SYNTHESIS AND REARRANGEMENTS OF IMIDAZOLO- AND TRIAZOLO-DIAZINES

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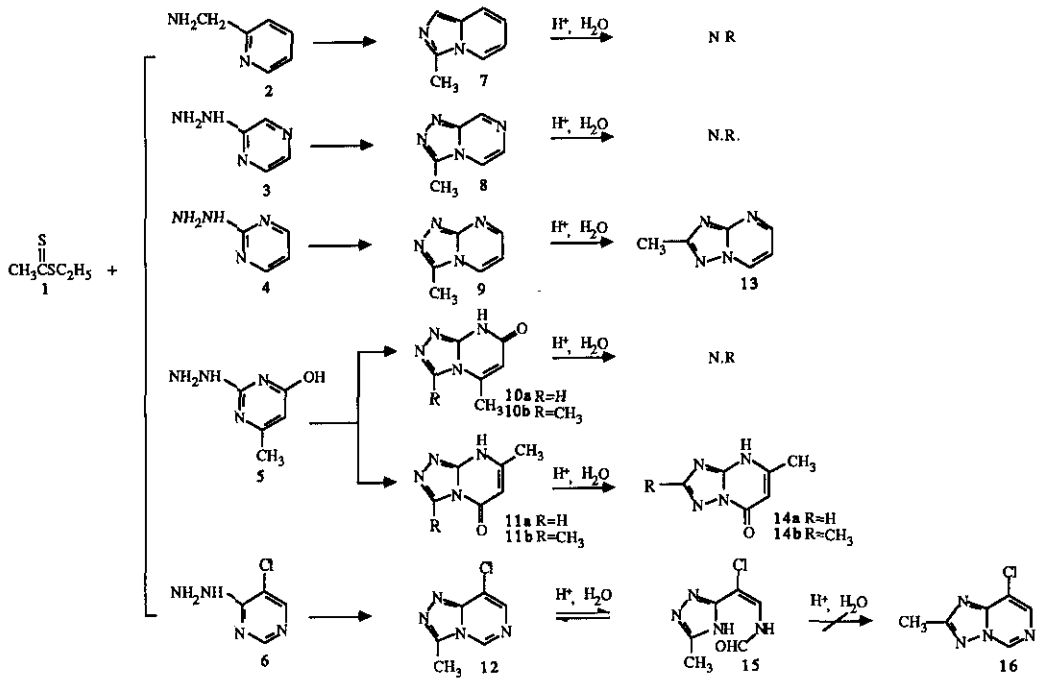
Abstract-3-Methylimidazolo[1,5-a]pyridine and 3-methyl-1,2,4-triazolo[4,3-a]-pyrazine were prepared by coupling ethyl dithioacetate with 2-(aminomethyl)-pyridine and 2-hydrazinopyrazine, respectively. Both compounds are stable in dilute acids and bases, unlike 3-methyl-1,2,4-triazolo[4,3-a]pyrimidine obtained by coupling the same dithioacetate with 2-hydrazinopyrimidine, which quickly undergoes a Dimroth type rearrangement. Coupling ethyl dithioacetate with 2-hydrazino-4-hydroxy-6-methylpyrimidine yielded a mixture of 3,5-dimethyl-1,2,4-triazolo[4,3-a]-7(8H)-pyrimidone and 3,7-dimethyl-1,2,4-triazolo[4,3-a]-5(8H)-pyrimidone, which were identified by 2D nmr. The last compound underwent a Dimroth rearrangement with acids to yield 2,5-dimethyl-1,2,4-triazolo[1,5-a]-7(4H)-pyrimidone, whereas the first did not. Finally, coupling ethyl dithioacetate with 5-chloro-4-hydrazinopyrimidine afforded 8-chloro-3-methyl-1,2,4-triazolo[4,3-c]pyrimidine, which upon treatment with acids underwent a reversible ring opening to afford 2-chloro-1-formamido-2-(5-methyl-1,3,4-triazolo-2-yl)ethene. The latter on pyrolysis gave the starting base without undergoing rearrangement.

INTRODUCTION

A number of nitrogen-bridged, purine-like C-nucleosides synthesized[1-6] for screening as antiviral or antitumor agents have been obtained by coupling hydrazino- or diamino-azines with benzyl 2,5-anhydro-6-O-benzoyl-D-allonothioimidate hydrochloride, 2,5-anhydro-6-O-benzoyl-D-glucono-thioimidate hydrochloride,[4] 2,6-anhydro-7-deoxy-3,4,5-tri-O-benzoyl-L-manno-heptonothioimidate hydrochloride,[5] or 2,5-anhydro-6-O-benzoyl-D-allonodithioate.[6] Some of these nucleosides were found to undergo Dimroth type rearrangements during their synthesis.[4,5] Because it is important to determine which base will withstand the reaction conditions leading to nucleoside formation, a number of purine-like bases were prepared and subjected to treatment with acids and bases. Bases which withstood this treatment without rearrangement were considered safe to incorporate in C-nucleoside molecules.

RESULTS AND DISCUSSION

Some nitrogen-bridged purine-like bases were prepared by coupling ethyl dithioacetate (1) with 2-(aminomethyl)pyridine (2) and 2-hydrazinopyrazine (3), as well as with three different hydrazinopyrimidines, namely, 2-hydrazinopyrimidine (4), 2-hydrazino-4-hydroxy-6-methylpyrimidine (5), and 5-chloro-4-hydrazinopyrimidine (6). The use of ethyl dithioacetate (1)[7] for coupling offered some advantage over previously used reagents, particularly in regard to the mild conditions needed. Refluxing ethyl dithioacetate (1) with 2-(aminomethyl)pyridine (2) in ethanol yielded N-[(2-pyridyl)methyl]thioacetamide, which was cyclized by refluxing with mercuric oxide and mercuric bromide in ethanol to afford 3-methylimidazo[1,5-a]pyridine (7) in 38% yield. The last compound had previously been prepared[8] by heating 2-(aminomethyl)pyridine (2) with excess acetic anhydride and acetic acid and cyclizing the resulting amide with phosphorus oxychloride. Although the yield of the amide was good, cyclization with phosphorus oxychloride reduced the overall yield significantly. Similarly, when 2-hydrazinopyrazine (3)[9,10] was refluxed with ethyl dithioacetate (1) in methanol, it gave 3-methyl-1,2,4-triazolo[4,3-a]pyrazine (8) in 22% yield. Compounds 7 and 8 are both stable in boiling acids, suggesting that their C-nucleosides could be safely prepared without fear of rearrangement.



The next purine-like base, 3-methyl-1,2,4-triazolo[4,3-a]pyrimidine (9), was obtained in 51% yield when 2-hydrazinopyrimidine (4)[11] was refluxed with ethyl dithioacetate (1) in propanol. Brown and Nagamatsu[12] prepared this compound by reacting 2-hydrazinopyrimidine (4) with triethyl orthoacetate and found that it rearranged to 2-methyl-1,2,4-triazolo[1,5-a]pyrimidine (13) upon refluxing in a mixture of acetic acid and sulfuric acid. Because the uv spectrum of the rearranged isomer differed markedly from that of the starting 3-methyl-1,2,4-triazolo[4,3-a]-pyrimidine (9), it was possible to follow the rearrangement spectrophotometrically. Ultraviolet spectra of 3-methyl-1,2,4-triazolo[4,3-a]pyrimidine (9) in hydrochloric acid (pH 2.55) were periodically recorded at room temperature. The absorption maximum of the starting material at 307 nm decreased, while that of the rearranged product at 277 nm increased and remained constant after 2 h (see Figure I). Apparently, the rearrangement of 3-methyl-1,2,4-triazolo[4,3-a]-pyrimidine (9) is not reversible, i.e., the rearranged isomer, 2-methyl-1,2,4-triazolo[1,5-a]-pyrimidine (13), does not revert to the starting base (9) when heated with acids, presumably because thermodynamically 13 is more stable than 9. The fact that 3-methyl-1,2,4-triazolo[4,3-a]-pyrimidine (9) readily rearranged with dilute acids and bases, suggests that C-nucleosides of this type would probably undergo rearrangement during their synthesis.

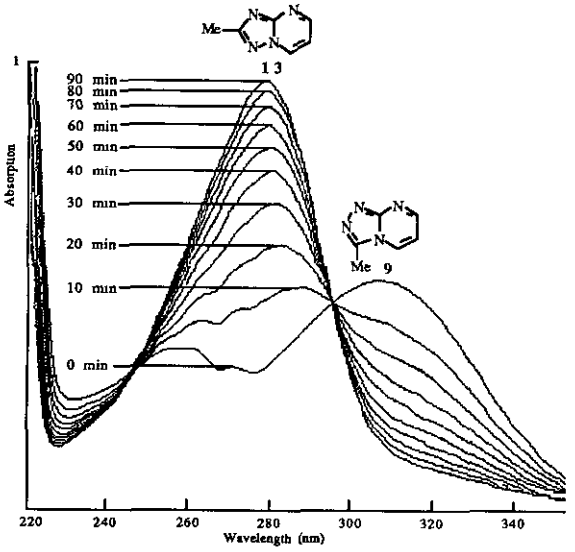
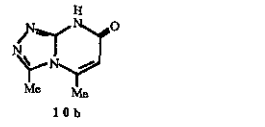


Figure I Uv spectra of solution of 3-methyl-1,2,4-triazolo[4,3-a]pyrimidine (9) in HCl (pH 2.55) recorded every 10 min at 20°C

The ^1H-nmr spectra of 3-methyl-1,2,4-triazolo[4,3-a]pyrimidine (**9**) and 2-methyl-1,2,4-triazolo-[1,5-a]pyrimidine (**13**) (see Table I) revealed that upon isomerization, the signals of the ring protons shifted to lower field, while those of the methyl protons shifted to higher field. The ^{13}C-nmr signals of the ring carbons and those of the methyl carbons in both isomers were sufficiently different to enable the recognition of the two isomers (see Table II).

When 2-hydrazino-4-hydroxy-6-methylpyrimdine (**5**) was refluxed with ethyl dithioacetate (**1**) in ethanol, it yielded two products, 3,5-dimethyl-1,2,4-triazolo[4,3-a]-7(8H)-pyrimidone (**10b**) and 3,7-dimethyl-1,2,4-triazolo[4,3-a]-5(8H)-pyrimidone (**11b**). The structure of the two isomers was determined unequivocally by 2D nuclear Overhauser effect spectroscopy (NOESY). In 2D NOESY spectra, the resonances along the diagonal correspond to the usual 1D spectra, while cross peaks (off diagonal resonances) connecting signals on the diagonal vertically and horizontally denote magnetization transfer between protons that are at close proximity to one another. Figures II and III show contour plots of 2D NOESY spectra of compounds **10b** and **11b**, respectively. The first shows cross peaks between *Me-3* and *Me-5* (see inset) and between the protons of the *Me-5* group and the low field H-6. These results agree with the assignment of a 3,5-dimethyl-1,2,4-triazolo-[4,3-a]-7(8H)-pyrimidone (**10b**) structure. Figure III, on the other hand, shows only one cross peak between Me-7 and H-6, as would be expected from 3,7-dimethyl-1,2,4-triazolo[4,3-a]-5(8H)-pyrimidone (**11b**).



10b

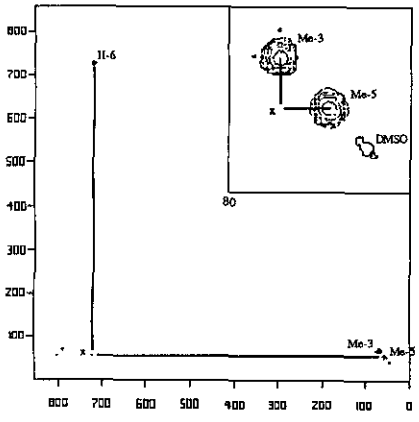
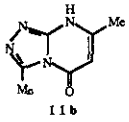


Figure II 2D NOESY spectra of 3,5-dimethyl-1,2,4-triazolo[4,3-a]-7(8*H*)-pyrimidone (50 MHz, in DMSO-d_6)



11b

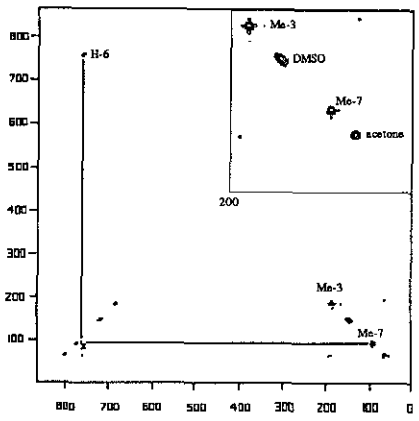
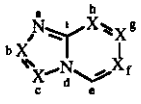


Figure III 2D NOESY spectra of 3,7-dimethyl-1,2,4-triazolo[4,3-a]-5(8*H*)-pyrimidone (50 MHz, in DMSO-d_6)

Table I. ^{1}H-NMR SPECTRA (200 MHz, DMSO-d_6, δ, J in Hz)

Compounds	*H_1*	*Me-2*	*Me-3*	*H_4*	*H_5*	*H_6*	*H_7*	*H_8*
7*	7.25 (s)		2.50 (s)**	8 02 (m)	——6 60 (m)——		7 45 (m)	
8			2.78 (s)		8.00 (d) $J_{5,6}$ 5.0	8.56 (dd) $J_{6,5}$ 5.0, $J_{6,8}$ 1.4	$J_{8,6}$ 1 4	9 42 (d)
9***			2.66 (s)		8 85 (dd) $J_{5,6}$ 7, $J_{5,7}$ 2	7.13 (q) $J_{6,5}$ 8, $J_{6,7}$ 4	8 70 (dd) $J_{7,6}$ 4, $J_{7,5}$ 2	
13***			2.54 (s)		9.34 (dd) $J_{7,6}$ 6, $J_{7,5}$ 2	7.32 (q) $J_{6,5}$ 8, $J_{6,7}$ 5	8 85 (dd) $J_{5,6}$ 5, $J_{5,7}$ 2	
10a			*H_3* 9.01 (s)		*Me-5* 2.31 (s)	5.68 (s)		
11a			*H_3* 8 84 (s)			6.00 (s)	2.48 (s)	
14a		*H_2* 8.23				5.86 (s)	2.36 (s)	
10b			2.63 (s)		*Me-5* 2 57 (s)	5.91 (s)		
11b			2.69 (s)			5.56 (s)	*Me-7* 2.23 (s)	
14b		2.34 (s)				5.77 (s)	*Me-7* 2.30 (s)	
12			2.56 (s)		9 78 (s)		8.52 (s)	

*60MHz **Lit. 16. ***60 MHz in lit. 11



X=N or C

Table II ^{13}C-NMR SPECTRA (50 MHz, DMSO-d_6, δ, J in Hz)

Compounds	*C_b*	*Me-b*	*C_c*	*Me-c*	*C_e*	*Me-e*	*C_f*	*C_g*	*Me-g*	*C_h*	*C_i*
9			142.1	9.8	131.9		108 5	152 3			154 0
13	165.2	14.6			136 6		110.2	154.7		154.7	
10b			150 2	13.3	160 2		96 2	143.3	21.3		157 5
11b			145.4	13.8	143 9	18 1	107.6	160.8			149 2
14b	155.5		14 2		150.8	18 6	98 1	160 6			151 0
12			142 3	14.1	125.7			117 9		140 3	150 1

The ^{1}H-nmr spectra of compounds **10b** and **11b** were quite similar to those of the parent bases 5-methyl-1,2,4-triazolo[4,3-a]-7(8H)-pyrimidone (**10a**) and 7-methyl-1,2,4-triazolo[4,3-a]-5(8H)-pyrimidone (**11a**), which were prepared by the method of Sirakawa[18] and VanAllan[19] (see Table I). The methyl group signals of the five membered ring in compounds **10b** and **11b** occupied roughly the same position, while those of the six membered ring were located at a much lower field. The ^{13}C-nmr spectra of compounds 3,5-dimethyl-1,2,4-triazolo[4,3-a]-7(8H)-pyrimidone (**10b**) and 3,7-dimethyl-1,2,4-triazolo[4,3-a]-5(8H)-pyrimidone (**11b**) are given in Table II. The ir spectra of compounds **10a,b** and **11a,b** all showed C=O stretching bands at 1680–1700 cm^{-1} and no OH bands, indicating that they exist in the keto forms. When treated with acids, compounds **11a** and **11b** underwent a Dimroth rearrangement to give 5-methyl-1,2,4-triazolo[4,3-a]-7(4H)pyrimidone (**14a**) and 2,5-dimethyl-1,2,4-triazolo[1,5-a]-7(4H)-pyrimidone (**14b**), whereas compounds **10a** and **10b** did not rearrange. This would suggest that nucleosides of type **10** can be prepared without rearrangement, whereas those of type **11** would probably undergo rearrangement during deblocking. 8-Chloro-3-methyl-1,2,4-triazolo[4,3-c]pyrimidine (**12**) was obtained in 57% yield by refluxing 5-chloro-4-hydrazinopyrimidine (**6**) with ethyl dithioacetate (**1**) in ethanol. Unlike 6-chloropurine, this compound resists catalytic hydrogenation or nucleophilic substitution with ammonia. π-Electron charge density calculations revealed that the charge at C-6 in 6-chloropurine is lower (0.60) than that at C-8 of 8-chloro-3-methyl-1,2,4-triazolo[4,3-c]pyrimidine (0.69). Heating compound **12** with acids resulted in opening of the six-membered ring and afforded a hydrate (**15**), which on pyrolysis gave the starting 8-chloro-3-methyl-1,2,4-triazolo[4,3-c]pyrimidine (**12**) without rearrangement. The hydrate (**15**) showed a carbonyl absorption band at 1680 cm^{-1} that was absent in the starting base (**12**). Its ^{1}H-nmr spectrum showed an aldehydic proton at 10.75 ppm, an imino proton at 7.52 ppm, and an amide proton at 7.40 ppm, and its ^{13}C-nmr spectrum showed a characteristic aldehydic carbon signal at 163.1 ppm. It was accordingly assigned a 2-chloro-1-formamido-2-(5-methyl-1,3,4-triazolo-2-yl)ethene structure (**15**). The fact that **15** reverted back to the starting heterocycle (**12**) instead of yielding a rearrangement product may be attributed to the greater stability of compound **12** compared to the rearrangement product (**16**). The isolation of hydrate **15** confirms the assumption that the Dimroth rearrangement of triazolopyrimidines is initiated by opening the six-membered ring.

EXPERIMENTAL

Corrected melting points were determined on a Kofler-block apparatus preheated to 10°C below the actual melting point and then heated at the rate of 1°C/min. Ms spectra were recorded with a Hewlett-Packard 5995 GC/MS spectrometer in the EI or CI modes. Ir spectra were measured on a Perkin-Elmer 735 spectrophotometer using KBr pellets. Uv spectra were recorded with a Perkin-Elmer 323 spectrophotometer. Uv spectral data are described as λ_{max} and λ_{min}, each followed by (log ε), and then the solvent. ^{1}H-Nmr spectra were recorded at 60 MHz on a Varian EM-360 spectrometer; at 80 MHz on a Bruker WP-80 spectrometer equipped with a 1180 data system and a 293A pulser; and at 200 MHz on a Varian XL 200. Tetramethylsilane (TMS) or sodium 4,4-dimethyl-4-silapentane-1-sulfonate (DSS) was used as the internal standard. ^{1}H-Nmr data are described as b, broad; s, singlet; t, triplet; d, doublet; dd, doublet of doublets; q, quartet; m, multiplet; followed by the coupling constant (J, in Hz), and the number of protons determined by integration. ^{13}C-Nmr spectra were recorded in the FT mode at 32°C on a Bruker WP-80 spectrometer at 20.1 MHz on a Varian XL 200 at 50 MHz. Nuclear Overhauser effect spectroscopy (NOESY) experiments were carried out at 200 MHz on a Varian XL 200. Microanalyses were performed by Spang Microanalytical Laboratory, Eagle Harbor, Michigan. The π-electron charge density was calculated by a Macintosh Plus computer using a Hückel Molecular Orbitals software by J. J. Farrel at Franklin, distributed by Kinko's Academic Courseware Exchange. Merck silica gel 60 (0.063-0.200 mm) was used for column chromatography. Ethyl dithioacetate was prepared by bubbling HCl in a solution of acetonitrile and ethanethiol in dry ether and treating the resulting acetothioimidate hydrochloride with H_2S in dry pyridine.[6,15]

N-[(2-Pyridyl)methyl]thioacetamide - A solution of 2-(aminomethyl)pyridine (2; 1.12 g, 10.4 mmol) and ethyl dithioacetate (1; 1.31 g, 11.0 mmol) in abs. EtOH (20 ml) was refluxed for 48 h, and then evaporated to dryness *in vacuo* to give a crystalline product. After two crystallizations from benzene-petroleum ether (bp 40-60°C), the colorless crystals (1.45 g) had mp 123-124°C (dec.), ν 3150 (NH), and 1160 cm^{-1} (C=S); ^{1}H-nmr ($CDCl_3$): δ 9.10 (b, 1H, NH), 8.60 (m, 1H, H-6), 7.70 (m, 1H, H-4), 7.30 (m, 2H, H-3,5), 4.90 (d, J 5.0, 2H, CH_2), and 2.68 (s, 3H, Me). Anal. Calcd for $C_8H_{10}N_2S$: C, 57.80; H, 6.06; N, 16.85; S, 19.29. Found: C, 57.74; H, 6.07; N, 16.77; S, 19.34.

3-Methylimidazo[1,5-a]pyridine (7) - (a) A suspension of N-[(2-pyridyl)methyl]thioacetanamide (164 mg, 1 mmol), mercuric bromide (22 mg, 0.06 mmol), and mercuric oxide (400 mg, 1.85 mmol) in EtOH (12 ml) was refluxed for 1 day, filtered through Celite, and evaporated to dryness *in vacuo*. The residue was dissolved in $CHCl_3$ (20 ml), washed successively with water (15 ml), 0.1N aq. EDTA solution (6 × 10 ml), and a saturated sodium chloride solution (10 ml), and then dried over

anhydrous sodium sulfate. After evaporation of the solvent, an oil (47 mg) was obtained which crystallized slowly on standing; mp 44-48°C (lit. mp 55°C),[8] its picrate had mp 219-221°C (dec.) (lit. mp 221°C (dec.)); λ_{max} 284 (3.73), 273 (3.76), 263 (3.58), λ_{min} 281 (3.53), 265 (3.58), 243 (3.08), in 95% EtOH; λ_{max} 308 (3.01), 280 (3.35), 269 (3.99), 259 (3.80), 230 (3.68), λ_{min} 289 (3.51), 276 (3.83), 262 (3.80), 246 (3.35) in 0.01N aq. HCl; λ_{max} 337 (3.33), 283 (3.86), 272 (3.92), 262 (3.76), λ_{min} 294 (2.68), 280 (3.70), 264 (3.76), and 243 nm (3.23) in 0.01N aq. NaOH.

(b) The same product (7) was also obtained by refluxing N-[(2-pyridyl)methyl]thioacetamide in a suspension of mercuric oxide and mercuric bromide in H_2O for 1 day or by stirring the same mixture in an ultrasonic bath at 10°C for 6 h (yield 38%).

3-Methyl-1,2,4-triazolo[4,3-a]pyrazine (8) - A solution of 2-hydrazinopyrazine (3; 330 mg, 3 mmol) and ethyl dithioacetate(1;360 mg, 3 mmol)in abs. MeOH (25 ml) was refluxed for 19 h and then concentrated to 5 ml in vacuo to afford a crystalline product (52 mg). The mother liquor afforded a 2nd crop (37 mg), bringing the total yield to 22%. An analytical sample obtained after two crystallizations from EtOH had mp 241-242°C (dec.) (lit. mp 239°C).[9] Anal. Calcd for $C_6H_6N_4$: C, 53.72; H, 4.51; N, 41.77. Found: C, 53.70; H, 4.58; N, 41.70.

3-Methyl-1,2,4-triazolo[4,3-a]pyrimidine (9) - A solution of 2-hydrazinopyrimidine (4) (330 mg, 3 mmol) and ethyl dithioate (1; 360 mg, 3 mmol) in dry n-propanol (25 ml) was refluxed for 2 days. Upon cooling to room temperature, the crystals (203 mg; 51%) were collected by suction, and recrystallized from 70% EtOH in colorless prisms, mp 255-255.5°C (lit. mp 251-253°C).[12]

2-Methyl-1,2,4-triazolo[1,5-a]pyrimidine (13) - A solution of 3-methyl-1,2,4-triazolo[4,3-a]-pyrimidine (9) (54 mg, 0.4 mmol) in AcOH (3 ml) containing a drop of conc. H_2SO_4 was heated at 70°C overnight. The acetic acid was evaporated under reduced pressure and the residue was coevaporated with H_2O (2 x 10 ml) to remove the last trace of acetic acid. The residue was redissolved in H_2O (20 ml) and extracted with $CHCl_3$ (3 x 15 ml). Upon concentration of the solvent, 30 mg (56%) of colorless crystals were obtained, which after recrystallization from 95% EtOH had mp 136.5-137°C (lit. mp 131-135°C);[12,18] EI/MS m/z 134 (100%, M), 106 (11%, $M-N_2$), and 93 (2%, $M-CH_2CN$). Anal. Calcd for $C_6H_6N_4$: C, 53.72; H, 4.51; N, 41.77. Found: C, 53.75; H, 4.44; N, 41.63.

Uv experiments: 3-Methyl-1,2,4-triazolo[4,3-a]pyrimidine (9) (0.4 mg) was dissolved in aq. 0.0027M HCl, and uv spectra measured at room temperature every 10 min (see Fig. I). Alternatively, an aqueous solution of 3-methyl-1,2,4-triazolo[4,3-a]pyrimidine (9; 2.99×10^{-6} M) and 2-hydrazinopyrimidine (3; 0.0029 M), was heated at 75°C in a water bath and uv spectra were measured every 4 h. The same changes in absorption were observed.

3,5-Dimethyl-1,2,4-triazolo[4,3-a]-7(8H)-pyrimidone (**10b**) - Ethyl dithioacetate (**1**; 366 mg, 3 mmol) and 2-hydrazino-4-hydroxy-6-methylpyrimidine (**5**; 420 mg, 3 mmol) were refluxed for 19 h in dry MeOH (35 ml) to afford 146 mg of a product mp 310-312°C (dec.) (lit. mp 309-310°C);[19] CI/MS, m/z 165 (100%, MH^+), 193 (33%, $M+Et^+$), EI/MS 165 (9.7%, MH^+), 164 (100%, M), 136 (45%, $M-N_2$), 42 (69%, $O=C=N^+$), and 41 (20%, $MeCN^+$); ν 3050 (Ar), 2910 (CH), and 1695 cm^{-1} (C=O). Anal. Calcd for $C_7H_8N_4O$: C, 51.21; H, 4.91; N, 34.13. Found: C, 51.20; H, 4.86; N, 33.90.

3,7-Dimethyl-1,2,4-triazolo[4,3-a]-5(8H)-pyrimidone (**11b**) - The mother liquor of the above reaction gave on concentration 123 mg of a yellowish product, which after recrystallization from 70% EtOH had mp 305-318°C (dec.) (lit. mp 310-311°C);[20] ν 1700 cm^{-1} (C=O). Anal. Calcd for $C_7H_8N_4O$: C, 51.21; H, 4.91; N, 34.13. Found: C, 51.33; H, 4.90; N, 34.04.

2,5-Dimethyl-1,2,4-triazolo[1,5-a]-7(4H)-pyrimidone (**14**) - A solution of compound **11b** (145 mg, 0.9 mmol) in HCl (60 ml) was refluxed for 10 h. After cooling to room temperature, it gave crystals (42 mg). An analytical sample, obtained by recrystallization from 70% EtOH, had mp 312-313°C (dec.) (lit. mp 311-313°C);[20] ν 1702 cm^{-1} (C=O). Anal. Calcd for $C_7H_8N_4O$: C, 51.21; H, 4.91; N, 34.13. Found: C, 51.15; H, 4.76; N, 33.84.

8-Chloro-3-methyl-1,2,4-triazolo[4,3-c]pyrimidine (**12**) - A solution of 5-chloro-4-hydrazinopyrimidine (**6**; 2.18 g, 15 mmol) and ethyl dithioacetate (**1**; 1.80 mg, 15 mmol) in EtOH (50 ml) was refluxed for 2 days. The solvent was removed *in vacuo* and the remaining solid crystallized from 95% EtOH in light yellowish-green needles (706 mg), mp 103-104°C. A 2nd crop (382 mg) brought the total yield to 1.44 g (57%). An analytical sample, obtained by recrystallization from 95% EtOH had mp 104-104.5°C; m/z 168 (100%, M) and 170 (33%, M + 1); λ_{max} 266 (3.77), 212 (4.59), and λ_{min} 233 nm (3.38) in 95% EtOH. Anal. Calcd for $C_6H_5ClN_4$: C, 42.75; H, 2.99; Cl, 21.03; N, 33.23. Found: C, 42.49; H, 2.94; Cl, 21.06; N, 33.13.

2-Chloro-1-formamido-2-(5-methyl-1,3,4-triazolo-2-yl)ethene (**15**) - A solution of 8-chloro-3-methyl-1,2,4-triazolo[4,3-c]pyrimidine (**12**) (145 mg, 0.86 mmol) in aq. 0.01N HCl (8 ml) was left at room temperature overnight. When 1N aq. HCl (1 ml) was added to bring the pH to 2, colorless crystals separated and were collected by suction (91 mg). The same product was also obtained by treatment with 0.1N aq. NaOH (yield 75%, mp 174.8-175°C). Recrystallization from 95% EtOH afforded an analytical sample, mp 178.5-179.5°C (dec.); ν 3420 (NH), 1680 cm^{-1} (C=O); λ_{max} 276 (4.45) in 95% EtOH; ^{1}H-nmr (200 MHz, $(CD_3)_2SO$)): δ 10.75 (s, 1H, CHO), 8.51 (s, 1H, H-3'), 7.52 (s, 1H, ArNH), 7.40 (b, 1H, (C=O)NH), and 2.44 (s, 3H, Me); ^{13}C-nmr (50 MHz): δ 163.1 (C-1',(CHO)), 159.6 (C-5), 154.3 (C-3), 128.0 (C-4'), 122.5 (C-3'), and 11.8 (Me). Anal. Calcd for $C_6H_7ClN_4O.H_2O$: C, 35.22; H, 4.43; Cl, 17.33; N, 27.38. Found: C, 35.29; H, 4.54; Cl, 17.25; N, 27.40.

Pyrolysis of 2-chloro-1-formamido-2-(5-methyl-1,3,4-triazolo-2-yl)ethene – The hydrate **15** was heated in a test tube at 190°C for 4 min. Steam condensed on the surface of the glass and a crystalline mass was formed on cooling; mp and mixed mp with 8-chloro-3-methyl-1,2,4-triazolo-[4,3-c]pyrimidine, 105°C. Both compounds had identical ir and uv spectra.

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