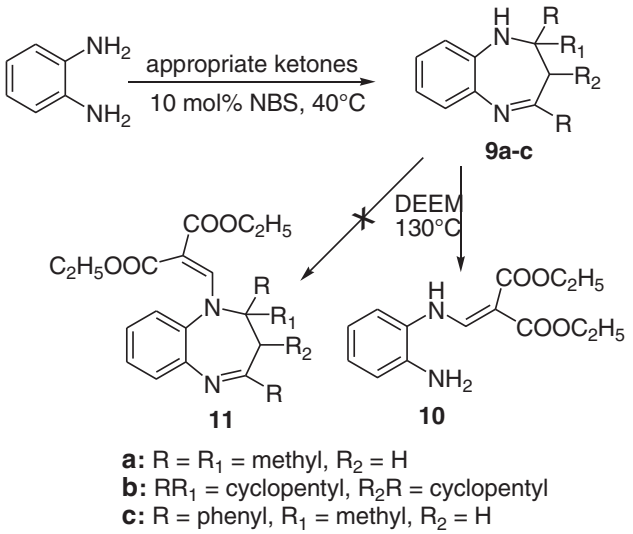
Figure 2. Diazepino[3,2,1-*ij*]quinoline and pyridoquinoxaline structures.

Scheme 1. Synthesis of ethyl 2,3,4,8-tetrahydro-2,8-dioxo-1*H*[1,4]diazepino [3,2,1-*ij*]quinoline-7-carboxylate **4**.

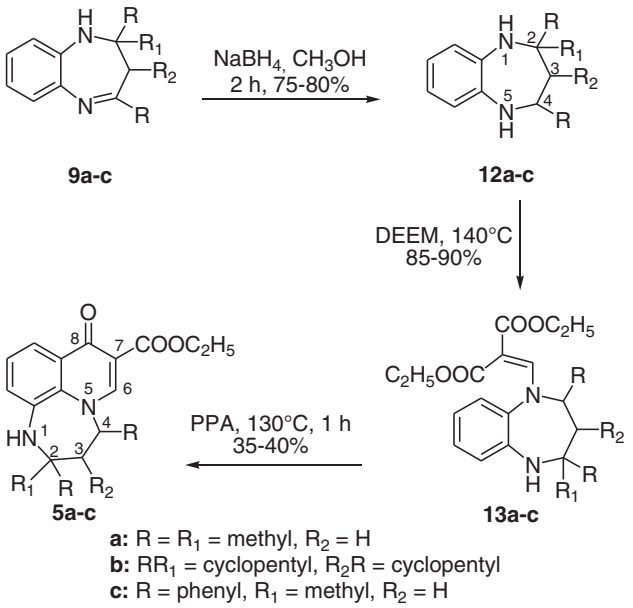


o-phenylenediamine simply by heating with aromatic (acetophenone), aliphatic acyclic (acetone), and cyclic ketones (cyclopentanone) in the presence of 2 mol% NBS as a catalyst [5]. Subsequent addition–elimination reaction with DEEM, in contrast to the synthesis of methylenemalonate **8**, did not produce **11** but underwent hydrolysis of

Scheme 2



Scheme 3. Synthesis of ethyl 2,3,4,8-tetrahydro-8-oxo-1*H*[1,4]diazepino [3,2,1-*ij*]quinoline-7-carboxylate **5a–c**.



the iminic carbon nitrogen double bond yielding diethyl 2-[(2-aminophenylamino)methylene]malonate **10**.

The alternative route to synthesize the target compounds **5a–c** as shown in Scheme 3 was achieved by reduction of carbon nitrogen double bond of compounds **9a–c** using sodium borohydride ($NaBH_4$) [6,7] to give 1,5-benzodiazepines **12a–c** in 75–80% yield. The transfer hydrogenation of prochiral imine **9b** furnished a mixture of *syn/anti* diastereomers (3/1) that were separated by column chromatography on silica gel to give the *syn*-isomer **12b** as major diastereomer. The NMR studies by NOE difference (NOEDIFF)

experiments confirmed the *syn*-conformation showing the presence of NOE enhancements between H-3 (δ = 2.39 ppm) and H-4 (δ = 4.43 ppm) protons. Furthermore, the saturation of H-4 (δ = 4.43 ppm) protons did not reveal NOE with the cyclopentyl hydrogens.

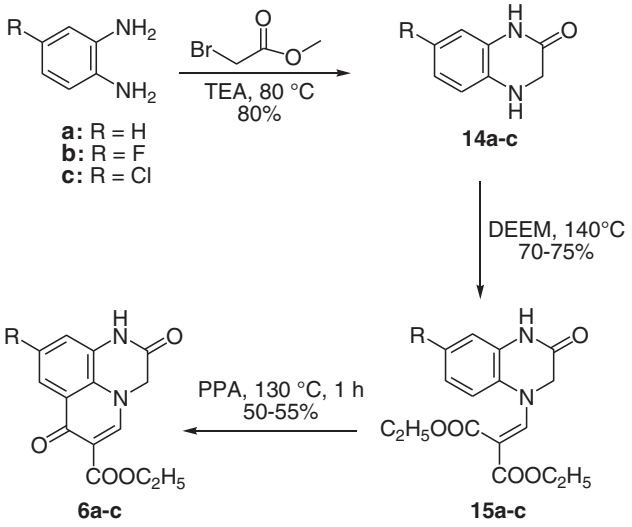
In the case of 1,5-benzodiazepine **12c** unexpectedly, the *syn*-diastereomer **12c** was the only compound obtained from hydrogenation by $NaBH_4$. The configuration of **12c** was assessed through NOEDIFF experiments. The saturation of C2-Me (δ = 1.64 ppm) protons resulted in NOE enhancements at H-4 (δ = 4.22 ppm), suggesting a *cis* relationship between the methyl at C-2 and H-4. The ^{1}H- and ^{13}C-NMR data of this compound fit completely to that reported in literature for the *syn*-isomer [8]. A possible reaction mechanism may be the transfer of hydride ion on the same side of the methyl group due to steric hindrance of the phenyl ring at C-2 position.

The 5-methylenemalonates **13a–c** were obtained from condensation with DEEM at 140°C for 2 h yielding **13a–c** (85–90%). The regioselective addition of DEEM at N-5 position was favored because of the less steric hindrance present at the 4-position than that of 2-position (Scheme 3). Subsequently, cyclization was achieved using PPA at 130°C in a short time to give target compounds **5a–c** in 35–40% yields [9,10]. The chemical identity of final compounds **5a–c** has been confirmed by ^{1}H-NMR and MS spectra. The NMR NOEDIFF studies were carried out on compounds **5a–c** to acquire information about the C-4 substituents. Compounds **5a–c** showed NOE enhancement from the position 6-CH to the 4-CH protons on the tricyclic nucleus, confirming the addition of methylmalonate chain on the NH close to the less steric hindrance carbon atom.

In this paper, we also report a simple method for the synthesis of ethyl pyrido[1,2,3-*de*]quinoxaline-6-carboxylates. Only few examples of 9-substituted-3,4-dihydroquinoxalin-2(1*H*)-ones have been reported in literature, and their synthesis has been generally carried out by using 2-nitrobenzenamine or 1-fluoro-2-nitrobenzene as starting materials [11–13].

As outlined in Scheme 4, treatment of *o*-phenylenediamines with methyl 2-bromoacetate in the presence of TEA at 80°C furnished the 3,4-dihydroquinoxalin-2(1*H*)-ones (**14a–c**) [12] in 80% yields. In analogy to the synthesis of previous tricycles, addition of DEEM to **14a–c** yielded (70–75%) diethyl [(3-oxo-3,4-dihydroquinoxalin-1(2*H*)-yl) methylene]malonates **15a–c**; this addition–elimination reaction is followed by cycloacylation in PPA at high temperature to yield the target compounds **6a–c**. The presence of (9-F, 9-Cl) on the quinoxaline nucleus, in compounds **6b** and **6c**, was confirmed by their ^{1}H-NMR spectra; in addition, ^{19}F-NMR resonances were well resolved for fluorine derivative **6b** that consisted of three signals at −114.070, −114.094, and −114.119 ppm with J_{HF} (H-8) = J_{HF} (H-9) = 10 Hz (equal intensity), which confirms the presence of fluorine on the 9-position. The biological activity of synthesized compounds would be reported in due course.

Scheme 4. Synthesis of ethyl 1,2,3,7-tetrahydro-2,7-dioxopyrido[1,2,3-de]quinoxaline-6-carboxylate **6a–c**.



EXPERIMENTAL

Reagent grade solvents were dried according to standard techniques. Sodium sulfate was used as a drying agent for water containing organic phases. All reported yields are of isolated products and are not optimized. Reactions were routinely monitored by TLC on silica gel (F245 Merck plates). Chromatographic spots were visualized by UV light. Purification of crude compounds and separation of reaction mixtures were carried out by column chromatography on silica gel 60 [230–400 mesh from Merck (Rome, Italy)]. Melting points (uncorrected) were determined in a 240 Buchi-Tottoli melting point apparatus (Butchi Italia S.R.L, Milano, Italy). Chemical shifts (δ) are reported in parts per million (ppm) relative to the solvent central peak. ^{1}H-NMR spectra were recorded at 200 or 400 MHz on a Bruker AC 200 spectrometer (Bruker Italia, Milano, Italy). ESI/MS was performed with an Agilent 1100 Series LC/MSD model (Agilent Technologies Italia S.P.A., Milano, Italy) in positive scan mode. The molecular weights from the MS spectra were in full agreement with the proposed chemical structures of target compounds. Elemental analysis data for final compounds were obtained from the micro-analytical laboratory of the Department of Chemistry, Ferrara University, and were within ±0.40 of the theoretical values for the formulas given.

Synthesis of 4,5-dihydro-1*H*-benzo[*b*][1,4]diazepin-2(3*H*)-one (7). A mixture of 1,2-phenyldiamine (0.018 mol) and 60% aqueous acrylic acid (0.027 mol) dissolved in water (3.5 mL) and conc. hydrochloric acid (3.5 mL) was stirred at 70°C for 3 h (TLC). The solvent was evaporated by distillation, basified with conc. ammonium hydroxide. The reaction mixture was partitioned between H_2O and ethyl acetate (EtOAc). The EtOAc layer was washed with brine and dried over Na_2SO_4. The solvent was evaporated under reduced pressure. The desired product was crystallized from EtOAc to afford 4,5-dihydro-1*H*-benzo[*b*][1,4]diazepin-2(3*H*)-one **7** (2 g, 68%) as pale white solid, mp 138°C, MS *m/z* 163 (MH^+). ^{1}H-NMR (200 MHz,

DMSO): δ 2.72 (t, J = 5.4 Hz, 2H, H-3); 3.65 (m, 2H, H-4); 4.10 (br s, 1H, NH); 7.02–6.70 (m, 4H); 7.99 (br s, 1H, CONH).

Synthesis of diethyl 2-[(1,2,3,4-tetrahydro-2-oxobenzo[*b*][1,4]diazepin-5-yl)methylene]malonate (8). A mixture of 4,5-dihydro-1*H*-benzo[*b*][1,4]diazepin-2(3*H*)-one **7** (0.8 g, 0.005 mol) and DEEM (1 g, 0.005 mol) was heated at 140°C for 1 h. The reaction mixture was poured into *n*-hexane, and the precipitate was collected by filtration to give the desired compound as a pale white solid (90%) that was filtered and used without purification in the next step.

Synthesis of ethyl 2,3,4,8-tetrahydro-2,8-dioxo-1*H*-[1,4]diazepino[3,2,1-ij]quinoline-7-carboxylate (4). A mixture of diethyl 2-((1,2,3,4-tetrahydro-2-oxobenzo[*b*][1,4]diazepin-5-yl) methylene)malonate **8** (1 g, 0.003 mol) and PPA (5 g) was heated at 130°C for 1 h. The mixture was poured into ice and water to form a white precipitate that was filtered and washed with cold water yielding (0.8 g, 95%) the target compound as a white solid, mp 295°C, MS *m*/*z* 287 (MH^+). *Anal*. Calcd for $C_{15}H_{14}N_2O_4$: C, 62.93; H, 4.93; N, 9.79. Found: C, 63.20; H, 4.72; N, 9.98. ^{1}H-NMR (200 MHz, DMSO): δ 1.28 (t, J = 7.2 Hz, 3H, CH_3-ester); 2.96 (t, J = 4.8 Hz, 2H, H-3); 4.23 (q, J = 7.2 Hz, 2H, CH_2-ester); 4.51 (t, J = 4.6 Hz, 2H, H-4); 7.50–7.25 (m, 2H); 8.10–8.00 (m, 1H): 8.53 (s, 1H, NH); 10.11 (br s, 1H, CONH). ^{13}C-NMR (100 MHz, DMSO): δ 14.3, 36.4, 52.2, 59.7, 108.5, 121.5, 124.5, 125.7, 129.0, 130.1, 130.6, 150.2, 164.3, 172.2, 173.7.

Synthesis of 2,3-dihydro-1*H*-benzo[*b*][1,4]diazepines (9). Compounds **9a–c** were obtained as described in literature [4].

General synthetic procedure for of 2,3,4,5-tetrahydro-1*H*-benzo[*b*][1,4]diazepine (12). A mixture of benzodiazepine **9** (0.02 mol), methanol (50 mL), and sodium borohydride (0.02 mol) was stirred at room temperature for 2 h (TLC) (for compound **12c**, the reaction mixture was stirred at 40°C for 8 h). Methanol was evaporated under reduced pressure, and the reaction mixture was partitioned between H_2O and ethyl acetate (EtOAc). The organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The resulting product was purified on silica gel column.

2,3,4,5-Tetrahydro-2,2,4-trimethyl-1H-benzo[b][1,4]diazepine (12a). Pale white solid (80%), mp 60–61°C, MS *m*/*z* 191 (MH^+). ^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.08 (s, 3H, CH_3-2); 1.22 (d, J = 6.4 Hz, 3H, CH_3-4); 1.32 (s, 3H, CH_3-2); 1.66–1.53 (m, 2H, H-3); 3.22 (m, 1H, H-4); 3.26 (br s, 2H, NH); 6.79–6.61 (m, 4H).

2,3,3a,4,9,10a-Hexahydro-1H-spiro[benzo[b]cyclopenta[e][1,4]diazepine-10,1′-cyclopentane] (12b). Pale yellow solid (75%), mp 70°C, MS *m*/*z* 243 (MH^+). ^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.2–2.7 (m, 15H); 3.5 (m, 1H, H-4); 4.00 (br s, 2H, NH); 6.61–6.70 (m, 4H).

2,3,4,5-Tetrahydro-2-methyl-2,4-diphenyl-1H-benzo[b][1,4]diazepine (12c). Pale white solid (80%), mp 132–133°C, MS *m*/*z* 315 (MH^+). ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.64 (s, 3H, CH_3-2); 1.88 (d d, J = 13.6 Hz, J = 2 Hz, 1H, H-3); 2.44 (m, 1H, H-3); 3.83 (br s, 2H, NH); 4.22 (d d, J = 13 Hz, J = 12 Hz, 1H, H-4); 6.83 (m, 4H); 7.46–7.25 (m, 8H); 7.73 (m, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 23.7, 55.4, 57.2, 57.7, 120.6, 122.3, 125.3, 126.7, 127.0, 127.7, 128.5, 128.8, 137.2, 139.7, 145.2, 150.3.

General synthetic procedure for diethyl 2-[(1,2,3,4-tetrahydro-2,2,4-trimethylbenzo[*b*][1,4]diazepin-5-yl)methylene]malonate (13a–c). Starting with 3,4,5-tetrahydro-2,2,4-trimethyl-1*H*-benzo [*b*][1,4]diazepines **12**, the title compounds were prepared in a manner analogous to that described for compound **8** in 85–90% yields. Compounds **13a–c** were used in the next step without purification.

General synthetic procedure for ethyl 2,3,4,8-tetrahydro-8-oxo-1*H*-[1,4]diazepino[3,2,1-*ij*]quinoline-7-carboxylate (5). Starting with diethyl 2-((1,2,3,4-tetrahydro-2,2,4-trimethylbenzo[*b*][1,4]diazepin-5-yl)methylene)malonates (**13a–c**), the title compounds were prepared in a manner analogous to that described for compound **4**.

Ethyl 2,3,4,8-tetrahydro-2,2,4-trimethyl-8-oxo-1H-[1,4]diazepino[3,2,1-ij]quinoline-7-carboxylate (5a). Purification on silica gel column: EtOAc : *n*-hexane 7/3, yellow solid (40%), mp 126°C, MS *m*/*z* 315 (MH^+). *Anal*. Calcd for $C_{18}H_{22}N_2O_3$: C, 68.77; H, 7.05; N, 8.91. Found: C, 69.07; H, 7.24; N, 8.72. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.16 (s, 3H, CH_3-2); 1.28 (s, 3H, CH_3-2); 1.41 (t, J = 7.2 Hz, 3H, CH_3-ester); 1.95 (m, 1H, H-3); 2.07 (d d, J = 14 Hz, J = 3.2 Hz, 1H, H-3); 3.46 (br s, 1H, NH); 4.39 (q, 2H, J = 7.6 Hz, CH_2-ester); 4.93 (m, 1H, H-4); 6.91 (m, 1H); 7.18 (m, 1H); 8.07 (m, 1H); 8.52 (s, 1H, H-6). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 14.5, 21.5, 30.2, 32.0, 46.7, 54.7, 60.0, 60.8, 109.5, 120.1, 123.76, 125.8, 138.0, 146.2, 166.7, 174.1.

Ethyl 3-oxo-9,10,11,11a-tetrahydro-3H,7H,8aH-spiro[cyclopenta[6,7][1,4]diazepino[3,2,1-ij]quinoline-8,1′-cyclopentane]-2-carboxylate (5b). Purification on silica gel column: EtOAc : *n*-hexane 1/1, pale yellow solid (35%), mp 109°C, MS *m*/*z* 367 (MH^+). *Anal*. Calcd for $C_{22}H_{26}N_2O_3$: C, 72.11; H, 7.15; N, 7.64. Found: C, 71.76; H, 6.87; N, 7.31. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.43 (t, J = 7.2 Hz, 3H, CH_3-ester); 1.58–2.04 (m, 14H); 2.39 (m, 1H, H-3); 3.72 (br s, 1H, NH); 4.39 (q, J = 7.2 Hz, 2H, CH_2-ester); 4.43 (m, 1H, H-4); 6.80 (m, 1H); 7.19 (m, 1H); 7.96 (m, 1H); 8.52 (s, 1H, H-6).

Ethyl 2,3,4,8-tetrahydro-2-methyl-8-oxo-2,4-diphenyl-1H-[1,4]diazepino[3,2,1-ij]quinoline-7-carboxylate (5c). Purification on silica gel column: EtOAc : *n*-hexane 8/2, pale white solid (40%), mp 150°C, MS *m*/*z* 439 (MH^+). *Anal*. Calcd for $C_{28}H_{26}N_2O_3$: C, 76.69; H, 5.98; N, 6.39. Found: C, 76.35; H, 5.76; N, 6.68. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.28 (t, J = 7.6 Hz, 3H, CH_3-ester); 1.64 (s, 3H, CH_3-2); 2.72 (d d, J = 15.2 Hz, J = 2 Hz, 1H, H-3); 3.37 (d d, J = 15.2 Hz, J = 8.4 Hz, 1H, H-3); 3.77 (br s, 1H, NH); 4.25 (q, J = 7.2 Hz, 2H, CH_2-ester); 5.99 (d d, J = 8.4 Hz, J = 1.6 Hz, 1H, H-4); 6.98 (m, 1H); 7.29–7.11 (m, 11H); 8.11 (s, 1H, H-6); 8.16 (m, 1H).

General synthetic procedure for 3,4-dihydroquinoxalin-2(1*H*)-one (14). Starting with (4-substituted)-*o*-phenylenediamine, the title compounds were prepared as described in literature [12].

3,4-Dihydroquinoxalin-2(1H)-one (14a). Purified on silica gel column (EtOAc : *n*-hexane 1/1), tan solid (55%), mp 127–129°C, MS *m*/*z* 149 (MH^+). ^{1}H-NMR (200 MHz, $CDCl_3$): δ 3.40 (br s, 1H, NH); 3.99 (s, 2H, CH_2); 6.93–7.20 (m, 4H); 8.92 (br s, 1H, NHCO).

6-Fluoro-3,4-dihydroquinoxalin-2(1H)-one (14b). Purified on silica gel column (EtOAc : *n*-hexane 8/2), tan solid (60%), mp 245–246°C, MS *m*/*z* 167 (MH^+). ^{1}H-NMR (200 MHz, $CDCl_3$): δ 3.68 (s, 2H, CH_2); 5.88 (br s, 1H, NH); 7.05–7.21 (m, 2H); 7.84 (m, 1H); 10.32 (br s, 1H, NHCO).

6-Chloro-3,4-dihydroquinoxalin-2(1H)-one (14c). Purified on silica gel column (EtOAc : *n*-hexane 1/1), tan solid (55%), mp 214–215°C, MS *m*/*z* 183 (MH^+). ^{1}H-NMR (200 MHz, $CDCl_3$): δ 3.65 (s, 2H, CH_2); 5.80 (br s, 1H, NH); 6.99–7.05 (m, 2H); 7.20 (m, 1H); 10.00 (br s, 1H, NHCO)

General synthetic procedure for diethyl 2-[(2,3-dihydro-2-oxoquinoxalin-4(1*H*)-yl)methylene]malonate (15). Starting with

3,4-dihydroquinoxalin-2(1*H*)-one (**14a–c**), the title compounds were prepared (70–75%) in a manner analogous to that described for compound **8**. Compounds **15a–c** were used in the next step without purification.

General synthetic procedure for ethyl 1,2,3,7-tetrahydro-2,7-dioxopyrido[1,2,3-*de*]quinoxaline-6-carboxylate (6). Starting with diethyl 2-((2,3-dihydro-2-oxoquinoxalin-4(1*H*)-yl) methylene)malonates **15a–c**, the title compounds were prepared in a manner analogous to that described for compound **4**.

Ethyl 1,2,3,7-tetrahydro-2,7-dioxopyrido[1,2,3-de]quinoxaline-6-carboxylate (6a). Purified on silica gel column (EtOAc : methanol 9/1), white solid. (55%), mp >300°C, MS *m/z* 273 (MH^+). *Anal.* Calcd for $C_{14}H_{12}N_2O_4$: C, 61.76; H, 4.44; N, 10.29. Found: C, 61.77; H, 4.45; N, 10.26. ^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.28 (t, *J* = 7 Hz, 3H, CH_3-ester), 4.17 (q, *J* = 7 Hz, 2H, CH_2-ester); 5.01 (s, 2H, CH_2-2); 7.37–7.15 (m, 2H); 7.71 (m, 1H); 8.51 (s, 1H, H-5); 11.16 (br s, 1H, NHCO). ^{13}C-NMR (100 MHz, DMSO): δ 14.3, 52.0, 59.8, 111.0, 116.6, 118.9, 125.2, 126.0, 127.6, 129.3, 147.2, 162.2, 164.3, 172.2.

Ethyl 9-fluoro-1,2,3,7-tetrahydro-2,7-dioxopyrido[1,2,3-de] quinoxaline-6-carboxylate (6b). Purified on silica gel column (EtOAc), white solid (50%), mp >300°C, MS *m/z* 291 (MH^+). *Anal*. Calcd for $C_{14}H_{11}FN_2O_4$: C, 57.93; H, 3.82; N, 9.65. Found: C, 57.96; H, 3.61; N, 9.62. ^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.27 (t, *J* = 7.4 Hz, 3H, CH_3-ester), 4.18 (q, *J* = 7.22 Hz, 2H, CH_2-ester); 5.02 (s, 2H, CH_2-2); 7.17–7.11 (m, 1H); 7.56–7.51 (m, 1H); 8.55 (s, 1H, H-5); 11.18 (br s, 1H, CONH). ^{16}F-NMR (397 MHz, DMSO): δ = −114.094 (t, 1 F, *J* = 10 Hz, F-9).

Ethyl 9-chloro-1,2,3,7-tetrahydro-2,7-dioxopyrido[1,2,3-de] quinoxaline-6-carboxylate (6c). Purified on silica gel column (EtOAc), white solid (50%), mp 292°C, MS *m/z* 307 (MH^+). *Anal*. Calcd for $C_{14}H_{11}ClN_2O_4$: C, 54.83; H, 3.62; N, 9.13. Found: C, 54.79; H, 3.60; N, 9.11. ^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.25 (t, *J* = 7.4 Hz, 3H, CH_3-ester), 4.18 (q, *J* = 7.2 Hz, 2H, CH_2-ester); 5.01 (s, 2H, CH_2-2); 7.13 (s, 1H); 7.71 (m, 1H); 8.51 (s, 1H); 11.16 (br s, 1H, NHCO).

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