Photoreduction of 5-Deazaflavins [1,3,9-Triaza-anthracene-2(3*H*),4(10*H*)-diones]

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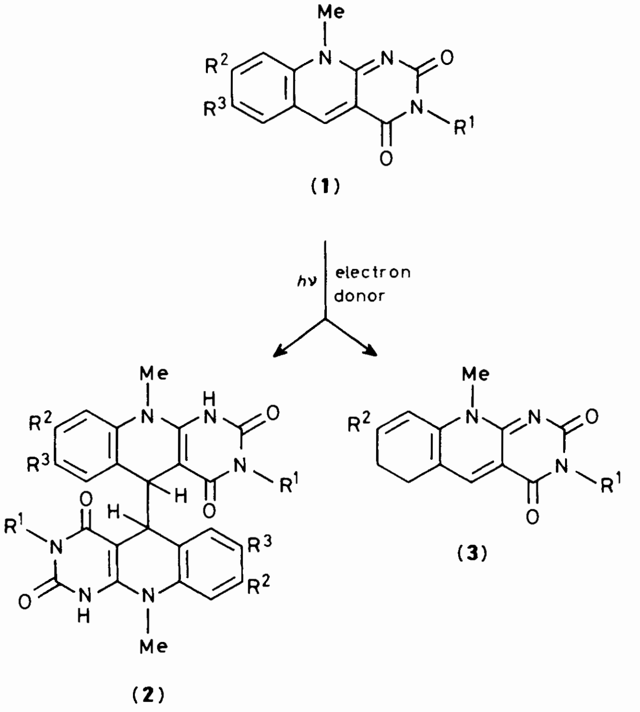
Prolonged illumination of 8-X-5-deazaflavins (X = NH_2 or NMe_2) in the presence of triethanolamine as electron donor leads to the formation of 6,7-dihydro-8-X-5-deazaflavins, while using ethylenediaminetetra-acetate or oxalate as electron donor, besides the 6,7-dihydro compound the dimeric product 5,5′-bis(1,5-dihydro-3-carboxymethyl-8-X-5-deazaflavin) is formed.

It has been shown[1] that prolonged illumination of 3-methyl- (**1a**) and 3,7,8-trimethyl-5-deazaflavin (**1b**) in the presence of oxalate or ethylenediaminetetra-acetate (EDTA) as electron donors leads to the formation of dimeric compounds (**2a**) and (**2b**) as final products of the photoreduction (Scheme 1). Recently we reported[2] the synthesis of novel water-soluble 5-deazaflavins [1,3,9-triaza-anthracene-2(3*H*),4(10*H*)-diones], containing at position 8 a strong electron donating group, *i.e.* 8-amino- (**1c**) or 8-dimethylamino-3-carboxymethyl-5-deazaflavin (**1d**). We were interested in the photoreduction of these compounds, since the presence of electron donating groups at position 8 might possibly change the path of the photoreduction. As the source of reducing equivalents we used oxalate, EDTA, or triethanolamine (TEA).

A deaerated solution of (**1c**) in water (pH 8), containing a 200-fold excess of TEA was exposed to a 20 W blue



a; R^1 = Me, R^2 = R^3 = H
b; R^1 = R^2 = R^3 = Me
c; R^1 = CH_2CO_2H, R^2 = NH_2, R^3 = H
d; R^1 = CH_2CO_2H, R^2 = NMe_2, R^3 = H

Scheme 1

Table 1. The dependence of the composition of the end-product on the electron donor used in the photoreduction of (**1c**) and (**1d**).

5-Deazaflavin	Electron donor	Ratio [½(**2**)] : [(**3**)]
(**1c**)	EDTA	67 : 33
(**1c**)	Oxalic acid	22 : 78
(**1c**)	TEA	0 : 100
(**1d**)	EDTA	13 : 87
(**1d**)	Oxalic acid	0 : 100
(**1d**)	TEA	0 : 100

fluorescent lamp (Sylvania F20T12-B) for several hours. U.v.–visible spectroscopic monitoring (Figure 1)† showed a decrease in the absorption maxima at 417 and 249 nm and the formation of a species with absorption maxima at 426 and 247 nm. Isosbestic points were found at 426, 340, 278, 231, and 216 nm. When the illumination was finished and air was admitted the spectrum remained unchanged.

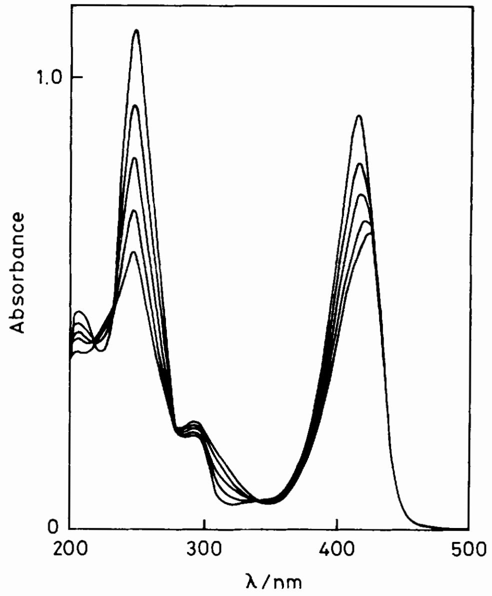


Figure 1. Photoreduction of (**1c**) (2×10^{-5} mol dm^{-3}) by TEA (4×10^{-3} mol dm^{-3}).

Since the photodimer, formed in the light-mediated conversion of 5-deazaflavin (**1a**) with oxalate, has a u.v. maximum at 312 nm and is slowly reoxidized by air in the dark,[1a,b] it is evident that the photoproduct originating from (**1c**) cannot be assigned a dimeric structure. To obtain more specific analytical data of the photoproduct the photoreduction was performed on a preparative scale by illuminating a solution of 30 mg of (**1c**) and 0.3 g of TEA in 100 ml of distilled water, which was continuously bubbled by argon, for 4 days. Isolation and characterization of the photoproduct by ^{1}H and ^{13}C n.m.r. and u.v.–visible spectroscopy, and mass spectrometry showed that it was the dihydro derivative (**3c**).‡ Although the formation of dihydro compounds has been observed in the photoreduction of a large variety of aromatic compounds,[3] hydrogenation across the C(6)–C(7) bond in 5-deazaflavin photochemistry is unprecedented. This unexpected formation of a 6,7-dihydro compound was also observed when (**1d**) was exposed to light in the presence of TEA under identical conditions; the compound being formed was assigned the structure (**3d**).‡

From these results it is evident that the presence of the amino or dimethylamino group at position 8 drastically influences the course of the photoreduction. No dimer formation occurs, but rather exclusive hydrogenation across the C(6)–C(7) bond. It has been shown[4,5] that in roseoflavin (**1**, R^1 = H, R^2 = NMe_2, R^3 = Me; C-5 replaced by N), an intramolecular charge transfer from the 8-dimethylamino group to the pteridine moiety occurs, which is even more significant in the triplet state. It is expected that in the triplet state of (**1c**) and (**1d**) a similar effect would be operative,

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† Spectra recorded after the fifth spectrum have been omitted because the isosbestic points were lost, apparently owing to some photodecomposition after prolonged illumination. The final spectrum, however, has its first absorption maximum at 426 nm. All spectra show at 248 nm a constant increase in intensity above the theoretical absorbance, caused by enhancement of the concentration of TEA relative to the reference due to the deaeration procedure.

‡ (**3c**): ^{1}H n.m.r. (300 MHz) in D_2O: δ 2.51 (m, 2H, 6-CH_2), 2.75 (m, 2H, 7-CH_2), 3.56 (s, 3H, 10-NMe), 4.41 (s, 2H, 3-NCH_2), 5.53 (s, 1H, H-9), and 7.59 (s, 1H, H-5); ^{13}C n.m.r. (300 MHz) in D_2O: δ 26.1 (C-6), 27.3 (C-7), 33.4 (10-NMe), 45.4 (3-NCH_2), 88.6 (C-9), 101.9 (C-5a), 119.1 (C-4a), 132.2 (C-5), 155.1 (C-8), 157.3 (C-9a), 158.9 (C-10a), and 164.8, 170.3, and 176.2 (3 × CO); field desorption mass spectrum: *m/z* 302 (M^+); $\lambda_{max.}$ (borate buffer, pH 8.0): 426 (log ε 4.50), 409 (sh.), 294 (3.95), 247 (4.18), and 229 nm (4.14). (**3d**): ^{1}H n.m.r. (300 MHz) in D_2O: δ 2.57 (m, 2H, 6-CH_2), 2.68 (m, 2H, 7-CH_2), 3.14 and 3.20 (6H, 8-NMe), 3.48 (s, 3H, 10-NMe), 4.35 (s, 2H, 3-NCH_2), 5.09 (s, 1H, H-9), and 7.44 (s, 1H, H-5); field desorption mass spectrum: *m/z* 330 (M^+); $\lambda_{max.}$ (borate buffer, pH 8.0): 438 (log ε 4.67), 419 (sh.), 303 (3.83), 251 (4.26), and 231 (4.16). Elemental analysis of both (**3c**) and (**3d**) could not be achieved owing to their instability during the purification procedures.

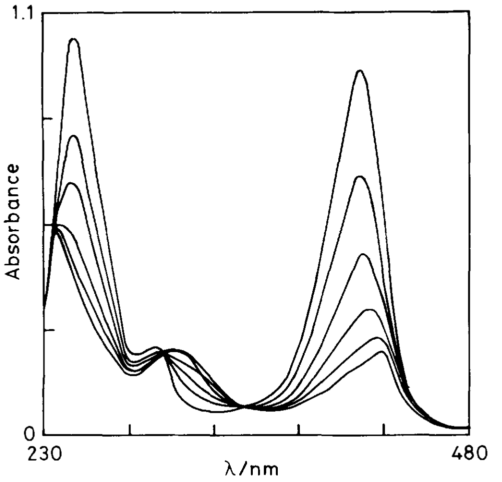

Figure 2. Photoreduction of (**1c**) (2×10^{-5} mol dm^{-3}) by EDTA (4×10^{-3} mol dm^{-3}).

which enhances the electrophilicity of the benzene ring and hence favours its reduction.

The use of other photoreducing agents such as oxalate and EDTA was also investigated.§ Irradiation of a deaerated solution of (**1c**) with blue light using either oxalate or EDTA as electron donors and monitoring the absorption spectrum (Figure 2, for EDTA) showed an absorption maximum at 426 nm, typical for the formation of (**3c**). However, the low intensity of this first absorption band, the hypsochromic shift of the absorption maximum at 249 nm, and the bathochromic shift of the absorption maximum at 295 nm, together with the observation of isosbestic points (452, 347, 300, and 236 nm) all show that this spectrum is completely different from that observed during the photoreduction of (**1c**) with TEA, and strongly indicates the formation of a second compound, which does not absorb above 380 nm. This compound is sensitive to air, since reoxidation to (**1c**) slowly occurs in the dark, when air is admitted to the solution. These spectroscopic and chemical properties point to the formation of dimer (**2c**). Similar observations were made with compound (**1d**).¶ In Table 1 the ratios between the formation of dimers (**2c**) and (**2d**) and 6,7-dihydro compounds (**3c**) and (**3d**), obtained in photoreduction of (**1c**) and (**1d**) with various electron donors, are summarized.

Table 1 shows that with the strongly electron donating dimethylamino group the reduction of the benzenoid ring is very strongly favoured. Since the amino group is a weaker electron donating group, the orientation to the benzenoid ring is less important, and in the photoreduction of (**1c**) with EDTA dimer formation even predominates.

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§ Irradiation experiments carried out in the absence of added reducing agent showed that self-reduction is negligible.

¶ No attempts were made to isolate (**2c**) and (**2d**) from the reaction mixtures for a more complete characterization, because reoxidation during the isolation procedure would be inevitable.