Keto-Enol Tautomerism. I. The Calorimetrical Determination of the Equilibrium Constant for Keto-Enol Tautomerism for Cyclopentanone

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The enol content of cyclopentanone was determined by calorimetrical measurement of the enthalpy of hydrolysis of cyclopentenyl methyl ether to cyclopentanone with the assumption that the thermodynamics of hydrolysis of any ROMe to ROH is the same as that for any other ROMe. The enthalpy of the ketonization of cyclopentenol was determined to be −7.87 kcal/mol in the liquid phase and −11.66 kcal/mol in the gas phase, at 25 °C. The enol content of cyclopentanone in the gas phase at 25 °C was found to be 2.5×10^{-7}%.

The equilibrium enol content of simple ketones (RR′HC·COR″: R, R′, and R″=H or allyl groups) is known to be very low, both in the neat substances and in aqueous solution. The enol content has been determined by several methods. Most of the measurements were based on the classical method in which the enol content was estimated by the rapid reaction of enol with bromine.

Schwarzenbach and Wittwer determined the enol content of cyclopentanone, cyclohexanone and acetone to be 0.0048, 0.02, and 0.00025%, respectively, by running a ketone solution of known concentration and a bromine solution of steadily increasing concentration at controlled rates through a reaction vessel and determining potentiometrically the moment at which excess bromine appears.[1]

Gero improved the bromine titration by the use of the most polar halogen available (iodine monochloride) instead of bromine, because the rate of the addition reaction is essential in order to obtain accurate information on the enol content. His values for cyclopentanone, cyclohexanone and acetone were 0.088, 1.2, and 0.00015 %, respectively.[2]

A careful work by Bell and Smith on the bromine titration[3] shows what large errors the method can lead to when the proper precautions are not taken. They found that the enol contents for cyclopentanone and cyclohexanone are, respectively, 0.0013 and 0.00041%, of which the latter is 3000 times as small as that reported by Gero.

Ultraviolet[4] and infrared[5] spectroscopy were also used as a mean of studying the keto-enol equilibria.

Calorimetry for Determining Equilibrium Constants for Keto-Enol Tautomerism. For simple ketones whose enol contents are relatively small, we planned to use an indirect method based on thermochemical measurements. This method is similar to that used by Sunner, who measured the heats of hydrolysis of *iso*-propenyl acetate and *m*-cresyl acetate.[6] He assumed that the heats of hydrolysis are identical for both of the esters and therefore claimed that the extra heat liberated in the hydrolysis of isopropenyl acetate is due to the subsequent ketonization of the initially formed enol. He got a value of the enthalpy change of 7 kcal/mol for ketonization in the liquid phase.

Jencks and co-workers have shown that the free energy of hydrolysis of ROAc's changes by 14.0±0.5 kcal/mol as R is changed from ethyl through phenyl and *p*-nitrophenyl to acetyl.[7] We believe that this method could be improved upon by eliminating the assumption that the heat of hydrolysis of one ROAc to ROH is the same as that of another. It is better to assume that the thermodynamic parameters of hydrolysis of any ROMe (or ROEt or ROPr-n, *etc.*) to ROH are approximately the same whether R is changed. In support of this assumption is the fact that as R is changed from methyl through phenyl to acetyl[8] the free energy of hydrolysis of ROMe changes by 1.7 kcal/mol.[9] Therefore, we shall measure the heats of hydrolysis of various enol methyl ethers and assume the heat of hydrolysis to ROH is the same as that for some ROMe for which the heat of hydrolysis is known reliably (and if possible for an ROMe that is structurally as closely related as possible to the enol methyl ether in question), *e.g.*,

$$\mathrm{CH_2{=}CROMe + H_2O \longrightarrow CH_3CRO + MeOH} \quad \Delta H_1 \quad (1)$$

$$\mathrm{R'OMe + H_2O \longrightarrow R'OH + MeOH} \quad \Delta H_2 \quad (2)$$

$$\mathrm{CH_2{=}CROMe + H_2O \longrightarrow CH_2{=}CROH + MeOH} \quad \Delta H_3 \quad (3)$$

$$\mathrm{CH_2{=}CROH \longrightarrow CH_3CRO} \quad \Delta H_4\ \text{(Ketonization)} \quad (4)$$

obviously

$$\Delta H_1 = \Delta H_3 + \Delta H_4\ \text{(Ketonization)}$$

Since it is assumed that ΔH_3 is equal to ΔH_2

$$\Delta H_4\ \text{(Ketonization)} = \Delta H_1 - \Delta H_2$$

Both ΔH_1 and ΔH_2 can be determined experimentally and therefore ΔH_4 (Ketonization) may be calculated.

The following four values are experimentally determined in order to get ΔH_1 in the liquid phase;

$$\mathrm{CH_2{=}CROMe(liq) + H_2O{\cdot}S + S \longrightarrow CH_3CRO{\cdot}S + CH_3OH{\cdot}S} \quad \Delta H_5 \quad (5)$$

$$\mathrm{H_2O(liq) + S \longrightarrow H_2O{\cdot}S} \quad \Delta H_6 \quad (6)$$

$$\mathrm{CH_3CRO(liq) + S \longrightarrow CH_3CRO{\cdot}S} \quad \Delta H_7 \quad (7)$$

$$\mathrm{CH_3OH(liq) + S \longrightarrow CH_3OH{\cdot}S} \quad \Delta H_8 \quad (8)$$

where S's are solvents. The actual reaction taking place in the calorimeter is represented by Eq. 5. In order to obtain the isothermal ideal hydrolysis reaction, as defined by Eq. 9 or 1, it is necessary to calculate as follows:

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Eq. 5+Eq. 6−Eq. 7−Eq. 8

$$CH_2{=}CROMe(liq) + H_2O(liq) \longrightarrow CH_3CRO(liq) + CH_3OH(liq) \quad \Delta H_9 = \Delta H_1 \quad (9)$$

Experimental

Water used in making up solutions in this study was double-distilled. Traces of potassium permanganate and potassium hydroxide were added to the distilled water before the second distillation. Baker Analyzed reagent grade tetrahydrofuran was distilled over ferrous sulfate.[10]

Cyclopentenyl Methyl Ether. The preparation of cyclopentanone dimethyl ketal was based on the method of Arbuzov and Mikhailova.[11] Cyclopentanone (168 g) and trimethyl orthoformate (212 g) were placed into a 1 l round-bottomed flask fitted with a magnetic stirrer, a condenser, and an ice bath. Six drops of concentrated sulfuric acid were added, and the reaction proved to be exothermic, causing the colorless mixture to become brown. The ice bath was removed after an hour, and the reaction allowed to continue overnight. After the reaction mixture was allowed to stir for an hour with solid potassium bisulfite (80 g) and then filtered, the product was fractionally distilled to give 204.3 g (78.5% yield) of cyclopentanone dimethyl ketal, bp 60—63 °C at 50 mmHg. Cyclopentenyl methyl ether was prepared by pyrolysis of cyclopentanone dimethyl ketal. The dimethyl ketal (108 g) was boiled overnight while resulting methanol collected, and the product was fractionated to give 52.3 g (64%) of cyclopentenyl methyl ether, bp 108—109 °C, which was found by gas chromatographic (GLC) analysis to be 90.5% pure. The purer product, 99.5%, was obtained by preparative GLC. The NMR spectrum showed at τ 5.77, a singlet (1H), assigned to the olefinic proton: τ 6.62, a singlet (3H), assigned to methoxy protons, τ 7.88, a multiplet (4H), assigned to allylic methylene protons; τ 8.22, a multiplet (2H), assigned to homoallylic methylene protons.

Calorimetric Measurements. The Bunsen ice calorimeter was used. The apparatus and the experimental procedure were similar to those described previously[12] with the following exception: the outer jacket (chamber C) was evacuated to insulate internal chambers A and B from the surrounding medium after draining of water.

In order to confirm its reliability, the apparatus was first used to determine the enthalpy of neutralization of sodium hydroxide with hydrochloric acid. Three determinations gave values of 14.45, 14.62, and 14.50 kcal/mol. The average value, 14.52±0.09 kcal/mol, is in good agreement with the reported values,[13–15] and is 5.6% smaller than the value that should have been obtained as calculated from the calorimetrically determined heat of dissociation of water at 0 °C and infinite dilution[16] and the heats of dilution[17] of sodium hydroxide, hydrochloric acid, and sodium chloride.

Determination of Heats of Hydrolysis for Cyclopentenyl Methyl Ether. In these studies an ampoule containing about 1 g of enol methyl ether was broken in a solution of 1.817 g of distilled water and 0.411 g of 96.5% sulfuric acid in 24.747 g of tetrahydrofuran [30 ml of 91.67% THF–H_2O (0.15 mol/l H_2SO_4)]. Five determinations of heat evolved gave values of 4367, 4417, 4521, 4380, and 4404 cal/mol. The average value was 4418±61 cal/mol.

The reaction solution was analyzed by GLC. The reaction solution of 0.175 g (1.78×10^{-3} mol) cyclopentenyl methyl ether in 5 ml of 91.67% THF–H_2O (0.15 M H_2SO_4), which is almost the same concentration as that used in the calorimetrical measurements, was analyzed on a 10% Carbowax and 2% KOH column (2 m). From the ratios of the area of cyclopentanone to that of THF and area of methanol to that of THF, concentrations of the products, methanol and cyclopentanone, were obtained as 1.82×10^{-3} mol and 1.72×10^{-3} mol which were 102 and 96.7%, respectively, compared with the theoretical yields.

The reaction solution of 0.146 g (1.49×10^{-3} mol) cyclopentenyl methyl ether in 25 ml of 91.67% THF–H_2O (0.15 M H_2SO_4) was also analyzed on a 5% Carbowax 20 M on Chromosorb P column (2 m). The ratio of the area of methanol to that of cyclopentanone gave 1 : 1.18 as the mole ratio calculated from the estimated standard values.

The reaction solution was analyzed by UV spectrometry. From the absorbance at 281 nm of 0.042 M solution of cyclopentenyl methyl ether in THF–H_2O (0.15 M H_2SO_4), the conversion was calculated to be 106, 97.7, and 107% (103% in the average).

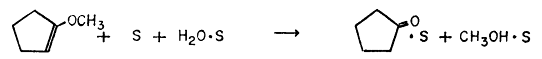
Determination of Heats of Solution for Cyclopentanone. In these studies an ampoule containing about 1—2 g of ketone was broken in a solution of 30 ml of 91.67% THF–H_2O (0.15 M H_2SO_4). Four determinations of heat absorbed gave values of 232, 319, 405, and 294 cal/mol. The average value was 312±72 cal/mol.

Determination of Heats of Solution for Methanol. In these studies an ampoule containing about 1 g of methanol was broken in a solution of 30 ml of 91.67% THF–H_2O (0.15 M H_2SO_4). Five determinations of heat evolved gave values of 21, 16, −8, 27, and 13 cal/mol. The average value was 14±13 cal/mol.

Determination of Heats of Solution for Water. In these studies an ampoule containing about 1 g of water was broken in a solution of 30 ml of 91.67% THF–H_2O (0.15 M H_2SO_4). Five determinations of heat evolved gave values of 198, 204, 190, 197, and 238 cal/mol. The average value was 206±19 cal/mol.

Discussion

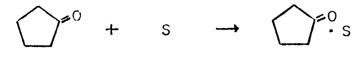
All values determined calorimetrically are as follows,



$$\Delta H_{10} = -4418 \pm 61 \text{ cal/mol} \quad (10)$$

$$H_2O + S \longrightarrow H_2O{\cdot}S$$

$$\Delta H_{11} = -206 \pm 19 \text{ cal/mol} \quad (11)$$

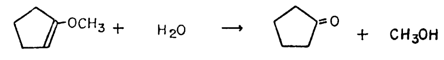


$$\Delta H_{12} = +312 \pm 72 \text{ cal/mol} \quad (12)$$

$$CH_3OH + S \longrightarrow CH_3OH{\cdot}S$$

$$\Delta H_{13} = +14 \pm 13 \text{ cal/mol} \quad (13)$$

where S's are solvents, and the ± figures are standard deviations. The actual reaction taking place in the calorimeter is represented by Eq. 10. In order to obtain the isothermal, ideal hydrolysis reaction (defined by Eq. 14) it is necessary to subtract Eq. 12 and 13 from 10 and to add 11. The following result is obtained.



$$\Delta H_{14} = -4950 \pm 165 \text{ cal/mol} \quad (14)$$

This value, −4950±165 cal/mol, is the heat of hydrolysis of the idealized reaction at 0 °C.

In order to obtain the heats of reaction at 25 °C, the

Kirchhoff's thermodynamic equation is used. The difference in the mean heat capacities at constant pressure of the products and reactants, ΔC_p, was estimated to be −4.9 cal/mol K.[18] Therefore, $\Delta H'_{14}$ (liq) = −5072±165 cal/mol, which is the heat of hydrolysis of the idealized reaction at 25 °C in the liquid phase for cyclopentenyl methyl ether, was obtained.

In order to calculate the heat of hydrolysis when both reactants and reaction are in the gaseous state it is necessary to know the heats of vaporization for all the compounds at 25 °C. The heat of vaporization of water, methanol,[20] cyclopentanone[22] and cyclopentenyl methyl ether[23] have been determined to be 10.47, 8.91, 9.67, and 9.4 kcal/mol, respectively.

The following five equations were used to calculate the heat of hydrolysis for cyclopentenyl methyl ether in the gas phase;

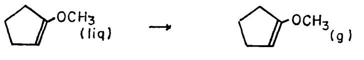
$$H_2O(liq) \longrightarrow H_2O(g)$$

$$\Delta H_{15} = +10.47\ \text{kcal/mol} \qquad (15)$$

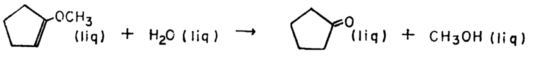
$$CH_3OH(liq) \longrightarrow CH_3OH(g)$$

$$\Delta H_{16} = +8.91\ \text{cal/mol} \qquad (16)$$

$$\Delta H_{17} = +9.67\ \text{kcal/mol} \qquad (17)$$



$$\Delta H_{18} = +9.4\ \text{kcal/mol} \qquad (18)$$



$$\Delta H_{19} = -5.07\ \text{kcal/mol} \qquad (19)$$

Then, −(15)+(16)+(17)−(18)+(19) gives the equation in the gaseous state. Therefore, $\Delta H'_{19}(g) = -6.36$ kcal/mol, which is the heat of hydrolysis for cyclopentenyl methyl ether at 25 °C in the gas phase, is obtained.

Heats of Ketonization. The hydrolysis of enol methyl ethers to ketones may be split into two consecutive steps, *viz.* the hydrolysis to enols, and the prototropic isomerization of enols to ketones:

$$R'R''C{=}CR'''OMe + H_2O \longrightarrow R'R''CHCOR''' + MeOH \quad \Delta H_{20} \qquad (20)$$

$$R'R''C{=}CR'''OMe + H_2O \longrightarrow R'R''C{=}CR'''OH + MeOH \quad \Delta H_{21} \qquad (21)$$

$$R'R''C{=}CR'''OH \longrightarrow R'R''CHCOR''' \quad \Delta H_{22}\ \text{(Ketonization)} \qquad (22)$$

A knowledge of the value of ΔH_{21} makes it possible to obtain a value of ΔH_{22} (ketonization), which is the reverse of the enolization reaction of ketones. The reaction for ΔH_{21} is of course not experimentally accessible; it is therefore necessary to estimate the accompanying change in enthalpy indirectly from the following reaction;

$$ROMe + H_2O \longrightarrow ROH + MeOH \quad \Delta H_{23} \qquad (23)$$

When R is methyl ΔH_{23} is 5.6 kcal/mol and when R is phenyl ΔH_{23} is 5.3 kcal/mol in the gas phase at 25 °C.[9] These two values were estimated to be 2.80 kcal/mol in the liquid phase.[24] Therefore, ΔH_{22} (Ketonization) can be obtained by $\Delta H_{20} - \Delta H_{23}$. In the liquid phase, value of ΔH_{22}(Ketonization) for cyclopentanone is −7.87 kcal/mol. In the gas phase, ΔH_{22} (Ketonization) for cyclopentanone can be estimated to be −11.66 kcal/mol, by taking the value of ΔH_{23} for phenyl which structurally resembles cyclopentenyl more than methyl does.

Free Energies for Ketonization. Benson and Buss have pointed out that entropies of compounds may be calculated reliably from structural contributions. Calculations, using the first-order approximation to the law of additivity of bond properties, gave +0.13 e.u. for the entropy of ketonization of cyclopentenol in the gas phase at 25 °C.[26,27] Therefore, free energy for the ketonization of cyclopentenol in the gas phase was −11.70 kcal/mol, which made the calculation of the equilibrium constant for the ketonization, K, and its reverse, $1/K$, which is the equilibrium constant for the enolization. They were 4.0×10^8 and 2.5×10^{-9}, respectively. Thus, the enol content of cyclopentanone was obtained to be $2.5 \times 10^{-7}\%$ in the gas phase at 25 °C.

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17) The heats of dilution used were determined at 25 °C. H. S. Harned and B. B. Owen, "The Physical Chemistry of Electrolytic Solutions," 3rd ed., Reinhold Publishing Corp., New York, N. Y. (1958), pp. 707, 708.

18) Mean heat capacities of water, methanol, and cyclo-

hexanone are 75.7, 78.2, and 177.8 J/K mol, respectively in the liquid phase.[19] Mean heat capacity of phenyl methyl ether, 200.8 J/K mol, was used instead of the value of cyclopentenyl methyl ether, and the value for cyclopentanone was taken as that cyclohexanone. To use the heat capacity of phenyl methyl ether for cyclopentenyl methyl ether may cause a large error, however, we believe that to take the value of cyclohexanone for cyclopentanone make this error minimized.

19) "International Critical Tables," Vol. 5, p. 106 (1929). Water: 4.220 at 0 °C, 4.210 at 5 °C, 4.199 at 10 °C, 4.190 at 15 °C, and 4.184 J/K g at 20 °C. Mean = 4.200 J/K g. Methanol: 2.37 at 0 °C, 2.51 J/K g at 20 °C, mean = 2.44 J/K g. Cyclohexanone: 1.812 J/K g at 15—18 °C. Phenyl methyl ether: 1.697 at 0 °C, 2.021 J/K g at 20—152 °C. Mean = 1.859 J/K g.

20) International Critical Tables, V. 5, p. 138 (1929). The heat of vaporization for methanol at 25 °C was calculated from that at 20 °C, 8.95 kcal/mol, and the heat capacities for the liquid and vapor, 80.3 J/K mol at 20 °C[19] and 43.9 J/K mol[21] at 25 °C, respectively.

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24) In order to calculate ΔH_3 in the liquid phase at 25 °C, the heat of vaporization of methyl ether, and of phenyl methyl ether were estimated from Klages equation[23] to be 4.55, 10.9 kcal/mol, respectively. Boiling points used were −23.6 °C for methyl ether and 155 °C for phenyl methyl ether.[25] The heat of vaporization of phenol was calculated to be 15.0 kcal/mol from another equation, $\Delta H_v = 6.8 + 0.045\,t$ kcal/mol, given by Klages where t is its normal boiling point, t °C. The boiling point is 182 °C. Those of water and methanol used were 10.47 and 8.95 kcal/mol,[20] respectively.

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27) The value of −2.5 for $\mathrm{C_{vi}}$–O bond was estimated from values of −16.4 and −14.3 for C–C and $\mathrm{C_{vi}}$–C, 12.9 and 13.8 for C–H and $\mathrm{C_{vi}}$–H, and −4.0 for C–O, respectively.