PREPARATION OF STEREOISOMERIC AMINO ALCOHOLS OF THE FURAN SERIES

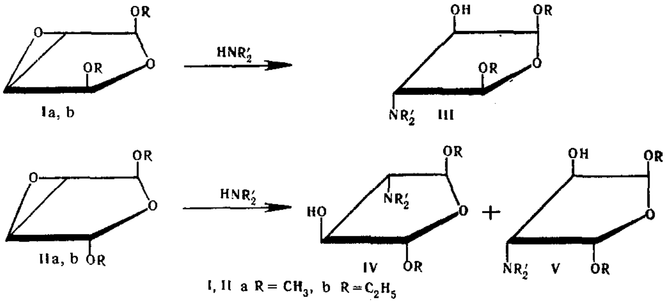
L. N. Kralinina, R. I. Kruglikova, and V. I. Bogomolova

Khimiya Geterotsiklicheskikh Soedinenii, Vol. 6, No. 3, pp. 299–301, 1970

UDC 541.634:547.723'722.6:543.422.4

The reaction of stereoisomers of 2,5-dialkoxy-3,4-epoxytetrahydrofuran with secondary amines has given stereoisomers of 2,5-dialkoxy-4-dialkylamino-3-hydroxytetrahydrofuran. Their configuration have been confirmed by IR spectroscopy.

In the search for new physiologically activity substances, stereoisomeric amino alcohols of the furan series have been obtained. We previously isolated individual isomers of 2,5-dialkoxy-3,4-epoxytetrahydrofuran and, on the basis of their NMR spectra and dipole moments, proposed configurational formulas I and II [1]. When these epoxides were heated for several hours with aqueous solutions of secondary amines, the epoxide rings opened and the corresponding amino alcohols were formed.



Epoxide I can give only one amino alcohol isomer III (in view of the fact that the opening of an α-oxide by nucleophilic reagents takes place as a trans addition and the hydroxyl group is located on the same side of the ring as the initial epoxide group). In actual fact, the action of various amines on 2,5-dimethoxy- and 2,5-diethoxy-3,4-epoxytetrahydrofuran to which configuration I is ascribed gave only one amino alcohol isomer III according to GLC analysis. The IR spectra of all the alcohols III obtained had a strong absorption band at 3570 cm^{-1}, which shows the presence of an intramolecular hydrogen bond and confirms configuration III.

In the opening of epoxide II by amines, two amino alcohols, IV and V, can theoretically be formed. Gas-chromatographic analysis showed that in this reaction two substances were formed in a ratio, by weight, of 95 : 5. Fractionation and crystallization gave a number of amino alcohols, in the IR spectra of which each had a strong absorption band at 3615 cm^{-1}, corresponding to a free hydroxyl, which permits these alcohols to be assigned configuration IV. The second component, the amount of which was ~5% of the mixture, could not be isolated. Thus, the addition of secondary amines to epoxide II takes place almost stereospecifically, obviously because of the influence of the neighboring alkoxide groups. The difference in the positions of the absorption bands of the free hydroxyl and the bound hydroxyl, $\Delta\nu_{OH}$, was 45 cm^{-1}. Taking into account literature information [2] on the correlation of $\Delta\nu_{OH}$ with the magnitude of the angle of twist between the functional groups (in the 1 and 2 positions), it may be concluded that in the compound obtained the furan ring has the half-chair form and the angle of twist between C_2—OR and C_3—OH bonds is approximately 40° (the possible limits of variation of the angle of twist for substiutents in the 1 and 2 positions of cyclopentane range from 0 to 48°).

EXPERIMENTAL

2,5-Dimethoxy-4-dimethylamino-3-hydroxytetrahydrofuran [3]. A mixture of 0.43 g of 2,5-dimethoxy-3,4-epoxytetrahydrofuran (I, R = CH_3) and 1.1 ml of 33% aqueous dimethylamine was heated in a sealed tube in a boiling water bath for 25 hr. Then it was extracted with chloroform, the extract was dried with magnesium sulfate, and the solvent was evaporated off in vacuo to give 0.48 g (78.5%) of 2,5-dimethoxy-4-dimethylamino-3-hydroxytetrahydrofuran, which, after recrystallization from n-hexane, had mp 93–94° C.

The other amino acids given in the table were obtained similarly.

2, 5-Dialkoxy-4-dialkylamino-3-hydroxytetrahydrofurans

Conformational formula	R	NR′₂	Bp, °C (mm)	n_D^{20}	Mp, °C	Mp of the methiodide	Empirical formula	Found, %			Calculated, %			IR spectrum ν, cm⁻¹
								C	H	N	C	H	N	
IV	CH_3	$N(CH_3)_2$	95—96 (0,3)	—	48—50	160—161	$C_8H_{17}NO_4$	50.57	8.71	7.12	50.29	8.90	7,33	3615
	CH_3	$N(C_2H_5)_2$	92—95 (0,2)	1.4552	—	152—154	$C_{10}H_{21}NO_4$	54.41	9.37	6.34	54.83	9.59	6,39	—
	CH_3	$N(C_3H_7)_2$	85—90 (0,4)	1.4612	—	129—131	$C_{12}H_{25}NO_4$	58.11	9.93	5.89	58.35	10.12	5,67	3615
	CH_3	NC_5H_{10}	—	—	77—78	170—171,5	$C_{11}H_{21}NO_4$	57.25	8.91	6.09	57.60	9.09	6,05	3610
	C_2H_5	$N(CH_3)_2$	—	—	47—48	155—156	$C_{10}H_{21}NO_4$	55.08	9.67	6.21	54.83	9.59	6,39	3615
	C_2H_5	NC_5H_{10}	—	—	101—103	144—145,5	$C_{13}H_{25}NO_4$	60.12	9.97	5.29	60.26	9.65	5,41	3612
III	CH_3	$N(CH_3)_2$	—	—	93—94	201—205	$C_8H_{17}NO_4$	50.59	8.81	7.18	50.29	8.90	7,33	3570
	CH_3	$N(C_3H_7)_2$	86—91 (0,45)	1.4572	—	143.5—144	$C_{12}H_{25}NO_4$	58.47	10.33	5.41	58.35	10.12	5,67	—
	CH_3	NC_5H_{10}	—	—	95.5—97	147—148	$C_{11}H_{21}NO_4$	57.47	9.25	6.25	57.60	9.09	6,05	3565
	C_2H_5	$N(CH_3)_2$	—	—	49—50	183.5—185	$C_{10}H_{21}NO_4$	54.63	9.71	6.61	54.83	9.59	6,39	3570
	C_2H_5	NC_5H_{10}	—	—	76—77	133.5—134	$C_{13}H_{25}NO_4$	60.07	9.93	5.29	60.26	9.65	5,41	3565

The GLC analysis of the products was carried out on a PAKhV-02 instrument (column 1 m × 6 mm, 10% Apiezon L on Celite, 135° C, rate of flow of helium 6 l/hr).

The IR spectra were recorded on an IKS-11 instrument using 0.01 M solutions of the product in CCl_4.

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15 August 1968

Lomonosov Moscow Institute of Fine Chemical Technology