A CONVENIENT SYNTHESIS OF PYRIMIDO[5,4-g]PTERIDINETETRONES

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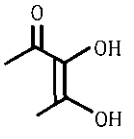
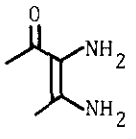
Abstract— The oxidation reactions of 5,6-diaminouracil derivatives with ferric chloride gave pyrimido[5,4-g]pteridinetetrones in good yield.

Various preparations of pyrimidopteridinetetrones have been reported[1-11] and discussion has been made as to the structures of 2,4,5,7(1H,3H,6H,8H)pyrimido-[5,4-g]pteridinetetrone (6)[6,9,10] and 2,4,6,8(1H,3H,5H,7H)pyrimido[4,5-g]pteridinetetrone (6')[3,9,10] Recently, we have been interested in the blue coloration reaction between 5,6-diamino-1,3-dimethyluracil (1a) and ferric ions,[12] and have found an improved method for preparation of 6a from the reaction. This synthetic method is based on the redox reaction, namely, it is well known that enediamines are readily oxidized, and in particular when they are conjugated with a carbonyl group, the enediamines turn out to be strong reducing agents like reductones (Scheme 1).[13] Although it has already been reported that 5,6-diaminouracil (1c) was converted to 6c by self-condensation, there was no description concerning oxidizing agents.[7] Hereupon, ferric ions were found to be useful oxidizing agents for this purpose.

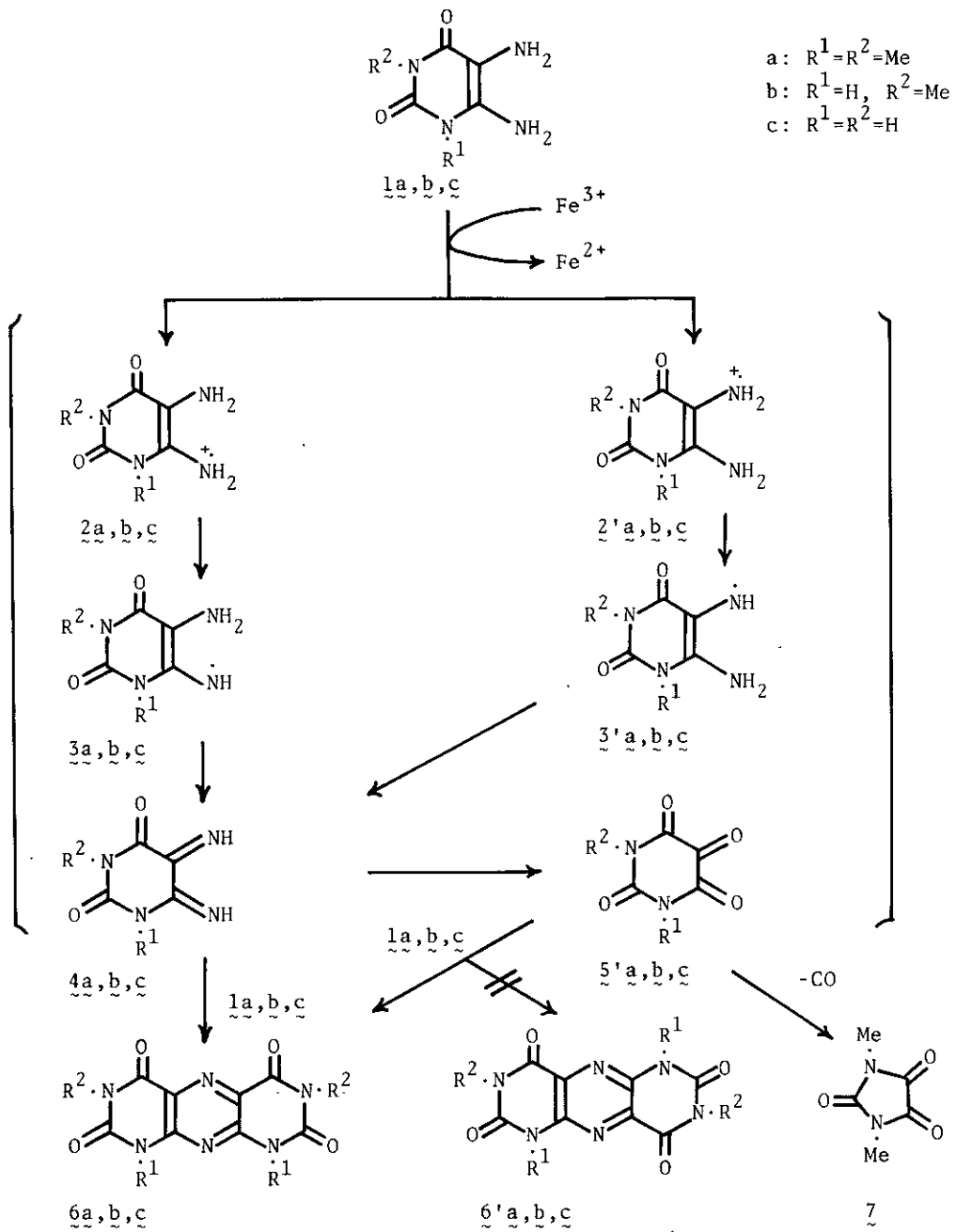


Reductone



Enediamine Reductone

Scheme 1


a: $R^1=R^2=Me$
b: $R^1=H$, $R^2=Me$
c: $R^1=R^2=H$
1a,b,c
Fe^{3+}
Fe^{2+}
2a,b,c
2'a,b,c
3a,b,c
3'a,b,c
4a,b,c
5'a,b,c
1a,b,c
1a,b,c
-CO
6a,b,c
6'a,b,c
7

Scheme 2

Ferric chloride was added to a suspension of 1a in water and the mixture was boiled for 5 min to precipitate 6a as bright yellow plates in 80% yield. The structure was determined by MS and IR spectra comparing with those of the authentic sample.[10] Reference-experiment (namely, in the abscence of ferric chloride) on the above reaction did not give 6a at all. In contrast, when ferric chloride was added to a solution of 1a in water and the mixture was boiled for 5 min, no precipitates occurred, but a bright yellow fluorescent solution was obtained. Extraction of the solution with chloroform and evaporation of the organic layer gave a yellow powder from which 1,3-dimethyl-2,4,5(1H,3H)-imidazolinetrione (7)[14] was isolated as only a stable compound.

We assumed the reaction mechanism as shown in Scheme 2. Ferric ions take on an electron from 1a to give 2a (or 2'a) which is converted to 4a through 3a (or 3'a). Both 4a and its hydrolyzed compound (5a) react with the starting enediamine 1a to give 6a by loss of ammonia and water, respectively. In fact, reaction of 1c with alloxane (5c) gave 6c.[6] Application of this method to other enediamine reductones gave similar results. We also tried the above method to N-substituted enediamines, and the results are now in press.[15]

EXPERIMENTAL[16]

1,3,6,8-Tetramethyl-2,4,5,7(1H,3H,6H,8H)pyrimido[5,4-g]pteridinetetrone (6a)---$FeCl_3$ $6H_2O$ (1.6 g, 5.9 mmol) was added to a suspension of 1a (monohydrate, 1 g, 5.3 mmol) in 50 ml of water, and the blue colored mixture was boiled for 5 min. At first, a clear solution was obtained, and then, plates were precipitated with evolution of gas. The plates were collected by filtration, and washed with 5% HCl solution, water, and ethanol. Yield, 0.65 g (80%), mp 390°C. Anal. Calcd. for $C_{12}H_{12}N_6O_4$: C, 47.37; H, 3.98; N, 27.62. Found: C, 47.41; H, 3.93; N, 27.78.

3,6-Dimethyl-2,4,5,7(1H,3H,6H,8H)pyrimido[5,4-g]pteridinetetrone (6b)---$FeCl_3 \cdot 6H_2O$ (0.8 g, 2.9 mmol) was added to a suspension of 1b (0.5 g, 3.2 mmol) in 25 ml of 1% HCl solution, and the blue colored mixture was treated by the same procedure described above to give 6b. Yield, 0.4 g (90%), mp>300°C. Anal. Calcd. for $C_{10}H_8N_6O_4$: C, 43.48; H, 2.92; N, 30.43. Found: C, 43.51; H, 2.83; N, 27.52.

1,3,6,8-Tetrahydro-2,4,5,7-pyrimido[5,4-g]pteridinetetrone (6c)---$FeCl_3 \cdot 6H_2O$ (0.3 g, 1.1 mmol) was added to a solution of hemisulfate of 1c (o.2 g, 1 mmol) in 120 ml of water, and the mixture was boiled for 8 min to precipitate crystals (6c). The crystals were collected by filtration, and washed with 5% HCl solution, water and ethanol. Yield, 0.08 g (61%), mp >300°C. Anal. Calcd. for $C_8H_4N_6O_4$: C, 38.72; H, 1.62; N, 33.87. Found: C, 38.81; H, 1.65; N, 33.93.

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16) IR and MS spectra were run on a JASCO IRA-1 spectrometer and a JEOL JMS-01S or DX-3000 (equipped with JMA-3000) spectrometers, respectively. Melting point for 6a was measured on a RIGAKU 8001 differential scanning calorimeter.

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