

A Novel One-electron Reduction System consisting of 1,5-Dihydro-5-deazaflavin and Flavinium. Application to the Reductive Repair of 1,3-Dimethylthymine Bromohydrin as a Model of a Damaged Nucleic Acid

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A novel one-electron transfer system consisting of 1,5-dihydro-5-deazaflavin (**2**) and flavinium (**3**) at room temperature has repaired efficiently 1,3-dimethylthymine bromohydrin (**1**), a model of a damaged nucleic acid, to give the original 1,3-dimethylthymine (**6**).

NADH and flavin work co-operatively as an electron bridge in many biological systems.¹ NADH apparently acts as a two-electron carrying shuttle, whereas flavin acts as both a one- and a two-electron carrying shuttle. Flavin can therefore function as an electron switch between NADH and iron, *e.g.* in a respiratory system, transferring one electron from NADH to iron. After consideration of this natural system, we attempted to construct an effective one-electron transfer system for use in synthetic organic chemistry. We have found that a combination of 1,5-dihydro-5-deazaflavin² and flavinium perchlorate³ in the presence of magnesium perchlorate can accomplish one-electron transfer very efficiently. We now report that the above novel system can repair reductively 1,3-dimethylthymine bromohydrin (**1**), a model of a damaged nucleic acid,⁴ to give the original 1,3-dimethylthymine (**6**) in high yield.

Recently, we have reported that (**1**) is repaired, giving (**6**), at high temperature or on irradiation with sunlight.⁵ The reaction was accelerated by radical initiator azoisobutyronitrile (AIBN) and prohibited by radical scavenger galvinoxyl. Therefore we proposed that the repair reaction proceeds *via* a radical process.⁵ Since this reaction included one-electron chemistry, it occurred to us that the use of the 1,5-dihydro-5-deazaflavin-flavinium system as an electron bridge may accomplish the reductive repair of (**1**).

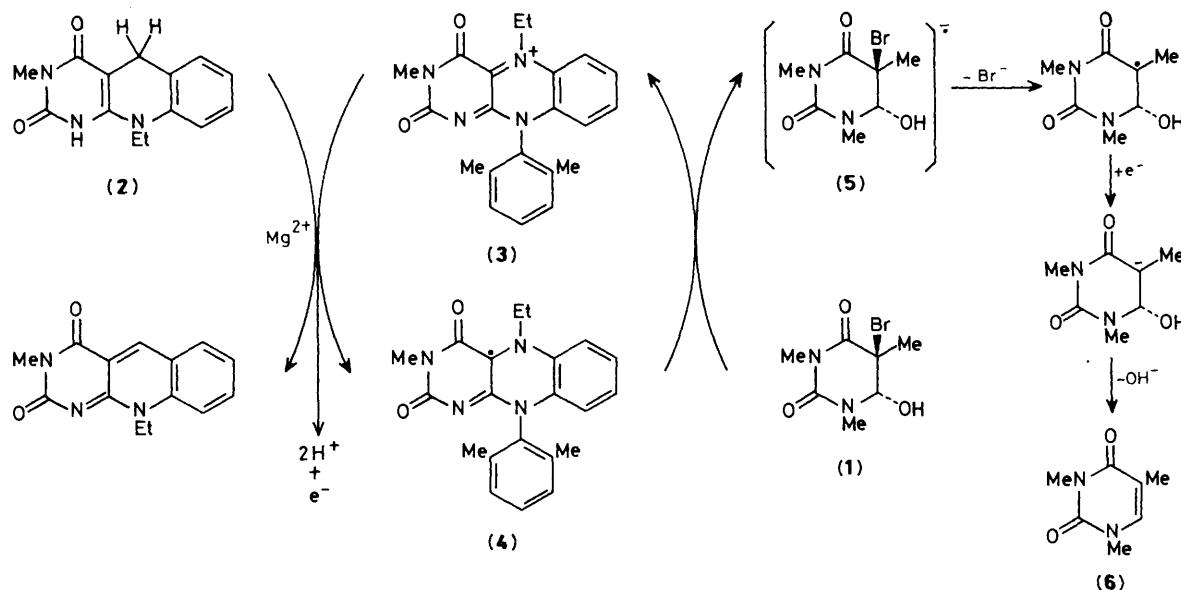
A typical procedure is as follows. 10-Ethyl-3-methyl-1,5-dihydro-5-deazaflavin (**2**) (0.096 mmol), 5-ethyl-3-methyl-10-(2,6-xylylidino)flavinium perchlorate (**3**) (0.096 mmol), and magnesium perchlorate (0.096 mmol) were added to a

solution of (**1**) (0.08 mmol) in acetonitrile (5 ml), and the solution was stirred under an argon atmosphere at room temperature for 3 days in the dark. The products were isolated by preparative t.l.c. As can be seen from Table 1, the repair reaction proceeded very smoothly to give the original (**6**) in high yield (entry 1). The results also showed that galvinoxyl

Table 1. The repair reactions of 1,3-dimethylthymine bromohydrin (**1**) by the 1,5-dihydro-5-deazaflavin (**2**)-flavinium (**3**) system.^a

Entry	Reagents (equiv.)	% Yield (6)	Recovery of (1)
1	(2) (1.2) (3) (1.2) Magnesium perchlorate (1.2)	88.7	0
2	(2) (1.2) (3) (1.2)	0	69.5
3	(2) (1.2) Magnesium perchlorate (1.2)	0	72.5
4	(2) (1.2) (3) (1.2) Magnesium perchlorate (1.2) Galvinoxyl (1.2)	0	58.0

^a All reactions conducted in acetonitrile, under an argon atmosphere, in the dark, at room temp. for 3 days.



Scheme 1. Proposed mechanism for the repair reaction of (**1**) by the (**2**)-(3) system.

could completely quench the reaction, the starting material being recovered in good yield (entry 4). The reaction did not proceed on omission of magnesium perchlorate (entry 2) or (3) (entry 3) from the system. The role of magnesium perchlorate appears to be to facilitate electron transfer from (2) to (3), because the reduced flavin radical (4) or its equivalent generated *in situ* by sodium hydrosulphite reduction of (3) could repair (1) under the same conditions, though in lower yield.

In Scheme 1, we propose a plausible mechanism for the repair of (1) by this novel one-electron reduction system. The reaction would be rationalised by the elimination of bromide ion from the bromohydrin radical anion (5) initially formed by one-electron transfer. There is a precedent for this type of carbon-bromine bond scission in the uracil series.⁶

The same repair reaction proceeds using an electron bridge consisting of natural NADPH and FMN (riboflavin 5'-phosphate), although in less than half the yield of our artificial system. These results suggest that this type of repair of thymine and thymidine bromohydrins may occur in living cells. Furthermore, this one-electron reduction may have considerable utility in organic synthesis as well as in bio-

mimetic reactions, because of the mildness of the conditions and the good yields obtained.

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