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SYNTHESES OF 3b,4,6,7-TETRAHYDRO-5H,9H-PYRAZINO [2,1-c] PYRROLO [1,2-a] [1,4] BENZODIAZEPINE, A VALUABLE PRECURSOR OF POTENTIAL CENTRAL NERVOUS SYSTEM AGENTS

Silvio Massa*, Antonello Mai, and Marino Artico
Dipartimento di Studi Farmaceutici, Facoltà di Farmacia,
Università degli Studi "La Sapienza", P.le Aldo Moro, 00185 Roma, Italy.

Federico Corelli*, and Maurizio Botta
Dipartimento Farmaco Chimico Tecnologico, Facoltà di Farmacia,
Via Banchi di Sotto 55, 53100 Siena, Italy.

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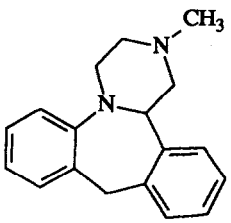
Abstract - Two alternative routes to 3b,4,6,7-tetrahydro-4H,9H-pyrazino [2,1-c] pyrrolo [1,2-a][1,4] benzodiazepine, a useful intermediate for the synthesis of potential antidepressant agents, are described. Though following conceptually different synthetic approaches, both procedures lead to the title compound in a simple and profitable way.

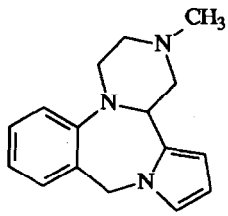
In the last few years much attention has been devoted to the development of safer antidepressant drugs having a lower incidence of extrapyramidal and cardiovascular side-effects. Prominent examples of such "non-classical" antidepressant agents are mianserin (1) and aptazapine (2), currently marketed in several countries and under clinical trials, respectively[1].

Following our research on new central nervous system agents with a pyrrole moiety[2], we have recently reported in brief the synthesis of 3b,4,6,7-tetrahydro-5-methyl-5H,9H-pyrazino [2,1-c] pyrrolo [1,2-a] [1,4] benzodiazepine (3)[3], a novel tetracyclic ring system which shares chemical features with both aptazapine (2) and compounds (4a) and (4b), which also have been claimed to possess psychotropic properties[4]. However, several new compounds, structurally related to (3), needed to be readily available for our pharmacological screening program. Accordingly, we sought to investigate synthetic routes to the nor-derivative of (3), namely 3b,4,6,7-

tetrahydro-5H,9H-pyrazino[2,1-c]pyrrolo[1,2-a][1,4]benzodiazepine (5), which could offer access to a homogeneous set of potential antidepressant agents through suitable derivatization reactions.



1



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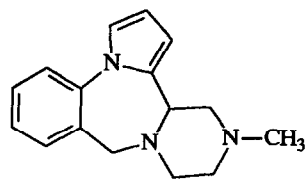

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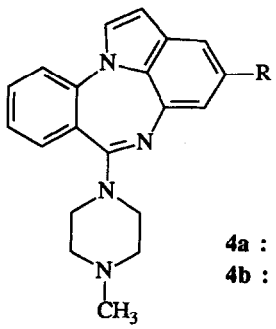
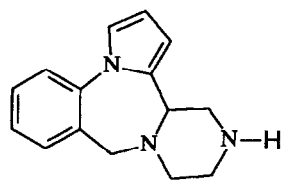


4a : R = Cl
4b : R = CH_3

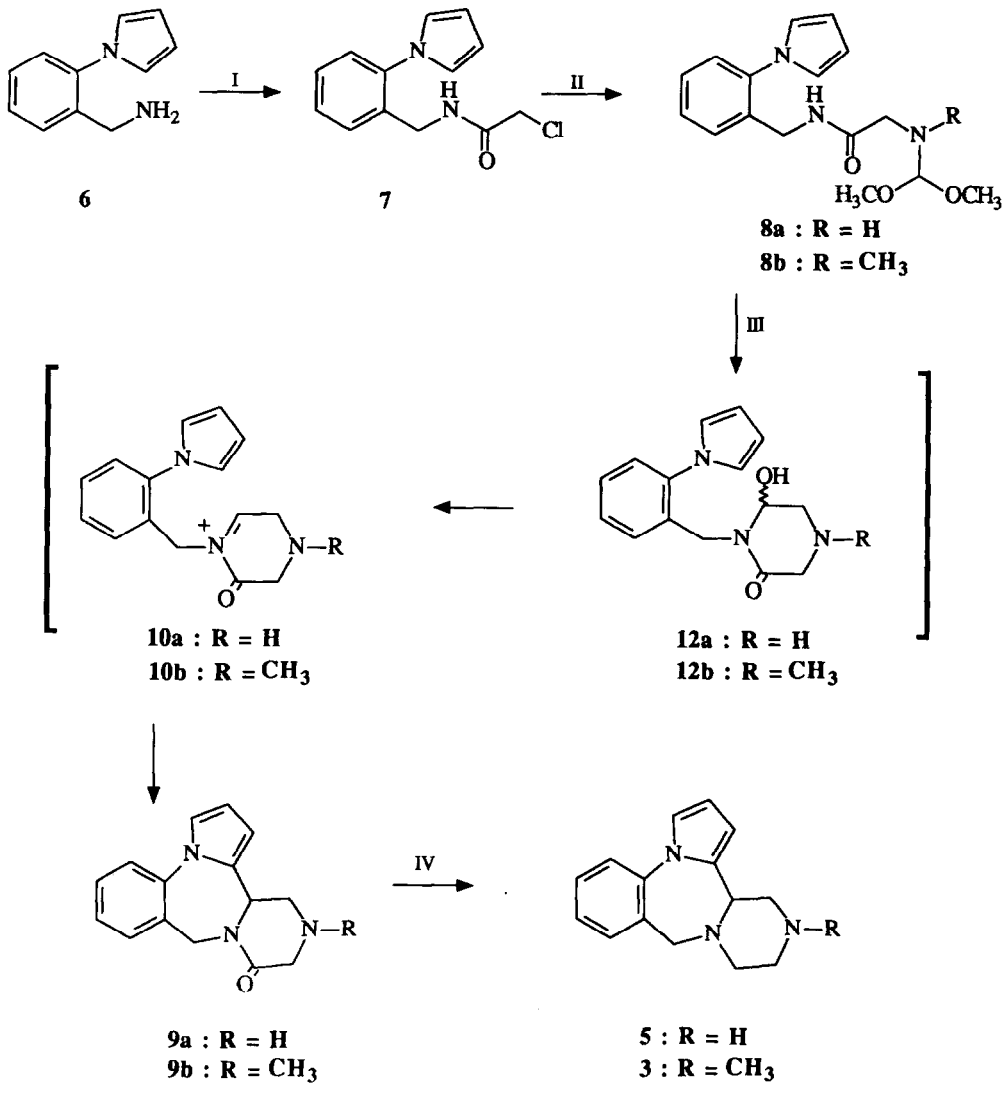


5

It is purpose of this paper to describe two alternative syntheses of this novel tetracyclic compound (5) and also to report the preparation of (3) in full experimental detail.

The synthetic approach to (5) we examined first (Scheme 1) is an extension of the one-pot double annelation procedure previously reported[3] for the preparation of (3). Thus, the known 1-(2-aminomethylphenyl)-1H-pyrrole (6)[5] was chloroacetylated to (7), which was in turn reacted with aminoacetaldehyde dimethyl acetal or methylaminoacetaldehyde dimethyl acetal in the presence of potassium carbonate to give the amidoacetals (8a) and (8b), respectively. Treatment with 37% hydrochloric acid in tetrahydrofuran directly transformed (8a) and (8b) into the tetracyclic derivatives (9a) and (9b) via π-cyclization of the intermediate iminium ions (10a) and (10b). Final reduction of (9a) and (9b) was best performed with lithium aluminum hydride/sulfuric acid (2:1)[6] to afford the required compounds (5) and (3) in a good overall yield.

Scheme 1

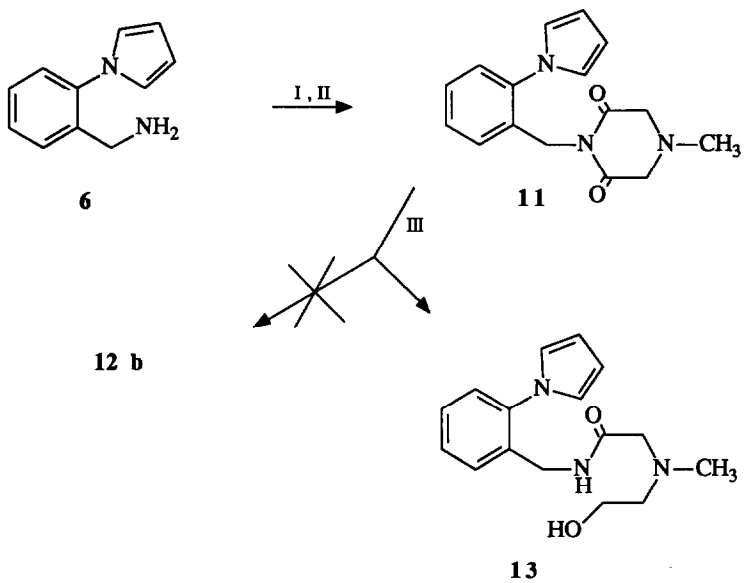


Reagents I: $ClCH_2COCl$, Et_3N; II: $RNHCH_2CH(OCH_3)_2$, K_2CO_3; III 37 % HCl; IV: LAH/H_2SO_4.

π-Cyclization of N-acyliminium ions is a well established[7] method for the preparation of even complex polycyclic compounds. Usually, such reactive species are generated by selective reduction of imide derivatives to hydroxy-

lactams[8], followed by acidic treatment, but this procedure is not free from shortcomings. In fact, our attempts to selectively reduce the imide (11) (Scheme 2) to the hydroxylactam (12b) suffered from overreduction leading to the open-chain hydroxyamide (13) as the main product. On the other hand, the double annelation procedure developed by us allows the direct one-pot synthesis of the tetracyclic derivatives (9a) and (9b) on a preparative scale starting from the readily obtained open-chain compounds (8a) and (8b). Other distinctive advantages of our method are that it does not require the preparation of elusive intermediates or the use of sophisticated reagents.

Scheme 2

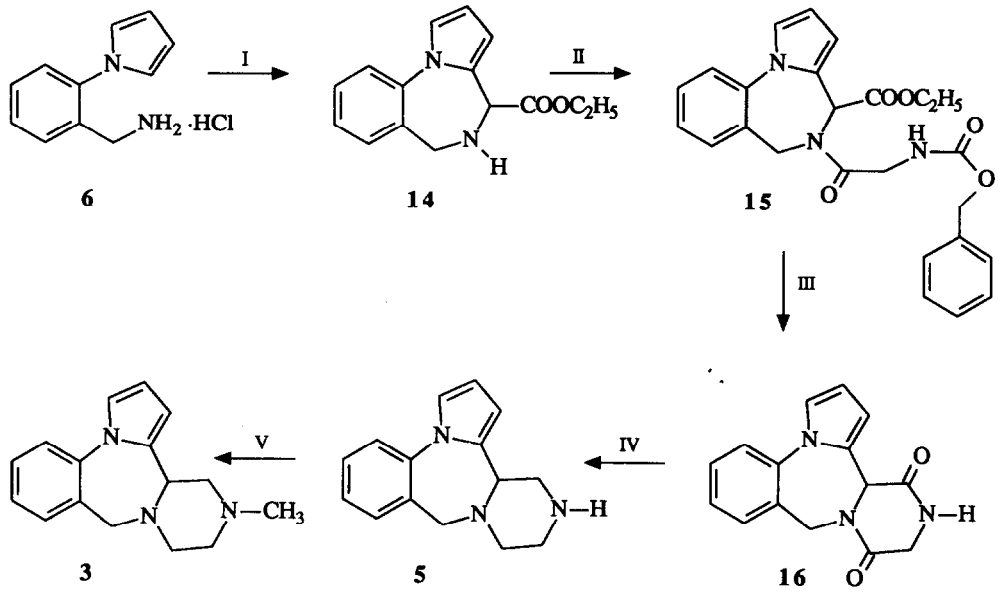


6 **11** **12 b** **13**

Reagents I: N-methyliminodiacetic anhydride ; II: acetic anhydride ; III: $NaBH_4$

Alternatively, (5) was obtained by a route involving as a key step the formation of a diketopiperazine ring by intramolecular cyclization of a conveniently substituted dipeptide derivative (Scheme 3). Pictet-Spengler condensation of (6) hydrochloride with ethyl 2-ethoxyglycolate[1d] provided 5,6-dihydro-4-ethoxycarbonyl-4H-pyrrolo [1,2-a][1,4] benzodiazepine (14). Such a compound could be actually regarded as a pyrrolobenzodiazepine skeleton involving an α-amino acid residue, whose acylation with benzyloxycarbonylglycine

Scheme 3



Reagents I: ethyl 2-ethoxyglycolate; II: benzyloxycarbonylglycine, EDCI ; III: H_2 , Pd / C ; IV: LAH, H_2SO_4; V: CH_2O, H_2, Pd /C.

was expected to furnish the protected dipeptide (15). In order to obtain this key intermediate in a simple and profitable way, we examined the reaction of (14) with both activated glycines (benzyloxycarbonylglycine p-nitrophenyl ester and benzyloxycarbonylglycine hydroxysuccinimido ester) and benzyloxycarbonylglycine in the presence of a number of condensing agents (1,1'-carbonyldiimidazole, dicyclohexylcarbodiimide, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride). Reaction between (14) and benzyloxycarbonylglycine in the presence of the water-soluble 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride as the condensing agent gave the best results as regard to either yield and purity of (15).

Deprotection of (15) could be easily accomplished by catalytic hydrogenolysis in the presence of 10% palladium on charcoal. In particular, when this reaction was performed in ethanol at 4 atm and 50°C for 8 h, the diketopiperazino derivative (16) was obtained directly in a good yield. Reduction of (16) also furnished 3b,4,6,7-tetrahydro-5H,9H-pyrazino [2,1-c] pyrrolo [1,2-a][1,4]

benzodiazepine (5). Finally, the actual usefulness of (5) as a synthetic intermediate was proved by its nearly quantitative transformation into (3) through a reductive alkylation reaction.

By comparing both number and yields of the involved steps as well as the required experimental conditions, the alternative synthetic routes described above appear to be essentially equivalent. Starting from the common precursor (6), both allow the preparation of (5) to be performed by experimentally simple and high-yielding procedures.

EXPERIMENTAL

Melting points were taken on a Büchi 530 apparatus and are uncorrected. IR spectra (Nujol mulls) were run on a Perkin-Elmer 297 spectrophotometer. ^{1}H-NMR spectra (90 MHz, TMS as an internal standard) were recorded on a Varian EM-390 instrument. Merck silica gel 60 and alumina 90 were used for chromatographic purifications. Thin layer chromatography (TLC) was performed by using aluminum baked silica gel plates (C.Erba Stratocrom SIF-254). Developed plates were visualized by UV light. Solvents were reagent grade and when necessary were purified and dried by standard methods. Concentration of solutions after reactions and extractions involved use of a rotary evaporator operating at reduced pressure of approximately 20 torr. Organic solutions were dried over anhydrous sodium sulfate. Elemental analyses were performed by Prof. A.Pietrogrande, Padova, Italy.

2-Chloro-N-[2-(1-pyrryl)phenylmethyl] acetamide (7) : To an ice-cooled solution of 1-(2-aminomethylphenyl)-1H-pyrrole (6)[5] (5.2 g, 0.03 mole) and triethylamine (3.6 g, 0.036 mole) in anhydrous THF (100 ml) a solution of chloroacetyl chloride (3.4 g, 0.03 mole) in the same solvent (10 ml) was gradually added. After stirring at room temperature for 2 h, the mixture was filtered and the clear solution so obtained was evaporated. The residue was taken up in ethyl acetate and washed with 2N hydrochloric acid, saturated solution of sodium hydrogen carbonate and water. Evaporation of the dried solution gave an oily residue, which was purified by column chromatography on silica gel eluting with chloroform to afford 5.5 g (74%) of (7), mp 80-82°C (from benzene:cyclohexane); IR : 3260 cm^{-1} (NH) and 1650 cm^{-1} (CO); ^{1}H-NMR($CDCl_3$) : δ 3.93 (s,2H,CH_2CO), 4.37 (d,2H,CH_2NH), 6.33 (m,2H,pyrrole β -protons), 6.4-6.7 (m,1H,NH), 6.78 (m,2H,pyrrole α -protons) and 7.2-7.5 ppm (m,4H,benzene protons). Anal.calcd. for $C_{13}H_{13}ClN_2O$: C 62.78, H 5.27, N 11.26, Cl 14.25; found: C 62.85, H 5.30, N 11.15, Cl 14.18.

2-[(2,2-Dimethoxyethyl)amino]-N-[2-(1-pyrryl)phenylmethyl] acetamide (8a): A solution of (7) (1.24 g, 0.005 mole) in dry DMF (3 ml) was dropped into a mixture of aminoacetaldehyde dimethyl acetal (0.63 g, 0.006 mole), anhydrous potassium carbonate (1.38 g, 0.01 mole) and dry DMF (7 ml). After heating at 90°C for 1 h while stirring, the mixture was cooled and diluted with water (100 ml) and ethyl acetate (30 ml). The organic layer was separated, washed with brine and dried. Removal of the solvent afforded a residue, which was chromatographed on a silica gel column eluting with ethyl acetate to yield (8a) (1.6 g; 60%), mp 68-70°C (from cyclohexane); IR : 3320 cm^{-1} (NH) and 1665 cm^{-1} (CO); ^{1}H-NMR ($CDCl_3$) : δ 1.53 (s,1H,amine NH), 2.53 (d,2H,$CH_2CH(OCH_3)_2$), 3.04 (s,2H,CH_2CO), 3.23 (s,6H,OCH_3), 4.1-4.4 (m,3H,$PhCH_2$ + $CH(OCH_3)_2$), 6.18 (m,2H,pyrrole β -protons), 6.70 (m,2H,pyrrole α -protons) and 7.1-7.5 ppm (m,5H,benzene protons + amide NH). Anal.calcd. for $C_{17}H_{23}N_3O_3$: C 64.33, H 7.30, N 13.24; found: C 64.25, H 7.33, N 13.16.

2-[N-(2,2-Dimethoxyethyl)-N-methylamino]-N'-[2-(1-pyrryl)phenylmethyl]acetamide (8b): Prepared from (7) in 84% yield following the same procedure reported for (8a); IR: 1665 cm^{-1} (CO); ^{1}H-NMR ($CDCl_3$): δ 2.30 (s,3H,NCH_3), 2.53 (d,2H,$CH_2CH(OCH_3)_2$), 3.07 (s,2H,CH_2CO), 3.22 (s,6H,OCH_3), 4.28-4.47 (m,3H,$PhCH_2$ + $CH(OCH_3)_2$), 6.32 (m,2H,pyrrole β-protons), 6.82 (m,2H,pyrrole α-protons)and 7.27-7.73 ppm (m,5H,benzene protons + NH). Anal.calcd. for $C_{18}H_{25}N_3O_3$: C 65.23, H 7.60, N 12.68; found: C 65.10, H 7.65, N 12.41.

3b,4,6,7-Tetrahydro-7-oxo-5H,9H-pyrazino[2,1-c]pyrrolo[1,2-a][1,4]benzodiazepine (9a) : A solution of (8a) (0.95 g, 0.003 mole) in THF (60 ml) was treated with 12N hydrochloric acid (12 ml) and stirred at room temperature for 20 h. The solution was concentrated in vacuo to a small volume, made basic by adding 2N sodium hydroxide and extracted with chloroform. The combined organic solution was dried and evaporated. After chromatographic purification on alumina column (chloroform as eluent), (9a) was obtained as a white solid (0.30 g, 40%), mp 168-170°C; IR : 3320 cm^{-1} (NH) and 1630 cm^{-1} (CO); ^{1}H-NMR ($CDCl_3$) : δ 1.85 (s,1H,NH), 3.37-3.80 (overlapped signals, 5H, piperazine methylene groups + half of the AB quartet due to the C-9 methylene group), 4.33 (dd, J = 9 and 6 Hz, 1H,C-3b proton), 5.46 (d,J = 13.5 Hz,1H,half of the AB quartet due to the C-9 methylene group), 6.2-6.4 (m,2H,pyrrole β-protons), 7.03 (m,1H,pyrrole α-proton) and 7.2-7.6 ppm (m,4H,benzene protons). Anal.calcd. for $C_{15}H_{15}N_3O$: C 71.13, H 5.97, N 16.59; found: C 71.21, H 5.90, N 16.46.

3b,4,6,7-Tetrahydro-5-methyl-7-oxo-5H,9H-pyrazino[2,1-c]pyrrolo[1,2-a][1,4]benzodiazepine (9b): Prepared as reported for (9a) starting from (8b). Yield: 80%. Mp 152-154°C (from ethanol); IR: 1630 cm^{-1} (CO); ^{1}H-NMR ($CDCl_3$): δ 2.37 (s,3H,CH_3), 2.73-3.62 (m,4H,piperazine methylene groups), 3.70 (d,J = 15 Hz,1H, half of the AB quartet due to the C-9 methylene groups), 4.50 (dd,J = 11 and 4.5 Hz,1H, C-3b proton), 5.53 (d,J = 15 Hz,1H, half of the AB quartet due to the C-9 methylene group), 6.23-6.43 (m,2H,pyrrole β-protons), 7.07 (m,1H,pyrrole α-proton) and 7.37-7.60 ppm (m,4H,benzene protons). Anal.calcd. for $C_{16}H_{17}N_3O$: C 71.88, H 6.41, N 15.72; found: C 71.76, H 6.42, N 15.60.

3b,4,6,7-Tetrahydro-5H,9H-pyrazino[2,1-c]pyrrolo[1,2-a][1,4]benzodiazepine (5): From (9a): To an ice-cooled suspension of lithium aluminum hydride (3.1 g, 0.08 mole) in anhydrous THF (100 ml) 100% sulfuric acid (3.92 g, 0.04 mole) was carefully added. After stirring for 30 min, a solution of (9a) (1.5 g, 0.006 mole) in anhydrous THF (20 ml) was dropped into the above suspension and stirring was maintained at 0-5°C for 2 h. The mixture was cooled to -15°C and quenched with 2N sodium hydroxide. After filtration and removal of the organic solvent the aqueous suspension was extracted with chloroform. Usual work-up afforded an oily product homogeneous by TLC analysis (SiO_2/chloroform : 2-propanol : triethylamine 4:1:1), which crystallized on treatment with diethyl ether to give (5) (1.12 g, 80%) as a white solid, mp 101-103°C; IR : 3210 cm^{-1} (NH); ^{1}H-NMR ($CDCl_3$) : δ 1.62 (s,1H,NH), 2.6-3.3 (m,7H, piperazine protons), 3.40 (d, J = 13.5 Hz,1H, half of the AB quartet due to the C-9 methylene group), 3.83 (d,J = 13.5 Hz,1H, half of the AB quartet due to the C-9 methylene group), 6.1-6.3 (m,2H,pyrrole β-protons), 6.93 (m,1H,pyrrole α-proton) and 7.2-7.5 ppm (m,4H,benzene protons). Anal.calcd. for $C_{15}H_{17}N_3$: C 75.28, H 7.16, N 17.56; found: C 75.33, H 7.15, N 17.52.
From (16): Following this procedure (5) was obtained from (16) in 89% yield.

3b,4,6,7-Tetrahydro-5-methyl-5H,9H-pyrazino[2,1-c]pyrrolo[1,2-a][1,4]benzodiazepine (3) : From (9b): Prepared in 89% yield by reduction of (9b) as described for (5).
From (5): To a solution of (5) (0.3 g, 1.25 mmole) in 95% ethanol (70 ml) were added 40% aqueous formaldehyde (0.1 ml) and 10% palladium on charcoal

(0.3 g). The mixture was hydrogenated in a Parr apparatus for 4 h at room temperature and 3 atm. Removal of the catalyst by filtration and evaporation of the solution afforded an oily residue. Purification by column chromatography (Al_2O_3/chloroform) gave (3) (0.3 g, 95%) whose analytical, spectral and chromatographic data were identical to those of a sample of (3) previously prepared by a different route[3].

4-Methyl-1-[2-(1-pyrryl)phenylmethyl] piperazine-2,6-dione (11): A mixture of N-methyliminodiacetic acid (2.94 g, 0.02 mole) and acetic anhydride (15 ml) was heated at 160°C (bath temperature) until a solution was obtained. Heating was mantained for 10 min more, then volatiles were evaporated off under reduced pressure. The brown oily residue was dissolved in dry benzene (20 ml) and this solution was dropped into a solution of (6) in 20 ml of the same solvent. After stirring at room temperature for 1 h, the precipitate was filtered and heated at 120°C with acetic anhydride (10 ml) for 20 min. The cooled mixture was poured into crushed ice (100 g) and made basic with 6N sodium hydroxide. The product was taken up in chloroform, the organic solution was dried and evaporated to give an oil, which was column chromatographed on alumina eluting with benzene:chloroform (1:1). The imide (11) was obtained (3.0 g; 54%) as a yellow oil; IR: 1735 and 1680 cm^{-1} (CO); ^{1}H-NMR ($CDCl_3$): δ 2.23 (s,3H,CH_3), 3.21 (s,4H,CH_2-N-CH_2), 4.73 (s,2H,Ph-CH_2-N), 6.17 (m,2H,pyrrole β-protons), 6.80 (m,2H,pyrrole α-protons) and 7.23 ppm (m,4H,benzene protons).

2-[N-(2-Hydroxyethyl)-N-methylamino] -N'-[2-(1-pyrryl)phenylmethyl] acetamide (13): To an ice-cooled solution of (11) (0.9 g, 0.0032 mole) in ethanol (10 ml) sodium borohydride (0.83 g, 0.026 mole) was added in three portions. The pH of the reaction was adjusted to 9-10 with some drops of 6N hydrochloric acid and the mixture was stirred for 1 h. A further portion of sodium borohydride (0.82 g, 0.026 mole) was added and the reaction was allowed to warm to room temperature during 1 h. Solvent was evaporated and the residue was partitioned between chloroform and water. The organic layer was dried and evaporated and the oily product was chromatographed on a silica gel column (5% ethanol in ethyl acetate as eluent) to afford oily (13) (0.4 g; 45%); IR: 3300 cm^{-1} (OH+NH) and 1640 cm^{-1} (CO); ^{1}H-NMR ($CDCl_3$): δ 2.20 (s,3H,CH_3), 2.43 (t,2H,NCH_2CH_2OH), 2.94 (s,2H,$COCH_2$), 3.15 (s,1H,OH), 3.47 (t,2H,NCH_2CH_2OH), 4.26 (d,2H,$PhCH_2NH$), 6.24 (m,2H,pyrrole β-protons), 6.73 (m,2H,pyrrole α-protons), 7.2-7.4 (m,4H,benzene protons) and 7.60 ppm (m,1H,NH). Anal.calcd. for $C_{16}H_{21}N_3O_2$: C 66.87, H 7.37, N 14.63; found: C 66.73, H 7.38, N 10.90.
Reduction of (11) with copper(II)chloride dihydrate (1.05 eq) and sodium borohydride (5-fold molar excess)[8a] gave a similar result.

5,6-Dihydro-4-ethoxycarbonyl-4H-pyrrolo [1,2-a] [1,4] benzodiazepine (14): A solution of (6) hydrochloride (27.1 g, 0.13 mole) and ethyl 2-ethoxyglycolate[1d] (29.9 g, 0.20 mole) in absolute ethanol (150 ml) was refluxed for 5 h, then cooled to room temperature. Addition of diethyl ether (400 ml) caused a precipitate to form, which was filtered, washed with diethyl ether and treated with 2N sodium hydroxide and chloroform. The organic layer was dried and evaporated to give (14) (23.3 g; 70%) as an oil which was used directly in the next step.

5,6-Dihydro-5-benzyloxycarbonylaminoacetyl-4-ethoxycarbonyl-4H-pyrrolo [1,2-a] [1,4] benzodiazepine (15): Benzyloxycarbonylglycine (1.15 g, 0.0055 mole) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.05 g, 0.0055 mole) were added in one portion to a pre-cooled (0-5°C) solution of 5,6-dihydro-4-ethoxycarbonyl-4H-pyrrolo [1,2-a][1,4] benzodiazepine (14) (1.28 g, 0.005 mole) in dichloromethane (50 ml). After stirring at 0-5°C for 1 h, then at room temperature for 4 h, the reaction mixture was washed

sequentially with 2N hydrochloric acid, water, saturated solution of sodium hydrogen carbonate and water again. The dried solution was evaporated and the residue was column chromatographed (SiO_2/ethyl acetate) to yield (15) (2.19 g, 98%) as a yellow oil; IR : 3400 cm^{-1} (NH), 1720 cm^{-1} (CO ester) and 1650 cm^{-1} (CO amide). Anal.calcd. for $C_{25}H_{25}N_3O_5$: C 67.10, H 5.63, N 9.39; found: C 66.98, H 5.60, N 9.49.

3b,4,6,7-Tetrahydro-4,7-dioxo-5H,9H-pyrazino[2,1-c]pyrrolo[1,2-a][1,4]benzodiazepine (16) : A solution of (15) (2.24 g, 0.005 mole) in 95% ethanol (200 ml) was hydrogenated in a Parr apparatus for 6 h at 50°C and 4 atm in the presence of 10% palladium on charcoal (0.3 g) as a catalyst. After filtration the solution was concentrated in vacuo to about 50 ml and stored in a cool place overnight. The solid precipitate was filtered and washed with diethyl ether. (16) weighted 0.67 g (50%) and had mp 213-214°C (from ethanol) ; IR : 3200 cm^{-1} (NH), 1675 and 1650 cm^{-1} (CO amide); ^{1}H-NMR (CF_3CO_2H) : δ 4.17 (d,J = 15 Hz,1H, half of the AB quartet due to the C-9 methylene group), 4.52 (s,2H,piperazine methylene group), 5.17 (d,J = 15 Hz, half of the AB quartet due to the C-9 methylene group), 5.53 (s,1H,C-3b proton), 6.40 (m,2H,pyrrole β -protons), 7.13 (m,1H,pyrrole α -proton), 7.47 (m,4H,benzene protons) and 8.45 ppm (s,1H,NH). Anal.calcd. for $C_{15}H_{13}N_3O_2$: C 67.40, H 4.90, N 15.72; found: C 67.25, H 4.86, N 15.58.

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REFERENCES

1. a) S.Ankier in "Progress in Medicinal Chemistry", Vol.23, G.P.Ellis and G.B.West, Eds., Elsevier, 1986, pp. 121-185; b) G.B.Cassano, L.Conti, L.Dell'Osso, and G.Massimetti, Adv.Biochem.Psychopharmacol., 1982, 32, 125; c) J.W.H.Watthey, T.Gavin, M.Desai, B.M.Finn, R.K.Rodebaugh, and S.L.Patt, J.Med.Chem., 1983, 26, 1116 and references cited therein; d) S.K.Boyer, G.Fitchett, J.W.F.Wasley, and G.Zaunius, J.Heterocyclic Chem., 1984, 21, 833.

2. a) M.Artico, F.Corelli, S.Massa, G.Stefancich, L.Avigliano, O.Befani, G.Marcozzi, S.Sabatini, and B.Mondovì, J.Med.Chem., 1988, 31, 802; b) F.Corelli, S.Massa, G.Stefancich, G.Ortenzi, M.Artico, G.C.Pantaleoni, G.Palumbo, D.Fanini, and R.Giorgi, Eur.J.Med.Chem.Chim.Ther., 1986, 21, 445; c) S.Massa, G.Stefancich, M.Artico, F.Corelli, and G.Ortenzi, Heterocycles, 1985, 23, 1417 and references cited therein.

3. S.Massa, A.Mai, and F.Corelli, Tetrahedron Lett., 1988, 29, 6471.

4. E.J.Glamkowski, and Y.Chiang, J.Heterocyclic Chem., 1987, 24, 1599.

5. G.W.H. Cheeseman, and M.Rafiq, J.Chem.Soc. (C), 1971, 2732.

6. H.C.Brown, and N.M.Yoon, J.Am.Chem.Soc., 1966, 88, 1464.

7. a) J.Klaver, H.Hiemstra, and W.N.Speckamp, Tetrahedron, 1988, 44, 6729 and references cited therein; b) S.Kano, Y.Yuasa, and S.Shibuya, Synthesis,

1984, 1071 and references cited therein.
8. a) D.Fréhel, and J.-P.Maffrand, Heterocycles, 1984, 22, 143; b) S.Cortes, and H.Kohn, J.Org.Chem., 1983, 48, 2246; c) J.D.Coyle, Synthesis, 1980, 403.