Tetrahedron Letters No.40, pp. 3547-3548, 1969. Pergamon Press. Printed in Great Britain.

PHOTOREDUCTION OF 4- AND 2-THIOURACIL AND 4-THIOURIDINE*

Eisuke Sato and Yuichi Kanaoka
Faculty of Pharmaceutical Sciences, Hokkaido University
Sapporo, Japan

(Received in Japan 14 July 1969; received in UK for publication 31 July 1969)

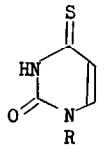
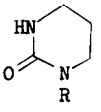
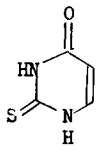
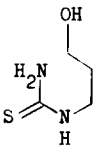
Recent attention has been drawn to the presence of sulfur-containing minor nucleotides in t-RNA; i.e., 4-thiouridine (2), 5-methoxycarbonylmethyl-2-thiouridine (3), 5-methylaminomethyl-2-thiouridine (4), 2-thiocytidine (4), and 2-methylthio-N^6-2-isopentenyladenosine (5).

In general, selective chemical modification is one of the most useful means to clarify correlation between sturcture and function of biopolymers. In an attempt to approach to elucidating the function of the minor nucleosides in the biological processes, this communication describes the selective reduction of 4- and 2-thiouracil and 4-thiouridine as model systems of these minor components.

Cerutti et al. recently reported that 4-thiouridine (Ib) is reduced to N-ribosyl-2-oxohexahydropyrimidine (IIb) with sodium borohydride in the dark (6). Earlier, Witkop et al. originally developed and introduced the ingeneous photoreduction method into the field of nucleic acids (7). In our preliminary experiments, this photoreduction was applied to 4-thio- uracil (Ia) using a 100 watt high pressure Hg lamp. Reduction of Ia proceeded far more rapidly than in the dark as measured spectroscopically. Also 2-thiouracil (III) was reduced similarly.

In order to realize the modification of minor, but not of major components, the selection of reaction conditions is required. This specific reduction of Ia (UVλ_{max} in H_2O : 328 mμ, log ε 4.2) in the presence of uracil (UVλ_{max} in H_2O : 260 mμ, log ε 3.9) involves the control of energies of exciting light source. Thus by employing a liquid filter, aqueous solution of potassium acid phthalate, Ia underwent rapid photo-dependent reduction, while uracil

* Heterocycles related to nucleotides. Part II. For Part I see ref.1.


(I)

(II)

(III)

(IV)

a: R= H

b: R= ribosyl

remained completely unchanged. Moreover, III (UVλ_{max} in H_2O : 270 mμ, log ε 4.1) was also reduced in a similar manner. In a preparative run, aqueous solution of Ia (50 mmoles) was treated with ten molar equivalents of sodium borohydride under irradiation at room temp for 12 hr. After silica gel chromatography, 2-oxohexahydropyrimidine (IIa) was obtained as a major product in 20% yield. On reduction of III for 4 hr., 2-thioureidopropanol (IV) was isolated in 22% yield. Finally, 4-thiouridine (Ib) was treated under the same conditions for 1 hr followed by acid hydrolysis to yield IIa in 15% yield.

The above results demonstrate that this photoreductive procedure may provide a potential method for a selective modification of sulfur-containing base moieties of nucleic acids without affecting major constituents. Further application of this method to nucleotide systems including 2-thiouridine and 2-thiocytosine is under investigation.

Acknowledgment We are grateful to Professor T.Ueda and Mr. T.Muneyama for helpful advice.

References

1. Y.Kanaoka,E.Sato,M.Aiura,O.Yonemitsu and Y.Mizuno,Tetrahedron Letters, Submitted.

2. M.N.Lipsett,J.Bol.Chem.,240,3975(1965); T.Seno,M.Kobayashi and S.Nishimura,Biochem.Biophy. Acta,169,80(1968).

3. L.Baczynskyj,K.Biemann and R.H.Hall,Science,159,1482(1968).

4. J.Carbon,H.David and M.H.Studire,Science,161,1146(1968).

5. F.Harada,H.J.Gross,F.Kimura,S.H.Chang,S.Nishimura and U.L.RajBhandary,Biochem.Biophys.Res. Comm.,33,299(1968), W.J.Burrows,D.J.Armstrong,F.Skoog,S.M.Hecht,J.T.A.Boyle,N.J.Leonard and J.Occolowitz,Science,161,691(1968).

6. P.Cerutti,J.W.Holt and N.Miller,J.Mol.Biol.,34,505(1968).

7. P.Cerutti,K.Ikeda and B.Witkop,J.Am.Chem.Soc.,87,2505(1965).