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SYNTHESIS OF CHLORINE-SUBSTITUTED NAPHTHO- AND BENZISOINDOLINIUM SALTS BY BASE-CATALYZED INTRAMOLECULAR CYCLIZATION OF AMMONIUM SALTS*

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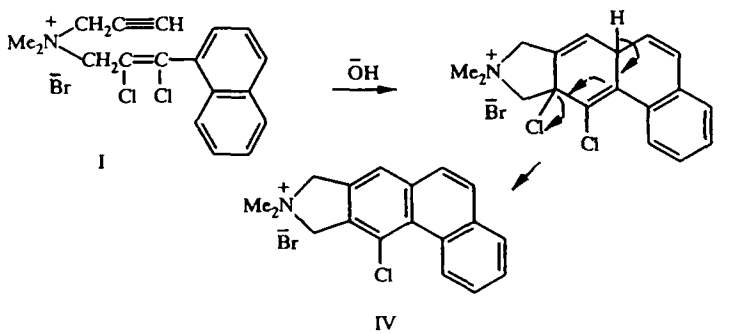
It was shown that ammonium salts containing a propargyl group together with 3-α-naphthyl-2,3-dichloroallyl or 3-p-tolyl-2,3-dichloroallyl groups undergo cyclization–dehydrochlorination in an aqueous alkaline medium, forming chlorine-substituted naphthisoindolinium and benzisoindolinium salts. If the 3-phenylpropargyl and 3-p-tolyl-2,3-dichloroallyl groups are both present in the molecule of the ammonium salt the latter group enters exclusively into cyclization as diene fragment.

Under the conditions of base catalysis quaternary ammonium salts containing a 3-*p*-chlorophenyl-2,3-dichloroallyl together with groups of the propargyl type undergo cyclization–dehydrochlorination [2]. While continuing investigations in this region we tried to compare the ability of the 3-α-naphthyl- and 3-*p*-tolyl-2,3-dichloroallyl groups to enter into cyclization as a diene component. For this purpose we studied the behavior of dimethylpropargyl(3-α-naphthyl-2,3-dichloroallyl)ammonium (I) and dimethylpropargyl- or dimethyl-3-phenylpropargyl(3-*p*-tolyl-2,3-dichloroallyl)ammonium bromides (II, III) toward aqueous alkali. It was shown that the salt (I) in the presence of 1.5 g-eq of aqueous alkali to one mole of the initial salt with moderate spontaneous heating undergoes cyclization–dehydrochlorination with the formation of 2,2-dimethyl-11-chloronaphth[2,1-*f*]isoindolinium bromide (IV) with a yield of 87%.



I

IV

The salts (II, III) also undergo cyclization–dehydrochlorination under the conditions of base catalysis, forming 2,2,7-trimethyl-4-chloro- and 2,2,6-trimethyl-4-phenyl-9-chlorobenz[*f*]isoindolinium bromides (V) and (II) with yields of 75 and 78%, respectively.

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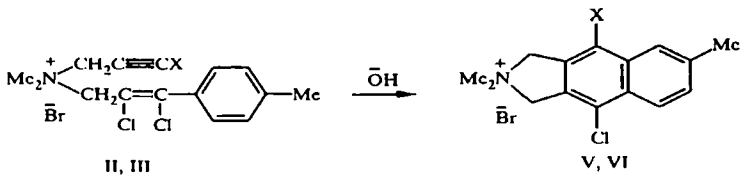

II, III

V, VI

II, V X = H; III, VI X = Ph

Spontaneous heating is not observed during the cyclization of the salts (II, III). In all cases the reaction mixture is heated at 70-75°C for 1 h in order to complete the process. By titration of an aqueous solution of the reaction mixture it was established that 1 g-atom of ionic halogen is formed to one mole of the initial salt.

The IR spectra of the cyclic salts (IV, V) do not contain absorption bands for the monosubstituted C≡C bond at 2140 and 3265 cm^{-1}, while the spectrum of the salt (VI) does not contain a band for the disubstituted C≡C bond at 2240 cm^{-1}. Characteristic bands for the *ortho*-, 1,2,3,4-, and pentasubstituted benzene rings at 770, 820, and 870 cm^{-1}, respectively, and also a band corresponding to the vibrations of the aromatic ring at 1600 cm^{-1} were found in the spectrum of the salt (IV). In the spectrum of the salt (V) there are characteristic absorption bands for the 1,2,4- and pentasubstituted benzene rings at 830, 870, and 880 cm^{-1} respectively and bands for the vibrations of the aromatic ring at 1550, 1590, and 1600 cm^{-1}. Bands at 820 and 880 cm^{-1} characteristic of the mono- and 1,2,4-disubstituted benzene rings and a band at 1600 cm^{-1} for the aromatic ring were found in the IR spectrum of the salt (VI).

As expected, the UV spectrum of the salt (IV) contains three α, β, and γ absorption bands characteristic of phenanthrenes, differing in intensity and vibrational structure. For phenanthrenes, as is known, the α band is always the most long-wave band, and the $\lambda\alpha > \lambda p > \lambda\beta$ relation is retained for these compounds [3, 4]. A similar pattern is observed in the spectrum of the salt (IV). The strong absorption bands of the salt (IV) have smaller logarithms of the molar extinction coefficients (2.65-2.50) than the absorption bands of the initial salt (I) (4.76-3.90). As a result of the conjugation of the *p*-tolyl substituent with the multiple bonds in the molecules of the initial salts (II) and (III) the absorption bands of the benzene ring are shifted toward the long-wave region. The characteristic absorption bands of the naphthalene ring were found in the UV spectra of the cyclic salts (V) and (VI).

The structure of the salt (V) is also confirmed by the PMR spectrum, in which signals for the $C_6H_4-C\underline{H}_3$ group (3H) at 2.71, the $N^+(C\underline{H}_3)_2$ group (6H) at 3.45 ppm, and the $N^+(C\underline{H}_2)_2$ group (4H) at 5.21 ppm and signals for the aromatic protons of $C_{10}H_4$ in the regions of 7.5-7.7 (2H) and 8.05-8.25 ppm (2H) respectively were found.

EXPERIMENTAL

The IR spectra were obtained on a UR-20 spectrometer for tablets in potassium bromide or in Vaseline oil. The UV spectra were obtained on a Specord UV-vis spectrophotometer in ethanol. The PMR spectra of the salt (V) were measured on a Bruker AC-200 instrument in DMSO-d_6 with HMDS as internal standard. The purity of the amines was established by GLC on an LKhM-72 chromatograph with a 1.6 × 4 mm column with 5% of OV-1 on Inerton Super (0.125-0.160) and with helium as carrier gas (50 ml/min) at 200-220°C. The purity of the salts (IV-VI) was determined by TLC on Silufol UV-254 plates in the 10:2:1:5 *n*-butanol–ethanol–water–acetic acid system with development by iodine vapor. The initial salts (I-III) were obtained with quantitative yields by the reaction of dimethyl(3-α-naphthyl-2,3-dichloroallyl)amine (VII) and dimethyl(3-*p*-tolyl-2,3-dichloroallyl)amine (VIII) with propargyl- and 3-phenylpropargyl bromides in acetonitrile. The data relating to the initial salts (I-III) and the cyclic salts (IV-VI) are given in Tables 1 and 2.

Dimethyl(3-α-naphthyl-2,3-dichloroallyl)amine (VII). We passed 2.5 g (35 mmole) of chlorine through a solution of 6.5 g (31 mmole) of dimethyl-3-α-naphthylpropargylamine in 6 ml of 36% HCl and 7 ml of water with cooling. The next day the solution was made alkaline with sodium carbonate and extracted with ether. After distilling the ether we obtained 5.6 g (64%) of the semicrystalline chromatographically pure amine (VII); bp 140-142°C (0.2-0.3 mm Hg), n_D^{20} 1.6100. IR spectrum, cm^{-1}: 740 (*o*- and 1,2,3-substituted arene), 1500, 1590, 1620 (conjugated C=C bond), 1697, 1940 (*o*-substituted arene), 1860, 1923 (1,2,3-substituted benzene ring), 3060 (CH_{arom}). Found %: C 64.76; H 5.60; N 4.95; Cl 25.66. $C_{15}H_{15}Cl_2N$. Calculated %: C 64.28; H 5.35; N 5.00; Cl 25.33.

TABLE 1. Initial Salts (I-III)

Compound	Empirical formula	Found, % / Calculated, %		mp, °C	IR spectrum, cm^{-1}	UV spectrum, λ_{max}, nm (log ε)
		N	Br			
I	$C_{18}H_{18}BrCl_2N$	3,62 / 3,79	20,42 / 20,05	153	730, 1600, 1620, 2120, 3030, 3070	225(4,76), 298(3,90
II	$C_{15}H_{18}BrCl_2N$	3,96 / 3,85	22,32 / 22,04	*	820, 840, 1580, 1620, 2130, 3060, 3090	235(5,11), 278(3,76), 285(3,81), 298(3,64), 312(2,78), 325(2,60)
III	$C_{21}H_{22}BrCl_2N$	3,38 / 3,18	17,85 / 18,22	*	840, 1590, 1620, 2240, 3040, 3070	205(4,05), 240 (4,20), 295(3,67), 310(2,78)

*The salt is hygroscopic.

TABLE 2. Cyclic Salts (IV-VI)

Compound	Empirical formula	Found, % / Calculated, %		mp, °C (from abs. ethanol)	R_f*	IR spectrum, cm^{-1}	UV spectrum, λ_{max}, nm (log ε)	Yield, %
		N	Br					
IV	$C_{18}H_{17}BrClN$	4,12 / 3,86	21,85 / 22,06	260	0,58	770, 820, 870, 1600, 3040, 3060	218(4,60), 258(4,89), 298(4,10), 305(4,08), 340(2,65), 345(2,64), 358(2,56)	87
V	$C_{15}H_{17}BrClN$	4,45 / 4,28	24,95 / 24,51	259	0,49	830, 870, 880, 1580, 1590, 1620, 3060	230(4,94), 270(4,00), 280(3,75), 300(3,52), 325(2,60)	73
VI	$C_{21}H_{21}BrClN$	3,65 / 3,47	20,23 / 19,87	232	0,52	810, 890, 1600, 1630, 3030	225(5,03), 240(5,12), 300(4,30)	75

*In the 10:2:1:5 *n*-butanol–ethanol–water–acetic acid system.

Dimethyl(3-*p*-tolyl-2,3-dichloroallyl)amine (VIII). By the chlorination of 6.3 g of a solution of 13 g (75 mmole) of dimethyl(3-*p*-tolylpropargyl)amine hydrochloride in 15 ml of 36% hydrochloric acid and 30 ml of water to absorption, we obtained after the treatment described in the previous experiment 9.8 g (53%) of the amine (VIII); bp 126°C (4 mm Hg), n_D^{20} 1.5510. Found, %: C 59.59; H 6.00; N 5.81; Cl 29.55. $C_{12}H_{15}Cl_2N$. Calculated, %: C 59.02; H 6.15; N 5.74; Cl 29.10. Picrate, mp 132-133°C. IR spectrum, cm^{-1}: 840 (*p*-substituted benzene ring), 1600 (conjugated C=C bond), 3040-3060 cm^{-1} (CH_{arom}).

General Method for the Cyclization of the Salts (I-III). To a solution of 3.1-9 mmole of the initial salt (I-III) in 4-9 ml of water [5-6 ml of ethanol is required to dissolve the salt (III) completely] we added 2.3-5 ml of a 2N solution of potassium hydroxide. (In each case the molar ratio of the salt and base was 1:1.5.) After the addition of aqueous alkali to the solution of the salt (I) moderate spontaneous heating was observed. (The temperature of the reaction mixture rose from 25°C to 45-50°C.) Spontaneous heating was not observed when the salts (II, III) were used. To complete the process the reaction mixture was heated at 70-75°C for 1 h. The next day in the case of the reaction of the salt (I) with potassium hydroxide the cyclic salt (IV) was isolated by filtration. To isolate the respective cyclic salts (V, VI) from the salts (II, III) the reaction mixture (after titration of the ionic halogen and extraction with ether, 2 × 30 ml) was acidified with hydrobromic acid to remove the products from possible side reactions, and the water was distilled under vacuum to dryness. The organic salt was extracted with absolute ethanol (1 × 40 ml). The cyclic salts (V, VI) were precipitated from the alkaline solution by the addition of an excess of ether.

In three cases it was established by titration that 0.95-1.0 g-atom of ionic halogen was formed to one mole of the salt.

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