Photochemical Intramolecular Cyclisation of Purine and Pyrimidine Nucleosides induced by an Electron Acceptor

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Irradiation of appropriately protected purine nucleosides (guanosine and adenosine) (**1**) and cytidine (**2a**) in the presence of pyrimido[5,4-*g*]pteridine *N*-oxide (**5**) with u.v.–visible light results in the exclusive formation of the corresponding 5′-*O*,8-cyclopurine nucleosides (**3**) and 5′-*O*,6-cyclocytidine (**4a**).

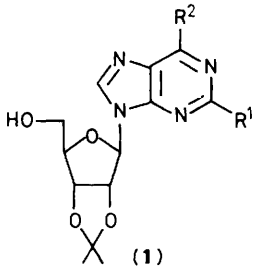
Photochemical reactions of purine and pyrimidine nucleosides have been investigated mainly as a chemical model for an understanding of irradiation damage in biological systems.[1] We now report that irradiation of appropriately protected purine nucleosides (**1**) and cytidine (**2a**) in the presence of pyrimido[5,4-*g*]pteridine *N*-oxide (**5**), which is a good electron acceptor,[2] with u.v.–visible light affords exclusively the corresponding 5′-*O*,8-cyclopurine nucleosides (**3**) and 5′-*O*,6-cyclocytidine (**4a**). The present reaction provides the first example of photoinduced intramolecular cyclisation of purine and pyrimidine nucleosides proceeding through charge-transfer (C.T.) complex formation† and also is of interest in

† It has been reported that the photochemical 5′-*O*-cyclisation of 2′-deoxyuridine to give 5′-*O*,6-cyclo-5,6-dihydro-2′-deoxyuridine proceeds as a minor process during photohydration under u.v. irradiation (254 nm); *cf.* J. Cadet, L.-S. Kan, and S. Y. Wang, *J. Am. Chem. Soc.*, 1978, **100**, 6715.

Table 1. Photochemical reaction of purine nucleosides (**1**) and the cytidine derivative (**2a**) with pyrimido[5,4-*g*]pteridine *N*-oxide (**5**).[a]

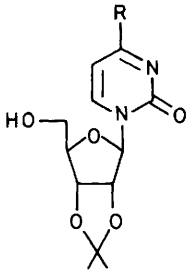
Nucleoside	Irradn. time/h	Conversion, %	Product (%)[b]	$\lambda_{max.}$/nm (ε)[c]
(**1a**)	0.5	80	(**3a**)[d] (70)	388 (118)
(**1b**)	0.5	21	(**3b**)[e] (18)	386 (59)
(**1c**)	0.5	22	(**3c**)[d] (20)	387 (65)
(**2a**)	1.5	8	(**4a**)[d] (7)	

[a] Reaction conditions: a mixture of nucleoside (1.0 mmol) and (**5**) (2.0 mmol) in dry acetonitrile was irradiated with a 400 W high-pressure mercury arc lamp through Pyrex at ambient temperature under argon. [b] Isolated yield. [c] Absorption of C.T. complex of the nucleoside with (**5**); nucleoside (**1**) and (**2a**) (25 mmol), (**5**) (0.5 mmol), in MeCN, at 25 °C. [d] Ref. 4. [e] M.p. 251—253 °C (from ethyl acetate).



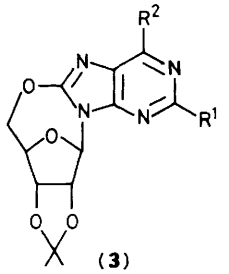
(**1**)

a; R^1 = NHCOPh, R^2 = OH
b; R^1 = H, R^2 = NHCOPh
c; R^1 = H, R^2 = NH_2



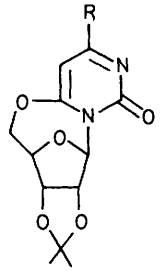
(**2**)

a; R = NHCOPh
b; R = OH



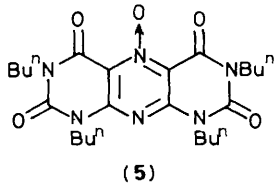
(**3**)

a; R^1 = NHCOPh, R^2 = OH
b; R^1 = H, R^2 = NHCOPh
c; R^1 = H, R^2 = NH_2

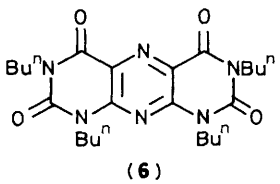


(**4**)

a; R = NHCOPh
b; R = OH



(**5**)



(**6**)

connection with reactions involving electron donor–acceptor interactions in biological substances.[3]

A mixture of the guanosine (**1a**) (1.0 mmol) and (**5**) (2.0 mmol) in dry acetonitrile was irradiated with a 400 W high-pressure mercury arc lamp through a Pyrex filter at ambient temperature under argon for 0.5 h. After removal of the solvent, the residue was chromatographed over silica gel to provide the cyclo compound (**3a**) in 70% yield, together with pyrimido[5,4-*g*]pteridine (**6**) and unchanged starting materials (**1a**) and (**5**). No other products were detected by t.l.c. The structures of (**3a**) and (**6**) were confirmed by spectral comparison with authentic samples.[2c,4]

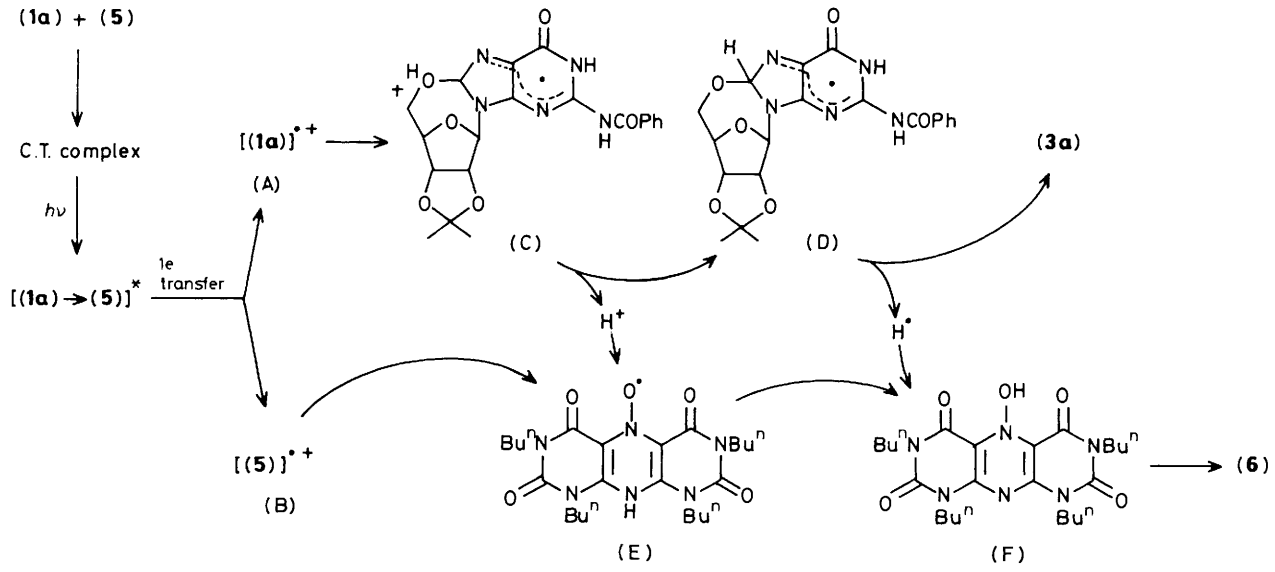
When the reaction was carried out in the absence of (**5**), the product (**3a**) was not obtained and the starting material (**1a**) was recovered unchanged. The 5′-*O*-cyclisation of (**1a**) in the presence of (**5**) did not proceed under thermal conditions (*e.g.*, reflux for 24 h). The difference spectrum ($\lambda_{max.}$ 388 nm) of the mixture of (**1a**) and (**5**) *vs.* (**5**)‡ in acetonitrile showed the presence of a C.T. interaction between (**1a**) and (**5**) in the ground state. A strong wavelength dependence was observed in the present photoreaction; irradiation at 388 nm (C.T. band) resulted in the maximum yield of (**3a**).

Analogous intramolecular oxidative 5′-*O*-cyclisation was also observed in the photoreaction of the adenosine derivatives (**1b**) and (**1c**) and cytidine derivative (**2a**) with (**5**) as summarised in Table 1. However, the cyclisation of 2′,3′-*O*-isopropylideneuridine (**2b**) to give 5′-*O*,6-cyclouridine (**4b**) did not proceed under conditions similar to those used for (**2a**). Thus, the ease of the reaction correlated well with the electron-donating capacity of the base moiety in the nucleosides employed.[5]

Taking these facts into consideration, a conceivable mechanism for the present photochemical 5′-*O*-cyclisation of (**1**) and (**2a**) in the presence of (**5**) leading to (**3**) and (**4a**) is outlined in Scheme 1 which illustrates the conversion of (**1a**) into (**3a**) as an example. The reaction could be initiated by the formation of a C.T. complex between (**1a**) and (**5**) in the ground-state followed by single-electron transfer (S.E.T.) from (**1a**) to (**5**) in an excited complex leading to the guanosinyl cation radical (A)[6] and the *N*-oxide anion radical (B). The intramolecular trapping of the cation radical (A) by the 5′-hydroxy group of the ribofuranosyl ring would give the cyclic guanosine cation radical (C). Proton uptake from (C) by (B) would generate the cyclic guanosine radical (D) and the nitroxyl radical (E). Hydrogen abstraction from the C(8)-position in (D) by (E) and subsequent dehydration of the resulting transient intermediate (F) would afford ultimately (**3a**) and (**6**).§ In agreement with the proposed S.E.T.

‡ $\lambda_{max.}$ (MeCN) of (**5**): 370 (ε 2.2 × 10^4), 270 (5.0 × 10^4), and 242 nm (3.2 × 10^4).

§ Another possible mechanism for the formation of (**3a**) and (**6**) involving the coupling of (D) and (E) can be considered. At present we have no evidence to rule out this mechanism.



Scheme 1

mechanism, the photochemical 5′-*O*-cyclisation of (**1a**) to give (**3a**) took place in moderate yields when tetracyanoethylene or dinitrobenzene, well-known electron acceptors,[7] were used in place of (**5**).

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