

## Acetylenic Derivatives of Crown Ethers

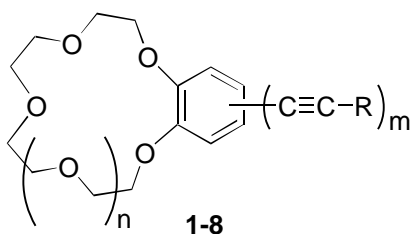
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Crown ethers are an extremely important class of the widely used and highly effective complexones and biologically active compounds [1]. On the other hand, it is known that many acetylenic derivatives also possess high biological activity [2].

In 1975 the Japanese investigators [3] discovered a new catalytic system ( $\text{PdCl}_2\text{-CuI-Et}_2\text{NH}$ ) for the cross-coupling of 1-alkynes with  $sp^2$ -halides. Still now this method is one of the best for preparing various derivatives of aryl- and hetarylacetylenes. However, only a few acetylenic derivatives of crown ethers are known. This situation is connected not with the absence of interest to the above compounds, but with the difficulties in preparing them. Actually, the Pd/Cu-catalyzed cross-coupling of 1-alkynes with the iodoarenes bearing electron-releasing substitutions (like  $\text{NR}_2$ , OR) is accompanied with a homo-coupling of alkynes and the reductive desiodination of iodoarenes. Sometimes side-reactions become the only reactions.

We investigated the possibility of applying the cross-coupling of 1-alkynes with iodocrown ethers for producing alkynylcrown ether. A mixture of iodo- or diiodocrown ether, terminal acetylene,  $\text{PdCl}_2(\text{PPh}_3)_2$ , CuI, and triethylamine is warmed at 80 °C for 2-5 h in an argon stream. Disubstituted alkynes **2-4** were obtained in 55-75% yields.



**1:** R = H, **2:** R = 4-Ph-C<sub>6</sub>H<sub>4</sub>, **3:** R = 4-CHO-C<sub>6</sub>H<sub>4</sub>,

**4:** R = C(OH)Me<sub>2</sub>, **5:** R = C≡C-C(OH)Me<sub>2</sub>,

**6:** R = CH<sub>2</sub>N(Et)<sub>2</sub>,

**7:** R = CH<sub>2</sub>N<img alt="piperidine ring" data-bbox="595 575 635 600"/>O, **8:** R = CH<sub>2</sub>N<img alt="piperidine ring" data-bbox="705 575 745 600"/>

n = 1,2; m = 1,2

Ethynyl crown ethers **1** are obtained by the Retro-Favorsky reaction. The boiling of the mixture of tertiary acetylenic alcohols **4**, and powdered KOH in dry toluene for 2-4 h affords **1** in 50-60% yields.

Taking into account the high biological activity of compounds bearing propargylamino fragment ( $\text{N-CH}_2\text{-C}\equiv\text{C}$ ), we carried out the aminoalkylation of alkynes **1**. Aminopropargylcrown ethers **6-8** are obtained by condensation of alkynes **1** with paraform and a secondary amine in the presence of the catalytic amounts of CuCl in boiling dioxane (1-2 h, 70-80%).

The typical reactions of terminal acetylenes are also demonstrated: the Cadiot-Chodkiewicz cross-coupling between 1-alkynes and 1-bromoalkynes, copper (I) halide catalyzed oxidative coupling of 1-alkynes.

### References:

- [1] E. Abel, G.E.M. Maguire, E.S. Meadows, O. Murillo, T. Jin, G.W. Gokel, *J. Am. Chem. Soc.* **1997**, *119*, 9061.
- [2] L. Brandsma, S.F. Vasilevsky, H.D. Verkruijsse, *Application of Transition Metal Catalysts in Organic Synthesis*; Springer-Verlag: Berlin, Heidelberg, New York, **1998**.
- [3] K. Sonogashira, Y. Tohda, N. Hagihara, *Tetrahedron Lett.* **1975**, *50*, 4467.