PROTON MAGNETIC RESONANCE SPECTRA AND CONFORMA-TIONAL PROPERTIES OF SPIRO[2.5]OCTAN-6-OL

A. S. ORAHOVATS, V. S. DIMITROV AND S. L. SPASSOV Institute of Organic Chemistry, Bulgarian Academy of Sciences, Sofia 13 (Bulgaria) (Received November 4th, 1969)

ABSTRACT

The free energy difference $(-\Delta G_0)$ for the axial-equatorial conformational equilibrium of spiro[2.5]octan-6-ol in CS₂ has been found with the aid of PMR spectra taken at low temperatures, to be 0.79 kcal mole⁻¹ at -75 °C. An Arrhenius activation energy of ring inversion of 14.4 ± 1.3 kcal mole⁻¹ has been obtained by the variable-temperature NMR total line-shape method.

INTRODUCTION

Interest in the influence of cyclohexane ring deformation on the conformational energy of the hydroxyl group¹⁻⁴ has led us to prepare spiro[2.5]octan-6-ol (I), a compound in which the ring might be expected to be additionally flattened as a result of the cyclopropane ring attached in the spiro position. The 6-hydroxy derivative was chosen, as the substituent is then relatively far from the ring junction. A significantly different value of the equilibrium constant for the equilibrium shown in Fig. 1 in comparison with that of cyclohexanol itself would be considered to be an indication of ring deformation.

While this work was in progress Stolow, Groom and McMaster⁵ reported among other values one of 0.7 kcal mole⁻¹ for the free energy difference for the equilibrium shown in Fig. 1, obtained by comparing the line-width of the tertiary proton measured at room temperature with those of suitable model compounds



Fig. 1. Axial-equatorial conformational equilibrium of spiro[2.5]octan-6-ol.

containing tertiary butyl groups. We report here the results obtained by a direct and more reliable method^{4,6} of studying such conformational equilibria, namely the low-temperature measurement of the NMR signal area for the C-6 protons of the "frozen" equatorial and axial conformers after deuteration at the C-5 and C-7 positions. A variable-temperature NMR study of the barrier to ring inversion using the total line-shape method was also undertaken.

RESULTS AND DISCUSSION

A room-temperature PMR spectrum of spiro[2.5]octan-5,5,7,7- d_4 -6-ol (II) is shown in Fig. 2. The tertiary proton signal undergoes broadening on cooling and, below -70 °C, becomes a well-separated doublet (Fig. 2, top). Some fine splitting due to CH-OH and CH-CD coupling, with a CH-OH coupling constant of 2.8 Hz, is also evident.



Fig. 2. PMR spectrum of spiro[2.5]octan-5,5,7,7-d₄-6-ol at 60 MHz.

The tertiary proton signal area from 29 spectra recorded in the temperature range of -55° to $-106 \,^{\circ}$ C was used to determine the ratio of the conformers. From it, a free energy difference of 0.79 kcal mole⁻¹ (at $-75 \,^{\circ}$ C) was calculated for the conformational equilibrium of II as depicted in Fig. 1. The mathematical treatment of the data by a computer-programmed least-squares method failed to reveal the existence of a systematic trend of the conformer ratio in the temperature interval studied, thus suggesting an entropy factor close to zero in agreement with recent results for cyclohexanols in aprotic solvents⁴.

The conformational energy of the hydroxyl group of II determined in this work falls well within the range of values obtained by various methods for cyclo-

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hexanols¹⁻⁴ (0.5–0.9 kcal mole⁻¹ at 25 °C) which suggests that the distortion of the six-membered ring in spiro[2.5]octan-6-ol·is relatively small. This result is in agreement with the observations reported by Uebel and Martin⁷ for the similar compound, 1,2-diaza-6-methyl-spiro[2.5]-1-octene, for which they found a conformational energy of the methyl group close to that in methylcyclohexanes.

The determination of the barrier to ring inversion of II was performed by the line-shape method⁸. The calculation of the theoretical spectra of the C-6 proton was carried out by a GIER computer using a Gier Algol 4 coded program based on the general equation for exchange between two unequally populated noncoupled sites (ref. 9, eqn. 4). The input of the program included the chemical shift difference between the tertiary proton signals of both conformers at slow exchange (33.5 Hz at 60 MHz), the mole fractions of the conformers N_a and N_e , the meanlife-time $\tau = \tau_a \tau_e / (\tau_a + \tau_e)$, and the "effective" relaxation time T_2 . The latter was adjusted so as to correspond to the experimental line width in the slow exchange spectra and the same value was used for calculations at higher temperatures. The comparison of the experimental and calculated spectra was made visually.

The Arrhenius parameters for ring inversion were obtained from a computer least-squares fit to the variation of the logarithm of the rate constant with the reciprocal of temperature. The calculated Arrhenius activation energy for the ring inversion of II and the logarithm of the frequency factor are 14.4 ± 1.3 kcal mole⁻¹ and 15.5 ± 1.3 sec⁻¹ respectively (standard deviations given). The values for the individual conformers calculated from the respective plots are within the error range of the above values.

The activation energy for ring inversion of spiro[2.5]octan-6-ol found in the present work is rather high compared with the values of 10–12 kcal mole⁻¹ obtained by various authors for cyclohexane¹⁰. This corresponds to the recent results of Anderson¹¹, according to which spiro-attached small rings in the 2-position of 1,3-dioxanes increase their inversion barriers. However, a better understanding of the effect of the attached cyclopropyl ring requires the determination of the inversion barrier of spiro[2.5]-octane itself.

EXPERIMENTAL

The PMR measurements were carried out on a JEOL JNM-C-60S spectrometer operating at 60 MHz, calibrated by the usual side-band technique. The lowtemperature measurements were performed with a JEOL JES-VT-2 Variable Temperature Controller. The temperatures were measured using a copper-constantan thermocouple calibrated against the methanol chemical shift and are believed to be accurate to within ± 3 °C. All spectra were taken using 5–10 % w/v solutions in carbon disulfide.

Synthesis

4-Benzoyloxycyclohexan-1-one¹³ was chosen as a starting material on the synthetic route to the alcohol I^{*}. The conversion of the keto group into a methylene group was accomplished by carrying out the Wittig reaction¹⁴ with methylene-triphenylphosphorane in dimethylsulfoxide. The 4-methylenecyclohexyl benzoate (b.p. 105 °C/0.13 mm) was obtained in 48 % yield.

The methylene alcohol (b.p. 100 °C/45 mm) obtained in 83 % yield on alkaline hydrolysis of the benzoate afforded, on treatment with methylene iodide and a zinc-copper couple according to the Simmons and Smith procedure¹⁵, the desired spiro[2.5]octan-6-ol (I) (m.p. 37 °C, b.p. 100 °C/27 mm) in 51 % yield. The 5,5,7,7-tetradeuteriospiro[2.5]octan-6-ol (II) was prepared by D₂O-exchange in spiro[2.5]octan-6-one (b.p. 93-4 °C/32 mm, semicarbazone m.p. 188-90 °C; obtained by chromic acid oxidation of I) and subsequent reduction with lithium aluminium hydride.

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^{*} The synthesis of I is described in detail in ref. 12.

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