Equilibrium between Hydroxycycloalkanones and Oxabicycloalkanols

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Hydroxycycloalkanones 1 of medium ring size (8 – 10) exist in a transannular tautomeric equilibrium with the corresponding oxabicycloalkan-1-ols 2, which represent hemiacetals. Normally, the bicyclic structures 2 predominate in solution although their portion decreases with increasing solvent polarity. A correlation of the Gibbs reaction enthalpies \( \Delta G (1 \rightarrow 2) \) with the solvent parameters \( E_T \) (30) is presented.

Key words: Hemiacetals, Hydroxyketones, Solvent Polarity, Transannular Tautomerism

Introduction

Several examples of (substituted) hydroxycycloalkanones 1 are known, which exist in a transannular tautomeric equilibrium with the corresponding oxabicycloalkan-1-ols 2 (Fig. 1). The oxygen bridge can span six-membered [1], seven-membered [2, 3], eight-membered [2 – 7], nine-membered [8], ten-membered [8 – 10] or possibly larger rings. The equilibrium can have a considerable influence on the reactions of the tautomers, in particular on the dehydration of 2 to yield anti-Bredt enol ethers [11, 12]. Such enol ether functionalities are present in numerous natural products and represent a synthetic challenge [12].

Results and Discussion

Results of an \textit{ab initio} calculation [13] of 5-hydroxycyclooctanone (1b) and its energetically favored hemiacetal, 9-oxabicyclo[3.3.1]nonan-1-ol (2b), prompted us to report our experimental study on the hydroxyketone/hemiacetal equilibria 1a – 1c \textleftrightarrow 2a – 2e (Fig. 2).

We used standard methods for the preparation of 1a/2a [3 – 7], 1b/2b [14], 1c/2c [4], and 1e/2e [10].
Table 1. $^1$H NMR signals of the OCH groups in $1a$–$2a$–$e$ and ratios $1/2$.

<table>
<thead>
<tr>
<th>Hydroxy-ketone</th>
<th>δ $^b$</th>
<th>Hemiacetal</th>
<th>δ $^b$</th>
<th>Solvent</th>
<th>Ratio $1/2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$1a$</td>
<td>3.70</td>
<td>$2a$</td>
<td>4.37</td>
<td>CDCl$_3$</td>
<td>22 : 78</td>
</tr>
<tr>
<td>$1b$</td>
<td>3.71</td>
<td>$2b$</td>
<td>4.38</td>
<td>CDCl$_3$</td>
<td>3 : 97</td>
</tr>
<tr>
<td>$1c$</td>
<td>3.70</td>
<td>$2c$</td>
<td>4.08</td>
<td>CDCl$_3$</td>
<td>4 : 96</td>
</tr>
<tr>
<td>$1d$</td>
<td>3.75</td>
<td>$2d$</td>
<td>4.00</td>
<td>CDCl$_3$</td>
<td>24 : 76</td>
</tr>
<tr>
<td>$1e$</td>
<td>3.83</td>
<td>$2e$</td>
<td>4.07</td>
<td>CDCl$_3$</td>
<td>45 : 55</td>
</tr>
</tbody>
</table>

The other signals, which belong to the CH$_2$ groups of $1$ and $2$, strongly overlap in the region $2.7 \leq \delta \leq 1.1$ ppm; $^b$ in CDCl$_3$ solution; $\delta$ values in ppm relative to TMS.

Table 2. $^{13}$C NMR data of the hydroxyketones $1a, c$–$e$ and the hemiacetals $2a$–$e$.

<table>
<thead>
<tr>
<th>Hydroxy-ketone</th>
<th>Hemi-acetal</th>
<th>Solvent</th>
<th>C=O</th>
<th>OC$_2$O</th>
<th>HCO</th>
<th>CH$_3$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$1a$</td>
<td>$2a$</td>
<td>CDCl$_3$</td>
<td>217.3</td>
<td>70.4</td>
<td>40.0, 39.2, 33.3, 30.3, 28.4</td>
<td>21.7</td>
</tr>
<tr>
<td>$2a$</td>
<td>$1b$</td>
<td>CDCl$_3$</td>
<td>108.1</td>
<td>75.6</td>
<td>41.4, 36.9, 36.1, 30.9, 23.6, 23.1</td>
<td></td>
</tr>
<tr>
<td>$2b$</td>
<td>$1c$</td>
<td>CD$_2$OD</td>
<td>93.4</td>
<td>72.4</td>
<td>36.1, 28.3, 20.7</td>
<td></td>
</tr>
<tr>
<td>$2c$</td>
<td>$1d$</td>
<td>CD$_2$OD</td>
<td>98.7</td>
<td>73.7</td>
<td>37.3, 37.2, 31.3, 28.8, 22.5, 21.2, 18.6</td>
<td></td>
</tr>
<tr>
<td>$2d$</td>
<td>$1e$</td>
<td>CD$_2$OD</td>
<td>96.2</td>
<td>73.6</td>
<td>37.6, 37.3, 32.6, 32.0, 27.8, 25.0, 21.7, 17.2</td>
<td></td>
</tr>
<tr>
<td>$2e$</td>
<td></td>
<td>CD$_2$OD</td>
<td>103.5</td>
<td>76.6</td>
<td>41.7, 34.6, 24.3, 23.9</td>
<td></td>
</tr>
</tbody>
</table>

$^a$ The portion of $1b$ was too small (~3 %) for a reliable measurement; $\delta$ values in ppm relative to TMS.

The new compounds $1d/2d$ were obtained by oxidation of cyclodecane-1,5-diol [15, 16] with Jones reagent (CrO$_3$, H$_2$SO$_4$).

The equilibria $1/2$ were determined by $^1$H and $^{13}$C NMR measurements. The relevant $^1$H NMR sig-
Experimental Section

The correlation coefficients for the linear relations are between 0.92 and 0.99, linearity of the correlations is not stringent. Further solvents have to be included in the study.

Conclusion

Cyclooctanones, -nonanones and -decanones 1a – 1e with hydroxy groups in 4-, 5- or 6-position show a transannular tautomerism to the corresponding hemiacetals 2a – 2e. The oxabicycloalkan-1-ols 2a – d represent the major components in the equilibria although their portion decreases with increasing solvent polarity. As an exception, 6-hydroxycyclodecanone (1d), in benzene still the minor component, is the pre-dominating tautomer in chloroform, dimethylsulfoxide and methanol. In large-ring hydroxyketones, with 12- and 15-membered rings, the transannular tautomerism does not play a role [18, 19]. The compounds studied here exhibit correlations between the Gibbs reaction enthalpies ΔG (1→2) and the solvent parameters ET (30).

Experimental Section

The 1H and 13C NMR spectra were obtained on Bruker AM 400 and ARX 400 instruments. A Finnigan MAT 95 spectrometer served for the FD MS measurement. The elemental analysis was obtained in the microanalytical laboratory of the Institute of Organic Chemistry of the University of Mainz.

Compounds 1a/2a [3–7], 1b/2b [14], 1e/2e [4] and 1e/2e [10] were obtained according to the literature.

5-Hydroxycyclodecanone (1d)/11-oxabicyclo[5.3.1]undecan-1-ol (2d)

To cyclodecane-1,5-diol [15, 16] (7.75 g, 45.0 mmol), dissolved in 200 mL of acetone, Jones reagent (2.0 g, 20 mmol CrO3, 3.5 mL conc. H2SO4, 15 mL ice water) was slowly added with stirring at 0 – 5 °C. After stirring for 1 h, the mixture was filtered and the filtrate evaporated. The residue was dissolved in CH2Cl2, and the solution was washed with water and dried (Na2SO4). Column chromatography (4 × 80 cm2 SiO2, petrol ether (b. p. 40 – 70 °C)/diethyl ether) gave 2.04 g (40 %) of an oil, which solidified in the refrigerator at 5 °C to a wax. The yields were higher when 1.5 equivalents of diol for 1 equivalent of Jones reagent were used, but the purification was then more difficult. – 1H NMR (CDCl3): δ = 4.00 (m, 1H, 7-H, 2d), 3.75 (m, 1H, 5-H, 1d), 2.70 – 22.0 (m, 4H, 2-H, 10-H, 1d), 2.01 – 1.05 (m, 28H, 3-H, 4-H, 6-H, 7-H, 8-H, 9-H, 9-H of 1d and 2-H, 3-H, 4-H, 5-H, 6-H, 8-H, 9-H, 10-H of 2d). According to the integration of the 1H NMR spectrum, the ratio 1d:2d amounts to 24 : 76 (in CDCl3). – 13C NMR signals: see Table 2. – MS (FD): m/z (%) = 170 (100) [M]+. – C10H18O2 (170.25): calcd. C 70.55, H 10.66; found C 70.91, H 10.38.

Measurement of the tautomeric equilibria

The 1H NMR signals of the methine protons H(COH) in 1a – e and HCO in 2a – e are well separated, so that repeated signal integration furnished reliable concentration ratios c(2)/c(1). An independent determination by 13C NMR spectroscopy was possible by the inverse-gated decoupling method [20].

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References


