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ω,ω'-Appended nucleo-base derivatives of hypericin

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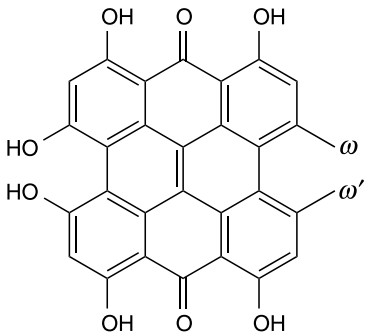
Abstract ω,ω'-Disubstituted hypericin derivatives with the nucleo-bases thymine, cytosine, and adenine in these positions were prepared starting from tri-*O*-methyl-ω-bromoemodin. The most promising derivative proved to be that with a thymine moiety. It displayed the best solubility of the three products together with a potency to produce singlet oxygen and/or reactive oxygen species comparable to the parent compound hypericin. In addition, although no specific interaction with *DNA* or poly(2′-deoxyadenylic acid) could be detected, it proved to be significantly better accumulating in the nucleus of prostatic cancer LNCaP cells than hypericin making it a promising candidate for a second-generation photodynamic hypericin agent.

Keywords Hypericin; Thymine; Oxidizing species; Prostatic cancer cells.

Introduction

Derivatization of hypericin (**1**; 1,3,4,6,8,13-hexahydroxy-10,11-dimethyl-phenanthro[1,10,9,8-*opqra*]-perylene-7,14-dione) is a major aim in the search for second-generation photodynamic agents [1]. This could be done either targeting a shift to absorption at longer wavelengths or with specific interaction functionality in mind. Here we present an investigation of the possibility to hybridize **1** with nucleo-bases to get a first access to hypericin derivatives potentially interacting with the complementary nucleo-bases of *DNA* or *RNA* by *Watson-Crick* pairing, or intercalation, or with other constituents of the cell nucleus.



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Results and discussion

Syntheses

To guarantee the extensively unperturbed photochemical properties of the hypericin residue derivatization with the nucleo-bases could be optimally undertaken at the ω,ω'-methyl groups of **1**. For this purpose, the appropriately modified emodin derivatives had to be prepared first in order to dimerize them in the next steps. This derivatization was envisaged to proceed best starting from the tri-*O*-methyl protected emodin bromomethyl derivative **2**. For the nucleo-base synthons we used the NH or NH_2 benzoyl-protected derivatives. Thus, **2** reacted with

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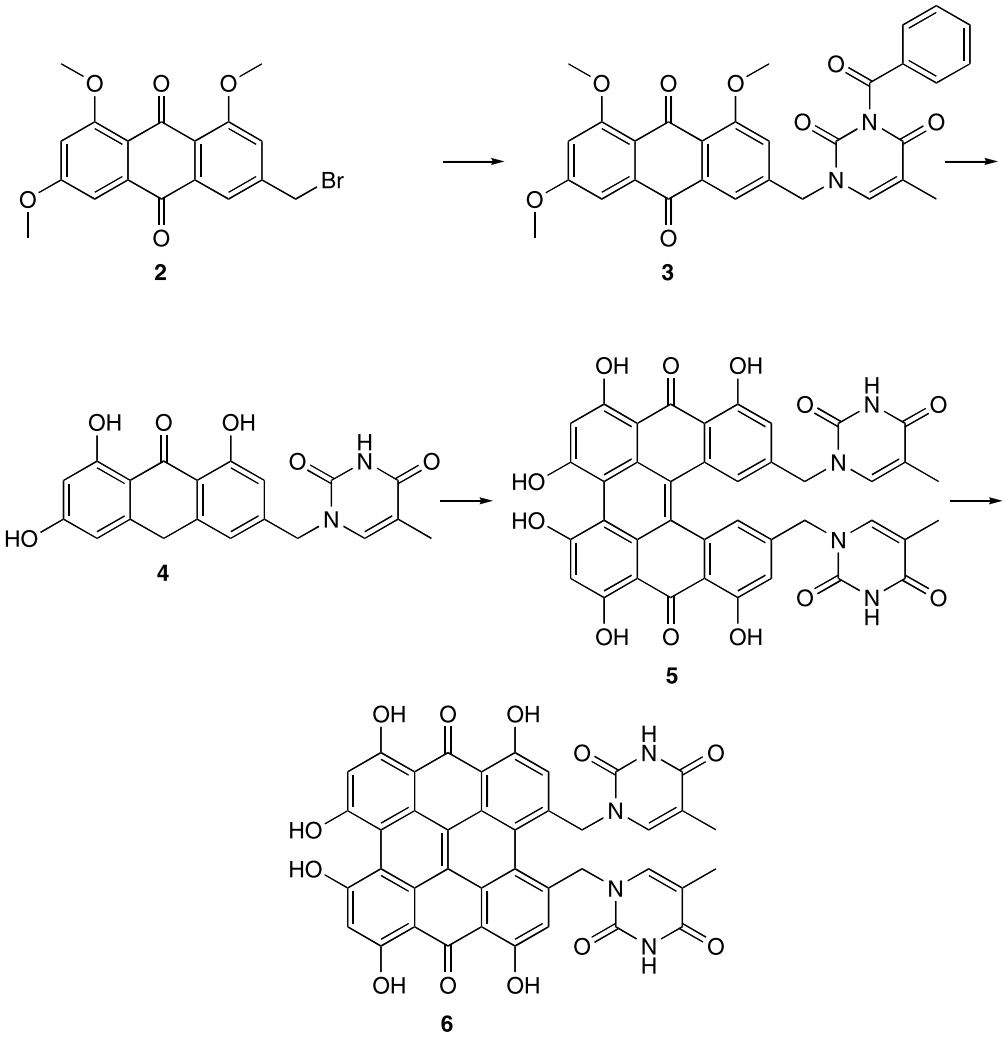
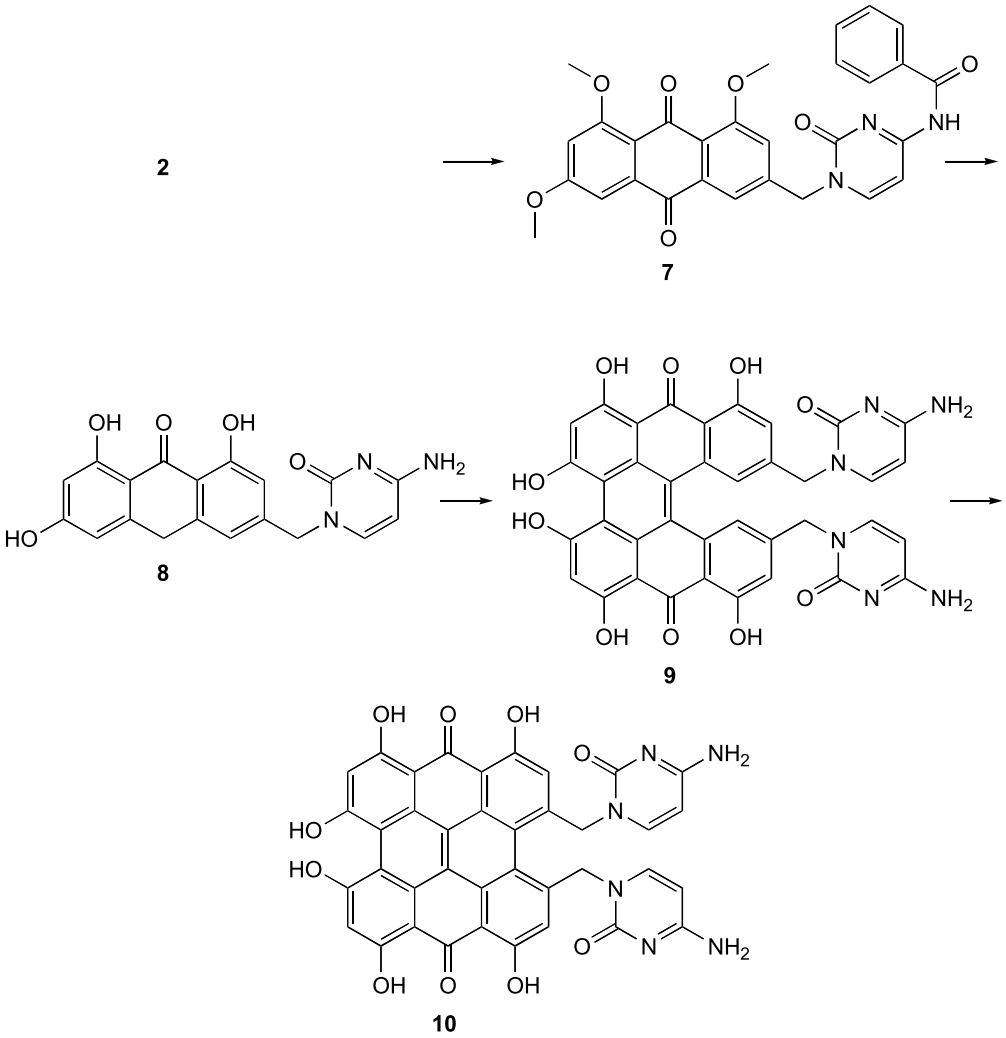


Scheme 1

3-benzoylthymine (prepared according to Ref. [2]) in presence of an excess of K_2CO_3 in *DMF* as the solvent to provide 69% of the corresponding emodin derivative **3** (Scheme 1). The latter could be deprotected and reduced in the common one-pot way [3] to the anthrone **4** with Sn(II) chloride in glacial acetic acid/HBr in 92% yield. The dimerization to the corresponding protohypericin derivative **5** with Fe(II) sulfate/pyridine-*N*-oxide in analogy to Ref. [4] was achieved with a yield of 88%. Photocyclization of this latter derivative **5** in acetone according to Ref. [4] then produced the targeted ω,ω'-thymine-disubstituted hypericin derivative **6** in 77% yield, thus providing an overall yield of **6** based on **2** of 43%.

Along the route described above for **6** the cytosine derivative **10** starting from **2** and *N*-benzoylcytosine [5] could be synthesized *via* **7**, **8**, and **9** (Scheme 2), although the reaction time in the first step had to be prolonged slightly. In the same way the adenine derivative **14** was advanced from **2** and *N*-benzoyladenine [6] *via* **11**, **12**, and **13** (Scheme 3) – both target compounds were obtained in yields comparable to the one of **6**. However, in the latter case the reaction time had to be prolonged considerably in the first step and KI had to be added as a catalyst to achieve the transformation. In addition, the photocyclizations were somewhat hampered by the low solubilities of the protohypericin derivatives and thus some added base or *DMSO*/*DMF* was necessary. Unfortunately, the guanineemodin derivative **15**, produced from **2** and *N*-benzoylguanine [7] (Scheme 4) under prolonged reaction time and addition of KI, could not be reduced to the anthrone derivative without excessive destruction.



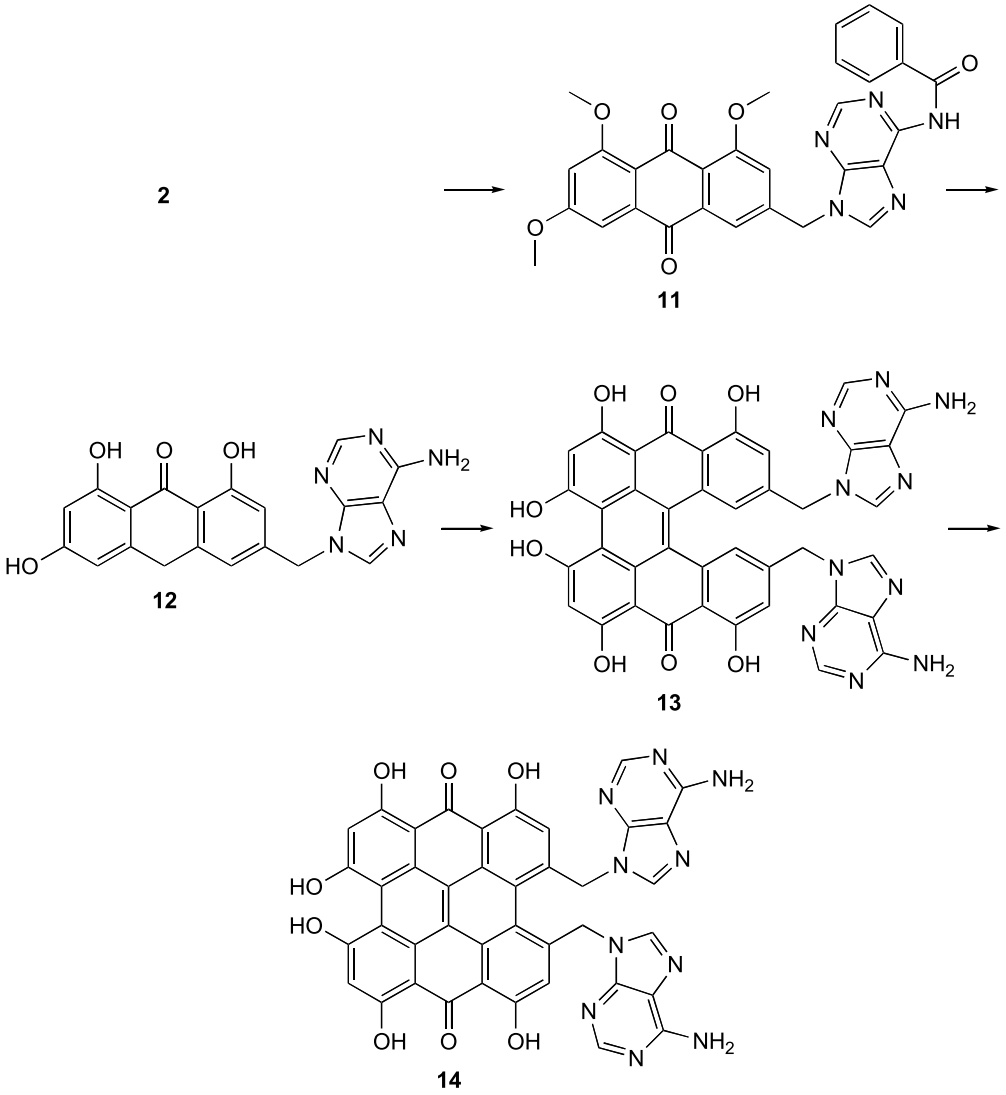
Scheme 2

Properties

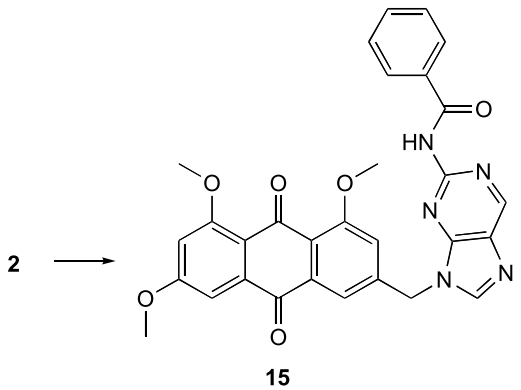
As expected for non-conjugated hybrids of hypericin (**1**) with other chromophores, the long wavelength absorption bands and fluorescence properties of the three compounds **6**, **10**, and **14** were very similar to the corresponding spectra of the parent compound **1**. However, the solubilities of these derivatives in common solvents were significantly reduced compared to **1**, with **6** as the most soluble one.

The light-induced production of singlet oxygen and oxidizing species as tested by the destruction of bilirubin-IXα according to Ref. [8] (Fig. 1) proved to be slightly lowered as compared to **1**, but is nevertheless appreciable. It might be stressed that in contrast to the thymine derivative **6** the cytosine and the adenine derivatives **10** and **14** initially provided a superior photo-destruction of bilirubin-IXα than hypericin (**1**) itself, but they are obviously (as judged from the irradiation time dependent decrease of the ''hypericin''-band absorption) slightly photodestructed themselves in the course of irradiation.

The interactions of the derivatives **6**, **10**, and **14** with calf thymus *DNA* and single strand poly(2′-deoxyadenylic acid) sodium salt (poly(d*A*)) were investigated according to Refs. [9, 10]. However, (*cf.* Exp. part) no changes in the absorption spectra of the hypericin derivatives, which would indicate a specific interaction like intercalation with *DNA* or *Watson-Crick* pairing of the thymine derivative **6** with poly(d*A*), could be observed. A possible explanation might be sought in the relatively high steric hindrance at the respective sites of the molecule as advanced by means of a MM2 force field calculation of the structure of **6** as shown in Fig. 2.



Scheme 3



Scheme 4

*Distribution of **6** in prostatic cancer cells*

The efficiency of a photosensitizer is not only dependent on its photochemical properties and its relative distribution between healthy tissue and tumor, but also on the subcellular distribution in malignant cells. The penetration of the photosensitizer into various cell compartments, especially the nucleus, plays an important role in its cytotoxic activity. Hypericin (**1**), which is usually accumulated in the cytoplasmic membrane, can penetrate these membranes and actually reach the inside of the nucleus after long term incubation, as it has been shown by *Miskovsky et al.* [11].

We decided to investigate the subcellular distribution of the thymine substituted hypericin derivative **6** compared to **1** in the prostatic carcinoma cell line LNCaP by means of fluorescence microscopy. The LNCaP cells were grown according to Ref. [12] and incubated in the dark with *DMSO* solutions of **6** or **1**. The final concentrations of **6** and **1** were set to

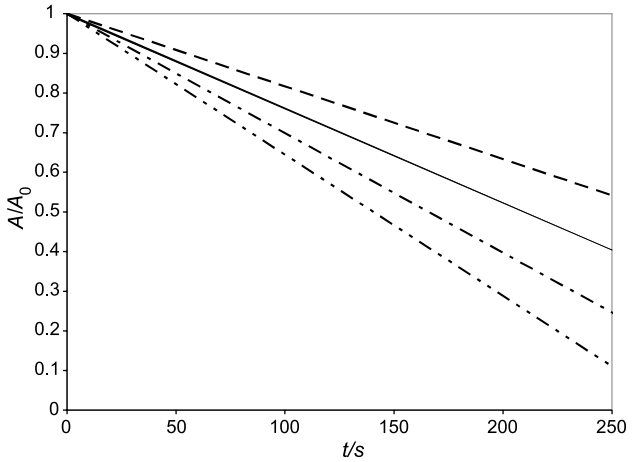


Fig. 1 Light-induced photodestruction of bilirubin-IXα sensitized by hypericin (**1**, —) and the nucleo-base substituted derivatives **6** (– –), **10** (– ·), and **14** (– · ·)

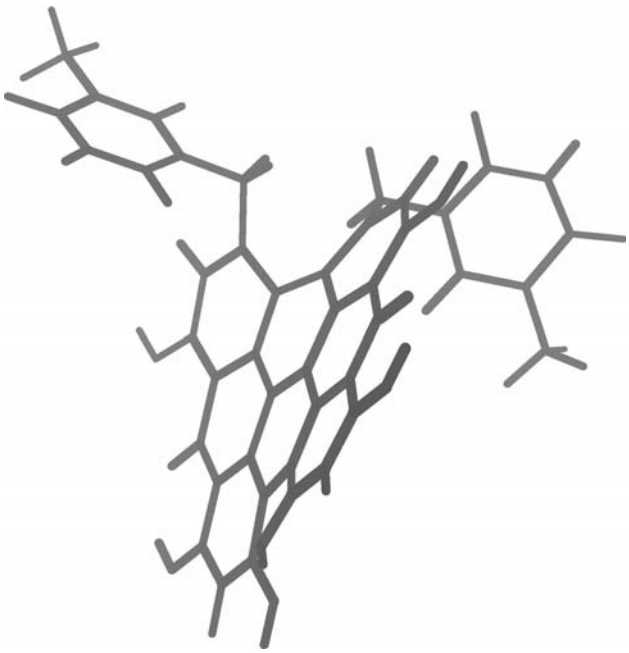


Fig. 2 Steric requirements by molecules of **6** as advanced by means of a MM2 force field calculation

1 μg/cm^3 and *DMSO* concentrations ranged from 0.1 to 1% (v/v) in the culture medium. During the incubation period light irradiation was strictly avoided to prevent a preliminary destruction of the cells or cell ingredients, and the dark toxicity of **6** and **1** is low enough for long incubation times. Measurements were taken after 4 and 24 h with a confocal fluorescence microscope – Fig. 3 provides an impression of the localization of **6** in the LNCaP cells.

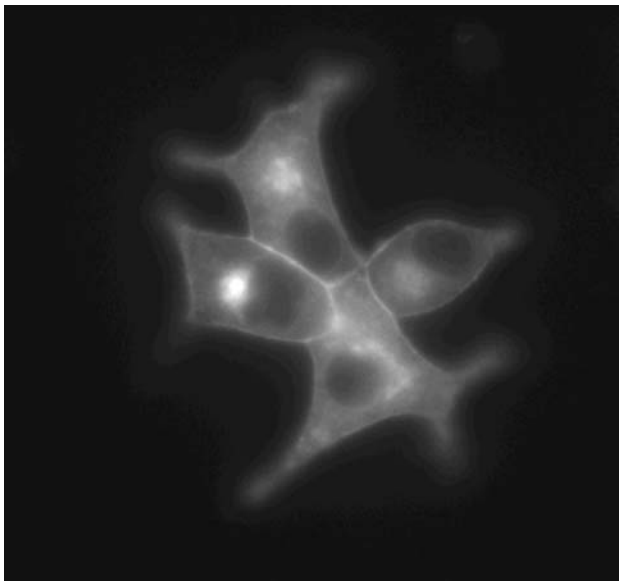


Fig. 3 LNCaP after 4 h incubation with **6**

The relative accumulation of **6** and **1** in the nucleus compared to the cytoplasmic membrane of the LNCaP cells was determined by measuring the intensity of fluorescence in the relevant regions. After 4 h incubation **6** was found in the nucleus with the median relative accumulation significantly higher compared to **1**. However, while the amount of **1** in the nucleus barely changed between the two incubation times, **6** showed a much higher accumulation in the nucleus after short-term incubation (*cf.* Fig. 4). Due to the higher concentration of **6** in the vital parts of the cell (like the nucleus) we also expect an increased cytotoxicity upon light irradiation compared to **1**, keeping in mind the almost equivalent photosensitizing properties of **6** and **1** as probed by the photodestruction of bilirubinate IXα.

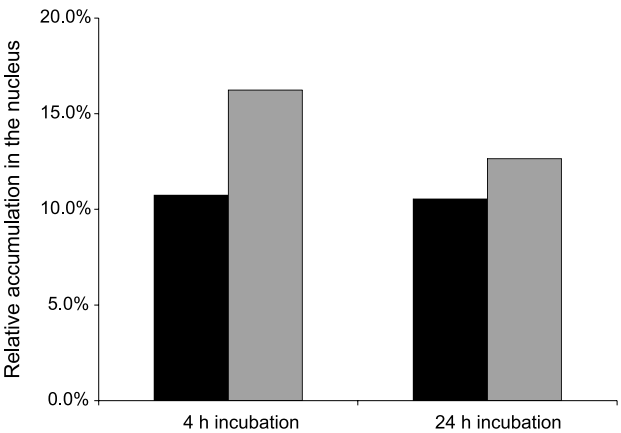


Fig. 4 Relative accumulation of **6** (*grey*) and **1** (*black*) in the nucleus of LNCaP cells after 4 and 24 h incubation

Conclusion

The synthesis of three of the four possible bis-ω,ω'-nucleo-base-hypericin derivatives **6**, **10**, and **14** substituted with the nucleo-bases thymine, cytosine, and adenine could be accomplished. The thymine derivative **6** proved to be the best soluble one and displayed photoproduction of singlet oxygen and/or reactive oxygen species comparable to the one of hypericin (**1**). Although no specific interaction with *DNA* or *Watson-Crick* base pairing with poly(2′-deoxyadenylic acid) could be detected it accumulated in the nucleus of prostatic cancer cells even better than **1**. Thus, it may constitute a novel potential second-generation hypericin derivative for photodynamic therapy.

Experimental

The products were characterized by means of mp (*Kofler* microscope, Reichert), NMR (Bruker Avance DPX 200 MHz or a Bruker Avance 500 MHz spectrometer using a TXI cryoprobe with *z*-gradient coil using standard pulse sequences as provided by the manufacturer. Typical 90° hard pulse durations were 8.2 μs (^{1}H) and 16.6 μs (^{13}C), 90° pulses in decoupling experiments were set to 67 μs. HSQC and HMBC experiments were optimized for decoupling constants of 145 Hz for single quantum correlations and 10 Hz for multibond correlations. The N*O*ESY mixing time was set to 400 ms), IR (Bruker Tensor 27, KBr), MS (Thermofinnigan LCQ Deca XP Plus or Hewlett Packard 59987 quadrupole instrument), fluorescence (Varian Carey Eclipse fluorescence instrument), and UV-Vis data (Varian Cary 100 Bio). Fluorescence quantum yields were calculated according to the comparative method of *Williams et al.* [13] using hypericin (**1**) as standard sample. Fluorescence microscopy was carried out on a LSM 510 Laser Module Axiovert 200 *M* fluorescence microscope.

Photocyclizations were carried out using a 700 W Hg high-pressure lamp with fluorescence screen (Philips). For the irradiation experiments a 300 W tungsten lamp (Philips) and a long-pass cut-off filter ($\lambda_{\text{cut-off}} > 570$ nm) were used. Thin layer chromatography (TLC) was performed on silica gel 60 F_{254} aluminum sheets (Merck). Column chromatography was carried out on silica gel (0.060–0.200 mm, pore diameter 6 nm), unless stated otherwise.

The production of singlet oxygen/oxidizing species by **1**, **2**, and **3** was monitored by bilirubin-IXα-degradation according to Ref. [8]. The long-wavelength absorption band intensities of the three compounds were made equal by adjusting concentrations to provide comparable light absorptions for all compounds.

DNA interaction experiments were carried out with calf thymus *DNA* (Sigma) and poly(2′-deoxyadenylic acid) sodium salt (poly(d*A*), Sigma) according to Refs. [9, 10] using H_2O (MilliQ 18 MΩ) + 10% *DMSO* (*v*/*v*). The concentration of calf thymus *DNA* was expressed in nucleotide/dm^3, determined spectrophotometrically by using an average molecular weight of 338 for a nucleotide and an extinction coefficient of $\varepsilon_{260} = 6600\,M^{-1}\,\text{cm}^{-1}$. Ratios of 1:40, 1:200, and 1:400 and measurements after 30 min, 2 and 24 h with stirring at 4°C in between were used. No change of the hypericin chromophore absorption spectra of **6**, **10**, and **14** as compared to a blind sample without *DNA* could be detected. The concentration for poly(d*A*) was expressed in nucleotide/dm^3 and determined spectrophotometrically by using an extinction coefficient of $\varepsilon_{260} = 9100\,M^{-1}\,\text{cm}^{-1}$ [9, 10]. In this case the relation between **6** and poly(d*A*) was 1:3 and 1:6 with measurements after 30 min, 2 and 24 h. Again, no change in the absorption spectrum of **6** could be detected.

6-(Bromomethyl)-1,3,8-trimethoxyanthracene-9,10-dione (**2**, $C_{18}H_{15}BrO_5$)

A mixture of 500 mg 1,3,8-trimethoxy-6-methyl-9,10-anthraquinone (1.85 mmol) [14], 317 mg 1,3-dibromo-5,5-dimethylhydantoin (1.11 mmol) (Aldrich), 10 mg dibenzoylperoxide (0.041 mmol), and 80 cm^3 CCl_4 was refluxed under Ar for 36 h. The reaction progress was controlled by means of NMR. The reaction mixture was evaporated, and the residue was washed with CCl_4 and hot H_2O. After purification by means of recrystallization from toluene/*EtOAc* = 2/1 and column chromatography (toluene/*EtOAc* = 1/1), 440 mg (1.12 mmol) **2** were obtained (61% yield). Mp 218–220°C; $R_f = 0.33$ ($CHCl_3$/*EtOAc* = 3/1), $R_f = 0.34$ (toluene/*EtOAc* = 1/1); ^{1}H NMR (500 MHz, *DMSO*-d_6, 30°C): $\delta = 7.76$ (s, ar-H5), 7.61 (s, ar-H7), 7.17 (d, $J = 2.3$ Hz, ar-H4), 6.98 (d, $J = 2.3$ Hz, ar-H2), 4.82 (s, 6-CH_2Br), 3.94 (s, 3-OCH_3), 3.91 (s, 8-OCH_3), 3.90 (s, 1-OCH_3) ppm; N*O*ESY (*DMSO*-d_6): 1-$OCH_3 \leftrightarrow$ ar-H2, 3-$OCH_3 \leftrightarrow$ ar-H2 and ar-H4, 8-$OCH_3 \leftrightarrow$ ar-H7, 6-CH_2Br $\leftrightarrow$ ar-H5 and ar-H7; ^{13}C NMR (125 MHz, *DMSO*-d_6, 30°C): $\delta = 182.8$ (C10), 179.6 (C9), 163.5 (C3), 161.1 (C1), 159.0 (C8), 144.0 (C6), 135.5 (C4a), 134.3 (C10a), 122.9 (C8a), 119.4 (C7), 118.8 (C5), 117.5 (C9a), 105.1 (C2), 102.4 (C4), 56.43 (1-OCH_3 or 8-OCH_3), 56.36 (8-OCH_3 or 1-OCH_3), 55.90 (3-OCH_3), 32.72 (6-CH_2Br) ppm; HMBC (*DMSO*-d_6): C1 $\leftrightarrow$ 1-OCH_3, ar-H2 and ar-H4, C2 $\leftrightarrow$ ar-H4, C3 $\leftrightarrow$ 3-OCH_3, ar-H2 and ar-H4, C4 $\leftrightarrow$ ar-H2, C5 $\leftrightarrow$ ar-H7 and 6-CH_2Br, C6 $\leftrightarrow$ ar-H7 and 6-CH_2Br, C7 $\leftrightarrow$ ar-H5 and 6-CH_2Br, C8 $\leftrightarrow$ 8-OCH_3 and ar-H7, C10 $\leftrightarrow$ ar-H4 and ar-H5, C4a $\leftrightarrow$ ar-H4, C8a $\leftrightarrow$ ar-H5 and ar-H7, C9a $\leftrightarrow$ ar-H2 and ar-H4, 6-CH_2Br $\leftrightarrow$ ar-H5 and ar-H7; HSQC data were according to structure; ESI-MS (CH_3OH + 1 vol% HCOOH, positive ion mode): $m/z = 392$ ($[M+H]^+$); IR (KBr): $\bar{\nu} = 3088$, 2941, 2840, 1774, 1708, 1663, 1597, 1566, 1464, 1426, 1349, 1324, 1252, 1220, 1206, 1163, 1135, 1071, 1020, 943, 849, 755 cm^{-1}; UV-Vis ($CHCl_3$): $\lambda_{\max} = 280$ (100), 403 (28) nm (rel. int.)

3-Benzoyl-5-methyl-1-((4,5,7-trimethoxy-9,10-dioxo-9,10-dihydroanthracen-2-yl)methyl)pyrimidine-2,4(1H,3H)-dione (**3**, $C_{30}H_{24}N_2O_2$)

A mixture of 63 mg **2** (0.163 mmol), 56 mg 3-benzoylthymine (0.244 mmol) [2], and 67 mg dried K_2CO_3 (0.489 mmol) was dissolved in 15 cm^3 *DMF*. After heating to 80°C under Ar

atmosphere the reaction mixture was stirred for 16 h. The solvent was evaporated and the residue was dissolved in $CHCl_3$. The organic layer was washed with water several times, dried ($MgSO_4$), and evaporated. The crude product was purified by means of column chromatography ($CHCl_3$/*Me*OH = 30/1) yielding 60.53 mg (69%) **3**. Mp 216–219°C; $R_f = 0.41$ ($CHCl_3$/*Me*OH = 9/1); ^{1}H NMR (500 MHz, *DMSO*-d_6, 30°C; note that here and throughout the descriptions we follow the numbering scheme of emodin and not the IUPAC enumeration as given with the name for the NMR assignments due to better comparison possibilities): $\delta = 1.96$ (s, 5′-CH_3), 3.95 (s, 8-OCH_3), 3.96 (s, 1-OCH_3), 3.97 (s, 3-OCH_3), 4.98 (s, 6-CH_2), 6.79 (d, $J = 1.9$ Hz, ar-H2), 7.14 (s, 6′-H), 7.28 (s, ar-H7), 7.33 (d, $J = 1.9$ Hz, ar-H4), 7.51 (m, ar-H4″), 7.64 (m, ar-H3″, ar-H5″), 7.73 (s, ar-H5), 7.93–7.94 (m, ar-H2″, ar-H6″) ppm; ^{13}C NMR (125 MHz, *DMSO*-d_6, 30°C): $\delta = 11.3$ (5′-CH_3), 50.2 (6-CH_2), 54.8 (3-OCH_3), 55.4 (1-OCH_3) 55.6 (8-OCH_3), 101.1 (C4) 104.3 (C2), 110.8 (C5′), 116.4 (C5), 116.6 (C7), 117.0 (C9a), 122.9 (C8a), 128.0 (C1″), 129.3 (C2″) 130.4 (C5″), 133.9 (C6″), 134.1 (C10a), 135.0 (C4a), 138.0 (C6′), 140.0 (C6), 149.0 (C2′), 159.3 (C8), 160.7 (C1), 161.6 (C4′), 162.9 (C3), 167.4 (*Bz*-C = O), 180.0 (C9), 182.6 (C10) ppm; N*O*ESY (*DMSO*-d_6, 30°C): ar-H2 ↔ 1-OCH_3 and 3-OCH_3, 6′-H ↔ 6-CH_2- and 5′-CH_3, ar-H4 ↔ 3-OCH_3, ar-H_7 ↔ 6-CH_2- and 8-OCH_3, ar-H5 ↔ 6-CH_2-; HMBC (*DMSO*-d_6, 30°C): 5′-CH_3 ↔ C6′. C5′ and C4′, 8-OCH_3 ↔ C8, 1-OCH_3 ↔ C1, 3-OCH_3 ↔ C3, 6-CH_2- ↔ C5, C6, C7 and C6′, ar-H2 ↔ C9a and C9, 6′-H ↔ C5′and C2′, ar-H7 ↔ C8 and C8a, ar-H4 ↔ C4a and C10, ar-H2″ ↔ *Bz*-C = O, ar-H5 ↔ C10a and C10; HSQC data were according to structure; ESI-MS (*Me*OH/$CHCl_3$ = 9/1 + 1 vol% HCOOH, positive ion mode): $m/z = 541$ ($[M + H]^+$); IR (KBr): $\bar{\nu} = 2925$, 2852, 1749, 1694, 1657, 1598, 1437, 1351, 1316, 1247, 1202, 1159, 1126, 1068, 1020, 997, 946, 910, 872, 817, 782, 752, 710 cm^{-1}; UV-Vis ($CHCl_3$): $\lambda_{max} = 402$ (100) nm (rel. int.).

3-Benzoyl-5-methyl-1-((4,5,7-trihydroxy-10-oxo-9,10-dihydroanthracen-2-yl)methyl)pyrimidine-2,4(1H,3H)-dione (**4**, $C_{20}H_{16}N_2O_2$)

An argon-flushed solution of 61 mg **3** (0.113 mmol) in 10 cm^3 glacial acetic acid was heated to reflux. Then 203 mg $SnCl_2 \cdot 2H_2O$ (0.9 mmol) in 4 cm^3 HBr (47%) were added drop-wise and refluxed for 90 min. The reaction mixture was poured into 15 cm^3 ice/water, the precipitate was separated by centrifugation, and washed with H_2O several times. The product was dried in vacuum and 40 mg **4** were isolated (92% yield). Mp 275°C (dec); $R_f = 0.45$ ($CHCl_3$/*Me*OH = 9/1); ^{1}H NMR (500 MHz, *DMSO*-d_6, 30°C): $\delta = 12.31$ (s, 8-OH), 12.29 (s, 1-OH), 11.35 (s, 3′-H), 10.85 (s, 3-OH), 7.63 (s, 6′-H), 6.83 (s, ar-H5), 6.74 (s, ar-H7), 6.43 (s, ar-H4), 6.24 (s, ar-H2), 4.86 (s, 6-CH_2), 4.36 (s, 4a-CH_2). 1.78 (s, 5′-CH_3) ppm; ^{13}C NMR (125 MHz, *DMSO*-d_6, 30°C): $\delta = 190.9$ (C9), 164.4 (C3), 164.2 (C1), 163.7 (C4′), 161.7 (C8), 151.0 (C2′), 144.6 (C6), 141.2 (C6′), 117.2 (C8a), 116.7 (C5), 113.2 (C7), 109.2 (C9a), 108.4 (C5′), 107.4 (C4), 100.5 (C2), 49.8 (6-CH_2-), 32.4 (C10), 11.9 (5′-CH_3) ppm; N*O*ESY (*DMSO*-d_6, 30°C): 8-OH ↔ ar-H7, 1-OH ↔ ar-H2, 3-OH ↔ ar-H4 and ar-H2, 6′-H ↔ 6-CH_2- and 5′-CH_3, ar-H5 ↔ 6-CH_2-, ar-H7 ↔ 6-CH_2; HMBC (*DMSO*-d_6, 30°C): 8-OH ↔ C8, 1-OH ↔ C1, 3-OH ↔ C3, 6′-H ↔ C2′, C4′, C5′ and 6-CH_2-, ar-H5 ↔ C10, C10a, C6 and 6-CH_2-, ar-H7 ↔ C6, C8 and C8a, ar-H4 ↔ C3, C4a and C10, ar-H2 ↔ C1, C3 and C9a, 6-CH_2- ↔ C5, C6, C7, C2′ and C6′, 4a-CH_2- ↔ C4, C4a, C5 and C10a, 5′-CH_3 ↔ C4′, C5′ and C6′; HSQC data were according to structure; ESI-MS (*Me*OH/$CHCl_3$ = 3/1 + 1 vol% NH_3, negative ion mode): $m/z = 379$ ($[M - H]^+$); IR (KBr): $\bar{\nu} = 3179$, 3033, 2926, 1687, 1624, 1601, 1478, 1435, 1379, 1244, 1171, 1064, 958, 911, 835, 798, 763, 723, 643 cm^{-1}; UV-Vis (*DMF*): $\lambda_{max} = 389$ (100), 371 (63) nm (rel. int.).

1,1′-(1,3,4,6,8,15-Hexahydroxy-7,16-dioxo-7,16-dihydrodibenzo[a,o]perylene-10,13-diyl)bis(methylene)bis(5-methylpyrimidine-2,4(1H,3H)-dione) (**5**, $C_{40}H_{26}N_4O_{12}$)

A light-protected mixture of 33 mg **4** (0.086 mmol), 1.2 mg $FeSO_4 \cdot 7H_2O$ (0.0043 mmol), and 45 mg pyridine-*N*-oxide (0.475 mmol) in 2.5 cm^3 dry pyridine and 0.2 cm^3 dry piperidine was stirred under Ar at 115°C for 1 h. After cooling to room temperature the mixture was poured into 16 cm^3 2 *N* HCl and stirred for another 30 min. The precipitate was centrifuged and washed three times with HCl (3%) and three times with H_2O. The residue was dried over P_2O_5 in vacuum and 29 mg **5** were obtained (88% yield). Due to its light-sensitivity isolation was only possible as a mixture with the light-induced sequel product **6**. Thus, characterization could only be achieved by mass spectrometry and UV-Vis spectrometry. Mp >350°C; ESI-MS (acetone + 1 vol% NH_3, negative ion mode): $m/z = 753$ ($[M - H]^+$); UV-Vis (acetone): $\lambda_{max} = 371$ (100), 555 (91), 590 (88) nm (rel. int.).

1,1′-(1,6,8,10,11,13-Hexahydroxy-7,14-dioxo-7,14-dihydrophenanthro[1,10,9,8-opqra]perylene-3,4-diyl)bis(methylene)-bis(5-methylpyrimidine-2,4(1H,3H)-dione) (**6**, $C_{40}H_{24}N_4O_{12}$)

A vigorously stirred solution of 147 mg **5** (0.195 mmol) in 2250 cm^3 acetone was irradiated for 150 min by means of a 700 W Hg high-pressure lamp with fluorescence screen. After evaporation of the solvent the residue was purified by means of column chromatography (Sephadex LH20 *Me*OH) and 113 mg **6** were obtained (77% yield). Due to its low solubility a complete structure determination by means of NMR experiments was not possible. Data for ^{13}C NMR are partly derived from 2D NMR experiments. Mp >350°C; $R_f = 0.80$ ($CHCl_3$/*Me*OH = 1/1), $R_f = 0.66$ (*THF*/petrol ether/*Me*OH = 7/1/1); ^{1}H NMR (500 MHz, *DMSO*-d_6, 30°C; note that hypericin enumeration is retained for NMR assignments for the hypericinoid compounds, instead of the IUPAC numbering): $\delta = 18.65$ (bs, 3-OH, 4-OH), 14.74 (s, 1-OH, 6-OH), 14.13 (s, 8-OH, 13-OH), 11.08 (s, 3′-NH, 3″-NH), 7.42 (s, ar-H9, ar-H12), 7.29 (s, 6′-H, 6″-H), 6.62 (s, ar-H2, ar-H5), 5.73 (d, $J = 15$ Hz, 10-CH_2-, 11-CH_2-), 4.98 (d, $J = 15$ Hz, 10-CH_2-, 11-CH_2-), 1.57 (s, 5′-CH_3, 5″-CH_3) ppm; ^{13}C NMR (125 MHz, *DMSO*-d_6, 30°C): $\delta = 184.8$ (C7, C14), 175.7 (C3, C4), 168.8 (C1, C6), 163.9 (C4′, C4″), 163.6 (C2′, C2″), 161.5 (C8, C13), 150.9 (C5′, C5″), 142.5 (C6′, C6″), 141.7 (C10, C11), 119.7 (C10a, C10b), 117.6 (C9, C12), 109.6 (C7a, C13a), 106.9 (C2, C5), 102.0 (C6a, C14a),

50.8 (10-CH_2-, 11-CH_2-), 12.9 (5′-CH_3, 5″-CH_3) ppm – C3a, C3b, C6b, C7b, C7c, C13b, C14b and C14c not visible; N*O*ESY (*DMSO*-d_6, 30°C): 10-CH_2- and 11-CH_2- ↔ 6′-H and 6″-H, 5′-CH_3 and 5″-CH_3 ↔ 6′-H and 6″-H; COSY (*DMSO*-d_6): 10-CH_2- and 11-CH_2- ↔ 10-CH_2- and 11-CH_2-; HMBC (*DMSO*-d_6): 1-OH and 6-OH ↔ C1 and C6, C6a and C14a, C2 and C5, 8-OH and 13-OH ↔ C8 and C13, C12 and C9, C7a and C13a, ar-H9 and ar-H12 ↔ C8 and C13, C10a and C10b, C7a and C13a, 6′-H and 6″-H ↔ C4′ and C4″, C5′and C5″, ar-H2 and ar-H5 ↔ C1 and C6, C6a and C14a, 10-CH_2- and 11-CH_2- ↔ C5′ and C5″, C10 and C11, C10a and C10b, 5′-CH_3 and 5″-CH_3 ↔ C2′ and C2″, C6′ and C6″; HSQC data were according to structure; ESI-MS (acetone/*Me*OH = 1/1, 1 vol% HCOOH, positive ion mode): $m/z = 753$ ($[M+H]^+$); IR (KBr): $\bar{\nu} = 3501$, 3064, 2925, 2854, 1684, 1586, 1550, 1497, 1430, 1374, 1244, 1186, 1114, 859, 785, 721 cm^{-1}; UV-Vis (*DMSO*, $c = 1.812 \cdot 10^{-5}$ mol dm^{-3}): λ_{max} (ε) = 603 (18433), 557 (8278), 345 (9437) nm ($dm^3\,mol^{-1}\,cm^{-1}$); UV-Vis (acetone, $c = 3.986 \cdot 10^{-5}$ mol dm^{-3}): λ_{max} (ε) = 600 (24561), 555 (12017) nm ($dm^3\,mol^{-1}\,cm^{-1}$); UV-Vis (*THF*, $c = 3.986 \cdot 10^{-5}$ mol dm^{-3}): λ_{max} (ε) = 605 (17612), 559 (9107) nm ($dm^3\,mol^{-1}\,cm^{-1}$); UV-Vis (*Et*OH (80%), $c = 3.986 \cdot 10^{-5}$ mol dm^{-3}): λ_{max} (ε) = 595 (17410), 551 (9057) nm ($dm^3\,mol^{-1}\,cm^{-1}$); fluorescence (*DMSO*, $c = 3.98 \cdot 10^{-8}$ mol dm^{-3}, $\lambda_{ex} = 550$ nm): λ_{em} (rel. int.) = 607 (100), 658 (30) nm, $\Phi_f = 0.11$; fluorescence (acetone, $c = 7.9 \cdot 10^{-8}$ mol dm^{-3}, $\lambda_{ex} = 550$ nm): λ_{em} (rel. int.) = 605(100), 657 (29) nm; fluorescence (*THF*, $c = 3.98 \cdot 10^{-8}$ mol dm^{-3}, $\lambda_{ex} = 550$ nm): λ_{em} (rel. int.) = 609 (100), 655 (31) nm; fluorescence (*Et*OH 80%, $c = 3.98 \cdot 10^{-8}$ mol dm^{-3}, $\lambda_{ex} = 550$ nm): λ_{em} (rel. int.) = 600 (100), 653 (34) nm.

N-(2-Oxo-1-((4,5,7-trimethoxy-10-oxo-9,10-dihydroanthracen-2-yl)methyl)-1,2-dihydropyrimidin-4-yl)benzamide (**7**, $C_{29}H_{23}N_3O_7$)

A mixture of 114 mg **2** (0.291 mmol), 88 mg benzoylcytosine [5] (0.408 mmol), and 100 mg K_2CO_3 (0.72 mmol) was dissolved in 60 cm^3 *DMF*. The Ar-flushed solution was heated to 80°C and stirred for 18 h. The solvent was evaporated, the residue was dissolved in $CHCl_3$, and washed with H_2O several times. The organic layer was dried ($MgSO_4$) and $CHCl_3$ was evaporated. The crude product was purified by column chromatography (silica gel, $CHCl_3$/*Me*OH = 15/1) and 127 mg **7** were obtained (83% yield). Mp 226–228°C; $R_f = 0.39$ ($CHCl_3$/*Me*OH = 15/1); ^{1}H NMR (500 MHz, *DMSO*-d_6, 30°C): $\delta = 11.21$ (bs, NH), 8.39 (d, 6′-H, J = 7 Hz), 8.01 (m, ar-H2″, ar-H6″), 7.63 (m, ar-H4″), 7.56 (s, ar-H5, ar-H7), 7.52 (m, ar-H3″, ar-H5″), 7.39 (d, 5′-H, J = 7 Hz), 7.16 (d, ar-H4, J = 3 Hz), 6.99 (d, ar-H2, J = 3 Hz), 5.17 (s, 6-CH_2-), 3.93 (s, 8-OCH_3), 3.91 (s, 1-OCH_3), 3.90 (s, 3-OCH_3) ppm; ^{13}C NMR (125 MHz, *DMSO*-d_6, 30°C): $\delta = 183.4$ (C10), 182.9 (C9), 179.7 (C4′), 167.3 (Bz-C = O), 163.4 (C3), 161.1 (C1), 159.0 (C8), 155.3 (C2′), 150.5 (C6′), 142.9 (C6), 135.6 (C4a), 134.1 (C10a), 132.7 (C1″), 132.6 (C4″), 128.6 (C2″), 128.5 (C3″), 124.6 (C6″), 122.8 (C8a), 118.5 (C7 or C5), 117.5 (C9a), 116.8 (C7 or C5), 104.4 (C2), 102.5 (C4), 96.5 (C5′), 56.4 (8-OCH_3) 56.3 (1-OCH_3), 55.9 (3-OCH_3), 52.5 (6-CH_2-) ppm; C5″ not visible; N*O*ESY (*DMSO*-d_6, 30°C): NH ↔ ar-H2″ and ar-H6″, 6′-H ↔ 5′-H and 6-CH_2-, ar-H5 and ar-H7 ↔ 6-CH_2-, 8-OCH_3 ↔ ar-H7, 1-OCH_3 ar-H2, 3-OCH_3 ↔ ar-H2 and ar-H4; HMBC (*DMSO*-d_6): NH ↔ *Bz*-C = O, 6′-H ↔ C2′and 6-CH_2, ar-H2″ and ar-H6″ ↔ C1″, C3″ and C5″, ar-H5 and ar-H7 ↔ C6, C10a, C8, C8a and 6-CH_2-, ar-H3″ and ar-H5″ ↔ C6″, C2″ and C4″, 5′-H ↔ C6′ and C4′, ar-H4 ↔ C10, C3 and C4a, ar-H2 ↔ C9, C1, C3 and C9a, 8-OCH_3 ↔ C8, 1-OCH_3 ↔ C1, 3-OCH_3 ↔ C3; HSQC data were according to structure; ESI-MS (*Me*OH + 1 vol% HCOOH, positive ion mode): $m/z = 526$ ($[M+H]^+$); IR (KBr): $\bar{\nu} = 3527$, 2941, 2840, 1669, 1599, 1565, 1487, 1458, 1353, 1323, 1248, 1070, 1018, 945, 753, 704 cm^{-1}; UV-Vis ($CHCl_3$): $\lambda_{max} = 400$ (16), 265 (100) nm (rel. int.).

4-Amino-1-((4,5,7-trihydroxy-10-oxo-9,10-dihydroanthracen-2-yl)methyl)pyrimidin-2(1H)-one (**8**, $C_{29}H_{23}N_3O_7$)

An Ar-flushed solution of 81 mg **7** (0.154 mmol) in 15 cm^3 glacial acetic acid was heated to reflux under vigorous stirring. Then 278 mg $SnCl_2 \cdot 2H_2O$ (1.23 mmol) dissolved in 10 cm^3 HBr (47%) was added dropwise. After 45 min the reaction mixture was poured into ice/water, stirred for another 30 min, and extracted with *Et*OA*c* three times. The organic layer was evaporated, the residue was suspended in water, and centrifuged. After the product was washed with H_2O two times and dried over P_2O_5 in vacuum 50 mg **8** were obtained (89% yield). According to NMR data **8** underwent tautomerization. Mp 243°C (dec); $R_f = 0.29$ ($CHCl_3$/*Me*OH = 15/1); ^{1}H NMR (500 MHz, *DMSO*-d_6, 30°C): $\delta = 12.30$ (s, 8-OH), 12.28 (s, 1-OH), 10.87 (s, 3-OH), 9.09 (bs, =NH), 8.05 (bs, 3′-H), 8.03 (d, 6′-H, J = 7.75 Hz), 6.87 (s, ar-H5), 6.78 (s, ar-H7), 6.43 (s, ar-H4), 6.24 (s, ar-H2), 6.03 (d, 5′-H, J = 7.75 Hz), 4.99 (s, 6-CH_2-), 4.35 (s, 2H, 10-H_2) ppm; ^{13}C NMR (125 MHz, *DMSO*-d_6, 30°C): $\delta = 191.0$ (C9), 165.3 (C3), 164.7 (C1), 161.8 (C8), 160.3 (C4′), 149.4 (C6′), 148.9 (C2′), 145.0 (C4a), 144.2 (C6), 142.6 (C10a), 117.4 (C5), 114.5 (C8a), 113.2 (C7), 108.5 (C9a), 107.5 (C4), 101.0 (C2), 94.1 (C5′) 51.4 (6-CH_2-), 32.5 (C10) ppm; N*O*ESY (*DMSO*-d_6, 30°C): 8-OH ↔ ar-H7, 1-OH ↔ ar-H2, 3-OH ↔ ar-H2 and ar-H4, N=H ↔ 5′-H, 6′H ↔ 5′H and 6-CH_2-, ar-H5 ↔ 10-H_2 and 6-CH_2-, ar-H7 ↔ 6-CH_2-; HMBC (*DMSO*-d_6): 8-OH ↔ C8, 1-OH ↔ C1, 3-OH ↔ C3, 6′-H ↔ C4′C5′and 6-CH_2-, ar-H5 ↔ C6, C10a, C10 and 6-CH_2-, ar-H7 ↔ C8, C8a and C6, ar-H4 ↔ C3, C4a and C10, ar-H2 ↔ C1, C3 and C9a, 6-CH_2- ↔ C6, C5, C7 and C6′, 10H_2 ↔ C8a, C9a, C10a, C4a, C4 and C5; HSQC data were according to structure; ESI-MS (*Me*OH + 1 vol% NH_3, negative ion mode): $m/z = 364$ ($[M-H]^+$).

10,13-Bis((4-amino-2-oxopyrimidin-1(2H)-yl)methyl)-1,3,4,6,8,15-hexahydroxydibenzo[a,o]perylene-7,16-dione (**9**, $C_{38}H_{24}N_6O_{10}$)

An Ar-flushed, light protected mixture of 60 mg **8** (0.164 mmol), 2.3 mg $FeSO_4 \cdot 7H_2O$ (0.008 mmol), and 86 mg pyridine-*N*-oxide (0.903 mmol) in 3.5 cm^3 dry pyridine and 0.3 cm^3 dry piperidine was heated to reflux and stirred for 1 h. Then the reaction mixture was cooled to room temperature, poured into 30 cm^3 2 *N* HCl, and stirred for 30 min. The

precipitate was centrifuged, washed three times with HCl (3%) and three times with H_2O. The residue was dried over P_2O_5 in vacuum and 28.4 mg **9** were obtained (48% yield). Due to its light sensitivity isolation was only possible as a mixture with the light induced following product **10**. Characterization could only be achieved by mass spectrometry and UV-Vis spectrometry. Mp >350°C; ESI-MS (*Me*OH + 1 vol% NH_3, negative ion mode): $m/z = 723$ ($[M-H]^+$); UV-Vis (acetone/*Me*OH = 3/1): $\lambda_{max} = 585$ (100), 550 (95) nm (rel. int.).

3,4-Bis((4-amino-2-oxopyrimidin-1(2H)-yl)methyl)-1,6,8,10,11,13-hexahydroxyphenanthro[1,10,9,8-opqra]-perylene-7,14-dione (**10**, $C_{38}H_{22}N_6O_{10}$)

A vigorously stirred solution of 25 mg **9** (0.0345 mmol) in 2000 cm^3 acetone/ethanol = 3/1 was irradiated for 120 min by means of a 700 W Hg high pressure lamp with fluorescence screen. The solvent was evaporated and the residue was dried over P_2O_5 in vacuum. The crude product was washed several times with $CHCl_3$ and 22 mg **10** were obtained (88% yield). Due to low solubility no ^{13}C and 2D NMR experiments were possible. Mp >350°C; ^1H NMR (500 MHz, *DMSO*-d_6, 30°C): $\delta = 18.63$ (bs, 3-OH, 4-OH), 14.72 (s, 1-OH, 6-OH), 14.10 (s, 8-OH, 13-OH), 7.78 (d, $J = 10$ Hz, 6′-H, 6″-H), 7.69 (d, $J = 10$ Hz, 5′-H, 5″-H), 7.36 (s, ar-H9, ar-H12), 6.62 (s, ar-H2, ar-H5), 4.92 (s, 10-CH_2-, 11-CH_2-) ppm, NH_2 not visible; ESI-MS (*Me*OH + 1 vol% NH_3, negative ion mode): $m/z = 721$ ($[M-H]^+$); IR (KBr): $\bar{\nu} = 3567$, 2925, 2854, 1733, 1684, 1653, 1457, 1374, 1271, 1176, 951, 776 cm^{-1}; UV-Vis (acetone/*Et*OH = 3/1): $\lambda_{max} = 600$ (100), 550 (25) nm (rel. int.); UV-Vis (*DMSO*, $c = 1.26 \cdot 10^{-4}$ mol dm^{-3}): λ_{max} (ε) = 602 (1968), 557 (1413) nm ($dm^3\,mol^{-1}\,cm^{-1}$); UV-Vis (*Et*OH 80% +1 vol% 50 m*M* NaOH, $c = 6.7 \cdot 10^{-6}$ mol dm^{-3}): λ_{max} (ε) = 595 (671), 551 (358) nm ($dm^3\,mol^{-1}\,cm^{-1}$); fluorescence (*DMSO*, $c = 1.25 \cdot 10^{-6}$ mol dm^{-3}, $\lambda_{ex} = 550$ nm): λ_{em} (rel. int.) = 607 (100), 656 (26) nm.

N-(9-((4,5,7-Trimethoxy-9,10-dioxo-9,10-dihydroanthracen-2-yl)methyl)-9H-purin-6-yl)benzamide (**11**, $C_{30}H_{23}N_5O_6$)

A mixture of 50 mg **2** (0.128 mmol), 86 mg benzoyladenine [6] (0.358 mmol), 35 mg K_2CO_3 (0.256 mmol), and 5 mg KI was dissolved in 50 cm^3 *DMF*. The Ar-flushed reaction mixture was heated to 80°C and stirred for 24 h. Then *DMF* was evaporated and the residue was dissolved in $CHCl_3$. The organic layer was washed with H_2O several times and dried ($MgSO_4$). After evaporation of the solvent and purification by means of column chromatography ($CHCl_3$/*Me*OH = 15/1) 38 mg **11** were obtained (54% yield). Mp 214–216°C; $R_f = 0.20$ ($CHCl_3$/*Me*OH = 15/1); ^1H NMR (500 MHz, *DMSO*-d_6, 30°C): $\delta = 11.16$ (bs, –NH–), 8.76 (s, 9′-H), 8.69 (s, 4′-H), 8.05 (m, *Bz*-H2″, *Bz*-H6″), 7.67 (s, ar-H5), 7.64 (m, *Bz*-H4″), 7.56 (m, *Bz*-H3″, *Bz*-H5″), 7.53 (s, ar-H7), 7.14, d, $J = 2.3$ Hz, ar-H4), 6.98 (d, $J = 2.3$ Hz, ar-H2), 5.65 (s, 6-CH_2–), 3.92 (s, 1-OCH_3), 3.91 (s, 8-OCH_3), 3.89 (s, 3-OCH_3) ppm; ^{13}C NMR (125 MHz, *DMSO*-d_6, 30°C): $\delta = 182.9$ (C10), 181.3 (C9), 165.3 (*Bz*-C = O), 163.5 (C1), 161.0 (C3), 159.1 (C8), 152.8 (C9′), 152.5 (C2′), 150.2 (C7′), 145.3 (C4′), 142.3 (C6), 132.9 (C1″) 132.4 (C2″, C6″), 132.2 (C4″), 128.8 (C3″, C5″), 127.8 (C4a), 125.4 (C6′), 122.7 (C10a), 121.8 (C8a), 118.8 (C5), 117.5 (C9a), 117.1 (C7), 105.4 (C2), 102.8 (C4), 56.2 (1-OCH_3), 56.0 (8-OCH_3), 55.8 (3-OCH_3), 46.5 (6-CH_2–) ppm; N*O*ESY (*DMSO*-d_6, 30°C): 6-CH_2– ↔ 9′-H, ar-H5 and ar-H7, ar-H2 ↔ 1-OCH_3 and 3-OCH_3, ar-H4 ↔ 3-OCH_3, ar-H7 ↔ 8-OCH_3; HMBC (*DMSO*-d_6): 9′-H ↔ C2′ and C7′, 4′-H ↔ C2′, C4′ and C6′, *Bz*-H2″ and *Bz*-H6″ ↔ *Bz*-C = O, C1″, C6″, C3″ and C5″, *Bz*-H4″ ↔ C3″ and C5″, ar-H5 ↔ C10, C6, C10a, C7 and 6-CH_2-, ar-H7 ↔ C9, C6, C8a and 6-CH_2–, ar-H4 ↔ C3, C4a, C9a and C2, ar-H2 ↔ C1, C3, C9a, 6-C*H*$_2$- ↔ cC9′ and C2, 1-OCH_3 ↔ C1, 8-OCH_3 ↔ C8, 3-OCH_3 ↔ C3; HSQC data were according to structure; ESI-MS (*Me*OH + 1 vol% HCOOH, positive ion mode): m/z = 550 ($[M+H]^+$); IR (KBr): $\bar{\nu} = 3503$, 3090, 2924, 2851, 1670, 1597, 1507, 1457, 1323, 1247, 1204, 1162, 1070, 1018, 946, 876, 799, 753 cm^{-1}; UV-Vis ($CHCl_3$): $\lambda_{max} = 403$ 403 (8), 281 (100) nm (rel. int.).

N-(9-((4,5,7-Trihydroxy-10-oxo-9,10-dihydroanthracen-2-yl)methyl)-9H-purin-6-yl)benzamide (**12**, $C_{20}H_{15}N_5O_4$)

An Ar-flushed solution of 42 mg **11** (0.0766 mmol) in 15 cm^3 glacial acetic acid and 5 cm^3 HBr (47%) was heated to reflux. Then 138 mg $SnCl_2 \cdot 2H_2O$ (0.612 mmol) in 5 cm^3 HBr (47%) was added and the reaction mixture was stirred for 90 min. After cooling to room temperature the reaction mixture was poured into ice/H_2O, stirred for another 30 min, and extracted with *Et*OA*c* several times. The organic layer was washed with 1 *N* NaOH and H_2O, dried ($MgSO_4$), and *Et*OA*c* was evaporated. The residue was dried in vacuum over P_2O_5 and 17 mg **12** were obtained (57% yield). Due to its rapid decomposition in *DMSO*-d_6, characterization by means of ^{13}C and 2D NMR experiments was not possible. Mp 272°C (dec); $R_f = 0.16$ ($CHCl_3$/*Me*OH = 15/1); ^1H NMR (500 MHz, *DMSO*-d_6, 30°C): $\delta = 12.89$ (bs, NH_2), 12.28 (s, 8-OH), 12.26 (s, 1-OH), 10.85 (s, 3-OH), 8.41 (s, 2′-H), 7.93 (s, 7′-H), 6.83 (s, ar-H5), 6.73 (s, ar-H7), 6.42 (s, ar-H4), 6.23 (s, ar-H2), 5.59 (s, 6-CH_2–), 4.32 (s, 10-H_2) ppm; ESI-MS (*Me*OH + 1 vol% NH_3, negative ion mode): $m/z = 388$ ($[M-H]^+$).

N,N′-(9,9′-(1,3,4,6,8,15-Hexahydroxy-7,16-dioxo-7,16-dihydrodibenzo[a,o]perylene-10,13-diyl)bis(methylene)bis-(9H-purine-9,6-diyl))dibenzamide (**13**, $C_{40}H_{24}N_{10}O_8$)

An Ar-flushed mixture of 17 mg **12** (0.0432 mmol), 0.6 mg $FeSO_4 \cdot 7H_2O$ (0.002 mmol), and 22.6 mg pyridine-*N*-oxide (0.238 mmol) in 2 cm^3 pyridine and 0.2 cm^3 piperidine was heated to reflux and stirred for 1 h. The reaction mixture was cooled to room temperature, poured into 20 cm^3 3 *N* HCl and stirred for another 30 min. The precipitate was centrifuged, washed three times with HCl (3%) and two times with H_2O. The product was dried in vacuum over P_2O_5 and 15 mg **13** were obtained (89% yield). Due to its light-sensitivity isolation was only possible as a mixture with the light-induced following product **14**. Characterization could only be achieved by mass spectrometry and UV-Vis spectrometry. Mp >350°C; ESI-MS (*Me*OH + 1 vol% NH_3, negative ion mode): $m/z = 771$ ($[M-H]^+$); UV-Vis (acetone/*Me*OH =

3/1 + 0.15 vol% NH_3 32%): $\lambda_{max} = 578$ (94), 548 (100) nm (rel. int.).

3,4-Bis((6-amino-9H-purin-9-yl)methyl)-1,6,8,10,11,13-hexahydroxyphenanthro[1,10,9,8-opqra]perylene-7,14-dione (**14**, $C_{40}H_{22}N_{10}O_8$)

A vigorously stirred solution of 14 mg **13** (0.018 mmol) in 2000 cm^3 acetone/*Me*OH = 1/1 and 3 cm^3 NH_3 (32%) was irradiated for 45 min by means of a 700 W Hg high pressure lamp with fluorescence screen. The solvent was evaporated and the residue was dried in vacuum over P_2O_5. After purification by washing the crude product several times with $CHCl_3$ 5 mg **14** were obtained (36% yield). Due to the instability and low solubility of the product a characterization by NMR experiments was not possible. Mp >350°C; $R_f = 0.0$ ($CHCl_3$/*Me*OH = 1/1); ESI-MS (*Me*OH + 1 vol% NH_3, negative ion mode): $m/z = 769$ ($[M-H]^+$); IR (KBr): $\bar{\nu} = 3447$, 2925, 2853, 1700, 1684, 1594, 1521, 1378, 1244, 847, 778 cm^{-1}; UV-Vis (acetone/*Me*OH = 1/1 + 0.15 vol% NH_3): $\lambda_{max} =$ 596 (100), 552 (70) 457 (84) nm (rel. int.); UV-Vis (*DMSO*, $c = 5.19 \cdot 10^{-5}$ mol dm^{-3}): λ_{max} (ε) = 602 (3892), 557 (3102) nm (dm^3 mol^{-1} cm^{-1}); UV-Vis (*Et*OH 80% +1 vol% 50 m*M* NaOH, $c = 5.6 \cdot 10^{-5}$ mol dm^{-3}): λ_{max} (ε) = 595 (3143), 551 (1946) 468 (2304) nm (dm^3 mol^{-1} cm^{-1}); fluorescence (*DMSO*, $c = 7.67$ 10^{-7} mol dm^{-3}, $\lambda_{ex} = 550$ nm): λ_{em} (rel. int.) = 606 (100), 651 (31) nm.

N-(6-Oxo-9-((4,5,7-trimethoxy-9,10-dioxo-9,10-dihydroanthracen-2-yl)methyl)-6,9-dihydro-1H-purin-2-yl)-benzamide (**15**, $C_{30}H_{23}N_5O_7$)

An Ar-flushed mixture of 100 mg **2** (0.256 mmol), 131 mg benzoylguanine [7] (0.513 mmol), 30 mg K_2CO_3 (0.217 mmol), and 5 mg KI in 50 cm^3 *DMF* was heated to 80°C and stirred for 24 h. After cooling to room temperature *DMF* was evaporated and the residue was dissolved in $CHCl_3$. The organic layer was washed with HCl (1%) and H_2O, dried ($MgSO_4$), and $CHCl_3$ was evaporated. The crude product was purified by column chromatography ($CHCl_3$/*Me*OH = 15/1) and 58 mg **15** were obtained (40% yield). Mp >350°C; $R_f = 0.47$ ($CHCl_3$/*Me*OH = 9/1); ^{1}H NMR (500 MHz, *DMSO*-d_6, 30°C): $\delta = 12.41$ (s, 5′-H), 11.91 (s, 6′-NH), 8.50 (s, 2′-H), 8.04 (m, *Bz*-H2″, *Bz*-H6″), 7.66 (m, ar-H5, *Bz*-H4″), 7.56 (m, *Bz*-H3″, *Bz*-H5″), 7.53 (s, ar-H7), 7.13 (s, ar-H4), 6.98 (s, ar · H2), 5.66 (s, 6-CH_2-), 3.91 (s, 1-OCH_3), 3.90 (s, 8-OCH_3), 3.89 (s, 3-OCH_3) ppm; ^{13}C NMR (125 MHz, *DMSO*-d_6, 30°C): $\delta = 185.0$ (C9), 184.8 (C10), 170.2 (*Bz*-C = O) 165.4 (C1), 163.0 (C3), 160.9 (C8), 146.4 (C2′), 145.0 (C6), 135.4 (C1″), 135.1 (C4″), 134.4 (C3″ or C5″), 130.5 (C3″ or C5″), 130.3 (C2″ or C6″), 129.2 (C2″ or C6″), 128.6 (C10a), 127.9 (C4a), 124.8 (C8a), 119.2 (C9a), 118.5 (C7), 117.4 (C5), 113.3 (C7a′), 106.6 (C2), 104.3 (C4), 57.5 (1-OCH_3), 57.2 (8-OCH_3), 56.7 (3-OCH_3), 50.6 (6-CH_2-) ppm, C3a′, C4′and C6′ could not be resolved; N*O*ESY (*DMSO*-d_6, 30°C): 6′-NH ↔ *Bz*-H2″ and *Bz*-H6″, ar-H7 ↔ 8-OCH_3, ar-H4 ↔ 3-OCH_3, ar-H2 ↔ 1-OCH_3 and 3-OCH_3, 6-CH_2- ↔ 2′-H, ar-H5 and ar-H7; HMBC (*DMSO*-d_6, 30°C): 2′-H ↔ C7a′, *Bz*-H2″ and *Bz*-H6″ ↔ *Bz*-C = O, C1″, C3″ and C5″, ar-H5 ↔ C10a and C7, ar-H7 ↔ C9, C6, C8 and C8a, ar-H4 ↔ C10, C3 and C4a, ar-H2 ↔ C1, C3 and C9a, 6-CH_2- ↔ C6, C2′, C5 and C7, 1-OCH_3 ↔ C1, 8-OCH_3 ↔ C8, 3-OCH_3 ↔ C3; HSQC data were according to structure; ESI-MS (*Me*OH + 1 vol% HCOOH, positive ion mode): $m/z = 566$ ($[M+H]^+$); IR (KBr): $\bar{\nu} = 3567$, 2924, 2848, 1918, 1705, 1664, 1597, 1560, 1507, 1458, 1380, 1251, 1068, 946, 874, 821, 755 cm^{-1}; UV-Vis ($CHCl_3$): $\lambda_{max} = 405$ 405 (24), 276 (100) nm (rel. int.).

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