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PHOTO-OXIDATION OF SULPHANILAMIDE TO BLUE PRODUCT

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ABSTRACT

Aqueous solutions of sulphanilamide undergo photolysis to produce several compounds including the blue oxidation product. The kinetics of the reaction leading to blue product has been studied and the apparant first-order rate constants for the formation of blue product at pH 1-11 have been calculated. Effect of certain antioxidants on this reaction at pH 7.0 and rates of inhibition have been determined. Ascorbic acid has been found to completely inhibit the formation of blue product. A reaction pathway for the photo-oxidation of sulphanilamide to blue product has been suggested. The blue product has been shown (James, 1940) to possess much higher antibacterial activity than sulphanilamide.

Introduction

Sulphanilamide is a photosensitizing drug which is known to cause pholotoxic and photoallergic reactions in patients (Epstein, 1941). Several photoproducts e.g. aniline, benzedine, sulphani5e acid, ammonium sulphate, 4-hydroxylaminobenzene-sulphonamide, 4,4'-azobenzene-disulphonamide, 4,4'-azoxybcnzenedisulphonamide result from the UV irradiation of aqueous sulphanilamide solutions (Epstein, 1941., Shinn, Main and Mellon, 1939., Pandula, Racz and Pajor, 1969., Pawlacryk, Turowska and Baranska, 1974., Pawlaczyk, Turowska, 1976., Ahmad and Ahmad, 1981). A number of reaction scheme have been proposed for the formation of some of these products on the basis of spin trapping studies (Chignell, Kalyanaraman, Mason, Sik, 1980., Chignell, Kalyanaraman, Sik and Mason, 1981). The formation of a blue oxidation product (Fox, Cline and Ottenberg, 1939) and purple/violet coloration (James, 1940., Rosenthal and Bauer, 1940) in photolysed solutions of sulphanilamide have been reported and a molecular formula of $C_{30}H_{25}O_2N5$ has been assigned to this product (Barkan Goldsmith, 1946). Aerobic photolysis of sulphanilamide may lead to azo and azoxy derivatives (Pandula, Racz and Pajor, 1969) or the blue product which is predominently formed in very dilute solutions i.e., 10^{-4}M (Ahmad, Ahmad and Zoha, 1973). In the present work an attempt has been made to evaluate the kinetics of this system and to outline the course of photolysis of sulphanilamide leading to the formation of the blue oxidation product.

Material and Method

A l0^{-4}M solution of sulphanilamide (BDH) was photolysed in a silica flask using a 30W Philips UV tube (88% emission at 254nm, the wavelength almost corresponding to the λ_{max} of sulphanilamide, 258nm) at pH 1-11 according to the method previously reported (Pawlaczyk, Turowska, 1976). The blue product was determined by its absorption in aqueous solution at 550nm (ε08700) Barkan, 1940).

Result and Discussion

Aqueous solutions of sulphanilamide (10^{-4}M) at pH 7.0 on UV irradiation, turned blue within 30 seconds with gradual increase in the intensity of the colour. A broad band appeared in the 500-650nm region with an absorption maximum at 550nm as reported earlier (Barkan, 1940) for the blue oxidation product of sulphanilamide. The product was assayed in solutions photolysed at pH 1-11 and the apparent first-order rate constants for its formation were calculated (Table-1).

Table-1: Formation of the blue oxidation product of sulphanilamide in photolysed solutions

pH	Apparent First-order rate constant (min. ^{1})
1	$4.44x10^4$
2	$7.08x10^4$
3	$7.89x10^4$
5	$7.90x10^4$
7	$7.50x10^4$
9	$7.87x10^4$
10	$7.15x10^4$
11	5.70x10

In order to observe the influence of pH on the formation of the blue product, log k were plotted against pH and the profile is shown in Fig.l. It appears that the formation of the blue product is independent of pH in the 3-9 range and the rate constants in this pH range are greater than those at the lower or higher pH values. This could be due to the ionisation of sulphanilamide in the higher acid-base region [pKa(SO_2NH_2)10.43,pKb(NH_2l l.64] (Northey, 1948).

The effect of some antioxidants (0.01%) was also studied on the inhibition of the photooxidation reaction of sulphanilamide. The apparent first-order rate constants for the formation of the blue product at pH 7.0 in presence of antioxidants are reported in Table-2. Ascorbic acid completely inhibits the formation of the blue product whereas the other antioxidants suppress the reaction in the following order: sodium mctabisulphitosodium sulphite >sodium thiosulphate>thiourea.The activity of ascorbic acid may be explained on the basis of its relatively higher redox potential (+ 0.40V).

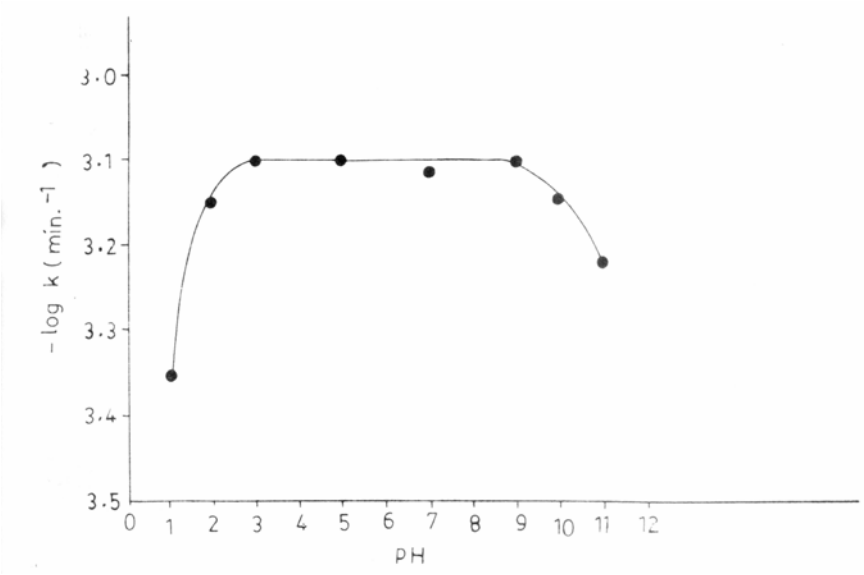

Fig.1 pH dependency of the formation of blue product.

Table-2: Formation of the blue oxidation product at pH 7.0 in presence of antioxidants

Antioxidant	Apparent First-order Rate constant (min.$^{-1}$)	Rate inhibition (%)
	7.50×10^{-4}	0
Thiourea	3.25×10^{-4}	57
Sodium thiosulphite	2.16×30^{-4}	71
Sodium sulphate	$1.08)(10^{-4}$	84
Sodium metabisulphite	0.77×10^{-4}	90
Ascorbic acid	0.00	100

A reaction pathway for the photolytic formation of the blue product of sulphanilamide may be presented (Fig.2).

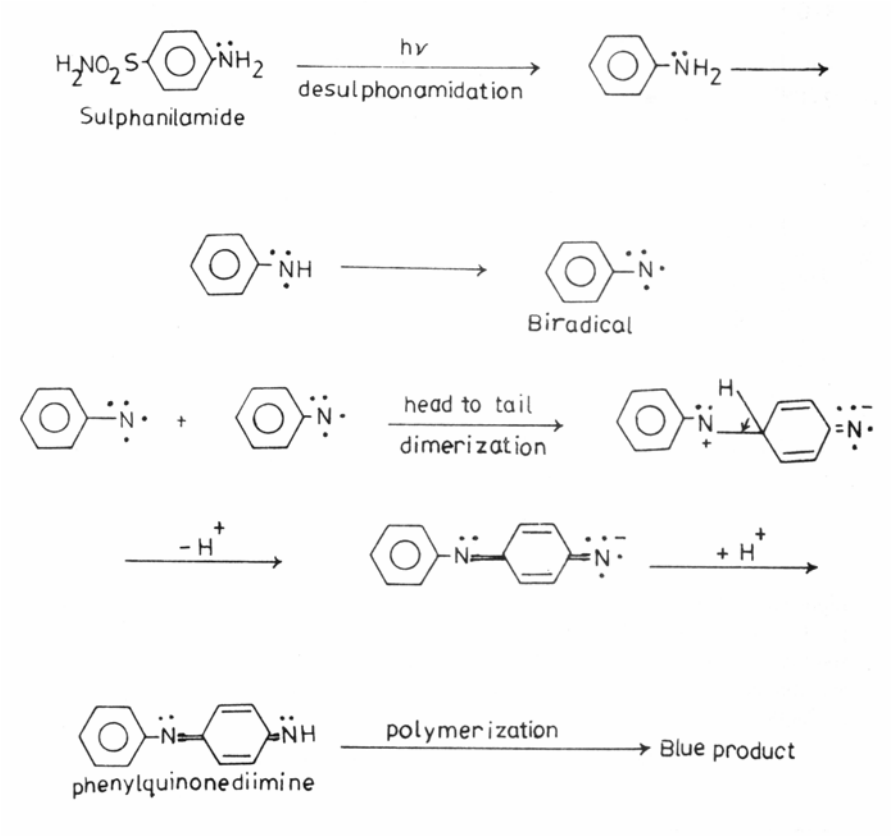

Fig.2 Photolysis of sulphanilamide to Blue Product.

Sulphanilamide on UV absorption is activated and transformed to the triplet state. The triplet state, by direct attack on the benzene ring, undergoes desulphonamidation (C-S bond energy 175 K. cal mole^{-1}) leading to the removal of the $-SO_2NH_2$ group (Rosenthal and Bauer, 1940). The species thus produced form biradicals by thhe loss of hydrogen atoms (N-H bond energy 86 K cal mole^{-1}). The head to tail dimerization of (he biradical leads to phenylquinonediimine which would polymerise to the blue product. The polymerisation of substituted imines to give deeply coloured products via a radical mechanism has been reported (Ginsburg, 1967). The participation of SO_2NH_2 and $C_6H_5NH_2$ redical in the photolysis sequence of sulphanilamide has been confirmed by spin trapping studies (Chignon, Kalyanaraman, Sik and Mason, 1981).

The photolysis of sulphanilamide to the blue product may be controlled by the

addition of suitable antioxidants as sulphanilamide can produce cynosis in patients due to its oxidation product (James, 1940). The blue product has been found to possess antibacterial activity approximately twenty five times that of sulphanilamide against streptococcus haemolyticus, staphylococcus aureus or pneumococcus type 1 (Barkan and Goldsmith, 1946). The higher antibacterial activity of the blue product may also result in higher toxicity and a need to suppress its photoformation when sulphanilamide or other sulphonamides are administered to patients.

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