Furan Ring Opening–Pyrrole Ring Closure: A New Route to Pyrrolo[1,2-*d*][1,4]benzodiazepin-6-ones

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Abstract: A new method for the synthesis of pyrrolo[1,2-*d*][1,4]benzodiazepines is described. The method is based on the acid-catalyzed recyclization of *N*-[2-(5-alkyl-2-furyl)phenyl]-2-aminoacetamides and permits the formation of both diazepine and pyrrole rings in one pot. The reaction proceeds via furan ring opening to give the diketone moiety followed by consecutive reactions of the free amino group with both carbonyl functions.

Key words: furans, ring opening, ring closure, fused-ring system, pyrrolo[1,2-*d*][1,4]benzodiazepines, Paal–Knorr reaction

Pyrrolo[1,4]diazepines represent an important class of compounds that are extensively utilized in pharmacology and medicine. Among them, the most frequently studied are the 'anthramycins' produced by *Streptomyces* sp.[1,2] These natural antitumor antibiotics are pyrrolo[2,1-*c*][1,4]benzodiazepine derivatives.[3] It is also known that pyrrolo[1,2-*a*][1,4]benzodiazepines exhibit a wide spectrum of biological activity.[4] On the other hand, pyrrolo[1,2-*d*][1,4]benzodiazepines are less well-studied,[5] though some of them reveal antiviral (including anti-HIV-1) activity.[5c]

Most known methods for the synthesis of pyrrolodiazepines are based on the annulation of a diazepine ring to pyrrole moiety.[6] To the best of our knowledge, only one method for the synthesis of pyrrolobenzodiazepines, based on the intramolecular Paal–Knorr reaction leading to the simultaneous formation of pyrrole and diazepine rings, has been hitherto described.[7] This approach is under-investigated, which is evidently related to the fact that the procedure for the synthesis of suitable 1,4-dicarbonyl compounds is quite time-consuming.

However, it is well known, that furan derivatives can serve as precursors of 1,4-diketones.[8] This feature of the furan ring has already been used in a two-step synthesis of pyrrolodiazepines.[4b,9] In this procedure, pyrrole derivatives were initially obtained and the diazepine ring was annulated in the next step. Recently, we have developed a simple and efficient method for the synthesis of pyrrolo[1,2-*a*][1,4]diazepines **1** which is based on the acid-catalyzed recyclization of the corresponding *N*-furfuryl-amides **2** (Scheme 1).[10] This process represents a domino reaction, in which the furan ring opening, pyrrole formation, and diazepine ring closure take place in one pot. Extending our research in this field, herein we present an application of this methodology to the synthesis of pyrrolo[1,2-*d*][1,4]benzodiazepines.

As starting compounds for the synthesis of pyrrolo[1,2-*d*][1,4]benzodiazepines, we have used 2-(2-aminoaryl)furans **3**, which were obtained according to the known, simple procedure.[11] Treatment of anilines **3a–f** with 2-(phthalimido)acetyl chloride (**4**) in benzene afforded amides **5a–f** (Scheme 2, Table 1). Refluxing compounds **5** in an ethanolic solution of hydrazine hydrate for a short time led to corresponding amines **6a–f**. The amines **6** were refluxed in a mixture of acetic acid and hydrochloric acid (5:1) for 40 minutes. Then, sodium hydrogen carbonate was added to the cooled reaction mixture in the amount which is required to neutralize hydrochloric acid only (if acetic acid was also neutralized, yields of the goal products dropped significantly). The target pyrrolodiazepines **8a–f** were isolated in moderate yields after reflux of the obtained reaction mixture for 20 minutes. It should be noted that moderate yields of the products **8** were caused by incomplete conversion of furans **6** into diketones **7**. Indeed, the starting compounds **6** can be isolated from the reaction mixture. A possible reason seems to be the conjugation of the furan and the aromatic ring. This fact is in accordance with the results obtained previously.[9c]

In summary, the proposed previously methodology of one-pot furan ring opening, pyrrole ring closure, and diazepine formation is a common approach to pyrrolodiaz-

Table 1 Yields of Compounds **5a–f**, **6a–f**, and **8a–f**

Entry	R^1	R^2	Products **5**, **6**, **8**	Yield (%)		
				5	**6**	**8**
1	H	Me	**a**	73	83	31
2	Me	Me	**b**	78	84	34
3	Cl	Me	**c**	85	88	36
4	OMe	Me	**d**	82	80	42
5	H	Et	**e**	84	82	30
6	Cl	Et	**f**	75	85	29

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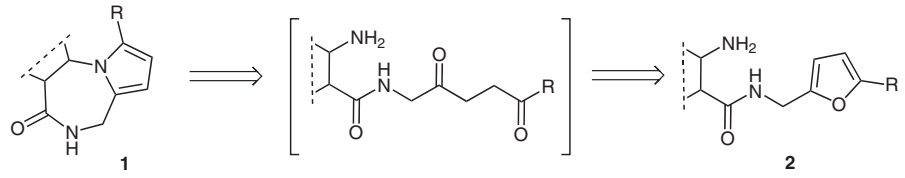
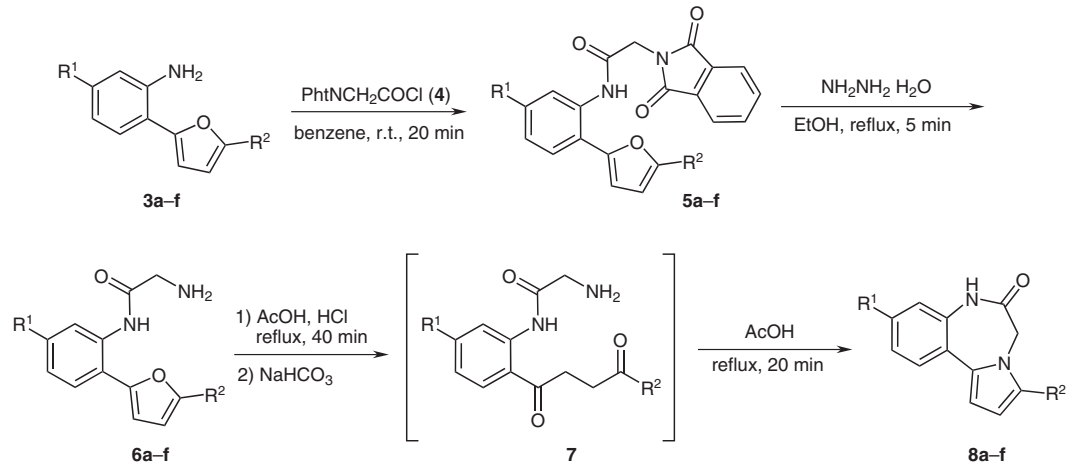


Scheme 1 A new method for the formation of pyrrolo[1,2-*a*][1,4]diazepine moiety via the furan ring opening–pyrrole ring closure sequence



Scheme 2 Synthesis of pyrrolo[1,2-*d*][1,4]benzodiazepin-6-ones **8a–f** from furans **3a–f**

epines. We showed here that it can be applied to the synthesis of pyrrolo[1,2-*d*][1,4]benzodiazepines.

NMR spectra were recorded with a Bruker DPX 300 (300 MHz for ^{1}H and 75 MHz for ^{13}C NMR) spectrometer at r.t.; measured with respect to the solvent [$CDCl_3$, δ = 7.25 (^{1}H), 77.2 (^{13}C); DMSO-d_6, δ = 2.50 (^{1}H), 39.5 (^{13}C)]. IR spectra were measured as KBr plates on a Bruker Alpha FT-IR spectrophotometer. Mass spectra were recorded on a Kratos MS-30 instrument with 70 eV electron-impact ionization at 200 °C. Melting points (uncorrected) were determined in capillaries with an Electrothermal 9100 capillary melting point apparatus. Column chromatography was performed on silica gel KSK (50–160 μm, LTD Sorbpolymer). All reactions were performed using freshly distilled and dry solvents. PE = petroleum ether.

Compounds **3** were synthesized according to the previously published procedure.[11]

N-[2-(5-Alkyl-2-furyl)phenyl]-2-(1,3-dioxo-1,3-dihydro-2*H*-isoindol-2-yl)acetamides 5a–f; General Procedure

A soln of 2-(phthalimido)acetyl chloride (**4**, 4.5 g, 20.1 mmol) in benzene (100 mL) was added dropwise under stirring to a soln of furan **3** (16 mmol) in benzene (25 mL) at r.t. The mixture was stirred at r.t. for 20 min (TLC monitoring). Then, it was poured into H_2O (150 mL), $NaHCO_3$ (4 g) was added, and the mixture was vigorously stirred for 30 min. The precipitate was collected by filtration, washed with H_2O (100 mL) and dried. The crude product was purified by flash chromatography (silica gel, 1,4-dioxane–PE, 3:1) and recrystallized (1,4-dioxane–PE, 2:1).

2-(1,3-Dioxo-1,3-dihydro-2*H*-isoindol-2-yl)-*N*-[2-(5-methyl-2-furyl)phenyl]acetamide (5a)

White solid; yield: 4.20 g (73%); mp 237–238 °C.

IR (KBr): 3225, 1730, 1667, 1548, 1536, 1416, 953, 760, 707 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.38 (s, 3 H, CH_3), 4.48 (s, 2 H, CH_2), 6.26 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 6.80 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 7.25–7.29 (m, 2 H, H_{Ar}), 7.36–7.40 (m, 1 H, H_{Ar}), 7.67–7.71 (m, 1 H, H_{Ar}), 7.86–7.90 (m, 2 H, H_{Pht}), 7.91–7.95 (m, 2 H, H_{Pht}), 9.92 (s, 1 H, NH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 13.3, 40.6, 108.2, 110.2, 123.2 (2 C), 126.0 (2 C), 126.4, 127.2, 127.9, 131.7 (2 C), 132.0, 134.6 (2 C), 148.4, 151.6, 165.5, 167.6 (2 C).

MS (EI, 70 eV): *m*/*z* (%) = 360 (100) [M$^+$], 284 (34), 267 (32), 237 (21), 226 (19), 207 (35), 200 (40), 172 (52), 160 (80), 101 (31), 82 (22), 76 (58), 59 (77), 57 (54), 43 (35).

Anal. Calcd for $C_{21}H_{16}N_2O_4$: C, 69.99; H, 4.48; N, 7.77. Found: C, 70.17; H, 4.57; N, 7.96.

2-(1,3-Dioxo-1,3-dihydro-2*H*-isoindol-2-yl)-*N*-[5-methyl-2-(5-methyl-2-furyl)phenyl]acetamide (5b)

White wool; yield: 4.67 g (78%); mp 248–249 °C.

IR (KBr): 3256, 1728, 1668, 1579, 1536, 1416, 952, 714 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.29 (s, 3 H, CH_3), 2.37 (s, 3 H, CH_3), 4.46 (s, 2 H, CH_2), 6.23 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 6.72 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 7.10 (d, *J* = 8.1 Hz, 1 H, H_{Ar}), 7.19 (s, 1 H, H_{Ar}), 7.56 (d, *J* = 8.1 Hz, 1 H, H_{Ar}), 7.86–7.90 (m, 2 H, H_{Pht}), 7.91–7.95 (m, 2 H, H_{Pht}), 9.86 (s, 1 H, NH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 13.3, 20.5, 40.6, 108.0, 109.4, 123.2 (2 C), 123.4, 125.9, 127.2, 128.2, 131.7 (2 C), 131.9, 134.6 (2 C), 136.7, 148.6, 151.2, 165.5, 167.6 (2 C).

MS (EI, 70 eV): *m*/*z* (%) = 374 (100) [M$^+$], 186 (47), 160 (30), 144 (13), 104 (14), 76 (33), 75 (18), 59 (35), 43 (58), 42 (34).

Anal. Calcd for $C_{22}H_{18}N_2O_4$: C, 70.58; H, 4.85; N, 7.48. Found: C, 70.42; H, 4.68; N, 7.45.

N-[5-Chloro-2-(5-methyl-2-furyl)phenyl]-2-(1,3-dioxo-1,3-dihydro-2*H*-isoindol-2-yl)acetamide (5c)

Pale beige solid; yield: 5.36 g (85%); mp 221–223 °C.

IR (KBr): 3245, 1724, 1668, 1578, 1533, 1418, 1097, 952, 715 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 2.37 (s, 3 H, CH_3), 4.50 (s, 2 H, CH_2), 6.27 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 6.85 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 7.34 (dd, *J* = 2.4, 8.7 Hz, 1 H, H_{Ar}), 7.49 (d, *J* = 2.4 Hz, 1 H, H_{Ar}), 7.68 (d, *J* = 8.7 Hz, 1 H, H_{Ar}), 7.86–7.90 (m, 2 H, H_{Pht}), 7.91–7.96 (m, 2 H, H_{Pht}), 10.06 (s, 1 H, NH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 13.3, 40.6, 108.3, 110.9, 123.3 (2 C), 126.3, 127.0, 127.5 (2 C), 130.9, 131.7 (2 C), 133.2, 134.6 (2 C), 147.4, 152.1, 165.9, 167.5 (2 C).

MS (EI, 70 eV): *m*/*z* (%) = 396/394 (34/100) [M^+], 186 (47), 160 (30), 144 (13), 104 (14), 76 (33), 75 (18), 59 (35), 43 (58), 42 (34).

Anal. Calcd for $C_{21}H_{15}ClN_2O_4$: C, 63.89; H, 3.83; N, 7.10. Found: C, 63.58; H, 3.89; N, 7.00.

2-(1,3-Dioxo-1,3-dihydro-2*H*-isoindol-2-yl)-*N*-[5-methoxy-2-(5-methyl-2-furyl)phenyl]acetamide (5d)
White wool; yield: 5.12 g (82%); mp 190–191 °C.

IR (KBr): 3249, 1725, 1669, 1583, 1541, 1416, 1293, 1237, 1036, 952, 715 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 2.36 (s, 3 H, CH_3), 3.75 (s, 3 H, OCH_3), 4.47 (s, 2 H, CH_2), 6.21 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 6.64 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 6.87 (dd, *J* = 2.7, 8.7 Hz, 1 H, H_{Ar}), 7.03 (d, *J* = 2.7 Hz, 1 H, H_{Ar}), 7.57 (d, *J* = 8.7 Hz, 1 H, H_{Ar}), 7.86–7.90 (m, 2 H, H_{Pht}), 7.91–7.95 (m, 2 H, H_{Pht}), 9.86 (s, 1 H, NH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 13.3, 40.6, 55.3, 107.9, 108.5, 112.2, 112.3, 123.2 (2 C), 127.4 (2 C), 131.7 (2 C), 133.4, 134.6 (2 C), 148.5, 150.8, 158.2, 165.5, 167.5 (2 C).

MS (EI, 70 eV): *m*/*z* (%) = 390 (100) [M^+], 347 (13), 299 (11), 264 (14), 246 (10), 203 (15), 160 (94), 89 (13), 59 (29), 43 (24).

Anal. Calcd for $C_{22}H_{18}N_2O_5$: C, 67.69; H, 4.65; N, 7.18. Found: C, 67.90; H, 4.74; N, 7.20.

2-(1,3-Dioxo-1,3-dihydro-2*H*-isoindol-2-yl)-*N*-[2-(5-ethyl-2-furyl)phenyl]acetamide (5e)
White solid; yield: 5.03 g (84%); mp 219–220 °C.

IR (KBr): 3257, 1730, 1667, 1535, 1415, 1287, 952, 760, 716 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 1.25 (t, *J* = 7.5 Hz, 3 H, CH_3), 2.73 (q, *J* = 7.5 Hz, 2 H, CH_2), 4.48 (s, 2 H, CH_2), 6.27 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 6.82 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 7.26–7.29 (m, 2 H, H_{Ar}), 7.37–7.40 (m, 1 H, H_{Ar}), 7.67–7.70 (m, 1 H, H_{Ar}), 7.86–7.90 (m, 2 H, H_{Pht}), 7.91–7.95 (m, 2 H, H_{Ar}), 9.92 (s, 1 H, NH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 12.1, 20.8, 40.6, 106.7, 110.0, 123.2 (2 C), 126.0, 126.1, 126.4, 127.2, 127.8, 131.7 (2 C), 132.0, 134.6 (2 C), 148.3, 157.1, 165.5, 167.5 (2 C).

MS (EI, 70 eV): *m*/*z* (%) = 374 (100) [M^+], 214 (14), 198 (29), 186 (68), 172 (29), 170 (29), 160 (45), 133 (45), 117 (21), 105 (32), 77 (40), 59 (19), 43 (18), 42 (20).

Anal. Calcd for $C_{22}H_{18}N_2O_4$: C, 70.58; H, 4.85; N, 7.48. Found: C, 70.52; H, 4.92; N, 7.39.

***N*-[5-Chloro-2-(5-ethyl-2-furyl)phenyl]-2-(1,3-dioxo-1,3-dihydro-2*H*-isoindol-2-yl)acetamide (5f)**
White wool; yield: 4.90 g (75%); mp 225–226 °C.

IR (KBr): 3246, 1724, 1674, 1577, 1531, 1417, 1265, 1197, 950, 716 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 1.25 (t, *J* = 7.5 Hz, 3 H, CH_3), 2.73 (q, *J* = 7.5 Hz, 2 H, CH_2), 4.50 (s, 2 H, CH_2), 6.29 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 6.86 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 7.34 (dd, *J* = 2.1, 8.7 Hz, 1 H, H_{Ar}), 7.50 (d, *J* = 2.1 Hz, 1 H, H_{Ar}), 7.69 (d, *J* = 8.7 Hz, 1 H, H_{Ar}), 7.86–7.90 (m, 2 H, H_{Pht}), 7.91–7.96 (m, 2 H, H_{Pht}), 10.06 (s, 1 H, NH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 12.0, 20.8, 40.6, 106.9, 110.7, 123.3 (2 C), 124.5, 126.2, 126.9, 127.6, 130.9, 131.7 (2 C), 133.2, 134.6 (2 C), 147.3, 157.5, 165.8, 167.5 (2 C).

MS (EI, 70 eV): *m*/*z* (%) = 410/408 (32/92) [M^+], 242 (62), 222 (67), 220 (100), 206 (30), 166 (15), 160 (96), 133 (20), 104 (25), 76 (10), 59 (17), 43 (59), 42 (34).

Anal. Calcd for $C_{22}H_{17}ClN_2O_4$: C, 64.63; H, 4.19; N, 6.85. Found: C, 64.54; H, 4.27; N, 7.02.

2-Amino-*N*-[2-(5-alkyl-2-furyl)phenyl]acetamides 6a–f; General Procedure
Hydrazine hydrate (4 mL) was added to a soln of amide **5** (8 mmol) in EtOH and the mixture was refluxed for 5 min (TLC monitoring). Then the mixture was evaporated under reduced pressure. CCl_4 (40 mL) was added to the residue and it was stirred vigorously. The obtained solid was collected by filtration and washed with CCl_4 (3 × 40 mL). The organic fractions were evaporated under reduced pressure. The residue was dissolved in EtOAc, passed through a pad of silica gel, and concentrated.

Amines **6a**,**b**,**e** were obtained as chromatographically pure light-yellow oils and used for the next step without additional purification. The compounds **6c**,**d**,**f** were recrystallized (EtOAc–PE, 1:1).

2-Amino-*N*-[5-chloro-2-(5-methyl-2-furyl)phenyl]acetamide (6c)
Cream plates; yield: 1.86 g (88%); mp 105–106 °C.

IR (KBr): 3412, 3258, 1673, 1574, 1515, 1456, 1411, 1260, 1028, 909, 815, 783 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.36 (s, 3 H, CH_3), 3.50 (s, 2 H, CH_2), 6.09 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 6.52 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 7.05 (dd, *J* = 2.1, 8.4 Hz, 1 H, H_{Ar}), 7.43 (d, *J* = 8.4 Hz, 1 H, H_{Ar}), 8.57 (d, *J* = 2.1 Hz, 1 H, H_{Ar}), 10.46 (s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.7, 45.6, 107.7, 109.2, 119.0, 121.1, 123.9, 127.9, 133.7, 134.7, 149.4, 152.4, 171.2.

MS (EI, 70 eV): *m*/*z* (%) = 266/264 (36/100) [M^+], 247 (30), 235 (29), 207 (77), 195 (38), 193 (42), 166 (70), 164 (59), 143 (40), 128 (32), 102 (27), 70 (22), 59 (29), 43 (43), 42 (45).

Anal. Calcd for $C_{13}H_{13}ClN_2O_2$: C, 58.99; H, 4.95; N, 10.58. Found: C, 59.11; H, 5.15; N, 10.74.

2-Amino-*N*-[5-methoxy-2-(5-methyl-2-furyl)phenyl]acetamide (6d)
Beige prisms; yield: 1.66 g (80%); mp 99–101 °C.

IR (KBr): 3406, 3277, 1690, 1575, 1517, 1474, 1422, 1301, 1169, 1031, 789 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.26 (s, 3 H, CH_3), 3.40 (s, 2 H, CH_2), 3.73 (s, 3 H, OCH_3), 5.97 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 6.30 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 6.57 (dd, *J* = 2.7, 8.7 Hz, 1 H, H_{Ar}), 7.31 (d, *J* = 8.7 Hz, 1 H, H_{Ar}), 8.10 (d, *J* = 2.7 Hz, 1 H, H_{Ar}), 10.41 (s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.6, 45.7, 55.4, 105.7, 107.4, 107.5, 110.6, 113.6, 128.3, 135.3, 150.4, 151.4, 159.6, 171.2.

MS (EI, 70 eV): *m*/*z* (%) = 260 (100) [M^+], 243 (12), 230 (20), 202 (47), 189 (50), 160 (84), 118 (18), 101 (19), 77 (17), 71 (31), 59 (43), 43 (73).

Anal. Calcd for $C_{14}H_{16}N_2O_3$: C, 64.60; H, 6.20; N, 10.76. Found: C, 64.82; H, 6.46; N, 10.99.

2-Amino-*N*-[5-chloro-2-(5-ethyl-2-furyl)phenyl]acetamide (6f)
Colorless prisms; yield: 1.90 g (85%); mp 64–65 °C.

IR (KBr): 3404, 3247, 1673, 1574, 1516, 1462, 1413, 1261, 1041, 820, 801, 781 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.27 (t, *J* = 7.5 Hz, 3 H, CH_3), 2.71 (q, *J* = 7.5 Hz, 2 H, CH_2), 3.50 (s, 2 H, CH_2), 6.10 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 6.54 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 7.06 (dd, *J* = 2.4, 8.4 Hz, 1 H, H_{Ar}), 7.44 (d, *J* = 8.4 Hz, 1 H, H_{Ar}), 8.56 (d, *J* = 2.4 Hz, 1 H, H_{Ar}), 10.50 (s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.0, 21.4, 45.6, 106.1, 109.1, 119.1, 121.1, 124.0, 128.0, 133.7, 134.7, 149.2, 158.1, 171.2.

MS (EI, 70 eV): *m*/*z* (%) = 280/278 (32/100) [M^+], 248 (32), 232 (32), 221 (87), 206 (48), 193 (59), 164 (40), 128 (29), 101 (22), 71 (33), 57 (31), 43 (46).

Anal. Calcd for $C_{14}H_{15}ClN_2O_2$: C, 60.33; H, 5.42; N, 10.05. Found: C, 60.19; H, 5.43; N, 9.89.

3-Alkyl-5*H*-pyrrolo[1,2-*d*][1,4]benzodiazepin-6(7*H*)-ones 8a–f; General Procedure

Concd HCl (5 mL) was added to a soln of amine **6** (6 mmol) in AcOH (25 mL), and the mixture was refluxed for 40 min (TLC monitoring). Then, $NaHCO_3$ (5 g) was added to the mixture and it was refluxed for 20 min, poured into H_2O (150 mL), and neutralized till pH ~7. The obtained solid was collected by filtration, washed with H_2O (50 mL), dried, and purified by flash chromatography (silica gel, benzene–PE, 1:1); compounds **8** were recrystallized (benzene–PE, 1:1).

3-Methyl-5*H*-pyrrolo[1,2-*d*][1,4]benzodiazepin-6(7*H*)-one (8a)

White wool; yield: 0.39 g (31%); mp 213–214 °C.

IR (KBr): 3189, 1700, 1514, 1402, 1027, 804, 747 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.36 (s, 3 H, CH_3), 4.48 (s, 2 H, CH_2), 6.06 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 6.33 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 7.02–7.05 (m, 1 H, H_{Ar}), 7.18–7.29 (m, 2 H, H_{Ar}), 7.54–7.57 (m, 1 H, H_{Ar}), 8.40 (s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.1, 47.9, 106.6, 108.6, 121.6, 125.1, 125.6, 127.5, 128.8, 129.6, 130.4, 132.6, 169.0.

MS (EI, 70 eV): *m*/*z* (%) = 212 (100) [M^+], 184 (34), 168 (12), 150 (13), 103 (33), 75 (18), 59 (14), 43 (26), 42 (51).

Anal. Calcd for $C_{13}H_{12}N_2O$: C, 73.57; H, 5.70; N, 13.20. Found: C, 73.47; H, 5.82; N, 13.30.

3,9-Dimethyl-5*H*-pyrrolo[1,2-*d*][1,4]benzodiazepin-6(7*H*)-one (8b)

Colorless needles; yield: 0.46 g (34%); mp 218–219 °C.

IR (KBr): 3192, 1694, 1523, 1400, 1027, 812, 750 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.36 (s, 6 H, 2 CH_3), 4.46 (s, 2 H, CH_2), 6.05 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 6.29 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 6.85 (d, *J* = 1.2 Hz, 1 H, H_{Ar}), 7.02 (dd, *J* = 1.2, 7.8 Hz, 1 H, H_{Ar}), 7.44 (d, *J* = 7.8 Hz, 1 H, H_{Ar}), 8.56 (s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.1, 21.0, 47.9, 105.9, 108.4, 121.9, 122.3, 126.6, 128.7, 129.1, 130.5, 132.5, 137.7, 169.1.

MS (EI, 70 eV): *m*/*z* (%) = 226 (100) [M^+], 198 (24), 113 (24), 59 (60), 56 (33), 43 (59), 42 (31).

Anal. Calcd for $C_{14}H_{14}N_2O$: C, 74.31; H, 6.24; N, 12.38. Found: C, 74.40; H, 6.12; N, 12.21.

9-Chloro-3-methyl-5*H*-pyrrolo[1,2-*d*][1,4]benzodiazepin-6(7*H*)-one (8c)

White solid; yield: 0.53 g (36%); mp 245–247 °C.

IR (KBr): 3180, 1696, 1578, 1509, 1405, 1102, 813, 750 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.36 (s, 3 H, CH_3), 4.47 (s, 2 H, CH_2), 6.06 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 6.32 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 7.02 (d, *J* = 2.1 Hz, 1 H, H_{Ar}), 7.18 (dd, *J* = 2.1, 8.4 Hz, 1 H, H_{Ar}), 7.48 (d, *J* = 8.4 Hz, 1 H, H_{Ar}), 7.96 (s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.1, 47.8, 107.0, 108.9, 121.4, 123.6, 125.9, 129.4, 129.9, 130.0, 132.8, 133.3, 168.5.

MS (EI, 70 eV): *m*/*z* (%) = 248/246 (33/100) [M^+], 219 (14), 217 (14), 205 (10), 203 (13), 76 (15), 71 (21), 43 (27), 42 (19).

Anal. Calcd for $C_{13}H_{11}ClN_2O$: C, 63.29; H, 4.49; N, 11.36. Found: C, 63.26; H, 4.42; N, 11.37.

9-Methoxy-3-methyl-5*H*-pyrrolo[1,2-*d*][1,4]benzodiazepin-6(7*H*)-one (8d)

Colorless needles; yield: 0.61 g (42%); mp 184–185 °C.

IR (KBr): 3215, 1690, 1616, 1581, 1522, 1468, 1281, 1242, 1038, 802, 751 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.35 (s, 3 H, CH_3), 3.82 (s, 3 H, OCH_3), 4.46 (s, 2 H, CH_2), 6.04 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 6.23 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 6.57 (d, *J* = 2.4 Hz, 1 H, H_{Ar}), 6.79 (dd, *J* = 2.4, 8.4 Hz, 1 H, H_{Ar}), 7.46 (d, *J* = 8.4 Hz, 1 H, H_{Ar}), 8.79 (s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.0, 47.8, 55.5, 105.3, 106.5, 108.2, 112.0, 118.1, 128.6, 130.0, 130.3, 133.8, 159.1, 169.1.

MS (EI, 70 eV): *m*/*z* (%) = 242 (100) [M^+], 227 (13), 213 (8), 200 (11), 198 (11), 43 (30), 42 (16).

Anal. Calcd for $C_{14}H_{14}N_2O_2$: C, 69.41; H, 5.82; N, 11.56. Found: C, 69.49; H, 5.92; N, 11.77.

3-Ethyl-5*H*-pyrrolo[1,2-*d*][1,4]benzodiazepin-6(7*H*)-one (8e)

Beige needles; yield: 0.41 g (30%); mp 159–160 °C.

IR (KBr): 3224, 1671, 1582, 1510, 1472, 1405, 1216, 1024, 748 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.19 (t, *J* = 7.5 Hz, 3 H, CH_3), 2.61 (q, *J* = 7.5 Hz, 2 H, CH_2), 4.36 (s, 2 H, CH_2), 5.98 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 6.25 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 6.93–6.96 (m, 1 H, H_{Ar}), 7.08–7.18 (m, 2 H, H_{Ar}), 7.44–7.47 (m, 1 H, H_{Ar}), 8.76 (s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.9, 19.8, 47.9, 106.7, 107.0, 121.9, 125.2, 125.8, 127.7, 129.0, 130.8, 132.9, 136.0, 169.4.

MS (EI, 70 eV): *m*/*z* (%) = 226 (67) [M^+], 211 (100), 183 (9), 45 (14), 43 (31), 41 (17).

Anal. Calcd for $C_{14}H_{14}N_2O$: C, 74.31; H, 6.24; N, 12.38. Found: C, 74.65; H, 6.51; N, 12.27.

9-Chloro-3-ethyl-5*H*-pyrrolo[1,2-*d*][1,4]benzodiazepin-6(7*H*)-one (8f)

Colorless needles; yield: 0.45 g (29%); mp 195–196 °C.

IR (KBr): 3184, 1697, 1573, 1509, 1458, 1401, 1098, 814, 796, 748 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.30 (t, *J* = 7.5 Hz, 3 H, CH_3), 2.71 (q, *J* = 7.5 Hz, 2 H, CH_2), 4.46 (s, 2 H, CH_2), 6.08 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 6.34 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 7.07 (d, *J* = 2.1 Hz, 1 H, H_{Ar}), 7.17 (dd, *J* = 2.1, 8.4 Hz, 1 H, H_{Ar}), 7.48 (d, *J* = 8.4 Hz, 1 H, H_{Ar}), 9.01 (s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.7, 19.6, 47.6, 106.9, 107.1, 121.5, 123.5, 125.8, 129.6, 129.8, 132.7, 133.5, 136.2, 169.0.

MS (EI, 70 eV): *m*/*z* (%) = 262/260 (24/65) [M^+], 247/245 (38/100), 231 (13), 210 (14), 182 (17), 181 (25), 154 (14), 130 (14), 43 (25).

Anal. Calcd for $C_{14}H_{13}ClN_2O$: C, 64.50; H, 5.03; N, 10.74. Found: C, 64.54; H, 4.90; N, 10.62.

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