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Determination of Hydride Affinities of Various Aldehydes and Ketones in Acetonitrile

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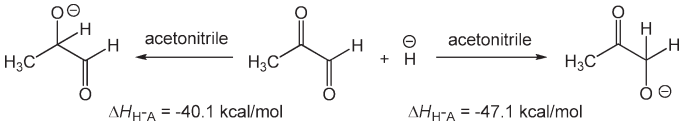
ABSTRACT



The hydride affinities of 21 typical aldehydes and ketones in acetonitrile were determined by using an experimental method, which is valuable for chemists choosing suitable reducing agents to reduce them. The focus of this paper is to introduce a very facile experimental method, which can be used to determine the hydride affinities of various carbonyl compounds in solution.

The reduction of aldehydes and ketones by the addition of a hydride ion is an issue of fundamental importance in chemistry and biochemistry. Consequently, there have been many studies of the reductions of various aldehydes and ketones with a wide variety of reagents.[1,2] Since the hydride affinity of aldehydes and ketones is one crucial thermodynamic parameter to scale the chemical activity of aldehydes and ketones for their reductions, there are many chemists who have contributed much time to examine the hydride affinities of aldehydes and ketones.[3,4] However, the available data related to the hydride affinities of aldehydes and ketones are all limited to the gas phase and most of them come from theory estimation using a computer.[3,4] No experimental method can be available to directly determine the hydride affinities of aldehydes and ketones in solution. The main reason is that the hydride ion solution is not available. Moreover, some side reactions, in general, appear during the reduction processes of aldehydes and ketones, which strictly hinder the development of an efficient experimental method. Since the theoretical results require further identification of experimental results and most reductions of aldehydes and ketones in research laboratories and industries all take place in solution, experimental data for hydride affinities of aldehydes and ketones in solution should be very important and urgently required.

In our previous paper,[5] we reported an efficient experimental method to determine the hydride affinity of various polarized olefins in acetonitrile by using *N*-methylacridinium perchloride as a hydride acceptor. But when we subsequently extended this method to determine the hydride affinity of aldehydes and ketones in dry acetonitrile, the extensions were all in failure. The reason is that *N*-methylacridinium perchloride is not an efficient hydride acceptor to the hydrides of aldehydes and ketones (alkoxide anions), but a good electrophilic agent to combine with the alkoxides (Scheme 1). The reason could be that the formed ether

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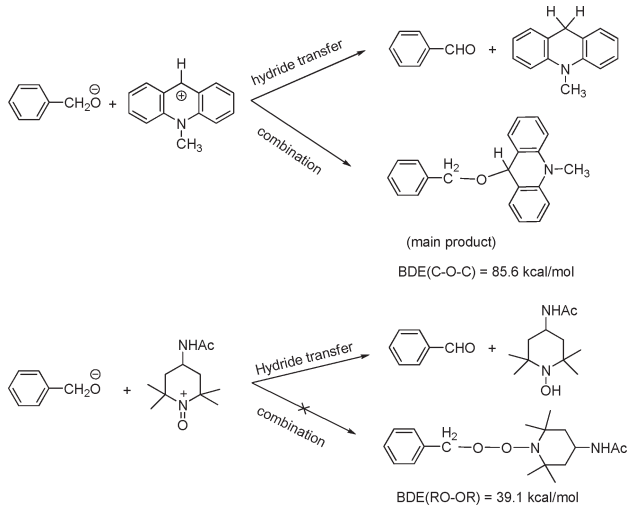
Scheme 1. Reaction Selectivities of the Hydrides of Aldehydes and Ketones with Oxoammonium and Acridinium in Acetonitrile



bond, R−O−R′, is a strong chemical bond [BDE(C−O) = 85.6 kcal/mol],[6] which indicates that carbenium ions cannot be used to determine the hydride affinity of aldehydes and ketones in solution according to the strategy applied in the previous paper.[5] Although we were frustrated in the determination of the hydride affinity of aldehydes and ketones in solution, we believe that organic oxygen cations should be a suitable agent for abstracting hydride anions from the hydrides of aldehydes and ketones in solution, because the peroxide bond (RO−OR′) is a weak chemical bond [BDE(O−O) = 39.1 kcal/mol],[6] which is unfavorable to the formation of peroxide products when the hydrides of aldehydes and ketones are treated with organic oxygen cations in solution. According to this idea, we finally found that 4-acetylamino-2,2,6,6-tetramethyl-piperidine-1-oxoammonium perchlorate ($TEMPO^+$) is quite a suitable hydride acceptor for abstracting hydride anions from the hydrides of aldehydes and ketones in acetonitrile without any side products, which can be used to determine the hydride affinity of various aldehydes and ketones in acetonitrile.[7] Herein we wish to report the detailed experimental results.

The hydride affinity of aldehydes and ketones (**X**) in acetonitrile in this work was defined as the enthalpy change of the aldehydes and ketones [$\Delta H_{H\text{-}A}(\mathbf{X})$] to capture a hydride ion in acetonitrile (eqs 1 and 2). According to eq 3, it is clear that the hydride affinity of aldehydes and ketones

(6) Luo, Y.-R. *Handbook of Bond Dissociation Energies in Organic Compounds*, 3rd ed.; Science Press: China, 2002.

(7) When the hydrides of aldehydes or ketones ($\mathbf{XH}^-$) were treated by $TEMPO^+$ in acetonitrile, it is found that the reactions took place by hydride transfer to yield the corresponding aldehydes or ketones (**X**) and TEMPOH quantitatively (eq 3), no side product ether was formed, which were identified by MS and ^1H NMR spectroscopy, and the rate of the hydride transfer is very fast. These experimental results indicate that $TEMPO^+$ as an efficient hydride acceptor completely met the criteria of calorimetric titration measurement to determine the hydride affinity of aldehydes and ketones in acetonitrile.

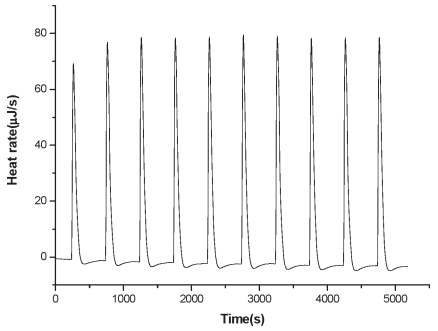
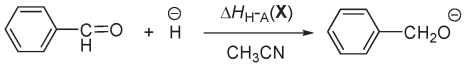


Figure 1. Isothermal titration calorimetry (ITC) for the reaction heat of alkoxide anion $\mathbf{6H}^-$ with 4-acetylamino-2,2,6,6-tetramethylpiperidine-1-oxoammonium perchlorate ($TEMPO^+$) in acetonitrile at 298 K. Titration was conducted by adding 10 μL of $TEMPO^+$ (1.75 mM) every 500 s into the acetonitrile containing the $\mathbf{6H}^-$ (ca. 20.0 mM), which was obtained in situ from the reactions of the corresponding saturated neutral compounds ($\mathbf{6H}_2$) with KH.

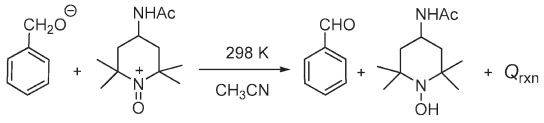
(**X**) in acetonitrile can be derived from the hydride affinity of $TEMPO^+$ and the reaction heat of $TEMPO^+$ with the hydrides of aldehydes and ketones ($\mathbf{XH}^-$) in acetonitrile (eq 4). In eq 4, Q_{rxn} is the reaction heat of eq 3 in acetonitrile, which can be determined by titration calorimetry (Figure 1); $\Delta H_{H^-A}(TEMPO^+)$ is the hydride affinity of $TEMPO^+$ in acetonitrile (−105.6 kcal mol^{-1}), which is available from the reaction heat of $TEMPO^+$ with BNAH. The hydride affinities of 21 typical aldehydes and ketones in acetonitrile and the corresponding Q_{rxn} in acetonitrile are summarized in Table 1.



(1)

(**X**) (**XH**$^-$)

$$\Delta H_{H\text{-}A}(\mathbf{X}) = \Delta H_f(\mathbf{XH}^-) - [\Delta H_f(\mathbf{X}) + \Delta H_f(H^-)] \quad (2)$$



(3)

(**XH**$^-$) ($TEMPO^+$) (**X**) (TEMPOH)

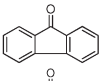
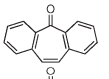
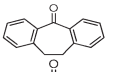
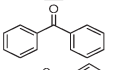
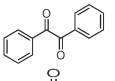
$$\Delta H_{H\text{-}A}(\mathbf{X}) = \Delta H_{H\text{-}A}(TEMPO^+) + Q_{rxn} \quad (4)$$

Table 1 shows that the hydride affinities of the 6 aldehydes (**1**−**6**) in acetonitrile range from −31.6 kcal/mol (**4**) to −47.1 kcal/mol (**5**) and the hydride affinities of the 15 ketones (**7**−**21**) in acetonitrile range from −28.9 kcal/mol for ketone **7** or **8** to −61.8 kcal/mol for ketone **17**. Since the hydride affinities of the aldehydes and ketones are all much smaller than those of the general carbocations, such as the benzyl cation [$\Delta H_{H\text{-}A}(PhCH_2^+)$ = −122.9 kcal/mol][9] in acetonitrile, these aldehydes and ketones should be all due to very weak hydride acceptors, which indicates that these aldehydes and ketones are quite difficult to reduce with mild organic reducing agents, such as BNAH (1-benzyl-1,4-dihydronicotinamide), HEH (Hantzsch

pyridine), and $AcrH_2$ (9,10-dihydroacridine), as well as with H_2, an extensively applied inorganic reducing agent in research laboratories and industry, without the aid of catalysts. Only quite strong inorganic hydride donors, such as $NaBH_4$ or $LiAlH_4$, can be chosen to reduce them efficiently. From eq 1, it is found that different from the reduction of benzyl cation by hydride anion, the reduction of aldehydes and ketones not only involves the formation of a new C−H σ-bond to release energy but also involves the dissociation of one C=O π-bond to consume energy. Hence, the hydride affinity magnitude of aldehydes and ketones in solution should be equal to the heterolytic dissociation energy of the newly formed C−H σ-bond minus the heterolytic dissociation energy of the broken C=O π-bond. Thus it is not difficult to understand why the hydride affinities of aldehydes and ketones are much smaller than that of the benzyl cation, since the hydride affinity of the benzyl cation does not involve the heterolytic dissociation of the C=O π-bond. From the three hydride affinities of benzaldehyde (−42.8 kcal/mol), acetophenone (−35.0 kcal/mol), and the benzyl cation (−122.9 kcal/mol),[8] it is clear that if the three C−H σ-bonds energies in the three compounds were postulated to be equal, the C=O π-bond heterolytic dissociation in benzaldehyde and acetophenone should be 80.1 and 87.9 kcal/mol, respectively. And the π-bond heterolytic dissociation energy of benzaldehyde is smaller than that of the corresponding acetophenone by 7.8 kcal/mol. The reason could be that the polarity of the aldehyde C=O double bond is larger than that of the ketone C=O double bond. In order to more accurately estimate the difference in hydride affinities between the aldehyde C=O double bond and ketone C=O double bond, the hydride affinities of aldehyde **5** and ketone **10** were compared, the result being that the hydride affinity of aldehyde **5** is more negative than that of ketone **10** by −7.0 kcal/mol. Since aldehyde **5** and ketone **10** are of the same structure, the −7.0 kcal/mol should be the intrinsic difference in hydride affinities between the aldehyde C=O double bond and ketone C=O double bond in acetonitrile.

If the data in Table 1 were examined in detail, the following findings can be obtained: (1) By comparing the hydride affinities of aromatic aldehyde **6** (−42.8 kcal/mol) and aliphatic aldehyde **2** (−33.8 kcal/mol), it is found that the hydride affinity of the aromatic aldehyde is larger than that of the aliphatic aldehyde by ca. 9 kcal/mol. Meanwhile, when the hydride affinities of aromatic ketone **12** (−35.0 kcal/mol) and aliphatic ketone **7** (−28.9 kcal/mol) were compared, it is found that the hydride affinity of the aromatic ketone is larger than that of the aliphatic ketone by ca. 6 kcal/mol. The two findings indicate that the π-bond heterolytic dissocialer than those of the corresponding aliphatic carbonyl compounds by 6−9 kcal/mol. The reason could be that π-electrons have a larger space to delocalize in aromatic carbonyl compounds. (2) When the hydride affinities of the 2-oxopropanal **5** (−47.1 kcal/mol) and the general propionaldehyde **3** (−34.4 kcal/mol) were

Table 1. Hydride Affinities of Carbonyl Compounds (**X**) and Reaction Heats (Q_{rxn}) of $\mathbf{XH}^-$ with $TEMPO^+$ in Acetonitrile (kcal/mol)

no	compds (**X**)	Q_{rxn} [a]	$\Delta H_{H\text{-}A}(\mathbf{X})$ [b]
	aldehydes		
1		66.3	-39.3
2		71.8	-33.8
3		71.2	-34.4
4		74.0	-31.6
5		58.5	-47.1
6		62.8	-42.8
	ketones		
7		76.7	-28.9
8		76.7	-28.9
9		70.1	-35.5
10		65.5	-40.1
11		54.9	-50.7
12		70.6	-35.0
13		56.7	-48.9
14		55.0	-50.6
15		56.4	-49.2
16		68.5	-37.1
17		43.8	-61.8
18		70.7	-34.9
19		69.1	-36.5
20		60.8	-44.8
21		58.9	-46.7

[a] Uncertainties were smaller than 1 kcal/mol in each case. [b] $\Delta H_{H\text{-}A}$ values were estimated from eq 4, taking $\Delta H_{H\text{-}A}(TEMPO^+) = -105.6$ kcal/mol, which was derived from the reaction heat (41.4 kcal/mol, which was determined in this work) of $TEMPO^+$ with BNAH in acetonitrile.[9]

(8) $\Delta H_{H\text{-}A}(PhCH_2^+) = \Delta G_{H\text{-}A}(PhCH_2^+) - 4.9$ in acetonitrile[10] and $\Delta G_{H\text{-}A}(PhCH_2^+) = -118.0$ kcal/mol, which is derived from Parker's work: Cheng, J.-P.; Handoo, K. L.; Parker, V. D. *J. Am. Chem. Soc.* **1993**, *115*, 2655.

(9) The hydride affinity of BNA^+ in acetonitrile was determined (−64.2 kcal/mol),[11] which has been supported by DuBois and co-workers' work (−63.9 kcal/mol);[12] the difference is smaller than the experimental error. It is worth noting that $\Delta H_{H\text{-}A}(BNA^+) = \Delta G_{H\text{-}A}(BNA^+) - 4.9$ in acetonitrile, which has been identified.[10] In this work, the value of −64.2 kcal/mol was chosen as the hydride affinity of BNA^+ in acetonitrile.

compared, it is found that the hydride affinity of 2-oxopropanal **5** is greater than that of the general propionaldehyde **3** by 12.7 kcal/mol. Meanwhile, when 1-oxo-propan-2-one **10** and the general acetone **7** were compared, it is found that the hydride affinity of 1-oxo-propan-2-one **10** (−40.1 kcal/mol) is greater than that of the general acetone **7** (−28.9 kcal/mol) by 11.2 kcal/mol. The two findings suggest that the contribution of the adjacent carbonyl substituent to the hydride affinity of aldehydes and ketones is more than 10 kcal/mol. The main reason could be that π-electrons can delocalize in an O=C−C=O system, and in addition, the oxygen atom at the end position can increase the polarization of vicinal carbonyl C=O double bond. But if ketone **11** and **7** can be compared, the result shows that the hydride affinity difference between ketone **11** (−50.7 kcal/mol) and ketone **7** (−28.9 kcal/mol) is 21.8 kcal/mol, which is much larger than 10 kcal/mol.[10] This result indicates that the contribution of the ester carboxyl group at the adjacent position to the hydride affinity of ketone is much greater than that of the general carbonyl group at the adjacent position to the hydride affinity of ketone. The main reason should be that the carboxyl group has a larger resonance orbit to accommodate the π-electrons from the vicinal carbonyl C=O double bond than the general carbonyl group. (3) When ketones **18** and **19** were examined, it is found that the hydride affinity of cyclohexanone **18** (−34.9 kcal/mol) is smaller than that of the corresponding cyclopentanone **19** (−36.5 kcal/mol) by ca. 2 kcal/mol. The reason is that the stretching force of cyclopentanone is larger than that of cyclohexanone, which makes the overlap of $2p_z$ orbitals for C=O π-bond formation in cyclopentanone become smaller than that in cyclohexanone. A similar result can be also found for the ketones **20** (−44.8 kcal/mol) and **21** (−46.7 kcal/mol). (4) When ketones **8** and **9** were compared, it is found that the hydride affinity of butan-2-one (−28.9 kcal/mol) is smaller than that of the corresponding but-3-en-2-one (−35.5 kcal/mol) by 6.6 kcal/mol, which suggests that the heterolytic C=O π-bond dissociation energy in **9** is smaller than that in **8** by 6.6 kcal/mol. It is evident that those important findings are all very valuable in the understanding of the nature of the C=O π-bond in various carbonyl compounds.

In summary, the hydride affinities of 21 aldehydes and ketones in acetonitrile were determined by an experimental method for the first time. The determined thermodynamic data should be not only very valuable for choosing suitable reducing agents to reduce aldehydes and ketones in research laboratories and industry but also useful for developing the structure theory of carbonyl compounds. After examining the data in Table 1, the following suggestions can be made: (1) Aldehydes and ketone are quite weak hydride acceptors; in general, the reductions need strong hydride donors and/or need the aid of suitable catalysts. (2) The hydride-accepting abilities of aldehydes are generally larger than those of the corresponding ketones by about 7 kcal/mol. (3) The hydride-accepting ability of the aromatic carbonyl compounds is greater than that of the corresponding aliphatic compounds by about 9 kcal/mol. (4) The hydride-accepting ability of the cyclic carbonyl compounds is larger than that of the corresponding open-chain carbonyl compounds by about 1−3 kcal/mol. (5) The hydride-accepting ability of the vicinal double carbonyl compounds is larger than that of the corresponding single carbonyl compounds by more than 10 kcal/mol. The most salient contribution of this paper is introducing an efficient experimental method, which can be used to determine the hydride affinities of various carbonyl and carboxyl compounds in solution.

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Supporting Information Available. Experimental details and some representative ITC spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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