

## Electronic Supplementary Information (ESI) for: Photoinduced water-chromophore electron transfer causes formation of guanosine photo-damages

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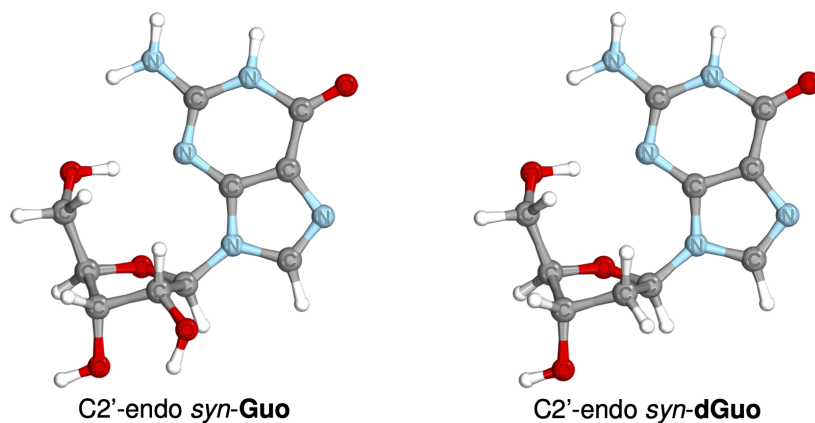
### Conformational spaces and ground-state geometries of guanine nucleosides

To find a preferred conformational arrangement of the chromophore moiety and sugar part in guanosine (**Guo**) and deoxyguanosine (**dGuo**) in a water solution, we performed an exploration of the conformational spaces of both nucleosides using the semi-empirical GFN2-xTB method<sup>1</sup> and the CREST<sup>2</sup> driver for the xTB program<sup>3</sup>. Next, we selected the energetically most stable structures for each nucleoside and reoptimized them using the PCM/ $\omega$ B97X-D/def2-TZVPP method. Our KS-DFT calculations indicate that the most stable ground-state structures in both cases (see Fig. S1) adopt the C2'-endo conformation of the sugar and the *syn* orientation of the nucleobase, which allows for the formation of the O5'-H $\cdots$ N3 intramolecular hydrogen bond. Consequently, we chose these KS-DFT optimized structures for further photochemical explorations of guanine nucleosides.

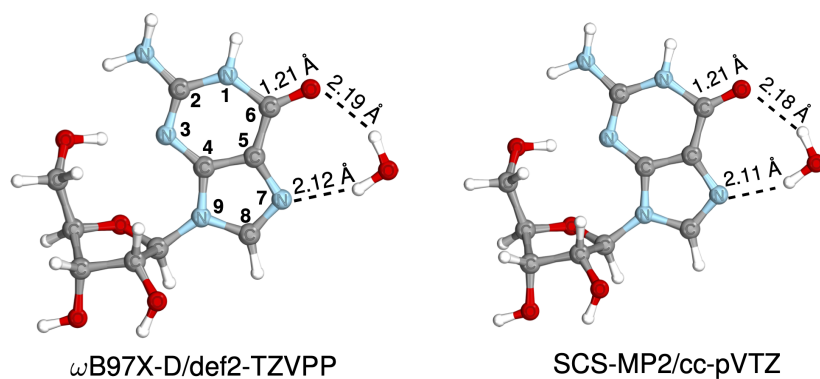
All ground-state calculations of the **Guo-H<sub>2</sub>O** cluster were performed using the  $\omega$ B97X-D/def2-TZVPP method and the photochemical properties were investigated using the SCS-MP2/SCS-ADC(2)/cc-pVTZ approach. Thus, to estimate the effect of the choice of method on the equilibrium ground-state structure of **Guo-H<sub>2</sub>O**, we optimized the latter geometry using the  $\omega$ B97X-D and SCS-MP2 methods. Fig. S2 presents complexes of guanosine with one explicit water molecule (**Guo-H<sub>2</sub>O**), which were optimized at the  $\omega$ B97X-D/def2-TZVPP and SCS-MP2/cc-pVTZ levels of theory. Both S<sub>0</sub> geometries are virtually identical, and it shows that the choice of method does not affect structural features of the S<sub>0</sub> geometry of **Guo-H<sub>2</sub>O**.

### Vertical excitation energies of guanine nucleosides

Vertical excitation energies of **Guo-H<sub>2</sub>O** and **dGuo-H<sub>2</sub>O** model systems, each including one explicit water molecule, (see Fig. S2) are presented in Tab. S1. The three lowest-lying excited states in both guanosine-water structures are virtually the same in the Franck-Condon region. Thus, we expect that the hydroxyl group on the C2' carbon does not affect the photophysical properties of guanine nucleosides. Furthermore, Tab. S1 presents two bright excited states (S<sub>1</sub> and S<sub>3</sub>) at  $\sim$ 5.13 and  $\sim$ 5.76 eV having substantial oscillator strengths. These two optically active states are characterized by locally excited (LE) <sup>1</sup> $\pi\pi^*$  transitions which are depicted in Fig. S3. In between those <sup>1</sup> $\pi\pi^*$  states, there is an S<sub>2</sub> dark state at 5.63 eV, which is marked by the <sup>1</sup> $n_O\pi^*$  transition (see Fig. S3). It is worth noting that the occupied n<sub>O</sub> orbital is delocalized on the carbonyl oxygen atom and a nearby water molecule, suggesting that the electronic structure of the water molecule may be involved in the <sup>1</sup> $n_O\pi^*$  excitation.



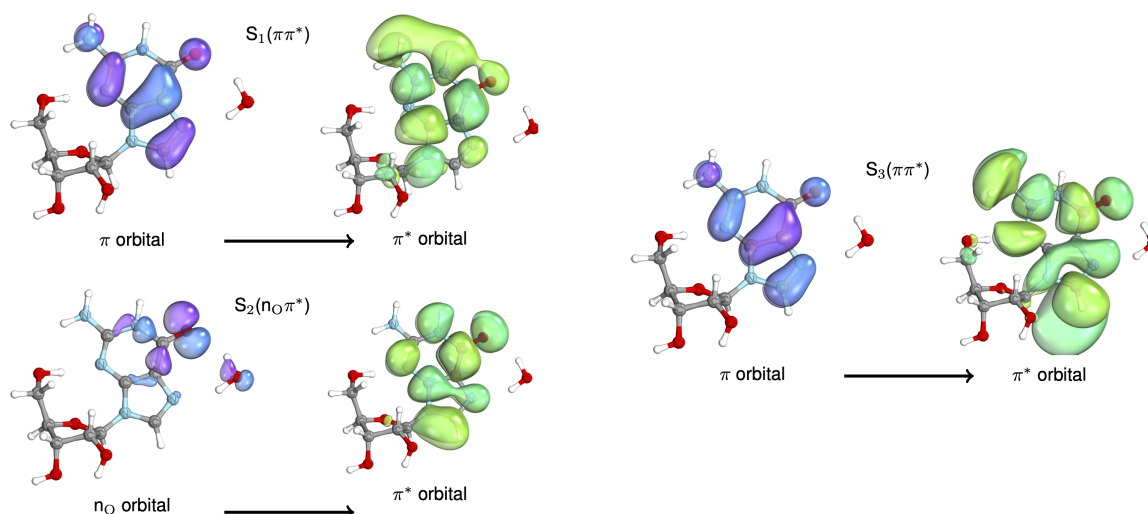
**Fig. S1** The equilibrium ground-state geometries of *syn* conformers of **Guo** and **dGuo** having the C2'-endo arrangement of the sugar moiety.



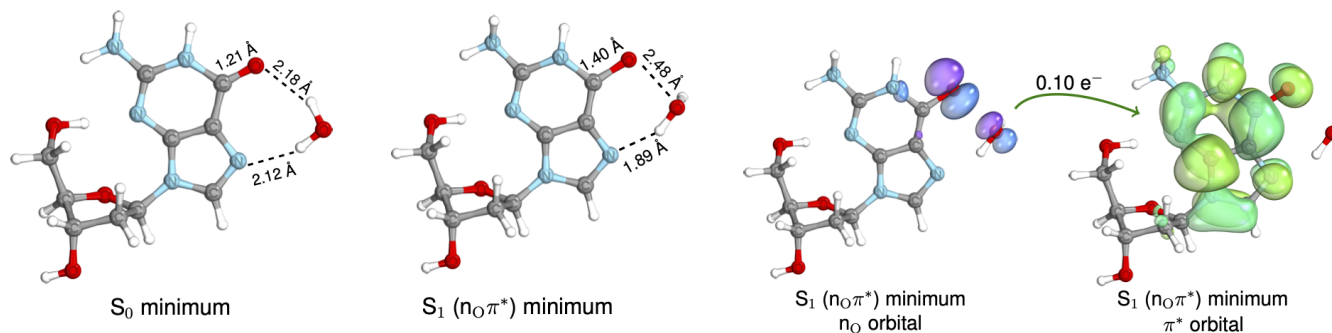
**Fig. S2** The equilibrium ground-state geometries of guanosine with one explicit water molecule found either using the  $\omega$ B97X-D/def2-TZVPP or SCS-MP2/cc-pVTZ method.

**Table S1** Vertical excitations energies (in eV) obtained at the SCS-ADC(2)/cc-pVTZ level of theory, assuming the  $S_0$  minimum-energy structures located using the  $\omega$ B97X-D/def2-TZVPP method. The character of electronic transitions was determined using natural transition orbitals.

State / Transition	$E_{exc}/[eV]$	$f_{osc}$	$\lambda/[nm]$
<b>Guo-H<sub>2</sub>O</b>			
S <sub>1</sub> $\pi\pi_{LE}^*$	5.13	$1.52 \times 10^{-1}$	242.2
S <sub>2</sub> $\pi\pi_{LE}^*$	5.63	$2.92 \times 10^{-1}$	219.4
S <sub>3</sub> $n_O\pi^*$	5.76	$2.11 \times 10^{-4}$	214.5
<b>dGuo-H<sub>2</sub>O</b>			
S <sub>1</sub> $\pi\pi_{LE}^*$	5.14	$1.71 \times 10^{-1}$	241.2
S <sub>2</sub> $n_O\pi^*$	5.63	$3.00 \times 10^{-4}$	220.2
S <sub>3</sub> $\pi\pi_{LE}^*$	5.74	$3.27 \times 10^{-1}$	216.0



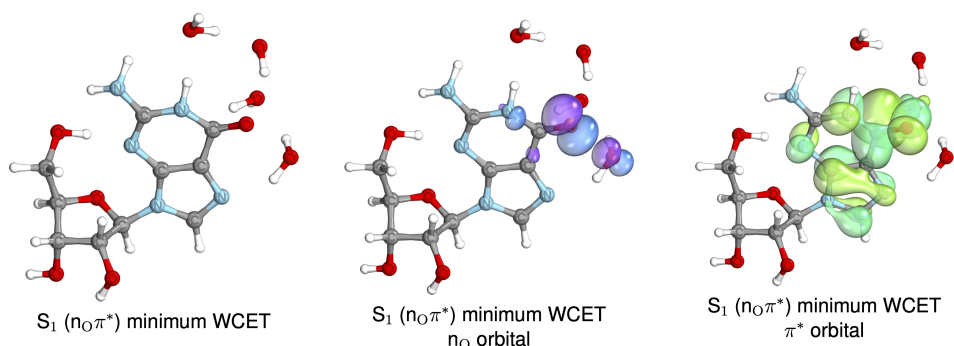
**Fig. S3** The natural transition orbitals present a molecular orbital character of the three lowest-lying excited states for **Guo-H<sub>2</sub>O**.



**Fig. S4** The  $S_0$  and  $S_1(n_O\pi^*)$  of **dGuo-H<sub>2</sub>O** are minimum-energy structures. The molecular orbitals involving in the  $S_1(n_O\pi^*)$  transition demonstrate a charge-transfer process of  $0.10 e^-$  from  $H_2O$  to the deoxynucleoside. Relevant distances between atoms are marked on geometries.

### Water-to-chromophore electron transfer in deoxyguanosine

The equilibrium ground-state structure of **dGuo-H<sub>2</sub>O** is presented in Fig. S4. The water molecule in the complex forms two strong hydrogen bonds with the carbonyl group (2.18 Å) and N7 atom (2.12 Å). The optimization of the  $S_1$  excited state yielded the  $^1n_O\pi^*$  minimum-energy structure presented in Fig. S4. The  $^1n_O\pi^*$  excited-state structure is characterized by the rearrangement of  $H_2O$  that results in the formation of the  $C6-O\cdots OH_2$  chalcogen bonding interaction, which consequently energetically stabilizes the  $^1n_O\pi^*$  excited state by  $\sim 1.20$  eV. In the  $S_1$  minimum, the  $O\cdots O$  intermolecular distance amounts to 2.48 Å, and the C6-O bond length is elongated to 1.40 Å in comparison with the corresponding ground-state structure. The chalcogen bonding interaction allows for an excited-state charge transfer (CT) of  $0.10 e^-$  from  $H_2O$  to the guanine part, and the CT process is demonstrated in Fig. S4 through the molecular orbitals participating in the  $^1n_O\pi^*$  transition. Furthermore, the discussed  $S_1$  structure of **dGuo-H<sub>2</sub>O**, having the CT character, is virtually the same as the  $S_1$  minimum located for **Guo-H<sub>2</sub>O** and described in the main article. Both  $S_1$  minimum-energy structures are consistent in terms of their structures and adiabatic excitation energies. Thus, it seems that the CT state could be attainable in the aqueous photochemistry of **Guo** and **dGuo**.

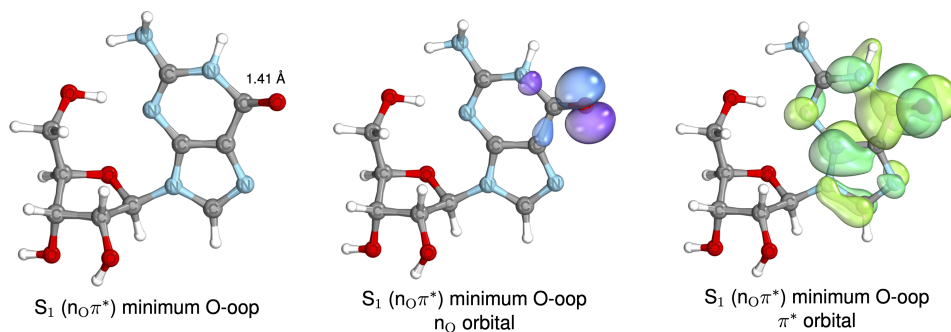


**Fig. S5** The  $S_1(n_O\pi^*)$  minimum-energy structure of guanosine with four explicit water molecules is marked by the  $O\cdots O$  chalcogen bonding interaction, assuming the excited-state optimization at the SCS-ADC(2)/cc-pVDZ level of theory. The shown molecular orbitals demonstrate a charge-transfer character of  $0.15 e^-$  from  $H_2O$  to the chromophore.

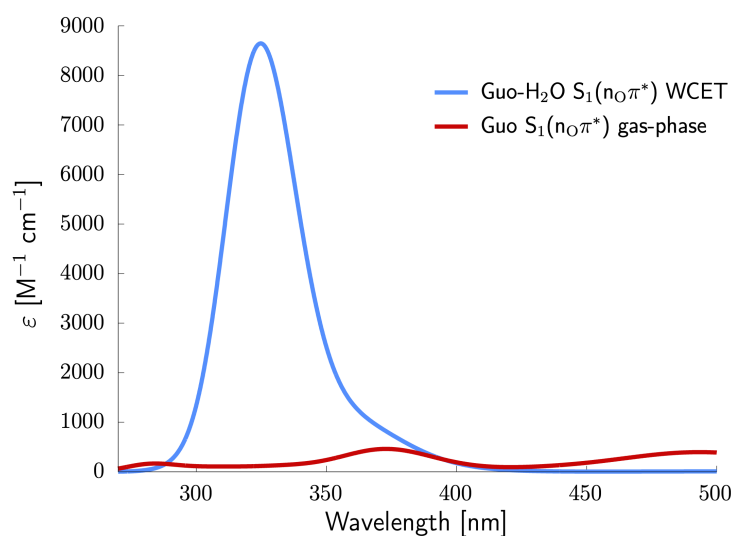
### $S_1(n_O\pi^*)$ structures of Guo- $H_2O$

In the main article, we discuss the  $S_1$  minimum-energy geometry of **Guo- $H_2O$**  having a charge-transfer character. This structure also possesses a chalcogen bonding interaction between the water molecule and the carbonyl oxygen atom. However, in such calculations, we added only a single quantum-mechanical water molecule that cannot reproduce the effect of the closest environment on the photoreactive carbonyl site of guanine nucleoside. Therefore, we added three additional explicit water molecules to our model system next to the carbonyl group and reoptimized the  $S_1$  minimum (see Fig. S5) using the SCS-ADC(2)/cc-pVDZ level of theory. Fig. S5 presents the  $S_1(n_O\pi^*)$  minimum-energy structure containing four explicit water molecules. Importantly, there is an  $O\cdots O$  chalcogen bonding contact of  $2.31 \text{ \AA}$  between the water molecule and the carbonyl oxygen atom, and the carbonyl bond is elongated to  $1.40 \text{ \AA}$ . Furthermore, the  $S_1$  minimum-energy geometry is characterized by out-of-plane displacement of the carbonyl group, which also originates from the excited-state interaction with the water molecule. In addition, the depicted molecular orbitals (see Fig. S5) participating in the  $S_1$  minimum are associated with an intermolecular charge-transfer character of  $0.15 e^-$  from the water molecule to the guanine moiety. The  $S_1$  structure of the extended water complex system resembles the  $S_1$  minimum found for the model system containing a single water molecule (Fig. 1 in the main article). Therefore, the results suggest that the intermolecular chalcogen bonding contact can be formed in an aqueous environment.

The  $S_1$  minimum-energy structure of the **Guo- $H_2O$**  complex containing one water molecule was used to simulate an excited-state absorption (ESA) spectrum, which in turn was compared to the recorded time-resolved spectra in the main article. The simulated ESA spectrum is characterised by an absorption band between 290-350 nm, which very well corresponds to the band recorded experimentally by Karunakaran *et al.*<sup>4</sup>. In contrast, the ESA spectrum of guanosine without any explicit water molecules simulated from the corresponding  $S_1(n_O\pi^*)$  minimum, does not exhibit and clear absorption features between 290 and 500 nm (see Fig. S6 and Fig. S7). Fig. S6 presents the  $S_1$  structure obtained using the SCS-ADC(2)/cc-pVTZ level of theory, and this geometry is also characterized by an evident out-of-plane displacement of the carbonyl oxygen atom. The carbonyl bond is also elongated to  $1.41 \text{ \AA}$ , which was also observed for the  $S_1$  minimum-energy structures discussed above. The presented molecular orbitals (see Fig. S6) associated with the  $S_1$  state show the  $^1n_O\pi^*$  character. In summary, our ESA spectra calculated for the  $S_1$  minima of microsolvated and isolated guanosine reinforce the hypothesis that the charge transfer character of the  $S_1$  minimum in aqueous guanosine has a spectral fingerprint in the range of 290-350 nm as according to the



**Fig. S6** The  $S_1$  minimum-energy structure of the gas-phase guanosine having an oxygen out-of-plane (O-oop) displacement. The depicted molecular orbitals show the  $^1n_O\pi^*$  character of the  $S_1$  geometry. The relevant distance between atoms is indicated.

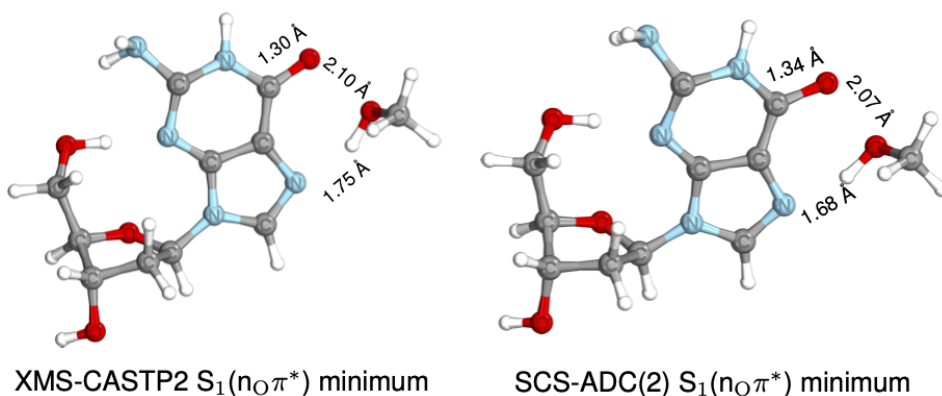


**Fig. S7** The excited-state absorption (ESA) spectra were simulated using the SCS-ADC(2)/cc-pVTZ method, assuming the  $S_1(n_O\pi^*)$  minimum-energy structures for **Guo-H<sub>2</sub>O** (solid blue line) and **Guo** (solid red line) systems obtained at the SCS-ADC(2)/cc-pVTZ level.

recorded experimental time-resolved spectrum.<sup>4,5</sup>

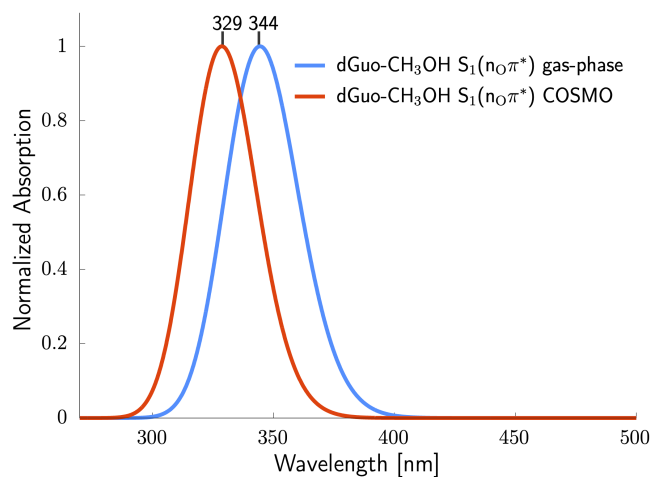
#### Methanol-to-chromophore electron transfer in deoxyguanosine

We located the  $S_1(n_O\pi^*)$  minimum-energy structure of **dGuo-CH<sub>3</sub>OH** (guanosine interacting with an MeOH molecule) using the XMS-CASPT2/SA-3-CASSCF(10,9)/cc-pVDZ level of theory (Fig. S8). This  $S_1$  minimum is characterized by the O...O chalcogen bonding interaction enabling a charge-transfer process of  $0.36 e^-$  from CH<sub>3</sub>OH to **dGuo**, obtained by means of the SCS-ADC(2)/cc-pVTZ method. Therefore, the observed extent of charge transfer is substantially higher than in the case of an explicit water molecule interacting analogously with the C=O group of guanosine. Furthermore, the  $S_1$  minimum of **dGuo-CH<sub>3</sub>OH** is characterized by the intermolecular O...O distance of 2.10 Å and the C6-O bond length equal to 1.30 Å in addition to a pyrimidalization of the C2 atom of the purine ring (Fig. S8). The XMS-CASPT2  $S_1(n_O\pi^*)$  structure of **dGuo-CH<sub>3</sub>OH** strongly resembles the corresponding SCS-ADC(2)  $S_1$  geometry (see Fig. 3 in the main article), and thus both XMS-CASPT2 and SCS-ADC(2)  $S_1$  minimum-energy structures are very consistent (see Fig. S8). The SCS-ADC(2)  $S_1$  minimum of **dGuo-CH<sub>3</sub>OH** was further

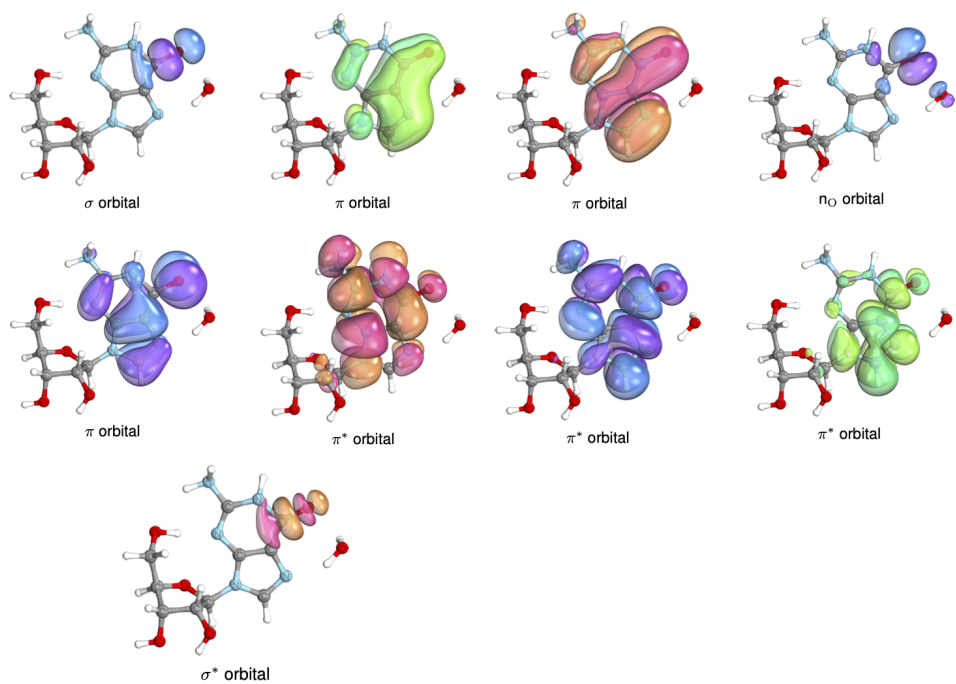


**Fig. S8** The  $S_1(n_O\pi^*)$  minimum-energy geometries were obtained at the SA-3-CASSCF(10,9)/XMS-CASPT/cc-pVDZ and SCS-ADC(2)/cc-pVTZ level of theory. Relevant distances are marked on these structures.

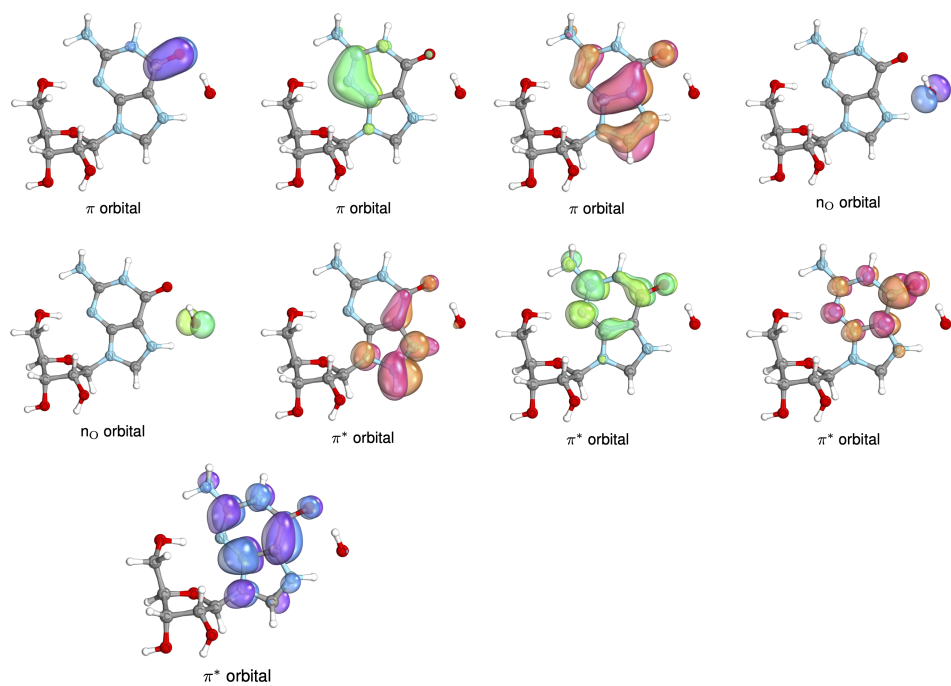
used to simulate the excited-state absorption (ESA) spectrum (Fig. S9) at the COSMO/SCS-ADC(2)/cc-pVTZ level of theory. To prepare the ESA spectrum, we took only the most intense electronic excitation and estimated a solvent-induced blueshift (15 nm) for the absorption band using the COSMO implicit solvent model. The ESA spectrum in the range of 290-350 nm (red line, Fig. S9) strongly resembles the simulated ESA spectrum for the  $S_1$  minimum of **dGuo-H<sub>2</sub>O** presented in the main article (Fig. 2). Moreover, both simulated ESA spectra are in good agreement with the corresponding experimental time-resolved spectra acquired for UV-excited deoxyguanosine in methanol.<sup>5</sup> Therefore, we suggest that this spectral feature can be considered a fingerprint for forming the excited-state chalcogen complex between guanosine and the methanol molecule.



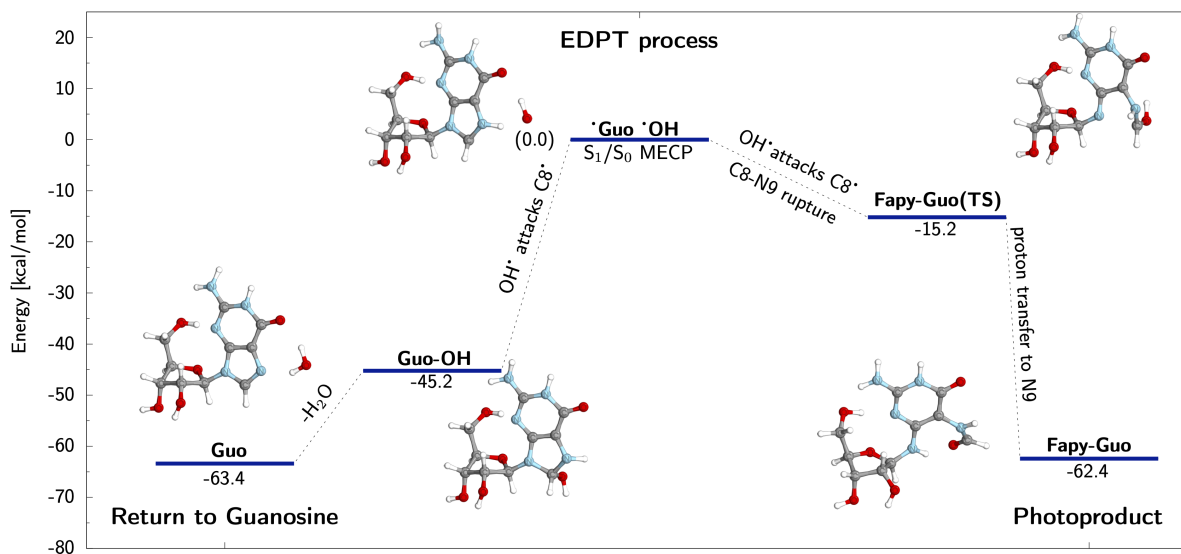
**Fig. S9** The simulated excited-state absorption spectra obtained using the most intense electronic excitation through the SCS-ADC(2)/cc-pVTZ method, assuming the SCS-ADC(2)  $S_1(n_O\pi^*)$  minimum-energy structure. While the blue line presents the most intense band of absorption for **dGuo-CH<sub>3</sub>OH**, the red line shows the same electronic excitation obtained using the COSMO implicit solvent model, assuming methanol solution, that enables estimating a solvent-induced shift of the absorption band.



**Fig. S10** The molecular orbitals were selected to build an active space in the SA-4-CASSCF(10,9)/XMS-CASPT2/cc-pVDZ optimization of the  $S_1(n_O\pi^*)$  minimum-energy structure for **Guo-H<sub>2</sub>O**.



**Fig. S11** The molecular orbitals were selected to build an active space in the SA-3-CASSCF(10,9)/XMS-CASPT2/cc-pVDZ optimization of the  $S_1(n_O\pi^*)/S_0$  minimum-energy conical intersection for **Guo-H<sub>2</sub>O**.



**Fig. S12** Starting from the EDPT  $S_1/S_0$  surface crossing, there are two ground-state routes, the first towards **Fapy-Guo** through the transition state geometry (**Fapy-Guo(TS)**), the second leading to the canonical structure of **Guo** that could be reachable through **Guo-OH** intermediate. All calculations were conducted using  $\omega$ B97X-D/PCM/def2-TZVPP method.

### Photoproducts of guanine nucleosides

The electron-driven proton transfer (EDPT) photorelaxation channel in **Guo-H<sub>2</sub>O** (Fig. 4 in the main article) enables radiationless deactivation to the electronic ground state through the EDPT  $S_1/S_0$  surface crossing. Consequently, the EDPT process can lead to the formation of the biradical structure containing **Guo•** as well as **OH•** radical. Hydroxyl radical is a highly mobile chemical species that could readily attack that the **Guo•** in the C8 position at which the excess electron is located. To provide mechanistic insights into hot ground-state reactions, we performed ground-state calculations based on Kohn-Sham density functional theory, assuming the EDPT  $S_1/S_0$  surface crossing (Fig. S12) as the starting point.

Fig. S12 demonstrates two plausible ground-state chemical pathways that can result in the formation of the possible photoproduct **Fapy-Guo** or reproduce the canonical structure of **Guo**. The radical recombination of **OH•** to the C8 atom of **Guo•** can entail the C8-N9 bond rupture that is shown as the optimized transition-state (TS) structure located 15.2 kcal/mol below the EDPT  $S_1/S_0$  MECP. Subsequently, the proton transfer from the hydroxyl group to the N9 atom of **Guo** leads to **Fapy-Guo** structure that is located 62.4 kcal/mol below the  $S_1/S_0$  MECP. It is worth to add that relative energies of **Guo-H<sub>2</sub>O** and **Fapy-Guo** are virtually the same (Fig. S12). It strongly suggests that **Fapy-Guo** should be a stable photoproduct. In addition, the ground-state chemical route shows that the UV-induced EDPT process plays a crucial role in a barrierless formation of the photoproduct. The radical recombination of the hydroxyl radical to the C8 atom of **Guo** could also result in the formation of a long-lived **Guo-OH** molecule that is located 45.2 kcal/mol below the EDPT  $S_1/S_0$  surface crossing. Such an intermediate could allow for the reproduction of **Guo** through releasing the water molecule. Furthermore, the **Guo-OH** intermediate could be a structural precursor of 8-oxo-**Guo** that is formed in trace amounts in the aqueous photochemistry of guanine nucleosides.<sup>6-8</sup> The vertical excitation energies of **Guo-OH** (Tab. 1 in the main article) show that there are energetically low-lying repulsive  $S_2$  and  $S_3$  excited states, both having a  $\pi\sigma^*$  character, which could enable



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the photodetachment of electron from the chromophore. This could lead to a reactive radical structure of **Guo-OH**, which may spontaneously undergo subsequent ground-state chemical reactions leading to the formation of 8-oxo-**Guo**. The UV-induced process would enable the formation of the radical cation that was previously proposed<sup>8</sup> as a key intermediate structure for 8-oxo-**dGuo**. The proposed chemical route to 8-oxo-**dGuo** formed in bulk water requires at least two photons, and it may explain the meager yields of this photoproduct.

## References

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