INDOLE DERIVATIVES

LXXVII.* SYNTHESIS OF 5-ARYLAZOINDOLES

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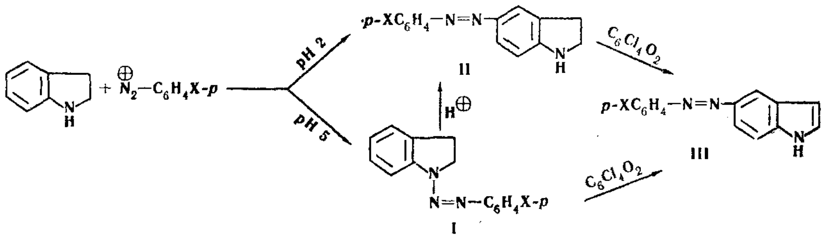
Depending on the pH, 1-(1-indolinyl)-3-aryltriazenes (I) or 5-arylazoindolines (II) are formed in the reaction of indoline with aryldiazonium salts. In acid media, I are rearranged to II. The dehydrogenation of I or II with chloranil gives 5-arylazoindoles.

In developing our research involving a study of azo compounds of the indole series [2, 3], we made an attempt to synthesize the as yet unknown 5-arylazoindoles using the indoline–indole method [4]. It is known [5] that 2-methylindoline forms triazenes with diazonium salts in buffered acetate solution, while coupling of 2-methylindoline with diazosulfanilic acid gives two compounds of unestablished structure, which are converted on reduction to the same 5-amino-2-methylindoline. 5-(p-Sulfophenylazo)-1-methylindoline has been described [4].



We have found that indoline (the base or the hydrochloride) reacts with diazonium salts at pH 5 to give satisfactory yields of triazenes (I). A certain amount of resinification is observed in this case, but quite pure substances [according to thin-layer chromatography (TLC)] are obtained when indoline hydrochloride is used. A 5-arylazoindoline (II), a triazene (I), and very small amounts of unknown compounds are formed in strongly acid media. The reaction proceeds very slowly and apparently depends on the character of the substituent in the diazo compound. When benzenediazonium chloride is used, the reaction is complete in about a week. Triazene I is detected by TLC in the first few days, and it can be isolated by column chromatography. In some cases ($X = CH_3$ and Cl), about a month is required for completion of the process, and we could not obtain the corresponding II ($X = NO_2$, OCH_3) from the indoline and diazotized p-nitroaniline and p-anisidine even after the mixture had stood for a month (I were isolated). Pronounced resinification occurs in acidic media.

Compounds II are apparently the products of the rearrangement of diazoamino compounds I, as Bamberger has already indicated [5], although he did not isolate the reaction products. In fact, 1-(1-indolinyl)-3-phenyltriazene (I, X = H) in alcohol solution in the presence of hydrochloric acid is converted to 5-phenylazoindoline (II, X = H) at about the same rate as in the formation of II (X = H) from indoline and benzenediazonium chloride.

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* See [1] for communication LXXVI.

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TABLE 1. 1-(1-Indolinyl)-3-aryltriazenes (I), 5-Arylazoindolines (II), and 5-Arylazoindoles (III)

Type of compound	X	Mp, °C	UV spectra		Empirical formula	Found, %			Calc., %			Yield, %
			λ_{max}, nm	lg ε		C	H	N	C	H	N	
I	H	74—76[a]	240 290 358	4,16 3,96 4,41	$C_{14}H_{13}N_3$	75,3	6,0	18,8	75,3	5,8	18,8	46
I	NO_2	171—172[b]	258 276 354	4,12 4,00 4,23	$C_{14}H_{12}N_4O_2$	62,8	4,5	20,7	62,6	4,5	20,9	62
I	OCH_3	90—91[b]	238 294 366	4,04 3,99 4,33	$C_{15}H_{15}N_3O$	71,3	6,0	16,3	71,1	5,9	16,2	45
II	H	79[a]	266—270 404—408	3,90 4,30	$C_{14}H_{13}N_3$	75,5	5,7	19,0	75,3	5,8	18,8	25
II	CH_3	135—136[b]	256—260 400—404	3,93 4,37	$C_{15}H_{15}N_3$	75,9	6,2	17,8	75,9	6,3	17,7	22
II	Cl	157[b]	268 416—420	3,98 4,38	$C_{14}H_{12}ClN_3$[c]	65,4	4,6	16,6	65,2	4,7	16,3	21
III	H	129[b]	272 350	4,17 4,10	$C_{14}H_{11}N_3$	76,0	5,0	19,0	76,0	4,9	19,0	60[d]
III	CH_3	169,5[b]	267—272 350—354	4,17 4,15	$C_{15}H_{13}N_3$	76,6	5,9	18,0	76,6	5,5	17,9	51
III	Cl	148[e]	270—272 354—356	4,23 4,16	$C_{14}H_{10}ClN_3$[f]	65,8	3,9	16,3	65,8	3,9	16,4	50
III	NO_2	224—226[b]	276 354	4,27 4,15	$C_{14}H_{10}N_4O_2$	63,0	4,0	21,2	63,1	3,7	21,0	19
III	OCH_3	138—138,5[b]	257—260 357—360	4,24 4,28	$C_{15}H_{13}N_3O$	71,5	5,0	16,5	71,7	5,2	16,7	20

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[a] From petroleum ether. [b] From benzene. [c] Found: Cl 13.4%. Calculated: Cl 13.8%. [d] By method A; the yield by method B was 22%. [e] From petroleum ether–benzene (2 : 1). [f] Found: Cl 14.1%. Calculated: Cl 13.9%.

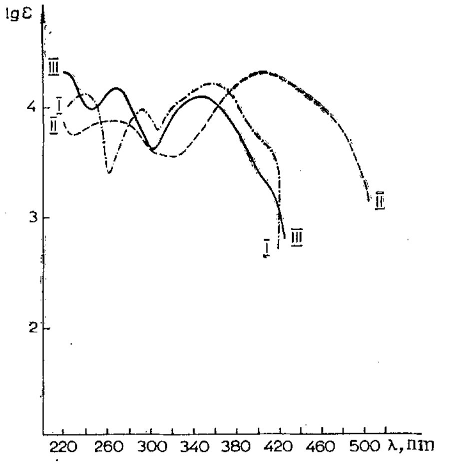

Fig. 1. UV spectra of 1-(1-indolinyl)-3-phenyltriazene (I), 5-phenylazoindoline (II), and 5-phenylazoindole (III).

The dehydrogenation of II (X = H, CH_3, Cl) with chloranil gave 5-arylazoindoles (III). After treatment of I (X = H) with an equimolar amount of chloranil, we unexpectedly isolated 5-phenylazoindole (III, X = H). Compounds I (X = NO_2, OCH_3) react similarly with chloranil. 5-Phenylazoindoline is obtained from I (X = H) in the presence of small amounts of chloranil. The conversion of triazenes to 5-arylazoindoles apparently occurs in two steps – rearrangement, probably catalyzed by tetrachlorohydroquinone, and dehydrogenation.

The UV spectra of I-III are presented in Fig. 1. In contrast to the spectra of II and III, the absorption band at 3400 cm^{-1} (ν_{NH}) is absent in the IR spectrum of I. The PMR spectrum of II (X = H) contains two triplets at 3.06 and 3.63 ppm with J = 3.5 Hz (methylene group protons). In the PMR spectrum of I (X = H), these triplets are shifted somewhat (3.18 and 4.21 ppm, with J = 3.5 Hz). They are not present in the PMR spectrum of III, but two doublets appear at 6.62 and 7.31 ppm with J = 1.5 Hz (the α and β protons of the pyrrole ring, respectively).

EXPERIMENTAL

The IR spectra of mineral oil suspensions were recorded with UR-10 and UR-20 spectrometers. The UV spectra of ethanol solutions were recorded with an SF-4A spectrometer. The PMR spectra of $CDCl_3$ and CD_3OD solutions were recorded with a JNM

4H-100 spectrometer with tetramethylsilane as the internal standard. Activity II aluminum oxide was used for column and thin-layer chromatography.

1-(1-Indolinyl)-3-phenyltriazene (I, X=H). A solution of 5.65 g (0.05 mole) of indoline in 125 ml of absolute ether was saturated with dry hydrogen chloride for 1 h. The precipitate was removed by suction filtration, washed with ether, and dried. Aniline [4.65 g (0.05 mole)] was dissolved in a mixture of 5 ml of concentrated hydrochloric acid and 35 ml of water, the solution was cooled to 0°, and 3.45 g (0.05 mole) of sodium nitrite in 10 ml of water was added with stirring to the solution. The excess nitrous acid was decomposed with urea, and the diazonium solution was filtered, treated with sodium acetate to pH 5, and allowed to stand at 0° for 0.5-1 h. Powdered indoline hydrochloride was then added in small portions with constant stirring in the course of 0.5-1 h, and the mixture was then stirred for another 2 h. The solid material was removed by filtration, dried, and chromatographed with elution of the yellow zone (with petroleum ether). The yield and characteristics of the reaction product are given in Table 1. This method was also used to obtain I ($X=NO_2$, OCH_3).

5-Phenylazoindoline (II, X=H). Powdered indoline hydrochloride [5.65 g (0.05 mole)] was added at pH 2 with constant stirring to a diazonium solution prepared from 4.65 g (0.05 mole) of aniline in 100 ml of water and 10 ml of hydrochloric acid and 3.45 g (0.05 mole) of sodium nitrite. A transparent solution formed initially, but a precipitate appeared after 15-20 min. The reaction mixture was stirred for 70 h. The precipitate was dissolved in 200 ml of alcohol, and the solution was filtered to remove the undissolved portion, neutralized with alcoholic sodium hydroxide solution, diluted with 500 ml of water, and extracted with three 70 ml portions of ether. The extract was dried, the ether was removed by distillation, and the residue was chromatographed with elution of the yellow zone (with petroleum ether). This method was also used to obtain II ($X=CH_3$, Cl) [with elution with petroleum ether–benzene (3 : 1)] (see Table 1).

Rearrangement of 1-(1-Indolinyl)-3-phenyltriazene to 5-Phenyl-azoindoline. A. A solution of 0.5 g (2 mmole) of I (X=H) in 10 ml of ethanol was mixed with 10 ml of 18% hydrochloric acid at 0°, and the mixture was held at this temperature for 7 days, after which it was poured over ice and neutralized with ammonium hydroxide. The precipitate was removed by filtration and chromatographed with elution by petroleum ether to give 0.10 g (20%) of 5-phenylazoindoline with mp 79°. This product did not depress the melting point of a genuine sample.

B. A mixture of 0.5 g (2 mmole) of I (X=H) and 0.05 g (0.2 mmole) of chloranil in 50 ml of p-xylene was heated on an oil bath at 110-115° for 3 h. The xylene was removed by distillation, and the residue was treated with 10% sodium hydroxide solution. The mixture was suction filtered, and the solid was chromatographed to give 0.10 g (20%) of 5-phenylazoindoline with mp 79°. This product did not depress the melting point of a genuine sample.

5-Phenylazoindole (III, X=H). A. A mixture of 0.50 g (2 mmole) of 5-phenylazoindoline and 0.62 g (2.5 mmole) of chloranil in 25 ml of p-xylene was refluxed on an oil bath for 5 h. The mixture was treated as in the method described above, and the yellow zone was chromatographed with petroleum ether–benzene (2 : 1). The yield and characteristics of the product are presented in Table 1. This method was also used to obtain indoles III ($X=CH_3$, Cl).

B. A mixture of 2.23 g (10 mmole) of 1-(1-indolinyl)-3-phenyltriazene and 2.46 g (10 mmole) of chloranil in 100 ml of xylene was heated on an oil bath at 110-115° for 2 h, at 150° for 5 min, and again at 110-115° for 2 h. The precipitate was treated with alkali and chromatographed. This method was also used to obtain indoles III ($X=NO_2$, OCH_3).

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