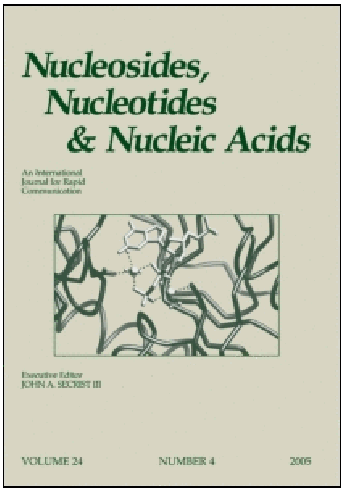

Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

A Short Synthesis of a Novel Ring-Expanded Purine and Its Nucleoside Analogue Containing the Imidazo[4,5-*e*][1,3]diazepine Ring Skeleton with Multiple Amino Substituents Attached to the 7-Membered Ring

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To cite this Article Wang, L. , Bhan, A. , Hosmane, R. S. and Guiles, R. D.(1994) 'A Short Synthesis of a Novel Ring-Expanded Purine and Its Nucleoside Analogue Containing the Imidazo[4,5-*e*][1,3]diazepine Ring Skeleton with Multiple Amino Substituents Attached to the 7-Membered Ring', Nucleosides, Nucleotides and Nucleic Acids, 13: 10, 2307 — 2320
To link to this Article: DOI: 10.1080/15257779408013222
URL: http://dx.doi.org/10.1080/15257779408013222

NUCLEOSIDES & NUCLEOTIDES, 13(10), 2307-2320 (1994)

A SHORT SYNTHESIS OF A NOVEL RING-EXPANDED PURINE AND ITS NUCLEOSIDE ANALOGUE CONTAINING THE IMIDAZO[4,5-*e*][1,3]DIAZEPINE RING SKELETON WITH MULTIPLE AMINO SUBSTITUENTS ATTACHED TO THE 7-MEMBERED RING

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ABSTRACT

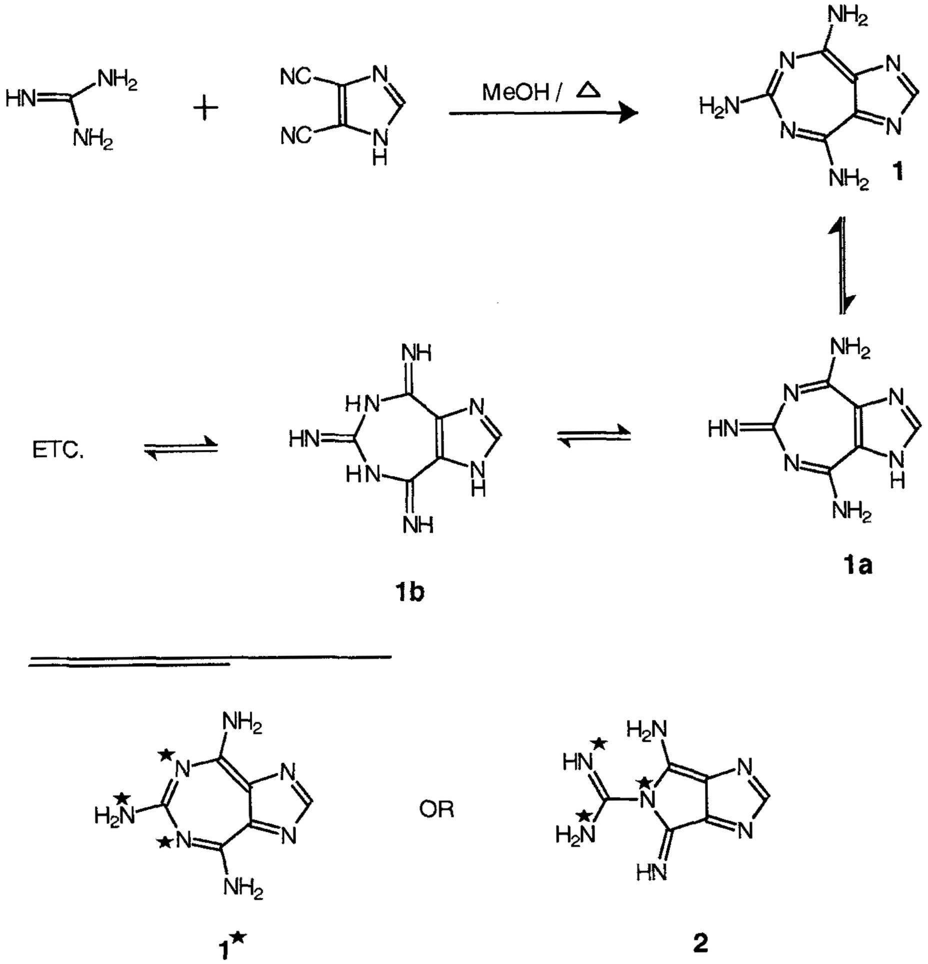
*The synthesis of 4,6,8-triaminoimidazo[4,5-e][1,3]diazepine (**1**) and its nucleoside analogue (**6**) are reported. The heterocycle was prepared in a single step by condensation of 4,5-dicyanoimidazole with guanidine. The 5,7-fused ring structure of **1** was distinguished from the other possible 5:5-fused isomer **2** by preparing the ^{15}N-labeled heterocycle (1^*) and exploring its ^{15}N-^{1}H coupling patterns in both ^{1}H and ^{15}N NMR spectra. These spectral patterns also enabled establishment of the triamino tautomeric form of **1** as assigned. Compound **1**, a novel ring-expanded ("fat") analogue of purine, is anticipated to be planar and aromatic as predicted by molecular modeling. The 1-benzyl analogue (**4**), a protocol for the ribosyl analogue **6**, was similarly prepared from 1-benzyl-4,5-dicyanoimidazole. The nucleoside **6** was prepared by the modified Vorbrüggen ribosylation of **1**. The position of ribosylation was unequivocally established by an unambiguous synthesis of **6** from condensation of 1-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl)-4,5-dicyanoimidazole (**7**) with guanidine in a solution of sodium methoxide in methanol. The nucleoside **7** was prepared by the Vorbrüggen ribosylation of 4,5-dicyanoimidazole.*

INTRODUCTION

Ring-expanded purine and ring-contracted pyrimidine nucleosides/-tides are potentially useful probes for nucleic acid metabolism, structure, and function. With their structural resemblance to natural purines or pyrimidines, they are a rich source of substrates/inhibitors of enzymes of nucleic acid metabolism and of those requiring energy cofactors ATP, CTP, etc. With their "fatter" or "slimmer" skeletal features as contrasted with the natural counterparts, these molecules may also be useful for investigations of steric and conformational constraints of nucleic acid double helices. Furthermore, from a chemical standpoint, studies relating to their structure, stability, aromaticity, acid-base property, and tautomerism would be interesting and rewarding. To this end, we have been pursuing the synthesis of a number of ring-expanded[1] and ring-contracted[2] purines and pyrimidine as well as their nucleoside and nucleotide analogues.

Most of the ring-expanded or ring-contracted purines or primidines that we have reported so far are xanthine or uracil analogues, bearing oxo functionalities in the 7- or 5-membered ring, respectively. Our earlier attempts to synthesize ring-expanded adenine analogues possessing amino substituents in the 7-membered ring only led to some novel opportunistic rearrangements.[3] We report herein our first successful synthesis of a 5:7-fused ring-expanded purine analogue that has multiple amino substituents attached to the 7-membered ring. The compound is highly stable, crystalline, is predicted to be flat by molecular modeling (QUANTA/ CHARMm),[4] and is aromatic by Hückel standards ($4n + 2\ \pi$ rule). By contrast, all of the ring-expanded heterocycles and nucleosides that we have hitherto reported[1] bear a puckered 7-membered ring. Also reported here is the synthesis of a nucleoside (**6**) derived from the above heterocycle, with a ribosyl moiety attached to the imidazole ring.

The target heterocycle, 4,6,8-triaminoimidazo[4,5-*e*][1,3]diazepine (**1**), was prepared in a single step by condensation of 4,5-dicyanoimidazole with guanidine (**Scheme I**). Initially, it was difficult to distinguish the product structure **1** from that of several other possible tautomeric forms, *e.g.* **1a** and **1b**, based on amino resonances in ^{1}H NMR alone. Although the amino groups appeared as three distinct singlets in the 7-8 δ region, each integrating for two protons, the usual peak broadning associated with amino proton absorptions did not immediately preclude the possibility of other tautomeric forms besides **1**, and for that matter, a possible isomeric structure **2** that has a unique, 5:5-fused, pyrrolo[4,5-*c*]-



SCHEME I

imidazole ring system. The tautomeric and isomeric ambiguities were, however, resolved by the following ^{15}N NMR studies.

Guanidine that had all three nitrogens labeled with ^{15}N, each with a 33.33% enrichment, was prepared by reaction of cyanoguanidine with $^{15}NH_4NO_3$ using the literature procedure for the unlabeled compound.[5] The labeled guanidine was then condensed in the usual manner with 4,5-dicyanoimidazole to obtain the labeled product **1***. The ^{1}HNMR of **1*** (see **Figure 1B**) indicated that while the two

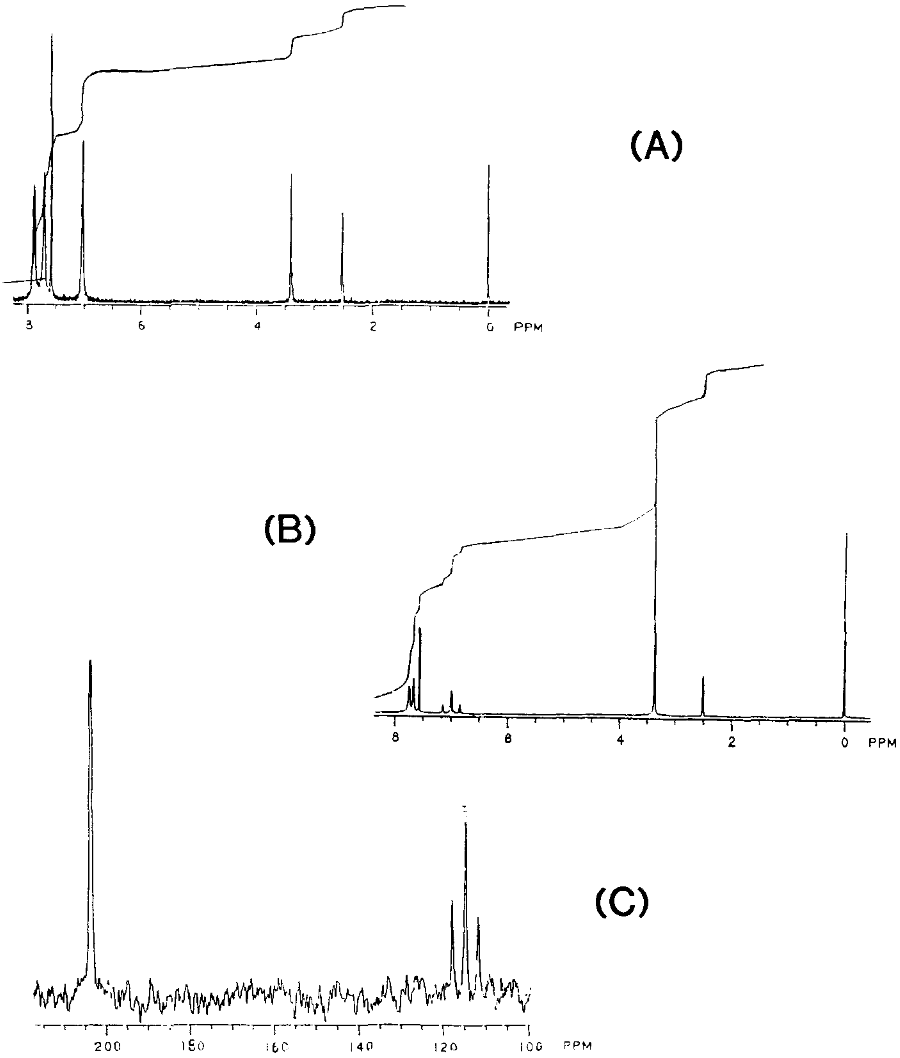
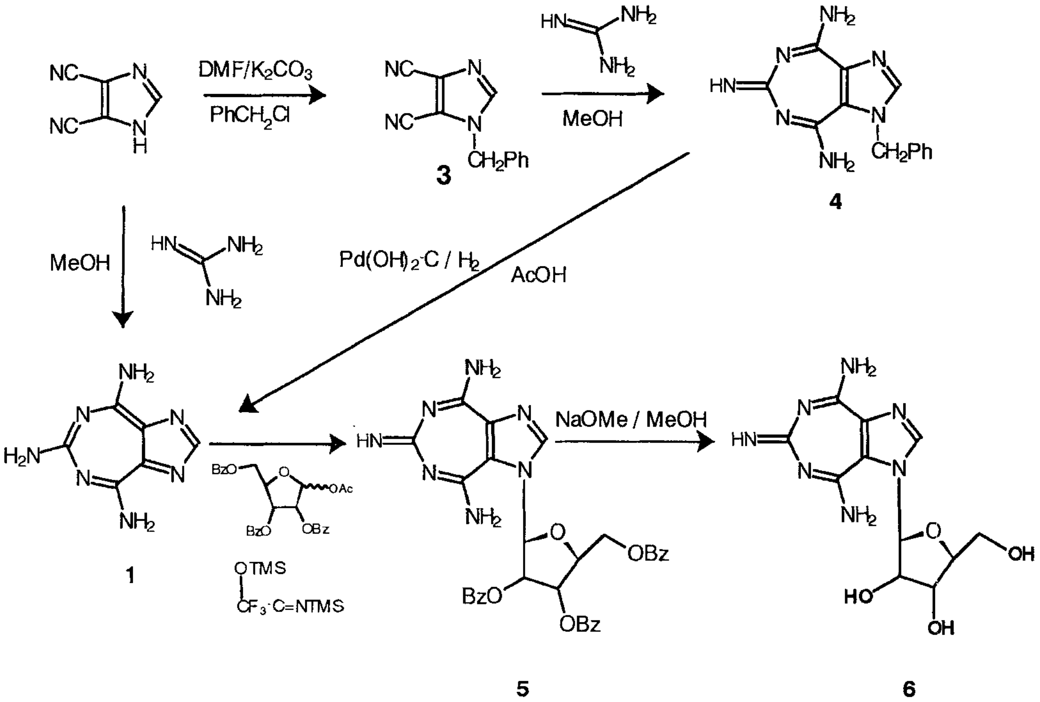


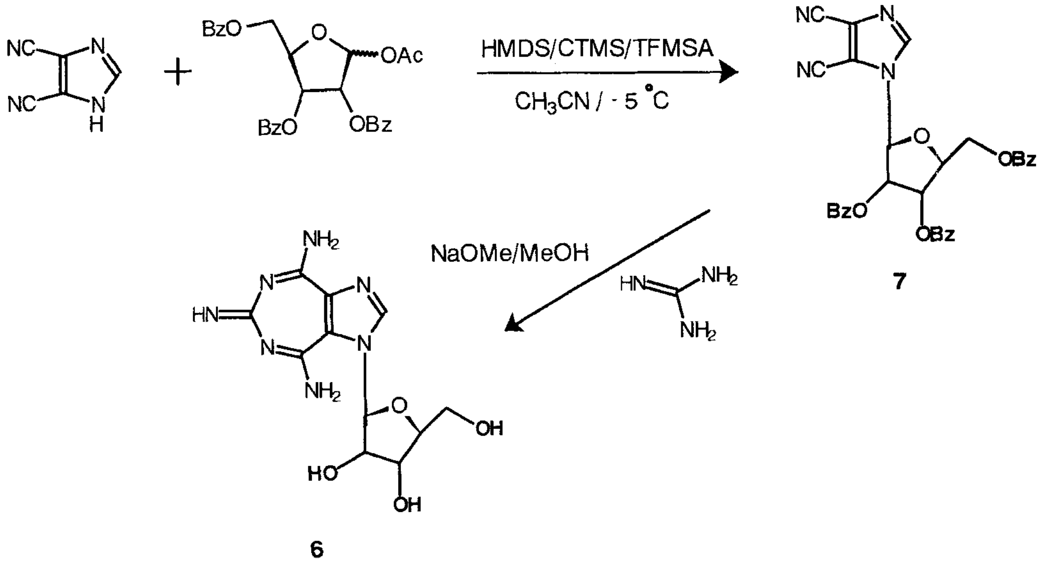
Figure 1: (**A**) The 300 MHz ^{1}H NMR of unlabeled **1**, (**B**) The 300 MHz ^{1}H NMR of ^{15}N labeled **1** with labeled N atoms shown with asterisks (see **Scheme I**), and (**C**) The 30 MHz ^{15}N NMR of ^{15}N labeled **1** with labeled N atoms shown with asterisks.

amino singlets of the original unlabeled material (**Figure 1A**) were still present at δ 7.66 and 7.74, the one in the higher region at δ 6.99 was now flanked by a smaller peak on either side, equidistant (~45 Hz) from the center peak. The combined peak integrations of the two small peaks corresponded to ~ one-third of the peak integration of the center peak. Apparently, the two small peaks are a doublet formed by the ^{15}N-^{1}H coupling of the $^{15}NH_2$ group with a coupling constant of $J = 90$ Hz. The observed relative peak integration of the doublet with respect to the center peak is as anticipated from the 33% ^{15}N-enrichment of the amino nitrogen atom. These results are consistent with structure **1*** but not with tautomers **1a*** or **1b***, or the isomer **2**. While structure **1a*** would also reveal a doublet centered around a singlet, the peak integration of the doublet would be be only half (i.e. one-sixth of the center peak) of what was actually observed. Similarly, structure **1b*** would have shown three doublets arising from ^{15}N-^{1}H coupling, each with a center peak corresponding to an unlabeled NH. Isomer **2**, on the other hand, would give rise to two additional doublets as compared with the unlabeled material, one with a one-third peak integration with respect to the center peak, and the other with a one-sixth. Finally, the ^{15}N NMR of the product (see **Figure 1C**) corroborated the above assignments by revealing a triplet at δ 114.57 corresponding to the labeled amino group, and a singlet at δ 203.46 corresponding to the two labeled ring nitrogen atoms. It should also be pointed out that while compound **1**, with its 10 π electrons, is aromatic by the Hückel rules, compound **2**, by contrast, would be considered antiaromatic as it has only 8 π electrons in its rings.

In order to serve as a protocol for the corresponding nucleoside analogues of **1**, 4,8-diamino-1-benzyl-6-iminoimidazo[4,5-*e*][1,3]diazepine (**4**) was analogously prepared (**Scheme II**) by condensation of 1-benzyl-4,5-dicyanoimidazole (**3**) with guanidine. This unambiguous synthesis of **4** from **3** was preferred over direct benzylation of **1** which could potentially yield multiple alkylation products. Compound **4** was conveniently debenzylated by catalytic hydrogenation in glacial acetic acid to give **1**. The modified Vorbrüggen ribosylation[1c,6] of **1**, using 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose, *N*,*O*-bis(trimethylsilyl)trifluoroacetamide and trimethylsilyl trifluoromethanesulfonate (TMS triflate), afforded the OH-protected nucleoside (**5**), which upon treatment with sodium methoxide/ methanol, gave the desired ribonucleoside (**6**). The structure of **6** was consistent with its spectral and microanalytical data. However, the depicted tautomeric form of **6** is only tentative as it could not be firmly established based solely on its ^{1}H NMR spectrum (deuterated dimethyl sulfoxide), which exhibited three D_2O-exchangeable singlets, two integrating for one proton each, and the third integrating for three protons.



SCHEME II



SCHEME III

The position of the sugar attachment in **6** was unequivocally established by an alternative synthesis of **6** from the reaction of 2',3',5'-tri-*O*-benzoyl-1-β-D-ribofuranosylimidazole-4,5-dinitrile (**7**) (**Scheme III**) with guanidine in a solution of sodium methoxide/methanol. The precursor **7** was prepared by the Vorbrüggen ribosylation[6] of 4,5-dicyanoimidazole with 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose.

EXPERIMENTAL

^{1}H, ^{13}C, and ^{15}N NMR spectra were recorded on a GE QE-300 instrument. The reported spectral data are relative to Me_4Si as an internal reference standard for ^{1}H and ^{13}C NMR spectra. For ^{15}N NMR, $^{15}NH_4Cl$ was employed as an external reference standard, and the chemical shifts are expressed after conversion to the liquid NH_3 scale, δ=0. Multiplicity is designated by the abbreviation, s = singlet, d = doublet, dd = doublet of doublets, t = triplet, q = quartet, m = multiplet, br = broad, app = apparent. Infrared spectra were obtained on a Perkin-Elmer 1420 ratio recording instrument. Ultraviolet spectra were recorded on a Gilford Response UV/VIS spectrophotometer. Elemental microanalyses were performed by Atlantic Microlab, Inc., Norcross, Georgia. Melting points are uncorrected. Dry solvents were prepared as follows: methanol, ether, toluene, and xylenes were distilled over sodium; acetonitrile was distilled from CaH_2, followed by distillation over P_2O_5.

4,6,8-Triaminoimidazo[4,5-*e*][1,3]diazepine (1)

Method A: By Condensation of 4,5-Dicyanoimidazole with Guanidine: Guanidine was liberated from guanidine hydrochloride (1.15 g, 12 mmol) by addition of a freshly prepared solution of sodium methoxide in methanol from sodium (0.28 g, 12 mg.atom), and stirring with ice-water cooling for 30 minutes. The precipitated sodium chloride was filtered off, and the filtrate was added to the solution of 4,5-dicyanoimidazole (1.18 g, 10 mmol) in methanol (25 mL). The reaction mixture was heated to reflux for 20 hours and cooled to room temperature. The solid separated was collected by filtration, and recrystallized from methanol. Yield 1.72 g (81%), mp >250 °C: ^{1}H NMR (DMSO-d_6) δ 7.73 (br s, 2 H, NH_2, exchangeable with D_2O); 7.65 (br s, 2 H, NH_2, exchangeable with D_2O), 7.55 (s, 1 H, imidazole CH), 6.99 (s, 2 H, NH_2, exchangeable with D_2O); ^{13}C NMR (DMSO-d_6) δ 164 (C=NH), 160 (C=N), 150 (C=C), 136.5 (imidazole CH); IR (KBr) υ_{max} 3300, 3010, 1600-1400 cm^{-1}.

Anal. Calcd. for $C_6H_7N_7$: C, 40.68; H, 3.98; N, 55.34. Found: C, 40.67; H, 4.02; N, 55.28.

Method B: By Debenzylation of 4,8-Diamino-1-benzyl-6H-6-imino-imidazo[4,5-e][1,3]diazepine (4) (vide infra): 4,8-Diamino-1-benzyl-6*H*-6-iminoimidazo[4,5-*e*][1,3]diazepine (**4**) (0.54 g, 2 mmol) was dissolved in glacial acetic acid (15 mL) in a hydrogenation bottle. Palladium hydroxide on carbon (20%, 80 mg) was added to the above solution, and the mixture was hydrogenated in a Parr hydrogenator at 40 psi for 16 hours. The catalyst was removed by filtration through Celite, and was washed with acetic acid (5 mL). The filtrate, along with the washings, was evaporated to dryness under reduced pressure to obtain a colorless residue. The residue was dissolved in cold water, filtered, and the filtrate was evaporated under reduced pressure. The resulting white solid was recrystallized from water. Yield 0.23 g, 64%, mp > 250 °C.

The spectral and analytical data of this compound were consistent with those of the compound obtained above by Method A.

^{15}N-Labeled 4,6,8-Triaminoimidazo[4,5-*e*][1,3]diazepine (1*)

^{15}N-Labeled guanidine nitrate, with a 33% ^{15}N enrichment at each of the guanidinium nitrogen atom [$^*NH_2$-C(=*NH)-$^*NH_2$•HNO_3], was prepared by the reaction of cyanoguanidine with 99% ^{15}N-enriched $^*NH_4NO_3$, employing the literature procedure for the unlabeled compound.[5] This labeled guanidine nitrate was employed in place of guanidine hydrochloride for condensation with 4,5-dicyanoimidazole to prepare **1***, using Method A described above.

4,8-Diamino-1-benzyl-6*H*-6-iminoimidazo[4,5-*e*][1,3]diazepine (4)

(a) 1-Benzyl-4,5-dicyanoimidazole (3): 4,5-Dicyanoimidazole (5.0 g, 42 mmol) was placed in a 250-mL three-necked, round-bottomed flask, equipped with a magnetic stirrer, a reflux condenser, a thermometer, and a $CaCl_2$ guard tube.

The solid was dissolved by addition of dimethylformamide (100 mL) with stirring. Anhydrous potassium carbonate (7.5 g, 54 mmol) was added slowly while stirring, followed by the addition of benzyl chloride (6.2 mL, 53 mmol), and the mixture was stirred at room temperature overnight. Then the reaction mixture was heated to 75 °C, and was allowed to stir at that temperature for 20 hours. The reaction mixture was cooled to room temperature, filtered to remove inorganic salts, and the filtrate was rotary evaporated to dryness. The residue was cooled in an ice-water bath, and the light yellow solid that separated was recrystallized from benzene. Yield 5.6 g (64%), mp 123-125 °C: ^{1}H NMR (DMSO-d_6) δ 8.57 (s, 1 H, imidazole CH), 7.46-7.30 (m, 5 H, Ph-H), 5.52 (s, 2 H, CH_2); ^{13}C NMR (DMSO-d_6) δ 145 (imidazole CH), 135 (*i*-C of Ph), 130 (*o*-C of Ph), 129 (*p*-C of Ph), 128 (*m*-C of Ph), 124 (C=C), 113 (C=C), 114 (CN), 109 (CN), 51 (CH_2); IR (KBr) 3100, 3020, 2200, 1560-1400, 1108, 902, 840, 800, 720, 690 cm^{-1}; UV (MeOH) λ_{max} 246, 207 nm.

(b) 4,8-Diamino-1-benzyl-6H-6-iminoimidazo[4,5-e][1,3]diazepine (4): Guanidine hydrochloride (1.15 g, 12 mmol) was added to a solution of sodium methoxide, freshly prepared by dissolving clean sodium metal (0.28 g, 12 mg.atom) in absolute methanol, and the mixture was stirred in an ice-water bath for 30 minutes. The precipitated sodium chloride was filtered off, and the filtrate was poured into a portion of the solution of 1-benzyl-4,5-dicyanoimidazole prepared above (2.08 g, 10 mmol) in 25 mL of methanol. The reaction mixture was heated to reflux for 20 hours, cooled to room temperature, and the precipitated solid was collected by filtration, and recrystallized from methanol. Yield 2.5 g (79%), mp 202-204 °C: ^{1}H NMR (DMSO-d_6) δ 8.12 (s, 1 H, imidazole CH), 7.32-7.20 (m, 9 H, five Ph-H + two NH_2, exchangeable with D_2O), 5.83 (s, 2 H, CH_2); ^{13}C NMR (DMSO-d_6) δ 158.2 (C=NH), 158.1 (C=N), 157.5 (C=N), 141.5 (imidazole CH), 139 (*i*-C of Ph), 133.2 (C=C), 133.0 (C=C), 129.5 (*o*-C of Ph), 128.4 (*p*-C of Ph), 128.2 (*m*-C of Ph), 49.0 (CH_2); IR (KBr) 3320, 3200, 1650, 1580, 1520, 1500, 1420, 1380, 900, 870 cm^{-1}; UV (MeOH) λ_{max} 248.0 nm (ε 3.4 x 10^4), (pH 0.54) 248.0 (ε 3.32 x 10^4), (pH 12.3) 212.5 (ε 1.82 x 10^5), 242.5 (ε 3.3 x 10^4).

Anal. Calcd. for $C_{13}H_{13}N_7$: C, 58.42; H, 4.90; N, 36.68. Found: C, 58.51; H, 4.89; N, 36.58.

4,8-Diamino-6*H*-6-imino-1-β-D-ribofuranosylimidazo[4,5-*e*][1,3]diazepine (6)

Method A*: *By Ribosylation of 4,6,8-triaminoimidazo[4,5-e][1,3]-diazepine (1)

(a) 4,8-Diamino-1-(2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl)-6H-6-iminoimidazo[4,5-e][1,3]diazepine (5). A 100-mL three-necked round-bottomed flask was flame-dried, and was fitted with a serum stopper, a magnetic stirring bar, and a N_2 gas inlet. It was charged with 4,6,8-triaminoimidazo[4,5-*e*][1,3]diazepine (**1**) (0.53 g, 3 mmol). Bis(trimethylsilyl)trifluoroacetamide (BTMSTFA) (4 mL, 15 mmol), pyridine (0.76 mL, 9.4 mmol), and acetonitrile (10 mL) were added, and the reaction mixture was stirred at room temperature overnight, during which time a near clear solution was formed. The solvent and excess reagents were evaporated at 30 °C (10 torr), and the residue was coevaporated with dry acetonitrile (2 x 10 mL). The residue was kept *in vacuo* until a syrup was formed. A flask fitted with a magnetic stirring bar and a dropping funnel was charged with 20 mL of dry acetonitrile, and cooled to -45 °C using acetonitrile-dry ice bath. 1-*O*-Acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (1.51 g, 3 mmol) and 0.7 ml of trimethylsilyl triflate were added with stirring. The reaction mixture was stirred for 10 hours. During this time, the temperature was slowly allowed to come to -10 - 0 °C. The cold reaction mixture was poured into a mixture of 50 mL of water and 100 mL of methylene chloride. The organic layer was separated and kept over anhydrous sodium bicarbonate for 3-4 hours. It was filtered and the filtrate was evaporated to dryness. The residue was dried in vacuum. The foam obtained was washed with ether, Yield 1.7g (90%). The foam solidified upon washing with a saturated solution of $NaHCO_3$, mp 181-183 °C: ^1H NMR (DMSO-d_6) δ 8.73 (s, 1 H, imidazole CH), 8.58 (br s, 1 H, NH, exchangeable with D_2O), 8.52 (s, 1 H, NH, exchangeable with D_2O), 8.22 (br s, 1 H, NH, exchangeable with D_2O), 8.15 (br s, 1 H, NH, exchangeable with D_2O), 7.99-7.38 (m, 16 H, 3 Ph + 1 NH exchangeable with D_2O), 6.77 (d, J = 3.4 Hz, 1 H, anomeric H), 6.21 (t, J = 3.9 Hz, 1 H, ribose CH), 5.98 (t, J = 5.9 Hz, 1 H, ribose CH), 4.92 (m, 1 H, ribose CH), 4.66 (m, 2 H, H-5'); ^{13}C NMR (DMSO-d_6) δ 165.98 (C=O), 165.09 (C=O), 164.98 (C=O), 163.99 (C=N), 157.92 (C=N), 152.24 (C=N), 141.86 (C=N), 139.50 (C=C), 139.10 (C=C), 130.09-128.12 (3 *i*-Ph, 6 *o*-Ph, 3 *p*-Ph), 126.6 (*m*-Ph), 123.26 (*m*-Ph), 118.99 (*m*-Ph), 88.96 (C-1'), 83.30 (C-2'), 79.75 (C-3'), 75.47 (C-4'), 70.36 (C-5'); UV (MeOH) λ_{max} 233 nm, (pH 0.53) 232.5, (pH 12.17) 213.5, 227.0.

Anal. Calcd. for $C_{32}H_{27}N_7O_7$: C, 61.83; H, 4.38; N, 15.77. Found: C, 61.69; H, 4.44; N, 15.67.

(b) 4,8-Diamino-6H-6-imino-1-β-D-ribofuranosylimidazo[4,5-e][1,3]-diazepine (6). To a solution of sodium methoxide that was freshly prepared by dissolving cleanly cut sodium metal (140 mg, 6.09 mg.atom) in 10 mL of methanol, was added a suspension of 4,8-diamino-1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-6*H*-6-imino-imidazo[4,5-e][1,3]diazepine (**5**), prepared above (0.64 g, 1.0 mmol) in 20 mL of methanol. The reaction mixture was stirred at room temperature overnight when a TLC (silica gel, $CHCl_3$:MeOH, 4:1) indicated no starting material. The reaction mixture was neutralized with 1N HCl to pH 6-6.5, followed by evaporation to dryness on a rotary evaporator. The solid residue was extracted with MeOH, filtered, and the filtrate was evaporated to dryness. The residue was redissolved in about 3 mL of water, and to the solution was added 2-propanol when a white solid separated. The solid was filtered and was recrystallized from a mixture of 2-propanol-water into colorless granules. Yield 0.2 g (85%), mp >250 °C: ^{1}H NMR (DMSO-d_6) δ 8.76 (br s, 1 H, exchangeable with D_2O, NH), 8.60 (s, 1 H, imidazole CH), 8.56 (s, 1 H, exchangeable with D_2O, NH), 8.46 (s, 1 H, exchangeable with D_2O, NH), 8.20 (s, 1 H, exchangeable with D_2O, NH), 8.17 (s, 1 H, exchangeable with D_2O, NH), 6.35 (br s, 1 H, exchangeable with D_2O, ribose OH), 6.0 (d, 1 H, J = 6.3 Hz, anomeric H), 5.43 (d, 1 H, J = 4.5 Hz, exchangeable with D_2O, ribose OH), 5.25 (t, 1 H, J = 5.4 Hz, exchangeable with D_2O, ribose OH), 4.35 (t, 1 H, H-2'), 4.06 (m, 2 H, H-3' and H-4'), 3.64 (m, 2 H, H-5'); ^{13}C NMR (DMSO-d_6) δ 163.94 (C=N), 157.79 (C=N), 152.16 (C=N), 140.52 (C=C), 138.13 (C=N), 126.58 (C=C), 89.31 (ribose C), 87.41 (ribose C), 76.27 (ribose C), 70.65 (ribose C), 61.03 (ribose C); UV (MeOH) λ_{max} 250.5 nm (ε 2.98 x 10^4), (pH 0.42) 250.6 (ε 1.46 x 10^4), (pH 12) 212 (ε 6.4 x 10^4), 244.5 (ε 2.4 x 10^4); MS (FAB) 310 (MH^+).

Anal. Calcd. for $C_{11}H_{15}N_7O_4$.2HCl: C, 34.71; H, 4.47; N, 25.77. Found: C, 34.87; H, 4.54; N, 25.70.

Method B: By Condensation of 4,5-Dicyano-1-β-D-ribofuranosylimidazole with Guanidine:

(a) 1-(2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl)-4,5-dicyanoimidazole (7): A solution of 4,5-dicyanoimidazole (354 mg, 3.0 mmol) and 1-*O*-acetyl-2,3,5-tri-*O*-

benzoyl-β-D-ribofuranose (1.51 g, 3 mmol) in acetonitrile (30 mL) was placed into a flame-dried, three-necked, 50-mL round-bottomed flask, equipped with a refluxing condenser, a magnetic stirrer, and a N_2 gas inlet. The solution was stirred in an ice-water bath for 5 minutes. Freshly distilled hexamethyldisilazane (HMDS) (0.7 mL, 3.3 mmol), freshly distilled chlorotrimethylsilane (CTMS) (0.45 mL, 3.6 mmol), and trifluoromethanesulfonic acid (TFMSA) (0.3 mL, 3.6 mmol) were consecutively added to the above solution. The resulting solution was stirred in an ice-water bath for 30 minutes. The reaction, as monitored by TLC (silica gel, toluene:acetic acid:water, 5:5:1), showed complete conversion to the product in 30 minutes. Methylene chloride (30 mL) was added to the reaction mixture, and was extracted with saturated aqueous $NaHCO_3$. The organic layer was separated, and the aqueous layer was once again extracted with methylene chloride (10 mL). The combined organic extracts were washed with saturated aqueous NaCl, dried over anhydrous $MgSO_4$, filtered, and the filtrate evaporated to dryness under reduced pressure to obtain a foam, which slowly crystallized upon standing. Yield 1.5 g (94%), mp 68-72 °C: ^{1}H NMR (DMSO-d_6) δ 8.68 (s, 1 H, imidazole CH), 7.92 (m, 5 H, Ph-H), 7.63 (m, 5 H, Ph-H), 7.40 (m, 5 H, Ph-H), 6.63 (d, J = 4.8 Hz, 1 H, H-1'), 6.06 (t, J = 5.1 Hz, 1 H, H-2'), 5.99 (t, 1 H, H-3'), 4.97 (q, 1 H, H-4'), 4.74 (dd, 2 H, H-5'); ^{13}C NMR (DMSO-d_6) δ 163 (C=O), 161 (C=O), 160.5 (C=O), 142.6 (imidazole CH), 135 (Ph-C), 134.8 (Ph-C), 134.4 (Ph-C), 130.4 (Ph-C), 130.2 (Ph-C), 130.0 (Ph-C), 129.8 (Ph-C), 129.7 (Ph-C), 129.5 (Ph-C), 129.4 (Ph-C), 129.3 (Ph-C), 129.0 (Ph-C), 124 (C=C), 113 (C≡N), 111.7 (C≡N), 109.2 (C=C), 89.8 (C-1'), 81.8 (C-2'), 75.5 (C-3'), 71.5 (C-4'), 64.2 (C-5').

Anal. Calcd. for $C_{31}H_{22}N_4O_7$: C, 66.19; H, 3.94; N, 9.96. Found: C, 66.20; H, 3.96; N, 9.76.

(b) 4,8-Diamino-6H-6-imino-1-β-D-ribofuranosylimidazo[4,5-e][1,3]-diazepine (6) : To a cold solution of freshly prepared sodium methoxide solution made by dissolving sodium metal (2.0 g, 87 mg.atom) in 50 mL of methanol, was added 1-(2,3,5-Tri-*O*-benzoyl-β-D-ribofuranosyl)-4,5-dicyanoimidazole (**7**) (2.0 g, 3.5 mmol), followed by guanidine hydrochloride (3.5 g, 36 mmol). The reaction mixture was heated at reflux overnight. A TLC of the reaction mixture (silica gel, $CHCl_3$:MeOH, 4:1) indicated complete consumption of the starting material and the presence of a new, UV-absorbing spot which had a lower R_f than the starting material. The reaction mixture was cooled and acidified to pH 6.5 with 1N HCl.

The solution was mixed with flash silica gel (4g, particle size 40-63 μm) and rotary evaporated to dryness. The silica gel-adsorbed compound was purified by flash chromatography on a column of flash silica gel of the same particle size as above. Elution with a mixture of $CHCl_3$:MeOH (4:1) removed most of the impurities present. The column was then eluted with methanol alone, and the appropriate UV-absorbing fractions were pooled, and evaporated to afford a solid which was recrystallized from 2-propanol to give white powder. Yield 0.45 g (40%), mp >250 °C. The spectral and analytical data of this compound were consistent with those of 4,8-Diamino-1-β-D-ribofuranosylimidazo[4,5-e][1,3]diazepine (**6**), prepared by Method A above.

ACKNOWLEDGMENTS

This research was supported by grants from the National Institutes of Health (#CA 36154 and #GM 49249) and the Maryland Industrial Partnerships (MIPS) program (#910). FAB mass spectral data were obtained at the Michigan State University Mass Spectral Facility which is supported, in part, by a grant (DRR-00480) from the Biotechnology Research Technology Program, National Center for Research Resources, National Institutes of Health.

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Received June 20, 1994
Accepted August 15, 1994