Keto-Enol Tautomerism. II.[1] The Calorimetrical Determination of the Equilibrium Constants for Keto-Enol Tautomerism for Cyclohexanone and Acetone

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The vapor phase enol contents of cyclohexanone and acetone were determined by calorimetric measurements of the enthalpies of hydrolysis of their corresponding enol methyl ethers to ketones and methanol in 91.67% THF–H_2O (0.15 M H_2SO_4). The relative order of enol content, together with cyclopentanone in our previous study, was cyclohexanone>cyclopentanone≧acetone, which was the same as that reported by Gero and by Schwarzenbach, but different from Bell's observed order (cyclopentanone>cyclohexanone>acetone). The enthalpies calculated from Benson's correlation of thermodynamic properties for the enolization reactions of these ketones and for the hydrolysis reactions of enol methyl ethers agreed with our relative ordering. Furthermore, data on reactions of compounds with 5- and 6-membered rings lead to the prediction that cyclohexanone contains more enol than cyclopentanone does. The kinetics of hydrolysis of enol methyl ethers was also discussed.

In an earlier paper[1] we described methods for determining the equilibrium enol content of simple ketones (RR'HC·COR": R, R', and R"=H or allyl groups) by calorimetric measurements of the enthalpies of hydrolysis of their corresponding enol methyl ethers to ketones and methanol, and by assuming that the thermodynamic parameters of hydrolysis of any ROMe to ROH are approximately the same whether R is changed. The enol content of cyclopentanone was obtained to be 2.5×10^{-7}% in the vapor phase at 25 °C.

The same method has been applied to cyclohexanone and acetone, and the relative order of enol content of these three ketone is discussed.

Experimental

Experiments which do not overlap with those reported in our previous paper[1] are described here.

Cyclohexenyl Methyl Ether. The preparation of cyclohexenyl methyl ether was analogous to that of cyclopentenyl methyl ether.[1] Pyrolysis of 43 g of cyclohexanone dimethyl ketal, bp 63—67 °C at 40 mmHg, gave 28.0 g (83% yield) of cyclohexenyl methyl ether, bp 140 °C, which was found by GLC analysis to be 92.2% pure. The purer product, 99.6%, was obtained by preparative GLC. Its NMR spectrum was identical with the reported spectra;[2] τ 5.5, a triplet (1H), assigned to the olefinic proton: τ 6.6, a singlet (3H), assigned to methoxy protons; τ 8.1, a multiplet (4H), assigned to allylic methylene protons; τ 8.5, a multiplet (4H), assigned to homoallylic methylene protons.

Isopropenyl Methyl Ether. The preparation of isopropenyl methyl ether was based on Kaufmann's method of preparation of propyl isopropenyl ether.[3] A mixture of 107 g of 2,2-dimethoxypropane, 7 g of quinoline, and 0.4 g of *p*-toluenesulfonic acid was allowed to reflux under a nitrogen blanket in a Todd distillation column and 34 g of the fraction boiling 34—52 °C was collected. This reaction was repeated in order to get more product. These mixtures were placed in a reflux set-up equipped with magnetic stirrer, condenser, and drying tube, and excess potassium metal carefully added through the condenser. After 2 h, the mixture was again distilled with the fraction boiling at 33.0—33.5 °C collected. This procedure was repeated to get the sufficiently pure (99.9%) isopropenyl methyl ether, bp 35.5 °C; [lit,[4] bp 35.2—35.6 °C/752 Torr, n_D^{20} 1.3824, d_4^{20} 0.7645]. NMR spectrum: τ 6.88, a singlet (2H), assigned to olefinic protons; 7.23, a singlet (3H), assigned to methoxy protons; τ 8.93, a singlet (2H), assigned to methyl protons.

Determination of Enthalpies of Hydrolysis for Enol Methyl Ethers. 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 24.847 g of tetrahydrofuran [30 ml of 91.67% THF–H_2O (0.15 mol/l H_2SO_4)].

Enthalpy of Hydrolysis of Cyclohexenyl Methyl Ether: Five determinations of heat evolved gave values of 2686, 2629, 2695, 2884, and 2888 cal/mol. The average value was 2756±121 cal/mol.

Ethalpy of Hydrolysis of Isopropenyl Methyl Ether: four determinations of heat evolved gave values of 5127, 5077, 5166, and 5174 cal/mol. The average value was 5136±44 cal/mol.

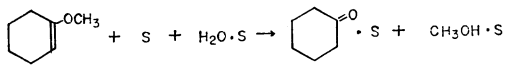
Determination of Heats of Solution for Ketones. In these studies an ampoule containing about 1—2 g of ketone was broken in a solution of 30 ml of 91.67% THF–H_2O (0.15 M H_2SO_4).

Enthalpy of Solution of Cyclohexanone: three determinations of heat absorbed gave values of 145, 170, and 162 cal/mol. The average value was 159±13 cal/mol.

Enthalpy of Solution of Acetone: five determinations of heat absorbed gave values of 162, 114, 145, 188, and 202 cal/mol. The average value was 162±35 cal/mol.

Results and Discussion

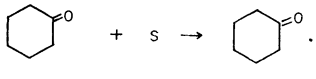
All values determined calorimetrically are as follows,



$$\Delta H_{1a} = -2756 \pm 121 \text{ cal/mol} \quad (1a)$$

$$CH_2{=}C(OCH_3)CH_3 + S + H_2O{\cdot}S \longrightarrow CH_3\overset{\overset{O}{\|}}{C}CH_3{\cdot}S + CH_3OH{\cdot}S$$

$$\Delta H_{1b} = -5136 \pm 44 \text{ cal/mol} \quad (1b)$$



$$\Delta H_{2a} = +159 \pm 13 \text{ cal/mol} \quad (2a)$$

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$$CH_3\overset{O}{\overset{\|}{C}}CH_3 + S \longrightarrow CH_3\overset{O}{\overset{\|}{C}}CH_3\cdot S$$

$$\Delta H_{2b} = +162 \pm 35 \text{ cal/mol} \quad (2b)$$

$$H_2O + S \longrightarrow H_2O\cdot S$$

$$\Delta H_3 = -206 \pm 19 \text{ cal/mol}^{1)} \quad (3)$$

$$CH_3OH + S \longrightarrow CH_3OH\cdot S$$

$$\Delta H_4 = +14 \pm 13 \text{ cal/mol}^{1)} \quad (4)$$

where S's are solvents, and the ± figures are standard deviations. In order to obtain the isothermal, ideal hydrolysis reaction it is necessary to subtract Eq. 2 and 4 from 1 and to add 3. Thus, the heats of hydrolysis of the idealized reaction in the liquid phase at 0 °C are −3135±166 and −5518±111 cal/mol for cyclohexenyl methyl ether and isopropenyl methyl ether, respectively.

These two values were corrected to those at 25 °C by following thermodynamic equation. Calculations[5] gave −3257±166 and −5745±111 cal/mol for cyclohexenyl and isopropenyl methyl ethers, respectively. These values are the heats of hydrolysis of the idealized reaction at 25 °C in the liquid phase.

In order to calculate the enthalpy 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. Those of water, methanol, cyclohexanone, acetone, cyclohexenyl methyl ether and isopropenyl methyl ether were 10.47, 8.91,[1] 10.61,[7] 7.61,[8] 10.62, and 6.68[9] kcal/mol, respectively. Therefore, the heats of hydrolysis for cyclohexenyl methyl ether and that for isopropenyl methyl ether at 25 °C in the gas phase were obtained to be −4.83 and −6.38 kcal/mol, respectively.

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. The heat of ketonization of RR'C=CR"OH can be estimated by assuming that, as carried out in the previous paper,[1] the heat of hydrolysis of RR'C=CR"-OMe to RR'C=CR"OH is the same as that of ROMe for which the heat of hydrolysis is known reliably to be 5.6 and 5.3 kcal/mol in gas phase when R is methyl and phenyl, respectively.[11] The heat of hydrolysis of ROMe was estimated to be 2.80 kcal/mol in the liquid phase.[1] Therefore, enthalpies of ketonization were −6.06 and −8.54 kcal/mol in the liquid phase for cyclohexanone and acetone, respectively. In the gas phase, depending on whether R is taken as methyl which is reasonable for isopropenyl, or phenyl which seems structurally a better model for cyclohexenyl, they were −10.13 and −11.98 kcal/mol for cyclohexanone and acetone, respectively.

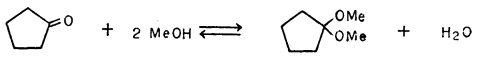
The entropies of ketonization of cyclohexenol and isopropenol were estimated to be +0.13 and −0.87 e.u., respectively, in the gas phase at 25 °C by calculations using the first-order approximation to the law of additivity of bond properties by Benson and Buss.[1,12] Therefore, free energies for the ketonization of cyclohexenol and isopropenol at 25 °C in the gas phase were −10.17 and −11.72 kcal/mol, respectively, 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 are summarized in Table 1, together with our previous study for cyclopentanone.[1]

Table 1. Equilibrium constant of ketonization, K, and enolization, $1/K$, in the gas phase at 25 °C

	K	$1/K$
Cyclopentanone[1]	4.0×10^{8}	2.5×10^{-9}
Cyclohexanone	3.0×10^{7}	3.3×10^{-8}
Acetone	4.2×10^{8}	2.4×10^{-9}

Kinetics of Reactions. It is interesting to note that one can find data from the literature to suggest that the reaction we studied should have been very rapid under our conditions. The hydrolysis of isopropenyl methyl ether was studied by Salomaa *et al.*[10] From their second-order rate constant at 25 and 35 °C in water, a second-order rate constant of 120 $M^{-1}\,s^{-1}$ may be calculated (from the Arrhenius equation) at 0 °C. In the presence of 0.15 M H_2SO_4 it would hydrolyze with a first-order rate constant of about 18 s^{-1} if the solvent was water. If the rate of protonation of the ether is the same in water and in 91.67% THF-8.33% water, then the half-life of the reaction we studied would be 0.04 s. Even if the real half-life is 1000 times as long as this, the reaction should be fast enough to study satisfactorily by the method we used. In the case of cyclohexenyl methyl ether, Lienhard and Wang have determined the second-order rate constant as 2810 $M^{-1}\,min^{-1}$ in water at 25 °C.[13] Similarly, it would give about 0.098 s for the half-life of the reaction in the presence of 0.15 M H_2SO_4 at 25 °C.

We must also be concerned as to whether there is any ketal present at the end of the reaction, due to the establishment of the following equilibrium. This



equilibrium was studied in aqueous methanol by Bell *et al.*[14] From their values of K at 10 and 25 °C, a value of 8.6×10^{-4} M^{-1} at 0 °C may be calculated. Starting with 0.35 M ether and 3.3 M water, $8.6\times10^{-4}=[\text{ketal}]\cdot[H_2O]/[\text{ketone}][MeOH]^2=[\text{ketal}]\cdot3/[0.35]^3$. Thus about 0.003% of the ketone would be in the form of ketal at equilibrium. This is certainly negligible. Similarly, in the cases of cyclohexanone and acetone, equilibrium constants of 2.14×10^{-2} for cyclohexanone and 9.3×10^{-4} for acetone at 0 °C were calculated from their values of K at 10 and 25 °C. These led to calculations that 0.058% and 0.0001%, respectively, would be in ketal forms at equilibrium.

Enol Contents of Ketones. Enol contents of cyclopentanone, cyclohexanone and acetone investigated by the auther are assembled in Table 2, together with the results by other workers for comparison. The most interesting phenomenon is the relative ordering of enol contents of cyclohexanone>cyclopentanone>acetone in the data by Schwarzenbach, Gero, and the author, which is the opposite tendency to that found by Bell, who reported that cyclopentanone contains more enol than does cyclohexanone.

Shechter and his co-workers have found that the rate

Table 2. Enol contents of ketones at 25 °C

Investigator	Compound Enol contents, %		
	Cyclohexanone	Cyclopentanone	Acetone
G. Schwarzenbach[15]	2.0×10^{-2},a)	4.8×10^{-3},a)	2.5×10^{-4},a)
A. Gero[16]	1.2b)	8.8×10^{-2},b)	1.5×10^{-4},b)
R. P. Bell[17]	4.1×10^{-4},c)	1.3×10^{-3},c)	$<10^{-4}$,c)
Author	3.3×10^{-6},d)	2.5×10^{-7},d)	2.4×10^{-7},d)
S. Sunner[18]	—	—	1.6×10^{-4},e)
J. Osugi[19]	2.0f)	—	4.0×10^{-2},f)
Calculated value	4.9×10^{-4},g)	—	2.8×10^{-6},g)

a) In aqueous solution. b) In 75% methanol–water. c) In aqueous solution. d) Idealized gas state. e) In 60% by volume ethanol–water. f) In toluene solution. g) Values calculated by the assumption of Lienhard and Wang.[13]

for enolization of cycloalkanones as a function of ring size is 6>8>5>7>4, and interpreted the rate order for acid-catalyzed enolization of cycloalkanones primarily on the basis of differences in steric requirements in conversion of the ketones to transition states having endocyclic unsaturated character.[20] If the rates of acid-catalyzed enolization of alkanones are related to the enol contents at equilibrium, cyclohexanone is considered to contain more enol than cyclopentanone.

Brown *et al.*[21] have reported that exocyclic double bonds stabilize a 5-membered ring and destabilize a 6-membered ring, and they made the generalization that reactions will proceed in such a manner as to favor the formation or retention of an exocyclic double bond in a 5-membered ring and to avoid the formation or retention of an exocyclic double bond in a 6-membered ring. It was also pointed out that reactions involving a change in coordination number from three to four proceed slowly in 5-membered and rapidly in 6-membered rings.

The proposal that an exocyclic double bond in 5-membered ring systems is more stable toward changes involving loss of the exocyclic double bond than the corresponding exocyclic double bond in 6-membered ring systems was supported by the higher heat of hydrogenation of cyclohexanone as compared to cyclopentanone; $\Delta H=-12.50$ kcal/mol for cyclopentanone and −15.42 for cyclohexanone.[22]

The generalization may be further illustrated by a consideration of the structures of the stable forms of the carbethoxy derivatives of cyclopentanone and cyclohexanone. The cyclopentanone derivative exists primarily in the form of the Keto derivative (5% enol) whereas the cyclohexanone compound exists primarily as the enol (57%) in 95% ethanol.[23]

In conclusion it may be reasonable to state that cyclohexanone contains more enol than cyclopentanone does. Heats of formation of three ketones and their enol forms in the gas phase at 25 °C were calculated by use of Benson and co-workers' second-order approximation which is the law of additivity of group properties. They were −53.10 kcal/mol for cyclohexanone, −45.50 for cyclopentanone, and −51.70 for acetone, and the values of their enol forms were −37.01, −27.56 and −31.40 kcal/mol, respectively. The differences for the reactions of enolization, $\Delta\Delta H^\circ_f$, were +16.1 kcal/mol for cyclohexanone, +17.94 for cyclopentanone and +20.30 for acetone, while our observed values were 10.13, 11.66 and 11.98 kcal/mol, respectively.[24]

Heats of formation of three enol ethers, their corresponding ketones and methanol in the gas phase at 25 °C were calculated by use of Benson and co-workers' group property approach. They were −40.50 kcal/mol for cyclohexenyl methyl ether, −31.09 for cyclopentenyl methyl ether, −34.90 for isopropenyl methyl ether, −53.10 for cyclohexanone, −45.50 for cyclopentanone, −51.70 for acetone, and −48.0 for methanol. From these values, heats of hydrolysis for the enol ethers were obtained. The calculated values, $\Delta\Delta H^\circ_f$, were −2.8 kcal/mol for cyclohexenyl methyl ether, −4.4 for cyclopentenyl methyl ether and −7.0 for isopropenyl methyl ether, while our observed values were −4.83, −6.36, and −6.38, respectively.[25] Heats of formation of enol ethers were also obtained from our values of ΔH for hydrolysis and other observed values.[24] They were −38.47 kcal/mol for cyclohexenyl methyl ether, −29.14 for cyclopentenyl methyl ether, and −35.52 for isopropenyl methyl ether in the gas phase at 25 °C.

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