Synthesis of 1,3,4-oxa(or thia)diazaheterocycles Starting from 2-(Pyrrol-1'-yl)phthalimide

Anita Guesdon, Alain Fogain-Ninkam, Bernard Decroix and Pierre Netchitaïlo*

Unité de Recherche en Chimie Organique et Macromoléculaire, Université du Havre, 25 rue Philippe Lebon, BP 540, 76058 LE HAVRE CEDEX, France

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1-(1,3-Dioxo-1,3-dihydro-*2H*-isoindol-2-yl)-1*H*-pyrrol-2 carbaldehyde **4** was synthesized by Vilsmeier-Haack reaction from 2-(pyrrol-1'-yl) phthalimide. Reduction of **4** by sodium borohydride, or action of Grignard reagents on **4** led to the corresponding alcohols **5** which were cyclized to pyrroloxadiazino isoindoles **1** by heating in the presence of silica gel. Transformation of the hydroxylactam **6** with acetic acid derivatives led to the esters **7** which gave, after saponification, pyrroloxa(or thia)diazepinoisoindolones **2** by intramolecular cyclization.

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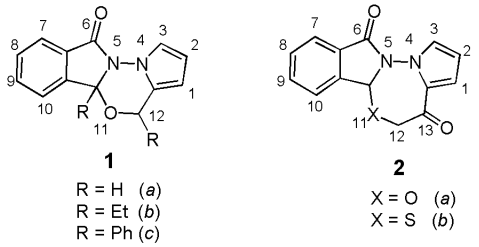
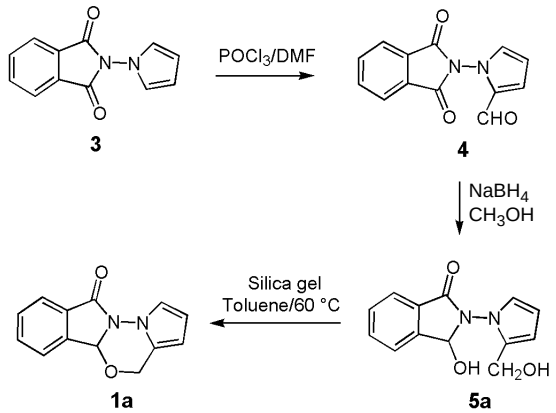
In the course of our research program concerning the synthesis of polyheterocycles with potential pharmacological activity we have reported the use of pyrrolyl isoindole or (pyrrol-1-ylmethyl)isoindole type compounds to lead to tetracyclic systems containing a pyridazine, imidazole, diazepine and thia-(or oxa)diazocine ring fused to pyrrole and isoindole [1a,b]. More recently, we focused our interest on the synthesis of fused dioxaza-ring compounds starting from *N*-hydroxyphthalimide to apply to these original molecules an exhaustive pharmacological investigation [2]. In an extension of these studies, we describe herein the synthesis of pyrrolo[1',2':4,5][1,3,4]oxadiazino-[2,3-*a*]isoindolones **1** and pyrrolo-[1',2':4,5][1,3,4]oxa-(or thia)diazepino[2,3-*a*]isoindolones **2** (Scheme 1).

Scheme 1



Scheme 2



Only little is known on the synthesis of [1,3,4]oxadiazino fused systems. For example, pyrrolidinoxadiazines and pyrrolidinoxadiazinoisoquinolines were obtained by condensation of β-hydroxyhydrazines and γ-chlorobutyraldehyde [3a,b] and pyranoxadiazines by conversion of diazetidines in acetone [4].

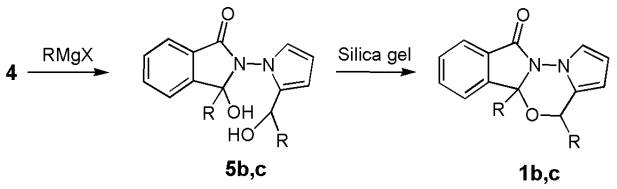
The key compound of the synthesis of oxadiazino derivatives **1** was the carbaldehyde **4** which was synthesized as depicted in Scheme 2.

1-Phthalimidopyrrole **3**, which was prepared by acidic condensation of 1-aminophthalimide with 2,5-diethoxytetrahydrofuran [5], was treated under Vilsmeier – Haack conditions leading to compound **4**. Reduction of **4** with sodium borohydride at 5° in methanol followed by hydrolysis with aqueous ammonium chloride led to the diol **5a** in good yield (82%). Attempts to cyclize compound **5a** in strong acid medium led only to polymerization products, a result which is consistent with the reported sensibility of pyrrole carboxaldehydes to acids [6]. Dehydration and cyclization of **5a** was most conveniently accomplished using silica gel in toluene at 65° since Lewis acids, dimethylsulfoxide or Mitsunobu conditions, which were readily used to lead to ethers from diols [7a-c], gave degradation or polymerization products. The yield was low (22%) as previously reported in the synthesis of pyrrolobenzoxazepine [8]. The ^{1}H nmr spectrum of the cyclic ether **1a** revealed the presence of a doublet of doublet for the H_3 proton characteristic of a monosubstituted pyrrole with usual coupling constants of 2.9 and 3.7 Hz. Furthermore the two protons attached to C_{12} are non equivalent and appear as two doublets at 5.07 and 5.18 ppm (J = 14.2 Hz). Finally, the signal of the proton H_{10b} appears as a singlet at 5.31 ppm.

In order to obtain substituted isomers of **5a** we have investigated the action of Grignard reagents on **4**. Previous studies performed in our laboratory on various *N*-substituted phthalimide derivatives bearing imide and ester functional groups have shown that the regioselectivity of addition of Grignard reagents depended on the nature of the *N*-substituent [9a,b].

Actually, action of ethyl- or phenylmagnesium bromide on **4** did not display any regioselectivity. Addition of one equivalent (or less) of Grignard reagents to **4** led, beside large amounts of starting material, to the diols **5b,c** expected through addition of two equivalents of reagent. Best results were obtained at low temperature (0°) when compound **4** dissolved in dichloromethane was reacted with a large excess (8 equivalents) of freshly prepared ethyl- and phenylmagnesium bromide for 2 hours. In these conditions **5b** and **5c** were prepared with moderate yields (51 and 71%, respectively). Attempts performed at room temperature gave complex mixtures of inseparable products probably through dehydration reactions of hydroxylactam and alcohol functions and/or polymerization reactions as previously reported [9b]. Cyclization of **5b,c** was conducted using the same conditions described above and led to C_{10b} substituted cyclic ethers **1b,c** in moderate yield (38-45%).

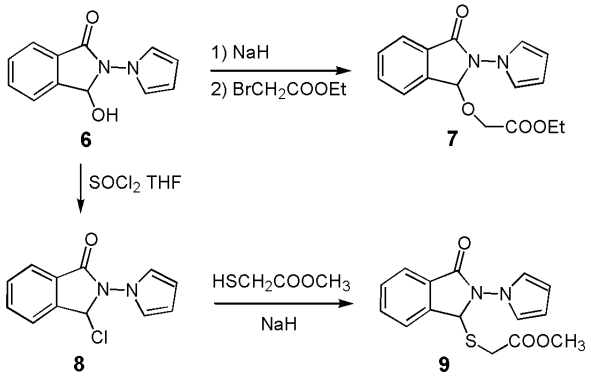
Scheme 3



The structure of compounds **1b,c** was supported by spectroscopic measurements as well as by microanalysis. In ^{1}H nmr spectra of **1b,c** it could be noted the disappearance of signals of exchangeable protons (two hydroxyl groups) which were present in spectra of **5b,c**.

Since we have previously shown that *N*-substituted hydroxyisoindolones can give glycolic or thioglycolic derivatives by nucleophilic substitution *via* an *N*-acyliminium ion [1b,10], we have considered the action of glycolic or thioglycolic acids on hydroxy(pyrrol-1-yl)phthalimide **6** [1a].

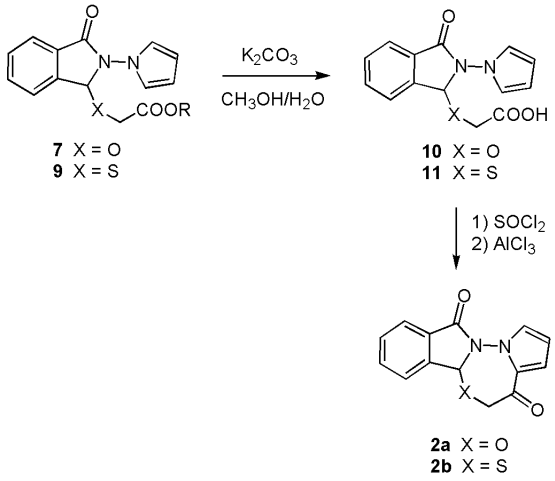
Scheme 4



The glycolic acid failed to react on **6** in acidic conditions as described before [1b], therefore, the carboxyethyloxyester derivative **7** was obtained by a nucleophilic substitution using ethyl bromoacetate and the alcoholate derivative from **6**. On the other hand, thioglycolic acid reacts directly on **6** in the presence of *p*-toluenesulfonic acid but give only low yields (20%) of the isoindolonethioglycolic acid **11**. Our best result was obtained if the hydroxylactam was treated with thionyl chloride in tetrahydrofuran and the resulting chlorolactam **8** submitted to the action of the thiolate anion generated by action of sodium hydride on methylthioglycolic ester (45% yield).

Saponification of the ester group of **7** and **9** led to the expected acids **10**, **11**. Intramolecular cyclization of the

Scheme 5



acid chloride derivatives under Friedel and Crafts conditions gave the pyrroloxa(ortha)diazepino isoindoles **2a** and **2b**. These compounds were characterised by their ^{1}H nmr spectra which exhibit the signals of the three protons of the monosubstituted pyrrole ring while ^{1}H nmr spectra of the starting acids show two symmetrical signals.

In conclusion, we have shown herein that 2-(pyrrol-1'-yl)phthalimide could constitue a versatile synthon to [1,3,4]oxa(thia)diaza systems fused to both isoindole and pyrrole rings. The 2-(2'-formylpyrrol-1'-yl)phthalimide **2** is an interesting intermediate and some other aspects of the reactivity of the formyl group of **2** are in progress, in particular the action of Wittig reagents.

EXPERIMENTAL

Melting points were determined on a Leitz hot plate apparatus and are uncorrected. The infrared spectra of solids (potassium bromide) were recorded on a Perkin Elmer FTIR paragon 1000 spectrometer. The ^{1}H and ^{13}C nmr spectra were recorded on a Bruker AC 200 instrument in deuteriochloroform solution except for compound **4**, **5a**, **10** and **11** (DMSO-d_6) and chemical shift (δ) are expressed in ppm relative to internal tetramethylsilane. Progress of the reactions was monitored by tlc on precoated plates of silica gel

60 F 254 (Merck) and the spots visualized using an ultraviolet lamp. Merck silica gel 60 F (70-300 mesh) was used for column chromatography. The elemental analyses were carried out by the microanalysis laboratory of INSA, Mont Saint Aignan, France.

1-(1,3-Dioxo-1,3-dihydro-2*H*-isoindol-2-yl)-1*H*-pyrrol-2-carbaldehyde (**4**).

To 0.75 ml (9.6 mmoles) of dimethylformamide at 10° was added 0.90 ml (9.6 mmoles) of phosphorus oxychloride. The mixture was kept at 5° with stirring during 15 minutes and then was diluted with 4 ml of 1,2-dichloroethane. A solution of 1.80 g (8.5 mmoles) of 1-(pyrrol-1'-yl)phthalimide in 4 ml of 1,2-dichloroethane was added. The reaction mixture was stirred at 65° during 20 hours, and after cooling at room temperature, a solution of 3.8 g (45 mmoles) of sodium acetate in 12 ml of water was added. The resulting mixture was refluxed 1 hour and extracted after cooling with dichloromethane (3 x 15 ml). The organic layer was washed with a saturated solution of sodium hydrogen carbonate, dried over magnesium sulfate and concentrated under reduced pressure. The residue was chromatographed using a mixture of dichloromethane and hexane (1/30) as eluent and afforded the carboxaldehyde **4** (50% yield), mp 200-202°, ir: 1732 and 1680 (C=O) cm^{-1}; ^1H nmr: δ 6.45 (dd, 1H, $H_{4'}$, J = 2.9, 4.3 Hz), 7.05 (multiplet, 1H, $H_{5'}$, J = 0.8, 1.9, 2.9 Hz), 7.10 (dd, 1H, $H_{3'}$, J = 1.9, 4.3 Hz), 7.8 (m, 2H, H_{arom}), 7.95 (m, 2H, H_{arom}), 9.50 (d, 1H, CHO, J = 0.8 Hz).

Anal. Calcd. for $C_{13}H_8N_2O_3$: C, 65.00; H, 3.36; N, 11.66. Found: C, 65.17; H, 3.54; N, 11.40.

2,3-Dihydro-3-hydroxy-2-[2'-(hydroxymethyl)pyrrol-1'-yl]-1*H*-isoindol-1-one (**5a**).

A mixture of **4** (3 g, 17 mmoles), sodium borohydride (1.34 g, 37.3 mmoles) in methanol (40 ml) was stirred at 5° for 2 hours. The solvent was evaporated under reduced pressure and the residue was hydrolyzed with a saturated solution of ammonium chloride (60 ml). The precipitate was collected, washed with water and recrystallized from hexane/ethylacetate (40/60) to give **5a** (3.3 g, 82%) as colorless crystals, mp 163-165°; ir: 3200 (OH), 1702 (C=O) cm^{-1}; ^1H nmr: δ 4.16-4.34 (m, 2H, CH_2O), 6.05-6.14 (m, 3H, H_3', H_4' and H_3), 6.80 (m, 1H, $H_{5'}$), 7.60-7.82 (m, 4H, H_{arom}).

Anal. Calcd. for $C_{13}H_{12}N_2O_3$: C, 63.93; H, 4.95; N, 11.47. Found: C, 63.77; H, 4.84; N, 11.67.

10b,12-Dihydropyrrolo[1',2':4,5][1,3,4]oxadiazino[2,3-*a*]isoindol-6-one (**1a**).

A mixture of **5a** (4 g, 22.6 mmoles) and 30 g of silica gel was stirred in 50 ml of toluene during 4 hours under reflux. The suspension was evaporated to dryness and the residue was chromatographed (ethylacetate/hexane 15/85) to afforded the cyclic compound **1a** (22% yield), mp 72-74°, ir: 1734 (C=O) cm^{-1}; ^1H nmr: δ 5.07 (d, 1H, H_{12}, J = 14.2 Hz), 5.18 (d, 1H, H_{12}, J = 14.2 Hz), 5.31 (s, 1H, H_{10b}), 5.95 (m, 2H, H_1 and H_2), 6.21 (dd, 1H, H_3, J = 2.9, 3.7 Hz), 7.43-7.65 (m, 3H, H_{arom}), 7.91 (m, 1H, H_{arom}), ^{13}C nmr: δ 69.3 (CH_2), 84.1 (CH), 100.6 (CH), 105.6 (CH), 117.1 (CH), 117.2 (C), 118.2 (C), 124.0 (CH), 124.5 (CH), 130.9 (CH), 133.2 (CH), 139.4 (C), 164.5 (C=O).

Anal. Calcd. for $C_{13}H_{10}N_2O_2$: C, 69.02; H, 4.45; N, 12.40. Found: C, 69.17; H, 4.74; N, 12.27.

Reduction of **4** with Grignard Reagents. General Procedure.

To a solution of **4** (1.0 g, 4 mmoles) in 15 ml of dry dichloromethane was added dropwise a solution of ethyl- or phenylbromide (32 mmoles) in dry ether. The mixture was stirred at 0° for 2 hours, quenched with 2 ml of water and filtered on celite. The organic layer was washed with 10 ml of saturated water, dried on magnesium sulfate and concentrated under reduced pressure. The oily residue was triturated with ether, the resulting precipitate was filtered and then recrystallized from ethanol.

3-Ethyl-2,3-dihydro-3-hydroxy-2-[2'-(1''-hydroxypropyl)-pyrrol-1'-yl]-1*H*-isoindol-1-one (**5b**).

This compound was obtained in a yield of 51%, mp 140°; ir: 3330 (OH), 1740 (C=O) cm^{-1}; ^1H nmr: δ 0.75 and 0.85 (t, 6H, $2CH_3$, J = 6.9 Hz), 1.70-2.09 (m, 4H, $2CH_2$), 3.02 (s, 2H, OH), 4.23 (t, 1H, CHOH, J = 6.9 Hz), 6.20 (m, 2H, $H_{3'}$ and $H_{4'}$), 6.60 (dd, 1H, $H_{5'}$, J = 2.1, 2.7 Hz), 7.47-7.83 (m, 4H, H_{arom}).

Anal. Calcd. for $C_{17}H_{20}N_2O_3$: C, 67.98; H, 6.71; N, 9.33. Found: C, 68.13; H, 6.79; N, 9.21.

2,3-Dihydro-3-hydroxy-2-[2'-(hydroxy)phenylmethyl]pyrrol-1'-yl]-3-phenyl-1*H*-isoindol-1-one (**5c**).

This compound was obtained in a yield of 71%, mp 176°; ir: 3316 and 3156 (OH), 1709 (C=O); ^1H nmr: δ 2.98 (s, 2H, OH), 5.45 (d, 1H, H_3, J = 1.1 Hz), 5.78 (m, 1H, H_{pyr}), 5.83 (m, 1H, H_{pyr}), 6.54 (m, 1H, $H_{5'}$), 7.28-7.96 (m, 14H, H_{arom}).

Anal. Calcd. for $C_{25}H_{20}N_2O_3$: C, 75.24; H, 5.08; N, 7.07. Found: C, 75.41; H, 5.29; N, 7.28.

10b,12-Diethyl-10b,12-dihydropyrrolo[1',2':4,5]oxadiazino-[2,3-*a*]isoindol-6-one (**1b**).

This compound was obtained in a yield of 35% using the same procedure as for compound **1a**, mp 144°; ir: 1742 (C=O) cm^{-1}; ^1H nmr: δ 0.64 and 0.97 (t, 6H, $2CH_3$, J = 7.5 Hz), 1.70-2.10 (m, 4H, $2CH_2$), 4.03 (t, 1H, H_{12}, J = 5.9 Hz), 6.02 (m, 1H, H_2), 6.21 (dd, 1H, H_1, J = 2.7, 3.2 Hz), 7.02 (dd, 1H, H_3, J = 1.1, 2.7 Hz), 7.53-7.94 (m, 4H, H_{arom}); ^{13}C nmr: δ 7.5 (CH_3), 9.7 (CH_3), 24.3 (CH_2), 30.1 (CH_2), 69.8 (CH), 93.7 (CH), 101.2 (CH), 106.7 (CH), 119.8 (CH), 123.0 (CH), 124.4 (CH), 128.9 (C), 129.9 (CH), 131.2 (C), 134.3 (CH), 145.4 (C), 169.3 (C=O).

Anal. Calcd for $C_{17}H_{18}N_2O_2$: C, 72.32; H, 6.43; N, 9.92. Found: C, 72.04; H, 6.18; N, 9.69.

10b,12-Dihydro-10b,12-diphenylpyrrolo[1',2':4,5][1,3,4]oxadiazino[2,3-*a*]isoindol-6-one (**1c**).

This compound was obtained in a yield of 38% using the same procedure as for compound **1a**, mp 187°; ir: 1749 (C=O) cm^{-1}; ^1H nmr: δ 5.47 (s, 1H, H_{12}), 5.50 (m, 1H, H_2), 6.08 (dd, 1H, H_1, J = 3.2, 4.3 Hz), 7.0 (dd, 1H, H_3, J = 1.6, 3.2 Hz), 7.26-7.60 (m, 14H, H_{arom}); ^{13}C nmr: δ 71.9 (CH), 92.9 (CH), 104.1 (CH), 106.8 (CH), 120.5 (CH), 120.6 (CH), 120.8 (CH), 124.5 (CH), 124.7 (C_{arom}), 127.7 (C), 127.9 (CH), 128.4 (CH), 128.5 (CH), 128.8 (CH), 129.0 (C_{arom}), 130.6 (C), 134.6 (C_{arom}), 136.7 (C), 138.1 (C), 146.5 (CH), 169.0 (C=O).

Anal. Calcd for $C_{25}H_{18}N_2O_2$: C, 79.35; H, 4.79; N, 8.46. Found: C, 79.16; H, 5.03; N, 8.48.

Ethyl 2,3-Dihydro-2-(pyrrol-1'-yl)-1*H*-isoindol-1-one-3-glycolate (**7**).

Sodium hydride (0.166 g, 6.9 mmoles) was added portionwise to a solution of the hydroxylactam **6** (6.25 mmoles) in anhydrous

tetrahydrofuran (25 ml) at room temperature. The mixture was stirred for 2 hours and a solution of ethyl bromoacetate (1.04 g, 6.5 mmoles) in tetrahydrofuran (7 ml) was slowly added. The mixture was refluxed overnight and the solvent was removed *in vacuo*. The residue was dissolved in dichloromethane, washed with brine and dried. After evaporation of the solvent the residue was purified by chromatography (dichloromethane) to give **7** as an oil (1.35 g, 70%), ir: 1734 and 1623 (C=O) cm^{-1}; ^1H nmr: δ 1.22 (t, 3H, CH_3, J = 7 Hz), 3.74 (d, 1H, OCH_2CO, J = 16.6 Hz), 4.03 (d, 1H, OCH_2CO, J = 16.6 Hz), 4.14 (q, 2H, OCH_2CH_3, J = 7 Hz), 5.99 (s, 1H, H_3), 6.23 (d, 2H, $H_{3'}$ and $H_{4'}$, J = 2.3 Hz), 6.74 (d, 2H, $H_{2'}$ and $H_{5'}$, J = 2.3 Hz), 7.50-7.66 (m, 2H, H_{arom}), 7.79-7.83 (m, 2H, H_{arom}).

Anal. Calcd. for $C_{16}H_{16}N_2O_4$: C, 63.99; H, 5.37; N, 9.33. Found: C, 63.74; H, 5.09; N, 9.06.

Methyl 2,3-Dihydro-2-(pyrrol-1'-yl)-1*H*-isoindol-1-one-3-thioglycolate (**9**).

A mixture of hydroxylactam **6** (2.2 g, 15 mmoles), thionyl chloride (1.5 equivalent) and two drops of dimethylformamide in anhydrous tetrahydrofuran (45 ml) was stirred at room temperature for 20 hours. After evaporation of the solvent *in vacuo*, the chlorolactam **8** was treated without purification as follows: a mixture of methylmercaptoacetate (18 mmoles) in anhydrous tetrahydrofuran (15 ml) was added to a suspension of sodium hydride (0.68 g, 17 mmoles) and was stirred at room temperature for 10 minutes. To this mixture was added slowly a solution of **8** in 20 ml of tetrahydrofuran. After 24 hours of stirring, the solvent was removed and the residue diluted with dichloromethane. The organic layer was washed with water, dried and after evaporation of the solvent the residue was flash-chromatographed (hexane/dichloromethane, 10/90) to give **9** as an oil (2.2 g, 48%), ir: 1731 and 1617 (C=O) cm^{-1}; ^1H nmr: δ 2.64 (d, 1H, CH_2S, J = 15.3 Hz), 2.90 (d, 1H, CH_2S, J = 15.3 Hz), 3.63 (s, 3H, CH_3), 6.14 (s, 1H, H_3), 6.29 (t, 2H, $H_{3'}$ and $H_{4'}$, J = 2.4 Hz), 6.82 (t, 2H, $H_{2'}$ and $H_{5'}$, J = 2.4 Hz), 7.55-7.71 (m, 3H, H_{arom}), 7.91-7.98 (m, 1H, H_{arom}).

Anal. Calcd. for $C_{15}H_{14}N_2O_3S$: C, 59.59; H, 4.67; N, 9.27. Found: C, 59.75; H, 4.79; N, 9.51.

Saponification of the Esters **7** and **9**.

General Procedure.

Potassium carbonate (1.2 g) was added to a suspension of ester **7** or **9** (5 mmoles) in a solution of methanol/water (5/1; 40 ml). The mixture was refluxed for 2 hours and then concentrated *in vacuo*. Water (5 ml) and dichloromethane (5 ml) were added to the residue and the organic layer was discarded. The aqueous layer was acidified with 10% aqueous hydrochloric acid until pH 3, the precipitate was collected and washed with water. Recrystallization from ethanol afforded the acids **10** or **11** as a white solid.

2,3-Dihydro-2-(pyrrol-1'-yl)-1*H*-isoindol-1-one-3-glycolic Acid (**10**).

This compound was obtained in a yield of 87%, mp 168-170°; ir: 3135 (OH), 1745 (COOH), 1695 (C=O) cm^{-1}; ^1H nmr: δ 3.72 (d, 1H, CH_2, J = 16.4 Hz), 3.93 (d, 1H, CH_2, J = 16.4 Hz), 6.17 (t, 2H, $H_{3'}$ and $H_{4'}$, J = 2.5 Hz), 6.24 (s, 1H, H_3), 6.99 (t, 2H, $H_{2'}$ and $H_{5'}$, J = 2.5 Hz), 7.63-7.71 (m, 1H, H_{arom}), 7.80-7.85 (m, 3H, H_{arom}).

Anal. Calcd. for $C_{14}H_{12}N_2O_4$: C, 61.76; H, 4.44; N, 10.29. Found: C, 61.52; H, 4.71; N, 10.45.

2,3-Dihydro-2-(pyrrol-1'-yl)-1*H*-isoindol-1-one-3-thioglycolic Acid (**11**).

This compound was obtained in a yield of 85%, mp 198-200°; ir: 3094 (OH), 1736 (COOH), 1692 (C=O) cm^{-1}; ^1H nmr: δ 2.84 (s, 2H, CH_2), 6.17 (t, 2H, $H_{3'}$ and $H_{4'}$, J = 2.1 Hz), 6.37 (s, 1H, H_3), 6.99 (t, 2H, $H_{2'}$ and $H_{5'}$, J = 2.1 Hz), 7.60-7.71 (m, 2H, H_{arom}), 7.77-7.87 (m, 2H, H_{arom}).

Anal. Calcd. for $C_{14}H_{12}N_2O_3S$: C, 58.32; H, 4.20; N, 9.72. Found: C, 58.58; H, 4.44; N, 9.88.

10b,12-Dihydropyrrolo[1',2':4,5][1,3,4]oxadiazepino[2,3-*a*]-isoindol-6,13-dione (**2a**).

To a mixture of the acid **10** (6 mmoles) in dry dichloromethane (25 ml) was added thionyl chloride (0.55 ml) under stirring. The mixture was refluxed for 2 hours, cooled and the solution was evaporated under reduced pressure. The residue was dissolved in dry dichloromethane (25 ml) and was added drop by drop to a stirred solution of aluminium trichloride (99.99%, 2.48 g, 19 mmoles) and dry dichloromethane (40 ml). At the end of the addition, stirring was continued for 1 hour. The solution was poured in cold water and decanted. The aqueous layer was extracted with dichloromethane (3x20 ml). The combined organic layers were successively washed with a 10% solution of sodium hydrogen carbonate and water, dried on magnesium sulfate and evaporated. The resulting solid was recrystallized from ethanol to give 1.05 g (70%) of compound **2a**, mp 196-198°; ir: 1727 and 1649 (C=O) cm^{-1}; ^1H nmr: δ 3.74 (d, 1H, OCH_2, J = 16.7 Hz), 4.04 (d, 1H, OCH_2, J = 16.7 Hz), 6.34 (s, 1H, H_{10b}), 6.42 (dd, 1H, H_2, J = 3.0, 4.3 Hz), 7.13 (dd, 2H, H_2 and H_3, J = 3.0, 4.3 Hz), 7.62-7.82 (m, 3H, H_{arom}), 7.91-7.95 (m, 1H, H_{arom}); ^{13}C nmr: δ 67.3 (CH_2), 85.8 (CH), 109.9 (CH), 116.5 (CH), 124.3 (CH), 124.8 (CH), 127.9 (CH), 130.2 (C), 131.0 (C), 131.2 (CH), 134.6 (CH), 138.0 (C), 166.1 (C=O), 187.5 (C=O).

Anal. Calcd. for $C_{14}H_{10}N_2O_3$: C, 66.13; H, 3.96; N, 10.72. Found: C, 66.42; H, 4.09; N, 11.02.

10b,12-Dihydropyrrolo[1',2':4,5][1,3,4]thiadiazepino[2,3-*a*]-isoindol-6,13-dione (**2b**).

This compound was obtained in a yield of 67%, starting from **11**, under the same conditions as for compound **2a**, mp 213-215°; ir: 1727 and 1646 (C=O) cm^{-1}; ^1H nmr: δ 2.79 (d, 1H, SCH_2, J = 16.1 Hz), 3.01 (d, 1H, SCH_2, J = 16.1 Hz), 6.07 (s, 1H, H_{10b}), 6.42 (dd, 1H, H_2, J = 2.7, 4.3 Hz), 7.03 (dd, 1H, H_1, J = 1.6, 2.7 Hz), 7.20 (dd, 1H, H_3, J = 1.6, 4.3 Hz), 7.56-7.67 (m, 2H, H_{arom}), 7.73-7.81 (m, 1H, H_{arom}), 7.91-7.95 (m, 1H, H_{arom}); ^{13}C nmr: δ 33.4 (CH_2), 64.0 (CH), 109.9 (CH), 117.8 (C), 117.9 (CH), 124.2 (CH), 124.4 (CH), 128.4 (CH), 130.0 (CH), 131.0 (C), 134.5 (CH), 141.9 (C), 166.2 (C=O), 184.5 (C=O).

Anal. Calcd. for $C_{14}H_{10}N_2O_2S$: C, 62.20; H, 3.73; N, 10.36. Found: C, 62.17; H, 3.94; N, 10.41.

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