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Synthesis and Stereochemistry of Some New Chiral Brominated 1,3-Dioxanes

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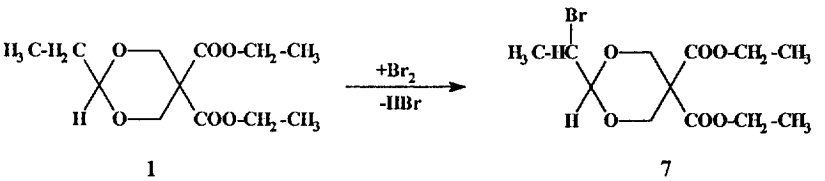
Abstract: The stereochemistry of some new 1,3-dioxanes with brominated chiral groups located in the (a)ketalic part of the heterocycle, obtained by a regioselective radicalic bromination reaction, was investigated by NMR methods. The experiments demonstrated the fixed or flipping structures of the compounds. The influence of the chiral carbon atoms was analyzed by means of the diastereotopicity of protons and carbon atoms. In the case of polychiral compounds, the diastereoselectivity of the bromi-nation reaction was studied.

INTRODUCTION

New saturated heterocyclic compounds were obtained by the regioselective bromination reaction (Scheme 1) of the 2,5-substituted 1,3-dioxanes **1-6** and **13-15**. The reaction was performed in good yields under conditions similar to those used by Giusti in the bromination reaction of some 1,3-dioxolanic derivatives.[1]

The investigations concerning the stereochemistry of these compounds follow configurational aspects pointing out the influences of the chirality of the molecules by means of the diastereotopicity of protons and carbon atoms and also determine using conformational analysis the rigidity or the flipping of the rings. The conformational status of the compounds **7-12** and **16-18** is correlated with the differences between the groups located in the 2 position of the heterocycle. If the substituents of the 1,3-dioxanic ring are different, the compounds are rigid and the conformation with the largest group in equatorial orientation is preferred. In the NMR spectra different signals for the axial and for the equatorial protons of the ring and for the protons and carbon atoms of the identical groups located at C-5 are recorded. Usually the equatorial C-4, C-6 protons are more deshielded than the axial ones, while in the case of the two identical groups located at C-5, the protons and the carbon atoms of the axial group are the more deshielded ones.[2-13] For the carbon atoms, situated in α to C-5, the deshielding is the result of the γ_{anti} effect.[6-13] If simultaneously, the groups in the 2 and 5 positions are identical, the compounds are flipping. As a result the protons and the carbon atoms of the

cycle and of the identical groups exist in similar average environment and for the chemical shifts of axial and equatorial positions unique mean values are recorded.



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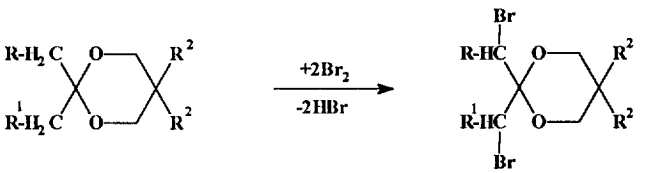
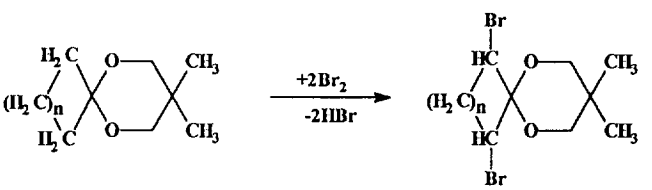


2	R= CH_3 ; R^1= H ; R^2= $COOC_2H_5$	8
3	R= CH_3 ; R^1= H ; R^2= CH_3	9
4	R= R^1= R^2= CH_3	10
5	R= R^1= C_6H_5 ; R^2= $COOC_2H_5$	11
6	R= R^1= C_2H_5 ; R^2= CH_3	12



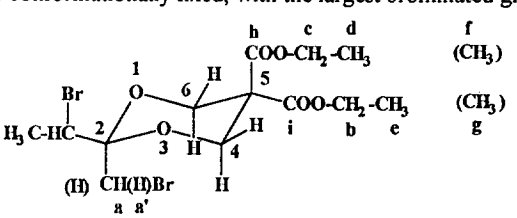
13	n= 2	16
14	n= 3	17
15	n= 4	18

Scheme 1

RESULTS AND DISCUSSION

Rigid compounds

Compounds **7-9** are conformationally fixed, with the largest brominated group in equatorial position:



The presence in compounds **7-9** of a chiral carbon atom entails the differentiation of positions 4 and 6 as diastereotopic ones. In the ^{1}H-NMR spectra (Table 1, Figure 1) two AB systems are observed and a

long range coupling between the diastereotopic equatorial protons located at C-4 and C-6 is measured: $^4J(7)$= 2.6 Hz ; $^4J(8)$= 2.2 Hz; $^4J(9)$= 1.6 Hz.

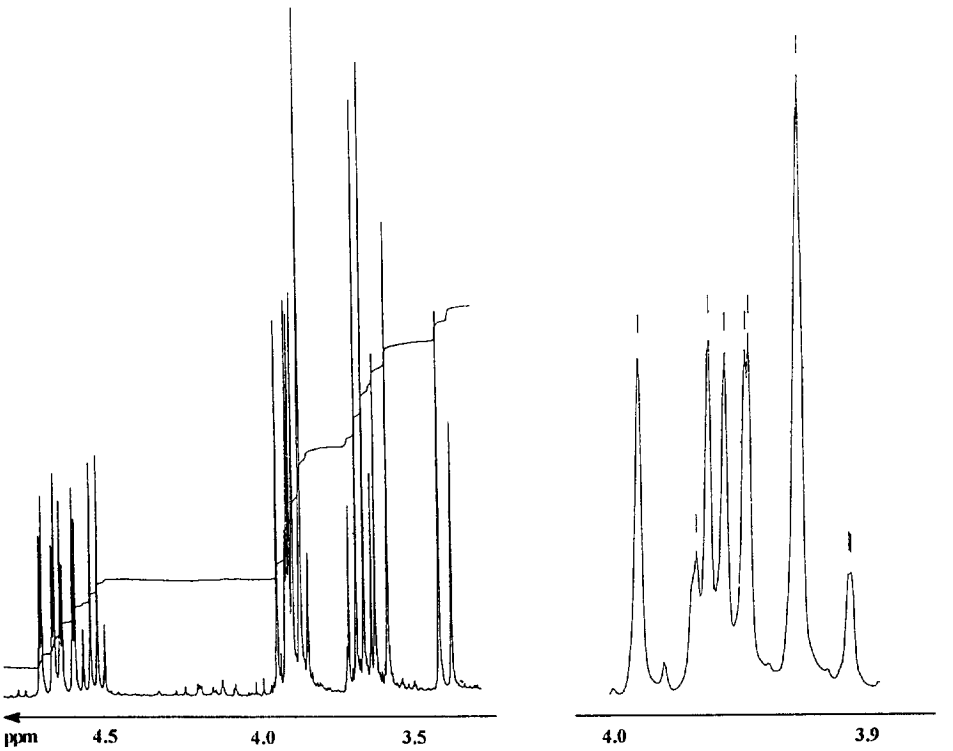


Figure 1. ^{1}H-NMR spectrum of compound **8** (fragment and detail).

Different signals for the diastereotopic protons belonging to the axial CH_2-Br group (a and a') are also recorded.

In order to achieve a more detailed NMR and stereochemical investigation of compounds **7-9** besides the usual ^{1}H and ^{13}C-NMR 1D spectra (Tables 1 and 2), the data offered by the 2D Homonuclear (**7-9**), 2D Heteronuclear (**7,8**) and N.O.E.Diff. (**9**) spectra were used.

So, in the ^{13}C-NMR spectrum of compound **7**, the signals of the two methylenic carbon atoms belonging to the esteric groups located at C-5 are fortuitously overlapped and their differentiation may be observed only in the 2D Heteronuclear spectrum when the ^{13}C-NMR spectrum signal of δ= 69.37 ppm is correlated with both the quartets belonging to the methylenic protons of the axial (δ_c= 4.02 ppm) and of the equatorial (δ_b= 3.72 ppm) esteric groups.

The spectra of compound **9** in $CDCl_3$ and C_6D_6 display significant overlaps of the signals corresponding to the axial and equatorial protons of the 1,3-dioxanic ring, their identification being possible only using N.O.E.Diff. spectra.

The method used involves the irradiation of the protons belonging to the groups located at C-5. The irradiation of the protons of the axial C-5 methyl group (δ=0.84 ppm in C_6D_6 ; δ=1.12 ppm in $CDCl_3$) influences only the equatorial protons at C-4 and C-6 (calculated N.O.E. 1.67 % in C_6D_6 and 1.12 % in $CDCl_3$) and the irradiation of the protons of the equatorial C-5 methyl group influences both equatorial and

Table 1. ^{1}H-NMR Data of Compounds **7-9**

Compound	Solvent	δ ppm											
		4ax	6ax	4eq	6eq	a	a'	b	c	d	e	f	g
7	C_6D_6	3.70	3.69	4.87	4.85	-	-	4.02	3.72	0.91	0.75	-	-
8	C_6D_6	3.97	3.95	4.57	4.54	3.71	3.55	3.94	3.78	0.87	0.78	-	-
9	C_6D_6	3.10	3.04	3.10	3.05	3.77	3.55	-	-	-	-	0.84	0.30
9	$CDCl_3$	3.61	3.57	3.50	3.49	3.94	3.87	-	-	-	-	1.12	0.83

Table 2. ^{13}C-NMR Data of Compounds **7-9**

Compound	Solvent	δ ppm									
		4	6	b	c	d	e	f	g	h	i
7	C_6D_6	61.87	61.67	69.37	69.37	13.96	13.70	-	-	167.52	166.57
8	C_6D_6	63.31	63.08	61.98	62.03	13.91	13.72	-	-	167.18	166.47
9	C_6D_6	70.73	70.54	-	-	-	-	22.68	21.68	-	-
9	$CDCl_3$	70.96	70.96	-	-	-	-	22.79	22.14	-	-

axial protons of the ring (calculated N.O.E. 2.00 % in C_6D_6 and 2.28 % in $CDCl_3$). The overlaps are now resolved:

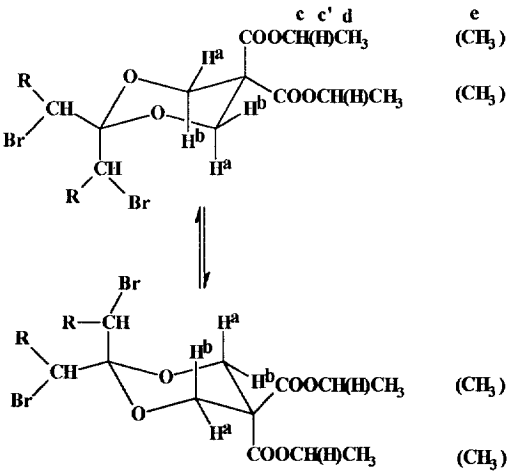
- in the spectrum run in C_6D_6 the signals of the axial and of the equatorial protons are overlapped and give only one singlet (δ=3.10 ppm) at C-4 and a very close AB system at C-6 (δ_{ax}=3.04 ; δ_{eq}=3.05 ppm). This quasi-identical deshielding of the equatorial and axial protons is due to the steric compression[14,15] exerted by the axial group at C-2 which determines the large deshielding of the axial protons of the fixed 1,3-dioxanic ring. Despite this unusual identity of the signals for axial and equatorial protons of an anancomeric 1,3-dioxanic compound, as a consequence of the influence of the chiral carbon atoms by means of the diastereotopicity of 4 and 6 position, the ^{1}H-NMR spectrum displays two signals for the ring protons ($\Delta\delta_{4\text{-}6}$= 0.05-0.06 ppm).

- in the spectrum run in $CDCl_3$, for the protons of the ring two AB systems are recorded. The peaks corresponding to the equatorial protons are overlapped (δ_{6eq}=3.49 ; δ_{4eq}=3.50 ppm) but the long range coupling of these diastereotopic protons due to the W arrangement of the bonds H^{eq}-C^4-C^5-C^6-H^{eq} can be measured (^{4}J=1.6 Hz). The axial protons are again more deshielded then the equatorial ones (δ_{6ax}=3.57 ;

δ_{4ax}=3.61 ppm).

Monocyclic flipping compounds

For compounds **10-12** with a flipping structure (Scheme 2), having two chiral carbon atoms, two cofigurational diastereomers are possible: a meso (R,S configuration for chiral carbon atoms) and a racemic d,l isomer (R,R or S,S configurations).



Scheme 2

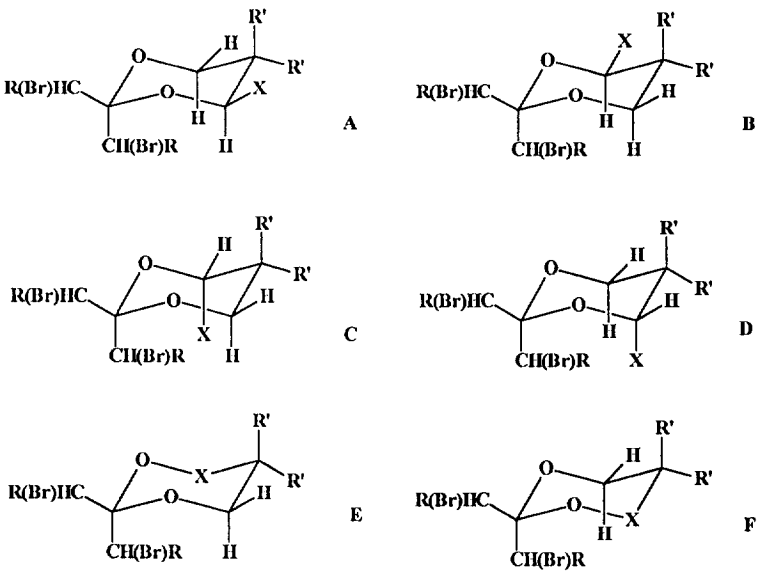
The identification of the diastereomers is made by NMR spectra taking into account the diastereotopicity of the carbon atoms and of the protons at C-4 and C-6.

Analyzing structures **A-F** (Scheme 3) resulted from compounds **10-12** by the substitution at C-4 or C-6 of a H or of the CH_2 group with another substituent X, and considering the flipping of the molecules, one can observe:

- if the d,l isomer is involved (R,R or S,S configurations) structures **A,C ; B,D** and **E,F** are identical the one which the other and structures **A** and **B** represent diastereomers. As a consequence, the identical protons 4a, 6a are diastereotopic with the identical protons 4b, 6b (Scheme 2), whereas C-4 and C-6 are not diastereotopic carbon atoms. In the ^{1}H-NMR spectra of these isomers two AB systems for the C-4, C-6 protons are recorded, whereas in the ^{13}C-NMR spectra only one peak for the carbon atoms of these positions is observed.

- if the meso isomer is considered (R,S configurations) the structures **A,D** are in enantiomeric relation as well as the **B** and **C** structures. Structures **A** and **B** represent diastereomers as well as the structures **E** and **F**. The diastereotopicity of C-4 and C-6 carbon atoms and of the identical protons 4a,4b with the identical protons 6a,6b is established. In the ^{1}H-NMR spectra of these isomers two singlets for the C-4, C-6 protons are recorded and also in the ^{13}C-NMR spectra two peaks for the diastereotopic C-4 and C-6 carbon atoms are identified.

As one can observe by analyzing the NMR spectra of compounds **10-12** (Figure 2), in the case of compound **11** only the d,l isomer is obtained. The high diastereoselectivity of the bromination reaction can be



Scheme 3

explained by an asymmetric induction of the first created chiral carbon atom. The first brominated benzyl group prefers the equatorial position and in the rigid monobrominated compound when the second bromine atom makes the substitution, it prefers the attack from the "re" face of the intermediary radical if the first brominated carbon atom has R configuration or the attack from the "si" face if the first chiral carbon atom has S configuration. These preferences are determinated by the relative positions of the phenyl groups which adopt in the intermediary radical an "antiparallel" orientation. This conformation does not permit the attack from one of the radical faces which is blocked (by the 1,3-dioxanic ring) and leads to the obtaining, when the second bromine atom is bonded, of only one of the possible configurations.

In compound **10** both diastereomers are obtained, as it is shown by the 1D and 2D Homo- and Heteronuclear NMR spectra. The ratio of the isomers was calculated from ^{1}H-NMR spectrum using the signals intensity. The average of the integrals of the signals of the two isomers measured for the ring protons and for the protons of the groups located at C-2 permits to estimate the ratio of 30% d,l and 70% meso isomer. The increased ratio of the meso isomer suggests the preference for an "antiparallel" orientation of the bromine atom of the equatorial group and the methyl group of the axial carbon atom which carries the radicalic reaction center in the intermediary radical of the second step of the bromination reaction.

In the case of compound **12** only the meso isomer was obtained. The high diastereoselectivity of the bromination reaction shows that the population of the conformation with the two ethyl groups of the two chiral carbon atoms in "antiparallel" orientation in the radical intermediary of the second step of the bromination reaction can be neglected in comparison with the population of the conformation in which the bromine atom of the equatorial group and the ethyl group of the axial radicalic carbon atom have an "antiparallel" orientation.

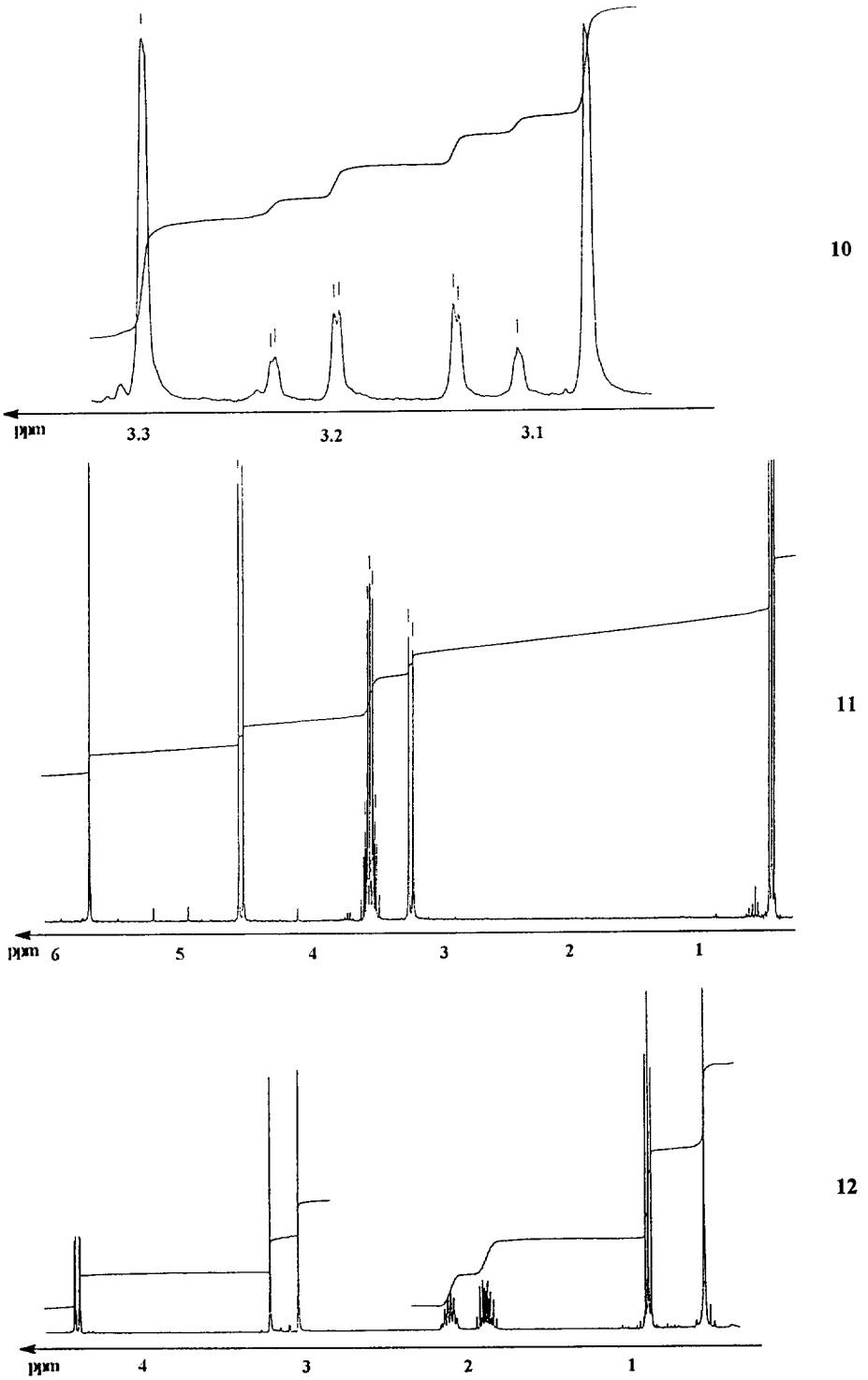


Figure 2. ^{1}H-NMR spectra of compounds **10** (detail), **11** (fragment) and **12**

The significant diastereoselectivity of the bromination reaction (Table 3) is correlated with the volume of the groups located at C-2 which determines the preference in the radicalic stage (of the second step of the bromination reaction) for one of the conformations involving these groups (in correlation with the chirality of the first brominated group too) and leads to the obtaining at the second chiral carbon atom of only one of the possible configurations.

Analyzing the NMR data for compounds **10-12** (Table 4, Figure 2), some facts have to be underlined. In the case of compound 11, for the protons a and b (Scheme 2) a very large value of the diastereotopicity, quite unusual ($\Delta\delta$=1.27 ppm) is observed. This large difference is due, probably, to the influences exerted by

Table 3. The Ratio of the Stereoisomers of Compounds **10-12**

Compound	Isomers ratio (from NMR spectra) %	
	d,l	meso
10	30	70
11	≈100	-
12	-	≈100

Table 4. ^{1}H- and ^{13}C-NMR Data of Compounds **10-12**

Nucleus	Compound	Isomer	δ ppm							
			4(a)	4(b)	6(a)	6(b)	c	c'	d	e
^{1}H	**10**	d,l	3.11	3.20	3.11	3.20	-	-	-	0.70
	11	d,l	3.37	4.65	3.37	4.65	3.69	3.67	0.68	-
	10	meso	3.29		3.06		-	-	-	0.72
	12	meso	3.31		3.13		-	-	-	0.68
^{13}C	**10**	meso	70.55		69.75		-		-	22.56
	12	meso	65.31		64.43		-		-	17.18
	10	d,l	70.27				-		-	22.56
	11	d,l	68.89				61.80		13.68	-

the phenyl groups which prefer an "antiparallel" orientation, with the shielding of one kind of protons (a) and the deshielding of the others (b) in both conformations resulted by the ring inversion (Scheme 2). Another remarkable feature is the presence in the ^{1}H-NMR spectrum of two different signals for the diastereotopic methylenic protons of the esteric groups (c,c') despite of the eight atoms distance between these protons and the chiral carbon atoms. After the decoupling with the vicinal protons the diastereotopicity was evaluated as

$\Delta\delta$=0.02 ppm and the geminal coupling constant (J=16.4 Hz) was measured.

In the ^{1}H-NMR spectrum of the diastereomers of compound **10**, a further splitting of the doublets of the diastereotopic protons a and b belonging to the d,l isomer (Figure 2) due to the coupling with the protons of the methyl groups located at C-5 is observed (^{4}J=0.90 Hz).

Spiranic flipping compounds

In the synthesis of compounds **16-18** only the d,l diastereomer is obtained (with a "trans" disposal of the bromine atoms). This result is supported by the ^{1}H- and ^{13}C-NMR spectra (Table 5, Figure 3) when only the characteristic signals for this isomer are obtained. In the analysis of the spectra the flipping of the 1,3-dioxanic ring (presented in Scheme 4 for compounds **16** and **17**) has to be considered.

The large diastereotoselectivity of the bromination reaction, a different case from the results reported for the bromination reaction of other spiroketals[16,17] can be explained like in the case of compound **10-12** by the asymmetric induction of the first brominated center which determines the attack of the second bromine atom from the "re" face of the intermediary radical if its configuration is R (with the obtaining of the R,R isomer) or from the "si" face if its configuration is S (resulting the S,S isomer).

Table 5. ^{1}H- and ^{13}C-NMR Data of Compounds **16-18**

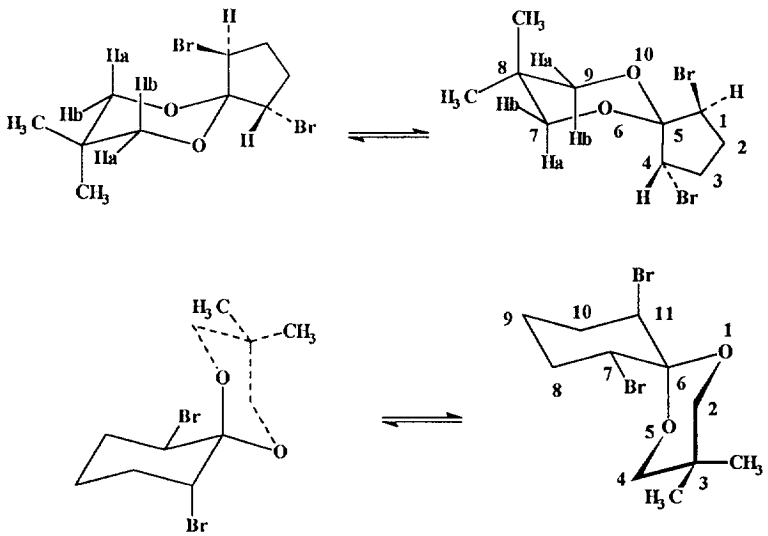
Nucleus	Compound	δ ppm		
		$C^{2,4(7,9)}$[a]	$C^{2,4(7,9)}$[b]	3(8)-CH_3
^{1}H	**16**	3.20	3.08	0.71
	17	3.25	3.13	0.78
	18	3.19	3.11	0.76
^{13}C	**16**	71.47		21.60
	17	69.86		22.58
	18	69.64		22.40

Note: The data for compound **17** are obtained from the spectra (^{1}H and ^{13}C) recorded at 70 °C.

The notations are presented in Scheme 4.

In the case of compound **17** the bromine atoms (located on the cyclohexanic ring) with a "trans" disposal have an axial-equatorial orientation. Both cyclohexanic and 1,3-dioxanic rings are flipping (Scheme 4) but the process is not so fast as in the case of monocyclic compounds **10-12** or the other two spiranic compounds **16** and **18**. As a consequence, in the ^{1}H-NMR spectrum run at room temperature the coalescence of the signals is recorded. A good resolution of the signals for the flipping compound is obtained in the spectrum run after increasing temperature when the flipping of the spiranic compound become faster (Figure 3). The NMR experiment at higher temperature was preferred to an experiment at low temperature because in the frozen spiranic compound, beside the chirality of the two brominated carbon atoms, the

chirality introduced by the spiro[5.5]undecanic skeleton has to be also considered[18,19] and the comparison with the other two spiranic compounds becomes unable.



Scheme 4

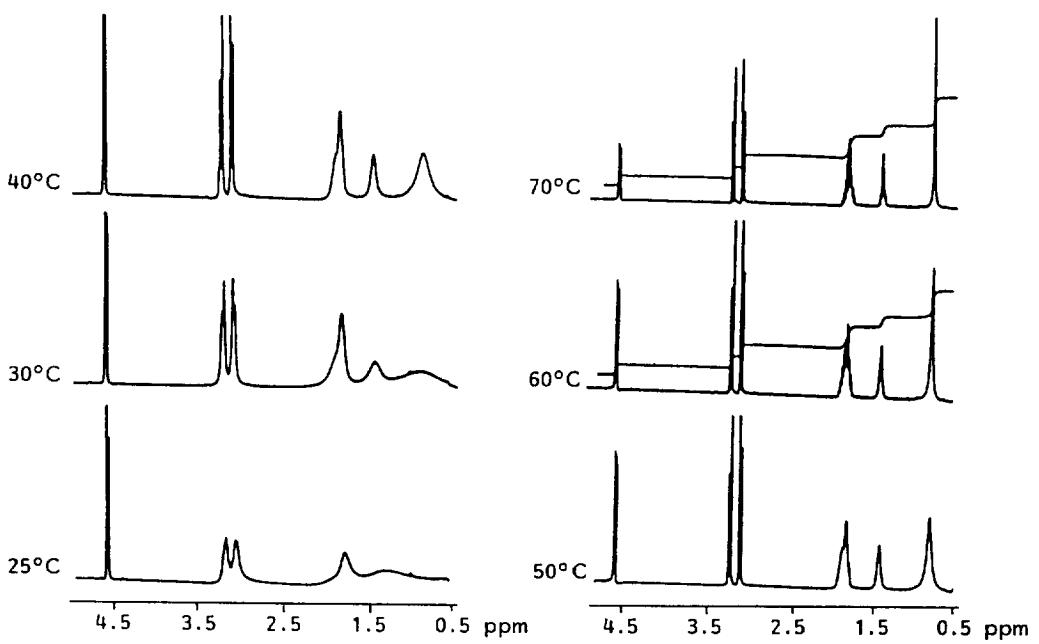


Figure 3. Variable temperature ^{1}H-NMR experiment for compound **17**.

The diastereotopicity ($\Delta\delta$) of the ring protons is evaluated as $0.01 < \Delta\delta < 0.06$ ppm for compounds **7-9** and as $0.09 < \Delta\delta < 1.27$ ppm for the d,l diastereomer of compounds **10, 11** and **16-18**.

As far as the C-4 and C-6 atoms are concerned their diastereotopicity is evaluated as $0.19 < \Delta\delta < 0.20$ ppm in the case of compounds **7-9** and as $0.80 < \Delta\delta < 0.88$ ppm in the case of the meso isomer of compounds **10** and **12**.

EXPERIMENTAL

^{1}H- and ^{13}C-NMR spectra were recorded at room temperature (excepting compound **17** when the spectra were run at 70 °C), in C_6D_6 or $CDCl_3$ solution in 5-mm tubes, on a Bruker AM 360 (for compounds 7-11) or on a Bruker AM 400 (for compounds 12,16-18)* Fourier transform NMR spectrometer equipped with an Aspect 3000 computer and with a dual ^{13}C-^{1}H probe head operating at 360 (400)* MHz for protons and 90 (100)* MHz for carbon atoms. No TMS was added, rather, shifts were referenced to the solvent line (C_6D_6 or $CDCl_3$). All coupling constants and chemical shifts are given with a precision of 0.1 Hz and 0.01 ppm.

The purity of liquid substances was checked by gas chromatography using a M9A chromatograph with a 2 m inox column with ϕ=2.2 mm packed with Carbowax 20M / Chromosorb W, a FID detector using Ar as carrier gas and with T_i=T_d=250 °C, T_c=120-160 °C.

M.p.s are uncorrected.

New compounds 7-12 and 16-18 general procedure: 0.1 mol (a)ketal and 100 ml dried ethylic ether were introduced in a four necked flask equipped with a reflux condenser, a mechanic stirring system, a thermometer and a dropping funnel. To this mixture cooled with an ice bath at 0-5 °C, the corresponding (0.1 or 0.2 mol) quantity of bromine was added drop by drop, under stirring, monitoring at the beginning the fading of the solution colour. When the addition of the bromine was finished the ice bath was removed and the stirring was continued four an hour and the temperature in the flask reached slowly the room value (20-25 °C). The ethylic ether and the resulted HBr were removed in vacuum (10-15 mm.col.Hg ; t < 50 °C). The raw product was purified by vacuum distillation (1-2 mm.col.Hg) or by crystallization from ethanol.

The synthesis and the stereochemistry of starting 1,3-dioxanes **1-6** and **13-15** were described elsewhere.[15,20-22]

2-α-Bromoethyl-5,5-bis(ethyloxycarbonyl)-1,3-dioxane 7. 10.33 g, yield 61%. Liquid, b.p.=154-156 ° C(1mm.col.Hg). ^{1}H-NMR(C_6D_6) δ 0.75[t,3H,J=7.1 Hz,5-COOCH$_2$C<u>H</u>$_3$(eq.)], 0.91[t,3H,J=7.1 Hz, 5-COOCH$_2$C<u>H</u>$_3$(ax.)], 1.52[d,3H,J=6.9 Hz,2-CH(Br)C<u>H</u>$_3$], 3.69[d,1H,J=11.5 Hz,C^6(ax.)], 3.70[d,1H, J=11.5 Hz,C^4(ax.)], 3.72[q,2H,J=7.1 Hz,5-COOC<u>H</u>$_2$CH$_3$(eq.)], 3.82[dq,1H,J=6.9 Hz,J=4.2 Hz, 2-C<u>H</u>(Br)CH$_3$], 4.02 [q,2H,J=7.1 Hz,5-COOC<u>H</u>$_2$CH$_3$(ax.)], 4.27(d,1H,J=4.2 Hz,C^2), 4.85[dd,1H,J=11.5 Hz,J=2.6 Hz, C^6(eq.)], 4.87 ppm[dd,1H,J=11.5 Hz,J=2.6 Hz,C^4(eq.)]. ^{13}C-NMR(C_6D_6) δ 13.70 [5-COOCH$_2$<u>C</u>H$_3$ (eq.)], 13.95[5-COOCH$_2$<u>C</u>H$_3$ (ax.)], 19.47[2-CH(Br)-<u>C</u>H$_3$], 46.94[2-<u>C</u>H(Br)-CH$_3$], 53.43(C^5), 61.67(C^6), 61.87 (C^4), 69.37[5-COO<u>C</u>H$_2$CH$_3$ (ax. and eq.)], 102.55(C^2), 166.57 [5-<u>C</u>OOCH$_2$CH$_3$ (eq.)], 167.52[5-<u>C</u>OOCH$_2$CH$_3$(ax.)]. Anal.Calcd. for $C_{12}H_{19}BrO_6$:C,42.29;H,5.64:Br, 23.55. Found: C,42.38;H,5.43;Br, 23.29.

2-α-Bromoethyl, 2-bromomethyl-5,5-bis(ethyloxycarbonyl)-1,3-dioxane 8. 14.47 g, yield 67%. Liquid, b.p.=188-190 °C(1mm.col.Hg). ^{1}H-NMR(C_6D_6) δ 0.78[t,3H,J=7.1 Hz,5-COOCH$_2$CH$_3$(eq.)], 0.87[t,3H, J=7.1 Hz,5-COOCH$_2$CH$_3$(ax.)], 1.57[d,3H,J=6.8 Hz,2-CH(Br)CH$_3$], 3.55[d,1H,J=11.8 Hz,2-CH(H)Br], 3.71[d,1H,J=11.8 Hz,2-CH(H)Br], 3.78[q,2H,J=7.1 Hz,5-COOCH$_2$CH$_3$(eq.)], 3.94[q,2H,J=7.1 Hz, 5-COOCH$_2$CH$_3$(ax.)], 3.95[d,1H,J=11.5 Hz,C^6(ax.)], 3.97[d,1H,J=11.5 Hz,C^4(ax.)], 4.46[q,1H,J=6.8 Hz,2-CH(Br)-CH$_3$], 4.54[dd,1H,J=11.8 Hz,J=2.6 Hz,C^6(eq.)], 4.57[dd,1H,J=11.8 Hz,J=2.6 Hz,C^4(eq.)]. ^{13}C-NMR(C_6D_6) δ 13.72[5-COOCH$_2$CH$_3$ (eq.)], 13.91[5-COOCH$_2$CH$_3$ (ax.)], 18.90[2-CH(Br)-CH$_3$], 28.38(2-CH$_2$Br), 49.66[2-CH(Br)-CH$_3$], 52.93(C^5), 61.98[5-COOCH$_2$CH$_3$ (eq.)], 62.03[5-COOCH$_2$CH$_3$ (ax.)], 63.08(C^6), 63.31(C^4), 97.78(C^2), 166.47[5-COOCH$_2$CH$_3$ (eq.)], 167.18[5-COOCH$_2$CH$_3$(ax.)]. Anal.Calcd. for $C_{13}H_{20}Br_2O_6$:C,36.13;H,4.66:Br,36.88. Found: C,36.39;H,4.88;Br,36.70.

2-α-Bromoethyl, 2-bromomethyl-5,5-dimethyl-1,3-dioxane 9. 11.85 g, yield 75%. Liquid, b.p.=142-144 °C(1mm.col.Hg). ^{1}H-NMR(C_6D_6) δ 0.30[s,3H,5-CH$_3$(eq.)], 0.84[s,3H,5-CH$_3$(ax.)], 1.66[d,3H,J=6.8 Hz,2-CH(Br)-CH$_3$], 3.04[d,1H,J=11.5 Hz,C^6(ax.)], 3.05[d,1H,J=11.5 Hz,C^6(eq.)], 3.10[s,2H,C^4(ax. and eq.)], 3.55[d,1H,J=11.6 Hz,2-CH(H)-Br], 3.77[d,1H,J=11.6 Hz,2-CH(H)-Br], 4.53[q,1H,J=6.8 Hz, 2-CH(Br)-CH$_3$]. ^{1}H-NMR($CDCl_3$) δ 0.83[s,3H,5-CH$_3$(eq.)], 1.12[s,3H,5-CH$_3$(ax.)], 1.83[d,3H,J=6.8 Hz,2-CH(Br)-CH$_3$], 3.49[d,1H,J=11.6 Hz,C^6(eq.)], 3.50[d,1H,J=11.6 Hz,C^4(eq.)], 3.57[d,1H,J=11.6 Hz, C^6(ax.)], 3.61[d,1H,J=11.6 Hz,C^4(ax.)], 3.87[d,1H,J=11.6 Hz,2-CH(H)-Br], 3.94[d,1H,J=11.6 Hz, 2-CH(H)-Br], 4.50[q,1H,J=6.8 Hz,2-CH(Br)-CH$_3$]. ^{13}C-NMR(C_6D_6) δ 19.43[2-CH(Br)-CH$_3$], 21.68 [5-CH$_3$(eq.)], 22.68[5-CH$_3$(ax.)], 28.94(2-CH$_2$Br), 29.15(C^5), 50.18[2-CH(Br)-CH$_3$], 70.54(C^6), 70.73(C^4), 97.28(C^2). ^{13}C-NMR($CDCl_3$) δ 19.28[2-CH(Br)-CH$_3$], 22.14[5-CH$_3$(eq.)], 22.79[5-CH$_3$(ax.)], 28.56(2-CH$_2$Br), 29.30(C^5), 49.69[2-CH(Br)-CH$_3$], 70.96(C^{4,6}), 97.00(C^2). Anal.Calcd. for $C_9H_{16}Br_2O_2$: C,34.20; H,5.10:Br,50.57. Found: C,33.98;H,5.33;Br,50.38.

2,2-Bis(α-bromoethyl)-5,5-dimethyl-1,3-dioxane 10. 10.06 g, (unseparated mixture of 30% d,l and 70% meso isomer) yield 61%. Liquid, b.p.=148-150 °C(1mm.col.Hg). ^{1}H-NMR(C_6D_6), **meso isomer signals:** δ 0.70(s ,6H,5-CH$_3$), 1.79[d,6H,J=7.1 Hz,2-CH(Br)-CH$_3$], 3.06(s,2H,C^6), 3.29(s,2H,C^4), 4.55[q,2H,J=7.1 Hz,2-CH(Br)-CH$_3$]; **d,l isomer signals:** δ 0.70(d,6H,J=0.9 Hz,5-CH$_3$), 1.69[d,6H,J=7.0 Hz, 2-CH(Br)-CH$_3$], 3.11 (d,2H,J=12.1 Hz,4-H$_a$,6-H$_a$), 3.20(d,2H,J=12.1 Hz,4-H$_b$,6-H$_b$), 4.55[q,2H,J=7.1 Hz, 2-CH(Br)-CH$_3$]. ^{13}C-NMR(C_6D_6), **meso isomer signals**: δ 21.83[2-CH(Br)-CH$_3$], 22.56(5-CH$_3$), 29.07 (C^5), 47.56[2-CH(Br)-CH$_3$], 69.75(C^6), 70.55(C^4), 99.30(C^2); **d,l isomer signals:** δ 21.24[2-CH(Br)-CH$_3$], 22.56(5-CH$_3$), 29.07(C^5), 47.26[2-CH(Br)-CH$_3$], 70.27(C^{4,6}), 90.30(C^2). Anal.Calcd. for $C_{10}H_{18}Br_2O_2$: C, 36.59; H,5.49:Br,48.38. Found: C,36.71;H,5.68;Br,48.11.

2,2-Bis(α-bromobenzyl)-5,5-bis(ethyloxycarbonyl)-1,3-dioxane (d,l) 11. 24.23 g, yield 85%. Solid, m.p = 131-132 °C. ^{1}H-NMR(C_6D_6) δ 0.68(t,6H,J=7.1 Hz,5-COOCH$_2$CH$_3$), 3.37(d,2H,J=12.1 Hz,4-H$_a$,6-H$_a$), 3.67[dq,2H,J=16.4 Hz,J=7.1 Hz,5-COOCH(H)-CH$_3$], 3.69[dq,2H,J=16.4 Hz,J=7.1 Hz,5-COOCH(H)-CH$_3$], 4.65(d,2H,J=12.1 Hz, 4-H$_b$,6-H$_b$), 5.78[s,2H,2-CH(Br)-C$_6$H$_5$], 6.85-7.52[m,10H,2-CH(Br)-C$_6$H$_5$]. ^{13}C-NMR(C_6D_6) δ 13.68(5-COOCH$_2$CH$_3$), 53.53(C^5), 55.95[2-CH(Br)-C$_6$H$_5$], 61.80(5-COOCH$_2$CH$_3$), 68.89(C^{4,6}), 100.19(C^2), 128.33,128.61,130.79,138.17[2-CH(Br)-C$_6$H$_5$], 167.68(COOCH$_2$CH$_3$). Anal. Calcd. for $C_{24}H_{26}Br_2O_6$: C,50.54; H,4.59:Br,28.02. Found: C,50.40;H,4.52;Br,28.23.

2,2-Bis(α-bromopropyl)-5,5-dimethyl-1,3-dioxane (meso) 12. 12.70 g, yield 71%. Solid: m.p.=86-87 °C. ^{1}H-NMR(C_6D_6) δ 0.68(d,6H,J=2.4 Hz,5-CH_3), 1.02[t,6H,J=7.2 Hz,2-CH(Br)-CH_2-C$\underline{H}_3$], 1.99[ddq,2H, J=11.2 Hz,J=11.1 Hz,J=7.2 Hz,2-CH(Br)-C$\underline{H}$(H)-CH_3], 2.22[ddq,2H,J=11.2 Hz,J=11.1 Hz,J=7.2 Hz,2-CH(Br)-CH($\underline{H}$)-CH_3], 3.13(s,2H,C^6), 3.31(s,2H,C^4), 4.45[dd,2H,J=11.2 Hz,J=2.4 Hz,2-C$\underline{H}$(Br)-CH_2-CH_3] ^{13}C-NMR(C_6D_6) δ 8.78[2-CH(Br)-CH_2-$\underline{C}H_3$], 17.18(5-CH_3), 21.94[2-CH(Br)-$\underline{C}H_2$-CH_3], 23.60(C^5), 52.14[2-$\underline{C}$H(Br)-CH_2-CH_3], 64.43(C^6), 65.31(C^4), 92.45(C^2). Anal.Calcd. for $C_{12}H_{22}Br_2O_2$: C,40.24; H, 6.19:Br,44.62. Found: C,40.05;H,6.33;Br,44.39.

1,4-Dibromo-8,8-dimethyl-6,10-dioxaspiro[4.5]decane (d,l) 16.12.13 g, yield 74%. Solid m.p.=66-67 °C. ^{1}H-NMR(C_6D_6) δ 0.71(d,6H,J=1.1 Hz,8-CH_3), 1.80-2.09(m,overlapped peaks,4H,$C^{2,3}$), 3.02(dd,2H,J=11.4 Hz,J=1.1 Hz,7-H_a,9-H_a), 3.20(dd,2H,J==11.4 Hz,J=1.1 Hz,7-H_b,9-H_b), 4.35(m,2H, $C^{1,4}$), ^{13}C-NMR (C_6D_6) δ 21.56(8-CH_3), 29.19(C^8), 30.88($C^{2,3}$), 48.47($C^{1,4}$), 71.47($C^{7,9}$), 103.95(C^5).Anal. Calcd. for $C_{10}H_{16}Br_2O_2$: C,36.61; H,4.91:Br,48.71. Found: C,36.36;H,5.13;Br,48.59.

7,11-Dibromo-3,3-dimethyl-1,5-dioxaspiro[5.5]undecane (d,l) 17. 14.02 g, yield 82%. Solid: m.p.=130-131 °C. ^{1}H-NMR(C_6D_6, 70 °C) δ 0.78(s,6H,3-CH_3), 1.35-1.45(m,2H,C^9), 1.75-1.95(m,4H,$C^{8,10}$), 3.13 (d,2H,J=11.5 Hz, 2-H_a,4-H_a), 3.20(d,2H,J=11.5 Hz,2-H_b,4-H_b), 4.65(dd,2H,J=7.6 Hz,J=4.3 Hz, $C^{7,11}$). ^{13}C-NMR(C_6D_6, 70 °C) δ 22.07(C^9), 22.58(3-CH_3), 29.32(C^3), 32.51($C^{8,10}$), 51.18($C^{7,11}$), 69.86 ($C^{2,4}$), 95.76(C^6).Anal.Calcd. for $C_{11}H_{18}Br_2O_2$: C,38.62; H,5.30:Br,46.71. Found: C,38.83;H,5.08; Br,46.96.

7,12-Dibromo-3,3-dimethyl-1,5-dioxaspiro[5.6]dodecane (d,l) 18. 14.77 g, yield 83%. Solid: m.p.=106-107 °C. ^{1}H-NMR(C_6D_6) δ 0.76(s,6H,3-CH_3), 1.38-1.54(m,overlapped peaks,4H,$C^{9,10}$), 1.91-2.01(m,overlapped peaks,4H,$C^{8,11}$), 3.11(d,2H,J=11.8 Hz,2-H_a,4-H_a), 3.19(d,2H,J=11.8 Hz,2-H_b,4-H_b), 4.72(dd,2H, J=3.6 Hz,J=8.2 Hz,$C^{7,12}$). ^{13}C-NMR(C_6D_6) δ 22.38(3-CH_3), 22.94($C^{9,10}$), 28.78(C^3), 29.83($C^{8,11}$),53.37 ($C^{7,12}$), 69.64($C^{2,4}$), 97.93(C^6). Anal.Calcd. for $C_{12}H_{20}Br_2O_2$: C,40.47; H,5.66: Br,44.87. Found: C,40.72; H,5.38;Br,44.90.

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