Furan Ring Opening–Pyrrole Ring Closure: Simple Route to 5-Alkyl-2-(aminomethyl)pyrroles

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Abstract: A simple route to 5-alkyl-2-(aminomethyl)pyrroles is proposed that is based on hydrolytic ring opening of 5-alkylfurfurylamines followed by pyrrole ring closure under Paal–Knorr conditions.

Key words: furans, ring opening, ring closure, pyrroles, polycycles

2-(Aminomethyl)pyrroles have a broad range of biological activities[1] and have been shown to be potential anti-inflammatory,[2] analgesic,[3] antidepressant,[4] antipsychotic,[5] or antitumor agents.[6] 2-(Aminomethyl)pyrroles have also been used in the treatment of attention-deficit hyperactive disorder;[7] they have also been used in the preparation of conformationally restricted peptidomimetics[8,9] and anion-binding receptors,[9,10] and for the synthesis of pyrrolodiazepines[11–13] and other bioactive molecules containing pyrrole units annulated to other heterocycles.[1i,13–15] The 2-(aminomethyl)pyrrole moiety is present in a variety of natural compounds such as porphobilinogen, an important intermediate in the biosynthesis of porphyrins, corrins, and chlorophylls.[16] 2-(Aminomethyl)pyrroles can be transformed into porphyrinogens,[17] pyrrodimethanes,[18] porphyrins, or porphocyanins.[19]

2-(Aminomethyl)pyrroles are usually synthesized by the reduction of the corresponding oximes,[1b,g,6a,9,10,20] nitriles,[1e,6a,19c,20b,21] azides,[1d,8b,12,14,22] or amides.[5a] Other approaches to 2-(aminomethyl)pyrroles include the reductive amination of pyrrole-2-carbaldehydes,[8d,23] the transformation of pyrrole-2-carbaldehydes into imines followed by addition of nucleophilic reagents,[24] aminoalkylation of pyrroles,[22b,25] nucleophilic substitution of bromine in 2-(bromomethyl)pyrroles,[5a,18a,26] and a variety of intramolecular condensation reactions.[8g,27]

One of the oldest and best-known methods for the synthesis of pyrroles is the Paal–Knorr reaction, i.e., the reaction of 1,4-diketones or their analogues with primary amines or ammonia.[28] However, the application of this approach to the synthesis of 2-(aminomethyl)pyrroles is very restricted,[1i,11,13] because of difficulties in preparing the necessary 1,4-diketones. 1-Phthalimido-2,5-diketones have been synthesized by a benzoin condensation-like addition of aldehydes to vinyl ketones in the presence of thiazolium salts as catalysts,[29] or by a three-step transformation of 2-(phthalimidomethyl)furans through formation of the corresponding 2,5-dimethoxy-2,5-dihydrofurans, ring opening, and double-bond hydrogenation.[11] An alternative route to these aminodiketones involves the reaction of *N*-(*tert*-butoxycarbonyl)glycine with potassium ethyl malonate followed by alkylation of the intermediate with a bromomethyl ketone.[1i] 1,4-Diketones can also be prepared by acid-catalyzed cleavage of a furan ring.[30]

When the starting furan contains a substituent that is appropriate for further transformation into an aminoalkyl group, a common sequence that involves cleavage of the furan ring followed by closure of the pyrrole ring can be used to provide an efficient synthesis of 2-(aminomethyl)pyrroles. Here, we describe an application of this approach to the transformation of 5-alkylfurfurylamines into the corresponding 5-alkyl-2-(aminomethyl)pyrroles by formation of 2-(phthalimidomethyl)furans as intermediates that undergo ring cleavage to give phthalimido diketones that are subjected to Paal–Knorr cyclization and removal of the phthalimide protecting group.

The starting *N*-furfurylphthalimides **3a–e** were synthesized in 65–79% yields by refluxing a mixture of the corresponding furfurylamine **1a–e**[31] with commercially available phthalic anhydride (**2**) in acetic acid for 15–30 minutes (Scheme 1).[11b] The furan ring can be subjected to acid-catalyzed cleavage by a variety of methods.[30] We used treatment with a mixture of acetic acid and hydrochloric acid, as we have shown that this method is efficient in a variety of furan recyclization reactions.[32] We found that furans **3b–d**, which have an alkyl group on the C5 atom, were transformed into the corresponding diketones **4b–d** in high yields when they were stirred in a mixture of acetic acid and hydrochloric acid at room temperature (Scheme 1). In contrast, under the same conditions imide **3a** failed to give **4a**, and instead of the diketone we obtained a resinous material, and when **3a** was heated to reflux in a mixture of the two acids, significant

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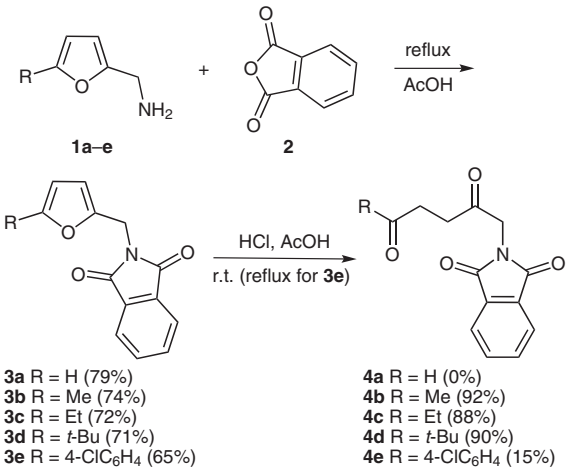
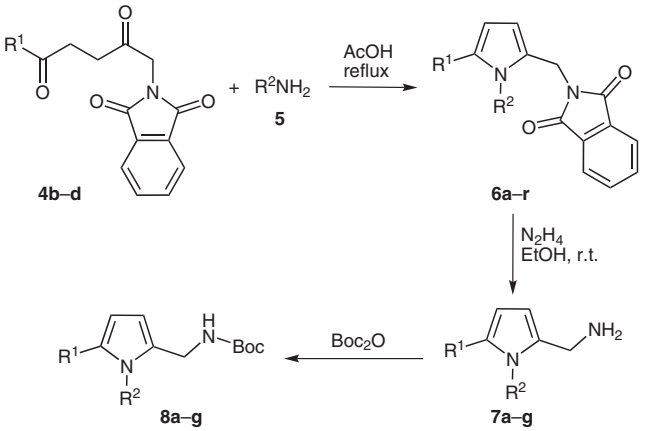
tarring occurred. We also found that the transformation of **3e** into **4e** was inefficient under these reaction conditions. At room temperature, the reaction was too slow, and only traces of **4e** were observed in the reaction mixture by TLC analysis after a solution of **3e** had been stirred in a mixture of acetic acid and hydrochloric acid for one week. By increasing the temperature, we were able to isolate **4e** in a small yield, but the conversion of **3e** was low even after refluxing the mixture for one day; increasing the reaction time had no effect on the efficiency of this reaction. We believe that in the case of **3e**, the reaction equilibrium is shifted toward the reagents side as a result of conjugation between the furan and chlorophenyl rings.



Scheme 1 Synthesis of *N*-furfurylphthalimides **3** and 1-phthalimido-2,5-diketones **4**

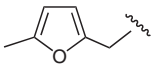
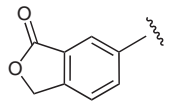
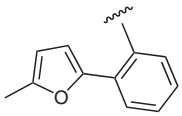
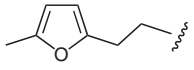
When mixtures of diketones **4b–d** with amines **5** were refluxed in acetic acid, the corresponding pyrroles **6a–r** were obtained (Scheme 2, Table 1). This transformation proceeded in moderate-to-good yields with aliphatic or aromatic amines, benzohydrazide, or 4-tolylsulfonohydrazide. Treatment of pyrroles **6a–g** with hydrazine hydrate in methanol at room temperature[33] gave the corresponding deprotected amines **7a–g**, which were characterized after transformation into the corresponding *N*-butoxycarbonyl derivatives **8a–g** (Scheme 2 and Table 1).

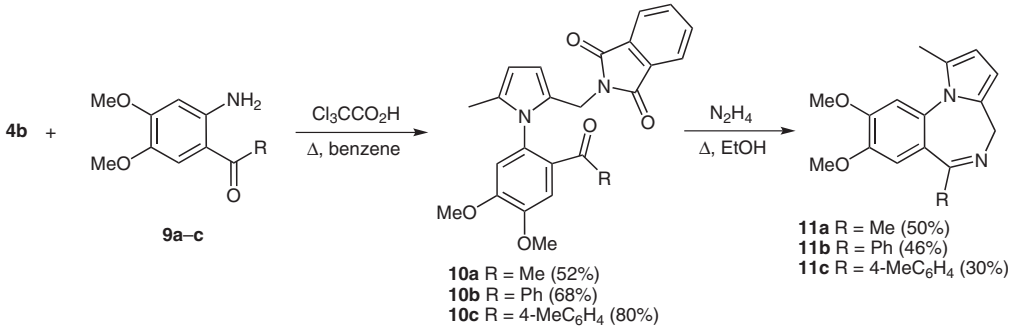


Scheme 2 Synthesis of 2-(phthalimidomethyl)pyrroles **6** by the Paal–Knorr reaction, and their transformation into the corresponding 2-[(*N*-butoxycarbonylamino)methyl]pyrroles **8**

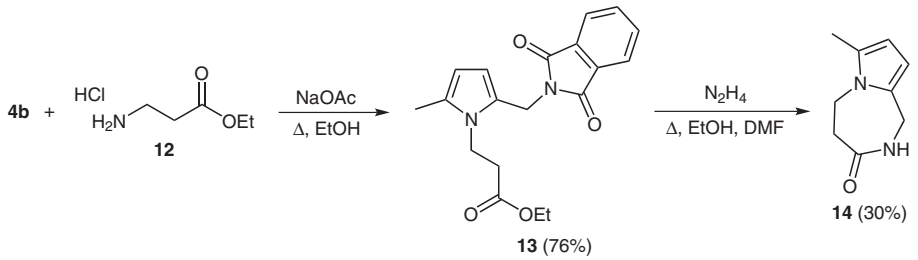
This approach was also used in the synthesis of pyrrolo[1,2-*a*][1,4]benzodiazepines **11a–c**. A solution of diketone **4b** in benzene was refluxed with anilines **9a–c** in the presence of catalytic amount of trichloroacetic acid to give the corresponding pyrroles **10a–c**. On heating with ethanolic hydrazine hydrate, pyrroles **10a–c** were transformed into the corresponding pyrrolo[1,2-*a*][1,4]benzodiazepines **11a–c** (Scheme 3).

Table 1 Synthesis of 2-(Phthalimidomethyl)pyrroles **6a–r** and 2-[(*N*-Butoxycarbonylamino)methyl]pyrroles **8a–g**

	R^1	R^2	Yield (%)			R^1	R^2	Yield (%)
			6	**8**				**6**
a	Me		85	82	**j**	Me	4-$O_2NC_6H_4$	68
b	Me	Bn	90	89	**k**	Me	4-$MeOC_6H_4$	84
c	Me	4-$F_3CC_6H_4$	83	72	**l**	Me	3-$MeOC_6H_4$	71
d	Me	*n*-Bu	78	63	**m**	Me	2,4-$(MeO)_2C_6H_3$	80
e	Me		80	67	**n**	Me		73
f	Me	NHC(O)Ph	90	76	**o**	Et	4-ClC_6H_4	78
g	Me	4-ClC_6H_4	85	88	**p**	*t*-Bu	4-ClC_6H_4	85
h	Me	$CH_2CH_2CO_2H$	55		**q**	Me	NHTs	82
i	Me	2-$F_3CC_6H_4$	83		**r**	Me		65



Scheme 3 Synthesis of pyrrolo[1,2-*a*][1,4]benzodiazepines **11**



Scheme 4 Synthesis of pyrrolo[1,2-*a*]diazepine **14** from diketone **4b** and β-glycine ethyl ester **12**

By using a similar procedure, we also prepared the pyrrolo[1,2-*a*]diazepine **14**. The diketone **4b**, on heating with β-glycine ethyl ester hydrochloride (**12**) in the presence of sodium acetate, gave the pyrrole **13**, which on treatment with hydrazine hydrate in ethanol and *N*,*N*-dimethylformamide gave the required product **14** (Scheme 4).[13]

To summarize, we have developed a simple and efficient method for the synthesis of 2-(aminomethyl)pyrroles from readily available furfurylamines. The approach permits the synthesis of *N*-alkyl- and *N*-arylpyrroles in good yields. The transformation is compatible with a variety of functional groups, including ketone, ester, and carboxy groups. 2-(Phthalimidomethyl)pyrroles containing a carbonyl function attached to the substituent at the nitrogen atom can be further transformed into pyrrolodiazepine derivatives by deprotection and cyclization in situ; this significantly broadens the value of the method.

NMR spectra were recorded on a Bruker DPX 300 spectrometer (300 MHz for ^{1}H; 75 MHz for ^{13}C NMR) at r.t.; the chemical shifts (δ) were measured in ppm with respect to the solvent ($CDCl_3$, ^{1}H: δ = 7.26 ppm, ^{13}C: δ = 77.13 ppm; DMSO-d_6, ^{1}H: δ = 2.50 ppm, ^{13}C: δ = 39.7 ppm). Coupling constants (*J*) are given in Hz. IR spectra were recorded by using KBr plates on InfraLUM FT-02 and InfraLUM FT-801 instruments. Mass spectra were recorded on a Kratos MS-30 instrument with EI ionization at 70 eV and 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 the reactions were carried out by using freshly distilled and dry solvents.

2-[(2-Furyl)methyl]-1*H*-isoindole-1,3(2*H*)-diones 3; General Procedure

A soln of furfurylamine **1** (90 mmol) and phthalic anhydride **2** (14.8 g, 100 mmol) in AcOH (15 mL) was refluxed for 20 min while the reaction was monitored by TLC. The mixture was poured into cold H_2O (150 mL) and neutralized with $NaHCO_3$ to pH ~7. The precipitate was filtered off, washed with cold H_2O, air dried, and recrystallized (EtOAc–PE).

2-[(5-Methyl-2-furyl)methyl]-1*H*-isoindole-1,3(2*H*)-dione (3b)

White solid; yield: 16.05 g (74%); mp 95 °C.

IR (KBr): 1717, 1560, 1465, 1421, 1387, 1334, 1219, 1089, 1023, 964, 787, 752, 711 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.21 (s, 3 H, Me), 4.78 (s, 2 H, CH_2), 5.85 (d, *J* = 3.0 Hz, 1 H, H_{Fur}), 6.22 (d, *J* = 3.0 Hz, 1 H, H_{Fur}), 7.66–7.72 (m, 2 H, H_{Pht}), 7.80–7.86 (m, 2 H, H_{Pht}).

MS (EI, 70 eV): *m/z* (%) = 241 (100) [M$^+$], 226 (12), 198 (31), 104 (14), 95 (32), 76 (36), 53 (16), 50 (43), 43 (45).

Anal. Calcd for $C_{14}H_{11}NO_3$: C, 69.70; H, 4.60; N, 5.81. Found: C, 69.83; H, 4.91; N, 5.79.

2-[(5-Ethyl-2-furyl)methyl]-1*H*-isoindole-1,3(2*H*)-dione (3c)

White solid; yield: 16.52 g (72%); mp 93 °C.

IR (KBr): 1715, 1433, 1397, 1314, 1195, 1109, 1019, 951, 804, 736 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.16 (t, *J* = 7.5 Hz, 3 H, CH_2CH_3), 2.57 (q, *J* = 7.5 Hz, 2 H, CH_2CH_3), 4.79 (s, 2 H, CH_2), 5.87 (d, *J* = 3.0 Hz, 1 H, H_{Fur}), 6.23 (d, *J* = 3.0 Hz, 1 H, H_{Fur}), 7.66–7.73 (m, 2 H, H_{Pht}), 7.81–7.87 (m, 2 H, H_{Pht}).

MS (EI, 70 eV): *m/z* (%) = 255 (100) [M$^+$], 240 (15), 226 (88), 198 (21), 108 (23), 104 (21), 78 (81), 65 (18), 50 (35), 43 (26).

Anal. Calcd for $C_{15}H_{13}NO_3$: C, 70.58; H, 5.13; N, 5.49. Found: C, 70.73; H, 5.06; N, 5.42.

2-[(5-*tert*-Butyl-2-furyl)methyl]-1*H*-isoindole-1,3(2*H*)-dione (3d)

White solid; yield: 17.83 g (71%); mp 93 °C.

IR (KBr): 1709, 1428, 1400, 1313, 1200, 1104, 949, 786, 733 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.21 (s, 9 H, *t*-Bu), 4.80 (s, 2 H, CH_2), 5.84 (d, *J* = 3.0 Hz, 1 H, H_{Fur}), 6.18 (d, *J* = 3.0 Hz, 1 H, H_{Fur}), 7.66–7.73 (m, 2 H, H_{Pht}), 7.81–7.88 (m, 2 H, H_{Pht}).

MS (EI, 70 eV): *m/z* (%) = 283 (45) [M^+], 268 (100), 226 (16), 160 (10), 121 (40), 104 (7), 77 (22), 50 (16), 43 (13).

Anal. Calcd for $C_{17}H_{17}NO_3$: C, 72.07; H, 6.05; N, 4.94. Found: C, 72.00; H, 6.12; N, 4.78.

2-{[5-(4-Chlorophenyl)-2-furyl]methyl}-1*H*-isoindole-1,3(2*H*)-dione (3e)

Beige solid; yield: 19.76 g (65%); mp 166 °C.

IR (KBr): 1705, 1424, 1400, 1316, 1092, 944, 829, 794, 732 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.89 (s, 2 H, CH_2), 6.44 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 6.53 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 7.29 (d, *J* = 9.0 Hz, 2 H, H_{Ar}), 7.53 (d, *J* = 9.0 Hz, 2 H, H_{Ar}), 7.68–7.74 (m, 2 H, H_{Pht}), 7.83–7.89 (m, 2 H, H_{Pht}).

MS (EI, 70 eV): *m/z* (%) = 339/337 (7/20) [M^+], 198 (64), 191 (62), 170 (37), 162 (33), 139 (30), 128 (45), 115 (30), 104 (53), 76 (100), 63 (24), 50 (69).

Anal. Calcd for $C_{19}H_{12}ClNO_3$: C, 67.57; H, 3.58; N, 4.15. Found: C, 67.35; H, 3.52; N, 4.11.

***N*-(2,5-Dioxoalkyl)-1*H*-isoindole-1,3(2*H*)-diones 4b–e; General Procedure**

An isoindoledione **3b–e** (40 mmol) was dissolved in a mixture of glacial AcOH (50 mL) and concd HCl (30 mL), and the mixture was stirred for 24 h (72 h for **4d**) at r.t. (reflux for **4e**), while the reaction was monitored by TLC. The mixture was then poured into cold H_2O (300 mL) and neutralized to pH ~7 with $NaHCO_3$. The precipitate was filtered off, washed with cold H_2O, air dried, and recrystallized (CH_2Cl_2–PE).

2-(2,5-Dioxohexyl)-1*H*-isoindole-1,3(2*H*)-dione (4b)

White solid; yield: 9.53 g (92%); mp 119 °C (Lit.[11a] 118–119.5 °C).

IR (KBr): 1721, 1680, 1414, 1228, 1192, 1092, 1042, 992, 971, 720 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.14 (s, 3 H, Me), 2.76 (s, 4 H, CH_2CH_2), 4.53 (s, 2 H, CH_2), 7.65–7.73 (m, 2 H, H_{Pht}), 7.77–7.85 (m, 2 H, H_{Pht}).

MS (EI, 70 eV): *m/z* (%) = 216 (2) [M^+ – 43], 160 (68), 133 (12), 104 (27), 99 (100), 76 (40), 71 (27), 50 (26), 43 (87).

2-(2,5-Dioxoheptyl)-1*H*-isoindole-1,3(2*H*)-dione (4c)

White solid; yield: 9.61 g (88%); mp 110 °C (Lit.[29] 109–110 °C).

IR (KBr): 1725, 1416, 1192, 1092, 1049, 969, 720 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.03 (t, *J* = 7.2 Hz, 3 H, CH_2CH_3), 2.44 (q, *J* = 7.2 Hz, 2 H, CH_2CH_3), 2.70–2.82 (m, 4 H, CH_2CH_2), 4.54 (s, 2 H, CH_2), 7.67–7.74 (m, 2 H, H_{Pht}), 7.80–7.87 (m, 2 H, H_{Pht}).

MS (EI, 70 eV): *m/z* (%) = 216 (6) [M^+ – 57], 160 (44), 133 (8), 113 (100), 104 (17), 95 (12), 85 (11), 77 (24), 57 (49), 50 (12).

2-(6,6-Dimethyl-2,5-dioxoheptyl)-1*H*-isoindole-1,3(2*H*)-dione (4d)

Colorless prisms; yield: 10.84 g (90%); mp 113 °C.

IR (KBr): 1716, 1419, 1315, 1192, 1071, 990, 907, 725 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.12 (s, 9 H, *t*-Bu), 2.73–2.78 (m, 2 H, CH_2), 2.82–2.86 (m, 2 H, CH_2), 4.55 (s, 2 H, CH_2), 7.67–7.74 (m, 2 H, H_{Pht}), 7.81–7.87 (m, 2 H, H_{Pht}).

MS (EI, 70 eV): *m/z* (%) = 244 (9) [M^+ – 57], 216 (28), 160 (45), 141 (100), 133 (11), 113 (84), 104 (25), 77 (37), 57 (74), 50 (22), 41 (80).

Anal. Calcd for $C_{17}H_{19}NO_4$: C, 67.76; H, 6.36; N, 4.65. Found: C, 67.73; H, 6.41; N, 4.50.

2-[5-(4-Chlorophenyl)-2,5-dioxopentyl]-1*H*-isoindole-1,3(2*H*)-dione (4e)

White solid; yield: 2.13 g (15%); mp 179 °C.

IR (KBr): 1721, 1681, 1414, 1088, 963, 818, 724 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.97 (t, *J* = 6.6 Hz, 2 H, CH_2), 3.31 (t, *J* = 6.6 Hz, 2 H, CH_2), 4.64 (s, 2 H, CH_2), 7.42 (d, *J* = 9.0 Hz, 2 H, H_{Ar}), 7.69–7.76 (m, 2 H, H_{Pht}), 7.82–7.90 (m, 4 H, H_{Pht}, H_{Ar}).

MS (EI, 70 eV): *m/z* (%) = 357/355 (1/3) [M^+], 197/195 (35/100), 160 (60), 141/139 (27/83), 133 (13), 111 (49), 104 (31), 76 (54), 50 (43).

Anal. Calcd for $C_{19}H_{14}ClNO_4$: C, 64.14; H, 3.97; N, 3.94. Found: C, 64.06; H, 3.89; N, 3.85.

2-[(1*H*-Pyrrol-2-yl)methyl]-1*H*-isoindole-1,3(2*H*)-diones 6a–q; General Procedure

A mixture of diketone **4** (11 mmol) and amine **5** (12 mmol) in AcOH (15 mL) was refluxed for 40–90 min while the reaction was monitored by TLC, then poured into cold H_2O (150 mL) and neutralized to pH ~7 with $NaHCO_3$. The product was extracted with CH_2Cl_2 (3 × 30 mL), and the combined organic fractions were washed with H_2O, dried (Na_2SO_4), and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel), and the solvent was evaporated to one third of the original volume and kept until the product crystallized.

2-({5-Methyl-1-[(5-methyl-2-furyl)methyl]-1*H*-pyrrol-2-yl}methyl)-1*H*-isoindole-1,3(2*H*)-dione (6a)

Eluent: CH_2Cl_2–PE (1:5); white solid; yield: 3.12 g (85%); mp 107 °C.

IR (KBr): 1707, 1426, 1388, 1326, 1196, 1089, 1020, 932, 786, 713 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.02 (s, 3 H, Me), 2. 21 (s, 3 H, Me), 4.89 (s, 2 H, CH_2), 5.15 (s, 2 H, CH_2), 5.69 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 5.83 (d, *J* = 3.3 Hz, 1 H, H_{Pyr}), 5.85 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 6.26 (d, *J* = 3.3 Hz, 1 H, H_{Pyr}), 7.63–7.70 (m, 2 H, H_{Pht}), 7.75–7.82 (m, 2 H, H_{Pht}).

MS (EI, 70 eV): *m/z* (%) = 334 (10) [M^+], 240 (12), 104 (4), 95 (100), 43 (20).

Anal. Calcd for $C_{20}H_{18}N_2O_3$: C, 71.84; H, 5.43; N, 8.38. Found: C, 71.91; H, 5.45; N, 8.20.

2-[(1-Benzyl-5-methyl-1*H*-pyrrol-2-yl)methyl]-1*H*-isoindole-1,3(2*H*)-dione (6b)

Eluent: CH_2Cl_2–PE (1:4); pale brown solid; yield: 3.27 g (90%); mp 127–128 °C.

IR (KBr): 1710, 1425, 1389, 1340, 1300, 1100, 934, 748, 711 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.12 (s, 3 H, Me), 4.74 (s, 2 H, CH_2), 5.28 (s, 2 H, CH_2), 5.95 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 6.36 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 6.69–6.72 (m, 2 H, H_{Ar}), 6.89–6.94 (m, 1 H, H_{Ar}), 7.03–7.08 (m, 2 H, H_{Ar}), 7.55–7.66 (m, 4 H, H_{Pht}).

MS (EI, 70 eV): *m/z* (%) = 330 (24) [M^+], 239 (100), 182 (10), 104 (7), 76 (14), 65 (27), 51 (11).

Anal. Calcd for $C_{21}H_{18}N_2O_2$: C, 76.34; H, 5.49; N, 8.48. Found: C, 76.06; H, 5.40; N, 8.47.

2-({5-Methyl-1-[4-(trifluoromethyl)phenyl]-1*H*-pyrrol-2-yl}methyl)-1*H*-isoindole-1,3(2*H*)-dione (6c)

Eluent: CH_2Cl_2–PE (1:5); white solid; yield: 3.51 g (83%); mp 124 °C.

IR (KBr): 1718, 1612, 1426, 1394, 1329, 1176, 1109, 951, 849, 713 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.99 (s, 3 H, Me), 4.63 (s, 2 H, CH_2), 5.96 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 6.22 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 7.41 (d, *J* = 8.1 Hz, 2 H, H_{Ar}), 7.64–7.79 (m, 6 H, H_{Ar} + H_{Pht}).

MS (EI, 70 eV): *m/z* (%) = 384 (41) [M^+], 238 (100), 222 (28), 196 (10), 168 (12), 145 (17), 130 (20), 105 (17), 76 (32), 50 (23).

Anal. Calcd for $C_{21}H_{15}F_3N_2O_2$: C, 65.62; H, 3.93; N, 7.29. Found: C, 65.40; H, 3.77; N, 7.39.

2-[(1-Butyl-5-methyl-1*H*-pyrrol-2-yl)methyl]-1*H*-isoindole-1,3(2*H*)-dione (6d)

Eluent: CH_2Cl_2–PE (1:10); pale brown solid; yield: 2.54 g (78%); mp 89–90 °C.

IR (KBr): 1701, 1427, 1394, 1342, 1090, 930, 749, 713 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.95 (t, *J* = 7.2 Hz, 3 H, Me), 1.35–1.49 (m, 2 H, CH_2), 1.52–1.64 (m, 2 H, CH_2), 2.19 (s, 3 H, CH_3), 4.00 (t, *J* = 7.5 Hz, 2 H, CH_2), 4.81 (s, 2 H, CH_2), 5.80 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 6.21 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 7.64–7.72 (m, 2 H, H_{Pht}), 7.76–7.84 (m, 2 H, H_{Pht}).

MS (EI, 70 eV): *m/z* (%) = 296 (100) [M^+], 254 (20), 239 (81), 150 (50), 136 (72), 130 (20), 107 (59), 94 (91), 76 (47), 50 (30).

Anal. Calcd for $C_{18}H_{20}N_2O_2$: C, 72.95; H, 6.80; N, 9.45. Found: C, 73.00; H, 6.86; N, 9.54.

2-{[5-Methyl-1-(3-oxo-1,3-dihydro-2-benzofuran-5-yl)-1*H*-pyrrol-2-yl]methyl}-1*H*-isoindole-1,3(2*H*)-dione (6e)

Eluent: CH_2Cl_2–PE (1:1); beige solid; yield: 3.27 g (80%); mp 163–164 °C.

IR (KBr): 1765, 1711, 1494, 1415, 1357, 1177, 1111, 1053, 995, 939, 718 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.96 (s, 3 H, Me), 4.60 (br s, 2 H, CH_2), 5.41 (s, 2 H, CH_2), 5.94 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 6.27 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 7.56–7.76 (m, 7 H, H_{Ar}).

MS (EI, 70 eV): *m/z* (%) = 372 (48) [M^+], 239 (14), 226 (100), 181 (18), 130 (16), 104 (15), 76 (37), 50 (26).

Anal. Calcd for $C_{22}H_{16}N_2O_4$: C, 70.96; H, 4.33; N, 7.52. Found: C, 70.79; H, 4.23; N, 7.48.

***N*-{2-[(1,3-Dioxo-1,3-dihydro-2*H*-isoindol-2-yl)methyl]-5-methyl-1*H*-pyrrol-1-yl}benzamide (6f)**

Eluent: CH_2Cl_2–PE (1:5); colorless prisms; yield: 3.55 g (90%); mp 217–218 °C.

IR (KBr): 3331, 1764, 1710, 1673, 1521, 1422, 1391, 1332, 1270, 1099, 930, 744, 706 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 2.00 (s, 3 H, Me), 4.58 (d, *J* = 15.0 Hz, 1 H, CH_AH_B), 4.69 (d, *J* = 15.0 Hz, 1 H, CH_AH_B), 5.79 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 6.05 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 7.51–7.57 (m, 2 H, H_{Ar}), 7.61–7.67 (m, 1 H, H_{Ar}), 7.76–7.84 (m, 4 H, H_{Pht}), 7.87–7.90 (m, 2 H, H_{Ar}), 11.27 (s, 1 H, NH).

MS (EI, 70 eV): *m/z* (%) = 359 (35) [M^+], 254 (25), 239 (81), 211 (12), 193 (16), 160 (10), 130 (19), 105 (97), 77 (100), 65 (14), 51 (57).

Anal. Calcd for $C_{21}H_{17}N_3O_3$: C, 70.18; H, 4.77; N, 11.69. Found: C, 70.12; H, 4.78; N, 11.51.

2-{[1-(4-Chlorophenyl)-5-methyl-1*H*-pyrrol-2-yl]methyl}-1*H*-isoindole-1,3(2*H*)-dione (6g)

Eluent: CH_2Cl_2–PE (1:6); white solid; yield: 3.28 g (85%); mp 159 °C.

IR (KBr): 1722, 1492, 1426, 1391, 1088, 1001, 949, 836, 732 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.97 (s, 3 H, Me), 4.61 (s, 2 H, CH_2), 5.92 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 6.19 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 7.20 (d, *J* = 8.7 Hz, 2 H, H_{Ar}), 7.43 (d, *J* = 8.7 Hz, 2 H, H_{Ar}), 7.64–7.71 (m, 2 H, H_{Pht}), 7.73–7.81 (m, 2 H, H_{Pht}).

MS (EI, 70 eV): *m/z* (%) = 352/350 (2/5) [M^+], 239 (15), 206/204 (34/100), 188 (14), 168 (18), 154 (27), 130 (22), 111 (19), 104 (16), 76 (47), 50 (33).

Anal. Calcd for $C_{20}H_{15}ClN_2O_2$: C, 68.48; H, 4.31; N, 7.99. Found: C, 68.32; H, 4.28; N, 8.18.

3-{2-[(1,3-Dioxo-1,3-dihydro-2*H*-isoindol-2-yl)methyl]-5-methyl-1*H*-pyrrol-1-yl}propanoic Acid (6h)

Eluent: CH_2Cl_2–PE (1:4); beige solid; yield: 1.89 g (55%); mp >250 °C (dec).

IR (KBr): 1720, 1436, 1400, 1328, 1300, 1088, 1120, 960, 748, 732, 712 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 2.15 (s, 3 H, Me), 2.55 (t, *J* = 7.8 Hz, 2 H, CH_2), 4.20 (t, *J* = 7.8 Hz, 2 H, CH_2), 4.73 (s, 2 H, CH_2), 5.66 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 5.83 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 7.77–7.90 (m, 4 H, H_{Pht}).

MS (EI, 70 eV): *m/z* (%) = 312 (100) [M^+], 297 (16), 239 (85), 166 (93), 152 (30), 130 (22), 120 (36), 104 (47), 94 (37), 76 (81), 65 (22), 50 (61).

Anal. Calcd for $C_{17}H_{16}N_2O_4$: C, 65.38; H, 5.16; N, 8.97. Found: C, 65.44; H, 4.82; N, 8.58.

2-({5-Methyl-1-[2-(trifluoromethyl)phenyl]-1*H*-pyrrol-2-yl}methyl)-1*H*-isoindole-1,3(2*H*)-dione (6i)

Eluent: CH_2Cl_2–PE (1:5); cream solid; yield: 3.51 g (83%); mp 128 °C.

IR (KBr): 1712, 1502, 1461, 1421, 1390, 1314, 1131, 1033, 768, 712 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.88 (s, 3 H, Me), 4.36 (d, *J* = 15.3 Hz, 1 H, CH_AH_B), 4.67 (d, *J* = 15.3 Hz, 1 H, CH_AH_B), 5.94 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 6.28 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 7.26–7.34 (m, 1 H, H_{Ar}), 7.58–7.70 (m, 4 H, H_{Pht}, H_{Ar}), 7.71–7.79 (m, 2 H, H_{Pht}), 7.80–7.87 (m, 1 H, H_{Ar}).

MS (EI, 70 eV): *m/z* (%) = 384 (18) [M^+], 238 (100), 222 (15), 168 (17), 145 (16), 130 (18), 105 (19), 76 (35), 50 (24).

Anal. Calcd for $C_{21}H_{15}F_3N_2O_2$: C, 65.62; H, 3.93; N, 7.29. Found: C, 65.84; H, 3.94; N, 7.46.

2-{[5-Methyl-1-(4-nitrophenyl)-1*H*-pyrrol-2-yl]methyl}-1*H*-isoindole-1,3(2*H*)-dione (6j)

Eluent: EtOAc–PE (1:5); yellow needles; yield: 2.70 g (68%); mp 203 °C.

IR (KBr): 1717, 1595, 1519, 1339, 1109, 941, 874 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.00 (s, 3 H, Me), 4.62 (s, 2 H, CH_2), 5.98 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 6.28 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 7.45 (d, *J* = 9.0 Hz, 2 H, H_{Ar}), 7.64–7.71 (m, 2 H, H_{Pht}), 7.72–7.79 (m, 2 H, H_{Pht}), 8.35 (d, *J* = 9.0 Hz, 2 H, H_{Ar}).

MS (EI, 70 eV): *m/z* (%) = 361 (5) [M^+], 239 (18), 215 (100), 199 (16), 167 (35), 154 (29), 130 (30), 104 (28), 76 (85), 50 (53).

Anal. Calcd for $C_{20}H_{15}N_3O_4$: C, 66.48; H, 4.18; N, 11.63. Found: C, 66.24; H, 4.22; N, 11.90.

2-{[1-(4-Methoxyphenyl)-5-methyl-1*H*-pyrrol-2-yl]methyl}-1*H*-isoindole-1,3(2*H*)-dione (6k)

Eluent: CH_2Cl_2–PE (1:6.5); pale yellow prisms; yield: 3.20 g (84%); mp 131–132 °C.

IR (KBr): 1718, 1516, 1426, 1392, 1292, 1251, 1189, 1113, 1027, 950, 837, 741, 709 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.96 (s, 3 H, Me), 3.85 (s, 3 H, OMe), 4.62 (s, 2 H, CH_2), 5.90 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 6.15 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 6.95 (d, *J* = 8.7 Hz, 2 H, H_{Ar}), 7.18 (d, *J* = 8.7 Hz, 2 H, H_{Ar}), 7.63–7.70 (m, 2 H, H_{Pht}), 7.73–7.81 (m, 2 H, H_{Pht}).

MS (EI, 70 eV): *m/z* (%) = 346 (40) [M^+], 239 (18), 200 (100), 184 (18), 130 (12), 77 (26), 50 (14).

Anal. Calcd for $C_{21}H_{18}N_2O_3$: C, 72.82; H, 5.24; N, 8.09. Found: C, 72.72; H, 5.26; N, 8.06.

2-{[1-(3-Methoxyphenyl)-5-methyl-1*H*-pyrrol-2-yl]methyl}-1*H*-isoindole-1,3(2*H*)-dione (6l)
Eluent: CH_2Cl_2–PE (1:6); cream solid; yield: 2.70 g (71%); mp 134 °C.

IR (KBr): 1718, 1597, 1394, 1326, 1243, 1180, 1114, 1031, 949, 857, 794, 747 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.00 (s, 3 H, Me), 3.76 (s, 3 H, OMe), 4.66 (s, 2 H, CH_2), 5.92 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 6.17 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 6.77–6.79 (m, 1 H, H_{Ar}), 6.83–6.86 (m, 1 H, H_{Ar}), 6.94–6.98 (m, 1 H, H_{Ar}), 7.32–7.37 (m, 1 H, H_{Ar}), 7.62–7.70 (m, 2 H, H_{Pht}), 7.72–7.81 (m, 2 H, H_{Pht}).

MS (EI, 70 eV): *m/z* (%) = 346 (34) [M^+], 239 (13), 200 (100), 184 (24), 130 (13), 77 (23), 50 (13).

Anal. Calcd for $C_{21}H_{18}N_2O_3$: C, 72.82; H, 5.24; N, 8.09. Found: C, 72.68; H, 5.12; N, 8.06.

2-{[1-(2,5-Dimethoxyphenyl)-5-methyl-1*H*-pyrrol-2-yl]methyl}-1*H*-isoindole-1,3(2*H*)-dione (6m)
Eluent: CH_2Cl_2–PE (1:6); cream solid; yield: 3.31 g (80%); mp 174 °C.

IR (KBr): 1714, 1510, 1422, 1390, 1277, 1229, 1099, 1048, 933, 806, 755, 729 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.92 (s, 3 H, Me), 3.48 (s, 3 H, OMe), 3.70 (s, 3 H, OMe), 4.56 (d, *J* = 15.3 Hz, 1 H, CH_AH_B), 4.69 (d, *J* = 15.3 Hz, 1 H, CH_AH_B), 5.94 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 6.28 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 6.73 (d, *J* = 3.0 Hz, 1 H, H_{Ar}), 6.82 (d, *J* = 9.0 Hz, 1 H, H_{Ar}), 6.93 (dd, *J* = 9.0 Hz, *J* = 3.0 Hz, 1 H, H_{Ar}), 7.61–7.68 (m, 2 H, H_{Pht}), 7.69–7.76 (m, 2 H, H_{Pht}).

MS (EI, 70 eV): *m/z* (%) = 376 (51) [M^+], 239 (14), 230 (100), 216 (37), 198 (14), 130 (13), 105 (12), 77 (23), 51 (15).

Anal. Calcd for $C_{22}H_{20}N_2O_4$: C, 70.20; H, 5.36; N, 7.44. Found: C, 69.95; H, 5.29; N, 7.38.

2-({5-Methyl-1-[2-(5-methyl-2-furyl)phenyl]-1*H*-pyrrol-2-yl}methyl)-1*H*-isoindole-1,3(2*H*)-dione (6n)
Eluent: CH_2Cl_2–PE (1:5); cream solid; yield: 3.18 g (73%); mp 126–127 °C.

IR (KBr): 1719, 1538, 1492, 1427, 1386, 1338, 1299, 1102, 1044, 935, 763, 713 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.81 (s, 3 H, Me), 1.99 (s, 3 H, Me), 4.41 (d, *J* = 15.3 Hz, 1 H, CH_AH_B), 4.55 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 4.66 (d, *J* = 15.3 Hz, 1 H, CH_AH_B), 5.63 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 6.02 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 6.41 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 7.21–7.24 (m, 1 H, H_{Ar}), 7.32–7.37 (m, 1 H, H_{Ar}), 7.45–7.50 (m, 1 H, H_{Ar}), 7.58 (s, 4 H, H_{Pht}), 7.77–7.81 (m, 1 H, H_{Ar}).

MS (EI, 70 eV): *m/z* (%) = 396 (100) [M^+], 353 (61), 250 (72), 236 (84), 221 (25), 206 (60), 191 (24), 180 (17), 105 (17), 76 (29), 59 (16).

Anal. Calcd for $C_{25}H_{20}N_2O_3$: C, 75.74; H, 5.08; N, 7.07. Found: C, 75.95; H, 4.99; N, 7.15.

2-{[1-(4-Chlorophenyl)-5-ethyl-1*H*-pyrrol-2-yl]methyl}-1*H*-isoindole-1,3(2*H*)-dione (6o)
Eluent: CH_2Cl_2–PE (1:2); white solid; yield: 3.13 g (78%); mp 119 °C.

IR (KBr): 1723, 1492, 1427, 1392, 1088, 1003, 950, 838, 730 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.06 (t, *J* = 7.5 Hz, 3 H, CH_2CH_3), 2.28 (q, *J* = 7.5 Hz, 2 H, CH_2CH_3), 4.60 (s, 2 H, CH_2), 5.94 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 6.22 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 7.21 (d, *J* = 8.7 Hz, 2 H, H_{Ar}), 7.43 (d, *J* = 8.7 Hz, 2 H, H_{Ar}), 7.64–7.71 (m, 2 H, H_{Pht}), 7.74–7.81 (m, 2 H, H_{Pht}).

MS (EI, 70 eV): *m/z* (%) = 366/364 (10/31) [M^+], 220/218 (33/100), 204/202 (12/35), 190/188 (13/38), 167 (59), 160 (17), 154 (30), 130 (34), 104 (34), 76 (81), 50 (52).

Anal. Calcd for $C_{21}H_{17}ClN_2O_2$: C, 69.14; H, 4.70; N, 7.68. Found: C, 69.00; H, 4.67; N, 7.66.

2-{[5-*tert*-Butyl-1-(4-chlorophenyl)-1*H*-pyrrol-2-yl]methyl}-1*H*-isoindole-1,3(2*H*)-dione (6p)
Eluent: CH_2Cl_2–PE (1:4); white solid; yield: 3.67 g (85%); mp 155–156 °C.

IR (KBr): 1714, 1492, 1422, 1390, 1319, 1092, 932, 840, 784, 732 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.08 (s, 9 H, *t*-Bu), 4.42 (s, 2 H, CH_2), 5.98 (d, *J* = 3.9 Hz, 1 H, H_{Pyr}), 6.12 (d, *J* = 3.9 Hz, 1 H, H_{Pyr}), 7.29 (d, *J* = 8.7 Hz, 2 H, H_{Ar}), 7.40 (d, *J* = 8.7 Hz, 2 H, H_{Ar}), 7.64–7.72 (m, 2 H, H_{Pht}), 7.74–7.82 (m, 2 H, H_{Pht}).

MS (EI, 70 eV): *m/z* (%) = 394/392 (9/26) [M^+], 379/377 (27/86), 232/230 (17/51), 215 (31), 180 (46), 160 (98), 130 (52), 104 (53), 77 (100), 50 (55).

Anal. Calcd for $C_{23}H_{21}ClN_2O_2$: C, 70.31; H, 5.39; N, 7.13. Found: C, 70.17; H, 5.27; N, 7.19.

***N*-{2-[(1,3-Dioxo-1,3-dihydro-2*H*-isoindol-2-yl)methyl]-5-methyl-1*H*-pyrrol-1-yl}-4-methylbenzenesulfonamide (6q)**
Eluent: CH_2Cl_2–PE (1:5); cream solid; yield: 3.69 g (82%); mp 222–223 °C.

IR (KBr): 3407, 1699, 1612, 1435, 1400, 1351, 1158, 1091, 897, 749 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.42 (s, 3 H, Me), 2.41 (s, 3 H, Me), 4.48 (d, *J* = 15.9 Hz, 1 H, CH_AH_B), 4.66 (d, *J* = 15.9 Hz, 1 H, CH_AH_B), 5.57 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 5.68 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 7.45 (d, *J* = 8.1 Hz, 2 H, H_{Ar}), 7.61 (d, *J* = 8.1 Hz, 2 H, H_{Ar}), 7.81–7.90 (m, 4 H, H_{Pht}), 11.12 (s, 1 H, NH).

MS (EI, 70 eV): *m/z* (%) = 409 (1) [M^+], 254 (64), 236 (15), 160 (14), 130 (39), 104 (27), 91 (93), 77 (100), 65 (55), 51 (29).

Anal. Calcd for $C_{21}H_{19}N_3O_4S$: C, 61.60; H, 4.68; N, 10.26; S, 7.83. Found: C, 61.93; H, 4.51; N, 9.97; S, 7.64.

2-({5-Methyl-1-[2-(5-methyl-2-furyl)ethyl]-1*H*-pyrrol-2-yl}methyl)-1*H*-isoindole-1,3(2*H*)-dione (6r)
A soln of diketone **4b** (2.86 g, 11 mmol) and 2-(2-furyl)ethanamine (1.38 g, 11 mmol) in EtOH (30 mL) was refluxed for 1 h (TLC monitoring). The solvent was evaporated and the residue was recrystallized (EtOAc–acetone) to give a white solid; yield: 2.50 g (65%); mp 137–138 °C.

IR (KBr): 1716, 1568, 1468, 1424, 1388, 1332, 1304, 1204, 1096, 1020, 932, 808, 780, 748 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.15 (s, 3 H, Me), 2.26 (s, 3 H, Me), 2.87 (t, *J* = 7.5 Hz, 2 H, CH_2), 4.29 (t, *J* = 7.5 Hz, 2 H, CH_2), 4.69 (s, 2 H, CH_2), 5.80 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 5.85 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 5.89 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 6.17 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 7.64–7.71 (m, 2 H, H_{Pht}), 7.76–7.84 (m, 2 H, H_{Pht}).

MS (EI, 70 eV): *m/z* (%) = 348 (42) [M$^+$], 253 (23), 241 (13), 201 (12), 160 (44), 106 (100), 94 (17), 79 (18), 65 (15), 53 (12).

Anal. Calcd for $C_{21}H_{20}N_2O_3$: C, 72.40; H, 5.79; N, 8.04. Found: C, 72.44; H, 5.66; N, 8.11.

2-[(*tert*-Butoxycarbonylamino)methyl]pyrroles 8; General Procedure

$N_2H_4 \cdot H_2O$ (5 mL) was added to a soln of compound **6** (6.0 mmol) in MeOH (40 mL), and the mixture was stirred at r.t. for 1 h while the reaction was monitored by TLC. The solvent was evaporated and H_2O (30 mL) was added to the residue and adjusted to pH ~5 with AcOH. The precipitate was filtered off and aq NH_3 was added to the filtrate to adjust the pH to ~10. The mixture was extracted with EtOAc (4 × 50 mL), and the combined organic fractions were washed with H_2O, dried (Na_2SO_4), and concentrated under reduced pressure. $(Boc)_2O$ (1.64 g 7.5 mmol) was added to the resulting 2-(aminomethyl)pyrrole, and the mixture was stirred at r.t. for 30 min (TLC monitoring). H_2O (30 mL) was added and the precipitate was filtered off, washed with H_2O, and air-dried. The residue was purified by column chromatography [EtOAc–PE (1:3)], and the solvents were evaporated under reduced pressure to give a crude product that was crystallized (PE).

***tert*-Butyl ({5-Methyl-1-[(5-methyl-2-furyl)methyl]-1*H*-pyrrol-2-yl}methyl)carbamate (8a)**

Colorless needles; yield: 1.50 g (82%); mp 75–76 °C.

IR (KBr): 3371, 1681, 1523, 1269, 1248, 1170, 1019, 938, 868, 773 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.43 (s, 9 H, *t*-Bu), 2.23 (s, 3 H, Me), 2.26 (s, 3 H, Me), 4.35 (d, *J* = 5.4 Hz, 2 H, CH_2), 4.82 (br t, *J* = 5.4 Hz, 1 H, NH), 4.91 (s, 2 H, CH_2), 5.81 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 5.85 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 5.97–6.02 (m, 2 H, H_{Pyr}, H_{Fur}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.3, 13.5, 28.3 (3C), 36.7, 40.6, 79.1, 105.8, 106.1, 107.6, 108.2, 128.3, 130.0, 148.9, 151.9, 155.4.

MS (EI, 70 eV): *m/z* (%) = 304 (7) [M$^+$], 153 (12), 95 (100), 57 (15).

Anal. Calcd for $C_{17}H_{24}N_2O_3$: C, 67.08; H, 7.95; N, 9.20. Found: C, 67.07; H, 8.23; N, 9.13.

***tert*-Butyl [(1-Benzyl-5-methyl-1*H*-pyrrol-2-yl)methyl]carbamate (8b)**

White solid; yield: 1.62 g (89%); mp 85 °C.

IR (KBr): 3371, 1684, 1523, 1450, 1359, 1246, 1165, 1020, 930, 860, 755 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.29 (s, 9 H, *t*-Bu), 2.00 (s, 3 H, Me), 3.99 (d, *J* = 5.7 Hz, 2 H, CH_2), 5.11 (s, 2 H, CH_2), 5.74 (d, *J* = 3.3 Hz, 1 H, H_{Pyr}), 5.85 (d, *J* = 3.3 Hz, 1 H, H_{Pyr}), 6.85–6.88 (m, 2 H, H_{Ar}), 7.10 (br t, *J* = 5.7 Hz, 1 H, NH), 7.18–7.31 (m, 3 H, H_{Ar}).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 12.1, 28.1 (3C), 36.0, 46.1, 77.6, 105.6, 106.8, 125.7 (2C), 126.7, 128.3, 128.5 (2C), 129.7, 139.0, 155.3.

MS (EI, 70 eV): *m/z* (%) = 300 (11) [M$^+$], 243 (39), 184 (23), 153 (47), 91 (100), 65 (17), 57 (35).

Anal. Calcd for $C_{18}H_{24}N_2O_2$: C, 71.97; H, 8.05; N, 9.33. Found: C, 71.97; H, 8.09; N, 9.23.

***tert*-Butyl ({5-Methyl-1-[4-(trifluoromethyl)phenyl]-1*H*-pyrrol-2-yl}methyl)carbamate (8c)**

White solid; yield: 1.33 g (72%); mp 128 °C (CH_2Cl_2–PE).

IR (KBr): 3340, 1675, 1530, 1325, 1166, 1120, 1069, 854, 765 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.28 (s, 9 H, *t*-Bu), 1.97 (s, 3 H, Me), 3.91 (d, *J* = 5.4 Hz, 2 H, CH_2), 5.89 (d, *J* = 3.3 Hz, 1 H, H_{Pyr}), 5.99 (d, *J* = 3.3 Hz, 1 H, H_{Pyr}), 6.96 (br t, *J* = 5.4 Hz, 1 H, NH), 7.51 (d, *J* = 8.4 Hz, 2 H, H_{Ar}), 7.85 (d, *J* = 8.4 Hz, 2 H, H_{Ar}).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 12.6, 28.1 (3C), 36.4, 77.5, 106.7, 107.6, 124.1 (q, J_{CF} = 272.6 Hz), 126.3 (2C, q, J_{CF} = 3.8 Hz), 128.1 (q, J_{CF} = 32.2 Hz), 128.7, 128.9 (2C), 130.3, 141.4, 155.0.

MS (EI, 70 eV): *m/z* (%) = 354 (7) [M$^+$], 297 (80), 253 (15), 238 (100), 226 (20), 154 (21), 145 (15), 94 (21), 57 (80).

Anal. Calcd for $C_{18}H_{21}F_3N_2O_2$: C, 61.01; H, 5.97; N, 7.91. Found: C, 61.11; H, 6.10; N, 7.97.

***tert*-Butyl [(1-Butyl-5-methyl-1*H*-pyrrol-2-yl)methyl]carbamate (8d)**

White solid; yield: 1.13 g (63%); mp 63–64 °C.

IR (KBr): 3358, 1684, 1518, 1361, 1244, 1167, 1026, 941, 864, 754 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.94 (t, *J* = 7.2 Hz, 3 H, Me), 1.30–1.40 (m, 2 H, CH_2), 1.44 (s, 9 H, *t*-Bu), 1.55–1.65 (m, 2 H, CH_2), 2.21 (s, 3 H, Me), 3.74–3.79 (m, 2 H, CH_2), 4.27 (d, *J* = 5.4 Hz, 2 H, CH_2), 4.58 (br s, 1 H, NH), 5.78 (d, *J* = 3.3 Hz, 1 H, H_{Pyr}), 5.93 (d, *J* = 3.3 Hz, 1 H, H_{Pyr}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.3, 13.8, 20.1, 28.3 (3C), 33.5, 36.9, 43.7, 79.3, 105.5, 107.1, 127.9, 129.4, 155.3.

MS (EI, 70 eV): *m/z* (%) = 266 (38) [M$^+$], 209 (80), 165 (25), 150 (70), 136 (25), 108 (26), 94 (61), 57 (93), 53 (21), 41 (100).

Anal. Calcd for $C_{15}H_{26}N_2O_2$: C, 67.63; H, 9.84; N, 10.52. Found: C, 67.41; H, 10.04; N, 10.36.

***tert*-Butyl {[5-Methyl-1-(3-oxo-1,3-dihydro-2-benzofuran-5-yl)-1*H*-pyrrol-2-yl]methyl}carbamate (8e)**

White solid; yield: 1.23 g (67%); mp 118 °C (CH_2Cl_2–PE).

IR (KBr): 3377, 1770, 1688, 1501, 1412, 1363, 1251, 1163, 1054, 995, 912, 863, 770 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.31 (s, 9 H, *t*-Bu), 2.00 (s, 3 H, Me), 4.06 (d, *J* = 5.4 Hz, 2 H, CH_2), 4.47 (br s, 1 H, NH), 5.38 (s, 2 H, CH_2), 5.94 (d, *J* = 3.3 Hz, 1 H, H_{Pyr}), 6.11 (d, *J* = 3.3 Hz, 1 H, H_{Pyr}), 7.54 (dd, *J* = 7.8 Hz, *J* = 1.8 Hz, 1 H, H_{Ar}), 7.60 (d, *J* = 7.8 Hz, 1 H, H_{Ar}), 7.77 (d, *J* = 1.8 Hz, 1 H, H_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.7, 28.1 (3C), 36.7, 69.5, 79.2, 106.7, 108.3, 123.2, 125.3, 127.0, 129.7, 130.6, 134.0, 139.2, 145.9, 154.8, 169.9.

MS (EI, 70 eV): *m/z* (%) = 342 (3) [M$^+$], 285 (34), 241 (83), 226 (95), 214 (19), 182 (21), 167 (24), 94 (28), 89 (19), 57 (100).

Anal. Calcd for $C_{19}H_{22}N_2O_4$: C, 66.65; H, 6.48; N, 8.18. Found: C, 66.71; H, 6.32; N, 8.22.

***tert*-Butyl {[1-(Benzoylamino)-5-methyl-1*H*-pyrrol-2-yl]methyl}carbamate (8f)**

White solid; yield: 1.39 g (76%); mp 140 °C (CH_2Cl_2–PE).

IR (KBr): 3298, 3161, 1700, 1666, 1547, 1277, 1166, 1056, 919, 863, 760 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.32 (s, 9 H, *t*-Bu), 2.03 (s, 3 H, Me), 3.96 (dd, *J* = 5.7 Hz, *J* = 15.3 Hz, 1 H, CH_AH_B), 4.03 (dd, *J* = 5.7 Hz, *J* = 15.3 Hz, 1 H, CH_AH_B), 5.75 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 5.84 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 6.85 (br t, *J* = 5.7 Hz, 1 H, NH), 7.50–7.57 (m, 2 H, H_{Ar}), 7.59–7.67 (m, 1 H, H_{Ar}), 7.93–7.99 (m, 2 H, H_{Ar}), 11.23 (s, 1 H, NH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 10.8, 28.2 (3C), 35.3, 77.7, 103.3, 104.4, 127.7 (2C), 128.3, 128.5 (2C), 129.2, 131.9, 132.2, 155.2, 166.0.

MS (EI, 70 eV): *m/z* (%) = 329 (2) [M$^+$], 228 (19), 213 (12), 152 (32), 122 (20), 105 (100), 77 (70), 57 (51), 51 (22).

Anal. Calcd for $C_{18}H_{23}N_3O_3$: C, 65.63; H, 7.04; N, 12.76. Found: C, 65.58; H, 7.18; N, 12.69.

tert-Butyl {[1-(4-Chlorophenyl)-5-methyl-1*H*-pyrrol-2-yl]methyl}carbamate (8g)

White solid; yield: 1.61 g (88%); mp 114 °C (CH_2Cl_2–PE).

IR (KBr): 3409, 1697, 1670, 1538, 1490, 1268, 1166, 1089, 1015, 874, 838, 762 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 1.31 (s, 9 H, *t*-Bu), 1.94 (s, 3 H, Me), 3.86 (d, *J* = 5.4 Hz, 2 H, CH_2), 5.85 (d, *J* = 3.3 Hz, 1 H, H_{Pyr}), 5.94 (d, *J* = 3.3 Hz, 1 H, H_{Pyr}), 6.94 (br t, *J* = 5.4 Hz, 1 H, NH), 7.30 (d, *J* = 8.7 Hz, 2 H, H_{Ar}), 7.54 (d, *J* = 8.7 Hz, 2 H, H_{Ar}).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 12.5, 28.2 (3C), 36.4, 77.5, 106.3, 107.0, 128.6, 129.2 (2C), 129.9 (2C), 130.2, 132.4, 136.6, 155.1.

MS (EI, 70 eV): *m/z* (%) = 322/320 (3/8) [M^+], 265/263 (34/100), 206/204 (30/90), 192 (20), 169 (21), 154 (43), 111 (15), 94 (25), 75 (20), 57 (80).

Anal. Calcd for $C_{17}H_{21}ClN_2O_2$: C, 63.65; H, 6.60; N, 8.73. Found: C, 63.53; H, 6.77; N, 8.69.

2-{[1-(2-Aroylphenyl)-5-methyl-1*H*-pyrrol-2-yl]methyl}-1*H*-isoindole-1,3(2*H*)-diones 10; General Procedure

Cl_3CCO_2H (0.6 g) was added to a soln of diketone **4b** (11 mmol) and amine **9** (11 mmol) in benzene (20 mL), and the mixture was refluxed for 40–90 min while the reaction was monitored by TLC. The mixture was then poured into cold H_2O (150 mL) and neutralized to pH ~7 with $NaHCO_3$. The product was extracted with benzene (3 × 30 mL), and the combined organic fractions were washed with H_2O, dried (Na_2SO_4), and concentrated under reduced pressure. The residue was purified by column chromatography [silica gel, EtOAc–PE (1:3)], and the solvent was evaporated to one third of its starting volume and kept until the product crystallized.

2-{[1-(2-Acetyl-4,5-dimethoxyphenyl)-5-methyl-1*H*-pyrrol-2-yl]methyl}-1*H*-isoindole-1,3(2*H*)-dione (10a)

Beige solid; yield: 2.40 g (52%); mp 179 °C.

IR (KBr): 1717, 1670, 1599, 1515, 1428, 1390, 1259, 1219, 1170, 1033, 949, 882, 794, 745, 711 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.78 (s, 3 H, Me), 1.92 (s, 3 H, Me), 3.83 (s, 3 H, OMe), 3.98 (s, 3 H, OMe), 4.55 (d, *J* = 15.6 Hz, 1 H, CH_AH_B), 4.63 (d, *J* = 15.6 Hz, 1 H, CH_AH_B), 5.96 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 6.19 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 6.73 (s, 1 H, H_{Ar}), 7.45 (s, 1 H, H_{Ar}), 7.65–7.73 (m, 2 H, H_{Pht}), 7.75–7.83 (m, 2 H, H_{Pht}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.4, 27.4, 34.0, 56.1, 56.3, 107.4, 109.1, 111.6, 112.4, 123.2 (2C), 127.1, 130.1, 130.3, 130.6, 131.9 (2C), 134.0 (2C), 148.9, 152.3, 167.4 (2C), 197.8.

MS (EI, 70 eV): *m/z* (%) = 418 (100) [M^+], 403 (30), 400 (60), 385 (24), 272 (75), 258 (54), 228 (60), 216 (81), 200 (20), 125 (16), 110 (17), 76 (19), 59 (37).

Anal. Calcd for $C_{24}H_{22}N_2O_5$: C, 68.89; H, 5.30; N, 6.69. Found: C, 68.69; H, 5.13; N, 6.68.

2-{[1-(2-Benzoyl-4,5-dimethoxyphenyl)-5-methyl-1*H*-pyrrol-2-yl]methyl}-1*H*-isoindole-1,3(2*H*)-dione (10b)

Pale yellow solid; yield: 3.60 g (68%); mp 181–182 °C.

IR (KBr): 1716, 1660, 1596, 1516, 1456, 1428, 1388, 1360, 1336, 1260, 1208, 1128, 1104, 1044, 940, 868, 720 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 1.84 (s, 3 H, Me), 3.53 (s, 3 H, OMe), 3.82 (s, 3 H, OMe), 4.42 (d, *J* = 15.6 Hz, 1 H, CH_AH_B), 4.48 (d, *J* = 15.6 Hz, 1 H, CH_AH_B), 5.59 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 5.83 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 6.79 (s, 1 H, H_{Ar}), 7.10 (s, 1 H, H_{Ar}), 7.44–7.51 (m, 2 H, H_{Ar}), 7.57–7.64 (m, 1 H, H_{Ar}), 7.68–7.73 (m, 2 H, H_{Ar}), 7.75–7.85 (m, 4 H, H_{Pht}).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 12.5, 34.0, 55.5, 55.9, 105.9, 108.4, 112.0, 113.4, 123.0 (2C), 127.7, 128.4 (2C), 129.0, 129.3 (2C), 130.0, 130.1, 131.5 (2C), 133.2, 134.4 (2C), 136.7, 148.0, 150.7, 167.0 (2C), 194.0.

MS (EI, 70 eV): *m/z* (%) = 480 (55) [M^+], 462 (70), 447 (10), 334 (57), 320 (26), 239 (45), 228 (76), 214 (15), 198 (18), 105 (100), 91 (17), 77 (21), 59 (12).

Anal. Calcd for $C_{29}H_{24}N_2O_5$: C, 72.49; H, 5.03; N, 5.83. Found: C, 72.47; H, 5.22; N, 5.66.

2-({1-[4,5-Dimethoxy-2-(4-methylbenzoyl)phenyl]-5-methyl-1*H*-pyrrol-2-yl}methyl)-1*H*-isoindole-1,3(2*H*)-dione (10c)

Beige solid; yield: 4.35 g (80%); mp 200 °C (EtOH–acetone).

IR (KBr): 1715, 1660, 1602, 1519, 1439, 1388, 1337, 1256, 1207, 1172, 1103, 1038, 940, 889, 864, 751, 714 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.92 (s, 3 H, Me), 2.39 (s, 3 H, Me), 3.67 (s, 3 H, OMe), 3.91 (s, 3 H, OMe), 4.56 (d, *J* = 15.6 Hz, 1 H, CH_AH_B), 4.63 (d, *J* = 15.6 Hz, 1 H, CH_AH_B), 5.76 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 6.08 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 6.76 (s, 1 H, H_{Ar}), 7.02 (s, 1 H, H_{Ar}), 7.21 (d, *J* = 8.1 Hz, 2 H, H_{Ar}), 7.62–7.79 (m, 6 H, H_{Pht}, H_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.7, 21.6, 34.3, 56.0, 56.2, 106.3, 109.2, 112.0, 113.3, 123.0 (2C), 127.8, 128.9 (2C), 129.9 (2C), 130.1, 130.7, 130.9, 132.1 (2C), 133.7 (2C), 134.5, 143.8, 148.0, 150.7, 167.4 (2C), 193.8.

MS (EI, 70 eV): *m/z* (%) = 494 (44) [M^+], 476 (16), 348 (19), 334 (32), 242 (57), 228 (22), 197 (12), 119 (100), 105 (82), 91 (26), 50 (14).

Anal. Calcd for $C_{30}H_{26}N_2O_5$: C, 72.86; H, 5.30; N, 5.66. Found: C, 72.79; H, 5.21; N, 5.61.

Substituted 8,9-Dimethoxy-1-methyl-4*H*-benzo[*f*]pyrrolo[1,2-*a*][1,4]diazepines 11; General Procedure

A mixture of compound **10** (5.0 mmol), $N_2H_4{\cdot}H_2O$ (2 mL), and EtOH (40 mL) was stirred at r.t. or the reflux temperature until homogeneous. Ethanolic HCl (33%) was added to adjust the pH to ~5. The precipitate was filtered off and the pH of the filtrate was adjusted to ~10 with aq NH_3. The product was extracted with $CHCl_3$ (5 × 50 mL), and the combined organic fractions were washed with H_2O and brine, dried (Na_2SO_4), and concentrated under reduced pressure. The residue was purified by column chromatography [silica gel, EtOAc–PE (1:4)]. The solvent was evaporated under reduced pressure to one third of its original volume, and the soln was kept until the product crystallized.

8,9-Dimethoxy-1,6-dimethyl-4*H*-pyrrolo[1,2-*a*][1,4]benzodiazepine (11a)

Reaction stirred at r.t. Pale yellow solid; yield 0.68 g (50%); mp 150–151 °C.

IR (KBr): 1628, 1608, 1516, 1448, 1420, 1372, 1312, 1252, 1208, 1172, 1044, 884, 796, 764 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.32 (s, 3 H, Me), 2.37 (s, 3 H, Me), 3.80 (d, *J* = 12.6 Hz, 1 H, CH_AH_B), 3.91 (s, 3 H, OMe), 3.95 (s, 3 H, OMe), 4.71 (d, *J* = 12.6 Hz, 1 H, CH_AH_B), 6.01 (d, *J* = 3.3 Hz, 1 H, H_{Pyr}), 6.04 (d, *J* = 3.3 Hz, 1 H, H_{Pyr}), 6.81 (s, 1 H, H_{Ar}), 6.97 (s, 1 H, H_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.4, 26.3, 48.0, 56.0, 56.1, 104.1, 108.0, 109.7, 110.1, 123.6, 127.7, 131.0, 135.4, 146.1, 149.6, 166.7.

MS (EI, 70 eV): *m/z* (%) = 270 (30) [M^+], 255 (100), 240 (33), 211 (27), 182 (11), 170 (16).

Anal. Calcd for $C_{16}H_{18}N_2O_2$: C, 71.09; H, 6.71; N, 10.36. Found: C, 71.08; H, 6.86; N, 10.49.

8,9-Dimethoxy-1-methyl-6-phenyl-4*H*-pyrrolo[1,2-*a*][1,4]benzodiazepine (11b)

Reaction stirred at r.t. White solid; yield 0.76 g (46%); mp 165–166 °C.

IR (KBr): 1604, 1564, 1516, 1448, 1424, 1364, 1312, 1252, 1208, 1176, 1128, 1044, 1028, 864, 796, 768 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.39 (s, 3 H, Me), 3.75 (s, 3 H, OMe), 3.96 (s, 3 H, OMe), 3.98 (d, *J* = 12.3 Hz, 1 H, CH_AH_B), 4.99 (d, *J* = 12.3 Hz, 1 H, CH_AH_B), 6.03 (d, *J* = 3.3 Hz, 1 H, H_{Pyr}), 6.05 (d, *J* = 3.3 Hz, 1 H, H_{Pyr}), 6.76 (s, 1 H, H_{Ar}), 6.89 (s, 1 H, H_{Ar}), 7.30–7.43 (m, 3 H, H_{Ph}), 7.56–7.63 (m, 2 H, H_{Ph}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.3, 48.6, 56.0, 56.1, 104.5, 107.8, 109.6, 112.7, 122.0, 127.7, 127.9 (2C), 129.3 (2C), 129.9, 133.0, 135.6, 139.8, 145.5, 149.9, 167.8.

MS (EI, 70 eV): *m/z* (%) = 332 (42) [M^+], 317 (100), 302 (15), 273 (10), 257 (27), 239 (10), 154 (11), 143 (10).

Anal. Calcd for $C_{21}H_{20}N_2O_2$: C, 75.88; H, 6.06; N, 8.43. Found: C, 75.67; H, 6.20; N, 8.27.

8,9-Dimethoxy-1-methyl-6-(4-methylphenyl)-4*H*-pyrrolo[1,2-*a*][1,4]benzodiazepine (11c)

Reaction stirred at reflux. White solid; yield 0.52 g (30%); mp 150–151 °C.

IR (KBr): 1603, 1519, 1451, 1415, 1363, 1254, 1207, 1129, 1048, 871, 825, 760 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.36 (s, 3 H, Me), 2.38 (s, 3 H, Me), 3.76 (s, 3 H, OMe), 3.95 (s, 3 H, OMe), 3.96 (d, *J* = 12.3 Hz, 1 H, CH_AH_B), 4.96 (d, *J* = 12.3 Hz, 1 H, CH_AH_B), 6.03 (d, *J* = 3.3 Hz, 1 H, H_{Pyr}), 6.05 (d, *J* = 3.3 Hz, 1 H, H_{Pyr}), 6.77 (s, 1 H, H_{Ar}), 6.87 (s, 1 H, H_{Ar}), 7.14 (d, *J* = 8.1 Hz, 2 H, H_{Ar}), 7.49 (d, *J* = 8.1 Hz, 2 H, H_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.3, 21.3, 48.5, 56.0, 56.1, 104.5, 107.8, 109.6, 112.9, 122.1, 127.7, 128.7 (2C), 129.3 (2C), 133.0, 135.7, 137.0, 140.0, 145.5, 149.8, 167.8.

MS (EI, 70 eV): *m/z* (%) = 346 (9) [M^+], 331 (100), 315 (11), 138 (15), 95 (20), 59 (40).

Anal. Calcd for $C_{22}H_{22}N_2O_2$: C, 76.28; H, 6.40; N, 8.09. Found: C, 76.29; H, 6.31; N, 8.20.

Ethyl 3-{2-[(1,3-Dioxo-1, 3-dihydro-2*H*-isoindol-2-yl)methyl]-5-methyl-1*H*-pyrrol-1-yl}propanoate (13)

A soln of diketone **4b** (2.6 g, 10 mmol), ester hydrochloride **12** (6.91 g, 45 mmol), and NaOAc (1.85 g, 22.5 mmol) in EtOH (40 mL) was refluxed for 4.5 h while the reaction was monitored by TLC. The mixture was poured into cold H_2O (200 mL), and the precipitate was filtered off, air-dried, and purified by column chromatography [silica gel, EtOAc–PE (1:3.5)]. The solvent was evaporated to one third of its original volume, and the soln was kept until the product crystallized.

White solid; yield: 2.59 g (76%); mp 118–119 °C.

IR (KBr): 1720, 1436, 1396, 1356, 1332, 1316, 1296, 1188, 1120, 1016, 960, 748, 740, 712 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.27 (t, *J* = 7.2 Hz, 3 H, CH_2CH_3), 2.20 (s, 3 H, Me), 2.62–2.67 (m, 2 H, CH_2), 4.16 (q, *J* = 7.2 Hz, 2 H, CH_2CH_3), 4.35–4.40 (m, 2 H, CH_2), 4.84 (s, 2 H, CH_2), 5.81 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 6.18 (d, *J* = 3.6 Hz, 1 H, H_{Pyr}), 7.64–7.72 (m, 2 H, H_{Pht}), 7.77–7.85 (m, 2 H, H_{Pht}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.3, 14.1, 33.2, 35.8, 39.0, 60.8, 106.7, 109.8, 123.2 (2C), 126.0, 128.8, 132.0 (2C), 133.9 (2C), 167.9 (2C), 170.9.

MS (EI, 70 eV): *m/z* (%) = 340 (29) [M^+], 253 (12), 239 (67), 193 (74), 180 (67), 160 (60), 147 (73), 130 (23), 120 (88), 108 (70), 93 (68), 76 (100).

Anal. Calcd for $C_{19}H_{20}N_2O_4$: C, 67.05; H, 5.92; N, 8.23. Found: C, 67.04; H, 5.92; N, 8.19.

7-Methyl-1,2,4,5-tetrahydro-3*H*-pyrrolo[1,2-*a*][1,4]diazepin-3-one (14)

A mixture of ester **13** (2 g, 6.0 mmol), DMF (6 mL), $N_2H_4 \cdot H_2O$ (2.5 mL), and EtOH (50 mL) was refluxed for 45 min (TLC monitoring). The solvent was then evaporated under reduced pressure and the residue was washed with $CHCl_3$ (3 × 30 mL). The combined organic fractions were washed with H_2O, dried (Na_2SO_4), and concentrated under reduced pressure. The residue was purified by column chromatography [silica gel, EtOAc–PE (1:3)], the solvent was evaporated under reduced pressure to one third of the original volume, and the soln was kept until the product crystallized.

White solid; yield: 0.52 g (30%); mp 194–195 °C.

IR (KBr): 3200, 1664, 1508, 1476, 1440, 1424, 1388, 1348, 1312, 1248, 1200, 1172, 1100, 776 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.19 (s, 3 H, Me), 2.90–2.94 (m, 2 H, CH_2), 4.00–4.05 (m, 2 H, CH_2), 4.31 (d, *J* = 5.7 Hz, 2 H, CH_2), 5.79 (d, *J* = 3.3 Hz, 1 H, H_{Pyr}), 5.85 (d, *J* = 3.3 Hz, 1 H, H_{Pyr}), 7.16 (br t, *J* = 5.7 Hz, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.2, 34.1, 39.3, 40.9, 105.3, 105.8, 126.9, 129.9, 174.3.

MS (EI, 70 eV): *m/z* (%) = 164 (60) [M^+], 162 (51), 149 (39), 136 (30), 120 (67), 109 (100), 106 (90), 95 (42), 93 (48), 77 (47), 66 (41), 59 (29), 55 (66), 42 (46).

Anal. Calcd for $C_9H_{12}N_2O$: C, 65.83; H, 7.37; N, 17.06. Found: C, 65.67; H, 7.30; N, 17.06.

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