2-Azidopyrrolo[2,1-*c*][1,4]benzodiazepines. Synthesis of the First Cyclic Amidine Derivatives

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We report the practical synthesis of the new 5-azidopyrrolo[2,1-*c*][1,2,4]triazolo[4,3-*a*][1,4]benzodiazepin-8-one and 11-alkylamino-2-azidopyrrolo[2,1-*c*][1,4]benzodiazepines *via* the corresponding hydroxy compounds.

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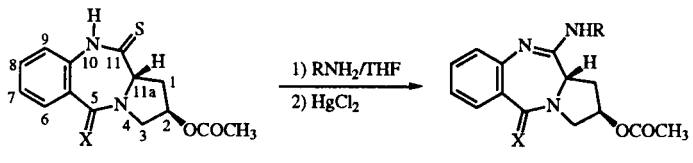
The pyrrolo[2,1-*c*][1,4]benzodiazepines such as anthramycin [1], tomaymycin [2] and sibiromycin [3] belong to a class of antitumor antibiotics which are biosynthetically derived from *Streptomyces species*. They are thought to exert their antitumor activity through covalent binding *via* a linkage of an amine moiety from the electrophilic carbinolamine-bearing C-11 position to an N-2 of guanine within the minor groove of DNA [4]. In spite of the importance of the carbinolamine functionality, we recently prepared cyclic amidines in the pyrrolo[2,1-*c*]-[1,4]benzodiazepine series [5]. Some of these amidines showed a good *in vitro* DNA binding [6,7]. However, they did not prove to be cytotoxic. In order to extend our study, and to try to improve the cytotoxicity in this series we introduced an azido substituent on the pyrrolidinic ring of these systems. We present in this paper the preparation of new tricyclic or tetracyclic 2-azidopyrrolo[2,1-*c*][1,4]benzodiazepines *via* the corresponding hydroxy compounds. We recently described the preparation of monothiolactams and dithiolactams of type **1**, **2** [8,9]. These thiolactams were synthesized to supplement the lack of reactivity of the corresponding dilactams. Treatment of the monothiolactam **1** with 5 equivalents of methylamine and cyclopentylamine in refluxing tetrahydrofuran, in the presence of 1.3 equivalents of mercuric chloride led in high yields to the cyclic amidines **3** and **4** respectively [10]. In the same manner, the dithiolactam **2**, by the action of cyclopentylamine, in the presence of 1.3 equivalents of mercuric chloride was converted to the cyclic amidine **5** (Scheme 1).

The 2-acetoxypyrrolo[2,1-*c*][1,4]benzodiazepines **3**, **4** and **5** were easily converted to the corresponding

Scheme 1



1, X = O

2, X = S

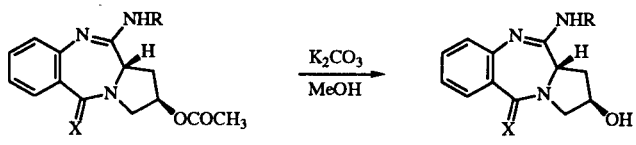
3, X = O, R = CH_3

4, X = O, R = cyclopentyl

5, X = S, R = cyclopentyl

2-hydroxy compounds **6**, **7** and **8** by the action of 1.5 equivalents of potassium carbonate in refluxing methanol. The amidine function was not affected by this reaction and no isomerization was noted (Scheme 2).

Scheme 2



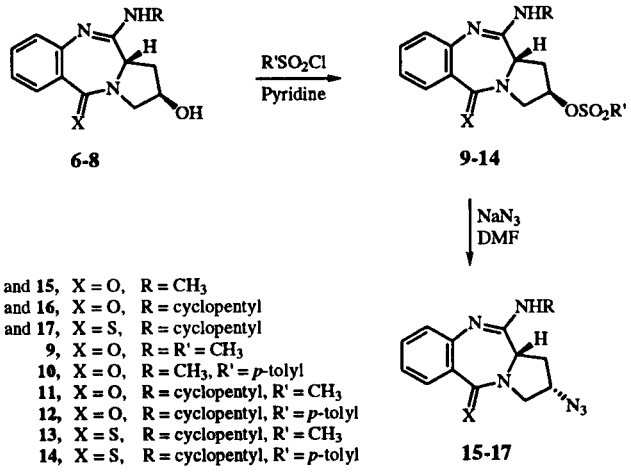
3-5 **6-8**

3 and **6**, X = O, R = CH_3
4 and **7**, X = O, R = cyclopentyl
5 and **8**, X = S, R = cyclopentyl

We recently described the preparation of azides from hydroxy compounds in the pyrrolo[2,1-*c*][1,4]benzodiazepine series [11]. Application of this pathway to the 11-alkylamino-2-hydroxypyrrolo[2,1-*c*][1,4]benzodiazepines **6**, **7** and **8** allowed us to obtain the azido amidines **15**, **16** and **17** in good yields (Scheme 3). The 2-hydroxypyrrolo[2,1-*c*][1,4]benzodiazepines **6**, **7** and **8** reacted with 1.6 equivalents of methanesulfonyl chloride to give the mesylates **9**, **11** and **13** in good yield. This reaction was accomplished in pyridine, at room temperature. In the same manner, the benzodiazepinic tosylates **10**, **12** and **14** were easily obtained from the compounds **6**, **7** and **8** by the action of 1.6 equivalents of *p*-toluenesulfonyl chloride in pyridine, at room temperature. Treatment of these mesylates or tosylates with 4 equivalents of sodium azide gave in good yields the 2-azidopyrrolo[2,1-*c*][1,4]benzodiazepines **15**, **16** and **17**. This reaction was accomplished in refluxing *N*,*N*-dimethylformamide during 4 hours. The amidine function did not react with sodium azide. Comparison of nmr spectra of the mesylates and the azido compounds showed that C_2 carbon was subjected to an inversion of configuration during this nucleophilic substitution.

We applicated this pathway to the 5-hydroxypyrrolo[2,1-*c*][1,2,4]triazolo[4,3-*a*][1,4]benzodiazepin-8-one **18** (Scheme 4). This compound was easily converted to the mesylate **19** or the tosylate **20** by the action of methanesul-

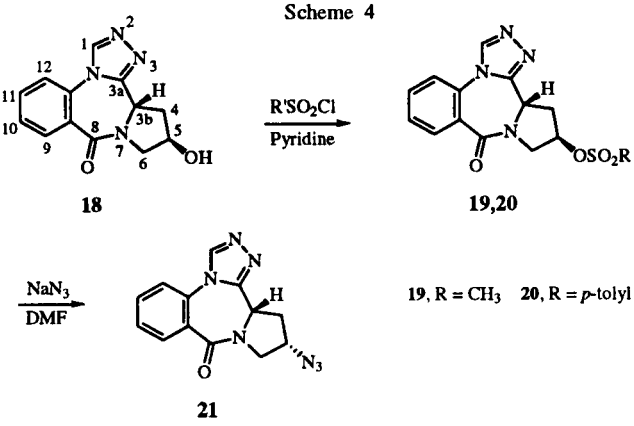
Scheme 3



6 and **15**, X = O, R = CH_3
7 and **16**, X = O, R = cyclopentyl
8 and **17**, X = S, R = cyclopentyl
9, X = O, R = R' = CH_3
10, X = O, R = CH_3, R' = *p*-tolyl
11, X = O, R = cyclopentyl, R' = CH_3
12, X = O, R = cyclopentyl, R' = *p*-tolyl
13, X = S, R = cyclopentyl, R' = CH_3
14, X = S, R = cyclopentyl, R' = *p*-tolyl

fonyl or *p*-toluenesulfonyl chloride respectively, in pyridine. The corresponding 5-azidopyrrolo[2,1-*c*][1,2,4]triazolo[4,3-*a*][1,4]benzodiazepin-8-one **21** was obtained by reaction of the mesylate **19** with sodium azide in refluxing *N,N*-dimethylformamide. According to the nmr spectra of compounds **19** and **21**, an inversion of configuration of the C_5 carbon occured during this nucleophilic substitution.

Scheme 4



19, R = CH_3 **20**, R = *p*-tolyl

The antitumor activity of compounds **7**, **15**, **16** and **21** was evaluated by the National Cancer Institute, Bethesda, Maryland and by the Institute of Cancer Research, Sutton, UK. However, none of these compounds showed any satisfactory result. Other products in this series are under investigation in a continuation of our structure-activity studies.

EXPERIMENTAL

General Methods.

Melting points were taken on a Köfler 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 LA 400 using TMS as an internal standard. Chemical shifts are reported in ppm downfield (δ) from TMS. The mass spectra were recorded on a Jeol JMS D-300. Experimental protocol for the synthesis of compound **18** is described in reference [10].

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

To a solution of (2*R*,11a*S*)-1,2,3,10,11,11a-hexahydro-2-acetoxy-5*H*-pyrrolo[2,1-*c*][1,4]benzodiazepin-5-one-11-thione (**1**) (8 g, 0.0276 mole) and methylamine in boiling tetrahydrofuran (80 ml), was added mercuric chloride (9.6 g, 0.0357 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 ethyl acetate (200 ml) and washed with an aqueous solution of sodium thiosulfate. The organic layer was dried (magnesium sulfate) and evaporated *in vacuo*. The white solid was recrystallized from ethanol to give 5.85 g (74%) of **3**, mp 203°; ir (potassium bromide): ν 3280 (NH), 1740 (C=O), 1630 (C=O), 1610 (C=N) cm^{-1}; ^{1}H-nmr (dimethyl sulfoxide-d_6): δ 7.80 (d, J_{H6H7} = 7.7 Hz, H_6), 7.45 (t, J_{H8H9} = J_{H8H7} = 7.6 Hz, H_8), 7.20-7.14 (m, NH, H_7 and H_9), 5.25 (m, H_{2b}), 4.24 (m, H_{11a}), 3.65 (d, J_{gem} = 12.2 Hz, H_{3a}), 3.31 (dd, J_{gem} = 12.3 Hz, J_{H3bH2b} = 4.1 Hz, H_{3b}), 2.80 (s, NCH_3), 2.75 (m, H_{1a}), 2.19 (m, H_{1b}), 2.05 (s, $COCH_3$); ms: m/z, 287 (31), 227 (18), 196 (48).

Anal. Calcd. for $C_{15}H_{17}N_3O_3$: C, 62.72; H, 5.92; N, 14.63. Found: C, 62.65; H, 6.08; N, 14.40.

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

The monothiolactam **1** (6 g, 0.0207 mole) was converted to **4** following the procedure for the preparation of **3**, using cyclopentylamine (10.2 ml, 0.1034 mole). This gave 4.95 g (70%) of **4** (white solid), mp 209° (acetonitrile); ir (potassium bromide): ν 3290 (NH), 1750 (C=O), 1640 (C=O), 1600 (C=N) cm^{-1}; ^{1}H-nmr (dimethyl sulfoxide-d_6): δ 7.82 (d, J_{H6H7} = 7.7 Hz, H_6), 7.45 (t, J_{H8H9} = J_{H8H7} = 7.8 Hz, H_8), 7.20 (m, NH), 7.18 (m, H_7 and H_9), 5.21 (m, H_{2b}), 4.24 (m, H_{11a}), 3.76-3.68 (m, CH and H_{3a}), 3.34 (dd, J_{gem} = 12.2 Hz, J_{H3bH2b} = 4.0 Hz, H_{3b}), 2.78 (m, H_{1a}), 2.33-1.65 (m, H_{1b} and 4 CH_2), 2.08 (s, CH_3).

Anal. Calcd. for $C_{19}H_{23}N_3O_3$: C, 66.86; H, 6.74; N, 12.32. Found: C, 66.93; H, 6.59; N, 12.18.

(2*R*,11a*S*)-1,2,3,11a-Tetrahydro-2-acetoxy-11-cyclopentylamino-5*H*-pyrrolo[2,1-*c*][1,4]benzodiazepine-5-thione (**5**).

The dithiolactam **2** (7 g, 0.0229 mole) was converted to **5** following the procedure for the preparation of **3**, using cyclopentylamine (11.3 ml, 0.1144 mole). This gave 5.85 g (72%) of **5** (yellow crystals), mp 214° (ether); ir (potassium bromide): ν 3280 (NH), 1750 (C=O), 1610 (C=N) cm^{-1}; ^{1}H-nmr (dimethyl sulfoxide-d_6): δ 8.03 (d, J_{H6H7} = 7.8 Hz, H_6), 7.42 (m, H_8 and NH), 7.20 (m, H_7 and H_9), 5.19 (m, H_{2b}), 4.20 (m, H_{11a}), 3.81 (m, CH), 3.67 (d, J_{gem} = 12.0 Hz, H_{3a}), 3.38 (dd, J_{gem} = 12.1 Hz, J_{H3bH2b} = 3.8 Hz, H_{3b}), 2.76 (m, H_{1a}), 2.25-1.67 (m, H_{1b} and 4 CH_2), 2.10 (s, CH_3); ms: m/z, 357 (16), 297 (42), 212 (28).

Anal. Calcd. for $C_{19}H_{23}N_3O_2S$: C, 63.86; H, 6.44; N, 11.76. Found: C, 64.01; H, 6.29; N, 11.58.

(2*R*,11a*S*)-1,2,3,11a-Tetrahydro-2-hydroxy-11-methylamino-5*H*-pyrrolo[2,1-*c*][1,4]benzodiazepin-5-one (**6**).

To a solution of (2*R*,11a*S*)-1,2,3,11a-tetrahydro-2-acetoxy-11-methylamino-5*H*-pyrrolo[2,1-*c*][1,4]benzodiazepin-5-one (**3**)

(6 g, 0.0209 mole) in methanol (60 ml), was added potassium carbonate (4.3 g, 0.0313 mole). The reaction mixture was stirred for 1 hour and evaporated to dryness under reduced pressure. The solid residue was taken up in water (80 ml) and extracted with ethyl acetate (2 x 90 ml). The organic layer was dried (magnesium sulfate) and evaporated to yield 4.15 g (81%) of **6** (white crystals), mp 182° (ether); ir (potassium bromide): ν 3340 (OH), 3270 (NH), 1640 (C=O), 1605 (C=N) cm^{-1}; ^{1}H-nmr (dimethyl sulfoxide-d_6): δ 7.80 (d, J_{H6H7} = 7.7 Hz, H6), 7.48 (t, J_{H8H9} = J_{H8H7} = 7.8 Hz, H_8), 7.20 (m, NH, H_7 and H_9), 5.20 (s, OH), 4.39 (m, H_{2b}), 4.03 (m, H_{11a}), 3.51 (d, J_{gem} = 12.1 Hz, H_{3a}), 3.36 (dd, J_{gem} = 12.1 Hz, J_{H3bH2b} = 4.4 Hz, H_{3b}), 2.76 (s, CH_3), 2.51 (m, H_{1a}) 2.04 (m, H_{1b}); ms: m/z, 245 (36), 227 (24), 196 (14), 164 (21).

Anal. Calcd. for $C_{13}H_{15}N_3O_2$: C, 63.67; H, 6.12; N, 17.14. Found: C, 63.78; H, 5.91; N, 17.30.

(2*R*,11a*S*)-1,2,3,11a-Tetrahydro-11-cyclopentylamino-2-hydroxy-5*H*-pyrrolo[2,1-*c*][1,4]benzodiazepin-5-one (**7**).

A mixture of (2*R*,11a*S*)-1,2,3,11a-tetrahydro-2-acetoxy-11-cyclopentylamino-5*H*-pyrrolo[2,1-*c*][1,4]benzodiazepin-5-one (**4**) (7 g, 0.0205 mole) and potassium carbonate (4.25 g, 0.0308 mole) in methanol (60 ml) was stirred at reflux for 1 hour. After evaporation of the solvent, the solid residue was taken up in water (100 ml). The resulting white solid was collected, dried (magnesium sulfate) and recrystallized from ethanol to give 4.8 g (78%) of **7**, mp 186°; ir (potassium bromide): ν 3330 (OH), 3250 (NH), 1640 (C=O), 1610 (C=N) cm^{-1}; ^{1}H-nmr (dimethyl sulfoxide-d_6): δ 7.75 (d, J_{H6H7} = 7.8 Hz, H_6), 7.33 (t, J_{H8H9} = J_{H8H7} = 7.7 Hz, H_8), 7.17 (s, NH), 7.08 (m, H_7 and H_9), 5.12 (s, OH), 4.34 (m, H_{2b}), 4.02 (m, CH), 3.96 (m, H_{11a}), 3.52 (d, J_{gem} = 12.0 Hz, H_{3a}), 3.43 (dd, J_{gem} = 12.0 Hz, J_{H3bH2b} = 4.3 Hz, H_{3b}), 2.54 (m, H_{1a}), 2.28-1.62 (m, H_{1b} and 4 CH_2); ms: m/z 299 (48), 281 (16), 195 (62).

Anal. Calcd. for $C_{17}H_{21}N_3O_2$: C, 68.22; H, 7.02; N, 14.05. Found: C, 68.04; H, 6.90; N, 13.87.

(2*R*,11a*S*)-1,2,3,11a-Tetrahydro-11-cyclopentylamino-2-hydroxy-5*H*-pyrrolo[2,1-*c*][1,4]benzodiazepine-5-thione (**8**).

The cyclic amidine **5** (5 g, 0.0140 mole) was converted to **8** using the procedure for the preparation of **6**. This gave 3.25 g (74%) of **8** (yellow crystals), mp 198° (2-propanol); ir (potassium bromide): ν 3340 (OH), 3250 (NH), 1620 (C=N) cm^{-1}; ^{1}H-nmr (dimethyl sulfoxide-d_6): δ 8.05 (d, J_{H6H7} = 7.8 Hz, H_6), 7.34 (t, J_{H8H9} = J_{H8H7} = 7.5 Hz, H_8), 7.18 (s, NH), 7.04 (m, H_7 and H_9), 5.18 (s, OH), 4.20 (m, H_{2b}), 3.98 (m, CH), 3.90 (m, H_{11a}), 3.53 (dd, J_{gem} = 11.9 Hz, J_{H3aH2b} = 2.1 Hz, H_{3a}), 3.41 (dd, J_{gem} = 12.0 Hz, J_{H3bH2b} = 4.3 Hz, H_{3b}), 2.58 (m, H_{1a}), 2.31-1.64 (m, H_{1b} and 4 CH_2).

Anal. Calcd. for $C_{17}H_{21}N_3OS$: C, 64.76; H, 6.66; N, 13.33. Found: C, 65.01; H, 6.41; N, 13.10.

(2*R*,11a*S*)-1,2,3,11a-Tetrahydro-11-methylamino-2-methylsulfonyloxy-5*H*-pyrrolo[2,1-*c*][1,4]benzodiazepin-5-one (**9**).

To an ice-cooled (0°) solution of methanesulfonyl chloride (1.75 ml, 0.0228 mole) in pyridine (40 ml) we added in small portions (2*R*,11a*S*)-1,2,3,11a-tetrahydro-2-hydroxy-11-methylamino-5*H*-pyrrolo[2,1-*c*][1,4]benzodiazepin-5-one (**6**) (3.5 g, 0.0143 mole). This solution was stirred at room temperature for 14 hours, poured into ice-water and extracted with ethyl acetate (2 x 90 ml). The organic layer was washed with water (60 ml), dried (magnesium sulfate) and evaporated to give 3.70 g (80%) of **9** (white crystals), mp 196° (ether); ir (potassium bromide): ν 3300 (NH), 1630 (C=O), 1600 (C=N) cm^{-1}; ^{1}H-nmr (dimethyl sulfoxide-d_6): δ 7.72 (d, J_{H6H7} = 7.8 Hz, H_6), 7.37 (t, J_{H8H9} = J_{H8H7} = 7.7 Hz, H_8), 7.20 (m, NH), 7.02 (m, H_7 and H_9), 5.10 (m, H_{2b}), 4.14 (m, H_{11a}), 3.82 (d, J_{gem} = 11.9 Hz, H_{3a}), 3.64 (dd, J_{gem} = 11.9 Hz, J_{H3bH2b} = 4.3 Hz, H_{3b}), 3.27 (s, SCH_3), 2.79 (d, J_{CH3NH} = 2.8 Hz, NCH_3), 2.64 (m, H_{1a}), 2.49 (m, H_{1b}); ms: m/z 323 (42), 291 (21), 195 (10).

Anal. Calcd. for $C_{14}H_{17}N_3O_4S$: C, 52.01; H, 5.26; N, 13.00. Found: C, 51.88; H, 5.44; N, 13.21.

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

The cyclic amidine **7** (4 g, 0.0134 mole) was converted to **11** using the procedure for the preparation of **9**. This gave 3.8 g (76%) of **11** (white solid), mp 192° (acetone); ir (potassium bromide): ν 3280 (NH), 1640 (C=O), 1610 (C=N) cm^{-1}; ^{1}H-nmr (dimethyl sulfoxide-d_6): δ 7.75 (d, J_{H6H7} = 7.8 Hz, H_6), 7.39 (t, J_{H8H9} = J_{H8H7} = 7.8 Hz, H_8), 7.10 (m, H_7, H_9 and NH), 5.02 (m, H_{2b}), 4.06 (m, H_{11a} and CH), 3.80 (m, H_{3a}), 3.61 (dd, J_{gem} = 11.9 Hz, J_{H3bH2b} = 4.1 Hz, H_{3b}), 3.19 (s, CH_3), 2.67 (m, H_{1a}), 2.43 (m, H_{1b}), 1.88-1.65 (m, 4 CH_2).

Anal. Calcd. for $C_{18}H_{23}N_3O_4S$: C, 57.29; H, 6.10; N, 11.14. Found: C, 57.12; H, 6.27; N, 10.96.

(2*R*,11a*S*)-1,2,3,11a-Tetrahydro-11-cyclopentylamino-2-methylsulfonyloxy-5*H*-pyrrolo[2,1-*c*][1,4]benzodiazepine-5-thione (**13**).

The cyclic amidine **8** (3 g, 0.0095 mole) was converted to **13** using the procedure for the preparation of **9**. This gave 2.8 g (75%) of **13** (yellow crystals), mp 210° (ether); ir (potassium bromide): ν 3275 (NH), 1610 (C=N) cm^{-1}; ^{1}H-nmr (dimethyl sulfoxide-d_6): δ 8.02 (d, J_{H6H7} = 7.7 Hz, H_6), 7.29 (t, J_{H8H9} = J_{H8H7} = 7.6 Hz, H_8), 7.12 (m, H_7, H_9 and NH), 5.05 (m, H_{2b}), 4.10 (m, H_{11a}), 3.98 (m, CH), 3.82 (d, J_{gem} = 11.8 Hz, H_{3a}), 3.64 (dd, J_{gem} = 11.8 Hz, J_{H3bH2b} = 3.9 Hz, H_{3b}), 3.07 (s, CH_3), 2.62 (m, H_{1a}), 2.45 (m, H_{1b}), 1.93-1.62 (m, 4 CH_2); ms: m/z 393 (52), 297 (18), 212 (32).

Anal. Calcd. for $C_{18}H_{23}N_3O_3S_2$: C, 54.96; H, 5.85; N, 10.69. Found: C, 55.09; H, 6.01; N, 10.48.

(3b*S*,5*R*)-3b,4,5,6-Tetrahydro-5-methylsulfonyloxy-8*H*-pyrrolo[2,1-*c*][1,2,4]triazolo[4,3-*a*][1,4]benzodiazepin-8-one (**19**).

The triazole **18** (3 g, 0.0117 mole) was converted to **19** using the procedure for the preparation of **9**. This gave 3.2 g (82%) of **19** (white solid), mp >260° (ethanol); ir (potassium bromide): ν 1640 (C=O), 1605 (C=N) cm^{-1}; ^{1}H-nmr (dimethyl sulfoxide-d_6): δ 9.22 (s, CH), 7.83 (d, J_{H9H10} = 7.8 Hz, H_9), 7.70-7.51 (m, H_{10}, H_{11} and H_{12}), 5.30 (m, H_{5b}), 4.78 (m, H_{3b}), 3.90 (d, J_{gem} = 12.2 Hz, H_{6a}), 3.69 (dd, J_{gem} = 12.1 Hz, J_{H6bH5b} = 4.1 Hz, H_{6b}), 3.37 (s, CH_3), 3.30 (m, H_{4a}), 2.71 (m, H_{4b}).

Anal. Calcd. for $C_{14}H_{14}N_4O_4S$: C, 50.29; H, 4.22; N, 16.76. Found C, 50.14; H, 4.39; N, 16.66.

(2*R*,11a*S*)-1,2,3,11a-Tetrahydro-11-methylamino-2-(*p*-tolylsulfonyloxy)-5*H*-pyrrolo[2,1-*c*][1,4]benzodiazepin-5-one (**10**).

To an ice-cooled (0°) solution of (2*R*,11a*S*)-1,2,3,11a-tetrahydro-2-hydroxy-11-methylamino-5*H*-pyrrolo[2,1-*c*][1,4]benzodiazepin-5-one (**6**) (3 g, 0.0122 mole) in pyridine (30 ml) we added in small portions *p*-toluenesulfonyl chloride (3.75 g, 0.0196 mole). This solution was stirred at room temperature for

15 hours and poured into ice-water. The precipitate was filtered, dried and recrystallized from acetonitrile to give 3.4 g (70%) of **10** (white solid), mp 206° (ethanol); ir (potassium bromide): ν 3320 (NH), 1640 (C=O), 1605 (C=N) cm^{-1}; ^1H-nmr (dimethyl sulfoxide-d_6): δ 7.85-7.78 (m, 3 H), 7.52-7.46 (m, 3 H), 7.18 (m, NH), 7.10 (m, 2 H), 5.13 (m, H_{2b}), 4.12 (m, H_{11a}), 3.84 (d, J_{gem} = 11.9 Hz, H_{3a}), 3.59 (dd, J_{gem} = 11.9 Hz, J_{H3bH2b} = 4.2 Hz, H_{3b}), 2.76 (d, J_{CH3NH} = 3.1 Hz, NCH_3), 2.68 (m, H_{1a}), 2.48 (m, H_{1b}), 2.45 (s, CCH_3).

Anal. Calcd. for $C_{20}H_{21}N_3O_4S$: C, 60.14; H, 5.30; N, 10.52. Found: C, 59.91; H, 5.43; N, 10.72.

(2*R*,11a*S*)-1,2,3,11a-Tetrahydro-11-cyclopentylamino-2-(*p*-tolylsulfonyloxy)-5*H*-pyrrolo[2,1-*c*][1,4]benzodiazepin-5-one (**12**).

The cyclic amidine **7** (3.5 g, 0.0117 mole) was converted to **12** using the procedure for the preparation of **10**. This gave 3.9 g (74%) of **12** (white solid), mp 201° (ether); ir (potassium bromide): ν 3250 (NH), 1635 (C=O), 1610 (C=N) cm^{-1}; ^1H-nmr (dimethyl sulfoxide-d_6): δ 7.80-7.69 (m, 3 H), 7.54-7.47 (m, 2 H), 7.33-7.20 (m, 3 H), 6.99 (m, NH), 4.98 (m, H_{2b}), 4.08 (m, H_{11a}), 3.99 (m, CH), 3.81 (d, J_{gem} = 12.1 Hz, H_{3a}), 3.64 (m, H_{3b}), 2.70 (m, H_{1a}), 2.47 (s, CH_3), 2.42 (m, H_{1b}), 1.90-1.68 (m, 4 CH_2); ms: m/z 453 (20), 280 (48), 196 (26).

Anal. Calcd. for $C_{24}H_{27}N_3O_4S$: C, 63.56; H, 6.04; N, 9.26. Found: C, 63.49; H, 5.92; N, 9.12.

(2*R*,11a*S*)-1,2,3,11a-Tetrahydro-11-cyclopentylamino-2-(*p*-tolylsulfonyloxy)-5*H*-pyrrolo[2,1-*c*][1,4]benzodiazepine-5-thione (**14**).

The cyclic amidine **8** (3 g, 0.0095 mole) was converted to **14** using the procedure for the preparation of **10**. This gave 3 g (68%) of **14** (yellow crystals), mp 218° (2-propanol); ir (potassium bromide): ν 3280 (NH), 1610 (C=N) cm^{-1}; ^1H-nmr (dimethyl sulfoxide-d_6): δ 8.04 (d, J_{H6H7} = 7.8 Hz, H_6), 7.76-7.70 (m, 2 H), 7.56-7.48 (m, 3 H), 7.34 (m, NH), 7.28-7.20 (m, 2 H), 5.01 (m, H_{2b}), 4.10 (m, H_{11a}), 3.86 (m, CH), 3.79 (d, J_{gem} = 12.0 Hz, H_{3a}), 3.63 (dd, J_{gem} = 11.9 Hz, J_{H3bH2b} = 4.2 Hz, H_{3b}), 2.63 (m, H_{1a}), 2.49 (s, CH_3), 2.40 (m, H_{1b}), 2.01-1.75 (m, 4 CH_2).

Anal. Calcd. for $C_{24}H_{27}N_3O_3S_2$: C, 61.41; H, 5.76; N, 8.95. Found: C, 61.30; H, 5.89; N, 9.06.

(3b*S*,5*R*)-3b,4,5,6-Tetrahydro-5-(*p*-tolylsulfonyloxy)-8*H*-pyrrolo[2,1-*c*][1,2,4]triazolo[4,3-*a*][1,4]benzodiazepin-8-one (**20**).

The triazole **18** (2 g, 0.0078 mole) was converted to **20** using the procedure for the preparation of **10**. This gave 2.25 g (70%) of **20** (white solid), mp >260° (acetone); ir (potassium bromide): ν 1630 (C=O), 1600 (C=N) cm^{-1}; ^1H-nmr (dimethyl sulfoxide-d_6): δ 9.13 (s, CH), 7.80-7.66 (m, 3 H), 7.53-7.45 (m, 3 H), 7.39-7.30 (m, 2 H), 5.26 (m, H_{5b}), 4.76 (m, H_{3b}), 3.88 (d, J_{gem} = 11.9 Hz, H_{6a}), 3.67 (dd, J_{gem} = 11.9 Hz, J_{H6bH5b} = 4.0 Hz, H_{6b}), 3.26 (m, H_{4a}), 2.72 (m, H_{4b}), 2.50 (s, CH_3); ms: m/z 410 (34), 242 (14), 200 (56).

Anal. Calcd. for $C_{20}H_{18}N_4O_4S$: C, 58.53; H, 4.39; N, 13.66. Found: C, 58.68; H, 4.18; N, 13.47.

(2*S*,11a*S*)-1,2,3,11a-Tetrahydro-2-azido-11-methylamino-5*H*-pyrrolo[2,1-*c*][1,4]benzodiazepin-5-one (**15**).

A solution of (2*R*,11a*S*)-1,2,3,11a-tetrahydro-11-methylamino-2-methylsulfonyloxy-5*H*-pyrrolo[2,1-*c*][1,4]benzodiazepin-5-one (**9**) (3 g, 0.0090 mole) and sodium azide (2.3 g, 0.0359 mole) in *N,N*-dimethylformamide (40 ml) was stirred at reflux for 4 hours. The cooled mixture was diluted with water (100 ml) and extracted with ethyl acetate (2 x 100 ml). The organic layer was dried (magnesium sulfate) and evaporated under reduced pressure. The white solid was recrystallized from ethanol to give 2 g (82%) of **15**, mp 187°; ir (potassium bromide): ν 3280 (NH), 2150 (N_3), 1630 (C=O), 1605 (C=N) cm^{-1}; ^1H-nmr (dimethyl sulfoxide-d_6): δ 7.76 (d, J_{H6H7} = 7.7 Hz, H_6), 7.40 (t, J_{H8H9} = J_{H8H7} = 7.6 Hz, H_8), 7.12-7.04 (m, NH, H_7 and H_9), 4.49 (m, H_{2a}), 4.08 (m, H_{11a}), 3.75 (dd, J_{gem} = 12.0 Hz, J_{H3aH2a} = 4.1 Hz, H_{3a}), 3.58 (d, J_{gem} = 11.9 Hz, H_{3b}), 2.81 (d, J_{CH3NH} = 2.9 Hz, CH_3), 2.61 (m, H_{1a}), 2.47 (m, H_{1b}); ms: m/z, 270 (56), 227 (20), 197 (32).

Anal. Calcd. for $C_{13}H_{14}N_6O$: C, 57.78; H, 5.18; N, 31.11. Found: C, 58.01; H, 5.07; N, 30.98.

(2*S*,11a*S*)-1,2,3,11a-Tetrahydro-2-azido-11-cyclopentylamino-5*H*-pyrrolo[2,1-*c*][1,4]benzodiazepin-5-one (**16**).

The mesylate **11** (2.5 g, 0.0066 mole) was converted to **16** using the procedure for the preparation of **15**. This gave 1.6 g (74%) of **16** (white solid), mp 185° (ether); ir (potassium bromide): ν 3290 (NH), 2120 (N_3), 1640 (C=O), 1605 (C=N) cm^{-1}; ^1H-nmr (dimethyl sulfoxide-d_6): δ 7.78 (m, H_6 and NH), 7.42 (t, J_{H8H9} = J_{H8H7} = 7.7 Hz, H_8), 7.15 (m, H_7 and H_9), 4.45 (m, H_{2a}), 3.90 (m, H_{11a} and CH), 3.47 (dd, J_{gem} = 11.9 Hz, J_{H3aH2a} = 4.2 Hz, H_{3a}), 3.38 (d, J_{gem} = 12.1 Hz, H_{3b}), 2.59 (m, H_{1a}), 2.33 (m, H_{1b}), 1.90-1.68 (m, 4 CH_2); ms: m/z 324 (38), 281 (12), 196 (38).

Anal. Calcd. for $C_{17}H_{20}N_6O$: C, 62.96; H, 6.17; N, 25.93. Found: C, 63.12; H, 6.08; N, 25.82.

(2*S*,11a*S*)-1,2,3,11a-Tetrahydro-2-azido-11-cyclopentylamino-5*H*-pyrrolo[2,1-*c*][1,4]benzodiazepine-5-thione (**17**).

The tosylate **14** (2.5 g, 0.0053 mole) was converted to **17** using the procedure for the preparation of **15**. This gave 1.35 g (74%) of **17** (yellow crystals), mp 201° (ethanol); ir (potassium bromide): ν 3280 (NH), 2110 (N_3), 1610 (C=N) cm^{-1}; ^1H-nmr (dimethyl sulfoxide-d_6): δ 8.02 (d, J_{H6H7} = 7.7 Hz, H_6), 7.30 (t, J_{H8H9} = J_{H8H7} = 7.6 Hz, H_8), 7.14-7.05 (m, NH, H_7 and H_9), 4.08-4.01 (m, H_{2a} and CH), 3.79 (m, H_{11a}), 3.48 (dd, J_{gem} = 12.0 Hz, J_{H3aH2a} = 4.4 Hz, H_{3a}), 3.39 (d, J_{gem} = 11.8 Hz, H_{3b}), 2.56 (m, H_{1a}), 2.28 (m, H_{1b}), 1.94-1.68 (m, 4 CH_2).

Anal. Calcd. for $C_{17}H_{20}N_6S$: C, 59.92; H, 5.88; N, 24.71. Found: C, 60.12; H, 6.01; N, 24.59.

(3b*S*,5*S*)-3b,4,5,6-Tetrahydro-5-azido-8*H*-pyrrolo[2,1-*c*]-[1,2,4]triazolo[4,3-*a*][1,4]benzodiazepin-8-one (**21**).

The mesylate **19** (2.5 g, 0.0075 mole) was converted to **21** using the procedure for the preparation of **15**. This gave 1.60 g (76%) of **21** (white solid), mp 251° (water); ir (potassium bromide): ν 2110 (N_3), 1630 (C=O), 1600 (C=N) cm^{-1}; ^1H-nmr (dimethyl sulfoxide-d_6): δ 9.11 (s, CH), 7.80 (d, J_{H9H10} = 7.8 Hz, H_9), 7.48 (t, J_{H11H12} = J_{H11H10} = 7.7 Hz, H_{11}), 7.20 (m, H_{12} and H_{10}), 5.20 (m, H_{5a}), 4.81 (m, H_{3b}), 3.78 (dd, J_{gem} = 12.3 Hz, J_{H6aH5a} = 4.2 Hz, H_{6a}), 3.49 (d, J_{gem} = 12.2 Hz, H_{6b}), 3.40 (m, H_{4a}), 2.71 (m, H_{4b}); ms: m/z 281 (41), 238 (16), 196 (28).

Anal. Calcd. for $C_{13}H_{11}N_7O$: C, 55.52; H, 3.91; N, 34.87. Found: C, 55.39; H, 4.03; N, 34.98.

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