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ARTICLE

A sodium ion-selective photosensitizer: Dibrominated F-BODIPY as a fluorescence imaging and therapeutic agent

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Herein, we report that the production of singlet oxygen ($^1O_2$) is exclusively regulated by sodium ions in aqueous solution by the use of a Na^+-selective photosensitizer (PS), a 2,6-dibrominated F-BODIPY dye equipped with benzo-15-crown-5. The PS showed an enhanced fluorescence quantum yield (Φ_f) and an enhanced singlet oxygen quantum yield (Φ_Δ) in the presence of Na^+. A detailed theoretical study uncovered the underlying photophysical pathways which are responsible for both functional characteristics of the PS, therapeutic and Na^+ imaging properties.

1 Introduction

Photodynamic therapy (PDT) is a non-invasive and very powerful method to kill cancer cells by singlet oxygen ($^1O_2$) generated through light and a photosensitizer (PS).[1,2] Several PSs, mainly porphyrin derivatives are approved for the PDT treatment for different types of cancer such as skin, lung, bladder, and breast cancer.[3] In malign breast cancer cells the pH value can be more acidic and the Na^+ level is up to five times higher than in benign cells (raising from around 20 mM to over 100 mM Na^+).[4] A very powerful and non-invasive but costly technique to visualise Na^+ in the human body is based on magnetic resonance imaging (MRI) of ^{23}Na.[5] A more cost-effective method to image Na^+ in vivo is the use of fluorescence spectroscopy.[6,7] For a precise identification and targeted light irradiation of tumor tissue, a fluorescence imaging-guided PDT is very helpful.[8,9] A further class of promising triplet PSs for PDT are based on boron-dipyrromethene (BODIPY) dyes,[10-12] when for instance substituted in 2,6-position with heavy atoms such as iodine[13,14,15] or bromine[16]. Two decades ago, the group of Akkaya et al. reported on 2,6-dibromo-substituted F-BODIPYs as triplet PSs to efficiently produce $^1O_2$.[16] Further, O'Shea et al. published a while ago, that the $^1O_2$ generation rate can be regulated by protons.[17] There, a photoinduced electron transfer (PET) is blocked by protonation of an amine donor.[17] Moreover, in a pioneering work Akkaya et al. showed that a PS consisting of 2,6-diiodo- and 3,5-dipyridylethenyl-substituted F-BODIPY equipped in *meso*-position with a benzo-15-crown-5 can modulate and enhance $^1O_2$ production by both H^+ and Na^+ in acetonitrile (ACN).[18] Meanwhile, some factors that control the $^1O_2$ efficiency have been uncovered such as pH, light, hydrogen peroxide, nucleic acids, proteins etc.[18-21]

In a recent study, we reported on a benzo-15-crown-5-equipped F-BODIPY dye **1a** (cf. Scheme 1) for a reliable fluorescence detection of Na^+ in the pH range from 3 to 10 by fluorescence enhancement caused by an off-switching of a PET by Na^+ in aqueous solution.[22] Herein, we now report on a detailed experimental and theoretical study of the regulation of $^1O_2$ exclusively by Na^+ and the fluorescence sensing of Na^+ by a PS in ACN and aqueous solution. Our overriding goal is to design a PS which shows an enhanced $^1O_2$ production as well as an enhanced fluorescence response only in malign, but not in benign tissue. As a trigger we selected the enhanced Na^+ level in breast cancer cells. By fine tuning the Na^+ complexing abilities of the Na^+-responsive PS (dissociation constant K_d) we aimed to manipulate the $^1O_2$ evolution and fluorescence response. We designed PS **1** to be both, a therapeutic and an imaging agent regulated by the enhanced Na^+ level in tumor tissue. PS **1** is a combination of the photostable triplet PS **2**,[23] a 2,6-dibromo-substituted F-BODIPY dye, and the pH-stable and Na^+-selective binding unit **3**, benzo-15-crown-5[24] (Figure 1).

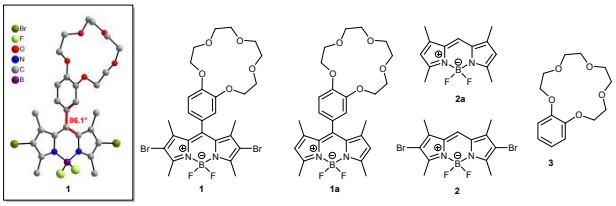

Figure 1 Studied Na^+-selective 2,6-dibrominated F-BODIPY PS **1** (left: molecular structure obtained from XRD) and reference compounds **1a**, **2**, **2a** and **3**. H atoms are omitted for clarity.

2 Results and discussion

A bromination at positions 2 and 6 of the F-BODIPY **1a**[22] ~~core~~ with *N*-bromosuccinimide (NBS) yielded the novel PS **1** in a moderate yield

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of 47%.[25] As ~~a~~ references, the F-BODIPYs ~~PS~~ **2** and **2a** without benzo-15-crown-5 moiety were synthesized as described.[26,22] Benzo-15-crown-5 (**3**) is commercially available. The novel PS **1** was characterized by ^{1}H and ^{13}C NMR spectroscopy as well as electrospray ionization mass spectrometry.[25] The molecular structure of **1** was confirmed by X-ray analysis (cf. Figure 1).[25] Single crystals of **1** were obtained by slow solvent evaporation (ethyl acetate/hexane, v/v, 1/1).

At first, we recorded UV/Vis absorption spectra of **1** and **2** in ACN (cf. Figure S2a). The absorption spectra of **1** and **2** are very similar, in the range from 350 nm to 550 nm, to each other. They show the most intense absorption band (S_0 to S_1 transition) with a local maximum (λ_{max}) at about 525 nm (vibronic 0–0 state) with a shoulder at about 490 nm (vibronic 0–1 state).[27] The molar extinction coefficients (ε_λ) at λ_{max} for **1** (77000 $M^{-1}cm^{-1}$) and **2** (75000 $M^{-1}cm^{-1}$) in ACN are comparable to each other, suggesting that the phenylic substituent in *meso*-position of the F-BODIPY in **1** does not significantly extend the π-electron system of the F-BODIPY chromophore. As found in the molecular structure of **1** the phenyl ring is almost orthogonal to the planar F-BODIPY core (dihedral angle 86.1°, cf. Figure 1) which electronically decouples the F-BODIPY from the benzo-15-crown-5. Then, we recorded UV/Vis absorption spectra of **1** and **2** (c_{dye} = 10^{-5} M and 10^{-6} M, respectively) in different ACN/water mixtures and found a good solubility of **1** and **2** up to a ACN/water mixture of 1/9 (v/v) (cf. Figures S2c, S2d, S2e and S2f), but **2** showed a blue shift of λ_{max} when the water amount was increased (cf. Figures 2d and 2f).[25] Thus, **2** is only an appropriate spectroscopic reference compound for **1** in ACN. Moreover, to ensure complete solubility of **1**, we decided for further investigation to use as an aqueous solution an ACN/water mixture of 1/3 (v/v). Further, the fluorescence emission maxima of **1** and **2** (c = 10^{-6} M) were also very similar to each other in ACN (539 nm (**1**) and 540 (**2**)) (cf. Figure S6a), but their fluorescence quantum yields (Φ_f) differ from each other (Φ_f = 0.010 (**1**), Φ_f = 0.207 (**2**)).[25] The low Φ_f value of **2** is caused by a heavy atom quenching effect which is typical for a triplet PS.[28] Probably, in **1** an additional quenching process, such as in **1a** (Φ_f = 0.258[22] in ACN(**1a**)), a reductive PET from the benzo-15-crown-5 (electron donor) to the excited and decoupled 2,6-dibrominated F-BODIPY core (electron acceptor) occurs.[29-31] Solvent effects on the Φ_f values for **1** are found because the reductive PET in **1** is more favorable in polar solvents (cf. Table S3).[25] The low Φ_f values of **1**, **1a** and **2** in polar solvents make them suitable candidates as PS to produce efficiently $^{1}O_2$ in ACN and aqueous solution. Then we monitored the $^{1}O_2$ production by recording the absorbance of 1,3-diphenylisobenzofuran (DPBF) as a singlet oxygen scavenger at 410 nm in ACN, aqueous solution (ACN/water, v/v, 1/3) and 1,4-dioxane/dimethyl sulfoxide (v/v, 99/1).[25] The following singlet oxygen quantum yields (Φ_Δ) were calculated: 0.199 ± 0.010 for **1** , 0.239 ± 0.010 for **1a** and 0.495 ± 0.092 for **2** in ACN, 0.527 ± 0.012 for **1**, 0.048 ± 0.002 for **1a** and 0.521 ± 0.014 for **2** in 1,4-dioxane/dimethyl sulfoxide (v/v, 99/1) as well as for **1** 0.126 ± 0.003 in aqueous solution (ACN/water, v/v, 1/3). The triplet PS **2** generates more $^{1}O_2$ than **1** and **1a** in ACN and exhibits very similar Φ_Δ values in both polar and non-polar solvents. The intersystem crossing (ISC) process in **2**, caused by the heavy atom effect of the two bromine atoms, results in a well populated triplet state (T_1), which is less dependent on the solvent polarity.[25,32] ~~and works more efficiently in polar solvents than in **1**.~~ The PS **1** exhibits a similar Φ_Δ value in non-polar environments to that of **2**, and shows a higher Φ_Δ value compared to its behaviour in more polar solvents. In contrast, **1a** displays the opposite trend: it has a higher Φ_Δ value in polar solvents and a lower Φ_Δ value in non-polar environments. In **1**, two deactivation pathways from the S_1 state to the T_1 state are conceivable. Firstly, ISC, which is typical for heavy atom containing triplet PS,[13,16,28] and secondly, a spin-orbit charge-transfer (SOCT)-ISC process, which ~~is~~ predominates in heavy atom-free triplet PS,[33,34,35,36] such as PET-based PS, where a charge-separated ^{1}CT state is formed and stabilized in polar solvents.[34] In general, the SOCT-ISC proceeds much faster than the ordinary ISC between π to π* states.[37] For the heavy atom-free triplet PS **1a**, we observed a higher Φ_Δ value in polar solvents compared to the reference F-BODIPY **2a** (Φ_Δ = 0.09 in ACN)[38]. This enhancement is likely due to a (SOCT)-ISC process facilitated by the polar environment. Moreover we observed similar Φ_Δ values for **1** and **1a** in ACN, indicating that in both PS, the SOCT-ISC is likely the predominant pathway from the ^{1}CT state to the T_1 state, in **1** the SOCT-ISC process likely predominates in polar solvents whereas conventional ISC is more dominant in non-polar environments.[25]

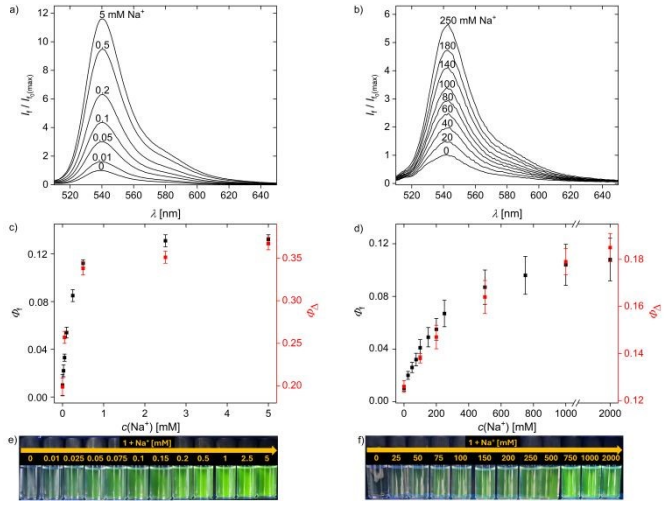

Figure 2 Fluorescence intensity (I_f) of **1** (c = 10^{-6} M, λ_{ex} = 500 nm) in the presence of different Na^+ concentrations a) in ACN and b) in ACN/water, (v/v, 1/3). Fluorescence quantum yields (Φ_f) (black) and singlet oxygen quantum yields (Φ_Δ) (red) of **1** in the presence of different Na^+ concentrations c) in ACN and d) in ACN/water (v/v, 1/3). Photographs under UV light (366 nm) of **1** (c = 10^{-6} M) in the presence of different Na^+ concentrations e) in ACN and f) in ACN/water (v/v, 1/3).

Further, we recorded UV/Vis absorption spectra of **1** (c = 10^{-5} M) in the presence of Na^+ in ACN and in an ACN/water mixture of 1/3 (v/v) (cf. Figures S3a and S3b). The absorption at 540 nm (λ_{max}) is nearly unaffected by Na^+. The complexation of Na^+ within the benzo-15-crown-5 in **1** can be observed by an enhanced blue-shift of the π→π* transition from around 280 nm to 270 nm, (cf. Figures S3a and S3b) which is typical for cation complexation of benzo-crown ethers.[39] Then, we measured the influence of Na^+ on the fluorescence intensity (I_f), Φ_f and Φ_Δ of **1** in ACN and aqueous solution (ACN/water, v/v, 1/3). The I_f of **1** is enhanced with increasing Na^+ concentrations in ACN and aqueous solution (ACN/water, v/v, 1/3) (cf. Figures 2a and 2b). The relative course of both titration curves (λ_{em} = 540 nm, cf. Figures S7b and S7d) is similar but the maximum FE is reached at different Na^+ concentrations, in ACN at 5 mM and in

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aqueous solution (ACN/water, v/v, 1/3) at 2 M, respectively. The fluorescence enhancement factor (*FEF*) induced by Na^+ in ACN is 11.6 ± 0.1 at 5 mM Na^+ and in ACN/water (v/v, 1/3) is 9.1 ± 0.5 at 2 M Na^+, respectively. We also observed an enhancement of the Φ_f values of **1** in the presence of different Na^+ concentrations in ACN and aqueous solutions (ACN/water, v/v, 1/3) (cf. Figure 2c and 2d, Tables S4 and S5). Here, we observed the highest Φ_f value for **1** at 5 mM Na^+ in ACN (Φ_f = 0.132 ± 0.004) and in aqueous solution (ACN/water, v/v, 1/3) at 2000 mM Na^+ (Φ_f = 0.108 ± 0.016). Probably, the FE is caused by blocking the PET process in **1** by Na^+, as also found for **1a** + Na^+.[22] Na^+ raises the oxidation potential of the PET electron donor benzo-15-crown-5 in ACN and aqueous solution.[40] Therefore, the reductive PET process in **1** + Na^+ becomes more unlikely as expressed by the Rehm-Weller equation.[30] Moreover, we also determined an enhanced Φ_Δ value for **1** in the presence of different Na^+ concentrations in both ACN and aqueous solution (ACN/water, v/v, 1/3), (cf. Figure 2c and 2d, Tables S1 and S2). We also observed the highest Φ_Δ value for **1** at 5 mM Na^+ in ACN (Φ_Δ = 0.367 ± 0.007) and in aqueous solution (ACN/water, v/v, 1/3) at 2000 mM Na^+ (Φ_Δ = 0.185 ± 0.006). Moreover, we determined for **1a** + 5 mM Na^+ a Φ_Δ value of 0.137 ± 0.006 in ACN which is close to the Φ_Δ value of 0.09 of **2a** in ACN[38]. Overall, we observed for **1** an enhancement of I_f, Φ_f and Φ_Δ by Na^+ and for **1a** an enhancement of I_f and Φ_f but a reduction of Φ_Δ by Na^+ in polar solvents.

Further, we calculated the limit of detection (LOD) from the fluorescence titration data of **1** + Na^+ (LOD = 3σ/m) in ACN and aqueous solution (ACN/water, v/v, 1/3).[25] The PS **1** shows a lower sensitivity towards Na^+ in ACN with a LOD of (9.45 ± 0.6) µM as in aqueous solution (ACN/water, v/v, 1/3) (11.5 ± 1.1) mM, respectively (cf. Figures S9a and S9b). We also found a good linear relationship between the fluorescence intensity of **1** + Na^+ in ACN and aqueous solution (ACN/water, v/v, 1/3) (from 0 mM to 0.14 mM Na^+, R^2 = 0.9966 (ACN), from 0 mM to 100 mM Na^+, R^2 = 0.9992 (ACN/water, v/v, 1/3), cf. Figures S9a and S9b) at 540 nm, respectively. More importantly, we calculated from the fluorescence intensity changes of **1** + Na^+ their dissociation constants (K_d) in ACN and in aqueous solution (ACN/water, v/v, 1/3) resulting in K_d values of (0.16 ± 0.02) mM and (209 ± 5) mM, respectively.[25] The latter K_d value of **1** + Na^+ in aqueous solution is biologically relevant, since it is close to the Na^+ level in malign breast cancer cells.[4] The K_d value of **1** + Na^+ is significantly lower in ACN than in aqueous solution caused by the fact that a solvent like ACN that does not coordinate strongly with Na^+ and a complexation of Na^+ within the benzo-15-crown-5 is less hampered. In addition to it, the slopes of the plots for **1** + Na^+ ($\log(c_{Na^+})$ *vs* $\log[(I_f-I_{fmin})/(I_{fmax}-I_f)]$) in ACN and aqueous solution (ACN/water, v/v, 1/3) were nearly 1 (cf. Figures S8a and S8b)[25], suggesting a 1:1 binding ratio between Na^+ and **1**.

Moreover, to elucidate the binding stoichiometry between **1** with $NaClO_4$ in solution, we carried out ^1H NMR experiments in CD_3CN (cf. Figure S12).[25] Thus, a 1:1 binding stoichiometry of **1** with $NaClO_4$ was confirmed by a Job's plot analysis (cf. Figures S13).[25] We observed a downfield shift of the benzo-15-crown-5 protons until one equivalent $NaClO_4$ in the ^1H NMR spectra of **1** (cf. Figure S12) assuming that Na^+ is coordinated within the benzo-15-crown-5 in **1**.

EPR experiments were carried out with 2,2,6,6-tetramethylpiperidine (TEMP) as a $^1O_2$ specific spin-trap agent.[25] It was added to **1** and **1** + 5 mM $NaClO_4$, and a strong EPR signal of 2,2,6,6-tetramethylpiperidinyloxyl (TEMPO) was observed after light irradiation in ACN (cf. Figure S30). We found for **1** + 5 mM $NaClO_4$ a two times higher intensity of the TEMPO signal at 336.58 mT than for **1** indicating that in the presence of Na^+ more $^1O_2$ is produced.

We further investigated the influence of varying aqueous pH values on the fluorescence performance of **1**.[25] **1** shows very stable invariant fluorescence emission signals in the pH value range from 3.04 to 10.04 (cf. Figure S11a). Moreover, we observed for **1** in ACN and aqueous solution (ACN/water, v/v, 1/3) over a time period of 360 min a relatively photostable fluorescence signal at 540 nm (cf. Figure S11b) meaning that the photobleaching of **1** is negligible.

To verify selectivity of **1** for Na^+ towards other important biological cations such as Li^+, K^+, NH_4^+, Mg^{2+}, Ca^{2+}, Mn^{2+}, Fe^{3+}, Cu^{2+} and Zn^{2+}, we measured the fluorescence intensities in the presence of these cations at their respective concentrations that are biologically relevant in aqueous solution (ACN/water, v/v, 1/3).[25] The fluorescence performance of **1** is only slightly impacted (cf. Figure S10), showing that **1** is a Na^+-selective fluorescent imaging tool.

Moreover, we tested the DNA cleavage activity of **1** (c = 200 µM) with plasmid DNA at pH 7.4 with or without green light irradiation in the absence or presence of NaCl (cf. Figure 3) or $NaClO_4$ (cf. Figure S28). Degradation of supercoiled DNA (form I) to open-circular/nicked (form II) and linear DNA (form III) was monitored via gel electrophoresis.[25] Under green light irradiation, we observed DNA cleavage by **1** (lane j) forming 69% DNA form II (single-strand breaks) and even 1% form III (double-strand breaks). When the sample was not irradiated, no cleavage activity of **1** was observed (lane d about 40% form II). Surprisingly, the cleavage activity is not enhanced by NaCl (lanes k and l, Figure 3) or $NaClO_4$ (Figure S28). Probably, the stabilisation of the negatively charged DNA double helix (phosphate backbone) by Na^+ due to electrostatic interactions[41] results in a lower DNA cleavage activity of **1**.

Further, we crystallized **1** with $NaClO_4$ in a molar ratio of 1 : 1 from a chloroform/acetonitrile (v/v, 3/1) mixture to get more insights on the binding characteristics of Na^+ within **1**. X-ray analysis provided the molecular structure of the Na^+ complex [Na(**1**)(ClO_4)] (cf. Figure 4). Na^+ is mainly coordinated by the five oxygen atoms of the benzo-15-crown-5 in **1** and shows a good fit-in-size into the cavity (cf. Figure 4a). Notably, the two symmetry-equivalent bridging perchlorate anions are disordered which influences the total number of coordination bonds of the Na^+ (cf. Figures S23 and S24). We also found an electronical decoupling of the F-BODIPY from the Na^+ complexed benzo-15-crown-5 unit because in the molecular structure of [Na(**1**)(ClO_4)] the phenyl ring is almost orthogonal to the planar F-BODIPY core (dihedral angle 82.2°, cf. Figure 4b).

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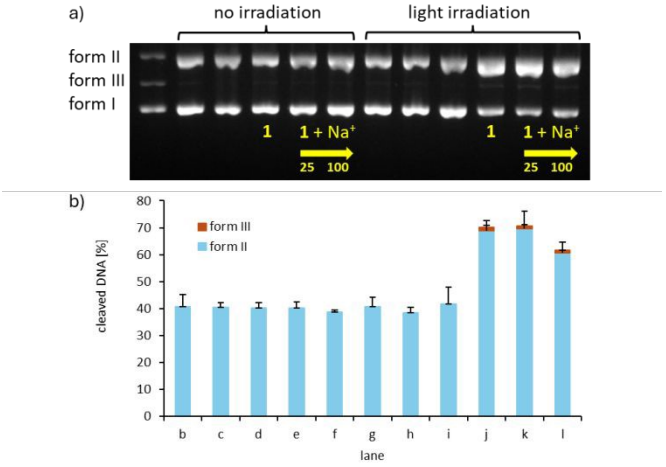

Figure 3 a) Nuclease activity towards plasmid DNA pBR322 (0.025 µg/µL) of PS **1** (*c* = 200 µM) in Tris buffer (5 mM, pH 7.4) w/wo NaCl (25 or 100 mM). Samples in lanes g-l were incubated for 50 min under irradiation by green light for 50 min whereas samples in lanes a-f were not irradiated. Lane a: DNA ladder (form I, II and III), lane b + g: DNA reference, lanes c + i: 100 mM NaCl, lanes d + j: **1**, lanes e + k: **1** + 25 mM NaCl, lanes f + l: **1** + 100 mM NaCl, lane h: 25 mM NaCl. b) Visualization of the extent of DNA cleavage in percent with standard deviation as error bars.

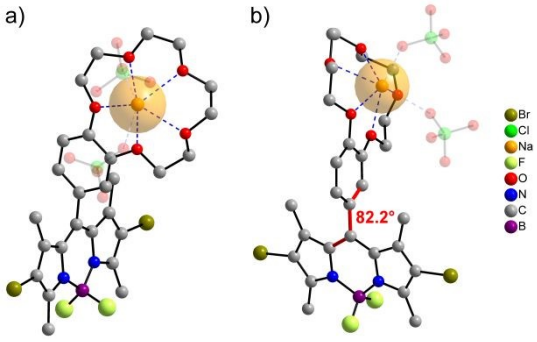

Figure 4 Molecular structure of [Na(**1**)ClO_4] with a space-filling model of Na (crystal radius[42] regarding coordination number). a) Front view and b) side view. H atoms are omitted for clarity.

Complementary to the experiments, we performed (time-dependent) density functional theory [(TD-)DFT] and singlet/triplet spin-orbit coupling (SOC) calculations of **1**, a dibromine-free F-BODIPY dye **1a** and **2** at the B3LYP/def2-TZVP level of theory[43-45] in ORCA 6.0[46].[25] The bright S_1 state of **1** in Figure 5c is given by a local transition on the BODIPY part from MO_{Dye} to the LUMO, while the optically dark ^{1}CT state shows strong charge transfer character from MO_{CT} to the LUMO. We find that the addition of Na^+ leads to an energetic stabilization of the MO_{CT}, while the two BODIPY-localized MOs remain mostly unaffected as shown in Figure 5d due to the greater spatial distance to the crown ether part of **1**. The excitation energy of the ^{1}CT state is thus increased relative to the bright S_1 state after Na^+ complexation in agreement with the reported experimental findings.[25] Furthermore, bromination leads to a one order of magnitude increase in the computed singlet/triplet SOCs of **1** compared to **1a** due to the heavy-atom effect of the bromine atoms.[25]

Overall, the fluorescence quenching observed for **1** is likely due to a reductive PET process. In polar solvents, a ^{1}CT state is formed and stabilized, and its conversion to T_1 state via a SOCT-ISC mechanism is probable. The resulting T_1 state subsequently generates a moderate amount of $^1O_2$ in polar solvents. Furthermore, we assume that Na^+ interrupts the reductive PET process in **1** in polar solvents, leading to an increase in the energy of the ^{1}CT state. As a result, population of the T_1 state via ISC, facilitated by the heavy atoms (bromine), becomes more favourable and efficient, thereby restoring both fluorescence and $^1O_2$ generation of the dibrominated F-BODIPY core (cf. Φ_f and Φ_Δ values of **2** in polar media). As a result we observed for **1** + Na^+ higher Φ_f and Φ_Δ values compared to **1** without Na^+ (cf. Figures 5a and 5b). The latter can lead to degradation of DNA under irradiation (cf. Figures 3a and 3b. Moreover, we found for the dibromine-free F-BODIPY dye **1a** in the presence of Na^+ also an enhanced Φ_f value but a reduced Φ_Δ value in polar solvents. The presence of Na^+ blocks the reductive PET process in **1a**, resulting in an elevation of the ^{1}CT energy level. This effectively restores the fluorescence of the dibromine-free F-BODIPY core, where intersystem crossing (ISC) is considered highly unlikely (cf. Figures S34a and 34b). To the best of our knowledge, this is the first report that only a cation, here Na^+, regulates $^1O_2$ evolution. The enhanced $^1O_2$ production by Na^+ can be useful to selectively kill malign cancer cells after irradiation when the K_d value of the Na^+-selective PS fits to the Na^+ levels in the cancer cells.

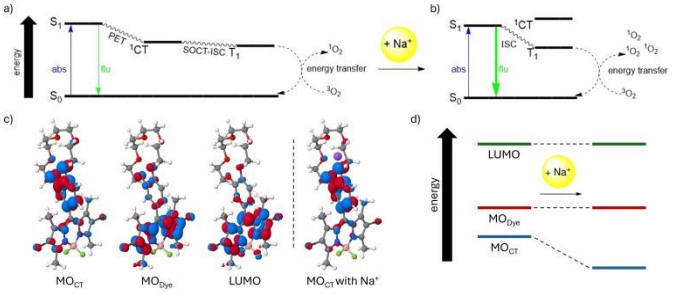

Figure 5 Jablonski diagram of the postulated mechanism of the photosensitized production of $^1O_2$ in the PS **1** in polar solvents a) without Na^+ and b) with Na^+. c) Molecular orbitals (MOs) of **1** corresponding to the S_1 and ^{1}CT excited states (see further explanations in the text). d) Relative MO energy level changes of **1** due to the addition of Na^+.

3 Conclusions

In summary, we synthesized the novel and Na^+ selective PS **1** consisting of a benzo-15-crown-5 and a dibrominated F-BODIPY dye shows a fluorescence signal which is photostable and invariant to a wide pH value range from 3.04 to 10.04. Further, **1** is a fluorescent tool with high Na^+ selectivity and Na^+ sensitivity, fast Na^+ response and the Na^+ induced fluorescence enhancement is even recognizable with the naked eye after irradiation with UV light. Moreover, we observed higher Φ_f and Φ_Δ values for **1** in the presence of Na^+ in polar solvents. The K_d value of **1** + Na^+ is (209 ± 5) mM in aqueous solution and fits better to the Na^+ level in malign cancer cells (around 100 mM Na^+) than to benign cells (around 20 mM Na^+).[4] PS **1** is a suitable therapeutic as well as a Na^+ imaging agent. **1** could be a useful PS for cancer therapy because **1** could image tumorous tissue,

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and targeted light irradiation would selectively kill cancer cells through $^1O_2$ generation. Currently, we are designing PSs applicable in PDT for a deeper tissue penetration by extending the π-system in position 2 and 5 of the F-BODIPY core to shift absorbance to the near-infrared (NIR) region.[47]

Author contributions

Thomas Schwarze: conceptualization, methodology, investigation, formal analysis, writing – original draft; Mazen Al Akrami: investigation, data curation; Julian Heinrich: formal analysis, data curation; Vinja Hergl: investigation; Alexandra Kelling: formal analysis; Eric Sperlich: formal analysis, visualisation, methodology; Tobias Sprenger: formal analysis; Nicolas Jahn: formal analysis, visualisation; Tillmann Klamroth: supervision; Nora Kulak: funding acquisition, supervision, writing – review & editing.

Conflicts of interest

The authors declare no conflict of interest.

Data availability

The data supporting this article have been included as part of the ESI.†

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- The data supporting this article have been included as part of the Supplementary Information.