Thiophene Systems. 4. Selective Syntheses of Thieno[3,4-*b*][1,4]- and [1,5]benzodiazepinones (1)

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Novel syntheses of thiophene fused tricyclic systems **1** and **2** are reported. The methods use intermediates 4-ethoxy-3-thiopheneamine, 4-ethoxy-3-thiophenecarbonyl azide and 4-ethoxy-3-thiophenecarbonyl chloride to effect selective, high yield syntheses of the target compounds in two steps. These methods allow preparation of thiophene systems without substitution at the normally reactive C-1 and C-3 positions.

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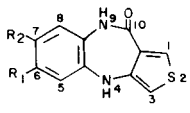
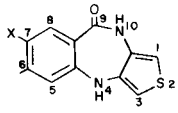
Discussion.

Recent interest in novel thieno[3,4-*b*]-fused tricyclic ring systems as potential CNS agents has been reported by several laboratories (1-4). In particular, we recently synthesized thieno[3,4-*b*][1,5]benzodiazepinones (**1**) and described the potential neuroleptic activity of some of their derivatives (2). Chakrabarti, *et al.*, reported the synthesis of **1a** by an alternate synthetic approach (3). Our initial (2) preparation of **1** suffered from a lack of selectivity



1



2

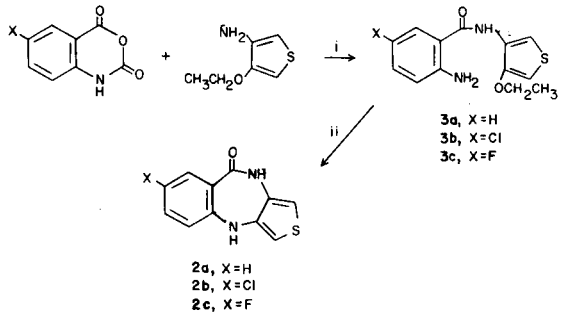
1a, R_1=H, R_2=F

for the formation of unsymmetrical lactams ($R_1 \neq R_2$) and a more stereo-controlled synthesis of **1** was required to facilitate development of these potential CNS agents. We also were interested in developing methods of synthesizing analogues of the isomeric 4*H*-thieno[3,4-*b*][1,4]benzodiazepinone (**2**) (also without substitution at C-1 and C-3) for the same purpose. A recently reported synthesis of unsubstituted **2** starting from bromonitrothiophenes (4) appeared inconvenient and not sufficiently general for our goals. We also hoped to utilize intermediates and techniques that we had previously reported (1,5) to prepare **1** and **2** selectively.

The thieno[3,4-*b*][1,4]benzodiazepin-9-(10*H*)one system (**2**) was prepared in several ways. In one approach, 4-ethoxy-3-thiopheneamine (5) was condensed with an appropriately substituted isatoic anhydride to provide aminoamides **3a-c** in good yields. We have previously noted that systems similar to **3** possess an enol ether-like moiety which is acid labile and subject to nucleophilic attack (1,5). Consequently, treatment of **3** with polyphosphoric acid led exclusively to intramolecular cyclization with the formation of the desired **2a-c**. This two-step procedure from literature compounds is the general procedure of choice to prepare useful quantities of **2**.

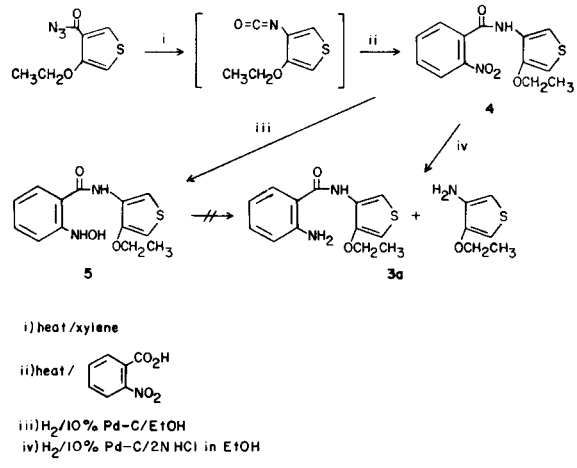
Synthesis of precusor **3a** could also be effected starting

SCHEME I



from 4-ethoxy-3-thiophenecarbonyl azide (5). In this procedure, thermal decomposition of the azide in an inert

SCHEME II



solvent led to the formation of the unisolated isocyanate which was trapped with *o*-nitrobenzoic acid to give nitro amide **4**. Hydrogenation of **4** using a variety of catalysts under neutral conditions led exclusively to hydroxylamine **5** which was inert to further reduction attempts. The desired amino amide **3a** could be formed, however, by hydrogenation of **4** in acidic media. Unfortunately, ethanolic hydrogen chloride, which was found to be the

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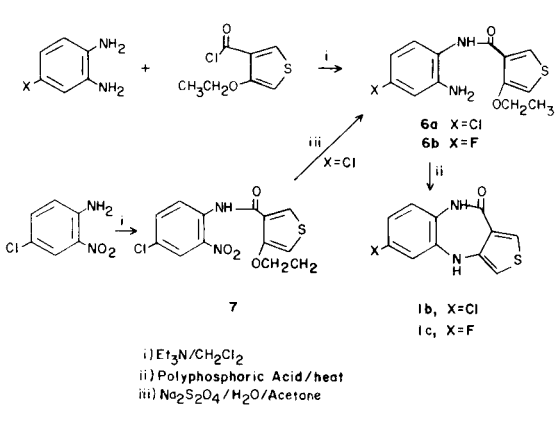
reaction medium leading to the best conversion to **3a**, caused some solvolysis of the amide linkage of **4** and/or **3a** leading to the formation of 4-ethoxy-3-thiopheneamine. Derivative **3a** prepared by this route was identical in all respects to the material prepared in Scheme I.

As these studies progressed, derivatives of **1** specifically substituted with halogen at C-6 were of particular interest and a selective synthesis of these compounds was developed. The original preparation of these systems involved non-controlled condensation of unsymmetrically substituted *o*-phenylenediamines with methyl tetrahydro-4-oxo-3-thiophenecarboxylate (6) which led to difficultly separated isomeric mixtures (2). More selective syntheses

SCHEME III



of **1** involved condensation of 4-ethoxy-3-thiophenecarbonyl chloride (1) with 4-chloro- or 4-fluoro-*o*-phenylenediamine which led exclusively to formation of desired amino amides **6a-b** respectively. Presumably, the mesomeric influence of the 4-halo substituent sufficiently enhances the nucleophilicity of the 1-amino moiety to give rise to the observed reaction exclusively. The outcome of this reaction was verified in the case of chloro system **6a** by alternative synthesis. Reaction of the acid chloride with 4-chloro-2-nitro aniline gave **7**. Sodium hydrosulfite reduction of **7** gave **6a** which was identical in all respects to material prepared by acylation of the diamine. Once again the acid lability of the enol ether linkage in **6a,b** was advantageously used in the conversion to the desired lactams **1b,c** respectively in excellent yields. Lactam **1b** was identical in all respects to material we previously reported (2).

The synthetic schemes represented herein allow preparation of the interesting thieno[3,4-*b*][1,4]- and [1,5]-benzodiazepinones (**1** and **2**) in useful quantities. The syntheses allow preparation of variously substituted derivatives selectively and without substitution in the 1-and 3-positions of the ring. Conversion of these lactams to biologically active, novel CNS agents is the subject of a future report from these laboratories (7).

Acknowledgement.

The authors wish to thank Dr. W. Gore and staff for measurement of spectral data and Mr. L. Brancone and staff for microanalytical data.

EXPERIMENTAL

Melting points were determined on a Mel-Temp capillary block melting point apparatus and are uncorrected. All compounds are homogeneous by thin layer chromatographic analysis using Whatman K5F (5 × 10 cm) silica gel analytical plates. ^{1}H Nmr measurements were obtained on a Varian Associates HA-100A spectrometer with tetramethylsilane as the internal standard.

2-Amino-*N*-(4-ethoxy-3-thienyl)benzamide (**3a**).

A solution of 3.2 g. (0.02 mole) of isatoic anhydride in 5 ml. of dimethylsulfoxide with a small amount of ground glass was stirred and heated at 120-128°. To this hot solution was added dropwise over 20 minutes a solution of 2.8 g. (0.02 mole) of 4-ethoxy-3-thiopheneamine (5) in 4 ml. of dimethylsulfoxide. The heating was continued for an additional 15 minutes and then the mixture was allowed to stand for 1 hour. The solution was poured into ice water and the mixture was extracted with chloroform. The extracts were dried, filtered and evaporated to an oil (6.6 g.). The oil was dissolved in methylene chloride and put through a cake of magnesium silicate. The filtrate was evaporated and the oily residue was crystallized from aqueous methanol to give 1.85 g. (35%) of **3a** as a tan solid, m.p. 89-94°; ^{1}H nmr (DMSO): δ 8.17 (brs, 1H, N*H*), 7.77 (d, 1H, thiophene-*H*), 7.3 (m, 2H), 6.70 (m, 2H, all Ar-*H*), 6.15 (d, 1H, thiophene-*H*), 5.52 (brs, 2H, NH_2), 4.09 (q, 2H, CH_2), 1.42 (t, 3H, CH_3).

Anal. Calcd. for $C_{13}H_{14}N_2O_2S$ (262.3): C, 59.52; H, 5.38; N, 10.68; S, 12.23. Found: C, 59.46; H, 5.14; N, 10.62; S, 11.82.

2-Amino-5-chloro-*N*-(4-ethoxy-3-thienyl)benzamide (**3b**).

In a similar manner to that described above, 21.3 g. (0.108 mole) of 6-chloroisatoic anhydride in 37 ml. of dimethylsulfoxide was treated with 15.4 g. (0.108 mole) of 4-ethoxy-3-thiopheneamine (5) in 30 ml. of dimethylsulfoxide. The product was converted to a white solid hydrochloride salt, 18.9 g. (59%), m.p. 185-186° dec. The hydrochloride was converted into the free base **3b** obtained as a white solid, m.p. 97-98°; ^{1}H nmr (DMSO): δ 9.64 (brs, 1H, N*H*), 8.03 (brs, 3H, $^+$NH_3), 7.68 (d, 1H, Ar-*H*), 7.58 (d, 1H, thiophene *H*), 7.32 (dd, 1H), 7.12 (d, 1H, both Ar-*H*), 6.56 (d, 1H, thiophene *H*), 4.08 (q, 2H, CH_2), 1.38 (t, 3H, CH_3).

Anal. Calcd. for $C_{13}H_{13}ClN_2O_2S$ (296.8): C, 52.62; H, 4.42; N, 9.44; S, 10.78; Cl, 11.95. Found: C, 52.23; H, 4.61; N, 9.47; S, 10.89; Cl, 11.69.

2-Amino-*N*-(4-ethoxy-3-thienyl)-5-fluorobenzamide (**3c**).

6-Fluoroisatoic anhydride (8) (13.9 g., 0.077 mole) in dimethylsulfoxide (20 ml.) was treated with 4-ethoxy-3-thiopheneamine (5) (11 g., 0.077 mole) in dimethylsulfoxide (25 ml.) by the procedure described above. The crude product was isolated as a dark colored solid, 14.7 (68%). This solid was converted to the hydrochloride 14 g. (57.5%), m.p. 177-178° dec., recrystallized from alcohol-ether and converted to the base **3c**, a white solid, 12.2 g. (56%), m.p. 95-97°; ^{1}H nmr (DMSO): δ 8.20 (brs, 1H, N*H*), 7.90 (d, 1H, thiophene *H*), 6.9 (m, 3H, Ar-*H*), 6.25 (d, 1H, thiophene *H*), 4.25 (q superimposed on brs, 4H, CH_2, NH_2), 1.50 (t, 3H, CH_3).

Anal. Calcd. for $C_{13}H_{13}FN_2O_2S$ (280.3): C, 55.70; H, 4.67; N, 10.00; S, 11.44; F, 6.78. Found: C, 55.69; H, 4.54; N, 10.03; S, 11.55; F, 6.90.

N-(4-Ethoxy-3-thienyl)-2-nitrobenzamide (**4**).

A solution of 11.8 g. (0.06 mole) of 4-ethoxy-3-thiophenecarbonyl azide (5) in 75 ml. of xylene was warmed at 95-100° for ½ hour at which time gas evolution had stopped. Then 12.0 g. (0.072 mole) of *o*-nitrobenzoic acid in 5-10 ml. of xylene was added. The mixture was stirred and refluxed for 60 hours, then cooled and filtered. The filtrate was washed several times with sodium bicarbonate solution, dried, filtered and evaporated to give 11.7 g. of an oily solid. Recrystallization from ethyl acetate-hexanes gave 6.3 g. (36%) of a tan solid, m.p. 108-112°. The analytical sample of **4** melted 112-114°; ^{1}H nmr (DMSO): δ 8.08 (m, 1H, Ar-*H*), 7.86 (d, 1H,

thiophene -*H*), 7.60 (m, 3H, Ar-*H*) 6.20 (d, 1H, thiophene -*H*), 6.20 (d, 1H, thiophene -*H*), 4.09 (q, 2H, C*H*$_2$), 1.39 (t, 3H, C*H*$_3$).

Anal. Calcd. for $C_{13}H_{12}N_2O_4S$ (292.3): C, 53.41; H, 4.14; N, 9.59; S, 10.97. Found: C, 53.07; H, 4.33; N, 9.58; S, 10.92.

N-(4-Ethoxy-3-thienyl)-*o*-hydroxylaminobenzamide (**5**).

Two g. (0.0069 mole) of *N*-(4-ethoxy-3-thienyl)-2-nitrobenzamide (**4**), 50 ml. of ethanol and 0.5 g. of 10% palladium/carbon was hydrogenated in a Parr shaker for 2 hours at which time no more hydrogen was absorbed. The mixture was filtered and the filtrate was evaporated to give an oily solid (0.5 g.). Purification through a column of silica gel and with recrystallization from methylene chloride-pet. ether gave 0.15 g. (8%) of **5** as a white solid, m.p. 106-107°. This solid is insoluble in acid and does not react with sodium nitrite, consistent with the presence of a hydroxylamine moiety; ^{1}H nmr (DMSO): δ 9.60 (brs, 1H, N*H*), 8.95 (d, 1H), 8.55 (d, 1H, NH, OH), 7.68 (m, 2H, Ar-H, thiophene *H*), 7.36 (m, 2H, Ar-*H*), 6.90 (m, 1H, Ar-*H*), 6.58 (d, 1H, thiophene *H*), 4.12 (q, 2H, C*H*$_2$), 1.36 (t, 3H, C*H*$_3$).

Anal. Calcd. for $C_{13}H_{14}N_2O_3S$ (278.3): C, 56.09; H, 5.07; N, 10.07; S, 11.52. Found: C, 56.14; H, 5.26; N, 9.91; S, 11.23.

2-Amino-*N*-(4-ethoxy-3-thienyl)benzamide (**3a**).

A mixture of 4.38 g. (0.015 mole) of *N*-(4-ethoxy-3-thienyl)-2-nitrobenzamide (**4**), 100 ml. of ethanol, 10 ml. of 2*N* alcoholic hydrogen chloride and 0.5 g. of 10% palladium/carbon was hydrogenated in a Parr shaker. After 3 hours, the mixture was filtered and the filtrate was evaporated to a glass (5 g.). Water (50 ml.) was added and the tan solid which separated was collected (1.3 g., m.p. 85-89°) and sublimed at 110-125°/0.1 mm to give 0.8 g. (20%) of a white solid, identical with **3a** prepared above. The aqueous filtrate was made alkaline and extracted with methylene chloride. From these extracts there was isolated 1.3 g. of 4-ethoxy-3-thiopheneamine (5) as an oil which was purified by distillation (b.p. 69°/0.4 mm,) and was identical in all respects to an authentic sample (5).

4*H*-Thieno[3,4-*b*][1,4]benzodiazepin-9-(10*H*)one (**2a**).

A mixture of 1.8 g. (0.007 mole) of 2-amino-*N*-(4-ethoxy-3-thienyl)-benzamide (**3a**) and 30 g. of polyphosphoric acid was warmed at 115-118° for 30 minutes. The mixture was cooled and poured into ice water layered with chloroform. The chloroform extracts were washed with water, dried (magnesium sulfate), filtered and the filtrate evaporated to give 1.1 g. (73%) of a yellow solid. The analytical sample of **2a** was obtained by sublimation at 140°/0.5 mm, as a yellow solid, m.p. 190-195° dec; ^{1}H nmr (DMSO): δ 9.99 (brs, 1H, N*H*), 8.22 (brs, 1H, N*H*), 7.72 (m, 1H), 7.25 (m, 1H), 6.7 (m, 2H, all Ar-*H*), 6.60 (d, 1H), 6.45 (d, 1H, both thiophene-*H*).

Anal. Calcd. for $C_{11}H_8N_2OS$ (216.3): C, 61.09; H, 3.73; N, 12.96; S, 14.83. Found: C, 61.12; H, 4.03; N, 12.39; S, 14.65.

7-Chloro-4*H*-thieno[3,4-*b*][1,4]benzodiazepin-9-(10*H*)one (**2b**).

A mixture of 2.96 g. (0.01 mole) of 2-amino-5-chloro-*N*-(4-ethoxy-3-thienyl)benzamide (**3b**) and 30 g. of polyphosphoric acid was heated in an oil bath at 120-123° for 30 minutes and then worked up as described above. A small sample of the crude product (2.2 g. 88%) was sublimed to give the analytical sample of **2b**, m.p. 203-205° dec.; ^{1}H nmr (DMSO): δ 10.28 (brs, 1H, N*H*), 8.48 (brs, 1H, N*H*), 7.69 (d, 1H), 7.30 (dd, 1H), 6.88 (d, 1H, all Ar-*H*), 6.44 (d, 1H), 6.38 (d, 1H, both thiophene-*H*).

Anal. Calcd. for $C_{11}H_7ClN_2OS$ (250.7): C, 52.71; H, 2.82; N, 11.18; S, 12.77; Cl, 14.15. Found: C, 53.00; H, 3.14; N, 10.92; S, 12.74; Cl, 13.57.

7-Fluoro-4*H*-thieno[3,4-*b*][1,4]benzodiazepin-9-(10*H*)one (**2c**).

A mixture of 2.8 g. (0.01 mole) of 2-amino-5-fluoro-*N*-(4-ethoxy-3-thienyl)benzamide (**3c**) and 30 g. of polyphosphoric acid was heated in an oil bath at 125° for 30 minutes and then worked up as described above. A sample of the crude product (2.0 g., 87%) was sublimed to give the analytical sample of **2c**, m.p. 195-200° dec.; ^{1}H nmr (DMSO): δ 10.16 (brs, 1H, N*H*), 8.22 (brs, 1H, N*H*), 7.46 (dd, 1H), 7.12 (td, 1H), 6.90 (dd, 1H, all Ar-*H*), 6.62 (d, 1H), 6.44 (d, 1H, both thiophene *H*).

Anal. Calcd. for $C_{11}H_7FN_2OS$ (234.3): C, 56.39; H, 3.01; N, 11.96; S, 13.69; F, 8.11. Found: C, 56.49; H, 3.43; N, 11.65; S, 13.37; F, 8.26.

2'-Amino-4-ethoxy-4'-fluoro-3-thiophenecarboxanilide (**6b**).

A solution of 32.9 g. (0.165 mole) of 4-ethoxy-3-thiophenecarboxylic acid chloride (1) in 220 ml. of methylene chloride was added dropwise to a cooled stirred solution of 20.8 g. (0.165 mole) of 4-fluoro-*o*-phenylenediamine and 23.6 ml. (0.165 mole) of triethylamine in 200 ml. of methylene chloride. The mixture was stirred for 24 hours and the solvent was evaporated. Water was added to the residue, the mixture was made alkaline with 1*N* sodium hydroxide and extracted several times with methylene chloride. The extracts were combined, dried over magnesium sulfate, filtered and evaporated to give the crude product as an orange solid. Recrystallization from methanol gave 36.8 g. (79.6%) of an off-white solid, m.p. 123-125°. The analytical sample of **6b** melted at 125-127°; ^{1}H nmr (DMSO): δ 9.00 (brs, 1H, N*H*), 8.16 (d, 1H, thiophene-*H*), 7.28 (m, 1H), 6.5 (m, 2H, all Ar-*H*), 6.38 (d, 1H, thiophene-*H*), 4.20 (q, 2H, C*H*$_2$), 4.0 (brs, 2H, N*H*$_2$), 1.50 (t, 3H, C*H*$_3$).

Anal. Calcd. for $C_{13}H_{13}FN_2O_2S$ (280.3): C, 55.70; H, 4.67; N, 10.00; S, 11.44; F, 6.78. Found: C, 55.11; H, 4.58; N, 10.08; S, 11.57; F, 7.10.

6b Hydrochloride.

This compound was obtained from ethyl acetate/ethanolic hydrogen chloride, tan solid, m.p. 175-177° dec.

Anal. Calcd. for $C_{13}H_{13}FNO_2S \cdot HCl$ (316.79): C, 49.29; H, 4.45; N, 8.84; F, 6.00; S, 10.12; Cl, 11.19. Found: C, 49.25; H, 4.48; N, 8.77; F, 6.17; S, 10.24; Cl, 11.28.

6-Fluoro-4,9-dihydro-10*H*-thieno[3,4-*b*][1,5]benzodiazepin-10-one (**1c**).

A mixture of 28 g. (0.1 mole) of 2'-amino-4-ethoxy-4'-fluoro-3-thiophenecarboxanilide (**6b**) and 300 g. of polyphosphoric acid was heated at 120-130° for 1.5 hours. The dark colored mass was poured into ice-water and then filtered. The solid was washed on the funnel with water, bicarbonate solution and water, and then dried to give 23.5 g. (100%) of a tan solid, m.p. 208-212° dec. The analytical sample of **1c** was obtained by recrystallization from aqueous methanol, m.p. 225-228° dec.; ^{1}H nmr (DMSO): δ 9.70 (brs, 1H, N*H*), 8.30 (brs, 1H, N*H*), 8.03 (d, 1H, thiophene-*H*), 6.9 (m, 3H, Ar-*H*), 6.55 (d, 1H, thiophene-*H*).

Anal. Calcd. for $C_{11}H_7FN_2OS$ (234.3): C, 56.39; H, 3.01; N, 11.96; S, 13.69; F, 8.11. Found: C, 56.06; H, 3.19; N, 11.69; S, 13.40; F, 8.11.

4'-Chloro-4-ethoxy-2'-nitro-3-thiophenecarboxanilide (**7**).

To a solution of 4.55 ml. (0.03175 mole) of triethylamine, 38 ml. of methylene chloride and 5.5 g. (0.03175 mole) of 4-chloro-2-nitroaniline was added dropwise over ½ hour a solution of 6.35 g. (0.03175 mole) of 4-ethoxy-3-thiophenecarbonyl chloride (1) in 40 ml. of methylene chloride. The mixture was stirred overnight and then filtered. The small amount of insoluble material on the funnel was washed with methylene chloride. The filtrate was evaporated to a sticky yellow solid which was recrystallized from ethanol to give 6.0 g. (58%) of a yellow solid, m.p. 140-143°. Recrystallization from 300 ml. of ethanol gave 5.3 g. of **7** as a yellow solid, m.p. 144-145°; ^{1}H nmr (DMSO): δ 11.35 (brs, 1H, N*H*), 8.82 (d, 1H), 8.20 (d, 1H, both Ar-*H*), 8.15 (d, 1H, thiophene-*H*), 7.57 (dd, 1H, Ar-*H*), 6.38 (d, 1H, thiophene-*H*), 4.29 (q, 2H, C*H*$_2$), 1.58 (t, 3H, C*H*$_3$).

Anal. Calcd. for $C_{13}H_{11}ClN_2O_4S$ (326.8): C, 47.78; H, 3.39; N, 8.57; S, 9.81; Cl, 10.85. Found: C, 47.40; H, 3.37; N, 8.42; S, 10.22; Cl, 10.81.

2'-Amino-4'-chloro-4-ethoxy-3-thiophenecarboxanilide (**6a**). (Method 1).

Seven and one-half g. (0.043 mole) of sodium hydrosulfite was added in portions to a solution of 3.3 g. (0.01 mole) of 4'-chloro-4-ethoxy-2'-nitro-3-thiophenecarboxanilide (**7**) in 33 ml. of acetone and 33 ml. of water. The mixture was warmed on a steam bath for 1 hour, then cooled and extracted 5 times with ether. The ether extracts were dried (sodium sulfate), filtered and evaporated to give 1 g. of an off-white solid, m.p. 158-162°. The aqueous layer (after the ether extractions) was stirred overnight with methylene chloride. This emulsion was filtered through diatomaceous earth and the organic layer was dried (sodium sulfate), filtered and

evaporated to give 0.3 g. of a solid. The two solids were combined (1.3 g., 45%) and recrystallized from ethanol to give 1 g. of **6a** m.p. 164-166°. A sample of this base was converted into the hydrochloride salt, m.p. 174-176° dec., identical in all respects to that prepared below; ^{1}H nmr (DMSO): δ 9.07 (brs, 1H, N*H*), 8.10 (d, 1H, thiophene-*H*), 7.48 (d, 1H), 6.86 (d, 1H), 6.70 (dd, 1H, all Ar-*H*), 6.48 (d, 1H, thiophene-*H*), 4.41 (brs, 2H, NH_2), 4.22 (q, 2H, CH_2), 1.52 (t, 3H, CH_3).

Anal. Calcd. for $C_{13}H_{13}ClN_2O_2S$ (296.8): C, 52.61; H, 4.41; N, 9.44; S, 10.81; Cl, 11.95. Found: C, 51.86; H, 4.46; N, 8.95; S 12.74; Cl, 11.47

2'-Amino-4'-chloro-4-ethoxy-3-thiophenecarboxanilide, Hydrochloride (**6a**) (Method 2).

A solution of 16.7 g. (0.117 mole) of 4-chloro-*o*-phenylenediamine, 16.5 ml. (0.117 mole) of triethylamine in 200 ml. of methylene chloride was stirred and cooled in an ice-bath as a solution of 23.4 g. (0.123 mole) of 4-ethoxy-3-thiophenecarbonyl chloride (1) in 156 ml. of methylene chloride was added dropwise. The mixture was stirred at room temperature overnight and then washed with water. The methylene chloride layer was extracted with 3*N* hydrochloric acid. As the acid was added to the organic layer a precipitate formed and was collected by filtration to give 25.9 g. (67%) of the hydrochloride as a tan solid, m.p. 173-174° dec. This material was used in the next step without further purification. A sample of the base prepared from this hydrochloride was the same as the base described above by mp and tlc.

Anal. Calcd. for $C_{13}H_{13}ClN_2O_2S$·HCl (333.2): C, 46.85; H, 4.23; N, 8.41; S, 9.62; Cl, 21.28. Found: C, 46.45; H, 4.24; N, 8.35; S, 9.59; Cl, 21.47.

6-Chloro-4,9-dihydro-10*H*-thieno[3,4-*b*][1,5]benzodiazepin-10-one (**1b**).

A mixture of 6 g. (0.018 mole) of 2'-amino-4'-chloro-4-ethoxy-3-thiophenecarboxanilide hydrochloride (**6a**) and 75 g. of polyphosphoric acid was stirred and warmed at 120-125° for 1 hour at which time no more starting material was present by tlc analyses. The dark colored solution was poured into ice-water and filtered. The solid was washed with water, bicarbonate solution, water and then dried to give 5 g. (100%) of a light brown solid, m.p. 241-262°. The crude material was recrystallized from methanol to give **1b** as a yellow solid, m.p. 277-280°, lit. (2) 279-281°, not depressed when mixed with an authentic sample of **2**; ^{1}H nmr (DMSO): δ 9.61 (brs, 1H, N*H*), 8.00 (brs, 1H, N*H*), 7.92 (d, 1H, thiophene-*H*), 6.85 (m, 3H, Ar-*H*), 6.44 (d, 1H, thiophene-*H*).

REFERENCES AND NOTES

(1) For the previous paper in this series see J. B. Press, N. H. Eudy and S. R. Safir, *J. Org. Chem.*, **45**, 497 (1980).

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