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ONE-POT SYNTHESIS OF 1-ALKYL-4,5-DIHYDRO-6H-PYRROLO[1,2-*a*]-[1,4]BENZODIAZEPIN-6-ONE

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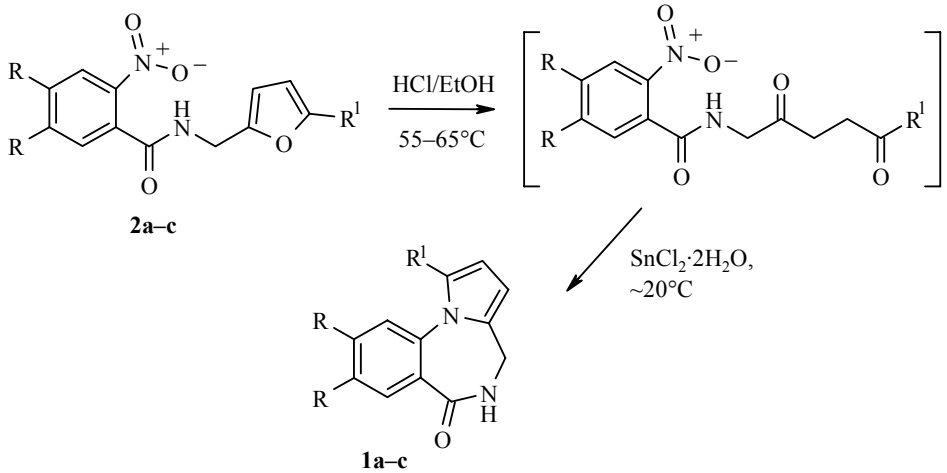
Annelated derivatives of [1,4]diazepine are well known due to the broad range of their biological activity. We have recently reported a synthesis of derivatives of pyrrolo[1,2-*a*][1,4]diazepine based on the acid-catalyzed recyclization of N-(5-methyl-2-furyl)-3-aminothieno[2,3-*b*]pyridinecarboxamides and N-(5-methyl-2-furyl)anthranilamides [1, 2]. This method involves the simultaneous formation of diazepine and pyrrole rings. The anthranilamides used in the reaction were obtained by the reduction of the corresponding *ortho*-nitrobenzamides.

In the present work, we present a one-pot synthesis of pyrrolo[1,2-*a*][1,4]benzodiazepinones **1a-c** directly from *o*-[N-(5-alkyl-2-furyl)methyl]nitrobenzamides **2a-c**.

The proposed method involves opening of the furan ring to form a 1,4-diketone and followed by reduction of the nitro group, leading to spontaneous intramolecular cyclization and formation of the pyrrolodiazepine system.



2a–c

1a–c

1,2 a R = H; R^1 = Me; **b** R =MeO, R^1=Me; **c** R = MeO, R^1=Et

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The ^{1}H NMR spectra were taken on a Bruker AM-300 spectrometer at 300 MHz in DMSO-d_6 with TMS as the internal standard. The electron impact mass spectra were taken on a MAT-112 mass spectrometer with direct inlet into the ion source. The ionizing energy was 70 eV.

Synthesis of Compounds 1a-c (General Method). Solution of gaseous hydrogen chloride in ethanol (20 ml) was added to a solution of nitroamide **2a-c** (5 mmol) in ethanol (20 ml) and the mixture obtained was maintained at 55-60°C until the starting reagent was completely consumed as indicated by thin-layer chromatographic monitoring. Then, $SnCl_2 \cdot 2H_2O$ (4.5 g, 20 mmol) was added to the reaction mixture and the suspension was stirred at room temperature for 10-14 h. The reaction mixture was diluted by adding 20-40 ml ethyl acetate. The precipitate was separated by filtration. The filtrate was evaporated and the residue was recrystallized from a mixture of ethyl acetate and petroleum ether.

1-Methyl-4,5-dihydro-6H-pyrrolo[1,2-*a*][1,4]benzodiazepine (1a) was obtained in 49% yield; mp 230-231°C (mp 230-231°C [2]). The ^{1}H NMR spectrum and mass spectrum were identical to those presented in our previous work [2].

8,9-Dimethoxy-1-methyl-4,5-dihydro-6H-pyrrolo[1,2-*a*][1,4]benzodiazepine (1b) was obtained in 50% yield; mp 195-196°C (mp 195-196°C [1]). The ^{1}H NMR spectrum and the mass spectrum were identical to those presented in our previous work [1].

1-Ethyl-8,9-dimethoxy-4,5-dihydro-6H-pyrrolo[1,2-*a*][1,4]benzodiazepine (1c) was obtained in 54% yield; mp 110-112°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.07 (3H, t, *J* = 7.6, $CH_2C\underline{H}_3$); 2.84 (2H, q, *J* = 7.6, $C\underline{H}_2CH_3$); 3.82 (3H, s, OCH_3); 3.85 (3H, s, OCH_3); 3.90-4.07 (2H, m, $C\underline{H}_2NH$); 5.96 (1H, d, *J* = 3.2, H pyrrole); 6.01 (1H, d, *J* = 3.2, H pyrrole); 6.92 (1H, s, H arom.); 7.26 (1H, s, H arom.); 8.40 (1H, br. s, NH). Mass spectrum, *m/z* (I_{rel}, %): 286 $[M]^+$ (100), 285 (10), 271 (19), 258 (10), 257 (80), 244 (12), 243 (18), 242 (73), 228 (31), 214 (12), 198 (20), 197 (16), 184 (29), 170 (12), 168 (10), 165 (14), 156 (13), 141 (16), 79 (10), 44 (17), 43 (31). Found, %: C 67.18; H 6.24; N 9.69. $C_{16}H_{18}N_2O_3$. Calculated, %: C 67.12; H 6.34; N 9.78.

REFERENCES

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