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USING OPTICALLY ACTIVE CHIRAL CROWN ETHER AT ENANTIOMERIC SEPARATION OF AMINES

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The synthesized *S*-enantiomer of the crown ether was used as an adsorbent to separate the racemic mixture of L-alanine ether of phenamine into individual diastereomers by column chromatography. Chromatographic separation occurred due to the formation of complexes of different stability between diastereomers and optically selective adsorbents on a "host-guest" principle. The separated diastereomers were converted into enantiomers by hydrolysis. The structure and optical activity of the synthesized crown ether and separated enantiomers were investigated by physicochemical methods.

Keywords: crown ether, enantiomers, diastereomer, chromatography, eluent, chirality.

doi

Introduction

In recent decades, supramolecular chemistry began to develop rapidly and spread to various fields of science. Conceptually, supramolecular chemistry has much in common, with of nanostructures is based on the principle of self-assembly and self-organization, and this is the essence of supramolecular assemblies. Supramolecular structures play a vital role in the functioning of living organisms. Their unique feature lies in the fact that they arise spontaneously, via hydrophobic interactions, electrostatic effects, which, in turn, immerge due to the interaction of functional groups of biomolecules with an aqueous medium and through non-covalent bonds, which play an important role in the formation of these structures [1]. All these natural supramolecular compounds, formed by self-assembly, are intended for the implementation of vital biological functions of living organisms [2].

So, synthetic analogues of such systems are very interesting, in term of its supramolecular properties, imitating the properties of naturally occurring systems [3]. The substitution of macrocycle's oxygen atoms by nitrogen atoms increases the complex formation ability, as the nitrogen atoms are softer bases. Crown ethers are able to bind the ions of transfer and rare earth

metals and ammonium [4]. Beside this, the synthesis of macroheterocycles, containing various functional groups in their molecule significantly affects the ability of these compounds to form supramolecular assemblies by means of non-covalent interactions [5].

After the discovery of crown compounds, the rapid development of supramolecular chemistry began and on their basis the "host-guest" type complexes were synthesized, capable of recognizing the obtained objects [6]. As a result, the use of crown ethers made it possible to separate the diastereoisomers. And this, in turn, gave an excellent opportunity to separate the enantiomers of chiral compounds of optical substances. Research in this area along with originality, has great perspective and importance in biochemistry and pharmaceuticals [7].

Taking into account the relevance of the topic, we have developed a chromatography method for the separation of optical isomers of physiologically active amines. Due to the presence of an asymmetric carbon atom, the crown ether (1,2,10,11-dibenzo-5-methyl-14-hydroxy-16-crown-5) (Figure 1) (I) [8] consists of a racemate containing two enantiomers. Using the method of Shabanov and Tong Kang Shon [9], we first performed method of the separation of these enantiomers by column chromatography.

For this purpose, racemic mixture of L(S)-alanine* of the crown ether has been separated into the individual diastereoisomers (*R,S*- and *S,S*-) by column chromatography. Individual diastereoisomers had been subjected to hydrolysis and obtained *S*- and *R*-enantiomers of crown ether.

Fig. 1. 1,2,10,11-dibenzo-5-methyl-14-hydroxy-16-crown-5.

Fig. 2. *S,S*- (II) and *R,S*- (III) enantiomers of crown ether with L(*S*) alanine.

S,S-diastereoisomer is held by adsorbent weakly (II), remains in the column, by washing with the eluent from the column comes easily.

As eluent it was taken aqueous-alcoholic solution (1:10). Diastereoisomers (*R,S*- and *S,S*-) are hydrolyzed in a basic medium to give the corresponding individual *R*- and *S*-enantiomers of phenamine [10]. The structures of the enantiomers was confirmed IR and NMR spectra.

*Note. In literature to name the optical isomers of alanine is using model DL-(Rozanov), in an article for the name of the optical isomers there had been used this model (DL) and SR- (Cannes-Ingold-Prelog) model [10].

Experimental part

Obtaining L-alanine ester of phenamine.

The ammonium salt of L(*S*)-alanine in the amount of 12.5 g, 1-phenyl-2-aminopropane in the amount of 13.5 g (0.1 mol) and 100 ml of

ethyl alcohol are mixed and boiled in a flask under reflux. Then the alcohol was removed in vacuo and a mixture of diastereoisomers was obtained. The sublimation temperature and the mixture yield are, respectively, 270°C, 98%.

In order to use the obtained *S*-enantiomer of the crown ether as an adsorbent, it is implanted on the surface of a silica gel (MSK) and filled into a 10×300 mm glass column. The thickness of the adsorbing layer should be 200 mm. An aqueous-alcoholic solution (1:2) of diastereoisomers of the racemate L(*S*)-alanine ester of phenamine passes through the surface of the adsorbent in a chromatographic column.

The mechanism of action of the *S*-enantiomer of crown ether as an adsorbent is that the hydrogen bond retains the diastereoisomers using column chromatography in cavities with different forces. Since the *R,S*-diastereoisomers are poorly retained in the cavities of crown ether (III), it comes first from the column.

Results of elemental analysis of diastereoisomers mixture: founded, %: C 55.32, H 8.03, N 10.81, Cl 13.59. C₁₂H₂₁N₂O₂Cl; calculated, %: 55.28%, H 8.06, N 10.75, Cl 13.63.

On chromatographic stand "Sulifol" confirmed that the selected sample for analysis consisted of mixture of two isomers.

Separation of mixtures diastereoisomers by chromatographic method. A mixture of diastereoisomers in an amount of 6.6 g is dissolved in a water-alcohol solution (3:1). The resulting solution was passed through a glass chromatographic column 300×10 mm in size. Chromatographic column is prepared in advance for this purpose.

The column is filled with MSK silica gel, on the surface of which optically active crown ether (I) is deposited using benzene. The separation process in a chromatographic column is controlled on a "Sulifol" plate. The first from the column comes *S*, *R*-diastereoisomer with a yield of 2.1 g. This isomer is not destroyed and does not melt. It sublimates at high temperatures.

Elemental analysis results of individual diastereomers: founded, %: C 55.41, H 8.09, N 10.84, Cl 13.35. C₁₂H₂₁N₂O₂Cl; calculated, %: C 55.28, H 8.06, N 10.75, Cl 13.63.

The yield of the second *S*,*S*-diastereoisomer is 18%. The obtained product is a crystal of white color and in a form of crystals doesn't differ from crystals of the *S*,*R*-diastereoisomer. It does not melt, does not destroyed and sublimates easily.

Elemental analysis results: founded, %: C 55.34, H 8.02, N 10.83, Cl 13.61. C₁₂H₂₁N₂O₂Cl; calculated, %: C 55.28, H 8.06, N 10.75, Cl 13.63.

Hydrolysis of *R*,*S*-diastereoisomer. Diastereoisomer in an amount of 6.6 g is dissolved in water and sodium hydroxide solution (1.0 mol) is added to the resulting solution until pH = 11 is reached. After cooling, the solution is extracted by toluene. Toluene is distilled off in vacuo and 1-phenyl-2-aminopropane is obtained with a yield of 57% and a boiling point

of 201–202⁰C. The physicochemical parameters of the obtained compounds do not differ from those given in the literature [11]. The structure and optical activity separated enantiomers were investigated by physicochemical methods [12].

Conclusion

Highly selective adsorbents (methyl- and hydroxy-substituted crown ethers) have been synthesized to be used in column chromatography for the separation of optical isomers. A chiral crown ether containing an asymmetric carbon atom in the macrocyclic ring was divided into enantiomers and used in a chromatographic column as an optically selective adsorbent. A way of the separation of phenamine into optical isomers by the method of column chromatography, which is of practical importance, has been developed. The racemic enantiomers of the compounds were converted into a mixture of diastereomers by crosslinking L(*S*)-alanine with them and separated into individual diastereomers using an appropriate adsorbent. Chromatographic separation occurred due to the formation of complexes of different stability between diastereomers and optically selective adsorbents on a "host-guest" principle. Diastereomers were turned into individual enantiomers by hydrolysis and reduction reactions. The structure of synthesized crown ether and separated enantio-

mers was investigated by NMR, mass-, FTIR spectroscopy methods. The optical induction of enantiomers was determined on an AUTOPOL III polarimeter.

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OPTİKİ AKTİV XİRAL KRAUN EFİRİN AMİNLƏRİN ENANTIOMER AYRILMASINDA TƏTBİQİ

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Rasemik qarışığın xromatoqrafik kolonkada ayrılması prosesində istifadə etmək üçün asimmetrik karbon atomuna malik xromatoqrafik metodla ayrılmış kraun efir sintez edilmişdir. Alınmış kraun efirin S-enantiomeri fenaminin L-alanin efiri rasematının fərdi diastereomerlərə ayrılması prosesində tətbiq edilmişdir. Xromatoqrafik ayrılma diastereomerlər və optiki seçici adsorbent arasında “sahib-qonaq” prinsipi ilə müxtəlif davamlılığa malik komplekslərin yaranması hesabına baş verir. Ayrılmış diastereomerlər hidroliz olunaraq enantiomerlərə çevrilmişdir. Sintez olunmuş kraun efirin və ayrılmış enantiomerlərin quruluşu və optiki aktivliyi fiziki-kimyəvi üsullarla təyin edilmişdir.

Açar sözlər: kraun efir, enantiomer, diastereomer, kolonkalı xromatoqrafiya, elyuent, xiralıq.

ПРИМЕНЕНИЕ ОПТИЧЕСКИ АКТИВНОГО ХИРАЛЬНОГО КРАУН-ЭФИРА ПРИ ЭНАНТИОМЕРНОМ РАЗДЕЛЕНИИ АМИНОВ

У.А.Гасанова, З.О.Гахраманова, П.Ф.Гусейнова

Для использования в процессе разделения рацемической смеси хроматографической колонке синтезирован краун-эфир с асимметричным атомом углерода, который отделяли хроматографическим методом. Полученный S-энантиомер краун-эфира был использован в качестве адсорбента в процессе разделения рацемата L-аланинового эфира фенамина на отдельные диастереомеры. Хроматографическое разделение происходит в результате образования комплексов различной стабильности между диастереомерами и оптически селективными адсорбентами по принципу “хозяин-гость”. Отдельные диастереомеры превращены в энантиомеры гидролизом. Структура и оптическая активность синтезированного краун-эфира и разделенных энантиомеров была исследована физико-химическими методами.

Ключевые слова: краун-эфир, энантиомер, диастереомер, колоночная хроматография, элюент, хиральный.