

NORRISH TYPE II ANALOGOUS PHOTODEGRADATION OF NEOPTERIN
AND BIOPTERIN TO 5,8 -DIHYDROPTERIN-6-ALDEHYDE

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Reports concerning the light sensitivity of pterin natural products are frequently found in the literature, e.g.¹⁻⁴. In order to prevent the formation of artefacts during work-up, isolation of these substances is usually carried out in the dark. In a few cases the final products of the aerobic photodegradation have been identified. Biopterin (6-(L-erythro-1,2-dihydroxypropyl)-pterin, 1a) yields pterin-6-carboxylic acid^{1,5} and ichthyopterin (7-hydroxybiopterin) leads to isoxanthopterin (7-hydroxypterin)^{3,4}.

The mechanism of these multistage photochemical reactions was not investigated further owing to difficulties attending the isolation of these natural substances and the small quantities consequently available. The successful large scale synthesis of very pure biopterin by a modified procedure^{6,7} has now enabled us to investigate these photochemical degradation processes for the first time.

When a 1.0×10^{-4} M solution of biopterin (1a) in phosphate buffer pH 10 was irradiated in the absence of oxygen with light of 365 nm wavelength, the absorption maximum at 362 nm disappeared (curve 1, Fig. 1) and a new maximum at 475 nm ($\lg \epsilon$ 3.13) was observed (curve 2, Fig. 1) instead. Admission of oxygen resulted in the formation of pterin-6-aldehyde 3 (curve 3, fig. 1) in a fast reaction (half live period < 1 sec); 3 was found to be identical with an authentic sample⁸ by tlc-, u.v.- and mass-spectroscopical comparison.

The second cleavage product was shown to be acetaldehyde by tlc comparison of its dinitrophenylhydrazone with authentic material. Steam distillation and u.v.-spectrophotometrical determination of the dinitrophenylhydrazone anion⁹ gave a yield of 69 %.

Compound 2 was tentatively assigned the structure 5,8-dihydro-pterin-6-aldehyde for the following reasons:

- a) 6-acetyl-1,3,7-trimethyl-5,8-dihydrolumazine, which was prepared electrochemically, showed a similar long wavelength absorption of low inten-

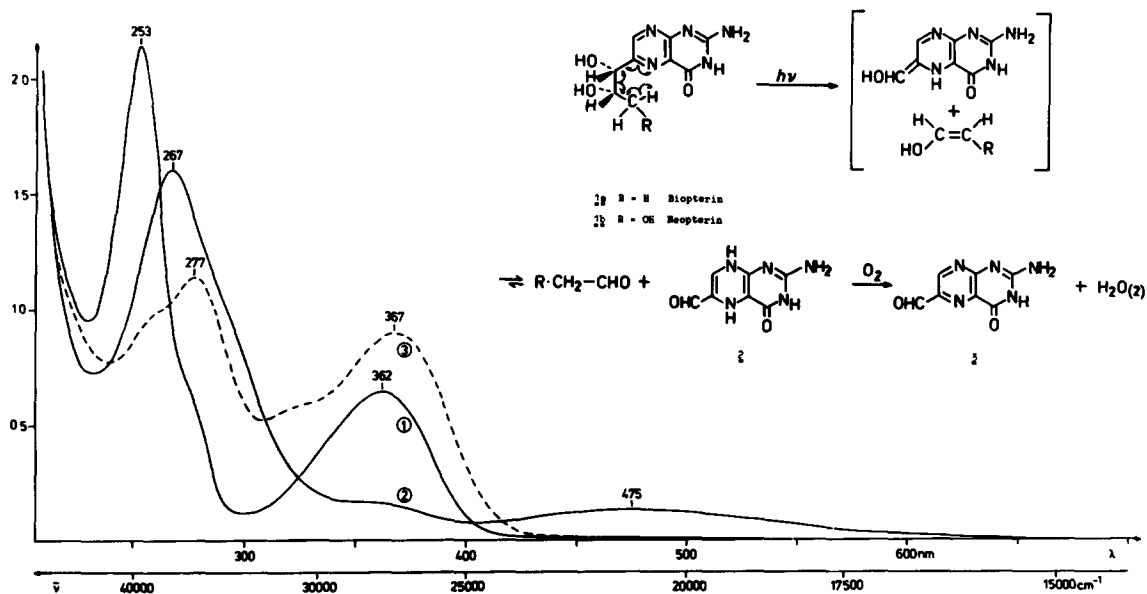


Fig. 1 - U.v.-spectra of biopterin and its photoproducts in buffer pH 10, 1.0×10^{-4} M. 1: biopterin (1a); 2: 5,8-dihydropterin-6-aldehyde (2), obtained from 1a on illumination ($\lambda = 365$ nm) in the absence of oxygen; 3: pterin-6-aldehyde (3) obtained from 2 on admission of oxygen.

sity at 488 nm¹⁰. This long wavelength absorption was also observed in the case of 1,4-dihydropyrazine derivatives (λ_{\max} 430 nm, $\lg \epsilon$ 3.1 - 3.4)¹¹.

- b) Compound 2 could be prepared also by the photoreduction of 3 in the presence of 1,4-cyclohexadiene-1-carboxylic acid. In the presence of this photosubstrate isoalloxazines are reduced to their 1,5-dihydro derivatives¹².
- c) Usually the 7,8-dihydro isomers are the more stable dihydropterin derivatives¹³. They are thought to be formed in most cases from the primarily formed formally antiaromatic 5,8-dihydro compounds by a 1,3-hydrogen shift¹³. In the case of compound 2 the 5,8-dihydro system is stabilized by the aldehyde function, which forms a vinylogous amide with the N(8)-H group.

Thus, the photoreaction proceeds like a Norrish type II cleavage, for which some examples are known in the heterocyclic series. Such reactions can occur

via a radical dealkylation mechanism as in the case of 2-butylquinoline¹⁴ or in a non-radical manner as is the case of 10-alkylisoalloxazine derivatives¹⁵. However, at the moment it is not possible to provide a detailed reaction mechanism in the pterin series.

The Norrish type II cleavage of biopterin proceeds with a quantum yield of 0.11 and was quenched to its half by 1.1×10^{-2} M iodide, whereas for the half quenching of the fluorescence (maximum at 455 nm) 5.4×10^{-2} M iodide was necessary. Therefore the participation of both singlet and triplet excited states can be postulated. The photoreaction is strongly pH-dependent: The anion reacts most easily, for the neutral species the quantum yield is only about one half, whereas the protonated compound 1 is stable photochemically. The fluorescence intensity shows a similar pH-dependence pattern to the quantum yield of the photodegradation: i.e., no fluorescence of the protonated form and strong fluorescence of the anion (the pK_a values of biopterin are 2.23 and 7.89⁶).

Neopterin (1b) was also photochemically degraded in a similar manner yielding 2 and possibly glycoaldehyde (not yet fully established). Surprisingly no reports about the photolability of neopterin were found in the literature. Experiments with this substance should be performed with careful exclusion of light.

The photoreactions described above proceed also in the presence of oxygen yielding the aldehyde 3 as the first product, which is relatively stable to oxygen. On further oxidation this aldehyde yields pterin-6-carboxylic acid as described in the literature^{1,5}.

Further photochemical degradation reactions of pterin natural products such as ichthyopterin are now being investigated.

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