STUDIES OF THE CHEMISTRY OF HETEROCYCLES

LIII.* DEAMINATION DURING THE ACIDOCHROMIC CYCLIZATION OF ARYLAMIDES OF DIARYLGLYCOLIC ACIDS

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In contrast to arylamides of N-benziloyl-p-aminobenzoic acid, the acidochromic cyclization of arylamides of N-benziloylanthranilic acid is accompanied by deamination and, regardless of the nature of the arylamide group, leads to the formation of 7-carboxy-3,3-diphenyl-2-ketoindoline.

It is known that 3,3-diarylhydroxyindoles are formed during the acidochromic cyclization of arylamides of diarylglycolic acids with retention of the substituents present in the arylamide residue [2]. In this paper, it is shown that this situation is not always observed in the case of the cyclization of arylamides with arylcarbamoyl substituents. Thus, as expected, 5-(N-phenylcarbamoyl)-3,3-diphenylhydroxyindole (XI) is formed by the action of concentrated H_2SO_4 on the anilide of N-benziloyl-p-aminobenzoic acid (Ia). At the same time, the cyclization of arylamides of N-benziloylanthranilic acid (Ib-d, Table 1) is accompanied by deamination, regardless of the nature of the arylamide group, and leads to the formation of the same product – 7-carboxy-3,3-diphenyl-2-ketoindoline (VII). It is interesting to note that the methyl ester of N-benziloylanthranilic acid (VIII) gives a cyclization product with retention of the substituent – 3,3-diphenyl-2-keto-7-methoxycarbonylindoline (IX). The structure of VII was proved by alternative synthesis by the cyclization of N-benziloylanthranilic acid (X). The latter was obtained by the saponification of VIII.

The ease of deamination during the cyclization of arylamides of anthranilic acid (Ib-d) and the stability of the phenylcarbamoyl group in the case of Ia indicate differences in the mechanisms of the transformations. The mechanism of the cyclization of Ia was discussed in [3]. Compounds Ib-d and concentrated H_2SO_4 initially give a halochromic cation (II) in which the electrophilic attack proceeds at the oxygen of the o-arylamido group rather than at the benzene ring. As a result, an unstable ammonium cation

TABLE 1. Arylamides of N-Benziloylaminobenzoic Acids*

Compound	R	Mp, °C (from benzene)	Empirical formula	N, %		Yield, %
				found	calc.	
Ia	C_6H_5	225–226†	$C_{27}H_{22}N_2O_3$	6,8	6,6	68
Ib	C_6H_5	204	$C_{27}H_{22}N_2O_3$	6,5	6,6	64
Ic	$2\text{-}CH_3C_6H_4$	173–174	$C_{28}H_{24}N_2O_3$	6,4	6,4	78
Id	$2\text{-}BrC_6H_4$	184–185	$C_{27}H_{21}BrN_2O_3$	5,7	5,6	75

*Obtained by the method in [2].

†From glacial acetic acid.

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*See [1] for communication LII.

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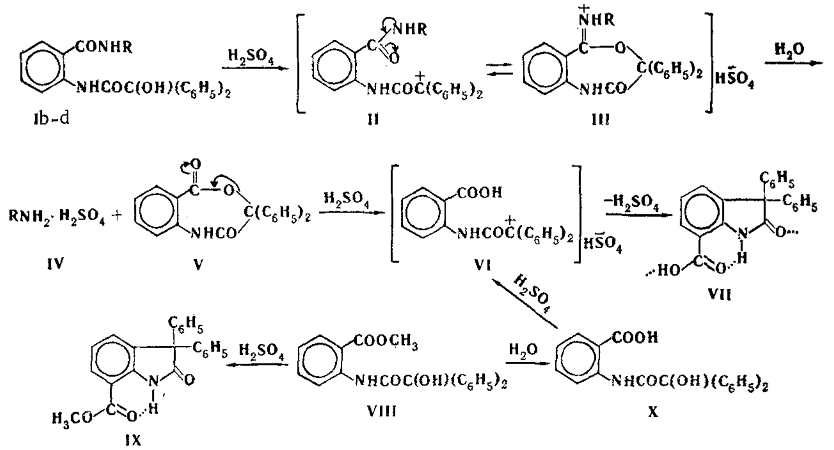
(III) is probably formed. The latter undergoes hydrolysis to give salt IV and lactone V.



The acidolysis of V generates cations VI in which the pyrrolidone ring is closed to give VII.

The structures of VII and its ester (IX) were confirmed by IR spectroscopy: a chelate structure is permitted for IX, while the spectrum of VII indicates the presence of intra- and intermolecular hydrogen bonds.

EXPERIMENTAL

Methyl N-Benziloylanthranilate (VIII). This compound was obtained in 61% yield by the general method in [2] as prisms (from glacial acetic acid) with mp 149°C. Found: N 3.8%. $C_{22}H_{19}NO_4$. Calculated: N 3.9%.

N-Benziloylanthranilic Acid (X). A 2 g (0.006 mole) sample of VIII was refluxed with 15 ml (0.07 mole) of 10% sodium hydroxide until it dissolved, and the solution was acidified with hydrochloric acid (1 : 1). The precipitate was removed by filtration and crystallized from aqueous ethanol to give 1.25 g (66%) of a product with mp 213° [4].

3,3-Diphenyl-5-(N-phenylcarbamoyl)hydroxyindole (XI). Concentrated H_2SO_4 was added to a solution of 4.3 g (0.016 mole) of Ia in 150 ml of glacial acetic acid until the red-brown coloration disappeared. The mixture was then poured into 300 ml of water, and the precipitate was removed by filtration and crystallized from ethanol to give 3.8 g (93.6%) of a product with mp 292°. Found: N 7.1%. $C_{27}H_{20}N_2O_2$. Calculated: N 6.9%.

3,3-Diphenyl-2-keto-7-methoxycarbonylindoline (IX). This compound was obtained in the same way as XI from VIII to give 58% of needles (from ethanol) with mp 227°. Found: N 4.3%. $C_{22}H_{17}NO_3$. Calculated: N 4.1%. IR spectrum: 1310 and 1130 (C−O−C), 1708 (lactam C=O), 1732 (ester C=O involved in an intramolecular hydrogen bond), 3400 and 3238 cm^{-1} (NH participating in the formation of a chelate bond [5]).

7-Carboxy-3,3-diphenyl-2-ketoindoline (VII). Concentrated H_2SO_4 was added to a solution of 4.5 g of Ib-d in 250 ml of glacial acetic acid until the appearance of a red-brown coloration ceased (~ 150 ml), and the mixture was poured into 500 ml of water. The precipitate was removed by filtration and crystallized from ethanol to give 80-97% of prisms with mp 255-256°. This compound was similarly obtained in 85% yield by cyclization of X. Found: N 4.1%. $C_{21}H_{15}NO_3$. Calculated: N 4.2%. The pK_a in 50% aqueous dioxane was 5.54. IR spectrum: 1732 and 1679 (C=O involved in intermolecular and intramolecular bonds), 2674 and 2555 (OH involved in intermolecular hydrogen bonds), 3356 and 3238 cm^{-1} (NH participating in the formation of chelate bonds [5]).

The IR spectra of KBr pellets containing 0.5% of the compounds were recorded with an IKS-14 spectrometer with LiF and NaCl prisms.

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