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REDUCTIVE SMILES REARRANGEMENT OF 1-[(5-CHLORO-2-NITROPHENYL)SULFONYL]-1*H*-PYRROLE-2-CARBOHYDRAZIDE TO 1-AMINO-6-CHLORO-2-(1*H*-PYRROL-2-YL)BENZIMIDAZOLE

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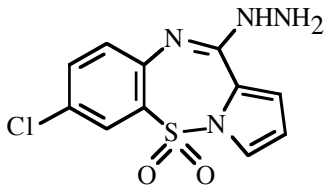
Abstract - Treatment of 1-[(5-chloro-2-nitrophenyl)sulfonyl]-1*H*-pyrrole-2-carbohydrazide with powdered iron in glacial acetic acid afforded 1-amino-6-chloro-2-(1*H*-pyrrol-2-yl)benzimidazole as the sole product. This compound was also obtained by iron-acetic acid reduction of 1-(5-chloro-2-nitrophenyl)-1*H*-pyrrole-2-carbohydrazide. Splitting of the sulfone group occurred only in the presence of the carbohydrazide group. In fact, iron-acetic acid reduction of 5-chloro-2-nitrophenyl 2-ethoxycarbonyl-1*H*-pyrrol-1-yl sulfone gave the expected 2-amino-5-chlorophenyl 2-ethoxycarbonyl-1*H*-pyrrol-1-yl sulfone. Treatment of this compound with hydrazine yielded the corresponding carbohydrazide, which failed cyclization when reacted with phosphorus pentoxide. Formation of 7-chloropyrrolo[1,2-*b*] [1,2,5]benzothiadiazepin-11(10*H*)-one 5,5-dioxide with loss of hydrazine was observed when the above amino hydrazide was reacted with 2-hydroxypyridine or with glacial acetic acid.

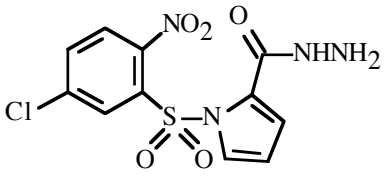
Pursuing searches aimed to synthesize novel tetracyclic ring systems containing a benzothiadiazepine moiety,[1-13] we planned a multistep procedure having 7-chloro-11-hydrazinopyrrolo[1,2-*b*][1,2,5]-benzothiadiazepine (**1**) as a key intermediate.

We supposed that treatment of 1-[(5-chloro-2-nitrophenyl)sulfonyl]-1*H*-pyrrole-2-carbohydrazide (**2**) with iron in acetic acid would undergo reduction of nitro group followed by cyclization to give the required tricyclic derivative (**1**). Therefore, we carried out the preparation of **2** by reacting 5-chloro-

2-nitrobenzenesulfonyl chloride with 2-trichloroacetyl-1*H*-pyrrole and treating the intermediate 1-[(5-chloro-2-nitrophenyl)sulfonyl]-2-trichloroacetyl-1*H*-pyrrole (**3**) with hydrazine hydrate (Scheme 1).



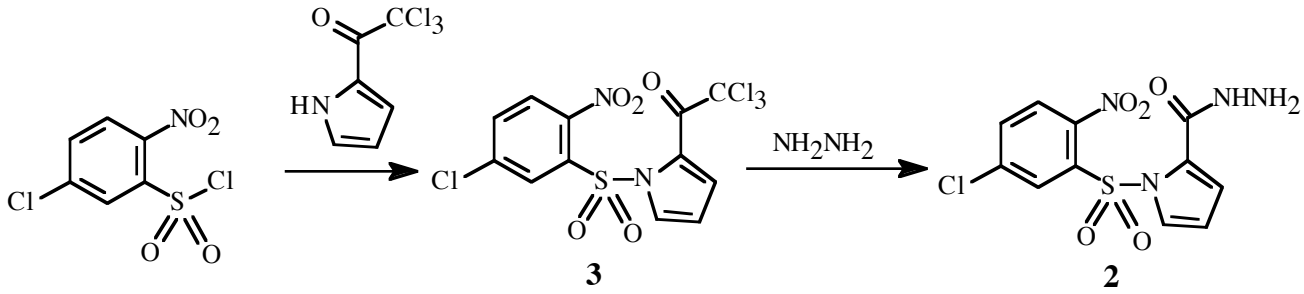
1



2

Contrary to the expectations, treatment of **2** with iron in acetic acid afforded as the sole product a bicyclic derivative, identified as 1-amino-6-chloro-2-(1*H*-pyrrol-2-yl)benzimidazole (**4**), instead of the required tricyclic hydrazino derivative (**1**) (Scheme 2).

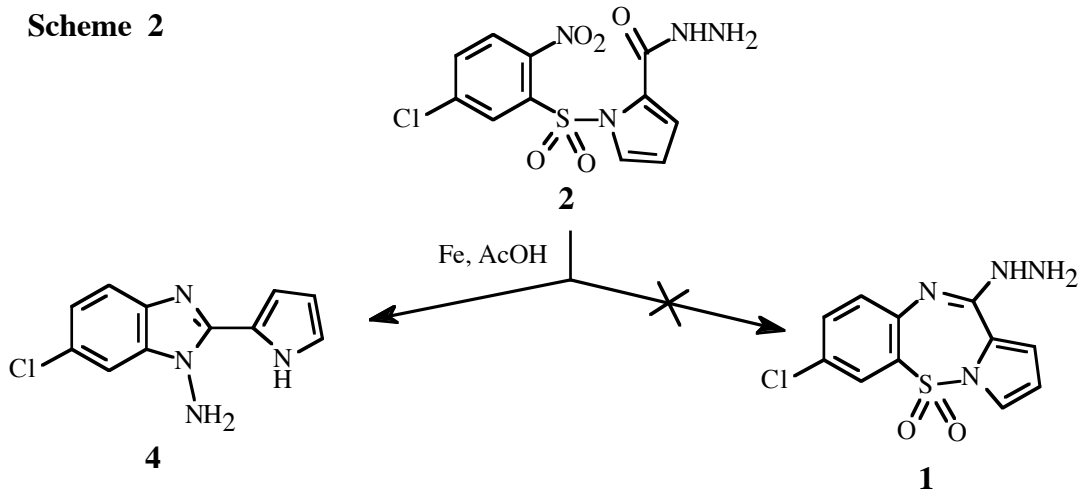
Scheme 1



3 **2**

The structure of **4** was deduced by the data of elemental analyses and NMR spectrum, and was ultimately confirmed by the crystallographic analysis (Figure 1).

Scheme 2



2 **4** **1**

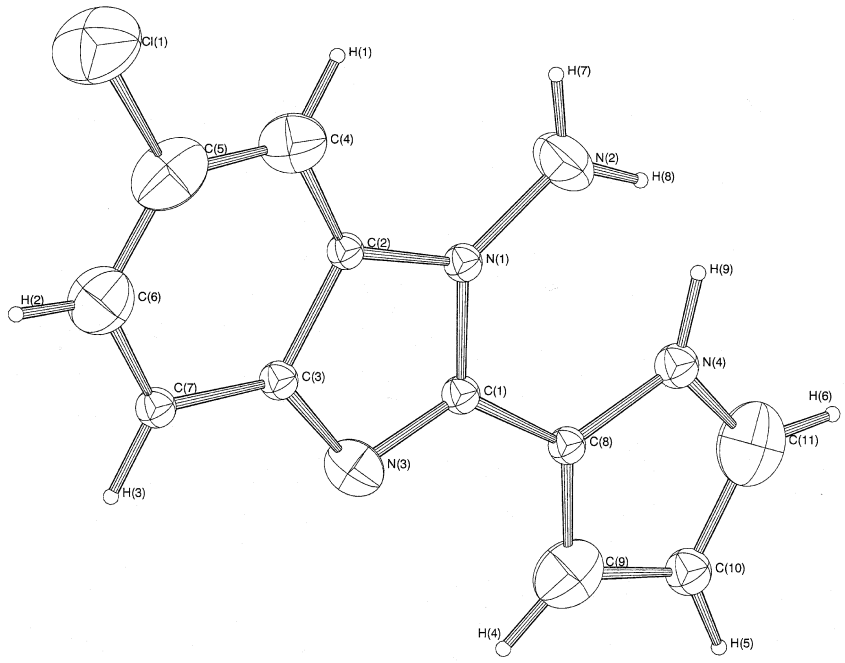
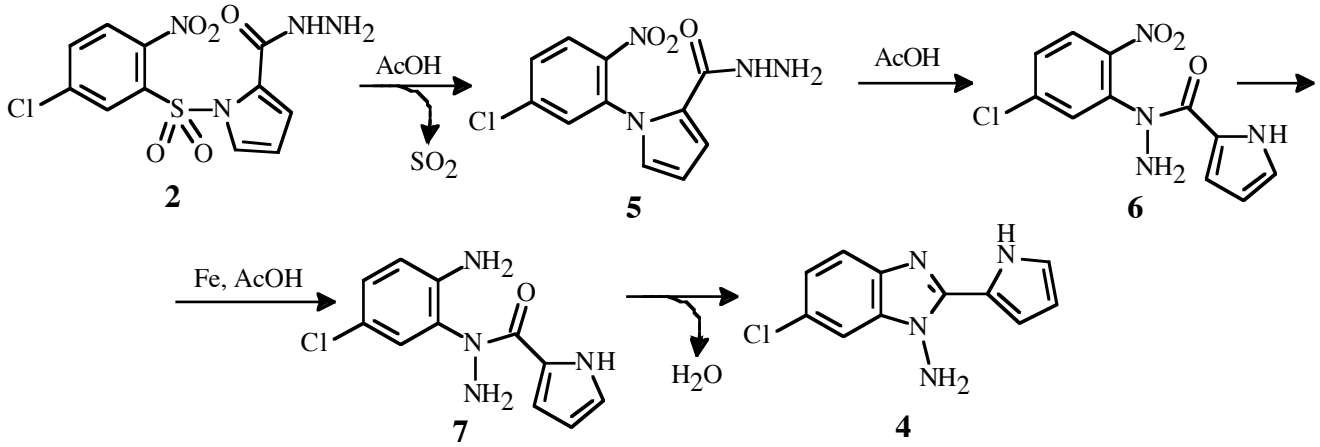


Figure 1. Molecular structure of compound (**4**) and labelling scheme draw with 30% thermal ellipsoids.

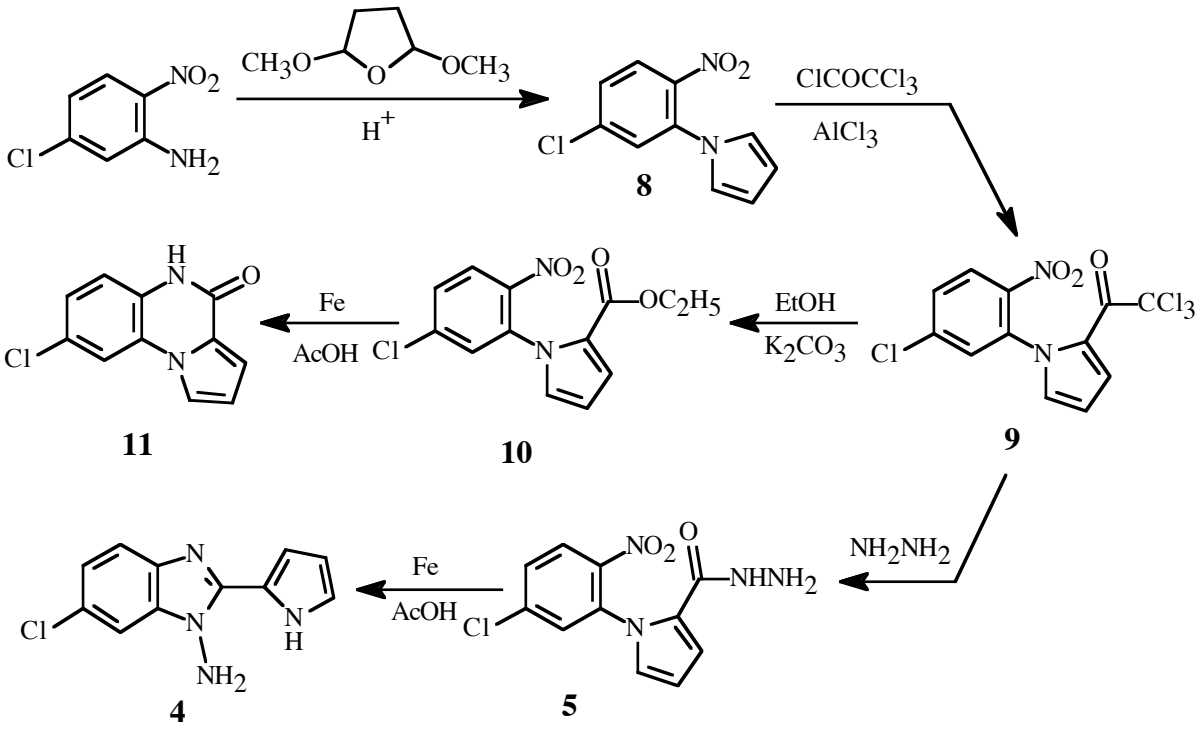
Formation of **4** could be explained hypothesizing the acid-catalyzed transformation of nitro sulfone (**2**) to the related 1-(5-chloro-2-nitrophenyl)-1*H*-pyrrole-2-carbohydrazide (**5**) with extrusion of the sulfone group, followed by the Smiles rearrangement of **5** to an intermediate (**6**). Reduction of nitro group to amino group with concomitant cyclization of an intermediate (**7**) would complete the synthetic pathway with formation of **4** (Scheme 3).

Scheme 3



Such a hypothetic sequence was supported by the following experiment. The reaction of 2,5-dimethoxytetrahydrofuran with 5-chloro-2-nitroaniline formed 1-(5-chloro-2-nitrophenyl)-1*H*-pyrrole (**8**),[16,17] whose treatment with trichloroacetyl chloride in the presence of aluminum trichloride furnished 1-(5-chloro-2-nitrophenyl)-2-trichloroacetyl-1*H*-pyrrole (**9**). Compound (**9**) was then condensed with hydrazine hydrate to afford **5** (Scheme 4). Reduction of **5** with iron-acetic acid gave **4** *via* the Smiles rearrangement, whereas the ester (**10**), obtained from **9**, furnished the pyrroloquinoxalinone (**11**) as the sole product of intramolecular cyclization.

Scheme 4

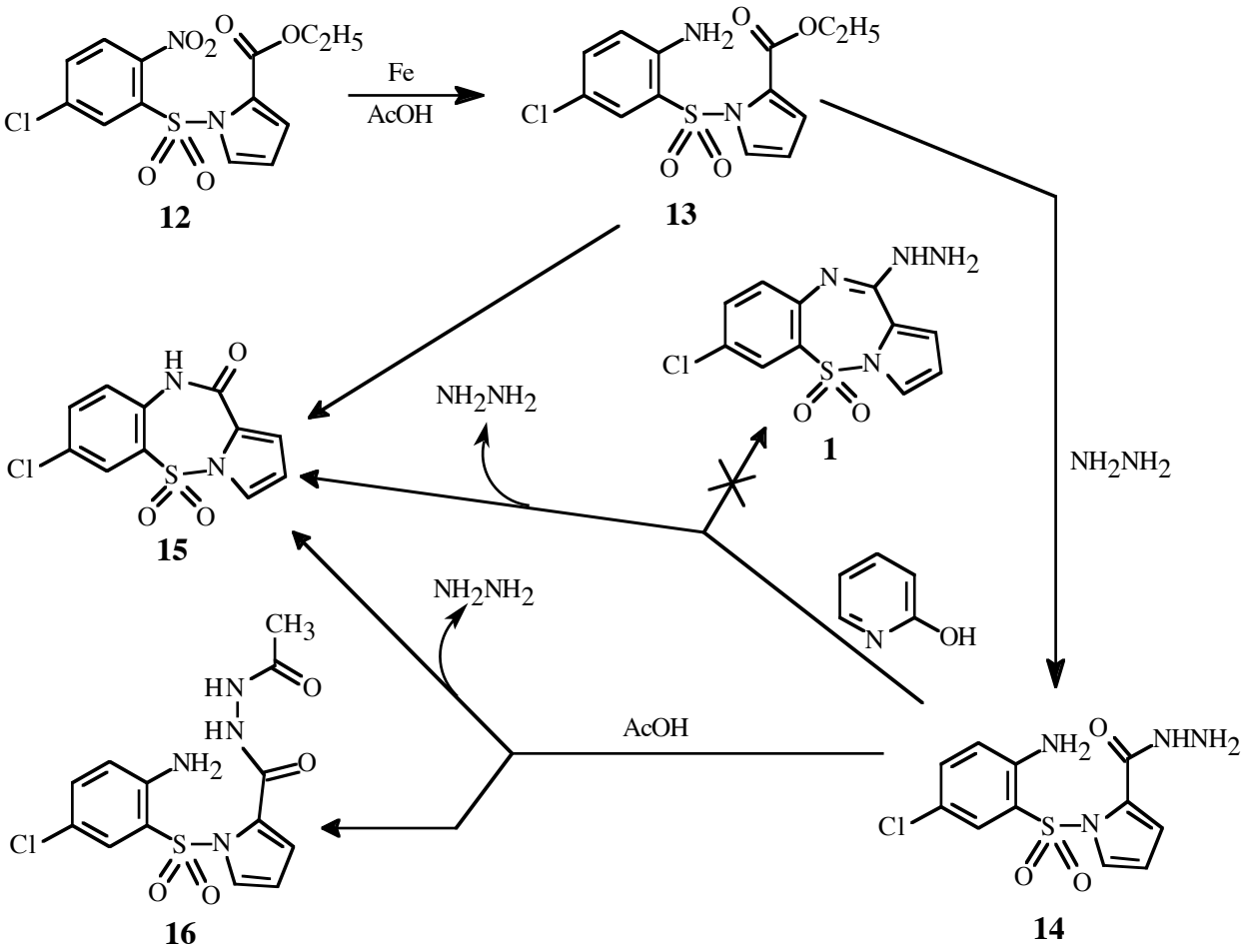


With the hope to avoid desulfonylation with consequent ring contraction, we attempted to synthesize **1** by cyclization of the hydrazide (**14**). In fact, according to Smiles rule (absence of nitro activating group *ortho* to sulfone), hydrazide (**14**), prepared from **13** (Scheme 5), did not undergo rearrangement neither in acetic acid nor on treatment with 2-hydroxypyridine, but led to the benzothiadiazepinone 5,5-dioxide (**15**) with loss of hydrazine in both cases.

Formation of the hydrazide (**16**) was observed as a side-product during treatment of **14** with acetic acid. Attempts to obtain **1** by reacting **14** with phosphorus pentoxide was uneffectual. Structure of **15** was confirmed by unambiguous synthesis involving cyclization of the ester (**13**).

The above results (Schemes 3-5) clarified that the formation of **4** from **2** occurrs only in the presence of the carbohydrazide group. In fact, the absence of the acyl hydrazide group only converted the nitroderivative (**12**) to the amino derivative (**13**). The presence of nitro group was absolutely determinant

Scheme 5



for the Smiles rearrangement because the hydrazide (**14**) did not suffer the rearrangement in acidic medium.

At the light of the above results, we can conclude that under iron-acetic acid reductive conditions **2** is firstly transformed into **5** with extrusion of sulfone group, then **5** undergoes the Smiles rearrangement leading to formation of an intermediate (**7**), which cyclizes to afford the benzimidazole (**4**).

Experimental

CHEMISTRY

Mp were determined on a Büchi 510 apparatus and are uncorrected. IR spectra were run on a Perkin-Elmer 1310 spectrophotometer. Band position and absorption ranges are given in cm^{-1}. ^1H NMR spectra were recorded on a Bruker AM-200 (200 MHz) FT spectrometer in the indicated solvent. Chemical shifts are expressed in δ units (ppm) from tetramethylsilane. Column chromatographies were packed with alumina Merck (70-230 mesh) and silica gel Merck (70-230 mesh). Aluminum oxide TLC cards Fluka (aluminum oxide precoated aluminum cards with fluorescent indicator at 254 nm) and silica gel TLC cards Fluka (silica

gel precoated aluminum cards with fluorescent indicator at 254 nm) were used for thin layer chromatography (TLC). Developed plates were visualized by spectroline ENF 260C/F UV apparatus. Organic solutions were dried over anhydrous sodium sulfate. Concentration and evaporation of the solvent after reaction or extraction was carried out on a rotary evaporator Büchi Rotavapor operating at reduced pressure. Elemental analyses were performed by laboratories of Dr. M. Zancato, Dipartimento di Scienze Farmaceutiche, University of Padova (Italy).

1-[(5-Chloro-2-nitrophenyl)sulfonyl]-2-trichloroacetyl-1*H*-pyrrole (3)

A solution of 2-trichloroacetyl-1*H*-pyrrole[14] (2.12 g, 10.00 mmol) in anhydrous tetrahydrofuran (21 mL) w as added dropwise into a well stirred mixture of potassium *tert*-butoxide (1.34 g, 12.00 mmol) and 18-crown-6 (0.29 g, 1.10 mmol) in the same solvent (21 mL). Stirring was maintained for 15 min, then the suspension formed was cooled to 0°C, while a solution of 5-chloro-2-nitrobenzenesulfonyl chloride[15] (2.56 g, 10.00 mmol) in anhydrous tetrahydrofuran (21 mL) was dropped onto. The solution was stirred at rt for 3.5 h, then concentrated to a small volume and the product was extracted with ethyl acetate. Combined organic extract was washed with brine and dried. Removal of the solvent furnished the crude product which was purified by chromatography on alumina column (chloroform as eluent) to yield **3** (1.64 g, 38%), mp 181-182°C (crystallization from toluene/cyclohexane); IR (nujol): ν 1680 cm^{-1}. ^1H NMR (deuteriochloroform): δ 6.51 (3 line m), 7.68-7.94 (m, 4H), 8.44 ppm (d, J = 2.0 Hz, 1H). *Anal*. Calcd for $C_{12}H_6N_2O_5Cl_4S$: C, 33.36; H 1.40; N, 6.48; Cl, 32.82; S, 7.42. Found: C, 33.52; H 1.44; N, 6.37; Cl, 32.66, S, 7.20.

1-[(5-Chloro-2-nitrophenyl)sulfonyl]-1*H*-pyrrole-2-carbohydrazide (2)

A solution of 1-[(5-chloro-2-nitrophenyl)sulfonyl]-2-trichloroacetyl-1*H*-pyrrole (3.00 g, 6.94 mmol) (**3**) in *N*,*N*-dimethylformamide (30 mL) was cooled to 0° C on an ice bath. 99% hydrazine hydrate (0.35 g, 6.94 mmol) was added, then reaction was stirred at 0°C for 30 min and at rt for 1 h. After dilution with water the mixture was extracted with ethyl acetate, and the extract was washed with brine and dried. Removal of the solvent gave a residue which was purified by passing through a silica gel column (ethyl acetate as eluent). The first fraction was discarded. Further elution with the same solvent and evaporation of collected eluates furnished **2** (0.77 g, 32%), mp 184-186°C (recrystallization from ethanol); IR (nujol): ν 1640, 3350, 3430 cm^{-1}. ^1H NMR (deuteriochloroform): δ 4.68 (br s, 2H, deuterium oxide exchangeable), 6.31 (3 line m, 1H), 6.71 (dd, J = 1.7 and 3.5 Hz, 1H), 7.60 (dd, J = 1.7 and 3.2 Hz, 1H), 7.69 (dd, J = 2.0 and 8.7 Hz, 1H), 7.78 (d, J = 8.7 Hz, 1H), 8.26 (d, J = 2.0 Hz, 1H), 10.12 (br s, 1H, deuterium oxide exchangeable). *Anal*. Calcd for $C_{11}H_9N_4O_5ClS$: C, 38.33; H 2.63; N, 16.25; Cl, 10.28; S, 9.30. Found: C, 38.21; H 2.61; N, 16.18; Cl, 10.33, S, 9.16.

1-(5-Chloro-2-nitrophenyl)-1*H*-pyrrole (8)

A solution of 5-chloro-2-nitroaniline (10.00 g, 57.95 mmol) and 2,5-dimethoxytetrahydrofuran (15.31 g, 115.84 mmol)[16,17] in glacial acetic acid (20 mL) was refluxed for 1 h, then evaporated to dryness. After

mixing with ice water and ethyl acetate, organic layers were combined, washed with brine and dried. Removal of the solvent gave **8** which was passed through a silica gel column (dichloromethane:petroleum ether 1:1 as eluent) to yield 12.26 g (95%), mp 77-78°C (crystallization from ligroin); ^{1}H NMR (deuteriochloroform): δ 6.37 (t, J = 2.1 Hz, 2H), 6.77 (t, J = 2.1 Hz, 2H), 7.38-7.51 (m, 2H), 7.83 ppm (d, J = 8.5 Hz, 1H). *Anal*. Calcd for $C_{10}H_7N_2O_2Cl$: C, 53.95; H 3.17; N, 12.58; Cl, 15.92. Found: C, 53.77; H 3.12; N, 12.70; Cl, 15.68.

1-(5-Chloro-2-nitrophenyl)-2-trichloroacetyl-1*H*-pyrrole (9)

Method A. Trichloroacetyl chloride (22.05 g, 121.28 mmo) was dropped onto an ice cooled solution of **8** (10.00 g, 44.93 mmol), 2,6-lutidine (13.00 g, 121.28 mmol) in anhydrous dioxane (100 mL). Reaction was refluxed for 3 h, then quenched on crushed ice and extracted with ethyl acetate. Organic extracts were combined, washed with brine and dried. Evaporation of the solvent left a residue which was purified by passing through a silica gel column (dichloromethane-petroleum ether 1:1 as eluent) to yield **9** (12.9 g, 78%), mp 152-154°C (recrystallization from ligroin); IR (nujol): ν 1660 cm^{-1}. ^{1}H NMR (deuteriochloroform): δ 6.51 (dd, J = 2.6 and 3.9 Hz, 1H), 7.04 (m, 1H), 7.44 (d, J = 2.0 Hz, 1H), 7.62 (dd, J = 2.0 and 8.6 Hz, 1H), 7.67 (m, 1H), 8.15 ppm (d, J = 8.6 Hz, 1H). *Anal*. Calcd for $C_{12}H_6N_2O_3Cl_4$: C, 39.17; H 1.64; N, 7.61; Cl, 38.54. Found: C, 39.08; H 1.55; N, 7.76; Cl, 38.56.
Method B. Trichloroacetyl chloride (7.27 g, 40.00 mmol) was added dropwise at rt to a suspension of anhydrous aluminum trichloride (10.67 g, 80.00 mmol) in 1,2-dichloroethane (125 mL). The solution was stirred for 10 min, then a solution of **8** (3.00 g, 13.48 mmol) in the same solvent (20 mL) was dropped. Reaction was stirred at rt overnight, then poured on crushed ice and diluted with dichloromethane. Organic layer was separated, washed with brine and dried. Removal of the solvent gave a residue which was purified by silica gel column chromatography (dichloromethane-petroleum ether 1:1 as eluent). First fraction returned 1.1 g (37%) of starting material (**8**); further elution with the same solvent furnished in sequence **9** (0.84 g, 17%) and 1-(5-chloro-2-nitrophenyl)-3-trichloroacetyl-1*H*-pyrrole (0.55 g, 11%), mp 132°C (crystallization from toluene/cyclohexane); IR (nujol): ν 1680 cm^{-1}. ^{1}H NMR (deuteriochloroform):δ 6.79 (dd, J = 2.2 and 3.1 Hz, 1H), 7.01 (dd, J = 1.7 and 3.1 Hz, 1H), 7.54 (d, J = 2.1 Hz, 1H), 7.60 (dd, J = 2.1 and 8.6 Hz, 1H), 7.75 (3 line m, 1H), 8.01 ppm (d, J = 8.6 Hz, 1H). *Anal*. Calcd for $C_{12}H_6N_2O_3Cl_4$: C, 39.17; H 1.64; N, 7.61; Cl, 38.54. Found: C, 38.91; H 1.58; N, 7.33; Cl, 38.30.

1-(5-Chloro-2-nitrophenyl)-1*H*-pyrrole-2-carbohydrazide (5)

A solution of 1-(5-chloro-2-nitrophenyl)-2-trichloroacetyl-1*H*-pyrrole (3.00 g, 6.94 mmol) (**9**) in *N*,*N*-dimethylformamide (30 mL) was cooled to 0° C on an ice bath. 99% hydrazine hydrate (0.35 g, 6.94 mmol) was added, then reaction was stirred at 0°C for 30 min and at rt for 1 h. After dilution with water the mixture was extracted with ethyl acetate, and the extract was washed with brine and dried. Removal of the solvent gave a residue which was purified by passing through a silica gel column chromatography (ethyl acetate as eluent). Evaporation of collected eluates furnished **5** (1.11 g, yield 65%), mp 155-156°C (recrystallization from toluene/cyclohexane); IR (nujol): ν 1605, 3310, 3390 cm^{-1}. ^{1}H NMR (dimethyl sulfoxide-d_6): δ 5.79 (br s, 2H, deuterium oxide exchangeable), 6.14 (m, 1H), 6.96 (u, 1H), 7.07 (u,

1H), 7.56 (dd, J = 2.1 and 9.0 Hz, 1H), 7.90-8.04 (m, 2H), 11.64 ppm (br s, 1H, deuterium oxide exchangeable). *Anal*. Calcd for $C_{11}H_9N_4O_3Cl$: C, 47.07; H 3.23; N, 19.96; Cl, 12.63. Found: C, 46.98; H 3.11; N, 20.03; Cl, 12.88.

1-Amino-6-chloro-2-(1*H*-pyrrol-2-yl)benzimidazole (4)

*From **2***. A solution of **2** (1.00 g, 2.90 mmol) in glacial acetic acid (21 mL) was heated at 60°C on oil bath, then treated portionwise with iron powder (1.00 g, 0.018 g-atom). Reaction mixture was stirred at 60°C for 1.5 h, then evaporated to dryness. Crushed ice and water were added to the residue while mixing for 10 min. After shaking with ethyl acetate, organic layers were collected, washed with brine and dried. Removal of the solvent gave the crude product which was purified by silica gel column chromatography (ethyl acetate as eluent) to yield **4** (0.59 g, 87%), mp 248-250°C (crystallization from toluene); IR (nujol): ν 3280, 3340 cm^{-1}.^{1}H NMR (dimethyl sulfoxide-d_6): δ 6.22 (br, 3H; 3 line m, 1H after deuterium oxide exchange), 6.98 (3 line m, 1H), 7.12-7.23 (m, 2H), 7.46-7.56 (m, 2H), 11.75 ppm (br s, 1H, deuterium oxide exchangeable). *Anal*. Calcd for $C_{11}H_9N_4Cl$: C, 56.78; H 3.90; N, 24.08; Cl, 15.24. Found: C, 56.96; H 3.82; N, 23.86; Cl, 15.19.

*From **5***. Compound (**5**) (1.00 g, 3.56 mmol) was dissolved in glacial acetic acid (21 mL), heated at 60°C and treated portion-wise with iron powder (1.00 g, 0.018 g-atom). After stirring for 1.5 h the mixture was evaporated and the residue triturated with crushed ice and water. Extraction with ethyl acetate and evaporation of collected extracts led to the crude product, which was purified by passing through a silica gel column (ethyl acetate as eluent) to afford pure **4** (0.75 g, 90 %).

Ethyl 1-(5-Chloro-2-nitrophenyl)-1*H*-pyrrole-2-carboxylate (10)

A mixture of **9** (2.55 g, 6.94 mmol), potassium carbonate (0.98 g, 7.08 mmol) and absolute ethanol (20 mL) was refluxed for 3 h. After concentration, the residue was diluted with water and extracted with ethyl acetate. The organic solution was shaken with brine, dried and the solvent evaporated. The crude residue was purified by chromatography on silica gel column (chloroform as eluent) to afford **10** (1.92 g, 77%), mp 120-121°C (recrystallization from toluene/cyclohexane), lit.,[8] mp 121-122°C.

8-Chloropyrrolo[1,2-*a*]quinoxalin-4(5*H*)-one (11)

Iron powder (6.00 g, 0.11 g-atom) was added portionwise to a solution of **10** (2.50 g, 8.48 mmol) in glacial acetic acid (25 mL), then reaction was stirred at 60°C for 3 h. Water (25 mL) and tetrahydrofuran (100 mL) were added while stirring at rt for 1 h and at 60°C for an additional h. Filtration of hot mixture and washing of solid on the filter with boiling tetrahydrofuran (50 mL) gave a clear solution, which was diluted to 1000 mL with water. The solid formed was separated by suction, washed with water and dried to yield pure **11** (1.7 g, 90%), mp >300°C (crystallization from ethanol); IR (nujol): ν 1645 cm^{-1}. ^{1}H NMR (dimethyl sulfoxide-d_6): δ 6.71 (3 line m, 1H), 7.06 (m, 1H), 7.22-7.40 (m, 2H), 8.20-8.30 (u, 2H), 11.38 ppm (br s, 1H, deuterium oxide exchangeable). *Anal*. Calcd for $C_{11}H_7N_2OCl$: C, 60.43; H 3.23; N, 12.81; Cl, 16.22. Found: C, 60.16; H 3.31; N, 12.79; Cl, 16.27.

1-[(2-Amino-5-chlorophenyl)sulfonyl]-1*H*-pyrrole-2-carbohydrazide (14)

A solution of 1-[(2-amino-5-chlorophenyl)sulfonyl]-2-ethoxycarbonyl-1*H*-pyrrole (**13**)[8] (0.63 g, 1.92 mmol) in ethanol (2.5 mL) and 99% hydrazine hydrate (2.5 mL, 51.44 mmol) was refluxed for 1 h, then quenched on crushed ice. After extraction with ethyl acetate the organic solution was shaken with brine and dried. Evaporation of the solvent furnished a residue which was purified by passing through a silica gel column (ethyl acetate as eluent) to give **14** (0.46 g, 77%), mp 174-175°C (recrystallization from ethanol at 4°C); IR (nujol): ν 1615, 1670, 3350, 3440 cm^{-1}. ^1H NMR (dimethyl sulfoxide-d_6): δ 4.46 (br s, 2H, deuterium oxide exchangeable), 6.31 (3 line m, 1H), 6.62 (br s, 2H, deuterium oxide exchangeable), 6.65 (dd, J = 1.4 and 3.4 Hz, 1H), 6.84 (d, J = 9.0 Hz, 1H), 7.37 (dd, J = 2.5 and 9.0 Hz, 1H), 7.72-7.83 (m, 2H), 9.63 ppm (br s, 1H, deuterium oxide exchangeable). *Anal.* Calcd for $C_{11}H_{11}N_4O_3ClS$: C, 41.98; H 3.52; N, 17.80; Cl, 11.26; S, 10.19. Found: C, 42.10; H 3.44; N, 17.66; Cl, 11.39, S, 9.95.

Ethyl 1-[(5-Chloro-2-nitrophenyl)sulfonyl]-1*H*-pyrrole-2-carboxylate (12)

A mixture of **3** (3.00 g, 6.94 mmol), potassium carbonate (2.87 g, 20.0 mmol) and absolute ethanol (20 mL) was refluxed for 3 h. After concentration, the residue was diluted with water and extracted with ethyl acetate. The organic solution was shaken with brine, dried and the solvent evaporated. The crude residue was purified by chromatography on silica gel column (chloroform as eluent) to afford **12** (2.34 g, 94 %), mp 97-98°C (recrystallization from cyclohexane); IR (nujol): ν 1670 cm^{-1}. ^1H NMR (deuteriochloroform): δ 1.22 (t, J = 7.1 Hz, 3H), 4.13 (q, J = 7.1 Hz, 2H), 6.39 (3 line m, 1H), 6.90 (m, 1H), 7.12 (dd, J = 1.6 and 3.8 Hz, 1H), 7.42 (d, J = 2.1 Hz, 1H), 7.56 (dd, J = 2.1 and 8.8 Hz, 1H), 8.08 ppm (d, J = 8.8 Hz, 1H). *Anal.* Calcd for $C_{13}H_{11}N_2O_4Cl$: C, 52.98; H 3.76; N, 9.51; Cl, 12.03. Found: C, 53.07; H 3.79; N, 9.39; Cl, 11.88.

1-[(2-Amino-5-chlorophenyl)sulfonyl]-1*H*-pyrrole-2-(*N*'-acetyl)carbohydrazide (16) and 15 from 14

A solution of **14** (0.40 g, 1.27 mmol) in glacial acetic acid (5 mL) was refluxed for 3 h, then evaporated to dryness. The residue was treated with crushed ice and extracted with ethyl acetate. Organic solution was washed with brine and dried. After evaporation of the solvent the residue was chromatographed on a silica gel column(chloroform-ethanol 9:1 as eluent). First eluate gave 7-chloropyrrolo[1,2-*b*]-[1,2,5]benzothiadiazepin-11(10*H*)-one 5,5-dioxide (**15**) (0.10 g, 28%), mp 277-279°C (crystallization from aqueous *N,N*-dimetylformamide), lit.,[8] mp 276-278°C. Further elution with the same solvent afforded 1-[(2-amino-5-chlorophenyl)sulfonyl]-1*H*-pyrrole-2-(*N*'-acetyl)carbohydrazide (**16**) (0.11 g, 24%) mp 177-178°C (crystallization from toluene); IR (nujol): ν 1640, 3210, 3280 cm^{-1}. ^1H NMR (dimethyl sulfoxide-d_6): δ 1.88 (s, 3H), 6.37 (3 line m, 1H), 6.52 (br s, 2H, deuterium oxide exchangeable), 6.76-6.92 (m, 2H), 7.36 (dd, J = 2.4 and 9.0 Hz, 1H), 7.72 (d, J = 2.4 Hz, 1H), 7.88 (unresolved, 1H), 9.98 and 10.17 ppm (two br s, 2H, deuterium oxide exchangeables). *Anal.* Calcd for

$C_{13}H_{13}N_4O_4ClS$: C, 43.76; H 3.67; N, 15.70; Cl, 9.94; S, 8.99. Found: C, 43.58; H 3.72; N, 15.81; Cl, 9.80, S, 9.12.

7-Chloropyrrolo[1,2-*b*][1,2,5]benzothiadiazepin-11(10*H*)-one 5,5-dioxide (15)

*From **13***. Cyclization of **13** to afford the tricyclic derivative (**15**) has been described in a previous work.[8]
*From **14***. A mixture of **14** (0.50 g, 1.59 mmol) and 2-hydroxypyridine (0.15 g, 1.59 mmol) was heated *in vacuo* at 180°C for 3 h. After cooling the residue was passed through a silica gel column (chloroform-ethanol 9:1 as eluent) to give **15** (0.17 g, 38%) as the unique product, mp 275-277°C (crystallization from aqueous *N,N*-dimethylformamide), lit.,[8] mp 276-278°C.

X-RAY CRYSTALLOGRAPHIC ANALYSIS

Crystal and experimental data are summarized in Table 1. Crystals of the compound (**4**), obtained from a solution of toluene were mounted on a Siemens P3 automatic four-circle diffractometer using graphite monochromatized Mo-radiation (λ Kα=0.71069Å). The cell parameters were refined by least squares from the angular positions of 32 reflections in the range 5.7< 2θ <32.0°. The data were measured at rt for 1.76< 2θ <35.07° from crystals with approximate dimension of 0.4x0.2x0.15 mm using a θ/2θ scan technique.

Table 1. Crystal Data and Structure Refinement for Compound (**4**)

Empirical formula	$C_{11}N_4C_{11}H_9$
Formula weight	232.67
Temperature, K	293(2)
Wavelength, Å	0.71069
Crystal system	Orthorombic
Space Group	P b c a
Unit cell dimensions	a (Ä) = 10.039 b (Å) = 23.125 c (Å) = 9.052 α (deg) = 90 β (deg) = 90 γ (deg) = 90
Volume, $Å^3$	2101.562
Z	8
Density (calculated), Mg/m^3	1.460
Absorption coefficient, mm^{-1}	0.340
F(000)	960
θ range for data collection, deg	1.76 - 35.07
Index ranges	$0 \le h \le 16, 0 \le k \le 37, 0 \le l \le 14$
Indipendent reflections	4669
Observed reflections	4669
Goodness-of-fit on F^2	0.07
Final R indices [I > 3σ(I)]	$R_1 = 0.057$, $wR_2 = 0.080$

The scan rate was automatically chosen according to the peak intensity in the range 3.0÷10.0°/min. and the background counts were taken with stationary crystal at each end of the scan and total background time to scan time ratio of 0.5.

The data were processed to yield values of I and σ(I). The intensities of three standard reflections, measured every 97 reflections throughout the data collections, show no decay. The values of I and σ(I) were corrected for Lorentz, polarization and shape anisotropy[18] effects. A total of 4669 independent reflections having Fo>3 σ(Fo) were processed by the direct methods program SIR97[19], which provided the complete structure. All non-hydrogen atoms were refined by full-matrix least squares methods with anisotropic thermal parameters. The hydrogen atoms where were idealized (C-H=.96Å)[20]. Each H atom was assigned the equivalent isotropic temperature factor of the parent atom and allowed to ride on it. The final difference Fourier map, with a root-mean-square deviation of electron density of 0.07 eÅ^3 showed no significant features. Atomic scattering factors were taken from literature.[21]

A perspective drawing of the molecule is shown in Figure 1, with the atomic numbering scheme. The crystal structure of the compound consists of one molecule in the asymmetric unit. The angle between the least mean square plane of the Benzimidazole and that of Pyrrole is 1.82(0.1). The distance of the Chlorine a tom to the least mean square plane of the Benzimidazole is 0.14. The geometry of the rings is in good agreement with the accepted values. Calculations were performed on the PC Pentium Windows NT of Istituto di Strutturistica Chimica CNR, using the SIR CAOS[22] and SIR97[19] structure determination packages.

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