Pyrrolothieno[1,4]Diazepines Part III: Synthesis of Amino, Hydrazino and Mercapto Derivatives

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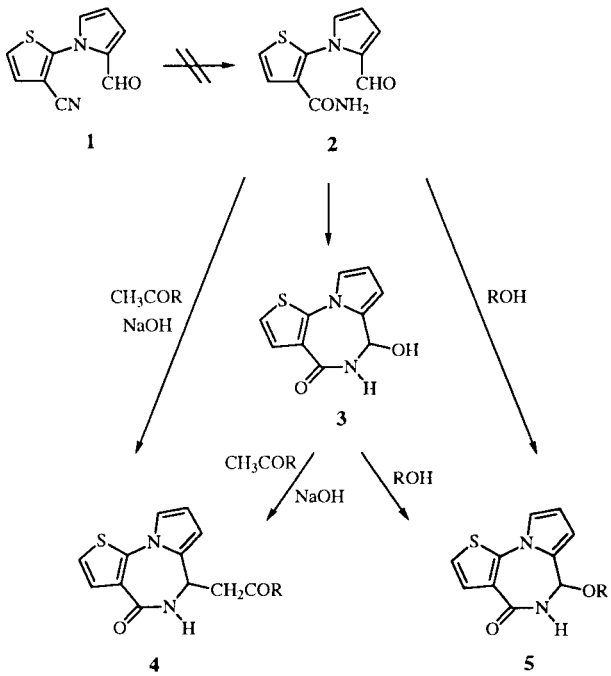
Received July 25, 1995

Treatment of 2-(2-formyl-1*H*-pyrrol-1-yl)-3-thiophenecarbonitrile by sodium percarbonate afforded, in a one-pot sequence and on a multigram scale, 5,6-dihydro-6-hydroxy-4*H*-pyrrolo[1,2-*a*]thieno-[3,2-*f*][1,4]diazepin-4-one whose reactivity towards various nucleophiles like amines, hydrazines and thiols was evaluated.

J. Heterocyclic Chem., **33**, 87 (1996).

During the course of our work concerning the synthesis of new [1,4]diazepines with potential therapeutic interest, we have recently described the access, starting from 2-(2-formyl-1*H*-pyrrol-1-yl)-3-thiophenecarbonitrile **1**, to 5,6-dihydro-4*H*-pyrrolo[1,2-*a*]thieno[3,2-*f*][1,4]diazepin-4-ones bearing on their C6 position either methyloxo or alkoxy groups (Scheme 1) [1,2].

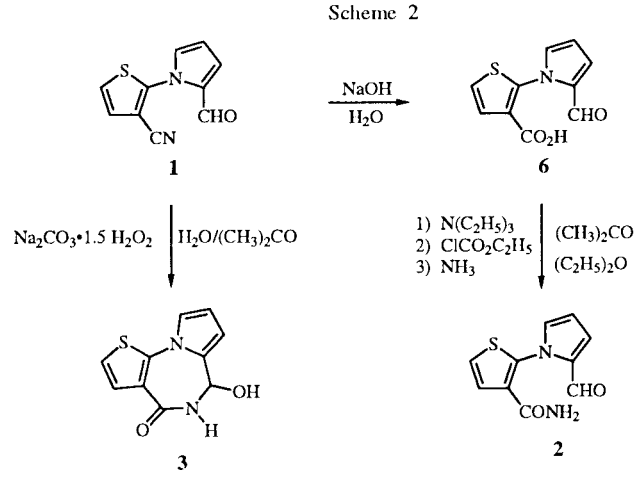
Scheme 1



The reaction pathway involved in this synthesis has been described and proceeded *via* the formylcarboxamide **2** and the hydroxydiazepinone **3** which both led to the substituted diazepinones **4** and **5** by treatment respectively with methyl ketones in alkaline medium or with various alcohols. In order to enlarge the potentialities of this system in the access to new heterocyclic derivatives, we undertook the study of its chemical reactivity towards other various nucleophiles like amines, hydrazines and thiols.

We have previously reported the access, starting from **1**, to the starting materials **2** and **3** (Scheme 2). This sequence, in 2 steps for **2**, in 3 steps for **3**, involved the intermediate formylcarboxylic acid **6**. Global yields were respectively 74% for **2** and 50% for **3**.

Scheme 2

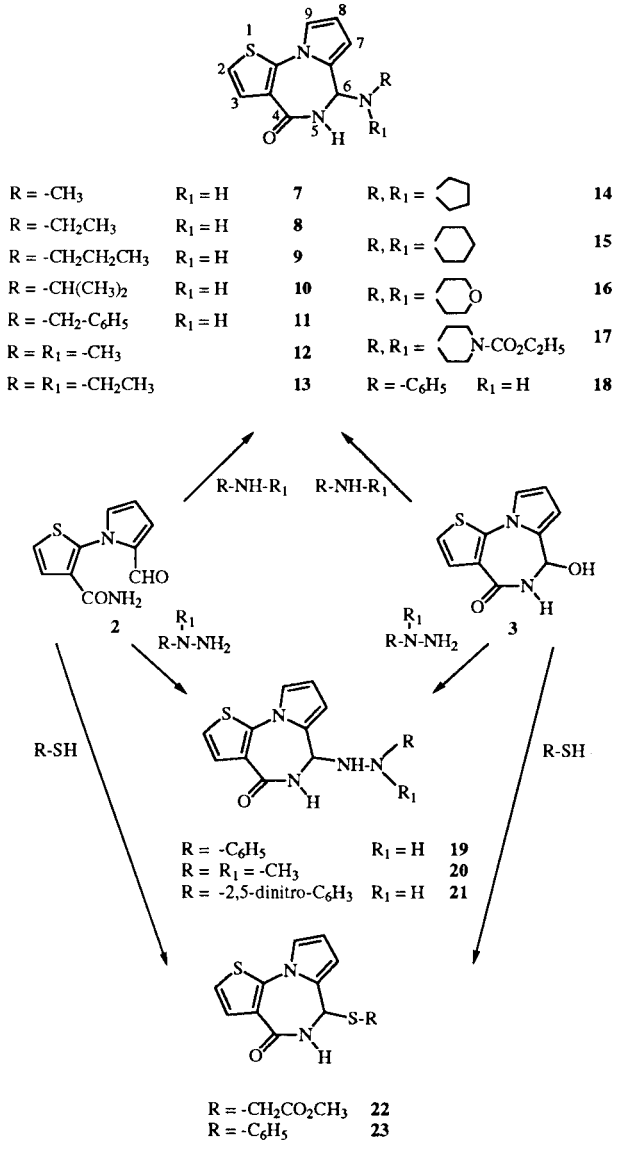


In order to prepare on a multigram scale these starting materials **2** and **3**, we turned to account for the present work a recent method of transformation of nitriles into amides using sodium percarbonate in a mixture of water-acetone [3]. Fortunately, treatment of **1** (50 g), according to this experimental process, did not lead to the expected formylcarboxamide **2** but gave directly in a one-pot sequence the hydroxydiazepinone **3** with a nearly quantitative yield (52 g, 95%).

The chemical reactivity of **2** and **3** towards various amines, hydrazines and thiols was evaluated and compared. These reactivities were identical and, in a similar manner as for the methyl ketones and the alcohols, treatments of **2** and **3** by these new nucleophiles led to the same products with similar yields (Scheme 3).

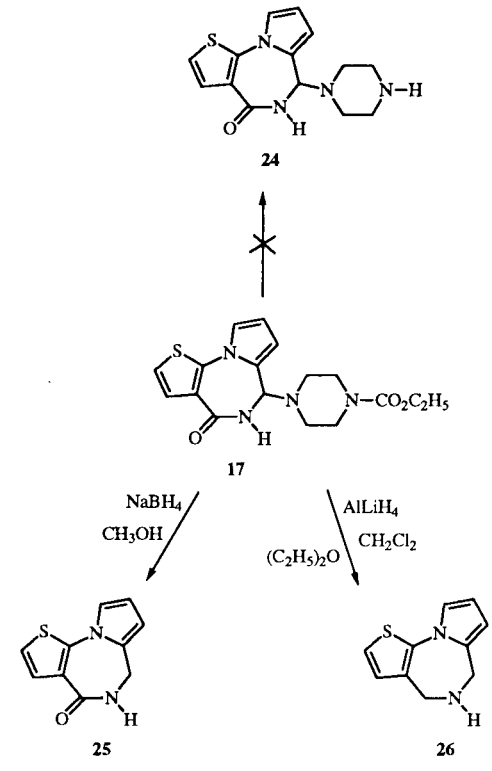
Owing to the facile preparation of **3** we demonstrated above, this starting material was used in preference to the formylcarboxamide **2** as new key intermediate. Thus, when **3** was treated with an excess of primary or secondary amine or hydrazine in water or in a mixture water/dioxane at room temperature, it gave the aminodiazepinones **7-18** and the hydrazinodiazepinones **19-21**. Sulfides **22** and **23** were obtained in a similar manner with respectively methylthioglycolate and thiophenol.

Scheme 3



All attempts aiming at hydrolyse of the protective group of the ethylpiperazinylcarboxylate **17** in alkaline or acidic medium failed and did not lead to the free base **24** (Scheme 4). However surprisingly, treatment of **17** with sodium borohydride in methanol under microwave irradiation yielded the new unsubstituted diazepinone **25**, while with lithium aluminohydride in ether, the hydrolysis of **17** was followed with the hydrogenation of the carbonyl group and afforded the previously described diazepine **26** [4]. The chemical reactivity of these systems will be reported in a future paper.

Scheme 4



EXPERIMENTAL

General Methods.

Melting points were determined on a Kofler bank and are uncorrected. Infrared spectra were recorded on a Philips PU 9716 apparatus and only noteworthy absorptions (reciprocal centimeters) are listed. Nmr spectra were recorded on a Jeol FX 200 using TMS as an internal standard. Chemical shifts are reported in ppm downfield (δ) from TMS.

5,6-Dihydro-6-hydroxy-4*H*-pyrrolo[1,2-*a*]thieno[3,2-*f*][1,4]-diazepin-4-one **3**.

A suspension of 2-(2-formyl-1*H*-pyrrol-1-yl)-3-thiophenecarbonitrile **1** (50 g, 0.25 mole) and sodium percarbonate (118 g, 0.75 mole) in a mixture of water (500 ml) and acetone (900 ml) was stirred at 50° for 90 minutes. Sodium percarbonate (118 g, 0.75 mole) was again added and stirring at 50° was maintained for another 90 minutes. Acetone was then removed under reduced pressure and the aqueous layer was cooled. The solid which precipitated was filtered, washed with water (100 ml), and dried to give **3** as colorless crystals (52 g, 95%) identical to the reference sample [1].

General Procedure for the Reaction of 5,6-Dihydro-6-hydroxy-4*H*-pyrrolo[1,2-*a*]thieno[3,2-*f*][1,4]diazepin-4-one **3** with Amines.

The appropriate amine was added to a suspension of 5,6-dihydro-6-hydroxy-4*H*-pyrrolo[1,2-*a*]thieno[3,2-*f*][1,4]diazepin-4-one **3** (1 g, 0.0045 mole) in water (50 ml) and the reaction mixture was stirred at room temperature for 12 hours. The solid which appeared was filtered off, washed with water (50 ml), dried and recrystallized to give **7-17**.

5,6-Dihydro-6-*N*-methylamino-4*H*-pyrrolo[1,2-*a*]thieno[3,2-*f*]-[1,4]diazepin-4-one **7**.

The reagent was methylamine (35% aqueous solution, 8 ml), colorless crystals (88%) had mp 168° (ether); ir (potassium bromide): 3320, 3250, 3170 (NH), 1635 (CO); ^{1}H-nmr (deuteriochloroform): 7.39 (d, $J_{H2\ H3}$ = 5.9 Hz, H2), 6.98 (m, H9), 6.91 (d, $J_{H3\ H2}$ = 5.9 Hz, H3), 6.81 (br s, NH), 6.31 (m, H8), 6.19 (m, H7), 5.03 (d, $J_{H6\ NH}$ = 5.4 Hz, H6), 2.53 (s, CH_3), 1.75 (br s, NH).

Anal. Calcd. for $C_{11}H_{11}N_3OS$: C, 56.63; H, 4.75; N, 18.01; S, 13.74. Found: C, 56.55; H, 4.73; N, 17.88; S, 13.69.

5,6-Dihydro-6-*N*-ethylamino-4*H*-pyrrolo[1,2-*a*]thieno[3,2-*f*]-[1,4]diazepin-4-one **8**.

The reagent was ethylamine (70% aqueous solution, 3 ml), colorless crystals (89%) had mp 156° (ether); ir (potassium bromide): 3300, 3240, 3140 (NH), 1630 (CO); ^{1}H-nmr (deuteriochloroform): 7.34 (d, $J_{H2\ H3}$ = 5.9 Hz, H2), 6.98 (m, H9), 6.92 (d, $J_{H3\ H2}$ = 5.9 Hz, H3), 6.76 (br s, NH), 6.31 (m, H8), 6.19 (m, H7), 5.15 (m, H6), 2.82 (m, CH_2), 1.74 (br s, NH), 1.11 (t, J = 7 Hz, CH_3).

Anal. Calcd. for $C_{12}H_{13}N_3OS$: C, 58.28; H, 5.30; N, 16.99; S, 12.96. Found: C, 58.26; H, 5.25; N, 16.99; S, 12.87.

5,6-Dihydro-6-*N*-propylamino-4*H*-pyrrolo[1,2-*a*]thieno[3,2-*f*]-[1,4]diazepin-4-one **9**.

The reagent was propylamine (3 ml), colorless crystals (85%) had mp 130° (ether); ir (potassium bromide): 3340, 3260, 3170 (NH), 1635 (CO); ^{1}H-nmr (deuteriochloroform): 7.39 (d, $J_{H2\ H3}$ = 5.9 Hz, H2), 6.98 (m, H9), 6.91 (d, $J_{H3\ H2}$ = 5.9 Hz, H3), 6.52 (br s, NH), 6.31 (m, H8), 6.18 (m, H7), 5.15 (m, H6), 4.82 (br s, NH), 2.73 (m, CH_2), 1.43 (m, CH_2), 0.88 (t, J = 7 Hz, CH_3).

Anal. Calcd. for $C_{13}H_{15}N_3OS$: C, 59.75; H, 5.78; N, 16.08; S, 12.27. Found: C, 59.63; H, 5.82; N, 15.95; S, 12.13.

5,6-Dihydro-6-*N*-isopropylamino-4*H*-pyrrolo[1,2-*a*]thieno-[3,2-*f*][1,4] diazepin-4-one **10**.

The reagent was isopropylamine (3 ml), yellow crystals (76%) had mp 152° (ether); ir (potassium bromide): 3330, 3250, 3170 (NH), 1625 (CO); ^{1}H-nmr (deuteriochloroform): 7.38 (d, $J_{H2\ H3}$ = 5.9 Hz, H2), 6.97 (m, H9), 6.92 (d, $J_{H3\ H2}$ = 5.9 Hz, H3), 6.83 (br s, NH), 6.31 (m, H8), 6.17 (m, H7), 5.20 (m, H6), 3.08 (m, CH), 1.75 (br s, NH), 1.07 (d, J = 7 Hz, 2 CH_3).

Anal. Calcd. for $C_{13}H_{15}N_3OS$: C, 59.75; H, 5.78; N, 16.08; S, 12.27. Found: C, 59.67; H, 5.88; N, 16.18; S, 12.12.

6-*N*-Benzylamino-5,6-dihydro-4*H*-pyrrolo[1,2-*a*]thieno[3,2-*f*]-[1,4]diazepin-4-one **11**.

The reagent was benzylamine (5 ml), colorless crystals (70%) had mp 148° (ether); ir (potassium bromide): 3340, 3220 (NH), 1635 (CO); ^{1}H-nmr (deuteriochloroform): 7.39 (d, $J_{H2\ H3}$ = 5.9 Hz, H2), 7.28 (m, 5 H arom), 6.98 (m, H9), 6.91 (d, $J_{H3\ H2}$ = 5.9 Hz, H3), 6.52 (br s, NH), 6.31 (m, H8), 6.18 (m, H7), 5.11 (d, $J_{H6\ NH}$ = 5.4 Hz, H6), 3.93 (q, J = 9 Hz, CH_2), 2.25 (br s, NH).

Anal. Calcd. for $C_{17}H_{15}N_3OS$: C, 66.00; H, 4.89; N, 13.58; S, 10.36. Found: C, 65.84; H, 4.91; N, 13.44; S, 10.55.

5,6-Dihydro-6-*N,N*-dimethylamino-4*H*-pyrrolo[1,2-*a*]thieno-[3,2-*f*][1,4]diazepin-4-one **12**.

The reagent was dimethylamine (40% aqueous solution, 5 ml), colorless crystals (63%) had mp 180° (ether); ir (potassium bromide): 3280, 3180 (NH), 1650 (CO); ^{1}H-nmr (deuteriochloroform): 7.38 (d, $J_{H2\ H3}$ = 5.9 Hz, H2), 6.99 (m, H9), 6.85 (d, $J_{H3\ H2}$ = 5.9 Hz, H3), 6.77 (br s, NH), 6.29 (m, H8), 6.21 (m, H7), 4.46 (d, $J_{H6\ NH}$ = 5.4 Hz, H6), 2.20 (s, 2 CH_3).

Anal. Calcd. for $C_{12}H_{13}N_3OS$: C, 58.28; H, 5.30; N, 16.99; S, 12.96. Found: C, 58.12; H, 5.22; N, 16.91; S, 13.09.

6-*N,N*-Diethylamino-5,6-dihydro-4*H*-pyrrolo[1,2-*a*]thieno-[3,2-*f*][1,4]diazepin-4-one **13**.

The reagent was diethylamine (3 ml), colorless crystals (65%) had mp 137° (ether); ir (potassium bromide): 3275, 3185 (NH), 1645 (CO); ^{1}H-nmr (deuteriochloroform): 7.37 (d, $J_{H2\ H3}$ = 5.9 Hz, H2), 6.98 (m, H9), 6.89 (d, $J_{H3\ H2}$ = 5.9 Hz, H3), 6.31 (m, H8 and NH), 6.19 (m, H7), 5.11 (d, $J_{H6\ NH}$ = 5.4 Hz, H6), 2.66 (m, 2 CH_2), 0.98 (t, J = 7 Hz, 2 CH_3).

Anal. Calcd. for $C_{14}H_{17}N_3OS$: C, 61.06; H, 6.22; N, 15.26; S, 11.64. Found: C, 60.99; H, 6.21; N, 15.31; S, 11.86.

5,6-Dihydro-6-(pyrrolidin-1-yl)-4*H*-pyrrolo[1,2-*a*]thieno[3,2-*f*]-[1,4]diazepin-4-one **14**.

The reagent was pyrrolidine (4 ml), colorless crystals (89%) had mp 176° (ether); ir (potassium bromide): 3280, 3180 (NH), 1645 (CO); ^{1}H-nmr (deuteriochloroform): 7.37 (d, $J_{H2\ H3}$ = 5.9 Hz, H2), 6.97 (m, H9), 6.83 (d, $J_{H3\ H2}$ = 5.9 Hz, H3), 6.71 (br s, NH), 6.27 (m, H8), 6.19 (m, H7), 4.64 (d, $J_{H6\ NH}$ = 5.4 Hz, H6), 2.64 (m, CH_2), 2.35 (m, CH_2), 1.65 (m, 2 CH_2).

Anal. Calcd. for $C_{14}H_{15}N_3OS$: C, 61.52; H, 5.33; N, 15.37; S, 11.73. Found: C, 61.65; H, 5.58; N, 15.46; S, 11.80.

5,6-Dihydro-6-(piperidin-1-yl)-4*H*-pyrrolo[1,2-*a*]thieno[3,2-*f*]-[1,4]diazepin-4-one **15**.

The reagent was piperidine (3 ml), colorless crystals (86%) had mp 150° (ether); ir (potassium bromide): 3270, 3190 (NH), 1650 (CO); ^{1}H-nmr (deuteriochloroform): 7.35 (d, $J_{H2\ H3}$ = 5.9 Hz, H2), 6.97 (m, H9), 6.85 (d, $J_{H3\ H2}$ = 5.9 Hz, H3), 6.62 (br s, NH), 6.28 (m, H8), 6.18 (m, H7), 4.65 (d, $J_{H6\ NH}$ = 5.4 Hz, H6), 2.63 (m, CH_2), 2.19 (m, CH_2), 1.39 (m, 3 CH_2).

Anal. Calcd. for $C_{15}H_{17}N_3OS$: C, 62.69; H, 5.96; N, 14.62; S, 11.16. Found: C, 62.43; H, 5.87; N, 14.50; S, 10.90.

5,6-Dihydro-6-(morpholin-1-yl)-4*H*-pyrrolo[1,2-*a*]thieno[3,2-*f*]-[1,4]diazepin-4-one **16**.

The reagent was morpholine (3 ml), colorless crystals (65%) had mp 180° (ether); ir (potassium bromide): 3280, 3200 (NH), 1645 (CO); ^{1}H-nmr (deuteriochloroform): 7.35 (d, $J_{H2\ H3}$ = 5.9 Hz, H2), 7.00 (m, H9), 6.93 (br s, NH), 6.86 (d, $J_{H3\ H2}$ = 5.9 Hz, H3), 6.29 (m, H8), 6.22 (m, H7), 4.53 (d, $J_{H6\ NH}$ = 5.4 Hz, H6), 3.47 (m, 2 CH_2), 2.50 (m, CH_2), 2.14 (m, CH_2).

Anal. Calcd. for $C_{14}H_{15}N_3O_2S$: C, 58.11; H, 5.22; N, 14.52; S, 11.08. Found: C, 58.13; H, 5.23; N, 14.64; S, 10.94.

5,6-Dihydro-6-(4-ethylpiperazin-1-ylcarboxylate)-4*H*-pyrrolo-[1,2-*a*]thieno[3,2-*f*][1,4]diazepin-4-one **17**.

The reagent was ethyl-4-piperazinecarboxylate (3 ml), colorless crystals (68%) had mp 200° (ether); ir (potassium bromide): 3280, 3180 (NH), 1690, 1650 (CO); ^{1}H-nmr (deuteriochloroform): 7.35 (d, $J_{H2\ H3}$ = 5.9 Hz, H2), 7.02 (m, H9), 6.87 (d, $J_{H3\ H2}$ = 5.9 Hz, H3), 6.85 (br s, NH), 6.29 (m, H8), 6.21 (m, H7), 4.65 (d, $J_{H6\ NH}$ = 5.4 Hz, H6), 4.07 (q, J = 7 Hz, CH_2), 3.34 (m, 2 CH_2), 2.46 (m, CH_2), 2.06 (m, CH_2), 1.26 (t, J = 7 Hz, CH_3).

Anal. Calcd. for $C_{17}H_{20}N_4O_3S$: C, 56.65; H, 5.59; N, 15.54; S, 8.89. Found: C, 56.43; H, 5.41; N, 15.34; S, 8.85.

5,6-Dihydro-6-*N*-phenylamino-4*H*-pyrrolo[1,2-*a*]thieno[3,2-*f*]-[1,4]diazepin-4-one **18**.

A solution of 5,6-dihydro-6-hydroxy-4*H*-pyrrolo[1,2-*a*]-thieno[3,2-*f*][1,4]diazepin-4-one **3** (1 g, 0.0045 mole) in dioxane (20 ml) was added to a mixture of aniline (5 ml) and sodium hydroxide (1*N* aqueous solution, 10 ml). The reaction mixture was stirred at room temperature for 6 hours and then poured into water (300 ml). The precipitate which appeared was filtered, washed with water (50 ml), dried and recrystallized to give **18** as colorless crystals (75%), mp 160° (ether); ir (potassium bromide): 3340, 3280, 3190 (NH), 1645 (CO); ^{1}H-nmr (deuteriochloroform): 7.39 (d, $J_{H2\ H3}$ = 5.9 Hz, H2), 7.18 (m, 2 H arom), 7.03 (m, H9), 6.96 (d, $J_{H3\ H2}$ = 5.9 Hz, H3), 6.85 (m, 1 H arom), 6.74 (m, 2 H arom), 6.64 (br s, NH), 6.35 (m, H8), 6.25 (m, H7), 5.88 (m, H6), 4.53 (br s, NH).

Anal. Calcd. for $C_{16}H_{13}N_3OS$: C, 65.07; H, 4.44; N, 14.23; S, 10.85. Found: C, 64.87; H, 4.56; N, 14.01; S, 11.10.

5,6-Dihydro-6-*N*-phenylhydrazino-4*H*-pyrrolo[1,2-*a*]thieno-[3,2-*f*][1,4]diazepin-4-one **19**.

Phenylhydrazine (2 ml) was added to a suspension of 5,6-dihydro-6-hydroxy-4*H*-pyrrolo[1,2-*a*]thieno[3,2-*f*][1,4]-diazepin-4-one **3** (1 g, 0.0045 mole) in water (50 ml). The reaction mixture was stirred at room temperature for 2 hours and the precipitate which appeared was filtered, washed with water (50 ml), dried and recrystallized to give **19** as grey crystals (71%), mp 158° (ether); ir (potassium bromide): 3460, 3320, 3280, 3150 (NH), 1660 (CO); ^{1}H-nmr (deuteriochloroform): 7.56 (d, $J_{H2\ H3}$ = 5.9 Hz, H2), 7.46 (m, 2 H arom), 7.20 (br s, NH), 7.18 (m, H3 and 1 H arom), 6.70 (m, H9, H8, H7 and 2 H arom), 6.54 (br s, NH), 6.38 (br s, NH), 5.33 (m, H6 and NH).

Anal. Calcd. for $C_{16}H_{14}N_4OS$: C, 61.92; H, 4.55; N, 18.05; S, 10.33. Found: C, 62.12; H, 4.66; N, 17.89; S, 10.43.

5,6-Dihydro-6-*N,N*-dimethylhydrazino-4*H*-pyrrolo[1,2-*a*]thieno-[3,2-*f*][1,4]diazepin-4-one **20**.

Dimethylhydrazine (2 ml) was added to a suspension of 5,6-dihydro-6-hydroxy-4*H*-pyrrolo[1,2-*a*]thieno[3,2-*f*][1,4]-diazepin-4-one **3** (1 g, 0.0045 mole) in water (30 ml). The reaction mixture was stirred at 50° for 30 minutes and then at room temperature for 12 hours. The solution was extracted by ether (3 x 100 ml). The organic layers were collected, dried over magnesium sulfate, filtered and the solvent was removed under reduced pressure to give **20** as pink crystals (85%), mp 116° (ethanol); ir (potassium bromide): 3280, 3140 (NH), 1675 (CO); ^{1}H-nmr (deuteriochloroform): 7.48 (d, $J_{H2\ H3}$ = 5.9 Hz, H2), 7.21 (m, H9), 6.94 (d, $J_{H3\ H2}$ = 5.9 Hz, H3), 6.79 (m, H8), 6.53 (m, H7), 6.38 (br s, NH), 5.52 (br s, NH), 5.15 (br s, H6).

Anal. Calcd. for $C_{12}H_{14}N_4OS$: C, 54.94; H, 5.38; N, 21.36; S, 12.22. Found: C, 54.71; H, 5.10; N, 21.10; S, 12.05.

5,6-Dihydro-6-*N*-(2,5-dinitrophenylhydrazino)-4*H*-pyrrolo-[1,2-*a*]thieno[3,2-*f*][1,4]diazepin-4-one **21**.

A solution of 5,6-dihydro-6-hydroxy-4*H*-pyrrolo[1,2-*a*]-thieno[3,2-*f*][1,4]diazepin-4-one **3** (1 g, 0.0045 mole) and of 2,5-dinitrophenylhydrazine (1 g, 0.0051 mole) in acetonitrile (150 ml) was stirred at 60° for 2 hours. The solvent was then removed under reduced pressure to give **21** as red crystals (66%), mp 238° (ether/acetone); ir (potassium bromide): 3270, 3120 (NH), 1650 (CO); ^{1}H-nmr (DMSO-d_6): 9.94 (br s, NH), 8.79 (m, 1 H arom and NH), 8.00 (d, $J_{H2\ H3}$ = 5.9 Hz, H2), 7.30 (m, 2 H arom), 7.19 (m, H9), 7.08 (d, $J_{H3\ H2}$ = 5.9 Hz, H3), 6.28 (m, H8 and H7), 5.85 (br s, NH), 5.54 (m, H6).

Anal. Calcd. for $C_{16}H_{12}N_6O_5S$: C, 48.10; H, 3.01; N, 21.00; S, 8.00. Found: C, 47.92; H, 2.98; N, 20.79; S, 8.02.

General Procedure for the Reaction of 5,6-Dihydro-6-hydroxy-4*H*-pyrrolo[1,2-*a*]thieno[3,2-*f*][1,4]diazepin-4-one **3** with Thiols.

The appropriate thiol (0.005 mole) was added to a solution of 5,6-dihydro-6-hydroxy-4*H*-pyrrolo[1,2-*a*]thieno[3,2-*f*][1,4]-diazepin-4-one **3** (1 g, 0.0045 mole) in acetonitrile (100 ml) and the reaction mixture was stirred at room temperature for 12 hours. The solvent was then removed under reduced pressure and the oily residue was crystallized by addition of petroleum ether to give **22** and **23**.

Methyl-5,6-Dihydro-4-oxo-4*H*-pyrrolo[1,2-*a*]thieno[3,2-*f*][1,4]-diazepin-6-thioglycolate **22**.

The reagent was methylthioglycolate (0.43 ml), colorless crystals (72%) had mp 158° (ether); ir (potassium bromide): 3360, 3280 (NH), 1730, 1645 (CO); ^{1}H-nmr (deuteriochloroform): 7.40 (d, $J_{H2\ H3}$ = 5.9 Hz, H2), 7.04 (m, H9), 6.92 (m, H3 and NH), 6.28 (m, H8 and H7), 5.94 (d, $J_{H6\ NH}$ = 7.3 Hz, H6), 3.76 (s, CH_3), 3.29 (d, $J_{Ha\ Hb}$ = 15.6 Hz, Ha), 3.06 (d, $J_{Hb\ Ha}$ = 15.6 Hz, Hb).

Anal. Calcd. for $C_{13}H_{12}N_2O_3S_2$: C, 50.64; H, 3.92; N, 9.08; S, 20.79. Found: C, 50.50; H, 3.83; N, 9.02; S, 20.95.

5,6-Dihydro-6-phenylthio-4*H*-pyrrolo[1,2-*a*]thieno[3,2-*f*][1,4]-diazepin-4-one **23**.

The reagent was thiophenol (0.50 ml), colorless crystals (78%) had mp 142° (ether); ir (potassium bromide): 3370, 3160 (NH), 1645 (CO); ^{1}H-nmr (deuteriochloroform): 7.40 (m, H2 and 5 H arom), 7.02 (m, H9), 6.95 (d, $J_{H3\ H2}$ = 5.9 Hz, H3), 6.60 (br s, NH), 6.26 (m, H8), 6.11 (m, H7), 5.73 (d, $J_{H6\ NH}$ = 6.8 Hz, H6).

Anal. Calcd. for $C_{16}H_{12}N_2OS_2$: C, 61.51; H, 3.87; N, 8.97; S, 20.52. Found: C, 61.32; H, 3.82; N, 9.13; S, 20.69.

5,6-Dihydro-4*H*-pyrrolo[1,2-*a*]thieno[3,2-*f*][1,4]diazepin-4-one **25**.

Sodium borohydride (0.84 g, 0.022 mole) was added portionwise to a solution of 5,6-dihydro-6-(4-ethoxycarbonylpiperazin-1-yl)-4*H*-pyrrolo[1,2-*a*]thieno[3,2-*f*][1,4]diazepin-4-one **17** (2 g, 0.0050 mole) in methanol (150 ml). The reaction mixture was stirred at room temperature for 15 minutes and then refluxed under microwave irradiation for 30 minutes. The solvent was then removed under reduced pressure and the solid residue was dissolved in water (200 ml). The precipitate which appeared was filtered, washed with water (50 ml), dried and recrystallized to

give **25** as colorless crystals (91%), mp 182° (ether); ir (potassium bromide): 3280, 3170 (NH), 1660 (CO); ^{1}H-nmr (deuteriochloroform): 7.39 (d, $J_{H2\ H3}$ = 5.9 Hz, H2), 6.95 (m, H3 and H9), 6.60 (br s, NH), 6.29 (m, H8), 6.13 (m, H7), 4.29 (d, $J_{CH_2\ NH}$ = 5.4 Hz, CH_2).

Anal. Calcd. for $C_{10}H_8N_2OS$: C, 58.81; H, 3.95; N, 13.72; S, 15.70. Found: C, 59.02; H, 3.87; N, 13.78; S, 15.65.

5,6-Dihydro-4*H*-pyrrolo[1,2-*a*]thieno[3,2-*f*][1,4]diazepine **26**.

A solution of 5,6-dihydro-6-(4-ethoxycarbonylpiperazin-1-yl)-4*H*-pyrrolo[1,2-*a*]thieno[3,2-*f*][1,4]diazepin-4-one **17** (2 g, 0.0050 mole) in dichloromethane (150 ml) was added dropwise to a suspension of lithium aluminium hydride (0.76 g, 0.02 mole) in ether (15 ml). The reaction mixture was stirred at room temperature for 20 minutes and then refluxed for 6 hours.

The solution was cooled and poored into iced-water (250 g). The suspension was filtered and the insoluble was washed with dichloromethane (200 ml). The filtrate was extracted with dichloromethane (200 ml) and the organic layers were collected, dried over calcium chloride and evaporated to dryness to give **26** as an yellow oil (86%), bp 170° (0.1 mm); ir (potassium bromide): 3310, 3210 (NH); ^{1}H-nmr (DMSO-d_6): 7.03 (d, $J_{H2\ H3}$ = 5.9 Hz, H2), 7.00 (m, H9), 6.71 (d, $J_{H3\ H2}$ = 5.9 Hz, H3), 6.08 (m, H8), 5.98 (m, H7), 4.05 (s, CH_2), 3.83 (s, CH_2), 3.32 (br s, NH).

Anal. Calcd. for $C_{10}H_{10}N_2S$: C, 63.15; H, 5.30; N, 14.73; S, 16.82. Found: C, 62.93; H, 5.59; N, 14.76; S, 16.59.

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