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Dedicated to Professor Ionel Haiduc
on the occasion of his 65th birthday

SYNTHESIS AND STEREOCHEMISTRY OF SOME NEW 1,3-DIOXANE DERIVATIVES OF α, β-UNSATURATED ALDEHYDES

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ABSTRACT. The synthesis and the stereochemistry of some new 1,3-dioxane derivatives obtained from α, β-unsaturated aldehydes are discussed. The NMR investigations revealed anancomeric structures and the equatorial orientation of the unsaturated substituent at C^2.

INTRODUCTION

The stereochemistry of 1,3-dioxane derivatives was intensively studied.

The free conformational enthalpy *(A* value) of different groups located at positions 2 and 5 have been measured[1-5] (Table 1).

Table 1.

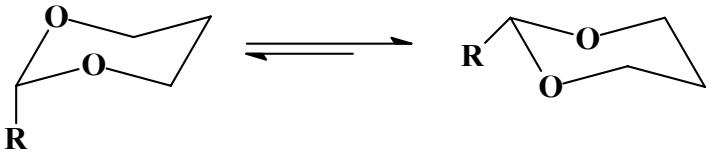
A values (kcal/mol) for alkyl groups located at positions 2 and 5 of the 1,3-dioxane ring

R	*A*
2-methyl	3.98-4.07
2-ethyl	4.04
2-i-propyl	4.17
2-phenyl	3.12
5-methyl	0.80-0.89

The highest *A* value for the methyl group bound to C^2 shows the capacity of methyl in this position to be a better "holding group" than the methyl located at C^5.

For 1,3-dioxane derivatives bearing alkyl or aryl groups at C^2, the characteristic conformational equilibrium is shifted toward the conformation exhibiting the substituent in equatorial orientation[6-12] (Scheme 2)

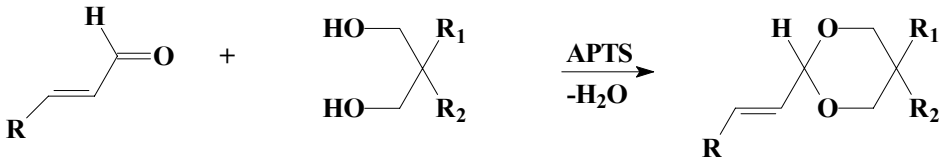
It has been considered of interest to study the stereochemistry of some new 1,3-dioxane derivatives obtained from α,β-unsaturated aldehydes and to determine the capacity of the unsaturated substituent at C^2 to be a "holding group" at this position.



Scheme 2

RESULTS AND DISCUSSIONS

New 1,3-dioxane derivatives have been obtained by the condensation reaction of *trans* α, β- unsaturated aldehydes with the appropiate 1,3-propanediols (Scheme 3).



$R = CH_3$	$R_1 = H$	$R_2 = CH_3$	**1**
$R = CH_3$	$R_1 = CH_3$	$R_2 = CH_3$	**2**
$R = C_6H_5$	$R_1 = H$	$R_2 = H$	**3**
$R = C_6H_5$	$R_1 = H$	$R_2 = CH_3$	**4**
$R = C_6H_5$	$R_1 = CH_3$	$R_2 = CH_3$	**5**
$R = C_6H_5$	$R_1 = COOC_2H_5$	$R_2 = COOC_2H_5$	**6**

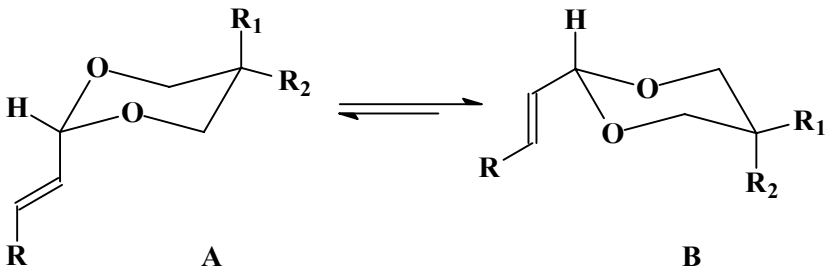
Scheme 3

Compounds **2, 3, 5** and **6** exist as unique diastereoisomer. For compounds **1** and **4** two diastereoisomers, *cis* and *trans*, are possible, depending on the relative position of R-CH=CH and R_2 groups located in positions 2 and 5 of the heterocycle (Scheme 4). For the *trans* isomer, the more stable conformer should be **B**, with both R and R_2 substituents in equatorial orientation (R_2 is of highest precedence).

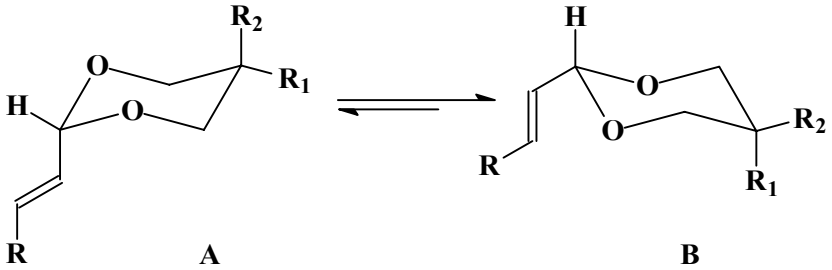
All the investigated compounds exhibit anancomeric structures.

For compounds displaying identical substituents in position 5 (**2, 3, 5** and **6**) the conformational equilibrium is shifted toward the conformer with the substituent at C^2 in equatorial orientation (Scheme 5).

The ^{1}H-NMR spectra of these compounds show different sets of signals for the axial and equatorial protons of the heterocycle and for the protons and carbon atoms of the similar groups located at C^5 (Table 2).

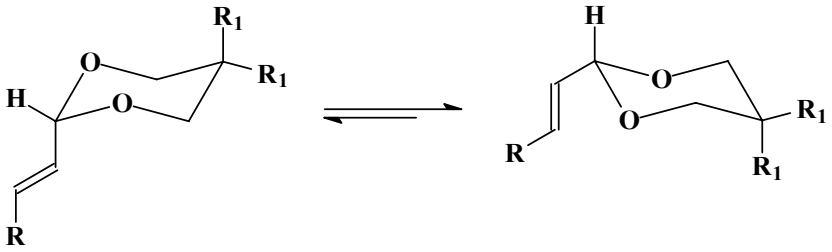


cis



trans

Scheme 4



Scheme 5

Table 2.

NMR data (δ, ppm) for the protons of positions 4, 5 and 6 of the 1,3-dioxane ring

Compound	Protons						
	4,6-eq.	4,6-ax.	Δδ	5-CH_3 eq.	5-CH_3 ax.	5-CH_2 eq.	5-CH_2 ax.
1	4.03	3.33	0.70	0.69	-	-	-
2	3.47	3.18	0.29	0.34	1.17	-	-
3	3.87	3.43	0.44	-	-	-	-
4	4.13	3.43	0.70	0.75	-	-	-
5	3.52	3.23	0.29	0.34	1.21	-	-
6	5.06	3.96	1.00	0.80	0.92	3.80	4.05

Compounds **1** and **4** were obtained as a mixture of two diastereoisomers, the *trans* one being the main product. For compound **4** the trans isomer was isolated and characterised.

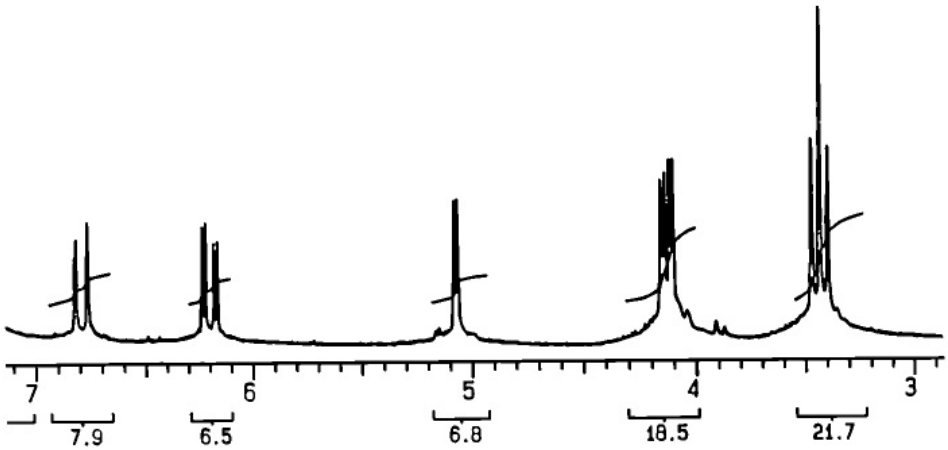


Figure 1

The ^{1}H-NMR spectrum of compound **4** (Figure1) displays different signals for the axial and equatorial protons at positions 4 and 6. The equatorial protons exhibit a doublet of doublet ($\delta_{4,6\text{-eq.}}$= 4.13 ppm, J = 11.5 Hz, J'= 4.6 Hz) due to a large geminal coupling and to a smaller coupling with the axial vicinal proton at position 5. The axial protons exhibit an overlapped doublet of doublet that gives a triplet ($\delta_{4,6\text{-ax.}}$= 3.43 ppm, J = J'= 11.5 Hz) The spectrum also exhibits a doublet for the axial proton located at C^2 ($\delta_{2\text{-ax.}}$= 5.07 ppm, J = 4.6 Hz), a doublet of doublet for the α-proton of the unsaturated substituent ($\delta_{CH\text{-}\alpha}$ = 6.20 ppm, J = 16.2 Hz, J'= 4.6 Hz) and a doublet for the β-proton ($\delta_{CH\text{-}\beta}$ = 6.79 ppm, J = 16.2 Hz).

The large values of the coupling constants involving the proton at position 5 demonstrate the axial orientation of this proton and the equatorial position of the methyl group at C^5. The values of the chemical shifts of the protons at position 2 and the missing of the characteristic long range coupling with the equatorial protons at positions 4 and 6 show the axial orientation of this proton.

CONCLUSIONS

The NMR investigations of compounds **1-6** bearing an unsaturated substituent at position 2 and one or two methyl groups at the position 5 of the 1,3-dioxanic ring revealed anancomeric structure. The unsaturated substituent located at position 2 prefers the equatorial position, being a good "holding group". In the compounds bearing two different substituents at C^5 (hydrogen and methyl), the methyl group also prefers the equatorial orientation.

EXPERIMENTAL

^{1}H- and ^{13}C-NMR spectra were recorded at room temperature, using $CDCl_3$ or C_6D_6 as solvent, in 5 mm tubes, on a Varian Gemini spectrometer, operating at 300 MHz for protons and at 75 MHz for carbon atoms. Melting points were measured with Electrothermal apparatus and are uncorrected.

New compounds **1-6**, general procedure

Stoechiometric amounts of 1,3-diol and carbonyl compound (0.05 mol) with catalytic amounts of *p*-toluenesulphonic acid (0.05 g) were solved in 100 ml benzene. The mixture were refluxed and the resulted water removed using a Dean-Stark trap. When 80% of the theoretical water was separated, after cooling at room temperature, the catalyst was neutralized (under stirring, 0.5 h) with sodium acetate powder in excess (0.1 g). The reaction mixture was washed twice with 50 ml water. The benzene was removed (after drying with sodium sulphate) and the 1,3-dioxanic compounds were purified by crystallisation or by vacuum distillation.

*5-methyl-2-(1-propenyl]-1,3-dioxane **1**.*
Liquid, b.p.= 50^{0}C (0.1 mm col. Hg). Yield 63.0 %. $C_8H_{14}O_2$, found C 67.39, H 10.02, required C 67.57, H 9.92
^{1}H RMN ($CDCl_3$, δ ppm) 0.69 (1H, d, J = 6.8 Hz, 5-CH_{3eq}), 1.69 (1H, dd, J = 6.6 Hz, J'=1.6 Hz, 2-CH=CH-C$\underline{H}_3$), 2.10 (1H, m, 5-ax), 3.33 (2H, overlapped dd, J = J'= 11.3 Hz, 4,6-H_{ax}), 4.03 (2H, dd, J = 11.3 Hz, J'= 4.6 Hz, 4,6-H_{eq}), 4.81 (1H, d, J = 5.2 Hz, 2-H_{ax}), 5.52 (1H, d, J = 5.2 Hz, J'=1.6 Hz, J''= 15.5 Hz, 2-C$\underline{H}$=CH-CH_3), 5.90 (1H, dq, J = 15.5 Hz, J'= 6.6 Hz, 2-CH=C$\underline{H}$-CH_3)

*5,5-dimethyl-2-(1-propenyl)-1,3-dioxane **2**.*
Liquid, b.p.= 55^{0}C (0.5 mm col.Hg). Yield=58.5 %. $C_9H_{17}O_2$, found C 69.11, H 10.19, required C 69.19, H 10.32
^{1}H RMN (C_6D_6, δ ppm) 0.34 (3H, s, 5-CH_{3eq}), 1.17 (3H, s, 5-CH_{3ax}), 1.50 (3H, ddd, J = .,4 Hz, J'= 1.6 Hz, J"=0.7 Hz, 2-CH=CH-C$\underline{H}_3$), 3.18 (2H, d, J = 11.5 Hz, 4,6-H_{ax}), 3.47 (2H, d, J = 11,5 Hz, 4,6-H_{eq}), 4.68 (1H, dd, J = 4.5 Hz, J'= 0.7 Hz, 2-H_{ax}), 5.78 (1H, m, 2-CH=C$\underline{H}$-CH_3), 5.94 (1H, dq, J = 6.4 Hz, J'= 15.6 Hz, 2-C$\underline{H}$=CH-CH_3), ^{13}C RMN (C_6D_6, δ ppm) 17.64 (2-CH=CH-$\underline{C}H_3$), 21.77 (5-CH_{3eq}), 23.16 (5-CH_{3ax}), 30.00 (C^5), 77.14($C^{4,6}$), 101.37 (C^2), 129.20 (2-$\underline{C}$H=CH-CH_3), 129.60 (2-CH=$\underline{C}$H-CH_3).

*2-[1-(2-phenyl)ethenyl]-1,3-dioxane **3**.*
Liquid, b.p.= 127 – 128^{0}C (0.5 mm col. Hg). Yield 57,0 %. $C_{12}H_{14}O_2$ found C 75.83, H 7.51, required C 75.76, H 7.42
^{1}H RMN (C_6D_6, δ ppm) 0.70 (1H, m, 5-H_{eq}), 1.83 (1H, tq, J $\approx$ J'= 12.5 Hz, J"= 7.6 Hz, 5-H_{ax}), 3.43 (2H, t, J = J =12.5 Hz, 4,6-H_{ax}), 3.87 (2H, dd, J = 12.5 Hz, J'=4.9 Hz, 4,6-H_{eq}), 4.99 (1H, d, J = 3,7 Hz, 2-H_{ax}), 6.38 (1H, dd, J = 2.5 Hz,

J'= 16.2 Hz, 2-C<u>H</u>=CH-C_6H_5), 6.88 (1H, d, J = 16.2 Hz, 2-CH=C<u>H</u>-C_6H_5), 7.0-7.30 (5H, m, aromatic protons) ^{13}C RMN (C_6D_6, δ ppm) 26.11 (C^5), 66.87 ($C^{4,6}$), 101.04(C^2), 127.12, 127.18, 128.10, 128.88, 132.78 (aromatic and vinylic carbon atoms), 136.84 (quaternary aromatic carbon atom).

5-methyl-2-[1-(2-phenyl)ethenyl]-1,3-dioxane ***4****.*
Liquid, b.p.= 140^{0}C (0.1 mm col. Hg). Yield 60.0 %. $C_{13}H_{16}O_2$, found C 76.32, H 7.98, required C 76.44, H 7.90
^{1}H RMN ($CDCl_3$, δ ppm) 0.75 (3H, d, J = 6.5 Hz, 5-CH_{3eq}), 2.18 (1H, m, 5-H_{ax}), 3.43 (2H, overlapped dd, J = J'= 11.5 Hz, 4,6-H_{ax}), 4.13 (2H, dd, J = 11.5 Hz, J'= 4.6 Hz, 4,6-H_{eq}), 6.79 (1H, d, J = 16.2 Hz, 2-CH=C<u>H</u>-C_6H_5), 7.20-7.50 (5H, m, aromatic protons), ^{13}C RMN ($CDCl_3$, δ ppm) 12.43 (5-CH_3), 29.40 (C^5), 73.37 ($C^{4,6}$), 100.47(C^2), 125.59 (2-CH=<u>C</u>H-C_6H_5), 133.40 2-<u>C</u>H=CH-C_6H_5), 126.87, 128.17, 128.56 (aromatic carbon atoms), 136.14 (1 quaternary aromatic carbon atom).

5,5-dimehyl-2-[1-(2-phenyl)etheny]-1,3-dioxane ***5***
Solid, m.p.= 55-56^{0}C. Yield 70,0%. $C_{14}H_{18}O_2$, found C 76.89 H 8.25, required C 77.03, H 8.31
^{1}H RMN (C_6D_6, δ ppm) 0.34 (3H, s, 5-CH_{3eq}), 1.21 (3H, s, 5-CH_{3ax}), 3.23 (2H, d, J = 11.1 Hz, 4,6-H_{ax}), 3.52 (2H, dd, J = 11.1 Hz, J'= 1.2 Hz, 4,6-H_{eq}), 4.93 (1H, dd, J = 1.2 Hz, J'= 4,2 Hz, 2-H_{ax}), 6.44 (1H, dd, J = 4.2 Hz, J'=17.2 Hz, 2-C<u>H</u>=CH-C_6H_5), 6.94 (1H, d, J = 17.2 Hz, 2-CH=C<u>H</u>-C_6H_5), 6.98-7.27 (5H, m, aromatic protons) ^{13}C RMN (C_6D_6, δ ppm) 21.75 (5-CH_{3eq}), 23.15 (5-CH_{3ax}), 30.10(C^5), 77.24 ($C^{4,6}$), 101.00 (C^2), 127.15 (2-CH=<u>C</u>H-C_6H_5), 132.98 (2-<u>C</u>H=CH-C_6H_5), 126.98, 128.18, 128.86 (tertiary aromatic carbons), 136.86 (quaternary aromatic carbon atom).

5,5-diethyloxycarbonyl-2-[1-(2-phenyl)ethenyl]-1,3-dioxane ***6***
Liquid, b.p.= 210-211^{0}C (0.5 mm col.Hg). Yield = 61,0%. $C_{18}H_{22}O_6$, found C 64.57, H 6.69, required C 64.66, H 6.63
^{1}H RMN (C_6D_6, δ ppm) 0.80 (3H, t, J = 7.1 Hz, 5-$COOCH_2C\underline{H}_{3eq}$), 0.92 (3H, t, J = 7.1 Hz, 5-$COOCH_2C\underline{H}_{3ax}$), 3.80 (2H, q, J =7.1 Hz, 5-$COOC\underline{H}_2CH_{3eq}$), 3.96 (2H, d, J = 11.5 Hz, 4,6-H_{ax}), 4.05 (2H, q, J = 7.1 Hz, 5-$COOC\underline{H}_2CH_{3ax}$), 4.93 (1H, dd, J = 1.2 Hz, J'= 4.5 Hz, 2-H_{ax}), 5.06 (2H, d, J = 11.5 Hz, 4,6-H_{eq}), 6.27 (1H, dd, J = 4.5 Hz, J'= 16.2 Hz, 2-C<u>H</u>=CH-C_6H_5), 6.80 (1H, d, J = 16.2 Hz, 2-CH=C<u>H</u>-C_6H_5), 7.00-7.30 (5H, m, aromatic protons) ^{13}C RMN (C_6D_6, δ ppm) 13.86 (5-$COOCH_2\underline{C}H_{3eq}$), 14.00 (5-$COOCH_2\underline{C}H_{3ax}$), 53.78 ($C^5$), 61.79 (5-$COO\underline{C}H_2CH_{3eq}$), 62.00 (5-$COO\underline{C}H_2CH_{3ax}$), 69.64 ($C^{4,6}$), 101.33 ($C^2$), 125.81 (2-<u>C</u>H=CH-C_6H_5), 133.79 (2-CH=<u>C</u>H-C_6H_5), 127.19, 128.39, 128.83 (tertiary aromatic carbon atoms), 136.46 (quaternary aromatic carbon atom), 167.11 (5-<u>C</u>$OOCH_2CH_{3eq}$), 167.91 (5-<u>C</u>$OOCH_2CH_{3ax}$).

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