STUDIES IN THE ALLOXAZINE AND ISOALLOXAZINE SERIES

XVIII. The Condensation of Symmetrical o-Aminoazobenzenes with Barbituric Acid*

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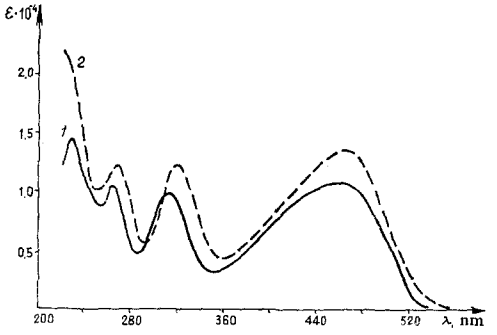
Alloxazine and lumichrome have been synthesized from symmetrical o-aminoazo compounds and barbituric acid. The yield of these compounds is considerably lower than when they are synthesized from unsymmetrical o-aminoazobenzenes and barbituric acid.

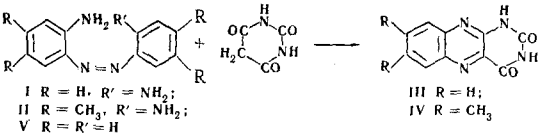
It has been shown previously [2, 3] that the condensation of unsymmetrical primary aromatic o-aminoazo



Absorption spectra (in ethanol); 1) 2,2'-diaminoazobenzene (I); 2) 2,2'-diamino-4,5,4',5'-tetramethylazobenzene (II).

compounds with barbituric acid gives alloxazines: 6-methylalloxazine, lumichrome, 7-aminoalloxazine, and 7-aminodesmethylumichrome.

In the present work we have investigated the possibility of synthesizing compounds of the alloxazine series by the condensation of barbituric acid with symmetrical aromatic o-aminoazo compounds in which the reactivity of the azo group might be different from that in the symmetrical compounds because of the countereffect of the conjugation of the ortho amino groups. It was found that the condensation of 2,2'-diaminoazobenzene (I) and 2,2'-diamino-4,5,4',5'-tetramethylazobenzene (II) with barbituric acid in n-butanol in the presence of acetic acid gave alloxazine (III) and natural lumichrome (IV), respectively, but in far lower yield. For comparison, III was synthesized from the unsymmetrical o-aminoazobenzene (V) and barbituric acid.



The marked decrease in the yield of the alloxazines III and IV (table) under monotypical reaction conditions indicates a definite deactivation of the azo bond and a hindrance to the reaction of the azo groups of the symmetrical o-aminoazobenzenes I and II with the active hydrogen atoms of the methylene group of barbituric acid. It is an interesting fact that in the formation of IV from II in the absence of acetic acid from the reaction mixture, the yield of IV rises slightly (from 7.5 to 21.0%), i.e., in this case acetic acid is perhaps a reaction inhibitor.

The structure of the compounds obtained, III and IV, was shown by the complete correspondence of their properties with those of the alloxazine and lumichrome synthesized by a known method [4, 5] from o-phenylenediamine and alloxan and from 1,2-diamino-4,5,dimethylbenzene and alloxan: by the absorption bands in the UV spectrum (in ethanol) with λ_{max} 242, 323, and 380 nm (for the alloxazine III) and with λ_{max} 250, 338, and 385 nm (for the lumichrome IV), and also by the results of paper chromatography, giving single spots with R_f 0.83 (bluish-white fluorescence for the alloxazine III) and with R_f 0.87 (yellow-green fluorescence for the lumichrome IV) in the pyridine–isobutanol–water–acetic acid (33:33:33:1) system.

2,2'-Diamino-4,5,4',5'-tetramethylazobenzene (II) was obtained from 4,5-diamino-o-xylene by the selective oxidation of one of the amino groups to an azo group with lead dioxide in absolute ether in analogy with the synthesis of 2,2'-diaminoazobenzene (I) from o-phenylenediamine according to Willstätter and Pfannenstiel [6]. The absorption spectrum of II in the UV region was identical with that of I with the small bathochromic shift (5–7 nm) characteristic for a

*For part XVII, see [1].

Yields of Alloxazines

Alloxazines	Initial o-aminoazo compounds	Yield of alloxazines
Alloxazine (III)	o-Aminoazobenzene (V)	84.2
	2,2'-Diaminoazobenzene (I)	43.0
Lumichrome (IV)	3,4-Dimethyl-6-(4'-tolylazo)aminobenzene	90.0[2]
	3,4-Dimethyl-6-(3',4'-dimethylphenylazo)-aminobenzene	83.5[2]
	2,2'-Diamino-4,5,4',5'-tetramethylazobenzene (II)	7.5

methylated compound, which confirms its structure as a symmetrical o-aminoazobenzene (figure).

EXPERIMENTAL

Alloxazine (III). A mixture of 1.0 g (0.005 mole) of o-aminoazobenzene (V) [7], 1.1 g (0.008 mole) of barbituric acid, 14.5 ml of n-butanol, and 2.4 ml of glacial acetic acid was heated to boiling for 6 hr. The precipitate that deposited was filtered off and washed with 30 ml of hot ethanol and 10 ml of boiling water. This gave 1.29 g (84.2%) of III, 97.0% pure.*

b) Under the same conditions, 0.3 g (0.0014 mole) of 2,2'-diaminoazobenzene (I) and 0.29 g (0.0023 mole) of barbituric acid gave 0.15 g (43.0%) of alloxazine 86.5% pure.

6,7-Dimethylalloxazine (IV). Under the conditions described above, 0.37 g (0.0014 mole) of 2,2'-diamino-4,5,4',5'-tetramethylazobenzene (II) and 0.29 g (0.0023 mole) of barbituric acid gave 0.062 g (7.5%) of IV 41.5% pure.

2,2'-Diamino-4,5,4',5'-tetramethylazobenzene (II). With vigorous stirring, 3.8 g of 4,5-diamino-1,2-xylene was added to a suspension of 30.0 g of lead dioxide in 350 ml of absolute ether. The mixture was heated to the boil for 2 hr. The lead oxide and unchanged lead dioxide were filtered off and the ether was distilled off from the filtrate, after which the residue was recrystallized from benzene. This gave 1.4 g (38.0%) of II with mp 212–214°C. Absorption spectrum (in ethanol): λ_{max} 268 nm (ε $1.23 \cdot 10^4$), 320 nm (ε $1.24 \cdot 10^4$), and 465 nm (ε $1.35 \cdot 10^4$). Found, %: C 71.68, 71.69; H 7.54, 7.72; N 20.40. Calculated for $C_{16}H_{20}N_4$, %: C 71.61; H 7.51; N 20.87.

*The UV absorption spectra was taken on an SF-4 spectrophotometer. The purity of the alloxazine was determined spectrophotometrically.

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