Axial and Helical Chirality of some Spiro-1,3-Dioxanes

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The diastereoisomerism of some spiro 1,3-dioxanes with axial chirality and of some trispiro derivatives exhibiting an axial and a hitherto unreported helical chirality for spiranic compounds is discussed.

Our interest in the synthesis of new spiro-1,3-dioxane derivatives led us to an investigation of some peculiar aspects of the stereochemistry of these compounds.

Few comments are available in the literature[1–5] concerning the study of axial chirality displayed by compounds with spiro[5.5]undecane structure substituted at positions 3 and 9.

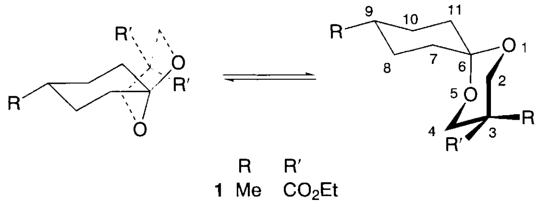
The spiranes **1–4**, with 1,5-dioxaspiro[5.5]undecane skeleta, show evidence of a semi-mobile structure. The cyclohexane ring has a chair conformation and an equatorial R alkyl group located at C(9) and is rigid (the ring inversion is frozen by the R alkyl group). On the other hand, the 1,3-dioxane ring, disubstituted at position 3 (by identical substituents R′) flips continuously at room temperature (Scheme 1).

These results have been inferred from high-field ^1H and ^{13}C NMR spectroscopic analysis carried out in C_6D_6.† The frozen inversion of the cyclohexane ring and the rapid inversion of the 1,3-dioxane ring lead to an enantiomeric interconversion (Scheme 1) as a consequence of the presence, in compounds **1–4**, of axial chirality [axis of chirality C(6)–C(9)].

For these compounds (**1–4**), the protons and the carbons at positions 2 and 4 are diastereotopic. Indeed, we can observe different signals for these diastereotopic protons and carbons (**1**: δ_H 4.51 and 4.59; δ_C 62.10 and 62.18. **2**: δ_H 4.47 and 4.57; δ_C 62.18 and 62.32. **3**: δ_H 3.32 and 3.40; δ_C 69.72 and 69.87. **4** δ_H 3.44 and 3.50; δ_C 69.79 and 70.00). So, the diastereotopicity of the protons is evaluated to be between 0.06 and 0.10 ($\Delta\delta_{H2,H4}$) and of the carbons to be between 0.06 and 0.21 ($\Delta\delta_{C2,C4}$).

Both of the stereochemical phenomena, that is, the mobility of the rings and the diastereotopicity of the 2 and 4 positions were revealed by a variable-temperature ^1H NMR experiment. The experiment (from 295 to 178 K) was carried out with compound **3** in deuteriated diethyl ether. When cooled to 183 K, the initial two singlets recorded at room temperature for the protons of the diastereotopic positions 2 and 4 (δ 3.41 and 3.45), were split into two well resolved AB systems (δ_{2e} = 3.57, δ_{2a} = 3.30; δ_{4e} = 3.72, δ_{4a} = 3.23) and the singlet (δ = 0.91) recorded at room temperature and assigned to the protons of C^3 methyl groups is also altered at low temperature into two singlets corresponding to the equatorial and axial (δ_e = 0.73 and δ_a = 0.89) methyl groups of the anancomeric 1,3-dioxane ring.

Furthermore, rather exciting results were obtained by a stereochemical study of trispiranes with a 7,11,18,21-tetraoxaspiro[5.2.2.5.2.2]henicosane skeleton. Thus, the trispiranes **5** and **6** also present a semi-mobile structure (Scheme 2), a feature which is similar to that observed for compounds **1–4**.



	R	R′
1	Me	CO_2Et
2	Bu^t	CO_2Et
3	Me	Me
4	Bu^t	Me

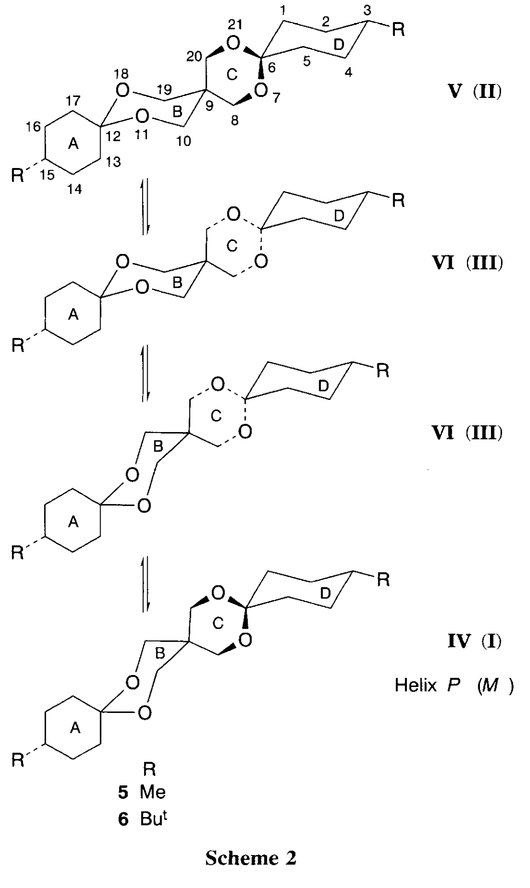
Scheme 1

This has been proved by their ^1H and ^{13}C NMR spectra in C_6D_6. The protons and the carbons of the diastereotopic positions 8(19) and 10(20) give two singlets (for **5**: δ_H 3.20 and 3.28; δ_C 63.37 and 63.53. **6**: δ_H 3.22 and 3.31; δ_C 63.45 and 63.68). The diastereotopicity of the protons and the carbon atoms are thus between 0.08 and 0.09 ppm [$\Delta\delta_{H8(19),H10(20)}$] and between 0.15 and 0.23 ppm [$\Delta\delta_{C8(19)C10(20)}$] respectively.

Compounds **5** and **6** present an inverting 1,3-dioxane middle section (B,C) and fixed terminal cyclohexane rings (A,D) bearing equatorial alkyl groups at positions 3 and 15.

A combined study by molecular-model observations and by NMR spectroscopy revealed that compounds **5** and **6** possess an axial chirality [axis of chirality C(3)–C(6) and C(12)–C(15)] and particularly, to the best of our knowledge, a helical chirality which has not been reported previously for spirane compounds. A spatial analysis by means of Dreiding models demonstrated that the helix returns to the original configuration after every eight hexaatomic cycles.

A variable-temperature (from 295 to 163 K) NMR analysis on compound **5** in deuteriated diethyl ether was performed. The two singlets [$\delta_{H8(19)}$ 3.64 and $\delta_{H10(20)}$ 3.68] belonging to the diastereotopic protons of the 1,3-dioxane rings, observed in the room temperature ^1H NMR spectrum, are transformed in the low-temperature spectra (*T* < 183 K) into four unresolved groups of signals located between δ 3.2 and 4.3 in agreement



R
5 Me
6 Bu^t

Scheme 2

with the differentiated equatorial and axial positions of the frozen 1,3-dioxane rings.

On the other hand the Eu chiral chelate, Eu(TFC)$_3$ in CDCl$_3$ solution does not separate the signals of the enantiomers of **5**, but determines the diastereotopicity of the geminal protons located at C(8)[C(19)] and C(10)[C(20)] respectively. The initial singlets (δ_1 = 3.66 and δ_2 = 3.73) are transformed into shifted AB systems, the most shielded one being well resolved (δ_{1a} = 4.00, δ_{1b} = 4.07, J = 12.0 Hz).

The stereoisomers of compounds **5** and **6** are presented in Table 1.

The inversion of the dioxane rings induces the interconversion of the isomers as shown in the equilibrium sequence given in Scheme 3.

This equilibrium is an unusual one, because it involves the interconversion between diastereoisomers having three elements of chirality but without the breaking of any bonds.

Table 1 Stereoisomers of compounds **5** and **6**

	Configuration			
Isomer	C(3)–C(6) axis	C(12)–C(15) axis	Helix	Enantiomer
I	*R*	*R*	*P*	**V**
II	*S*	*S*	*P*	**IV**
III	*R(S)*	*S(R)*	*P*	**VI**
IV	*R*	*R*	*M*	**II**
V	*S*	*S*	*M*	**I**
VI	*S(R)*	*R(S)*	*M*	**III**

$$\mathbf{I} \rightleftharpoons \overset{\text{Helix } M}{\mathbf{III}} \rightleftharpoons \mathbf{II} \qquad \mathbf{IV} \rightleftharpoons \overset{\text{Helix } P}{\mathbf{VI}} \rightleftharpoons \mathbf{V}$$

Scheme 3

At room temperature, the product is isolated as a racemic mixture because the change of helical chirality is possible only if the whole molecule is rebuilt. However once formed, the helix preserves its initial structure (*P* or *M* configuration).

Compounds **4**[6] and **6**[7] have been previously described and compounds **1–3** and **5** are new;[8] their syntheses will be described elsewhere.

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Footnote

† NMR spectra were obtained on a Bruker AM 400 spectrometer (with an Aspect 3000 calculator) operating at 400 MHz for ^{1}H and 100 MHz for ^{13}C. No SiMe$_4$ was added; chemical shifts were measured against the solvent peak.

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