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Syntheses, Photochemical Properties, and Tautomerism of Intramolecularly *Friedel-Crafts* Acylated Hypericin Derivatives[#]

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Summary. Intramolecularly *Friedel-Crafts* acylation carried out on the hypericin moiety provided a new class of 9,12-dicarbonyl substituted hypericin derivatives as potential candidates for photodynamic therapy (PDT). Focusing on cyclopentanone and cyclohexanone condensed derivatives, investigations concerning the chemical and photochemical properties as well as the tautomerism of these compounds were performed.

Keywords. Phenanthroperylenequinones; Semiempirical calculations; Anthraquinones; Photodynamic therapy.

Introduction

Among the naturally occurring phenanthroperylenequinones, hypericin (1,3,4,6,8,13-hexahydroxy-9,12-dimethylphenanthro[1,10,9,8-*opqra*]perylene-7,14-dione, **1**) is of special interest as it is one of the most powerful photosensitizers found in nature [1]. Due to its broad anticancer and antiviral activity [2–4] intensive research has been undertaken in the syntheses of second generation photodynamically active hypericin derivatives with improved solubility, enhanced ability to generate singlet oxygen and/or reactive oxygen species, and a bathochromically shifted absorption maximum into the wavelength range of common medicinal lasers ($\lambda_{max} \geq 620$ nm) [5–7].

[#] Dedicated to Prof. Dr. *Albert Eschenmoser* on occasion of his 80th birthday

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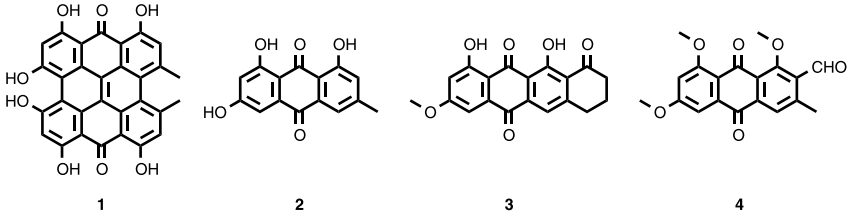


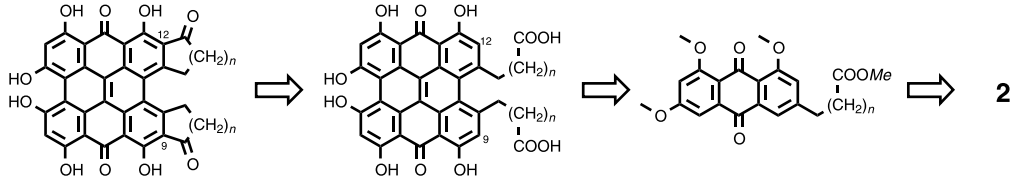
Fig. 1. Constitutions of hypericin (**1**), emodin (**2**), 10,12-dihydroxy-8-methoxy-1,2,3,4-tetrahydronaphtacene-1,6,11-trione (**3**), and 1,6,8-trimethoxy-2-formyl-3-methyl-9,10-anthraquinone (**4**)

Following this quest, we have now investigated the synthesis of a new class of 9,12-dicarbonyl substituted hypericin derivatives. These compounds are interesting targets, as the carbonyl group might exert a bathochromic effect as well as it should not interfere with the photosensitization processes. Because modifications of the perimeter of the hypericin skeleton are hardly possible (exceptions so far are the halogenation and sulfonation [7–9]), functionalizations have to be usually carried out on the precursor emodin (1,3,8-trihydroxy-6-methyl-9,10-anthraquinone, **2**) followed by dimerization to the corresponding hypericin derivative [10]. We have recently reported the syntheses of the 2-carbonyl substituted anthraquinones 10,12-dihydroxy-8-methoxy-1,2,3,4-tetrahydronaphtacene-1,6,11-trione (**3**) [11] and 1,6,8-trimethoxy-2-formyl-3-methyl-9,10-anthraquinone (**4**) [12], both possessing a promising bathochromic shift in comparison to the corresponding methyl ethers of **2** (Fig. 1).

Unfortunately, the insufficient regioselectivity encountered in the synthesis of **3** [11] as well as the observed decarbonylation of **4** (similar to such reactions reported in Ref. [13]) under the strong acidic and reducing dimerization conditions necessary, made the synthons **3** and **4** of limited value for a direct dimerization. To overcome these problems, we investigated the synthesis of 9,12-acylated hypericin derivatives *via* an intramolecular *Friedel-Crafts* acylation carried out on the hypericin moiety itself. Thus, we herein report our efforts in the syntheses of the first regioselectively *Friedel-Crafts* acylated hypericin derivatives and the chemical, photochemical, and spectroscopic properties as well as the tautomerism of these interesting 9,12-dicarbonyl substituted derivatives.

Results and Discussions

It has already been mentioned, that reactions on the hypericin skeleton are normally hardly possible. However, due to the failure of dimerization experiments on



Scheme 1

the 2-carbonyl substituted emodin derivatives **3** and **4**, it became necessary to carry out at least the final *Friedel-Crafts* acylation on the hypericin moiety. Scheme 1 shows the retrosynthetic strategy for the introduction of the carbonyl group in positions 9 and 12 of the hypericin skeleton starting from **2**.

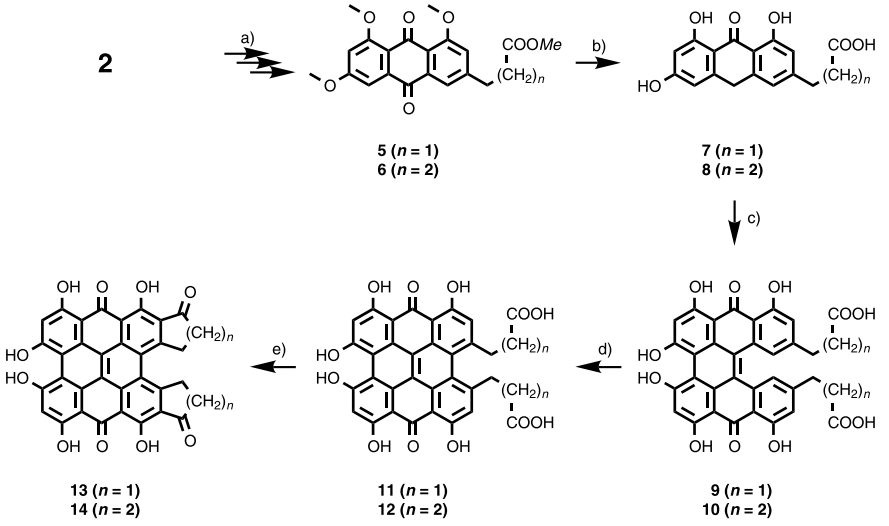
To keep the number of reaction steps to be carried out on the stage of the hypericin skeleton to a minimum, we intended to synthesize the corresponding carboxyalkylemodin derivatives followed by subsequent dimerization to the carboxyalkylhypericin derivatives. Leaving only one possible position available for an electrophilic attack by an intramolecular *Friedel-Crafts* acylation, these compounds should be the perfect synthons for the syntheses of 9,12-dicarbonyl substituted hypericin derivatives.

Syntheses

Focusing on 5- and 6-membered ring systems, we started from the recently prepared methyl 3-(1,6,8-trimethoxy-9,10-anthraquinon-3-yl)propionate (**5**) and methyl 3-(1,6,8-trimethoxy-9,10-anthraquinon-3-yl)butyrate (**6**) [11]. Dimerization to the corresponding hypericin derivatives was carried out in three steps. First, a combined deprotection/reduction with HBr (47%)/*Ac*OH and $SnCl_2 \cdot H_2O$ under reflux (carried out in analogy to Ref. [14]) yielded the corresponding anthrons **7** (74%) and **8** (66%). Both compounds were fully characterized on basis of their IR, UV-Vis, mass, and NMR spectra, particularly by 2D NMR experiments. Subsequent treatment of **7** and **8** with $FeSO_4 \cdot 7H_2O$, pyridine-*N*-oxide, pyridine, and piperidine (following Ref. [10]) yielded the light-sensitive protohypericins **9** (88%) and **10** (85%). Due to their instability, in particularly in solution, **9** and **10** were directly used without purification for the photocyclization to the desired carboxyalkylhypericin derivatives **11** and **12**. After washing of the resulting green residues with $CHCl_3$, **11** was obtained in 84% and **12** in 93% yield. Both compounds were characterized by means of their IR, UV-Vis, mass, and ^{1}H-NMR spectra.

With only one possible position left for an electrophilic attack, the intramolecular *Friedel-Crafts* acylations of the acids **11** and **12** were carried out in polyphosphoric acid (*PPA*) between 70–75°C in the dark. Best conversions and yields were obtained with a reaction time of 3 h in case of the 5-membered and 2.5 h in case of the 6-membered ring system. As both compounds showed a very low solubility in common organic solvents (*e.g.*, $CHCl_3$, acetone, *Me*OH), separations from the remaining educt were easily possible by washings with acetone, giving **13** in 75% and **14** in 87% yield. Due to their rather low solubility, characterization of both compounds, but especially in the case of the nearly insoluble **13**, turned out to be quite problematic. In the case of **14**, which is the better soluble one (*e.g.*, in *DMSO* or *DMF*), evidence for the successful cyclization was obtained by means of mass, UV-Vis, IR, and also ^{1}H NMR spectroscopy. However, in the case of **13**, no NMR spectra could be obtained, and therefore characterization of this compound was only possible by means of MS, UV-Vis, and IR experiments.

Accordingly, the new 9,12-dicarbonyl substituted hypericin derivatives **13** and **14** could be synthesized in four step syntheses from the anthraquinones **5** and **6** in overall yields of 41% (**13**) and 45% (**14**) (Scheme 2).



a) according to Ref. [11]; b) $SnCl_2 \cdot 2H_2O$/HBr(47%)/*Ac*OH, reflux; c) $FeSO_4 \cdot 7H_2O$/pyridine-*N*-oxide/pyridine/piperidine; d) *hν*, acetone; e) *PPA*, 70-75°C

Scheme 2

Chemical and Photochemical Properties

As already mentioned, the main motives in the syntheses of new photodynamically active hypericin derivatives are an improved solubility, an enhanced ability for the generation of singlet oxygen and/or reactive oxygen species, and a bathochromically shifted absorption maximum.

Unfortunately, the novel derivatives **13** and **14** show a rather low solubility in common solvents. As mentioned earlier, the 5-membered ring compound **13** was nearly insoluble and also the 6-membered ring compound **14** was only sparingly soluble in commonly good solvents like *DMSO* or *DMF*. Thus, both compounds failed the demand for an improved solubility.

Due to this low solubility, also measurements of the UV-Vis spectra were rather difficult. In particular, in the case of **13** only a spectrum of a very diluted solution in pyridine (assuming the predominance of the monodeprotonated pyridinium salt of **13**) was possible. Unfortunately, and in contrast to what could be expected from the bathochromic shift of the emodin analogue **3** [11], this compound showed only a minor bathochromic shift of its main absorption wavelength ($\lambda_{max} = 603$ nm) in comparison to **1** ($\lambda_{max} = 601$ nm). In the case of the better soluble **14**, reasonable UV-Vis spectra were obtained in pyridine and in *DMSO*. In both solvents, these spectra showed a rather broad absorption maximum at about 600 nm with a characteristic shoulder at about 630 nm. As it was not obvious whether this broad shoulder is really a characteristic property of this compound, or may result from a *pH*-dependent deprotonation behaviour or a complex tautomerism, a spectrophotometric acid–base titration experiment on **14** was carried out as well as semiempirical calculations with respect to the tautomerism of **13** and **14**.

The results of the titration experiments in 80% aqueous *DMSO* with H_2SO_4 and tetrabutylammonium hydroxide (*TBAH*) (carried out in analogy to Ref. [15]) are

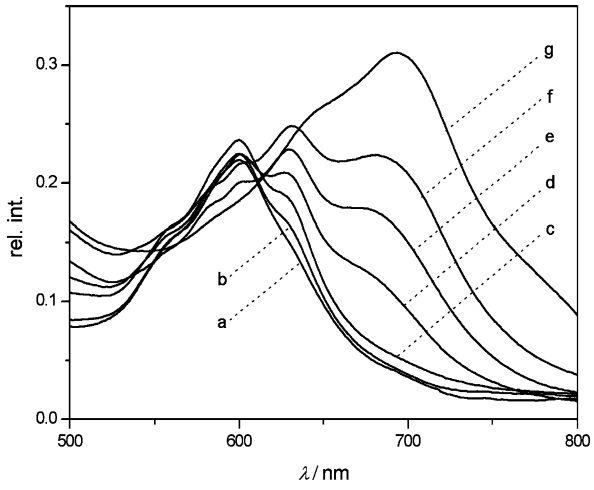
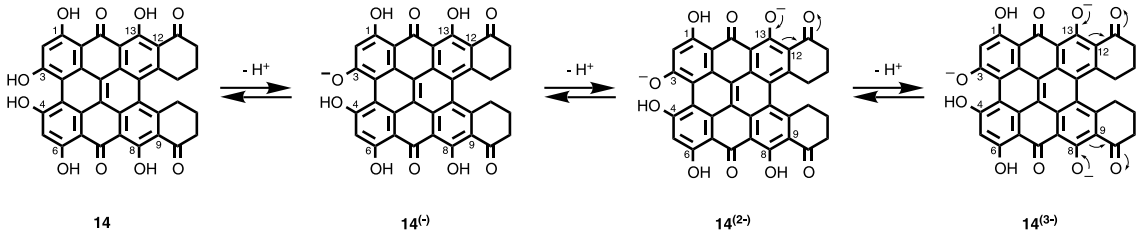


Fig. 2. Absorption spectra of **14** in 80% aqueous *DMSO* at $pH = 0.9$ (a), 1.9 (b), 4.9 (c), 8.6 (d), 10.5 (e), 11.6 (f), and 14.5 (g)

shown in Fig. 2. It was found, that the shoulder at 630 nm disappears at $pH < 1.0$, but increases at higher pH (≥ 8.6). Then a third species (absorbing at about 670 nm) becomes predominant at a $pH > 11.6$. As the *bay*-hydroxyl groups of **1** are known to be quite acidic ($pK_a \sim 2.0$ [16, 17]), the presence of the nondeprotonated form of **14** at $pH < 1.9$ can be assumed. Due to the fact that this spectrum shows a similar λ_{max} as the one in pyridine, where the monodeprotonated species $\mathbf{14}^{(-)}$ should be predominant, it is obvious, that the absorption spectra of **14** and $\mathbf{14}^{(-)}$ are very similar. As the second *bay*-hydroxyl group is highly stabilized by the deprotonated one, the presence of the shoulder at 630 nm at $pH \geq 1.9$ may be assigned to the deprotonation of the 8- and/or 13-*peri*-hydroxyl group. In the case of **14** both groups should possess an increased acidity in comparison to those of **1** ($pK_a \sim 11$ [17]), as the corresponding phenolates (either dideprotonated $\mathbf{14}^{(2-)}$ or also trideprotonated $\mathbf{14}^{(3-)}$) appear to be highly stabilized by the additional 9,12-carbonyl groups (*cf.* Scheme 3). Thus, it seems reasonable that $\mathbf{14}^{(2-)}/\mathbf{14}^{(3-)}$ are also present in the pH-range of 1.9–11.6 with estimated pK_a-values in the order of 5. At $pH > 11.6$ a further deprotonation step was observable, easily explained by a deprotonation of the 1- and/or 6-*peri*-hydroxyl group. Accordingly, the characteristic shoulder at 630 nm in the spectra of **14** in *DMSO* and pyridine may be due to the protonation/deprotonation behaviour of the *peri*-hydroxyl groups of **14**. Anyway, although the absorption maximum itself is only at about 600 nm, the UV-Vis



Scheme 3

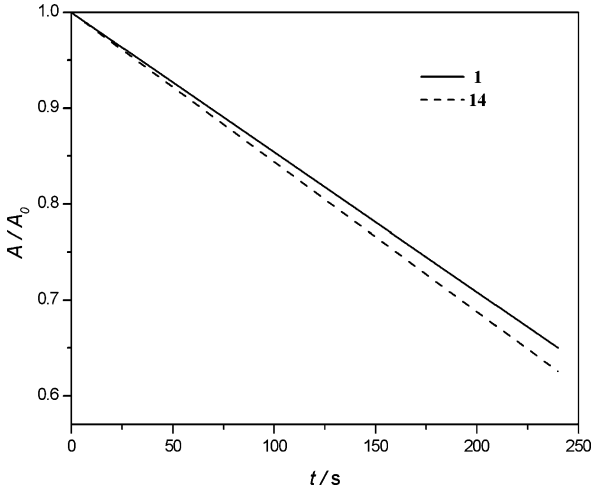


Fig. 3. Hypericin derivative sensitized photooxidation of bilirubin IXα in aerated 80% aqueous ethanol upon irradiation at $\lambda > 570$ nm; normalized absorption (A/A_0) *vs.* time of solutions of disodium bilirubinate IXα with the pyridinium salt of **1** or the pyridinium salt of **14**

spectrum of **14** still shows a quite broad, and maybe useful absorption characteristic, reaching into the wavelength range of common medicinal lasers, even under rather acidic conditions.

For the possible application of **14** in photodynamic therapy (PDT), it was important to investigate the ability of **14** for the generation of singlet oxygen and/or reactive oxygen species. As the hypericin sensitized destruction of bilirubin has been established as a rapid experiment to assess the sensitized production of singlet oxygen and/or reactive oxygen species [2, 18], the sensitized destruction of bilirubin by the mono-pyridinium salt of **14** was compared with that of the mono-pyridinium salt of **1** (Fig. 3). Use of the pyridinium salt was necessary, as **14** had no proper solubility in 80% aqueous ethanol. Accordingly, bilirubin destruction by **14** turned out to be even slightly more efficient than in the case of the reference experiment, which proves that the carbonyl groups introduced in positions 9 and 12 do not interfere with the sensitization processes making **14** a potential candidate for PDT. Due to its low solubility, bilirubin destruction by **13** could not be investigated but could be assumed to be comparably efficient.

Semiempirical Calculations

To clarify the role of tautomerism of **13** and **14**, investigations by means of semiempirical calculations (AM1) were carried out. According to previous calculations by a variety of methods on hypericin (**1**) it is known that ten different tautomers are possible for **1** were the $Q^{7,14}$ tautomer ($Q^{m,n}$ denotes the type of tautomer by indicating the carbonyl positions in superscripts) represents the most stable one [19–24]. For each tautomer of **1** two conformations, namely the ''propeller'' and ''butterfly'' conformations, might exist.

Due to two more carbonyl groups there are 45 tautomers possible in the case of **13** and **14**. Calculations were executed on the propeller conformation only because

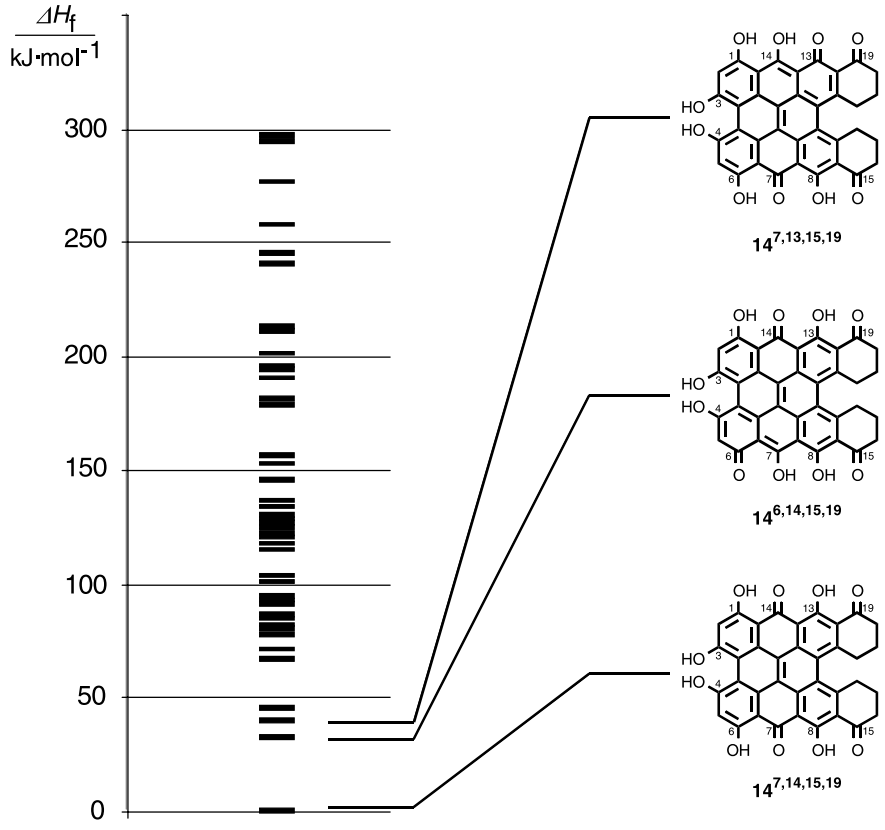


Fig. 4. Relative stability of the 45 possible tautomers of **14** normalized to the energetically most favored one, with the three most stable ones being $\mathbf{14}^{7,14,15,19}$, $\mathbf{14}^{6,14,15,19}$, and $\mathbf{14}^{7,13,15,19}$

the butterfly conformers proved to be of higher energy in selected cases. For **14** all 45 tautomers were investigated. Results on selected tautomers of **13** showed similar results.

As a summary, Fig. 4 presents the heats of formation of the tautomers of **14** which are possible in principle normalized to the most stable one and the structures of the three energetically most favored ones. The lowest heat of formation was found in the case of $\mathbf{14}^{7,14,15,19}$ which is stabilized by 32.6 kJ/mol compared to $\mathbf{14}^{6,14,15,19}$. Comparison of the heats of formation of these tautomers showed, that the most important influence on stability is the degree of aromaticity, which is optimal in the case of the $Q^{7,14}$ tautomer. As the number of quinoid rings increases the heat of formation increases concomitantly. Accordingly, the 7,14-quinoid tautomers of **13** and **14** appear to be the most stable ones, thus excluding tautomerism to be responsible for the characteristic UV-Vis spectra.

Conclusion

Syntheses of 9,12-dicarbonyl substituted hypericin derivatives **13** and **14** were achieved in good yields following an intramolecular *Friedel-Crafts* acylation strategy. Unfortunately, both derivatives showed rather low solubilities and insufficient

bathochromic shifts of their long wavelength absorption maxima. However, in contrast to the unsubstituted **1**, the cyclohexanone condensed **14** has a very broad absorption maximum reaching into the wavelength range of common medicinal lasers. Furthermore, the pyridinium salt of **14** possesses a rather good solubility and also an enhanced ability for the generation of singlet oxygen and/or reactive species, thus making this compound a potential candidate for further investigations towards PDT.

Experimental

Solvents were of p.a. quality unless stated otherwise. Melting points were measured on a *Kofler* melting point microscope (Reichert, Vienna). NMR spectra were recorded on a Bruker Avance DRX 500 MHz spectrometer using a TXI cryoprobe with *z*-gradient coil. 2D NMR experiments were performed 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 coupling constants of 145 Hz for single quantum correlations and 10 Hz for multi-bond correlations. The N*O*ESY mixing time was set to 400 ms. IR and UV-Vis were recorded using a Bruker Tensor 27 and Varian Cary 100 Bio UV-Vis instrument. Mass spectra were recorded on a Thermo Finnigan LCQ Deca XP-Plus. Semiempirical calculations were performed at the SGI Origin 3800 of the ZID at the Johannes Kepler University of Linz with AM1 [25] using geometry inputs from MM3 [26].

3-(9,10-Dihydro-1,3,8-trihydroxy-9-oxoanthracen-6-yl)propanoic acid (**7**, $C_{17}H_{14}O_6$)

An Ar-flushed solution of 150 mg **5** (0.39 mmol) in 35 cm^3 glacial *Ac*OH was heated to reflux. Then 700 mg (3.142 mmol) $SnCl_2 \cdot 2H_2O$ dissolved in 15 cm^3 HBr (47%) were added and refluxed for 60 min. The solution was poured on ice/H_2O, filtrated, and washed with H_2O giving 90 mg **7** (74%). Mp $\geq$ 254°C (decomp); $R_f = 0.05$ ($CHCl_3$:*Et*O*Ac* = 4:1); IR (KBr): $\bar{\nu} = 3556$, 3506, 3160, 2923, 2853, 1712, 1625, 1599, 1486, 1469, 1396, 1380, 1293, 1211, 1163, 1062, 763 cm^{-1}; ^{1}H NMR (500 MHz, *DMSO*-d_6, 30°C): $\delta = 2.58$ (t, $J = 7.32$ Hz, –CH_2–COO–), 2.84 (t, $J = 7.32$ Hz, ar-CH_2–), 4.32 (s, ar-CH_2-ar), 6.23 (s, ar-H2), 6.43 (s, ar-H4), 6.73 (s, ar-H7), 6.85 (s, ar-H5), 10.80 (s, 3-OH), 12.16 (bs, –COOH), 12.22 (s, 8-OH), 12.35 (s, 1-OH) ppm; N*O*ESY (*DMSO*-d_6): 8-OH ↔ ar-H7, 3-OH ↔ ar-H4 and ar-H2, –CH_2– ↔ ar-H5 and ar-H4, ar-CH_2 ↔ ar-H5, ar-H7, and –CH_2–COO–; ^{13}C NMR (125 MHz, *DMSO*-d_6, 30°C): $\delta = 30.4$ (ar-CH_2–), 32.3 (ar-CH_2-ar), 34.1 (–*C*H_2–COOH), 101.2 (C2), 107.3 (C4), 108.4 (C9a), 113.3 (C8a), 114.4 (C7), 119.3 (C5), 142.0 (C10a), 144.9 (C4a), 150.1 (C6), 161.6 (C8), 164.5 (C1), 164.9 (C3), 173.4 (–COOH), 191.3 (C9) ppm; HMBC (*DMSO*-d_6): C1 ↔ ar-H2 and 1-OH, C3 ↔ ar-CH_2–, ar-H2, and ar-H4, C4a ↔ ar-CH_2-ar, C6 ↔ ar-CH_2–, C8 ↔ ar-H7 and 8-OH, C8a ↔ ar-H7 and ar-H5, C9a ↔ ar-H2 and ar-H4, C10 ↔ ar-H4 and ar-H5, C10a ↔ ar-CH_2-ar, ar-CH_2 ↔ –CH_2–COO–, –COO– ↔ –CH_2–COO–; HSQC data were according to structure; ESI-MS (*Me*OH + 1 vol-% NH_3, negative ion mode): $m/z = 313$ ([M-H]$^-$); UV-Vis ($CHCl_3$): λ_{max} (rel. int.) = 272 (64), 304 (57), 357 (100) nm.

4-(9,10-Dihydro-1,3,8-trihydroxy-9-oxoanthracen-6-yl)butyric acid (**8**, $C_{18}H_{16}O_6$)

An Ar-flushed solution of 100 mg (0.251 mmol) **6** in 20 cm^3 glacial *Ac*OH was heated to reflux. Then 451 mg (2.01 mmol) $SnCl_2 \cdot 2H_2O$ dissolved in 7.3 cm^3 HBr (47%) were added and the mixture was refluxed for 60 min. The solution was poured on ice/H_2O, centrifuged, and washed with H_2O giving 55 mg **8** (66%). Mp $\geq$203°C (decomp); $R_f = 0.12$ ($CHCl_3$:*Et*O*Ac* = 4:1); IR (KBr): $\bar{\nu} = 3568$, 3504, 2925, 2855, 1703, 1625, 1601, 1484, 1379, 1273, 1245, 1159, 1056, 914, 870, 797 cm^{-1}; ^{1}H NMR

(500 MHz, *DMSO*-d_6, 30°C): $\delta = 1.82$ (m, 2H, $-CH_2-CH_2-CH_2-$), 2.24 (t, $J = 7.02$ Hz, $-CH_2-$COOH), 2.61 (t, $J = 7.63$ Hz, ar-CH_2-), 4.33 (s, ar-CH_2-ar), 6.23 (s, ar-H2), 6.43 (s, ar-H4), 6.69 (s, ar-H7), 6.81 (s, ar-H5), 10.80 (s, 3-OH), 12.03 (bs, –COOH), 12.22 (s, 8-OH), 12.36 (s, 1-OH) ppm; N*O*ESY (*DMSO*-d_6): 8-OH ↔ ar-H7, 3-OH ↔ ar-H4 and ar-H2, $-CH_2-$ ↔ ar-H5 and ar-H4, ar-CH_2 ↔ ar-H5, ar-H7, and $-CH_2-$; ^{13}C NMR (125 MHz, *DMSO*-d_6, 30°C): $\delta = 25.5$ ($-CH_2-CH_2-CH_2-$), 32.1 (ar-CH_2-ar), 33.1 ($-CH_2-$COOH), 34.7 (ar-CH_2-), 101.0 (C2), 107.4 (C4), 108.7 (C9a), 113.3 (C8a), 114.6 (C7), 119.2 (C5), 142.2 (C10a), 145.1 (C4a), 150.9 (C6), 161.8 (C8), 164.6 (C1), 165.2 (C3), 174.2 (–COOH), 191.2 (C9) ppm; HMBC (*DMSO*-d_6): C1 ↔ ar-H2 and 1-OH, C3 ↔ ar-H2, ar-H4, 3-OH, and ar-CH_2-, C4a ↔ ar-H4, ar-H2, and ar-CH_2-ar, C6 ↔ ar-H5 and ar-H7, C8 ↔ ar-H7 and 8-OH, C8a ↔ ar-H7 and ar-H5, C9a ↔ ar-H2 and ar-H4, C10 ↔ ar-H4 and ar-H5, C10a ↔ ar-H5 and ar-CH_2-ar, ar-CH_2 ↔ $-CH_2-CH_2-COO-$, $-COO-$ ↔ $-CH_2-COO-$; HSQC data were according to structure; ESI-MS (*Me*OH + 1 vol-% NH_3, negative ion mode): $m/z = 327$ ($[M-H]^-$); UV-Vis ($CHCl_3$): λ_{max} (rel. int.) = 272 (71), 304 (55), 357 (100) nm.

10,13-Bis(carboxyethyl)-1,3,4,6,8,15-hexahydroxydibenzo[ao]perylene-7,16-dione (**9**, $C_{34}H_{22}O_{12}$)

A mixture of 70 mg (0.223 mmol) **7**, 3.1 mg (0.011 mmol) $FeSO_4 \cdot 7H_2O$, 113 mg (1.186 mmol) pyridine-*N*-oxide, 1.2 cm^3 dry pyridine, and 111 mm^3 dry piperidine was stirred under Ar in the dark at 115°C for 1 h. After cooling to room temperature, the mixture was poured into 6 cm^3 2*N* HCl and stirred for further 30 min at room temperature (in the dark). After centrifugation the residue was washed three times with HCl (3%), three times with H_2O, and dried over P_2O_5 yielding 60 mg **9** (88%) as a black solid. Mp >350°C; ESI-MS (*Me*OH + 1 vol-% NH_3, negative ion mode): $m/z = 621$ ($[M-H]^-$); UV-Vis (acetone): λ_{max} (rel. int.) = 550 (100), 584 (96) nm. Due to its instability, crude **9** was directly used for the subsequent photocyclisation to **11** without further purification.

10,13-Bis(carboxypropyl)-1,3,4,6,8,15-hexahydroxydibenzo[ao]perylene-7,16-dione (**10**, $C_{36}H_{26}O_{12}$)

A mixture of 50 mg (0.152 mmol) **8**, 2.7 mg (0.0074 mmol) $FeSO_4 \cdot 7H_2O$, 78.7 mg (0.827 mmol) pyridine-*N*-oxide, 1 cm^3 dry pyridine, and 80 mm^3 dry piperidine was stirred under Ar in the dark at 115°C for 1 h. After cooling to room temperature, the mixture was poured into 8 cm^3 2*N* HCl and stirred for further 30 min at room temperature (in the dark). After centrifugation the residue was washed three times with 3% HCl, three times with H_2O, and dried over P_2O_5 yielding 42 mg **10** (85%) as a black solid. Mp >350°C; ESI-MS (*Me*OH + 1 vol-% NH_3, negative ion mode): $m/z = 649$ ($[M-H]^-$); UV-Vis (acetone): λ_{max} (rel. int.) = 549 (100), 581 (95) nm. Due to its instability, crude **10** was directly used for the subsequent photocyclisation to **12** without purification.

10,11-Bis(carboxyethyl)-1,3,4,6,8,13-hexahydroxyphenanthro[1,10,9,8-opqra]perylene-7,14-dione (**11**, $C_{34}H_{20}O_{12}$)

A solution of 60 mg (0.096 mmol) crude **9** in 1500 cm^3 acetone was irradiated for 35 min by means of a 700 W Hg high pressure lamp with fluorescence screen (Philips) under stirring and air admission. After evaporation of the solvent and washing of the resulting residue with $CHCl_3$ 50 mg **11** (84%) were obtained. The purity of **11** was judged from the ^{1}H NMR spectrum to be ≥90%. Mp >350°C; $R_f = 0.11$ ($CHCl_3$:*Me*OH = 3:1); ^{1}H NMR (500 MHz, *DMSO*-d_6, 30°C): $\delta = 6.59$ (s, 2H, ar-H), 7.58 (s, 2H, ar-H), 11.97 (bs, 2H, –COOH), 14.08 (s, 2H, 1-OH and 6-OH or 8-OH and 13-OH), 14.71 (s, 2H, 8-OH and 13-OH or 1-OH and 6-OH) ppm, $-CH_2-$ not observable due to low solubility and solvent overlap, 3-OH and 4-OH not observable; ^{13}C NMR and 2D NMR not possible due to low solubility; IR (KBr): $\bar{\nu} = 3478$, 2929, 2857, 1713, 1613, 1588, 1463, 1417, 1225, 1185, 1112,

847, 752 cm^{-1}; ESI-MS (*Me*OH + 1 vol-% NH_3, negative ion mode): $m/z = 619$ ($[M–H]^-$); UV-Vis (acetone, $c = 8 \cdot 10^{-5}$ mol · dm^{-3}): λ_{max} (ε) = 515 (1900), 553 (4300), 597 (8300) nm (dm^3 · mol^{-1} · cm^{-1}); UV-Vis (*Me*OH, $c = 8 \cdot 10^{-5}$ mol · dm^{-3}): λ_{max} (ε) = 547 (3100), 589 (6100) nm ($dm^3 \cdot mol^{-1} \cdot cm^{-1}$); fluorescence (acetone, $c = 8 \cdot 10^{-7}$ mol · dm^{-3}, $\lambda_{ex} = 550$ nm): λ_{em} (rel. int.) = 603 (100), 651 (27) nm; fluorescence (*Me*OH, $c = 8 \cdot 10^{-7}$ mol · dm^{-3}, $\lambda_{ex} = 550$ nm): λ_{em} (rel. int.) = 597 (100), 644 (30) nm.

10,11-Bis(carboxypropyl)-1,3,4,6,8,13-hexahydroxyphenanthro[1,10,9,8-opqra]perylene-7,14-dione (**12**, $C_{36}H_{24}O_{12}$)

A solution of 42 mg (0.064 mmol) **10** in 1000 cm^3 acetone was irradiated for 45 min by means of a 700 W Hg high pressure lamp with fluorescence screen (Philips) under stirring and air admission. After evaporation of the solvent and washing with $CHCl_3$ 39 mg **12** were obtained (93%). The purity of **12** was judged from the ^1H NMR spectrum to be ≥90%. Mp >350°C; $R_f = 0.17$ ($CHCl_3$: *Me*OH = 3 : 1); ^1H NMR (500 MHz, *DMSO*-d_6, 30°C): $\delta = 6.59$ (s, 2H, ar–H), 7.49 (s, 2H, ar–H), 11.90 (bs, 2H, –COOH), 14.12 (s, 2H, 1-OH and 6-OH or 8-OH and 13-OH), 14.73 (s, 2H, 8-OH and 13-OH or 1-OH and 6-OH) ppm, $–CH_2–$ not observable due to low solubility and solvent overlap, 3-OH and 4-OH not observable, ^{13}C NMR and 2D NMR not possible due to low solubility; IR (KBr): $\bar{\nu} = 3455$, 2928, 2858, 1722, 1710, 1613, 1585, 1463, 1413, 1228, 1183, 1110, 891, 749 cm^{-1}; ESI-MS (*Me*OH + 1 vol-% NH_3, negative ion mode): $m/z = 647$ ($[M–H]^-$); UV-Vis (acetone, $c = 7.4 \cdot 10^{-5}$ mol · dm^{-3}): λ_{max} (ε) = 514 (2000), 552 (5500), 597 (11400) nm ($dm^3 \cdot mol^{-1} \cdot cm^{-1}$); UV-Vis (*Me*OH, $c = 7.4 \cdot 10^{-5}$ mol · dm^{-3}): λ_{max} (ε) = 510 (1400), 546 (4100), 589 (8200) nm ($dm^3 \cdot mol^{-1} \cdot cm^{-1}$); fluorescence (acetone, $c = 7 \cdot 10^{-7}$ mol · dm^{-3}, $\lambda_{ex} = 550$ nm): λ_{em} (rel. int.) = 603 (100), 651 (27) nm; fluorescence (*Me*OH, $c = 7 \cdot 10^{-7}$ mol · dm^{-3}, $\lambda_{ex} = 550$ nm): λ_{em} (rel. int.) = 596 (100), 643 (30) nm.

1,3,4,6,8,13-Hexahydroxy-9,10-(1-oxotrimethylene)-11,12-(3-oxotrimethylene) phenanthro[1,10,9,8-opqra]perylene-7,14-dione (**13**, $C_{34}H_{16}O_{10}$)

A solution of 10 mg (0.016 mmol) **11** in 4 cm^3 *PPA* was stirred at 75°C for 3 h, poured on ice/H_2O, reduced on vacuum until a precipitate was formed, cooled down in the fridge, centrifuged, and washed acid free (first with a saturated NaCl solution, then with H_2O). The residue was triturated with acetone (purification from remaining educt) yielding 7 mg crude **13** (75%). Mp >350°C; IR (KBr): $\bar{\nu} = 3459$, 2945, 2913, 1713, 1614, 1588, 1463, 1419, 1265, 1227, 1185, 1112, 847, 751 cm^{-1}; ESI-MS (*DMF* + 10 vol-% NH_3, negative ion mode): $m/z = 583$ ($[M–H]^-$); UV-Vis (pyridine, $c \sim 3 \cdot 10^{-5}$ mol · dm^{-3}): λ_{max} (rel. int.) = 588 (52), 603 (100) nm; fluorescence (pyridine, $c \sim 7 \cdot 10^{-7}$ mol · dm^{-3}, $\lambda_{ex} = 550$ nm): λ_{em} (rel. int.) = 609 (100), 659 (27) nm. Due to its very limited solubility, no characterisation by NMR spectra was possible.

1,3,4,6,8,13-Hexahydroxy-9,10-(1-oxotetramethylene)-11,12-(4-oxotetramethylene)phenanthro[1,10,9,8-opqra]perylene-7,14-dione (**14**, $C_{36}H_{20}O_{10}$)

A solution of 10 mg (0.015 mmol) **12** in 4 cm^3 *PPA* was stirred at 70°C for 2.5 h, poured on ice/H_2O, reduced on vacuum until a precipitate was formed, put in the fridge, centrifuged, and washed acid free (first with a saturated NaCl solution, then with H_2O). The residue was dried over P_2O_5 yielding 8 mg **14** (87%). Mp >350°C; ^1H NMR (500 MHz, *DMSO*-d_6, 30°C): $\delta = 6.62$ (s, 2H, ar–H), 14.69 (s, 2H, 1-OH and 6-OH or 8-OH and 13-OH), 15.25 (s, 2H, 8-OH and 13-OH or 1-OH and 6-OH), 18.48 (s, 1H, 3-OH or 4-OH) ppm, $–CH_2–$ not observable due to low solubility and solvent overlap, ^{13}C NMR and 2D NMR not possible due to low solubility; IR (KBr): $\bar{\nu} = 3455$, 2925, 2856, 1611, 1537, 1416, 1177, 1103, 997, 830 cm^{-1}; ESI-MS (*DMSO*:*Me*OH = 1:3 + 1 vol-% NH_3, negative ion mode):

$m/z = 611$ ([M–H]$^-$); UV-Vis (pyridine, $c \sim 3 \cdot 10^{-5}$ mol · dm^{-3}): λ_{max} (rel. int.) = 602 (100) with a characteristic shoulder at 631 (50) nm; UV-Vis (*DMSO*, $c \sim 5 \cdot 10^{-5}$ mol · dm^{-3}): λ_{max} (rel. int.) = 568 (76), 601 (100) with a characteristic shoulder at 630 (66) nm; fluorescence (pyridine, $c \sim 3 \cdot 10^{-6}$ mol · dm^{-3}, $\lambda_{ex} = 550$ nm): λ_{em} (rel. int.) = 608 (100), 657 (34) nm; fluorescence (*DMSO*, $c = 5.44 \cdot 10^{-6}$ mol · dm^{-3}, $\lambda_{ex} = 550$ nm): λ_{em} (rel. int.) = 615 (100), 657 (56) nm.

The pyridinium salt of **14** was prepared by dissolving 5 mg **14** in 5 cm^3 pyridine and evaporation of the solvent.

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