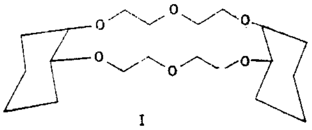
INTERACTION OF cis-DIASTEREOMERS OF DICYCLOHEXANO-18-CROWN-6 WITH MALEIC ANHYDRIDE AND SOME "SMALL" POLAR MOLECULES

E. V. Ganin, S. A. Kotlayar,
G. S. Musienko, M. S. Fonar',
M. S. Salakhov, A. A. Dvorkin,
and Yu. A. Simonov

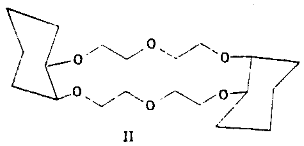
UDC 548.736:547.898'594.3:541.634

The cis-anti-cis diastereomer of dicyclohexano-18-crown-6 with maleic anhydride or formamide gives a crystalline complex of ratio 1:2. The three-dimensional structure of the former was found from x-ray studies. The formation of complexes was used for the separation of the individual cis-syn-cis and cis-anti-cis diastereomers from a mixture. Crystallization of a cis-anti-cis diastereomer from DMFA, DMSO, and N-methylpyrrolidine gave a high melting form.

The interaction of the sterically hindered ortho-nitroanilines and the cis-syn-cis (I) or cis-anti-cis (II) diastereomer of cyclohexano-18-crown-6 yields a crystalline complex only with the II isomer; this can be explained by steric factors [1]. The complex is stabilized by hydrogen bonding (N—H...O) between two atoms of the nitroaniline ("guest") and one of the diastereomer II ("host").



I



II

Maleic anhydride possesses similar properties, and forms a complex with the 18-crown-6 [2], but dimethyl- and dichloromaleic, succinnic, and phthalic anhydrides, and also N-phenylmaleic imide and hydrazide do not form this type of complex.

To explain the interactions of components of the complex, and to show how the molecule of maleic anhydride affects the conformation of the macrocycle, we carried out an x-ray study of the complex (III), obtained from the diastereomer II and two molecules of maleic anhydride.

From the nature of the reaction, the complex can be assigned to the "host-guest" type [3], in which the guest possesses a proton-donor group H—C (see Fig. 1). The present work is the first example of evidence of an interaction of the type C—H...O in a complex. Previously, the existence of such an interaction was only weakly established for the complex of maleic anhydride with sterically hindered 18-crown-6 [2] based on indirect data obtained from NMR and IR spectra and from dipole moment measurements. In [3, 4] for example, complexes consisting of 1:2 18-crown-6 with dimethylacetylene carboxylate and dimethylsulfone are also explained by the interaction C—H...O.

The following are properties of the complex III: 1) the heterocyclic anhydride ring is almost perpendicular to the average plane of the six oxygen atoms of the diastereomer II — the dihedral angle between them is 102.5°; (Figure, top, following page.) 2) a shortened contact (H...O) between the maleic anhydride and the diastereomer II; $H_{(1)}...O_{(1)} = 2.51$; $H_{(1)}...O_{(7)} = 2.72$; $H_{(2)}...O_{(2)} = 2.7$; $H_{(2)}...O_{(7)} = 2.75$ Å (total van der Walls radii for H and O is 2.69 Å) [5 – p. 86]). The interaction is weak; however, the position of the atoms $H_{(1)}$ and $H_{(2)}$ above the plane of the ring II produces a significant change in their conformation.

All-Union Scientific-Research and Project Institute of Monomers, Tula 300600. Institute of Applied Physics, Academy of Sciences of the Moldavian SSR, Kishinev 277028. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 10, pp. 1329-1332, October, 1989. Original article submitted May 18, 1988.

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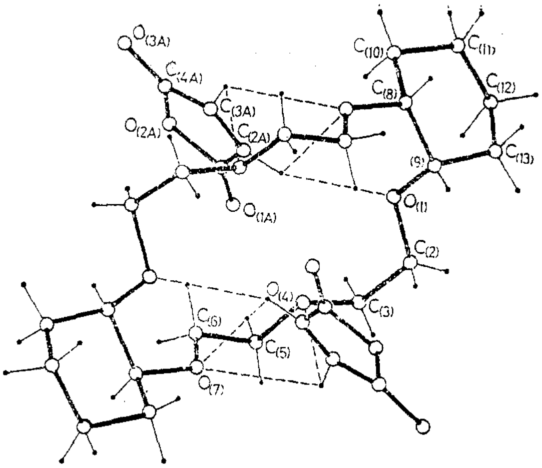

Structure of complex III

position of the atoms $H_{(1)}$ and $H_{(2)}$ above the plane of the ring II produces a significant change in their conformation.

The first of these factors is due to the decrease in the repulsion between the unshared electron pair on the oxygen atoms in maleic anhydride and crown-ether II, and also between these p-electrons and the C=C bond. Furthermore, such an arrangement guarantees maximum drawing together of "guest" hydrogen atoms and "host" oxygen atoms. Apparently, only one of the interactions noted in 2) is significant and for this the H...O distance is less than the total van der Waals radii. Nevertheless, together these interactions cause considerable conformational rearrangement of the diastereomer II, which is characterized by six gauche-rotamers at the C—C bonds and ten trans- and two gauche-rotamers at the C—O bonds. Such a conformation differs from that found for the free diastereomer II.

The distances in the crown-ether II are normal and have average values of 1.49 for C—C and 1.42 Å for C—O; the mean values for the angles are 109.6° for the carbon atoms and 113.0° for oxygen. In the chair conformation, cyclohexane substituents have average C—C distances of 1.53 Å and C—C—C angles of 111.2°. The geometry of the "guest" in the complex III appears to be similar to that in the starting maleic anhydride [6]. In the crystal structure, molecular complexes are held by van der Waals forces.

Thus, the absence of mutual packing carriers of the "guest" and "host" in the complex III appears to be the same as in the ortho-nitroanilines [1], and is a necessary condition for the formation of the molecular complex. As maleic anhydride offers no obvious steric hindrance to the formation of the complex with the diastereomer I, the important factor of formation of the complex III appears to be the greater degree of symmetry (C_1) of this complex [7].

Crystallization of the diastereomers I and II from acetonitrile [8] did not result in selective interaction. The complex mixture of diastereomers I and II obtained from acetonitrile did not have a constant melting point, and the polar composition "host-guest" varied from 1:3 to 1:1. Interaction with DMFA, DMSO, and N-methylpyrrolidone gave no separable mixture with diastereomers I and II. It should be noted that the diastereomer II crystallizes from these solvents as a higher-melting form [9] without formation of a complex. Selective interaction of the diastereomer II with formation of the complex "host-guest," 1:2 (IV) was observed when it was crystallized from formamide, which gives a similar complex with 18-crown-6 [10]. Bonding in the complex IV exists apparently through N—H...O interaction involving the formamide NH_2 group and oxygen atoms of the oxyethylene ring diastereomer II.

Formation of crystalline complexes III and IV has been used for the preparative separation of the diastereomers I and II formed as a result of catalytic hydrogenation of dibenzo-18-crown-6 on a ruthenium catalyst [9, 11].

EXPERIMENTAL

IR spectra of the compounds in KBr pellets were recorded on an IKS-29 spectrophotometer. PMR spectra were taken on a Tesla BS-467 (60 MHz) in $CDCl_3$, using TMS as internal standard.

TLC was carried out on Silufol UV-254 plates in methanol-chloroform, (1:8)-(1:10), visualized with UV light and ninhydrin.

A single crystal of the complex III with linear dimensions 0.2 × 0.3 × 0.4 mm was used for the x-ray analysis. The crystal was triclinic with unit cell parameters a = 9.745(4), b = 9.602(3), c = 8.745(4) Å; α = 65.38(3), β = 99.79 (3), γ = 89.47(3)°; space group symmetry P1, elemental composition $C_{28}H_{40}O_{12}$, d_{calc} = 1.29 g/cm³. Experimental data were obtained on a PED-4M diffractometer (MoK_α-radiation, θ/2θ-scanning, θ_{max} = 50°). There were 1247 reflections with $I \geq 2\sigma(I)$. The structure was determined by direct methods using the program MULTAN on an EVM SM-4 computer; the symmetry was lowered to P1. A refinement was carried out using the centrosymmetric space group and anisotropic temperature factors for the nonhydrogen atoms which led to an R factor of 0.055 (R_w = 0.036). Atomic coordinates, interatomic distances, and bond angles are given in [12].

Complex of cis-anti-cis-Diastereomer of Dicyclohexano-18-crown-6 with Maleic Anhydride (composition 1:2) (III). The diastereomer II (0.74g; 2 mmole) and maleic anhydride (0.39g; 4 mmole) were dissolved in benzene (3 ml) at 80°C. When cooled to 15°C, crystals separated and were filtered off to give 0.75g (66%) of the complex III, mp 83-85°C. IR spectrum: 2970-2830 (C—H), 1840, 1760 (C=O), 1100 cm^{-1} (C—O—C). PMR spectrum: 1.62 m, 3.62 s (36H, CH, CH_2, CH_2O – diastereomer II); 7.06 s ppm (4H, HC=CH). When the diastereomer I was used, no crystalline complex was obtained.

Separation of the Diastereomers I and II with Maleic Anhydride. A mixture of the diastereomers I and II (14.9 g; 0.04 mole) and maleic anhydride (5.9 g; 0.06 mole) was dissolved in benzene (25 ml) at 80°C. The crystalline complex which separated out at 5°C was filtered off, washed with benzene and heated with 30% NaOH (15 ml). The oily product was extracted with $CHCl_3$ (30 ml), the extract washed with water (30 ml), 3% HCl (30 ml), and again with water (30 ml). The extract was evaporated and the residue recrystallized from hexane (10 ml) to give the diastereomer II (4.3 g; 29%), mp 68-70°C. The filtrate, obtained after separation of the complex III, was treated analogously and after a final crystallization from diethyl ether (10 ml) yielded 3 g (20%) of the diastereomer I mp 61-62°C.

Complex of cis-anti-cis-Diastereomer of Dicyclohexano-18-crown-6 with Formamide (composition 1:2) (IV). The diastereomer II (0.74 g; 2 mmole) was dissolved in formamide (3 ml) at 100°C. When cooled to 20°C crystals separated and were filtered off to give 0.6 g (65%) of the complex IV, mp 85-87°C. IR spectrum: 3450 (H—N), 2940-2850 (H—C), 1665 (C=O), 1100 cm^{-1} C—O—C). PMR spectrum: 1.3 m, 3.60 s (36H, CH, CH_2, CH_2O – diastereomer II); 8.07 d ppm (4H, NH_2). When the diastereomer I was used, no crystalline complex was obtained.

Crystallization under these conditions of the diastereomer II in DMFA, DMSO, and N-methylpyrrolidone gave a high-melting form (mp 83-84°C) in 50-60% yield [9].

Separation of the Diastereomer II with Formamide. A mixture of the diastereomers I and II (112 g; 0.3 mole) was crystallized from 110 ml, then 100 ml of formamide. The crystals of the complex IV obtained were dissolved in 3% HCl (50 ml), then water (3 × 100 ml). The chloroform was evaporated off, and the residue recrystallized from hexane (50 ml) to give 36 g(32%) of the diastereomer II, mp 68-70%C.

Constants and IR spectra of the obtained diastereomers corresponded with known data [9].

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MECHANISM OF RECYCLIZATION OF FURANS TO THIOPHENES AND SELENOPHENES UNDER ACID CATALYSIS.

1. KINETIC STUDIES OF THE REACTION OF 2,5-DIALKYLFURANS WITH HYDROGEN SULFIDE IN THE PRESENCE OF HYDROCHLORIC ACID

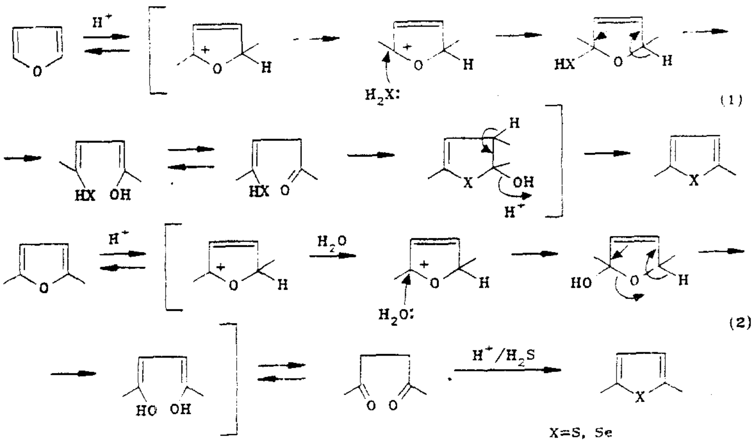
S. P. Voronin, T. I. Gubina,
I. A. Markushina, and V. G. Kharchenko

UDC 547.739'732'722.04:541.127

The transformation of 2,5-dialkylfurans to thiophenes by reaction with hydrogen sulfide in the presence of hydrochloric acid was studied. The reaction was found to be first order with respect to the furan; the rate of consumption of the furan did not change with increasing length of one of the alkyl substituents. Recyclization in the presence of acid proceeds in two independent directions: through the formation of an intermediate dicarbonyl compound, and by direct conversion of the furan to a thiophene. Kinetic data showed that the reaction occurs mainly by the second route.

Earlier we reported the acid-catalyzed recyclization of furans to thiophenes and selenophenes [1-4]. The aim of the present round of work is to study the mechanism of this chemical change.

Based on existing experimental and literature data [2, 3] the following reaction mechanism was proposed:



The important step in scheme (1) is the protonation of the α-carbon atom of the furan ring, and this is followed by nucleophilic attack by a hydrogen sulfide or a hydrogen selenide molecule, leading in the end to the formation of thiophene or selenophene.

When the process was carried out in the presence of concentrated acid (HCl, $HClO_4$), i.e., with a competing nucleophile (a water molecule) present, in addition to the desired reaction product, the 1,4-dicarbonyl compound was also formed [3]. Based on this, we proposed that

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N. G. Chernyshevskii State University, Saratov 410026. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 10, pp. 1333-1337, October, 1989. Original article submitted April 20, 1988.

0009-3122/89/2510-1113$12.50