

The Reductive Repair of 1,3-Dimethylthymine
Bromohydrin into 1,3-Dimethylthymine by
1,5-Dihydro-5-deazaflavin or 1,4-Dihydroquinoline
Taishin Akiyama, Kiyoshi Tanaka and Fumio Yoneda*

Faculty of Pharmaceutical Sciences, Kyoto University,
Yoshida, Sakyo-ku, Kyoto 606, Japan
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The reductive conversion of 1,3-dimethylthymine bromohydrin into 1,3-dimethylthymine by 10-ethyl-3-methyl-1,5-dihydro-5-deazaflavin or 1-benzyl-3-carbamoyl-1,4-dihydroquinoline has been achieved in the presence of trifluoroacetic acid.

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As we have recently reviewed [1], 1,5-dihydro-5-deazaflavin derivatives are regarded as a model of NADH and can be used for the biomimetic reductions of several kinds of substrates. Thus, the reduction of carbonyl compounds to the corresponding alcohols [2,3], the α -amino acids synthesis by the reductive amination [4], and the specific 1,4-reduction of α,β -unsaturated carbonyl compounds [5] have successively been achieved. Furthermore, the latter reaction was successfully applied to the 1,4-reduction of chrysolimial or dehydroiridodial to give (\pm)-iridodial [6].

In the present communication, we report the reductive conversion of 1,3-dimethylthymine bromohydrin (**1**) into 1,3-dimethylthymine (**2**) by 10-ethyl-3-methyl-1,5-dihydro-5-deazaflavin (**3**) [2] in the presence of trifluoroacetic acid. Additionally, we describe that another NADH model, 1-benzyl-3-carbamoyl-1,4-dihydroquinoline (**4**) [7], can also reduce **1** into **2** under the same conditions.

A mixture of **1** (1 eq) and **3** (1.2 eq) in anhydrous acetonitrile was stirred in the presence of a small amount of trifluoroacetic acid under argon atmosphere at room temperature for 2 hours in the dark. The reaction mixture was evaporated *in vacuo* and the residue was purified by preparative tlc to give **2** in 91% yield. It is noted that this is considered to be a model reaction of the reductive repairs of oxidatively damaged nucleic acids, because **1** is a model

compound of the thymidine bromohydrin induced by oxidative bromination of thymidine with haloperoxidase in the presence of potassium bromide and hydrogen peroxide [8]. Without 1 or trifluoroacetic acid, this reaction did not proceed at all, giving the starting material **1** (34-49%) and decomposition products even after 3 days. Therefore, the reaction would be initiated by the protonation toward **1**, followed by the transfer of electron from **3** and elimination of bromo anion, as depicted in Scheme 1. This type of carbon-bromine bond scission is preceded in the uracil series [9].

The conversion of **1** into **2** was likewise realized by **4** in the presence of trifluoroacetic acid in 93% yield. Furthermore, the combination of sodium dithionite and trifluoroacetic acid converted **1** into **2** in high yield under the same conditions. In this case also the presence of trifluoroacetic acid as a proton source was necessary for the reaction.

EXPERIMENTAL

The Repair Reaction of **1** to **2** with **3**.

To a solution of **1** (20 mg, 0.076 mmole) in acetonitrile (5 ml) was added **3** (24 mg, 0.092 mmole) and trifluoroacetic acid (0.2 ml) and the mixture was stirred under argon atmosphere at room temperature for 2 hours in the dark. The reaction mixture was evaporated *in vacuo* and the residue was purified by preparative tlc (methanol:chloroform = 5:95) to give **2** in 91%.

The Repair Reaction of **1** to **2** with **4**.

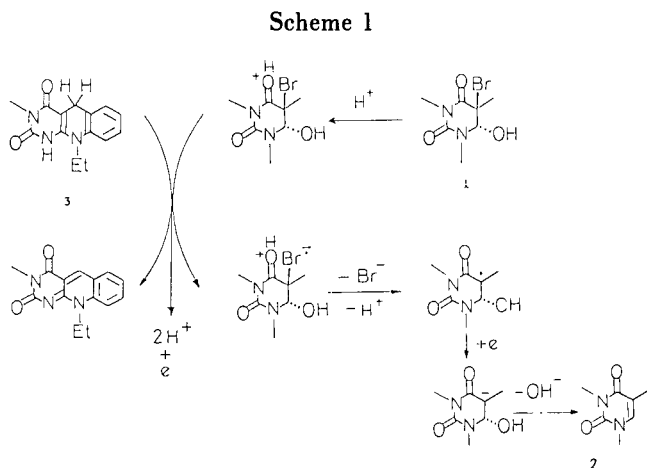
To a solution of **1** (20 mg, 0.076 mmole) in acetonitrile (5 ml) was added **4** (26 mg, 0.092 mmole) and trifluoroacetic acid (0.2 ml) and the mixture was treated in the same way as above to give **2** in 93%.

The Repair Reaction of **1** to **2** with Sodium Dithionite.

To a solution of **1** (20 mg, 0.076 mmole) in acetonitrile (5 ml) was added sodium dithionite (16 mg, 0.092 mmole) and trifluoroacetic acid (0.2 ml) and the mixture was treated in the same way as above to give **2** in almost quantitative yield.

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