Articles

Enolization Enthalpies for Aliphatic Carbonyl and Thiocarbonyl Compounds

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The enolization enthalpies at 0 and 298 K for nine aliphatic carbonyl and nine aliphatic thiocarbonyl compounds have been determined from ab initio CBS-4 (complete basis set fourth-order) model calculations. The enolization enthalpies for the aliphatic carbonyl compounds were found to be 9−24 kcal/mol, but they were about 8−11 kcal/mol higher than those for the corresponding thiocarbonyl compounds. The lower enolization enthalpies for the thiocarbonyl compounds are attributed to the >C═S being much weaker than the >C═O double bond strength. The enolization enthalpies for the cycloketones and thiocycloketones were found to be significantly dependent upon the size of the cyclic ring. The solvent effects on the enolization enthalpy have also been discussed.

Introduction

Enols have been widely suggested as reactive intermediates in a wide variety of organic and biological reactions.[1,2] The enolization of simple aldehydes and ketones is known to be negligible.[1,2] For example, the enol tautomer concentration for most simple aldehydes and ketones was found to be less than 1 ppm (parts per million).[2] In contrast, thioaldehydes and thioketones are generally unstable in solution. They are ready to tautomerize into the corresponding thioenols provided that they have α-enolizable hydrogen atom(s).[3]

Although the thermodynamic information for the enolization of many aldehydes and ketones is available,[1,2,10,11] the thermodynamic information for the enolization of the related thioaldehydes and thioketones is scarce in the literature.[4] In the present paper, with the aid of ab initio CBS-4 (complete basis set fourth-order) model calculations,[5] we wish to report the enolization enthalpies (ΔH) at 0 and 298 K for nine aliphatic carbonyl and nine aliphatic thiocarbonyl compounds in the gas phase.

Calculations

All of the ab initio CBS-4 theoretical calculations were carried out using Gaussian 94,[6] and the details of the calculations have been discussed in the previous papers.[5] The thermodynamic quantities such as homolytic bond dissociation enthalpies (BDEs), proton affinities, electron affinities, and ionization potentials obtained from the ab initio CBS-4 model calculations have been shown to agree within ±2 kcal/mol (mean absolute deviation) with the experimental results.[5] Recently, we have shown that the BDEs of the C−H bonds adjacent to various radical centers, as calculated from the CBS-4 method, also agree within ±2 kcal/mol with the related experimental results.[7a] The calculated C−H BDEs in various fluorinated hydrocarbons were also found to agree within ±2 kcal/mol with the experimental results.[7b]

The enolization enthalpies (ΔH) for the carbonyl (Scheme 2) and thiocarbonyl (Scheme 3) compounds at 0 and 298 K are readily obtained from the formation enthalpies of the keto tautomers (ΔH_{keto}) and the corresponding enol tautomers (ΔH_{enol}) as calculated from the CBS-4 method.[5,8] The calculated total energies, formation enthalpies, and atomization energies for the keto and enol tautomers are all summarized in Table 1. The enolization enthalpies for the nine aliphatic carbonyl compounds and the nine aliphatic thiocarbonyl compounds were calculated by using the data given in Table 1, and the results, together with the available experimental results, are summarized in Tables 2 and 3, respectively.

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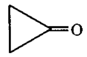
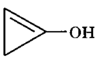
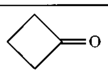
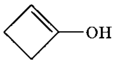
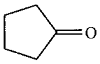
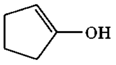
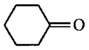
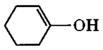
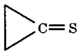
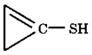
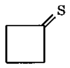
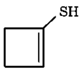
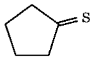
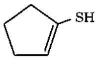
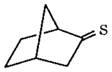
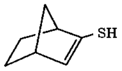
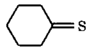
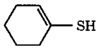
Table 1. Calculated Total Energies and Formation Enthalpies and Atomization Energies for the Keto and Enol Tautomers

Neutral	E_{tol} (0K)^a	$\Delta H(0K)^b$	$\Delta H(298K)^c$	$D_0{}^d$
CH_3CHO	-153.609418	-38.73	-41.34	-644.20
CH_2=CH(OH)	-153.590609	-26.92	-29.73	-632.40
CH_3COCH_3	-192.858219	-50.28	-54.55	-929.00
$CH_3C(OH)$=CH_2	-192.839963	-38.82	-43.19	-917.54
$CH_3COCH_2CH_3$	-232.098026	-56.18	-61.80	-1208.15
CH_2=C(OH)CH_2CH_3	-232.077844	-43.52	-49.48	-1195.48
E-$CH_3C(OH)$=$CHCH_3$	-232.079094	-44.30	-49.94	-1196.47
Z-$CH_3C(OH)$=$CHCH_3$	-232,080557	-45.22	-50.79	-1197.19
$CH_3COCH(CH_3)_2$	-271,336754	-61.41	-68.62	-1486.62
$CH_3C(OH)$=$C(CH_3)_2$	-271.322017	-52.16	-59.00	-1477.38
$CH_3COCH(CH_2CH_3)_2$	-349.809752	-69.07	-79.26	-2040.78
$CH_3C(OH)$=$C(CH_2CH_3)_2$	-349.800396	-63.20	-73.34	-2034.91
	-191.602060	2.99	0.04	-772.46
	-191.563999	26.88	24.09	-748.58
	-230.873540	-22.79	-27.38	-1071.49
	-230.848332	-6.97	-11.43	-1055.67
	-270.144173	-48.04	-54.53	-1369.98
	-270.122017	-34.13	-40.37	-1356.08
	-309.387303	-56.03	-64.30	-1651.22
	-309.369616	-44.93	-52.89	-1640.12
CH_3CSCH_3	-515.438446	5.44	1.44	-879.96
$CH_3C(SH)$=CH_2	-515.433288	8.68	4.62	-876.72
$CH_3C(=S)CH_2CH_3$	-554.676341	0.73	-4.86	-1157.91
E-$CH_3C(SH)$=$CHCH_3$	-554.673041	2.80	-2.44	-1155.84
Z-$CH_3C(SH)$=$CHCH_3$	-554.674919	1.63	-3.62	-1157.02
	-514.192891	52.05	49.28	-730.08
	-514.169328	66.84	64.37	-715.29
	-553.455451	31.87	27.44	-1023.51
	-553.447224	37.03	32.74	-1018.34
	-592.726934	6.09	-0.24	-1322.54
	-592.722663	8.77	2.73	-1319.86
	-670.019166	4.39	-4.10	-1767.46
	-670.007834	11.50	3.24	-1760.35
$CH_3CSCHCMe_2$	-593.918815	-6.85	-13.98	-1438.74
$CH_3C(SH)$=CMe_2	-593.921076	-8.27	-14.91	-1440.16
	-631.972937	-3.71	-11.85	-1605.58
	-631.969165	-1.34	-9.13	-1603.21

^{a} Total energy at 0 K, in hartree. 1 hartree; = 627.5095 kcal/mol. ^{b} Formation enthalpy at 0 K, in kcal/mol. ^{c} Formation enthalpy at 298 K, in kcal/mol. ^{d} Atomization energy at 0 K, in kcal/mol.

Results and Discussion

Aldehydes and Ketones. Examination of the calculated enolization enthalpies[9] in Table 2 shows that the keto tautomer of acetone is 11.4 kcal/mol more stable than the corresponding enol tautomer in the gas phase at 298 K, suggesting that there is only about 4 ppb (parts per billion) concentration of the enol tautomer for acetone in the gas phase at the temperature of 298 K. Our calculated results agree very well with the enolization enthalpy (13.9 ± 2 and 12 ± 2 kcal/mol) of acetone as estimated from the gas-phase experimental data.[10,11] Interestingly, the enolization enthalpy for cyclohexanone (11.1 and 11.4 kcal/mol at 0 and 298 K) was found to be similar to those for acetone and 2-butanone (Table 2).

There are two possible enolization products for the methylene hydrogen (italic) atoms of 2-butanone ($CH_3COC\mathit{H}_2CH_3$) as shown in Scheme 1. The enolization enthalpy was calculated to be 11.0 kcal/mol when (*Z*)-2-hydroxyl-2-butene was formed as the enolization product, but it was 11.9 kcal/mol when (*E*)-2-hydroxyl-2-butene was formed as the enolization product. The slight different enolization enthalpies could be attributed to the less steric hindrance in (*Z*)-2-hydroxyl-2-butene than in (*E*)-2-hydroxyl-2-butene because of the relatively larger size of methyl group than hydroxyl group. The steric hindrance between the two methyl groups in (*Z*)-2-butene was believed to be responsible for the about 1.5 kcal/mol less stability of (*Z*)-2-butene than (*E*)-2-butene.[12] There is only one enolization product for the tertiary hydrogen (italic) atom of 3-methyl-2-butanone ($CH_3COC\mathit{H}Me_2$), and the calculated enolization enthalpy was found to be 9.6 kcal/mol (Table 2).

The relatively higher stabilities of the keto than the corresponding enol tautomers are clearly associated with the >C═O being much stronger than the >C═C< double bond strength (Scheme 2).[13] For example, the average bond dissociation enthalpy (179 kcal/mol) of the >C═O

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(9) The calculated enolization enthalpies (Schemes 2 and 3) are expected to equal the corresponding enolization free energies within ±1 kcal/mol since the enolization entropies of the keto and enol tautomers are similar. For example, the calculated enolization free energies of acetone and cyclopropanone are 12.1 and 23. 3 kcal/mol at 298 K, whereas the corresponding enolization enthalpies are 11.4 and 24.1 kcal/mol (Table 2) at 298 K, respectively.

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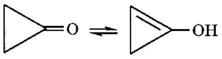
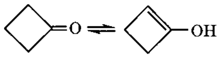
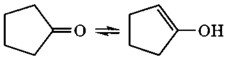
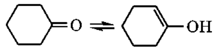
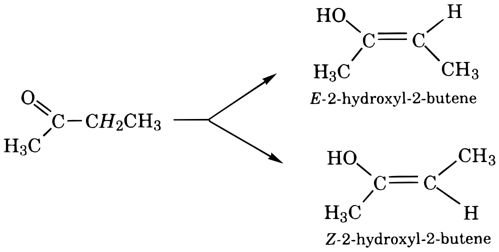
Table 2. Enolization Enthalpies for the Aliphatic Carbonyl Compounds

substrate	ΔH_0[a]	ΔH_{298}[d]	ΔG_{298}(sol.)[g]
$CH_3CHO \rightleftharpoons CH_2{=}CH(OH)$	11.6	11.6	8.5
$CH_3COCH_3 \rightleftharpoons CH_2{=}C(OH)CH_3$	11.5	11.4 (13.9 ± 2)[e]; (12 ± 2)[f]	11.4
$CH_3COCH_2CH_3 \rightleftharpoons CH_3C(OH){=}CHCH_3$	11.9 (*E*-)[b] 11.0 (*Z*-)[c]	11.9 (*E*-)[b] 11.0 (*Z*-)[c]	10.3[h]
$CH_3COCH(CH_3)_2 \rightleftharpoons CH_3C(OH){=}C(CH_3)_2$	9.3	9.6	10.0
$CH_3COCH_2CH_3 \rightleftharpoons CH_2{=}C(OH)CH_2CH_3$	12.6	12.3	12.0
	23.9	24.1	
	15.8	16.0	
	13.9	13.7	10.9
	11.1	11.4	8.7

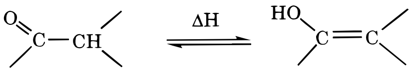
[a] In kcal/mol, enolization enthalpy at 0 K as calculated from the CBS-4 model. [b] (*E*)-2-Hydroxyl-2-butene is formed as the enolization product. [c] (*Z*)-2-Hydroxyl-2-butene is formed as the enolization product. [d] In kcal/mol, enolization enthalpy at 298 K as calculated from the CBS-4 model. [e] Reference 10. [f] Reference 11. [g] In kcal/mol, enolization free energies determined from the aqueous solution.[2] The related aqueous enolization enthalpies are about 1 kcal/mol higher than the enolization free energies listed in this column.[15] [h] The enolization product is a mixture of the *Z*- and *E*-isomers.

Scheme 1



double bond is about 40 kcal/mol higher than that (140 kcal/mol) of the >C=C< double bond.[13]

Scheme 2



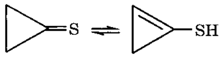
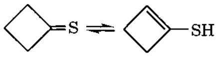
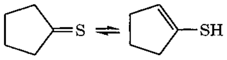
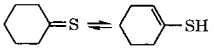
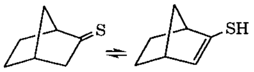
More interestingly, the enolization enthalpies of cycloketones were found to increase progressively from 11.4 to 13.7 to 16.0 to 24.1 kcal/mol at 298 K when the cyclic ring changes from six to five to four to three members. The progressive increase of the enolization enthalpy can be attributed to the increasing difficulty to form the unsaturated cyclic ring due to the shrinkage of the ring size.[14] This explains why the enolization enthalpy increment (2.3 kcal/mol) from cyclohexanone to cyclopentanone is much smaller than that (8.1 kcal/mol) from cyclobutanone to cyclopropanone.

It is worth noting that the calculated (gas-phase) enolization enthalpy of acetone was found to be fortuitously close to that observed in the aqueous solution (Table 2).[2,15] Also, the gas-phase enolization enthalpies for 2-butanone ($CH_3COCH_2CH_3$) and 3-methyl-2-butanone ($CH_3COCHMe_2$) were found to be close to those reported from the aqueous solution measurements (Table 2). The similar gas-phase and aqueous enolization enthalpies imply that the aqueous solvation effects for the keto tautomers of these ketones are not significantly different from those for the corresponding enol tautomers, and as a result they cancel each other.

On the other hand, the gas-phase enolization enthalpies of acetaldehyde, cyclopentanone, and cyclohexanone were found to be about 2−3 kcal/mol higher than those reported from the aqueous solution (Table 2).[2] The slightly lower aqueous solution enolization enthalpies for acetaldehyde and cycloketones are presumably due to the larger aqueous solvation effects for the corresponding enol tautomers than for the keto tautomers since the solvation effects for the enol tautomers were known to be more sensitive to the steric hindrance.[10]

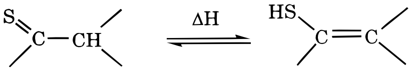
Thioaldehydes and Thioketones. The enolization of the thiocarbonyl compounds is shown in Scheme 3, and the calculated enolization enthalpies for nine aliphatic thiocarbonyl compounds are all summarized in Table 3.

Table 3. Enolization Enthalpies for the Aliphatic Thiocarbonyl Compounds

substrate (keto tautomer)	ΔH_0[a]	ΔH_{298}[d]
$CH_3CHS \rightleftharpoons CH_2{=}CH(SH)$	2.2	2.2
$CH_3CSCH_3 \rightleftharpoons CH_2{=}C(SH)CH_3$	3.2	3.2
$CH_3CSCH_2CH_3 \rightleftharpoons CH_3C(SH){=}CHCH_3$	2.1 (*E*-)[b] 0.90 (*Z*-)[c]	2.4 (*E*-)[b] 1.2 (*Z*-)[c]
$CH_3CSCH(CH_3)_2 \rightleftharpoons CH_3C(SH){=}C(CH_3)_2$	-1.42	-0.93
	14.8	15.1
	5.2	5.3
	2.7	3.0
	2.4	2.7
	7.1	7.3

[a] In kcal/mol, enolization enthalpy at 0 K as calculated from the CBS-4 model. [b] (*E*)-2-Mercapto-2-butene is formed as the enolization product. [c] (*Z*)-2-Mercapto-2-butene is formed as the enolization product. [d] In kcal/mol, enolization enthalpy at 298 K as calculated from the CBS-4 model.

Scheme 3



Examination of Table 3 shows that the enolization enthalpies for the acyclic aliphatic thioaldehyde and thioketones are in the range of −1 to 3 kcal/mol at 298 K, which are about 8 to 11 kcal/mol less than those for the corresponding carbonyl compounds. Our calculated results agree very well with the experimental results; the enolization equilibrium constants for thioketones were estimated to be at least 10^6 time larger than those for the corresponding ketone analogues.[3e] The equilibrium constant differences indicate that the thioketones in energy are at least 8.2 kcal/mol less stable than the

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(14) Harnisch, J.; Baumgartel, O.; Szeimies, G.; van Meerssche, M.; Germain, G.; Declercq, J. *J. Am. Chem. Soc.* **1979**, *101*, 3370.

corresponding ketones at 298 K. The smaller enolization enthalpies for the thiocarbonyl compounds are clearly associated with the much weakness of the >C=S compared to the >C=O double bond strength.[4,8,16] For example, the bond dissociation enthalpy of the >C=S double bond in $H_2C{=}S$ was found to be 125 kcal/mol, whereas the bond dissociation enthalpy of the >C=O double bond in $H_2C{=}O$ was found to be 179 kcal/mol.[8]

The enolization enthalpy for the methylene hydrogen (italic) atoms of 2-butanethione ($CH_3CSC\mathit{H}_2CH_3$) is 2.4 kcal/mol when (*E*)-2-mercapto-2-butene was formed as the enolization product, but it is 1.2 kcal/mol when (*Z*)-2-mercapto-2-butene was formed as the enolization product. The enolization enthalpy difference is similar, but slightly larger than that for the methylene hydrogen atoms of 2-butanone as shown in Scheme 1. More significantly, the enolization enthalpy for the tertiary hydrogen (italic) atom of 3-methyl-2-butanethione ($CH_3CSC\mathit{H}Me_2$) was found to be −1.42 and −0.93 kcal/mol at 0 and 298 K, respectively. The *negative* enolization enthalpy indicates that the thioketo tautomer of 3-methyl-2-butanethione is thermodynamically *less* stable than the corresponding thioenol tautomer. The enolization enthalpy is expected to decrease for the introduction of the α-methyl group(s) due to the stabilization on the conjugated carbon−carbon double bond of the thioenol tautomer, but the related stabilization of the α-methyl group(s) on the carbonyl double bond of keto tautomer or the thiocarbonyl double bond of thioketo tautomer should be negligible because of the separation of the methylene group. Apparently, the enolization enthalpies for the thiocarbonyl compounds with α-phenyl group(s) would be even *more negative* than that of 3-methyl-2-butanethione because of the much larger resonance stabilizing nature of the conjugated aromatic system. Indeed, a survey of the related literature shows that this is essentially what happens. For example, the thioenols with α-phenyl group(s) were found to be the sole tautomers observed.[3e,17]

Examination of Table 3 shows that the enolization enthalpies of thiocyclohexanone and thiocyclopentanone are close to those of thioaldehyde and thioacetone. They are also similar to the enolization enthalpy of 2-butanethione when (*E*)-2-mercapto-2-butene was formed as the enolization product. Comparison of the enolization enthalpies of the cycloketones (Table 2) and thiocycloketones (Table 3) indicates that the enolization enthalpies for the cycloketones are also about 8−11 kcal/mol higher than those of the corresponding thiocycloketones even though the enolization enthalpies for the cycloketones and thiocycloketones are significantly dependent upon the size of the cyclic ring, and are also much higher than those of the corresponding acyclic analogues. This provides the additional evidence to show that the significant enolization enthalpy increase for the cycloketones and thiocycloketones with the shrinkage of the ring size is caused by the difficulty for the formation of a carbon−carbon double bond in a smaller cyclic ring.

The much lower enolization enthalpies for the thiocarbonyl compounds imply that there would be much higher thioenol tautomer concentrations compared to the corresponding carbonyl compounds, but the direct measurements of the enolization equilibrium constants for the thiocarbonyl compounds will still be very difficult because the thioenol structures were known to be unstable, and they easily dimerize or trimerize.[3,17] For example, the most stable form of thioacetone is trithiane, which is believed to be formed from the trimerization of the corresponding thioenol tautomer of thioacetone.[18]

The enolization enthalpy of thionorbornanone (bicyclo[2.2.1]heptane-2-thione) was found to be 7.1 and 7.3 kcal/mol at 0 and 298 K, respectively (Table 3), which is about 4−5 kcal/mol higher than those of thiocyclopentanone and thiocyclohexanone. The higher enolization enthalpy for thionorbornanone is no doubt due to the much larger ring strain to form the thioenol >C=C< double bond in the related bicyclic system,[19] which makes the thioenol tautomer less stable. Our calculated results agree very well with the experimental observation, which showed that only less than 1% of the thioenol tautomer to be present for thionorbornanone.[3d]

In an earlier section, we mentioned that the gas-phase enolization enthalpies for acyclic ketones are close to those reported from the aqueous solution, but the gas-phase enolization enthalpies for acetaldehyde and cycloketones are a few kcal/mol lower than those reported from the aqueous solution measurements since the enol tautomers are more sensitive to the aqueous solvation than their keto tautomers.[10,11] Therefore, it is conceivable that the aqueous solution enolization enthalpies for the thioacetaldehyde and thiocycloketones would also be a few kcal/mol lower than the related gas-phase enolization enthalpies. In other words, the aqueous solution enolization enthalpies for thioacetaldehyde and thiocycloketones would be even a few kilocalories/mole lower than the calculated gas-phase enolization enthalpies as summarized in Table 3.

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[15] The enolization entropy of acetone in aqueous solution was reported to be about 3.5 cal/K·mol,[11] suggesting that the aqueous solution enolization enthalpy of acetone is only about 1 kcal/mol higher than the corresponding enolization free energy.

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