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STUDY OF THE BEHAVIOR OF DIALKYL(3-CHLORO-2-BUTENYL)(3-p-CHLOROPHENYLPROPARGYL)AMMONIUM SALTS IN AQUEOUS ALKALINE MEDIUM. SYNTHESIS OF 2,2-DIALKYL-6-CHLORO-4-METHYL-BENZ[f]ISOINDOLINIUM CHLORIDE SALTS*

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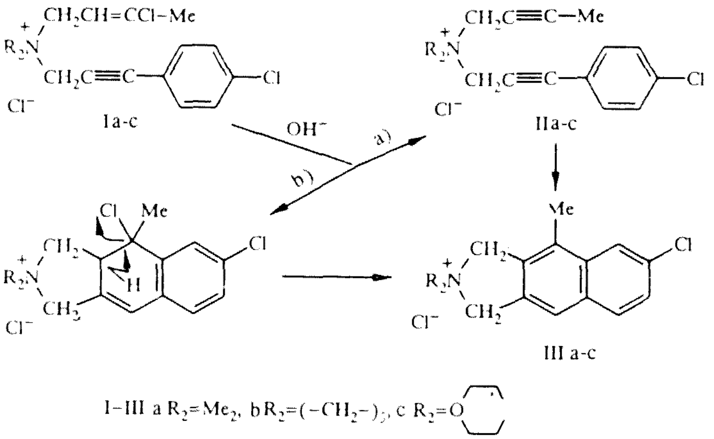
Dialkyl-(3-chloro-2-butenyl) (3-p-chlorophenylpropargyl) ammonium salts undergo dehydrochlorination solution with the formation of condensed analogs of isoindolinium salts.

It was shown previously that quaternary ammonium salts containing a 3-chloro-2-butenyl group in addition to a 3-α-naphthylpropargyl group undergo dehydrochlorination – cyclization in aqueous alkaline solution [2]. The present work is devoted to a study of the behavior of the dialkyl-(3-chloro-2-butenyl)(3-chlorophenylpropargyl)ammonium chlorides (Ia-c) towards aqueous alkali.

As is evident from the scheme there are two pathways (a and b) for the formation of the cyclization products (IIIa-c) differing in the sequence of the cyclization and dehydrochlorination stages. According to pathway *a* the initial salts are first dehydrochlorinated, then the dehydrochlorination products (IIa-c) are cyclized. According to pathway b cyclization precedes dehydrochlorination.



The interaction of salts (Ia-c) with 1.5 g-eq aqueous alkali has been studied at room temperature in order to clarify the sequence of these reactions.

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TABLE 1. Results of the Reaction of Salts (Ia-c) with 1.5 g-eq Aqueous Alkali at Room Temperature

Compound	Empirical formula	mp, °C	Reaction time, h	Amount of ionic halide formed, %	Yield of (IIa-c) and (IIIa-c) mixture, %	IR spectrum, cm^{-1}
Ia	$C_{15}H_{18}NCl_3$	91	24	27	60	825, 840, 875, 1550, 1570, 1605, 2255...2265
			48	40		
			72	53		
			96	53		
			168	65		
			3	32*		
			21	58		
			48	82		
Ib	$C_{18}H_{22}NCl_3$	134	2	37	69	825, 840, 875, 1510, 1605, 2245, 3060
			24	63		
			96	73		
			120	87		
Ic	$C_{17}H_{20}NCl_3O$	152	2	62	72	825, 830, 875, 1505, 1600, [illegible], 3060
			4	75		
			24	87		

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*Ratio of salt–KOH was 1:1.7.

TABLE 2. Results of the Interaction of the Salts (Ia-c) with 1.5 g-eq Aqueous Alkali on Heating (2 h at 80-85°C)

Initial salt	IR spectrum, cm^{-1}	UV spectrum, λ_{max}, nm, (log ε)	Cyclization product, empirical formula, mp, °C (R_f)	IR spectrum, cm^{-1}	UV spectrum, λ_{max}, nm, (log ε)	% ionic halogen formed	Yield, %
Ia	830, 960, 1550, 1595, 1670, 2245, 3030	208 (4,66), 250 (4,64), 278 (3,04), 286 (2,84)	IIIa $C_{15}H_{17}NCl_2$ (244...246) (0,45)	825, 875, 1505, 1605, 3025, 3065	235 (5,60), 265 (3,83), 278 (3,92), 285 (3,97), 300 (3,84), 315 (2,80), 330 (2,69)	95	65
Ib	840, 960, 1550, 1600, 1670, 2240, 3030	207 (4,70), 258 (4,68), 278 (3,34), 283 (3,0)	IIIb $C_{18}H_{21}NCl_2$ (273...275) (0,3)	820, 870, 890, 1500, 1605, 3050	235 (5,56), 255 (3,82), 278 (3,93), 285 (3,98), 300 (3,84), 315 (2,90), 330 (2,78)	97	64
Ic	825, 1590, 1660, 1805, 2240, 3030, 3070	265 (3,83), 278 (3,92), 285 (3,98), 300 (3,84), 315 (2,80), 330 (2,69)	IIIc $C_{17}H_{19}NCl_2O$ (294...296) (0,59)	825, 875, 1505, 1605, 3040, 3060	265 (3,83), 278 (3,92), 285 (3,98), 300 3,85), 315 (2,80), 330 (2,69)	98	66

It is seen from the data in Table 1 that under the conditions indicated above 0.65, 0.87, and 0.87 g-at halogen per g-mole salt respectively pass into the ionic state and as a result a mixture is formed of products of dehydrochlorination , viz. the dialkyl-(2-butynyl)(3-p-chlorophenylpropargyl)ammonium salts (IIa-c), and of cyclization, viz. the 2,2-dialkyl-6-chloro-4-methylbenz[f]isoindolinium salts (IIIa-c), in overall yields of 60, 69, and 72% respectively. According to TLC data and IR spectral analysis the salts (IIa-c) predominates in the mixture, not having had time to cyclize. It was shown using salt (Ic) as an example, that (IIc) underwent cyclization completely after standing the mixture in aqueous alkali for five days.

It must be noted that the salt (Ic) is also present in insignificant amount in the mixture of salts (IIa) and (IIIa). It was shown that on reacting salt (Id) with 1.7 g-eq aqueous alkali at room temperature the rate of forming ionic halogen is increased (see Table 1), and even the trace of the initial salt (Ia) was absent from the mixture of salts (IIa) and (IIIa).

On heating the salts (Ia-c) at 40-45°C for 2 h 0.86, 0.92, and 0.95 g-atom ionic halogen were formed per g-mole salt and in this case also a mixture of salts (IIa-c) and (IIIa-c) were formed in overall yields of 63, 65, and 73% respectively. Separation of them by fractional crystallization failed. The salts (IIa-c) were completely cyclized by adding 0.2 g-eq aqueous alkali to the mixture of salts (IIa-c) and (IIIa-c) and keeping he mixture at room temperature for some days and subsequently heating it at 70-75°C (2-2.5 h). The products (IIIa-c) were obtained in a pure state in 65-66% yield on heating the salts (Ia-c) with 1.5 g-eq aqueous alkali for 2 h at 80-85%,

Products of nucleophilic fission, viz. dialkyl-(3-chlorophenylpropargylamines [3], are formed in 10-13 and 20-25% yield both at room temperature and on heating the salts (Ia-c) in aqueous alkali to 40-45°C and 80-85°C respectively. Vinylacetylene and chloroprene were detected qualitatively.

It has therefore been established from the data that in aqueous alkali the dehydrochlorination of salts (Ia-c) precedes cyclization.

The absorption bands for a trisubstituted $C \equiv C$ bond, characteristic of the salts (Ia-c), were absent from the IR spectra of the mixtures of salts (IIa-c) and (IIIa-c). Absorption bands were detected for disubstituted $C \equiv C$ bond at 2255-2265 cm^{-1} and a 1,4-substituted ring at 840 cm^{-1}, characteristic of salts (IIa-c), and also absorption bands for a 1,2,4- and a pentasubstituted benzene ring at 825 and 875 cm^{-1} respectively, characteristic of the salts (IIIa-c, and the absorption bands of the aromatic ring at 1505, 1605, and 3025 cm^{-1}.

The absorption bands for a disubstituted $C \equiv C$ bond at 2235-2265 cm^{-1}, characteristic of the initial salts (Ia-c) and salts (IIa-c), were absent from the IR spectra of the cyclic salts (IIIa-c). Absorption bands were detected for 1,2,4-substituted and pentasubstituted benzene rings at 825 and 875 cm^{-1} respectively and for the aromatic ring at 2505, 1605, and 3025 cm^{-1}.

There were three types of absorption bands α, ρ and β in the UV spectra of the salts (Ia-c) and (IIIa-c) differing in intensity and vibrational structure. As expected, the presence of a chlorine atom and a benzene ring substituted with a triple bond in the salts (Ia-c) leads to an increase in the molar extinction coefficient of the absorption bands and to their displacement towards the long wave region of the spectrum (Table 2). Due to the presence of a naphthalene ring in salts (IIIa-c) all the absorption bands in the UV spectra are shifted bathochromically. The ρ-band is shifted bathochromically more strongly than the α-band (see Table 2). The latter is still the furthest long wave band (300, 315, 330 nm) and has the least value of logarithm molar extinction coefficient at 3.84, 2.8, and 2.7 respectively. The ratio $\lambda\alpha/\lambda\rho$, as for all catacondensed hydrocarbons, is almost constant and equal to ~ 1.15 [4].

A series of investigations was carried out in the seventies by A. T. Babayan and collaborators with the aid of establishing the sequence of cyclization and dehydrochlorination reactions of ammonium salts containing a 3-vinyl- and 3-phenylpropargyl group in addition to a 3-chloro-2-butenyl group [5, 6]. Based on the data obtained for the reaction of cis- and trans-dimethyl(3-chloro-2-butenyl)(3-vinylpropargyl)ammonium chlorides with aqueous alkali, the authors concluded that the 3-chloro-2-butenyl group is directly involved in the cyclization as a group of the allyl tape. This is in agreement with literature data according to which the cyclization of salts with a 3-alkenylpropargyl group, irrespective of the character of the β,γ-unsaturated group, takes place under base-catalysis conditions with evolution of heat even at room temperature [7].

The high yield of 2,2,4-trimethylbenz[f]isoindolinium chloride obtained from trans-dimethyl-(3-chloro-2-butenyl)-(3-phenylpropargyl) ammonium salts was ascribed by the authors to the reaction conditions (molar ratio salt:KOH of 1:3, extended storage at room temperature of 72 h, and additional heating at 38-40°C for 1 h with subsequent heating on an oil bath). In the authors' opinion, the salt being tested in cyclized under these conditions with the direct participation of the 3-chloro-2-butenyl fragment as a group of the allyl type. However the authors did not attempt to isolate and identify the intermediate salt before heating on the oil bath, which would have permitted the actual pathway of forming the cyclic salt to be established.

In addition it is known that the cyclization of salts containing a 3-arylpropargyl group together with a group of the allyl type is effected under base-catalysis conditions only on heating at 90-92°C [7].

EXPERIMENTAL

The IR spectra were taken on a UR 20 spectrometer in KBr disks or in Nujol mulls. The UV spectra were taken in ethanol on a Specord UV-VIS instrument. The TLC was carried out on Silufol UV-254 plates in the system n-butanol–ethanol–water–acetic acid, 8:2:3:1:, and visualization with iodine vapor.

The salts (Ia-b) were obtained quantitatively by the interaction of dialkyl-3-p-chlorophenylpropargylamines with 1,3-dichloro-2-butene in acetonitrile on heating to 90-92°C for 2-3 h for salts (Ib,c) but in the case of (Ia) the reaction occurs with evolution of heat. The salts (Ia-c), their cyclization products (IIa-c), and the salts (IIa-c) are described for the first time. The physicochemical characteristics of the salts mentioned are given in Table 1 and 2.

The data of elemental analysis for Cl and N for the salts corresponded to calculated values.

General Procedure for the Reaction of Salts (Ia-c) with 1.5 g-eq Aqueous Alkali

A (at room temperature). A 2.3 N solution of KOH (2.6 ml) was added to a solution of the salt (Ia-c) (4 mmole) being tested in water (3-4 ml) (molar ratio of salt:base 1:1.5).

After standing at room temperature for 72 h in the case of salt (Ia) and 24 h in the case of (Ib) and (Ic) 0.65, 0.71, and 0.87 g-atom ionic halogen were formed per g-mole salt respectively. The reaction mixture was extracted with ether. Amine (10-14%) was detected in the ether extract by titration.

The solution was acidified with hydrochloric acid and the solvent distilled off in vacuum to dryness. The mixtures of salts (IIa-c) and (IIIa-c) were extracted with ethanol and were precipitated from the alcoholic solution with absolute ether. The ether extract was washed with hydrochloric acid. Dialkyl-3-p-chlorophenylpropargylamines were isolated by making the hydrochloric acid solution alkaline and extracting with ether [3]. Identification of the amines was effected by chromatography with authentic specimens.

B (on heating at 80-85°C). A 2.3 N solution of potassium hydroxide (2.6 ml) was added to a solution of the initial salt (4 mmole) in water (3-4 ml), the ratio salt:alkali being 1:1.5. The solution was heated for 2 h at 80-85°C. The formation of 0.95-0.98 g-atom ionic halogen per g-mol salt was established by titration. The aqueous solution was then extracted with ether. The presence of 20, 24, and 28% amine respectively was established in the ether extract by titration. The solution was acidified with hydrochloric acid and the solvent distilled off in vacuum to dryness. The 2,2-dialkyl-6-chloro-4-methylbenz[f]isoindolinium salts (IIIa-c) were extracted from the residue with absolute ethanol. The salts were isolated by filtration or by ether precipitation of the alcoholic solution. The dialkyl(3-p-chlorophenylpropargyl)amines were obtained from the ether extract by the usual method.

Interaction of the Mixtures of Salts (IIa-c) and (IIIa-c) with a Catalytic Amount of Aqueous Alkali on Heating to 75-80°C. A 2.3 N solution of KOH (0.43 ml) was added to a solution of the mixture of salts (IIa-c) and (IIIa-c) (4.9 mmole) in water (3.4 ml) the ratio of salt:alkali being 5:1. The solution was heated at 75-80°C for 2-2.5 h. The solution was then extracted with ether. The cyclic salts (IIIa-c) were isolated from the aqueous solution by the usual treatment (see method B) and gave no depression of melting point when mixed with the salts obtained on cyclizing salts (Ia-c) in aqueous alkali by heating to 80-85°C.

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