SYNTHESIS AND STEREOCHEMISTRY OF SOME NEW DERIVATIVES OF 1,5-DIOXASPIRO[5.5]UNDECANE

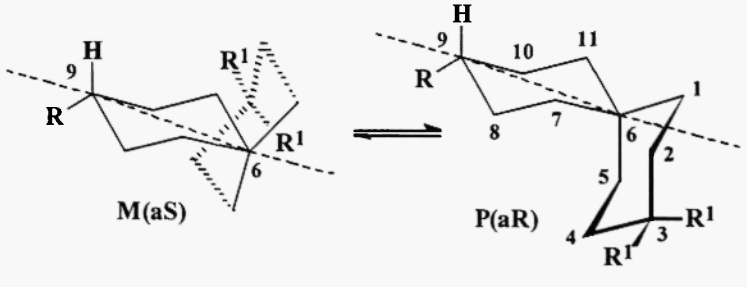
Ion Grosu[a]*, Gerard Plé[b], Clementina Mesaros[a] and Sorin Mager[a]

[a]"Babes-Bolyai" University, Organic Chemistry Department, 11 Arany Janos str., RO-3400 Cluj-Napoca, Romania
[b]Universite de Rouen et IRCOF, Laboratoire associé au CNRS DO-464, Faculté des Sciences de Rouen, 76821 Mont Saint-Aignan, Cedex, France

Abstract: The stereoisomerism of some spiro-1,3-dioxanes obtained from substituted cyclohexanones and 2-methyl-2-ethyl-1,3-propanediol is discussed on the basis of the helical chirality of the 1,5-dioxaspiro[5.5]undecane skeleton and of the data of conformational analysis. The influence of the flexibility of the rings on the representative number of isomers and on their NMR spectra is commented. The isomers (diastereomers and enantiomers) of some peculiar compounds were separated by gas chromatography using chiral columns.

INTRODUCTION

In previous papers (1-5) the stereochemistry of some saturated heterocyclic spiro compounds with six membered rings have been investigated using Dreiding models and NMR experiments. The helical disposition of the cycles in a polyspiro skeleton with six-membered rings has been revealed. The helix exhibiting P or M configuration can turn identical with itself after each fourth six-membered ring. The axial chirality of spiro compounds with six-membered rings is also different to the usual case of allenes or spiro compounds with planar rings. This type of spiranes exhibits axial chirality even if the different substitution is made only at one of the extremities of the spiro skeleton. The axis C^6-C^9 (Scheme 1) is a chiral element despite the identical substituents located in the position 3. The reference groups are H and R at C^9 and the whole identically substituted ring (that can be in front or behind the axis) at C^6. The flipping of the symmetrically substituted ring results into an enantiomeric inversion (this spiro compound exhibits helical chirality too, the helix begins to be built and in the process both chiral elements change their configurations).



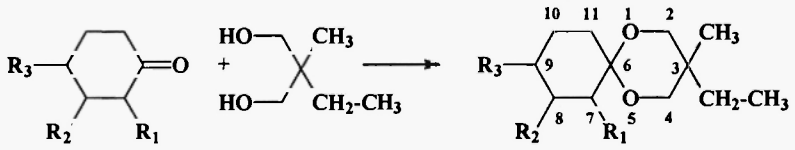
Scheme 1

On the other hand the data of conformational analysis show small values for the conformational free enthalpies of the substituents located in the position 5 of the 1,3-dioxane (6). These values for the methyl and ethyl groups (6-8) are close and unexpectedly the conformational free enthalpy of the ethyl group is somewhat smaller than that measured for the methyl group. As a consequence in anancomeric 5-ethyl,5-methyl-1,3-dioxanes (bearing a "holding group" in the positions 2 or 4) the methyl group prefers the equatorial orientation. The difference between the conformational free enthalpies of these two groups (Me and Et) is too small to induce the anancomericity of the 1,3-dioxane ring and the derivatives of 5-ethyl-5-methyl-1,3-dioxane displaying identical substituents in the other positions of the heterocycle (2 or 4) show flipping structures.

It was considered of interest to develop studies on the stereochemistry of some peculiar spiro 1,3-dioxanes that are bearing in the aliphatic part of the heterocycle two different substituents (Me and Et) without inducing the anancomericity of the ring.

RESULTS AND DISCUSSION

New spiro-1,3-dioxanes have been obtained by the acetalization reaction of some substituted cyclohexanones with 2-ethyl-2-methyl-1,3-propanediol (Scheme 2).



R_1=R_2=R_3=H **1**

R_1=R_2=H, R_3=CH_3 **2**

R_1=R_2=H, R_3=t-C_4H_9 **3**

R_1=R_3=H, R_2=CH_3 **4**

R_2=R_3=H, R_1=CH_3 **5**

Scheme 2

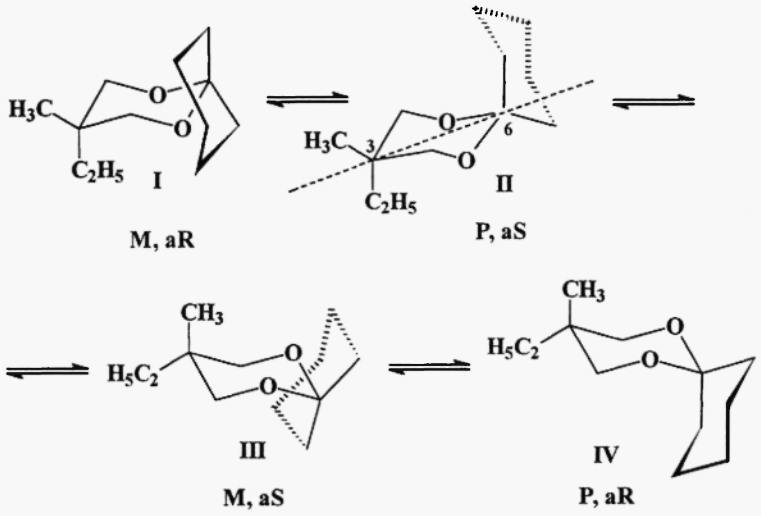
Compound **1** exhibits a flexible structure, both cyclohexane and 1,3-dioxane rings are flipping (Scheme 3). The difference between the conformational free enthalpies of the two substituents of the heterocycle is too small to induce the anancomericity of this ring.

Compound **1** shows at the same time helical and axial chirality. The axis C_3-C_6 is a chiral element, the reference groups being Me, Et at C_3 and the whole cyclohexane ring (that can be in face or behind the axis of chirality) at C_6. Four stereoisomers, within two diastereomers (D_1: structures I, II and D_2: structures III and IV) are possible. The flipping of the cyclohexane ring results into an enantiomeric inversion, whereas the flipping of the heterocycle equilibrates the two diastereomers.

The flexibility of the molecules determines the recording in the NMR spectra of only one set of signals. The chemical shifts reflect the average of the magnetic environments of the protons (or carbon atoms) in the four possible structures (I-IV). The positions 2 and 4 are rendered equivalent by the flipping of the rings, but the geminal protons are diastereotopic (despite of the flipping of the rings, the mean magnetic environments for the proR and proS protons of these positions are different). The ^{1}H-NMR spectrum of compound **1** exhibits for the protons of the heterocycle an AB

system with a large coupling constant and close values of the chemical shifts (δ=3.39, δ =3.32 ppm, J=11.2 Hz, Figure 1a, Table 1).

The ^{13}C NMR spectrum exhibits only one signal (δ=67.97 ppm) for the carbon atoms C^2 and C^4 proving the equivalence of these two positions as a result of the flipping of the spiro skeleton.



Scheme 3

Table1. NMR data (δ, ppm) for compounds **1-5**.

Compound	Position of protons					Position of carbon atoms	
	2	4	3-CH_3	3-CH_2-CH_3	3-CH_2-CH_3*	2	4
1	3.32, 3.39		0.72	0.67	1.25	67.97	
2	3.38, 3.45	3.28, 3.37	0.72	0 67	1.264, 1.267	68.22	67.98
3	3.41, 3.47	3.29, 3.37	0.73	0.68	1.28	68.31	68.02
4**	3.401, 3.467	3.27, 3.34	0.706	0.672	1.207, 1.216	68.11	68.01
	3.408, 3.474	3.30, 3.36	0.757	0.682	1.292, 1.298		
5**	3.27(eq), 3.53(ax)	3.24(eq), 3.35(ax)	0.37(eq)	0.76(ax)	1.63(ax)	68.23	67.20
	3.37(eq), 3.48(ax)	3.34(eq), 3.35(ax)	1.07(ax)	0.56(eq)	0.83(eq)	68.40	67.35

* The diastereotopicity of the protons belonging to the methylene group of the substituent 3-CH(H')-CH_3 is observed for compounds **2** and **4**

** The spectrum shows signals for two independent diastereoisomers; but a correlation for all the signals is not possible.

Compounds **2** and **3** display semiflexible structures, the cyclohexane ring being anancomeric (the substituents of position 9 are "holding groups"), whereas the 1,3-dioxane ring is flipping. The flexibility of the heterocycle induces a diastereomeric equilibration (V ⇌ VI; VII ⇌ VIII, Scheme 4).

Compounds **2** and **3** show three chiral elements: the axes C_3-C_6 (a_1) , C_6-C_9 (a_2) and the helix. Four of the possible (eight) isomers display the substituent of position 9 in equatorial orientation (Scheme 4). The flipping of the 1,3-

dioxane ring does not change the configurations of all the chiral elements, so in the process one diastereomer is passed into the other one. For changing one enantiomer into the other one the whole spiro skeleton has to be rebuilt.

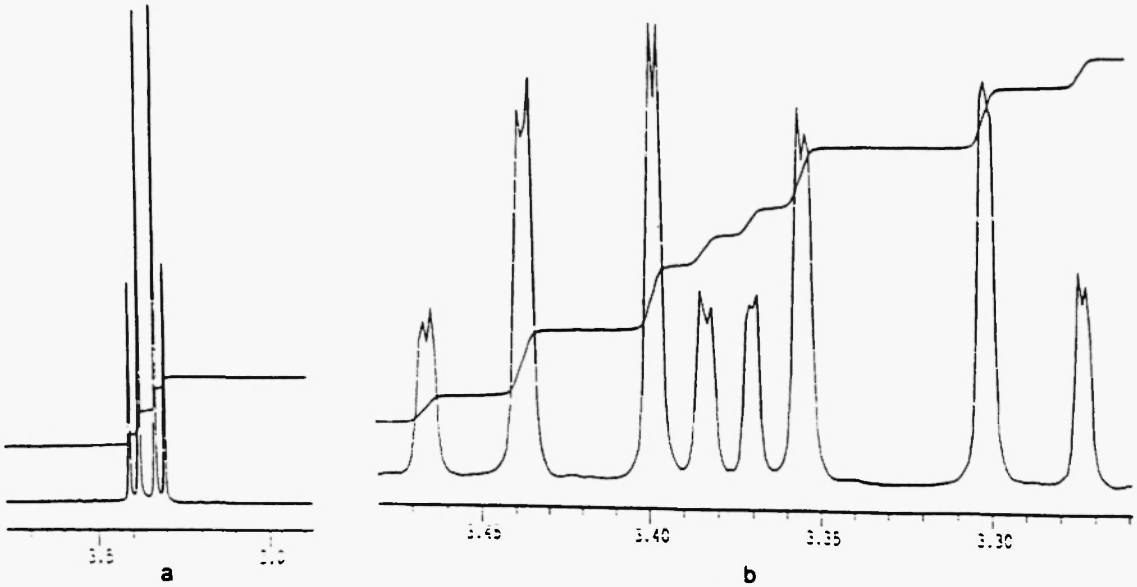
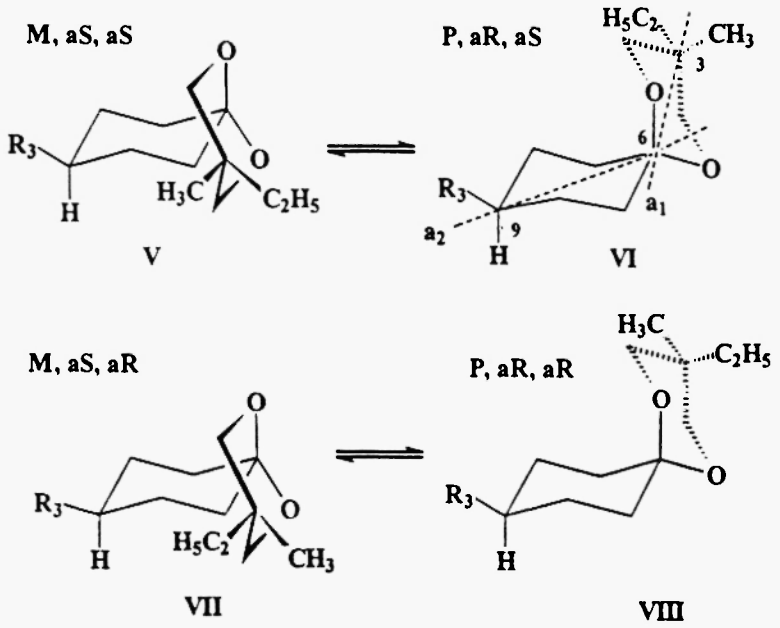


Figure 1. NMR spectra (fragments) of compounds **1** (a) and **2** (b)



R_3=CH_3 (**2**); R_3=*t*-C_4H_9 (**3**)

Scheme 4

The ^{1}H NMR spectra (Table 1) of compounds **2** and **3** are more complex showing different signal for the equatorial and axial protons of the cyclohexane ring and for the protons of the positions 2 and 4 of the heterocycle (these positions are rendered diastereotopic by the chirality of the molecule). As an example the ^{1}H NMR spectrum of compound

2 (Figure 1b) exhibits for the protons of positions 2 and 4 two well resolved AB systems (δ_2=3.45, δ_2'-3.38 and δ_4=3.37, δ_4'=3.28 ppm) corresponding to the diastereotopic positions 2 and 4 and to the diastereotopic (proR and proS) protons of each of these positions. The further splitting of the signals is due to the long range coupling (^{4}J=0.9 Hz) between the protons of the diastereotopic positions 2 and 4. Despite the recording of four signals for the protons of the positions 2 and 4 these ones do not correspond to the axial or equatorial positions, the average magnetic environments (structures I-IV), as a consequence of the chirality of the molecule are all different. The diastereotopicity of the positions 2 and 4 has been also observed in the ^{13}C NMR spectrum of this compound, two signals (δ_2=68.22 and δ_4=67.98 ppm) for the carbon atoms of these positions being recorded. The values of the diastereotopicities for the protons ($\Delta\delta_{2\text{-}4}$=0.06-0.09 ppm) and for the carbon atoms ($\Delta\delta_{2\text{-}4}$=0.24-0.29 ppm) of the positions 2 and 4 are close to the values reported for other chiral 1,3-dioxane compounds (1-3,5,9-11).

Compound **4** displays a semiflexible structure with an anancomeric carbocycle and a flipping heterocycle. The compound shows three chiral elements: a chiral carbon atom (C^8), a chiral axis (C_3-C_6) and the helicity of the spiro skeleton. Eight stereoisomers (Table 2), within four diastereomers (D_1: IX, XVI; D_2: X, XV; D_3: XI, XIV and D_4: XII, XIII) are possible

Table 2. The possible stereoisomers of compound **4** in correlation with the configurations of its chiral elements.

Chiral carbon atom	Axis C^3-C^6	Helix	Isomer
R	aR	P	IX
R	aR	M	X
R	aS	P	XI
R	aS	M	XII
S	aR	P	XIII
S	aR	M	XIV
S	aS	P	XV
S	aS	M	XVI

The flipping of the heterocycle equilibrates diastereomers $D_1 \rightleftharpoons D_4$ and $D_2 \rightleftharpoons D_3$ (IX $\rightleftharpoons$ XII, X $\rightleftharpoons$ XI, XIII $\rightleftharpoons$ XVI, XIV $\rightleftharpoons$ XV, Scheme 5 shows only the equilibria involving the spirane resulted by the acetalization of the R configured ketone). The compound exhibits at room temperature only two independent diastereomers noted arbitrarily with A (D_1, D_4) and B (D_2, D_3). This result was deduced from the NMR and gas-chromatographic investigations of the compound. The chromatogram (Figure 2a) obtained using a chiral column, exhibits three peaks, one of them corresponding to overlapped signals. The peaks belonging to the enantiomers of each independent diastereomer were very well separated R_F(A)=69.17, R_F(A)'=69.70 and R_F(B)=69.70, R_F(B)'=70.53 min., whereas the two peaks belonging to the different diastereomers are overlapped [R_F(A)'=R_F(B)=69.70]. The two diastereomers are obtained in a ratio (A, B) close to equimolecular (48.5 and 51.5 %).

In the ^{1}H NMR spectrum two sets of signals belonging to the two independent diastereisomers of the compound have been recovered (Table 1). The signals of the two isomers exhibit close values of the chemical shifts in agreement with the small structural differences between these diastereoisomers (e.g. for the methyl group located in the position 3 two singlets δ=0.70 and δ'=0.75 ppm). The protons of the 1,3-dioxane ring show two doublets of doublets for each

diastereomer. These signals correspond to the proR and proS protons of the diastereotopic positions (of the spiro skeleton) 2 and 4.

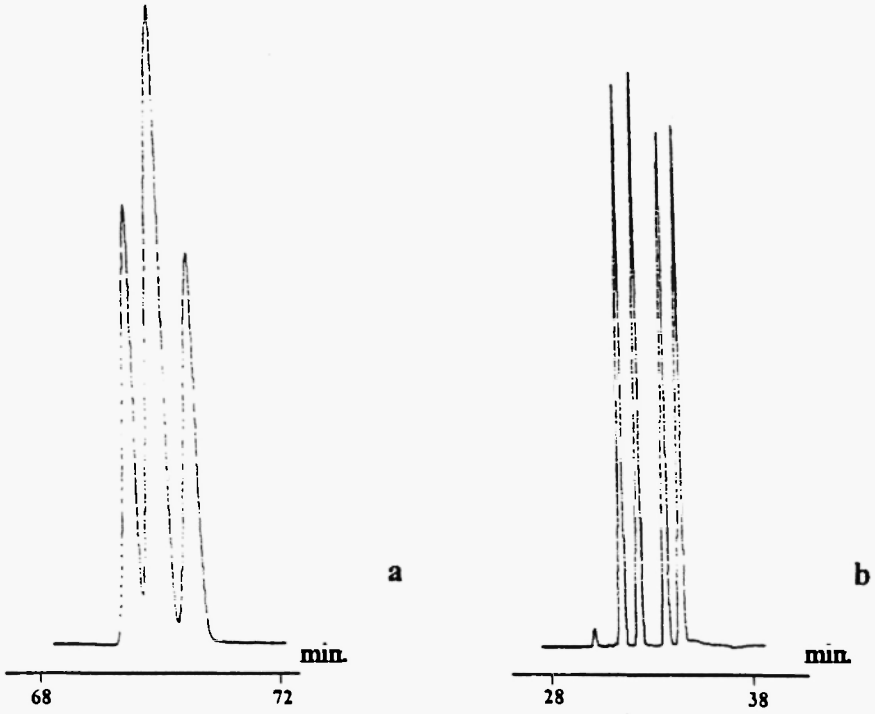
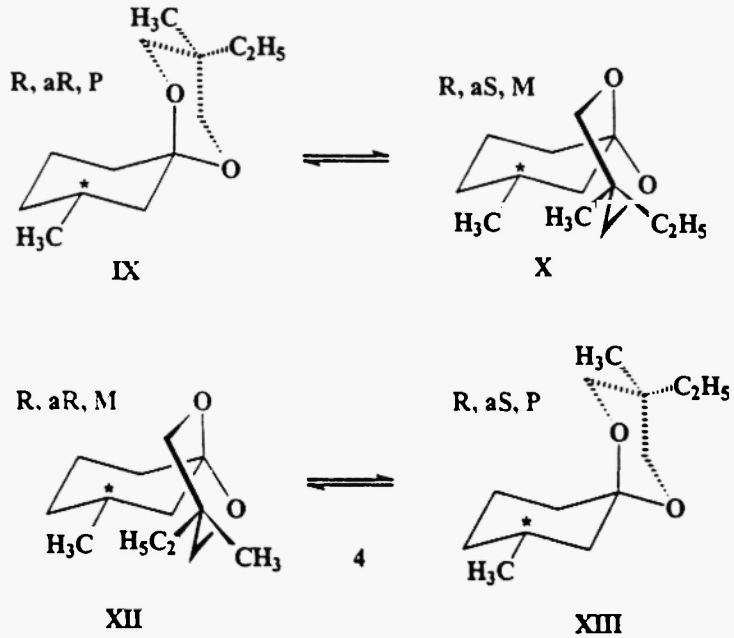


Figure 2. The chromatograms of compounds 4 (a) and 5 (b).



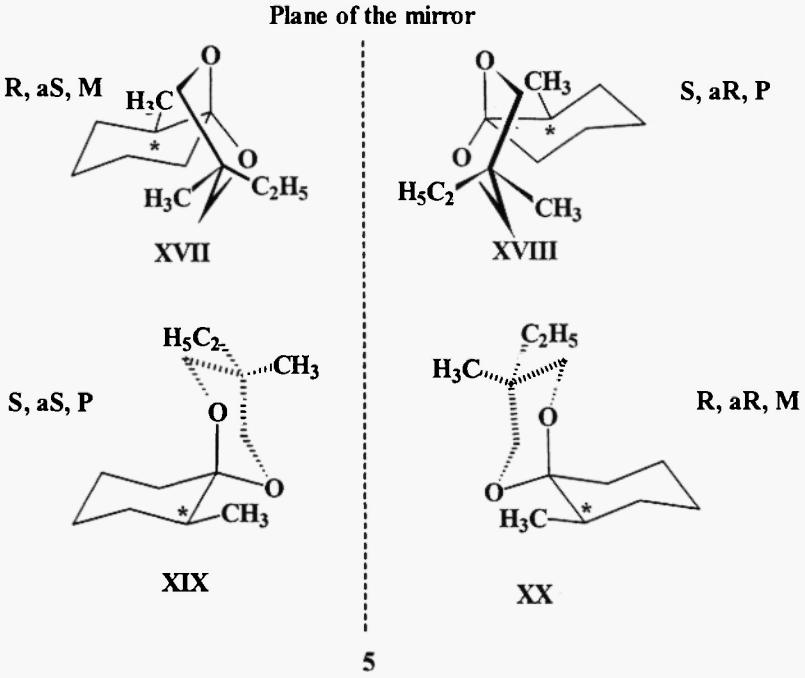
Scheme 5

The diastereotopicity of the positions 2 and 4 leads to the recording in the ^{13}C NMR spectrum of two different signals (for each diastereomer) for the carbon atoms of these positions (Table 1).

Compound **5** exhibits a different stereochemistry than the previously investigated compounds. Both cyclohexane and 1,3-dioxane rings are anancomeric. The conformational equilibria for the flipping of the heterocycle are shifted towards the structures displaying M, R and P, S configurations for the helix (the spiro skeleton) and of the chiral carbon atom (C^7). The configuration of the chiral carbon atom induces a specific configuration of the spiro skeleton (R→M and S→P) that corresponds to a disposition of the heterocycle on the opposite side with the methyl group located on the chiral carbon atom. Theoretically, in correlation with the three chiral elements of the molecule (chiral carbon atom, axis of chirality and the helicity) eight stereoisomers are possible (as for compound **4**, Table 2), but as a consequence of the conformational behaviour (starting from racemic 2-methylcyclohexanone) only four representative isomers are obtained (Table 3, Scheme 6). These isomers are two diastereomers noted arbitrarily with D_1 (XVIII, XIX). and D_2 (XVII, XX). Each of these diastereoisomers is a pair of enantiomers. One of these isomers exhibits the ethyl group in equatorial position (D_2), whereas the other one shows an equatorial methyl group (D_1).

Table 3. The possible stereoisomers of compound **5** in correlation with the configurations of its chiral elements.

Chiral carbon atom	Axis C^3-C^6	Helix	Isomer
R	aR	M	XVII
R	aS	M	XVIII
S	aR	P	XIX
S	aS	P	XX



5

Scheme 6

These results have been obtained by the NMR and gas chromatographic investigations of the compound. The chromatogram (Figure 2b) obtained on a chiral column showed very well separated peaks for each diastereoisomer as

well as for the enantiomers of these ones [$R_F(D_1)$=31.97, $R_F(D_1)'$=32.62 and $R_F(D_2)$=33.61, $R_F(D_2)'$=34.20 min.]. The ratio of the two diastereomers is 52.3% D_1 and 47.7 % D_2, in agreement with the small differences between the conformational free enthalpies of the methyl and ethyl groups located in position 5 of the 1,3-dioxane ring shows the higher preference of the methyl group (as of the ethyl one) for the equatorial orientation.

The ^1H NMR spectrum of compound **5** (mixture of two diastereomers) is different to the spectra of the other investigated compounds. The differences among the chemical shifts of the protons of the heterocycle are higher in agreement with the axial or equatorial orientations of these ones. Significant differences are observed for the protons of the groups located in the position 3 of the spirane. In one diastereoisomer the methyl group is equatorial (δeq=0.37 ppm) whereas in the other one it is axial giving a more deshielded signal (δax=1.07 ppm). High differences have been recorded between the signals of the protons of the ethyl group belonging to the two diastereomers that group being axial in the major one [$\delta(CH_2)$=1.63 and $\delta(CH_3)$=0.76 ppm] and equatorial in the minor one [$\delta(CH_2)$=0.83 and $\delta(CH_3)$=0.56].
The axial or equatorial positions of the methyl and ethyl groups in the two diastereomers of compound 5 leads to the recording of higher differences between the chemical shifts of the carbon atoms of these groups in the two diastereomers too (Table 1)

CONCLUSIONS

The stereochemistry of the derivatives of 3-ethyl-3-methyl-1,5-dioxaspiro[5.5]undecane is correlated with the position of the substituent of the carbocycle. If this substituent is in the other extremity of the spiro skeleton (position 9) the compound exhibits semiflexible structure and is represented by only one independent diastereoisomer, while if the substituent is located in the position 8 or 7 the compound shows two independent diastereomers, in the first case both with semiflexible structure (substituent at C^8) and in the second case (substituent at C^7) both anancomeric. The stereoisomerism of the compounds was discussed considering the helicity and the axial chirality of the spiro skelata.

EXPERIMENTAL

^1H-and ^{13}C-NMR spectra were recorded at room temperature, using C_6D_6 as solvent, in 5 mm tubes, on a Bruker AM 400 Fourier transform NMR spectrometer, equipped with a dual ^{13}C-^1H head, operating at 400 MHz for protons and 100 MHz for carbon atoms. The gas-chromatographic separations were performed on a Kontron Instruments apparatus on a silica capillary chiral column of 15m (Supelco β-Dex-120) filled up with a film of β-cyclodextrine, using a temperature program from 60 to 140°C with a temperature gradient of 2°/min and a gas-vector of He (0.7 bar).
M.ps were measured with Electrothermal melting point apparatus and are uncorrected.

*Compounds **1-5**, general procedure.* - Equimolecular amounts of 1,3-diol and carbonyl compound (0.1 mol) with catalytic amounts of p-toluenesulphonic acid (0.1 g) were solved in 200 ml benzene. The mixture was refluxed and the water resulted in the reaction was 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 CH_3-COONa powder in excess (0.2 g). The reaction mixture was washed twice with 100 ml water. After drying (with Na_2SO_4) the benzene was removed and the spiro-1,3-dioxane compounds were purified by vacuo distillation (1 mmcol.Hg) or by crystallization from ethanol.

3-Ethyl-3-methyl-1,5-dioxaspiro[5.5]undecane 1. Liquid, b.p.=100-101 °C (1mm col.Hg). Yield 50%. Anal. Calcd for $C_{12}H_{22}O_2$: C, 72.68, H, 11.18. Found: C, 72.82, H, 11.30. ^{1}H NMR δ (C_6D_6) 0.67(3H, t, J=7.7 Hz, 3-CH_2-CH_3), 0.72(3H, s, 3-CH_3), 1.25(2H, q, J=7.7 Hz, 3-CH_2-CH_3), 1.30(2H, m, 9-H), 1.49-1.55(4H, overlapped peaks, 8-H, 10-H), 1.74-1.79(4H, overlapped peaks, 7-H, 11-H), 3.32(2H, d, J=11.2 Hz, 2-H, 4-H) and 3.39 ppm (2H, d, J=11.2 Hz, 2-H, 4-H). ^{13}C NMR δ (C_6D_6) 7.23(3-CH_2-CH_3), 18.86(3-CH_3), 22.66(3-CH_2-CH_3), 25.90(C^9), 27.80($C^{8,10}$), 32.42(C^3), 32.50(C^7), 32.98(C^{11}), 67.97($C^{2,4}$) and 97.47 ppm (C^6).

3-Ethyl-3,9-dimethyl-1,5-dioxaspiro[5.5]undecane 2. Liquid, b.p.=100-101 °C (1mm col.Hg). Yield 50%. Anal. Calcd for $C_{13}H_{24}O_2$: C, 73.54, H, 11.39. Found: C, 73.73, H, 11.51. ^{1}H NMR δ (C_6D_6) 0.67(3H, t, J=7.5 Hz, 3-CH_2-CH_3), 0.72(3H, s, 3-CH_3), 0.87(3H, d, J=7.0 Hz, 9-CH_3), 1.264(1H, q, J=7.5 Hz, 3-CH(H)-CH_3), 1.267(1H, q, J=7.5 Hz, 3-CH(H)-CH_3), 1.30-1.49(5H, overlapped peaks, 8-H, 9-H, 10-H), 2.20-2.31(4H, overlapped peaks, 7-H, 11-H), 3.28(1H, dd, J=11.2, J'=0.7 Hz, 4-H), 3.37(1H, dd, J=11.2, J'=0.7 Hz, 4-H), 3.38(1H, dd, J=11.2, J'=0.7 Hz, 2-H) and 3.45 ppm (1H, dd, J=11.2, J'=0.7 Hz, 2-H). ^{13}C NMR δ (C_6D_6) 7.25(3-CH_2-CH_3), 18.86(3-CH_3), 21.67(9-CH_3), 27.79(3-CH_2-CH_3), 30.96($C^{8,10}$), 30.96(C^3), 31.93(C^7), 32.06(C^9), 32.47(C^{11}), 67.98(C^4), 68.22(C^2) and 97.49 ppm (C^6).

9-*t*-Butyl-3-Ethyl-3-methyl-1,5-dioxaspiro[5.5]undecane 3. Liquid, b.p.=100-101 °C (1mm col.Hg). Yield 50%. Anal. Calcd for $C_{16}H_{30}O_2$: C, 75.54, H, 11.89. Found: C, 75.41, H, 11.76. ^{1}H NMR δ (C_6D_6) 0.68(3H, t, J=7.6 Hz, 3-CH_2-CH_3), 0.73(3H, s, 3-CH_3), 0.84[9H, s, 9-C(CH_3)$_3$], 0.95(1H, m, 9-H), 1.28(2H, q, J=7.6 Hz, 3-CH_2-CH_3), 1.30-1.60(4H, overlapped peaks, 8-H, 10-H), 1.80-1.94(4H, overlapped peaks, 7-H, 11-H), 3.29(1H, d, J=11.3 Hz, 4-H), 3.37(1H, d, J=11.3 Hz, 4-H), 3.41(1H, d, J=11.3 Hz, 2-H) and 3.47 ppm (1H, d, J=11.3 Hz, 2-H). ^{13}C NMR δ (C_6D_6) 7.27(3-CH_2-CH_3), 18.86(3-CH_3), 23.42($C^{8\,10}$), 27.50[9-C(CH_3)$_3$], 27.78(3-CH_2-CH_3), 29.50(C^3), 32.03[9-C(CH_3)$_3$], 32.52(C^7), 33.12(C^{11}), 47.74(C^9), 68.02(C^4), 68.31(C^2) and 97.44 ppm (C^6).

3-Ethyl-3,8-dimethyl-1,5-dioxaspiro[5.5]undecane 4. Liquid, b.p.=100-101 °C (1mm col.Hg). Yield 50%. Anal. Calcd for $C_{13}H_{24}O_2$: C, 73.54, H, 11.39. Found: C, 73.69, H, 11.47. ^{1}H NMR δ (C_6D_6), mixture of two diastereoisomers: 0.672, 0.687(3H, t, J=7.5 Hz, 3-CH_2-CH_3), 0.706, 0.757(3H, s, 3-CH_3), 0.848, 0.854(3H, d, J=6.6 Hz, 8-CH_3), 1.009, 1.022[1H, t (overlapped dd), J=J'=12.6 Hz, 7-H_{ax}], 1.207, 1.216(1H, q, J=7.5 Hz, 3-CH(H)-CH_3), 1.292, 1.298(1H, q, J=7.5 Hz, 3-CH(H)-CH_3), 1.30(1H, overlapped peaks, 11-H_{ax}), 1.43-1.62(5H, overlapped peaks, 9-H_{ax},9-H_{eq}, 10-H_{ax}), 1.78(1H, overlapped peaks, 8-H_{ax}), 2.21-2.36(2H, overlapped peaks, 7-H_{eq}, 11-H_{eq}), 3.276, 3.303(1H, dd, J=11.2, J'=0.5 Hz, 4-H), 3.347, 3.361(1H, dd, J=11.2, J'=0.5 Hz, 4-H), 3.401, 3.408(1H, dd, J=11.2, J'=0.5 Hz, 2-H) and 3.467, 3.474 ppm (2H, dd, J=11.2, J'–0.5 Hz, 2-H). ^{13}C NMR δ (C_6D_6) 7.21, 7.27(3-CH_2-CH_3), 18.83, 18.91(3-CH_3), 22.16(8-CH_3), 22.22(C^9), 27.74, 27.88(3-CH_2-CH_3), 28.88(C^8), 31.68, 32.17($C^{8,10}$), 32.45(C^3), 34.63(C^7), 41.22, 41.70(C^{11}), 68.01(C^4), 68.11(C^2) and 98.02 ppm (C^6).

3-Ethyl-3,7-dimethyl-1,5-dioxaspiro[5.5]undecane 2. Liquid, b.p.=100-101 °C (1mm col.Hg). Yield 50%. Anal. Calcd for $C_{13}H_{24}O_2$: C, 73.54, H, 11.39. Found: C, 73.40, H, 11.54. ^{1}H NMR δ (C_6D_6) 0.37[3H, s, 3-CH_3(eq)]*, 0.56[3H, t, J=7.4 Hz, 3-CH_2-CH_3(eq)]**, 0.76[3H, t, J=7.4 Hz, 3-CH_2-CH_3(ax)]*, 0.83[2H, q, J=7.4 Hz, 3-CH_2-CH_3(eq)]**, 1.07[3H, s, 3-CH_3(ax)]**, 1.23, 1.27(3H, d, J=6.7 Hz, 7-CH_3), 1.63[2H, q, J=7.4 Hz, 3-CH_2-CH_3(ax)]*, 1.11-1.79(7H, overlapped peaks, 7-H_{ax}, 8-H_{ax+eq}, 9-H_{ax+eq}, 10-H_{ax}, 11-H_{ax}), 2.32-2.43(2H, overlapped peaks, 7-H_{eq}, 11-H_{eq}), 3.24, 3.34(1H, dd, J=11.5, J'=2.0 Hz, 4-H_{eq}), 3.29, 3.35(1H, d, J=11.5, Hz, 4-H_{ax}), 3.27, 3.37(1H, dd, J=11.5, J'=2.0 Hz, 2-H_{eq}) and 3.48, 3.53 ppm (1H, d, J=11.5, Hz, 2-H_{ax}). ^{13}C NMR δ (C_6D_6) 6.69[3-CH_2-CH_3(eq)]**, 7.62[3-CH_2-CH_3(ax)]*, 14.06(7-CH_3), 18.22[3-CH_3(eq)]*,

19.41[3-CH_3(ax)]**, 22.78(C^9), 24.98(C^{10}), 26.80[3-CH_2-CH_3(eq)]**, 27.30[3-CH_2-CH_3(ax)]*, 28.63(C^8), 30.85(C^{11}), 32.09, 32.14(C^3), 40.14(C^7), 67.20, 67.35(C^4), 68.23, 68.40(C^2) and 98.48, 98.66 ppm (C^6).

* and ** signals identified to belong to diastereoisomer D_1 and D_2, respectively

REFERENCES

(1) I. Grosu, S. Mager, G. Plé and M. Horn, J. Chem. Soc. Chem. Commun. 167 (1995).

(2) I. Grosu, S. Mager and G. Plé, J. Chem. Soc. Perkin Trans. 2 1351 (1995).

(3) I. Grosu, S. Mager, G. Plé, R. Martinez, M. Horn and R. R. Gavino,. Monatsh. Chem. **126**, 1021 (1995).

(4) I. Grosu, S. Mager, G. Ple and E. Mesaroş, Tetrahedron **52**, 12783 (1996).

(5) I. Grosu, S. Mager, R. Martinez, B.C. Camacho, G. Plé and C. Mesaros, Rev. Roum. Chim. submitted.

(6) M. J. O. Anteunis, D. Tavernier and F. Borremans, Heterocycles **4**, 293 (1976).

(7) F.G. Riddell and M. J. T. Robinson, Tetrahedron **23**, 3417 (1967).

(8) E. L. Eliel and M. C. Knoeber, J. Am. Chem. Soc. **90**, 3444 (1968).

(9) T. A. Crabb, M. Porssa and E. Elmore, Magn. Reson. Chem. **29**, 613 (1991).

(10) I. Grosu, G. Plé and S. Mager, Tetrahedron **51**, 2659 (1995).

(11) I. Grosu, S. Mager, G. Plé, R. Martinez, L. Muntean and E. Mesaros, Heterocycles **41**, 2233 (1995).

Received on April 24, 1997