Pyrrolothieno[1,4]diazepines. Part IV. First Synthesis of Pyrrolo-[1,2-*a*]thieno[2,3-*f*][1,4]diazepine Derivatives

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Treatment of 3-(2-formyl-1*H*-pyrrol-1-yl)-2-thiophenecarboxamide by various nucleophiles like methyl ketones, amines, alcohols, thiols or acetates led to new 5,6-dihydro-4*H*-pyrrolo[1,2-*a*]thieno-[2,3-*f*][1,4]diazepines.

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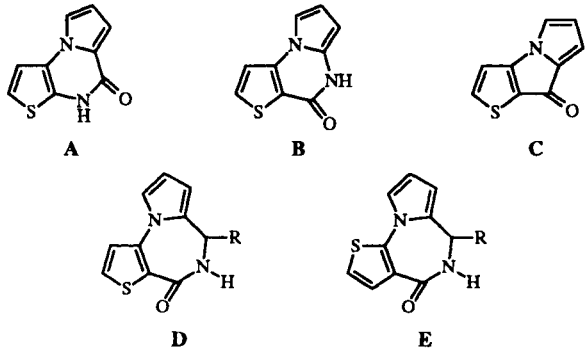
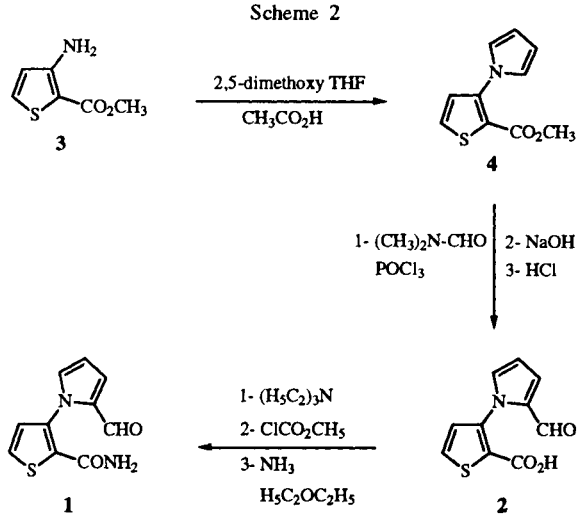
Scheme 1



During the course of our work concerning the involvement of 3-(pyrrol-1-yl)thiophene derivatives in the synthesis of new heterocyclic systems with potential therapeutic interest, we have described, during the past several years, the preparation of pyrrolothienopyrimidines **A** [1], pyrrolothieno-pyrazines **B** [2] and pyrrolothienopyrrolizines **C** [3] (Scheme 1). We wish herein to complete this study and to report routes to new 5,6-dihydro-4*H*-pyrrolo[1,2-*a*]thieno[2,3-*f*]-diazepin-4-ones **D**, positional isomers of the thieno[3,2-*f*]-diazepines **E** we furthermore recently described [4,5].

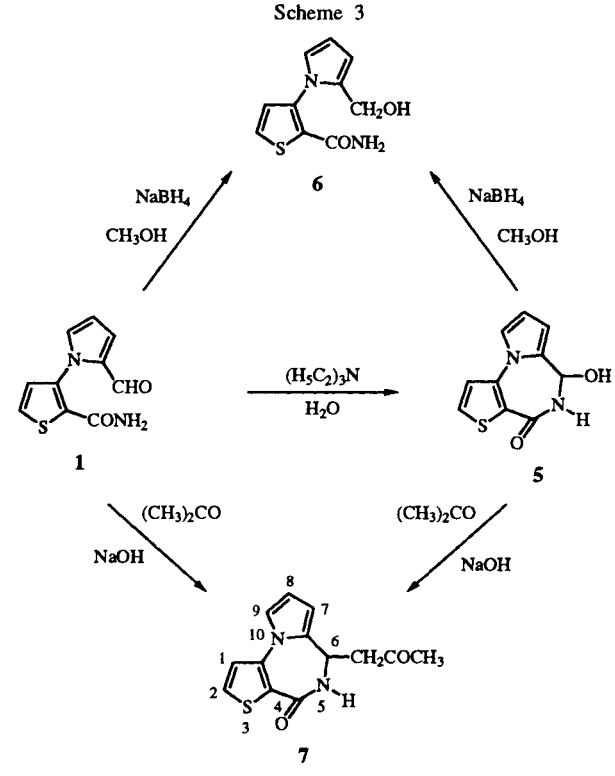
Scheme 2



The starting material involved in the synthesis of **D** was 3-(2-formyl-1*H*-pyrrol-1-yl)-2-thiophenecarboxamide **1** whose synthesis was achieved, *via* a mixed anhydride, by treatment of the formylcarboxylic acid **2** with triethylamine, ethyl chloroformate and ammonia successively (Scheme 2). We previously reported a route to **2** starting from methyl 3-amino-2-thiophenecarboxylate **3**, involving first a Clauson-Kaas reaction leading to **4** [1], which was then formylated and saponified in a one-step sequence [2].

In a similar manner as for the isomeric series [4], the formylcarboxamide **1** was cyclized with 67% yield by treatment with triethylamine in water leading to the hydroxydiazepinone **5** (Scheme 3). The chemical reactiv-

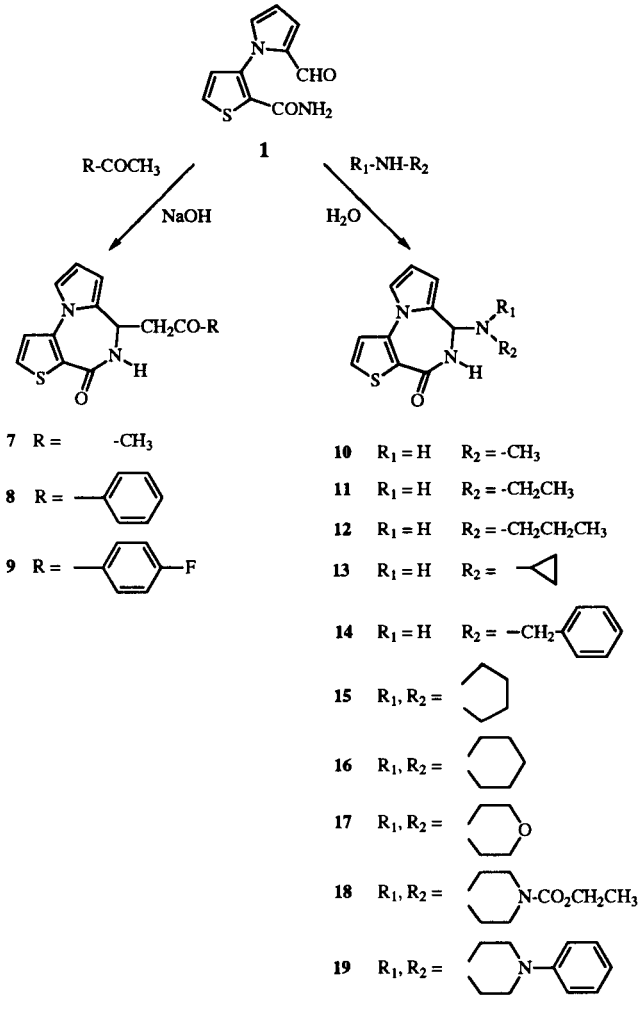
Scheme 3



ity of **1** and **5** in solution was identical and we consider them as two entities of the same compound in equilib-

rium. Thus, treatment of **1** or **5**, with sodium borohydride in methanol under microwave irradiation, led in both cases and in the same yields (60%) to the hydroxymethylcarboxamide **6**.

Scheme 4



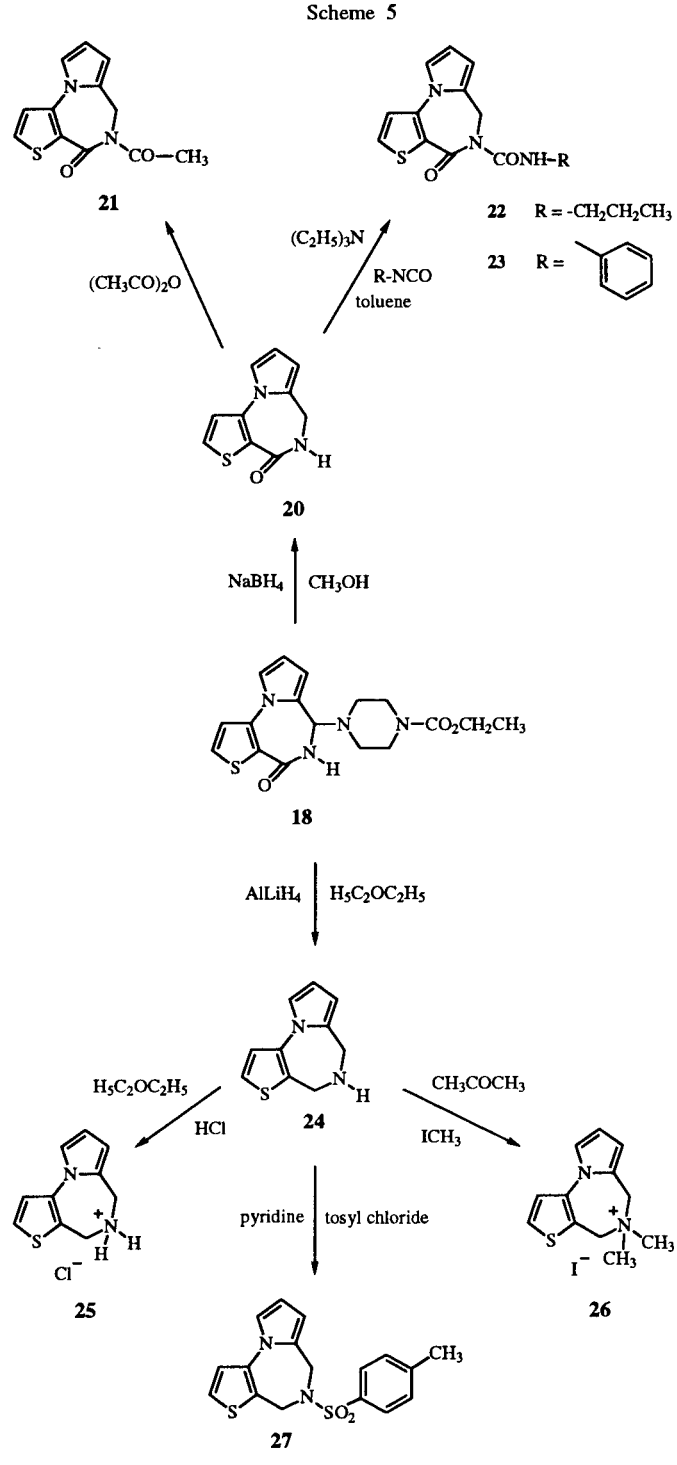
On the other hand, nucleophiles reacted in a similar manner with **1** and **5** and for example their treatment at room temperature with acetone in presence of sodium hydroxide led to the unique 6-acetonyldiazepinone **7** in 60% yield. All further reactions involving nucleophiles have been achieved starting from **1**.

This preparation of oxomethyldiazepinones has been extended to phenacyl **8** and 4-fluorophenacyl **9** derivatives by treatment of **1** in alkaline medium with acetophenone and 4-fluoroacetophenone respectively (Scheme 4).

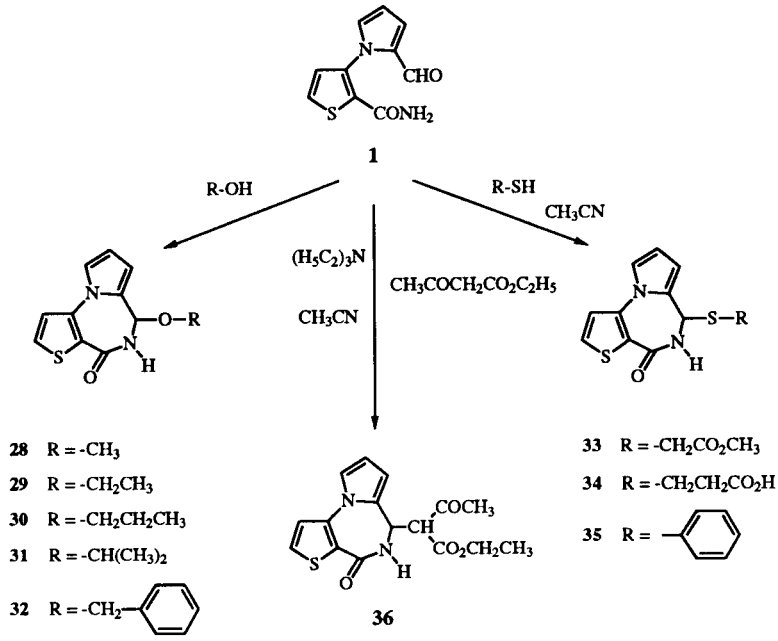
On the other hand, reaction at room temperature of an aqueous solution of **1** with various primary amines in excess led to the precipitation of the 6-aminodiazepinones **10-14**. This reaction failed with aromatic amines due to their weak basicity and hydrosolubility. Secondary amines led under the same conditions to the formation of diazepines **15-19**.

All attempts to hydrolyse the protective group of the ethyl piperazinylcarboxylate **18** in alkaline or acidic medium failed. However, in a similar manner as that for the isomeric series [6] treatment of **18** with sodium borohydride in methanol under microwave irradiation led to the unsubstituted diazepinone **20** in 89% yield, while with lithium aluminohydride in ether the hydrolysis of **18** was

Scheme 5



Scheme 6



followed by hydrogenation of the carbonyl and afforded the new diazepine **24** in 64% yield (Scheme 5).

Reactivity of the lactam nitrogen of **20** was evaluated against acetic anhydride and isocyanates. The reactions furnished the acetyl **21**, the propylaminocarbonyl **22** and the anilinocarbonyl **23** diazepinones, respectively.

On the other hand, the free base **24** was allowed to react with hydrochloric acid in ether and with iodomethane in acetone yielding the hydrochloride **25** and the methiodide **26** respectively, while treatment of **24** with tosyl chloride in pyridine afforded the 5-(*N*-tosyl)-substituted diazepine **27**.

In a similar manner as for methyl ketones and amines, treatment of **1** with alcohols at reflux temperature or with thiols in acetonitrile at room temperature led to the alkoxy **28-32** and thio **33-35** diazepinones respectively (Scheme 6). Finally, ethyl acetoacetate in the presence of triethylamine reacted with **1** in acetonitrile solution to give the ethyl diazepinylacetoacetate **36** in 47% yield, while similar reactions never took place in the isomeric thieno-[3,2-*f*]diazepine series.

EXPERIMENTAL

General Methods.

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

3-(2-Formyl-1*H*-pyrrol-1-yl)-2-thiophenecarboxamide **1**.

Triethylamine (14 ml, 0.1 mole) was added at 0° to a stirred mixture of 3-(2-formyl-1*H*-pyrrol-1-yl)thiophene-2-carboxylic acid **2** (20 g, 0.092 mole) in ether (600 ml). After 10 minutes, ethyl chloroformate (9.6 ml, 0.1 mole) was added dropwise to the reaction mixture at 0°. After 20 minutes, the insoluble material was filtered and ammonia was bubbled into the filtrate at 0° for 30 seconds. The precipitate was filtered, washed with ether and recrystallized to give **1** as colorless crystals (84%), mp 164° (ether); ir (potassium bromide): 3460, 3320, 3270, 3100 (NH_2), 1675, 1655 (CO); ^{1}H-nmr (deuteriochloroform): 9.59 (s, CHO), 7.55 (d, $J_{H5\ H4}$ = 5.4 Hz, H5), 7.19 (dd, $J_{H3'\ H4'}$ = 3.4 Hz, $J_{H3'\ H5'}$ = 1.5 Hz, H3'), 7.05 (m, H4 and H5'), 6.52 (dd, $J_{H4'\ H3'}$ = 3.4 Hz, $J_{H4'\ H5'}$ = 2.9 Hz, H4'), 5.39 (brs, NH_2).

Anal. Calcd. for $C_{10}H_8N_2O_2S$: C, 54.53; H, 3.66; N, 12.72; S, 14.56. Found: C, 54.71; H, 3.58; N, 12.79; S, 14.43.

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

Triethylamine (0.63 ml, 0.0045 mole) was added to a solution of 3-(2-formyl-1*H*-pyrrol-1-yl)-2-thiophenecarboxamide **1** (1 g, 0.0045 mole) in water (20 ml). The reaction mixture was then stirred at room temperature for 2 hours. The precipitate which appeared was filtered, washed with water, dried and recrystallized to give **5** as yellow crystals (67%), mp 172° (ether); ir (potassium bromide): 3520 (OH), 3420, 3280 (NH), 1640 (CO); ^{1}H-nmr (DMSO-d_6): 9.00 (d, $J_{NH\ H6}$ = 4.4 Hz, NH), 7.87 (d, $J_{H2\ H1}$ = 5.4 Hz, H2), 7.49 (d, $J_{H1\ H2}$ = 5.4 Hz, H1), 7.37 (dd, $J_{H9\ H8}$ = 2.9 Hz, $J_{H9\ H7}$ = 1.5 Hz, H9), 6.24 (m, H7, H8 and OH), 5.65 (dd, $J_{H6\ NH}$ = 4.4 Hz, $J_{H6\ OH}$ = 3.6 Hz, H6).

Anal. Calcd. for $C_{10}H_8N_2O_2S$: C, 54.53; H, 3.66; N, 12.71; S, 14.56. Found: C, 54.38; H, 3.48; N, 13.01; S, 14.85.

3-(2-Hydroxymethyl-1*H*-pyrrol-1-yl)-2-thiophenecarboxamide **6**.

Method A .

Sodium borohydride (0.68 g, 0.018 mole) was added portionwise to a solution of 3-(2-formyl-1*H*-pyrrol-1-yl)-2-thiophenecarboxamide **1** (1 g, 0.0045 mole) in methanol (200 ml). The reaction mixture was stirred for 15 minutes at room temperature and then refluxed for 30 minutes under microwave conditions. The solvent was removed under reduced pressure and the solid residue was taken up in water (150 ml). The solution was extracted twice with ether (2 x 100 ml) and the organic layers were collected and dried over magnesium sulfate. The solvent was evaporated to give a solid which was recrystallized to give **6** as colorless crystals (60%), mp 122°; ir (potassium bromide): 3460 (OH), 3330, 3270, 3160 (NH), 1670 (CO); ^{1}H-nmr (DMSO-d_6): 7.82 (d, $J_{H5\,H4}$ = 5.4 Hz, H5), 7.45 and 5.85 (2 br s, NH_2), 7.15 (d, $J_{H4\,H5}$ = 5.4 Hz, H4), 6.82 (m, H5'), 6.19 (m, H3' and H4'), 4.24 (d, $J_{CH2\,OH}$ = 4.4 Hz, CH_2), 3.32 (d, $J_{OH\,CH2}$ = 4.4 Hz, OH).

Anal. Calcd. for $C_{10}H_{10}N_2O_2S$: C, 54.04; H, 4.53; N, 12.60; S, 14.42. Found: C, 54.30; H, 4.44; N, 12.56; S, 14.26.

Method B.

The same procedure as for method A was applied to 5,6-dihydro-6-hydroxy-4*H*-pyrrolo[1,2-*a*]thieno[2,3-*f*][1,4]diazepin-4-one **5** (1 g, 0.0045 mole) to give **6** (60%).

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

Method A.

3-(2-Formyl-1*H*-pyrrol-1-yl)-2-thiophenecarboxamide **1** (1 g, 0.0045 mole) was added to a mixture of acetone (20 ml) in aqueous sodium hydroxide solution (4%, 20 ml). The reaction mixture was stirred at room temperature for 3 hours. Acetone was removed under reduced pressure and the residue was poured into water (100 ml). The precipitate which appeared was filtered, washed with water (50 ml), dried and recrystallized to give **7** as colorless crystals (60%), mp 268° (propan-2-ol); ir (potassium bromide): 3270, 3150 (NH), 1700, 1640 (CO); ^{1}H-nmr (DMSO-d_6): 8.34 (d, $J_{NH\,H6}$ = 4.4 Hz, NH), 7.96 (d, $J_{H2\,H1}$ = 5.4 Hz, H2), 7.46 (d, $J_{H1\,H2}$ = 5.4 Hz, H1), 7.30 (dd, $J_{H9\,H8}$ = 2.9 Hz, $J_{H9\,H7}$ = 1.5 Hz, H9), 6.24 (dd, $J_{H8\,H7}$ = 3.4 Hz, $J_{H8\,H9}$ = 2.9 Hz, H8), 6.10 (dd, $J_{H7\,H8}$ = 3.4 Hz, $J_{H7\,H9}$ = 1.5 Hz, H7), 4.66 (m, H6), 3.16 (d, $J_{CH2\,H6}$ = 6.8 Hz, CH_2), 2.17 (s, CH_3).

Anal. Calcd. for $C_{13}H_{12}N_2O_2S$: C, 59.99; H, 4.65; N, 10.77; S, 12.30. Found: C, 59.78; H, 4.72; N, 10.64; S, 11.96.

Method B.

The same procedure as for method A was applied to 5,6-dihydro-6-hydroxy-4*H*-pyrrolo[1,2-*a*]thieno[2,3-*f*][1,4]diazepin-4-one **5** (1 g, 0.0045 mole) to give **7** (60%).

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

3-(2-Formyl-1*H*-pyrrol-1-yl)-2-thiophenecarboxamide **1** (1 g, 0.0045 mole) was added to a mixture of acetophenone (2 ml) in an aqueous sodium hydroxide solution (4%, 20 ml). The reaction mixture was heated at 70° for 1 hour and then poured into water (150 ml). The precipitate which appeared was filtered, washed with water (50 ml), dried and recrystallized to give **8** as colorless crystals (15%), mp 214° (ether); ir (potassium bromide): 3280, 3170 (NH), 1690, 1655 (CO); ^{1}H-nmr (DMSO-d_6): 8.35 (br s, NH), 7.94 (m, H2' and H6'), 7.89 (d, $J_{H2\,H1}$ = 5.4 Hz, H2), 7.57 (m, H1, H3', H4' and H5'), 7.25 (dd, $J_{H9\,H8}$ = 2.9 Hz, $J_{H9\,H7}$ = 1.5 Hz, H9), 6.15 (m, H7 and H8), 4.80 (m, H6), 3.35 (d, $J_{CH2\,H6}$ = 6.8 Hz, CH_2).

Anal. Calcd. for $C_{18}H_{14}N_2O_2S$: C, 67.07; H, 4.38; N, 8.69; S, 9.93. Found: C, 66.99; H, 4.44; N, 8.69; S, 10.20.

5,6-Dihydro-6-(4'-fluorophenacyl)-4*H*-pyrrolo[1,2-*a*]thieno-[2,3-*f*][1,4]diazepin-4-one **9**.

This compound was obtained as for **8**, starting from 3-(2-formyl-1*H*-pyrrol-1-yl)-2-thiophenecarboxamide **1** (1 g, 0.0045 mole) and 4-fluoroacetophenone (2 ml), to give **9** as yellow crystals (16%), mp 250° (ether); ir (potassium bromide): 3280, 3180 (NH), 1670, 1630 (CO); ^{1}H-nmr (DMSO-d_6): 8.61 (d, $J_{NH\,H6}$ = 4.4 Hz, NH), 7.77 (d, $J_{H2\,H1}$ = 5.4 Hz, H2), 7.12 (m, H9, H2' H3', H5' and H6'), 7.02 (d, $J_{H1\,H2}$ = 5.4 Hz, H1), 6.12 (dd, $J_{H8\,H7}$ = 3.4 Hz, $J_{H8\,H9}$ = 2.9 Hz, H8), 5.86 (dd, $J_{H7\,H8}$ = 3.4 Hz, $J_{H7\,H8}$ = 1.5 Hz, H7), 4.62 (m, H6), 3.39 (m, CH_2).

Anal. Calcd. for $C_{18}H_{13}N_2O_2FS$: C, 63.51; H, 3.84; F, 5.58; S, 9.41. Found: C, 63.29; H, 3.65; F, 5.39; S, 9.62.

General Procedure for the Reaction of 3-(2-Formyl-1*H*-pyrrol-1-yl)-2-thiophenecarboxamide **1** with Amines.

The appropriate amine was added to a suspension of 3-(2-formyl-1*H*-pyrrol-1-yl)-2-thiophenecarboxamide **1** (1 g, 0.0045 mole) in water (20 ml) and the reaction mixture was stirred at room temperature for 4 hours. The solid which appeared was filtered off, washed with water (50 ml), dried and recrystallized to give **10-19.**

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

The reagent was methylamine (35% aqueous solution, 3 ml); colorless crystals (60%) had mp 146° (ether); ir (potassium bromide): 3320, 3250, 3180 (NH), 1625 (CO); ^{1}H-nmr (DMSO-d_6): 8.63 (d, $J_{NH\,H6}$ = 4.4 Hz, NH), 7.84 (d, $J_{H2\,H1}$ = 5.4 Hz, H2), 7.40 (d, $J_{H1\,H2}$ = 5.4 Hz, H1), 7.32 (m, H9), 6.21 (m, H7 and H8), 4.86 (d, $J_{H6\,NH}$ = 5.4 Hz, H6), 3.30 (br s, NH), 2.20 (s, CH_3).

Anal. Calcd. for $C_{11}H_{11}N_3OS$: C, 56.63; H, 4.75; N, 18.01; S, 13.74. Found: C, 56.38; H, 4.51; N, 17.91; S, 13.48.

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

The reagent was ethylamine (70% aqueous solution, 3 ml); colorless crystals (72%) had mp 152° (ether); ir (potassium bromide): 3290, 3150 (NH), 1630 (CO); ^{1}H-nmr (deuteriochloroform): 7.59 (d, $J_{H2\,H1}$ = 5.4 Hz, H2), 7.17 (d, $J_{H1\,H2}$ = 5.4 Hz, H1), 7.03 (dd, $J_{H9\,H8}$ = 2.9 Hz, $J_{H9\,H7}$ = 1.5 Hz, H9), 6.71 (br s, NH), 6.31 (dd, $J_{H8\,H7}$ = 3.4 Hz, $J_{H8\,H9}$ = 2.9 Hz, H8), 6.18 (dd, $J_{H7\,H8}$ = 3.4 Hz, $J_{H7\,H9}$ = 1.5 Hz, H7), 5.16 (d, $J_{H6\,NH}$ = 5.4 Hz, H6), 2.82 (m, CH_2), 1.68 (br s, NH), 1.09 (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, 58.21; H, 5.26; N, 16.78; S, 12.78.

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

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): 7.58 (d, $J_{H2\,H1}$ = 5.4 Hz, H2), 7.16 (d, $J_{H1\,H2}$ = 5.4 Hz, H1), 7.03 (dd, $J_{H9\,H8}$ = 2.9 Hz, $J_{H9\,H7}$ = 1.5 Hz, H9), 6.60 (br s, NH), 6.31 (dd, $J_{H8\,H7}$ = 3.4 Hz, $J_{H8\,H9}$ = 2.9 Hz, H8), 6.18 (dd, $J_{H7\,H8}$ = 3.4 Hz, $J_{H7\,H9}$ = 1.5 Hz, H7), 5.15 (d, $J_{H6\,NH}$ = 5.4 Hz, H6), 2.68 (m, CH_2), 1.66 (br s, NH), 1.47 (m, CH_2), 0.87 (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, 59.67; H, 5.70; N, 16.15; S, 12.13.

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

The reagent was cyclopropylamine (3 ml); colorless crystals (86%) had mp 185° (ether); ir (potassium bromide): 3340, 3260, 3150 (NH), 1630 (CO); ^{1}H-nmr (DMSO-d_6): 8.67 (br s, NH), 7.84 (d, $J_{H2\ H1}$ = 5.4 Hz, H2), 7.42 (d, $J_{H1\ H2}$ = 5.4 Hz, H1), 7.30 (m, H9), 6.20 (m, H8 and H7), 5.04 (m, H6), 2.83 (br s, NH), 2.09 (m, CH), 0.26 (m, 2 CH_2).

Anal. Calcd. for $C_{13}H_{13}N_3OS$: C, 60.21; H, 5.05; N, 16.20; S, 12.36. Found: C, 60.47; H, 5.30; N, 15.97; S, 12.10.

6-*N*-Benzylamino-5,6-dihydro-4*H*-pyrrolo[1,2-*a*]thieno[2,3-*f*]-[1,4]diazepin-4-one **14**.

The reagent was benzylamine (5 ml); colorless crystals (65%) had mp 161° (ether); ir (potassium bromide): 3340, 3200 (NH), 1630 (CO); ^{1}H-nmr (DMSO-d_6): 8.80 (br s, NH), 7.88 (d, $J_{H2\ H1}$ = 5.4 Hz, H2), 7.46 (d, $J_{H1\ H2}$ = 5.4 Hz, H1), 7.30 (m, H9 and 5H arom), 6.25 (m, H8), 6.16 (m, H7), 4.99 (m, H6), 3.70 (m, CH_2), 2.83 (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, 65.85; H, 5.16; N, 13.39; S, 10.27.

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

The reagent was pyrrolidine (4 ml); colorless crystals (93%) had mp 191° (ether); ir (potassium bromide): 3260, 3190 (NH), 1630 (CO); ^{1}H-nmr (deuteriochloroform): 7.52 (d, $J_{H2\ H1}$ = 5.4 Hz, H2), 7.16 (d, $J_{H1\ H2}$ = 5.4 Hz, H1), 7.03 (m, H9), 6.72 (br s, NH), 6.27 (m, H8), 6.18 (m, H7), 4.61 (m, H6), 2.63 (m, CH_2), 2.27 (m, CH_2), 1.63 (m, 2 CH_2).

Anal. Calcd. for $C_{14}H_{15}N_3OS$: C, 61.52; H, 5.54; N, 15.37; S, 11.73. Found: C, 61.62; H, 5.41; N, 15.35; S, 11.79.

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

The reagent was piperidine (1 ml); colorless crystals (89%) had mp 178° (ether); ir (potassium bromide): 3260, 3170 (NH), 1640 (CO); ^{1}H-nmr (deuteriochloroform): 7.50 (d, $J_{H2\ H1}$ = 5.4 Hz, H2), 7.36 (br s, NH), 7.13 (d, $J_{H1\ H2}$ = 5.4 Hz, H1), 7.02 (m, H9), 6.28 (m, H8), 6.17 (m, H7), 4.64 (m, H6), 2.56 (m, CH_2), 2.15 (m, CH_2), 1.35 (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, 62.65; H, 5.96; N, 14.57; S, 11.20.

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

The reagent was morpholine (1 ml); colorless crystals (92%) had mp 198° (ether); ir (potassium bromide): 3270, 3170 (NH), 1640 (CO); ^{1}H-nmr (deuteriochloroform): 7.54 (d, $J_{H2\ H1}$ = 5.4 Hz, H2), 7.14 (d, $J_{H1\ H2}$ = 5.4 Hz, H1), 7.11 (br s, NH), 7.06 (m, H9), 6.29 (m, H8), 6.22 (m, H7), 4.56 (d, $J_{H6\ NH}$ = 5.4 Hz, H6), 3.47 (m, 2 CH_2), 2.56 (m, CH_2), 2.10 (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, 57.92; H, 5.23; N, 14.46; S, 10.95.

5,6-Dihydro-6-(4-ethylpiperazin-1-ylcarboxylate)-4*H*-pyrrolo[1,2-*a*]thieno[2,3-*f*][1,4]diazepin-4-one **18**.

The reagent was ethyl 1-piperazinecarboxylate (2 ml); colorless crystals (80%) had mp 180° (ether/petroleum ether); ir (potassium bromide): 3260, 3160 (NH), 1690, 1640 (CO); ^{1}H-nmr (deuteriochloroform): 7.53 (d, $J_{H2\ H1}$ = 5.4 Hz, H2), 7.23 (br s, NH), 7.14 (d, $J_{H1\ H2}$ = 5.4 Hz, H1), 7.06 (m, H9), 6.30 (m, H8), 6.21 (m, H7), 4.60 (d, $J_{H6\ NH}$ = 5.4 Hz, H6), 4.07 (q, J = 7 Hz, CH_2), 3.24 (m, 2 CH_2), 2.48 (m, CH_2), 2.06 (m, CH_2), 1.21 (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, 56.76; H, 5.48; N, 15.47; S, 8.78.

5,6-Dihydro-6-(4-phenylpiperazin-1-yl)-4*H*-pyrrolo[1,2-*a*]-thieno[2,3-*f*][1,4]diazepin-4-one **19**.

A mixture of 3-(2-formyl-1*H*-pyrrol-1-yl)-2-thiophenecarboxamide **1** (2 g, 0.009 mole) and 1-phenylpiperazine (1.8 ml, 0.012 mole) in water (40 ml) was heated at 45° for 30 minutes and then stirred at room temperature for 4 hours. The precipitate which appeared was filtered, washed with water (50 ml), dried and recrystallized to give **19** as colorless crystals (76%), mp 150° (ether); ir (potassium bromide): 3300, 3220 (NH), 1690, 1645 (CO); ^{1}H-nmr (deuteriochloroform): 7.50 (d, $J_{H2\ H1}$ = 5.4 Hz, H2), 7.14 (m, H1, H9, NH and 2 H arom), 6.84 (m, 3 H arom), 6.30 (m, H8), 6.25 (m, H7), 4.64 (d, $J_{H6\ NH}$ = 5.4 HZ, H6), 2.97 (m, 2 CH_2), 2.76 (m, CH_2), 2.31 (m, CH_2).

Anal. Calcd. for $C_{20}H_{20}N_4OS$: C, 65.91; H, 5.53; N, 15.37; S, 8.80. Found: C, 65.61; H, 5.59; N, 15.08; S, 8.62.

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

Sodium borohydride (0.84 g, 0.022 mole) was added portionwise to a solution of 5,6-dihydro-6-(4-ethylpiperazin-1-ylcarboxylate)-4*H*-pyrrolo[1,2-*a*]thieno[2,3-*f*][1,4]diazepin-4-one **18** (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 recristallized to give **20** as colorless crystals (89%), mp 191° (ether); ir (potassium bromide): 3230, 3160 (NH), 1635 (CO); ^{1}H-nmr (deuteriochloroform): 7.60 (d, $J_{H2\ H1}$ = 5.4 Hz, H2), 7.16 (d, $J_{H1\ H2}$ = 5.4 Hz, H1), 7.01 (dd, $J_{H9\ H8}$ = 2.9 Hz, $J_{H9\ H7}$ = 1.5 Hz, H9), 6.29 (dd, $J_{H8\ H7}$ = 3.4 Hz, $J_{H8\ H9}$ = 2.9 Hz, H8), 6.12 (dd, $J_{H7\ H9}$ = 3.4 HZ, $J_{H7\ H9}$ = 1.5 Hz, H7), 4.71 (br s, NH), 4.32 (d, $J_{CH2\ NH}$ = 5.1 Hz, CH_2).

Anal. Calcd. for $C_{10}H_8N_2CS$: C, 58.81; H, 3.95; N, 13.72; S, 15.70. Found: C, 58.70; H, 3.97; N, 13.64; S, 15.54.

5-Acetyl-5,6-dihydro-4*H*-pyrrolo[1,2-*a*]thieno[2,3-*f*][1,4]-diazepin-4-one **21**.

A mixture of 5,6-dihydro-4*H*-pyrrolo[1,2-*a*]thieno[2,3-*f*]-[1,4]diazepin-4-one **20** (0.5 g, 0.0024 mole) in acetic anhydride (20 ml) was refluxed for 2 hours. The solution was then evaporated to dryness under reduced pressure and the oily residue was dissolved in ether (150 ml). The organic layer was washed with water (3 x 50 ml), separated and dried over magnesium sulfate. The solvent was then removed under reduced pressure and the solid residue was recrystallized to give **21** as yellow crystals (66%), mp 157° (ether); ir (potassium bromide): 1695, 1660 (CO); ^{1}H-nmr (DMSO-d_6): 8.19 (d, $J_{H2\ H1}$ = 5.4 Hz, H2), 7.56 (d, $J_{H1\ H2}$ = 5.4 Hz, H1), 7.43 (dd, $J_{H9\ H8}$ = 2 9 Hz, $J_{H9\ H7}$ = 1.5 Hz, H9), 6.26 (m, H8 and H7), 4.82 (br s, CH_2), 2.36 (s, CH_3).

Anal. Calcd. for $C_{12}H_{10}N_2O_2S$: C, 58.52; H, 4.09; N, 11.37; S, 13.02. Found: C, 58.48; H, 4.17; N, 11.20; S, 13.05.

5,6-Dihydro-5-*N*-propylaminocarbonyl-4*H*-pyrrolo[1,2-*a*]-thieno[2,3-*f*][1,4]diazepin-4-one **22**.

Propylisocyanate (0.58 ml, 0.0053 mole) was added to a mixture of 5,6-dihydro-4*H*-pyrrolo[1,2-*a*]thieno[2,3-*f*][1,4]diazepin-4-one **20** (1 g, 0.0049 mole) and triethylamine (1.4 ml, 0.0098 mole) in toluene (200 ml). The reaction mixture was refluxed for 2 hours and the solvent was then removed under reduced pressure. The solid residue was triturated in ether (200 ml), filtered, dried and recrystallized to give **22** as colorless crystals (63%), mp 120° (ether); ir (potassium bromide): 3290 (NH), 1690, 1625 (CO); ^{1}H-nmr (DMSO-d_6): 8.79 (t, $J_{NH\ CH2}$ = 5 Hz, NH), 8.14 (d, $J_{H2\ H1}$ = 5.4 Hz, H2), 7.52 (d, $J_{H1\ H2}$ = 5.4 Hz, H1), 7.40 (dd, $J_{H9\ H8}$ = 2.9 Hz, $J_{H9\ H7}$ = 1.5 Hz, H9), 6.28 (m, H8 and H7), 4.90 (br s, CH_2), 3.17 (m, CH_2), 1.48 (m, CH_2), 0.86 (t, J = 7 Hz, CH_3).

Anal. Calcd. for $C_{14}H_{15}N_3O_2S$: C, 58.11; H, 5.22; N, 14.52; S, 11.08. Found: C, 58.15; H, 5.19; N, 14.48; S, 11.16.

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

This compound was obtained as for **22**, starting from 5,6-dihydro-4*H*-pyrrolo[1,2-*a*]thieno[2,3-*f*][1,4]diazepin-4-one **20** (1 g, 0.0049 mole), triethylamine (1.4 ml, 0.0098 mole) and phenylisocyanate (0.5 ml, 0.0054 mole) in toluene (200 ml), as colorless crystals (63%), mp 176° (ether); ir (potassium bromide): 3260, 3220 (NH), 1710 (CO); ^{1}H-nmr (DMSO-d_6): 10.85 (s, NH), 8.21 (d, $J_{H2\ H1}$ = 5.4 Hz, H2), 7.55 (m, H1, H2' and H6'), 7.45 (dd, $J_{H9\ H8}$ = 2.9 Hz, $J_{H9\ H7}$ = 1.5 Hz, H9), 7.34 (m, H3' and H5'), 7.06 (m, H4'), 6.32 (m, H8 and H7), 5.00 (br s, CH_2).

Anal. Calcd. for $C_{17}H_{13}N_3O_2S$: C, 63.14; H, 4.05; N, 12.99; S, 9.91. Found: C, 63.07; H, 4.08; N, 13.07; S, 9.92.

5,6-Dihydro-4*H*-pyrrolo[1,2-*a*]thieno[2,3-*f*][1,4]diazepine **24**.

A solution of 5,6-dihydro-6-(4-ethylpiperazin-1-ylcarboxylate)-4*H*-pyrrolo[1,2-*a*]thieno[2,3-*f*][1,4]diazepin-4-one **18** (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 poured into iced-water (250 ml). The suspension was filtered and the insoluble material 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 **24** as a yellow oil (64%); ir (potassium bromide): 3300, 3220 (NH); ^{1}H-nmr (deuteriochloroform): 7.18 (d, $J_{H2\ H1}$ = 5.4 Hz, H2), 7.10 (d, $J_{H1\ H2}$ = 5.4 Hz, H1), 7.02 (m, H9), 6.17 (m, H8), 6.06 (m, H7), 4.25 (s, CH_2), 3.98 (s, CH_2), 1.70 (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, 62.95; H, 5.52; N, 14.78; S, 16.53.

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

A solution of 5,6-dihydro-4*H*-pyrrolo[1,2-*a*]thieno[2,3-*f*]-[1,4]diazepine **24** (3 g, 0.016 mole) in ether (60 ml) was bubbled with an hydrochloric acid gas flow for 30 seconds at room temperature. The precipitate which appeared was filtered, washed with ether (100 ml) and recrystallized to give **25** as colorless crystals (96%), mp 260° (propan-2-ol); ir (potassium bromide): 2900-2470 ($^+NH_2$); ^{1}H-nmr (DMSO-d_6): 9.95 (br s, $^+NH_2$), 7.77 (d, $J_{H2\ H1}$ = 5.4 Hz, H2), 7.40 (d, $J_{H1\ H2}$ = 5.4 Hz, H1), 7.33 (dd, $J_{H9\ H8}$ = 2.9 Hz, $J_{H9\ H7}$ = 1.5 Hz, H9), 6.43 (dd, $J_{H7\ H8}$ = 3.4 Hz, $J_{H7\ H9}$ = 1.5 Hz, H7), 6.27 (dd, $J_{H8\ H7}$ = 3.4 Hz, $J_{H8\ H9}$ = 2.9 Hz, H8), 4.17 (s, CH_2), 4.09 (s, CH_2).

Anal. Calcd. for $C_{10}H_{11}N_2SCl$: C, 52.98; H, 4.89; N, 12.36; Cl , 15.64. Found: C, 53.20; H,4.98; N, 12.67; S, 15.46.

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

Iodomethane (2 ml) was added to a solution of 5,6-dihydro-4*H*-pyrrolo[1,2-*a*]thieno[2,3-*f*][1,4]diazepine **24** (1 g, 0.005 mole) in acetone (20 ml). The reaction mixture was stirred at room temperature for 2 hours and then allowed to stand for 6 hours. The precipitate which appeared was filtered, washed with ether (50 ml) and recrystallized to give **26** as yellow crystals (51%), mp 260° (acetone); ^{1}H-nmr (DMSO-d_6): 7.94 (d, $J_{H2\ H1}$ = 5.4 Hz, H2), 7.51 (d, $J_{H1\ H2}$ = 5.4 Hz, H1), 7.44 (dd, $J_{H9\ H8}$ = 2.9 Hz, $J_{H9\ H7}$ = 1.5 Hz, H9), 6.64 (dd, $J_{H7\ H8}$ = 3.4 Hz, $J_{H7\ H9}$ = 1.5 Hz, H7), 6.36 (dd, $J_{H8\ H7}$ = 3.4 Hz, $J_{H8\ H9}$ = 2.9 Hz, H8), 4.40 (s, CH_2), 4.36 (s, CH_2), 3.18 (s, 2 CH_3).

Anal. Calcd. for $C_{12}H_{15}N_2SI$: C, 41.62; H, 4.36; N, 8.08; S, 9.26; I, 36.65. Found: C, 41.44; H,4.32; N, 8.12; S, 9.29; I, 36.28.

5,6-Dihydro-5-S-tosyl-4*H*-pyrrolo[1,2-*a*]thieno[2,3-*f*]-[1,4]diazepine **27**.

Tosyl chloride (1 g, 0.0053 mole) was added to a solution of 5,6-dihydro-4*H*-pyrrolo[1,2-*a*]thieno[2,3-*f*][1,4]diazepine **24** (1 g, 0.0053 mole) in pyridine (10 ml). The reaction mixture was stirred at room temperature for 1 hour. The solvent was then removed under reduced pressure and the oily residue was dissolved in ether (150 ml). The organic layer was washed with water (2 x 50 ml), separated, dried over magnesium sulfate and evaporated to dryness. The solid residue was recrystallized to give **27** as yellow crystals (22%), mp 165° (ether); ^{1}H-nmr (deuteriochloroform): 7.65 (m, H2' and H6'), 7.21 (m, H2, H3' and H5'), 6.97 (d, $J_{H1\ H2}$ = 5.4 Hz, H1), 6.82 (m, H9), 6.14 (m, H8 and H7), 4.47 (s, CH_2), 4.39 (s, CH_2), 2.38 (s, CH_3).

Anal. Calcd. for $C_{17}H_{16}N_2O_2S_2$: C, 59.28; H, 4.68; N, 8.13; S, 18.62. Found: C, 59.21; H, 4.72; N, 8.05; S, 18.44.

General Procedure for the Reaction of 3-(2-Formyl-1*H*-pyrrol-1-yl)-2-thiophenecarboxamide **1** with Alcohols.

3-(2-Formyl-1*H*-pyrrol-1-yl)-2-thiophenecarboxamide **1** (1 g, 0.0045 mole) was dissolved in the appropriate alcohol (30 ml) and the solution was refluxed for 1 hour. The alcohol was then removed under reduced pressure to give a solid residue which was recrystallized to give **28-32**.

5,6-Dihydro-6-methoxy-4*H*-pyrrolo[1,2-*a*]thieno[2,3-*f*]-[1,4]diazepin-4-one **28**.

The reagent was methanol; colorless crystals (92%) had mp 172° (methanol); ir (potassium bromide): 3250 (NH), 1650 (CO); ^{1}H-nmr (deuteriochloroform): 7.56 (d, $J_{H2\ H1}$ = 5.4 Hz, H2), 7.47 (br s, NH), 7.20 (d, $J_{H1\ H2}$ = 5.4 Hz, H1), 7.10 (m, H9), 6.30 (m, H7 and H8), 5.35 (d, $J_{H6\ NH}$ = 5.4 Hz, H6), 3.30 (s, CH_3).

Anal. Calcd. for $C_{11}H_{10}N_2OS$: C, 56.39; H, 4.30; N, 11.95; S, 13.68. Found: C, 56.62; H, 4.09; N, 11.81; S, 13.48.

5,6-Dihydro-6-ethoxy-4*H*-pyrrolo[1,2-*a*]thieno[2,3-*f*]-[1,4]diazepin-4-one **29**.

The reagent was ethanol; colorless crystals (86%) had mp 148° (ethanol); ir (potassium bromide): 3260, 3180 (NH), 1635 (CO); ^{1}H-nmr (deuteriochloroform): 7.57 (d, $J_{H2\ H1}$ = 5.4 Hz, H2), 7.43 (br s, NH), 7.18 (d, $J_{H1\ H2}$ = 5.4 Hz, H1), 7.08 (m, H9), 6.29 (m, H7 and H8), 5 46 (d, $J_{H6\ NH}$ = 5.4 Hz, H6), 3.57 (m, CH_2), 1.08 (t, J = 7 Hz, CH_3).

Anal. Calcd. for $C_{12}H_{12}N_2O_2S$: C, 58.05; H, 4.87; N, 11.28; S, 12.91. Found: C, 57.83; H, 4.80; N, 11.20; S, 12.79.

5,6-Dihydro-6-propoxy-4*H*-pyrrolo[1,2-*a*]thieno[2,3-*f*]-[1,4]diazepin-4-one **30**.

The reagent was propan-1-ol; colorless needles (86%) had mp 164° (ether); ir (potassium bromide): 3300 (NH), 1645 (CO); ^{1}H-nmr (deuteriochloroform): 7.90 (br s, NH), 7.56 (d, $J_{H2\ H1}$ = 5.4 Hz, H2), 7.17 (d, $J_{H1\ H2}$ = 5.4 Hz, H1), 7.08 (m, H9), 6.28 (m, H7 and H8), 5.45 (d, $J_{H6\ NH}$ = 5.4 Hz, H6), 3.42 (m, CH_2), 1.45 (m, CH_2), 0.71 (t, J = 7 Hz, CH_3).

Anal. Calcd. for $C_{13}H_{14}N_2O_2S$: C, 59.52; H, 5.38; N, 10.68; S, 12.22. Found: C, 59.59; H, 5.33; N, 10.72; S, 12.08.

5,6-Dihydro-6-methylethoxy-4*H*-pyrrolo[1,2-*a*]thieno[2,3-*f*]-[1,4]diazepin-4-one **31**.

The reagent was propan-2-ol; colorless crystals (80%) had mp 160° (propan-2-ol); ir (potassium bromide): 3260, 3170 (NH), 1640 (CO); ^{1}H-nmr (deuteriochloroform): 7.56 (d, $J_{H2\ H1}$ = 5.4 Hz, H2), 7.38 (br s, NH), 7.17 (d, $J_{H1\ H2}$ = 5.4 Hz, H1), 7.07 (m, H9), 6.28 (m, H7 and H8), 5.56 (d, $J_{H6\ NH}$ = 5.4 Hz, H6), 3.81 (m, CH), 1.07 (d, J = 7 Hz, 2 CH_3).

Anal. Calcd. for $C_{13}H_{14}N_2O_2S$: C, 59.52; H, 5.38; N, 10.68; S, 12.22. Found: C, 59.44; H, 5.30; N, 10.62; S, 12.06.

6-Benzyloxy-5,6-dihydro-4*H*-pyrrolo[1,2-*a*]thieno[2,3-*f*]-[1,4]diazepin-4-one **32**.

The reagent was benzyl alcohol in acetonitrile solution (1%, 50 ml); colorless crystals (60%) had mp 179° (ether); ir (potassium bromide): 3270, 3190 (NH), 1645 (CO); ^{1}H-nmr (deuteriochloroform): 7.58 (d, $J_{H2\ H1}$ = 5.4 Hz, H2), 7.42 (br s, NH), 7.27 (m, H1 and 5 H arom), 7.08 (m, H9), 6.26 (m, H7 and H8), 5.47 (d, $J_{H6\ NH}$ = 5.4 Hz, H6), 4.52 (s, CH_2).

Anal. Calcd. for $C_{17}H_{14}N_2O_2S$: C, 65.79; H, 4.55; N, 9.02; S, 10.33. Found: C, 65.51; H, 4.71; N, 9.22; S, 10.56.

General Procedure for the Reaction of 3-(2-Formyl-1*H*-pyrrol-1-yl)-2-thiophenecarboxamide **1** with Thiols.

The appropriate thiol (0.005 mole) was added to a solution of 3-(2-formyl-1*H*-pyrrol-1-yl)-2-thiophenecarboxamide **1** (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. The solid was recrystallized to give **33-35.**

Methyl 5,6-Dihydro-4-oxo-4*H*-pyrrolo[1,2-*a*]thieno[2,3-*f*]-[1,4]diazepin-6-thioglycolate **33**.

The reagent was methylthioglycolate (0.43 ml); colorless crystals (68%) had mp 158° (ether); ir (potassium bromide): 3270, 3160 (NH), 1715, 1645 (CO); ^{1}H-nmr (deuteriochloroform): 7.62 (d, $J_{H2\ H1}$ = 5.4 Hz, H2), 7.18 (d, $J_{H1\ H2}$ = 5.4 Hz, H1), 7.10 (dd, $J_{H9\ H8}$ = 2.9 Hz, $J_{H9\ H7}$ = 1.5 Hz, H9), 6.94 (d, $J_{NH\ H6}$ = 7 Hz, NH), 6.30 (dd, $J_{H8\ H7}$ = 3.4 Hz, $J_{H8\ H9}$ = 2.9 Hz, H8), 6.26 (dd, $J_{H7\ H8}$ = 3.4 Hz, $J_{H7\ H9}$ = 1.5 Hz, H7), 5.94 (d, $J_{H6\ NH}$ = 7.0 Hz, H6), 3.77 (s, CH_3), 3.28 (d, $J_{Ha\ Hb}$ = 15.4 Hz, Ha), 3.04 (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, 50.55; H, 3.87; N, 8.97; S, 20.71.

5,6-Dihydro-4-oxo-4*H*-pyrrolo[1,2-*a*]thieno[2,3-*f*][1,4]diazepin-6-yl-*S*-(3-thio)propionic Acid **34**.

The reagent was 3-thiopropionic acid (0.45 ml); colorless crystals (43%) had mp 190° (ether); ir (potassium bromide): 3450 (OH), 3240 (NH), 1700, 1610 (CO); ^{1}H-nmr (DMSO-d_6): 12.20 (br s, OH), 9.13 (d, $J_{NH\ H6}$ = 7 Hz, NH), 7.94 (d, $J_{H2\ H1}$ = 5.4 HZ, H2), 7.50 (d, $J_{H1\ H2}$ = 5.4 HZ, H1), 7.42 (m, H9), 6.28 (m, H7 and H8), 5.78 (d, $J_{H6\ NH}$ = 7.0 Hz, H6), 2.50 (m, 2 CH_2).

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, 50.53; H, 3.89; N, 9.09; S, 20.69.

5,6-Dihydro-6-phenylthio-4*H*-pyrrolo[1,2-*a*]thieno[2,3-*f*]-[1,4]diazepin-4 one **35**.

The reagent was thiophenol (0.50 ml); colorless needles (72%) had mp 178° (ether); ir (potassium bromide): 3270, 3160 (NH), 1645 (CO); ^{1}H-nmr (deuteriochloroform): 7.65 (d, $J_{H2\ H1}$ = 5.4 Hz, H2), 7.30 (m, 5 H arom), 7.21 (d, $J_{H1\ H2}$ = 5.4 Hz, H1), 7.09 (m, H9), 6.75 (d, $J_{NH\ H6}$ = 7 Hz, NH), 6.24 (dd, $J_{H8\ H7}$ = 3.4 Hz, $J_{H8\ H9}$ = 2.9 Hz, H8), 6.14 (m, H7), 5.79 (d, $J_{H6\ NH}$ = 7.0 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, 61.70; H, 3.96; N, 9.10; S, 20.54.

Ethyl 5,6-Dihydro-4-oxo-4*H*-pyrrolo[1,2-*a*]thieno[2,3-*f*][1,4]-diazepin-6-yl-(2-aceto)acetate **36**.

Ethyl acetoacetate (2 ml) and triethylamine (0.5 ml, 0.007 mole) were added to a solution of 3-(2-formyl-1*H*-pyrrol-1-yl)-2-thiophene carboxamide **1** (1 g, 0.0045 mole) in acetonitrile (100 ml). The reaction mixture was stirred at room temperature for 12 hours. The solvent was then removed under reduced pressure and the oily residue was dissolved in water (200 ml). The precipitate which appeared was filtered, washed with water (50 ml), dried and recrystallized to give **36** as colorless crystals (47%), mp 196° (ether); ir (potassium bromide): 3270, 3200 (NH), 1710, 1635 (CO); ^{1}H-nmr (deuteriochloroform): 7.65 (d, $J_{H2\ H1}$ = 5.4 Hz, H2), 7.20 (d, $J_{H1\ H2}$ = 5.4 Hz, H1), 7.04 (m, H9), 6.62 (d, $J_{NH\ H6}$ = 7.4 Hz, NH), 6.28 (dd, $J_{H8\ H7}$ = 3.4 Hz, $J_{H8\ H9}$ = 2.9 Hz, H8), 6.11 (m, H7), 5.16 (dd, $J_{H6\ CH}$ = 9.7 Hz, $J_{H6\ NH}$ = 7.4 Hz, H6), 4.25 (q, J = 7 Hz, CH_2), 4.13 (d, $J_{CH\ H6}$ = 9.7 Hz, CH), 1.91 (s, CH_3), 1.29 (t, J = 7 Hz, CH_3).

Anal. Calcd. for $C_{16}H_{16}N_2O_4S$: C, 57.82; H, 4.85; N, 8.43; S, 9.65. Found: C, 57.75; H, 4.78; N, 8.37; S, 9.85.

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