

Synthesis and characterization of 6-(hydroxymethyl)-14,16-dimethyl-13,14,16,17-tetrahydro-6H-13,17-epiminodibenzo[e,-l][1,4]dioxacyclotridecin-15(7H)-one

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Abstract

New 6-(hydroxymethyl)-14,16-dimethyl-13,14,16,17-tetrahydro-6H-13,17-epiminodibenzo[e,l][1,4]dioxacyclotridecin-15(7H)-one (**2a**) was synthesized in good yield by the Petrenko-Kritchenko reaction of 2,2'-(3-hydroxypropane-1,2-diyl)bis(oxy)bisbenzaldehyde (**1a**) with diethyl ketone in the mixture of ethanol and acetic acid as solvent in the presence of ammonium acetate. The compounds were characterized by elemental analyses, IR, ¹H-NMR, ¹³C-NMR and mass spectrometry.

Keywords: Petrenko-Kritchenko condensation; macrocyclic compound; bisaldehyde.

Introduction

Crown ethers constitute one of the most important classes of macrocyclic compounds [1]. The study of crown ethers has largely contributed to the development of Host-Guest and molecular recognition chemistry [2]. The syntheses of many different types of new aza crown ethers have attracted researchers' attention due to their

widespread applications in biology, supra-molecular chemistry, new materials, medicine and the chemical industry [3-5]. Also, the presence of aza crown ethers including a piperidone moiety in a single macrocyclic molecule could increase the potential of biological activity of such derivatives [1,6]. Therefore, because of the numerous areas of chemistry where

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aza-macrocyclic complexes are main key, the preparation of new macrocyclic ligands with ever more elaborate structures is also a vital area of research [7,8]. In this paper, we synthesized and characterized new 6-(hydroxymethyl)-14,16-dimethyl-13,14,16,17-tetrahydro-6H-13,17-epiminodibenzo[e,l][1,4]

dioxacyclotridecin-15(7H)-one (2a).

Aza crown macrocycle was synthesized by Petrenko-Kritchenkocondensation of bisaldehyde(1a) and diethyl ketone in the presence of ammonium acetate (NH₄OAC). The chemical structure of newly synthesized compounds was characterized by FT-IR, NMR and mass spectroscopy and their purities were also confirmed by elemental analyses.

Experimental

General

Melting points were measured by an Electrothermal digital 9200 melting point apparatus and the results were uncorrected. IR spectra were recorded in the region 400-4000 cm⁻¹ on a Shimadzu Varian Model-4300 FT-IR spectrophotometer using KBr discs. The ¹H and ¹³C-NMR spectra were recorded in CDCl₃ on a Bruker-Avance DRX-400 and 75 spectrometers using TMS as an internal standard. Chemical

shifts are given in ppm () relative to tetramethylsilane. Mass spectra were recorded on a GC-MS Shimadzu QP1000PX Mass Spectrometer. Elemental analyses (C, H and N) were performed on a Perkin-Elmer 240C analyzer.

Synthesis of 2,2'-((3-hydroxypropane-1,2-diyl)bis(oxy))-bisbenzaldehyde (1a)

To the stirred solution of salicylaldehyde (24.4 g, 0.2mol) in hot ethanol was added sodium hydroxide (8 g, 0.2mol) in absolute ethanol (100 mL). The mixture was warmed and 2,3-dibromo-1-propanol (10.28 mL, 0.1mol) was added. To produce a homogeneous solution, sufficient ethanol (300 mL) was then added. The progress of the reaction was monitored by thin layer chromatography (TLC). The solution was refluxed under nitrogen for 100 h and then cooled and let stand at 0°. The cream-colored crystals produced were washed with water and recrystallized from ethanol. The resulting crystals were collected by filtration and dried in vacuum desiccators over P₄O₁₀.

Cream crystals; m.p: 109-110 °C, - yield: 84%; IR (KBr): 3466 (OH), 2875 (CHO), 1682 (C=O) cm⁻¹. ¹H-NMR (400 MHz, CDCl₃): δ= 10.2 (s, 2H, H-

7), 7.02-7.8 (m, 6H, H-3, 4, 5), 6.96 (s, 2H, H-2) 4.520 (m, 2H, H-8), 4.317 (d, 1H, H-9), 3.9 (s, 2H, H-10), 2 (s, 1H, OH) ppm. $^{13}\text{C-NMR}$ (100 MHz, CDCl_3): = 190.25 (C, C-7), 160 (C, C-1), 134 (CH, C-3), 130.3 (CH, C-5), 122.11 (C, C-6), 119.08 (CH, C-4), 114.7 (CH, C-2), 80 (CH, C-9), 73 (CH, C-8), 64.3 (CH, C-10) ppm; MS: m/z (%) = 300 (100) [M^+]. Anal. calcd for $\text{C}_{17}\text{H}_{16}\text{O}_5$ (300.31): C, 67.85; H, 5.37; O, 26.54. Found: C, 67.55; H, 5.06; O, 26.20 %.

Synthesis of 6-(hydroxymethyl)-14,16-dimethyl-13,14,16,17-tetrahydro-6H-13,17-epiminodibenzo[e,l][1,4]dioxacyclotridecin-15(7H)-one(2a)

A mixture of **1** (1 g, 3 mmol), diethyl ketone (0.22 g, 3 mmol) and ammonium acetate (0.3 g, 4 mmol) in ethanol (20 mL) and acetic acid (4 mL) solution were heated for 7 h under reflux. The reaction solution was then concentrated. The residue mixture was treated with a saturated solution of sodium carbonate (30 mL) and extracted with chloroform (15 mL). The extract was dried with MgSO_4 ; the solvent was distilled off, and the solution was chromatographed on SiO_2 . A hexane-ethyl acetate (1:1) eluent was

used to separate 2.1 g (34%) from this aza crown as snow-white crystals.

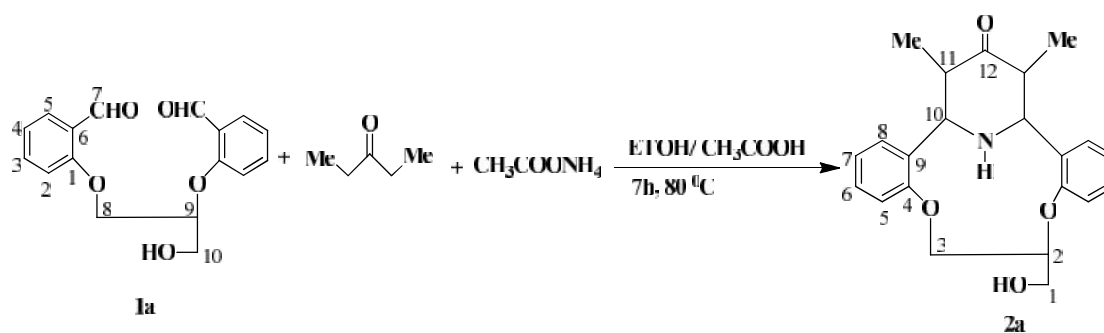
White crystals; m.p: 265°C. IR (KBr): 3377, 1701, 750.3 cm^{-1} . $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ = 7.2-6.7 (m, 8H, H-5, 6, 7,8), 4.6 (m, 2H, H-3), 4.3 (s, 1H, H-2), 4.1 (d, 2H, H-1), 3.6 (t, 2H, H-10), 3.1 (m, 2H, H-11), 1.6 (s, 2H, OH and NH), 0.88 (d, 6H, CH_3) ppm. $^{13}\text{C-NMR}$ (100 MHz, CDCl_3): δ = 212 (C, C-12), 155.7 (C, C-4), 131.2 (CH, C-8), 128.7 (CH, C-6), 124.5 (C, C-9), 121.3 (CH, C-7), 111.28 (CH, C-5), 77 (CH, C-2), 70.17 (CH, C-3), 70.1 (CH, C-1), 67.9 (CH, C-11), 49.8 (CH, C-10), 11.6 (CH, CH_3) ppm. MS: m/z (%) = 368 (25), 283 (50), 121 (100), 91 (25). Anal. Calcd. For $\text{C}_{22}\text{H}_{25}\text{NO}_4$ (367.44): C, 81.01; H, 5.48; N, 3.71; O, 17.2. Found: C, 81.07; H, 5.42; N, 3.81; O, 17.3 %.

Results and discussion

6-(hydroxymethyl)-14,16-dimethyl-13,14,16,17-tetrahydro-6H-13,17-epiminodibenzo[e,l][1,4]-dioxacyclotridecin-15(7H)-one (**2a**) ligand was successfully synthesized by Petrenko-Kritchenkocondensation of bisaldehyde (**2a**) and diethyl ketone in the presence of ammonium acetate (Scheme 1). Mechanistically, it is reasonable to assume that the first step

may involve Claisen-Schmidt condensation of bisaldehyde (**1a**) and diethyl ketone to aldol adducts [9]. Then, Petrenko-Kritchenko condensation of aldol adduct with ammonium acetate leading to the final product, 6-(hydroxymethyl)-14,16-dimethyl-13,14,16,17-tetrahydro-6H-13,17-epiminodibenzo[e,l][1,4]-dioxacyclotridecin-15(7H)-one (**2a**) [10]. The spectroscopic data of this aza crown by IR, $^1\text{H-NMR}$, $^{13}\text{C-NMR}$ and elemental analysis are in full accordance with the proposed structures. The IR spectra of the aza-crown ether display absorption bands at 3547, 3377 and 1701 cm^{-1} , which is characteristic of (OH), (NH) and (CO) bonds. In the $^1\text{H-NMR}$ spectrum of this

aza crown, two protons H_{10} and H_{11} appear at 3.65 and 3.16 ppm as adoublet signal with coupling constants equal 7.6 Hz, which indicates the transpositions of Me and Ar substituents in a piperidine moiety. Two protons of OH and NH were observed at 1.6 ppm. $^{13}\text{C-NMR}$ spectra of this compound showed peaks in the region of 11.69 (CH_3), 67.98 (C-11), 49.85 (C-10), 70.138 (C-1), 77 (C-2), 70.170 (C-3) and 212.126 (C-12) ppm, which are in good agreement with the probable structures. Mass spectral fragments of new synthesized aza crown agree with the proposed structure. The elemental analysis of this ligand showed good agreements with calculated values of % C, H and N.



Scheme 1. Synthesis of 6-(hydroxymethyl)-14,16-dimethyl-13,14,16,17-tetrahydro-6H-13,-17-epiminodibenzo[e,l][1,4]dioxacyclotridecin-15(7H)-on

Conclusion

In the present study, a new family of crown ethers containing piperidine ring has been synthesized and characterized

by spectral data (IR, $^1\text{H-NMR}$, $^{13}\text{C-NMR}$ & Mass) and elemental analysis studies.

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