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SYNTHESIS OF DIBENZOAZACROWN ETHERS INCLUDING A γ-PIPERIDONE MOIETY

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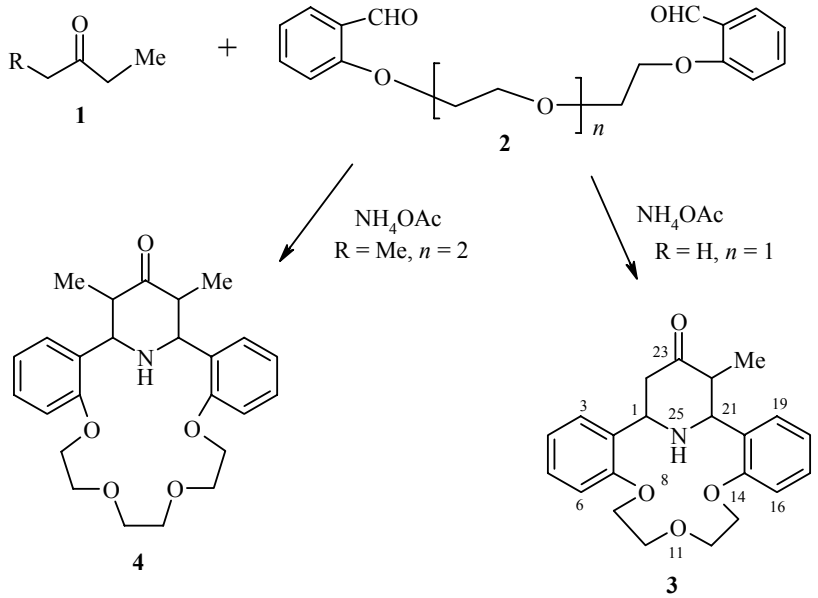
Use of substituted γ-piperidones is promising for synthesis of various heterocycles [1] and biologically active compounds [2]. In particular, azacrown ethers including a piperidone moiety have not been obtained before now. At the same time, combining such moieties in a single molecule is quite interesting from the standpoint of studying their mutual effect on complex formation, the reactivity of the γ-piperidone portion of the molecule, and also enhancing the potential for bioactivity of various derivatives. In this connection, our goal was to synthesize 2,6-diaryl-substituted γ-piperidones in which the aryl moieties are linked to each other by a polyethylene oxide chain. However, attempts to synthesize 2,6-di(2-hydroxyphenyl)piperidones by the Petrenko–Kritchenko method (condensation of dialkyl ketones **1** with salicylic aldehyde [3]) followed by their conversion to azacrown ethers (etherification by the Pedersen method [4]) proved to be ineffective because of the very low yields. So in order to achieve our goal, we decided to try a different approach: direct condensation of dialkyl ketones **1** with polyethers **2** in the presence of ammonium acetate.



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As a result of this method, we were able to obtain the desired azacrown ethers **3** and **4** in 40 and 26% yield respectively. Their structure was confirmed by NMR, mass spectrometry, and X-ray diffraction data (the X-ray diffraction data will be published in a separate communication). Thus we have developed a preparative method for synthesis of the first representatives of dibenzopiperidono-14-azacrown-4 and dibenzopiperidono-17-azacrown-5 ethers, which allows us to begin studying their chemical properties, chelating abilities, and synthesis of potentially biologically active derivatives of this novel group of azacrown ethers.

The ^{1}H NMR spectra were recorded on a Bruker WP-400 (400 MHz) spectrometer in $CDCl_3$, internal standard TMS; the mass spectra (electron impact) were recorded on a Finnigan MAT Incos 50 mass spectrometer (70 eV).

22-Methyl-8,11,14-trioxa-25-azatetracyclo[19.3.10^{2,7}.0^{15,20}]pentacosa-2,4,6,15(20),16,18-hexaen-23-one (3). A solution of ether **2** (*n* = 1) (5 g, 16 mmol), butan-2-one (**1**, R = H) (1.3 g, 16 mmol), and ammonium acetate (1.57 g, 20 mmol) in a mixture of EtOH (15 ml) and AcOH (3 ml) was refluxed for 5 h. The solvents were evaporated and a saturated solution of sodium carbonate (50 ml) was added to the residue, and it was extracted with chloroform (3 × 30 ml). The combined extracts were dried with $MgSO_4$, the solvent was driven off, and the residue was separated by column chromatography on alumina gel, eluting with a 1:1 ethyl acetate–hexane mixture. 2.36 g (40%) of compound **3** was isolated; mp 232-233°C (EtOH). IR spectrum (KBr), ν, cm^{-1}: 3302 (NH), 1696 (C=O). ^{1}H NMR spectrum, δ, ppm (*J* , Hz): 0.82 (3H, d, *J* = 5.7, CH_3); 2.57 (2H, dd, *J* = 13.5 and *J* = 2.2, H-24); 3.29 (1H, br. s, NH); 3.36 (1H, m, H-22); 3.49 (1H, m, H-21); 3.84-4.25 (9H, m, H-1,9,10,12,13); 6.77 (2H, d, *J* = 8.14, H-6, 10); 6.85 (2H, br. s, H-4,18); 7.09-7.20 (4H, m, H-3,6,17,19). Mass spectrum, *m*/*z* (I_{rel}, %): 367 $[M]^+$. Found, %: C 71.57; H 7.01; N 3.68. $C_{22}H_{25}NO_4$. Calculated, %: C 71.91; H 6.86; N 3.81.

25,27-Dimethyl-8,11,14,17-tetraoxa-28-azatetracyclo[22.3.1.0^{2,7}.0^{18,23}]octacosa-2,4,6,18(23),19,21-hexaen-26-one (4) was obtained similarly from ketone **1** (R = Me) and ether **2** (*n* = 2). Yield 26%; mp 168°C (EtOH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.88 (6H, d, *J* = 6.53, CH_3); 2.81 (2H, m, H-24,27); 3.5 (1H, br. s, NH); 3.61-3.81 (8H, m, H-10,12,13,15); 4.01-4.09 (4H, m, H-9,16); 4.39 (2H, d, *J* = 10.9, H-1,24); 6.76 (2H, d, *J* = 8.0, H-6,16); 6.94 (2H, t, *J* = 7.56 and *J* = 7.52, H-4,21); 7.14 (2H, t, *J* = 8.0 and *J* = 7.52, H-5,20); 7.53 (2H, d, *J* = 7.56, H-3,22). Mass spectrum, *m*/*z* (I_{rel}, %): 425 $[M]^+$ (91), 424 (7), 410 (8), 397 (35), 383 (19), 368 (64), 340 (57), 310 (24), 264 (25), 161 (46), 149 (48), 131 (68), 121 (100), 119 (42), 91 (57), 77 (40). Found, %: C 70.13; H 7.53; N 3.05. $C_{25}H_{31}NO_5$. Calculated, %: C 70.57; H 7.34; N 3.29.

REFERENCES

1. V. Baliah, R. Jeyaraman, and L. Chandrasekaran, *Chem. Rev.*, **83**, 379 (1983).
2. A. T. Soldatenkov, A. N. Levov, Zh. A. Mamyrbekova, N. M. Kolyadina, I. G. Mobio, Yu. I. Naumov, A. I. Komarova, and Le Tuan Anh, *Khim.-Farm. Zh.*, **38**, 16 (2004).
3. K. V. Vatsuro and G. L. Mishchenko, *Name Reactions in Organic Chemistry* [in Russian], Khimiya, Moscow (1976), p. 314.
4. M. Hiraoka, *Crown Compounds* [Russian translation], Mir, Moscow (1986), p. 363.