A Novel Rearrangement of 1-(2-Aminoaryl)imidazoles

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6-Ethyl-2,4-bis(1*H*-imidazol-1-yl)pyrimidin-5-amine was found to undergo a novel rearrangement in the presence of acetic anhydride. The structure of the rearrangement product was deduced using a combination of one- and two-dimensional nmr methods. Confirmation of the structure was obtained by unambiguous synthesis of a reduced analog and establishment of the identity of this material with material prepared by reduction of the rearrangement product. Examination of three related cases indicated that the rearrangement process is significant only when both positions adjacent to the aryl amino group are substituted.

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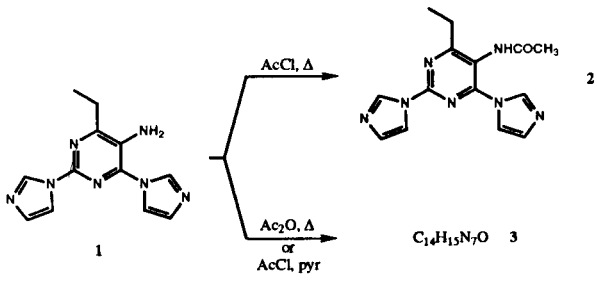
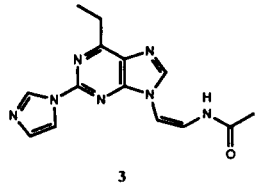
We recently needed to prepare acetamide **2** for use in our vascular drug discovery program [1,2]. We chose to prepare the acetamide by way of acetylation of the corresponding pyrimidinamine **1**, as shown in Scheme 1. Although we found that this acetylation can easily be carried out by heating **1** in acetyl chloride at reflux, we were surprised to discover in the course of our studies that if we instead treated **1** with hot acetic anhydride, or with acetyl chloride in pyridine, a very different product **3** was obtained. Compound **3** is produced cleanly and in good yield as the sole product of the acetic anhydride reaction. We were intrigued by this unexpected result, and therefore decided to undertake the determination of the structure of **3**.

Scheme 1



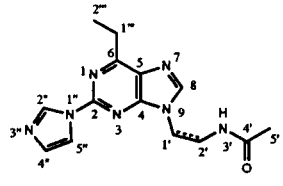


3

The molecular formula of **3** was shown to be $C_{14}H_{15}N_7O$ by both elemental analysis and FAB mass spectroscopy, in which an $[M+H]^+$ molecular ion of 298 was observed. The proton nmr spectrum of **3** showed the presence of an acetamide, an ethyl group, and one imidazole, together with three unexplained resonances: a doublet at 6.21 ppm, a double doublet at 7.08 ppm, and a singlet at 8.53 ppm. The amide NH proton was split into a doublet. On the basis of these data we proposed that **3** has the structure shown below, in which the imidazole at the 4-position of the pyrimidine has been opened by the adjacent amine to form a purine substituted by an acetamidoethylene group. The resonances at 6.21 and 7.08 ppm were assigned to the two ethylene protons, and that at 8.53 was assigned to the purine H-8. The proton nmr spectrum of **3** can be found in Table 1, together with a numbering scheme which will be used to refer to individual assignments.

Table 1

Proton and Carbon NMR Chemical Shifts for Compounds **3** and **4**.



	compound 3		compound 4	
position	^1H	^{13}C	^1H	^{13}C
2	—	148.7	—	148.4
4	—	151.6	—	151.8
5	—	130.2	—	130.4
6	—	163.6	—	163.5
8	8.53	145.7	8.48	146.1
1'	6.21	100.8	4.33	43.2
2'	7.08	122.0	3.53	38.3
3'	9.82	—	7.97	—
4'	—	167.9	—	169.5
5'	1.92	22.4	1.68	22.4
2"	8.57	135.4	8.64	135.5
4"	7.13	130.0	7.14	129.8
5"	7.94	116.7	8.01	116.7
1"'	3.17	25.5	3.14	25.7
2"'	1.43	11.8	1.40	11.9

Two dimensional nOe spectroscopy [3] was used to confirm the spatial arrangement of the purine substituents.

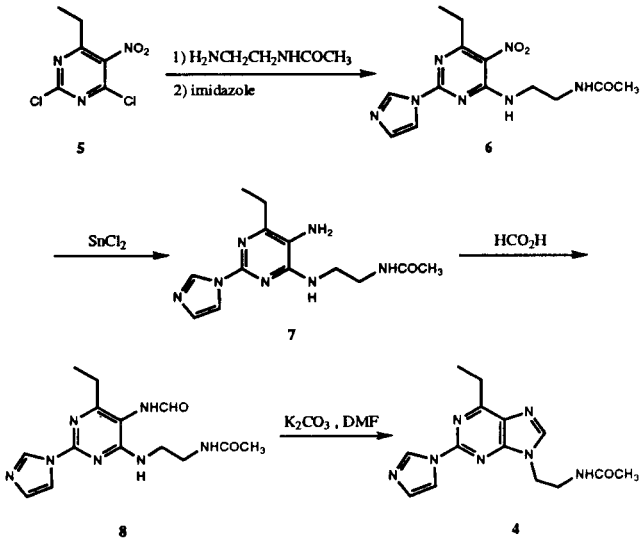
In addition to the expected correlations within the ethyl, imidazole, and acetamidoethylene subunits, correlations were observed between the purine H-8 and the NH and H-1' protons of the acetamidoethylene sidechain. These results served to substantiate the proposed structure.

The carbon nmr spectrum of **3**, reported in Table 1, provided further support for this structure. The purine C-8 resonance at 145.7 ppm and the two ethylene resonances at 100.8 and 122.0 ppm are notable supporting features in the spectrum. The carbon assignments were arrived at on the basis of chemical shifts and multiplicities as determined by APT spectroscopy [4]. Proton-carbon correlation spectroscopy [5] aided the assignment of several of the non-quaternary carbons. All of the possible direct one-bond couplings were observed in this way; however, the pairs of proton resonances at 7.08 and 7.13 ppm and 8.53 and 8.57 ppm were insufficiently resolved to allow unequivocal assignment of the attached carbons (resonating at 122.0 and 130.0 ppm and 135.4 and 145.7 ppm, respectively).

In order to assign these carbons as well as the five quaternary carbons, we made use of long-range heteronuclear correlation spectroscopy optimized for two- and three-bond couplings of 8 Hz. Several of these long-range correlations were of particular value and are worthy of note. The correlation observed between the protons of the ethyl group at 1.43 and 3.17 ppm with purine carbon C-6 at 163.6 ppm allowed the assignment of this quaternary carbon. The correlation between the ethylene H-1' proton at 6.21 ppm and the adjacent C-2' carbon at 122.0 ppm made the assignment of this carbon possible, which also resolved one of the two ambiguities mentioned above, and allowed the assignment of the 130.0 ppm resonance to the imidazole C-4". The other ambiguity was resolved by the observation of a correlation between the imidazole H-4" proton at 7.13 ppm and the imidazole C-2" carbon at 135.4 ppm, allowing this carbon assignment as well as the assignment of the 145.7 ppm resonance to the purine C-8. Finally, correlations between the purine H-8 proton at 8.53 ppm and the purine C-4 and C-5 carbons at 151.6 and 130.2 ppm, respectively, made possible these assignments.

As a final confirmation of the proposed structure we prepared compound **4**, the dihydro analog of **3**, by an unambiguous route. The synthesis is detailed in Scheme 2. Thus, dichloronitropyrimidine **5** was treated in a one-pot procedure first with *N*-acetylethylenediamine and then with imidazole to give the product of the double displacement reaction **6**. Tin(II) chloride [6] reduction of **6** afforded the amine **7**, which was converted to the corresponding formamide with refluxing formic acid [7]. Exposure of **7** to the aqueous cyclization conditions reported by Kamiya and coworkers [7] led in this case to extensive hydrolysis of the formamide; however, treatment of **7** with potassium carbonate in anhydrous dimethylformamide gave the desired purine **4** in high yield. Compound **4** was found to be identical in all respects to material obtained by hydrogenation of **3**.

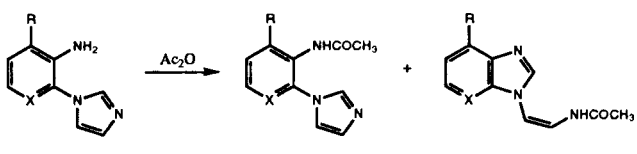
Scheme 2



The proton and carbon nmr spectra of **4** are reported in Table 1. The assignments of the carbon spectrum were determined as described above for compound **3**, with the simplification that all non-quaternary carbons could be assigned directly from one-bond proton-carbon correlation spectrum, due to the absence of non-resolved proton resonances. The quaternary carbons were assigned using long-range correlation spectroscopy as described above.

In order to determine the generality of this unusual acetic anhydride mediated rearrangement, we examined several related cases as shown in Scheme 3. We found that treatment of 1-(2-aminophenyl)imidazole **9a** with acetic anhydride over long reaction periods led to the production of complex mixtures of products in which acetylation had taken place on the imidazole as well as the amine; however, no evidence was seen for the production of the rearranged product **11a**. This result is consistent with previous reports of the acetylation of **9a** [8]. Acetic anhydride treatment of **9b** led to complex reaction mix-

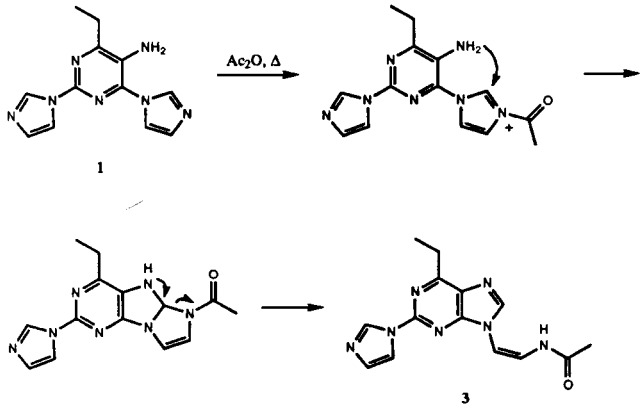
Scheme 3



tures as well, although in this case analysis of the crude product by proton nmr suggested the presence of **11b** to the extent of approximately 3% of the reaction mixture. In contrast to the above results, we found that reaction of **9c** with acetic anhydride afforded exclusively the rearranged product **11c** in 85% yield.

In light of the above findings, we propose that in cases where approach to the amino group is hindered by flanking substituents, an abnormal acylation takes place under the acetic anhydride reaction conditions. This reaction pathway is shown in Scheme 4. Nucleophilic attack at the 2-position of the imidazole by the amino group followed by bond reorganization and the appropriate proton shifts leads to the observed product **3**. Under the more strongly acidic acetyl chloride conditions the imidazole is protonated, effectively protecting it from acylation so that normal acetylation of the amino group takes place.

Scheme 4



In summary, we have found that 1-(2-aminoaryl)imidazoles undergo a novel rearrangement in the presence of acetic anhydride, and we have determined the structure of the rearrangement products by a combination of nmr spectroscopy and synthesis. This rearrangement is reminiscent of the acid catalyzed rearrangement of *N*-acylbenzimidazole arylhydrazones reported by Cusmano and Macaluso [9]. In their study, the imidazole portion of the benzimidazole is opened by one of the hydrazone nitrogens to give a triazolium salt. However, the rearrangement which we have reported in this paper, in which an imidazole ring is opened in such a way as to give a new imidazole ring fusion elsewhere in the molecule, is to the best of our knowledge unprecedented in the literature.

EXPERIMENTAL

Melting points were recorded on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were recorded on a Sargent-Welch 3-300 or a Beckman Acculab 2 infrared spectrometer as potassium bromide pellets. The nmr spectra were recorded at 300 MHz on a Varian XL-300 spectrometer operating at 299.945 MHz for proton observation. Chemical shifts are reported in parts per million (δ) downfield from an internal standard of tetramethylsilane. Elemental analyses were performed by Galbraith Laboratories, Microlit Laboratories, or the Berlex Analytical Section. All solvents and reagents were used as supplied unless otherwise noted. Solid products were routinely dried at 60° under reduced pressure for a minimum of 12 hours. Reactions were monitored by thin-layer chromatography on silica gel (Merck) and alumina (Merck); plates were visualized by uv, iodine, and iodoplatinate reagent.

NMR Spectroscopy.

Samples of compounds **3** and **4** for carbon, nOe, and heteronuclear correlation spectroscopy were prepared in DMSO-d_6 at a concentration of approximately 10 mg/ml. The nOe spectra were acquired using the method of States and coworkers [3]. The data were collected as 1024 x 512 data points with a spectral width of 3661.7 Hz in both frequency domains. A mixing time of 1.5 seconds was used during the acquisition. The data were processed using Gaussian apodization and zero-filled to 2048 x 2048 points.

APT spectra were obtained as reported by Patt and Shoolery [4]. Heteronuclear correlation spectra were carried out as described by Bax and Morris [5]. The spectra were acquired as 2048 x 256 data points with spectral widths of 2589.3 and 16501.7 Hz in F_2 and F_1, respectively. The data were processed using Gaussian apodization and zero-filled to 4096 x 512 points. One-bond couplings were optimized for an average coupling of 140 Hz; 8 Hz was used as the coupling in the long-range correlation spectra.

6-Ethyl-2,4-bis(1*H*-imidazol-1-yl)pyrimidin-5-amine (**1**).

A stirred solution of 30.00 g of 2,4-dichloro-6-ethyl-5-nitropyrimidine [10] in 200 ml of acetonitrile was cooled to -5°, and to this mixture a solution of 45.95 g (0.675 mole) of imidazole in 200 ml of acetonitrile was added at such a rate as to maintain the temperature of the mixture at 0°. After the addition was complete the mixture was allowed to warm to room temperature, and stirring was continued for 18 hours. The solvent was removed by evaporation, and the residue was dissolved in 400 ml of methylene chloride and washed five times with saturated aqueous sodium bicarbonate. The organic phase was dried over sodium sulfate and evaporated to give 40.10 g (100%) of 6-ethyl-2,4-bis(1*H*-imidazol-1-yl)-5-nitropyrimidine as a yellow solid which was used immediately in the next step.

A solution of 38.50 g (0.135 mole) of 6-ethyl-2,4-bis(1*H*-imidazol-1-yl)-5-nitropyrimidine in 500 ml of acetonitrile was added dropwise over 2 hours to a stirred suspension of 182.10 g (0.809 mole) of tin(II) chloride dihydrate in 500 ml of acetonitrile under a nitrogen atmosphere at 0°. After the addition was complete, the mixture was stirred at room temperature for 1 hour and then at reflux for 5 hours. The solvent was evaporated and the residue was suspended in 300 ml of ethanol. Sodium bicarbonate (29.16 g) was added, and the mixture was stirred for 2 hours. The mixture was filtered through Celite, and the filter cake was washed thoroughly with ethanol and methylene chloride:2-propanol (3:1). The filtrates were evaporated, the residue was dissolved in 500 ml of methanol:methylene chloride (1:1), filtered, and evaporated. Trituration of the residue with hot ace-

tonitrile afforded 22.20 g (64%) of the title compound as a white solid, mp 232-233°; ir: ν 3350, 1665, 1590, 1490, 1480, 1445 cm^{-1}; ^1H nmr ($DMSO_6$ δ 1.27 (t, 3H), 2.82 (quar, 2H), 5.43 (s, 2H), 7.09 (d, 1H), 7.19 (d, 1H), 7.83 (d, 1H), 7.87 (d, 1H), 8.37 (s, 1H), 8.48 (s, 1H).

Anal. Calcd. for $C_{12}H_{13}N_7$: C, 56.46; H, 5.13; N, 38.41. Found: C, 56.23; H, 4.99; N, 38.53.

N-[2,4-Bis(1*H*-imidazol-1-yl)-6-ethylpyrimidin-5-yl]acetamide (**2**).

A solution of 6-ethyl-2,4-bis(1*H*-imidazol-1-yl)pyrimidin-5-amine (**1**) (16.10 g, 0.063 mole) in 600 ml of acetyl chloride was heated at reflux for four days, after which the excess acetyl chloride was removed by distillation. The residue was taken up in 300 ml of 2 *M* aqueous sodium hydroxide, and the *p*H of the mixture was adjusted to 9.0 with additional sodium hydroxide. The resulting precipitate was collected by filtration and washed with water and ether. The crude product was recrystallized twice from ethanol to yield 8.70 g (46%) of the title compound as an ethanol solvate, mp 227-229°; ir: ν 3131, 1590, 1566, 1239, 1009 cm^{-1}; ^1H nmr (DMSO-d_6): δ 1.26 (t, 3H), 2.10 (s, 3H), 2.83 (quar, 2H), 7.17 (s, 2H), 7.93 (s, 1H), 8.06 (s, 1H), 8.56 (s, 1H), 8.72 (s, 1H), 9.99 (s, 1H).

Anal. Calcd. for $C_{14}H_{15}N_7O \cdot 0.20\ C_2H_6O$: C, 56.42; H, 5.33; N, 31.99. Found: C, 56.31; H, 5.28; N, 31.96.

(*Z*)-*N*-[2-[6-Ethyl-2-(1*H*-imidazol-1-yl)-9*H*-purin-9-yl]-ethenyl]acetamide (**3**).

A solution of 6-ethyl-2,4-bis(1*H*-imidazol-1-yl)pyrimidin-5-amine (**1**) (2.20 g, 9.76 mmoles) in 11 ml of acetic anhydride was heated at 50° for 8 hours. The excess acetic anhydride was removed by distillation and the residue was taken up in 2 *M* aqueous sodium hydroxide. The *p*H of the mixture was adjusted to 8.0 and the resulting precipitate was collected by filtration and washed with water and ether. The crude product was recrystallized from ethanol to afford 1.76 g (61%) of the title compound as a white solid, mp 221-222°; ir: ν 3440, 1716, 1671, 812 cm^{-1}; ^1H nmr (DMSO-d_6): δ 1.43 (t, 3H), 1.92 (s, 3H), 3.17 (quar, 2H), 6.20 (d, 1H), 7.08 (dd, 1H), 7.12 (s, 1H), 7.94 (s, 1H), 8.53 (s, 1H), 8.56 (s, 1H), 9.80 (br d, 1H); fab ms: m/z 298 $(M+H)^+$, 256, 215.

Anal. Calcd. for $C_{14}H_{15}N_7O$: C, 56.56; H, 5.08; N, 32.98. Found: C, 56.38; H, 5.12; N, 33.07.

N-[2-[[4-Ethyl-2-(1*H*-imidazol-1-yl)-5-nitropyrimidin-6-yl]-amino]ethyl]acetamide (**6**).

A suspension of 7.15 g (0.070 mole) of *N*-acetylethylenediamine and 9.05 g (12.2 ml, 0.070 mole) of diisopropylethylamine in 200 ml of acetonitrile was cooled to -50° under an atmosphere of argon, and to this mixture was added dropwise over 30 minutes a solution of 15.54 g (0.070 mole) of 2,4-dichloro-6-ethyl-5-nitropyrimidine [10] in 50 ml of methylene chloride. The mixture was stirred at -50° for 2 hours, and then was warmed to 0° over 1.5 hours, after which 23.83 g (0.350 mole) of imidazole was added. The mixture was stirred at room temperature for 20 hours, after which it was partitioned between 500 ml of water and 600 ml of methylene chloride. Some of the product precipitated and was collected by filtration. The organic phase was washed with saturated aqueous sodium bicarbonate and brine, dried over sodium sulfate, and evaporated to a residue, which was triturated with ether and acetonitrile and combined with the first precipitate. Recrystallization of the combined solids from acetonitrile gave 19.10 g (85%) of the title compound as a yellow solid, mp 184-186°; ir: ν 1613, 1467, 1430, 1239, 1052 cm^{-1}; ^1H nmr (DMSO-d_6): δ 1.27 (t, 3H), 1.75 (s, 3H), 2.89 (quar, 2H), 3.28 (m, 2H), 3.61 (quar, 2H), 7.14 (s, 1H), 8.00 (s, 1H), 8.06 (br t, 1H), 8.66 (s, 1H), 8.75 (br t, 1H).

Anal. Calcd. for $C_{13}H_{17}N_7O_3$: C, 48.90; H, 5.37; N, 30.70. Found: C, 49.28; H, 5.34; N, 30.83.

N-[2-[[5-Amino-4-ethyl-2-(1*H*-imidazol-1-yl)pyrimidin-6-yl]-amino]ethyl]acetamide (**7**).

A suspension of 15.97 g (0.050 mole) of *N*-[2-[[4-ethyl-2-(1*H*-imidazol-1-yl)-5-nitropyrimidin-6-yl]amino]ethyl]acetamide (**6**) and 56.41 g (0.250 mole) of tin(II) chloride dihydrate in 250 ml of ethanol was heated at reflux for 3 hours. The mixture was cooled, poured onto a mixture of 900 ml of 1 *M* aqueous sodium hydroxide, 400 ml of methylene chloride, and 200 ml of 2-propanol, and stirred for 15 minutes. The layers were separated, 2 *M* aqueous sodium hydroxide was added to the aqueous phase to dissolve some residual solids, and the aqueous phase was extracted twice with methylene chloride:2-propanol (3:1). The combined organics were washed with 2 *M* aqueous sodium hydroxide, dried over sodium sulfate, and evaporated to a residue, which was triturated with hot acetonitrile to afford 12.95 g (90%) of the title compound as an off-white solid hemihydrate, mp 203-205°; ir: ν 1657, 1608, 1485, 1429, 1341, 1052 cm^{-1}; ^1H nmr (DMSO-d_6): δ 1.16 (t, 3H), 1.80 (s, 3H), 2.53 (quar, 2H), 3.27 (dt, 2H), 3.42 (dt, 2H), 4.54 (s, 2H), 6.99 (t, 1H), 7.00 (s, 1H), 7.81 (s, 1H), 8.03 (br t, 1H), 8.42 (s, 1H).

Anal. Calcd. for $C_{13}H_{19}N_7O \cdot 0.5\ H_2O$: C, 52.34; H, 6.76; N, 32.86. Found: C, 52.41; H, 6.53; N, 32.54.

N-[2-[[4-Ethyl-5-(formylamino)-2-(1*H*-imidazol-1-yl)pyrimidin-6-yl]amino]ethyl]acetamide (**8**).

N-[2-[[5-Amino-4-ethyl-2-(1*H*-imidazol-1-yl)pyrimidin-6-yl]-amino]ethyl]acetamide (**7**) (12.00 g, 0.0415 mole) was suspended in 300 ml of 95-97% formic acid and 15 ml of water, and the mixture was heated to reflux for 1 hour. The mixture was cooled, the formic acid was evaporated, and the residue was evaporated from 100 ml of water and twice from 100 ml of ethanol to yield 13.96 g (93%) of the title formamide as a formic acid salt, which was sufficiently pure for further use. In order to obtain a sample for characterization a portion of the salt was suspended in saturated aqueous sodium bicarbonate, extracted three times with methylene chloride: 2-propanol (3:1), and the organic phases were dried over sodium sulfate and evaporated. Recrystallization of the residue from methanol: acetonitrile (1:1) gave a pure sample, ir: ν 1662, 1607, 1483, 1431, 1336, 1050 cm^{-1}; ^1H nmr (DMSO-d_6): δ 1.14 (t, 3H), 1.81 (s, 3H), 2.47 (quar, 2H), 3.24 (quar, 2H), 3.40 (quar, 2H), 7.07 (s, 1H), 7.48 (t, 1H), 7.92 (s, 1H), 8.00 (t, 1H), 8.24 (s, 1H), 8.56 (s, 1H), 9.43 (s, 1H).

N-[2-[6-Ethyl-2-(1*H*-imidazol-1-yl)-9*H*-purin-9-yl]ethyl]-acetamide (**4**).

To a suspension of 12.43 g (0.0342 mole) of *N*-[2-[[4-ethyl-5-(formylamino)-2-(1*H*-imidazol-1-yl)pyrimidin-6-yl]amino]ethyl]acetamide formic acid salt (**8**) in 100 ml of anhydrous dimethylformamide was added 5.73 g (0.0415 mole) of potassium carbonate, and the mixture was heated to 150° under an atmosphere of argon. After 2 hours the mixture was cooled, diluted with 300 ml of water, and extracted four times with methylene chloride:2-propanol (3:1). The organic phase was

dried over sodium sulfate and evaporated to a residue, which was triturated with ether and then recrystallized from acetonitrile to give 7.42 g, (72%) of the title compound as a white solid, mp 176-178°; ir: ν 3069, 1682, 1591, 1474, 1201, 1053 cm^{-1}; ^1H nmr (DMSO-d_6): δ 1.40 (t, 3H), 1.68 (s, 3H), 3.14 (quar, 2H), 3.53 (dt, 2H), 4.33 (t, 2H), 7.14 (s, 1H), 7.97 (br t, 1H), 8.01 (s, 1H), 8.48 (s, 1H), 8.64 (s, 1H).

Anal. Calcd. for $C_{14}H_{17}N_7O$: C, 56.18; H, 5.72; N, 32.75. Found: C, 56.29; H, 5.77; N, 32.82.

The title compound was also prepared by hydrogenation of (*Z*)-*N*-[2-[6-ethyl-2-(1*H*-imidazol-1-yl)-9*H*-purin-9-yl]ethenyl]-acetamide (**3**). A suspension of 200 mg (0.672 mmole) of **3** and 100 mg of 10% palladium on carbon in 40 ml of ethanol was shaken on a Parr apparatus under 50 psi of hydrogen for 7 hours. The catalyst was removed by filtration and the solvent was evaporated to give 170 mg (84%) of **4** as a white solid, mp 168-170°. The spectra obtained for this material were identical with those obtained for the material prepared by the route described above.

(*Z*)-*N*-[2-(7-Methylimidazo[4,5-*b*]pyridin-3-yl)ethenyl]-acetamide (**11c**).

2-(1*H*-Imidazol-1-yl)-4-methylpyridin-3-amine (**9c**) was prepared in 35% yield as a white solid using the method used to prepare compound **1**. This compound was characterized by nmr spectroscopy only and was submitted immediately to the rearrangement conditions, ^1H nmr (acetic acid-d_4): δ 2.32 (s, 3H), 7.31 (d, 1H), 7.73 (m, 2H), 7.88 (d, 1H), 9.04 (m, 1H).

Compound **9c** was heated in acetic anhydride as described for the preparation of compound **3**. After washing the crude material with ether, the title compound was obtained as a white solid in 85% yield, mp 140-142°; ir: ν 3524, 3074, 1675, 1613, 1086 cm^{-1}; ^1H nmr (DMSO-d_6): δ 2.01 (s, 3H), 2.60 (s, 3H), 6.32 (d, 1H), 6.79 (dd, 1H), 7.21 (d, 1H), 8.28 (d, 1H), 8.47 (s, 1H), 10.95 (d, 1H); fab ms: m/z 217 $(M+H)^+$, 175, 134.

Anal. Calcd. for $C_{11}H_{12}N_4O$: C, 61.10; H, 5.59; N, 25.91. Found: C, 60.75; H, 5.82; N, 25.77.

Attempted Rearrangement of 2-(1*H*-imidazol-1-yl)benzenamine (**9a**).

2-(1*H*-Imidazol-1-yl)benzenamine (**9a**) [11] was subjected to the acetic anhydride rearrangement conditions as described for the preparation of **3**. Examination of the crude reaction mixture by ^1H nmr showed the presence of several mono- and diacylated materials, including *N*-[2-(1*H*-imidazol-1-yl)phenyl]acetamide (**10a**) [8]; no evidence for the presence of the rearranged product **11a** could be found by examining the spectrum in the 6-7 ppm region.

Attempted Rearrangement of 2-(1*H*-imidazol-1-yl)pyridin-3-amine (**9b**).

2-(1H-Imidazol-1-yl)pyridine-3-amine (**9b**) [1] was subjected to the acetic anhydride rearrangement conditions as described for the preparation of **3**. Examination of the crude reaction mixture by ^1H nmr revealed a complex mixture of mono- and diacylated materials; signals at 6.33 (d) and 6.84 (dd) ppm suggested the presence of the rearranged product **11b** in the crude material. Compound **11b** was judged to make up approximately 3% of the total crude mixture based on integration of these nmr resonances.

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