SYNTHESIS OF CHLORINE-CONTAINING BENZISOINDOLINIUM SALTS BY BASE-CATALYZED INTRAMOLECULAR CYCLIZATION OF AMMONIUM SALTS*

É. O. Chukhadzhyan, L. A. Manasyan, and A. T. Babayan

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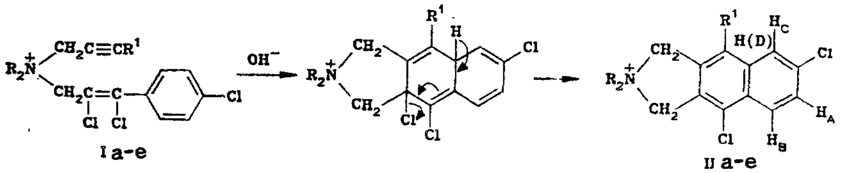
It was shown that dialkylpropargyl/3-(p-chlorophenyl)-2,3-dichloroallyl/ammonium salts in an aqueous alkali medium undergo cyclization-dehydrochlorination to give chlorine-containing benzisoindolinium salts. When the ammonium salt contains simultaneously 3-phenyl (or vinyl)propargyl and 3-(p-chlorophenyl)-2,3-dichloroallyl groups, only the latter enters into the cyclization as the diene fragment.

It has been previously reported that quaternary ammonium salts that contain a 3-phenyl-2,3-dichloroallyl group along with groups of the propargyl type in the presence of aqueous alkali form chlorobenzisoindolinium salts in almost quantitative yields [2]. It was established that cyclization of the indicated salts precedes dehydrochlorination [3].

Continuing our research in this area we have observed that in an aqueous alkaline medium salts with a 3-(p-chlorophenyl)-2,3-dichloroallyl group quite smoothly undergo cyclization-dehydrochlorination with the formation of benzisoindolinium salts with two chlorine atoms in the benzene rings.



I a-e

II a-e

I, IIa,c,e $R=CH_3$, b,d $R=C_2H_5$; a,b $R^1=H$, c,d $R^1=C_2H_5$, e $R^1=CH=CH_2$

It was established that when the quaternary ammonium salt contains 3-phenyl (or vinyl)-propargyl and 3-(p-chlorophenyl)-2,3-dichloroallyl groups, exclusively the latter enters into the cyclization as the diene fragment; this indicates its higher reactivity as compared with 3-phenyl (or vinyl) propargyl groups.

The starting dialkyl(3-p-chlorophenyl)-2,3-dichloroallyl)amines were synthesized by chlorination of hydrochloric acid solutions of dialkyl(3-p-chlorophenyl)propargyl/amines. Starting salts Ia-e were obtained in quantitative yields by the reaction of the starting amines with the corresponding halides. Data pertaining to salts Ia-e and their cyclization-dehydrochlorination products IIa-e are presented in Tables 1 and 2.

EXPERIMENTAL

The IR spectra of KBr pellets or mineral oil suspensions of the compounds were obtained with a UR-20 spectrometer. The UV spectra of solutions in ethanol were recorded with a specord UV-vis spectrophotometer. The PMR spectra were obtained with a Perkin–Elmer R12B spectrometer (60 MHz). The purity of the substances was established by GLC with an LKhM-72 chromatograph with a 1.5 m × 4 mm column packed with 5% OV-1 impregnated with INERTON-Super (0.125-0.160) and helium as the carrier gas (50 ml/min) at 180°C, as well as by TLC on

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Institute of Organic Synthesis, Academy of Sciences of the Armenian SSR, Yerevan 375094.
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TABLE 1. Starting Salts Ia-e

Compound	mp,* °C	IR spectrum, cm⁻¹	UV spectrum, λ_{max}, nm (log ε)	Found, %		Empirical formula	Calc., %	
				N	Hal		N	Hal
Dimethylpropargyl** bromide Ia	158...159	825, 840, 1590, 2140, 3265	235 (4,92), 280 (3,64), 290 (3,68)	3,9	20,6	$C_{14}H_{15}BrCl_3N$	3,7	20,9
Diethylpropargyl** bromide Ib	110...111	730, 780, 1590, 1620, 2125, 3060, 3090, 3160	205 (4,56), 260 (4,33)	3,6	18,7	$C_{16}H_{19}BrCl_3N$	3,4	19,4
Dimethyl(3-phenylpropargyl)** bromide Ic	136...137	840, 1580, 1595, 1620, 2240, 3060, 3090	205 (4,06), 247 (3,90)	3,3	17,9	$C_{20}H_{19}BrCl_3N$	3,1	17,4
Diethyl(3-phenylpropargyl)** bromide Id	110	1600, 1620	205 (4,45), 240 (4,20)	2,9	16,3	$C_{22}H_{23}BrCl_3N$	2,9	16,4
Dimethyl(3-vinylpropargyl)** chloride	159...160	1600, 2250, 3030	205 (4,30), 230 (4,73)	3,9	9,7	$C_{16}H_{17}BrCl_4N$	3,8	9,6

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*The salts were recrystallized from absolute ethanol.

**-(3-(p-chlorophenyl)-2,3-dichloroallyl) ammonium.

TABLE 2. Cyclic Products IIa-e

Compound	mp,* °C	IR spectrum, cm⁻¹	UV spectrum, λ_{max}, nm (log ε)	Found, %		Empirical formula	Calc., %		Formation of ionic Hal, %	Yield, %
				N	Hal		N	Hal		
4,7-Dichloro-2,2-dimethyl** bromide IIa	236...237	835, 870, 885, 1570, 1595, 1620	235 (4,94), 268 (4), 285 (3,72), 300 (3,58), 325 (2,60)	4,1	22,9	$C_{14}H_{14}BrCl_2N$	4,0	23,0	95	93
4,7-Dichloro-2,2-diethyl** bromide IIb	211...212	805, 810, 825, 870, 885, 1575, 1605, 1630	225 (4,87), 240 (4,93), 300 (3,98)	4,0	21,1	$C_{16}H_{18}BrCl_2N$	3,7	21,3	84	85
6,9-Dichloro-4-phenyl-2,2-dimethyl** bromide IIc	271...272	820, 890, 1580, 1605, 1630, 3030	225 (5,03), 240 (5,11), 300 (4,30)	3,4	19,3	$C_{20}H_{18}BrCl_2N$	3,3	18,9	82	87
6,9-Dichloro-4-phenyl-2,2-diethyl** bromide IId	250...251	810, 870, 1600, 1620	240 (5,05), 300 (4)	3,2	17,4	$C_{22}H_{22}BrCl_2N$	3,1	17,7	100	79
6,9-Dichloro-4-vinyl-2,2-dimethyl** chloride IIe	265...266	820, 890, 1605, 3030	240 (4,72), 300 (2,75)	4,6	10,9	$C_{16}H_{16}Cl_3N$	4,3	10,8	82	70

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*The salts were recrystallized from ethanol.

**Benz[f]isoindolinium

Silufol UV-254 in an n-butanol—ethanol—water—acetic acid system (10:2:1:5) with development by iodine vapors.

Dimethyl[3-(p-chlorophenyl)-2,3-dichloroallyl]amine. Chlorination of a solution of 4 g (21 mmoles) of dimethyl[3-(p-chlorophenyl)propargyl]amine hydrochloride in 4 ml of 36% hydrochloric acid and 5 ml of water with 2 g of chlorine gave 3.6 g (62%) of chromatographically pure dimethyl[3-(p-chlorophenyl)-2,3-dichloroallyl]amine with a GLC retention time of 7.5 min, bp 109-110°C (0.2 mm Hg), and n_D^{20} 1.5650. IR spectrum: 840 (p-substituted aromatic ring), 1600 (conjugated C=C), 3040, 3050, 3060 cm^{-1} (aromatic ring C—H). Found, %: C 49.7; H 4.6; N 5.2. $C_{11}H_{12}Cl_3N$. Calculated, %: C 49.9; H 4.5; N 5.3. The picrate had mp 140°C (from ethanol). Found, %: N 11.4. $C_{17}H_{15}Cl_3N_4O_7$. Calculated, %: N 11.4.

Diethyl[3-(p-chlorophenyl)-2,3-dichloroallyl]amine. Chlorination of a solution of 15 g (68 mmoles) of diethyl[3-(p-chlorophenyl)propargyl]amine hydrochloride in 15 ml of 36% hydrochloric acid and 15 ml of water with 6 g of chlorine gave 9.5 g (52%) of chromatographically pure diethyl[3-(p-chlorophenyl)-2,3-dichloroallyl]amine with GLC retention time of 8.2 min, bp 125-126°C (0.3 mm Hg), and n_D^{20} 1.5500. IR spectrum: 830 (p-substituted aromatic ring), 1600 (conjugated C=C), 3030, 3060 cm^{-1} (aromatic ring C—H). Found, %: C 53.2; H 5.6; N 4.7. $C_{13}H_{16}Cl_3N$. Calculated, %: C 53.3; H 5.5; N 4.8. The picrate had mp 94-95°C (from ethanol). Found, %: N 10.9. $C_{19}H_{19}Cl_3N_4O_7$. Calculated, %: N 10.7.

General Method for the Cyclization of Salts I to Salts II. A 6-mmole sample of 2 N KOH solution was added to a solution of 5 mmoles of the starting salt, and the temperature of the reaction mixture rose from 25°C to 60°C as a result of spontaneous heating. The cyclic substances that crystallized when the mixtures were allowed to stand at room temperature were isolated in 70-93% yields by filtration. the amount of ionic halogen was determined by titration of the aqueous solution. The products had the following R_f values: 0.58 (IIa), 0.58 (IIb), 0.55 (IIc), 0.61 (IId), and 0.50 (IIe). PMR spectrum of IIa: 3.18 (6H, d, CH_3), 4.75 (4H, s, CH_2), 7.22 (1H, dd, H_A, J = 9.3, J = 2.0 Hz), 7.81 (1H, d, H_B, J = 9.3 Hz), 7.45 (1H, br, H_D), 7.55 ppm (1H, d, H_C, J = 2.0 Hz).

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