

# Intramolecular Cyclization of Furfuryl 2-Propynyl Ether

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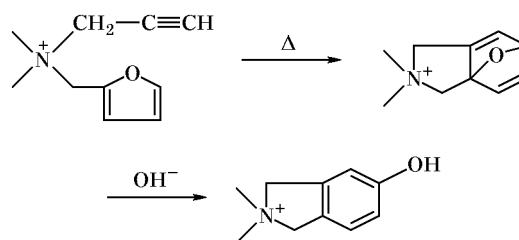
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**Abstract**—Intramolecular cyclization of furfuryl 2-propynyl ether in the presence of a catalytic amount of potassium *tert*-butoxide in *tert*-butyl alcohol gives 3a,6-epoxy-1,3-dihydro-6*H*-isobenzofuran. The cyclization is presumed to be favored by preliminary isomerization of the 2-propynyl group into allenyl. Heating of the cyclization product with excess potassium *tert*-butoxide in *tert*-butyl alcohol results in cleavage of the epoxy bridge with formation of 6-hydroxy-1,3-dihydroisobenzofuran.

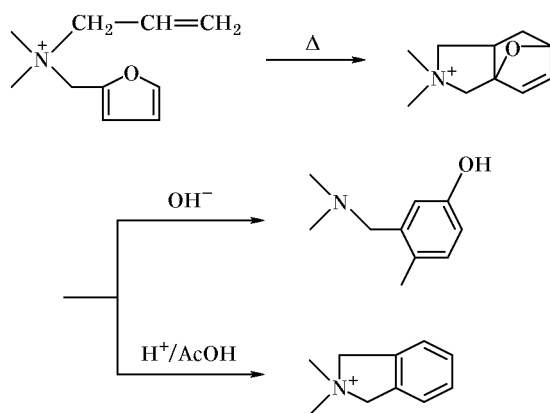
Intramolecular version of the Diels–Alder reaction provides a convenient, economic, and stereocontrollable route to natural compounds and substances possessing a wide spectrum of useful properties [1–3]. Important are cyclizations involving a furan ring which constitutes the key fragment in many natural products [4]. Tagmazyan *et al.* previously reported that dialkyl(allyl)furfurylammonium salts undergo quantitative intramolecular cyclization to give 2,2-dialkyl-5,7a-epoxytetrahydroisobenzofuran salts. The cyclization occurs on heating the substrate both in aqueous solution [5] and without a solvent [6]. Dehydration of the cyclization product in the presence of acetic acid yields the corresponding 2,2-dialkyldihydroisobenzofuran salt, and treatment with aqueous alkali leads to dialkylaminomethyl derivatives of phenol [6] (Scheme 1). The same authors obtained 2,2-dialkyl-5-hydroxydihydroisobenzofuran salt by alkaline cleavage of the cyclization product derived

from dialkyl(furfuryl)-2-propynylammonium salt [7] (Scheme 2). Successful intramolecular Diels–Alder reactions were also reported for carboxamides having an *N*-allyl group together with *N*-furfuryl [8].

Scheme 2.



Scheme 1.

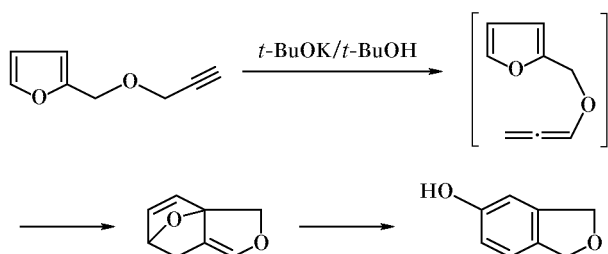


The present communication reports the results of studying intramolecular cyclization of furfuryl 2-propynyl ether in the presence of potassium *tert*-butoxide in *tert*-butyl alcohol. It was found previously that thermal cyclization of allyl and 2-propynyl furfuryl ethers requires drastic conditions [9]. This was explained in terms of electronic interactions between the lone electron pair on the oxygen atom and the  $\pi$ -system of the triple bond which is not involved in the cyclization [10]. Therefore, elimination of such interaction should favor intramolecular cyclization.

By heating on a boiling water bath of furfuryl 2-propynyl ether in *tert*-butyl alcohol containing a catalytic amount of potassium *tert*-butoxide, 47% of the corresponding cyclization product, 3,6a-epoxy-1,3-dihydro-6*H*-isobenzofuran, was obtained. Presumably, the cyclization is favored by preliminary isomerization of the 2-propynyl group into allenyl,

which can be promoted by potassium *tert*-butoxide (Scheme 3). The latter either reduces or completely eliminates the above intramolecular electronic interaction, thus making the cyclization possible under relatively mild conditions.

Scheme 3.



Treatment of furfuryl 2-propynyl ether in *tert*-butyl alcohol with 3 equiv of potassium *tert*-butoxide at 85–90°C (reaction time 10 h) leads to formation of 65% of 5-hydroxy-1,3-dihydroisobenzofuran, presumably via cleavage of the epoxy bridge in the intermediate intramolecular Diels–Alder adduct (Scheme 3).

#### EXPERIMENTAL

The IR spectra were recorded on a UR-20 spectrometer from samples dispersed in mineral oil. The  $^1\text{H}$  NMR spectra were obtained on a Perkin–Elmer-30 instrument (300 MHz) in  $\text{CDCl}_3$  using tetramethylsilane as internal reference.

**3a,6-Epoxy-1,3-dihydro-6H-isobenzofuran.** A mixture of 1.5 g (11 mmol) of furfuryl 2-propynyl ether, 0.2 g of potassium *tert*-butoxide, and 0.05 g of hydroquinone was heated for 5 h at 80–85°C under argon. The mixture was cooled and washed with dry diethyl ether. The precipitate was dissolved in 5 ml of anhydrous alcohol, and the solution was poured into 50 ml of dry diethyl ether. Yield 0.7 g (45%), mp 181–183°C. IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 1030, 1080, 1630, 3010.  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 3.8–4.5 m (5H,  $2\text{CH}_2\text{O}$ , OCH), 5.7–6.8 m (3H,  $\text{CH}=\text{CH}$ ,  $\text{CH}=\text{}$ ).

**5-Hydroxy-1,3-dihydroisobenzofuran.** A solution of 3.4 g of potassium *tert*-butoxide in 100 ml of *tert*-

butyl alcohol and 0.1 g of hydroquinone were added to 3 g (22 mmol) of furfuryl 2-propynyl ether. The mixture was heated with stirring for 10 h on a boiling water bath (90–95°C). It was then cooled, acidified with 40% hydrobromic acid to a weakly acidic reaction, and evaporated to dryness. The residue was extracted with alcohol to obtain 1.95 g (65%) of 5-hydroxy-1,3-dihydroisobenzofuran. IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 810, 830, 1200, 1470, 1560, 1810, 3030; 3320–3400.  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 5.05–5.13 m ( $2\text{CH}_2$ ), 6.8–7.1 m (3H), 7.7 s (1H). Found, %: C 70.41; H 5.72.  $\text{C}_8\text{H}_8\text{O}_2$ . Calculated, %: C 70.59; H 5.89.

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