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## STEREOCHEMISTRY OF THE IODOCYCLIZATION OF UNSATURATED

### ALCOHOLS

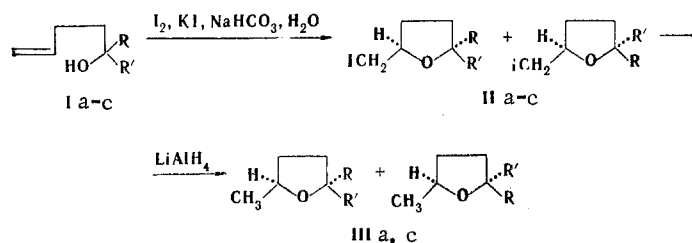
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The corresponding tetrahydrofuran derivatives were obtained by iodination of  $\delta,\epsilon$ -unsaturated alcohols containing substituents attached to the  $\alpha$ -carbon atom. The effect of substituents on the stereochemistry of the products and the rate of iodination of the unsaturated alcohols were studied.

Electrophilic heterocyclization of  $\delta,\epsilon$ -unsaturated alcohols is widely used for the synthesis of derivatives of tetrahydrofuran and tetrahydropyran [1, 2].

In a continuation of our research on electrophilic heterocyclization [3, 4] we have studied the effect of substituents attached to the  $\alpha$ -carbon atom of  $\delta,\epsilon$ -unsaturated alcohols on the rate of their iodination and the stereochemistry of the cyclization products.



I-III a R=H, R'=CH<sub>3</sub>; I-II b R=C<sub>2</sub>H<sub>5</sub>, R'=CH<sub>3</sub>; I-III c R=C<sub>6</sub>H<sub>5</sub>, R'=H

The cyclization of alcohol Ia may lead to derivatives of both tetrahydrofuran and tetrahydropyran. The PMR spectrum of the reaction product indicates the formation of only a five-membered heteroring. Two well-resolved doublets at 1.75 and 1.81 ppm (with an intensity ratio of 7:3) with J = 6 Hz, which are related to nonequivalent 2-CH<sub>3</sub> groups of cis- and trans-2-methyl-5-iodomethyltetrahydrofuran (IIa), are a characteristic feature of this spectrum.

Because of the development of chiral centers in the IIa molecule, the protons of the CH<sub>2</sub>I substituent turn out to be diastereotopic and form a complex multiplet (2H) centered at

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TABLE 1. Kinetic and Activation Parameters for the Iodocyclization of Unsaturated Alcohols Ia-c

R	R'	$k_{20}^{\circ}$ , liters/mole-sec	$E^{\ddagger}$ , kcal/mole	$-\Delta S^{\ddagger}$ , eu	$\lg A$
H	CH <sub>3</sub>	4,9±0,3	11,01±1,0	19,9±3,6	8,8
C <sub>2</sub> H <sub>5</sub>	CH <sub>3</sub>	13,5±1,0	10,5±1,3	19,6±3,6	8,9
C <sub>6</sub> H <sub>5</sub>	H	34,1±1,5	9,2±0,9	22,1±3,4	8,4

3.81 ppm. The two other methylene groups (3- and 4-CH<sub>2</sub>) absorb at 2.1-2.9 ppm. The protons of the CH-O groups give signals at 4.3-4.9 ppm.

In the case of IIb one can form a judgment regarding the ratio of the diastereomers from the intensities of the singlets of the 2-CH<sub>3</sub> groups at 1.45 and 1.50 ppm (45:55). Magnetic nonequivalence of the diastereotopic protons of the CH<sub>2</sub>I group (2H, 3.45 ppm) is manifested in this case also.

We were unable to separate the mixture of IIa diastereomers. We obtained a mixture of cis- and trans-2,5-dimethyltetrahydrofuran (IIIa) in a ratio of 1:2 (judging from the intensities of the doublets of the methyl groups [5] at 1.13 and 1.05 ppm) by reduction of this mixture with LiAlH<sub>4</sub> in absolute ether.

The product of iodination of Ic decomposes upon distillation in vacuo. For identification, it was reduced with LiAlH<sub>4</sub> to 2-methyl-5-phenyltetrahydrofuran (IIIc). On the basis of the ratio of the intensities of the doublets of the 2-CH<sub>3</sub> group in the PMR spectrum of IIIc at 1.41 and 1.48 ppm, the ratio of the cis and trans isomers is 64:36.

The yields of cis-tetrahydrofurans increase as the volume of substituent R in Ia-c increases. The preponderant formation of the cis isomer in the iodocyclization and chloromercuration [2] of Ic can be explained by the effect of vertical stabilization by the phenyl group of the transition state involved in ring formation [6]. To confirm this explanation we investigated the kinetics of the formation of Ia-c.

It follows from Table 1, in which the kinetic and activation parameters for the iodination of Ia-c are presented, that the rate of iodination increases as the volume of the substituents attached to the α-carbon atom increases. The maximum rate is observed in the case of the iodination of Ic. The activation energy and entropy of Ic do not contradict the expressed assumption regarding stabilization by the phenyl group of the transition state involved in ring formation.

Thus at least two factors, viz., the state of the conformational equilibrium in the starting alcohols and the electronic effects of stabilization of the transition state involved in ring formation, affect the rate of iodocyclization of unsaturated alcohols.

#### EXPERIMENTAL

The IR spectra were recorded with a UR-20 spectrometer. The PMR spectra of solutions of the compounds in CCl<sub>4</sub> were recorded with a BS-487C spectrometer (80 MHz) with tetramethylsilane as the internal standard.

Unsaturated alcohols Ia,c were obtained by reduction of the corresponding ketones with LiAlH<sub>4</sub> in absolute ether. The constants of the alcohols obtained were in agreement with the literature data [2]. The PMR spectra of Ia-c are presented in Table 2.

3-Methyl-5-hepten-3-ol (Ib). This compound was obtained in 54% yield by reaction of ethylmagnesium bromide with 1-hexen-5-one and had bp 34-35°C (2 mm),  $n_D^{20}$  1.4420, and  $d_4^{20}$  0.8469. IR spectrum: 1640 (C=C) and 3450 cm<sup>-1</sup> (OH). Found: C 74.5; H 12.3%; MR<sub>D</sub> 40.1. C<sub>8</sub>H<sub>16</sub>O. Calculated: C 74.9; H 12.6%; MR<sub>D</sub> 40.3.

The method used to iodinate alcohols Ia-c was similar to that employed for the iodocyclization of 4-penten-2-ol [1].

2-Methyl-5-iodomethyltetrahydrofuran (IIa). This compound was obtained in 92% yield and had bp 39-41°C (1 mm) and  $n_D^{20}$  1.5205. PMR spectrum: 4.4-4.9 (2H, m), 3.81 (2H, m), 1.9-2.1 (4H, m), and 1.75 and 1.81 ppm (3H, doublets). IR spectrum: 1085 cm<sup>-1</sup> (C-O-C). Found: I 56.1%. C<sub>6</sub>H<sub>11</sub>IO. Calculated: I 56.2%.

TABLE 2. Chemical Shifts in the PMR Spectra of Unsaturated Alcohols Ia-c

Compound	$\delta$ , ppm						
	R	2-R'	3-H	4-H	5-H	6-H	2-OH
1a	3,93	1,33	1,68	2,28	5,95	5,15	4,23
1b	CH <sub>2</sub> 1,65 CH <sub>3</sub> 1,10	1,38	1,65	2,28	5,95	5,15	2,88
1c	7,13	4,66	1,93	1,93	5,60	4,33	4,97

2-Methyl-2-ethyl-5-iodomethyltetrahydrofuran (IIb). This compound was obtained in 94% yield and had pb 45-47°C (1 mm),  $n_D^{20}$  1.5028, and  $d_4^{20}$  1.4149. PMR spectrum: 4.25 (1H, m), 3.45 (2H, m), and 1.45 and 1.50 ppm (3H, singlets). IR spectrum: 1090  $\text{cm}^{-1}$  (C-O-C). Found: I 49.1%;  $\text{MR}_D$  53.2.  $\text{C}_8\text{H}_{16}\text{IO}$ . Calculated: I 49.8%;  $\text{MR}_D$  53.6.

The reduction of iodomethyl derivatives IIa,c was carried out with  $\text{LiAlH}_4$  in absolute ether.

2,5-Dimethyltetrahydrofuran (IIIa) [5]. This compound was obtained in 65% yield and had bp 92-94°C.

2-Phenyl-5-methyltetrahydrofuran (IIIc) [2]. This compound was obtained by reduction of the product of iodination of Ic. PMR spectrum: 7.42 (5H, s), 4.17-5.30 (2H, m), 2.30 (4H, m), and 1.41 and 1.48 ppm (3H, doublets).

The kinetic measurements were made in a phosphate buffer (0.2 mole/liter) at pH 6.3-7.5 and unsaturated alcohol and iodine concentrations of  $(2.5-5.0) \cdot 10^{-3}$  mole/liter and potassium iodide concentrations of 0.1-1.0 mole/liter by the method in [1].

According to the experimental data obtained, the iodocyclization of Ia-c is described by the second-order kinetic equation

$$-d[\text{I}_2]/dt = k_2[\text{HC}] \cdot [\text{I}_2],$$

where [UA] is the analytical concentration of the unsaturated alcohol, and  $[\text{I}_2]$  is the concentration of molecular iodine.

The kinetic and activation data on the iodination of Ia-c are presented in Table 1.

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