IODONIUM DERIVATIVES OF HETEROCYCLIC COMPOUNDS

III.* PREPARATION AND PROPERTIES OF IODONIUM DERIVATIVES OF INDOLE

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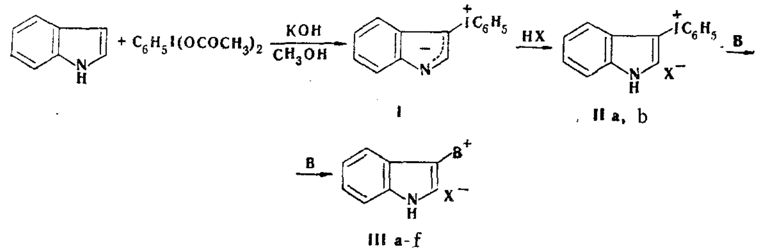
Reaction of indole with phenyl iodosoacetate in alkaline media leads to the unstable β-phenyliodonioindole betaine, the more stable tosylate and fluoborate of which were used for the introduction of a pyridine, quinoline, and isoquinoline molecule into the β-position of indole to give the corresponding tosylates and fluoborates of β-(N-pyridinio)-, β-(N-quinolinio)-, and β-(N-isoquinolinio)indole. Intramolecular charge transfer from the donor indole system to the acceptor onium systems is detected from the UV spectral data. The acidity constants of a number of β-onium derivatives of indole were determined by spectrophotometry.

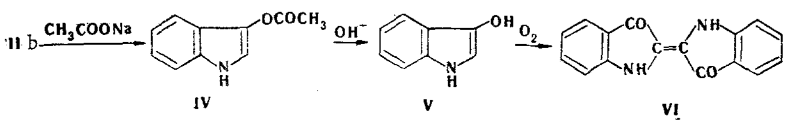
In previous papers one of us [2] mentioned the possibility of obtaining β-phenyliodonioindole betaine (I). In the present research we have made a more detailed study of the phenyliodonation of indole and have studied some properties of phenyliodonium derivatives of indole.

Reaction of indole with phenyl iodosoacetate gave, in good yield, the unstable β-phenyliodonioindole betaine (I), which is inclined to undergo electrification and spontaneous decomposition (even explosively on grinding). Treatment of betaine I with equimolar amounts of p-toluenesulfonic acid and fluoboric acid gives the relatively more stable β-phenyliodonioindole tosylate and fluoborate (IIa,b), which can be stored for several days in the cold in the dark.



a B=N-pyridyl X=TsO; b B=N-pyridyl X=BF₄; c B=N-isoquino X=TsO; d B=N-isoquinolyl X=BF₄; e B=N-quinolyl X=BF₄; f B=N-quinolyl X=ClO₄.

One should have anticipated that electrophilic attack would occur in the β-position of the indole molecule [3]. In fact, treatment of IIb with sodium acetate and subsequent alkaline hydrolysis of acyloxy derivative IV gives indoxyl (3-hydroxyindole) (V), which gives indigo (VI) on oxidation by air oxygen; this unambiguously proves the formation of I during phenyliodonation of indole.



Substitution of the phenyliodonium group to give the corresponding tosylates and fluoborates (IIIa-e) occurs in the reaction of II with nucleophilic reagents – pyridine, isoquinoline, and quinoline. β-(N-quin-

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*See [1] for communication II.

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TABLE 1. Characteristics of the Onium Derivatives of Indole

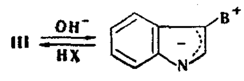
Compound	mp, deg °C	Empirical formula	Found, %			Calc., %			IR spectrum (2800-3600), cm^{-1}	pK_a in 50% ethanol	Yield, %
			N	S	Hal	N	S	Hal			
I	99—100	$C_{14}H_{10}IN$	4,5		I 39,6	4,4		I 39,7			70
IIa	102—103 ^{a}	$C_{21}H_{18}INO_3S$	3,0	6,3	I 25,8	2,9	6,5	I 25,8			85
IIb	95 ^{a}	$C_{14}H_{11}BF_4IN$			I 31,2			I 31,2	3363s, 3137m		81
IIIa	177—179 ^{b}	$C_{20}H_{18}N_2O_3S$	7,8	8,5		7,6	8,7		3137s, 3105s, 3084s, 3064s, 3041s, 2996m, 2971m, 2933m, 2913m, 2881w	13,31±0,05	98
IIIb	157—158 ^{b}	$C_{13}H_{11}BF_4N_2$	9,8		F 26,7	9,9		F 26,9	3381s, 3143m, 3129m, 3079w		72
IIIc	200—202 ^{a}	$C_{24}H_{20}N_2O_3S$	7,0	7,4		6,7	7,7		3135s, 3097s, 3050s, 2989m, 2963m, 2928s, 2871m	~13,3	96
IIId	218—220 ^{b}	$C_{17}H_{13}BF_4N_2$	8,5		F 22,9	8,4		F 22,9	3345s, 3126m, 3089w, 3064w	~13,2	76
IIIe	168—172 ^{c}	$C_{17}H_{13}BF_4N_2 \cdot {}^1/_2H_2O$	8,1		F 22,4	8,2		F 22,3	3363s, 3137m, 3076w	12,60±0,06	60
IIIf	207—209 ^{c}	$C_{17}H_{13}ClN_2O_4$	8,2		Cl 10,3	8,1		Cl 10,3	3285s, 3119m, 3084w, 3053w	12,60±0,07	50

Note: ^{a}Reprecipitation from ethanol solution by the addition of ether. ^{b}From ethanol. ^{c}From water.

olino)indole tosylate was converted, without isolation, to perchlorate IIIf. Thus it was shown to be possible to prepare a number of β-onium derivatives of indole through its iodonium derivatives. We were unable to obtain a sulfonium derivative in the reaction of II with dimethyl sulfide. Attempts to obtain the corresponding onium betaines from salts III were also unsuccessful, since resinification occurs on treatment of them with alkali solution. A similar phenomenon is also known in the hydrolysis of α-pyridinium salts of indole [4], which are obtained by reaction of β-substituted indoles with N-bromosuccinimide and pyridine.

The band of the stretching vibrations of the N—H bond of the onium derivatives in the IR spectra (Table 1) are shifted to the low-frequency region as compared with unsubstituted indole [5] (3390 cm^{-1}); this is due to the electron-acceptor properties of the onium groupings, since it is known that electron-acceptor substituents, particularly in the β-position of the indole ring, markedly lower the absorption frequency of the N—H group [5].

The onium derivatives of indole were also characterized by the UV spectra of the compounds in aqueous and aqueous ethanol solutions in media with various pH values (Figs. 1-4). As compared with the spectra of indole and its derivatives [6, 7], the introduction of onium groupings into the β-position of indole causes the appearance of new absorption maxima at 300-500 nm. The characteristic absorption bands of the pyridinium, quinolinium, and isoquinolinium systems [7] are changed. The absorption maxima of III at 350-400 nm (Figs. 2-4) are mainly associated with electron transfer from the donor indole system to the pyridinium, quinolinium, and isoquinolinium systems. The absorption maxima in the long-wave region (at 450-550 nm) of the ammonium derivatives of indole in strongly alkaline media (pH > 12), in which the betaine forms of these compounds (VII) are formed, are associated with intramolecular transfer of charge from the indole anion to the onium system. In the case of betaine I, the absorption maximum at 344 nm is evidence for intramolecular charge transfer.



VII

Judging from the absorption maxima, the onium systems that we investigated are arranged in the following order with respect to their acceptor properties: quinolinium (492 nm) > isoquinolinium (486) > pyridinium (453) > phenyliodonium (344). The same order is also observed for the onium betaines of β-dicarbonyl compounds [8-10], only in this case the quinolinium betaines display a greater bathochromic shift of the long-wave maximum than the isoquinolinium derivatives (on the average, a shift of 16 nm). The VII system is evidently coplanar, and the indole portion of the molecule interacts more with the onium portion.

The onium betaines of indole display solvatochromism: the long-wave maximum is shifted bathochromically as the polarity of the solvent decreases (Table 2).

The acidity constants of some onium derivatives of indole in aqueous ethanol solutions (Table 1) were determined by a spectrophotometric method [8]. The values of the constants of IIb and IIIc are approximate, since these compounds are unstable in alkaline

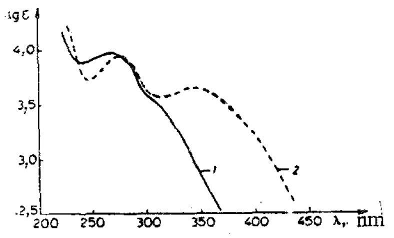


Fig. 1. UV spectra of IIb in 50% ethanol: 1) pH 1-10; 2) pH ~14.

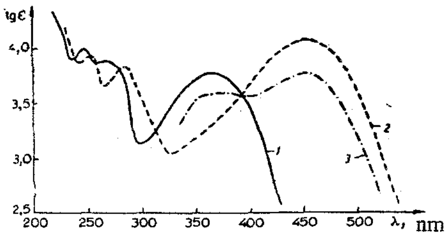


Fig. 2. UV spectra of IIIa in 50% ethanol: 1) pH 0-10; 2) pH > 14; 3) pH ~ 14.

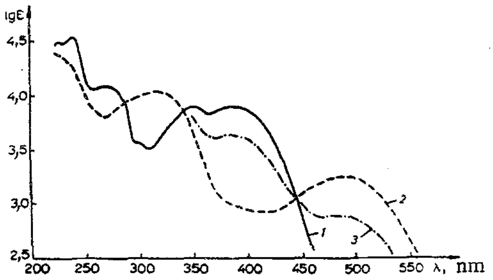


Fig. 3. UV spectra of IIIf in 50% ethanol: 1) pH 0-10; 2) pH ~ 14; 3) pH 12.2.

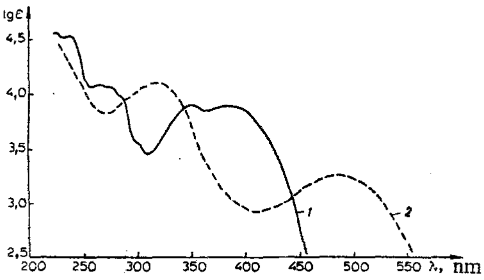


Fig. 4. UV spectra of IIIc in 50% ethanol: 1) pH 0-11; 2) pH ~ 14.

TABLE 2. Solvatochromism of β-Onium Betaines of Indole

Compound	λ_{max}, nm (lg ε)		
	1 N KOH in water	1 N KOH in 50% ethanol	1 N KOH in 90% ethanol
IIb	333 (3,50)*	344 (3,63)	360 (3,65)
IIIa	427 (3,93)	453 (4,07)	476 (4,08)

*Contains 2% ethanol.

media. Since there are no data in the literature regarding the acidity of indole and one cannot determine it by a simple spectrophotometric method (pK > 14), we cannot draw any accurate conclusions regarding the effect of onium groupings on the NH acidity of indole. It is known that the acidity of pyrazoles increases by 4.7-5 orders of magnitude [11] when a phenyliodonium group is introduced into the 4 position. Assuming a similar effect for indole, one can roughly estimate the acidity of indole in 50% ethanol as pK_a ~ 17.

EXPERIMENTAL

The IR spectra of Nujol suspensions of the compounds were recorded with an IKS-14A spectrometer. The UV spectra were recorded with SFD-2 and Specord UV-vis spectrophotometers. The pH values of buffered solutions were measured with an LPM-60M pH meter by means of a glass electrode paired with a silver chloride flow electrode. The optical densities of IIb and IIIc in alkaline media were extrapolated to "zero" time.

β-Phenyliodonioindole Betaine (I). A solution of 4.7 g (0.04 mole) of indole and 11.2 g (0.2 mole) of potassium hydroxide in 40 ml of methanol was cooled to 0-5°, and 12.9 g (0.04 mole) of finely ground phenyl iodosoacetate [13] was added in small portions with vigorous stirring in the course of 1.5 h. After all of the phenyl iodosoacetate had been added, stirring at 0-5° was continued for another 1.5 h. Betaine I (a yellow crystalline substance) was then removed by filtration, washed successively on the filter with a small amount of cold methanol and chloroform, and air dried (do not grind – it may decompose explosively!). It is recommended that the product be used immediately for the subsequent reactions, since it decomposes rapidly on storage. In work with sizeable amounts of betaine I, it should not be dried completely but used immediately after washing with chloroform. The yield was 9.0 g (70%).

β-Phenyliodonioindole Tosylate (IIa). A suspension of 9.6 g (0.03 mole) of I in 30 ml of ethanol was cooled in ice water, and 5.7 g (0.03 mole) of p-toluenesulfonic acid monohydrate was added in portions with stirring. Colorless IIa gradually precipitated from the yellow solution. The reaction mixture was diluted with 30 ml of absolute ether, and the precipitate was removed by filtration and washed on the filter with ether to give 12.5 g of a product with mp 94-95° (dec.).

β-Phenyliodonioindole Fluoborate (IIb). A 3.2 g (0.01 mole) sample of betaine I was added in portions with stirring to 10 ml of an ice water-cooled 1 N solution of fluoboric acid in ethanol. The resulting dark solution was diluted with 50 ml of absolute ether and allowed to stand at 0-5° for 1 h for crystallization. The colorless crystals of IIb were washed with ether to give 3.3 g of a product with mp 91° (dec.).

β-(N-Pyridinio)- and β-(N-Isoquinolinio)indole Tosylates (IIIa,c) and β-(N-Quinolinio)indole Perchlorate (IIIf). A mixture of 2.45 g (0.005 mole) of IIa and 4 ml of pyridine, isoquinoline, or quinoline was heated on a water bath for 15 min, after which the cooled solutions were diluted with 30 ml of absolute ether and allowed to stand at 0-5° for 12 h. The precipitated IIIa and IIIc were removed by filtration and washed on the filter with ether. The ether layer was poured off from the oily β-(N-quinolinio)indole tosylate, and 15 ml of water and 2 ml of perchloric acid were added to the residue. The reaction mixture was allowed to stand for another day, after which it was heated to the boiling point, treated with activated charcoal, and refluxed for 5 min. The hot solution was filtered, and the filtrate was cooled. The bright-yellow precipitate of IIIf was removed by filtration.

β-(N-Pyridinio)-, β-(N-Isoquinolinio)-, and β-(N-Quinolinio)indole Fluoborates (IIIb,d,e). A mixture of 2.0 g (0.005 mole) of IIb and 3-4 ml of pyridine, isoquinoline, or quinoline was heated on a boiling-water bath for 10 min. The solutions of IIIb and IIIe were cooled and diluted with 15 ml of absolute ether. Compound IIIb was allowed to stand at 0-5° for 12 h, after which the light-yellow crystalline precipitate, with mp 144-153° was removed by filtration. Compound IIIe was isolated as a dark oil; the ether was decanted, the residue was treated with 5 ml of absolute ethanol, and the greenish-yellow precipitate of IIIe was removed by filtration after 2 h. A greenish-yellow precipitate with mp 180-185° was isolated from the solution of IIId after cooling.

Conversion of IIb to Indigo. A mixture of 0.82 g (0.002 mole) of IIb and 0.16 g (0.002 mole) of sodium acetate was refluxed in 5 ml of ethanol for 30 min, after which 0.11 g (0.002 mole) of potassium hydroxide was added, and the mixture was refluxed for 5 min. It was then cooled, and 20 ml of water was added to the solution. Air was bubbled through the solution to accelerate oxidation. The resulting blue precipitate was removed by filtration to give 0.2 g (76%) of a product with mp 389° (from nitrobenzene) (mp 390-392° [14]).

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