¹H NMR Investigations on the Conformation of the Spirodioxolanes Derived from Vicinal Diols II[†]—The Ketal of Cyclohexanone and Racemic 1,2-Propanediol

C. Csunderlik, T. Chirilă* and R. Bacaloglu

Department of Organic Chemistry, Traian Vuia Polytechnic Institute, Timişoara 1900, Rumania

The methylene, methine and methyl protons at C-2 and C-3 from the dioxolane moiety in 2-methyl-1,4dioxaspiro[4.5]decane constitute an ABMX₃ coupling system. The analysis data obtained and, also, the application of the Karplus rule to the value of the J(AB) vicinal coupling constant, confirm the axial orientation of the A methine proton and the pseudoequatorial orientation of the B methylene proton. These findings agree with a 'half-chair' conformation of the 1,3-dioxolane ring.

INTRODUCTION

The conformation of the dioxolane ring in 2,2-gemdisubstituted 1,3-dioxolanes (A), bearing a CH_2Z group at C-4, has probably a 'half-chair' geometry (C₂ symmetry). This assumption is considered to be quite valid for 1,3-dioxolanes,² in spite of critical remarks on such an apparent oversimplification.^{3,4} The ¹H NMR parameters and the orientation of the two methine hydrogens in a related compound were necessary for the determination of the orientation of the methine hydrogen at C-4, and of the methylene hydrogens at C-5, in the 4-substituted 1,3-dioxolanes A. An analysis of 2,3-dimethyl-1,4-dioxaspiro[4.5]decane (1), as a simple model for the A system, has been previously carried out.¹ The conformation of 2methyl-1,4-dioxaspiro[4.5]decane (2) has now been investigated by ¹H NMR spectroscopy and, to complete the conclusions, by ¹³C NMR spectroscopy.

2 Was obtained as an equilibrium mixture of the 2a and 2b conformers by acid catalysed ketalization of cyclohexanone with a racemic mixture (R+S) of 1,2-propanediol (Scheme 1).



The methyl group in 2a, with an equatorial orientation, is energetically more favoured than the axial methyl in 2b, as assumed for 5-membered rings.⁵

Although there are many reports on the cyclic acetalization (ketalization) of 1,2-propanediol,⁶⁻¹⁰ the diastereoisomerism of the reaction products are not so well investigated.^{2,3,11-15} These investigations suggest that 2a will prevail at equilibrium at room temperature, and the following analysis provides further evidence for this phenomenon.



Scheme 1

*Author to whom correspondence should be addressed at: ICECHIM-CCMP Research Laboratory, The Solventul Laboratory, spl. Titulescu 31, Timişoara 1900, Rumania. † For Part I, see Ref. 1.

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EXPERIMENTAL

Synthesis

A mixture of 1,2-propanediol (152.2 g, 2 mol), cyclohexanone (215.9 g, 2.2 mol), p-toluenesulphonic acid (1.5 g) and benzene (200 ml) was heated in a 100 ml three necked flask provided with a stirrer, Dean-Stark trap (with condenser) and thermometer. The mixture was refluxed for 2 h, by which time the temperature had reached 105 °C and 37 ml of water had collected in the trap. After neutralization with 3 g potassium hydroxide, filtration and distillation on a Vigreux column, 257.8 g (yield 82.5%) of a clear and colourless liquid of the pure spirodioxolane **2** resulted: b.p. 43-44 °C/4 mm and 48 °C/5.5 mm; n_D^{25} , 1.450; d_4^{25} , 0.9833 g ml⁻¹. Elem. Anal: found C, 69.43 %, H, 10.60 %; calc. C, 69.19 %, H, 10.32 %. This analysis was carried out with a Perkin-Elmer 240 B automatic analyser.

NMR spectra

The ¹H NMR spectra of **2** were recorded on a Tesla BS 487 C spectrometer (80 MHz), using TMS as internal standard and c. 0.2 M solutions in carbon tetrachloride, at 25 °C, with a sweep width of 5 Hz cm⁻¹ and a sweep rate of 1 Hz s⁻¹. The line frequencies and intensities were obtained by averaging the results of five measurements.

The ¹³C NMR spectra were recorded on a JEOL JNM-FX 60 Q Fourier transform spectrometer at 15 MHz, in 30% v/v chloroform- d_1 solutions, at 25 °C, using TMS as internal standard. The flip angle was 45°, and pulse repetition times of 3 s were applied. The number of accumulations was 560–1000, and the spectral width was 2800 Hz; the data capacity was 8 K.

RESULTS AND DISCUSSIONS

The three dioxolane ring protons and the exocyclic methyl protons in 2 form an ABMX₃ system (Fig. 1 (a)).

Similar coupling systems have already been described for some related compounds. Thus, for instance, in compounds **3** ($R^1 = R^2 = Me$; R = COOK, COOMe, CD₂OH, etc.)¹⁶ and also in **3** ($R^1 = R = Me$, $R^2 = H$; $R^1 = t$ -Bu, $R^2 = H$, R = Me),³ the three protons form ABC systems. In compounds **4** (n = 4-8, and 12), the same protons form ABX systems.¹⁷



Figure 1. The coupling paths in the stable conformers of 1 and 2. (a) In the 2a conformer; (b) in conformer (4e,5e') of *trans*-1.

In the ¹H NMR spectrum of 2, the ABM lines appear as two multiplets between 3.32 and 4.35 ppm, and the X_3 signals as a doublet at 1.24 ppm $[{}^{3}J(H, CH_{3}) = J(AX) = 5.50 \text{ Hz}]$. By irradiating the X₃ region the lower field multiplet becomes an approximate ABM system, which can be analysed as an ABX system.¹⁸ The spectral lines were completely assigned and the chemical shifts could, thus, be calculated $(\delta,ppm)\!:\!4.11$ (A), 3.95 (B) and 3.32 (M). The low field signal (δ_A) is easily assigned to the methine proton at C-2. The other two signals, corresponding to the two methylene protons at C-3, were assigned only by comparison with the chemical shifts of the methine protons at C-2 and C-3 in the 'trans' isomer of 1, with an axial orientation which has been already demonstrated.1 The chemical shift of the axial methine protons in this compound was found to be 3.56 ppm; accordingly, the pseudoaxial proton (H-M) in 2 is assigned to δ 3.32 ppm, and the pseudoequatorial proton (H-B), to δ 3.95 ppm. The values calculated for the spin-spin coupling constants are: J(AB) = 5.65 Hz, J(AM) = 8.40 Hz and J(BM) = -8.40 Hz.

Using this parameter set $[\delta_A, \delta_B, \delta_M, J(AB), J(AM), J(BM)$ and the signs of these coupling constants], the ABM type spectrum was calculated and simulated. Good agreement was observed between the simulated and experimental decoupled spectra.

Couplings in the ABM system

The large difference between the J(AB) and J(AM) vicinal coupling constants is explicable only if the **2a** conformer prevails at equilibrium in the mixture. In this conformer, the ϕ_{23}^{AB} and ϕ_{23}^{AM} dihedral angles must be quite different, while in **2b** these angles have almost the same value. If the **2b** conformer was dominant in the mixture, the above mentioned coupling constants should be smaller and almost equal. In addition, the value of J(AM) is very close to J(AA') = 8.21 Hz from **1** where the A' proton is axial¹ (Fig. 1(b)). The A proton in **2** is in a similar conformational environment and, consequently, must be axial, i.e. as in the more favoured **2a** conformer.

Using the Karplus equation ¹⁹⁻²¹ for the estimation of the ϕ_{23}^{AB} dihedral angle by means of the J(AB) value (5.65 Hz), and taking into account the orientation of the electronegative endocyclic oxygen atoms (the vicinal coupling constant for a zero value of the dihedral angle, J^0 , was between 7 and 10 Hz), the dihedral angle was estimated to be between 25 and 45°. Thus, the pseudoequatorial orientation of H-B is fully demonstrated.

Couplings in the ABMX₃ system

The value of J(AX) is 5.50 Hz, which is normal for the vicinal couplings between a methyl group attached to cyclic systems and endocyclic methine protons.

The long-range J(MX) and J(BX) coupling constants describe typical 1,3-gauche methyl-proton interactions. It is known that these interactions are

characterized by small²² and negative²³ coupling constants. The negative sign is probably due to a particular type of spin-spin coupling mechanism.²⁴ The absolute value of J(MX) was directly calculated from the experimental spectrum (0.30 Hz). This value is greater than that (0.147 Hz) of the similar coupling constant, J(AX'), in the stable conformer of 1^1 and supports Bothner-By and Naar-Colin's hypothesis²⁵ concerning the simultaneous increase of the long-range coupling constant with the increase in the vicinal coupling constant involving the same structural sequence.

The non-zero value for J(MX) is also an argument for the fact that conformer **2**a prevails at equilibrium in the reaction product. Anteunis and Alderweireldt showed¹³ that this spin-spin coupling occurred only in the Z diastereoisomer of 2,4-dimethyl-1,3-dioxolane (**3**, $R = R^1 = Me$, $R^2 = H$) which has an equatorially oriented methyl group at C-4. This orientation is also found in **2**a.



Figure 2. The ¹H NMR spectrum of the coupling path CH_3 — CH_-CH_2 — from the **2a** conformer; coupled (ABMX₃). (a) Observed spectrum; (b) calculated spectrum.

An ABMX₃ spectrum was simulated to confirm the deduced set of parameters. For this purpose, a reasonable value of -0.30 Hz was taken for J(BX) and the spectrum was computed with the NMR-LAOCN-4A program.^{26,27} The calculated and observed spectra are presented in Fig. 2.

¹³C NMR Spectra

The proton noise decoupled ¹³C NMR spectra of the **1** and **2** compounds (see Table 1) do not offer new information on the conformation of these molecules. The downfield shift (2–4 ppm) of the C-5 signal, (Table 1), compared with 2-alkyl substituted 1,3-dioxolanes,²⁸ however, should be noted and also the large downfield shift (c. 6 ppm) of the C-2 and C-3 signals in **1**, probably caused by the *trans-e,e'* position of the two methyl groups.^{29,30}

CONCLUSIONS

The investigation of the 1,3-dioxolane moiety in the ¹H NMR spectrum of 2-methyl-1,4-dioxaspiro[4.5]decane, corresponding to an ABMX₃ coupling system, was possible from the results of the previous analysis of the related 2,3-dimethyl-1,4dioxaspiro[4.5]decane spectrum. The application of computer simulation techniques led to the determination of all NMR parameters. These values, and also the results of the specific application of the Karplus equation to the vicinal coupling constants, have indicated that the conformer possessing an equatorial methyl group is dominant at equilibrium.

All data are in good accord with a 'half-chair' geometry for the 1,3-dioxolane ring conformation.

Table 1. The ¹³C NMR chemical shifts in the spectra of the spirodioxolanes, 1 and 2

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| | Chemical shifts in ppm (TMS) | | | | | | | | | |
| Compound | C-2 | C-3 | C-5 | C-6 | C-7 | C-8 | C-9 | C-10 | 2-CH ₃ | 3-CH₃ |
| 1 | 77.86 | 77.86 | 108.12 | 36.91 | 23.86 | 25.27 | 23.86 | 36.91 | 17.00 | 17.00 |
| 2 | 71.58 | 70.4 9 | 109.22 | 35.45 | 23.91 | 25.27 | 24.04 | 36.77 | 18.73 | |
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