STUDY OF PROTONATION AND DEUTERIUM EXCHANGE OF CARBAZOLES IN TRIFLUOROACETIC ACID–1,2-DICHLOROETHANE

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The protonation of the aromatic ring of 9-methylcarbazole under the influence of trifluoroacetic acid in 1,2-dichloroethane was established by spectrophotometry. Deuterium exchange between 9-methylcarbazole and deuterotrifluorotrifluoroacetic acid was evaluated quantitatively by means of mass spectrometry and the PMR spectra. Highly deuterated carbazole and 9-methylcarbazole were obtained for the first time.

We have shown [1] that trifluoroacetic acid (TFAA) accelerates the trifluoroacetylation of 9-methylcarbazole (Ib) by trifluoroacetic anhydride in 1,2-dichloroethane (DCE).

The aim of the present research was to study the reaction of Ib with TFAA in the absence of trifluoroacetic anhydride. It is known that TFAA, owing to its high acidity, is capable of protonating [2] and acylating [3, 4] several aromatic compounds and, in the presence of oxygen, of oxidizing condensed arenes [5].

On the basis of data from the PMR spectra recorded in HSO_3F at 30°C, Hakka and coworkers [6] concluded that the heteroatom of Ib undergoes protonation [6]. In their opinion, this is also related to weaker acids, viz., sulfuric acid and TFAA; they ascribe the band with λ_{max} 258 nm in the UV spectrum of a solution of Ib in 96% sulfuric acid to the absorption of the N-protonated form.

A yellow coloration, which is characterized by a new band with λ_{max} 430 nm in the electronic absorption spectrum (Fig. 1), appears when carbazole Ib is added to solutions of TFAA in DCE. The specific electrical conductivity increases by an order of magnitude in this case (Fig. 2); this indicates an increase in the number of ionic particles in solution. As the indicator of C protonation of Ib in a TFAA–DCE mixture we used anthracene, the protonation of which has been studied in various acids; the band with λ_{max} 408 nm in its electronic spectrum in solution in HF is related to the absorption of the BH^+ form [7]. We found that this same band appears in the UV spectrum of anthracene under the conditions of protonation of Ib. On the basis of the data that we obtained and the literature data we assigned the band with λ_{max} 430 nm in the electron spectrum of a solution of carbazole Ib in a TFAA–DCE mixture to the absorption of the C-protonated form. Let us note that attempts to record the signals of the methylene protons of the BH^+ form of Ib in the PMR spectrum in the TFAA–DCE system were unsuccessful both at room temperature and at −40°C, evidently because of rapid proton exchange and an insufficiently high concentration of protonated Ib.

In order to confirm our conclusion, it seemed of interest to ascertain the principal pathway and degree of deuterium exchange in Ib under the conditions of its C protonation. According to the data in [8], carbazole Ib is only slightly active with respect to acid-catalyzed hydrogen exchange. The action of CF_3COOD on a solution of carbazole Ib in DCE at room temperature for 1 day gave a mixture of deutero isomers IIb (Table 1). The percentage of deuterium in the mixture, determined by mass spectrometry, was 15.5% of the overall number of hydrogen atoms in the molecule, which corresponds to the replacement, on the average, of 1.7 H atoms in the carbazole Ib molecule by deuterium. Only 27.6% of the overall amount of the substance is involved in the fraction of polydeuterated isomers that contain three or more D atoms in the molecule. The same percentage of deuterium was obtained from the data from the PMR spectrum of a mixture in which the following three signals were recorded: 3.56 ppm (s, NCH_3), 6.87-7.38 ppm

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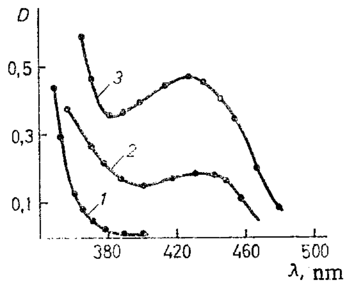


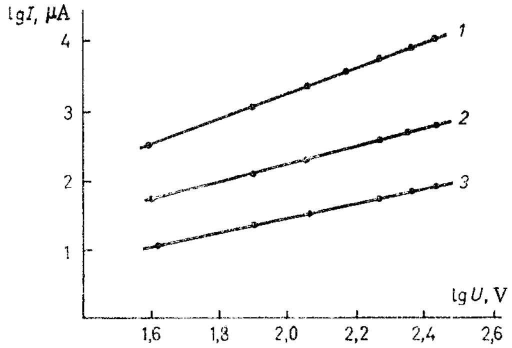


Fig. 1   Fig. 2

Fig. 1. Electronic absorption spectra of Ib: 1) when c = 1•10^{-3} mole/liter in DCE; in a TFAA–DCE mixture; 2) when c = 1•10^{-3} mole/liter; 3) when c = 3•10^{-1} mole/liter.

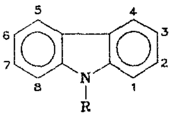
Fig. 2. Volt–ampere characteristics of the solutions: 1) DCE; 2) DCE–TFAA mixture (3 moles/liter); 3) solution of Ib in solution (2) (3•10^{-1} mole/liter); κ_1 = 0.3•10^{-6}, κ_2 = 1.8•10^{-6}, and κ_3 = 22•10^{-6} Ω^{-1}•cm^{-1}.

TABLE 1. Isotopic Composition and Conditions for Obtaining Deuterocarbazoles

Compound	No. of D atoms	M⁺	Amt. of the deutero isomer, %	Av. No. of D atoms	Reaction conditions
IIb	0	181	16,0	1,7	CF_3COOD, DCE, 20°, 24 h
	1	182	26,9		
	2	183	29,0		
	3	184	15,9		
	4	185	10,6		
	5	186	0,5		
	6	187	0,5		
	7	188	0,1		
	8	189	—		
	9	190	—		
IIa	0	167	1,9	6,0	CF_3COOD, DCE, 120°C, 6 h, threefold exchange
	1	168	2,1		
	2	169	1,8		
	3	170	4,5		
	4	171	5,8		
	5	172	13,2		
	6	173	28,3		
	7	174	24,1		
	8	175	16,0		
	9	176	2,1		
IIIb	0	181	—	6,3	Methylation [12] of IIa
	1	182	—		
	2	183	0,4		
	3	184	2,3		
	4	185	3,5		
	5	186	17,4		
	6	187	31,7		
	7	188	27,9		
	8	189	16,6		
	9	190	—		

(m, aromatic H), and 7.83 ppm (m, 4-H, 5-H) with an intensity ratio of 3:4.8:1.5, respectively. This means that for each pair of molecules of the deutero isomers of the mixture there is only one D atom located in the $C_{(4)}$ or $C_{(5)}$ position, i.e., approximately half of the molecules of the mixture of IIb contains a D atom in one of these equivalent positions, whereas the rest of the D atoms are distributed in other positions.

The bulk of the deuterium is evidently concentrated in the 3 and 6 positions; this is in agreement with the usual pathway of electrophilic substitution in carbazoles [9]. Thus, in the IR spectrum (Fig. 3) of a mixture of IIb one observes a significant decrease in the intensities of the bands of the out-of-plane deformation vibrations of the C–H bonds of the carbazole ring



Ia R=H; b R=CH$_3$

(725 and 760 cm^{-1}), and a band at 820 cm^{-1}, which is characteristic for 3- and 3,6-substituted carbazoles, and a new band at 525 cm^{-1}, which is evidently due to the deformation vibrations of the C—D bonds [10], appear in the IR spectrum (Fig. 3) of the IIb mixture. We assigned the new low-intensity band at 2275 cm^{-1} to the stretching vibrations of the aromatic ring (calculated frequency ν = 2190 cm^{-1} [10]).

The results obtained are in agreement with the data in [11], in which it was shown that 100% HSO_3F or TFAA give rise to protonation of the nitrogen atom of triphenylamine and pronounced retardation of hydrogen exchange in the phenyl rings and that, in media with lower acidity, such as TFAA—CCl_4, one observes rapid exchange of the D atoms in the para positions relative to the nitrogen atom.

In a further study of deuterium exchange we observed that carbazole Ib, when it is maintained with CF_3COOD in DCE at room temperature for 1 month, contains, on the average, 16.3% D atoms (PMR), i.e., the deuterium distribution in the mixture obtained in the case of deuterium exchange for 1 day is apparently close to the equilibrium value. Heating carbazole Ib with CF_3COOD in DCE at 110°C gives a product that contains 18.2% D atoms, which corresponds to substitution, on the average, of 18.2% D atoms; however, an increase in the temperature also leads to the formation of resins.

In contrast to its methyl analog Ib, carbazole Ia does not give side products under the conditions of deuterium exchange with CF_3COOD in DCE even at 120°C. After threefold successive reaction of Ia with CF_3COOD under these conditions, we obtained a mixture of deutero isomers IIa (Table 1). The percentage of D atoms in the product amounted to 65.8%, which corresponds to replacement of, on the average, six H atoms in carbazole Ia by deuterium; 94% of the overall amount of the substance accounts for the polydeuterated isomers that contain three or more deuterium atoms. The IR spectrum of product IIa (in mineral oil), recorded immediately after its preparation, is characterized by very weak absorption in the region of deformation vibrations of the C—H bond at 700-800 cm^{-1}, and intense band at 525 cm^{-1} (δCD), a weak band at 2295 cm^{-1} (νCD), and a band of medium intensity at 3440 cm^{-1} (νNH). The latter circumstance can be explained by rapid exchange of a D atom by the H atom attached to the heteroatom of carbazole IIa under the influence of moisture in the process of preparation of a sample for spectral measurements.

By methylation of the mixture of deutero isomers IIa under interphase conditions [12] we obtained a mixture of IIIb which, according to the mass-spectral data (Table 1), did not contain carbazole Ib and the products of its monodeuteration. This fact, as yet, remains unexplainable and requires special study. The percentage of D atoms in the sample amounts to 57%, and the average number of D atoms in the molecule is 6.3. These results are in good agreement with the data from the PMR spectrum of IIIb, which contains three signals with an intensity ratio of 3:1:0.6, from which it follows that, on the average, only three H atoms in the C$_{(4)}$

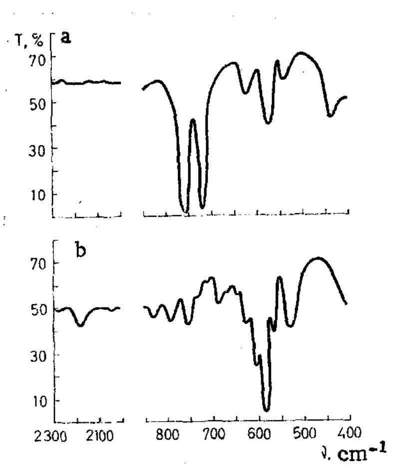
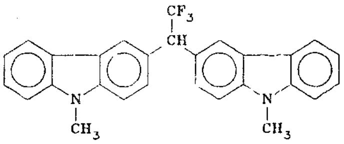


Fig. 3. IR spectra: a) Ib; b) mixture of deutero isomers IIb.

or C$_{(5)}$ position account for the five molecules of the IIIb mixture. Since the signal of the 4-H and 5-H protons in the PMR spectrum of the IIIb mixture has the form of a singlet, we concluded that all of the 3-H and 6-H protons in this product are replaced by deuterium.

We observed that the reaction of TFAA with carbazole Ib, even at room temperature, is not limited only to protonation and hydrogen exchange. Thus, from a solution of Ib in a TFAA—DCE mixture after 3 days (at 20°C), we isolated, in 4% yield, 1,1-bis(3-carbazolyl-9-methyl)-2,2,2-trifluoroethylidene (IV), the structure of which was established from data from the IR and PMR spectra and mass spectrometry, and a certain amount of resin.



IV

EXPERIMENTAL

The UV spectra of solutions of the compounds in DCE ($c = 6 \cdot 10^{-3}-3 \cdot 10^{-1}$ mole/liter for carbazole Ib) were recorded with an SF-16 spectrophotometer. The IR spectra of mineral oil suspensions were recorded with a UR-20 spectrometer. The PMR spectra were recorded with a Tesla BS-487c spectrometer (80 MHz) with hexamethyldisiloxane (HMDS) as the internal standard. The mass spectra were recorded with an MKh-1310 mass spectrometer with a system for direct introduction of the samples at an ionizing-electron voltage of 20 eV. The electrical conductivities of the solutions were measured at 20°C by the well-known two-electrode method [13]. The current in the circuit was recorded by means of a B7-27A digital voltmeter.

We obtained 95% CF_3COOD (according to the PMR spectral data) by the addition of D_2O to a cooled (to —40°C) sample of trifluoroacetic acid and fractionation at 72°C. The anthracene was recrystallized twice from benzene and had mp 214-216°C. Carbazole Ib was purified by fractionation *in vacuo* and recrystallization from hexane and had mp 88.5-89°C. Carbazole Ia was recrystallized from toluene and had mp 242-244°C. Deuterium exchange was carried out in sealed ampuls in DCE, twice distilled over P_2O_5, and then over granulated potassium hydroxide. The substrate—CF_3COOD molar ratio was 1:10. Products IIb and IIIb were recrystallized from hexane, and product IIa was crystallized from the reaction mixture by cooling and analyzed without any additional workup.

1,1-Bis(3-carbazolyl-9-methyl)-2,2,2-trifluoroethylidene (IV). A 10-ml (130 mmole) sample of TFAA was added to a solution of 4 g (22 mmole) of carbazole Ib in 10 ml of DCE, and the mixture was maintained at room temperature for 3 days. It was then washed with water until the washings were neutral with respect to litmus and dried with granulated $CaCl_2$. Separation was carried out by means of column chromatography on activity II Al_2O_3 by elution with benzene—hexane (1 1). This procedure gave 0.4 g (4%) of IV with mp 109-110°C (from hexane) and R_f 0.37 [Silufol, benzene—hexane (1:1)]. IR spectrum: 1260, 1120 (C—F), 820, 760, 730 cm^{-1} (aromatic C—H). PMR spectrum (CCl_4): 3.50 (6H, s, NCH_3), 4.87 (1H, q, $CHCF_3$, J_{HF} = 10 Hz), 6.75-7.37 (5H, m, aromatic H), and 7.75-8.80 ppm (4H, m, 4-H, 5-H). Found, %: C 75.5, H 2.5, F 13.0, N 6.5. M^+ 442. $C_{28}H_{21}F_3N_2$. Calculated, %: C 76.0, H 2.5, F 12.8, N 6.3.

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TRANSFORMATIONS OF SOME ALKALOIDS OF THE CARBOLINE SERIES UNDER THE INFLUENCE OF ALKALI

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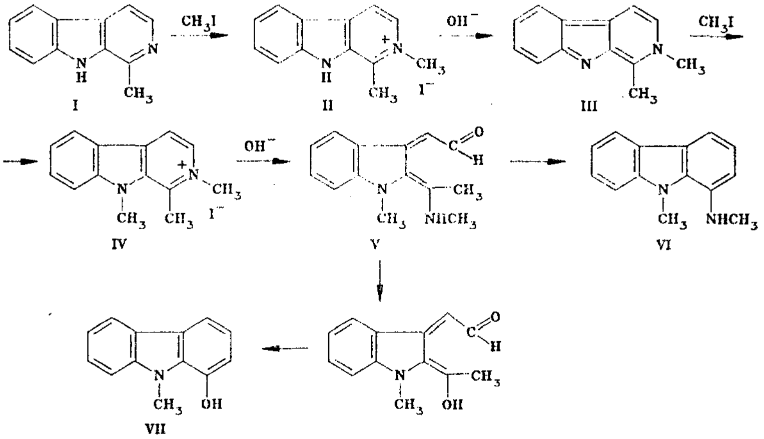
The reaction of quaternized forms of two alkaloids of the β-carboline series — harman and brevicarine — with alkali was investigated. It was established that, under the reaction conditions, the harman derivative undergoes recyclization of the pyridine part of the molecule, whereas in the analogous brevicarine derivative the pyridine ring does not undergo transformations.

The β-carboline ring is included in the composition of many natural and synthetic alkaloids with hypotensive, anti-inflammatory, and antipyretic activity [1-3]. These properties of derivatives of the group of isomeric carbolines for decades have led to the unflagging interest of chemists and pharmacologists, who have set out to search for new methods for the synthesis of these systems and to study their biological activity. The problems relating to the reactivities of carboline derivatives and their transformations under the influence of various agents have not been studied, although the presence in their structures of a π-deficient pyridine ring condensed with a typical π-surplus system (the indole fragment) makes it possible to expect the manifestation of interesting chemical properties, one of which may be the transformation of the ring under the influence of nucleophiles. The study of the transformation of these systems under the influence of nucleophiles, particularly the hydroxide



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