Synthesis and *in vitro* Evaluation of Some New Pyrimidines and Related Condensed Ring Systems as Potential Anticancer Agents

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Several new pyrimidines **6-11**, **18-20**, furo-, thieno-, and pyrrolo[2,3-*d*]pyrimidines **3**, **8**, **12**, triazolo-[4,3-*a*]pyrimidines **14**, **15**, **16** and tetrazolo[1,5-*a*]pyrimidine **17** were prepared from the known intermediate 5-(2-hydroxyethyl)-6-methyl-2-thiouracil (**2**). Compound **7** (4-chloro-5-(2-chloroethyl)-2-methylthio-6-methyl-pyrimidine) exhibited weak antitumor activity *in vitro*.

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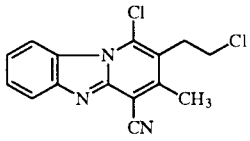
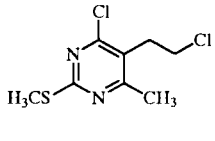
Previously we have described the synthesis of 1-chloro-2-(2-chloroethyl)-3-methylpyrido[1,2-*a*]benzimidazole-4-carbonitrile (NSC 649900, Figure 1), a compound which showed good activity and subpanel selectivity against leukemia cell lines, *in vitro* [1]. This led to the synthesis and testing of 6-(2-chloroethyl)-7-methylimidazo[1,2-*a*]-pyrimidin-5(1*H*)-one (NSC 660341) and related derivatives; however, their test results were discouraging [2]. In view of selecting simpler chemical structures having a similar substitution pattern to NSC 649900, we now report the synthesis and antineoplastic activity of 4-chloro-5-(2-chloroethyl)-2-methylthio-6-methyl-pyrimidine **7** (NSC 660335, Figure 1). This compound could be regarded as a bioisisteric counter part of the 1-chloro-2-(2-chloroethyl)-3-methylpyridine moiety in NSC 649900. Some furo-, thieno-, and pyrrolo[2,3-*d*]pyrimidines **3**, **5**, **8**, **12**, triazolo[4,3-*d*]pyrimidines **14**, **15**, **16**, and tetrazolo[1,5-*a*]pyrimidine **17**, as well as 2-pyrazolylpyrimidines **19**, **20** were also proposed (Schemes 1 and 2) in order to study their potential anticancer activity. Many furo- and pyrrolopyrimidines have also been allocated in the literature as antitumor agents [3-6].



NSC 649900



7 (NSC 660335)

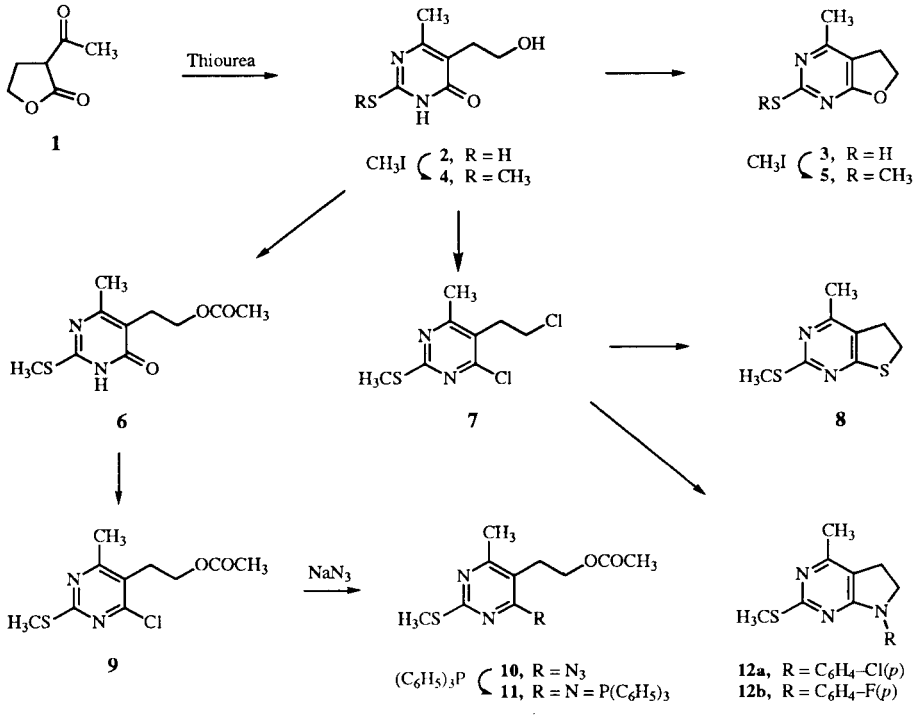
Figure 1.

Thiouracil **2**, the starting material for the synthetic sequences depicted in Scheme 1, has been previously prepared by reacting 2-acetylbutyrolactone (**1**) with thiourea in the presence of sodium methoxide [7-8]. In the present investigation compound **2** was obtained in an almost identical yield by replacing sodium methoxide with triethylamine. The reaction of **2** with thionyl chloride followed by sodium carbonate treatment led to the furo[2,3-*a*]pyrimidine **3**. The latter compound has been previously prepared by treatment of **2** with thiourea in the presence of hydrogen bromide and subsequent treatment with sodium hydroxide [9]. The methylmercapto compounds **4** and **5** were prepared by reacting **2** or **3** with methyl iodide in the presence of sodium methoxide, respectively. Acetylation of **4** was carried out in refluxing acetic anhydride to produce compound **6**. The chloro compounds **7** and **9** were prepared by refluxing **4** or **6** with phosphorus oxychloride, respectively. The dichloro compound **7** gave rise to the thieno[2,3-*d*]pyrimidine **8** on treatment with thiourea in refluxing ethanol or to the pyrrolo[2,3-*d*]pyrimidines **12a,b** on reaction with the selected amines. Reacting the monochloro compound **9** with sodium azide gave the 4-azido derivative **10**, which was converted to the phosphinimine derivative **11** upon treatment with triphenylphosphine.

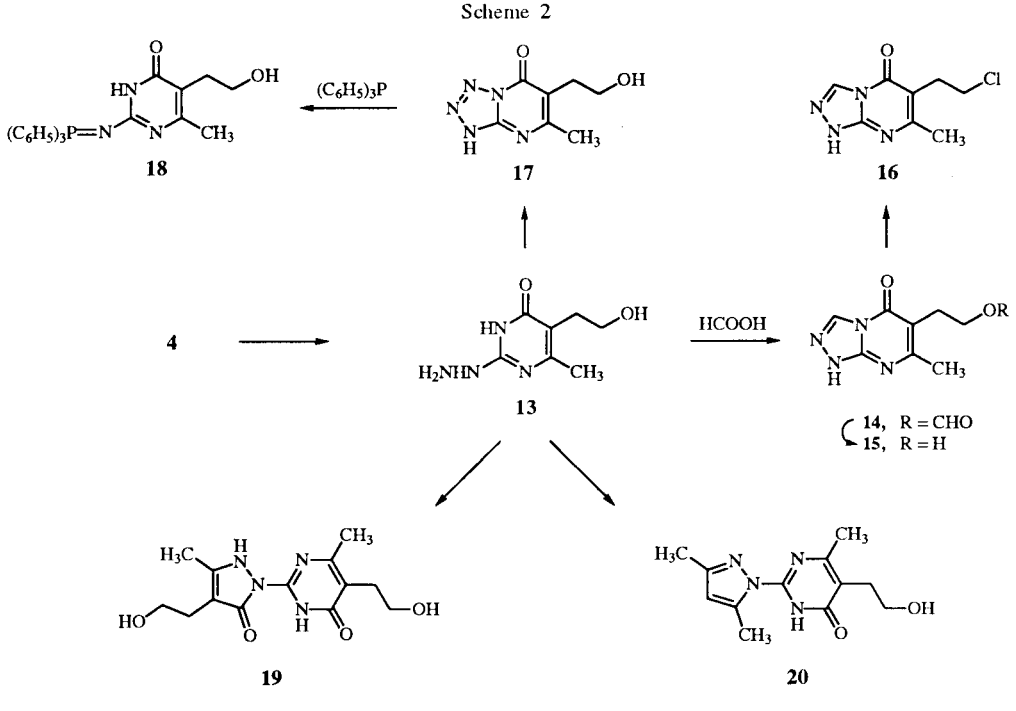
Scheme 2 outlines the chemical transformations carried out with the 2-hydrazinouracil **13**, which was prepared from **4** and hydrazine hydrate in refluxing ethanol. Refluxing **13** with formic acid resulted in the 6-(2-formyloxyethyl)-7-methyl-1*H*,5*H*-1,2,4-triazolo[4,3-*a*]pyrimidin-5-one (**14**), which was hydrolyzed to the 6-(2-hydroxyethyl) derivative **15** with sodium carbonate. Subsequent reaction of **15** with phosphorus oxychloride gave the 6-(2-chloroethyl) derivative **16**. Treatment of **13** with sodium nitrite in acidic medium gave the tetrazolo[1,5-*a*]pyrimidine **17** which reacted with triphenyl phosphine to give 2-phosphinimine derivative **18** with the evolution of nitrogen. The 2-(pyrazol-1-yl)pyrimidine derivatives **19** and **20** were obtained by condensing **13** with 2-acetylbutyrolactone (**1**) or acetylacetone, respectively.

Compounds **7-9**, **11**, **12a**, **14**, **16**, **17**, **19** and **20** were submitted to the National Cancer Institute for testing in its new *in vitro* disease oriented antitumor screen [10]. Out of these compounds, only 4-chloro-5-(2-chloroethyl)-2-methylthio-6-methylpyrimidine (**7**, NSC 660335), exhibited weak antineoplastic activity against CCRF-CEM, K-562 and MOLT-4 cell lines from leukemia, COLO-205 and DHCT-116 cell lines from colon cancer and LOXIMVI and M14

Scheme 1



Scheme 2



cell lines from melanoma panels. Thus despite its close relationship to the 1-chloro-2-chloromethyl-3-methylpyridine counterpart present in NSC 649900 (Figure 1), it is not superior to NSC 649900 in activity. The selected compounds were also screened for anti-HIV activity in cultures of CEM cells but were inactive [10].

EXPERIMENTAL

Melting points were determined in open-glass capillaries on a Gallenkamp melting point apparatus and are uncorrected. The ir spectra were recorded on a Perkin-Elmer 298 spectrophotometer using samples in potassium bromide discs. The ^{1}H nmr spectra

were recorded on a Varian Gemini 200 at 200 MHz using hexadeuteriodimethyl sulfoxide as solvent (unless otherwise specified) and tetramethylsilane (TMS) as the internal standard. Microanalyses were performed on a Carlo Erba 1106 analyzer.

5-(2-Hydroxyethyl)-6-methyl-2-thiouracil (**2**).

A mixture of 2-acetylbutyrolactone (**1**) (10.8 ml, 100 mmoles) and thiourea (7.6 g, 100 mmoles) was refluxed with absolute ethanol (100 ml) in presence of triethylamine (27.8 ml, 200 mmoles) for 15 hours. Excess solvent was removed under vacuum and the residue was stirred with water (100 ml), neutralized carefully with hydrochloric acid to *p*H 3 and the product was filtered, washed with water and dried, yield 9.0 g (48%), mp 257-259° (aqueous dimethylformamide), reported 257-258° [7], 260-265° [8]; ir: ν 3500-2200 bm 1650 s, 1550 m, 1440 w cm^{-1}; ^1H nmr: δ 2.15 (s, 3H, CH_3), 2.45 (t, 2H, CH_2), 3.4 (t, 2H, CH_2OH), 4.6 (t, 1H, O*H*), 13.1 & 13.3 (S*H* + N*H*).

Anal. Calcd. for $C_7H_{10}N_2O_2S$: C, 45.14; H, 5.41; N, 15.04; S, 17.22. Found: C, 45.35; H, 5.79; N, 14.96; S, 17.42.

5,6-Dihydro-4-methyl-2-thiofuro[2,3-*d*]pyrimidine (**3**).

Thionyl chloride (0.5 ml) was added to a stirred suspension of **2** (0.56 g, 3 mmoles) in benzene (30 ml) and the mixture was refluxed for 2 hours. After cooling, the product was filtered, washed with benzene, stirred with (2%) sodium carbonate solution (20 ml) for 2 hours, refiltered, washed with water and dried, yield 0.5 g (99%), mp 212-214° dec (ethanol); ir: ν 2900 m, 1580 s, 1470 m, 1420 s cm^{-1}; ^1H nmr: δ 2.4 (s, 3H, CH_3), 3.2 (t, 2H, CH_2), 4.65 (t, 2H, CH_2O).

Anal. Calcd. for $C_7H_8N_2OS$: C, 49.98; H, 4.79; N, 16.65. Found: C, 50.02; H, 4.41; N, 16.73.

5-(2-Hydroxyethyl)-6-methyl-2-methylthiopyrimidin-4(3*H*)-one (**4**).

A stirred suspension of **2** (7.44 g, 40 mmoles) in sodium methoxide solution (40 mmoles) in methanol (50 ml) was treated with methyl iodide (2.5 ml, 40 mmoles) and the reaction mixture was refluxed for 1 hour during which a clear solution was formed followed by separation of white crystalline product. It was filtered, washed with ethanol and dried, yield 7.2 g (90%), mp 198-199° (dimethylformamide); ir: ν 3500-2100 bm, 1650 s, 1580 w, 1550 m, 1470 m, 1420 w cm^{-1}; ^1H nmr: δ 2.2 (s, 3H, CH_3), 2.45 (s, 3H, SCH_3), 2.55 (t, 2H, CH_2), 3.45 (t, 2H, CH_2OH).

Anal. Calcd. for: $C_8H_{12}N_2O_2S$: C, 47.98; H, 6.04; N, 13.99. Found: C, 48.15; H, 5.88; N, 14.35.

5,6-Dihydro-4-methyl-2-methylthiofuro[2,3-*d*]pyrimidine (**5**).

This compound was similarly prepared by reacting **3** (0.68 g, 4 mmoles) with methyl iodide (0.25 ml, 4 mmoles) in presence of sodium methoxide. The product was obtained after removal of the solvent, addition of water, neutralization with hydrochloric acid and cooling, yield 0.36 g (50%), mp 58-60° (benzene-ether); ir: ν 2920 w, 1580 s, 1470 m, 1420 cm^{-1}; ^1H nmr (deuteriochloroform): δ 2.3 (s, 3H, CH_3), 2.5 (s, 3H, SCH_3), 3.15 (t, 2H, CH_2), 4.65 (t, 2H, CH_2O).

Anal. Calcd. for $C_8H_{10}N_2OS$: C, 52.73; H, 5.53; N, 15.37. Found: C, 52.51; H, 5.48; N, 15.38.

5-(2-Acetyloxyethyl)-6-methyl-2-methylthiopyrimidin-4(3*H*)-one (**6**).

This compound was prepared by refluxing **4** (4.0 g, 20 mmoles) in acetic anhydride (30 ml) for 1 hour. After cooling, the reaction mixture was treated with ethanol, left over night and the product was filtered, washed with ethanol and dried, yield 3.2 g (66%), mp 195-197° (ethanol); ir: ν 2960 w, 1750 s, 1740 s, 1650 s, 1540 m, 1450 w cm^{-1}; ^1H nmr: δ 2.2 (s, 3H, CH_3), 2.25 (s, 3H, CH_3CO), 2.45 (s, 3H, SCH_3), 2.7 (t, 2H, CH_2), 4.1 (t, 2H, CH_2O).

Anal. Calcd. for $C_{10}H_{14}N_2O_3S$: C, 49.57; H, 5.82; N, 11.56. Found: C, 49.80; H, 5.70; N, 11.49.

4-Chloro-5-(2-chloroethyl)-6-methyl-2-methylthiopyrimidine (**7**).

This compound was prepared by refluxing **3** (7.0 g, 35 mmoles) with phosphorus oxychloride (50 ml) for 2 hours. Excess phosphorus oxychloride was removed under vacuum and the remaining oily residue was stirred with cold water to obtain a yellowish product which was filtered, washed with water and dried, yield 6.4 g (77%), mp 64-65° (ether-petroleum ether); ir: ν 1550 m, 1550 m, 1450 m, 1420 w cm^{-1}; ^1H nmr (deuteriochloroform, 360 MHz): δ 2.55 (s, 3H, CH_3), 2.6 (s, 3H, SCH_3), 3.3 (t, 2H, CH_2), 3.7 (t, 2H, CH_2Cl).

Anal. Calcd. for $C_8H_{10}Cl_2N_2S$: C, 40.52; H, 4.25; Cl, 29.90; N, 11.81. Found: C, 40.18; H, 4.23; Cl, 29.63; N, 11.52.

5,6-Dihydro-2-methylthio-4-methylthieno[2,3-*d*]pyrimidine (**8**).

A solution of **7** (0.95 g, 4 mmoles) and thiourea (0.3 g, 4 mmoles) in ethanol (15 ml) was refluxed in presence of anhydrous sodium carbonate (0.53 g, 5 mmoles) for 2 hours. After removal of ethanol and addition of water, the product was filtered, washed with water and dried, yield 0.62 g (78%), mp 66° (ethanol-water); ir: ν 2920 w, 1560 s, 1530 s, 1430 m cm^{-1}; ^1H nmr (deuteriochloroform): δ 2.35 (s, 3H, CH_3), 2.55 (s, 3H, SCH_3), 3.15-3.45 (m, 4H, 2 CH_2).

Anal. Calcd. for $C_8H_{10}N_2S_2$: C, 48.45; H, 5.08; N, 14.13. Found: C, 48.72; H, 5.18; N, 13.75.

5-(2-Acetyloxyethyl)-4-chloro-6-methyl-2-methylthiopyrimidine (**9**).

This compound was prepared, as described under compound **7**, by refluxing **6** (2.42 g, 10 mmoles) with phosphorous oxychloride (20 ml), yield 2.4 g (92%), mp 35-37° (ether-petroleum ether); ir: ν 2900 w, 1740 s, 1550s, 1510 s, 1470 w, 1420 w cm^{-1}; ^1H nmr (deuteriochloroform): δ 2.0 (s, 3H, CH_3), 2.45 (s, 3H, CH_3CO), 2.55 (s, 3H, SCH_3), 3.05 (t, 2H, CH_2), 4.2 (t, 2H, CH_2O).

Anal. Calcd. for $C_{10}H_{13}ClN_2O_2S$: C, 46.06; H, 5.03; N, 10.74. Found: C, 46.13; H, 5.14; N, 10.32.

4-Azido-5-(2-acetyloxyethyl)-6-methyl-2-methylthiopyrimidine (**10**).

This compound was prepared by stirring **9** (1.3 g, 5 mmoles) with sodium azide (0.39 g, 6 mmoles) in dimethylformamide (15 ml) at room temperature for 5 hours and then at 60° for an additional 5 hours. The reaction mixture was then stirred with ice water until a solid product was formed, yield 1.2 g (90%), mp 56-59° (ether-petroleum ether); ir: ν 2950 m, 2140 s, 1730 s, 1590 s, 1540 m, 1450 s, 1410 w cm^{-1}; ^1H nmr: δ 2.0 (s, 3H, CH_3), 2.65 (s, 3H, CH_3CO), 2.85 (s, 3H, SCH_3), 3.35 (t, 2H, CH_2), 4.4 (t, 2H, CH_2O).

Anal. Calcd. for $C_{10}H_{13}N_5O_2S$: C, 44.93; H, 4.90; N, 26.20. Found: C, 44.95; H, 4.93; N, 25.81.

5-(2-Acetyloxyethyl)-6-methyl-2-methylthio-4-triphenylphosphoranylideneaminopyrimidine (**11**).

A solution of **10** (1.07 g, 4 mmoles) and triphenylphosphine (1.57 g, 6 mmoles) in benzene (20 ml) was refluxed with stirring for 5 hours. Excess benzene was removed under vacuum and the residue was treated with ether-petroleum ether. After cooling, the white crystalline product was separated, yield 1.9 g (95%), mp 116-118° (benzene-ether); ir: ν 3000 w, 1735 s, 1550 s, 1510 m, 1480 w, 1410 s cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.75 (s, 3H, CH_3), 2.0 (s, 3H, CH_3CO), 2.35 (s, 3H, SCH_3), 3.15 (t, 2H, CH_2), 4.4 (t, 2H, CH_2O), 7.4-7.8 (m, 15 Ar*H*).

Anal. Calcd. for $C_{28}H_{28}N_3O_2PS$: C, 67.05; H, 5.63; N, 8.38. Found: C, 67.12; H, 5.57; N, 8.17.

7-(4-Chlorophenyl)-5,6-dihydro-4-methyl-2-methylthio-7*H*-pyrrolo[2,3-*d*]pyrimidine (**12a**).

A solution of **7** (2.37 g, 10 mmoles) and 4-chloroaniline (2.55 g, 20 mmoles) was refluxed with acetonitrile (10 ml) in an oil bath for 30 minutes. Acetonitrile was then evaporated and the reaction mixture was heated at 150° until solidification of the product (30-45 minutes). After cooling, the product was stirred with water and neutralized with sodium carbonate solution. It was filtered, washed with water and dried, yield 2.8 g (96%), mp 169-171° (acetonitrile); ir: ν 1620 s, 1600 w, 1560 w, 1510 m cm^{-1}; ^1H nmr: δ 2.2 (s, 3H, CH_3), 2.5 (s, 3H, SCH_3), 3.05 (t, 2H, CH_2), 4.1 (t, 2H, CH_2N), 6.95 & 7.9 (2 dd, 4 Ar*H*).

Anal. Calcd. for $C_{14}H_{14}ClN_3S$: C, 57.63; H, 4.84; Cl, 12.15; N, 14.40. Found: C, 57.33; H, 4.87; Cl, 12.37; N, 14.38.

7-(4-Fluorophenyl)-5,6-dihydro-4-methyl-2-methylthio-7*H*-pyrrolo[2,3-*d*]pyrimidine (**12b**).

This compound was similarly prepared from **7** (2.37 g, 10 mmoles) and 4-fluoroaniline (1.9 ml, 20 mmoles), yield 2.7 g (98%), mp 162-164° (acetonitrile); ir: ν 1615 s, 1600 w, 1580 w, 1550 m, 1500 s cm^{-1}; ^1H nmr: δ 2.2 (s, 3H, CH_3), 2.5 (s, 3H, SCH_3), 3.05 (t, 2H, CH_2), 4.1 (t, 2H, CH_2N), 7.3 & 7.9 (2dd, 4 Ar*H*).

Anal. Calcd. for $C_{14}H_{14}FN_3S$: C, 61.07; H, 5.12; N, 15.26; S, 11.64. Found: C, 61.23; H, 5.37; N, 15.04; S, 11.62.

2-Hydrazino-5-(2-hydroxyethyl)-6-methylpyrimidin-4(3*H*)-one (**13**).

This compound was prepared by refluxing compound **4** (3.72 g, 20 mmoles) with hydrazine hydrate (3 ml) in ethanol (20 ml) for 10 hours. Aftes cooling, the product was filtered, washed with ether and dried, yield 3.1 g (84%), mp 227° (dimethylformamide); ir: ν 3500-2200 bm, 1650 s, 1570 w, 1480 w cm^{-1}; ^1H nmr: δ 2.15 (s, 3H, CH_3), 2.5 (t, 2H, CH_2), 3.45 (t, 2H, CH_2OH), 4.6 (t, 1H, OH).

Anal. Calcd. for $C_7H_{12}N_4O_2$: C, 45.64; H, 6.57, N, 30.42. Found: C, 45.69; H, 6.48; N, 30.46.

6-(2-Formyloxyethyl)-7-methyl-1*H*,5*H*-1,2,4-triazolo-[4,3-*a*]pyrimidin-5-one (**14**).

Compound **13** (1.11 g, 6 mmoles) was refluxed with formic acid (10 ml) for 5 hours. Excess formic acid was removed under vacuum and the remaining solid was treated with acetonitrile, filtered and dried, yield 1.0 g (75%), mp 198-200° (ethanol-petroleum ether); ir: ν 3120 s, 3000-2100 bm, 1730 s, 1670 s, 1630 s, 1460 w, 1420 w cm^{-1}; ^1H nmr: δ 2.35 (s, 3H, CH_3), 2.8 (t, 2H, CH_2), 4.2 (t, 2H, CH_2O), 8.2 (s, 1H, CHO), 9.0 (s, 1H at C-3).

Anal. Calcd. for $C_9H_{10}N_4O_3$: C, 48.65; H, 4.54; N, 25.21. Found: C, 48.55; H, 4.64; N, 25.34.

6-(2-Hydroxyethyl)-7-methyl-1*H*,5*H*-1,2,4-triazolo[4,3-*a*]-pyrimidin-5-one (**15**).

This compound was prepared by stirring compound **14** (2.22 g, 10 mmoles) with (10%) solution of sodium carbonate (20 ml) for 10 hours and neutralizing the formed sodium salt with 2*N* hydrochloric acid, yield 1.2 g (72%), mp 250-252° (ethanol); ir: ν 3500-2100 bm, 1685 s, 1635 s, 1580 s, 1510 w, 1430 w cm^{-1}; ^1H nmr: δ 2.4 (s, 3H, CH_3), 2.65 (t, 2H, CH_2), 3.5 (t, 2H, CH_2OH), 4.6 (t, 1H, OH), 8.95 (s, 1H at C-3).

Anal. Calcd. for $C_8H_{10}N_4O_2$: C, 49.48; H, 5.19; N, 28.85. Found: C, 49.48; H, 5.20; N, 29.02.

6-(2-Chloroethyl)-7-methyl-1*H*,5*H*-1,2,4-triazolo[4,3-*a*]pyrimidin-5-one (**16**).

This compound was prepared by refluxing **15** (1.94 g, 10 mmoles) with phosphorus oxychloride (20 ml) for 4 hours. The product was obtained after removal of the excess phosphorus oxychloride and neutralization with a cold solution of sodium carbonate, yield 1.4 g (66%), mp 198-199° (ethanol); ir: ν 3160 s, 3100-2000 bm, 1690 s, 1630 s, 1570 s, 1470 m, 1440 m, 1420 w cm^{-1}; ^1H mnr: δ 2.4 (s, 3H, CH_3), 2.95 (t, 2H, CH_2), 3.7 (t, 2H, CH_2Cl), 9.0 (s, 1H at C-3).

Anal. Calcd. for $C_8H_9ClN_4O$: C, 45.19; H, 4.27; Cl, 16.67; N, 26.35. Found: C, 45.22; H, 4.49; Cl, 16.77; N, 26.11.

6-(2-Hydroxyethyl)-5-methyl-4*H*,7*H*-tetrazolo[1,5-*a*]pyrimidin-7-one (**17**).

To a cold stirred solution of **13** (0.55 g, 3 mmoles) in 2*N* hydrochloric acid (10 ml), a solution of sodium nitrite (0.41 g, 6 mmoles) in water (10 ml) was added dropwise and the reaction mixture was then stirred in ice bath for 1 hour. The separated product was filtered, washed with water and dried, yield 0.5 g (85%), mp 234-235° dec (ethanol); ir: ν 3500-3200 s, 3150-2200 bm, 1680 s, 1580 m, 1530 s, 1460 w cm^{-1}; ^1H nmr: δ 2.45 (s, 3H, CH_3), 2.65 (t, 2H, CH_2), 3.55 (t, 2H, CH_2OH), 4.65 (bs, 1H, OH).

Anal. Calcd. for $C_7H_9N_5O_2$: C, 43.08; H, 4.65; N, 35.88. Found: C, 43.36; H, 4.73; N, 36.29.

5-(2-Hydroxyethyl)-2-triphenylphosphoranylideneamino-6-methylpyrimidin-4(3*H*)-one (**18**).

This compound was prepared by reacting **17** (0.39 g, 2 mmoles) with triphenylphosphine (1.05 g, 4 mmoles) in refluxing toluene for 5 hours. After cooling the product was filtered, washed with benzene and dried, yield 0.85 g (99%), mp 238-239° (benzene); ir: ν 3500-2500 bm, 1620 s, 1550 s, 1490 w cm^{-1}; ^1H nmr: δ 1.8 (s, 3H, CH_3), 2.4 (t, 2H, CH_2), 3.35 (t, 2H, CH_2OH), 4.55 (t, H, OH), 7.5-7.9 (m, 15 Ar*H*), 11.1 (s, 1H, N*H*).

Anal. Calcd. for $C_{25}H_{24}N_3O_2P$: C, 69.92; H, 5.63; N, 9.78. Found: C, 70.09; H, 5.61; N, 9.70.

2-[4-(2-Hydroxyethyl)-3-methyl-2*H*-5-oxopyrazolidin-1-yl]-5-(2-hydroxyethyl)-6-methylpyrimidin-4(3*H*)-one (**19**).

This compound was prepared by heating a mixture of **13** (1.84 g, 10 mmoles) and 2-acetylbutyrolactone (**1**) (2.15 ml, 20 mmoles) in an oil bath at 140° for 1 hour.After cooling and addition of ether the product was filtered, yield 2.0 g (68%), mp 175-177° (benzene-ethanol); ir: ν 3700-2500 bm, 1650 s, 1600 s, 1430 w cm^{-1}; ^1H nmr: δ 2.2 (s, 3H, CH_3), 2.3 (s, 3H, CH_3), 2.35

(t, 2H, CH_2), 2.6 (t, 2H, CH_2), 3.5 (2t, 4H, 2 CH_2OH).

Anal. Calcd. for $C_{13}H_{18}N_4O_4$: C, 53.05; H, 6.16; N, 19.04. Found: C, 52.98; H, 6.15; N, 18.75.

2-(3,5-Dimethylpyrazol-1-yl)-5-(2-hydroxyethyl)-6-methylpyrimidin-4(3*H*)-one (**20**).

This compound was similarly prepared from **13** (1.84 g, 10 mmoles) and acetylacetone (2.0 ml, 20 mmoles), yield 1.9 g (77%), mp 163-165° (benzene); ir: ν 3420 s, 3300-2600 bm, 1650 s, 1610 m, 1500 s, 1410 w cm^{-1}; ^1H nmr (deuteriochloroform): δ 2.25 (s, 3H, CH_3 of pyrimidine), 2.35, 2.65 (2 s, 6H, 2 CH_3 of pyrazole), 2.85 (t, 2H, CH_2), 3.85 (t, 2H, CH_2OH), 6.0 (s, 1H at C-4 of pyrazole).

Anal. Calcd. for $C_{12}H_{16}N_4O_2$: C, 58.05; H, 6.50; N, 22.57. Found: C, 57.99; H, 6.56; N, 22.48.

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