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Pyrimidine Derivatives and Related Compounds. XLIV.[1] Thermolysis of 6-Azido-1,3-dimethyluracil to a Pyrimido[5,4-*g*]pteridine Derivative

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Thermolysis of 6-azido-1,3-dimethyluracil (**1**) in formamide gave 1,3,6,8-tetramethylpyrimido[5,4-*g*]pteridine-2,4,5,7(1*H*,3*H*,6*H*,8*H*)-tetrone (**3**), while the same reaction in *N*,*N*-dimethylformamide (DMF) gave 3-(5-amino-1,3-dimethyluracil-6-yl)-4,6-dimethyl-[1,2,3]triazolo[4,5-*d*]pyrimidine-5,7(4*H*,6*H*)-dione (**4**), which was converted into **3** in refluxing formamide. Compound **4** was also obtained by the treatment of **1** with 4,6-dimethyl[1,2,3]triazolo[4,5-*d*]pyrimidine-5,7(4*H*,6*H*)-dione (**5**) in refluxing DMF. The mechanism of these reactions is discussed.

Keywords——thermolysis; 6-azido-1,3-dimethyluracil; pyrimido[5,4-*g*]pteridine; triazolo[4,5-*d*]pyrimidine; aziridine intermediate

Thermolysis and photolysis of organic azides have been studied from a number of points of view, the objectives being mainly synthetic or mechanistic.[2] In our previous papers,[3,4] we have reported that the photolysis of 6-azido-1,3-dimethyluracils in the presence of various nucleophiles gave 6-alkylamino-5-aminouracils, lumazines, fervenulins, 1,3,5-triazepines, and 5-acylamino-6-chlorouracils which cannot be obtained by the thermochemical process. These results prompted us to investigate the thermolysis of 6-azido-1,3-dimethyluracil (**1**). To our knowledge, there has been no report concerning the thermochemical decomposition of **1** except for that of Senga *et al.*[5] who reported the isomerization of **1** in the presence of alkyl halides to give [1,2,3]triazolo[4,5-*d*]pyrimidines. In this paper, we describe the thermolysis of **1** in various solvents without nucleophiles.

Thus, refluxing of **1** in formamide for 15 min gave 1,3,6,8-tetramethylpyrimido[5,4-*g*]-pteridine-2,4,5,7(1*H*, 3*H*, 6*H*, 8*H*)-tetrone (**3**) in 40% yield. The structure of **3** was easily established from its spectral data, reported by Yoneda *et al.*[6] On the other hand, it is known that irradiation of **1** in methanol gives 1,3,5,7-tetramethylpyrimido[4,5-*g*]pteridine-2,4,6,8-(1*H*, 3*H*, 5*H*, 7*H*)-tetrone (**2**).[7] The above results indicate that **1** shows different behavior according to the conditions used. When **1** was refluxed in *N*,*N*-dimethylformamide (DMF) in place of formamide, an unexpected product, 3-(5-amino-1,3-dimethyluracil-6-yl)-4,6-dimethyl[1,2,3]triazol[4,5-*d*]pyrimidine-5,7-(4*H*, 6*H*)-dione (**4**), was obtained in 70% yield. The structure of **4** was clarified by its conversion into **3**. Thus, a solution of **4** in formamide was refluxed for 15 min to give **3** (70% yield), which was also prepared by photolysis of **4** in tetrahydrofuran (THF). Additionally, when a mixture of **1** and 1,3-dimethyl[1,2,3]triazolo-[4,5-*d*]pyrimidine (**5**) in DMF was refluxed for 1 h, **4** was obtained in 85% yield as a sole product. This suggests the intermediacy of **5** in the mechanism .

A possible mechanism for the formation of **3** and **4** is shown in Chart 2. First, both isomerization[5] of **1** to a triazole (**5**) and loss of nitrogen from **1** giving an azirine (**9**) proceed competitively. Subsequent nucleophilic addition of **5** to **9** affords an aziridine intermediate (**10**), followed by ring cleavage to give the product (**4**) as described previously.[4] Further heating in formamide or irradiation of **4** would cause a cyclization to **3** *via* a 1,3-biradical or carbene intermediate.[8]

The thermolysis described above was considerably affected by the solvent used. When **1** was heated in tetralin at 150°C, 6-amino-1,3-dimethyluracil (**6**) was obtained. Similar treatment of **1** in nitrobenzene did not give any definite product but, in dimethylaniline, bis(6-

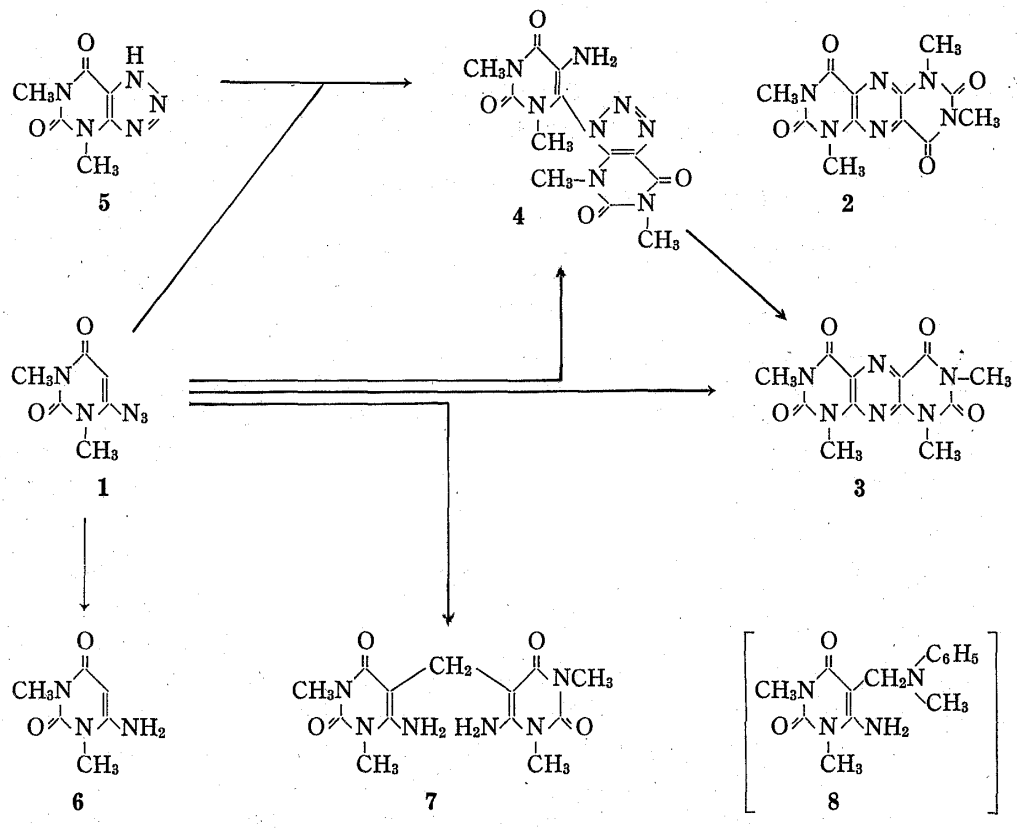

Chart 1

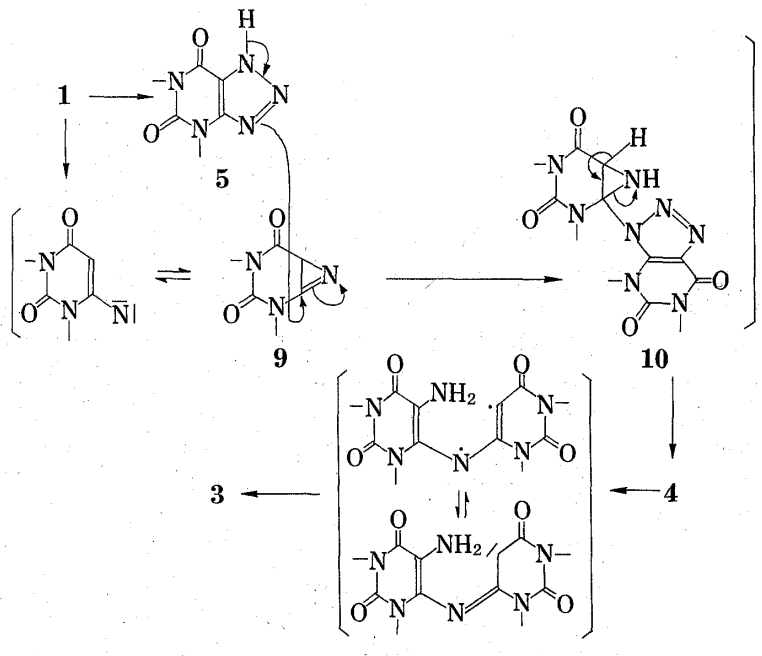

Chart 2

amino-1,3-dimethyluracil-5-yl)methane (**7**) was obtained in 89% yield. The structure was confirmed by direct comparison with an authentic sample.[9] This reaction presumably involves the formation of a Mannich type base (**8**)[10] and **6** as intermediates and their condensation.

Experimental

All melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. Infrared (IR) spectra were taken on a Hitachi 215 instrument from KBr pellets. Proton magnetic resonance spectra were recorded on a Hitachi Perkin-Elmer R-20B spectrometer with tetramethylsilane as an internal reference. Irradiation was carried out at 25—30°C in a flask fitted with a Pyrex-jacketed immersion lamp. The light source was a Riko-UVL 100 W high-pressure mercury arc lamp.

1,3,6,8-Tetramethylpyrimido[5,4-*g*]pteridine-2,4,5,7(1H,3H,6H,8H)-tetrone (3)——a) A solution of 1 g (5.5 mmol) of **1**[4] in 10 ml of formamide was refluxed for 15 min. After cooling, the mixture was diluted with water and allowed to stand overnight. The resulting precipitate was collected by filtration and recrystallized from DMF to give 0.34 g (40%) of **3**, which was identical with an authentic sample.[6] mp>300°C.

b) A solution of 0.5 g (1.5 mmol) of **4** in 5 ml of formamide was refluxed for 15 min. The mixture was treated in the manner described above to give **3** in 70% yield.

c) A solution of 0.5 g (1.5 mmol) of **4** in 250 ml of methanol was irradiated for 3 h. After removal of the solvent by evaporation, the residue was recrystallized from DMF to give **3** in 80% yield.

3-(5-Amino-1,3-dimethyluracil-6-yl)-4,6-dimethyl[1,2,3]triazolo[4,5-*d*]pyrimidine-5,7(4H,6H)-dione (4)——a) A solution of 1 g (5.5 mmol) of **1** in 10 ml of DMF was refluxed for 30 min. After removal of the solvent by evaporation, the residue was treated with ethanol. The resulting precipitate was collected by filtration and recrystallized from water to give 0.64 g (70%) of **4** as pale yellow prisms. mp 229°C; NMR (DMSO-d_6) δ 2.90, 3.28, 3.30 and 3.47 (each 3H, each s, each N–CH_3), 4.81 (2H, br s, NH_2, deuterium exchangeable): IR (KBr) 3350 and 3430 cm^{-1} (NH_2). *Anal.* Calcd for $C_{12}H_{14}N_8O_4$: C, 43.20; H, 4.03; N, 33.59. Found: C, 43.48; H, 4.18; N, 33.33.

b) A mixture of 0.5 g (2.8 mmol) of **1** and 0.5 g (2.8 mmol) of **5**[11] in 10 ml of DMF was refluxed for 1 h. After removal of the solvent by evaporation, the residue was treated with ethanol. The resulting precipitate was collected by filtration and recrystallized from water to give 0.8 g (85%) of **4** which was identical with the product obtained above.

c) A solution of 0.5 g (2.8 mmol) of **1** and 1.0 g (5.5 mmol) of **5** in 250 ml of THF was irradiated for 3 h. After removal of the solvent by evaporation, the residue was treated with ethanol and allowed to stand overnight. The resulting precipitate was filtered off and recrystallized from water to give **4** in 60% yield.

6-Amino-1,3-dimethyluracil (6)——A solution of 0.5 g (2.8 mmol) of **1** in 10 ml of tetralin was heated at 150°C for 5 min. After cooling, the mixture was diluted with petroleum benzine. The resulting precipitate was collected by filtration and recrystallized from acetonitrile to give 0.39 g (90%) of **6**, which was identical with an authentic sample.[12]

Bis(6-amino-1,3-dimethyluracil-5-yl)methane (7)——A solution of 1.0 g (5.5 mmol) of **1** in 5 ml of dimethylaniline was refluxed for 5 min. Excess petroleum ether was added to the reaction mixture. The resulting precipitate was filtered off and recrystallized from DMF to give 0.8 g (90%) of colorless needles, which were identical with an authentic sample.[9] mp>300°C; NMR (CF_3CO_2H) δ 3.57 and 3.68 (each 6H, each s, each N–$CH_3\times2$), 3.73 (2H, s, CH_2): IR (KBr) 3140 and 3410 cm^{-1} (NH_2).

References and Notes

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