

THE REDUCTIVE REPAIR OF ADENINE-1-OXIDE DERIVATIVES TO ADENINE DERIVATIVES BY γ -GLUTAMYL-CYSTEINYLGLYCINE (GLUTATHIONE)

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Adenine-1-oxide derivatives were reductively repaired by γ -glutamylcysteinylglycine (glutathione) under irradiation with a sunlamp to give the corresponding adenine derivatives.

KEYWORDS adenine-1-oxide; glutathione; reduction; photolysis

Previous papers have shown that adenine derivatives are easily oxidized by neutral hydrogen peroxide¹⁻³⁾ and by ionizing radiation⁴⁾ to give the corresponding adenine-1-oxide derivatives and their peroxides. In biological system also adenine-1-oxide is generated within the DNA when exposed to hydrogen peroxide.⁵⁾ The adenine-1-oxide derivatives are sensitive to ultraviolet- and gamma-irradiation, which induce two main chemical changes; one is direct loss of oxygen and the other is rearrangement of the oxygen to the adjacent carbon, giving isoguanine derivatives.⁶⁾ Recently we have studied the organic chemistry in the damage and repair of nucleic acids and their components, particularly thymine derivatives.⁷⁻¹⁰⁾

In the present paper, we describe the reductive repair of adenine-1-oxide derivatives to the corresponding adenine derivatives by glutathione (GSH) under irradiation with a sunlamp. 9-Ethyladenine-1-oxide (**1**) (0.1 mmol) and GSH (**2**) (0.5 mmol) were dissolved in phosphate buffer (pH 7.0) (5 ml) and the solution was stirred in an argon atmosphere at room temperature under irradiation with a sunlamp (2380 lux). As the reaction progressed, the chemical yields of 9-ethyladenine (**3**)¹²⁾ were monitored by h.p.l.c. The products were identified by their isolation with preparative t.l.c. It is significant that the rearranged product, 9-ethylisoguanine (**6**), was not detected (Chart 1). The results are summarized in Table I. Irradiation without GSH gave no appreciable yield of (**3**) (21% yield after 6 days) and the treatment with GSH in the dark gave only a trace of the product.

Table I. Repair Reaction of 9-Ethyladenine-1-oxide (**1**) to 9-Ethyladenine (**3**) by GSH under Irradiation with a Sunlamp (2380 lux)

Reagent	Yield (%) of (3)			
	1 day	2 days	4 days	6 days
GSH (10 eq)	17	35	70	81
Cystein HCl (10 eq)	10	25	44	59
Sunlight alone	10	13	17	21
GSH (10 eq) in the dark	0	0	0.5	1

As seen in Table II, the repair yields from (**1**) to (**3**) were somewhat proportional to the amount of GSH. The reducing ability of GSH was considered to depend on the thiol function of cystein in tripeptide GSH. In fact, cystein hydrochloride under irradiation with a sunlamp repaired (**1**) to give (**3**),

although in lower yield than GSH. The other reducing agents included in biological systems, such as flavin, deazaflavin, pterin, ascorbic acid and Cu^+ , were all ineffective for the above repair, even under irradiation with a sunlamp.

Adenosine-1-oxide (4)¹³ was also repaired under the same conditions as above to give the adenosine (5) in 60% yield after 6 days, without forming isoguanosine (7).

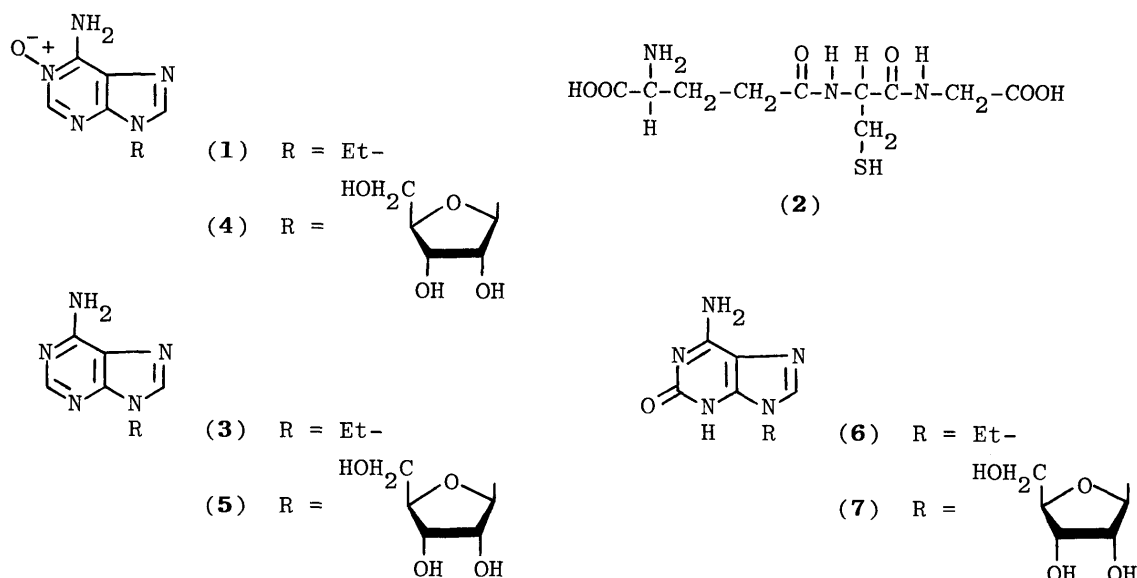


Chart 1

Table II. Repair Reaction of 9-Ethyladenine-1-oxide (1) to 9-Ethyladenine (3) with Variable Amounts of GSH under Irradiation with a Sunlamp (2380 lux)

GSH	Yield (%) of (3)			
	1 day	2 days	4 days	6 days
1 eq	9	19	35	47
2 eq	11	25	49	65
5 eq	13	31	59	72
10 eq	15	35	70	81

The reaction would be initiated by the electron transfer from GSH (2) to adenine-1-oxides, accompanied by protonation and then dehydration to give the corresponding adenines (Chart 2). The formation of thiyl radicals is well known in the photolysis of mercaptans.¹⁴⁾ Since glutathione is involved in almost all kinds of living cells, this type of repair reaction of the adenine-1-oxide derivatives could occur in live bodies under certain circumstances.

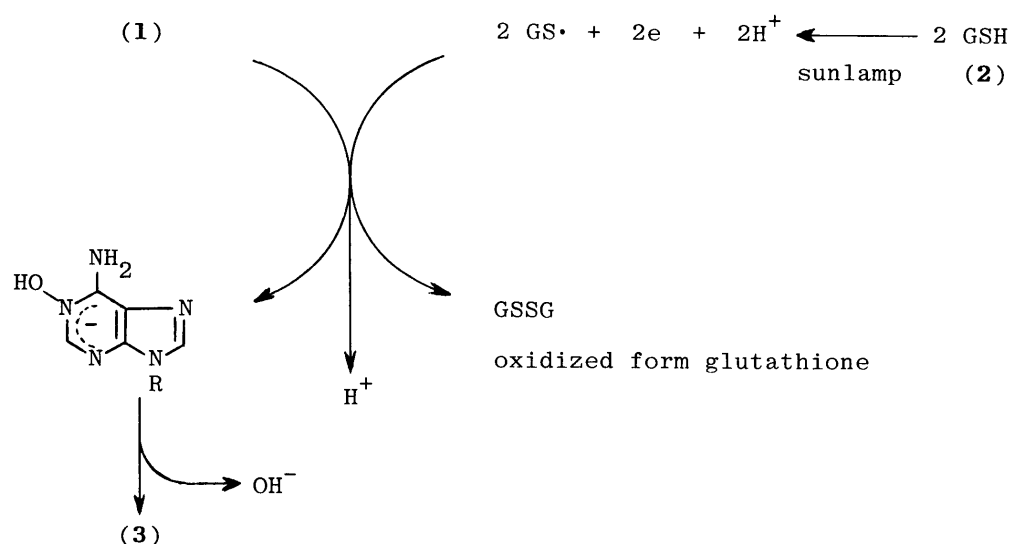


Chart 2

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