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On the Mechanism of Intramolecular Cyclization of Dialkyl(2-propynyl)[3-alkenyl(or aryl)-2-propynyl]-ammonium Salts

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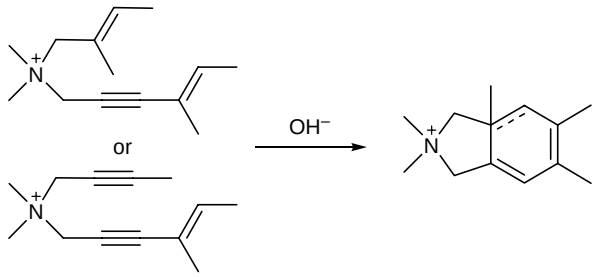
Abstract—Given are experimental data indicating that base-catalyzed intramolecular cyclization of ammonium salts containing a 2-propynyl-like group together with a 3-alkenyl- or 3-aryl-2-propynyl group follows a concerted mechanism involving the 3-alkenyl- or 3-aryl-2-propynyl moiety as π^4-fragment.

We previously showed that ammonium salts containing β,γ-unsaturated groups and various 4-en-2-ynyl fragments on the nitrogen atom readily undergo base-catalyzed intramolecular cyclization (like Diels–Alder reaction) to afford 2,2-dialkylisoindolium or 2,2-dialkyldihydroisoindolium salts and their fused analogs in almost quantitative yield [1–7] (Scheme 1).

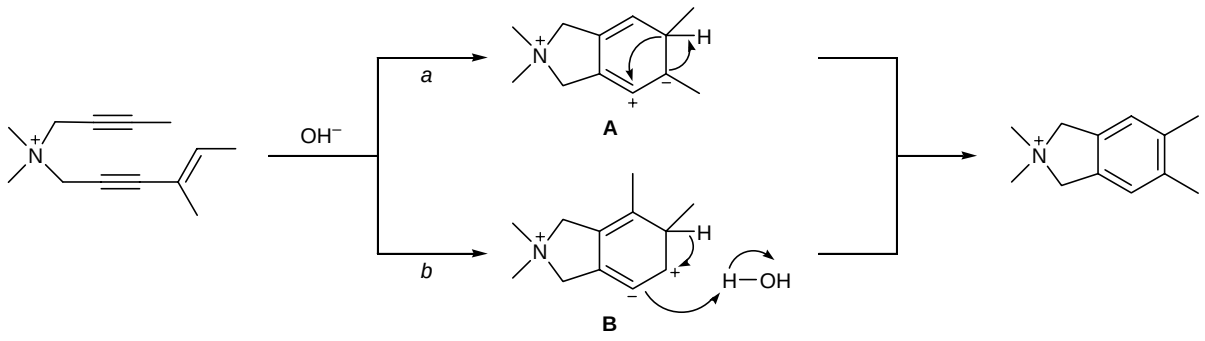
Scheme 1.



Two schemes were proposed for cyclization of the above systems [1, 3, 8–15]. According to the first of these, the cyclization involves intermediate formation of species **A** or **B** which undergoes fast aromatization via hydride (pathway *a*) or proton transfer (pathway *b*; Scheme 2). The other scheme includes isomerization of the 3-alkenyl- or 3-aryl-2-propynyl group to allenyl fragment, cyclization of the salt thus formed, and aromatization of the latter to dihydroisoindole derivative (Scheme 3). Scheme 3 is consistent with published data on cyclization of acetylenic compounds [16–20]. For example, base-catalyzed intramolecular cyclization of compounds with the general formula $X(CH_2C{\equiv}CC_6H_5)_2$ (X = CH_2, S, NCH_3, O), as well as of allyl and 2-propynyl ethers derived from 3-isopropenyl-2-propynyl and 3-phenyl-2-propynyl alcohols, was presumed to be preceded by isomerization into the corresponding α-allenyl derivative [16–18].

With the goal of establishing the true mechanism of the cyclization, Babayan and co-workers previously performed kinetic studies using UV spectroscopy [8–15]. However, this method did not allow the authors to detect formation of intermediate species, in

Scheme 2.



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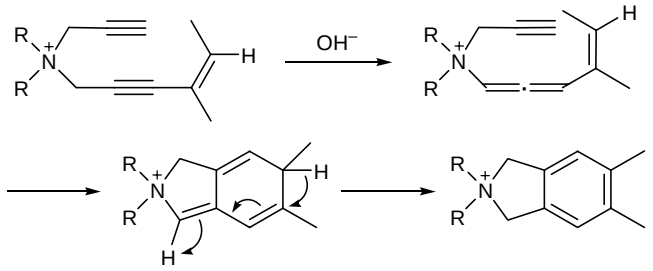
particular salts containing an allene moiety. On the basis of the effects of structural and external factors on the rate of cyclization, the authors presumed that the second scheme is more probable.

Scheme 3.



In the present work we made an attempt to elucidate the mechanism of cyclization of quaternary ammonium salts containing a β,γ-unsaturated group together with a 3-alkenyl- or 3-aryl-2-propynyl radical on the nitrogen atom. The study was performed using IR spectroscopy, and we found optimal conditions for the cyclization to occur in water-resistant cells (CaF_2). As substrates we used dimethyl(2-propynyl)(3-vinyl-2-propynyl)ammonium, dimethyl(3-phenyl-2-propynyl)-(2-propynyl)ammonium, diethyl(3-phenyl-2-propynyl)-(2-propynyl)ammonium, dicyclohexyl(3-phenyl-2-propynyl)(2-propynyl)ammonium, 4-(3-phenyl-2-propynyl)-4-(2-propynyl)morpholinium, dimethylbis(3-phenyl-2-propynyl)ammonium, and diethylbis(3-phenyl-2-propynyl)ammonium salts **I**–**VII**.

I **II–VII**

II, R = Me, X = H; **III**, R = Et, X = H; **IV**, R = *cyclo*-C_6H_{11}, X = H; **V**, R_2N = morpholino, X = H; **VI**, R = Me, X = Ph; **VII**, R = Et, X = Ph.

In all cases, the IR spectra of aqueous solutions of salts **I**–**VII** were initially recorded, a 2 N solution of potassium hydroxide was added, the mixture was quickly stirred and placed into a spectrophotometric cell, and the progress of reaction was monitored following variations in the IR spectra.

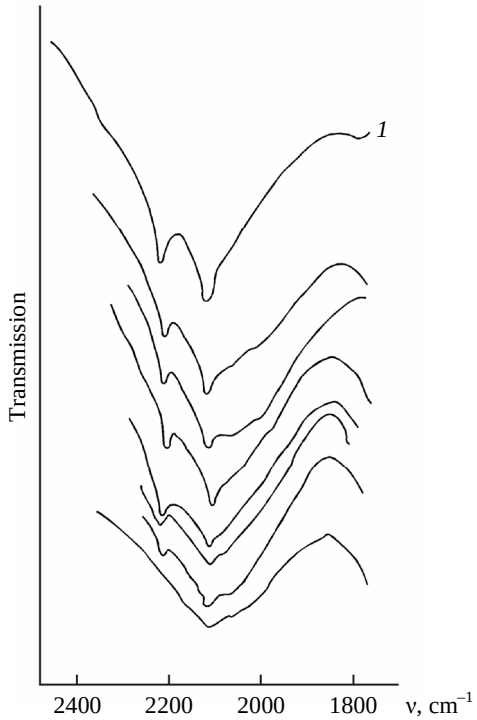
Had the cyclization followed Scheme 2, the IR spectra recorded during the process would display absorption in the region 1940–1960 cm^{-1}, typical of allene fragment. However, in the cyclization of salts **I**–**VII**, the IR spectra contained only absorption bands due to disubstituted (2220–2240 cm^{-1}) and monosubstituted triple bonds (2110–2130 cm^{-1}; compounds **I**–**V**), whose intensity gradually decreased. In no case absorption assignable to allene group was detected.

It might be presumed that we failed to detect α-allene fragment because of very fast cyclization with participation of that group. To verify this assumption we examined the behavior of trimethyl(3-phenyl-2-propynyl)ammonium bromide (**VIII**), which cannot undergo cyclization, in the presence of a catalytic amount of aqueous alkali. We observed no absorption typical of an allene fragment, while the band belonging to disubstituted acetylene moiety did not change its position and intensity. Figure illustrates variation of the IR spectral pattern during cyclization of salt **V**. It is seen that the spectra recorded at different moments lack absorption band assignable to allene moiety.

Thus the results of our IR studies led us to conclude that the cyclization of ammonium salts having a 2-propynyl group together with a 3-alkenyl- or 3-aryl-2-propynyl moiety follows a concerted mechanism which directly involves the enyne group as π^4-fragment, i.e., according to Scheme 2.

EXPERIMENTAL

The IR spectra of salts **I**–**III**, **VI**, and **VII** were recorded on a UR-20 spectrometer, and the spectra of **IV** and **V** were obtained on a Specord IR75 instrument.



IR monitoring of the cyclization of 4-(3-phenyl-2-propynyl)-4-(2-propynyl)morpholinium salt **V**: (*1*) initial spectrum.

Salts **I**–**VII** were synthesized according to the procedures described in [1–3]; salt **VIII** was prepared by alkylation of dimethyl(3-phenyl-2-propynyl)amine with methyl bromide in anhydrous diethyl ether. Potassium hydroxide of chemically pure grade was used.

A 2 N aqueous solution of potassium hydroxide, 0.04–0.08 ml, was added to a 15–20% solution of salt **I**–**VIII**, 0.2 ml. The mixture was transferred into a spectrophotometric cell, and the progress of the reaction was monitored following variation of the IR spectral pattern. While preparing solutions of poorly soluble salts **II**, **VI**, and **VII**, a few drops of ethanol were added.

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