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SYNTHESIS OF β,γ-UNSATURATED AMINES OF THE TETRAHYDROPYRAN SERIES

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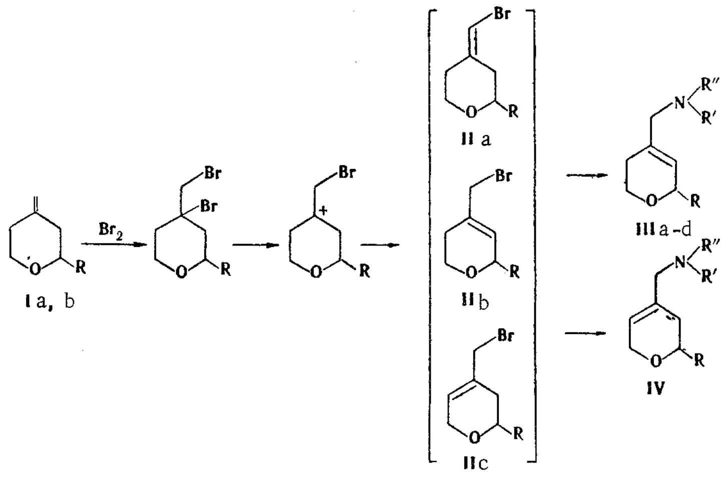
Dibromides of 4-methylenetetrahydropyran and 4-methyldihydro-2H-pyran were synthesized and subjected to reaction with excess amounts of amines to give β,γ-unsaturated amines of the tetrahydropyran series, the structure of which was proved on the basis of data from gas—liquid chromatography and PMR and IR spectroscopy.

In a continuation of our earlier research [1, 2] we have shown that 4-methylenetetrahydropyran and 4-methyldihydro-2H-pyran and their 2-isopropyl derivatives, which were isolated from mixtures of the isomers by preparative gas—liquid chromatography (GLC), form dibromides readily in high yields. The dibromides react with excess amounts of amines to give unsaturated amino derivatives in high yields.

It is assumed that the carbonium ion formed by heterolysis of the tertiary bromine atom is stabilized primarily by ejection of β protons from the heteroring rather than by ejection of the acidic protons of the bromomethyl group. The resulting intermediate unsaturated halide IIb (IIc) then reacts via the well-known scheme [3].



I a R=H; b R=i-C_3H_7; III R=H; a $R'=R''=C_2H_5$; b $R'=R''=C_4H_9$; c $R'+R''=(CH_2)_5$; d $R'+R''=(CH_2CH_2)_2O$; IV R=i-C_3H_7, $R'=R''=C_2H_5$

The structure of amines III was proved on the basis of data from GLC and IR and PMR spectroscopy. Absorption at 1678 cm^{-1}, which is characteristic for a trisubstituted double bond [4], is observed in the IR spectra of IIIa-d. The signal of a hydrogen atom attached to a double bond shows up distinctly at 5.5 ppm in the PMR spectra of these compounds. A signal from the protons of an NCH_2 group at 2.8 ppm, a triplet signal from the protons of a 6-CH_2 group at 3.7 ppm, and a multiplet signal of a 2-CH_2 group at 4.0 ppm are also observed. A similar result is obtained when an alkyl substituent is introduced in the α position of pyran system: We observed the formation of only the IV isomer (by GLC), the IR spectrum of

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TABLE 1. Dibromo Derivatives of Tetrahydropyrans

Compound	bp, °C (mm) (mp, °C)	n_D^{20}	d_4^{20}	Found, %			Empirical formula	Calc., %			Yield, %
				C	H	Br		C	H	Br	
I a	81—84 (2)	1,5395	1,7884	28,2	4,0	61,8	$C_6H_{10}Br_2O$	27,9	3,9	62,0	90
I b	92—94 (2)	1,5235	1,5485	36,2	5,0	53,7	$C_9H_{16}Br_2O$	36,0	5,3	53,3	78
Va	79—82 (2) (27)	—	—	28,9	3,3	62,6	$C_6H_{10}Br_2O$	27,9	3,9	62,0	92
Vb	92—95 (2)	1,5245	1,5499	36,5	5,2	53,0	$C_9H_{16}Br_2O$	36,0	5,3	53,3	77

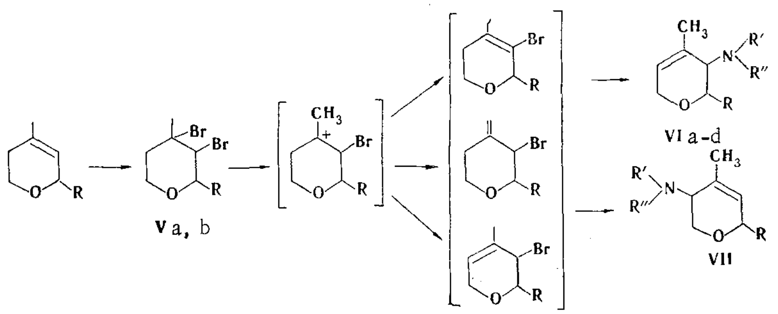
TABLE 2. Amino Derivatives of Dihydropyrans

Compound	bp, °C (mm)	n_D^{20}	d_4^{20}	Found, %			Empirical formula	Calculated, %			Yield, %
				C	H	N		C	H	N	
IIIa	86—89 (10)	1,4690	0,9214	71,0	10,8	8,1	$C_{10}H_{19}NO$	71,0	11,2	8,3	76
IIIb	100—101 (1)	1,4655	0,8929	74,5	12,3	6,2	$C_{14}H_{27}NO$	74,7	12,0	6,2	71
IIIc	112—114 (19)	1,4940	0,9887	72,6	10,1	7,7	$C_{11}H_{19}NO$	72,9	10,5	7,7	75
IIId	91—92 (3)	1,4968	1,0641	65,6	9,2	7,9	$C_{10}H_{17}NO_2$	65,6	9,3	7,6	86
IV	120—122 (25)	1,4645	0,9229	73,6	11,7	6,4	$C_{13}H_{25}NO$	73,9	11,8	6,6	57
VIa	83—84 (11)	1,4700	0,9211	70,7	11,1	8,3	$C_{10}H_{19}NO$	71,0	11,2	8,3	87
VIb	108,5 (2)	1,4668	0,8979	74,4	12,0	6,1	$C_{14}H_{27}NO$	74,7	12,0	6,2	68
VIc	106—107 (10)	1,4950	0,9887	72,8	10,0	8,1	$C_{11}H_{19}NO$	72,9	10,5	7,7	66
VId	89—90 (2,5)	1,4972	1,0646	65,3	9,2	8,1	$C_{10}H_{17}NO_2$	65,6	9,3	7,6	93
VII	103—104 (11)	1,4635	—	73,7	11,7	6,7	$C_{13}H_{25}NO$	73,9	11,8	6,6	58

which contains absorption at 1678 cm^{-1} (a trisubstituted C=C bond). The PMR spectrum of amine IV does not contain the triplet signal at 3.7 ppm that is related to 6-CH_2 protons in the spectra of systems of the III type, and the multiplet structure of the signals at 5.5 and 4.05 ppm (one and two protons, respectively) indicates the presence of an $OCH_2CH=$ fragment in the molecule.

In other words, during deprotonation of the intermediate cationoid particles the more sterically accessible proton leaves the system.

Observable correlations between the strucdure of the bromides subjected to the reaction and the resulting reaction products were also observed in the reaction of 3,4-dibromo-4-methyltetrahydropyran and its 2-isopropyl derivative with amines.



V a R=H; b R=i-C_3H_7; VI R=H; a R'=R''=C_2H_5; b R'=R''=C_4H_9; c R'+R''=$(CH_2)_5$; d R'+R''=$(CH_2CH_2)_2O$; VII R=i-C_3H_7, R'=R''=C_2H_5

The IR spectra of VIa-d (R = H) contain absorption at 1680 cm^{-1}, which is characteristic for a trisubstituted C=C bond. The following signals, in addition to the signals of NR'R'' groups, are observed in the PMR spectra of these systems: 1.70 (=CCH_3, m) and 3.9 ppm (2-CH_2, m). The hydrogen atoms in the 5 and 6 position give the spectral patterns that are characteristic for a spin system of the ABX type [3.40 (A), 4.00 (B), and 5.65 ppm (X); J_{AB} = 11.8, J_{AX} = 3.9, and J_{BX} = 2.3 Hz].

According to the GLC data, VII (R = iso-C_3H_7) contains two peaks. This is possibly associated with the existence of two isomeric forms relative to the position of the double bond in the ring (i.e., VI and VII). However, the possibility that this pattern is due to cis-trans isomerism of the substituents is not excluded. The PMR spectrum of this compound also indicates the existence of at least two isomeric structures. Unfortunately, the PMR spectrum recorded at 60 MHz proved to be extremely complex and did not enable us to make a choice between the possible structures.

EXPERIMENTAL

The PMR spectra of solutions of the compounds in CCl_4 were recorded with a Perkin Elmer R-12B spectrometer (60 MHz) with tetramethylsilane as the internal standard. The purity and identity of the synthesized substances were determined by GLC with an LKhM-8MD chromatograph equipped with a catharometer and a 2-m long column filled with 5% SE-30 cm Chromaton N-AW-HMDS; the carrier-gas (helium) flow rate was 40-60 ml/min, and the temperature ranged from 120 to 170°C. The isomeric di- and tetrahydropyrans were separated with a preparative chromatograph equipped with 3.3 m by 5 mm columns filled with 15% PEG-20M on Chromaton N-AW-HMDS; the carrier-gas (helium) flow rate was 80-90 ml/min, and the temperature ranged from 100 to 120°C.

Dibromo Derivatives of Tetrahydropyrans. A solution of 50 mmole of bromine in 15 ml of CCl_4 was added dropwise to an ice-cooled mixture of 50 mmole of the di- or tetrahydropyran derivative in 15 ml of CCl_4, after which the CCl_4 was removed by distillation, and the residue was distilled *in vacuo* to isolate the tetrahydropyran dibromides (Table 1).

Amino Derivatives of Dihydropyrans. A 150-mmole sample of the secondary amine was added to 50 mmole of the dibromo derivative of the di- or tetrahydropyran in 90 ml of benzene, and the mixture was refluxed for 20-24 h. It was then treated with hydrochlric acid, and the mixture was extracted with ether. The ether extract was worked up to give 5-12% (22-25% in the case of diethylamine) of the starting dibromide. The aqueous layer was made alkaline with potassium carbonate and extracted with ether, and the amine fraction was distilled *in vacuo* to give the amino derivatives of the dihydropyran, some physicochemical constants of which are presented in Table 2. The yields presented are based on the converted bromides.

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