

STEREOCHEMISTRY AND NMR SPECTRA OF SOME NEW 5-METHYL-2,2-SUBSTITUTED-1,3-DIOXANES

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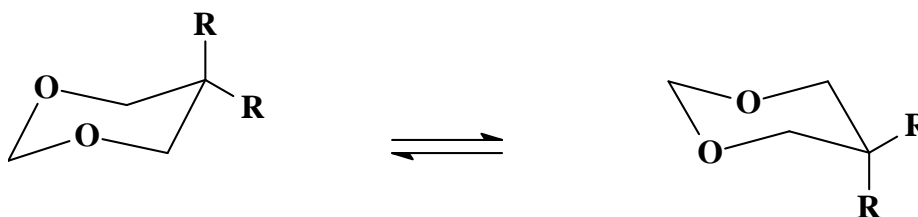
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ABSTRACT. The synthesis, stereochemistry and NMR spectra of some new 2,2- substituted-5-methyl-1,3-dioxanes are reported.

INTRODUCTION

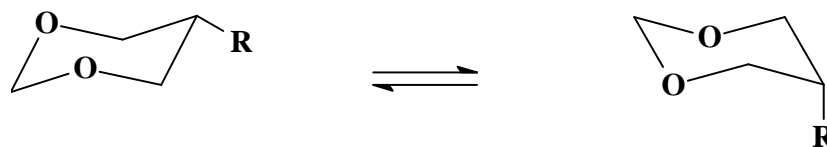
The 2 and/or 5-substituted-1,3-dioxanes display flipping or anancomeric structures, in correlation with the nature of the substituents. The compounds bearing identical substituents in the 5-position, exhibit flipping structure, with a rapid inversion of the heterocycle (Scheme1)¹⁻¹²

Scheme 1



Their NMR spectra exhibit unique signals for the axial and equatorial positions of the protons of the heterocycle and for the axial and equatorial positions of the protons and carbon atoms of the similar substituents.

For the monosubstituted 5-alkyl-1,3-dioxane derivatives, the conformational analysis revealed anancomeric structures, despite the fact that the value of the conformational free enthalpy is quite small (in comparison with the largest value for the alkyl groups located at the 2-position, e.g. $\Delta G^0_{\text{Me(position 2)}} = 3,98 \text{ kcal/mol}^{12}$, $\Delta G^0_{\text{Me(position 5)}} = 0,83 \text{ kcal/mol}^{13}$). The conformational equilibria are shifted towards the conformer having the alkyl substituent equatorially placed (Scheme 2)



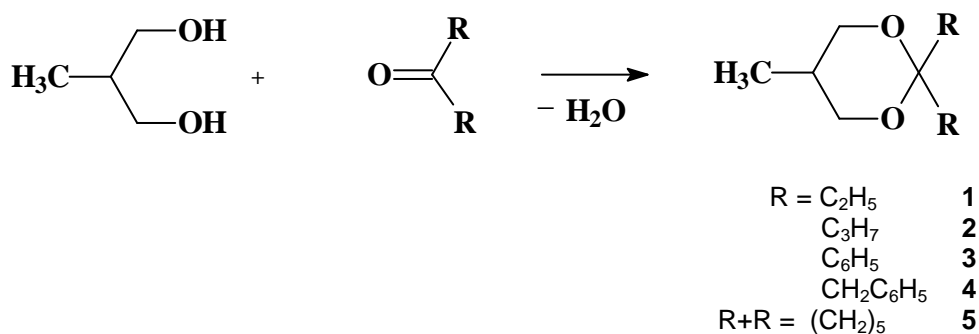
Scheme 2

The NMR spectra of these compounds exhibit different signals for the axial and equatorial protons of the 1,3-dioxane ring and for the protons and the carbon atoms of the equatorial and axial identical groups located in it.

It was considered of interest to study by means of NMR spectra the stereochemistry of some new 5-methyl-1,3-dioxanes bearing homomorphic groups in the position 2.

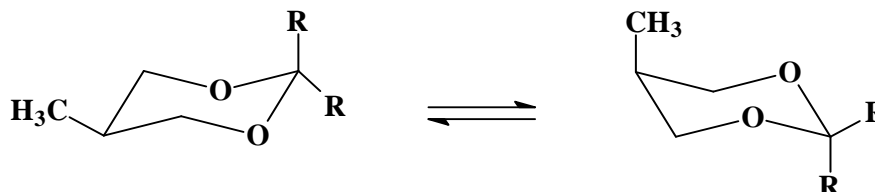
RESULTS AND DISCUSSION

New 1,3-dioxane compounds (**1-5**) have been obtained by the condensation reaction between 2-methyl-1,3-propanediol and symmetric ketones (Scheme 3):



Scheme 3

All the investigated compounds exhibit anancomeric structures, the conformational equilibria being shifted towards the conformations that display the 5-methyl group in equatorial orientation (Scheme 4):



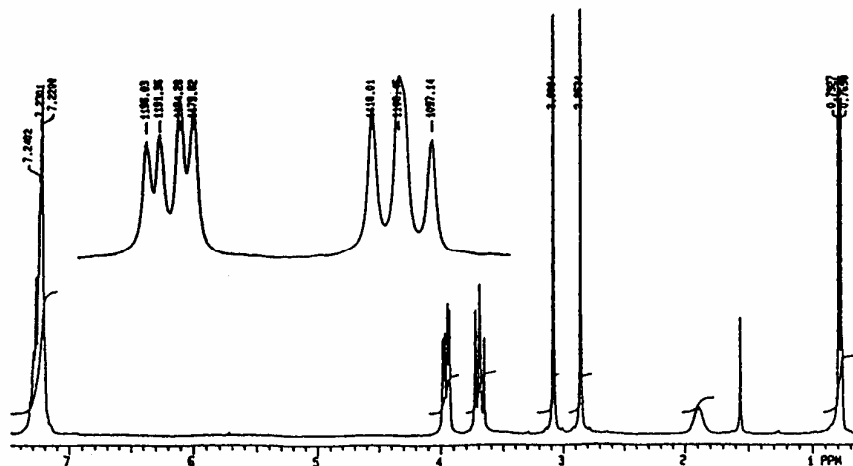
Scheme 4

The spectra of all these compounds exhibit different signals for the axial and equatorial orientations of the protons of the 1,3-dioxane ring and of the protons and carbon atoms of the identical alkyl groups located at the position 2 (Table 1).

Table 1¹H and ¹³C-NMR data for compounds 1-5

Comp.	¹ H-NMR			¹³ C-NMR			
	4,6-H _{ax}	4,6-H _{eq}	5-CH ₃	C ²	C ^{4,6}	C ⁵	5-CH ₃
1	3.22	3.58	0.44	100.59	65.56	23.18	13.28
2	3.28	3.60	0.47	100.16	65.61	29.43	13.35
3	3.42	3.77	0.31	-	67.72	29.57	13.01
4	3.69	3.95	0.78	100.17	66.01	28.94	13.27
5	3.59	3.25	0.44	97.12	64.96	29.32	12.88

As an example, the ¹H-NMR spectrum for compound 4 (Figure 1) displays different signals for the axial and equatorial protons at positions 4 and 6. The equatorial protons exhibit a doublet of doublet ($\delta_{4,6\text{ eq}} = 3.95$ ppm) due to a large geminal coupling constant ($J = 11.7$ Hz) and to a smaller coupling with the vicinal axial proton at position 5 ($^3J = 4.6$ Hz). The axial protons exhibit an overlapped doublet of doublet that gives a triplet ($\delta_{4,6\text{ ax}} = 3.69$ ppm; $^2J = ^3J = 11.7$ Hz). The spectrum also exhibits two singlets ($\delta = 2.85$ and $\delta = 3.08$ ppm) corresponding to the axial, respectively equatorial methylene protons of the benzyl groups, a multiplet ($\delta = 1.88$ ppm) for the axial proton at the position 5, a doublet ($\delta = 0.78$ ppm) for the protons of the equatorial methyl group and a multiplet ($\delta = 7.23$ ppm) for the aromatic protons.

**Fig.1.** ¹H-NMR Spectrum of compound 4

CONCLUSIONS

The NMR investigations of compounds **1-5** bearing similar substituents at position 2 and a methyl group at the position 5 of the 1,3-dioxane ring revealed anancomeric structures despite the smaller A values of the alkyl groups located in the aliphatic part of the heterocycle.

EXPERIMENTAL

^1H - and ^{13}C -NMR spectra were recorded at room temperature, using 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 1-5, 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 of benzene. The mixture was refluxed and the resulted water 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_3COONa powder in excess (0.2 g). The reaction mixture was washed twice with 100 ml water. The benzene was removed (after drying with Na_2SO_4) and the 1,3-dioxanic compounds were purified by crystallisation from ethanol or by vacuum distillation.

2,2-Diethyl-5-methyl-1,3-dioxane 1

Liquid, b.p.=186 $^{\circ}\text{C}$. Yield 54%. $\text{C}_9\text{H}_{18}\text{O}_2$, found C 69.33, H 11.07; required C 68.35, H 11.39%

^1H -NMR (C_6D_6): δ 0.44 (3H, d, $J = 6.7$ Hz, 5- $\text{CH}_{3\text{eq}}$), 0.86 (3H, t, $J = 7.5$ Hz, 2- $\text{CH}_2\text{CH}_{3\text{ax}}$), 1.05 (3H, t, $J = 7.5$ Hz, 2- $\text{CH}_2\text{CH}_{3\text{eq}}$), 1.62 (2H, q, $J = 7.5$ Hz, 2- $\text{CH}_2\text{CH}_{3\text{ax}}$), 1.77 (2H, q, 2- $\text{CH}_2\text{CH}_{3\text{eq}}$), 1.84-1.97 (H, m, 5- H_{ax}), 3.22 (2H, t, overlapped dd, $J = J' = 11.8$ Hz, 4,6- H_{ax}), 3.61 (2H, dd, $J = 11.8$ Hz, $J' = 4.7$ Hz, 4,6- H_{eq})

^{13}C -NMR (C_6D_6): δ 7.65 (2- $\text{CH}_2\text{CH}_{3\text{ax}}$), 8.17 (2- $\text{CH}_2\text{CH}_{3\text{eq}}$), 13.28 (5- CH_3), 23.18 (C^5), 29.39 (2- $\text{CH}_2\text{CH}_{3\text{ax}}$), 29.52 (2- $\text{CH}_2\text{CH}_{3\text{eq}}$), 65.61 ($\text{C}^{4,6}$), 100.59 (C^2)

5-Methyl-2,2-dipropyl-1,3-dioxane 2

Liquid, b.p.=206 $^{\circ}\text{C}$. Yield 61%. $\text{C}_{11}\text{H}_{22}\text{O}_2$, found C 70.28, H 11.96; required C 70.96, H 11.82%

^1H -NMR (C_6D_6): δ 0.47 (3H, d, $J = 6.8$ Hz, 5- $\text{CH}_{3\text{eq}}$), 0.88-0.97 (6H, overlapped peaks, 2- $\text{CH}_2\text{CH}_2\text{CH}_{3(\text{ax+eq})}$), 1.30-1.80 (9H, overlapped peaks, 2- $\text{CH}_2\text{CH}_2\text{CH}_{3(\text{ax+eq})}$ + 5- H_{ax}), 3.28 (2H, t, overlapped dd, $J = J' = 11.8$ Hz, 4,6- H_{ax}), 3.60 (2H, dd, $J = 11.8$ Hz, $J' = 4.6$ Hz, 4,6- H_{eq})

^{13}C -NMR (C_6D_6): δ 13.35 (5- CH_3), 14.74 (2- $\text{CH}_2\text{CH}_2\text{CH}_{3\text{ax}}$), 14.82 (2- $\text{CH}_2\text{CH}_2\text{CH}_{3\text{eq}}$), 16.76 (2- $\text{CH}_2\text{CH}_2\text{CH}_{3\text{ax}}$), 17.34 (2- $\text{CH}_2\text{CH}_2\text{CH}_{3\text{eq}}$), 29.43 (C^5), 33.57 (2- $\text{CH}_2\text{CH}_2\text{CH}_{3\text{ax}}$), 39.69 (2- $\text{CH}_2\text{CH}_2\text{CH}_{3\text{eq}}$), 65.61 ($\text{C}^{4,6}$), 100.16 (C^2)

5-Methyl-2,2-diphenyl-1,3-dioxane 3

Solid, m.p. = 150⁰C. Yield 66%. C₁₇H₂₂O₂, found C 81.03, H 6.82; required C 80.31, H 6.82%

¹H-NMR (C₆D₆): δ 0.31 (3H, d, J = 6.6 Hz, 5-CH_{3eq}), 1.81 (H, m, 5-H_{ax}), 3.42 (2H, t, overlapped dd, J = J' = 11.3 Hz, 4,6-H_{ax}), 3.77 (2H, dd, J = 11.3 Hz, J' = 4.2 Hz, 4,6-H_{eq}), 7.0-7.80 (10H, m)

¹³C-NMR (C₆D₆): δ 13.01 (5-CH₃), 29.57 (C⁵), 67.72 (C^{4,6}), 126.48, 128.08, 128.39, 128.92 (aromatic carbon atoms)

2,2-Dibenzyl-5-methyl-1,3-dioxane 4

Solid, m.p.=58⁰C. Yield 76%. C₁₉H₂₂O₂, found C 81.40, H 7.63; required C 80.85, H 7.80%

¹H-NMR (C₆D₆): δ 0.78 (3H, d, J = 6.9 Hz, 5-CH_{3eq}), 1.88 (H, m, 5-H_{ax}), 2.85 (2H, s, CH_{2ax}), 3.08 (2H, s, CH_{2eq}), 3.69 (2H, t, overlapped dd, J = J' = 11.7 Hz, 4,6-H_{ax}), 3.95 (2H, dd, J = 11.7 Hz, J' = 4.6 Hz, 4,6-H_{eq}), 7.23 (10H, m)

¹³C-NMR (C₆D₆): δ 13.27 (5-CH₃), 28.94 (C⁵), 38.17 (CH₂Ph_{ax}), 43.22 (CH₂Ph_{eq}), 66.01 (C^{4,6}), 100.17 (C²), 126.36, 126.48, 127.86, 128.20, 130.86, 131.41, 137.31, 137.54 (aromatic carbon atoms)

3-Methyl-1,5-dioxaspiro[5.5]undecane 5

Solid, m.p.=66⁰C. Yield 57%. C₁₀H₁₈O₂, found C 70.01, H 10.86; required C 70.59, H 10.60 %

¹H-NMR (C₆D₆): δ 0.44 (3H, d, J = 6.8 Hz, 3-CH_{3eq}), 1.30 (2H, m, H⁹), 1.43 (2H, m, H⁸), 1.59 (2H, m, H¹⁰), 1.73 (3H, m, overlapped peaks, H⁷, H³), 1.78 (2H, m, H¹¹), 3.25 (2H, t, overlapped dd, J = J' = 11.9 Hz, 2,4-H_{ax}), 3.59 (2H, dd, J = 11.9 Hz, J' = 4.8 Hz, 2,4-H_{eq})

¹³C-NMR (C₆D₆): δ 12.88 (3-CH₃), 22.52, 22.64 (C^{8,10}), 25.89 (C⁹), 29.10 (C^{7,11}), 29.32 (C³), 64.96 (C^{2,4}), 97.12 (C⁶)

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