N^6-Substituent Effect on the Photooxidation of 2′,3′-*O*-Isopropylideneadenosines with a Pyrimido[5,4-*g*]pteridinetetraone *N*-Oxide. Chemical Evidence for the Generation and Reactivity of Adenosyl Cation Radicals

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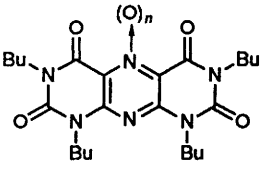
A comparative study on the photooxidation of 2′,3′-*O*-isopropylideneadenosine **1a** and its N^6-benzoyl, N^6-monomethyl, and N^6,N^6-dimethyl derivatives, **1b–d**, with a pyrimido[5,4-*g*]pteridinetetraone *N*-oxide (PPO) was carried out. The ease of photooxidative consumption of the adenosines by the PPO is in the order of **1d** > **1c** > **1a** > **1b**, which is parallel to their oxidation-peak potentials. Although substrates **1a** and **1b** underwent oxidative intramolecular cyclisation to the corresponding 5′-*O*,8-cycloadenosines, **2a** and **2b**, even in low yield, substrates **1c** and **1d** were exclusively oxidised at the N^6-methyl group to give the corresponding N^6-formyl derivatives, **3** and **4**, together with minor amounts of demethylated products, **1a** and **1c**. The present observations provide chemical evidence for the generation and reactivity of adenosyl cation radicals.

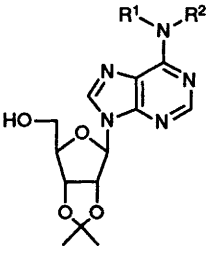
In a preliminary communication,[1] we have described how 2′,3′-*O*-isopropylideneadenosine **1a** and its N^6-benzoyl derivative **1b** undergo photooxidative cyclisation leading to the corresponding 5′-*O*,8-cycloadenosines, **2a** and **2b**, in the presence of an electron acceptor such as the pyrimido[5,4-*g*]pteridinetetraone *N*-oxide PPO.† The thermal oxidative cyclisation of compounds **1a**, **1b** and the N^6, N^6-dimethyl derivative **1d** to the corresponding cycloadenosines, **2a**, **2b** and **2c**, with lead tetra-acetate (LTA) has been also demonstrated.[2,3] In the last case, a significant accelerative effect of the N^6-benzoyl group on the oxidative cyclisation was observed and suggested the occurrence of an intramolecular oxidative nucleophilic substitution involving two-electron oxidation which arises from the preferential co-ordination of lead ion at the N^7-position.‡

In the photooxidation of the adenosines with PPO, however, no accelerative effect of the N^6-benzoyl group should be observed if the oxidation involves an initial single-electron-transfer (SET) process as a rate-determining step as proposed previously.[1]

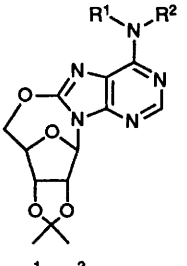
In this context, the N^6-substituent effect on the photooxidation of the adenosine derivatives, **1a**, **1b** and **1d**, and 2′,3′-*O*-isopropylidene-(N^6-methyl-adenosine **1c** by PPO was investigated in comparison with the case of LTA-oxidation. The experimental results showed that the ease of the photooxidation is in the order **1d** > **1c** > **1a** > **1b** which is in sharp contrast to the case of LTA-oxidation. Regioselectivity in the photooxidation was also observed: substrates **1a** and **1b** underwent the photooxidative intramolecular cyclisation to the corresponding 5′-*O*,8-cycloadenosines **2a** and **2b**. On the other hand, N^6-methyl-substituted derivatives **1c** and **1d** were oxidised exclusively at the N^6-position to give the corresponding N^6-formyl derivatives **3** and **4**, together with the N^6-demethylated products **1a** and **1c**. The present results are well rationalised in terms of the generation of adenosyl cation radicals by an initial SET in an excited state and provide insights for the reactivity of adenosyl radical species, which is important from the biological and chemical viewpoints.[5]



n = 1; **PPO**
n = 0; **PP**



1a; $R^1 = R^2 = H$
1b; R^1 = COPh, $R^2 = H$
1c; R^1 = Me, $R^2 = H$
1d; $R^1 = R^2$ = Me
3; R^1 = CHO, $R^2 = H$
4; R^1 = CHO, R^2 = Me



2a; $R^1 = R^2 = H$
2b; R^1 = COPh, $R^2 = H$
2c; $R^1 = R^2$ = Me

A mixture of compound **1a** [λ_{max} 258 (ε/dm^3 mol^{-1} cm^{-1} 1.6 × 10^4) nm] (1.0 mmol dm^{-3}) and PPO [λ_{max} 370 (2.2 × 10^4) nm] (2.0 mmol dm^{-3}) in dry acetonitrile was irradiated with a 400 W high-pressure mercury arc lamp through a $BiCl_3$ solution filter (>355 nm) at ambient temperature under argon for 4 h to give the 5′-*O*,8-cycloadenosine **2a** in 26% yield, together with recovery of

† Pyrimido[5,4-*g*]pteridinetetraone *N*-oxide PPO has been shown to function efficiently as an electron acceptor and as an agent for oxygenation or dehydrogenation under photochemical conditions, *cf.* ref. 6.

‡ The relative increase in the nucleophilicity of the imidazole ring nitrogen (N^7) in comparison with the pyrimidine ring nitrogen (N^1) by virtue of introduction of the N^6-acyl group has been observed (*cf.* ref. 18). Oxidative cyclisation of adenosines in an analogous manner has also been observed when *N*-halogenosuccinimides (in acetic acid) and copper(II) chloride (in acetonitrile) are used as an oxidant (see ref. 4).

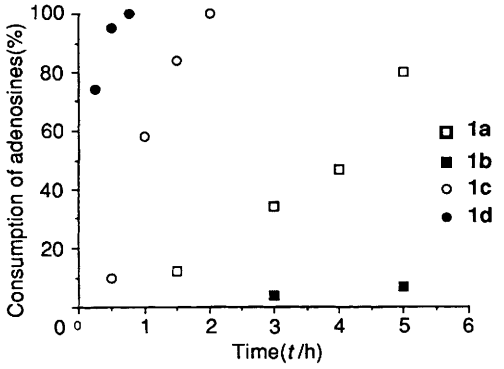


Fig. 1 Consumption of adenosines **1a–d** in the photooxidation by pyrimido[5,4-*g*]pteridinetetraone *N*-oxide (PPO) as a function of reaction time. Reaction conditions: a mixture of substrate **1a–d** (1.0 mmol dm^{-3}) and PPO (2.0 mmol dm^{-3}) in dry acetonitrile was irradiated under argon.

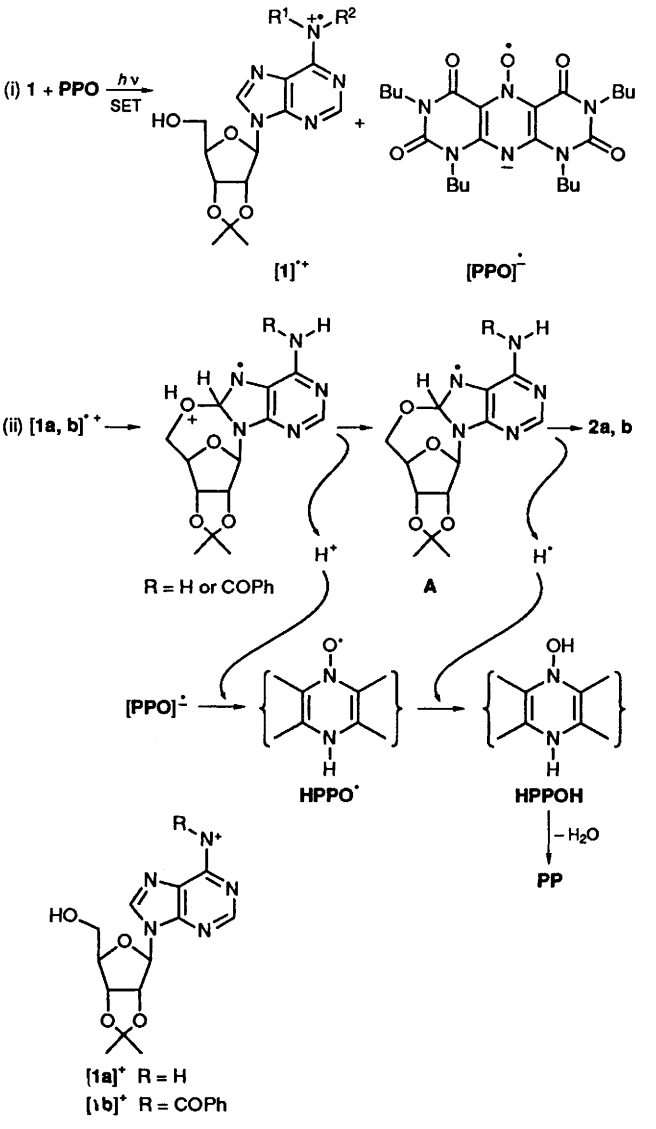
substrate **1a**. In the case of substrate **1b**, compound **2b** was obtained in only 5% yield after irradiation for 5 h.

The photoreaction of substrate **1c** with PPO under analogous conditions occurred with ease and gave N^6-formyl derivative **3** and N^6-demethylated product **1a** in 63 and 4% yield, respectively, after irradiation for 1.5h. Photooxidation of substrate **1d** by PPO took place more smoothly to give N^6-formyl-N^6-methyl derivative **4** and demethylated product **1c** in 73 and 14% yield, respectively, after irradiation for 0.5 h, together with small amounts of compounds **3** and **1a**. The structure of the N^6-formyl derivatives **3** and **4** was assigned by high-resolution mass spectrometry (HRMS) and spectral data and were confirmed by independent syntheses. It is worthwhile to note from the mechanistic viewpoint that, in the cases of substrates **1c** and **1d**, no formation of the corresponding 5′-*O*,8-cycloadenosines (*cf.* **2c**) was observed. In the above photoreactions, PPO was effectively consumed to give the parent pyrimido[5,4-*g*]pteridinetetraone (PP).

Fig. 1 plots the consumption of the adenosines **1a–d** in the photoreaction with PPO under the same conditions as a function of reaction time. The results clearly indicate that the photooxidative consumption of the adenosines occurs easily in the order **1d** > **1c** > **1a** > **1b**, which is in sharp contrast to the order **1b** > **1a** > **1c** > **1d** in the LTA-oxidation[3] and accommodates the oxidation peak potentials [E^{ox}p(V *vs* standard calomel electrode, SCE), in acetonitrile] of the adenosines, *i.e.*, 1.60 for **1a**; 1.82 for **1b**; 1.44 for **1c**; 1.40 for **1d**.

The *N*-oxide PPO is very stable to UV irradiation in dry acetonitrile. Addition of substrate **1d** to the solution of PPO and irradiation with UV-visible light resulted in the smooth consumption of PPO with concentration dependence, implicating an appreciable interaction between PPO and substrate **1d** in the photoreaction. In fact, a very weak charge-transfer (CT) interaction between compound **1d** and PPO was observed in acetonitrile: a difference spectrum of the mixture of a large excess of **1d** and PPO *vs.* PPO in acetonitrile showed the CT absorption band at around 388 nm. However, wavelength-dependence experiments showed that the consumption of PPO in the photoreaction occurs most efficiently on irradiation at around 365 nm, which is near the longest UV absorption band of PPO.

Taking the above results and other demonstrations in the photochemical reactivity of PPO[6] into consideration, the initial stage of the photoreaction of substrates **1a–d** with PPO



Scheme 1

evidently involves an SET from **1a–d** to an excited PPO (partially in an excited CT-complex) to give adenosyl cation radical [**1**]$^{\bullet+}$ and *N*-oxide anion radical [PPO]$^{\bullet-}$ [see reaction (*i*) in Scheme 1],* although the efficiency of the SET and the successive reaction modes depend upon the nature of the N^6-substituents of the substrate **1**.

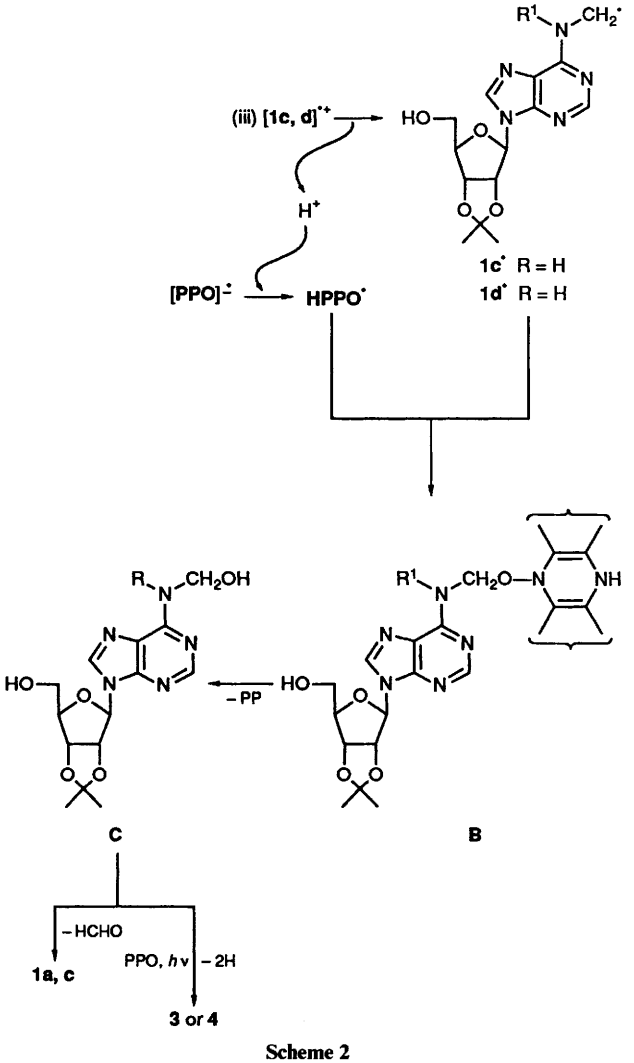
In the case of substrates **1a** and **1b**, the formation of the 5′-*O*,8-cycloadenosines, **2a** and **2b**, occurred as the sole oxidation process. Thus, the cation radical [**1a**, **b**]$^{\bullet+}$ gives a radical intermediate **A** *via* intramolecular trapping at C-8 by the 5′-hydroxy group of the adenosine. Hydrogen abstraction from C-8 in **A** by HPPO$^{\bullet}$ and subsequent dehydration of the resulting transient intermediate HPPOH would afford ultimately **2a**, **b** and PP [see reaction (*ii*) in Scheme 1]. An alternative route for the oxidative cyclisation of **1a**, **b** to **2a**, **b** involving deprotonation from the N^6-position of [**1a**, **b**]$^{\bullet+}$ followed by a single-electron oxidation to generate nitrenium ion [**1a**, **b**]$^{+}$ cannot be ruled out completely, since deprotonation from the nitrogen of arylamine cation radicals is possible in acetonitrile.[7]

In the case of substrates **1c** and **1d**, oxidation on the N^6-methyl group involving demethylation and conversion into the N^6-formyl group occurred concurrently, *i.e.*, no conversion of the N^6-formyl derivatives, **3** and **4**, into the demethylated products **1a**, **c** under the conditions employed, and product distributions during the photoreactions confirmed this aspect.

* The structures of the radical species in Schemes 1 and 2 are presented for convenience by one of canonical structures in their resonance hybrids.

The oxygen atom inserted into the photo-products **3** and **4** might originate from a small amount of water or molecular oxygen contained in the reaction medium. In order to rule out this possibility, the photoreaction of compound **1d** with ^{18}O-labelled *N*-oxide[6] was examined. When a mixture of compound **1d** and the ^{18}O-labelled PPO was irradiated under conditions similar to those of the foregoing case, almost quantitative ^{18}O-incorporation into the N^6-formyl group of the major product **4** was observed. This fact clearly indicates that the inserted oxygen atom of the product **4** originates from the *N*-oxide oxygen of PPO. A stoicheiometric study showed that two equimolar amounts of PPO were required for the formation of products **3** and **4** in the photo-oxidations of substrates **1c** and **1d** by PPO.

On the basis of the above facts and complete conversion of PPO into PP, a plausible reaction sequence for the formation of the N^6-formyl derivative **3** or **4** and N^6-demethylated products **1a**, **c** in the photooxygenation of compounds **1c**, **d** by PPO is outlined as shown in Scheme 2 [see reaction (*iii*).



Scheme 2

Proton abstraction from the radical cation [**1c**, **d**]$^{\bullet+}$ by [PPO]$^{\bullet-}$ generates aminomethyl radical **1c**, **d**$^{\bullet}$ and a nitroxyl radical HPPO$^{\bullet}$ which couple together to give a transient intermediate **B**. Heterolytic fragmentation of the N–O bond in **B** leads to the formation of PP and N^6-carbinolamine **C**. Subsequent elimination of formaldehyde from **C** as a minor process results in the formation of the demethylated products **1a**, **c**. Photochemical dehydrogenation of **C** by PPO *via* the reaction pathway analogous to the case of compounds **1c**, **d** affords the N^6-formyladenosine **3** or **4** as a major product.

A number of previous observations have shown that N–H deprotonation of the cation radical derived from secondary dialkylamines is often favoured over loss of an α-CH proton in nonpolar solvents (*e.g.*, benzene), whereas in polar solvents (*e.g.*, acetonitrile) α-CH proton loss takes place to give α-aminoalkyl radicals.[8–11] The N^6-demethylation and N^6-formyl formation in **1c** under the conditions employed are consistent with the fact that the proton loss of the initially formed cation radical [**1c**]$^{\bullet+}$ occurs preferably to produce the thermodynamically stable aminoalkyl radical **1c**$^{\bullet}$.

In the photoreaction of **1d** with PPO, formation of the N^6-formyl deivative **4** occurred in a major pathway which is in sharp contrast to the case of *N*,*N*-dimethylaniline: no formation of the corresponding *N*-formyl derivative was observed in the photooxidation of *N*,*N*-dimethylaniline by PPO.[12] Therefore, the carbinolamine intermediate **C** seems to be fairly stable toward photochemical dehydrogeneration by PPO.

Endo and Zemlicka[13] reported that N^6,N^6-dimethyladenosine was oxidised by ruthenium tetraoxide to give the corresponding N^6-formyl-N^6-methyl derivative together with minor amount of N^6-demethylated product and proposed a mechanism which is entirely different from that of the photochemical oxidation with PPO. The present results in the photooxidation of substrate **1d** by PPO are of novelty in the mechanistic viewpoint and also of interest in connection with the enzymatic demethylation of puromycin.[14]

The generation of adenosyl cation radicals by the use of the powerful oxidants such as $SO_4^{\bullet-}$ and OH$^{\bullet}$ and their reactivities in aqueous solution have been studied mainly from the viewpoint of radiation damage to DNA components.[15]. In addition to these studies, the present study provides further chemical evidence for the generation and reactivity of adenosyl cation radicals based on experimental observations concerning the efficiency and regioselectivity in the photooxidation of adenosine and its N^6-substituted derivatives by PPO. Extension of this observation in purinyl cation radical chemistry * to the chemical modification of purine nucleosides is in progress.

Experimental

Irradiations were carried out at ambient temperature with a Riko Rotary Photochemical Reactor (400 W high-pressure mercury arc lamp, Riko Kagaku Sangyo) though a $BiCl_3$ solution filter (>355 nm) under argon. A grating monochrometer (JASCO CRM-FA spectroirradiator) with 2 kW Xe lamp and a 4 nm bandwidth was used for the wavelength-dependence experiments. The spectroscopic measurements were performed with the following instruments: UV absorption spectra with a Shimadzu-260 spectrophotometer; ^1H NMR spectra with a JEOL JNX-270 (270 MHz) spectrometer with tetramethylsilane as internal standard and *J*-values in Hz; high-resolution and mass spectra with a JEOL JMS D-300 machine operating at 70 eV. TLC analyses were performed on silica gel plates (Merck, art 5715) with benzene–ethyl acetate (5:2) for the assay of pyrimido[5,4-*g*]pteridine derivatives; ethyl acetate–methanol (30:1) for the assay of adenosine derivatives as developer, and TLC-scanning was carried out with a Shimadzu CS-9000 dual-wavelength flying-spot scanner (detection: 370 nm for the assay of the pyrimido[5,4-*g*]pteridine derivatives; 270 nm for the assay of the adenosines). Column chromatographic separation was accomplished on silica gel (Wakogel C-300).

* A guanosine derivative has been shown to undergo analogous photo-oxidation by PPO (see ref. 1).

Materials.—1,3,7,9-Tetrabutylpyrimido[5,4-*g*]pteridine-2,4,6,8(1*H*,3*H*,7*H*,9*H*)-tetraone 5-oxide (PPO),[16] 1,3,7,9-tetrabutylpyrimido[5,4-*g*]pteridine-2,4,6,8(1*H*,3*H*,7*H*,9*H*)-tetraone (PP),[17] 2′,3′-*O*-isopropylideneadenosine **1a**,[18] N^6-benzoyl-2′,3′-*O*-isopropylideneadenosine **1b**,[18] 2′,3′-*O*-isopropylidene-N^6-methyladenosine **1c**,[18] and 2′,3′-*O*-isopropylidene-N^6,N^6-dimethyladenosine **1d**[18] were prepared according to the known methods, respectively.

Photochemical Reactions of the Adenosines **1a–d** *with PPO.*—(a) *Consumption of* **1a–d** *in the photoreaction.* A solution of **1a–d** (5.0×10^{-6} mol) and PPO (4.9 mg, 1.0×10^{-5} mol) in dry acetonitrile (5 cm^3) was irradiated externally. The reaction mixture was sampled every 15 min for 5 h. Consumption of substrates **1a–d** and PPO during the irradiation was estimated by TLC densitometry. The consumptions of substrates **1a–d** [for **1a**: 12% (after 1.5 h), 34 (3 h), 47 (4 h) and 80 (5 h); for **1b**: 4% (after 3 h) and 7% (5 h); for **1c**: 10% (after 30 min), 58 (1 h), 84 (1.5 h) and 100 (2 h); for **1d**: 74% (after 15 min), 95 (30 min) and 100 (45 min)] were plotted in Fig. 1 as a function of irradiation time. The consumption yields of PPO were as follows: for **1a**: 15% (after 1.5 h, based on the employed PPO), 41 (3 h), 64 (4 h) and 87 (5 h); for **1b**: 6% (after 3 h) and 10 (5 h); for **1c**: 10% (after 30 min), 63 (1 h), 98 (1.5 h) and 100 (2 h); for **1d**: 77% (after 15 min), 97 (30 min) and 100 (45 min). TLC analyses of the reaction mixtures showed almost quantitative conversion of the consumed PPO (R_f 0.27) into PP (R_f 0.35), respectively.

(b) *Photoreaction of the adenosines* **1a** *and* **1b** *with PPO.* A solution of substrate **1a** (30.7 mg, 1.0×10^{-4} mol) in dry acetonitrile (100 cm^3) containing PPO (97.7 mg, 2.0×10^{-4} mol) was irradiated externally for 4 h. TLC analyses of the reaction mixture showed 64% consumption of PPO and the formation of PP (almost quantitative yield) and 2′,3′-*O*-isopropylidene-5′-*O*,8-cycloadenosine **2a** (R_f 0.14, 26%) with recovery of **1a** (R_f 0.08, 53%).

Under conditions analogous to the case of compound **1a**, irradiation of a mixture of **1b** (41.2 mg, 1.0×10^{-4} mol; R_f 0.20) and PPO (97.7 mg, 2.0×10^{-4} mol) was carried out for 5 h to give N^6-benzoyl-2′,3′-*O*-isopropylidene-5′-*O*,8-cycloadenosine **2b** (R_f 0.39, 5%) and PP (10%, based on the employed PPO).

The structures of the products **2a**, **b** were confirmed by spectral comparison with authentic samples[1] after column chromatographic separation using chloroform–methanol (50:1) as eluent.

(c) *Photoreaction of the adenosines* **1c** *and* **1d** *with PPO.* A solution of substrate **1c** (32.1 mg, 1.0×10^{-4} mol) and PPO (97.7 mg, 2.0×10^{-4} mol) in dry acetonitrile (100 cm^3) was irradiated externally for 1.5 h. TLC analyses of the reaction mixture showed 84% consumption of **1c** (R_f 0.15) and the formation of two products (R_f 0.36 and 0.08) together with PP (97% based on the employed PPO). After removal of the solvent under reduced pressure, the residue was subjected to column chromatography and elution with chloroform–methanol (50:1) to isolate the less polar product, which was N^6-formyl-2′,3′-*O*-isopropylideneadenosine **3** (21 mg, 63%) as a powder, and polar product **1a** (2 mg, 4%). The product **1a** was identical in every respect with an authentic sample. The structure of product **3** was assigned by microanalytical spectral data (Found: M^+, 335.1192. $C_{14}H_{17}N_5O_5$ requires M, 335.1210); *m/z* 335 (M^+, 1%), 320 ($M^+ - 15$, 6), 290, 277, 218, 164 (100) and 135; ν_{max}(KBr)/cm^{-1} 1715 (C=O); λ_{max}(MeOH)/nm 271 and 218; δ_H($CDCl_3$) 1.39 (3 H, s, CMe), 1.67 (3 H, s, CMe), 3.8–4.0 (2 H, m, 5′-H_2), 4.57 (1 H, br, 4′-H), 5.13 (1 H, m, 3′-H), 5.23 (1 H, t, *J* 5, 2′-H), 5.99 (1 H, d, *J* 4, 1′-H), 8.40 (1 H, s, 8- or 2-H), 8.64 (1 H, s, 2- or 8-H), 9.96 (1 H, d, *J* 10, NHC*H*O) and 10.27 (1 H, br d, *J* 10, deuterium exchangeable N*H*CHO).

Under conditions similar to those in the foregoing case, irradiation of a mixture of substrate **1d** (33.6 mg, 1.0×10^{-4} mol) and PPO (97.7 mg, 2.0×10^{-4} mol) in dry acetonitrile (100 cm^3) was carried out for 30 min to give N^6-formyl-2′,3′-*O*-isopropylidene-N^6-methyladenosine **4** (73%) as a viscous oil, R_f 0.56), **1c** (14%), **3** (2%) and **1a** (1%) together with PP (97%, based on the employed PPO) and the remaining **1d** (5%, R_f 0.36). The structure of the product **4** was assigned by microanalytical and spectral data (Found: M^+, 349.1341. $C_{15}H_{19}N_5O_5$ requires M, 349.1363); *m/z* 349 (M^+, 2%), 334 ($M^+ - 15$, 3), 321, 306, 291, 260, 232, 206, 178 (10) and 149 (100); λ_{max}(MeOH)/nm 277 and 214; ν_{max}(KBr/cm^{-1} 1722 (C=O); δ_H($CDCl_3$) 1.43 (3 H, s, CMe), 1.70 (3 H, s, CMe), 3.52 (3 H, br s, NMe), 3.8–4.0 (2 H, m, 5′-H_2), 4.56 (1 H, br, 4′-H), 5.14 (1 H, m, 3′-H), 5.24 (1 H, d, *J* 5, 2′-H), 5.93 (1 H, d, *J* 5, 1′-H), 8.04 (1 H, s, 8-H), 8.68 (1 H, s, 2-H) and 10.50 (1 H, s, NCHO).

(d) *Concentration-dependence of the photoreaction of* **1d** *with PPO.* A solution of substrate **1d** (1.0, 2.0 or 4.0 mmol dm^{-3}) in dry acetonitrile containing PPO (2.0 mmol dm^{-3}) was irradiated under the same conditions for 30 min. TLC analyses of the reaction mixtures showed that the consumption rate of PPO depended upon the concentration of **1d** in the medium. Consumption of PPO and yields of the photo-products were as follows. The consumption of PPO: 90% (based on the employed PPO) in the case of the molecular quotient **1d**/PPO = 1/2; 96% in the case of **1d**/PPO = 1/1; 100% in the case of **1d**/PPO = 2/1. Product (yield, based on the employed PPO): **4** (37%) and **1c** (7%) in the case of **1d**/PPO = 1/2; **4** (38%) and **1c** (10%) in the case of **1d**/PPO = 1/1; **4** (41%), **1c** (21%) and **1a** (1%) in the case of **1d**/PPO = 2/1.

Independent Syntheses of N^6*-Formyladenosines* **3** *and* **4**.—A solution of the adenosine **1a** (76.9 mg, 2.5×10^{-4} mol) in formic acid (99% purity; 1.0 cm^3) and acetic anhydride (1.0 cm^3) was stirred at room temperature for 1 day. After removal of the solvent under reduced pressure, the residual oil was subjected to column chromatography with chloroform–acetone (10:1) as eluent to isolate N^6,5′-*O*-diformyl-2′,3′-*O*-isopropylideneadenosine[19] as a viscous oil, *m/z* 364 ($M^+ + 1$, 6%), 348 ($M^+ - 15$, 15), 335, 320, 305, 246 (100), 218 and 192 (97); λ_{max}(MeOH)/nm 271 and 216; ν_{max}(film)/cm^{-1} 1715 (C=O); δ_H($CDCl_3$) 1.42 (3 H, s, CMe), 1.66 (3 H, s, CMe), 4.3–4.5 (2 H, m, 5′-H_2), 4.56 (1 H, br, 4′-H), 5.12 (1 H, dd, *J* 3 and 6, 3′-H), 5.46 (1 H, dd, *J* 2 and 6, 2′-H), 6.26 (1 H, d, *J* 2, 1′-H), 8.08 (1 H, s, OCHO), 8.62 (1 H, s, 8- or 2-H), 8.71 (1 H, s, 2- or 8-H), 9.98 (1 H, d, *J* 10, NCHO) and 11.11 (1 H, br d, *J* 10, deuterium exchangeable N*H*CHO)] (30 mg, 33%), **3** (trace) and 5′-*O*-formyl-2′,3′-*O*-isopropylideneadenosine[19,20] as a powder, *m/z* 335 (M^+, 4%), 320 ($M^+ - 15$, 10), 290, 287, 218 and 164 (100); λ_{max}(MeOH)/nm 259 and 217; ν_{max}(film)/cm^{-1} 1724 (C=O) and 1644; δ_H($CDCl_3$) 1.41 (3 H, s, CMe), 1.63 (3 H, s, CMe), 4.3–4.5 (2 H, m, 5′-H_2), 4.52 (1 H, br, 4′-H), 5.13 (1 H, dd, *J* 3 and 6, 3′-H), 5.49 (1 H, dd, *J* 2 and 6, 2′-H), 6.12 (1 H, d, *J* 2, 1′-H), 6.20 (2 H, br, deuterium exchangeable NH_2), 7.89 (1 H, s, 2-H), 8.02 (1 H, s, OCHO) and 8.34 (1 H, s, 8-H)] (50 mg, 60%).

Under conditions analogous to those in the foregoing case, formylation of substrate **1c** (80.4 mg, 2.5×10^{-4} mol) was carried out to give N^6,5′-*O*-diformyl-2′,3′-*O*-isopropylidene-N^6-methyladenosine as a viscous oil, *m/z* 377 (M^+, 2%), 362 ($M^+ - 15$, 4), 349, 334, 319, 304, 260, 232 and 148 (100); λ_{max}(MeOH)/nm 277 and 206; ν_{max}(film)/cm^{-1} 1725 (C=O) and 1691 (C=O); δ_H($CDCl_3$) 1.42 (3 H, s, CMe), 1.65 (3 H, s, CMe), 3.59 (3 H, s, NMe), 4.3–4.5 (2 H, m, 5′-H_2), 4.52 (1 H, br, 4′-H), 5.11 (1 H, dd, *J* 3 and 6, 3′-H), 5.47 (1 H, dd, *J* 2 and 6, 2′-H), 6.20 (1 H, d, *J* 2, 1′-H), 8.02 (1 H, s, OCHO), 8.08 (1 H, s, 8-H), 8.71 (1 H, s, 2-H) and 10.47 (1 H, s, NCHO)] (40 mg, 42%), **4** (6 mg, 7%), 5′-*O*-formyl-2′,3′-*O*-isopropylidene-N^6-methyladenosine as a powder, *m/z* 349 (M^+, 10%), 334 ($M^+ - 15$, 7), 304, 291, 232 and 178 (100); λ_{max}(MeOH)/nm 265 and 216; ν_{max}-

(film)/cm^{-1} 1725 (C=O) and 1625; $\delta_H(CDCl_3)$ 1.40 (3 H, s, CMe), 1.62 (3 H, s, CMe), 3.19 (3 H, br s, NMe), 4.3–4.5 (2 H, m, 5′-H_2), 4.50 (1 H, br, 4′-H), 5.13 (1 H, dd, *J* 3 and 6, 3′-H), 5.50 (1 H, dd, *J* 2 and 6, 2′-H), 6.11 (1 H, d, *J* 2, 1′-H), 6.23 (1 H, br, deuterium exchangeable NH), 7.83 (1 H, s, 8-H), 8.01 (1 H, s, OCHO) and 8.40 (1 H, s, 2-H)] (41 mg, 47%).

The above N^6,5′-*O*-diformyladenosines were treated with refluxing ethanol overnight to remove the 5′-*O*-formyl group. The compounds obtained almost quantitatively were identical in every respect with the photo-products **3** and **4**, respectively.

Charge-transfer (CT) Interaction between the Adenosines **1a–d** *and PPO.*—The CT-complex formation between substrates **1a–d** and PPO was observed in the difference UV-visible absorption spectra of a mixture of PPO (5.0×10^{-4} mol dm^{-3}) and a substrate **1a–d** (2.5×10^{-2} mol dm^{-3}) *vs.* PPO (5.0×10^{-4} mol dm^{-3}) in dry acetonitrile. The observed CT-bands were 387 (ε 65 dm^3 mol^{-1} cm^{-1}) nm for **1a**, 386 (ε 59 dm^3 mol^{-1} cm^{-1}) nm for **1b**, 386 (ε 40 dm^3 mol^{-1} cm^{-1}) nm for **1c** and 388 (ε 60 dm^3 mol^{-1} cm^{-1}) nm for **1d**.

Wavelength-dependence Experiments for the Photochemical Oxidation of the Adenosine **1d** *by PPO.*—A solution of compound **1d** (1.0×10^{-4} mol dm^{-3}) and PPO (2.0×10^{-4} mol dm^{-3}) in dry acetonitrile was degassed carefully and irradiated with light of various wavelengths (301–504 nm; $\sim 3.3 \times 10^5$ *J* m^{-2}. The consumption of PPO and yields of the major product **4** were determined by TLC densitometry. The results were as follows. Consumption of PPO (wavelength, nm): 25 (327), 64 (353), 21 (380), 2 (406) and 2% (432); yields of **4** (wavelength, nm): 23 (327), 60 (353), 21 (380), 0 (406) and 0% (432).

Photoreaction of Compound **1d** *with* ^{18}O-*Labelled PPO.*—A solution of substrate **1d** (23.6 mg, 7.0×10^{-5} mol) and ^{18}*O*-labelled PPO[5] (48.9 mg, 1.0×10^{-4} mol, ^{18}O-content ~ 20%) in dry acetonitrile (50 cm^3) was irradiated externally for 30 min under conditions similar to those in the foregoing case. ^{18}O-Content (~20%) of the oxidation product **4** was determined by mass spectral analysis after column chromatographic separation.

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