

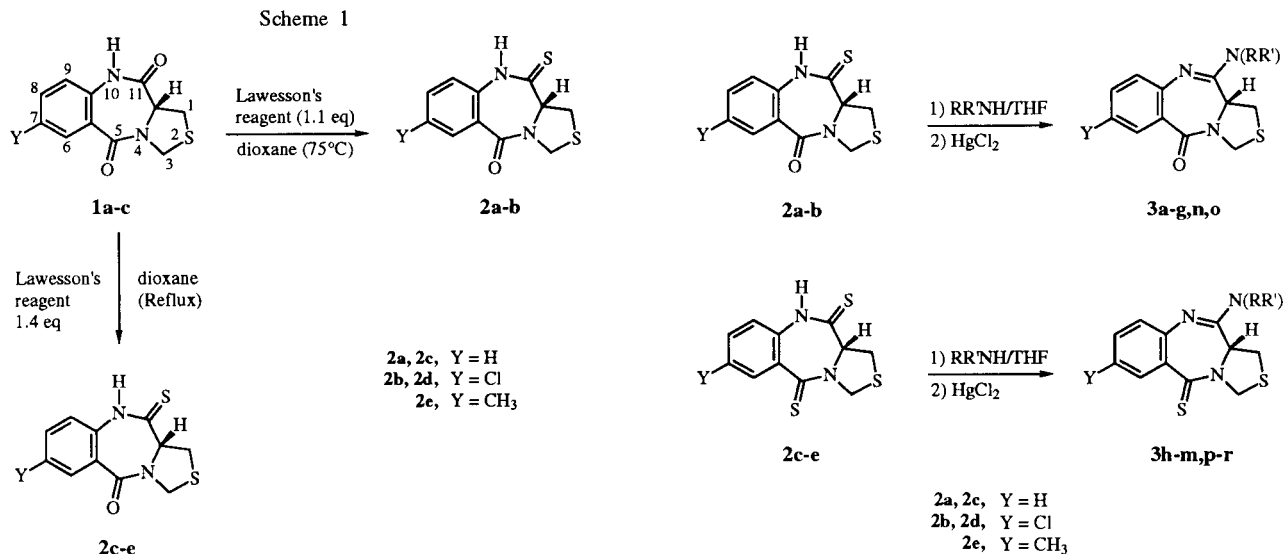
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Received June 30, 1995

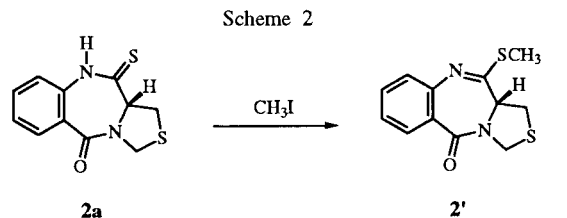
Reactivity of 1,2,3,10,11,11a-hexahydro-5*H*-thiazolo[4,3-*c*][1,4]benzodiazepin-5-one-11-thione and 1,2,3,10,11,11a-hexahydro-5*H*-thiazolo[4,3-*c*][1,4]benzodiazepine-5,11-dithione was evaluated against various amines. The synthetic pathways involved in these reactions which led to new thiazolo[4,3-*c*]-[1,4]benzodiazepine amidines are described.

*J. Heterocyclic Chem.*, **32**, 1741 (1995).

The pyrrolo[2,1-*c*][1,4]benzodiazepines (PBD) such as anthramycin, tomaymycin, neothramycins A and B are thought to exert their antitumor activity [1] through covalent binding *via* an aminor linkage from the electrophilic carbinolamine-bearing C-11 position to an N-2 of guanine within the minor groove of DNA [2]. In view of the importance of the carbinolamine functionality, Foloppe and Rault have recently developed a synthesis of new PBD N-10 C-11 amidine derivatives [3] [4]. Some of these amidines showed good DNA binding [5] [6]. In order to extend our study to the thiazolo[4,3-*c*][1,4]benzodiazepine series we first prepared thiolactams and dithiolactams from several 1,2,3,10,11,11a-hexahydro-5*H*-thiazolo[4,3-*c*]-[1,4]benzodiazepine-5,11-diones **1** (Scheme 1). The thiolactams and dithiolactams **2** were selectively obtained. The action of 1.1 equivalents of Lawesson's reagent on dilactam **1** in dioxane at 75° led to monothiolactams **2a,b**, while **1** in the presence of 1.4 equivalent of Lawesson's reagent in refluxing dioxane led to dithiolactams **2c-e**.

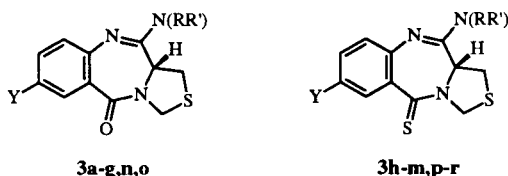


The methyliminothioether **2'** obtained by the action of methyl iodide on the thiolactam **2a** was unreactive towards amines in refluxing solvents. The preparation of amidines always required the same procedure. The monothiolactam or dithiolactam **2** was dissolved in tetrahydrofuran or acetone with 5 equivalents of primary or secondary amine (dimethylamine) and the solution was stirred at 55°; 1.3 equivalents of mercuric chloride was added. A black precipitate of mercuric sulfide immediately appeared (Scheme 2). Application of this pathway to various amines gave the corresponding amidines **3** in good yield (Scheme 3). Treatment of **3e** with thionyl chloride in refluxing chloroform gave the chloroethylamidine **4**. This compound was obtained by a nucleophilic substi-



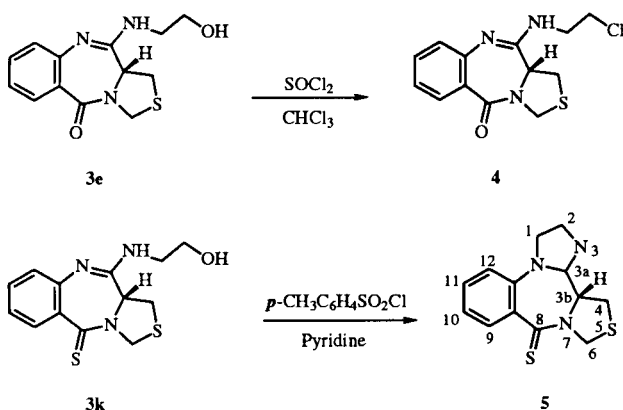
tution of hydroxy by chloride. On the other hand treatment of **3k** with *p*-toluenesulfonic acid chloride gave the tetracyclic compound **5** (Scheme 4). This structure was supported by the absence of NH and OH absorptions in the ir spectrum. The <sup>1</sup>H nmr spectrum showed no deuterable signal. This structure was also confirmed by mass spectrum and elemental analysis.

Scheme 3



- 3a,h**, Y = H, R = CH<sub>3</sub>, R' = H  
**3b,j**, Y = H, R = R' = CH<sub>3</sub>  
**3c,i**, Y = H, R = cyclopentyl, R' = H  
**3n,p**, Y = Cl, R = cyclopentyl, R' = H  
**3d**, Y = H, R = 3,4-dichlorobenzyl, R' = H  
**3e,k**, Y = H, R = CH<sub>2</sub>CH<sub>2</sub>OH, R' = H  
**3o,q**, Y = Cl, R = CH<sub>2</sub>CH<sub>2</sub>OH, R' = H  
**3f,l**, Y = H, R = CH<sub>2</sub>CH<sub>2</sub>N(CH<sub>3</sub>)<sub>2</sub>, R' = H  
**3g**, Y = H, R = CH<sub>2</sub>CO<sub>2</sub>Et, R' = H  
**3m**, Y = H, R = CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>N(CH<sub>3</sub>)<sub>2</sub>, R' = H  
**3r**, Y = CH<sub>3</sub>, R = CH<sub>2</sub>CH<sub>2</sub>OH, R' = H

Scheme 4



## EXPERIMENTAL

### General Methods.

Melting points were taken on a Kofler block 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 using TMS as an internal standard. Chemical shifts are reported in ppm downfield ( $\delta$ ) from TMS.

1,2,3,10,11,11a-Hexahydro-5*H*-thiazolo[4,3-*c*][1,4]benzodiazepin-5-one-11-thione (**2a**).

A solution of 1,2,3,10,11,11a-hexahydro-5*H*-thiazolo[4,3-*c*][1,4]benzodiazepine-5,11-dione (**1a**) (30 g, 0.128 mole) and Lawesson's reagent (57 g, 0.141 mole) in dioxane (300 ml) was heated at 75°. After 3 hours the mixture was cooled and the yellow solid was collected, dried and recrystallized from dioxane to yield 19.5 g (61%) of **2a**, mp 234°; ir (potassium bromide):  $\nu$  3140 (NH), 1605 (C=O) cm<sup>-1</sup>; <sup>1</sup>H-nmr (dimethyl sulfoxide-*d*<sub>6</sub>):  $\delta$  12.67 (s, NH), 7.89 (d,  $J_{\text{H6H7}} = 8.29$  Hz, H<sub>6</sub>), 7.59 (t,  $J_{\text{H8H9}} = J_{\text{H8H7}} = 7.83$  Hz, H<sub>8</sub>), 7.29 (m, H<sub>7</sub> and H<sub>9</sub>), 4.87 (d,  $J_{\text{gem}} = 11.84$  Hz, H<sub>3a</sub>), 4.61 (m, H<sub>11a</sub>), 4.51 (d,  $J_{\text{gem}} = 11.66$  Hz, H<sub>3b</sub>), 4.12 (d,  $J_{\text{gem}} = 11.49$  Hz, H<sub>1a</sub>), 3.41 (m, H<sub>1b</sub>).

*Anal.* Calcd. for C<sub>11</sub>H<sub>10</sub>N<sub>2</sub>O<sub>2</sub>S<sub>2</sub>: C, 52.78; H, 4.03; N, 11.19. Found: C, 53.01; H, 4.21; N, 11.01.

1,2,3,10,11,11a-Hexahydro-7-chloro-5*H*-thiazolo[4,3-*c*][1,4]benzodiazepin-5-one-11-thione (**2b**).

1,2,3,10,11,11a-Hexahydro-7-chloro-5*H*-thiazolo[4,3-*c*][1,4]benzodiazepine-5,11-dione (**1b**) (15 g, 0.056 mole) was converted to **2b** using the procedure for the preparation of **2a**. This gave 10.5 g (66%) of **2b** (yellow solid), mp 242°; ir (potassium bromide):  $\nu$  3180 (NH), 1610 (C=O) cm<sup>-1</sup>; <sup>1</sup>H-nmr (dimethyl sulfoxide-*d*<sub>6</sub>):  $\delta$  12.65 (s, NH), 7.80 (d,  $J_{\text{H6H8}} = 2.45$  Hz, H<sub>6</sub>), 7.69 (dd,  $J_{\text{H8H9}} = 8.54$  Hz,  $J_{\text{H8H6}} = 2.44$  Hz, H<sub>8</sub>), 7.34 (d,  $J_{\text{H9H8}} = 8.79$  Hz, H<sub>9</sub>), 4.81 (d,  $J_{\text{gem}} = 10.74$  Hz, H<sub>3a</sub>), 4.68 (m, H<sub>11a</sub>), 4.64 (d,  $J_{\text{gem}} = 10.55$  Hz, H<sub>3b</sub>), 4.06 (d,  $J_{\text{gem}} = 10.44$  Hz, H<sub>1a</sub>), 3.32 (m, H<sub>1b</sub>).

*Anal.* Calcd. for C<sub>11</sub>H<sub>9</sub>N<sub>2</sub>O<sub>2</sub>S<sub>2</sub>Cl: C, 46.39; H, 3.19; N, 9.84. Found: C, 46.22; H, 3.38; N, 10.08.

1,2,3,10,11,11a-Hexahydro-5*H*-thiazolo[4,3-*c*][1,4]benzodiazepine-5,11-dithione (**2c**).

A solution of 1,2,3,10,11,11a-Hexahydro-5*H*-thiazolo[4,3-*c*][1,4]benzodiazepine-5,11-dione (**1a**) (25 g, 0.107 mole) and Lawesson's reagent (60.4 g, 0.149 mole) in dioxane (300 ml) was heated at reflux for 5 hours. The reaction mixture was cooled and the yellow precipitate was collected, recrystallized from dioxane to yield 17.5 g (61%) of **2c**, mp 252°; ir (potassium bromide):  $\nu$  3140 (NH) cm<sup>-1</sup>; <sup>1</sup>H-nmr (dimethyl sulfoxide-*d*<sub>6</sub>):  $\delta$  12.75 (s, NH), 8.15 (d,  $J_{\text{H6H7}} = 8.21$  Hz, H<sub>6</sub>), 7.61 (t,  $J_{\text{H8H9}} = J_{\text{H8H7}} = 7.85$  Hz, H<sub>8</sub>), 7.32 (m, H<sub>7</sub> and H<sub>9</sub>), 5.12 (d,  $J_{\text{gem}} = 11.48$  Hz, H<sub>3a</sub>), 4.98 (m, H<sub>11a</sub> and H<sub>3b</sub>), 4.08 (d,  $J_{\text{gem}} = 11.71$  Hz, H<sub>1a</sub>), 3.51 (m, H<sub>1b</sub>).

*Anal.* Calcd. for C<sub>11</sub>H<sub>10</sub>N<sub>2</sub>S<sub>3</sub>: C, 49.60; H, 3.78; N, 10.52. Found: C, 49.80; H, 4.01; N, 10.29.

1,2,3,10,11,11a-Hexahydro-7-chloro-5*H*-thiazolo[4,3-*c*][1,4]benzodiazepine-5,11-dithione (**2d**).

1,2,3,10,11,11a-Hexahydro-7-chloro-5*H*-thiazolo[4,3-*c*][1,4]benzodiazepine-5,11-dione (**1b**) (15 g, 0.056 mole) was converted to **2d** using the procedure for the preparation of **2c**. This gave 11.5 g (68%) of **2d** (yellow crystals), mp >260° (2-propanol); ir (potassium bromide):  $\nu$  3165 (NH) cm<sup>-1</sup>; <sup>1</sup>H-nmr (dimethyl sulfoxide-*d*<sub>6</sub>):  $\delta$  12.76 (s, NH), 8.07 (d,  $J_{\text{H6H8}} = 2.16$  Hz, H<sub>6</sub>), 7.64 (dd,  $J_{\text{H8H9}} = 8.26$  Hz,  $J_{\text{H8H6}} = 2.31$  Hz, H<sub>8</sub>), 7.26 (d,  $J_{\text{H9H8}} = 7.91$  Hz, H<sub>9</sub>), 5.05 (m, H<sub>3a</sub> and H<sub>11a</sub>), 4.90 (d,  $J_{\text{gem}} = 10.45$  Hz, H<sub>3b</sub>), 4.03 (d,  $J_{\text{gem}} = 11.72$  Hz, H<sub>1a</sub>), 3.51 (m, H<sub>1b</sub>).

*Anal.* Calcd. for C<sub>11</sub>H<sub>9</sub>N<sub>2</sub>S<sub>3</sub>Cl: C, 43.92; H, 3.02; N, 9.31. Found: C, 44.10; H, 3.21; N, 9.15.

1,2,3,10,11,11a-Hexahydro-7-methyl-5*H*-thiazolo[4,3-*c*][1,4]benzodiazepine-5,11-dithione (**2e**).

1,2,3,10,11,11a-Hexahydro-7-methyl-5*H*-thiazolo[4,3-*c*][1,4]

benzodiazepine-5,11-dione (**1c**) (10 g, 0.0403 mole) was converted to **2e** using the procedure for the preparation of **2c**. This gave 7.6 g (67%) of **2e** (yellow solid), mp 250° (acetone); ir (potassium bromide):  $\nu$  3190 (NH)  $\text{cm}^{-1}$ ;  $^1\text{H-nmr}$  (dimethyl sulfoxide- $d_6$ ):  $\delta$  12.66 (s, NH), 7.96 (s,  $\text{H}_6$ ), 7.38 (d,  $\text{J}_{\text{H}_8\text{H}_9} = 8.11$  Hz,  $\text{H}_8$ ), 7.15 (d,  $\text{J}_{\text{H}_9\text{H}_8} = 7.94$  Hz,  $\text{H}_9$ ), 5.06 (d,  $\text{J}_{\text{gem}} = 11.12$  Hz,  $\text{H}_{3a}$ ), 4.85 (m,  $\text{H}_{11a}$  and  $\text{H}_{3b}$ ), 3.91 (d,  $\text{J}_{\text{gem}} = 11.44$  Hz,  $\text{H}_{1a}$ ), 3.41 (m,  $\text{H}_{1b}$ ), 2.28 (s,  $\text{CH}_3$ ).

*Anal.* Calcd. for  $\text{C}_{12}\text{H}_{12}\text{N}_2\text{S}_3$ : C, 51.40; H, 4.31; N, 9.99. Found: C, 51.23; H, 4.49; N, 9.74.

1,2,3,11a-Tetrahydro-11-alkylamino-5H-thiazolo[4,3-c][1,4]-benzodiazepin-5-ones **3a-g**.

#### General Procedure.

To a solution of 1,2,3,10,11,11a-hexahydro-5H-thiazolo[4,3-c]-[1,4]benzodiazepin-5-one-11-thione (**2a**) (1 g, 0.004 mole) and the appropriate amine (5 equivalents) in tetrahydrofuran (40 ml), we added at 55° mercuric chloride (1.4 g, 0.0052 mole). The reaction mixture was stirred for 1 hour at 55°, filtered and evaporated to dryness under reduced pressure. The oily residue was taken up in ethyl acetate (100 ml), washed with aqueous sodium thiosulfate (2 x 100 ml), dried (magnesium sulfate) and evaporated *in vacuo*. The solid residue was recrystallized to give **3a-g**.

1,2,3,11a-Tetrahydro-11-methylamino-5H-thiazolo[4,3-c]-[1,4]benzodiazepin-5-one (**3a**).

With monomethylamine, white crystals (77%) were obtained, mp 166° (ether); ir (potassium bromide):  $\nu$  3320 (NH), 1640 (C=O), 1610 (C=N)  $\text{cm}^{-1}$ ;  $^1\text{H-nmr}$  (dimethyl sulfoxide- $d_6$ ):  $\delta$  7.73 (d,  $\text{J}_{\text{H}_6\text{H}_7} = 8.3$  Hz,  $\text{H}_6$ ), 7.39 (t,  $\text{J}_{\text{H}_8\text{H}_9} = \text{J}_{\text{H}_8\text{H}_7} = 6.84$  Hz,  $\text{H}_8$ ), 7.16 (s, NH), 7.01 (m,  $\text{H}_7$  and  $\text{H}_9$ ), 4.72 (d,  $\text{J}_{\text{gem}} = 10.26$  Hz,  $\text{H}_{3a}$ ), 4.53 (d,  $\text{J}_{\text{gem}} = 10.23$  Hz,  $\text{H}_{3b}$ ), 4.25 (m,  $\text{H}_{11a}$ ), 3.58 (d,  $\text{J}_{\text{gem}} = 12.68$  Hz,  $\text{H}_{1a}$ ), 3.34 (m,  $\text{H}_{1b}$ ), 2.8 (s,  $\text{CH}_3$ ); ms:  $m/z$ , 247 (12), 218 (15), 142 (21).

*Anal.* Calcd. for  $\text{C}_{12}\text{H}_{13}\text{N}_3\text{OS}$ : C, 58.28; H, 5.30; N, 16.99. Found: C, 58.09; H, 5.08; N, 17.09.

1,2,3,11a-Tetrahydro-11-dimethylamino-5H-thiazolo[4,3-c][1,4]benzodiazepin-5-one (**3b**).

With dimethylamine, white crystals (72%) were obtained, mp 174° (ether); ir (potassium bromide):  $\nu$  1630 (C=O), 1615 (C=N)  $\text{cm}^{-1}$ ;  $^1\text{H-nmr}$  (dimethyl sulfoxide- $d_6$ ):  $\delta$  7.78 (d,  $\text{J}_{\text{H}_6\text{H}_7} = 7.83$  Hz,  $\text{H}_6$ ), 7.40 (t,  $\text{J}_{\text{H}_8\text{H}_9} = \text{J}_{\text{H}_8\text{H}_7} = 7.31$  Hz,  $\text{H}_8$ ), 7.06 (m,  $\text{H}_7$  and  $\text{H}_9$ ), 4.79 (d,  $\text{J}_{\text{gem}} = 10.25$  Hz,  $\text{H}_{3a}$ ), 4.57 (d,  $\text{J}_{\text{gem}} = 10.21$  Hz,  $\text{H}_{3b}$ ), 4.45 (m,  $\text{H}_{11a}$ ), 3.56 (d,  $\text{J}_{\text{gem}} = 12.63$  Hz,  $\text{H}_{1a}$ ), 3.39 (m,  $\text{H}_{1b}$ ), 3.06 (s, 2  $\text{CH}_3$ ); ms:  $m/z$ , 261 (21), 228 (52), 175 (31).

*Anal.* Calcd. for  $\text{C}_{13}\text{H}_{15}\text{N}_3\text{OS}$ : C, 59.75; H, 5.78; N, 16.08. Found: C, 60.01; H, 5.57; N, 16.32.

1,2,3,11a-Tetrahydro-11-cyclopentylamino-5H-thiazolo[4,3-c]-[1,4]benzodiazepin-5-one (**3c**).

With cyclopentylamine, yellow crystals (85%) were obtained, mp 189° (2-propanol); ir (potassium bromide):  $\nu$  3300 (NH), 1620 (C=O), 1605 (C=N)  $\text{cm}^{-1}$ ;  $^1\text{H-nmr}$  (dimethyl sulfoxide- $d_6$ ):  $\delta$  7.72 (d,  $\text{J}_{\text{H}_6\text{H}_7} = 8.27$  Hz,  $\text{H}_6$ ), 7.36 (t,  $\text{J}_{\text{H}_8\text{H}_9} = \text{J}_{\text{H}_8\text{H}_7} = 8.04$  Hz,  $\text{H}_8$ ), 7.06 (m,  $\text{H}_7$  and  $\text{H}_9$ ), 6.64 (s, NH), 4.72 (d,  $\text{J}_{\text{gem}} = 10.69$  Hz,  $\text{H}_{3a}$ ), 4.55 (d,  $\text{J}_{\text{gem}} = 10.39$  Hz,  $\text{H}_{3b}$ ), 4.23 (m,  $\text{H}_{11a}$ ), 4.11 (d,  $\text{J}_{\text{gem}} = 10.81$  Hz,  $\text{H}_{1a}$ ), 3.74 (m, CH), 3.36 (m,  $\text{H}_{1b}$ ), 1.8 (m, 4  $\text{CH}_2$ ).

*Anal.* Calcd. for  $\text{C}_{16}\text{H}_{19}\text{N}_3\text{OS}$ : C, 63.76; H, 6.35; N, 13.94.

Found: C, 63.77; H, 6.60; N, 13.69.

1,2,3,11a-Tetrahydro-11-(3,4-dichlorobenzylamino)-5H-thiazolo[4,3-c][1,4]benzodiazepin-5-one (**3d**).

With 3,4-dichlorobenzylamine, white crystals (68%) were obtained, mp 202° (ether); ir (potassium bromide):  $\nu$  3255 (NH), 1630 (C=O), 1615 (C=N)  $\text{cm}^{-1}$ ;  $^1\text{H-nmr}$  (dimethyl sulfoxide- $d_6$ ):  $\delta$  7.78-7.01 (m, 7 H), 6.84 (m, NH), 4.65 (d,  $\text{J}_{\text{gem}} = 10.32$  Hz,  $\text{H}_{3a}$ ), 4.47 (d,  $\text{J}_{\text{gem}} = 10.21$  Hz,  $\text{H}_{3b}$ ), 4.19 (m,  $\text{H}_{11a}$ ), 3.95 (d,  $\text{J}_{\text{gem}} = 9.72$  Hz,  $\text{H}_{1a}$ ), 3.51 (m,  $\text{CH}_2$ ), 3.35 (m,  $\text{H}_{1b}$ ); ms:  $m/z$  392 (38), 232 (23), 216 (8).

*Anal.* Calcd. for  $\text{C}_{18}\text{H}_{15}\text{N}_3\text{OCl}_2$ : C, 55.11; H, 3.85; N, 10.71. Found: C, 55.30; H, 4.02; N, 10.87.

1,2,3,11a-Tetrahydro-11-(2-hydroxyethylamino)-5H-thiazolo[4,3-c][1,4]benzodiazepin-5-one (**3e**).

With 2-aminoethanol, white crystals (74%) were obtained, mp 182° (acetonitrile); ir (potassium bromide):  $\nu$  3445 (OH), 3220 (NH), 1625 (C=O), 1605 (C=N)  $\text{cm}^{-1}$ ;  $^1\text{H-nmr}$  (dimethyl sulfoxide- $d_6$ ):  $\delta$  7.72 (d,  $\text{J}_{\text{H}_6\text{H}_7} = 8.07$  Hz,  $\text{H}_6$ ), 7.39 (t,  $\text{J}_{\text{H}_8\text{H}_9} = \text{J}_{\text{H}_8\text{H}_7} = 7.98$  Hz,  $\text{H}_8$ ), 7.20 (m, NH), 7.05 (m,  $\text{H}_7$  and  $\text{H}_9$ ), 4.82 (m, OH), 4.69 (d,  $\text{J}_{\text{gem}} = 10.02$  Hz,  $\text{H}_{3a}$ ), 4.53 (d,  $\text{J}_{\text{gem}} = 9.97$  Hz,  $\text{H}_{3b}$ ), 4.18 (m,  $\text{H}_{11a}$ ), 4.02 (d,  $\text{J}_{\text{gem}} = 7.84$  Hz,  $\text{H}_{1a}$ ), 3.68 (m,  $\text{CH}_2$ ), 3.40 (m,  $\text{CH}_2$ ), 3.36 (m,  $\text{H}_{1b}$ ); ms:  $m/z$ , 277 (21), 259 (12), 158 (28).

*Anal.* Calcd. for  $\text{C}_{13}\text{H}_{15}\text{N}_3\text{O}_2\text{S}$ : C, 56.30; H, 5.45; N, 15.15. Found: C, 56.52; H, 5.24; N, 14.89.

1,2,3,11a-Tetrahydro-11-[2-(*N,N*-dimethylamino)ethylamino]-5H-thiazolo[4,3-c][1,4]benzodiazepin-5-one (**3f**).

With *N,N*-dimethylethylenediamine, orange crystals (73%) were obtained, mp 201° (ethanol); ir (potassium bromide):  $\nu$  3310 (NH), 1630 (C=O), 1600 (C=N)  $\text{cm}^{-1}$ ;  $^1\text{H-nmr}$  (dimethyl sulfoxide- $d_6$ ):  $\delta$  7.76 (d,  $\text{J}_{\text{H}_6\text{H}_7} = 8.01$  Hz,  $\text{H}_6$ ), 7.42 (t,  $\text{J}_{\text{H}_8\text{H}_9} = \text{J}_{\text{H}_8\text{H}_7} = 8.04$  Hz,  $\text{H}_8$ ), 7.08 (m,  $\text{H}_7$  and  $\text{H}_9$ ), 6.92 (m, NH), 4.71 (d,  $\text{J}_{\text{gem}} = 10.25$  Hz,  $\text{H}_{3a}$ ), 4.57 (d,  $\text{J}_{\text{gem}} = 10.74$  Hz,  $\text{H}_{3b}$ ), 3.61 (m,  $\text{H}_{11a}$ ), 3.42 (d,  $\text{J}_{\text{gem}} = 6.11$  Hz,  $\text{H}_{1a}$ ), 3.36 (m,  $\text{CH}_2$ ), 3.17 (m,  $\text{H}_{1b}$ ), 2.54 (m,  $\text{CH}_2$ ), 2.21 (s, 2  $\text{CH}_3$ ).

*Anal.* Calcd. for  $\text{C}_{15}\text{H}_{20}\text{N}_4\text{OS}$ : C, 59.19; H, 6.62; N, 18.41. Found: C, 59.25; H, 6.56; N, 18.59.

1,2,3,11a-Tetrahydro-11-(ethylcarboxymethylamino)-5H-thiazolo[4,3-c][1,4]benzodiazepin-5-one (**3g**).

With glycine ethyl ester, white crystals (62%) were obtained, mp 238° (2-propanol); ir (potassium bromide):  $\nu$  3150 (NH), 1735 (C=O), 1625 (C=O), 1595 (C=N)  $\text{cm}^{-1}$ ;  $^1\text{H-nmr}$  (dimethyl sulfoxide- $d_6$ ):  $\delta$  7.84 (d,  $\text{J}_{\text{H}_6\text{H}_7} = 7.79$  Hz,  $\text{H}_6$ ), 7.68 (t,  $\text{J}_{\text{H}_8\text{H}_9} = \text{J}_{\text{H}_8\text{H}_7} = 8.29$  Hz,  $\text{H}_8$ ), 7.49 (m, NH), 7.26 (m,  $\text{H}_7$  and  $\text{H}_9$ ), 4.84 (d,  $\text{J}_{\text{gem}} = 9.91$  Hz,  $\text{H}_{3a}$ ), 4.71 (d,  $\text{J}_{\text{gem}} = 9.84$  Hz,  $\text{H}_{3b}$ ), 4.20 (d,  $\text{J} = 5.87$  Hz,  $\text{CH}_2$ ), 3.92 (m,  $\text{H}_{11a}$ ), 3.80 (d,  $\text{J}_{\text{gem}} = 8.95$  Hz,  $\text{H}_{1a}$ ), 3.56 (q,  $\text{J}_{\text{CH}_2\text{CH}_3} = 7.2$  Hz,  $\text{CH}_2$ ), 3.37 (m,  $\text{H}_{1b}$ ), 1.21 (t,  $\text{J}_{\text{CH}_3\text{CH}_2} = 7.13$  Hz,  $\text{CH}_3$ ); ms:  $m/z$ , 319 (30), 247 (15), 218 (45).

*Anal.* Calcd. for  $\text{C}_{15}\text{H}_{17}\text{N}_3\text{O}_3\text{S}$ : C, 56.42; H, 5.33; N, 13.16. Found: C, 56.23; H, 5.13; N, 13.29.

1,2,3,11a-Tetrahydro-11-alkylamino-5H-thiazolo[4,3-c][1,4]-benzodiazepine-5-thiones **3h-m**.

#### General Procedure.

To a solution of 1,2,3,10,11,11a-hexahydro-5H-thiazolo[4,3-c]-[1,4]benzodiazepine-5,11-dithione (**2b**) (1 g, 0.0037 mole) and the appropriate amine (5 equivalents) in tetrahydrofuran (50 ml)

stirred at 55°, we added mercuric chloride (1.3 g, 0.0049 mole). The reaction mixture was stirred for 1.5 hour at 55° and filtered. The solvent was then removed under reduced pressure. The oily residue was taken up in ethyl acetate (120 ml), washed with aqueous sodium thiosulfate (2 x 100 ml), dried (magnesium sulfate) and evaporated *in vacuo*. The solid residue was recrystallized to give **3h-m**.

1,2,3,11a-Tetrahydro-11-methylamino-5*H*-thiazolo[4,3-*c*][1,4]benzodiazepine-5-thione (**3h**).

With monomethylamine, yellow crystals (68%) were obtained, mp 202° (2-propanol); ir (potassium bromide):  $\nu$  3250 (NH), 1630 (C=N)  $\text{cm}^{-1}$ ;  $^1\text{H-nmr}$  (dimethyl sulfoxide- $d_6$ ):  $\delta$  8.45 (d,  $J_{\text{H6H7}} = 8.27$  Hz,  $\text{H}_6$ ), 7.97 (t,  $J_{\text{H8H9}} = J_{\text{H8H7}} = 8.30$  Hz,  $\text{H}_8$ ), 7.67 (m,  $\text{H}_7$  and  $\text{H}_9$ ), 5.51 (d,  $J_{\text{gem}} = 10.11$  Hz,  $\text{H}_{3a}$ ), 5.32 (d,  $J_{\text{gem}} = 10.02$  Hz,  $\text{H}_{3b}$ ), 5.07 (m, NH), 4.09 (m,  $\text{H}_{11a}$ ), 3.32 (d,  $J_{\text{gem}} = 8.47$  Hz,  $\text{H}_{1a}$ ), 3.12 (m,  $\text{H}_{1b}$ ), 2.83 (s,  $\text{CH}_3$ ).

*Anal.* Calcd. for  $\text{C}_{12}\text{H}_{13}\text{N}_3\text{S}_2$ : C, 54.75; H, 4.94; N, 15.97. Found C, 54.91; H, 4.71; N, 16.08.

1,2,3,11a-Tetrahydro-11-dimethylamino-5*H*-thiazolo[4,3-*c*][1,4]benzodiazepine-5-thione (**3i**).

With dimethylamine, white crystals (71%) were obtained, mp 185° (ether); ir (potassium bromide):  $\nu$  1590 (C=N)  $\text{cm}^{-1}$ ;  $^1\text{H-nmr}$  (dimethyl sulfoxide- $d_6$ ):  $\delta$  8.08 (d,  $J_{\text{H6H7}} = 7.82$  Hz,  $\text{H}_6$ ), 7.39 (t,  $J_{\text{H8H9}} = J_{\text{H8H7}} = 7.32$  Hz,  $\text{H}_8$ ), 7.05 (m,  $\text{H}_7$  and  $\text{H}_9$ ), 5.19 (d,  $J_{\text{gem}} = 11.72$  Hz,  $\text{H}_{3a}$ ), 5.01 (d,  $J_{\text{gem}} = 11.31$  Hz,  $\text{H}_{3b}$ ), 4.51 (m,  $\text{H}_{11a}$ ), 3.72 (d,  $J_{\text{gem}} = 8.01$  Hz,  $\text{H}_{1a}$ ), 3.31 (m,  $\text{H}_{1b}$ ), 2.89 (s, 2  $\text{CH}_3$ ); ms:  $m/z$  277 (13), 232 (21), 186 (9).

*Anal.* Calcd. for  $\text{C}_{13}\text{H}_{15}\text{N}_3\text{S}_2$ : C, 56.29; H, 5.45; N, 15.15. Found: C, 56.08; H, 5.36; N, 14.92.

1,2,3,11a-Tetrahydro-11-cyclopentylamino-5*H*-thiazolo[4,3-*c*][1,4]benzodiazepine-5-thione (**3j**).

With cyclopentylamine, yellow crystals (69%) were obtained, mp 213° (2-propanol); ir (potassium bromide):  $\nu$  3315 (NH), 1610 (C=N)  $\text{cm}^{-1}$ ;  $^1\text{H-nmr}$  (dimethyl sulfoxide- $d_6$ ):  $\delta$  8.07 (d,  $J_{\text{H6H7}} = 8.30$  Hz,  $\text{H}_6$ ), 7.42 (t,  $J_{\text{H8H9}} = J_{\text{H8H7}} = 7.34$  Hz,  $\text{H}_8$ ), 7.03 (m,  $\text{H}_7$  and  $\text{H}_9$ ), 6.69 (d,  $J_{\text{NHCH}} = 6.83$  Hz, NH), 5.11 (d,  $J_{\text{gem}} = 11.71$  Hz,  $\text{H}_{3a}$ ), 4.76 (d,  $J_{\text{gem}} = 10.41$  Hz,  $\text{H}_{3b}$ ), 4.45 (m,  $\text{H}_{11a}$ ), 4.03 (m, CH), 3.78 (d,  $J_{\text{gem}} = 9.51$  Hz,  $\text{H}_{1a}$ ), 3.54 (m,  $\text{H}_{1b}$ ), 1.7 (m, 4  $\text{CH}_2$ ); ms:  $m/z$  317 (14), 248 (31), 232 (16).

*Anal.* Calcd. for  $\text{C}_{16}\text{H}_{19}\text{N}_3\text{S}_2$ : C, 60.53; H, 6.03; N, 13.24. Found: C, 60.27; H, 6.09; N, 13.48.

1,2,3,11a-Tetrahydro-11-(2-hydroxyethylamino)-5*H*-thiazolo[4,3-*c*][1,4]benzodiazepine-5-thione (**3k**).

With 2-aminoethanol, grey crystals (73%) were obtained, mp 204° (ether); ir (potassium bromide):  $\nu$  3405 (OH), 3250 (NH), 1605 (C=N)  $\text{cm}^{-1}$ ;  $^1\text{H-nmr}$  (dimethyl sulfoxide- $d_6$ ):  $\delta$  8.07 (d,  $J_{\text{H6H7}} = 8.30$  Hz,  $\text{H}_6$ ), 7.39 (t,  $J_{\text{H8H9}} = J_{\text{H8H7}} = 7.67$  Hz,  $\text{H}_8$ ), 7.06 (m,  $\text{H}_7$  and  $\text{H}_9$ ), 6.83 (m, NH), 5.14 (d,  $J_{\text{gem}} = 11.72$  Hz,  $\text{H}_{3a}$ ), 4.85 (m, OH), 4.73 (d,  $J_{\text{gem}} = 11.32$  Hz,  $\text{H}_{3b}$ ), 4.49 (m,  $\text{H}_{11a}$ ), 3.72 (d,  $J_{\text{gem}} = 8.14$  Hz,  $\text{H}_{1a}$ ), 3.60 (m,  $\text{CH}_2$ ), 3.49 (m,  $\text{CH}_2$ ), 3.31 (m,  $\text{H}_{1b}$ ).

*Anal.* Calcd. for  $\text{C}_{13}\text{H}_{15}\text{N}_3\text{O}_2\text{S}_2$ : C, 53.22; H, 5.15; N, 14.32. Found: C, 53.36; H, 4.93; N, 14.06.

1,2,3,11a-Tetrahydro-11-[2-(*N,N*-dimethylamino)ethylamino]-5*H*-thiazolo[4,3-*c*][1,4]benzodiazepine-5-thione (**3l**).

With *N,N*-dimethylethylenediamine, white crystals (81%) were obtained, mp 210° (2-propanol); ir (potassium bromide):  $\nu$

3205 (NH), 1590 (C=N)  $\text{cm}^{-1}$ ;  $^1\text{H-nmr}$  (dimethyl sulfoxide- $d_6$ ):  $\delta$  8.10 (d,  $J_{\text{H6H7}} = 7.91$  Hz,  $\text{H}_6$ ), 7.41 (t,  $J_{\text{H8H9}} = J_{\text{H8H7}} = 7.79$  Hz,  $\text{H}_8$ ), 7.06 (m,  $\text{H}_7$  and  $\text{H}_9$ ), 6.85 (m, NH), 5.14 (d,  $J_{\text{gem}} = 11.72$  Hz,  $\text{H}_{3a}$ ), 4.79 (d,  $J_{\text{gem}} = 11.72$  Hz,  $\text{H}_{3b}$ ), 4.51 (m,  $\text{H}_{11a}$ ), 3.60 (m,  $\text{H}_{1a}$  and  $\text{H}_{1b}$ ), 3.43 (m,  $\text{CH}_2$ ), 2.46 (t,  $J_{\text{CH}_2\text{CH}_2} = 6.84$  Hz,  $\text{CH}_2$ ), 2.07 (s, 2  $\text{CH}_3$ ); ms:  $m/z$  320 (12), 275 (19), 234 (15).

*Anal.* Calcd. for  $\text{C}_{15}\text{H}_{20}\text{N}_4\text{S}_2$ : C, 56.22; H, 6.29; N, 17.48. Found: C, 56.15; H, 6.20; N, 17.52.

1,2,3,11a-Tetrahydro-11-[2-(*N,N*-dimethylamino)propylamino]-5*H*-thiazolo[4,3-*c*][1,4]benzodiazepine-5-thione (**3m**).

With *N,N*-dimethylpropylenediamine, white crystals (72%) were obtained, mp 221° (ethanol); ir (potassium bromide):  $\nu$  3190 (NH), 1625 (C=N)  $\text{cm}^{-1}$ ;  $^1\text{H-nmr}$  (dimethyl sulfoxide- $d_6$ ):  $\delta$  8.05 (d,  $J_{\text{H6H7}} = 7.83$  Hz,  $\text{H}_6$ ), 7.43 (t,  $J_{\text{H8H9}} = J_{\text{H8H7}} = 7.78$  Hz,  $\text{H}_8$ ), 7.05 (m,  $\text{H}_7$  and  $\text{H}_9$ ), 6.89 (m, NH), 5.11 (d,  $J_{\text{gem}} = 11.43$  Hz,  $\text{H}_{3a}$ ), 4.81 (d,  $J_{\text{gem}} = 11.33$  Hz,  $\text{H}_{3b}$ ), 4.49 (m,  $\text{H}_{11a}$ ), 3.51 (d,  $J_{\text{gem}} = 4.89$  Hz,  $\text{H}_{1a}$ ), 3.31 (m,  $\text{H}_{1b}$  and  $\text{CH}_2$ ), 2.43 (m,  $\text{CH}_2$ ), 2.13 (s, 2  $\text{CH}_3$ ), 1.99 (m,  $\text{CH}_2$ ).

*Anal.* Calcd. for  $\text{C}_{16}\text{H}_{22}\text{N}_4\text{S}_2$ : C, 57.45; H, 6.63; N, 16.75. Found C, 57.26; H, 6.46; N, 16.54.

1,2,3,11a-Tetrahydro-11-alkylamino-7-chloro-5*H*-thiazolo[4,3-*c*][1,4]benzodiazepin-5-ones **3n-o**.

General Procedure.

A solution of 1,2,3,10,11,11a-hexahydro-7-chloro-5*H*-thiazolo[4,3-*c*][1,4]benzodiazepin-5-one-11-thione (**2c**) (1 g, 0.0035 mole) and the appropriate amine (5 equivalents) in acetone (50 ml) was heated at 55°. We added mercuric chloride (1.2 g, 0.0046 mole) to the reaction mixture and it was allowed to stirring for 1 hour at 55°. Then the mixture was filtered and the acetone evaporated. The oily residue was taken up in chloroform (100 ml) and washed with aqueous solution of sodium thiosulfate (2 x 100 ml). The organic layer was dried (calcium chloride) and evaporated under reduced pressure. The solid obtained was recrystallized to give **3n-o**.

1,2,3,11a-Tetrahydro-11-cyclopentylamino-7-chloro-5*H*-thiazolo[4,3-*c*][1,4]benzodiazepin-5-one (**3n**).

With cyclopentylamine, yellow crystals (71%) were obtained, mp 216° (ethyl acetate); ir (potassium bromide):  $\nu$  3220 (NH), 1630 (C=O)  $\text{cm}^{-1}$ ;  $^1\text{H-nmr}$  (dimethyl sulfoxide- $d_6$ )  $\delta$  7.61 (d,  $J_{\text{H6H8}} = 1.95$  Hz,  $\text{H}_6$ ), 7.37 (dd,  $J_{\text{H8H9}} = 8.30$  Hz,  $J_{\text{H8H6}} = 2.01$  Hz,  $\text{H}_8$ ), 6.96 (d,  $J_{\text{H9H8}} = 8.32$  Hz,  $\text{H}_9$ ), 6.72 (d,  $J_{\text{NHCH}} = 6.87$  Hz, NH), 4.65 (d,  $J_{\text{gem}} = 10.26$  Hz,  $\text{H}_{3a}$ ), 4.47 (d,  $J_{\text{gem}} = 10.25$  Hz,  $\text{H}_{3b}$ ), 4.20 (m,  $\text{H}_{11a}$  and CH), 3.74 (d,  $J_{\text{gem}} = 11.02$  Hz,  $\text{H}_{1a}$ ), 3.32 (m,  $\text{H}_{1b}$ ), 1.73 (m, 4  $\text{CH}_2$ ).

*Anal.* Calcd. for  $\text{C}_{16}\text{H}_{18}\text{N}_3\text{OSCl}$ : C, 57.22; H, 5.40; N, 12.51. Found: C, 57.13; H, 5.44; N, 12.46.

1,2,3,11a-Tetrahydro-11-(2-hydroxyethylamino)-7-chloro-5*H*-thiazolo[4,3-*c*][1,4]benzodiazepin-5-one (**3o**).

With 2-aminoethanol, yellow crystals (80%) were obtained, mp 172° (2-propanol); ir (potassium bromide):  $\nu$  3390 (OH), 3300 (NH), 1620 (CO), 1595 (C=N)  $\text{cm}^{-1}$ ;  $^1\text{H-nmr}$  (dimethyl sulfoxide- $d_6$ ):  $\delta$  7.65 (d,  $J_{\text{H6H8}} = 2.02$  Hz,  $\text{H}_6$ ), 7.43 (dd,  $J_{\text{H8H9}} = 7.95$  Hz,  $J_{\text{H8H6}} = 1.99$  Hz,  $\text{H}_8$ ), 7.13 (m, NH), 7.01 (d,  $J_{\text{H9H8}} = 8.01$  Hz,  $\text{H}_9$ ), 4.79 (m, OH), 4.71 (d,  $J_{\text{gem}} = 9.78$  Hz,  $\text{H}_{3a}$ ), 4.54 (d,  $J_{\text{gem}} = 9.88$  Hz,  $\text{H}_{3b}$ ), 4.28 (m,  $\text{H}_{11a}$ ), 3.62 (m,  $\text{H}_{1a}$  and  $\text{CH}_2$ ), 3.38 (m,  $\text{H}_{1b}$  and  $\text{CH}_2$ ); ms:  $m/z$  311 (34), 293 (21), 252 (16).

*Anal.* Calcd. for  $\text{C}_{13}\text{H}_{14}\text{N}_3\text{O}_2\text{SCl}$ : C, 50.08; H, 4.53; N, 13.48. Found: C, 50.30; H, 4.56; N, 13.36.

1,2,3,11a-Tetrahydro-11-alkylamino-7-chloro-5*H*-thiazolo[4,3-*c*][1,4]benzodiazepine-5-thiones **3p-q**.

#### General Procedure.

A solution of 1,2,3,10,11,11a-hexahydro-7-chloro-5*H*-thiazolo[4,3-*c*][1,4]benzodiazepine-5,11-dithione (**2d**) (1 g, 0.0033 mole) and the appropriate amine (5 equivalents) in tetrahydrofuran (50 ml) was heated at 55°. Mercuric chloride (1.15 g, 0.0043 mole) was added and the mixture was allowed to stirring for 1 hour at 55°. The reaction mixture was filtered and the solvent removed. The residue was taken up in ethyl acetate (100 ml) and washed with an aqueous solution of sodium thiosulfate (2 x 100 ml). The organic layer was dried (magnesium sulfate) and evaporated under reduced pressure. The solid residue obtained was recrystallized to give **3p,q**.

1,2,3,11a-Tetrahydro-11-cyclopentylamino-7-chloro-5*H*-thiazolo[4,3-*c*][1,4]benzodiazepine-5-thione (**3p**).

With cyclopentylamine, yellow crystals (64%) were obtained, mp 223° (2-propanol); ir (potassium bromide):  $\nu$  3310 (NH), 1605 (C=N)  $\text{cm}^{-1}$ ;  $^1\text{H-nmr}$  (dimethyl sulfoxide- $d_6$ ):  $\delta$  8.01 (d,  $J_{\text{H6H8}} = 2.93$  Hz, H<sub>6</sub>), 7.35 (dd,  $J_{\text{H8H9}} = 6.89$  Hz,  $J_{\text{H8H6}} = 2.84$  Hz, H<sub>8</sub>), 6.95 (d,  $J_{\text{H9H8}} = 7.01$  Hz, H<sub>9</sub>), 6.82 (d,  $J_{\text{NHCH}} = 6.83$  Hz, NH), 5.07 (d,  $J_{\text{gem}} = 11.21$  Hz, H<sub>3a</sub>), 4.72 (d,  $J_{\text{gem}} = 11.12$  Hz, H<sub>3b</sub>), 4.48 (m, H<sub>11a</sub>), 4.05 (m, CH), 3.77 (d,  $J_{\text{gem}} = 12.08$  Hz, H<sub>1a</sub>), 3.51 (m, H<sub>1b</sub>), 1.75 (m, 4 CH<sub>2</sub>).

*Anal.* Calcd. for C<sub>16</sub>H<sub>18</sub>N<sub>3</sub>S<sub>2</sub>Cl: C, 54.61; H, 5.16; N, 11.94. Found: C, 54.83; H, 5.22; N, 12.02.

1,2,3,11a-Tetrahydro-11-(2-hydroxyethylamino)-7-chloro-5*H*-thiazolo[4,3-*c*][1,4]benzodiazepine-5-thione (**3q**).

With 2-aminoethanol, white crystals (71%) were obtained, mp 192° (ether); ir (potassium bromide):  $\nu$  3350 (OH), 3265 (NH), 1605 (C=N)  $\text{cm}^{-1}$ ;  $^1\text{H-nmr}$  (dimethyl sulfoxide- $d_6$ ):  $\delta$  8.04 (d,  $J_{\text{H6H8}} = 2.70$  Hz, H<sub>6</sub>), 7.41 (dd,  $J_{\text{H8H9}} = 6.98$  Hz,  $J_{\text{H8H6}} = 2.64$  Hz, H<sub>8</sub>), 7.19 (t,  $J_{\text{NHCH}_2} = 2.63$  Hz, NH), 6.97 (d,  $J_{\text{H9H8}} = 7.03$  Hz, H<sub>9</sub>), 5.12 (d,  $J_{\text{gem}} = 11.22$  Hz, H<sub>3a</sub>), 4.76 (m, H<sub>3b</sub> and OH), 4.55 (m, H<sub>11a</sub>), 3.65 (m, H<sub>1a</sub> and CH<sub>2</sub>), 3.46 (m, H<sub>1b</sub>), 3.31 (m, CH<sub>2</sub>).

*Anal.* Calcd. for C<sub>13</sub>H<sub>14</sub>N<sub>3</sub>OS<sub>2</sub>Cl: C, 47.63; H, 4.30; N, 12.82. Found: C, 47.62; H, 4.42; N, 13.03.

1,2,3,11a-Tetrahydro-11-(2-hydroxyethylamino)-7-methyl-5*H*-thiazolo[4,3-*c*][1,4]benzodiazepine-5-thione (**3r**).

To a solution of 1,2,3,10,11,11a-hexahydro-7-methyl-5*H*-thiazolo[4,3-*c*][1,4]benzodiazepine-5,11-dithione (**2e**) (1 g, 0.0036 mole) and 2-aminoethanol (1 ml, 0.018 mole) in tetrahydrofuran (50 ml), we added at 55°, mercuric chloride (1.2 g, 0.0046 mole). The reaction mixture was stirred for 1 hour, then filtered and tetrahydrofuran was removed under reduced pressure. The solid residue was taken up in chloroform (120 ml), washed with an aqueous solution of sodium thiosulfate. The organic layer was dried (calcium chloride) and evaporated *in vacuo*. The yellow solid was recrystallized in ether to give 0.75 g (68%) of **3r**, mp 174° (ether); ir (potassium bromide):  $\nu$  3350 (OH), 3280 (NH), 1615 (C=N)  $\text{cm}^{-1}$ ;  $^1\text{H-nmr}$  (dimethyl sulfoxide- $d_6$ ):  $\delta$  7.86 (d,  $J_{\text{H6H8}} = 2.41$  Hz, H<sub>6</sub>), 7.20 (dd,  $J_{\text{H8H9}} = 7.81$  Hz,  $J_{\text{H8H6}} = 2.49$  Hz, H<sub>8</sub>), 7.04 (m, NH), 6.92 (d,  $J_{\text{H9H8}} = 7.75$  Hz, H<sub>9</sub>), 5.11 (d,  $J_{\text{gem}} = 10.93$  Hz, H<sub>3a</sub>), 4.95 (m, OH), 4.75 (d,  $J_{\text{gem}} = 10.61$

Hz, H<sub>3b</sub>), 4.53 (m, H<sub>11a</sub>), 3.53 (m, H<sub>1a</sub> and 2 CH<sub>2</sub>), 3.38 (m, H<sub>1b</sub>); ms:  $m/z$  307 (18), 199 (23).

*Anal.* Calcd. for C<sub>14</sub>H<sub>17</sub>N<sub>3</sub>OS<sub>2</sub>: C, 54.70; H, 5.57; N, 13.67. Found: C, 54.45; H, 5.41; N, 13.48.

1,2,3,11a-Tetrahydro-11-(2-chloroethylamino)-5*H*-thiazolo[4,3-*c*][1,4]benzodiazepin-5-one (**4**).

To a solution of 1,2,3,11a-tetrahydro-11-(2-hydroxyethylamino)-5*H*-thiazolo[4,3-*c*][1,4]benzodiazepin-5-one (**3e**) (0.8 g, 0.0029 mole) in chloroform (40 ml) we added thionyl chloride (0.3 ml, 0.0043 mole). The solution was stirred for 1 hour to reflux and the chloroform was removed *in vacuo*. The solid residue was taken up in a 5% ammonia solution (100 ml) and extracted with ethyl acetate (2 x 100 ml). The organic layer was washed with water (80 ml), dried (magnesium sulfate) and evaporated. The yellow solid was recrystallized in ether to give 0.7 g (81%) of **4**, mp 190°; ir (potassium bromide):  $\nu$  3360 (NH), 1630 (C=O), 1600 (C=N)  $\text{cm}^{-1}$ ;  $^1\text{H-nmr}$  (dimethyl sulfoxide- $d_6$ ):  $\delta$  7.84 (d,  $J_{\text{H6H7}} = 7.32$  Hz, H<sub>6</sub>), 7.51 (t,  $J_{\text{H8H9}} = J_{\text{H8H7}} = 7.31$  Hz, H<sub>8</sub>), 7.39 (m, H<sub>7</sub>, H<sub>9</sub> and NH), 4.68 (d,  $J_{\text{gem}} = 10.01$  Hz, H<sub>3a</sub>), 4.53 (d,  $J_{\text{gem}} = 9.95$  Hz, H<sub>3b</sub>), 4.41 (m, H<sub>11a</sub>), 3.69 (m, H<sub>1a</sub> and 2 CH<sub>2</sub>), 3.43 (m, H<sub>1b</sub>); ms:  $m/z$  295 (8), 231 (18).

*Anal.* Calcd. for C<sub>13</sub>H<sub>14</sub>N<sub>3</sub>OSCl: C, 52.79; H, 4.74; N, 14.21. Found: C, 52.91; H, 4.80; N, 14.34.

1,2,3b,4,5,6-Hexahydro-8*H*-thiazolo[4,3-*c*][1,3]imidazo[1,2-*a*][1,4]benzodiazepine-8-thione (**5**).

To a solution of 1,2,3,11a-tetrahydro-11-(2-hydroxyethylamino)-5*H*-thiazolo[4,3-*c*][1,4]benzodiazepine-5-thione (**3k**) (1.2 g, 0.0041 mole) in pyridine (30 ml), we added over a period of 10 minutes at 0° *p*-toluenesulfonyl chloride (1.25 g, 0.0065 mole). After the addition was complete, the solution was stirred at 0° for 30 minutes and allowed to warm to room temperature overnight. The mixture was poured into water and extracted with ethyl acetate (2 x 100 ml). The organic layer was dried (magnesium sulfate) and evaporated to yield 0.7 g (62%) of **5** (white solid), mp 235° (ether); ir (potassium bromide):  $\nu$  1625 (C=N)  $\text{cm}^{-1}$ ;  $^1\text{H-nmr}$  (dimethyl sulfoxide- $d_6$ ):  $\delta$  7.89 (d,  $J_{\text{H6H7}} = 8.02$  Hz, H<sub>6</sub>), 7.42 (t,  $J_{\text{H8H9}} = J_{\text{H8H7}} = 7.79$  Hz, H<sub>11</sub>), 7.12 (m, H<sub>10</sub> and H<sub>12</sub>), 5.21 (d,  $J_{\text{gem}} = 11.43$  Hz, H<sub>6a</sub>), 4.87 (m, H<sub>6b</sub> and H<sub>3b</sub>), 3.51 (m, H<sub>4a</sub> and CH<sub>2</sub>), 3.33 (m, H<sub>4b</sub> and CH<sub>2</sub>); ms:  $m/z$  275 (6), 234 (11).

*Anal.* Calcd. for C<sub>13</sub>H<sub>13</sub>N<sub>3</sub>S<sub>2</sub>: C, 56.70; H, 4.76; N, 15.26. Found: C, 56.95; H, 4.57; N, 15.08.

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