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Thiourea-Enhanced Flavin Photooxidation of Benzyl Alcohol

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Abstract: Upon irradiation, flavin oxidises 4-methoxybenzyl alcohol to the corresponding aldehyde using aerial O_2 as the terminal oxidant. We have observed that this reaction is significantly accelerated by the presence of thiourea. A series of thiourea-functionalised flavins has been prepared from flavin isothiocyanates and their photocatalytic efficiencies have been monitored by NMR. The alcohol photooxidation proceeds rapidly and cleanly with high turnover numbers of up to 580, exceeding previously reported performances. A likely mechanistic rationale for the more than 30-fold acceleration of the photo–redox reaction by thiourea has been derived from spectroscopic, electrochemical, and kinetic studies. Thus, thiourea acts as an electron-transfer mediator for the initial photooxidation of 4-methoxybenzyl alcohol by the excited flavins. This mechanism has similarities to electron-relay mechanisms in flavoenzymes, for which cysteine sulfenic acid intermediates are proposed. The observation that thiourea mediates flavin photo–redox processes is valuable for the design of more sophisticated photocatalysts based on Nature's best redox chromophore.

Keywords: flavins · photooxidation · redox chemistry · thiourea

Introduction

Flavins are Nature's beloved redox co-factors.[1,2] They occur in a number of enzymes which are responsible for some of the most essential biochemical processes, mostly in the form of flavin adenine dinucleotide (FAD) or flavin mononucleotide (FMN) co-factors. Their redox properties, reactivity, and selectivity for the desired process are fine-tuned by substitution, non-covalent interactions, and the presence of the surrounding protein, and their function can therefore be tailored to the required task. Their reactivity increases further upon irradiation, making them strong oxidising agents.[3–6]

A large number of flavoenzyme models, usually designed to simulate a particular feature of the protein in a minimised system, have been studied.[7–29] Most studies of this type have been focussed on changes of the flavin chromophore redox potentials caused by non-covalent interactions. However, examples in which the modification of flavin reactivity has been applied to chemical catalysis are less common.[30–39]

In this work, we report flavin molecules functionalised with a thiourea group,[40–42] which, it was envisaged, would reversibly bind substrates of photooxidation reactions to keep them in the vicinity of the excited chromophore. The aim was to increase the electron-transfer efficiency by making the process intramolecular rather than diffusion-controlled.[33,34,43] To investigate possible effects of thiourea functionalisation, the activity of the new flavin molecules in the photooxidation of 4-methoxybenzyl alcohol in air has been studied.[44]

Results and Discussion

The new compounds were synthesised according to the Kuhn protocol.[45] The preparation of 4,5-dimethyl-1,2-dinitrobenzene (**1**) was optimised to obtain the starting material in sufficient quantities (see the Supporting Information). Heating the dinitro compound **1** with 3-oxabut-1-yl amine, 2-(*tert*-butyloxycarbonylamino)ethyl amine, or symmetrical 3,6-dioxaoctyl-1,8-diyl diamine led to *N*-substituted 2-nitroanilines **2**–**4** (Scheme 1). The glycol chains increase the solubility of the target molecules in polar solvents, and the amino groups could be converted into thiourea moieties at a later stage. Although 3,6-dioxaoct-1,8-diyl diamine was not mono-protected, two-fold substitution was not observed. However, the side chain amino group disturbs the course of the cyclocondensation reaction of the phenylene–diamine

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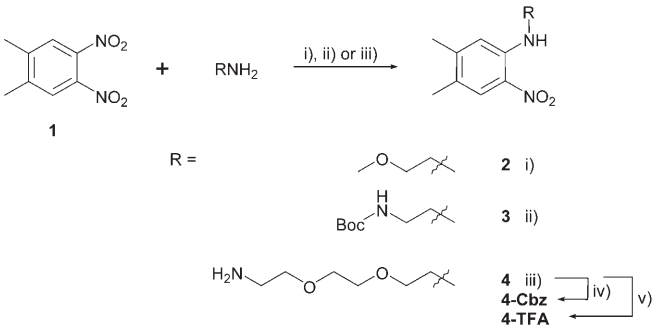
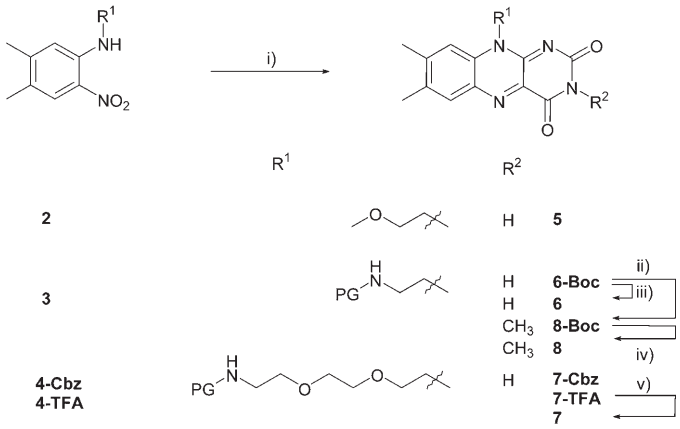
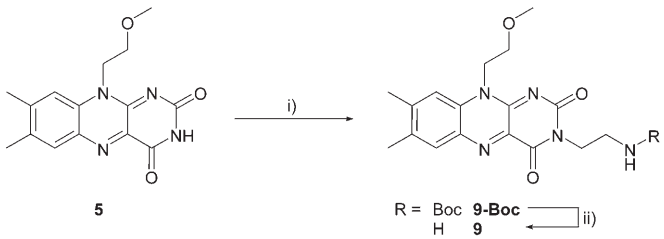


Scheme 1. *ipso*-Substitution of dinitro compound **1** with amines and protection of the side chain amino group. i) 3-Oxabut-1-yl amine (neat), 80 °C, 6 h, 99 %; ii) pyridine, 24 h, 90 °C, 46 %; iii) ethanol, reflux, 62 h, 51 %; iv) Cbz-Cl, TEA, dichloromethane, RT, 30 min, 64 %; v) Ethyl trifluoroacetate (ETFA), TEA, methanol, RT, 24 h, 83 %.



Scheme 2. Completion of flavin synthesis. i) 1) H_2 (g), 10 % palladium on activated charcoal, acetic acid (compounds **2**, **3**, and **4-TFA**), or tin(II) chloride, ethanol, reflux, 72 h (compound **4-Cbz**); 2) alloxane hydrate, boric acid, acetic acid, RT, 50 % (**5**), 47 % (**6-Boc**), 71 % (**7-Cbz**), 48 % (**7-TFA**); ii) dimethyl sulfate, caesium carbonate, DMF (dry), RT, overnight, 53 %; iii) HCl, diethyl ether, chloroform, RT, overnight, 83 %; iv) HCl, diethyl ether, chloroform, RT, overnight, 100 %; v) aqueous HCl (6 M), 90–95 °C, 90 min, 100 %.



Scheme 3. Synthesis of 3-(2′-aminoeth-1′-yl) flavin (**9**). i) 2-(*tert*-Butyloxycarbonylamino)eth-1-yl bromide, K_2CO_3, NaI, DMF (dry), RT, 3 d, 54 %; ii) HCl, diethyl ether, RT, 95 %.

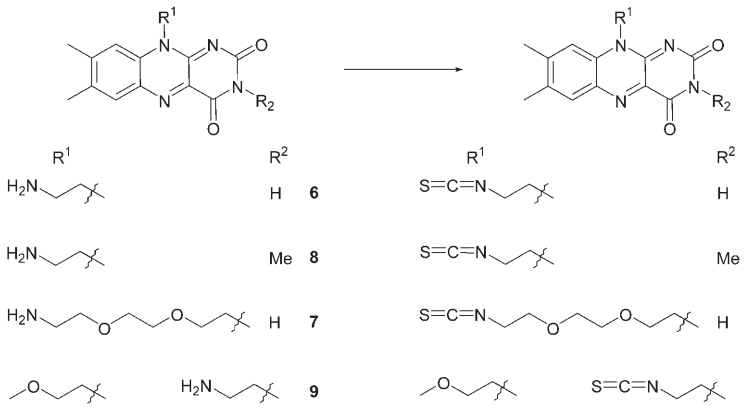
intermediate with alloxane hydrate, and so had to be protected to enable completion of the flavin synthesis. The flavin skeleton is sensitive to bases,[46,47] hence protective groups that require removal by base were unsuitable. Suitable protection was ensured by benzyloxycarbonyl and trifluoroacetyl groups.

The synthesis of the flavin skeleton was completed by reduction of the remaining nitro group and cyclocondensation of the resulting phenylene–diamine intermediates with alloxane hydrate in the presence of boric acid. In this way, flavins **5**, **6-Boc**, **7-Cbz**, and **7-TFA** were obtained (Scheme 2). Flavin **6-Boc** was *N*-methylated with dimethyl sulfate to give the corresponding analogue **8-Boc**. *tert*-Butyl carbamates **6-Boc** and **8-Boc** were cleaved with hydrogen chloride to afford 10-(2′-aminoethyl) flavins **6·HCl** and **8·HCl**. Unfortunately, the benzyloxycarbonyl protective group of flavin **7-Cbz** could not be removed by any of the usual methods.[48,49] Cleavage of the trifluoroacetamide **7-TFA** in a strongly acidic environment[50] led to the quantitative formation of aminoglycol flavin **7·HCl**.

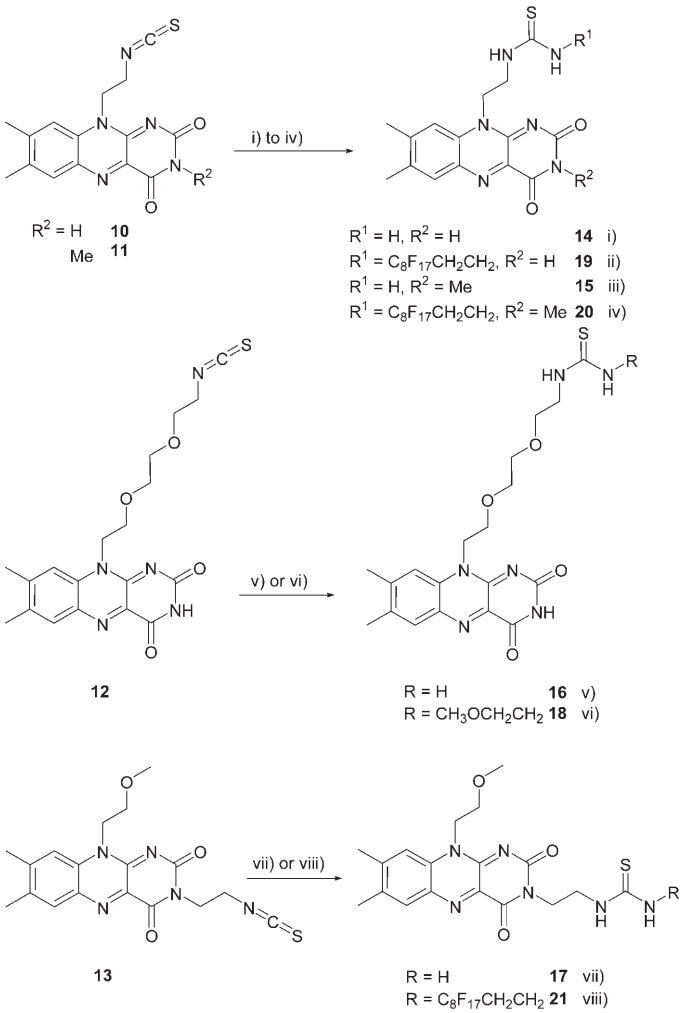
Flavin **5** was *N*-alkylated with 2-(*tert*-butyloxycarbonylamino)ethyl bromide (Scheme 3). Cleavage of *tert*-butyl carbamate **9-Boc** with hydrogen chloride yielded the corresponding 3-(2′-aminoeth-1′-yl) flavin **9·HCl**. Amines **6–9** were then converted into the corresponding isothiocyanates **10–13** by reaction with thiophosgene in a two-phase solvent mixture (Scheme 4). The reactions were clean and rapid, and very good yields of the isothiocyanates were obtained.

The reaction of isothiocyanates with amines leads to the formation of substituted thioureas.[40,51] Flavin isothiocyanates **10–13** show high reactivity, and the corresponding thioureas were obtained in excellent yields.

Passing gaseous ammonia through solutions of the respective isothiocyanates led to the mono-substituted thioureas **14–17** (Scheme 5), which were less soluble than the starting



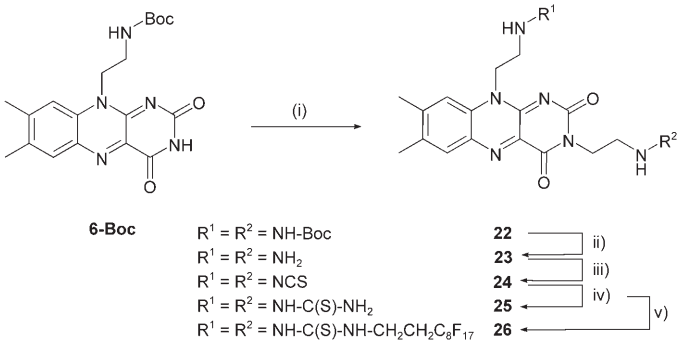
Scheme 4. Synthesis of isothiocyanates **10–13**. Thiophosgene, dichloromethane, calcium carbonate, water, RT, 87 % (**10**), 79 % (**11**), 97 % (**12**), 89 % (**13**).



Scheme 5. Synthesis of thioureas **14**–**21** from isothiocyanates **10**–**13**. i) NH_3 (g), methanol, RT, 3 h, 76%; ii) perfluorooctylethyl amine, TEA, chloroform, reflux, overnight, 68%; iii) NH_3 (g), chloroform, RT, 2 h, 68%; iv) perfluorooctylethyl amine, TEA, chloroform, reflux, overnight, 79%; v) NH_3 (g), chloroform, RT, 3 h, 44%; vi) 3-oxabut-1-yl amine, chloroform, reflux, 2.5 h, 100%; vii) NH_3 (g), chloroform, RT, 3 h, 100%; viii) perfluorooctylethyl ammonium chloride, TEA, reflux, 18 h, 67%.

materials and could be isolated in yields of 44–100% by filtration or trituration. Reactions with primary amines led to *N*,*N*′-substituted thioureas **18**–**21**. A hydrophilic chain (thiourea **18**) or fluorophilic chain (thioureas **19**–**21**) was introduced to increase the solubility of the molecules in hydrophilic or fluorophilic solvents, respectively.

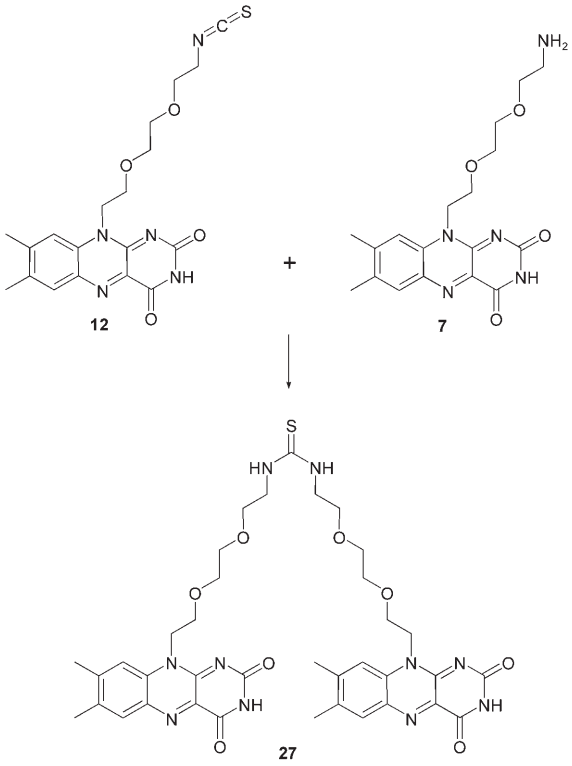
Flavins containing two thiourea groups were prepared starting from flavin **6-Boc**, which was alkylated with 2-(*tert*-butyloxycarbonylamino)ethyl bromide to afford flavin **22** (Scheme 6). Removal of both Boc protective groups led to bis(2′-aminoethyl) flavin dihydrochloride **23·2HCl** in quantitative yield. Two-fold reaction with thiophosgene under the conditions mentioned above led to bis(isothiocyanatoethyl) flavin **24**. Reaction of both isothiocyanate groups with ammonia gave compound **25** containing two mono-substituted thiourea groups, and reaction with perfluorooctylethyl



Scheme 6. Synthesis of flavin–bis-thioureas **25** and **26**. i) 2-(*tert*-Butyloxycarbonylamino)eth-1-yl bromide, K_2CO_3, NaI, DMF (dry), 3 d, 52%; ii) HCl, diethyl ether, methanol, RT, overnight, 100%; iii) thiophosgene, dichloromethane, calcium carbonate, water, overnight, 81%; iv) NH_3 (g), methanol, chloroform, 100%, RT, 1 h; v) perfluorooctylethyl amine, TEA, chloroform, reflux, 51%.

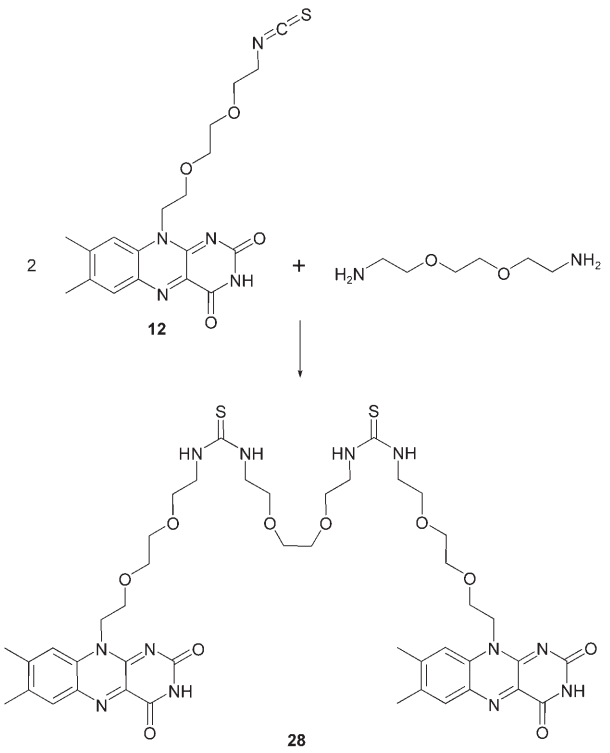
amine yielded compound **26** containing two *N*,*N*′-substituted thiourea groups.

The reaction of isothiocyanate **12** with aminoglycol flavin **7** (Scheme 7) and two-fold reaction of isothiocyanate **12**



Scheme 7. Synthesis of bis-flavin **27**. TEA, chloroform, reflux, 22 h, 100%.

with 3,6-dioxaoct-1,8-diyl diamine (Scheme 8) yielded bis-flavins **27** and **28**, respectively, containing one and two thiourea groups and a glycol linker of varying length, both in high yields.[21,26,37]



Scheme 8. Synthesis of bis-flavin **28**. Chloroform, reflux, 8 h, 93%.

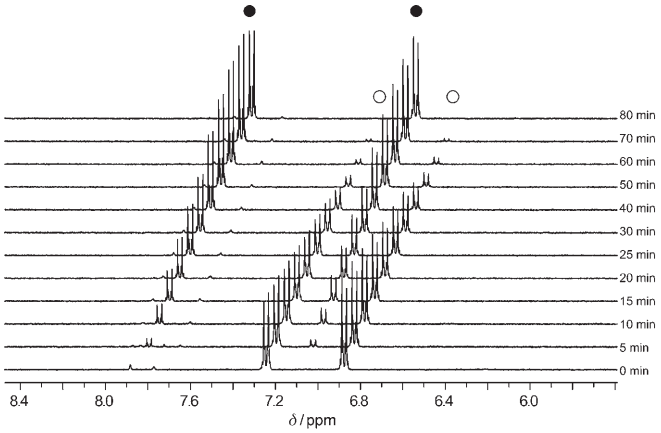


Figure 1. Stack plot of the aromatic region of the ^{1}H NMR spectra recorded during the irradiation of 4-methoxybenzyl alcohol in the presence of 10-thioureidoglycol flavin **16**. Perspective view of the spectra is used (no change of the chemical shift of the signals). ○: 4-methoxybenzyl alcohol aromatic signals; ●: 4-methoxybenzaldehyde aromatic signals. Resonance signals in the baseline noise belong to flavin. Initial concentration of 4-methoxybenzyl alcohol 2×10^{-3} M; concentration of flavin 2×10^{-4} M. Recorded on a Bruker spectrometer at working frequency 400 MHz using 64 transitions.

Flavin-mediated photooxidation of 4-methoxybenzyl alcohol to the corresponding aldehyde using aerial oxygen as terminal oxidant was chosen as the model reaction to study the catalytic activity of the new flavin–thiourea compounds. Other photocatalysts, such as titanium dioxide, can also mediate this oxidation, but they require intense UV irradiation.[52] The catalytic flavin cycle starts with the oxidised form of flavin, which is irradiated with visible light ($\lambda =$ 440 nm; the absorption maximum of flavin is in the visible region). The excited chromophore is a strong oxidising agent,[3–6] and accepts electrons and protons in a stepwise manner from the benzyl alcohol substrate. The aldehyde is formed, along with the reduced flavin, which rapidly reacts with oxygen dissolved in the reaction mixture to yield the hydroperoxide intermediate. The hydroperoxide intermediate then instantaneously releases hydrogen peroxide and regenerates the oxidised flavin, thus completing the catalytic cycle.[53,54] The oxidation of benzyl alcohol to benzaldehyde by oxygen is an exothermic process, but it does not proceed in the absence of flavin or light. The efficiency of the flavin photooxidation increases if substrate-binding sites are present in the vicinity of the chromophore,[23,33,34] and the experiments described herein were performed with the aim of clarifying the effect of thiourea substituents on the photooxidation process.

The reactions were monitored in a mixture of [D_3]acetonitrile and [D_6]dimethyl sulfoxide (98:2 v/v) by ^{1}H NMR.[55] Upon irradiation, the intensity of the resonance signals corresponding to the benzyl alcohol decreased, while benzaldehyde resonance signals appeared (Figure 1, Table 1) in a very clean conversion. At the concentrations used (flavin 2×10^{-4} M, 4-methoxybenzyl alcohol 2×10^{-3} M), the resonance signals of the photocatalysts are observed only as minor peaks in the baseline noise. Hydrogen peroxide was not detected by NMR, presumably due to fast deuterium exchange with the solvent.[56]

In the absence of flavin, light, or oxygen, or in the presence of thiourea alone, the reaction did not proceed (Table 1, entries 17–20).[57] Using simple flavins **5**, **30**, and **31** (Scheme 9), which do not contain a thiourea group, some amount of the product was formed, but the conversion remained very low (entries 11, 12, and 16). Bis-flavins **27** and **28** (entries 13 and 14) were not very efficient either, presumably due to steric factors or unproductive excimer formation.[25] Thiourea groups attached at the 3- or 10-position led to similar rate enhancements: 3-(2′-thioureidoethyl) flavin **17** oxidised 64% of the alcohol within 60 min, while 10-(2′-thioureidoethyl) flavin **14** oxidised 47% of the alcohol in this time (cf. entries 2 and 4). The distance of the thiourea group from the chromophore was found to play a significant role.[58] With the thiourea group located at the end of the dioxaoctyl chain (catalyst **16**) the conversion reached 92%, while with a short ethylene spacer (catalyst **14**) only 47% conversion was observed (cf. entries 1 and 4).

The flavin–thiourea photocatalysts remained active for several subsequent cycles (Figure 2). At hourly intervals, the conversion of 4-methoxybenzyl alcohol to the aldehyde was determined by ^{1}H NMR, and an aliquot of concentrated alcohol stock solution was added to restore the initial alcohol-to-sensitiser ratio. While high conversion within 1 h was observed in the first cycles, the activity of the photocatalyst subsequently decayed due to photodecomposition of the flavin chromophore.

Table 1. Results of flavin-mediated photooxidations of 4-methoxybenzyl alcohol to 4-methoxybenzaldehyde.

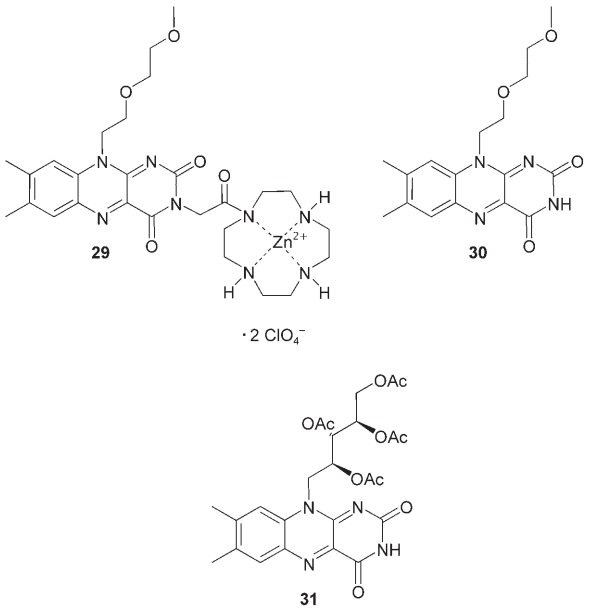
Entry	Flavin photocatalyst [mol L^{-1}]	4-Methoxybenzyl alcohol [mol L^{-1}]	Substrate/catalyst ratio	Irradiation time [h]	Conversion [%]	TON	TOF [h^{-1}]	Quantum yield Φ (×100)
			flavin-catalysed photooxidations					
1	**16** (2×10^{-4})	2×10^{-3}	10:1	1	92	9.2	9.2	0.93
2	**17** (2×10^{-4})	2×10^{-3}	10:1	1	64	6.4	6.4	0.65
3	**19** (3×10^{-5})	2×10^{-3}	70:1	1	64	45	45	0.65
4	**14** (2×10^{-4})	2×10^{-3}	10:1	1	47	4.7	4.7	0.48
5	**18** (2×10^{-4})	2×10^{-3}	10:1	1	41	4.1	4.1	0.42
6	**15** (2×10^{-4})	2×10^{-3}	10:1	1	40	4.0	4.0	0.41
7	**21** (2×10^{-4})	2×10^{-3}	10:1	1	39	3.9	3.9	0.40
8	**25** (5×10^{-5})	2×10^{-3}	40:1	1	27	11	11	0.27
9	**29** (2×10^{-4})	2×10^{-3}	10:1	1	25	2.5	2.5	0.25
10	**20** (2×10^{-5})	2×10^{-3}	100:1	1	20	20	20	0.20
11	**5** (2×10^{-4})	2×10^{-3}	10:1	1	9	0.9	0.9	0.09
12	**31** (2×10^{-4})	2×10^{-3}	10:1	1	7	0.7	0.7	0.07
13	**27** (2×10^{-4})	2×10^{-3}	10:1	1	6	0.6	0.6	0.06
14	**28** (2×10^{-4})	2×10^{-3}	10:1	1	6	0.6	0.6	0.06
15	**26** (1×10^{-5})	2×10^{-3}	200:1	1	3	6	6	0.03
16	**30** (2×10^{-4})	2×10^{-3}	10:1	1	2	0.2	0.2	0.02
			experiments without light, oxygen, or flavin					
17	**16** (2×10^{-4})	2×10^{-3}	10:1	1[a]	5	0.5	0.5	0.05
18	**16** (2×10^{-4})	2×10^{-3}	10:1	1[b]	0	–	–	–
19	None	2×10^{-3}	N/A	1	0	–	–	–
20	None[c]	2×10^{-3}	N/A	1	0	–	–	–
			experiments with lower catalyst loading					
21	**16** (2×10^{-4})	2×10^{-2}	100:1	16	84[d]	87	5.4	0.55
22	**16** (2×10^{-5})	2×10^{-3}	100:1	156	61	61	0.4	0.004
23	**16** (2×10^{-4})	2×10^{-1}	1000:1	96	50[e]	580	6.0	0.006
			stoichiometric mixtures of flavin and thiourea and miscellaneous experiments					
24	**5** (2×10^{-4})[c]	2×10^{-3}	10:1	1	91	9.1	9.1	0.92
25	**30** (2×10^{-4})[c]	2×10^{-3}	10:1	1	95	9.5	9.5	0.97
26	**31** (2×10^{-4})[c]	2×10^{-3}	10:1	0.5	89	8.9	18	1.81
27	**30** (2×10^{-4})[f]	2×10^{-3}	10:1	1	99	9.9	9.9	1.01
28	**5** (2×10^{-4})[g]	2×10^{-3}	10:1	1	3	0.3	0.3	0.03

[a] The reaction mixture was thoroughly purged with argon prior to irradiation. [b] Instead of irradiation, the reaction mixture was left to stand in the dark. [c] Thiourea (2×10^{-4} M) was added to the reaction mixture. [d] Mixture of 4-methoxybenzaldehyde (81%) and *p*-anisic acid (3%). [e] Mixture of 4-methoxybenzaldehyde (42%) and *p*-anisic acid (8%). [f] *N*,*N*,*N*′,*N*′-Tetramethylthiourea (2×10^{-4} M) was added to the reaction mixture. [g] Urea (2×10^{-4} M) was added to the reaction mixture.

To further probe the activity of the most efficient compound **16**, experiments with higher substrate-to-photocatalyst ratios were carried out (Table 1, entries 21–23). Regardless of whether the concentration of the substrate was increased or the concentration of the flavin sensitiser was lowered to reach the higher ratio, the reaction was significantly slower and longer irradiation times were therefore required. Nevertheless, unprecedented turnovers were observed: using a mere 0.1 mol% of the flavin photocatalyst, a total conversion of 50% after 4 d of irradiation was observed. 4-Methoxybenzaldehyde (42%) was in this case accompanied by *p*-anisic acid (8%), the product of a subsequent oxidation, which was not observed in the experiments employing 10 mol% of flavin sensitiser, even after prolonged irradiation of the fully converted reaction mixtures or of mixtures with authentic 4-methoxybenzaldehyde. This result corresponds to a TON of 580, significantly exceeding the highest turnover hitherto reported for this reaction.[33] Fluorophilic catalysts **19** and **20** and bis-thiourea catalysts **25** and **26** (entries 3, 8, 10, and 15) were not sufficiently soluble to test their efficiencies at 2×10^{-4} M. However, they were highly active even at lower concentrations, especially compound **19**, which oxidised 64% of the substrate while present at 1.5 mol%, thus achieving a turnover frequency (TOF) of 45 h^{-1}.

Surprisingly, the covalent linkage between the flavin chromophore and the thiourea group was not decisive for the catalytic activity. Mixtures of related flavin molecules not bearing a covalently-linked thiourea group with stoichiometric amounts of thiourea worked comparably well (Table 1, entries 24–26). This made us revise the hypothesis of reversible non-covalent binding of the substrate to the thiourea group. Indeed, addition of 4-methoxybenzyl alcohol to the most active catalyst, **16**, did not cause any quenching of the flavin fluorescence and induced no changes in the UV/Vis spectrum, suggesting no direct binding between the substrate and the thiourea group. This assumption was supported by ^{19}F NMR titration of 2-fluorobenzyl alcohol with flavin–thiourea **16**. Upon addition of the flavin–thiourea, no change in the chemical shift of the fluorine nucleus was observed, again indicating no direct interaction.

To assess whether the presence of thiourea influences the redox potential of the flavin through hydrogen binding, as observed in natural flavoenzymes and models thereof,[15,16,20,21,24,59–65] the reduction potentials of 10-thioureidoglycol flavin **16** and 10-(3′,6′-dioxahept-1′-yl) flavin **30** were determined by cyclic voltammetry (see the Supporting Information). These measurements revealed a shift of the reduction potential by +90 mV for flavin–thiourea **16** as compared to **30**. This shift is not as pronounced as those for related flavin molecules that catalyse the oxidation of 4-methoxybenzyl alcohol less efficiently (e.g., the reduction potential of compound **29** is shifted by +200 mV compared to that of compound **30**),[33] and so cannot be cited to justify the high activity in the oxidation reactions. To disprove a hydrogen-bond-mediated change in the redox potential of the



Scheme 9. Flavin molecules that do not contain a thiourea group, used for comparison.

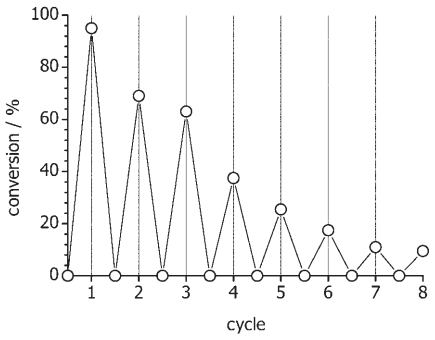
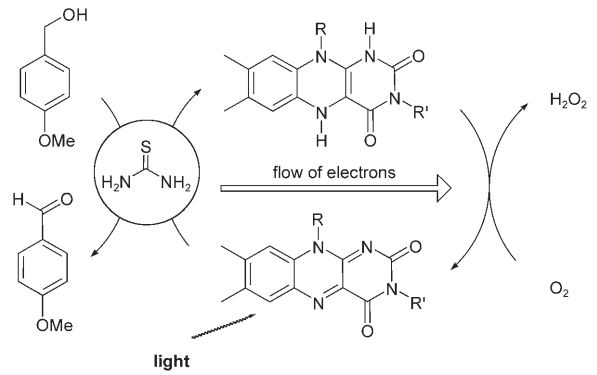


Figure 2. Repeated oxidation of 4-methoxybenzyl alcohol. Conditions: flavin–thiourea **16** 2×10^{-4} M, 4-methoxybenzyl alcohol 2×10^{-3} M before every cycle (1 h). Products accumulated in the reaction mixture.

flavin as the origin of the increased reactivity in alcohol photooxidation, experiments were carried out using mixtures of 10-(3′,6′-dioxahept-1′-yl) flavin **30** with either thiourea or *N*,*N*,*N*′,*N*′-tetramethylthiourea, and these gave comparable results (Table 1, cf. entries 25 and 27).

Another potential effect of thiourea, which is a mild organic base, is deprotonation of the alcohol, making it more electron-rich and facilitating its oxidation. However, although thiourea is more basic than alcohols in aqueous environments, the situation changes in organic media due to less effective solvation of the alcoholate anion, making deprotonation by thiourea virtually impossible.[66,67]

Having disproved the hypotheses described above, we turned our attention to the possibility that thiourea functions as an electron mediator between the substrate and the flavin moiety, and assists the chromophore in bringing the oxidation about (Scheme 10). To assess whether electron transfer between the flavin unit and thiourea and other entities participating in the system is thermodynamically feasible, the relevant redox potentials were determined by cyclic voltammetry and ΔG values for the electron-transfer reactions were calculated using the Rehm–Weller equation (Supporting Information).[68,69] It was found that the excited flavin can indeed oxidise either the alcohol ($\Delta G = -29$ kJ mol^{-1}) or thiourea ($\Delta G = -100$ kJ mol^{-1}). The reduced form of the flavin may also reduce thiourea ($\Delta G = -55$ kJ mol^{-1}) or be re-oxidised by oxygen ($\Delta G = -35$ kJ mol^{-1}); however, the rate-determining step is the oxidation of the substrate, not the re-oxidation of the reduced form of the flavin, as only the oxidised form can be observed in UV spectra recorded during the reaction. Thiourea must therefore exert its positive effect on the oxidation of the substrate. The ability of thiourea to enhance the reactivity of flavin may stem from its propensity to be oxidised to highly reactive (radical) intermediates.[70–72] Accordingly, urea, which cannot tautomerise to the isourea form[73] that is necessary to enable oxidation,[74] does not increase the efficiency of the flavin photocatalyst (Table 1, entry 28). The situation may be analogous to that in certain oxidases, which contain a stabilised sulfenic acid based on the cysteine side chain in the vicinity of the flavin-dependent active site.[75–80]



Scheme 10. Proposed catalytic cycle for the thiourea-mediated photooxidation of 4-methoxybenzyl alcohol.

The effect of thiourea on the reaction rate is a diffusion-controlled process rather than a photochemical reaction within a non-covalent assembly. When an excess of thiourea with respect to the flavin is used, the oxidation proceeds significantly more rapidly than in the case of a stoichiometric mixture of flavin and thiourea. In addition, the difference in photocatalyst efficiency between covalently tethered thiourea and stoichiometric mixtures of flavin and thiourea is small.

Conclusion

Flavin–thioureas **14**–**21** and **25**–**28** have been prepared by the Kuhn synthesis and the application of isothiocyanate chemistry. The photocatalysts have been successfully applied to the oxidation of 4-methoxybenzyl alcohol to 4-methoxybenzaldehyde using aerial oxygen as the terminal oxidising

agent. The activities of some of the catalysts exceeded those of known systems and high TONs of up to 580 were observed. The presence of thiourea, either covalently bound to a flavin derivative or added stoichiometrically, led to a 30-fold increase in the quantum yield of the reaction in some cases. Our investigations have revealed that thiourea presumably acts as an efficient electron mediator between the photoactive flavin chromophore and the substrate.

Experimental Section

General: 10-(3′-Oxabut-1′-yl) flavin **5**,[81] 10-[2′-(*tert*-butyloxycarbonylamino)eth-1′-yl] flavin **6-Boc**,[17] 10-(2′-aminoeth-1′-yl) flavin **6**,[17] 2-perfluorooctylethyl amine,[82] 2-(*tert*-butyloxycarbonylamino)ethyl bromide,[83] and (3′,6′-dioxahept-1′-yl) flavin **30**[33] were prepared by known methods. Flavin–zinc(II)–cyclene **29** was a gift from Dr. Radek Cibulka. All other chemicals were purchased from commercial suppliers, checked by ^{1}H NMR spectrometry, and then used as received. Solvents were distilled before use and dried by standard methods if required by the experimental procedure. Dry *N*,*N*-dimethylformamide was purchased from Fluka. Thin-layer chromatography (TLC) was carried out on silica gel 60 F_{254} coated aluminium sheets (Merck) or on pre-coated Polygram SIL G/UV_{254} plastic sheets (Macherey-Nagel, Düren, Germany), with detection under 254 nm or 333 nm UV light, by the naked eye (flavins are intensely yellow-coloured), or by staining with ninhydrin solution. Preparative thin-layer chromatography (PTLC) was carried out on home-made glass plates (20×20 cm) coated with silica gel 60 GF_{254} (20 g, Merck). Column chromatography was carried out on silica gel Geduran 60 (Merck) or silica gel 60 M (Macherey-Nagel). Flash chromatography was carried out on silica gel 60 A, 0.035–0.070 mm, from Acros. Nuclear magnetic resonance spectra were recorded on a Bruker spectrometer equipped with a robotic sampler at 300 MHz (^{1}H NMR) or 75 MHz (^{13}C NMR), unless otherwise indicated. Tetramethylsilane (TMS) was used as an external standard. Electron-impact (EI-MS) and chemical ionisation (CI-MS) mass spectra were measured on a Finnigan TSQ 710 spectrometer, and electrospray ionisation (ES-MS) mass spectra were measured on a ThermoQuest Finnigan TSQ 7000 spectrometer. All determinations by high-resolution mass spectrometry (HR-MS) were performed on a ThermoQuest Finnigan MAT 95 spectrometer. Elemental compositions (C, H, N, S) of the new compounds were determined either by HR-MS or by combustion elemental analysis. Melting points were measured with a Büchi SMP-20 melting point apparatus using a glass capillary tube immersed in heated silicon oil, and are uncorrected. UV/Vis spectra were recorded on a Varian Cary 50 Bio UV/Vis spectrometer with reference to air. Fluorescence spectra were recorded on a Varian Cary Eclipse fluorescence spectrophotometer.

Kinetic experiments: Kinetic experiments were carried out in a mixture of [D_3]acetonitrile and [D_6]dimethyl sulfoxide (98:2, v/v). The latter was required to improve the solubility of the flavin–thiourea photocatalysts. A typical reaction mixture, prepared in an NMR tube,[84] contained the flavin derivative (2×10^{-3} M) and 4-methoxybenzyl alcohol (2×10^{-4} M) and had a total volume of 1 mL. The reaction mixture was prepared under aerobic conditions, but the solution was not additionally saturated with oxygen. The reaction mixture was irradiated by means of a light-emitting diode with an emission wavelength of 440 nm and an electric power of 6 W. The NMR tube was placed vertically above the aperture of the LED. The optical path using this set-up was about 73 mm. The reaction mixture was irradiated for the desired time, and then the ^{1}H NMR spectrum of the mixture was recorded using a Bruker spectrometer with a working frequency of 400 or 300 MHz using 64 transitions to achieve a better signal-to-noise ratio and hence more accurate integration. Sodium 3-(trimethylsilyl)-2,2,3,3-tetradeuteropropionate (TSP, 2×10^{-3} M) was used as an internal standard. The concentrations of the substrate and product were derived from the areas under the peaks of the aromatic doublets (see Figure 1) by comparison with the integral value of the trimethylsilyl peak of the TSP internal standard. The quantum yield was estimated by standard ferrioxalate actinometry.[85]

Cyclic voltammetry: Cyclic voltammograms were recorded on an Autolab potentiostat, using a glassy carbon working electrode, a platinum auxiliary electrode, and a saturated calomel reference electrode (SCE). The auxiliary electrolyte was 0.1 M tetrabutylammonium tetrafluoroborate, the solvent was a mixture of acetonitrile and dimethyl sulfoxide (98:2, v/v), and the analytes were present at a concentration of 1 mM. Solutions were degassed with a stream of argon prior to the measurements and were maintained under a gentle stream of argon during acquisition of the voltammograms; a step potential of 0.1 V s^{-1} was used.

***N*-(3′-Oxabut-1′-yl)-4,5-dimethyl-2-nitroaniline (2)**: Dinitrobenzene **1** (2.94 g, 15 mmol) was dissolved in 3-oxabut-1-yl amine (25 mL) and the reaction mixture was heated to 80 °C for 6 h. It was then diluted with dichloromethane (100 mL) and washed with water (2×100 mL) and brine (100 mL); the organic phase was dried over magnesium sulfate and concentrated to dryness in vacuo. The product (brown oil) partially solidified upon drying (3.35 g, 99 %); ^{1}H NMR ($CDCl_3$): $\delta=2.14$ (s, 3H; CH_3-4), 2.23 (s, 3H; CH_3-5), 3.40 (s, 3H; CH_3-4′), 3.42–3.47 (m, 2H; CH_2-1′), 3.65 (m, 2H; CH_2-2′), 6.60 (s, 1H; H-6), 7.87 (s, 1H; H-3), 8.07 ppm (br s, 1H; NH); ^{13}C NMR ($CDCl_3$): $\delta=18.4$, 20.6 (2×CH_3), 42.6 (CH_2), 58.9 (CH_3), 70.4 (2×CH_2), 114.0 (CH), 124.4 (quaternary C), 126.3 (CH), 129.8, 143.9, 147.1 ppm (3×quaternary C); CI-MS: *m*/*z* (%): 225.1 (100) $[M+H]^+$, 195.2 (60) $[M+H-NO]^+$.

***N*-(8′-Amino-3′,6′-dioxaoct-1′-yl)-4,5-dimethyl-2-nitroaniline (4)**: The procedure used was analogous to that described by Sawhney et al.[86] Thus, dinitro compound **1** (6.0 g, 30 mmol) was dissolved in ethanol (3 L). 1,8-Diamino-3,6-dioxaoctane (23.8 g, 160 mmol, 5.3 equiv) was added and the reaction mixture was heated to reflux for 62 h. It was then concentrated in vacuo, and the residue was redissolved in dichloromethane. This solution was extracted with dilute hydrochloric acid, and the aqueous phase was separated and neutralised with dilute sodium hydroxide solution. The resulting solution was extracted with dichloromethane, the organic phase was separated and concentrated, and the residue was co-evaporated with toluene and dried to obtain a red oil (4.6 g, 51 %). $R_f=0.17$ (CH_2Cl_2/MeOH/TEA 50:2:1); ^{1}H NMR ($CDCl_3$): $\delta=2.15$ (s, 3H; CH_3-4), 2.24 (s, 3H; CH_3-5), 2.86, 3.52, 3.66, 3.77 (4×m, 12H in total; 6×CH_2 glycol), 6.61 (s, 1H; H-6), 7.90 (s, 1H; H-3), 8.13 ppm (br s, 1H; Ar-NH-); ^{13}C NMR ($CDCl_3$): $\delta=18.6$, 20.7 (2×CH_3), 41.1, 42.7, 69.1, 70.3, 70.6, 71.7 (6×CH_2), 114.2 (CH), 117.8, 124.6 (2×quaternary C), 126.5 (CH), 144.1, 147.3 (2×quaternary C); ES-MS: *m*/*z* (%): 298.2 (100) $[M+H]^+$; HR-MS (EI-MS): *m*/*z*: calcd for $C_{14}H_{23}N_3O_4$ $[M]^{+\cdot}$: 297.1689; found: 297.1689 (delta 0.00 ppm).

***N*-[8′-(Benzyloxycarbonylamino)-3′,6′-dioxaoct-1′-yl]-4,5-dimethyl-2-nitroaniline (4-Cbz)**: The procedure used was analogous to that described by Nicola et al.[87] Thus, free amine **4** (650 mg, 2.2 mmol) was dissolved in dry dichloromethane (100 mL). A solution of benzyl chloroformate (380 mg, 2.2 mmol, 1 equiv) in dry dichloromethane (50 mL) was added dropwise. Triethylamine (0.75 mL) was added to the reaction mixture and the reaction was monitored by TLC (mobile phase CH_2Cl_2/MeOH/TEA 50:2:1; staining with ninhydrin). After 30 min, the spot due to the starting material ($R_f=0.17$) was no longer visible. The reaction mixture was concentrated in vacuo, the residue was dissolved in the minimum volume of methanol, and this solution was applied to four PTLC plates. The mixture was separated using the aforementioned eluent system, and the appropriate zone ($R_f=0.58$) was thoroughly extracted with chloroform. The extract was concentrated in vacuo and the residue was dried to yield a red oil (610 mg, 64 %). $R_f=0.58$ ($CHCl_2$/MeOH/TEA 50:2:1); ^{1}H NMR ($CDCl_3$): $\delta=2.13$ (s, 3H; CH_3-4), 2.22 (s, 3H; CH_3-5), 3.41, 3.55, 3.63, 3.77 (4×m, 12H in total; 6×CH_2 glycol), 5.05 (s, 2H; CH_2Ph), 5.44 (br s, 1H; H-8′), 6.57 (s, 1H; H-6), 7.30 (m, 5H; Ph), 7.86 (s, 1H; H-3), 8.13 ppm (s, 1H; NH aniline); ^{13}C NMR ($CDCl_3$): $\delta=18.6$, 20.7 (2×CH_3), 42.7 (CH_2Ph), 65.1, 66.6, 69.1, 70.2, 70.3, 70.5 (6×CH_2 glycol), 114.2 (CH aniline), 124.5 (quaternary C), 126.4 (CH aniline), 126.8 (quaternary C), 128.0, 128.5, 130.0 (3×CH phenyl), 137.7, 144.0, 147.3 (4×quaternary C), 156.5 ppm (C=O); EI-MS (70 eV): *m*/*z* (%): 91.1 (100) $[C_7H_7]^+$, 179.1 (62) $[ArNH=CH_2]^+$, 431.2 (5) $[M]^{+\cdot}$; elemental analysis

calcd (%) for $C_{22}H_{29}N_3O_6$: C 61.24, H 6.77, N 9.74; found: C 61.44, H 6.91, N 9.65.

***N*-[8′-(Trifluoroacetamido)-3′,6′-dioxaoct-1′-yl]-4,5-dimethyl-2-nitroaniline (4-TFA)**: Free amine **4** (5.8 g, 20 mmol) was dissolved in methanol (200 mL), and ethyl trifluoroacetate (13 g, 92 mmol, 4.6 equiv) and triethylamine (11 g, 0.11 mol, 5.4 equiv) were added to the solution. The mixture was stirred at ambient temperature and the progress of the reaction was monitored by TLC (mobile phase CH_2Cl_2/MeOH/TEA 50:2:1). After 24 h, the spot due to the starting material (R_f=0.17) was no longer visible. The reaction mixture was concentrated in vacuo, the residue was redissolved in dichloromethane (100 mL), and this solution was washed with water (3×100 mL). The organic phase was separated, concentrated in vacuo, and the residue was dried to yield a red oil (6.5 g, 83%). R_f= 0.46 ($CHCl_2$/MeOH/TEA 50:2:1); ^{1}H NMR ($CDCl_3$): δ=2.10 (s, 3H; CH_3-4), 2.20 (s, 3H; CH_3-5), 3.43, 3.53, 3.60, 3.63, 3.72 (5×m, 12H in total; 6×CH_2 glycol), 6.57 (s, 1H; H-6), 7.42 (brs, 1H; -NH-CO-), 7.81 (s, 1H; H-3), 8.15 ppm (br, 1H; Ar-NH-); ^{19}F NMR ($CDCl_3$): δ= −76.4 ppm; ES-MS: *m*/*z* (%): 394.2 (100) $[M+H]^+$; EI-MS: *m*/*z* (%): 393.3 (100) $[M]^{+\bullet}$; HR-MS: *m*/*z*: calcd for $C_{16}H_{22}F_3N_3O_5$ $[M]^{+\bullet}$: 393.1512; found: 393.1509 (delta −0.76 ppm).

10-[8′-(Benzyloxycarbonylamino)-3′,6′-dioxaoct-1′-yl]-7,8-dimethylbenzo[*g*]pteridine-2,4-dione (7-Cbz): The reduction procedure used was analogous to one reported in the literature.[88,89] Thus, *o*-nitroaniline **4-Cbz** (430 mg, 1 mmol) was dissolved in ethanol (100 mL), and tin(II) chloride dihydrate (1.7 g, 7.5 mmol, 7.5 equiv) was added. The mixture was heated to reflux and the progress of the reaction was monitored by TLC (CH_2Cl_2/MeOH/TEA 50:2:1). After 72 h, the spot due to the starting material (R_f=0.58) was no longer visible. The reaction mixture was concentrated in vacuo and the residue was redissolved in ethyl acetate. This solution was washed with 2 M sodium hydroxide solution; the organic phase was separated, dried over magnesium sulfate, and concentrated in vacuo, and the residue was dried. The crude reduction product was dissolved in acetic acid (25 mL), and alloxane hydrate (1.1 g, 6.9 mmol, 6.9 equiv) and boric acid (1 g, 16 mmol, 16 equiv) were added. The flask was wrapped in aluminium foil and the mixture was stirred at ambient temperature for 22 h. It was then diluted with water (25 mL) and extracted with dichloromethane (50 mL). The organic phase was concentrated in vacuo and the residue was co-evaporated with toluene to remove traces of water and acetic acid. The crude product was dissolved in the minimum volume of methanol and separated on four PTLC plates (CH_2Cl_2/MeOH/TEA 50:2:1, eluting twice). The appropriate zone (R_f=0.43) was extracted with methanol, the extract was concentrated in vacuo, and the residue was dried. Yield: 360 mg (71%) of an orange solid; R_f=0.43 (CH_2Cl_2/MeOH/TEA 50:2:1, eluted twice); m.p. 232 °C (decomp); ^{1}H NMR ($CDCl_3$): δ=2.41 (s, 3H; CH_3-7), 2.50 (s, 3H; CH_3-8), 3.31, 3.47, 3.55, 3.97 (4×m, 8H in total; 4×CH_2 glycol), 4.86 (br, 2H; CH_2-2′), 5.06 (s, 2H; $PhCH_2$), 5.30 (br, 2H; CH_2-1′), 7.15–7.38 (m, 5H; Ph), 7.66 (s, 1H; H-9), 7.97 ppm (s, 1H; H-6); a ^{13}C NMR spectrum could not be recorded due to the very low solubility of the title compound in organic solvents; EI-MS: *m*/*z* (%): 242.0 (100) [*M*−side chain]$^{+\bullet}$, 507.2 (5) $[M]^{+\bullet}$;[90] elemental analysis calcd (%) for $C_{26}H_{29}N_5O_6$: C 61.53, H 5.76, N 13.80; found: C 61.33, H 5.84, N 13.85.

7,8-Dimethyl-10-[8′-(trifluoroacetamido)-3′,6′-dioxaoct-1′-yl]benzo[*g*]pteridine-2,4-dione (7-TFA): Trifluoroacetamide **4-TFA** (2 g, 5 mmol) was dissolved in acetic acid (60 mL), and palladium on activated charcoal (10% Pd/C, 1 spatula load) was added. The reaction mixture was placed in an autoclave, which was flushed three times with hydrogen and then filled to 50 bar. The reaction mixture was stirred at ambient temperature for 16 h. It was then filtered through Celite to remove the catalyst, and the filtrate was transferred to a round-bottomed flask. Alloxane hydrate (2.1 g, 13 mmol, 2.6 equiv) and boric acid (7 g, 0.11 mol, 22 equiv) were added to the filtrate. The flask was wrapped in aluminium foil and the reaction mixture was stirred at ambient temperature for 6 d. It was then concentrated in vacuo, the residue was dissolved in water (300 mL), and this solution was extracted with dichloromethane (2×250 mL). The separated organic phases were combined, dried over anhydrous magnesium sulfate, and concentrated in vacuo, and the residue was dried to yield orange crystals (1.13 g, 48%). R_f=0.27 (CH_2Cl_2/MeOH/TEA 50:2:1), R_f=0.65 ($CHCl_3$/MeOH/AcOH 77.5:15:7.5); m.p. 215 °C (decomp); ^{1}H NMR ([D$_6$]DMSO): δ=2.40 (s, 3H; CH_3-7), 2.50 (s, 3H; CH_3-8), 3.25–3.46 (m, 8H; 4×CH_2 glycol), 3.81 (t, *J*=5.9 Hz, 2H; CH_2-2′), 4.78 (t, *J*=5.9 Hz, 2H; CH_2-1′), 7.85 (s, 1H; H-9), 7.88 (s, 1H; H-6), 9.47, 11.33 ppm (2×brs, 2×1H; 2×NH); a ^{13}C NMR spectrum could not be recorded due to the very low solubility of the title compound in organic solvents; ES-MS: *m*/*z* (%): 470.3 (100) $[M+H]^+$; elemental analysis calcd (%) for $C_{20}H_{22}F_3N_5O_5$: C 51.17, H 4.72, F 12.14, N 14.92; found: C 51.34, H 4.87, N 14.83.

10-[2′-(*tert*-Butyloxycarbonylamino)eth-1′-yl]-3,7,8-trimethylbenzo[*g*]pteridine-2,4-dione (8-Boc): Flavin **6-Boc** (0.8 g, 2.1 mmol) was dissolved in dry DMF (80 mL). Caesium carbonate (0.9 g, 2.8 mmol, 1.3 equiv) and dimethyl sulfate (2.7 g, 2 mL, 21 mmol, 10 equiv) were added, and the mixture was stirred overnight at ambient temperature in the dark. The suspension was then diluted with chloroform (250 mL) and washed sequentially with water (3×100 mL), 5% aqueous NH_3 solution (100 mL), and further water (100 mL). The organic phase was separated, dried over magnesium sulfate, and concentrated in vacuo. The crude product was purified by column chromatography ($CHCl_3$/MeOH 20:1) to yield an orange solid (0.44 g, 53%). R_f=0.38 ($CHCl_3$/MeOH 20:1); m.p. 232 °C (decomp); ^{1}H NMR ([D$_6$]DMSO): δ=1.21 (s, 9H; Boc), 2.41 (s, 3H; CH_3-7), 2.51 (s, 3H; CH_3-8), 3.28 (s, 3H; CH_3-3), 3.41 (m, 2H; CH_2-1′), 4.67 (t, *J*=5.8 Hz, 2H; CH_2-2′), 6.99 (t, *J*=5.8 Hz, 1H; NH), 7.87 (s, 1H; H-9), 7.95 ppm (s, 1H; H-6); ^{13}C NMR ([D$_6$]DMSO): δ=18.8, 20.9, 28.0, 28.2 (4×CH_3), 37.0, 44.1 (2×CH_2), 77.9 (quaternary C), 116.2, 131.0 (CH), 131.5, 134.2, 135.8, 135.9, 146.5, 148.9, 155.1, 155.8, 159.7 ppm (9× quaternary C); ES-MS: *m*/*z* (%): 300.1 (55) $[M+H-Boc]^+$, 344.1 (65) $[M+H-C_4H_8]^+$, 400.2 (100) $[M+H]^+$, 422.2 (20) $[M+NH_4]^+$, 438.2 (15) $[M+K]^+$.

10-(2′-Aminoeth-1′-yl)-3,7,8-trimethylbenzo[*g*]pteridine-2,4-dione (8): Flavin **8-Boc** (100 mg, 0.25 mmol) was dissolved in chloroform (25 mL), and HCl in diethyl ether (3 mL) was added dropwise. The reaction mixture was stirred overnight at ambient temperature, and was then concentrated in vacuo to leave a yellow solid to yield the hydrochloride salt of the title compound (84 mg, 100%). R_f=0.00 ($CHCl_3$/MeOH 20:1); m.p. 257 °C (decomp); ^{1}H NMR ([D$_6$]DMSO): δ=2.42 (s, 3H; CH_3-7), 2.54 (s, 3H; CH_3-8), 3.19–3.21 (m, 2H; CH_2-2′), 3.29 (s, 3H; CH_3-3), 4.92 (t, *J*= 6.5 Hz, 2H; CH_2-1′), 7.99 (s, 1H; H-9), 8.06 (s, 1H; H-6), 8.18 ppm (brs, 3H; NH_3^+); a ^{13}C NMR spectrum could not be measured due to the extremely low solubility of the title compound; ES-MS: *m*/*z* (%): 300.1 (100) $[M+H]^+$.

10-(8′-Amino-3′,6′-dioxaoct-1′-yl)-7,8-dimethylbenzo[*g*]pteridine-2,4-dione (7): Trifluoroacetamide **7-TFA** (1.1 g, 2.3 mmol) was dissolved in a 6 M aqueous solution of HCl (200 mL, ca. 1.2 mol, ca. 520 equiv), and the reaction mixture was heated to 90–95 °C with monitoring by TLC ($CHCl_3$/MeOH/AcOH 77.5:15:7.5). After 90 min, the spot due to the starting material (R_f=0.65) was no longer visible. The reaction mixture was then concentrated in vacuo and the residue was dried (dark-brown oil) to yield **7·HCl** (940 mg, 100%). R_f=0.04 ($CHCl_3$/MeOH/AcOH 77.5:15:7.5); ^{1}H NMR (CD_3OD): δ=2.46 (s, 3H; CH_3-7), 2.58 (s, 3H; CH_3-8), 3.06 (t, *J*=4.9 Hz, 2H; CH_2-8′), 3.60–3.68 (m, 6H; 3×CH_2 glycol), 4.00 (t, *J*=5.6 Hz, 2H; CH_2-2′), 5.00 (t, *J*=5.6 Hz, 2H; CH_2-1′), 7.86 (s, 1H; H-9), 7.91 ppm (s, 1H; H-6); ^{13}C NMR (CD_3OD): δ=19.5, 21.4 (2×CH_3), 40.7, 46.3, 68.0, 68.7, 71.3, 71.8 (6×CH_2), 118.1 (CH), 132.5, 133.3, 138.9, 139.0, 141.3, 149.7, 151.7, 158.4 (8×quaternary C), 172.8 ppm (CH); ES-MS: *m*/*z* (%): 374.3 (100) $[M+H]^+$; HR-MS (EI-MS): *m*/*z*: calcd for $C_{18}H_{23}N_5O_4$ $[M+H]^+$: 374.1828; found: 374.1834 (delta 1.69 ppm).

3-[2′-(*tert*-Butyloxycarbonylamino)eth-1′-yl]-7,8-dimethyl-10-(3″-oxabut-1″-yl)benzo[*g*]pteridine-2,4-dione (9-Boc): Flavin **5** (1.2 g, 4 mmol, 1 equiv) was dissolved in dry DMF (150 mL) at 80 °C. After cooling the solution to ambient temperature, potassium carbonate (2.8 g, 20 mmol, 5 equiv) was added and the mixture was stirred for 30 min. A solution of 2-(*tert*-butyloxycarbonylamino)ethyl bromide (2.3 g, 10 mmol, 2.5 equiv) in DMF (5 mL) was added dropwise, followed by sodium iodide (0.9 g, 6 mmol, 1.5 equiv). The reaction mixture was stirred at ambient temperature for 1 d. Another portion of the bromide (2.3 g, 10 mmol, 2.5 equiv) was then added, and the reaction mixture was stirred for a further 2 d at

ambient temperature. It was then concentrated in vacuo, the residue was redissolved in dichloromethane (400 mL), and this solution was washed with aqueous sodium hydrogen carbonate solution (250 mL), water (250 mL), and brine (250 mL). The organic phase was separated, dried over magnesium sulfate, and concentrated in vacuo. The remaining dark oil was purified by column chromatography (AcOEt/MeOH 20:1), giving the title product as a yellow solid (950 mg, 54%). R_f=0.42 (AcOEt/MeOH 10:1); m.p. 176°C (decomp); ^{1}H NMR ([D$_6$]DMSO): δ=1.32 (s, 9H; Boc), 2.40 (s, 3H; CH$_3$-7), 2.51 (s, 3H; CH$_3$-8), 3.19–3.21 (m, 2H; CH$_2$-2′), 3.24 (s, 3H; CH$_3$-4″), 3.76 (t, J=5.6 Hz, 2H; CH$_2$-1″), 3.96 (t, J=5.9 Hz, 2H; CH$_2$-1′), 4.83 (t, J=5.6 Hz, 2H; CH$_2$-2″), 6.82 (t, J=5.9 Hz, 1H; NH), 7.89 (s, 1H; H-9), 7.95 ppm (s, 1H; H-6); ^{13}C NMR ([D$_6$]DMSO): δ=18.8, 20.7, 28.2 (3×CH$_3$), 37.7, 40.9, 43.8 (3×CH$_2$), 58.5 (CH$_3$), 68.4 (CH$_2$), 77.6 (quaternary C), 116.8, 130.8 (2×CH), 131.4, 133.9, 136.0, 136.4, 146.5, 148.8, 154.8, 155.7, 159.7 ppm (9×quaternary C); ES-MS: m/z (%): 388.1 (65) [M+H−C$_4$H$_8$]$^+$, 444.2 (100) [M+H]$^+$.

3-(2′-Aminoeth-1′-yl)-7,8-dimethyl-10-(3″-oxabut-1″-yl)benzo[*g*]pteridine-2,4-dione (9): Flavin **9-Boc** (0.85 g, 1.9 mmol) was dissolved in dichloromethane (150 mL), and HCl in diethyl ether (10 mL) was added dropwise. The reaction mixture was stirred for 15 h at ambient temperature. The brown precipitate that formed was collected by filtration and dried to yield **9·HCl** (0.69 mg, 95%). R_f=0.00 (AcOEt/MeOH 10:1); m.p. 150°C (decomp); ^{1}H NMR ([D$_6$]DMSO): δ=2.41 (s, 3H; CH$_3$-7), 2.51 (s, 3H; CH$_3$-8), 3.07–3.09 (m, 2H; CH$_2$-2′), 3.24 (s, 3H; CH$_3$-4″), 3.79 (t, J=5.5 Hz, 2H; CH$_2$-1″), 4.16 (t, J=5.9 Hz, 2H; CH$_2$-1′), 4.87 (t, J=5.8 Hz, 2H; CH$_2$-2″), 7.94 (s, 1H; H-9), 7.94–7.96 (br, 3H; NH$_3^+$), 7.96 ppm (s, 1H; H-6); ^{13}C NMR ([D$_6$]DMSO): δ=18.8, 20.7 (2×CH$_3$), 37.3, 39.9, 44.0 (3×CH$_2$), 58.5 (CH$_3$), 68.4 (CH$_2$), 117.0, 130.8 (CH), 131.4, 133.9, 136.3, 136.4, 146.8, 148.9, 154.9, 160.2 ppm (8×quaternary C); ES-MS: m/z (%): 344.1 (100) [M+H]$^+$.

General Procedure 1 for the preparation of isothiocyanates 10–13 and 24: The flavin was dissolved in water and calcium carbonate (2.5 equiv) was added. The solution was then added to a rapidly stirred solution of thiophosgene (2 equiv) in dichloromethane, prepared by diluting a 0.1 M stock solution in dichloromethane, at 0°C. The reaction mixture was stirred overnight at ambient temperature. It was then diluted with dichloromethane, and the organic phase was separated, washed with water, dried over magnesium sulfate, and concentrated in vacuo. If required, the crude product was purified by chromatography.

10-(2′-Isothiocyanatoeth-1′-yl)-7,8-dimethylbenzo[*g*]pteridine-2,4-dione (10): Preparation according to GP 1 starting from **6·HCl** (150 mg) yielded **10** as an orange solid (130 mg, 87%). R_f=0.39 (AcOEt/MeOH 10:1); m.p. 182°C (decomp); ^{1}H NMR ([D$_6$]DMSO): δ=2.41 (s, 3H; CH$_3$-7), 2.50 (s, 3H; CH$_3$-8), 4.14 (t, J=5.8 Hz, 2H; CH$_2$-2′), 4.95 (t, J=5.8 Hz, 2H; CH$_2$-1′), 7.92 (s, 1H; H-9), 8.00 (s, 1H; H-6), 11.37 ppm (s, 1H; NH); ES-MS: m/z (%): 328 (100) [M+H]$^+$.

10-(2′-Isothiocyanatoeth-1′-yl)-3,7,8-trimethylbenzo[*g*]pteridine-2,4-dione (11): Preparation according to GP 1 starting from **8·HCl** (109 mg) yielded **11** as an orange solid (88 mg, 79%). R_f=0.35 (CHCl$_3$/MeOH 20:1); m.p. 195°C (decomp); ^{1}H NMR (CDCl$_3$): δ=2.46 (s, 3H; CH$_3$-7), 2.59 (s, 3H; CH$_3$-8), 3.52 (s, 3H; CH$_3$-3), 4.17 (t, J=5.8 Hz, 2H; CH$_2$-2′), 4.97 (t, J=5.6 Hz, 2H; CH$_2$-1′), 7.55 (s, 1H; H-9), 8.09 ppm (s, 1H; H-6); ^{13}C NMR ([D$_6$]DMSO): δ=18.8, 20.6, 30.0 (3×CH$_3$), 41.9, 42.8 (2×CH$_2$), 116.3 (CH), 130.8 (quaternary C), 131.1 (CH), 133.9, 136.0, 136.3, 146.9, 148.9, 155.0, 159.6 (7×quaternary C). The signal of the isothiocyanate group was not observed, presumably due to a long relaxation time; ES-MS: m/z (%): 342.1 (100) [M+H]$^+$.

10-(8′-Isothiocyanato-3′,6′-dioxaoct-1′-yl)-7,8-dimethylbenzo[*g*]pteridine-2,4-dione (12): Preparation according to GP 1 starting from **7·HCl** (100 mg) yielded **12** as an orange solid (98 mg, 97%). R_f=0.84 (CHCl$_3$/MeOH/AcOH 77.5:15:7.5); m.p. 178°C (decomp); NMR signals could be completely assigned with the help of 2D experiments (NOESY, HMBC, HSQC) and reported data for analogous compounds;[91] ^{1}H NMR (600 MHz, CDCl$_3$): δ=2.45 (s, 3H; CH$_3$-7), 2.56 (s, 3H; CH$_3$-8), 3.57–3.62 (m, 8H; CH$_2$-4′, -5′, -7′, -8′), 4.04 (t, J=5.5 Hz, 2H; CH$_2$-2′), 4.95 (t, J=5.5 Hz, 2H; CH$_2$-1′), 7.73 (s, 1H; H-9), 8.03 (s, 1H; H-6), 8.58 ppm (s, 1H; H-3); ^{13}C NMR (150 MHz, CDCl$_3$): δ=19.5 (CH$_3$-7), 21.5 (CH$_3$-8), 45.3 (C-4′), 45.6 (C-1′), 67.9 (C-2′), 69.2, 70.6, 70.8 (C-5′, -7′, -8′), 132.1 (C-9a), 132.4 (C-6), 133.0 (NCS), 135.0 (C-5a), 136.0 (C-4a), 137.1, 148.1 (C-7, -8), 150.4 (C-10a), 155.1, 159.6 (C-2, -4), 166.8 ppm (C-9); EI-MS: m/z (%): 91.2 (100) [C$_7$H$_7$]$^+$, 242.2 (98) [M−side chain]$^{+\cdot}$, 415.3 (5) [M]$^{+\cdot}$;[90] ES-MS: m/z (%): 416.1 (100) [M+H]$^+$; HR-MS (EI-MS): m/z: calcd for C$_{19}$H$_{21}$N$_5$O$_4$S [M]$^{+\cdot}$: 415.1314; found: 415.1320 (delta −1.39 ppm).

3-(2′-Isothiocyanatoeth-1′-yl)-7,8-dimethyl-10-(3″-oxabut-1″-yl)benzo[*g*]pteridine-2,4-dione (13): Preparation according to GP 1 starting from **9·HCl** (0.6 g) yielded **13** as a yellow solid (0.54 g, 89%). R_f=0.33 (AcOEt); m.p. 190–193°C; ^{1}H NMR ([D$_6$]DMSO): δ=2.41 (s, 3H; CH$_3$-7), 2.51 (s, 3H; CH$_3$-8), 3.24 (s, 3H; CH$_3$-4″), 3.77 (t, J=5.8 Hz, 2H; CH$_2$-1″), 3.95 (t, J=5.9 Hz, 2H; CH$_2$-1′), 4.20 (t, J=5.8 Hz, 2H; CH$_2$-2′), 4.84 (t, J=5.6 Hz, 2H; CH$_2$-2″), 7.91 (s, 1H; H-9), 7.96 ppm (s, 1H; H-6); ^{13}C NMR ([D$_6$]DMSO): δ=18.8, 20.7 (2×CH$_3$), 40.0, 42.8, 44.0 (3×CH$_2$), 58.5 (CH$_3$), 68.3 (CH$_2$), 116.9, 130.8 (2×CH), 131.5, 134.1, 136.0, 136.2, 146.8, 149.0, 154.4, 159.6 ppm (8×quaternary C); the signal of the isothiocyanate group was not observed, presumably due to a long relaxation time; EI-MS: m/z (%): 242.2 (100) [M−CH$_2$OCH$_2$CH$_2$−CH$_2$CH$_2$-NCS]$^{+\cdot}$, 385.2 (5) [M]$^{+\cdot}$.[90]

General Procedure 2 for the preparation of flavin photocatalysts bearing a primary thiourea group (14–17 and 25): The flavin was dissolved in chloroform and gaseous NH$_3$ was passed through the solution for 3 h. The precipitate was collected by filtration and purified by trituration or chromatography as required.

7,8-Dimethyl-10-(2′-thioureidoeth-1′-yl)benzo[*g*]pteridine-2,4-dione (14): Preparation according to GP 2 starting from **10** (60 mg) yielded **14** as a yellow solid (48 mg, 76%). M.p. 178°C (decomp); ^{1}H NMR ([D$_6$]DMSO): δ=2.40 (s, 3H; CH$_3$-7), 2.48 (s, 3H; CH$_3$-8), 3.78 (m, 2H; CH$_2$-2′), 4.71 (m, 2H; CH$_2$-1′), 7.16 (brs, 2H; NH$_2$), 7.72 (m, 1H; NH), 7.87 (s, 1H; H-9), 8.14 (s, 1H; H-6), 11.27 ppm (s, 1H; H-3); ^{13}C NMR ([D$_6$]DMSO): δ=18.8, 20.6 (2×CH$_3$), 39.5, 43.6 (2×CH$_2$), 116.5, 130.8 (2×CH), 131.5, 133.7, 135.8, 136.8, 146.5, 150.3, 155.6, 159.9, 183.8 ppm (9×quaternary C); ES-MS: m/z (%): 345.0 (100) [M+H]$^+$; elemental analysis calcd (%) for C$_{15}$H$_{16}$N$_6$O$_2$S: C 52.31, H 4.68, N 24.40, S 9.31; found: C 52.55, H 4.53, N 24.51, S 9.20.

3,7,8-Trimethyl-10-(2′-thioureidoeth-1′-yl)benzo[*g*]pteridine-2,4-dione (15): Preparation according to GP 2 starting from **11** (50 mg) yielded **15** as a yellow solid (36 mg, 68%). R_f=0.70 (CHCl$_3$/MeOH 7:1); m.p. 252°C (decomp); ^{1}H NMR ([D$_6$]DMSO): δ=2.38 (s, 3H; CH$_3$-7), 2.47 (s, 3H; CH$_3$-8), 3.29 (s, 3H; CH$_3$-3), 3.77 (m, 2H; CH$_2$-2′), 4.70 (m, 2H; CH$_2$-1′), 7.18 (m, 2H; NH$_2$), 7.75 (m, 1H; NH), 7.87 (s, 1H; H-9), 8.14 ppm (s, 1H; H-6); ^{13}C NMR ([D$_6$]DMSO): δ=18.8, 20.7, 28.0 (3×CH$_3$), 39.5, 43.6 (2×CH$_2$), 116.5, 130.8 (2×CH), 131.5, 133.7, 135.8, 136.8, 146.5, 150.3, 155.6, 159.9, 183.8 ppm (9×quaternary C); ES-MS: m/z (%): 357.1 (100) [M−H$^+$]$^-$, 417.2 (65) [M+AcO]$^-$, 471.1 (55) [M+TFA]$^-$; HR-MS (EI-MS): calcd for C$_{16}$H$_{19}$N$_6$O$_2$S [M]$^{+\cdot}$: 359.1290; found: 359.1297 (delta −1.89 ppm).

7,8-Dimethyl-10-(3′,6′-dioxa-8′-thioureidooct-1′-yl)benzo[*g*]pteridine-2,4-dione (16): Preparation according to GP 2 starting from **12** (0.5 g) yielded **16** as a brown solid (230 mg, 44%). R_f=0.60 (CHCl$_3$/MeOH/AcOH 77.5:15:7.5); m.p. 170°C (decomp); ^{1}H NMR ([D$_6$]DMSO): δ=2.40 (s, 3H; CH$_3$-7), 2.50 (s, 3H; CH$_3$-8), 3.35–3.56 (m, 8H; CH$_2$-4′, -5′, -7′, -8′), 3.81 (t, J=5.9 Hz, 2H; CH$_2$-2′, 4.80 (t, J=5.5 Hz, 2H; CH$_2$-1′), 7.01 (brs, 2H; NH$_2$), 7.54 (brs, 1H; N*H*-C(S)NH$_2$), 7.88 (s, 2H; CH-6, -9), 11.33 ppm (s, 1H; H-3); ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ=18.8, 20.6 (2×CH$_3$), 43.8 (CH$_2$), 44.0 (CH$_2$-1′), 66.7 (CH$_2$-2′), 69.0, 69.5, 70.1 (3×CH$_2$), 116.8, 130.7 (2×CH), 131.4 (C-9a), 133.7 (C-5a), 135.8, 136.0, 137.1, 146.2, 155.6, 159.9 (6×quaternary C), 182.9 ppm (C=S); ES-MS: m/z (%): 433.1 (100) [M+H]$^+$; ES-MS: m/z (%): 431.1 (100) [M−H]$^+$, 467.1 (50) [M+Cl]$^-$, 491.3 (24) [M+AcO]$^-$; HR-MS (EI-MS): m/z: calcd for C$_{19}$H$_{24}$N$_6$O$_4$S [M]$^{+\cdot}$: 432.1580; found: 432.1575 (delta 1.10 ppm).

3-(2′-Thioureidoeth-1′-yl)-10-(3″-oxabut-1″-yl) flavin (17): Preparation according to GP 2 starting from **13** (100 mg) yielded 104 mg (100%) of **17** as an orange solid; R_f=0.30 (AcOEt/MeOH 10:1); m.p. 171°C (decomp); ^{1}H NMR ([D$_6$]DMSO): δ=2.39 (s, 3H; CH$_3$-7), 2.49 (s, 3H; CH$_3$-8), 3.24 (s, 3H; CH$_3$-4″), 3.66 (br, 2H; CH$_2$-1′), 3.76 (t, J=5.6 Hz, 2H; CH$_2$-1″), 4.03 (br, 2H; CH$_2$-2′), 4.82 (t, J=5.5 Hz, 2H; CH$_2$-2″), 6.98, 7.62 (2×s, 3H in total; NH), 7.88 (s, 1H; H-9), 7.90 ppm (s, 1H; H-6); ^{13}C NMR ([D$_6$]DMSO): δ=18.8, 20.7 (2×CH$_3$), 39.5, 42.1, 43.9 (3×

CH_2), 58.5 (CH_3), 68.3 (CH_2), 116.8, 130.8 (2×CH), 131.4, 133.9, 136.1, 136.2, 146.6, 148.8, 154.9, 159.7, 183.5 ppm (9×quaternary C); ES-MS: *m/z* (%): 403.1 (100) $[M+H]^+$; HR-MS (EI-MS): calcd for $C_{18}H_{22}N_6O_3S$ $[M]^{+\cdot}$: 402.1474; found: 402.1479 (delta −1.22 ppm).

General Procedure 3 for the preparation of *N,N′*-substituted flavin–thiourea compounds 18–21 and 26–28: The flavin isothiocyanate was dissolved in chloroform, and the appropriate amine (2.5 equiv) and TEA (2 equiv) were added. The reaction mixture was heated to reflux under TLC control until complete conversion was indicated. The mixture was then concentrated in vacuo and the crude product was purified by chromatography if required.

10-(9′,11′-Diaza-3′,6′,14′-trioxa-10′-thioxopentadec-1′-yl)-7,8-dimethylbenzo[*g*]pteridine-2,4-dione (18): Preparation according to GP 3 starting from **12** (20 mg) yielded **18** as an orange solid (24 mg, 100%). R_f=0.69 ($CHCl_3$/MeOH/AcOH 77.5:15:7.5); m.p. 178°C (decomp); NMR signals were assigned in analogy to those of the isothiocyanate **12** and with the help of HMBC and HSQC experiments; ^{1}H NMR ($CDCl_3$): δ=2.43 (s, 3H; CH_3-7), 2.54 (s, 3H; CH_3-8), 3.14–3.72 (m, 15H; CH_2-4′, -5′, -7′, -8′, -12′, -13′), 4.05 (br, 2H; CH_2-2′), 4.99 (br, 2H; CH_2-1′), 7.59 (s, 1H; H-9), 8.01 ppm (s, 1H; H-6); ^{13}C NMR (100 MHz, $CDCl_3$): δ=19.5 (CH_3-7), 21.6 (CH_3-8), 44.3 (C-4′), 44.9 (C-1′), 58.5 (C-15′), 70.1, 70.3, 70.6, 70.9, 71.5, 71.5 (C-2′, -5′, -7′, -8′, -12′, -13′), 116.0 (C-9), 131.5 (C-9a), 132.6 (C-6), 135.1 (C-5a), 136.0 (C-4a), 137.3, 148.3 (C-7, -8), 150.5 (C-10a), 156.5, 159.7 (C-2, -4), 183.1 ppm (C=S); ES-MS: *m/z* (%): 491.3 (100) $[M+H]^+$; HR-MS (LSI-MS): *m/z*: calcd for $C_{22}H_{31}N_6O_5S$ $[M+H]^+$: 491.2077; found: 491.2086 (delta −1.90 ppm).

10-(3′,5′-Diaza-8′,8′,9′,9′,10′,10′,11′,11′,12′,12′,13′,13′,14′,14′,15′,15′,15′-heptadecafluoro-4′-thioxopentadec-1′-yl)-7,8-dimethylbenzo[*g*]pteridine-2,4-dione (19): Preparation according to GP 3 starting from isothiocyanate **10** (50 mg) yielded **19** as a yellow solid (82 mg, 68%). M.p. 237°C (decomp); ^{1}H NMR ([D$_6$]DMSO): δ=2.38 (s, 3H; CH_3-7), 2.46 (br, 5H; CH_3-8, CH_2), 3.50–4.00 (m, 4H; 2×CH_2), 4.72 (m, 2H; CH_2), 7.78 (t, *J*=5.4 Hz, 1H; NH), 7.88 (s, 1H; H-9), 8.03 (s, 1H; H-6), 11.37 ppm (s, 1H; H-3); a ^{13}C NMR spectrum could not be measured to the extremely low solubility of the title compound; ^{19}F NMR ([D$_6$]DMSO): δ=−125.2 (m, 2F), −122.6 (m, 2F), −121.9 (m, 2F), −121.2 (m, 6F), −112.7 (m, 2F), −79.7 ppm (t, *J*=9.5 Hz, 3F; CF_3); ES-MS: *m/z* (%): 791.2 (100) $[M+H]^+$; HR-MS (LSI-MS): *m/z*: calcd for $C_{25}H_{20}F_{17}N_6O_2S$ $[M+H]^+$: 791.1097; found: 791.1102 (delta 0.64 ppm).

10-(3′,5′-Diaza-8′,8′,9′,9′,10′,10′,11′,11′,12′,12′,13′,13′,14′,14′,15′,15′,15′-heptadecafluoro-4′-thioxopentadec-1′-yl)-3,7,8-trimethylbenzo[*g*]pteridine-2,4-dione (20): Preparation according to GP 3 starting from isothiocyanate **11** (15 mg) yielded 28 mg (79%) of **20** as an orange solid; m.p. 208°C (decomp); ^{1}H NMR ([D$_6$]DMSO): δ=2.37 (s, 3H; CH_3-7), 2.45 (br, 5H; CH_3-8, CH_2), 3.30 (s, 3H; CH_3-3), 3.52–3.98 (m, 4H; 2×CH_2), 4.69 (m, 2H; CH_2), 7.79 (t, *J*=5.4 Hz, 1H; NH), 7.89 (s, 1H; H-9), 8.05 (s, 1H; H-6); a ^{13}C NMR spectrum could not be measured due to the extremely low solubility of the title compound; ^{19}F NMR ($CDCl_3$): δ=−126.6 (m, 2F), −123.9 (m, 2F), −123.2 (m, 2F), −122.4 (m, 2F), −122.1 (m, 2F), −114.2 (m, 2F), −81.2 (t, *J*=9.8 Hz, 3F); ES-MS: *m/z* (%): 805.2 (100) $[M+H]^+$; HR-MS (LSI-MS): *m/z*: calcd for $C_{26}H_{22}F_{17}N_6O_2S$ $[M+H]^+$: 805.1253; found: 805.1281 (delta −3.42 ppm).

3-(3′,5′-Diaza-8′,8′,9′,9′,10′,10′,11′,11′,12′,12′,13′,13′,14′,14′,15′,15′,15′-heptadecafluoro-4′-thioxopentadec-1′-yl)-7,8-dimethyl-10-(3″-oxabut-1″-yl)benzo[*g*]pteridine-2,4-dione (21): Preparation according to GP 3 starting from isothiocyanate **13** (40 mg) yielded **21** as an orange solid (59 mg, 67%). R_f=0.63 (CH_2Cl_2/MeOH 10:1); m.p. 186°C (decomp); ^{1}H NMR ($CDCl_3$): δ=2.45 (s, 3H; CH_3-7), 2.55 (m, 5H; CH_3-8 and CH_2-6′), 3.27 (s, 3H; CH_3-4″), 3.65 (m, 2H; CH_2-2′), 3.91 (t, *J*=5.1 Hz, 2H; CH_2-1″), 3.99 (m, 2H; CH_2-7′), 4.30 (t, *J*=6.2 Hz, 2H; CH_2-1′), 4.91 (t, *J*=5.1 Hz, 2H; CH_2-2″), 7.71 (s, 1H; H-9), 8.04 ppm (s, 1H; H-6); ^{13}C NMR ($CDCl_3$): δ=19.6, 21.8 (2×CH_3), 30.6, 40.6, 40.7, 45.6, 45.7 (5×CH_2), 59.3 (CH_3), 69.5 (CH_2), 117.0, 132.1 (2×CH), 132.2, 134.9, 135.4, 137.6, 137.6, 148.6, 148.8, 156.5, 160.5 ppm (9×quaternary C); ^{19}F NMR ($CDCl_3$): δ=−126.7 (m, 2F), −124.0 (m, 2F), −123.3 (m, 2F), −122.5 (m, 4F), −122.2 (m, 2F), −114.3 (t, *J*=13.5 Hz, 2F; CF_2-8′), −81.3 ppm (t, *J*=9.8 Hz, 3F; CF_3-16′); ES-MS: *m/z* (%): 849.3 (100) $[M+H]^+$; HR-MS (EI-MS): *m/z*: calcd for $C_{28}H_{25}F_{17}N_6O_6S$ $[M]^{+\cdot}$: 848.1437; found: 848.1438 (delta −0.07 ppm).

3,10-Bis[2′-(*tert*-butyloxycarbonylamino)eth-1′-yl]-7,8-dimethylbenzo[*g*]-pteridine-2,4-dione (22): Flavin **6-Boc** (300 mg, 0.78 mmol, 1 equiv) was dissolved in dry DMF (40 mL) at 80°C. The solution was allowed to cool to ambient temperature, whereupon potassium carbonate (540 mg, 3.9 mmol, 5 equiv) was added and the mixture was stirred for 30 min. 2-(*tert*-Butyloxycarbonylamino)ethyl bromide (520 mg, 2.3 mmol, 3 equiv) and sodium iodide (180 mg, 1.2 mmol, 1.5 equiv) were then added, and the reaction mixture was stirred at ambient temperature. After stirring for 1 d and then again after 2 d, further portions of the bromide (520 mg, 2.3 mmol, 3 equiv each) were added. After 3 d, the reaction mixture was diluted with chloroform (300 mL), washed with aqueous sodium hydrogen carbonate solution (100 mL), water (3×100 mL), and brine (100 mL), and the organic phase was concentrated in vacuo. Compound **22** was isolated by flash chromatography ($CHCl_3$/MeOH 15:1) to yield an orange solid (210 mg, 52%). R_f=0.34 ($CHCl_3$/MeOH 15:1); m.p. 136°C (decomp); ^{1}H NMR ([D$_6$]DMSO): δ=1.24 (s, 9H; *t*Bu), 1.34 (s, 9H; *t*Bu), 2.41 (s, 3H; CH_3-7), 2.50 (s, 3H; CH_3-8), 3.19 (d, *J*=6.0 Hz, 2H; CH_2-2′), 3.40 (d, *J*=5.8 Hz, 2H; CH_2-2′), 3.96 (t, *J*=6.0 Hz, 2H; CH_2-1′), 4.66 (t, *J*=5.6 Hz, 2H; CH_2-1′), 6.83 (t, *J*=5.8 Hz, 1H; NH), 7.03 (t, *J*=5.8 Hz, 1H; NH), 7.89 (s, 1H; H-9), 7.95 ppm (s, 1H; H-6); ^{13}C NMR ([D$_6$]DMSO): δ=18.8, 20.8, 27.9, 28.1 (4×CH_3), 36.9, 37.8, 40.8, 43.9 (4×CH_2), 77.5, 77.8 (2×quaternary C), 116.1, 130.9 (2×CH), 131.3, 134.0, 135.7, 135.8, 146.5, 148.7, 154.7, 155.6, 155.8, 159.6 ppm (10×quaternary C); ES-MS: *m/z* (%): 429.2 (25) $[M+H-Boc]^+$, 473.3 (35) $[M+H-Bu]^+$, 529.3 (100) $[M+H]^+$, 551.4 (40) $[M+Na]^+$.

3,10-Bis(2′-aminoeth-1′-yl)-7,8-dimethylbenzo[*g*]pteridine-2,4-dione (23): Flavin **22** (150 mg, 0.29 mmol) was dissolved in methanol (30 mL), and HCl in diethyl ether (3 mL) was added dropwise. The reaction mixture was stirred overnight at ambient temperature. It was then concentrated in vacuo and the yellow-brownish residue was dried to yield **23·2 HCl** (114 mg, 100%). R_f=0.00 ($CHCl_3$/MeOH 15:1); m.p. 268°C (decomp); ^{1}H NMR ([D$_6$]DMSO): δ=2.42 (s, 3H; CH_3-7), 2.55 (s, 3H; CH_3-8), 3.07 (d, *J*=5.5 Hz, 2H; CH_2-2′), 3.18 (d, *J*=5.2 Hz, 2H; CH_2-2′), 4.18 (t, *J*=5.9 Hz, 2H; CH_2-1′), 4.97 (t, *J*=6.6 Hz, 2H; CH_2-1′), 7.97 (s, 1H; H-9), 8.13 (brs, 3H; NH_3), 8.30 (s, 1H; H-6), 8.57 ppm (brs, 3H; NH_3); ^{13}C NMR ([D$_6$]DMSO): δ=18.8, 20.5 (2×CH_3), 35.8, 37.1, 38.5, 41.2 (4×CH_2), 116.3 (CH), 130.5 (quaternary C), 131.2 (CH), 134.2, 136.4, 136.5, 147.6, 149.4, 154.9, 160.0 ppm (7×quaternary C); ES-MS: *m/z* (%): 329.1 (100) $[M+H]^+$.

3,10-Bis(2′-isothiocyanatoeth-1′-yl)-7,8-dimethylbenzo[*g*]pteridine-2,4-dione (24): Preparation according to GP 1 starting from **23·2 HCl** (114 mg) yielded **24** as a yellow solid (95 mg, 81%). R_f=0.35 ($CHCl_3$/MeOH 25:1); m.p. 140°C (decomp); ^{1}H NMR ($CDCl_3$): δ=2.47 (s, 3H; CH_3-7), 2.60 (s, 3H; CH_3-8), 3.91 (t, *J*=6.3 Hz, 2H; CH_2-2′), 4.19 (t, *J*=5.6 Hz, 2H; CH_2-2′), 4.43 (t, *J*=6.3 Hz, 2H; CH_2-1′), 4.99 (t, *J*=5.9 Hz, 2H; CH_2-1′), 7.57 (s, 1H; H-9), 8.10 ppm (s, 1H; H-6); ^{13}C NMR ($CDCl_3$): δ=18.8, 20.9 (2×CH_3), 40.4, 42.0, 42.3, 43.8 (4×CH_2), 115.6 (CH), 131.1 (quaternary C), 132.0 (CH), 134.6, 135.0, 137.6, 148.6, 149.4, 155.4, 159.9 ppm (7×quaternary C); the signals of the isothiocyanate groups were not observed, presumably due to a long relaxation time; ES-MS: *m/z* (%): 413.1 (100) $[M+H]^+$.

7,8-Dimethyl-3,10-bis(2′-thioureidoeth-1′-yl)benzo[*g*]pteridine-2,4-dione (25): Preparation according to GP 2 starting from isothiocyanate **24** (60 mg) yielded 65 mg (100%) of **25** as an orange-red solid; R_f=0.30 ($CHCl_3$/MeOH 10:1); m.p. 235°C (decomp); ^{1}H NMR ([D$_6$]DMSO): 2.42 (s, 3H; CH_3-7), 2.50 (s, 3H; CH_3-8), 3.67–3.69 (m, 4H; 2×CH_2), 4.06 (m, 2H; CH_2-2′), 4.76 (m, 2H; CH_2-1′), 6.98–7.77 (m, 6H; NH and NH_2 groups), 7.95 (s, 1H; H-9), 8.21 ppm (s, 1H; H-6); a ^{13}C NMR spectrum could not be measured due to the extremely low solubility of the title compound; ES-MS: *m/z* (%): 447.2 (100) $[M+H]^+$; HR-MS (LSI-MS): *m/z*: calcd for $C_{18}H_{23}N_8O_2S_2$ $[M+H]^+$: 447.1385; found: 447.1372 (delta −3.00 ppm).

3,10-Bis[2′-(3′,5′-diaza-8′,8′,9′,9′,10′,10′,11′,11′,12′,12′,13′,13′,14′,14′,15′,15′,15′-heptadecafluoro-4′-thioxopentadec-1′-yl)eth-1′-yl]-7,8-dimethylbenzo[*g*]pteridine-2,4-dione (26): Preparation according to GP 3 starting from isothiocyanate **24** (60 mg) yielded a red solid (99 mg, 51%). R_f=

0.50 ($CHCl_3$/MeOH 10:1); m.p. 211 °C (decomp); ^1H and ^{13}C NMR spectra could not be measured due to the extremely low solubility of the title compound; ^{19}F NMR ([D$_6$]DMSO): $\delta = -125.4$ (m, 4F), −122.6 (m, 4F), −122.0 (m, 4F), −121.2 (m, 12F), −112.8 (m, 4F), −79.7 (m, 6F); ES-MS: *m/z* (%): 1339.2 (100) $[M+H]^+$, 1361.2 (15) $[M+Na]^+$; elemental analysis calcd (%) for $C_{38}H_{28}F_{34}N_8O_2S_2$: C 34.09, H 2.11, F 48.25, N 8.37, S 4.79; found: C 34.31, H 1.95, N 8.24, S 4.91.

Bis-flavin 27: Preparation according to GP 3 starting from isothiocyanate **12** (40 mg) and amine **7·HCl** (80 mg) yielded **27** as an orange solid (76 mg, 100%). $R_f = 0.62$ ($CHCl_3$/MeOH/AcOH 77.5:15:7.5); m.p. 165 °C (decomp); ^1H NMR ($CDCl_3$): $\delta = 2.44$ (s, 6H; CH_3-7), 2.56 (s, 6H; CH_3-8), 3.59–3.72 (m, 16H; CH_2-4′, -5′, -7′, -8′, -12′, -13′, -15′, -16′), 4.05 (t, J = 5.1 Hz, 4H; CH_2-2′, -18′), 4.11 (t, J = 5.1 Hz, 4H; CH_2-1′, -19′), 7.02 (br s, 2H; H-9′, -11′), 7.64 (s, 2H; H-9), 7.99 (s, 2H; H-6), 9.38 ppm (br s, 2H; H-3); a ^{13}C NMR spectrum could not be measured due to the very low solubility of the compound; ES-MS: *m/z* (%): 395.3 (14) $[M+2H]^{2+}$, 414.3 (21) $[M+H+K]^{2+}$, 798.4 (100) $[M+H]^+$, 811.4 (47) $[M+Na]^+$, 827.3 (4) $[M+K]^+$; elemental analysis calcd (%) for $C_{37}H_{44}N_{10}O_8S$: C 56.33, H 5.62, N 17.75, S 4.06; found: C 56.47, H 5.42, N 17.91, S 4.05.

Bis-flavin 28: Preparation according to GP 3 starting from isothiocyanate **12** (60 mg) and 3,6-dioxaoct-1,8-diyl diamine yielded **28** as an orange solid (66 mg, 93%). $R_f = 0.55$ ($CHCl_3$/MeOH/AcOH 77.5:15:7.5); m.p. 117 °C (decomp); ^1H NMR ($CDCl_3$): $\delta = 2.42$ (s, 6H; CH_3-7), 2.55 (s, 6H; CH_3-8), 3.54–3.87 (m, 28H; glycol CH_2 groups), 4.05 (br, 4H; CH_2-2′, -29′), 4.95 (br, 4H; CH_2-1′, -30′), 7.07 (br, 2H; H-3), 7.66 (s, 2H; H-9), 7.95 (s, 2H; H-6), 8.39 ppm (br, 4H; H-9′, -11′, -20′, -22′); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 19.4$, 21.5, 45.3, 67.7, 69–72 (unresolved glycol CH_2 groups), 132.2, 136.3, 138.8, 148.2 ppm. Due to low solubility of the compound, the ^{13}C NMR spectrum was reconstructed from HSQC and HMBC experiments. The signals of the remaining carbon atoms could therefore not be observed; ES-MS: *m/z* (%): 490.5 (100) $[M+2H]^{2+}$, 491.5 (22) $[M+H+Na]^{2+}$, 979.5 (72) $[M+H]^+$, 1001.5 (23) $[M+Na]^+$; HR-MS (EI-MS): *m/z*: calcd for $C_{44}H_{59}N_{12}O_{10}S_2$ $[M+H]^+$: 979.3919; found 979.3882 (delta 3.73 ppm).

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[1] S. O. Mansoorabadi, C. J. Thibodeaux, H. Liu, *J. Org. Chem.* **2007**, *72*, 6329–6342.
[2] V. Massey, *Biochem. Soc. Trans.* **2000**, *28*, 283–296.
[3] *Chemistry and Biochemistry of Flavoenzymes* (Ed.: F. Müller), CRC, Boca Raton, **1991**.
[4] B. J. Fritz, S. Kasai, K. Matsui, *Photochem. Photobiol.* **1987**, *45*, 113–117.
[5] A. Bowd, P. Byrom, J. B. Hudson, J. H. Turnbull, *Photochem. Photobiol.* **1968**, *8*, 1–10.
[6] B. König, M. Pelka, H. Zieg, T. Ritter, H. Bouas-Laurent, R. Bonneau, J.-P. Desvergne, *J. Am. Chem. Soc.* **1999**, *121*, 1681–1687.
[7] B. J. Jordan, G. Cooke, J. F. Garety, M. A. Pollier, N. Kryvokhyzha, A. Bayir, G. Rabani, V. M. Rotello, *Chem. Commun.* **2007**, 1248–1250.
[8] J. B. Caroll, B. J. Jordan, H. Xu, B. Erdogan, L. Lee, L. Cheng, C. Tiernan, G. Cooke, V. M. Rotello, *Org. Lett.* **2005**, *7*, 2551–2554.
[9] M. Gray, A. J. Goodman, J. B. Carroll, K. Bardon, M. Markey, G. Cooke, V. M. Rotello, *Org. Lett.* **2004**, *6*, 385–388.
[10] S. M. Butterfield, C. M. Goodman, V. M. Rotello, M. L. Waters, *Angew. Chem.* **2004**, *116*, 742–745; *Angew. Chem. Int. Ed.* **2004**, *43*, 724–727.
[11] Y.-M. Legrand, M. Gray, G. Cooke, V. M. Rotello, *J. Am. Chem. Soc.* **2003**, *125*, 15789–15795.
[12] G. Cooke, *Angew. Chem.* **2003**, *115*, 5008–5018; *Angew. Chem. Int. Ed.* **2003**, *42*, 4860–4870.
[13] F. Guo, B. H. Chang, C. J. Rizzo, *Bioorg. Med. Chem. Lett.* **2002**, *12*, 151–154.
[14] C. Behrens, M. Ober, T. Carell, *Eur. J. Org. Chem.* **2002**, 3281–3289.
[15] B. König, M. Pelka, R. Reichenbach-Klinke, J. Schelter, J. Daub, *Eur. J. Org. Chem.* **2001**, 2297–2303.
[16] A. Niemz, V. M. Rotello, *Acc. Chem. Res.* **1999**, *32*, 44–52.
[17] J. Butenandt, R. Epple, E.-U. Wallenborn, A. P. M. Eker, V. Gramlich, T. Carell, *Chem. Eur. J.* **2000**, *6*, 62–72.
[18] V. M. Rotello, *Curr. Opin. Chem. Biol.* **1999**, *3*, 747–751.
[19] R. Deans, V. M. Rotello, *J. Org. Chem.* **1997**, *62*, 4528–4529.
[20] E. Breinlinger, A. Niemz, V. M. Rotello, *J. Am. Chem. Soc.* **1995**, *117*, 5379–5380.
[21] H. A. Staab, P. Kirsch, M. F. Zipplies, A. Weinges, C. Krieger, *Chem. Ber.* **1994**, *127*, 1653–1665.
[22] T. Akiyama, F. Simeno, M. Murakami, F. Yoneda, *J. Am. Chem. Soc.* **1992**, *114*, 6613–6620.
[23] I. Tabushi, M. Kodera, *J. Am. Chem. Soc.* **1987**, *109*, 4734–4735.
[24] S. Shinkai, N. Honda, Y. Ishikawa, O. Manabe, *J. Am. Chem. Soc.* **1985**, *107*, 6286–6292.
[25] M. F. Zipplies, H. A. Staab, *Tetrahedron Lett.* **1984**, *25*, 1035–1038.
[26] Y. Yano, E. Ohya, *J. Chem. Soc. Perkin Trans. 2* **1984**, 1227–1230.
[27] S. Shinkai, T. Yamashita, Y. Kusano, O. Manabe, *J. Am. Chem. Soc.* **1982**, *104*, 563–568.
[28] G. Blankenhorn, *Eur. J. Biochem.* **1975**, *50*, 351–356.
[29] N. J. Leonard, R. F. Lambert, *J. Org. Chem.* **1969**, *34*, 3240–3248.
[30] A. A. Lindén, M. Johansson, N. Hermanns, J.-E. Bäckvall, *J. Org. Chem.* **2006**, *71*, 3849–3853.
[31] A. A. Lindén, N. Hermanns, S. Ott, L. Krüger, J.-E. Bäckvall, *Chem. Eur. J.* **2005**, *11*, 112–119.
[32] Y. Imada, H. Iida, S.-I. Murahashi, T. Naota, *Angew. Chem.* **2005**, *117*, 1732–1734; *Angew. Chem. Int. Ed.* **2005**, *44*, 1704–1706.
[33] R. Cibulka, R. Vasold, B. König, *Chem. Eur. J.* **2004**, *10*, 6223–6231.
[34] O. Wiest, C. B. Harrison, N. J. Saettel, R. Cibulka, M. Sax, B. König, *J. Org. Chem.* **2004**, *69*, 8183–8185.
[35] Y. Imada, H. Iida, S. Ono, S.-I. Murahashi, *J. Am. Chem. Soc.* **2003**, *125*, 2868–2869.
[36] M. J. H. Moonen, M. W. Fraaije, I. M. C. M. Rietjens, C. Laane, W. J. H. van Berkel, *Adv. Synth. Catal.* **2002**, *344*, 1023–1035.
[37] S.-I. Murahashi, S. Ono, Y. Imada, *Angew. Chem.* **2002**, *114*, 2472–2474; *Angew. Chem. Int. Ed.* **2002**, *41*, 2366–2368.
[38] S.-I. Murahashi, T. Oda, Y. Masui, *J. Am. Chem. Soc.* **1989**, *111*, 5002–5003.
[39] S. Shinkai, Y.-i. Ishikawa, O. Manabe, *Chem. Lett.* **1982**, *11*, 809–812.
[40] For a recent review on thiourea-based organocatalysts, see: S. J. Connon, *Chem. Eur. J.* **2006**, *12*, 5418–5427.
[41] For examples of guest binding by thiourea-containing molecules, see: a) C. Roussel, M. Roman, F. Andreoli, A. Del Rio, R. Faure, N. Vanthuyne, *Chirality* **2006**, *18*, 762–771; b) T. Gunnlaugsson, A. P. Davis, J. E. O'Brien, M. Glynn, *Org. Biomol. Chem.* **2005**, *3*, 48–56; c) G. V. Oshovsky, W. Verboom, R. H. Fokkens, D. N. Reinhoudt, *Chem. Eur. J.* **2004**, *10*, 2739–2748; d) Z.-Y. Zeng, Y.-B. He, J.-L. Wu, L.-H. Wei, X. Liu, L.-Z. Meng, X. Yang, *Eur. J. Org. Chem.* **2004**, 2888–2893; e) U. Boas, A. J. Karlsson, B. F. M. de Waal, E. W. Meijer, *J. Org. Chem.* **2001**, *66*, 2136–2145; f) K. H. Lee, J.-I. Hong, *Tetrahedron Lett.* **2000**, *41*, 6083–6087; g) K. A. Haushalter, J. Lau, J. D. Roberts, *J. Am. Chem. Soc.* **1996**, *118*, 8891–8896.
[42] For examples of colourimetric sensors based on thiourea-containing molecules, see: a) J. V. Ros-Lis, R. Martínez-Mánez, F. Sancenón, J. Soto, K. Rurack, H. Weisshoff, *Eur. J. Org. Chem.* **2007**, 2449–2458; b) D. A. Jose, D. K. Kumar, B. Ganguly, A. Das, *Org. Lett.* **2004**, *6*, 3445–3448.

[43] J. Svoboda, B. König, *Chem. Rev.* **2006**, *106*, 5413–5430.
[44] Oxidations of alcohols to aldehydes are important synthetic transformations, and environmentally more benign processes which use hydrogen peroxide or aerial oxygen as terminal oxidant are desired. See: a) K. Van Aken, L. Strekowski, L. Patiny, *Beilstein J. Org. Chem.* **2006**, *2*, 3; b) C. L. Hill, *Nature* **1999**, *401*, 436–437; c) P. T. Anastas, J. C. Warner, in *Green Chemistry: Theory and Practice*, Oxford University Press, Oxford, **1998**.
[45] For the synthesis of riboflavin, vitamin B_2, see: R. Kuhn, F. Weygand, *Chem. Ber.* **1935**, *68*, 1282–1288, and references therein.
[46] T. Harayama, Y. Tezuka, T. Taga, F. Yoneda, *Tetrahedron Lett.* **1984**, *25*, 4015–4018, and references therein.
[47] S. B. Smith, T. C. Bruice, *J. Am. Chem. Soc.* **1975**, *97*, 2875–2881.
[48] For examples of catalytic hydrogenation or the action of hydrobromic acid in acetic acid, see: a) N. S. Chowdari, C. F. Barbas III, *Org. Lett.* **2005**, *7*, 867–870; b) M. Drag, J. Oleksyszyn, *Tetrahedron Lett.* **2005**, *46*, 3359–3362; c) K. Senten, P. van der Veken, I. De Meester, A.-M. Lambeir, S. Scharpé, A. Haemers, K. Augustyns, *J. Med. Chem.* **2004**, *47*, 2906–2916; d) A. Mucha, M. Pawełczak, J. Hurek, P. Kafarski, *Bioorg. Med. Chem. Lett.* **2004**, *14*, 3113–3116; e) A. P. Owens, A. Nadin, A. C. Talbot, E. E. Clarke, T. Harrison, H. D. Lewis, M. Reilly, J. D. J. Wrigley, J. L. Castro, *Bioorg. Med. Chem. Lett.* **2003**, *13*, 4143–4145.
[49] P. G. M. Wuts, T. W. Green, in *Green's Protective Groups in Organic Synthesis*, Wiley, Hoboken, **2006**.
[50] Modification of a procedure of C. Vergne, M. Bois-Choussy, R. Beugelmans, J. Zhu, *Tetrahedron: Asymmetry* **1997**, *8*, 391–398.
[51] J. L. Jiménez Blanco, P. Bootello, J. M. Benito, C. Ortiz Mellet, J. M. García Fernandez, *J. Org. Chem.* **2006**, *71*, 5136–5143.
[52] For the photocatalytic oxidation of 4-methoxybenzyl alcohol to the aldehyde using titanium dioxide, see: G. Palmisano, S. Yurdakal, V. Augugliaro, V. Loddo, L. Palmisano, *Adv. Synth. Catal.* **2007**, *349*, 964–970.
[53] V. Massey, *J. Biol. Chem.* **1994**, *269*, 22459–22462.
[54] K. C. Jones, D. P. Ballou, *J. Biol. Chem.* **1986**, *261*, 2553–2559.
[55] To exclude any kinetic deuterium isotope effect on the course of the reaction, analogous experiments were performed in undeuterated solvents and analysed by HPLC, which gave identical results.
[56] N. A. Stephenson, A. T. Bell, *Anal. Bioanal. Chem.* **2005**, *381*, 1289–1293.
[57] In the absence of oxygen, conversion of up to 10% would be still observed, even if the cycle did not proceed, because the flavin is initially in the active oxidised form.
[58] F. Y.-H. Wu, R. E. MacKenzie, D. B. McCormick, *Biochemistry* **1970**, *9*, 2219–2224.
[59] K.-Y. Yang, R. P. Swenson, *Biochemistry* **2007**, *46*, 2289–2297.
[60] M. Ghanem, G. Gadda, *Biochemistry* **2006**, *45*, 3437–3447.
[61] R. Singh, Geetanjali, C. R. Babu, *Chem. Biodiversity* **2005**, *2*, 429–446.
[62] S. Watanabe, N. Kosaka, S.-i. Kondo, Y. Yano, *Bull. Chem. Soc. Jpn.* **2004**, *77*, 569–574.
[63] Y. Yano, *Antioxid. Redox Signaling* **2001**, *3*, 899–909.
[64] T. D. Carson, S.-W. Tam-Chang, H. E. Beck, *Antioxid. Redox Signaling* **2001**, *3*, 731–736.
[65] Y. Yin, N. S. Sampson, A. Vrielink, P. I. Lario, *Biochemistry* **2001**, *40*, 13779–13787.
[66] F. G. Bordwell, *Acc. Chem. Res.* **1988**, *21*, 456–463.
[67] W. N. Olmstead, Z. Margolin, F. G. Bordwell, *J. Org. Chem.* **1980**, *45*, 3295–3299.
[68] D. Rehm, A. Weller, *Ber. Dtsch. Chem. Ges.* **1969**, *73*, 834–839.
[69] F. Scandola, V. Balzani, G. B. Schuster, *J. Am. Chem. Soc.* **1981**, *103*, 2519–2523.
[70] S. V. Torti, H. Akimoto, K. Lin, M. E. Billingham, F. M. Torti, *J. Mol. Cell. Cardiol.* **1998**, *30*, 1173–1180.
[71] J. K. Grady, Y. Chen, N. D. Chasteen, D. C. Harris, *J. Biol. Chem.* **1989**, *264*, 20224–20229.
[72] W.-X. Athena Guo, D. M. Ziegler, *Anal. Biochem.* **1991**, *198*, 143–148.
[73] The thiourea–isothiourea tautomerisation is induced by light. See: a) A. Macijewski, R. P. Steer, A. Mickiewicz, *Chem. Rev.* **1993**, *93*, 67–98; b) L. Lapinski, H. Rostkowska, A. Khvorostov, M. J. Nowak, *Phys. Chem. Chem. Phys.* **2003**, *5*, 1524–1529; c) H. Rostkowska, L. Lapinski, A. Khvorostov, M. J. Nowak, *J. Phys. Chem. A* **2003**, *107*, 6373–6380.
[74] G. S. Misra, U. D. N. Bajpai, J. Trekoval, *Rev. Macromol. Chem. Phys.* **1984**, *C24*, 335–353.
[75] A. Claiborne, H. Miller, D. Parsonage, R. P. Ross, *FASEB J.* **1993**, *7*, 1483–1490.
[76] A. Claiborne, R. P. Ross, D. Parsonage, *Trends Biochem. Sci.* **1992**, *17*, 183–186.
[77] J. S. O'Donnel, A. L. Schwan, *J. Sulfur Chem.* **2004**, *25*, 183–211.
[78] F. A. Davis, L. A. Jenkins, R. L. Billmers, *J. Org. Chem.* **1986**, *51*, 1033–1040.
[79] F. A. Davis, R. L. Billmers, *J. Am. Chem. Soc.* **1981**, *103*, 7016–7018.
[80] W. S. Allison, *Acc. Chem. Res.* **1976**, *9*, 293–299.
[81] R. Epple, E.-U. Wallenborn, T. Carell, *J. Am. Chem. Soc.* **1997**, *119*, 7440–7451.
[82] a) A. Gheorghe, *Dissertation*, Universität Regensburg, **2006**; b) H. Trabelsi, F. Szönyi, N. Michelangeli, A. Cambon, *J. Fluorine Chem.* **1994**, *69*, 115–117; c) F. Szönyi, F. Guennouni, A. Cambon, *J. Fluorine Chem.* **1991**, *55*, 85–92.
[83] N. Sakai, D. Gerard, S. Matile, *J. Am. Chem. Soc.* **2001**, *123*, 2517–2524.
[84] Norel-507 HP tubes, fully transparent to 440 nm light, were used.
[85] S. L. Murov, *Handbook of Photochemistry*, Marcel Dekker, New York, **1973**.
[86] S. N. Sawhney, D. W. Boykin, *J. Heterocycl. Chem.* **1979**, *16*, 397–400.
[87] M. Nicola, G. Gaviraghi, M. Pinza, G. Pifferi, *J. Heterocycl. Chem.* **1981**, *18*, 825–829.
[88] Z.-L. Zhou, S. M. Kher, S. X. Cai, E. R. Whittemore, S. A. Espitia, J. E. Hawkinson, M. Tran, R. M. Woodward, E. Weber, J. F. Keana, *Bioorg. Med. Chem.* **2003**, *11*, 1769–1780.
[89] M. Rangarajan, J. S. Kim, S.-P. Sim, A. Liu, L. F. Liu, E. J. LaVoie, *Bioorg. Med. Chem.* **2000**, *8*, 2591–2600.
[90] For a detailed discussion on flavin fragmentation in EI-MS measurements, see: P. Brown, C. L. Hornbeck, J. R. Cronin, *Org. Mass Spectrom.* **1972**, *6*, 1383–1399.
[91] C. G. van Schagen, F. Müller, *Helv. Chim. Acta* **1978**, *61*, 3139–3142.

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