Synthesis and Photophysical Properties of a Deazaflavin-Bridged Porphyrinatoiron(III) That Mimics the Interaction of a Deazaflavin Inhibitor with the Heme-Thiolate Cofactor of Cytochrome P450 3A4

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Cytochrome P450 3A4 metabolizes a majority of administered therapeutic agents in the human liver. We recently reported the synthesis of a new inhibitor, **1**, whose binding to and displacement from the active site of CYP 3A4 can be conveniently followed by the associated changes in fluorescence intensity. Here we report the synthesis of a bichromophoric compound, **6**, in which deazaflavin was strapped over the distal side of a porphyrinatoiron(III) complex to mimic the envisaged enzyme–inhibitor interaction within the active site. Femtosecond pump–probe and fluorescence spectroscopies were used to study the photophysical processes of **6**. Rapid intramolecular energy transfer and enhanced intersystem-crossing processes induced by the high-spin Fe^{III} central ion are responsible for the complete suppression of deazaflavin fluorescence in **6**. Fluorescence quenching is less efficient in the iron-free analogue of **6**, *i.e.*, in **21**.

1. Introduction. – Cytochrome P450 3A4 (CYP 3A4), a heme–thiolate protein, is one of the most important P450s in the human liver [1]. The ability of CYP 3A4 to metabolize a majority of administered therapeutic agents accounts for the large number of documented drug–drug interactions associated with CYP 3A4 inhibition [2]. It is therefore of great importance to know the affinity of new drug candidates to CYP 3A4 at an early stage, in order to determine their potential as inhibitors, and to evaluate their influence on the metabolism of co-administered drugs. Some particular features of CYP 3A4 make it difficult to achieve this goal. Though X-ray structures are now available from truncated CYP 3A4 [3], these pictures provide no clues on how the enzyme accepts substrates as different as, *e.g.*, erythromycin and nifedipine, how the active site accommodates more than one substrate [4], and why partial inhibition and even activation is observed when pairs of drugs are co-incubated [5].

Our group has recently reported [6] the synthesis of a new inhibitor **1** that displayed favourable IC_{50} values in the range of 1–4 μM for three characteristic substrates of CYP 3A4 such as testosterone (**2**), midazolam (**3**), and nifedipine (**4**) (*Fig. 1*). The binding of **1** to the active site of CYP 3A4 and its displacement by other substrates can be followed by the associated change in the intensity of the deazaflavin fluorescence [7], such that a screening for drugs that might cause drug–drug interactions requires neither the determination of substrate turnover nor product analyses.

From these experiments, it was suggested [6] that the fluorescence of **1** is quenched upon binding to CYP 3A4 due to an interaction such as that shown in structure **5** of the

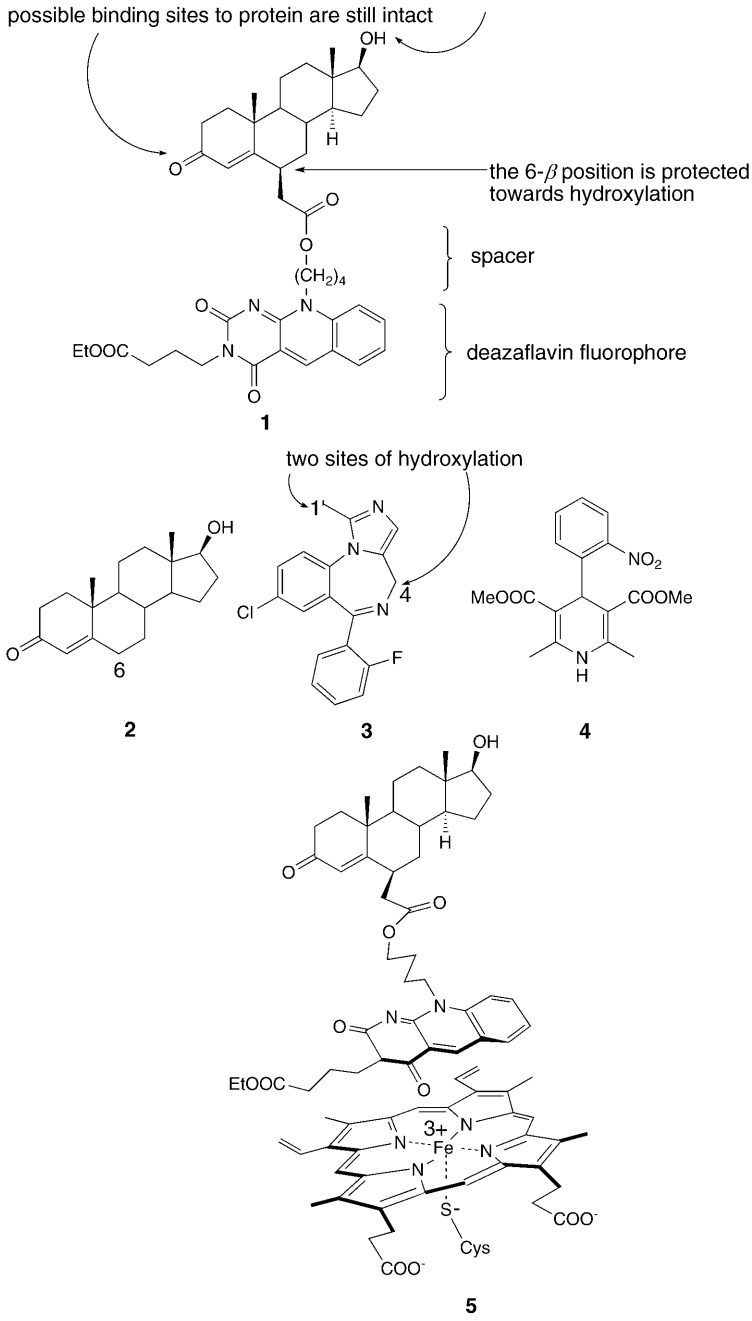


Fig. 1. *The new inhibitor* **1**, *substrates* **2**–**4** [8], *and the envisaged orientation of* **1** *towards the cofactor of CYP 3A4 as shown in structure* **5**

Fig. 1. We now report our efforts to understand the origin of this fluorescence quenching by means of the model system **6** (see *Scheme*).

2. Results and Discussion. – The target molecule **6** contains a thiolato ligand, which coordinates to iron(III) and mimics the cysteine S^- ion of native P450s [1]. The opposite face of the porphyrin is strapped with the deazaflavin chromophore *ca.* 4.5 Å above the porphyrin plane; the complete system models the envisaged interaction of the fluorescent chromophore of the inhibitor **1** with the cofactor of CYP 3A4, as in **5**.

The porphyrin **7** was prepared as described previously [9]. The synthesis of the deazaflavin strap started with commercially available **8** and **9**, which were converted to **10** and **11**, respectively, by adaptation of known procedures [10], the latter *via* intermediates **12**–**15**. Condensation of **10** and **11** furnished **16**, which was cyclized to the deazaflavin derivative **17**. *N*-Alkylation of **17** led to **18** [11] which, after saponification [12], gave the diacid **19** that was converted to the activated ester **20**, ready for macrocyclization with the diamino-porphyrin **7**. Iron was inserted into the resulting doubly bridged porphyrin **21** to form the desired product **6** (*Scheme*).

No fluorescence was detected from a solution of the porphyrinatoiron(III) **6** in MeCN by using a conventional fluorescence spectrometer. This result, though it did confirm the concept, nevertheless came as a surprise, because binding of **1** to cytochrome P450 3A4 leaves a residual fluorescence of *ca.* 20% of the intensity of that of **1** in the absence of enzyme [6]. Three intramolecular processes for fluorescence quenching may be envisaged to occur in the dyad **6** [13]: *i*) resonance energy transfer, *ii*) electron transfer, and *iii*) enhanced intersystem crossing (ISC) induced by the high-spin Fe^{III} centre. The last process is not operative in iron-free **21**.

The fluorescence properties of deazaflavin **18**, porphyrin **7**, and dyad **21** in degassed MeCN solution were recorded with a streak camera following sub-picosecond excitation at 388 or 310 nm. The measured lifetimes are collected in *Table 1* together with the wavelengths of selected absorption and emission maxima.

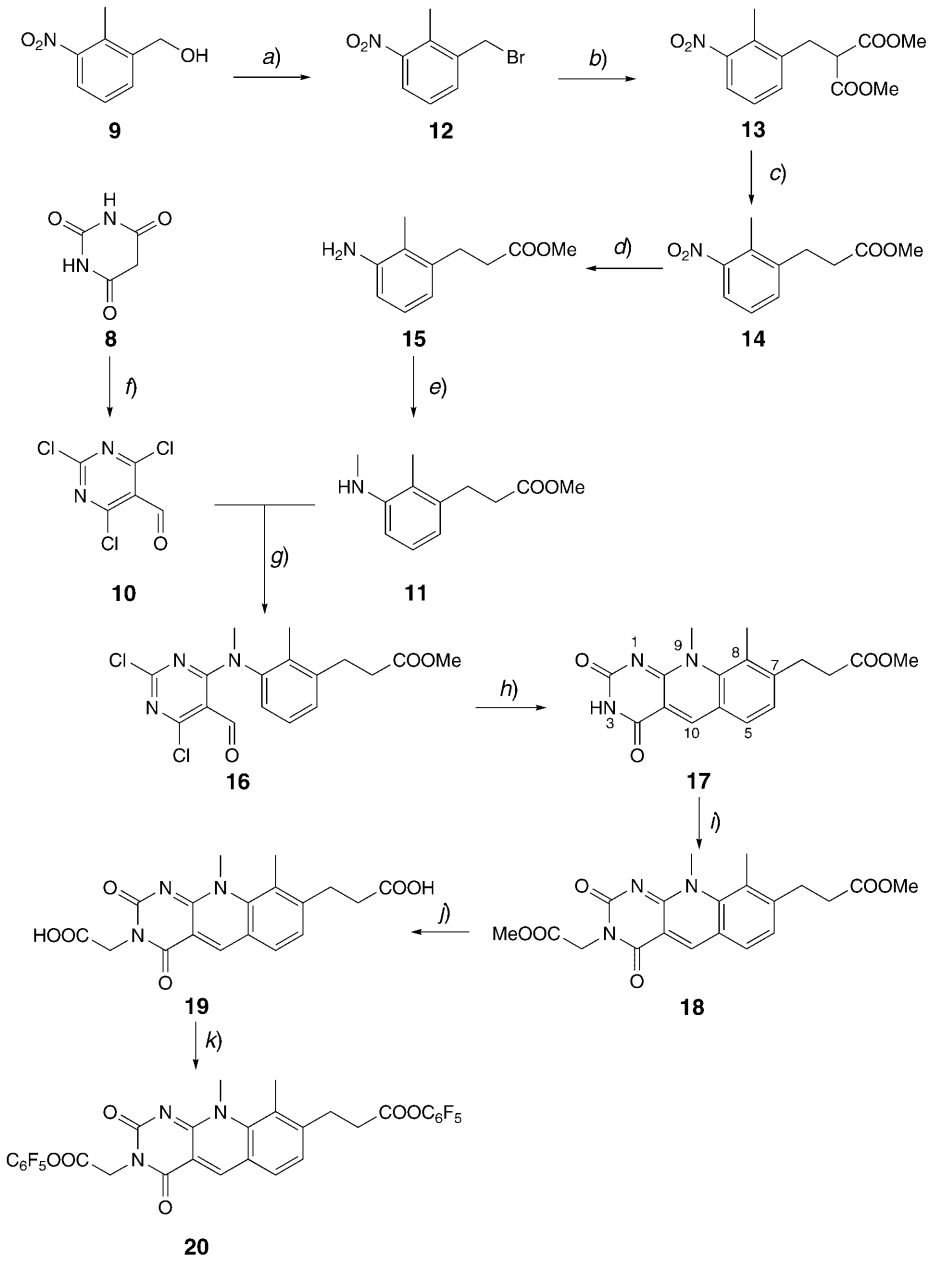
Table 1. *Absorption and Emission Properties of* **18**, **7**, *and* **21** *in Degassed MeCN*

	Absorption	Fluorescence			
	λ_{max}/nm	emission λ_{max}/nm	excitation λ_{max}/nm	lifetime τ/ns (475 nm)[a])	lifetime τ/ns (698 nm)[b])
18	265, 339, 403	475	403	3.0 ± 0.2	
7	414, 509, 544, 576, 630	631, 698	414	–	10.3 ± 0.4
21	348, 414, 510, 544, 577, 634	635, 700	414	–	2.3 ± 0.2
18 + **7**[c])				2.2 ± 0.2	9.4 ± 0.4

[a]) Deazaflavin unit. [b]) Porphyrin unit. [c]) 10^{-3} M each.

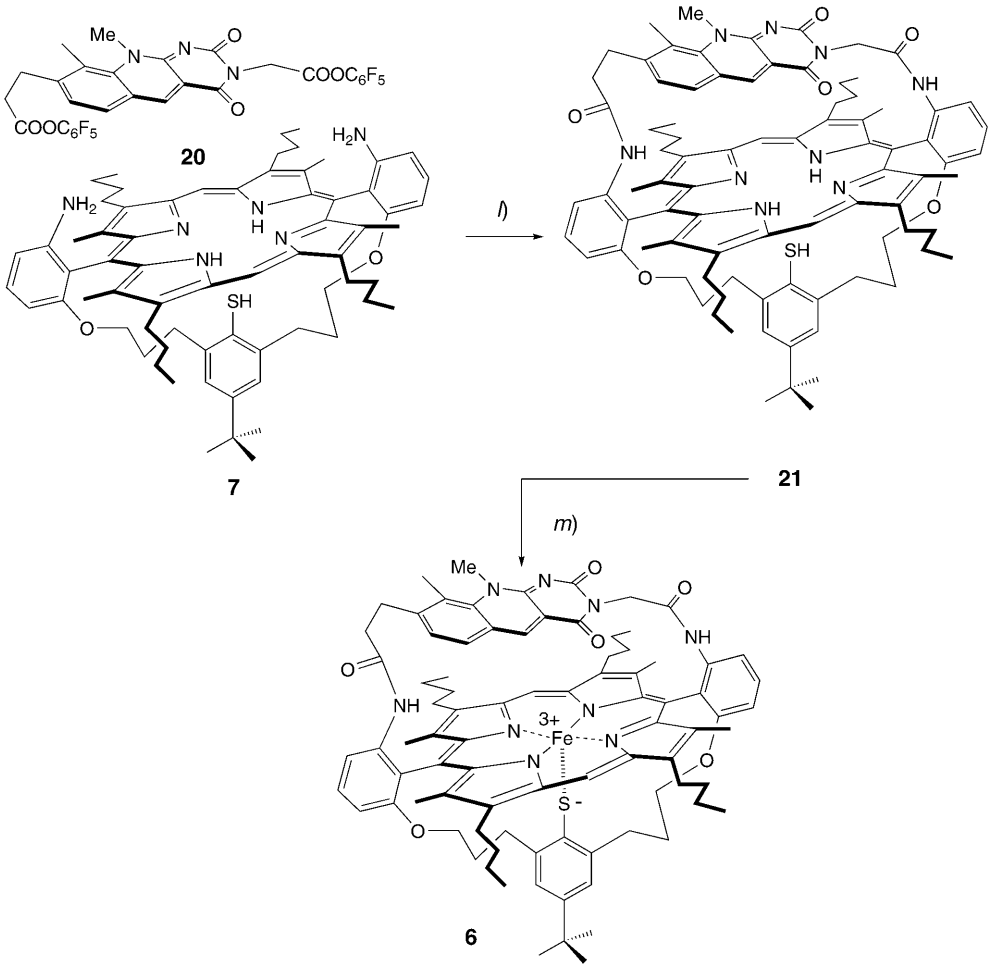
We introduce the following notation to characterize the electronic states of the dyads **21** and **6**: The letter P is used for the porphyrin moiety, P_{Fe} for porphyrinatoiron(III), and F for the deazaflavin unit, thus, **21** = P – F and **6** = P_{Fe} – F. The lowest locally excited singlet and triplet states of the P and F moieties are designated as $^1P^*$

Scheme. *Synthesis of the Doubly Bridged Porphyrinatoiren* **6**



a) PBr_3, Et_2O, r.t. → 50°, 1 h. *b*) NaH, $CH_2(COOMe)_2$, DMSO, 0° → r.t., 45 min, **12**, r.t., 45 min. *c*) LiI, DMF/H_2O 9:1, 160°, 7 h. *d*) 5% Pd/C, H_2, 1 bar, EtOH, r.t., 4 h. *e*) NaH, MeI, r.t., 45 min. *f*) DMF, $POCl_3$, 0°, 15 min, **8**, 100°, 4 h. *g*) CH_2Cl_2, 100°, 5 min. *h*) CF_3COOH (98%), 60°, 1 h. *i*) K_2CO_3, $BrCH_2COOMe$, DMF, r.t., 10 h. *j*) $LiOH \cdot H_2O$, THF/H_2O 3:2, r.t., 1 h. *k*) *N*-[3-(dimethylamino)propyl]-*N*′-ethylcarbodiimide hydrochloride (EDC·HCl), C_6F_5OH, DMF, r.t., 1 h. *l*) **20** (2.5 equiv.), dry DMF, 100°, 4 h; 37%. *m*) 2,6-Lutidine (20 equiv.), $FeBr_2$ (14 equiv.), dry toluene, 120°, 45 min; 89%.

Scheme (cont.)



and ^{3}P* and ^{1}F* and ^{3}F*, respectively. Charge-transfer states of dyad **21** are denoted as $P^{+\bullet} - F^{-\bullet}$ and $P^{-\bullet} - F^{+\bullet}$.

The fluorescence lifetimes measured at the two emission maxima of the metal-free porphyrin **7** (631 and 698 nm) were equal and independent of the excitation wavelength. Emission from the locally excited deazaflavin chromophore of the iron-free dyad **21**, P – ^{1}F*, was not detectable. Following excitation of the deazaflavin chromophore of **21**, *i*) resonance energy transfer to the porphyrin forming ^{1}P* – F, or *ii*) electron transfer yielding the charge-separated state $P^{+\bullet} - F^{-\bullet}$ may be considered. The fluorescence emission of deazaflavin **18**, λ_{max} 475 nm, overlaps well with the Q-band absorption of porphyrin **7**, λ_{max} 509 nm (*Fig. 2*). Thus, intramolecular energy transfer between the two chromophores of **21**, *i.e.*, from locally excited deazaflavin to the porphyrin moiety, P – ^{1}F* → ^{1}P* – F, is expected to be rapid.

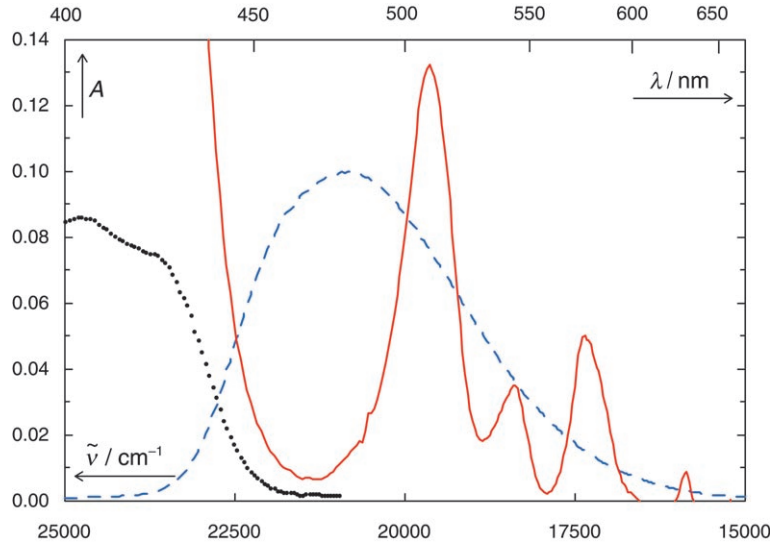


Fig. 2. *Spectral overlap between the Q-band absorbance A* (——) *of porphyrin* **7** ($1\cdot10^{-5}$ M, 1-cm path length) *and the* (uncorrected) *fluorescence emission* (– – – –) *of deazaflavin diester* **18**. The absorbance *A* (·····) of **18** ($1\cdot10^{-5}$ M, 1-cm path length) is shown on the left.

The reverse energy transfer $^1P^* - F \rightarrow P - {}^1F^*$ cannot occur because this would be highly endothermic. Yet, the fluorescence lifetime of dyad **21** in the porphyrin locally excited state $^1P^* - F$ is much shorter than that of porphyrin **7**. Also, diffusional quenching of the fluorescence of **7** is observed when 10^{-3} M deazaflavin **18** is added to the solution (*Table 1*). These quenching processes are attributed to electron transfer, $^1P^* - F \rightarrow P^{+\bullet} - F^{-\bullet}$. Similar behavior has been reported for porphyrin–quinone systems [14]; their fluorescence lifetimes increase by an order of magnitude when the quinone moieties are reduced. To evaluate the energetic feasibility of electron transfer processes in **21**, we determined electrochemical potentials E° in MeCN (*Table 2*). The standard reduction potentials of the quinones in the porphyrin–quinone cyclophanes, $E^\circ(Q/Q^{-\bullet}) = -0.72$ to -1.45 V [15], are comparable to that of deazaflavin **18**, $E^\circ(F/F^{-\bullet}) = -0.98$ V.

Table 2. *Standard Electrochemical Potentials* E° (*vs.* SCE) *of Compounds* **6**, **7**, **18**, *and* **21** *Determined by Differential Pulse Voltammetry in MeCN with 0.1*M *$LiClO_4$*. P = porphyrin moiety, F = deazaflavin unit.

	Redox couple	E°/V		Redox couple	E°/V
18	$E^\circ(F^{+\bullet}/F)$	*ca.* +1.93[a])	**21**	$E^\circ(P^{+\bullet}/P)$	+0.73
	$E^\circ(F/F^{-\bullet})$ [16]	−0.98		$E^\circ(F/F^{-\bullet})$	−0.91
7	$E^\circ(P^{+\bullet}/P)$	+0.68		$E^\circ(P/P^{-\bullet})$	−1.31
	$E^\circ(P/P^{-\bullet})$	−1.07	**6**	$E^\circ(P^{+\bullet}/P)$	+0.84
				$E^\circ(F/F^{-\bullet})$	−1.10
				$E^\circ(P/P^{-\bullet})$	−1.55

[a]) Irreversible.

Combination of these data with the excitation energy of **21**[1]) shows that intramolecular electron transfer from the locally excited porphyrin of dyad **21**, $^1P^* - F$, to generate the charge transfer state $P^{+\bullet} - F^{-\bullet}$ is energetically feasible: $\{E^\circ(P^{+\bullet}/P) - E^\circ(F/F^{-\bullet})\}e - E_{0-0}(^1P^* - F) = \{0.73 - (-0.91) - 1.96\}$ eV $= -0.32$ eV[2]). On the other hand, the reverse electron transfer, $^1P^* - F \rightarrow P^{-\bullet} - F^{+\bullet}$, would be strongly endothermic: $\{E^\circ(F^{+\bullet}/F) - E^\circ(P/P^{-\bullet})\}e - E_{0-0}(^1P^* - F) = \{1.93 - (+1.31) - 1.96\}$ eV $= +1.28$ eV. An energy diagram for the deactivation processes occurring after excitation of **21** is shown in *Fig. 3*.

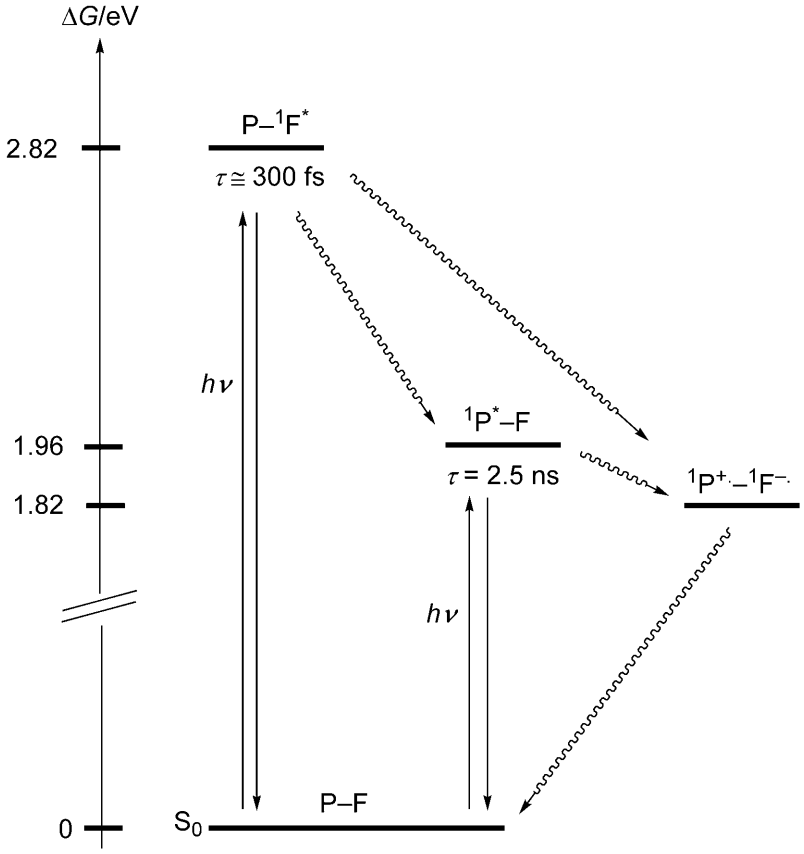


Fig. 3. *Energy diagram and possible deactivation processes following excitation of the deazaflavin-bridged porphyrin* **21**. P = porphyrin moiety, F = deazaflavin unit.

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[1]) The positions of the first absorption and emission bands (634 and 635 nm, resp., *Table 1*) define the energy $E_{0-0}(^1P^* - F)$ as 1.96 eV.

[2]) The *Coulomb* attraction C for stabilization of the charge-transfer complex $P^{+\bullet} - F^{-\bullet}$ is neglected: $C/e \approx 14.4/(\varepsilon R)$ V/pm ≈ 0.04 V, assuming an average distance between the charges $R \approx 500$ pm and a dielectric constant $\varepsilon = 100$ for MeCN.

Fluorescence emission from the charge-transfer state $P^{+\bullet} - F^{-\bullet}$ is not observed, presumably due to the low transition moment for radiative back electron transfer. The pump–probe spectra of **7**, **21**, and **18** shown in *Fig. 4* appear within the laser pulse. Assignment of the transient spectrum obtained with **21** to the locally excited singlet $^1P^* - F$ is strongly supported by its similarity with that obtained with the porphyrin **7** and by the fact that its lifetime of *ca.* 2.5 ns is consistent with the fluorescence lifetime of **21**.

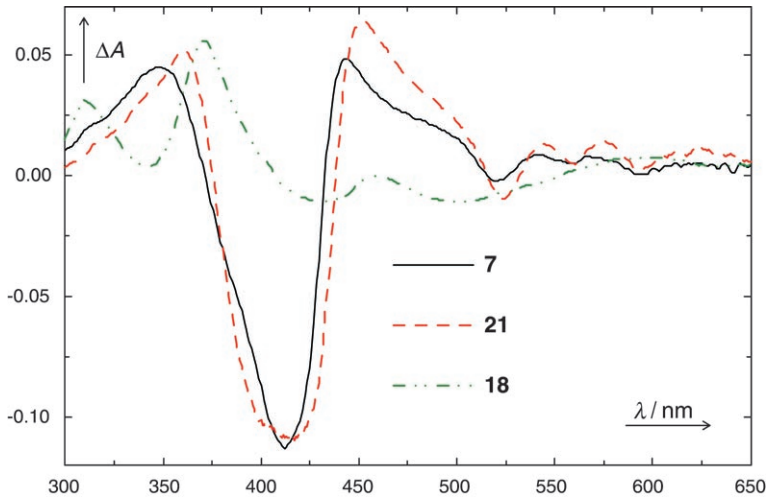

Fig. 4. *Pump–probe spectra taken 1 ps after excitation of porphyrin* **7** (——), **21** (– – –), *and deazaflavin* **18** (–••–••) *in MeCN*

We now turn to the dyad **6** with the porphyrinatoiron(III) complex, which did not exhibit any fluorescence, so that information could only be gained from the transient absorption spectra (*Fig. 5*). Immediately after the excitation, two main features of the porphyrin excited state, namely strong bleaching at 405 nm and absorption at 460 nm, appeared. These features were similar to those obtained with the iron-free dyad **21** (*Fig. 4*). The subsequent changes were, however, complex and differed substantially from those observed with **21**.

Previous studies [17] have shown that excited porphyrinatoiron(III) complexes relax very rapidly (*ca.* 50 fs) to their ground states, presumably due to the presence of several low-lying charge-transfer states. *Franzen* and co-workers recently reported that ultra-fast iron-to-porphyrin charge transfer is initiated by excitation of haemoglobins [18]. Porphyrin-to-iron back charge transfer subsequently produces a low-lying electronic state with a non-equilibrium d-orbital population on the Fe-atom. Such charge-transfer reactions may also occur in **6**. Moreover, the pump pulse initially excites both chromophores of **6**. The spectra detected immediately after the excitation of **6** are thus attributed to a combination of porphyrin and deazaflavin excited singlet states with, possibly, a contribution from an iron-to-porphyrin charge-transfer state.

The strong bleaching at 405 nm, which is due to depletion of the ground state of **6**, partially (*ca.* 50%) recovers rapidly, $\tau \approx 750$ fs, and then more slowly, $\tau \approx 11$ ps (*ca.*

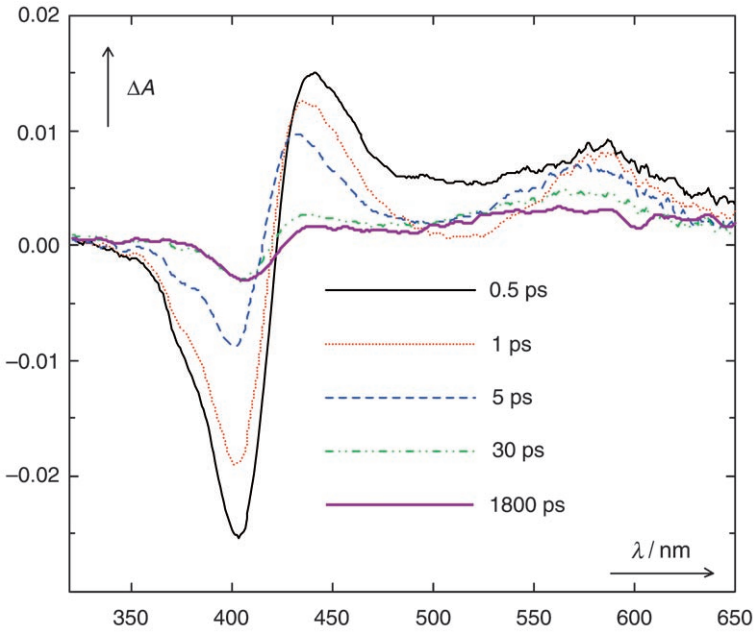

Fig. 5. *Pump–probe spectra taken at various delays after excitation of* **6** *in MeCN at 288 nm*

40%). Full recovery of the porphyrin ground state takes longer than 2 ns. The very broad initial absorption ranging from 430 to 650 nm decays within 200 fs around 500 nm, while a new broad band appears around 570 nm with a risetime of *ca.* 750 fs. Porphyrin triplets are known to exhibit broad absorbance centred around 600 nm [19]. We therefore attribute the long-lived, 570-nm transient to the porphyrin triplet state of **6**, $^3P_{Fe}^* - F$, and the 750-fs kinetics to the lowest singlet state of **6**, $^1P_{Fe}^* - F$, which decays by a combination of ISC to $^3P_{Fe}^* - F$ and radiationless conversion [17][18]. No significant signal was detected at 680 nm, where the porphyrin radical cation usually displays its absorbance [19–21], *i.e.*, formation of a $P_{Fe}^{+\cdot} - F^{-\cdot}$ charge-transfer state was not observed.

All synthetic porphyrinatoiron(III) complexes carrying a thiolato ligand coordinated to the Fe-atom are high-spin [22]. The unusually fast intersystem crossing of $^1P_{Fe}^* - F$ is, therefore, attributed to a substantial interaction of the d-electrons of Fe^{III} with the unpaired electrons of the porphyrin singlet state $^1P_{Fe}^* - F$.

Our tentative assignments of the observed processes are summarized in the energy diagram of *Fig. 6*. Here, the energy of the deazaflavin triplet, $P_{Fe} - {}^3F^*$, $E_{0-0} = 2.58$, was assumed to be equal to that of 3,10-dimethyl-5-deazaflavin [23] and that of the porphyrin triplet, $^3P_{Fe}^* - F$, equal to that of tetraarylporphyrinatometals, $E_{0-0} = 1.50$ [24].

3. Conclusions. – Compound **6** was studied as a model system for the interaction of the deazaflavin inhibitor **1** and native CYP 3A4. To mimic the enzyme–inhibitor interaction within the active site, deazaflavin was strapped over the distal side of a porphyrinatoiron(III). A new synthetic approach for 8-alkylated deazaflavins was developed.

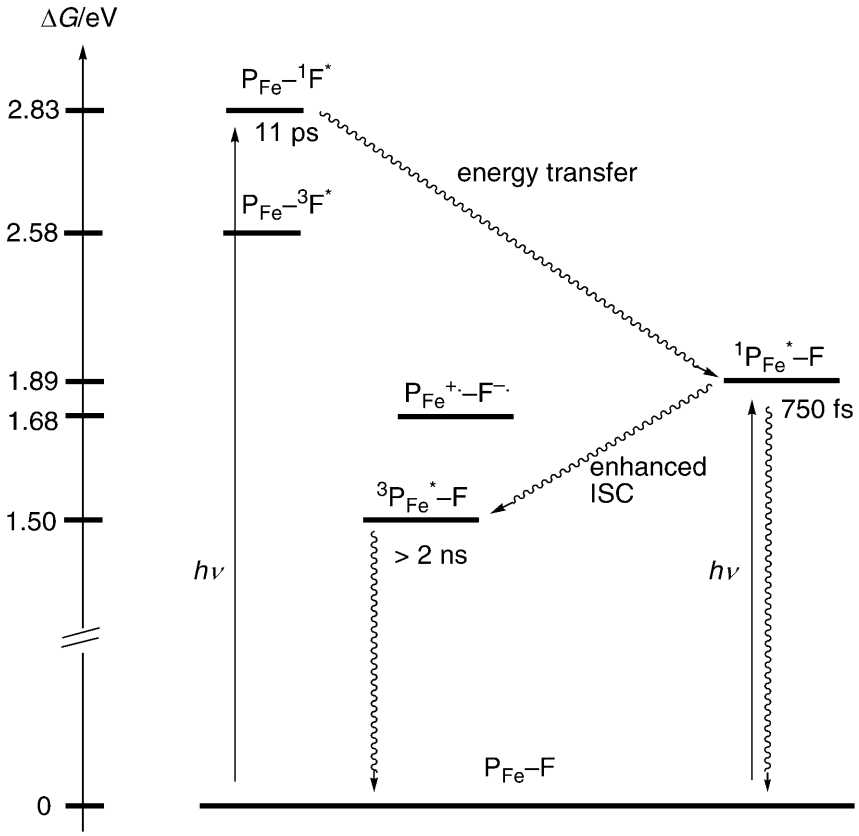

Fig. 6. *Energy diagram and radiationless transitions following excitation of the deazaflavin-bridged iron porphyrin* **6**. P = porphyrin moiety, F = deazaflavin unit.

Compound **6** was synthesized in 26 steps comprising the synthesis of diamino–porphyrin **7**, followed by coupling with deazaflavin active ester **18** to provide the iron-free compound **21** and, after iron(III) insertion, the model compound **6**. A study of the electrochemical and the time-resolved optical properties of compounds **21** and **6** showed that the mechanism of fluorescence quenching differs strongly in the two dyads. Radiationless deactivation of the locally excited deazaflavin of the iron-free compound **21**, $P-{}^1F^*$, proceeds either by electron transfer forming a charge-separated state, $P^{+\bullet}-F^{-\bullet}$, or by energy transfer to the porphyrin unit, ${}^1P^*-F$, or both.

The presence of a high spin, paramagnetic iron(III) is responsible for the complete suppression of fluorescence in model compound **6**. It is suggested that the locally excited state ${}^1P_{Fe}^*-F$, that is formed by excitation of the porphyrin moiety of **6** and, in part, by energy transfer from $P_{Fe}-{}^1F^*$, has a lifetime of only 750 fs due to rapid radiationless relaxation and enhanced ISC to ${}^3P_{Fe}^*-F$.

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Experimental Part

General. Chemicals were purchased from *Aldrich*, *Sigma*, or *Fluka* and were used without further purification, if not otherwise stated. Solvents were purified by standard procedures. TLC: *Merck* precoated silica gel *60 F_{254}* glass plates (0.25-mm layer); *Merck RP-18 F_{254s}* glass plates (0.25-mm layer). Column chromatography (CC): *Merck* silica gel *60* (0.04–0.063 mm); visualization by UV light (254 nm) and fluorescence (366 nm); FC = flash chromatography. UV/VIS Spectra: *Hewlett-Packard 8452A* spectrophotometer; λ in nm (ε). Fluorescence spectra: *ISA Jobin Yvon-Spex Fluoromax-2*; λ in nm. IR Spectra: *Perkin-Elmer FTIR-1600* spectrophotometer; absorptions in cm^{-1}. ^{1}H- (250, 400, 500, and 600 MHz) and ^{13}C-NMR (400 and 500 MHz) Spectra: in $CDCl_3$, *Bruker av250*, *DPX-NMR*, *Bruker DRX-500*, and *Bruker DRX-600* instruments; at 298 K if not otherwise stated; δ in ppm, coupling constants J in Hz. EI- or FAB-MS: *Varian-VG-70-250* or *Bruker Esquire3000+* for ESI-MS; in m/z (rel. %). Elemental analysis: *Perkin-Elmer 240* analyzer.

Picosecond Pump–Probe Spectroscopy. Ti:Sa Laser system *Clark MXR CPA-2001* (775 nm, pulse energy 0.8 mJ, full width at half maximum (*fwhm*) 150 fs, operating frequency 426 Hz). Part of the beam was fed into a *Clark-MXR NOPA*. The output at 540 nm was frequency-doubled to 270 nm and, after compression, provided pump pulses with an energy of 1 μJ and $<$100 fs pulse width. A probe beam continuum (300–680 nm) was produced by focusing part of the 775-nm beam 1 mm in front of a CaF_2 crystal of 2 mm path length. The detection system has been described [25]. Two-photon absorption is observed when the pump and probe pulses coincide at the sample. The *fwhm* of the two-photon absorption in H_2O was 180 fs, which provides a measure of the time resolution of the detection system. Typically, several hundred spectra were collected and averaged for each delay. The translation stage allowed for a maximum time delay of 1.8 ns for the probe beam.

Time-Resolved Fluorescence Spectroscopy. Hamamatsu-C5680 streak camera equipped with a with *Chromex-250IS* polychromator unit. Excitation laser pulses (pulse length 140 fs) centred at 310 nm were provided by frequency doubling of the *Clark-MXR-NOPA* output. The excitation beam was focused into the 1-mm sample cell under 45° angle, providing front-side excitation. Incident fluorescence light was collimated and then focused into the polychromator. The *C5680* unit recorded the time and spectrally resolved fluorescence. The optical grating was chosen to allow recording fluorescence spectra in 300-nm windows from 250 to 1100 nm. Typically, 500 scans were averaged after electronic jitter and background corrections. A reflection of the excitation laser beam was recorded for use in a reconvolution procedure, which improved the lifetime resolution. All samples for the time-resolved spectroscopy were carefully degassed by four freeze-pump-thaw cycles to a final pressure of *ca.* 10^{-4} Torr.

Differential Pulse Voltammetry. Eco-Chemie-BV-μAutolab type *II* potentiostat; data were collected by a three-electrode technique comprising a working electrode (glassy carbon), a counter electrode (Pt-net), and a reference electrode (Ag-wire). Electrolyte: 0.1M $LiClO_4$ in degassed MeCN. Ferrocene (Fc^+/Fc = +0.41 V *vs.* SCE (saturated calomel electrode) in MeCN [26]) was used as an internal reference. Standard electrode potentials E° are given *vs.* SCE; for conversion to NHE (normal hydrogen electrode) add 0.241 V [27]. All compounds except deazaflavin gave reversible waves for the potentials quoted.

2,4,6-Trichloropyrimidine-5-carboxaldehyde (**10**). To DMF (9.6 ml, 124.8 mmol), $POCl_3$ (48 ml, 524.2 mmol) was added dropwise at 0°. After 15 min stirring at 0°, **8** (8.02 g, 62.4 mmol) was added. After 4 h stirring at 100°, the mixture was directly evaporated. The residue was dissolved in ice-cooled H_2O. The precipitate was filtered, washed with H_2O, and purified by FC (CH_2Cl_2): 7.82 g (59%). Colorless crystals. M.p. 131–132°. R_f 0.48 (CH_2Cl_2). IR (KBr): 2833.7*w*, 1706.3*s*, 1525.9*s* 1499.0*s*, 1299.5*m*, 1118.7*m*, 885.9*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 10.41 (*s*, 1 H). ^{13}C-NMR (400 MHz, $CDCl_3$): 184.95; 164.433; 123.97. EI-MS: 208.9 (100, $[M+1]^+$), 173.9 (10, $[M-Cl]^+$), 146.9 (5), 120 (11), 85 (23). Anal. calc. for C_5HCl_3O (211.44): C 28.40, H 0.48, N 13.25, O 7.57; found: C 28.45, H 0.49, N 13.19, O 7.70.

1-(Bromomethyl)-2-methyl-3-nitrobenzene (**12**). To a soln. of **9** (20.0 g, 120 mmol) in Et_2O (200 ml), PBr_3 (18.6 ml, 197 mmol) was added dropwise at r.t. After stirring 1 h at 50°, the soln. was cooled to r.t. and hydrolyzed with H_2O (50 ml). The aq. layer was extracted with Et_2O, the combined org. phase dried (Na_2SO_4) and concentrated, and the residue purified by FC (CH_2Cl_2): **12** (27.4 g, 99%). Light yellow crystals. M.p. 42–43°. R_f 0.74 (CH_2Cl_2). IR (KBr): 3079.5*w*, 1525.5*s*, 1454.0*m*, 1357.2*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.71 (*d*, J = 8.1, 1 H); 7.54 (*d*, J = 7.6, 1 H); 7.30 (*t*, J = 8.1, 1 H); 4.54 (*s*, 2 H); 2.51 (*s*, 3 H).

^{13}C-NMR (400 MHz, $CDCl_3$): 151.96; 139.07; 134.31; 131.97; 127.24; 124.78; 30.99; 14.87. EI-MS 229.0 (6, M^+), 214.0 (6, $[M-Me]^+$), 183.0 (1, $[M-NO_2]^+$), 150.1 (100, $[M-Br]^+$), 132.1 (7), 103.1 (42), 77.1 (20), 51.0 (11). Anal calc. for $C_8H_8BrNO_2$ (230.06): C 41.77, H 3.51, N 6.09; found: C 41.76, H 3.30, N 6.04.

Dimethyl 2-[(2-Methyl-3-nitrophenyl)methyl]propanedionate (**13**). To a soln. of NaH (13.1 g, 328 mmol) in DMSO (150 ml), $CH_2(COOMe)_2$ (38 ml, 328 mmol) was added dropwise under cooling in an ice bath. Then **12** (15.1 g, 65.6 mmol) was added at r.t. within 45 min. The soln. was poured into ice-cooled H_2O (200 ml). The precipitate was filtered, washed with H_2O, and dried *in vacuo*: **13** (10.7 g, 58%). Colorless crystals. M.p. 81–83°. R_f 0.40 (CH_2Cl_2). IR (KBr): 2953.1*w*, 2360.2*m*, 1731.0*s*, 1531.3*s*, 1434.9*s*, 1355.6*s*, 1293.3*m*, 1228.0*m*, 1159.6*m*, 1020.7*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.63 (*dd*, $^3J=8.1$, $^5J=1.0$, 1 H); 7.38 (*d*, $J=7.1$, 1 H); 7.24 (*d*, $J=7.8$, 1 H); 3.71 (*s*, 6 H); 3.65 (*t*, $J=7.6$, 1 H); 3.33 (*d*, $J=7.6$, 2 H); 2.45 (*s*, 3 H). ^{13}C-NMR (400 MHz, $CDCl_3$): 169.16; 151.95; 139.23; 134.04; 130.90; 126.81; 123.23; 53.17; 52.20; 32.67; 15.10. FAB-MS 282 (100, $[M+H]^+$), 265 (7), 250 (14), 218 (36), 150 (20), 137 (30). Anal. calc. for $C_{13}H_{15}NO_6$: C 55.51, H 5.38, N 4.98, O 34.13; found: C 55.55, H 5.25, N 4.95, O 33.97.

Methyl 2-Methyl-3-nitropbenzenepropanoate (**14**). To a soln. of **13** (9.3 g, 33 mmol) in DMF (50 ml) and H_2O (5 ml), LiI (13.2 g, 98 mmol) was added. After stirring 7 h at 160°, the soln. was cooled to r.t. and hydrolyzed with H_2O (300 ml). The aq. layer was extracted with CH_2Cl_2, the combined org. phase dried (Na_2SO_4) and concentrated, and the residue purified by FC (AcOEt/hexane 2:1): **14** (5.6 g, 76%). Yellow oil. R_f 0.37 (AcOEt/hexane 2:1). IR (NaCl): 3088.9*w*, 3000.0*w*, 2952.9*m*, 1737.5*s*, 1605.6*w*, 1527.4*s*, 1438.1*m*, 1355.7*s*, 1294.4*m*, 1261.1*m*, 1211.1*m*, 1171.9*m*, 1088.1*m*, 1027.0*w*, 988.9*w*, 905.6*w*, 877.8*w*, 833.3*w*, 806.7*w*, 772.0*w*, 733.4*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.52 (*dd*, $^3J=8.1$, $^5J=1.0$, 1 H); 7.33 (*d*, $J=7.1$, 1 H); 7.18 (*t*, $J=7.8$, 1 H); 3.62 (*s*, 3 H); 2.98 (*t*, $J=8.1$, 2 H); 2.55 (*t*, $J=8.1$, 2 H); 2.35 (*s*, 3 H). ^{13}C-NMR (400 MHz, $CDCl_3$): 172.99; 151.83; 141.92; 133.19; 130.42; 126.78; 122.53; 52.06; 40.32; 28.93; 14.89. EI-MS: 223.0 (3, M^+), 206.1 (19), 192.1 (17, $[M-OMe]^+$), 174.1 (76), 164.1 (41, $[M-COOMe]^+$), 146.1 (49), 132.1 (100), 115.1 (28), 103.1 (30), 91.1 (44), 77.1 (25), 59.1 (17), 39.1 (14). Anal. calc. for $C_{11}H_{13}NO_4$ (223.23): C 59.19, H 5.87, N 6.27, O 28.67; found: C 58.96, H 5.82, N 6.26, O 28.81.

Methyl 3-Amino-2-methylbenzenepropanoate (**15**). A mixture of 5% Pd/C, **14** (5.4 g, 24.3 mmol), and 95% EtOH (100 ml) was shaken for 4 h under H_2 at r.t. The soln. was filtered over *Celite*, the latter washed with EtOH, and the filtrate diluted with H_2O. The aq. layer was extracted with CH_2Cl_2, the combined org. phase dried (Na_2SO_4) and concentrated, and the residue purified by FC (AcOEt/hexane 1:1): **15** (3.6 g, 76%). Colorless crystals. M.p. 45–46°. R_f 0.33 (AcOEt/hexane 1:1). IR (KBr): 3452.9*m*, 3374.2*m*, 3002.9*w*, 2950.4*m*, 1731.1*s*, 1635.1*m*, 1587.1*m*, 1472.9*m*, 1437.0*m*, 1369.0*m*, 1291.0*m*, 1250.0*m*, 1195.1*m*, 1167.1*m*, 1083.0*m*, 782.8*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 6.96 (*t*, $J=7.6$, 1 H); 6.63 (*d*, $J=7.6$, 1 H); 6.60 (*d*, $J=8.1$, 1 H); 4.00–3.50 (br., 2 H); 3.69 (*s*, 3 H); 2.94 (*t*, $J=8.3$, 2 H); 2.56 (*t*, $J=8.3$, 2 H); 2.12 (*s*, 3 H). ^{13}C-NMR (400 MHz, $CDCl_3$): 173.88; 144.94; 139.81; 126.82; 120.94; 120.20; 114.29; 52.01; 35.35; 29.54; 12.85. EI-MS 193.1 (100, M^+), 162.1 (16, $[M-OMe]^+$), 134.1 (68, $[M-COOMe]^+$), 120.1 (65, $[M-CH_2COOMe]^+$), 106.1 (34, $[M-CH_2CH_2COOMe]^+$), 77.1 (11). Anal calc. for $C_{11}H_{15}NO_2$ (193.25): C 68.37, H 7.82, N 7.25, O 16.56; found: C 68.25, H 7.77, N 7.15, O 16.60.

Methyl 2-Methyl-3-(methylamino)benzenepropanoate (**11**). To a suspension of **15** (5.0 g, 25.9 mmol) and NaH (683 mg, 28.5 mmol) in dry DMF (75 ml), MeI (2 ml, 31 mmol) was added within 30 min at r.t. After stirring further 15 min at r.t., the sol. was diluted with H_2O, and 1M NaOH was added until a pH of *ca.* 11 was reached. The aq. layer was extracted with CH_2Cl_2, the combined org. phase dried (Na_2SO_4) and concentrated, and the residue purified by FC (AcOEt/hexane 1:1): **11** (2.6 g, 64%). Light yellow oil. R_f 0.47 (AcOEt/hexane 1:1). IR (NaCl): 3438.4*m*, 2948.0*m*, 2360.8*w*, 1733.9*s*, 1590.2*s*, 1511.1*m*, 1477.9*m*, 1433.3*m*, 1361.1*w*, 1287.1*m*, 1160.3*m*, 1105.6*w*, 1027.8*w*, 778.2*w*. ^{1}H-NMR (250 MHz, $CDCl_3$): 7.14 (*t*, $J=7.8$, 1 H); 6.65 (*d*, $J=7.7$, 1 H); 6.56 (*d*, $J=8.1$, 1 H); 3.80–3.70 (br., 1 H); 3.73 (*s*, 3 H); 3.01 (*t*, $J=7.5$, 2 H); 2.93 (*s*, 3 H); 2.60 (*t*, $J=7.7$, 2 H); 2.12 (*s*, 3 H). ^{13}C-NMR (400 MHz, $CDCl_3$): 173.97; 147.75; 139.10; 127.07; 120.20; 118.72; 108.45; 52.04; 35.54; 31.56; 29.77; 12.59. EI-MS 207.1 (100, M^+), 176.1 (15, $[M-OMe]^+$), 160.0 (6), 148.1 (51, $[M-COOMe]^+$), 134.1 (32), 120.0 (36), 91.0 (9). Anal. calc. for $C_{12}H_{17}NO_2$ (207.27): C 69.54, H 8.27, N 6.76, O 15.44; found: C 69.06, H 8.30, N 6.81, O 15.15.

Methyl 3-[(5-Formyl-2,6-dichloropyrimidin-4-yl)methylamino]-2-methylbenzenepropanoate (**16**). To a soln. of **11** (1.00 g, 4.8 mmol) in dry CH_2Cl_2 (25 ml), **10** (1.02 g, 4.8 mmol) was added in portions. After stirring for 5 min at 100°, the soln. was cooled to r.t., and H_2O was added, followed by 1M NaOH until a

pH of *ca.* 11 was reached. The aq. layer was extracted with CH_2Cl_2, the combined org. phase dried (Na_2SO_4) and concentrated, and the residue purified by FC (AcOEt/hexane 1:1): **16** (1.55 g, 85%). Colorless crystals. M.p. 83–85°. R_f 0.54 (AcOEt/hexane 1:1). IR (KBr): 2992.9*w*, 2949.9*w*, 2844.0*w*, 1739.8*s*, 1700.1*s*, 1437.0*m*, 1396.8*m*, 1341.1*m*, 1279.1*m*, 1234.6*m*, 1134.1*m*, 1091.3*m*, 1045.5*m*, 1021.8*m*, 982.3*m*, 885.5*m*. ^{1}H-NMR (500 MHz, $CDCl_3$): 9.20 (br., 1 H); 7.20–7.10 (*m*, 2 H); 6.86 (br., 1 H); 3.69 (*s*, 3 H); 3.41 (br., 3 H); 2.99 (*td*, *J* = 7.1, 2.6, 2 H); 2.62 (*td*, *J* = 7.9, 3.4, 2 H); 2.18 (*s*, 3 arom. H). ^{13}C-NMR (500 MHz, $CDCl_3$): 185.48; 173.06; 162.16; 159.74; 143.74; 142.20; 140.05; 134.05; 134.00; 129.48; 127.82; 124.49; 51.81; 40.51; 34.13; 28.68; 13.98. EI-MS 381.0 (100, M^+), 366.0 (70, $[M-Me]^+$), 352.0 (80), 346.0 (43, $[M-Cl]^+$), 322.0 (58, $[M-COOMe]^+$), 306.0 (34), 294.0 (40, $[M-CH_2CH_2COOMe]$), 278.0 (52), 264.0 (36), 115.0 (32), 91.1 (31). Anal. calc. for $C_{17}H_{17}Cl_2N_3O_3$ (382.25): C 53.42, H 4.48, N 10.99, O 12.56; found: C 53.48, H 4.45, N 10.93, O 12.27.

Methyl 8,9-Dimethyl-10-deazaisoalloxazine-7-propanoate (= *Methyl 2,3,4,10-Tetrahydro-9,10-dimethyl-2,4-dioxopyrimido[4,5-*b*]quinoline-8-propanoate*; **17**). To **16** (1.42 g, 3.7 mmol), 98% CF_3COOH (10 ml) was added. After stirring for 1 h at 60°, the soln. was cooled to r.t. and poured on ice-cooled H_2O (200 ml). The aq. layer was extracted with CH_2Cl_2 until the layer was colorless, the combined org. phase dried (Na_2SO_4), and evaporated, and the residue purified by FC (CH_2Cl_2/MeOH 9:1): **17** (1.18 g, 98%). Yellow crystals. M.p. > 300°. R_f 0.31 (CH_2Cl_2/MeOH 9:1). UV/VIS ($CHCl_3$): 269 (100), 343 (43), 404 (41). Fluor. ($CHCl_3$): 474. IR (KBr): 3144.4*w*, 3012.2*w*, 2800.0*w*, 2366.7*w*, 1737.1*w*, 1704.5*m*, 1664.4*m*, 1623.0*s*, 1594.4*m*, 1552.0*m*, 1527.7*m*, 1482.1*w*, 1413.7*w*, 1377.8*w*, 1344.4*w*, 1228.8*m*, 1175.2*w*. ^{1}H-NMR (250 MHz, $CDCl_3$): 8.84 (*s*, 1 H); 8.46 (br., 1 H); 7.71 (*d*, *J* = 8.2, 1 H); 7.40 (*d*, *J* = 8.1, 1 H); 4.15 (*s*, 3 H); 3.74 (*s*, 3 H); 3.22 (*t*, *J* = 7.9, 2 H); 2.75 (*t*, *J* = 7.5, 2 H); 2.67 (*s*, 3 H). ^{13}C-NMR (500 MHz, CH_3-COOD): 174.73; 164.34; 161.33; 160.91; 151.75; 145.50; 145.31; 130.56; 128.31; 127.32; 123.74; 114.77; 52.68; 43.81; 34.54; 30.45; 18.98. EI-MS 327.1 (37, M^+), 296.0 (6, $[M-OMe]^+$), 268.1 (100, $[M-COOMe]^+$), 254.0 (10, $[M-CH_2COOMe]^+$), 225.1 (9). Anal. calc. for $C_{17}H_{17}N_3O_4$ (327.34): C 62.38, H 5.23, N 12.84; found: C 62.00, H 5.31, N 12.26.

Methyl 3-[(Methoxycarbonyl)methyl]-8,9-dimethyl-10-deazaisoalloxazine-7-propanoate (= *Methyl 2,3,4,10-Tetrahydro-3-(2-methoxy-2-oxoethyl)-9,10-dimethyl-2,4-dioxopyrimido[4,5-*b*]quinoline-8-propanoate*; **18**). To a suspension of **17** (1.13 g, 3.5 mmol) and K_2CO_3 (2.67 g, 19.3 mmol) in dry DMF (15 ml), $BrCH_2COOMe$ (3.2 ml, 34.5 mmol) was added. After stirring for 10 h at r.t., the clear soln. was diluted with H_2O. The aq. layer was extracted with CH_2Cl_2, the org. phase dried (Na_2SO_4) and concentrated, and the residue purified by FC (CH_2Cl_2/MeOH 9:1): **18** (900 mg, 65%). Yellow crystals. M.p. 218–220°. R_f 0.39 (CH_2Cl_2/MeOH 95:5). UV/VIS ($CHCl_3$): 267 (100), 343 (35), 405 (31). Fluor. ($CHCl_3$): 477. IR (KBr): 2927.0*m*, 2367.2*w*, 1752.2*s*, 1733.3*s*, 1699.5*m*, 1650.0*m*, 1616.6*s*, 1531.7*s*, 1433.4*s*, 1369.8*m*, 1322.6*w*, 1209.5*s*, 1066.7*w*, 966.7*w*, 933.0*w*, 796.2*m*. ^{1}H-NMR (500 MHz, $CDCl_3$): 8.77 (*s*, 1 H); 7.65 (*d*, *J* = 8.1, 1 H); 7.33 (*d*, *J* = 8.1, 1 H); 4.83 (*s*, 2 H); 4.07 (*s*, 3 H); 3.74 (*s*, 3 H); 3.69 (*s*, 3 H); 3.17 (*t*, *J* = 8.0, 2 H); 2.71 (*t*, *J* = 8.0, 2 H); 2.62 (*s*, 3 H). ^{13}C-NMR (500 MHz, $CDCl_3$): 172.54; 168.6; 161.69; 159.18; 156.39; 149.50; 144.03; 143.13; 129.10; 126.42; 125.21; 121.85; 52.38; 52.00; 42.71; 42.14; 33.85; 29.54; 18.96. EI-MS: 399.1 (57, M^+), 368.1 (12, $[M-OMe]^+$), 340.1 (100, $[M-COOMe]^+$), 280.1 (19, $[M-COOMe]^+$), 225.1 (8). Anal. calc. for $C_{20}H_{21}N_3O_6$ (399.41): C 60.14, H 5.30, N 10.52, O 24.04; found: C 57.88, H 5.24, N 10.02, O 24.61.

3-(Carboxymethyl)-8,9-dimethyl-10-deazaisoalloxazine-7-propanoic Acid (= *3-(Carboxymethyl)-2,3,4,10-tetrahydro-9,10-dimethyl-2,4-dioxopyrimido[4,5-*b*]quinoline-8-propanoic Acid*; **19**). To a suspension of **18** (400 mg, 1 mmol) in THF/H_2O 6:4 (10 ml), $LiOH \cdot H_2O$ (210 mg, 5 mmol) was added. After stirring for 1 h at r.t., the soln. was diluted with H_2O (10 ml). Then 1M HCl was added until a pH of *ca.* 3 was reached and the soln. was concentrated. The residue was directly purified by reversed-phase CC (H_2O/MeCN 3:1): **19** (252 mg, 68%). Yellow crystals. M.p. 291–292°. R_f 0.74 (H_2O/MeCN 3:1). UV/VIS (MeOH): 229 (82), 264 (100), 343 (32), 401 (26). Fluor. (MeOH): 476. IR (KBr): 2933.3*w*, 2361.1*s*, 1727.8*s*, 1694.4*s*, 1670.3*s*, 1586.4*s*, 1536.4*s*, 1483.3*m*, 1452.4*m*, 1411.1*m*, 1377.8*w*, 1338.9*w*, 1311.1*w*, 1250.0*w*, 1208.3*s*, 927.4*w*. ^{1}H-NMR (250 MHz, $CDCl_3$): 13.00–12.00 (br., 2 H); 8.98 (*s*, 1 H); 7.91 (*d*, *J* = 7.9, 1 H); 7.47 (*d*, *J* = 8.0, 1 H); 4.55 (*s*, 2 H); 3.98 (*s*, 3 H); 3.08 (*t*, *J* = 7.4, 2 H); 2.65 (*t*, *J* = 8.0, 2 H); 2.62 (*s*, 3 H). ^{13}C-NMR (500 MHz, (D_6)DMSO): 173.7; 169.6; 161.3; 158.9; 155.5; 150.3; 143.4; 143.0; 128.9; 126.2; 125.4; 121.5; 112.9; 42.1; 41.8; 33.6; 29.3; 18.4. EI-MS 371.2 (100, M^+), 340.1 (12),

326.2 (57, $[M-COOH]^+$), 312.2 (29, $[M-CH_2COOH]^+$), 283.2 (28), 266.1 (45), 252.1 (9), 237.1 (9). Anal. calc. for $C_{18}H_{17}N_3O_6$ (371.35): C 58.22, H 4.61, N 11.32, O 25.85; found: C 57.62, H 4.73, N 11.05, O 26.32.

Pentafluorophenyl 3-{[(Pentafluorophenoxy)carbonyl]methyl}-8,9-dimethyl-10-deazaisoalloxazine-7-propanoate (= *Pentafluorophenyl 2,3,4,10-Tetrahydro-9,10-dimethyl-2,4-dioxo-3-[2-oxo-2-(pentafluorophenoxy)ethyl]pyrimido[4,5-*b*]quinoline-8-propanoate*; **20**). To **19** (170 mg, 0.46 mmol) and EDC·HCl (263 mg, 1.37 mmol) in dry DMF (5 ml), C_6F_5OH (253 mg, 1.37 mmol) was added. After stirring for 1 h at r.t., the soln. was diluted with H_2O. The aq. layer was extracted with CH_2Cl_2, the combined org. phase dried (Na_2SO_4) and concentrated, and the residue recrystallized from CH_2Cl_2/hexane: **20** (267 mg, 83%). Yellow crystals. R_f 0.85 (CH_2Cl_2/MeOH 9:1). UV/VIS ($CHCl_3$): 266 (100), 342 (3), 406 (33). Fluor. ($CHCl_3$): 472. IR (KBr): 2926.7*w*, 1782.5*m*, 1700.3*m*, 1654.6*s*, 1628.6*m*, 1603.8*w*, 1559.7*w*, 1520.4*s*, 1419.8*w*, 1366,7*w*, 1314.5*w*, 1252.5*w*, 1148,3*m*, 1111.1*m*, 1001.2*s*, 796.3*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 8.85 (*s*, 1 H); 7.72 (*d*, *J* = 8.1, 1 H); 7.41 (*d*, *J* = 8.1, 1 H); 5.20 (*s*, 2 H); 4.10 (*s*, 3 H); 3.32 (*t*, *J* = 7.6, 2 H); 3.10 (*t*, *J* = 7.6, 2 H); 2.68 (*s*, 3 H).

*19-(*tert*-Butyl)-46-mercapto-41,43-dimethyl-45,47-(2,8,12,18-tetrabutyl-3,7,13,17-tetramethyl-21*H,*23*H*-porphine-5,15-diyl)-13,25-dioxa-2,4,7,31,41-pentaazaheptacyclo[33.5.3.1^{4,40}.1^{8,12}.1^{17,21}.1^{26,30}.0^{38,42}]heptatetraconta-1,8,10,12(47),17,19,21(46),26,28,30(45),35,37,39,42-tetradecaene-3,6,32,44-tetrone* (**21**). To a soln. of **7** (58 mg, 0.055 mmol) in dry and degassed DMF (1ml), **20** (97 mg, 0.138 mmol) was added. After stirring for 4 h at 100°, the soln. was cooled to r.t. and diluted with CH_2Cl_2 and sat. $NaHCO_3$ soln. The aq. layer was extracted with CH_2Cl_2, the combined org. phase dried (Na_2SO_4) and evaporated, and the crude product purified by CC (CH_2Cl_2/MeOH 95:5 + 1% Et_3N): 28.0 mg **21** (37%). Pink solid. R_f 0.33 (CH_2Cl_2/MeOH 95:5 + 1% Et_3N). UV/VIS ($CHCl_3$): 269 (47), 346 (31), 415 (100), 513 (9), 546 (4), 583 (4). Fluor. (MeOH): 476. ^{1}H-NMR (600 MHz, toluene, 345 K): 10.14 (br., 2 H); 9.05 (*d*, *J* = 8.8, 1 H); 8.93 (*d*, *J* = 8.8, 1 H); 8.77 (*s*, 1 H); 7.95 (*s*, 1 H); 7.70 (*m*, 2 H); 6.70 (*m*, 2 H); 6.15–6.05 (*m*, 2 H); 5.80 (*d*, *J* = 7.7, 1 H); 4.46 (*s*, 2 H); 4.41 (*s*, 1 H); 4.18 (*d*, *J* = 7.9, 1 H); 4.10–3.80 (*m*, 8 H); 3.27 (*t*, *J* = 4.6, 2 H); 3.17 (*t*, *J* = 4.4, 2 H); 2.74 (br., 12 H); 2.50–2.40 (*m*, 2 H); 2.40–2.10 (*m*, 8 H); 2.12 (*s*, 3 H); 1.90–1.70 (*m*, 8 H); 1.18 (*t*, *J* = 7.1, 6 H); 1.10 (*t*, *J* = 7.3, 6 H); 1.05–0.95 (*m*, 2 H); 0.84 (*s*, 9 H); 0.70 (*m*, 2 H); 0.57 (*m*, 2 H); 0.28 (*s*, 3 H); 0.26 (*m*, 2 H); 0.17 (*m*, 2 H); −2.57 (*s*, 1 H); −2.87 (*s*, 1 H); −3.02 (*s*, 1 H). ESI-MS (MeOH): 1386.5 (100, M^+).

*[19-(*tert*-Butyl)-46-(mercapto-*κ*S)-41,43-dimethyl-45,47-(2,8,12,18-tetrabutyl-3,7,13,17-tetramethyl-21*H,*23*H*-porphine-5,15-diyl-*κ*N^{21},*κ*N^{22},*κ*N^{23},*κ*N^{24})-13,25-dioxa-2,4,7,31,41-pentaazaheptacyclo[33.5.3.1^{4,40}.1^{8,12}.1^{17,21}.1^{26,30}.0^{38,42}]heptatetraconta-1,8,10,12(47),17,19,21(46),26,28,30(45),35,37,39,42-tetradecaene-3,6,32,44-tetronato(3-)]iron* (**6**). To **21** (7.8 mg, 5.6 μmol) in dry and degassed toluene (3 ml), 2,6-lutidine (= 2,6-dimethylpyridine; 13 μl, 0.112 mmol) was added. After heating to 120°, dry and degassed $FeBr_2$ (17.2 mg, 0.078 mmol) was added. After stirring for 45 min at 120°, the soln. was cooled to r.t., poured on *Celite*, and washed until the filtrate was colorless. The soln. was evaporated and the crude product purified by CC (toluene/THF 2:1): **6** (6.5 mg, 89%). Brown solid. R_f 0.41 (toluene/THF 2:1). UV/VIS ($CHCl_3$): 269 (68), 346 (49), 406 (100), 510 (br., 15). ESI-MS (MeOH): 1439.5 (50, M^+), 1462.5 (100, $[M+Na]^+$).

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