Chemistry of 5-Pyrimidinecarboxaldehydes

Lawrence Bell*, H. Michael McGuire and G. Andrew Freeman

Wellcome Research Laboratories, Department of Organic Chemistry, Burroughs Wellcome Co., Research Triangle Park, North Carolina 27709

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Selective hydrolysis of 2-amino-4,6-dichloro-5-pyrimidinecarboxaldehyde, **2**, gave 2-amino-4-chloro-1,6-dihydro-6-oxo-5-pyrimidinecarboxaldehyde, **5**. The oxime of **2** rearranged to 2-amino-4-chloro-1,6-dihydro-6-oxo-5-pyrimidinecarbonitrile, **8**. Reaction of **8** with 4-phenylbutylamine resulted in the displacement of the 4-chloro atom to give compound **9**. Hydrolysis of the cyano function of **9** gave amides **12**, **13**, and **14** depending on reaction conditions. A discussion of the ^{1}H-nmr spectrum of 2-amino-1,6-dihydro-6-oxo-4-[(4-phenylbutyl)amino]-5-pyrimidinecarboxcaldehyde, **6**, is presented.

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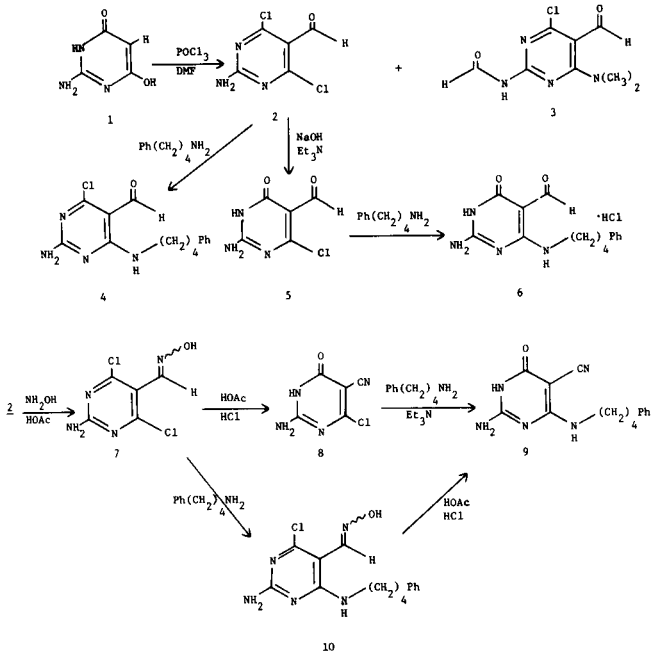
The Vilsmeier-Haack reaction is useful in the preparation of 5-pyrimidinecarboxaldehydes, introducing a formyl group directly onto the 5 position of a preformed pyrimidine. By this method, Klötzer and Herberz reported (1) the preparation of 2-amino-4,6-dichloro-5-pyrimidinecarboxaldehyde, **2**, in 28% yield from 2-amino-6-hydroxy-4(3*H*)-pyrimidinone, **1** (Scheme I). The dichloroaldehyde, **2** was sought by us as a useful starting material in developing synthetic routes to other 5-pyrimidinecarboxaldehydes and related compounds, some of which (Scheme I) are multifunctional intermediates potentially useful in the synthesis of bicyclic compounds.

Scheme I



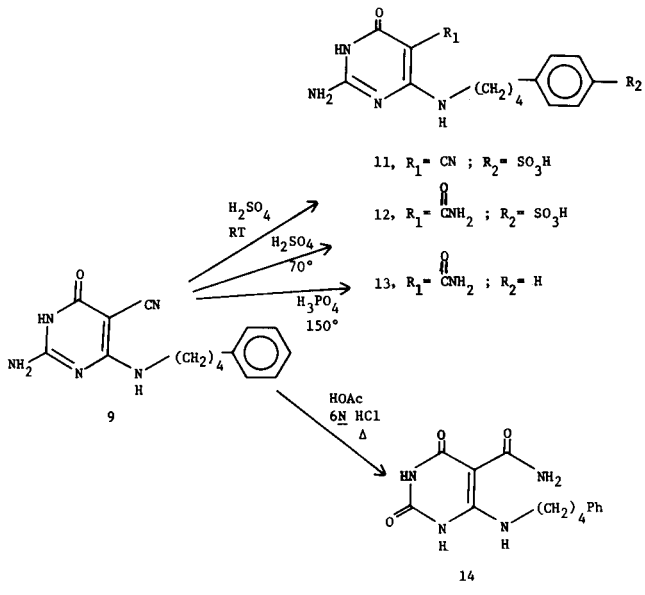
In our hands the formylation-chlorination of **1**, using dimethylformamide-phosphorus oxychloride, gave **2** in 51% yield. Another product of the reaction in low yield was the previously unreported *N*-[4-chloro-6-(dimethylamino)-5-formyl-2-pyrimidinyl]formamide, **3**. Treatment of **2** with methanolic 4-phenylbutylamine gave a 53% yield of the 4-chloro-6-substituted amino derivative **4**; treatment of a refluxing aqueous solution of **2** with one equivalent of sodium hydroxide gave 2-amino-4-chloro-1,6-dihydro-6-oxo-5-pyrimidinecarboxaldehyde, **5**, in 70% yield. Reaction of **5** with 4-phenylbutylamine gave the 6-substituted aminopyrimidine, **6**, isolated as its hydrochloride salt. Treatment of **2** with hydroxylamine hydrochloride in acetic acid gave the oxime derivative **7**. Treatment of the oxime **7** with anhydrous hydrochloric acid in distilled acetic acid gave 2-amino-4-chloro-1,6-dihydro-6-oxo-5-pyrimidinecarbonitrile, **8**. Attempts to prepare **8** from **7** under a variety of other conditions, including acetic acid, acetic acid/one drop of concentrated hydrochloric acid, sodium hydroxide in 95% ethanol, or refluxing sodium methoxide in methanol gave no reaction.

The reaction of the oxime **7** with 4-phenylbutylamine gave the 4-chloro-6-phenylbutylamine oxime **10**. Oxime **10** in hydrogen chloride-acetic acid gave 2-amino-1,6-dihydro-6-oxo-4-[(4-phenylbutyl)amino]-5-pyrimidinecarbonitrile, **9**. This compound was also prepared by the displacement of the 4-chloro group of **8** with 4-phenylbutylamine.

The mechanism of the transformation, oxime to nitrile, is proposed to occur *via* an unstable intermediate isoxazole which undergoes rearrangement to the nitrile **8** (2). The stability of oxime **7** is in contrast to the reported facile rearrangement of the 2-H analog of **7** in acetic acid (2).

Attempted hydrolysis of the 5-pyrimidinecarbonitrile **9** with concentrated sulfuric acid at room temperature (3) gave only the sulfonated nitrile **11**, Scheme II. Elevation of the reaction temperature to 70° resulted in the formation of the amide **12**. Further hydrolysis of the amide **12** to a carboxylic acid could not be effected with either sulfuric acid or sodium hydroxide (4). Treatment of **89** with 100% phosphoric acid (5) at 150° for 3 hours hydrolyzed the 5-cyano group to the amide **13**. Hydrolysis of compound **9** with 6*N* hydrochloric acid gave the uracil amide **14**.

Scheme II



The nmr spectra of compounds **6, 13**, and **14**, indicate considerable restruction in the degree of rotation about the pyrimidine-carbonyl bond. This restriction is assumed to be caused by strong hydrogen bonding between the carbonyl group in the 5-position and the ortho substituents on the ring.

The aldehyde proton signal of the 5-pyrimidinecarboxaldehyde **6** is a doublet at δ 8.3 (J = 15). This splitting was investigated by proton decoupling experiments. In the 100 MHz spectrum (Figure 1), the aldehyde proton (labeled a) is a doublet, the 6-amino proton (labeled b) is a complex multiplet and the methylene protons adjacent to the 6-nitrogen (labeled c) also show up as a multiplet. Decoupling the aldehyde signal converts the N-H multiplet (b) to a triplet. Decoupling the N-H signal converts the aldehyde proton signal to a singlet and the adjacent methylene signal to a triplet. Finally, decoupling the methylene signal converts the N-H signal to a doublet with a J value of 15 Hz, which matches the J value of the aldehyde doublet.

Interestingly, 15 Hz, is also the J value for *trans* olefin protons and as is shown, hydrogen bonding between the amino hydrogen and the aldehyde oxygen gives the coupled protons a "*trans*" relationship.

The nmr spectra of both compounds **13** and **14** show that the 5-amide protons are non-equivalent. This non-equivalence is assumed to be due to the hydrogen bonding interactions between the amide carbonyl group and the 4-amino proton and between one of the amide protons and the 6-oxo function. Two six-membered rings can readily be formed by these hydrogen bonding interactions.

EXPERIMENTAL

Physical Data.

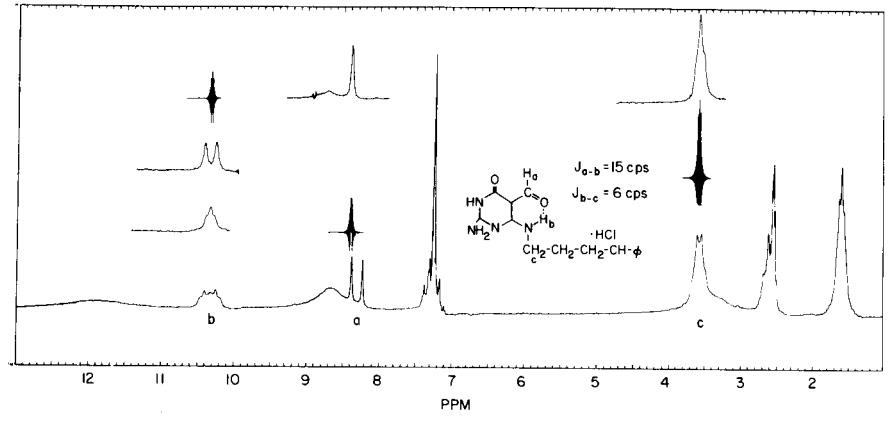
Melting points were determined with a Thomas-Hoover melting-point apparatus or Mel-temp hot stage and are uncorrected; ir spectra were obtained in a Perkin Elmer 237B grating spectrophotometer in Nujol; uv spectra were recorded on a Cary Model 118; ^{1}H nmr spectra were recorded on a Varian T-60 or a Varian XL-100-15 spectrometer in DMSO-d_6 with TMS (δ 0.00 ppm) as an internal standard. Compound purity was checked by tlc. Mass spectra were determined on a Varian MAT 731 double focusing mass spectrometer. All solvents were evaporated on a Büchi Rotavapor evaporator under water-aspirator pressure using a water bath set at 35-60°.

2-Amino-4,6-dichloro-5-pyrimidinecarboxaldehyde (**2**) and *N*-[4-Chloro-6-(dimethylamino)-5-formyl-2-pyrimidinyl]formamide (**3**).

Phosphorus oxychloride (108 ml, 1.18 moles) was cooled in an ice-water bath to ~5°. Dry dimethylformamide (35 ml) was added slowly with stirring over 15 minutes to the phosphorus oxychloride. A white precipitate formed during the addition. The reaction mixture was warmed gently to dissolve the precipitate and produce a clear solution to which was added 2-amino-6-hydroxy-4(3*H*)-pyrimidinone, **1**, (28 g, 0.22 mole, Aldrich Chem. Co.) in small portions with stirring over a period of 30-40 minutes. Heating the mixture on a steam bath for ~5 hours gave a dark red-brown solution. About 15 ml of excess phosphorus oxychloride was

Figure 1

100mc NMR Decoupling Experiment on 2-Amino-5-formyl-4-hydroxy-6-(4-phenylbutylamino) pyrimidine hydrochloride



removed by distillation *in vacuo*, leaving a dark red-brown viscous oil. The oil was mixed with 1500 ml of crushed ice and allowed to stand at room temperature overnight; the resulting mixture consisted of a red-orange solution and a yellow-brown solid. The solid was collected by filtration. The filtrate was treated with concentrated ammonium hydroxide in portions to pH ~ 7 (235 ml of ammonium hydroxide required). The yellow-brown precipitate which formed was collected by filtration. The combined precipitates were vacuum dried at room temperature overnight and then extracted with hot ethyl acetate (6 × 400 ml) leaving a brown insoluble residue which was discarded. Upon cooling, a yellow precipitate formed in the combined ethyl acetate extracts and filtration gave 21.8 g of 2-amino-4,6-dichloro-5-pyrimidinecarboxaldehyhde, **2**, (51% yield). Recrystallization from ethyl acetate gave 15 g of pure **2**, mp > 130° dec; nmr (DMSO-d_6): δ 8.5 (s, broad, 2, -N*H*), 10.1 (s, 1, -C*H*O); uv (95% ethanol): λ max (ε × 10^3) 283 nm (13.6), 239 (9.4).

Anal. Calcd. for $C_5H_3Cl_2N_3O$: C, 31.28; H, 1.57; N, 21.89; Cl, 36.93. Found: C, 31.04; H, 1.72; N, 21.83; Cl, 37.17.

A second precipitate which formed in the aqueous ammonium hydroxide filtrate after several days was filtered and the yellow solid was vacuum dried at room temperature for 3 days. Recrystallization from 1,2-dichloroethane gave 2.0 g of **3** (4% yield): mp 190-193.5° dec; nmr (DMSO-d_6): δ 3.05 (s, 6, -N(CH_3)$_2$), 9.30 (d, 1, J ≅ 4.5 Hz, O*H*CN-H), 10.05 (s, 1, C-C*H*O), 11.05 (d, 1, J ≅ 4.5 Hz, OHC-N-*H*); uv (95% ethanol): λ max (ε × 10^3) 325 nm (6.8), sh 272 (18.1), 253 (32.5).

Anal. Calcd. for $C_6H_5ClN_4O_2$: C, 42.03; H, 3.97; N, 24.51; Cl, 15.51. Found: C, 41.99; H, 3.90; N, 24.40; Cl, 15.66.

2-Amino-4-chloro-6-[(4-phenylbutyl)amino]-5-pyrimidinecarboxaldehyde (**4**).

A solution of **2** (3.64 g, 0.019 mole), triethylamine (2.6 ml, 0.019 mole), 4-phenylbutylamine (2.97 g, 0.02 mole, Aldrich Chem. Co.), and 75 ml of methanol was refluxed for 2 hours. The methanol was removed on a rotary evaporator to give a yellow solid. Three recrystallizations from 95% ethanol gave 3.08 g (53% yield) of the desired product **4**, mp 115.5-118°; nmr (DMSO-d_6): δ 1.55 (m, 4, -CH$_1$CH_2CH_2 CH$_2$-), 2.6 (m, partial overlap with DMSO-H, 2, -CH$_2$-CH_2-Ar), 3.5 (m, partial overlap with water, 2, -NH-CH_2-CH$_2$-), 7.22 (s, 5, -PH), 7.6 (s, broad, 2, -NH_2), 9.2 (t, 1, -N*H*-CH$_2$-), 9.9 (s, 1, -C*H*O); uv (95% ethanol): λ max (δ × 10^3) 3.35 nm (14.3).

Anal. Calcd. for $C_{15}H_{17}ClN_4O$: C, 59.11; H, 5.62; N, 18.38; Cl, 11.63. Found: C, 58.98; H, 5.80; N, 18.13; Cl, 11.79.

2-Amino-5-chloro-1,6-dihydro-6-oxo-5-pyrimidinecarboxaldehyde (**5**).

2-Amino-4,6-dichloro-5-pyrimidinecarboxaldehyde (1.92 g, 0.01 mole) and triethylamine (6.9 ml, 0.05 mole) were dissolved in 1500 ml of refluxing water. Sodium hydroxide (60 ml, 0.017*N*) was slowly added to the refluxing pyrimidine solution over a period of 1 hour. The reaction solution was refluxed for another 30 minutes, tlc (1:1 chloroform:ethyl ether) showed no starting material remaining. The warm solution was treated with 25 ml of 2*N*- acetic acid and then cooled in an ice-water bath to produce a light yellow precipitate. Filtration and vacuum drying at 80° gave 1.58 g (86%) of product. Recrystallization from water yielded the analytical sample (as its monohydrate), mp > 190° dec; nmr (DMSO-d_6: δ 7.9 (s, very broad, 2, -NH_2), 9.9 (s, 1, -C*H*O), 11.6 (s, 1, *H*-N); uv (95% ethanol): λ max (ε × 10^3) 313 nm (18.8), 244 (7.9).

Anal. Calcd. for $C_5H_4ClN_3O_2$·H_2O: C, 31.35; H, 3.16; N, 21.93; Cl, 18.51. Found: C, 31.69; H, 3.00; N, 21.89; Cl, 18.16.

2-Amino-1,6-dihydro-6-oxo-4-[(4-phenylbutyl)amino]-5-pyrimidinecarboxaldehyde (**6**).

A sample of **5** (0.159 g, 0.0009 mole) was mixed with 20 ml of methanol, triethylamine (0.14 ml, 0.001 mole) and 4-phenylbutylamine (0.149 g, 0.001 mole). After refluxing for 5 hours the hot reaction mixture was filtered. The filtrate was evaporated to dryness and the residue was dissolved in 110 ml of boiling 1*N* hydrochloric acid. The solution was evaporated to dryness under reduced pressure and the residue was extracted with 50 ml of boiling chloroform. Filtration of the hot chloroform mixture gave 0.1 g of insoluble material. Recrystallization of this material from 100 ml of boiling 1*N* hydrochloric acid gave 44 mg (15% yield) of pure **6**: mp 274-278° dec; nmr (DMSO-d_6): δ 1.6 (m, 4, -CH$_2$CH_2CH_2CH$_2$-), 2.5 (m, 2, -CH$_2$-CH_2Ar), 3.6 (m, 2, -NHCH_2CH$_2$-), 7.24 (s, 5, ArH), 8.3 (d, J = 15, 1, -C*H*O), 8.75 (s, broad, 2, -NH_2), 10.2 (m, 1, -N*H*-CH$_2$-), 11.0 (s, very broad, 1, N*H*); uv (95% ethanol): λ max (ε × 10^3) 309 nm (24.9), 260 (2.9), sh 224 (12.3).

Anal. Calcd. for $C_{15}H_{18}N_4O_2$·HCl: C, 55.81; H, 5.93; N, 17.36; Cl, 10.98. Found: C, 55.75; H, 6.06; N, 17.14; Cl, 10.89.

2-Amino-4,6-dichloro-5-pyrimidinecarboxaldehyde Oxime (**7**).

A sample of **2** (9.6 g, 0.05 mole) was mixed with 1100 ml glacial acetic acid and warmed slightly to dissolve most of the starting material. After cooling the mixture to room temperature, a solution of hydroxylamine hydrochloride (3.82 g, 0.055 mole) in 700 ml of absolute ethanol was added slowly to the stirred acetic acid mixture over a period of ~ 2 hours. A yellow precipitate formed and was collected by filtration. Recrystallization of the crude product from a large volume of 95% ethanol gave 6.28 g (61% yield) of pure **7**, mp ~ 150° dec; nmr (DMSO-d_6): δ 7.75 (s, broad, 2, -NH_2), 8.1 (s, 1, -C*H*=NO), 11.6 (s, 1, =NO*H*); uv (95% ethanol): λ max (ε × 10^3) 268 nm (16.9), sh 306 (4.9).

Anal. Calcd. for $C_5H_4Cl_2N_4O$: C, 29.01; H, 1.95; N, 27.06; Cl, 34.25. Found: C, 29.36; H, 2.05; N, 27.08; Cl, 34.31.

2-Amino-4-chloro-1,6-dihydro-6-oxo-5-pyrimidinecarbonitrile (**8**).

The oxime, **7**, (0.828 g, 0.004 mole) was dissolved in 100 ml of hot freshly distilled glacial acetic acid with stirring. The acetic acid had been distilled at atmospheric pressure through a 25 cm Vigreux column under anhydrous conditions, bp 114-116°. Anhydrous hydrogen chloride gas (Matheson) was bubbled into the hot reaction solution for ~ 1 minute and the solution was refluxed overnight. The cooled reaction mixture was filtered to remove a small amount of brown precipitate and the filtrate was evaporated under reduced pressure to dryness. Two recrystallizations of the residue from water gave 0.209 g (28% yield) of **8** as a 3/4 hydrate: mp > 350° dec; ir (Nujol): 2230 cm^{-1} (-C≡N); uv (95% ethanol): λ max (ε × 10^3) 300 nm (13.6), 233.5 (10.1).

Anal. Calcd. for $C_5H_3ClN_4O$·3/4 H_2O: C, 32.63; H, 2.46; N, 30.44; Cl, 19.26. Found: C, 32.93; H, 2.97; N, 30.01; Cl, 18.99.

2-Amino-1.6-dihydro-6-oxo-4-[(4-phenylbutyl)amino]-5-pyrimidinecarbonitrile (**9**).

The 6-phenylbutylamino oxime **10** (3.2 g, 0.01 mole) was dissolved in 100 ml of hot freshly distilled glacial acetic acid with stirring. Anhydrous hydrogen chloride gas (Matheson) was bubbled into the hot reaction solution for ~ 2 minute and the solution was refluxed overnight. The reaction solution was evaporated under reduced pressure to a brown oil. Two recrystallizations from 95% ethanol gave light yellow crystalline product, **9**, 1.40 g (49% yield): mp 209-215° dec. Another recrystallization from 95% ethanol gave the analytical sample, mp 213-215.5° dec; ir (Nujol), 2215 cm^{-1} (-C≡N); nmr (DMSO-d_6): ~ 1.3-1.7 (m, 4, CH$_2$-CH_2-CH_2-CH$_2$), 2.5 (m, 2, -CH$_2$-CH_2-Ph), 3.4 (m, 2, -NH-CH_2-CH$_2$), 6.8-7.2 (m, 3, -NH_2 and -N*H*-CH$_2$-), 7.3 (s, 5, Ar*H*), 10.3 (s, broad, 1, *H*N-); uv (95% ethanol): λ max (ε × 10^3) 273 nm (13.3), 228 (44.2).

Anal. Calcd. for $C_{15}H_{17}N_5O$: C, 63.59; H, 6.05; N, 24.72. Found: C, 63.68; H, 6.11; N, 24.78.

Compound **9** was also prepared by reaction of the chlorocyanopyrimidine **8** with 4-phenylbutylamine. The dichloro oxime **7** (0.828 g, 0.004 mole) was rearranged to the nitrile **8** as described above. Following removal of the reaction solvent (acetic acid) under reduced pressure, the crude product **8** was suspended in 25 ml of absolute ethanol and the ethanol was removed by evaporation under reduced pressure. After repeating the ethanol addition-evaporation the residue was suspended in 400 ml of absolute ethanol and 5.5 ml (4.04 g, 0.04 mole) of triethylamine was added. This mixture was then treated with 4-phenylbutylamine (0.67 g, 0.0045 mole). After refluxing on a steam bath for 24 hours the reaction solution was allowed to stand at room temperature for several days. Filtration and evaporation of the ethanol under reduced pressure gave a

viscous oil. Recrystallization of the oil from 50 ml of 1,2-dichloroethane gave 0.295 g of pure **9** (25% yield based on **7**). The tlc behaviour (silica gel, 9:1 chloroform:methanol) of this material was identical to that of compound **9** prepared from **10**.

2-Amino-4-chloro-6-[(4-phenylbutyl)amino]-5-pyrimidinecarboxaldehyde Oxime (**10**).

The dichloro oxime, **7** (2.07 g, 0.01 mole) was almost completely dissolved in 2 ℓ of hot absolute ethanol containing triethylamine (2.0 g, 0.02 mole). 4-Phenylbutylamine (1.49 g, 0.01 mole) was added and the reaction solution was refluxed on a steam bath for 2 hours and then kept at room temperature overnight. The ethanol was evaporated under reduced pressure and the residue was recrystallized from 20 ml of 1,2-dichloroethane. The crude product was extracted with 100 ml of boiling ethyl acetate and the mixture filtered ot remove the insoluble triethylamine hydrochloride. The ethyl acetate filtrate was evaporated under reduced pressure to dryness and the residue was recrystallized from 50 ml of 1,2-dichloroethane to give 2.08 g (66% yield) of pure **10**, mp 156-159°; nmr (DMSO-d_6): δ 1.3-1.8 (m, 4, -$CH_2CH_2CH_2CH_2$-), 2.6 (m, 2, -CH_2-CH_2-Ar), 3.5 (m, 2, -NH-CH_2-CH_2-), 6.85 (s, broad, 2, -NH_2), 7.15 (s, 5, ArH), 8.2-8.5 (overlapping s and m, 2, -N*H*CH_2- and CH=NOH), 8.35 (s, 1, C*H*=NOH); uv (95% ethanol): λ max (ε × 10^3) sh 319 nm (12.7), 308.5 (15.8), 280 (13.0), 226 (27.5).

Anal. Calcd. for $C_{15}H_{18}ClN_5O$: C, 56.34; H, 5.67; N, 21.90; Cl, 11.09. Found: C, 56.34; H, 5.68; N, 22.00; Cl, 11.10.

4-[4-[(2-Amino-5-cyano-1,6-dihydro-6-oxo-4-pyrimidinyl)amino]butyl]benzenesulfonic Acid (**11**).

The nitrile **9** (0.14 g, 0.0005 mole) was stirred with 2.5 ml concentrated sulfuric acid at room temperature for 1 hour giving a yellow solution. The solution was poured into a 50 ml beaker which was half-filled with crushed ice. A yellow precipitate formed immediately and the mixture was allowed to stand at room temperature until all of the ice had melted. Filtration gave 0.158 g (79% yield) of pure **11** (isolated as a dihydrate), mp 257-266° dec; ir (Nujol): 2230 cm^{-1} (-C≡N); nmr (DMSO-d_6): δ 7.0-7.8 (aromatic protons show an AA'BB' quartet which indiates *para* substitution of the ring); uv (95% ethanol): λ max (ε × 10^3) 273 nm (14.3), 228 (51.2).

Anal. Calcd. for $C_{15}H_{17}N_5O_4S$: C, 45.10; H, 5.29; N, 17.53. Found: C, 45.01; H, 5.29; N, 17.58.

4-[4-[[2-Amino-5-(aminocarbonyl)-1,6-dihydro-6-oxo-4-pyrimidinyl]amino]butyl]benzenesulfonic Acid (**12**).

The nitrile **9** (0.849 g, 0.003 mole) was stirred with 15 ml of concentrated sulfuric acid and heated to 70° for 2 hours. The resulting dark yellow solution was poured onto 100 ml of crushed ice and a yellow precipitate formed. The mixture was allowed to stand at room temperature until the ice melted; filtration gave a sticky solid. This solid was treated with 50 ml of boiling 95% ethanol and filtered hot, giving 0.99 g (87% yield) of crude product. Recrystallizaiton from 1:1 ethanol: water gave analytically pure product **12**, mp 295-300° dec; a field desorption mass spectrum of **12** was run at an emitter current of 20 mA, based peak (M^+, 1) mass 382, molecular ion (93% of base) M^+ = 381; uv (95% ethanol): λ max (ε × 10^3) 273 nm (14.1), 224.5 (46.3).

Anal. Calcd. for $C_{15}H_{19}N_5O_4S$: C, 47.24; H, 5.02; N, 18.36. Found: C, 47.39; H, 5.15; N, 18.34.

2-Amino-1,6-dihydro-6-oxo-4-[(4-phenylbutyl)amino]-5-pyrimidinecarboxamide (**13**).

The nitrile, **9**, (0.274 g, 0.00097 mole) was mixed with an estimated 3-5 g of orthophosphoric acid (crystalline, 100% phosphoric acid, Matheson, Colemen, and Bell). This acid is very hygroscopic and could not be weighed accurately. The reaction mixture was heated at 150° for 3½ hours giving a clear solution which was poured into ~20 ml of crushed ice. A white precipitate formed immediately. After the ice melted the solid was collected by filtration and recrystallized from isopropanol to give 0.12 g of crude **13**. The mother liquor was evaporated to dryness and the residue was chromatographed on a 10 g column of silica gel with 18:1 chloroform:methanol giving an additional 0.11 g of **13**. The combined samples were recrystallized from 1:1 ethanol:water giving 0.13 g (44% yield) of pure **13**, mp 253-259° dec; nmr (DMSO-d_6): δ 1.55 (m, 4, -$CH_2CH_2CH_2CH_2$-), 2.6 (m, 2, -CH_2CH_2-Ph), 3.4 (m, 2, -NH-CH_2CH_2-), 6.7 (d, 1, -CONH*H*), 6.7 (s, broad, overlaps amide proton signal, 2, -NH_2), 9.05 (d, 1, -CONH*H*, 10.2 (s, 1, N*H*), 10.45 (t, 1, -N*H*-CH_2-); uv (95% ethanol): λ max (ε × 10^3) 273.5 nm (15.9), 230 (42.1).

Anal. Calcd. for $C_{15}H_{19}N_5O_2$: C, 59.79; H, 6.36; N, 23.24. Found: C, 59.85; H, 6.59; N, 22.86.

1,2,3,4-Tetrahydro-2,4-dioxo-6-[(4-phenylbutyl)amino]-5-pyrimidinecarboxamide (**14**).

The nitrile **9** (0.283 g, 0.001 mole) was dissolved in a warm solution of 10 ml of 6*N* hydrochloric acid and 7 ml of glacial acetic acid. After refluxing for 3 days, the solution was cooled and a white precipitate formed. Filtration gave 0.117 g of crude product (39% yield) and recrystallization from 95% ethanol gave analytically pure **14**, mp 273-278.5°; nmr (DMSO-d_{16}): δ 1.55 (m, 4, -CH_2-$CH_2CH_2CH_2$-), 2.5 (m, 2, -CH_2-CH_2-Ph), 3.35 (m, 2, -NH-CH_2-CH_2-), 7.0 (d, J = 4 Hz, 1, -CONH*H*), 7.25 (s, 5, Ar*H*), 9.0 (d, J = 4 Hz, 1, -CONH*H*H), 10.7 (s, 1, N-*H*), 10.8 (s, 1, N-*H*), 11.35 (t, 1, -N*H*-CH_2-); uv (95% ethanol): λ max (ε × 10^3) 264 nm (22.7).

Anal. Calcd. for $C_{15}H_{18}N_4O_3$: C, 59.59; H, 6.00; N, 18.53. Found: C, 59.82; H, 6.04; N, 18.72.

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