Hydride Affinities

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A Facile Experimental Method To Determine the Hydride Affinity of Polarized Olefins in Acetonitrile**

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Reductions of various unsaturated compounds, such as olefins, alkynes, ketones, aldehydes, and imines in solution by hydride reagents ($NaBH_4$, $LiAlH_4$, NADH, etc.) to the corresponding saturated compounds are fundamental reactions[1] that have been extensively applied in organic syntheses.[2] The thermodynamics and kinetics of reduction of unsaturated compounds are not only dependent on the hydride-donating ability (hydricity) of the hydride reagents, but also on the hydride-accepting ability (hydride affinity) of the unsaturated compounds (hydride acceptors). Hence, the hydride affinity of unsaturated compounds should be an important clue to select suitable reducing agents for their efficient reduction and to perform detailed thermodynamic analyses on the reduction mechanisms. Examination of past publications on this subject shows that, although much attention has been paid to determining hydricity of reducing agents (hydride donors) and the hydricity values of many reducing agents have been accurately determined,[3] no reports have been made on the determination of hydride affinity of unsaturated organic compounds, especially in solution. The main reason could be that the state free energy or state enthalpy of the free hydride anion in solution is not available, and this strictly limits the experimental methods that can be efficiently applied for the direct determination of the hydride affinities of unsaturated compounds in solution. Several years ago, we embarked on a major project to experimentally determine the hydride affinity scale of various unsaturated compounds in organic solvents. Herein we report a facile and efficient experimental method to determine the hydride affinity of polarized olefins **1** in acetonitrile.

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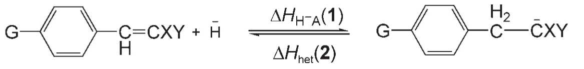
The hydride affinity of olefins **1** [$\Delta H_{\mathrm{H^-A}}(\mathbf{1})$] is defined in this work as the enthalpy change in the reaction of olefin **1** with free hydride ion to form carbanion **2** at 25 °C [Eq. (1)].

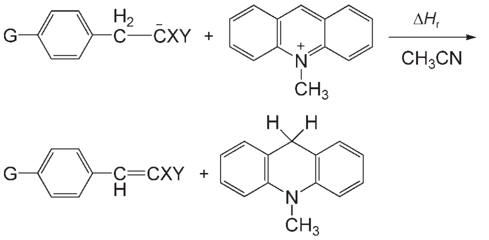


1 **2** (1)

According to the definition of hydride affinity of **1** [Eq. (2)], it is clearly difficult to directly determine the hydride affinity of the olefins [$\Delta H_{\mathrm{H^-A}}(\mathbf{1})$] in solution by an experimental method because the enthalpy of the free hydride ion in solution is not available.

$$\Delta H_{\mathrm{H^-A}}(\mathbf{1}) = H(\mathbf{2}) - [H(\mathrm{H^-}) + H(\mathbf{1})] \tag{2}$$

However, examining Equation (1) shows that the hydride affinity of olefins is simply equal to the heterolytic $\mathrm{C_\beta{-}H}$ bond dissociation energy of the corresponding carbanion **2** of **1** [$\Delta H_{\mathrm{het}}(\mathbf{2})$] by switching the sign [Eq. (5)]. This grants efficient and facile access to determining the hydride affinity of olefins **1** in solution according to the enthalpy change in the reaction of the corresponding carbanion **2** with the strong hydride acceptor *N*-methylacridinium [$\mathrm{AcrH^+}$; Eqs. (3) and (4)]. In Equation (5), ΔH_{r} is the enthalpy change of the reaction [Eq. (3)], which can be obtained by titration calorimetry;[5] $\Delta H_{\mathrm{het}}(\mathrm{AcrH_2})$ is the heterolytic C9–H bond dissociation energy of 9,10-dihydroacridine ($\mathrm{AcrH_2}$) in solution, which we have determined previously.[5]



(3)

$$\Delta H_{\mathrm{r}} = \Delta H_{\mathrm{het}}(\mathbf{2}) - \Delta H_{\mathrm{het}}(\mathrm{AcrH_2}) \tag{4}$$

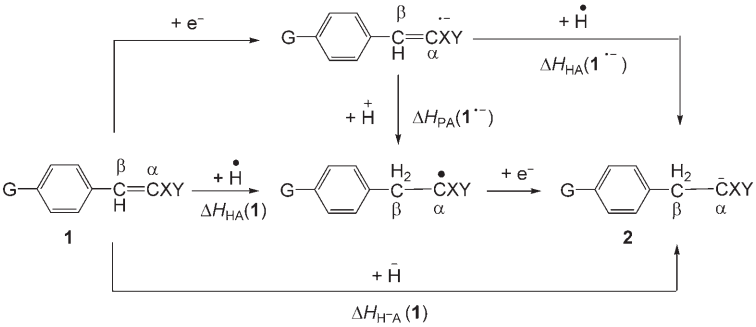
$$\Delta H_{\mathrm{H^-A}}(\mathbf{1}) = -\Delta H_{\mathrm{het}}(\mathbf{2}) = -[\Delta H_{\mathrm{r}} + \Delta H_{\mathrm{het}}(\mathrm{AcrH_2})] \tag{5}$$

Herein, the hydride affinity scales of four types of polarized olefins **1a–d**, which have been extensively applied in organic syntheses,[6] were examined in acetonitrile solution. The hydride affinities of **1a–d** are summarized in Table 1. The enthalpy changes of the reactions of **2a–d** with $\mathrm{AcrH^+}$ [Eq. (3)] and the standard redox potentials of the relevant species are listed in the Supporting Information.

Table 1: Hydride and hydrogen affinities of olefins **1**, as well as proton affinities and hydrogen affinities of the radical anions $\mathbf{1}^{\bullet-}$ in acetonitrile [kcal mol^{-1}].[a]

G	$\Delta H_{\mathrm{H^-A}}(\mathbf{1})$[b]	$\Delta H_{\mathrm{HA}}(\mathbf{1})$[c]	$\Delta H_{\mathrm{PA}}(\mathbf{1}^{\bullet-})$[d]	$\Delta H_{\mathrm{HA}}(\mathbf{1}^{\bullet-})$[e]
1a (X=CN, Y=CN)				
$\mathrm{CH_3O}$	−60.4	−42.6	−25.3	−70.1
$\mathrm{CH_3}$	−60.6	−42.7	−24.1	−69.0
H	−61.0	−42.6	−22.8	−68.1
Cl	−61.6	−42.8	−20.4	−66.2
Br	−61.5	−42.7	−20.1	−65.9
$\mathrm{CF_3}$	−62.6	−43.2	−16.6	−63.0
$\mathrm{NO_2}$	−63.0	−43.0	−13.5	−60.5
1b (X=CN, Y=$\mathrm{CO_2Et}$)				
$\mathrm{CH_3O}$	−58.1	−40.9	−27.4	−71.6
$\mathrm{CH_3}$	−58.4	−41.0	−26.5	−70.8
H	−59.0	−41.3	−24.9	−69.6
Cl	−59.4	−41.2	−22.6	−67.8
Br	−59.5	−41.3	−22.7	−67.8
$\mathrm{CF_3}$	−60.3	−41.5	−19.0	−64.8
$\mathrm{NO_2}$	−60.8	−41.6	−15.8	−61.9
1c (X=CN, Y=$\mathrm{CONH_2}$)				
$\mathrm{CH_3O}$	−55.1	−38.6	−30.2	−73.7
$\mathrm{CH_3}$	−55.3	−38.6	−28.9	−72.5
H	−55.7	−38.7	−26.9	−70.8
Cl	−56.6	−39.2	−24.4	−68.8
Br	−56.7	−39.2	−24.5	−68.9
$\mathrm{CF_3}$	−57.2	−39.1	−20.8	−65.7
$\mathrm{NO_2}$	−57.7	−39.1	−17.7	−63.2
1d (X=$\mathrm{CO_2Et}$, Y=$\mathrm{CO_2Et}$)				
$\mathrm{CH_3O}$	−52.8	−36.9	−31.6	−74.4
$\mathrm{CH_3}$	−53.1	−37.0	−30.7	−73.8
H	−53.7	−37.3	−29.1	−72.5
Cl	−54.2	−37.4	−27.0	−70.8
Br	−54.3	−37.5	−27.8	−71.0
$\mathrm{CF_3}$	−55.0	−37.6	−23.8	−68.2
$\mathrm{NO_2}$	−55.7	−37.8	−21.6	−66.4

[a] Relative uncertainties were estimated to be smaller than or close to 1 kcal mol^{-1} in each case. [b] $\Delta H_{\mathrm{H^-A}}(\mathbf{1})$ was estimated from Equation (5), taking $\Delta H_{\mathrm{het}}(\mathrm{AcrH_2}) = 81.1$ kcal mol^{-1} from reference [5]. [c] Estimated from Equation (6) with $E^\circ(\mathrm{H^{0/-}}) = -1.137$ V vs. $\mathrm{Fc^+/Fc^0}$ (Fc = ferrocen).[9] [d] Estimated from Equation (7) with $E^\circ(\mathrm{H^{+/0}}) = -2.307$ V vs. $\mathrm{Fc^+/Fc^0}$.[9] [e] Estimated from Equation (8) with $E^\circ(\mathrm{H^{+/0}}) = -2.307$ V vs. $\mathrm{Fc^+/Fc^0}$.



Scheme 1. Possible pathways of the reduction of **1** by hydride.

As the reductions of olefins **1** by hydride ions could involve multistep hydride-transfer mechanism, such as $\mathrm{e^-{-}H^+{-}e^-}$, $\mathrm{e^-{-}H}$, $\mathrm{H{-}e^-}$, and so on (Scheme 1),[7] it is evident that the hydrogen affinity of olefins **1**, $\Delta H_{\mathrm{HA}}(\mathbf{1})$, as well as proton affinity and hydrogen affinity of the corresponding radical carbanion of the olefins $\mathbf{1}^{\bullet-}$, $\Delta H_{\mathrm{PA}}(\mathbf{1}^{\bullet-})$ and $\Delta H_{\mathrm{HA}}(\mathbf{1}^{\bullet-})$, are also very important for elucidating the reduction mechanism. In this work, their values were also estimated according to Equations (6)–(8), which were derived from appropriate thermodynamic cycles (see Supporting Information).[8] The results are also summarized in Table 1.

$$\Delta H_{\mathrm{HA}}(\mathbf{1}) = \Delta H_{\mathrm{H^-A}}(\mathbf{1}) - F[E^{\circ}(\mathrm{H}^{0/-}) - E^{\circ}(\mathbf{2}^{0/-})] \quad (6)$$

$$\Delta H_{\mathrm{PA}}(\mathbf{1}^{\cdot-}) = \Delta H_{\mathrm{H^-A}}(\mathbf{1}) + F[E^{\circ}(\mathbf{1}^{0/-}) - E^{\circ}(\mathrm{H}^{0/-})] - F[E^{\circ}(\mathrm{H}^{+/0}) - E^{\circ}(\mathbf{2}^{0/-})] \quad (7)$$

$$\Delta H_{\mathrm{HA}}(\mathbf{1}^{\cdot-}) = \Delta H_{\mathrm{H^-A}}(\mathbf{1}) - F[E^{\circ}(\mathrm{H}^{0/-}) - E^{\circ}(\mathbf{1}^{0/-})] \quad (8)$$

Table 1 shows that the hydride affinities of olefins **1** in acetonitrile range from −60.4 to −63.0 kcal mol^{-1} for **1a**, from −58.1 to −60.8 kcal mol^{-1} for **1b**, from −55.1 to −57.7 kcal mol^{-1} for **1c**, and from −52.8 to −55.7 kcal mol^{-1} for **1d**. The hydride affinities of olefins **1** decrease in the order **1a** > **1b** > **1c** > **1d.**[10] Among the 28 olefins, **1a** (G = NO_2) is the strongest oxidant ($\Delta H_{\mathrm{H^-A}} = -63.0$ kcal mol^{-1}) and the easiest to reduce; **1d** (G = CH_3O) should be the weakest oxidant ($\Delta H_{\mathrm{H^-A}} = -52.8$ kcal mol^{-1}) and the most difficult to reduce.

The hydride affinities of olefins **1**[10] are much smaller than those of the corresponding primary benzylic carbonium ions in acetonitrile solution (e.g., −106, −112, −118, and −121 kcal mol^{-1} for 4-$CH_3OC_6H_4CH_2^+$, 4-Me$C_6H_4CH_2^+$, $C_6H_5CH_2^+$, and 4-Cl$C_6H_4CH_2^+$, respectively),[11] but slightly smaller than or close to that of NAD$^+$ models (NADH = nicotinamide adenine dinucleotide) in acetonitrile (e.g., −64.2 kcal mol^{-1} for BNA$^+$ and −66.9 to −72.6 kcal mol^{-1} for (G)PNA$^+$; G = CH_3O, CH_3, H, Cl, Br, and CF_3),[4] which indicates that olefins **1**, like the NAD$^+$ models, are not strong hydride acceptors. Thus, if these olefins are to be efficiently reduced, only stronger reducing agents such as $NaBH_3(CN)$ (ΔH_{het}(B−H) = 45.0 kcal mol^{-1} in acetonitrile)[12] should be chosen. Weak reducing agents, such as *N*-benzyl-1,4-dihydronicotinamide (BNAH) and *N*-phenyl-1,4-dihydronicotinamide (PNAH), can not be used to reduce them in nonprotic solvents, as is well supported by experimental results.

Examining reaction (1) shows that, unlike the reduction of benzylic carbonium ions by hydride, the reduction of olefins **1** by hydride does not only involve the formation of a new C−H σ bond to release energy, but also dissociation of one C=C π bond to consume energy. Hence, the magnitude of the olefin hydride affinities 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=C π bond. Thus, it is easy to understand why the hydride affinity scale of olefins **1** is much smaller than that of the corresponding primary benzylic carbonium ions, since the hydride affinities of the primary benzylic carbonium ions do not involve the heterolytic dissociation energy of the broken C=C π bond.

From the same viewpoint, we also can explain why the hydride affinity scale of olefins **1** is close to or slightly smaller than that of NAD$^+$ models in the same solvent: The reason is that the reduction of the NAD$^+$ models by hydride, like the reduction of the olefins, also involves dissociation of one π bond in the pyridine ring. This leads to the valuable prediction that the hydride affinities of carbonyl compounds such as ketones and aldehydes should all be close to those of the corresponding olefins **1** in the same solvent.

In Table 1, the hydrogen affinities of olefins **1** in acetonitrile range from −42.6 to −43.0 kcal mol^{-1} for **1a**, from −40.9 to −41.6 kcal mol^{-1} for **1b**, from −38.6 to −39.1 kcal mol^{-1} for **1c** and from −36.9 to −37.8 kcal mol^{-1} for **1d**. These values are all close to or slightly larger than the average hydrogen affinities of typical olefins in the gas phase (−35.2 kcal mol^{-1}),[13] which means that the hydrogen affinities of olefins **1** determined in this work should be reasonable and reliable, and the same should hold true for their hydride affinities in acetonitrile. The hydrogen affinities of olefins **1** are smaller than the corresponding hydride affinities by about 18 kcal mol^{-1}, that is, olefins **1** should prefer hydride to the neutral hydrogen atom.

Proton and hydrogen affinities of the radical anions of olefins ($\mathbf{1}^{\cdot-}$) in acetonitrile range from −25.3 to −13.5 and from −70.1 to −60.5 kcal mol^{-1} for $\mathbf{1}^{\cdot-}$, from −27.4 to −15.8 and from −71.6 to −61.9 kcal mol^{-1} for $\mathbf{1b}^{\cdot-}$, from −30.2 to −17.7 and from −73.7 to −63.2 kcal mol^{-1} for $\mathbf{1c}^{\cdot-}$, and from −31.6 to −21.6 and from −74.4 to −66.4 kcal mol^{-1} for $\mathbf{1d}^{\cdot-}$, respectively (Table 1). Thus, the proton affinities of radical anions $\mathbf{1}^{\cdot-}$ are much smaller than the corresponding hydrogen affinities, by about 45 kcal mol^{-1}, which suggests that these radical anions are strong acceptors of the neutral hydrogen atom but weak proton acceptors. Conceivably, if reduction of olefins **1** by a hydride donor were initiated by single-electron transfer, hydrogen-atom transfer in the second step to the formed $\mathbf{1}^{\cdot-}$ should be much easier than proton transfer to the same radical anion. Since the hydrogen-atom affinities of $\mathbf{1}^{\cdot-}$ all are large (−60.5 to −74.4 kcal mol^{-1}), hydrogen-atom transfer could be extremely fast and possibly diffusion-controlled. We conclude that the e^-–$H^{\cdot}$ sequence of hydride transfer should be most likely among the possible multistep mechanisms for reduction of olefins **1** by hydride if the reactions were initiated by single-electron transfer.

The effect of the α substituents X and Y on the hydride affinity $\Delta H_{\mathrm{H^-A}}(\mathbf{1})$ (slope of −17.7, see Supporting Information) is much larger than that of the remote substituent G (slope of −2.56). Electron-withdrawing groups increase the hydride affinity, while electron-donating groups decrease it, that is, the hydride affinities of olefins **1** are mainly dependent on the stability of carbanions **2**, since α-Y(X) is closer to the center of negative charge than G. By using a similar method, the effects of α-substituents X and Y and remote substituent G on $\Delta H_{\mathrm{HA}}(\mathbf{1})$, $\Delta H_{\mathrm{PA}}(\mathbf{1}^{\cdot-})$, and $\Delta H_{\mathrm{HA}}(\mathbf{1}^{\cdot-})$ can also easily be elucidated (see Supporting Information).

In summary, the hydride affinities of 28 polarized olefins **1** in acetonitrile were determined by an experimental method, while the hydrogen-atom affinities of **1** and the proton affinity and hydrogen-atom affinity of the radical anions $\mathbf{1}^{\cdot-}$ were estimated by using thermodynamic cycles according to Hess' law. These thermodynamic data should be very valuable when choosing suitable reducing agents for olefins and carrying out detailed thermodynamic analysis of the reduction mechanism. This paper not only reports the hydride affinities of polarized olefins in solution for the first time, but also offers a facile and efficient experimental method to determine the hydride affinities of unsaturated organic compounds such as ketones, aldehydes, and imines in solution, which have also not yet been reported. The detailed hydride affinities of some imines will be disclosed in a forthcoming paper.

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