

Nanda M. Brahme and Walter T. Smith, Jr.*

Department of Chemistry, University of Kentucky,
Lexington, Kentucky 45006-0055
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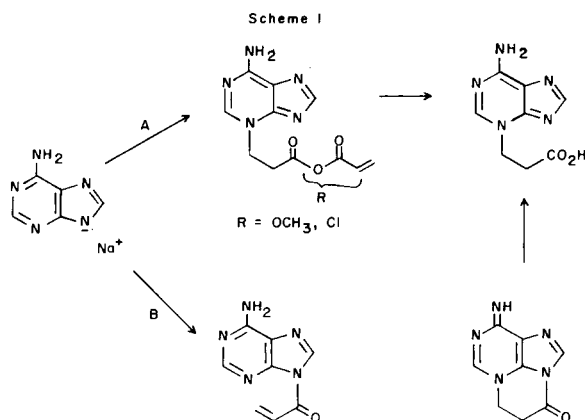
In our attempts to prepare polymerizable derivatives of nucleic acid bases, we investigated the reaction of adenine (**1**) and 9-(cyanoethyl)adenine (**4**) with acrylic anhydride and acryloyl chloride. Reactions of adenine with methyl acrylate and vinyl acrylate were also examined. The results show that these reactions are solvent dependent and the intermediate acryloyladenine **3** can undergo a facile intramolecular Michael reaction to form **7**.

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Acryloyl derivatives of several nucleotides have been prepared *via* their reactions with acrylic anhydride [1-3]. However, treatment of adenine with acrylic anhydride gave a cyclized product **7** under anhydrous conditions (dry DMSO, 60°, 24 hours) and gave 3-carboxyethyladenine (**8**) under aqueous basic conditions (sodium hydroxide, 25°, 17 hours). With acryloyl chloride, adenine gave (**8**) under anhydrous conditions (dry DMF, 25°, 18 hours) and also under aqueous basic conditions (sodium hydroxide, 25°, 2 hours). The precursor of **7** was likely 6-acryloylaminopurine (**3**), which underwent cyclization *via* an intramolecular Michael reaction at N-7. Cyclization at N-7 was probably energetically more favorable than the alternative mode (*i.e.*, cyclization at N-1), since cyclization at N-7 retained the aromaticity of the pyrimidine ring in adenine. The assigned cyclic structure **7** was consistent with the spectral properties and elemental analysis. In addition, the hydrolysis product of **7** was found to be identical with an independently prepared 7-(carboxyethyl)adenine (**10**). Similar cyclic derivatives of xanthenes have been prepared through alkylation reactions [4].

The identity of **8** was established from its uv and ¹H nmr spectra. In purine chemistry the uv spectrum (absorbance maximum and extinction coefficient at acidic and basic pH) and the ¹H nmr spectrum (magnitude of the chemical shift difference between 2-CH and 8-CH) are often used to distinguish several isomeric alkyl purines [5,6].

Formation of **8** could proceed *via* a direct Michael reaction between the adenine sodium salt and acrylic anhydride, followed by the solvolysis of the mixed anhydride (Pathway A). Alternatively, an intermediate 9-(acryloyl)adenine could undergo an intramolecular Michael reaction at N-3 followed by the solvolytic ring cleavage (Pathway B). These two pathways are shown in Scheme 1. In an attempt to distinguish between these two possible pathways, we examined the reaction between adenine and methyl acrylate in DMSO and also in aqueous sodium hydroxide. As expected, only the Michael adducts were isolated. Previously reported base catalyzed (sodium ethoxide/ethanol) Michael additions of adenine to acrylonitrile and methyl

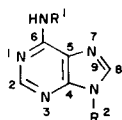


acrylate had given only the N-9 isomers **4** and **6** respectively [7]. In contrast, we obtained an isomeric mixture of N-9 (**4** and **6**) and N-7 (**9** and **11**) Michael adducts in the ratio 2:1 [8]. The observed preference for N-9 isomer was perhaps indicative of higher N-9 tautomer population of adenine. This is consistent with the recently reported nmr studies on the tautomer ratios in purine [9]. Under the aqueous sodium hydroxide conditions, the same reaction gave only N-3 isomer **8**. Since methyl acrylate cannot acryloylate adenine, it follows that **8** was formed through hydrolysis of the Michael adduct between adenine and methyl acrylate. We therefore conclude that the formation of **8**, in the reactions of adenine with acrylic anhydride and acryloyl chloride in aqueous sodium hydroxide, was by pathway A.

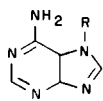
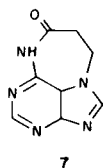
An anomalous result was obtained when adenine was allowed to react with acryloyl chloride in dry DMF (Note: DMF was chosen instead of DMSO because the latter reacted with acryloyl chloride). Instead of the expected cyclic product **7**, the product obtained was **8**. A simple solvent effect (DMF *vs* DMSO) was ruled out since, when DMF was used the reaction between adenine and acrylic anhydride still produced **7**. Clearly, this reaction needs further investigation.

Unlike methyl acetate, vinyl acetate can be used as an acetylating agent. Indeed, vinyl acetate gave **2** when reacted with adenine in DMSO. Treatment of adenine with vinyl acrylate in DMSO gave the expected cyclic product **7**. Thus, a better leaving group (vinyloxy *versus* methoxy) facilitates acylation reaction in comparison to the Michael addition. In aqueous sodium hydroxide no reaction occurred. Apparently, the hydrolysis of vinyl acrylate to acrylic acid was rapid enough to prevent any significant formation of the Michael adduct.

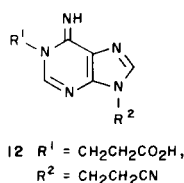
In order to prevent the cyclization of the acryloyladenine intermediate, we explored reactions of acrylic anhydride and acryloyl chloride with 2-(cyanoethyl)adenine (**4**). Similar reactions of 9-alkyladenines with chloroacetic anhydride have been reported [10,11]. Under the reaction conditions employed, we obtained a 1,9-disubstituted adenine derivative **12**. Thus, although the cyclization was prevented at N-7 position due to the cyanoethyl group on N-9, the initially formed acryloyl derivative underwent cyclization at N-1 position. However, this six-membered ring opened during the work-up (aqueous crystallization) to give **12**. Direct alkylation of **4** at N-1 position has been shown to occur [12], but **4** did not react with either acrylonitrile or methyl acrylate under our reaction conditions (DMSO, 60°, 6 hours and DMF, reflux, 12 hours). Hence the possibility that **12** was formed directly *via* a Michael addition at N-1 was ruled out.



- 1 $R^1 = R^2 = H$
- 2 $R^1 = COCH_3, R^2 = H$
- 3 $R^1 = COCHCH_2, R^2 = H$
- 4 $R^1 = H, R^2 = CH_2CH_2CN$
- 5 $R^1 = H, R^2 = CH_2CH_2CO_2Et$
- 6 $R^1 = H, R^2 = CH_2CH_2CO_2Me$



- 9 $R = CH_2CH_2CN$
- 10 $R = CH_2CH_2CO_2H$
- 11 $R = CH_2CH_2CO_2Me$



EXPERIMENTAL

Melting points were recorded on a Fisher-Johns melting point apparatus and are uncorrected. The ir spectra were recorded on a Beckman IR 20A-X infrared spectrophotometer. The uv spectra were recorded on a

Beckman model 26 spectrophotometer. Proton nmr spectra were recorded on either a Varian T-60 spectrometer, a Varian FT-80 spectrometer, a Varian EM-390 spectrometer in DMSO- d_6 with TMS as internal standard or in sodium deuterioxide/deuterium oxide with sodium 3-(trimethylsilyl)-1-propane-1-sulfonate (DSS) as internal standard; chemical shifts are reported in parts per million, and signals are described as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet). Mass spectra were recorded on a Hitachi Perkin-Elmer RMU-6E mass spectrometer. Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tennessee, and Atlantic Microlab, Inc., Atlanta, Georgia. Thin-layer chromatograms were run on either silica gel CF-254 plates or alumina GF-254 plates (Analtech, thickness 0.25 mm).

7,8-Dihydro[1,4]diazepino[1,2,3-gh]purine-9(10H)-one (7). A.

To a solution of adenine (2.7 g, 20 mmoles) in 50 ml of freshly distilled dry DMSO was added acrylic anhydride (4 ml, 35 mmoles) dropwise. The solution was stirred in an oil bath at 60° for 24 hours. A solid formed and was separated by filtration, washed with 5 ml of 95% ethanol and 10 ml of acetone, and dried under suction to give a yellowish solid (0.73 g, 19%), mp, did not melt below 300°. In four different runs under identical conditions, the yield varied from 19 to 25%. The product was recrystallized from water, one charcoal treatment was given, to give colorless crystals (0.5 g, 13%), mp did not melt below 300°; 1H nmr (sodium deuterioxide/deuterium oxide): 60 MHz, 2.4-2.9 (m, 2, $OCCH_2$), 3.95-4.4 (m, 2, NCH_2), 7.85 (s, 1, 8-CH), 8.1 (s, 1, CH); ms: m/e 189 (M^+), 161 ($M^+ - CO$), 135 (adenine), 108 (135 - HCN); ir: 1680 cm^{-1} (CO); uv: λ max, pH 1.6, 281 nm (ϵ , 19,100), 300 nm (s), pH 6.8, 285 nm (ϵ , 17,600), 295 nm (s) (ϵ , 13,500), pH 12.3, 273 nm (ϵ 11,200), 284 nm (s).

Anal. Calcd. for $C_8H_7N_5O$: C, 50.79; H, 3.70; N, 37.04. *Found:* C, 50.36; H, 4.11; N, 36.76.

B.

To a solution of adenine (1.35 g, 10 mmoles) in 20 ml of dry DMSO was added vinyl acrylate (2.4 ml, 24 mmoles). The solution was stirred at 60° for 24 hours. A solid formed and was separated by filtration, washed with acetone, and dried under suction to give a slightly yellow solid (0.6 g, 32%). The product was recrystallized from water, one charcoal treatment was given, to give colorless crystals (0.5 g, 26%), mp, did not melt below 300°. The spectral properties were identical to those described under method A.

3-(Carboxyethyl)adenine (8). A.

To a stirred solution of adenine (0.675 g, 5 mmoles) in 80 ml of freshly distilled, dry DMF was added acryloyl chloride (1.2 ml, 15 mmoles) dropwise. The cloudy solution was stirred at room temperature for 18 hours. A solid formed and was separated by filtration, washed with acetone, dried under suction to give a yellowish solid (0.42 g, 40%), mp, 185-190° dec. It was recrystallized from 1:1 water-ethanol to give colorless crystals (0.32 g, 31%), mp 273-275° dec. Analysis (tlc, silica gel, 1:1 chloroform-methanol, 1-butanol-acetic acid-water), showed that the product was homogeneous; 1H nmr (sodium deuterioxide-deuterium oxide): 60 MHz, 2.4-2.88 (t, 2, $OCCH_2$), 3.9-4.4 (t, 2, NCH_2), 7.68 (s, 1, 8-CH), 7.92 (s, 1, 2-CH); ms: m/e 207 (M^+), 189 ($M^+ - H_2O$), 135 (adenine), 108 (135 - HCN), 81 (108 - HCN); ir: 3300-2800 (broad, carboxylic OH), 1700 (CO); uv: λ max, pH 1, 275 nm (ϵ 17,000), pH 12, 273 nm (ϵ , 12,200).

Anal. Calcd. for $C_8H_9N_5O_2 \cdot 0.25H_2O$: C, 45.38; H, 4.52; N, 33.08. *Found:* C, 45.64; H, 4.42; N, 33.08.

B.

To a chilled solution of adenine (1.35 g, 10 mmoles) in 10 ml of 1 N sodium hydroxide was added acrylic anhydride (2 ml, 18 mmoles) dropwise. The solution was stirred for 17 hours at room temperature. A solid formed and was separated by filtration, washed with water and acetone, and dried under suction to give a white solid (0.74 g, 36%), mp 250-270° dec. Analysis (tlc, silica gel, 1:1 chloroform-methanol), showed that the product was contaminated with traces of adenine. It was then suspended in 50 ml of hot 1:1 water-ethanol for 30 minutes. It was separated by filtration, washed with acetone, and dried under suction to give a dry pro-

duct (0.6 g, 30%), mp 260-265° dec. Analysis (tlc, silica gel, 1:1 chloroform-methanol, 4:1:1 1-butanol-acetic acid-water, 6.9:0.1:3 2-propanol-acetic acid-water), showed that the product was now homogeneous. It was recrystallized from 1:1 water-ethanol to give colorless crystals (0.4 g, 19%), mp 270-272° dec. Spectral properties were identical to those described under method A.

C.

To a chilled solution of adenine (1.35 g, 10 mmole) in 10 ml of 1 *N* sodium hydroxide was added methyl acrylate (1.1 ml, 12 mmoles) dropwise. The solution was stirred at room temperature for 24 hours. A solid formed and was separated by filtration, washed with acetone, and dried under suction to give a white solid (1 g, 48%), mp 200-210° dec; Analysis (tlc, silica gel), 1:1 chloroform-methanol, showed that the product was contaminated with unreacted adenine. The product was separated from adenine by extraction with 1:1 water-ethanol as described under method B to give a tlc pure product (0.65 g, 31%), mp 250-260° dec. It was then recrystallized from 1:1 water-ethanol to give colorless crystals (0.4 g, 19%), mp 270-274° dec. Spectral properties were identical to those described under method A.

D.

To a chilled solution of adenine (1.35 g, 10 mmoles) in 10 ml of 1 *N* aqueous sodium hydroxide was added acryloyl chloride (1 ml, 12 mmoles) dropwise. The solution was stirred at room temperature for 2 hours. A solid was formed and was separated by filtration, washed with acetone, and dried under suction to give a white solid (1 g, 48%), mp 220-240° dec. It was recrystallized from 1:1 water-ethanol to give colorless crystals (0.6 g, 29%), mp 270-272° dec. Spectral properties were identical to those described under method A.

7-(Carboxyethyl)adenine (10). A.

7,8-Dihydro[1,4]diazepino[1,2,3-*gh*]purine-9(10*H*)-one (0.189 g, 1 mmole) was dissolved in 2 ml of 1 *N* sodium hydroxide and was heated in an oil bath at 60° for 7 hours. The solution was acidified to pH 5 (pH-paper) using concentrated hydrochloric acid. A solid was formed and was removed by filtration, washed with 10 ml of acetone and dried under suction to give a white product (0.196 g, 95%), mp, did not melt below 300°. It was recrystallized from 1:2 water-ethanol to give colorless crystals (0.16 g, 78%), mp, did not melt below 300°. Analysis (tlc, silica gel, 1:1 chloroform-methanol, 4:1:1 1-butanol-acetic acid-water), showed that the product was homogenous. Spectral properties were as follows; ¹H nmr (sodium deuteriooxide-deuterium oxide): 90 MHz, 2.55-2.75 (t, 2, OCCH₂), 4.2-4.4 (t, 2, NCH₂), 7.84 (s, 1, 8-CH), 7.91 (s, 1, 2-CH); ms: *m/e* 207 (M⁺), 189 (M⁺ - H₂O), 161 (189 - CO), 135 (adenine), 108 (135 - HCN); ir: 3450-2500 (broad, carboxylic OH), 1700 (CO); uv: λ max, pH 1.2, 274 nm (ε 11,200), pH 12.5, 270 nm (ε, 8,800).

Anal. Calcd. for C₈H₈N₅O₂: C, 46.38; H, 4.35; N, 33.82. Found: C, 45.88; H, 4.46; N, 34.67.

B.

A solution of 7-(carbomethoxyethyl)adenine (0.024 g, 0.11 mmole) in 5 ml of 3 *N* hydrochloric acid was heated on a steam bath for 4 hours. The solution was adjusted to pH 4 (pH-paper) using saturated aqueous sodium hydroxide solution. This acidified solution showed a single spot on tlc (silica gel, 1:1 chloroform-methanol). The solution was evaporated to dryness to give a residue (0.9 g) which was extracted with 2.5 ml of distilled water. The residue after extraction (0.038 g) was still contaminated with sodium chloride but was used without further purification. It was identical to the product prepared by method A on tlc (silica gel and alumina, 1:1 chloroform-methanol, 4:1:1 1-butanol-acetic acid-water). The spectral properties were also identical to those described under method A.

Isomeric Mixture of 9- and 7-(Cyanoeethyl)adenines 4 and 9.

To a solution of adenine (1.35 g, 10 mmoles) in 20 ml of hot DMSO was added acrylonitrile (2 ml, 30 mmoles). The solution was stirred in an oil bath at 60° for 24 hours. Solvent was removed *in vacuo* to give a dry yellowish solid (1.82 g, 97%), mp 243-245°.

Analysis (tlc, silica gel, 1:1 chloroform-methanol, 4:1:1 1-butanol-acetic acid-water, 6.9:0.1:3 2-propanol-acetic acid-water), showed that this product was a mixture of two products and was completely free of adenine. The mixture of products was separated by column chromatography as described below.

A solution of 0.46 g of the product in 40 ml of hot 1:1 methanol-water was cooled to room temperature. The crystals formed were separated by filtration, washed with acetone, and dried under suction to give a white powder (0.18 g, 39% recovery), mp 255-258°, (lit mp of 9-(cyanoethyl)adenine, 255-257° [7]). Spectral properties of this product were identical to that of 9-(cyanoethyl)adenine.

To the filtrate was added 0.5 g of silica gel (grade 950, mesh size 60-200) and the slurry was allowed to sit for 12 hours. Solvent was then removed *in vacuo* to give dry silica gel on which the product was adsorbed. The silica gel was slurried with 10 ml of 7:3 chloroform-methanol and was poured on top of a column of silica gel (20 g, grade 950, mesh size 60-200) and eluted with 7:3 chloroform-methanol. Thirty-six fractions were collected, each of 10-15 ml. Fractions 1-9 showed a fast-moving single spot, fractions 10-19 showed two spots, fractions 20-36 showed a slow-moving single spot on the tlc (silica gel, 7:3 chloroform-methanol). Fractions 1-9 were combined and evaporated to dryness to give a white product which was recrystallized from 1:1 ethanol-water (0.1 g, 21% recovery), mp 255-257°. Spectral properties were identical to that of 9-(cyanoethyl)adenine. Fractions 20-36 were combined and evaporated to dryness to give another white product (0.082 g, 18% recovery), mp, did not melt below 300°. This product was identified as 7-(cyanoethyl)adenine from its spectral properties which were as follows; ¹H nmr (DMSO-*d*₆): 60 MHz 2.85-3.08 (t, 2, NCCH₂), 4.48-4.71 (t, 2, NCH₂), 6.72 (broad, 2, NH₂), 7.83 (s, 1, 8-CH), 7.93 (s, 1, 2-CH); ms: *m/e* 188 (M⁺), 160, 148 (M⁺ - CH₂CN), 135 (adenine), 121 (148 - HCN), 108 (135 - HCN); ir: 3340 (NH₂), 3150 (NH₂), 2250 (CN); uv: λ max, pH 1.2, 274 nm (ε 11,300), pH 12.5, 269 nm (ε, 9,200).

Anal. Calcd. for C₈H₈N₆·0.15H₂O: C, 50.33; H, 4.38; N, 44.02. Found: C, 50.48; H, 4.26; N, 43.80.

Isomeric Mixture of 9- and 7-(Carbomethoxyethyl)adenines 6 and 11.

Adenine (1.35 g, 10 mmoles) was dissolved in 20 ml of freshly distilled dry DMSO. The solution was stirred in an oil bath at 60° and to it was added methyl acrylate (2.7 ml, 30 mmoles). Stirring was continued for 24 hours and then DMSO was removed *in vacuo* to give a slightly wet residue. The residue was suspended in 20 ml of acetone for 1 hour, separated by filtration, and dried under suction to give a white solid (1.97 g, 89%). Analysis (tlc, silica gel, 1:1 chloroform-methanol, 4:1:1 1-butanol-acetic acid-water), showed that this solid was free of the starting material and contained two products. The mixture was separated by column chromatography as described below.

The mixture of products (0.41 g) was dissolved in 40 ml of 1:1 (methanol-water) and was concentrated to 20 ml. Silica gel (0.5 g, grade 950, mesh size 60-200) was added to this solution and the suspension was stored at room temperature overnight. Solvent was removed *in vacuo* to give dry silica gel on which the products were adsorbed. It was slurried in 10 ml of 9:1 chloroform-methanol and poured on the top of the silica gel column (20 g, grade 950, mesh size 60-200). Elution was done with 9:1 chloroform-methanol and 23 fractions of 10 ml each were collected. All these fractions showed a single spot on tlc (silica gel), 9:1 chloroform-methanol. This was the fast-moving spot from the product mixture. The fractions 1-23 were combined and evaporated to dryness to give a white powdery product which was recrystallized from 1:1 ethanol-water (0.2 g, 49% recovery), mp 184-185°. This was identified as 9-isomer from the spectral properties which were as follows; ¹H nmr (DMSO-*d*₆): 60 MHz, 2.74-3.1 (t, 2, OCCH₂), 3.52 (s, 3, OCH₂), 4.16-4.55 (t, 2, NCH₂), 7.0-7.42 (broad, 2, NH₂), 8.12 (s, 1, 8-CH), 8.18 (s, 1, 2-CH); ms: *m/e* 221 (M⁺), 206 (M⁺ - CH₃), 190 (M⁺ - OCH₃), 178, 162 (190 - CO), 148 (162 - CH₂), 135 (adenine), 108 (135 - HCN); ir: 3290 (NH₂), 1735 (CO); uv: λ max, pH 1.3, 259 nm (ε 14,400), pH 12.4, 261 nm (ε 14,300).

Anal. Calcd. for C₉H₁₁N₅O₂·0.2H₂O: C, 48.08; H, 5.11; N, 31.15. Found: C, 48.27; H, 4.96; N, 31.02.

Elution was further continued with chloroform-methanol, 8:2, 7:3, 5:5,

100 ml each and fractions 24 to 29, each of 50 ml, were collected. These fractions were concentrated to 5 ml and examined on tlc (silica gel, 9:1 chloroform-methanol). Fractions 24 and 25 showed two spots whereas fractions 26-29 showed a single slower moving spot. Fractions 26-29

were combined and evaporated to dryness to give dry, white product (0.05 g, 12% recovery), mp, did not melt below 300°. This was identified as a 7-isomer from its spectral properties; ¹H nmr (DMSO-d₆): 60 MHz, 2.7-3.05 (t, 2, OCCH₂), 3.6 (s, 3, OCH₃), 4.4-4.8 (t, NCH₂), 6.55-6.94 (broad, 2, NH₂), 7.95 (two closely spaced singlets, 2, 8-CH and 2-CH); ms: m/e 221 (M⁺), 190 (M⁺ - OCH₃), 162 (190 - CO), 148 (162 - CH₂), 135 (adenine), 108 (135 - CN); ir (potassium bromide): 3320 (NH₂), 3140 (NH₂), 1730 (CO); uv: λ max, pH 1.3, 274 nm (ε, 13,000), pH 12.5, 270 nm (ε, 8,500).

Anal. Calcd. for C₉H₁₁N₅O₂: C, 48.87; H, 5.01; N, 31.67. Found: C, 48.42; H, 4.97; N, 31.40.

6-Acetylaminopurine (2).

To a solution of adenine (1.35 g, 10 mmoles) in 25 ml of freshly distilled, dry DMSO was added vinyl acetate (1.6 ml, 17.5 mmoles). The solution was stirred in an oil bath at 60° for 24 hours. A solid was formed and was separated by filtration, washed with 95% ethanol, acetone, and dried under suction to give a white solid (0.81 g, 46%). The product was crystallized from water to give colorless crystals (0.6 g, 34%), mp 260-300° partial decomposition, (lit mp >260° [13]); ¹H nmr (trifluoroacetic acid): 90 MHz, 1.98 (s, 3, CH₃), 8.32 (s, 2, 8-CH and 2-CH); ms: m/e 177 (M⁺), 135 (adenine), 108 (135 - HCN); ir: 3350 (NH), 1695 (CO); uv (water): λ max, 279 nm.

1-(Carboxyethyl)-9-(cyanoethyl)adenine (12).

To a solution of 9-(cyanoethyl)adenine (2.54 g, 13.5 mmoles) in 30 ml of dry DMSO was added acrylic anhydride (3.1 ml, 27 mmoles). The solution was stirred in an oil bath at 60° for 6 hours. A solid formed after storing the solution overnight at room temperature. The solid was separated by filtration, washed with 95% ethanol and acetone, and dried under suction to give a yellow solid (1.37 g, 39%). The product was recrystallized from water. Several charcoal treatments were needed to decolorize the solution, finally colorless crystals were obtained. The crystals were separated by filtration, washed with acetone, and dried under suction to give a powdery solid (0.9 g, 26%), mp 198-200° partial decomposition, 210-214° complete decomposition. Analysis (tlc, silica gel, 1:1 chloroform-methanol, 4:1:1 1-butanol-acetic acid-water), and 6.9:0.1:3 2-propanol-acetic acid-water), showed that the product was homogeneous; ¹H nmr (sodium deuterioxide-deuterium oxide): 90 MHz, 2.5-2.78 (m, 2, NCCH₂), 3.49-3.81 (m, 2, CH₂CO₂H), 4.1-4.52 (m, 4, 1-NCH₂ and 9-NCH₂), 8.0 (s, 1, 8-CH), 8.13 (s, 1, 2-CH); ms: m/e 260 (M⁺) was not observed, 188 (M⁺ - C₂H₄ and CO₂), 148 (188 - CH₂CN), 135 (adenine), 108 (135 - HCN); ir: 3400-2800 (broad, carboxylic OH), 2250 (CN), 1690 (CO); uv: λ max, pH 1.9, 261 nm (ε, 14,800), pH 12, 261 nm (ε, 11,700), 268 nm (s) (ε, 11,300).

Anal. Calcd. for C₁₁H₁₂N₆O₂·0.25H₂O: C, 49.90; H, 4.76; N, 31.74. Found: C, 50.00; H, 4.83; N, 31.63.

1-(Carboxyethyl)-9-(cyanoethyl)adenine Hydrochloride (12).

To a solution of 9-(cyanoethyl)adenine (1.88 g, 10 mmoles) in 40 ml of

dry DMF was added acryloyl chloride (2.5 ml, 30 mmole). The solution was refluxed for 12 hours. A solid separated from the solution when chilled in ice water. This was separated by filtration, washed with acetone, and dried under suction to give a dry solid (0.76 g, 26%). The product was recrystallized from water, two charcoal treatments were given, to give colorless crystals (0.68 g, 23%), mp 170° turned yellow, 198-203° slow decomposition. Analysis (tlc, silica gel, 1:1 chloroform-methanol, 4:1:1 1-butanol-acetic acid-water, 6.9:0.1:3 2-propanol-acetic acid-water), showed that the product was homogeneous. Spectral properties were as follows; ¹H nmr (sodium deuterioxide-deuterium oxide): 90 MHz, 2.7-2.91 (m, 2, NCCH₂), 3.6-3.9 (m, 2, CH₂CO₂H), 4.24-4.74 (m, 4, 1-NCH₂ and 9-NCH₂), 8.11 (s, 1, 8-CH), 8.21 (s, 1, 2-CH); ms: identical to that described above; ir: 3400 (OH), 2250 (CN), 1730 (CO); uv: λ max, pH 1.7, 261 nm (ε 12,300), pH 12.4, 261 nm (ε 11,800), 268 (s) (ε 11,800).

Anal. Calcd. for C₁₁H₁₃ClN₆O₂·0.05H₂O: C, 42.96; H, 4.65; N, 27.32. Found: C, 42.66; H, 4.82; N, 27.48.

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