HETEROCYCLES, Vol. 75, No. 11, 2008, pp. 2713 - 2722. © The Japan Institute of Heterocyclic Chemistry
Received, 12th May, 2008, Accepted, 27th June, 2008, Published online, 3rd July, 2008. COM-08-11436

NEW METHOD OF SYNTHESIS OF 5,6-DIHYDRO-4*H*-PYRROLO[1,2-*a*]-[1,4]BENZODIAZEPINES

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Abstract - 2,5-Dimethoxy-2-(dimethoxymethyl)tetrahydrofuran **1** reacted with anthranilic acid alkyl esters **2** in boiling acetic acid to give 2-(2-formylpyrrol-1-yl)benzoic acid esters **3**. The reductive amination of **3** with primary arylalkylamines **4** led to 2-{2-[(arylalkylamino)methyl]pyrrol-1-yl}-benzoic acids esters **5**. Heating of the aminoesters **5** in xylene under reflux resulted in 5-(arylalkyl)-4,5-dihydro-6*H*-pyrrolo[1,2-*a*][1,4]benzodiazepin-6-ones **7**. Lactams **7** were reduced by lithium aluminum hydride in toluene and ether solutions to give 5-(arylalkyl)-5,6-dihydro-4*H*-pyrrolo[1,2-*a*][1,4]benzo-diazepines **8**. The solid products **8** were recrystallized and the liquid ones were transformed into their salts with oxalic acid.

INTRODUCTION

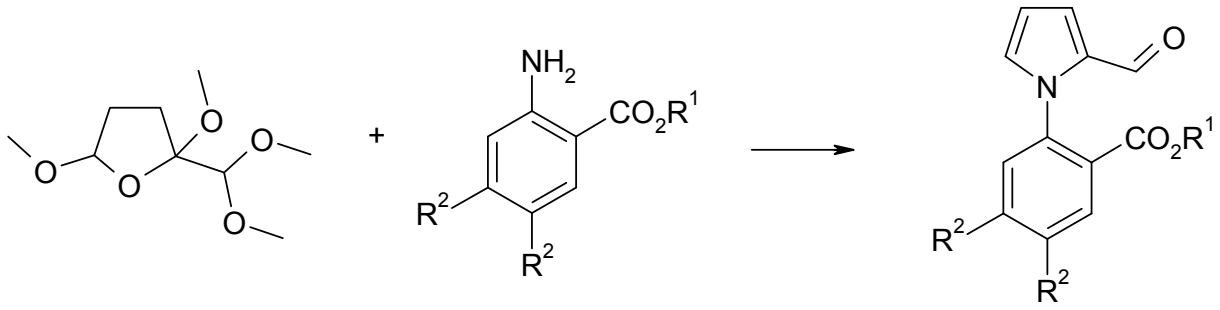
2,5-Dialkoxytetrahydrofuranes are widely used compounds in synthetic heterocyclic chemistry.[1] The presence of an additional reactive acetal group in these furan systems allows to exploit them in obtaining pyrrolo[1,2-*a*]pyrazines[2] and pyrrolo[1,2-*a*]diazepines[3] derivatives, which can be used in the synthesis of novel physiologically active substances.[4,5] In particular, pyrrolo-[1,2-*a*][1,4]benzodiazepines were described as CNS active agents with antidepressant, neuropsychopharmacological activities.[6] According to these examples, differently substituted pyrrolo[1,2-*a*][1,4]benzodiazepines represent promising synthetic targets. Several synthetic approaches based on Mannich reaction between 1-(2-aminomethylphenyl)-1*H*-pyrrole and

aldehydes or ketones were developed.[7,8] Ilyn reported a synthetic route to carboxamide derivatives of pyrrolo[1,2-*a*][1,4]benzodiazepine based on a four-component Ugi reaction.[9] Corelli described the ring closure of 2-(2-hydroxyiminomethyl-1*H*-pyrrol-1-yl)benzene-carboxylates using reductive conditions to obtain 4,5-dihydro-6*H*-pyrrolo[1,2-*a*][1,4]-benzodiazepin-6-ones.[10]

The present work aimed at the synthesis of 5,6-dihydro-4*H*-pyrrolo[1,2-*a*][1,4]benzodiazepines focusing on a specific furan intermediate with an exocyclic acetal group, 2,5-dimethoxy-2-(dimethoxymethyl)tetrahydrofuran (acetal **1**). This method allowed a new strategy in terms of the possible substituents around the core scaffold.

RESULTS AND DISCUSSION

The key compound, Acetal **1**, was synthesized by a 3 step sequence of reactions starting from furan-2-carbaldehyde.[11,12] Acetal **1** reacted with anthranilic acid alkyl esters **2** in boiling acetic acid to give 2-(2-formylpyrrol-1-yl)benzoic acid esters **3** (Scheme 1).The optimum reaction conditions were found to be 3 h reflux and a 10% excess of **1**.



1 **2** **3a-c**

3a, R^1 = Me, R^2 = H

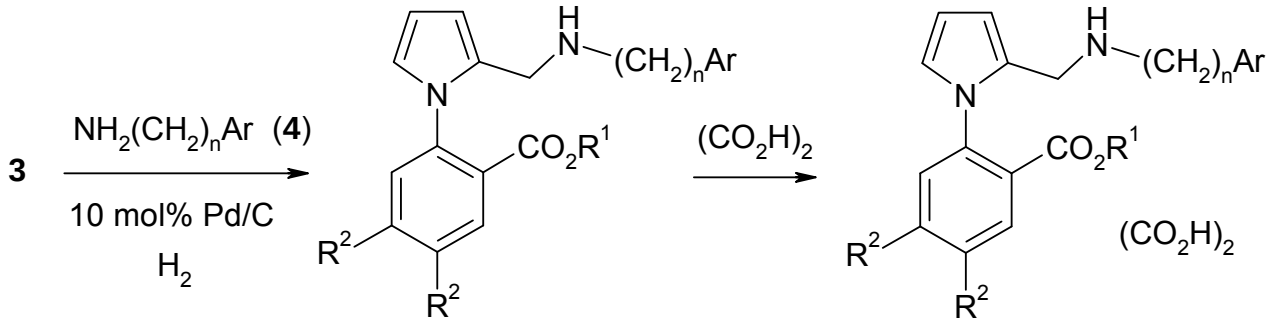
3b, R^1 = Et, R^2 = H

3c, R^1 = Me, R^2 = OMe

Scheme 1

In the process of this reaction the acetal **1**, containing three reactive centers, began to hydrolyze by acid catalysis, starting with the less stable endocyclic ketal group. Simultaneously, the resulting carbocation reacted with the amine group of compound **2** to give the intermediate forming the five-membered cycle. After elimination of water and methanol aromatization led to the pyrrole. The remaining 2-dimethoxymethyl group was then transformed into the aldehyde.

The reductive amination of aldehydoesters **3** with primary arylalkylamines **4** by palladium on coal (10% Pd) led to 2-{2-[(arylalkylamino)methyl]pyrrol-1-yl}benzoic acids esters **5** (Scheme 2).



6a, R^1 = Et, R^2 = H, n = 2, Ar = Ph
6b, R^1 = Et, R^2 = H, n = 2, Ar = $Ph(OMe)_2$-3,4
6c, R^1 = Me, R^2 = OMe, n = 2, Ar = $Ph(OMe)_2$-3,4
6d, R^1 = Me, R^2 = OMe, n = 1, Ar = $Ph(OMe)_2$-3,4
6e, R^1 = Me, R^2 =H, n = 1, Ar = $Ph(OMe)_2$-3,4

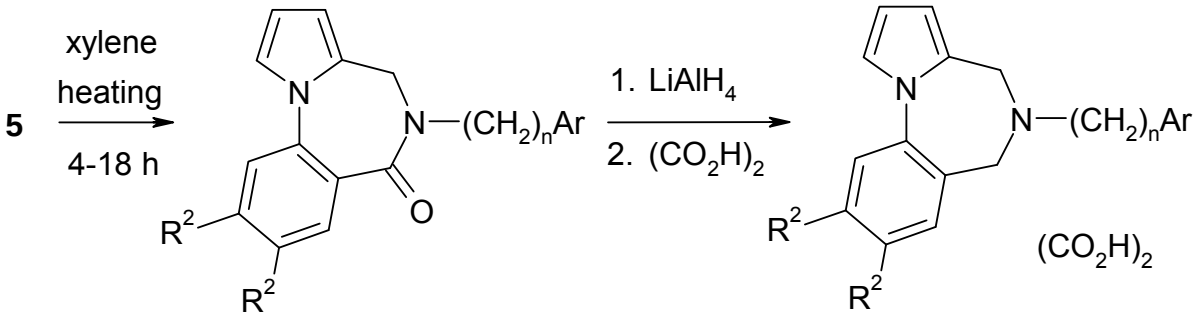
Scheme 2

The reactions were carried out in ethanol solutions and the products **6** were isolated as salts with oxalic acid.

Aminoesters **5** either obtained via reductive amination without isolation or by the treatment of oxalates with potassium carbonate were heated in xylene under reflux to yield the desired 5-(arylalkyl)-4,5-dihydro-6*H*-pyrrolo[1,2-*a*][1,4]benzodiazepin-6-ones **7** (Scheme 3). The process of cyclization was controlled by thin-layer chromatography. The time of lactamization depended on the character of R^1 and R^2 substitutents and on the structure of the arylalkyl group, ranging from 4 to 18 h. The reaction time showed a good correlation with theoretical information on the rate of lactamization according to electronic properties of specific groups. For example, the replacement of protons by methoxy groups, possessing a rather high +M effect, in the benzene ring (R^2) led to a reduction of the reaction rate by half due to the lower partial positive charge at the carbonyl carbon. Also the rate of cyclization was lower for the replacement of methyl by ethyl in the ester group (CO_2R^1) due to an increased +I effect of the alkoxy group.

Lactams **7** were reduced by lithium aluminum hydride in toluene and ether solutions to give the corresponding 5-(arylalkyl)-5,6-dihydro-4*H*-pyrrolo[1,2-*a*][1,4]benzodiazepines **8**. The solid

products **8d** and **8e** were recrystallized and the liquid ones **8a-c** were transformed into their salts with oxalic acid.



7a-e **8a-d**

7a, 8a, R^2 = H, n = 2, Ar = Ph
7b, 8b, R^2 = H, n = 2, Ar = $Ph(OMe)_2$-3,4
7c, 8c, R^2 = OMe, n = 2, Ar = $Ph(OMe)_2$-3,4
7d, 8d, R^2 = OMe, n = 1, Ar = $Ph(OMe)_2$-3,4
7e, 8e R^2 = H, n = 1, Ar = $Ph(OMe)_2$-3,4

Scheme 3

Thus, as a result of our work, a new and convenient method of synthesis of *N*-arylalkyl-substituted pyrrolo[1,2-*a*][1,4]benzodiazepines **7** and **8** was developed. It has considerable advantages in comparison with previously reported procedures.[8,13,14] Based on readily available starting materials and providing high yields this new method has the potential to be used in the synthesis of many other derivatives of this heterocyclic system.

EXPERIMENTAL

^{1}H NMR spectra were determined on a Bruker AC-250 spectrometer in DMSO-d_6 or $CDCl_3$ as solvent and TMS as internal standard. Analytical thin-layer chromatography (TLC) was performed on Merck silica gel 60 F_{254}, using aluminum plates with UV-detection and toluene/acetone/heptane/triethylamine (14:9:3:1) as eluent.

Preparation of alkyl 2-(2-formyl-1*H*-pyrrol-1-yl)benzenecarboxylates (3). General procedure.

A solution of 2,5-dimethoxy-2-(dimethoxymethyl)tetrahydrofuran **1** (0.22 mol) and 2-aminobenzoic acid alkyl ester **2** (0.2 mol) in acetic acid (160 mL) was refluxed for 3 h. The reaction mixture was distilled to dryness. The residue was dissolved in toluene, washed with water, purified by column chromatography (alumina gel, toluene) and evaporated. Solids were washed with toluene and liquid products were distilled.

Methyl 2-(2-formyl-1*H*-pyrrol-1-yl)benzenecarboxylate (3a). Orange oil; yield 70%; bp 140-143 ºC at 1.5 mm Hg; n_D^{25} = 1.6021; mp 53 ºC (lit.,[6] mp 53-55 ºC).

Ethyl 2-(2-formyl-1*H*-pyrrol-1-yl)benzenecarboxylate (3b). Orange oil; yield 74%; bp 150-152 ºC at 1 mm Hg; n_D^{25} = 1.5870. ^{1}H NMR ($CDCl_3$, δ, ppm): 1.13 (t, *J* = 6.8 Hz, 3H, CH_3); 4.12 (q, *J* = 6.8 Hz , 2H, CH_2); 6.42 (m, 1H, H-4); 6.98 (m, 1H, H-5); 7.11 (m, 1H, H-3); 7.32 (d, *J* = 7.6 Hz, 1H, 3`-H); 7.58 (m, 2H, 4`,5`-H); 8.05 (d, *J* = 8.0 Hz, 1H, 6`-H); 9.48 (s, 1H, COH).

Methyl 4,5-dimethoxy-2-(2-formyl-1*H*-pyrrol-1-yl)benzenecarboxylate (3c). Yellow crystals; yield 75%; mp 124-125 ºC; R_f = 0.69. ^{1}H NMR ($CDCl_3$, δ, ppm): 3.64 (s, 3H, CO_2CH_3); 3.88 (s, 3H, 5`-$OCH_3$); 3.97 (s, 3H, 4`-OCH_3); 6.40 (m, 1H, H-4); 6.76 (s, 1H, H-6`); 6.95 (m, 1H, H-5); 7.09 (m, 1H, H-3); 7.54 (s, 1H, H-3`); 9.46 (s, 1H, COH).

Preparation of alkyl 2-{2-[(arylalkylamino)methyl]pyrrol-1-yl}benzenecarboxylates hydrogenoxalates (6). General procedure.

To a solution of alkyl 2-(2-formyl-1*H*-pyrrol-1-yl)benzenecarboxylate **3** (30.0 mmol) and arylalkylamine (30.0 mmol) in EtOH (80 mL) 0.5 g of palladium on coal (10% Pd) was added. The reaction mixture was hydrogenated at atmospheric pressure until the theoretical quantity of hydrogen was absorbed. The catalyst was filtered off and a hot solution of oxalic acid (37.0 mmol) in EtOH was added to the filtrate to give crystals on cooling. The products were recrystallized from EtOH.

Ethyl 2-{2-[(phenethylamino)methyl]pyrrol-1-yl}benzenecarboxylate hydrogenoxalate (6a). White crystals; yield 81%; mp 140-142 ºC; R_f = 0.51. ^{1}H NMR (DMSO-d_6, δ, ppm): 1.01 (t, *J* = 6.7 Hz, 3H, CH_3); 2.86 (m, 2H, C$\underline{H}_2$-Ph); 2.99 (m, 2H, NH-C$\underline{H}_2$-CH_2); 3.92 (q, *J* = 6.7 Hz, 2H, C$\underline{H}_2$-CH_3); 4.08 (s, 2H, C$\underline{H}_2$-Pyr); 6.21 (m, 1H, 4-H); 6.52 (m, 1H, 3-H); 6.80 (m, 1H, 5-H); 7.10-7.38 (m, 5H, PhH); 7.50 (d, *J* = 7.6 Hz, 1H, 3`-H); 7.67 (m, 2H, 4`,5`-H); 7.88 (d, *J* = 7.3 Hz, 1H, 6`-H). *Anal.* Calcd for $C_{22}H_{24}N_2O_2.C_2H_2O_4$ (438.49): C, 65.74; H, 5.98; N, 6.39. Found: C 65.56; H 6.20; N 6.24.

Ethyl 2-{2-[(3,4-dimethoxyphenethylamino)methyl]pyrrol-1-yl}benzenecarboxylate hydrogenoxalate (6b). White crystals; yield 85%; mp 163-165 ºC; R_f = 0.47. ^{1}H NMR (DMSO-d_6, δ, ppm): 1.01 (t, *J* = 6.7 Hz, 3H, CH_3); 2.75 (m, 2H, C$\underline{H}_2$-Ph); 2.94 (m, 2H, NH-C$\underline{H}_2$-CH_2); 3.70 (s, 6H, 2OCH_3); 3.90 (q, *J* = 6.7 Hz, 2H, C$\underline{H}_2$-CH_3); 4.07 (s, 2H, C$\underline{H}_2$-Pyr); 6.22 (m, 1H, 4-H); 6.50 (m, 1H, 3-H); 6.64 (d, *J* = 8.3 Hz, 1H, 6``-H); 6.74 (s, 1H, 2``-H); 6.77 (m, 1H, 5-H); 6.83 (d, *J* = 8.3 Hz, 1H, 5``-H); 7.48 (d, *J* = 7.7 Hz, 1H, 3`-H); 7.66 (m, 2H, 4`,5`-H); 7.87 (d, *J* = 7.3 Hz, 1H, 6`-H). *Anal.* Calcd for $C_{24}H_{28}N_2O_4.C_2H_2O_4$ (498.54): C, 62.64; H, 6.07; N 5.62. Found: C 62.55; H 6.20; N 5.88.

Methyl 2-{2-[(3,4-dimethoxyphenethylamino)methyl]pyrrol-1-yl}-4,5-dimethoxybenzenecarboxylate hydrogenoxalate (6c). White crystals; yield 82%; mp 154-155 ºC; R_f = 0.44. ^{1}H NMR (DMSO-d_6, δ, ppm): 2.72 (m, 2H, C$\underline{H}_2$-Ph); 2.97 (m, 2H, NH-C$\underline{H}_2$-CH_2); 3.51 (s, 3H, CO_2CH_3); 3.72 (s, 6H, 3``-OCH & 4``-OCH_3); 3.79 & 3.83 (2s, 6H, 3`-$OCH_3$ & 4`-OCH_3); 4.01 (s, 2H, C$\underline{H}_2$-Pyr); 6.19 (m, 1H, 4-H); 6.42 (m, 1H, 3-H); 6.63 (d, *J* = 8.4 Hz, 1H, 6``-H); 6.73 (m, 2H, 5-H & 2``-H); 6.82 (d, *J* = 8.4 Hz, 1H, 5``-H); 7.00 (s, 1H, 3`-H); 7.38 (s, 1H, 6`-H). *Anal.* Calcd for $C_{25}H_{30}N_2O_6.C_2H_2O_4$ (544.57): C, 59.55; H, 5.92; N, 5.14. Found: C 59.32; H 6.14; N 5.29.

Methyl 2-{2-[(3,4-dimethoxybenzylamino)methyl]pyrrol-1-yl}-4,5-dimethoxybenzenecarboxylate hydrogenoxalate (6d). White crystals; yield 87%; mp 174-176 ºC; R_f = 0.39. ^{1}H NMR (DMSO-d_6, δ, ppm): 3.55 (s, 3H, CO_2CH_3); 3.67 & 3.73 (2s, 6H, 3``-OCH & 4``-OCH_3); 3.79 & 3.85 (2s, 6H, 3`-$OCH_3$ & 4`-OCH_3); 3.95 (s, 2H, CH_2-Ph); 4.03 (s, 2H, C$\underline{H}_2$-Pyr); 6.17 (m, 1H, 4-H); 6.44 (m, 1H, 3-H); 6.73 (m, 1H, 6``-H); 6.82 (m, 2H, 2``-H & 5-H); 6.95 (m, 1H, 5``-H); 6.99 (s, 1H, 3`-H); 7.30 (s, 1H, 6`-H). *Anal.* Calcd for $C_{24}H_{28}N_2O_6.C_2H_2O_4$ (530.53): C, 58.86; H, 5.70; N, 5.28. Found: C 58.95; H 5.80; N 5.33.

Methyl 2-{2-[(3,4-dimethoxybenzylamino)methyl]pyrrol-1-yl}benzenecarboxylate hydrogenoxalate (6e). White crystals; yield 85%; mp 132-134 ºC; R_f = 0.45. ^{1}H NMR (DMSO-d_6, δ, ppm): 3.55 (s, 3H, CO_2CH_3); 3.69 (s, 6H, 2OCH_3); 3.94 (s, 2H, CH_2-Ph); 4.07 (s, 2H, C$\underline{H}_2$-Pyr); 6.21 (m, 1H, 4-H); 6.48 (m, 1H, 3-H); 6.81 (m, 3H, 5-H, 6``-H & 5``-H); 6.97 (s, 1H, 2``-H); 7.43 (d, *J* = 7.5 Hz, 1H, 3`-H); 7.62 (m, 2H, 4`,5`-H); 7.87 (d, *J* = 7.2 Hz, 1H, 6`-H). *Anal.* Calcd for $C_{22}H_{24}N_2O_4.C_2H_2O_4.0.5\ H_2O$ (479.49): C, 60.12; H, 5.68; N 5.84. Found: C 60.09; H 5.67; N 5.82.

Preparation of 5-(arylalkyl)-4,5-dihydro-6*H*-pyrrolo[1,2-*a*][1,4]benzodiazepin-6-ones (7). General procedure.

Alkyl 2-{2-[(arylalkylamino)methyl]pyrrol-1-yl}benzenecarboxylate hydrogenoxalate **6** (15.0 mmol) was added to a solution of K_2CO_3 (35.0 mmol) in water (30 mL). The free base was

extracted with toluene and the organic layer was washed with water and evaporated. The residue was dissolved in xylene and refluxed for 4-18 h (monitored by TLC). The solution was evaporated to dryness and the residue was recrystallized from aqueous EtOH.

5-Phenethyl-4,5-dihydro-6*H*-pyrrolo[1,2-*a*][1,4]benzodiazepin-6-one (7a). The compound was prepared using 8 h reaction time as white crystals; yield 84%; mp 103-105 ºC; R_f = 0.70. ^{1}H NMR ($CDCl_3$, δ, ppm): 2.94 (t, *J* = 7.6 Hz, 2H, C$\underline{H}_2$-Ph); 3.63 & 3.97 (2m, 2H, C$\underline{H}_2$-CH_2-Ph); 3.95 & 4.24 (2d, *J* = 15.8 Hz, 2H, (4)CH_2); 6.08 (dd, ^3J = 3.4 Hz, ^4J = 1.6 Hz, 1H, 3-H); 6.26 (dd, *J* = 3.4 Hz, *J'* = 3.0 Hz, 1H, 2-H); 7.02 (dd, ^3J = 3.0 Hz, ^4J = 1.6 Hz, 1H, 1-H); 7.15-7.37 (m, 7H, PhH & 7-H & 9-H); 7.51 (ddd, ^3J = 8.5 Hz, $^3J'$ = 7.1 Hz, ^4J = 1.6 Hz, 1H, 8-H); 7.96 (dd, ^3J = 8.5 Hz, ^4J = 1.6 Hz, 1H, 7-H). *Anal.* Calcd for $C_{20}H_{18}N_2O$ (302.38): C, 79.44; H, 6.00; N, 9.26. Found: C 79.41; H 6.09; N 8.99.

5-(3,4-Dimethoxyphenethyl)-4,5-dihydro-6*H*-pyrrolo[1,2-*a*][1,4]benzodiazepin-6-one (7b). The compound was prepared using 8 h reaction time as white crystals; yield 83%; mp 121-122 ºC; R_f = 0.60. ^{1}H NMR ($CDCl_3$, δ, ppm): 2.90 (t, *J* = 7.6 Hz, 2H, C$\underline{H}_2$-Ph); 3.67 & 3.97 (2m & s, 8H, C$\underline{H}_2$-CH_2-Ph, 3'-(OCH_3) & 4'-(OCH_3)); 3.97 & 4.27 (2d, *J* = 15.7 Hz, *J* = 16 Hz, 2H, (4)CH_2); 6.10 (dd, ^3J = 3.4 Hz, ^4J = 1.6 Hz, 1H, 3-H); 6.26 (dd, *J* = 3.4 Hz, *J'* = 3.0 Hz, 1H, 2-H); 6.7-6.85 (m, 3H, 2`-H & 5`-H & 6`-H); 7.03 (dd, ^3J = 3.0 Hz, ^4J = 1.6 Hz, 1H, 1-H); 7.15-7.34 (m, 2H, 10-H & 9-H); 7.51 (ddd, ^3J = 8.3 Hz, $^3J'$ = 7.6 Hz, ^4J = 1.6 Hz, 1H, 8-H); 7.98 (dd, ^3J = 8.35 Hz, ^4J = 1.6 Hz, 1H, 7-H). *Anal.* Calcd for $C_{22}H_{22}N_2O_3$ (362.43): C, 72.91; H, 6.12; N, 7.73. Found: C 73.16; H 6.20; N 7.87.

5-(3,4-Dimethoxyphenethyl)-8,9-dimethoxy-4,5-dihydro-6*H*-pyrrolo[1,2-*a*][1,4]benzodiazepin-6-one (7c). The compound was prepared using 13 h reaction time as white crystals; yield 85%; mp 119-120 ºC; R_f = 0.51. ^{1}H NMR ($CDCl_3$, δ, ppm): 2.88 (m, 2H, C$\underline{H}_2$-Ph); 3.64 & 3.95 (2m, 2H, C$\underline{H}_2$-CH_2-Ph); 3.84 (s, 6H, 3`-$OCH_3$ & 4`-OCH_3); 3.94 (2s, 6H, 8-OCH_3 & 9-OCH_3); 3.97 & 4.28 (2d, *J* = 15.6 Hz, 2H, (4)CH_2); 6.13 (dd, ^3J = 3.4 Hz, ^4J = 1.5 Hz, 1H, 3-H); 6.27 (dd, *J* = 3.4 Hz, *J'* = 2.8 Hz, 1H, 2-H); 6.70-6.80 (m, 4H, 2`-H & 5`-H & 6`-H & 10-H); 7.00 (dd, ^3J = 2.8 Hz, ^4J = 1.5 Hz, 1H, 1-H); 7,46 (s, 1H, 7-H). *Anal.* Calcd for $C_{24}H_{26}N_2O_5$ (422.49): C, 68.23; H, 6.20; N, 6.63. Found: C 67.93; H 6.40; N 6.60.

5-(3,4-Dimethoxybenzyl)-8,9-dimethoxy-4,5-dihydro-6*H*-pyrrolo[1,2-*a*][1,4]benzodiazepin-6-one (7d). The compound was prepared using 18 h reaction time as white crystals; yield 70%; mp 154-156 ºC; R_f = 0.52. ^{1}H NMR ($CDCl_3$, δ, ppm): 3.77 (s, 3H, 3`-$OCH_3$); 3.87 (s, 3H, 4`-OCH_3); 3.94 (s, 3H, 8-OCH_3); 3.97 (s, 3H, 9-OCH_3); 4.05 & 4.24 (2d, *J* = 15.5 Hz, 2H, (4)CH_2); 4.54 & 4.93 (2d, *J* = 15.8 Hz, 2H, C$\underline{H}_2$-Ph); 5.89 (dd, ^3J = 3.4 Hz, ^4J = 1.6 Hz, 1H, 3-H); 6.22 (dd,

J = 3.4 Hz, *J'* = 3.2 Hz, 1H, 2-H), 6.74 (d, *J* = 1.9 Hz, 1H, 5`-H); 6.80 (s, 1H, 10-H); 6.83 (s, 1H, 2`-H); 6.85 (d, *J* = 1.9 Hz, 1H, 6`-H); 7.00 (dd, ^3J = 3.2 Hz, ^4J = 1.6 Hz, 1H, 1-H); 7.52 (s, 1H, 7-H). *Anal.* Calcd for $C_{23}H_{24}N_2O_5$ (408.46): C, 67.63; H, 5.92; N, 6.86. Found: C 67.66; H 6.14; N 6.90.

5-(3,4-Dimethoxybenzyl)-4,5-dihydro-6*H*-pyrrolo[1,2-*a*][1,4]benzodiazepin-6-one (7e). The compound was prepared using 4 h reaction time as white crystals; yield 74%; mp 130-131 ºC; R_f = 0.60. ^{1}H NMR ($CDCl_3$, δ, ppm): 3.77 (s, 3H, 3`-$OCH_3$); 3.86 (s, 3H, 4`-OCH_3); 4.04 & 4.23 (2d, *J* = 15.5 Hz, 2H, (4)CH_2); 4.53 & 4.92 (2d, *J* = 15.8 Hz, 2H, C$\underline{H}_2$-Ph); 5.90 (dd, ^3J = 3.4 Hz, ^4J = 1.6 Hz, 1H, 3-H); 6.22 (dd, *J* = 3.4 Hz, *J'* = 3.2 Hz, 1H, 2-H), 6.75 (d, *J* = 1.9 Hz, 1H, 5`-H); 6.83 (s, 1H, 2`-H); 6.86 (d, *J* = 1.9 Hz, 1H, 6`-H); 7.04 (dd, ^3J = 3.2 Hz, ^4J = 1.6 Hz, 1H, 1-H); 7.35 (m, 2H, 8-H & 10H); 7.37 (d, 1H, 7-H); 7.53 (m, 1H, 9-H); 8.04 (d, *J* = 8.1 Hz, 1H, 7-H). *Anal.* Calcd for $C_{21}H_{20}N_2O_3$ (348.40): C, 72.40; H, 5.79; N, 8.04. Found: C 71.98; H 5.76; N 8.15.

Preparation of 5,6-Dihydro-4*H*-pyrrolo[1,2-*a*][1,4]benzodiazepines (8). General procedure. To a stirred suspension of lithium aluminum hydride (1 g) in dry Et_2O a solution of 4,5-dihydro-6*H*-pyrrolo[1,2-*a*][1,4]benzodiazepin-6-one **7** (7.0 mmol) in dry Et_2O (20 mL) and dry toluene (40 mL) was added dropwise. Then the reaction mixture was refluxed for 5 h. 1 mL of a 20% solution of NaOH and 8 mL of water were added dropwise, the solution was decanted from the precipitate and evaporated. The solid products were recrystallized from EtOH. The liquid compounds were dissolved in EtOH (8 mL) and a hot solution of oxalic acid (8.0 mmol) in EtOH (6 mL) was added. After cooling the precipitate was filtered off and recrystallized from EtOH.

5-Phenethyl-5,6-dihydro-4*H*-pyrrolo[1,2-*a*][1,4]benzodiazepine hydrogenoxalate (8a). White crystals; yield 91%; mp 176-177 ºC. ^{1}H NMR (DMSO-d_6, δ, ppm): 3.08 (m, 2H, C$\underline{H}_2$-Ph); 3.23 (m, 2H, N-C$\underline{H}_2$); 3.98 (s, 2H, (6)CH_2); 4.12 (s, 2H, (4)CH_2); 6.31 (m, 1H, 3-H); 6.52 (m, 1H, 2-H); 7.20-7.46 (m, 7H, PhH, 1-H, 7-H); 7.61 (m, 3H, 8.9,10-H). *Anal.* Calcd for $C_{20}H_{20}N_2.C_2H_2O_4.0{,}5\ H_2O$ (387.45): C, 68.20; H, 5.98; N, 7.23. Found: C 68.26; H 6.00; N 7.35.

5-(3,4-Dimethoxyphenethyl)-5,6-dihydro-4*H*-pyrrolo[1,2-*a*][1,4]benzodiazepine hydrogenoxalate (8b). White crystals; yield 94%; mp 164-166 ºC. ^{1}H NMR (DMSO-d_6, δ, ppm): 3.00 (m, 2H, C$\underline{H}_2$-Ph); 3.21 (m, 2H, N-C$\underline{H}_2$); 3.70 & 3.72 (2s, 6H, 3'-OCH_3 & 4'-OCH_3); 4.00 (s, 2H, (6)CH_2); 4.10 (s, 2H, (4)CH_2); 6.31 (m, 1H, 3-H); 6.50 (m, 1H, 2-H); 6.80 (d, *J* = 7.6 Hz, 1H, 6`-H); 6.89 (d, *J* = 7.6 Hz, 1H, 5`-H); 6.91 (s, 1H, 2`-H); 7.32 (m, 1H, 1-H); 7.41 (m, 1H, 7-H); 7.60 (m, 3H, 8,9,10-H). *Anal.* Calcd for $C_{22}H_{24}N_2O_2.C_2H_2O_4$ (438.49): C; 65.74; H, 5.98; N 6.39. Found: C 65.84; H 6.19; N 6.45.

5-(3,4-Dimethoxyphenethyl)-8,9-dimethoxy-5,6-dihydro-4*H*-pyrrolo[1,2-*a*][1,4]benzodiazepine hydrogenoxalate (8c). White crystals; yield 94%, mp 199-200 ºC. ^{1}H NMR (DMSO-d_6, δ, ppm): 3.02 (m, 2H, C$\underline{H}_2$-Ph); 3.22 (m, 2H, N-C$\underline{H}_2$); 3.72 & 3.74 (2s, 6H, 3'-OCH_3 & 4'-OCH_3); 3.79 & 3.86 (2s, 6H, 8-OCH_3 & 9-OCH_3); 3.98 (m, 2H, (6)CH_2); 4.05 (m, 2H, (4)CH_2); 6.29 (m, 1H, 3-H); 6.45 (m, 1H, 2-H); 6.82 (d, *J* = 7.8 Hz, 1H, 6`-H); 6.88 (d, *J* = 7.8 Hz, 1H, 5`-H); 6.91 (s, 1H, 2`-H); 7.19 (s, 1H, 7-H); 7.23 (s, 1H, 10-H); 7.38 (m, 1H, 1-H). *Anal*. Calcd for $C_{24}H_{28}N_2O_4.C_2H_2O_4$ (498.54): C, 62.64; H, 6.07; N, 5.62. Found: C 62.77; H 6.26; N 5.56.

5-(3,4-Dimethoxybenzyl)-8,9-dimethoxy-5,6-dihydro-4*H*-pyrrolo[1,2-*a*][1,4]benzozepine (8d). White crystals; yield 91%; mp 148-149 ºC; R_f = 0.56. ^{1}H NMR ($CDCl_3$, δ, ppm): 3.38 (s, 2H, (6)CH_2); 3.49 (s, 2H, C$\underline{H}_2$-Ph); 3.62 (s, 2H, (4)CH_2); 3.88 (2s, 6H, 3`-$OCH_3$ & 4`-OCH_3); 3.9 (s, 6H, 8-OCH_3 & 9-OCH_3); 6.21 (m, 1H, 3-H); 6.28 (m, 1H, 2-H); 6.85 (m, 1H, 5`-H); 6.91-7.01 (m, 6H, 1,2`,5`,6`,7,10-H). *Anal*. Calcd for $C_{23}H_{26}N_2O_4$ (394.47): C, 70.03; H, 6.64; N, 7.10. Found: C 69.94; H 6.74; N 7.41.

5-(3,4-Dimethoxybenzyl)-5,6-dihydro-4*H*-pyrrolo[1,2-*a*][1,4]benzodiazepine (8e).
White crystals; yield 90%; mp 111-113 ºC; R_f = 0.66. ^{1}H NMR ($CDCl_3$, δ, ppm): 3.50 (s, 4H, (6)CH_2 & C$\underline{H}_2$-Ph); 3.64 (s, 2H, (4)CH_2); 3.91 (2s, 6H, 3`-$OCH_3$ & 4`-OCH_3); 6.26 (m, 1H, 3-H); 6.31 (m, 1H, 2-H); 6.79-7.06 (m, 4H, 1,2`,5`,6`-H); 7.25-7.46 (m, 4H, 7,8,9,10-H). *Anal*. Calcd for $C_{21}H_{22}N_2O_2$ (334.42): C, 75.42; H, 6.63; N, 8.38. Found: C 75.31; H 6.65; N 8.47.

ACKNOWLEDGEMENTS

This work was funded by EFRE grants from the EU and by grants from the Free State of Saxony (project no. 10843).

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