# 6-Amino-1,8-dihydroimidazo[4,5-*e*][1,3]diazepin-4(5*H*)-one, a ring expanded analogue of guanine

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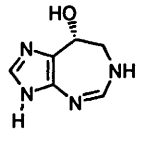
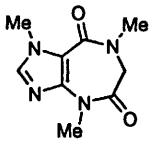
**The preparation of 6-amino-1,8-dihydroimidazo[4,5-*e*][1,3]diazepin-4(5*H*)-one (15), an analogue of guanine which has a seven-membered ring in place of the usual six-membered ring, is described. Cyclization to form the aminodiazepine ring involves reaction of amide and isothiourea groups in a suitably substituted imidazole precursor. The method is also shown to be applicable to the synthesis of an acyclonucleoside derivative (20).**

## Introduction

Purine analogues in which a seven-membered ring replaces the pyrimidine ring have aroused considerable interest since the discovery of the first such naturally occurring ring system (**1**) as the aglycon of the nucleoside antibiotic coformycin.[1] Many studies have been directed toward construction of this imidazo[4,5-*d*][1,3]diazepine ring, including a recent asymmetric synthesis.[2] The imidazo[4,5-*e*][1,4]diazepine ring system has also been extensively explored since the first report of a caffeine analogue (**2**) in 1980.[3] In contrast, imidazo[4,5-*e*]-[1,3]diazepines have received very little attention. In 1990 we reported the synthesis of the xanthine analogue **3**,[4] and the triamino compound **4** and its nucleoside were recently reported by Hosmane.[5] Herein we report the synthesis and characterization of a guanine analogue based on this ring system.



**1**



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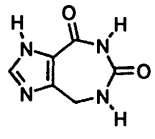

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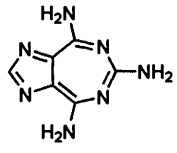
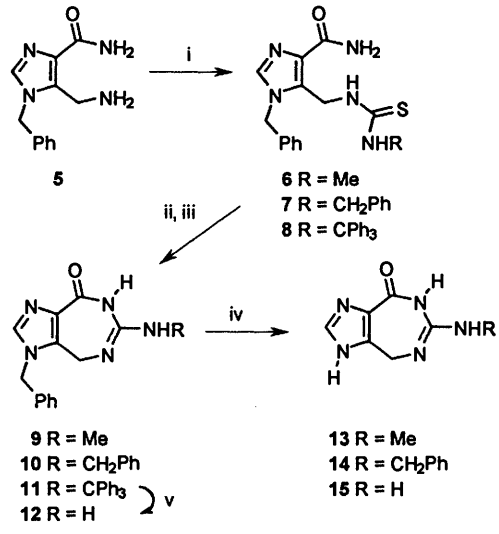


**4**

## Results and discussion

Our approach to the functionalized seven-membered ring involves ring closure of a thiourea and is analogous to a conventional approach to the six-membered ring of guanine.[6] Thus the amine **5**[4] (Scheme 1), protected on the imidazole ring with a benzyl group, was treated with methyl isothiocyanate to yield the thiourea **6**. Methylation on sulfur was achieved by treating the thiourea with sodium hydride and iodomethane in DMF. Ring closure was then most conveniently accomplished by adding another equivalent of sodium hydride to this solution and warming, although the intermediate methyl isothiourea could be isolated and treated with sodium ethoxide to give the same product. This was characterized as 1-benzyl-1,8-dihydro-6-methylaminoimidazo[4,5-*e*][1,3]diazepin-4(5*H*)-one (**9**) on the basis of proton and carbon magnetic resonance spectroscopy and elemental analysis. Comparison of the $^{13}C$ NMR spectra of thiourea **6** and diazepine **9** shows that the




**Scheme 1** *Reagents:* i, RNCS; ii, MeI, NaH; iii, NaH, heat; iv, $H_2$, $Pd(OH)_2$ on C; v, $CF_3CO_2H$

low field signal at $\delta$ 181.9 assigned to the thiocarbonyl group has been replaced by a signal at $\delta$ 149.8 consistent with the new guanidine functional group. In the proton NMR in [$^2H_6$]dimethyl sulfoxide ([$^2H_6$]DMSO), the appearance of the resonances for the methyl group as a doublet, the NH as a quartet, and the ring methylene group as a singlet confirm the tautomeric structure as that shown. Further evidence for the presence of the basic guanidine group in the product is the strong downfield shift of these signals when the spectrum is obtained in $CD_3CO_2D$. It is also of interest to note that the signals for the C-5 side chain in thiourea **6** are very broad at room temperature, presumably due to conformational isomerism, but become sharp at higher temperature. In contrast, the spectrum of the rigid diazepine **9** is sharp at room temperature. As in our earlier synthesis of the xanthine analogue,[4] catalytic hydrogenolysis over 20% palladium on carbon was used to remove the benzyl protecting group yielding diazepine **13**.

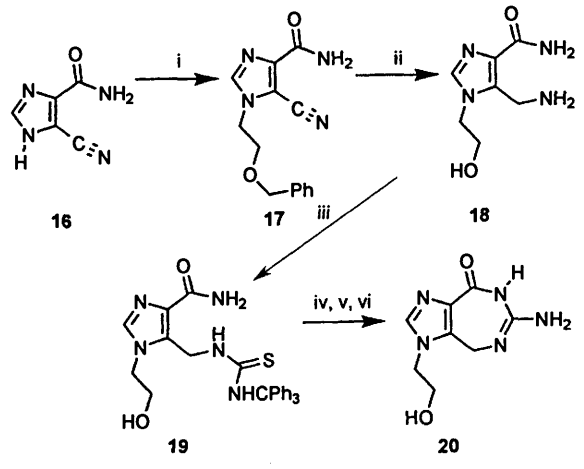
Having demonstrated that the seven-membered ring could be established in this way, we next used benzyl isothiocyanate to prepare thiourea **7**, and subjected it to ring closure by the same procedure to produce diazepine **10**. We had hoped to be able to remove both benzyl groups simultaneously to prepare the unsubstituted diazepine **15**, the desired guanine analogue, but were disappointed to find that only the benzyl group on the imidazole ring could be removed by catalytic hydrogenolysis. The 6-benzylaminodiazepine **14** was isolated and characterized. Preliminary experiments gave some indication that a poor yield

of **15** could be obtained by debenzylation with aluminum chloride,[7] but an improved procedure that might be applicable to a future nucleoside synthesis was sought.

The successful synthesis of guanine analogue **15** was accomplished using a trityl protecting group. Reaction of the amine **5** with trityl isothiocyanate gave thiourea **8** as the only product when the reaction was carried out in dioxane. In more polar solvents tritylation of the amine was a significant side reaction, as has been reported for other amines.[8] Methylation of **8** followed by ring closure gave diazepine **11**, from which the trityl group was easily removed by treatment with trifluoroacetic acid to yield the diazepine **12**.

6-Amino-1,8-dihydroimidazo[4,5-*e*][1,3]diazepin-4(5*H*)-one (**15**) was prepared from either **11** or **12** by catalytic hydrogenolysis. After separation of the catalyst, evaporation of the solvent (acetic acid), and removal of trityl alcohol if necessary, the diazepine was dissolved in water and the pH was adjusted to 10 by addition of sodium carbonate. The neutral form of the diazepine separated from the solution as a white precipitate and was isolated in moderate yield. Proton and carbon NMR spectra, and elemental analysis were consistent with the expected structure. A small sample was dissolved in dilute hydrochloric acid and titration with sodium hydroxide was used to determine two p$K_a$ values, 2.6 for the imidazole ring nitrogen and 7.2 for the acylguanidine functional group in the seven-membered ring. The latter value is comparable to the p$K_a$ of 7.0 observed for benzoylguanidine.[9] The proton NMR spectrum in [$^2H_6$]DMSO was also observed to vary with pH. Solutions of diazepine **15** in $D_2O$ were prepared at various pD values by adding $P_2O_5$ or sodium carbonate. The chemical shift of the proton at C-2 was found to be $\delta$ 7.7 at pH 10, 7.85 at pH 6, and 8.8 at pH 2. The large downfield shift between pH 6 and pH 2 is consistent with the second protonation taking place on the imidazole ring nitrogen. In our initial preparations of **15** we had observed large differences in the chemical shift assigned to H-2 depending on the method used for isolation of the diazepine. This was presumably due to the presence of mixtures of protonated and unprotonated species. Eventually we discovered that the most effective method for isolation of pure diazepines was precipitation from sodium carbonate treated solutions.

Preparation of a simple acyclonucleoside analogue of **15** was accomplished by applying the same series of reactions to the (2-hydroxyethyl)imidazole **18** (Scheme 2). This was prepared from




**Scheme 2** *Reagents:* i, $PhCH_2OCH_2CH_2OTs$, $K_2CO_3$; ii, $H_2$, Pd on C; iii, $Ph_3CNCS$; iv, MeI, NaH; v, NaH, heat; vi, $CF_3CO_2H$

5-cyanoimidazole-4-carboxamide (**16**) by alkylation with benzyloxyethyl toluene-*p*-sulfonate to give **17**, and reduction of **17** by catalytic hydrogenation. The regiochemistry of the alkylation was confirmed by $^{13}C$ NMR.[10] The benzyl group was required to prevent intramolecular reaction of a free hydroxy group with the cyano group under the basic reaction conditions used for the alkylation. Reaction of amine **18** with trityl isothiocyanate gave thiourea **19** as the only product in excellent yield when the reaction was carried out in dioxane. Ring closure, under the conditions described previously, and detritylation with trifluoroacetic acid gave the (2-hydroxyethyl)diazepine **20**.

## Experimental

Melting points were obtained on a Laboratory Devices Mel-Temp apparatus and are uncorrected. NMR spectra were obtained on a Varian VXR-300 spectrometer. Chemical shifts ($\delta$) are reported in ppm downfield from $Me_4Si$ and *J* values are given in Hz. Microanalyses were performed by Desert Analytics, Tucson, Arizona.

### *N*-(1-Benzyl-4-carbamoylimidazol-5-yl)methyl-*N'*-methylthiourea 6

Amine **5**[4] (3.4 g, 15 mmol) was dissolved in *N*,*N*-dimethylformamide (DMF) (50 ml), methyl isothiocyanate (1.5 g, 20 mmol) was added, and the solution was stirred at room temperature for 1.5 h. DMF was evaporated under vacuum and the residue was crystallized from aqueous ethanol to yield thiourea **6** (4.3 g, 95%), mp 205–206 °C, (Found: C, 55.4; H, 5.7; N, 23.0. Calc. for $C_{14}H_{17}N_5OS$: C, 55.4; H, 5.65; N, 23.1%); $\delta_H$(300 MHz; [$^2H_6$]DMSO; 70 °C) 2.81 (3 H, d, *J* 5, $CH_3$), 4.69 (2 H, d, *J* 6, $CH_2NH$), 5.43 (2 H, s, $PhCH_2$), 7.18–7.38 (7 H, $C_6H_5$ and 2 × NH), 7.81 (1 H, s, 2-H), 7.90 (2 H, br, 2 × NH); $\delta_C$(75 MHz; [$^2H_6$]DMSO; 70 °C) 30.8, 35.7, 47.6, 126.8, 127.6, 128.6, 131.9, 132.4, 136.8, 137.2, 165.6, 181.8.

### *N*-(1-Benzyl-4-carbamoylimidazol-5-yl)methyl-*N'*-benzylthiourea 7

The acetic acid salt of amine **5** (2.9 g, 10.4 mmol) was dissolved in water (80 ml) and ethanol (120 ml), benzyl isothiocyanate (5.5 ml, 42 mmol) was added, and the mixture was stirred at room temperature for 16 h. The precipitate was collected by filtration, washed with ethanol, and dried to yield thiourea **7** (3.67 g, 90%). An analytical sample, mp 179–181 °C, was obtained by recrystallization from aqueous ethanol (Found: C, 63.4; H, 5.3; N, 18.8. Calc. for $C_{20}H_{21}N_5OS$: C, 63.3; H, 5.6; N, 18.5%); $\delta_H$(300 MHz; [$^2H_6$]DMSO; 70 °C) 4.65 (2 H, d, *J* 6, $NHCH_2Ph$), 4.85 (2 H, d, *J* 6, $CH_2NH$), 5.44 (2 H, s, $PhCH_2$), 7.13–7.38 (12 H, 2 × $C_6H_5$ and 2 × NH), 7.73 (1 H, s, 2-H), 7.91 (1 H, br, NH), 8.40 (1 H, br, NH); $\delta_C$(75 MHz; [$^2H_6$]DMSO; 70 °C) 35.8, 47.0, 47.6, 126.3, 126.6, 126.8, 127.3, 127.7, 128.3, 131.7, 132.5, 136.4, 136.8, 138.6, 165.1, 181.7.

### *N*-(1-Benzyl-4-carbamoylimidazol-5-yl)methyl-*N'*-tritylthiourea 8

Amine **5** (1.5 g, 6.6 mmol) was dissolved in warm dioxane (90 ml). After allowing the solution to cool, trityl isothiocyanate[8] (6.0 g, 19.8 mmol) was added and the solution was stirred at room temperature for 3 h. The white precipitate was collected by filtration and recrystallized from ethanol to yield thiourea **8** (2.8 g, 81%), mp 205–206 °C (Found: C, 72.0; H, 5.5; N, 13.1. Calc. for $C_{32}H_{29}N_5OS$: C, 72.3; H, 5.5; N, 13.2%); $\delta_H$(300 MHz; [$^2H_6$]DMSO) 4.75 (2 H, br d, $CH_2NH$), 5.35 (2 H, s, $PhCH_2$), 7.11–7.36 (23 H, 4 × $C_6H_5$ and 3 × NH), 7.74 (1 H, s, 2-H), 8.22 (1 H, br, NH); $\delta_C$(75 MHz; [$^2H_6$]DMSO) 36.5, 47.8, 71.3, 126.4, 126.6, 127.4, 127.5, 128.5, 128.6, 131.7, 133.2, 136.8, 136.9, 143.9, 164.7, 181.1.

### 1-Benzyl-1,8-dihydro-6-methylaminoimidazo[4,5-*e*][1,3]-diazepin-4(5*H*)-one 9

The thiourea **6** (0.9 g, 3 mmol) was dissolved in DMF (30 ml). Sodium hydride (60%, 0.13 g, 3.3 mmol) and methyl iodide (0.3 ml, 4.8 mmol) were added and the mixture was stirred at room temperature for 1 h. Excess methyl iodide was evaporated *in*

*vacuo* and more sodium hydride (0.15 g, 3.8 mmol) was added. The solution was stirred at 70 °C for 2 h then concentrated *in vacuo*. Water was added to the residue and the precipitate was collected, washed with water, and dried to yield diazepine **9** (0.5 g, 62%). An analytical sample, mp 246–247 °C, was obtained by crystallization from ethanol after addition of dilute aqueous sodium carbonate (Found: C, 62.5; H, 5.6; N, 26.2. Calc. for $C_{14}H_{15}N_5O$: C, 62.4; H, 5.6; N, 26.0%); $\delta_H$(300 MHz; [$^2H_6$]DMSO) 2.49 (3 H, d, *J* 5, N-Me), 4.22 [2 H, s, C(8)$H_2$], 5.30 (2 H, s, PhC$H_2$), 5.71 (1 H, q, *J* 5, NHMe), 7.18–7.39 (5 H, $C_6H_5$), 7.84 (1 H, s, 2-H), 9.19 [1 H, br, N(5)H]; $\delta_H$(300 MHz; $CD_3CO_2D$) 2.99 (3 H, s, N-Me), 4.68 [2 H, s, C(8)$H_2$], 5.40 (2 H, s, PhC$H_2$), 7.22–7.44 (5 H, $C_6H_5$), 8.08 (1 H, s, 2-H); $\delta_C$(75 MHz; [$^2H_6$]DMSO) 28.6, 38.9, 47.3, 126.9, 127.7, 128.7, 131.7, 136.9, 138.3, 139.2, 149.8, 162.4; $\delta_C$(75 MHz; $CD_3CO_2D$) 29.7, 36.3, 50.1, 128.0, 129.5, 130.2, 131.8, 135.7, 137.6, 141.7, 155.0, 161.0.

**1-Benzyl-6-benzylamino-1,8-dihydroimidazo[4,5-*e*][1,3]-diazepin-4(5*H*)-one 10**

To a solution of the thiourea **7** (1.14 g, 3 mmol) and sodium hydride (60%, 0.2 g, 5 mmol) in DMF (30 ml) was added methyl iodide (0.3 ml, 4.8 mmol). The solution was stirred at room temperature for 1 h then concentrated *in vacuo*. The residue was dissolved in 2 M sodium ethoxide in ethanol (30 ml). The solution was heated under reflux for 1 h. The solvent was evaporated under vacuum and the residue was triturated with water. The solid was collected by filtration, washed with water, and dried to yield diazepine **10** (1.17 g, 99%), mp 240 °C (Found: C, 69.3; H, 5.8; N, 19.9. Calc. for $C_{20}H_{19}N_5O$: C, 69.55; H, 5.5; N, 20.2%); $\delta_H$(300 MHz; [$^2H_6$]DMSO) 4.18 [2 H, d, *J* 5, N(6)C$H_2$], 4.23 [2 H, s, C(8)$H_2$], 5.30 [2 H, s, N(1)C$H_2$], 6.22 [1 H, t, *J* 5, N(6)H], 7.16–7.36 (10 H, 2 × $C_6H_5$), 7.84 (1 H, s, 2-H), 9.20 [1 H, br s, N(5)H]; $\delta_C$(75 MHz; [$^2H_6$]DMSO) 38.8, 45.2, 47.4, 126.6, 126.9, 127.2, 127.7, 128.1, 128.8, 131.7, 137.0, 138.5, 139.2, 139.7, 149.1, 162.5.

**1-Benzyl-1,8-dihydro-6-tritylaminoimidazo[4,5-*e*][1,3]-diazepin-4(5*H*)-one 11**

This compound (3.37 g, 86% yield) was prepared from thiourea **8** (4.2 g, 7.9 mmol) by the same procedure used to prepare **9**. An analytical sample, mp 208–209 °C, was obtained by recrystallization from aqueous ethanol (Found: C, 75.9; H, 5.65; N, 13.9. Calc. for $C_{32}H_{27}N_5O{\cdot}\frac{1}{2}H_2O$: C, 75.9; H, 5.6; N, 13.8); $\delta_H$(300 MHz; [$^2H_6$]DMSO) 3.70 [2 H, s, C(8)$H_2$], 5.21 (2 H, s, PhC$H_2$), 6.87 [1 H, br s, N(6)H], 6.97–7.32 (20 H, 4 × $C_6H_5$), 7.78 (1 H, s, 2-H), 9.47 [1 H, br s, N(5)H]; $\delta_C$(75 MHz; [$^2H_6$]DMSO) 38.7, 46.9, 70.5, 126.0, 126.3, 127.1, 127.4, 128.6, 128.7, 131.5, 137.0, 138.5, 138.8, 145.4, 146.8, 162.6.

**6-Amino-1-benzyl-1,8-dihydroimidazo[4,5-*e*][1,3]diazepin-4(5*H*)-one 12**

Trityl derivative **11** (1.5 g, 3 mmol) was dissolved in trifluoroacetic acid (15 ml) and the solution was stirred at room temperature for 16 h. The solvent was evaporated, water was added, and the solid was removed by filtration. The pH of the filtrate was adjusted to 10 by adding sodium hydroxide. The precipitate was collected by filtration, washed with water, and dried to yield diazepine **12** (0.6 g, 78%), mp 294–295 °C (Found: C, 61.2; H, 5.1; N, 27.5. Calc. for $C_{13}H_{13}N_5O$: C, 61.2; H, 5.1; N, 27.4%); $\delta_H$(300 MHz; $CD_3CO_2D$) 4.63 [2 H, s, C(8)$H_2$], 5.40 (2 H, s, PhC$H_2$), 7.22–7.43 (5 H, $C_6H_5$), 8.08 (1 H, s, 2-H): $\delta_C$(75 MHz; $CD_3CO_2D$) 36.2, 50.1, 128.0, 129.5, 130.2, 131.6, 135.8, 137.3, 141.7, 156.1, 160.9.

**1,8-dihydro-6-methylaminoimidazo[4,5-*e*][1,3]diazepin-4(5*H*)-one 13**

Benzyl derivative **9** (0.5 g, 1.9 mmol) was dissolved in glacial acetic acid (100 ml), 20% palladium hydroxide on carbon (0.5 g) was added, and the mixture was shaken under hydrogen (55 psi) for 48 h. The catalyst was removed by filtration and the solvent was evaporated under vacuum. The residual glass was dissolved in the minimum volume of water and the pH of the solution was adjusted to 10 by addition of solid sodium carbonate. The crystalline product which separated after standing was filtered, washed with cold water, and dried to yield diazepine **13** (0.21 g, 64%), mp 246 °C (Found: C, 47.2; H, 5.15; N, 39.4. Calc. for $C_7H_9N_5O$: C, 46.9; H, 5.1; N, 39.1%); $\delta_H$(300 MHz; $CD_3CO_2D$) 3.02 (3 H, s, $CH_3$), 4.76 [2 H, s, C(8)$H_2$], 8.11 (1 H, s, 2-H); $\delta_C$(75 MHz; $CD_3CO_2D$) 29.7, 39.4, 124.4, 140.7, 143.9, 154.9, 159.3.

**6-Benzylamino-1,8-dihydroimidazo[4,5-*e*][1,3]diazepin-4(5*H*)-one 14**

This compound (0.45 g, 59% yield) was prepared from benzyl derivative **10** (1.04 g, 3 mmol) by the same method used for the preparation of **13**. The analytical sample had mp 220 °C (decomp.) (Found: C, 60.9; H, 5.1; N, 27.1. Calc. for $C_{13}H_{13}N_5O$: C, 61.2; H, 5.1; N, 27.4%); $\delta_H$(300 MHz; $CD_3CO_2D$) 4.58 (2 H, s, PhC$H_2$), 4.70 [2 H, s, C(8)$H_2$], 7.22–7.38 (5 H, $C_6H_5$), 8.11 (1 H, s, 2-H); $\delta_C$(75 MHz; $CD_3CO_2D$) 39.4, 47.4, 124.6, 128.6, 129.1, 129.8, 135.5, 140.8, 144.1, 154.3, 159.4.

**6-Amino-1,8-dihydroimidazo[4,5-*e*][1,3]diazepin-4(5*H*)-one 15**

This compound (0.18 g, 48% yield) was prepared from the fully protected compound **11** by the same method used for the preparation of **13**. The analytical sample had mp 272 °C (decomp.) (Found: C, 43.75; H, 4.25; N, 42.7. Calc. for $C_6H_7N_5O$: C, 43.6; H, 4.3; N, 42.4%); $\delta_H$(300 MHz; $CD_3CO_2D$) 4.71 [2 H, s, C(8)$H_2$], 8.11 (1 H, s, 2-H); $\delta_C$(75 MHz; $CD_3CO_2D$) 39.4, 124.6, 140.8, 143.0, 155.9, 159.2.

**1-(2-Benzyloxyethyl)-5-cyanoimidazole-4-carboxamide 17**

5-Cyanoimidazole-4-carboxamide **16** (3.8 g, 28 mmol) was dissolved in DMF (60 ml). Potassium carbonate (7.6 g) and 2-benzyloxyethyl toluene-*p*-sulfonate [11] (10.3 g, 33.6 mmol) were added, and the mixture was stirred at room temperature for 16 h. The mixture was poured into ice–water (120 ml). The white precipitate was collected, washed with water, and dried to yield **17** (5.35 g, 71%). An analytical sample, mp 184–185 °C, was obtained after recrystallization from ethanol (Found: C, 61.9; H, 5.1; N, 20.65. Calc. for $C_{14}H_{14}N_4O_2$: C, 62.2; H, 5.2; N, 20.7%); $\delta_H$(300 MHz; [$^2H_6$]DMSO) 3.75 (2 H, t, *J* 5, $CH_2CH_2O$), 4.35 (2 H, t, *J* 5, $CH_2CH_2O$), 4.48 (2 H, s, PhC$H_2$), 7.19–7.34 (5 H, $C_6H_5$), 7.58 (1 H, br, NH), 7.70 (1 H, br, NH), 8.09 (1 H, s, 2-H); $\delta_C$(75 MHz; [$^2H_6$]DMSO) 46.4, 67.6, 71.6, 105.7, 110.6, 127.1, 127.4, 128.1, 137.7, 141.2, 144.3, 161.4.

**5-Aminomethyl-1-(2-hydroxyethyl)imidazole-4-carboxamide 18**

Cyanoimidazole **17** (2.4 g, 9 mmol) was dissolved in glacial acetic acid (100 ml). 10% Palladium on carbon (0.4 g) was added and the mixture was shaken under hydrogen (40 psi) for 16 h. The mixture was filtered, and the filtrate was concentrated. The residue was coevaporated with water and the solid (2.0 g, 89%) was recrystallized from aqueous ethanol to give an analytical sample of amine **18** as its acetate salt, mp 199–201 °C (Found: C, 44.0; H, 6.7; N, 22.7. Calc. for $C_9H_{16}N_4O_4$: C, 44.3; H, 6.6; N, 22.9%); $\delta_H$(300 MHz; [$^2H_6$]DMSO) 1.85 (3 H, s, $CH_3$-$CO_2^-$), 3.63 (2 H, t, *J* 5, $CH_2CH_2OH$), 3.76 (br, $NH_3^+$ and OH), 3.95 (2 H, s, $CH_2NH_3^+$), 4.07 (2 H, t, *J* 5, $CH_2CH_2OH$), 7.07 (1 H, br s, NH), 7.32 (1 H, br s, NH), 7.58 (1 H, s, 2-H); $\delta_C$(75 MHz; [$^2H_6$]DMSO) 21.5, 33.4, 46.7, 60.7, 131.3, 136.1, 136.3, 165.3, 172.2.

***N*-[4-Carbamoyl-1-(2-hydroxyethyl)imidazol-5-yl]methyl-*N'*-tritylthiourea 19**

This compound (6.62 g, 98% yield) was prepared from the amine **18** by the same method used for the preparation of **8**. The analytical sample had mp 196–197 °C (Found: C, 66.5; H, 5.5; N, 14.3. Calc. for $C_{27}H_{27}N_5O_2S$: C, 66.8; H, 5.6; N, 14.4); $\delta_H$(300 MHz; [$^2H_6$]DMSO) 3.54 (2 H, q, *J* 5, $CH_2CH_2OH$), 4.09 (2 H, t, *J* 5, $CH_2CH_2OH$), 4.82 (2 H, br d, $CH_2NH$), 4.94 (1

H, t, *J* 5, OH), 7.05–7.28 (18 H, 3 × $C_6H_5$ and 3 × NH), 7.57 (1 H, s, 2-H), 8.20 (1 H, br, NH); $\delta_C$(75 MHz; [$^2H_6$]DMSO) 36.7, 47.2, 60.3, 71.3, 126.5, 127.4, 128.5, 131.7, 132.6, 136.8, 143.9, 164.8, 181.0.

**6-Amino-1,8-*dih*ydro-1-(2-hydroxyethyl)imidazo[4,5-*e*][1,3]-diazepin-4(5*H*)-one 20**

This compound was prepared in 40% overall yield from the thiourea **19** by the same reaction sequence used for the preparation of **12**. The analytical sample had mp 278 °C (decomp.) (Found: C, 44.3; H, 5.4; N, 32.2. Calc. for $C_8H_{11}N_5O_2 \cdot \frac{1}{2}H_2O$: C, 44.0; H, 5.5; N, 32.1%); $\delta_H$(300 MHz; $CD_3CO_2D$) 3.92 (2 H, t, *J* 5, $CH_2CH_2O$), 4.32 (2 H, t, *J* 5, $CH_2CH_2O$), 4.76 [2 H, s, C(8)$H_2$], 8.06 (1 H, s, 2-H); $\delta_C$(75 MHz; $CD_3CO_2D$) 36.4, 48.8, 62.0, 131.1, 138.5, 142.0, 156.4, 161.2.

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