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## Synthesis and Study of the Structure of the Reaction Products Formed from Cyclopenta[c]quinolinium Quarternary Salts and p-Dimethylaminobenzaldehyde

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**Abstract**—The presence of active methylene group in the molecules of cyclopenta[c]quinolinium quarternary salts permitted to obtain products of their reaction with p-dimethylaminobenzaldehyde. Structures of the reaction products were established from <sup>1</sup>H and <sup>13</sup>C NMR spectral data using the correlation spectra. The effect of substituents at nitrogen on the visible absorption spectra was studied. The investigation of formation of the frontier orbitals in the reaction products by quantum chemical calculations revealed the reason of the coloration of the dyes synthesized.

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The presence of saturated five- and six-membered cycles along with the pyridine fragment in the structure of heterocyclic compounds is a real sign of their biological activity [1]. Studies of the effect of various substituents on different types of activity requires a broad set of compound containing versatile substituents in the pharmacophore fragments of molecules.

Recent studies permitted the establishment of the conditions of the reaction between secondary aromatic amines, formaldehyde, and cyclopentanone in the butanol-1-nitrobenzene mixture acidified with perchloric acid leading to the easy one-pot formation of the cyclopenta[*c*]quinolinium quarternary salts [2].

With the purpose of establishing the reactivity of the obtained quarternary cyclopenta[c]quinolinium salts we performed the quantum chemical calculations of charges and electronic density distribution on the carbon atoms [3] by PM3 method, the most suitable among the semiempiric procedures (Table 1). The presence in the structures under investigation of the negative charge and an exess electronic density in the position 1 of the compounds obtained makes them interesting nucleophilic reagents which may enter in the reactions of nucleophilic substitution at the carbonyl group of aromatic aldehydes. The substituents at the nitrogen do not affect significantly the charge of the methylene group located in the  $\gamma$ -position of the pyridinium cycle.

The reaction of the corresponding cyclopenta[*c*]quinolinium salts **I–VI** with equimolar amount of *p*dimethylaminobenzaldehyde in boiling acetic anhydride leads to the formation of colored compounds **VII-XII** according to the following scheme.

 $<sup>\</sup>begin{array}{c} R^{1} \begin{array}{c} 9 \\ 8 \\ 7 \\ 6 \end{array} \begin{array}{c} 9 \\ 9a \\ 9b \\ 3a \\ 7 \\ 6 \end{array} \begin{array}{c} 3a \\ 3a \\ 4 \\ 8 \\ R \end{array}$ 

<sup>&</sup>lt;sup>†</sup> Deceased.



 $R^{1} = H, R = CH_{3}$  (I), (A) (VII),  $R = C_{2}H_{5}, R^{1} = H$  (II), (A) (VIII),  $R = CH_{2}C_{6}H_{5}, R^{1} = H$  (III), (A) (IX),  $R = C_{6}H_{5}, R^{1} = H$  (IV), (A) (X),  $R = C_{6}H_{5}, R^{1} = H$  (IV), (A) (XI), R = 5,6-(CH<sub>2</sub>)<sub>3</sub>,  $R^{1} = H$  (VI), (A) (XII).

The reaction mixture was treated with diethyl ether and the product was crystallized from ethanol. The characteristics of the compounds obtained, their visible absorption spectra, and <sup>1</sup>H NMR spectra are presented in Table 2.

Evidently formula **A** is more probable because the methylene group located in the  $\gamma$ -position to the pyridinium nitrogen atom must be more active, still the formation of the structure **B** cannot be rejected. For establishing the structure of the dye synthesized we recorded its <sup>1</sup>H and <sup>13</sup>C NMR spectra and carried out the experiments of homonuclear (COSY, NOESY) and

heteronuclear <sup>1</sup>H–<sup>13</sup>C HMQC and HMBC correlations. The interesting specific feature of the <sup>1</sup>H NMR spectrum of the dye obtained is the extreme downfield location of one of doublets of the aromatic protons (9.52 ppm). Attribution of this signal as well as of the others belonging to the aromatic protons follows from the COSY spectrum (Fig. 1).

A doublet at 9.52 ppm is the spin–spin coupling partner for the triplet at 7.67 ppm. Therefore the downfield doublet must be attributed to the  $H^5$  proton of the benzoquinoline fragment. Most probably the downfield location of the signal is connected with the

**Table 1.** Atomic charges and HOMO  $\pi$ -electronic density calculated by PM3 method for N-substituted cyclopenta[c]quinolines

R	$\mathbf{R}^1$	Atomic charges					HOMO $\pi$ -electronic density				
		Ν	$C_{9b}$	$C_1$	$C_4$	C <sub>3</sub>	Ν	$C_{9b}$	$C_1$	$C_4$	C <sub>3</sub>
CH <sub>3</sub>	Н	0.465	0.072	-0.075	-0.121	-0.045	0.365	0.316	0.121	0.384	0.150
$C_2H_5$	Н	0.448	0.072	-0.075	-0.125	-0.044	0.362	0.315	0.120	0.386	0.149
$CH_2-C_6H_5$	Н	0.456	0.071	-0.075	-0.129	-0.045	0.006	0.003	0.001	0.001	0.000
$C_6H_5$	Н	0.592	0.058	-0.071	-0.118	-0.044	0.351	0.311	0.102	0.329	0.109
$C_6H_5$	(CH=CH) <sub>2</sub>	0.589	0.038	-0.078	-0.096	-0.049	0.245	0.086	0.046	0.254	0.072

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Comp. no.	R	$R^1$	mp	Yield, %	Found N, %	Formula	Calculated N, %	$\lambda_{max}$ , nm (log $\epsilon$ )	<sup>1</sup> H MR spectrum, δ, ppm
VII	CH <sub>3</sub>	Н	232	79	6.67	C <sub>22</sub> H <sub>23</sub> ClN <sub>2</sub> O <sub>4</sub>	6.75	559 (3.36)	6.79 (2H, Ph), 7.50–7.52 (2H, Ph), 7.8 (3H, Ph), 8.62 (1H, Ph), 8.92 (1H, 4-CH), 7.82 (1H, C=C), 2.50 (2H, 2-CH <sub>2</sub> ), 2.80(3H, N-CH <sub>3</sub> ), 3.08 [6H, N(CH <sub>3</sub> ), 3.34 (2H, 3-CH <sub>3</sub> )
VIII	C <sub>2</sub> H <sub>5</sub>	Н	141	60	6.55	C <sub>23</sub> H <sub>25</sub> ClN <sub>2</sub> O <sub>4</sub>	6.53	565 (3.40)	6.75 (2H, Ph), 6.93–7.43 (2H, Ph), 8.47–8.57 (2H, Ph), 9.20 (1H, 4- CH), 7.90 (1H, C=C), 2.50 (2H, 2- CH <sub>2</sub> ), 2.85 (2H, 3-CH <sub>2</sub> ), 5,0 (2H, N-CH <sub>2</sub> ), 1,7 (3H, CH <sub>3</sub> , 5-Et), 3,10 (6H, N(CH <sub>3</sub> ) <sub>2</sub> )
IX	CH <sub>2</sub> -C <sub>6</sub> H <sub>5</sub>	Н	244– 246	95	5.68	$C_{28}H_{27}ClN_2O_4$	5.71	560 (3.50)	6.80 (2H, Ph), 7.32 (5H, Ph) 7.60 (2H, Ph), 8.34–8.8 (2H, Ph), 9.45 (1H, 4-CH), 7.90 (1H, C=C), 2.50 (2H, 2-CH <sub>2</sub> ), 3.13 (2H, 3-CH <sub>2</sub> ), 3.09 [6H, N(CH <sub>3</sub> ) <sub>2</sub> ], 4.15 (2H, CH <sub>2</sub> -Ph)
X	C <sub>6</sub> H <sub>5</sub>	Н	272	93	5.75	$C_{27}H_{25}ClN_2O_4$	5.87	583 (3.56)	6.80 (2H, Ph), 7.55 (5H, Ph), 7.62 (2H, Ph), 7.80 (2H, Ph), 8.00 (2H, Ph), 9.16(1H, 4-CH), 7.73 (1H, C=C), 2.50 (2H, 2-CH <sub>2</sub> ), 3.45 (2H, 3-CH <sub>2</sub> ), 3.10 [6H, N(CH <sub>3</sub> ) <sub>2</sub> ]
XI	C <sub>6</sub> H <sub>5</sub>	8,9- (CH=CH) <sub>2</sub>	162– 163	95	5.35	C <sub>31</sub> H <sub>27</sub> ClN <sub>2</sub> O <sub>4</sub>	5.32	582 (3.74)	6.81 (2H, Ph), 7.81 d (5H, Ph), 7.41 (2H, Ph), 7.67–8.17 (3H, Ph), 8.34 (2H, Ph), 9.52 (1H, Ph), 9.10 (1H, 4-CH), 7.81 (1H, C=C), 3.42 (4H, 2,3-CH <sub>2</sub> ), 3.03 [6H, N(CH <sub>3</sub> ) <sub>2</sub> ]
XII	5,6-(CH <sub>2</sub> ) <sub>3</sub>	Н	128– 130	86	6.29	C <sub>24</sub> H <sub>26</sub> ClN <sub>2</sub> O	6.35	554 (3.27)	6,78 (2H, Ph), 7,55 (2H, Ph), 7,88 (2H, Ph), 8,69 (1H, Ph), 9,09(1H, 4- CH), 7,84 (1H, C=C), 2,50 (2H, 2- CH <sub>2</sub> ), 3,32 (4H, 2,3-CH <sub>2</sub> ), 4.82 (2H, CH <sub>2</sub> ), 2.33 (2H, CH <sub>3</sub> ), 3.13 (2H, CH <sub>3</sub> ), 3.08 [6H, N(CH <sub>3</sub> ) <sub>2</sub> ]

Table 2. Characteristics of 1-(p-dimethylaminobenzylidene) cyclopenta[c]quinolinium derivatives

spatial proximity to the exocyclic double bond of this compound. In the <sup>13</sup>C NMR spectrum of product **XI** the number of signals corresponds to the assumed formula of the compound. The attribution of signals can be made on the basis of correlations observed in the two-dimentional HMQC and HMBC spectra. Coordinates of cross-peaks found in these spectra are presented in Table 3.

The attribution of signals of the protonated carbon atoms follows from the heteronuclear correlations through one chemical bond in HMQC spectrum. Note that for some signals these correlations were not found because of the small intensity of the corresponding cross-peaks. In this case the attribution was carried out on the basis of the assembly of correlations through 2– 3 chemical bonds observed in HMBS spectra similarly to the nonprotonated carbon atoms. Most important HMBC correlations forming the basis for attribution of signals are shown by arrows.

On the basis of structural formula of compound XI the presence of significant spatial hindrances in the molecule may be suggested. But it is not the case. The



Fig. 1. COSY spectrum of compound XI.

Table 3. Cross-peak coordinates in the HMQC and HMBC spectra found for product XI

l TT	<sup>13</sup> C measurement, ppm						
'H measurement, ppm	HMQC	НМВС					
9.52	126.76	130.30; 132.51; 122.66					
9.10	142.37	159.12; 141.20; 141.49; 138.56					
8.34							
8.17		136.58; 132.51; 128.28; 128.53					
7.81	137.52	159.12; 141.49; 133.03; 131.17; 127.69; 126.76; 132.51					
7.67		129.90; 128.28					
7.41	133.03	151.77; 137.52; 133.03					
7.33	117.67	122.66; 132.51					
6.81	112.66	112.66; 123.49					
3.42	31.02; 28.18	159.12; 136.56					
3.03	40.00	151.77; 40.00; 112.62					



computer simulation of this substance by the molecular mechanics MM+ method shows that the fivemembered ring of the heterocyclic system has the *envelope* structure. In this case the exocyclic double bond deviates from the plane of the benzoquinoline fragment by an angle exceeding 30°C. Such spatial arrangement of the above-described molecule is confirmed by the absence of a noticeable Overhouser effect between the olefin proton giving signal at 7.81 ppm and the proton at 9.52 ppm in the NOESY spectrum.

The analysis of electron absorption spectra of the colored products obtained revealed the presence of a relatively strong absorption band at 560–580 nm. Compounds with alkyl substituents exhibited the maximum of the absorption band at about 560 nm with insignificant deviations, while for the products containing aromatic substituents the maximum was observed at 580 nm.

Studies of formation of molecular orbitals of the compounds prepared by the reaction of quarternary salts with *p*-dimethylaminobenzaldehyde were carried out by quantum chemical calculations. The formation of frontier orbitals in the molecules of dyes synthesized results from the interaction of orbitals of the



Fig. 2. Formation of frontier orbitals in the molecule of dye.

**Table 4.** Energies of frontier moleculer orbitals

Molecular orbital	Salt II	<i>p</i> -dimethylamino- benzaldehyde	Dye VIII		
LUMO+1	-4.882	0.388	-3.876		
LUMO	-5.558	-0.168	-5.149		
НОМО	-13.142	-8.273	-10.208		
HOMO-1	-13.961	-9.989	-11.879		
НОМО-2	-14.518	-10.408	-12.302		
LUMO-HOMO	7.584	8.104	5.059		

quarternary salts and *p*-dimethylaminobenzaldehyde. In the molecules of cyclopenta[c]quinolinium cations the orbital energy is lower, while in the molecules of aldehydes it is higher (Fig. 2). HOMO of the dve molecule is formed mainly from HOMO of aldehyde because the energy of its orbital is higher. The decrease in energy of this orbital by 1.9 eV occurs mainly because of the transition from a neutral molecule to the molecule of cationic type. The energy of the aldehyde HOMO-1 corresponding to HOMO-2 in the dye molecule also decreases by 2.4 eV (see Table 4). LUMO of the dye is formed mainly from the LUMO of the salt. The energy of the latter slightly increases (by 0.4 eV) due to the interaction with the aldehyde orbitals. The difference in the energy between HOMO and LUMO in the molecule of dve becomes smaller resulting in the appearance of an absorption band at about 550 nm which relates to the first singlet transition from HOMO to LUMO. The next singlet transitions occur in the UV spectral range (365 and 300 nm).

## EXPERIMENTAL

UV spectra of the ethanol solutions of substances were taken on a Specord M-40 spectrometer. <sup>1</sup>H NMR spectra were registered on a Varian Mercury-400 spectrometer (400 MHz) in DMSO- $d_6$  with respect to internal TMS.

Cyclopenta[*c*]quinolinium perchlorates **I-VI** were prepared according to the procedure [3].

1-(*p*-Dimethylaminobenzylidene)-5-methyl-2,3-dihydrocyclopenta[*c*]quinolinium perchlorate (VII). An equimolar mixture of salt II and *p*-dimethylaminobenzaldehyde was heated in acetic anhydride for 0.5 h at 130°C. The appearance and deepening of the coloration of the reaction mixture was observed. After a day of storage the obtained precipitate was treated with ether and crystallized from aqueous ethanol (1:1). Compounds VIII–XII were obtained analogously. The properties of the reaction products and their spectral characteristics are presented in Table 2.

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