Thermodynamic Diagnosis of the Properties and Mechanism of Dihydropyridine-Type Compounds as Hydride Source in Acetonitrile with "Molecule ID Card"

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Received: November 23, 2009; Revised Manuscript Received: December 19, 2009

A series of 45 dihydropyridine-type organic compounds as hydride source were designed and synthesized. The thermodynamic driving forces (defined as enthalpy changes or redox potentials in this work) of the dihydropyridines to release hydride anions, hydrogen atoms (hydrogen for short), and electrons in acetonitrile, the thermodynamic driving forces of the radical cations of the dihydropyridines to release protons and hydrogens in acetonitrile, and the thermodynamic driving forces of the neutral pyridine-type radicals of the dihydropyridines to release electron in acetonitrile were determined by using titration calorimetry and electrochemical methods. The rates and activation parameters of hydride transfer from the dihydropyridines to acridinium perclorate, a well-known hydride acceptor, were determined by using UV−vis absorption spectroscopy technique. The relationship between the thermodynamic driving forces and kinetic rate of the hydride transfer was examined. Thermodynamic characteristic graph (TCG) of the dihydropyridines as an efficient "Molecule ID Card" was introduced. The TCG can be used to quantitatively diagnose or predict the characteristic chemical properties of the dihydropyridines and their various reaction intermediates. The mechanism of hydride transfer from the dihydropyridines to acridinium perclorate was diagnosed and elucidated by using the determined thermodynamic parameters and the activation parameters.

Introduction

Organic hydride compounds (organic hydrides for short in this paper) are one class of very important organic compounds that can provide hydride anions in chemical and biochemical reactions.[1] Because they play very important roles in the processes of biological reductions and bioantioxidations, natural organic hydrides, such as NAD(P)H, $FADH_2$, F420 coenzyme, tetrahydrofolate, and ascorbic acid (vitamin C), have been the focus of interest for many chemists and biochemists in the past several decades.[2−6] Recently, man-made organic hydrides have been also attracting extensive and increasing attention of chemists and biochemists, the main reason is that the man-made organic hydrides have many important roles and extensive applications in various chemical fields, e.g., as models of some important natural organic hydrides to examine the mechanisms of hydride transfer from the natural organic hydrides in vivo;[7−20] as organic reducing agents to take the place of inorganic hydrides, e.g., $NaBH_4$, $LiAlH_4$, etc. to efficiently reduce various unsaturated organic compounds, such as olefins, aldehydes, ketones, epoxy compounds, and imines;[21−25] as hydrogen-stored materials to release hydrogen gas by reacting with protonic acids;[26] as functional molecular blocks to construct various molecule devices,[27−29] and as various molecular probes to explore the essence of living phenomena,[30,31] etc. In fact, studies on man-made organic hydrides have made the *chemistry of organic hydrides* a new and hot field of chemistry.[32] By examining the publications on the man-made organic hydrides, it is found that among the various man-made organic hydrides, dihydropyridine and its various derivatives as a class of dihydropyridine-type organic hydrides have received much more special attention of chemists and biochemists than the others.[33−35] The advantages of dihydropyridine-type organic hydrides are the following: (i) dihydropyridine-type organic hydrides have the same or similar active center structure as the natural NAD(P)H coenzymes, which make the man-made dihydropyridine-type organic hydrides usable as models of NAD(P)H to mimic NAD(P)H reduction in vivo; (ii) man-made dihydropyridine-type organic hydrides can be easily synthesized in the laboratory on a large scale; and (iii) man-made dihydropyridine-type organic hydrides like natural NAD(P)H are easy to recycle for use. But, from past publications on man-made dihydropyridine-type organic hydrides, it is clear that, although there have been a lot of various man-made dihydropyridine-type organic hydrides designed and synthesized in the laboratory, and applications of them as organic reducing agents, hydrogen-storage materials, and molecule probe, etc., and they have been extensively investigated, the fundamental thermodynamic parameters, especially the thermodynamic driving forces of the organic hydrides to release hydride anions in solution, have not been systematically investigated; in fact, no thermodynamic driving forces of the dihydropyridine-type organic hydrides to release hydride anion in solution has been available from the literature until now except a few NAD(P)H models.[9f,36] It is evident that the terrible lack of knowledge about the thermodynamic driving forces of the man-made dihydropyridine-type organic hydrides must cause a lot of difficulties to predict the relative activity order of the extensively existing dihydropyridine-type organic hydrides as reducing agents, to design new dihydropyridine-type organic hydrides with higher power of releasing hydride anion, and to develop the application of the dihydropyridine-type organic hydrides as new hydride source, etc. The key reason for the lack of thermodynamic parameters until now is that no appropriate methods including efficient experimental method and reliable theoretical method have been established. Several years ago, we embarked on a major project to experimentally

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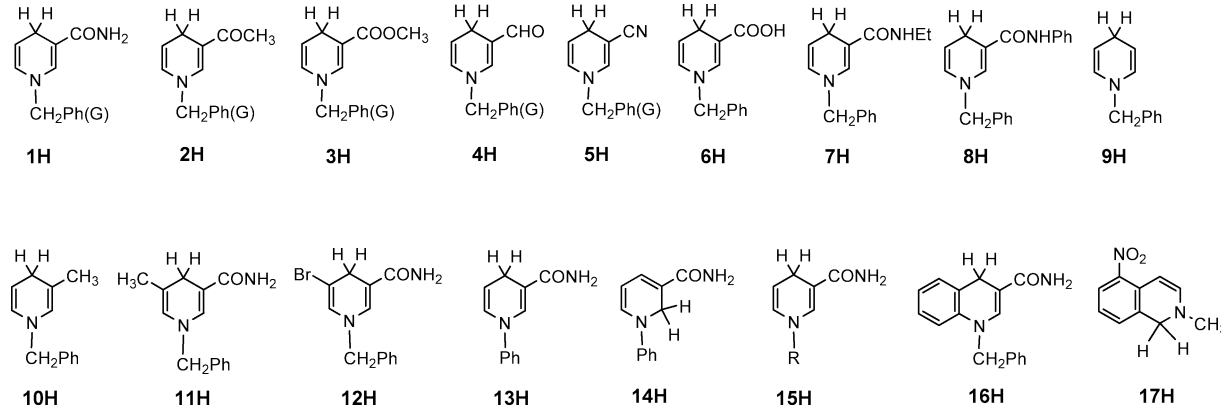
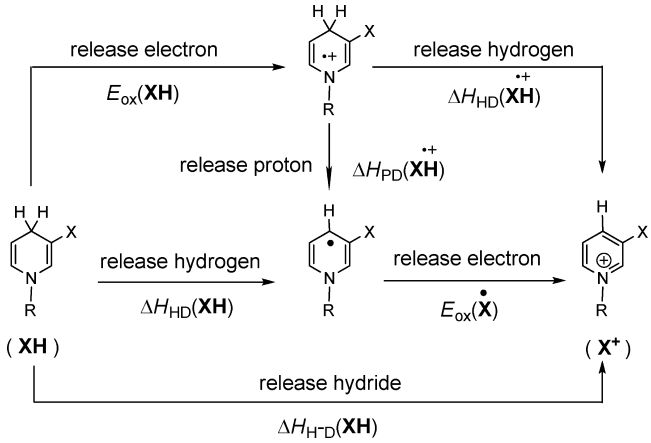
10.1021/jp911137p
Published on Web 01/14/2010

SCHEME 1: Structures of the Dihydropyridine-Type Organic Hydrides (XH) Examined in This Work



SCHEME 2: Possible Pathways of the Dihydropyridine-Type Organic Hydrides (XH) to Release Hydride Anions



determine the thermodynamic driving forces of various natural and man-made organic hydrides to release hydride anions in solution; one of the main purposes was to develop the thermodynamic driving force scale of various organic hydrides to release hydride anions in solution.[9f,35,37] In this work, 45 dihydropyridine-type organic hydrides (**XH**) (Scheme 1) were designed and synthesized and the thermodynamic driving forces of them to release hydride anions in acetonitrile were examined systematically.

As the process of the dihydropyridine-type organic hydrides (**XH**) to release hydride anions could involve multistep mechanisms, such as $e^-{-}H^+{-}e^-$, $e^-{-}H^{\bullet}$, and $H^{\bullet}{-}e^-$ (Scheme 2),[8−20] the thermodynamic driving forces of **XH** to release hydrogen atoms, the thermodynamic driving forces of $\mathbf{XH}^{\bullet+}$ to release protons and to release hydrogen atoms and the thermodynamic driving forces of $\mathbf{X}^{\bullet}$ to release electrons in solution are also very important and urgently required for chemists and biochemists to elucidate the hydride transfers mechanism and to predict and diagnose the characteristic chemical properties of the various reaction intermediates of **XH**. In this work, these thermodynamic parameters were also examined.

Results

The 45 dihydropyridine-type organic hydrides (**XH**) were synthesized in this work according to conventional and convenient synthetic strategies,[38,39] and the target products were identified by ^{1}H NMR and MS; the detailed synthetic routes are provided in the Supporting Information. Oxidation potentials of the 45 dihydropyridine-type organic hydrides (**XH**) and their corresponding pyridine-type neutral radicals ($\mathbf{X}^{\bullet}$) were determined in acetonitrile by using electrochemical methods CV and OSWV (Figures 1 and 2), and the detailed experimental results are summarized in Table 1. The molar enthalpy changes (ΔH_r) of hydride transfer from the dihydropyridine-type organic hydrides **XH** to 9-phenylxanthium perclorate ($PhXn^+ClO_4^-$) (eq

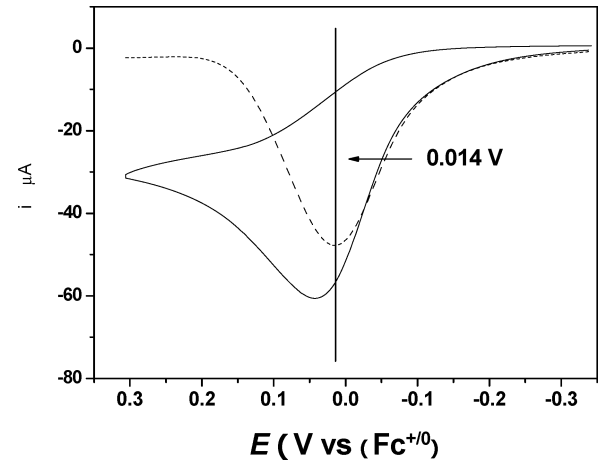


Figure 1. Cyclic voltammogram (CV) and Osteryong square wave voltammogram (OSWV) of **9H** in anhydrous deaerated acetonitrile solution containing 0.1 M $(n\text{-Bu})_4NPF_6$ as supporting electrolyte: CV graph (full line), OSWV graph (dashed line).

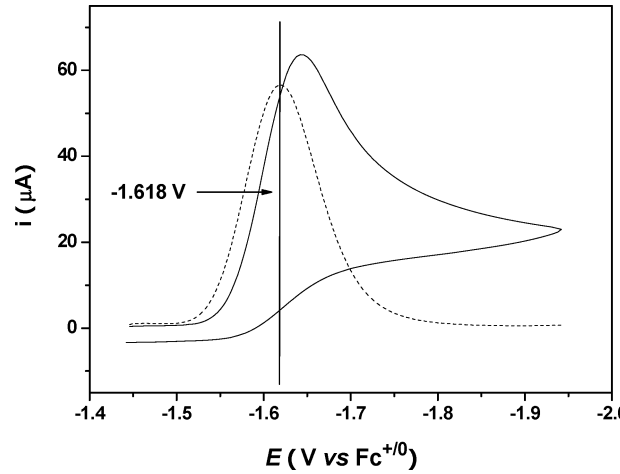


Figure 2. Cyclic voltammogram (CV) and Osteryong square wave voltammogram (OSWV) of $\mathbf{9}^+$ in anhydrous deaerated acetonitrile solution containing 0.1 M $(n\text{-Bu})_4NPF_6$ as supporting electrolyte: CV graph (full line), OSWV graph (dashed line).

TABLE 1: Reaction Enthalpy Changes of Hydride Transfer from XH to $PhXn^+ClO_4^-$ in Acetonitrile (kcal mol^{-1}) and Oxidation Potentials of XH and $X^•$ in Acetonitrile (V versus $Fc^{+/0}$), Measured by Using CV and OSWV Methods, Respectively

org hydrides (**XH**)	ΔH_r[a]	E_{ox}(**XH**)[b]		E_{ox}($X^•$)[b]	
		CV	OSWV	CV	OSWV
1H					
p-CH_3O	−33.7	0.241	0.204	−1.463	−1.432
p-CH_3	−33.2	0.253	0.211	−1.458	−1.427
p-H	−32.6	0.259	0.219	−1.448	−1.419
p-F	−32.5	0.266	0.224	−1.445	−1.415
p-Cl	−31.8	0.279	0.237	−1.436	−1.407
p-CN	−30.5	0.311	0.268	−1.405	−1.374
2H					
p-CH_3O	−30.6	0.338	0.302	−1.369	−1.329
p-CH_3	−30.3	0.351	0.312	−1.36	−1.318
p-H	−29.7	0.361	0.323	−1.347	−1.310
p-F	−29.6	0.366	0.329	−1.341	−1.306
p-Cl	−29.2	0.381	0.344	−1.326	−1.295
p-CN	−27.8	0.408	0.370	−1.295	−1.265
3H					
p-CH_3O	−31.9	0.374	0.337	−1.394	−1.363
p-CH_3	−31.6	0.385	0.348	−1.389	−1.355
p-H	−31.0	0.402	0.361	−1.37	−1.341
p-F	−30.9	0.406	0.365	−1.366	−1.339
p-Cl	−30.2	0.413	0.375	−1.359	−1.329
p-CN	−28.9	0.438	0.401	−1.325	−1.295
4H					
p-CH_3O	−27.1	0.443	0.407	−1.217	−1.187
p-CH_3	−26.7	0.455	0.418	−1.213	−1.181
p-H	−26.3	0.470	0.431	−1.207	−1.176
p-F	−26.2	0.476	0.434	−1.203	−1.172
p-CN	−24.2	0.508	0.471	−1.169	−1.139
5H					
p-CH_3O	−26.6	0.490	0.454	−1.224	−1.195
p-CH_3	−26.2	0.501	0.464	−1.216	−1.187
p-H	−25.5	0.517	0.479	−1.202	−1.175
p-F	−25.4	0.522	0.484	−1.200	−1.171
p-Cl	−24.4	0.531	0.495	−1.191	−1.159
p-CN	−22.9	0.557	0.521	−1.159	−1.131
6H	−29.3	0.390	0.370	−1.380	−1.352
7H	−33.0	0.233	0.199	−1.485	−1.463
8H	−30.9	0.303	0.259	−1.393	−1.340
9H	−43.8	0.038	0.014	−1.642	−1.618
10H	−48.8	−0.070	−0.094	−1.710	−1.682
11H	−35.3	0.170	0.142	−1.478	−1.458
12H	−28.6	0.394	0.370	−1.406	−1.386
13H	−28.0	0.363	0.332	−1.154	−1.125
14H	−29.5	0.251	0.222	−1.154	−1.125
15H (R =)					
CH_3	−36.1	0.170	0.136	−1.492	−1.470
Et	−35.3	0.176	0.136	−1.500	−1.480
pr	−36.0	0.167	0.136	−1.490	−1.468
i-pr	−35.6	0.180	0.150	−1.508	−1.484
n-butyl	−35.5	0.168	0.140	−1.687	−1.464
16H	−21.0	0.380	0.348	−1.046	−1.000
17H	−22.9	0.150	0.115	−0.959	−0.924

[a] ΔH_r obtained from the reaction heat of eq 3 by switching the sign; the latter was measured by titration calorimetry in acetonitrile at 25 °C. The data given in kcal/mol were average values of at least three independent runs. The reproducibility is ±0.5 kcal mol^{-1}. [b] Measured by CV and OSWV methods in acetonitrile at 25 °C, the unit in volts vs $Fc^{+/0}$ and reproducible to 5 mV or better.

3) were measured by using titration calorimetry in acetonitrile (Figure 3), the detailed experimental results are also listed in Table 1.

The thermodynamic driving force of the dihydropyridine-type organic hydrides (**XH**) to release hydride anions in acetonitrile

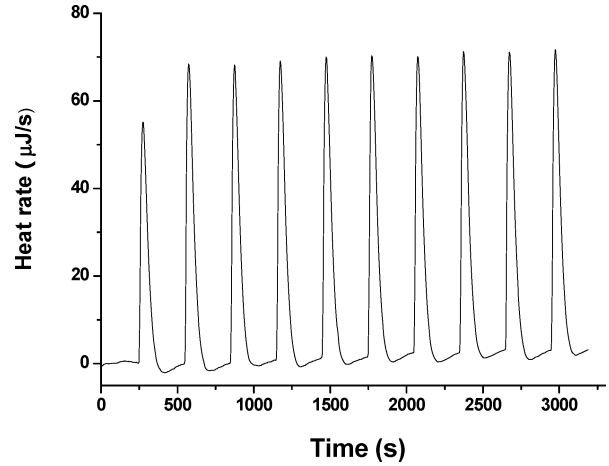
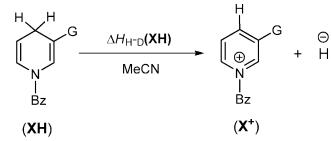


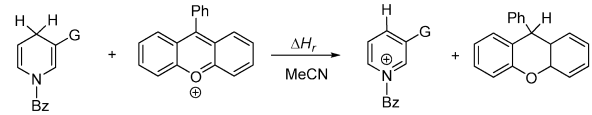
Figure 3. Isothermal titration calorimetry (ITC) for the reaction heat of **2H** (G = H) with 9-phenylxanthylium perclorate ($PhXn^+ClO_4^-$) in acetonitrile at 298 K. Titration was conducted by adding 10 μL of $PhXn^+ClO_4^-$ (3.27 mM) every 300s into the acetonitrile containing **2H** (G = H) (ca. 12.08 mM).

in this work was defined as the enthalpy changes of **XH** to release hydride anions in acetonitrile (eqs 1 and 2), which can be obtained from the reaction enthalpy change of the hydride transfer from **XH** to 9-phenylxanthylium perclorate ($PhXn^+ClO_4^-$) in acetonitrile (eqs 3 and 4). In eq 4, ΔH_r is the enthalpy change of the reaction of eq 3 in acetonitrile, which can be determined by using titration calorimetry (Figure 3); $\Delta H_{H^-A}(PhXn^+)$ is the hydride affinity of $PhXn^+$ in acetonitrile (i.e., the molar enthalpy change of $PhXn^+$ to obtain hydride anions in acetonitrile), which is available from our previous work (−96.8 kcal/mol).[40] The detailed enthalpy changes of the 45 **XH** to release hydride anions in acetonitrile are summarized in Table 2.



(1)

$$\Delta H_{H^-D}(\mathbf{XH}) = H_f(\mathbf{X}^+) + H_f(H^-) - H_f(\mathbf{XH}) \quad (2)$$



(3)

$$\Delta H_{H^-D}(\mathbf{XH}) = \Delta H_r - \Delta H_{H-A}(PhXn^+) \quad (4)$$

The thermodynamic driving forces of **XH** to release hydrogen atoms and the thermodynamic driving forces of $\mathbf{XH}^{•+}$ to release protons and to release hydrogen atoms in acetonitrile are also defined as the corresponding enthalpy changes of **XH** to release hydrogen atoms and of $\mathbf{XH}^{•+}$ to release protons and to release hydrogen atoms in acetonitrile, respectively. It is evident that these enthalpy change values can be used to measure hydrogen-donating abilities of **XH** and proton-donating and hydrogen-donating abilities of $\mathbf{XH}^{•+}$, respectively. In order to obtain the enthalpy change values of the 45 **XH** to release hydrogen atoms in acetonitrile and the enthalpy change values of the 45 $\mathbf{XH}^{•+}$ to release protons and to release hydrogen atoms in acetonitrile, three thermodynamic cycles were constructed according to the chemical process of **XH** to release hydride anions in acetonitrile (Scheme 3). From the three thermodynamic cycles, three eqs

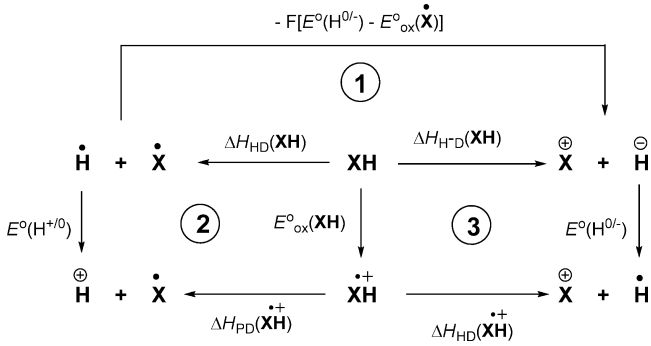
TABLE 2: Molar Enthalpy Changes of XH to Release Hydride Anions and Hydrogen Atoms and Molar Enthalpy Changes of $XH^{\bullet+}$ To Release Hydrogen Atoms and Protons (kcal mol^{-1}) as Well as Oxidation Potentials of XH and $X^{\bullet}$ in Acetonitrile (V versus $Fc^{+/0}$)

XH	$\Delta H_{H^-D}(XH)^a$	$\Delta H_{HD}(XH)^b$	$\Delta H_{HD}(XH^{\bullet+})^b$	$\Delta H_{PD}(XH^{\bullet+})^b$	$E^\circ_{ox}(XH)^c$	$E^\circ_{ox}(X^{\bullet})^c$
1H						
p-CH_3O	63.1	69.9	32.2	12.0	0.204	−1.432
p-CH_3	63.6	70.3	32.5	12.2	0.211	−1.427
p-H	64.2	70.7	32.9	12.4	0.219	−1.419
p-F	64.3	70.7	32.9	12.3	0.224	−1.415
p-Cl	65.0	71.2	33.3	12.6	0.237	−1.407
p-CN	66.3	71.8	33.9	12.4	0.268	−1.374
2H						
p-CH_3O	66.2	70.6	33.0	10.5	0.302	−1.329
p-CH_3	66.5	70.7	33.1	10.3	0.312	−1.318
p-H	67.1	71.1	33.4	10.4	0.323	−1.310
p-F	67.2	71.1	33.4	10.3	0.329	−1.306
p-Cl	67.6	71.2	33.4	10.1	0.344	−1.295
p-CN	69.0	72.0	34.2	10.2	0.370	−1.265
3H						
p-CH_3O	64.9	70.1	30.9	9.1	0.337	−1.363
p-CH_3	65.2	70.2	31.0	9.0	0.348	−1.355
p-H	65.8	70.5	31.3	9.0	0.361	−1.341
p-F	65.9	70.6	31.3	8.9	0.365	−1.339
p-Cl	66.6	71.0	31.7	9.2	0.375	−1.329
p-CN	67.9	71.5	32.4	9.1	0.401	−1.295
4H						
p-CH_3O	69.7	70.9	34.1	8.3	0.407	−1.187
p-CH_3	70.1	71.1	34.2	8.3	0.418	−1.181
p-H	70.5	71.4	34.3	8.3	0.431	−1.176
p-F	70.6	71.4	34.4	8.2	0.434	−1.172
p-CN	72.6	72.6	35.5	8.5	0.471	−1.139
5H						
p-CH_3O	70.2	71.5	33.5	7.9	0.454	−1.195
p-CH_3	70.6	71.8	33.7	7.9	0.464	−1.187
p-H	71.3	72.2	34.0	7.9	0.479	−1.175
p-F	71.4	72.2	34.0	7.8	0.484	−1.171
p-Cl	72.4	72.9	34.8	8.3	0.495	−1.159
p-CN	73.9	73.8	35.7	8.5	0.521	−1.131
6H	67.5	72.5	32.7	10.7	0.370	−1.352
7H	63.8	71.3	33.0	13.5	0.199	−1.463
8H	65.9	70.6	33.7	11.4	0.259	−1.340
9H	53.0	64.1	26.5	10.6	0.014	−1.618
10H	48.0	60.6	23.9	9.5	−0.094	−1.682
11H	61.5	68.9	32.0	12.4	0.142	−1.458
12H	68.2	73.9	33.4	12.2	0.370	−1.386
13H	68.8	68.5	34.9	7.7	0.332	−1.125
14H	67.3	67.0	36.0	8.7	0.222	−1.125
15H (R =)						
CH_3	60.7	68.4	31.3	12.0	0.136	−1.470
Et	61.5	69.4	32.1	13.1	0.136	−1.480
pr	60.8	68.5	31.5	12.1	0.136	−1.468
i-pr	61.3	69.3	31.6	12.6	0.150	−1.484
n-butyl	61.4	68.9	31.9	12.5	0.140	−1.464
16H	75.8	72.6	41.5	11.4	0.348	−1.000
17H	73.9	69.0	44.9	12.5	0.115	−0.924

[a] $\Delta H_{H^-D}(XH)$ values were derived from eq 4, taking $\Delta H_{H^-A}(PhXn^+) = 96.8$ kcal/mol in acetonitrile from ref 40 the uncertainties are all smaller than 1 kcal mol^{-1}. [b] $\Delta H_{HD}(XH)$, $\Delta H_{PD}(XH^{\bullet+})$, and $\Delta H_{HD}(XH^{\bullet+})$ were estimated from eqs 5−7, respectively, taking $E^o(H^{+/0}) = -2.307$ (V versus $Fc^{+/0}$), $E^o(H^{0/-}) = -1.137$ (V versus $Fc^{+/0}$), which was derived from Parker's work[42] adjusted to versus $Fc^{+/0}$ by adding −0.537 V. Relative uncertainties were estimated to be smaller than or close to 1 kcal/mol in each case. [c] The standard oxidation potential values of **XH** and $X^{\bullet}$ in acetonitrile were all derived from the experimental results by using OSWV method, because OSWV has been verified to be a more exact electrochemical method for evaluating the standard one-electron redox potentials of analyte with irreversible electrochemical processes than CV.[9f,43]

5−7[41] were formed according to Hess' law, respectively. In eqs 5−7, $\Delta H_{H^-D}(XH)$ and $\Delta H_{HD}(XH)$ are the enthalpy changes of **XH** to release hydride anions and to release hydrogen atoms in acetonitrile, respectively; the $\Delta H_{PD}(XH^{\bullet+})$ and $\Delta H_{HD}(XH^{\bullet+})$ are the enthalpy changes of $XH^{\bullet+}$ to release protons and to release hydrogen atoms in acetonitrile, respectively; $E^o(X^{+/0})$, $E^o(XH^{+/0})$, $E^o(H^{0/-})$, and $E^o(H^{+/0})$ are the standard redox potentials of X^+, **XH**, H^+, and H^- in acetonitrile, respectively. Evidently, it is not difficult to obtain the enthalpy change of **XH** to release hydrogen atoms, the enthalpy changes of $XH^{\bullet+}$ to release protons and to release hydrogen atoms in acetonitrile, if only $\Delta H_{H^-D}(XH)$, $E^o(X^{+/0})$, $E^o(XH^{+/0})$, $E^o(H^{0/-})$, and $E^o(H^{+/0})$ are available. In fact, $\Delta H_{H^-D}(XH)$ can be available from the above work (Table 1), the standard redox potentials of $E^o(H^{0/-})$ and $E^o(H^{+/0})$ can be obtained from the literature,[42] and $E^o(X^{+/0})$ and $E^o(XH^{+/0})$ can be obtained from experimental measurements

SCHEME 3: Three Thermodynamic Cycles Constructed on the Basis of the Chemical Process of XH to Release Hydride Anion in Acetonitrile



(Table 1). The detailed values of $\Delta H_{HD}(\mathbf{XH})$, $\Delta H_{PD}(\mathbf{XH}^{\bullet+})$, and $\Delta H_{HD}(\mathbf{XH}^{\bullet+})$ of the 45 dihydropyridine-type organic hydrides in acetonitrile are also summarized in Table 2.

$$\Delta H_{HD}(\mathbf{XH}) = \Delta H_{H-D}(\mathbf{XH}) - F[E^{o}_{ox}(\mathbf{X}^{\bullet}) - E^{o}(H^{0/-})] \quad (5)$$

$$\Delta H_{HD}(\mathbf{XH}^{\bullet-}) = \Delta H_{HD}(\mathbf{XH}) - F[E^{o}_{ox}(\mathbf{XH}) - E^{o}(H^{+/0})] \quad (6)$$

$$\Delta H_{HD}(\mathbf{XH}^{\bullet+}) = \Delta H_{H-D}(\mathbf{XH}) - F[E^{o}_{ox}(\mathbf{XH}) - E^{o}(H^{0/-})] \quad (7)$$

The kinetics of hydride transfer from **XH** to acridinium perclorate ($AcrH^+ClO_4^-$), a well-known hydride acceptor, were conveniently monitored with stopped-flow or general UV−vis absorption spectra by following the time dependence of the absorbance at $\lambda_{max} = 415$ nm for the $AcrH^+ClO_4^-$ with **XH** in more than 20-fold excess (Figure 4). The pseudo-first-order rate constants were calculated by Guggenheim's method.[44] The second-order rate constant (k_2) at different temperature between 298 and 318 K are given in Table 3, which were derived from plots of the pseudo-first-order rate constants versus the concentrations of **XH**. Eyring activation parameters, activation enthalpy ($\Delta H^{\neq}$) and activation entropy ($\Delta S^{\neq}$), for the hydride transfer from **XH** to $AcrH^+ClO_4^-$ are summarized in Table 4; they were derived from Eyring plots of $\ln(k_2/T)$ versus the reciprocal of the absolute temperature ($1/T$), respectively.

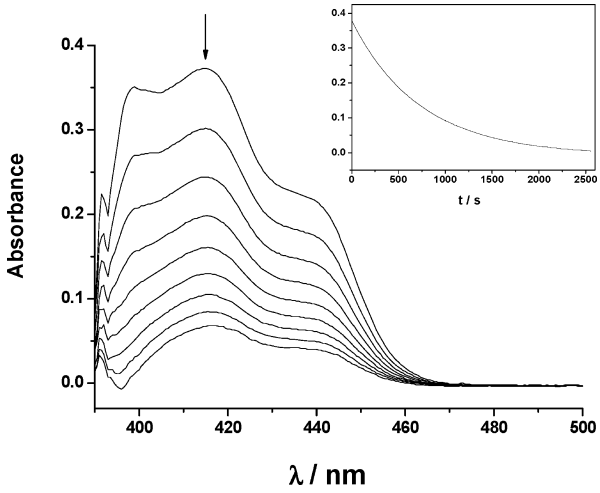


Figure 4. UV−vis spectra change obtained from the reaction of **4H** (2 mM) with $AcrH^+ClO_4^-$ (0.1 mM) in dry acetonitrile at 298 K at 3 min intervals (going downward). Inset: the time-resolved spectrum at $\lambda_{max} = 415$ nm.

TABLE 3: Dependence of the Hydride Transfer Rates from XH to $AcrH^+ClO_4^-$ in Acetonitrile on the Reaction Temperature

	k_2 (M^{-1} s^{1-})[a]				
dihydropyridines	298 K	303 K	308 K	313 K	318 K
1H					
p-CH_3O	97.0	109.3	125.7	147.2	170.4
p-CH_3	83.6	93.5	108.2	133.3	150.0
p-H	76.1	86.7	101.0	117.5	135.7
p-F	71.6	83.2	91.7	101.6	118.3
p-Cl	51.6	61.5	69.4	78.4	89.3
p-CN	25.8	27.6	31.1	36.8	41.4
2H					
p-CH_3O	25.5	36.3	44.5	53.1	64.4
p-CH_3	23.8	33.4	41.4	49.8	59.5
p-H	17.7	21.2	26.1	31.7	36.4
p-F	14.9	20.4	23.5	29.5	34.5
p-Cl	12.8	16.9	19.3	24.5	29.2
p-CN	9.81	12.5	13.6	16.4	19.9
3H					
p-CH_3O	41.8	51.3	66.0	75.3	87.5
p-CH_3	38.0	49.7	61.2	70.3	82.4
p-H	31.0	36.9	46.4	54.9	66.1
p-F	24.5	32.4	38.4	46.2	54.5
p-Cl	21.7	27.4	32.6	39.0	45.8
p-CN	9.91	13.8	17.4	21.9	27.3
4H					
p-CH_3O	0.842	0.999	1.20	1.36	1.66
p-CH_3	0.771	0.867	0.982	1.12	1.23
p-H	0.597	0.752	0.919	1.09	1.32
p-F	0.518	0.649	0.774	0.896	1.10
p-CN	0.238	0.315	0.406	0.501	0.602
5H					
p-CH_3O	0.668	0.823	0.968	1.25	1.37
p-CH_3	0.641	0.777	0.885	1.03	1.16
p-H	0.455	0.553	0.652	0.755	0.850
p-F	0.332	0.389	0.457	0.531	0.612
p-Cl	0.161	0.204	0.254	0.296	0.359
p-CN	0.092	0.114	0.134	0.151	0.192
6H	25.8	31.4	40.1	48.8	59.4
7H	83.4	95.8	106.3	122.3	144.6
8H	43.8	52.1	63.5	77.1	86.0
9H	1.90×10^4	2.36×10^4	2.79×10^4	3.38×10^4	3.96×10^4
10H	2.61×10^4	3.17×10^4	3.77×10^4	4.45×10^4	5.10×10^4
11H	91.3	107.1	125.7	149.2	171.3
12H	1.65	1.88	2.28	2.73	3.35
13H	4.62	5.53	6.30	7.18	7.68
14H	3.63	4.22	4.49	5.18	5.66
15H					
CH_3	288	347	388	463	514
Et	238	303	357	423	477
pr	281	352	387	444	511
i-pr	102	130	150	175	204
n-butyl	343	415	472	576	656
16H	0.52	0.62	0.74	0.86	1.03
17H	3.02	3.28	3.47	3.75	3.97

[a] Second-order rate constants k_2 were obtained from the corresponding pseuso-first-order rate constants by the linear correlation against the concentration of the **XH**, the experimental error is within 5%.

Discussion

Thermodynamic Driving Force Scale of the Dihydropyridine-Type Organic Hydrides (XH) To Release Hydride Anions in Acetonitrile. It is well-known that the standard-state enthalpy change of **XH** to release hydride anions is a very important thermodynamic parameter of **XH**, which can be used to scale the power of **XH** to donate hydride anions. From Table 2, it is found that the enthalpy changes of the 45 **XH** in

TABLE 4: Comparison of Activation Parameters of Hydride Transfer from XH to $AcrH^+$ and Thermodynamic Driving Forces of XH to Release Hydride Anions in Acetonitrile

dihydropyridines	$\Delta H_{H^-T}(\mathbf{XH})^a$	$\Delta H^{\ddagger}(H^-T)^b$	$\Delta S^{\ddagger}(H^-T)^c$	$-T\Delta S^{\ddagger}(H^-T)^d$	$\Delta G^{\ddagger}(H^-T)^e$
1H					
p-CH_3O	63.1	4.8	−33.6	10.0	14.8
p-CH_3	63.6	5.1	−32.6	9.7	14.8
p-H	64.2	4.9	−33.6	10.0	14.9
p-F	64.3	3.9	−36.9	11.0	14.9
p-Cl	65.0	4.4	−35.8	10.7	15.1
p-CN	66.3	4.0	−38.7	11.5	15.6
2H					
p-CH_3O	66.2	7.8	−25.8	7.7	15.5
p-CH_3	66.5	7.8	−25.9	7.7	15.5
p-H	67.1	6.3	−31.6	9.4	15.8
p-F	67.2	7.1	−29.2	8.7	15.8
p-Cl	67.6	7.0	−30.0	9.0	15.9
p-CN	69.0	5.8	−34.7	10.3	16.1
3H					
p-CH_3O	64.9	6.4	−29.6	8.8	15.2
p-CH_3	65.2	6.6	−29.3	8.7	15.3
p-H	65.8	6.6	−29.7	8.8	15.4
p-F	65.9	6.8	−29.4	8.8	15.5
p-Cl	66.6	6.3	−31.1	9.3	15.6
p-CN	67.9	8.8	−24.6	7.3	16.1
4H					
p-CH_3O	69.7	5.7	−39.9	11.9	17.6
p-CH_3	70.1	3.9	−46.2	13.8	17.6
p-H	70.5	6.8	−36.9	11.0	17.8
p-F	70.6	6.3	−38.7	11.5	17.8
p-CN	72.6	8.1	−34.1	10.2	18.3
5H					
p-CH_3O	70.2	6.4	−37.9	11.3	17.7
p-CH_3	70.6	4.9	−43.1	12.8	17.7
p-H	71.3	5.3	−42.4	12.6	17.9
p-F	71.4	5.2	−43.4	12.9	18.1
p-Cl	72.4	6.9	−39.1	11.7	18.5
p-CN	73.9	6.0	−43.3	12.9	18.9
6H	67.5	7.4	−27.5	8.2	15.9
7H	63.8	4.5	−34.9	10.4	14.8
8H	65.9	6.0	−31.1	9.3	15.2
9H	53.0	6.2	−18.2	5.4	11.6
10H	48.0	5.7	−19.2	5.7	11.5
11H	61.5	5.4	−31.6	9.4	14.8
12H	68.2	6.1	−37.1	11.1	17.2
13H	68.8	5.8	−36.2	10.8	16.6
14H	67.3	3.9	−41.9	12.5	16.4
15H					
CH_3	60.7	4.8	−31.0	9.2	14.1
Et	61.5	5.9	−27.8	8.3	14.2
pr	60.8	4.8	−31.2	9.3	14.1
i-pr	61.3	5.8	−30.0	8.9	14.7
n-butyl	61.4	5.5	−28.5	8.5	14.0
16H	75.8	5.8	−40.6	12.1	17.9
17H	73.9	2.0	−49.8	14.8	16.8

[a] $\Delta H_{H^-D}(\mathbf{XH})$ is enthalpy change of **XH** to release hydride anion in acetonitrile, the unit is kcal mol^{-1}. [b] From the slope of the Eyring plots, the unit is kcal mol^{-1}. [c] From the intercept of the Eyring plot; the unit is cal mol^{-1} K^{-1}. [d] The unit is kcal mol^{-1}. [e] From the equation $\Delta G^{\ddagger} = \Delta H^{\ddagger} - T\Delta S^{\ddagger}$, the unit is kcal mol^{-1}.

acetonitrile range from 48.0 kcal/mol for **10H** to 75.8 kcal/mol for **16H**. Because the enthalpy changes of the 45 **XH** in acetonitrile all are not quite large, generally much smaller than that of toluene in acetonitrile (118.0 kcal/mol),[45] the dihydripyridine-type organic hydrides **XH** especially with strongly electron-donating groups should belong to good hydride donors, which indicates that the 45 dihydripyridine-type organic hydrides **XH** can construct a very useful organic hydrides library whose thermodynamic driving forces all are available, and from this organic hydrides library chemists can choose an organic hydride donor as the suitable organic reducing agent for organic syntheses. In the organic hydrides library, **10H** is the strongest organic hydride donor, the power to donate hydrides is close to or even larger than those of some metal hydrides in acetonitrile, such as $HCo(dppe)_2$ (49.1 kcal/mol),[46] $[HNi(dmpe)_2]^+$ (51 kcal mol^{-1}),[46] $CpMoH(PMe_3)(CO)_2$ (55 kcal mol^{-1}),[47] $CpMoH(PMe_3)(CO)_2$ (58 kcal mol^{-1}),[47] $[HCo(dppe)_2]^+$ (59.7 kcal mol^{-1} kcal mol^{-1}),[48] $[H_2Co(dppe)_2]^+$ (60 kcal/mol),[48] $[HNi(dmpp)_2]^+$ (65.1 kcal mol^{-1}),[46] and $[HNi(depp)_2]^+$ (67 kcal/mol).[46] In order to intuitively compare the powers of the dihydropyridine-type organic hydrides to donate hydride anions and make chemists easily choose suitable dihydropyridine-type organic hydrides as reducing agents, the 19 typical dihydripyridine-type organic

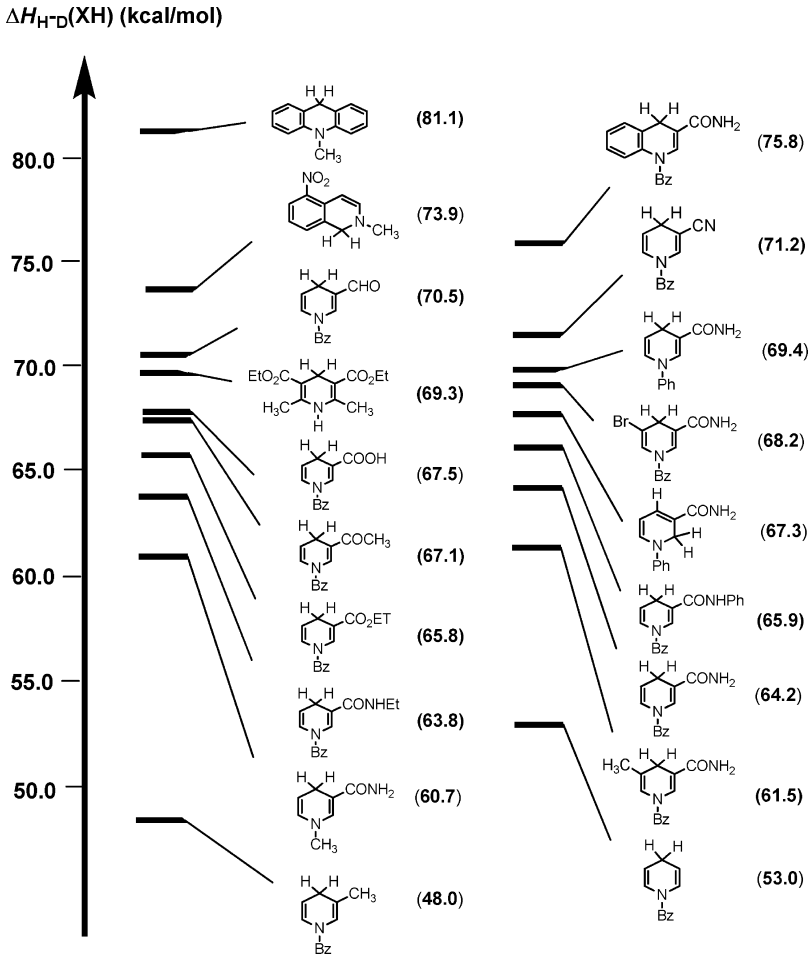


Figure 5. Comparison of thermodynamic driving forces of some typical dihydropyridine-type organic hydrides (**XH**) to release hydride anions in acetonitrile.

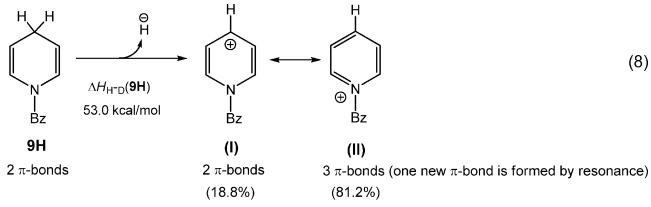
hydrides were ranked together according to their enthalpy change values to release hydride anions in acetonitrile (Figure 5).

From Figure 5, it is found that the hydride-donating ability of the dihydropyridine-type organic hydrides is not only dependent on the nature and number of the substituents on the dihydropyridine ring but also dependent on the aromaticity of the dihydropyridine system as well as on the structure of dihydropyridines. If the enthalpy change values of the dihydropyridine-type organic hydrides **1H**-**10H** are examined, it is found that electron-donating groups, such as methyl and methoxyl groups, can significantly increase the hydride-donating ability; but electron-withdrawing groups, such as CN and CHO, decrease the hydride-donating ability, and the contribution order of the substituents to the hydride-donating ability of the dihydropyridine-type organic hydrides is CH_3 > H > CONHEt > $CONH_2$ > CO_2Et > CONHPh > $COCH_3$ > COOH > CHO > CN. If the hydride-donating abilities of **13H** and **14H** are compared, it is found that the hydride-donating ability of 1,2-dihydropridine is larger than that of the corresponding 1,4-dihydropridine by 1.5 kcal mol^{-1}, which means that the state free energy of the 1,2-dihydropyridine is higher than that of the corresponding 1,4-dihydropyridine by 1.5 kcal mol^{-1}. The reason could be that the intramolecular tension of the 1,2-dihydropyridine is larger than that of the corresponding 1,4-dihydropyridine, which makes the hydrogen atom at the 2-position in the 1,2-dihydropyridine to be easier to escape as hydride anions. If the hydride-donating abilities of **1H** and **16H** are compared, it is found that the hydride-donating abilities of **1H** is larger than that of **16H** by 11.6 kcal mol^{-1}; i.e., the merger of benzene unit into the pyridine ring can decrease the hydride-donating ability of the dihydropyridine by 11.6 kcal mol^{-1}.

In order to dig up the root resulting in the good hydride-donating abilities of the dihydropyridine-type organic hydrides, the product structure of the dihydropyridine-type organic hydrides to release hydride anions is examined. From eq 1, it is found that the process of **9H** to release hydride anions does not only involve the dissociation of one old C−H bond to consume energy but also involves the formation of one new C═N π-bond to release energy; i.e., the magnitude of enthalpy change values of the dihydropyridine-type organic hydrides to release hydride anions should be equal to the heterolytic dissociation energy of the old C−H σ-bond minus the heterolytic dissociation energy of the C═N π-bond newly formed. Thus, it is easy to understand why the powers of the dihydropyridine-type organic hydrides to release hydride anions in acetonitrile are generally quite large, the reason is that, during the hydride transfer from the organic hydrides, formation of new C═N π-bond on the pyridine ring can release energy to promote the hydride anions to leave.

In order to quantitatively examine the contribution of the formed π-bond in the product to the hydride-donating abilities of the organic hydrides, the thermodynamic driving forces of **9H** and toluene[49] to release hydride anions in acetonitrile are compared (see eqs 8 and 9). From eqs 8 and 9, it is found that the hydride-donating abilities of **9H** (53.0 kcal/mol) are larger than that of toluene in acetonitrile (118.0 kcal/mol)[45] by 65.0 kcal mol^{-1}. Since 65.0 kcal/mol is smaller than the heterolytic

dissociation energies of C═N π-bonds of some neutral pyridine derivatives (80 kcal mol^{-1}),[50] it is clear that the contribution of the resonance structure II of $\mathbf{9}^+$ to the natural structure of $\mathbf{9}^+$ could not be 100%,[51] which means that the contribution of the resonance structure I to the natural structure of $\mathbf{9}^+$ can not be neglected. According to the heterolytic dissociation energy of C═N π-bond in acetonitrile solution (80 kcal mol^{-1}),[50] and the difference of the hydride-donating abilities between **9H** and toluene in acetonitrile, the contribution of resonance structures II and I to the natural structure of $\mathbf{9}^+$ can be estimated; the result is 81.2% and 18.8% from the resonance structures II and I, respectively, which means that the natural structure of $\mathbf{9}^+$ should resemble the idealized Lewis-type resonance structure with the three π-bonds on the pyridine ring (**II**) much more than the resonance structure I. This result suggests that $\mathbf{9}^+$ should be a stable chemical species, because the chemical bonds for all atoms in the resonance structure II of $\mathbf{9}^+$ are sufficient. As for the dihydropyridines **1H** and **16H**, the contribution of the resonance structure II of $\mathbf{1}^+$ to the natural structure of $\mathbf{1}^+$ and the contribution of the resonance structure II of $\mathbf{16}^+$ to the natural structure of $\mathbf{16}^+$ can be estimated by using the same method as described above; the result is 67.4% (eq 10) and 52.7% (eq 11), respectively. Since the contribution of the resonance structure II of $\mathbf{1}^+$ to the natural structure of $\mathbf{1}^+$ is larger than that of the resonance structure II of $\mathbf{16}^+$ to the natural structure of $\mathbf{16}^+$ by about 14.4%,[52] it is not difficult to understand why the hydride-donating ability of **1H** is larger than that of **16H** by 11.6 kcal/mol.



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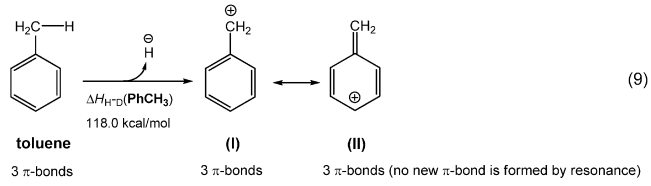

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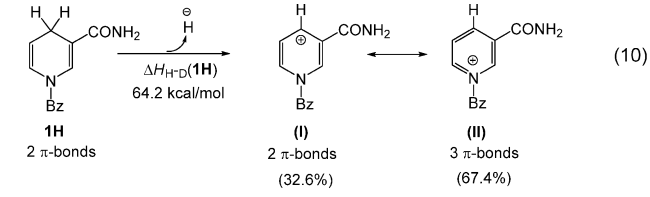

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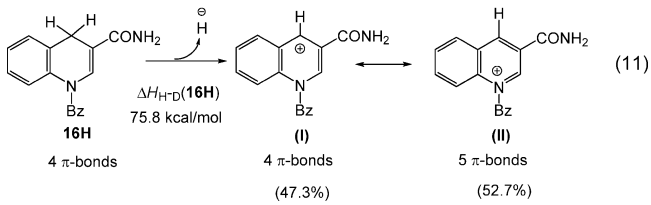


(11)

Thermodynamic Driving Forces of the Dihydropyridine-type Organic Hydrides (XH) To Release Hydrogen Atoms in Acetonitrile. From the second column in Table 2, it is clear that the enthalpy change scales of the 45 dihydropyridine-type

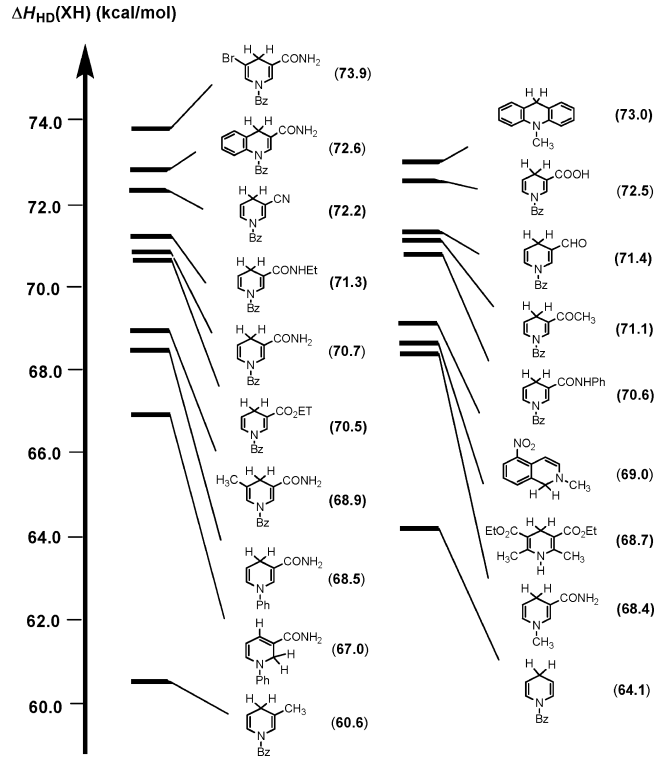
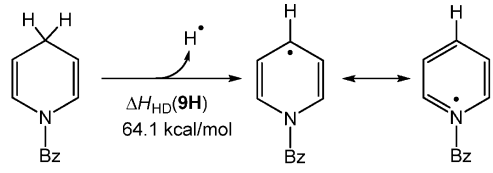


Figure 6. Comparison of thermodynamic driving forces of some typical dihydropyridine-type organic hydrides (**XH**) to release a hydrogen atom in acetonitrile.

organic hydrides **XH** to release hydrogen atoms in acetonitrile range from 60.6 kcal mol^{-1} for **10H** to 73.9 kcal mol^{-1} for **12H**. Since the enthalpy change values of the 45 **XH** all are significantly lower than that of vitamin E (79.3 kcal mol^{-1}),[53] the 45 dihydropyridine-type organic hydrides all belong to good hydrogen atom donors, which means that the 45 organic hydrides all can be used as good antioxidants to quench some well-known radicals, such as O$^\bullet$ (102.8 kcal mol^{-1}),[54] HO$^\bullet$ (118.8 kcal mol^{-1}),[54] HOO$^\bullet$ (87.8 kcal mol^{-1}),[55] *i*-$C_3H_7OO^\bullet$ (85.1 kcal mol^{-1}),[56] PhS$^\bullet$ (83.5 kcal mol^{-1}),[57] RSS$^\bullet$ (70.0 kcal mol^{-1}),[58] and TEMPO$^\bullet$ (71.2 kcal mol^{-1}).[59] But for the radical of $O_2^\bullet$ (48.2 kcal mol^{-1}),[60] the 45 dihydropyridine-type organic hydrides all have no work to quench it. In order to more intuitively compare the powers of the organic hydrides to donate hydrogen atoms and make one easily choose the dihydropyridine-type organic hydrides as suitable antioxidants, 19 typical dihydropyridine-type organic hydrides were ranked in order according to the values of the enthalpy changes in acetonitrile (Figure 6). From Figure 6, it is found that the substituent at the pyridine ring has evident effect on the hydrogen-atom-donating ability of the organic hydrides and generally, the electron-drawing groups, such as cyano, can decrease the hydrogen-donating ability, but electron-donating groups, such as methyl, can increase the hydrogen-donating ability, which suggests that the neutral pyridine-type radicals $\mathbf{X}^\bullet$ should be due to electron-deficient radicals.

In order to examine the actual structure of $\mathbf{X}^\bullet$, the thermodynamic driving forces of **9H** and toluene to release hydrogen atoms in acetonitrile are compared (see eqs 12 and 13). From eqs 12 and 13, it is found that the hydrogen-atom-donating ability of **9H** (64.1 kcal mol^{-1}) is larger than that of toluene in acetonitrile (90.1 kcal mol^{-1})[48] by 26.0 kcal mol^{-1}. Since the homolytic dissociation energy of C═N

π-bond on the neutral pyridine ring has been estimated to be about 66 kcal mol^{-1},[50] the contribution of resonance structures II and I to the actual structure of **9**$^{\bullet}$ can be estimated according to the difference between the enthalpy change of **9H** to release hydrogen atoms (64.1 kcal mol^{-1}) and the homolytic dissociation energy of C=N π-bond (66 kcal mol^{-1}); the result is 39.4% and 60.6% for the resonance structures II and I, respectively, which means that the actual structure of **9**$^{\bullet}$ should resemble the idealized Lewis-type resonance structure I with two π-bonds on the pyridine ring rather than the idealized Lewis-type resonance structure II with three π-bonds on the pyridine ring, which means that **9**$^{\bullet}$ should primarily belongs to carbon radical rather than nitrogen radical. Since the carbon atom at 4-position in the resonance structure I is lacking a chemical bond, **9**$^{\bullet}$ should be a very active radical, but the activity should be markedly smaller than that of the benzyl radical, because the contribution of the resonance structure I to the actual structure of **9**$^{\bullet}$ is merely 60.6%.



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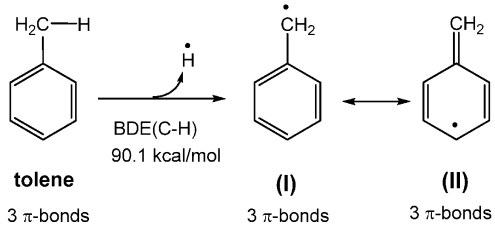


(13)

Thermodynamic Driving Forces of Radical Cations of the Dihydropyridine-Type Organic Hydrides (XH$^{\bullet+}$) To Release Hydrogen Atoms and To Release Protons in Acetonitrile. As is well-known, radical cations of organic hydrides (**XH**$^{\bullet+}$) are one of the most important reaction intermediates of the organic hydrides as organic reducing agents, when the hydride transfer is initiated by electron transfer. Since the enthalpy changes of the radical cations to release hydrogen atoms and protons can not only be used to quantitatively scale the characteristic chemical properties of the radical cations but also to diagnose the mechanism of the hydride transfer from the organic hydrides, it is necessary to examine and compare the enthalpy changes of the radical cations to release hydrogen atoms and to release protons. From columns 4 and 5 in Table 2, we found that the enthalpy change scales of the 45 **XH**$^{\bullet+}$ to release hydrogen atoms and to release protons range from 23.9 to 44.9 kcal mol^{-1} and from 7.7 to 13.5 kcal mol^{-1}, respectively. According to the enthalpy change values of the 45 **XH**$^{\bullet+}$ to release hydrogen atoms (23.9−44.9 kcal/mol), it is conceived that the radical cations of the dihydropyridine-type organic hydrides should be very strong hydrogen atom donors, and the hydrogen-atom-donating abilities of the 45 **XH**$^{\bullet+}$ all are larger than that of the well-known HOO$^{\bullet}$, a very strong hydrogen atom donor in acetonitrile (48.2 kcal mol^{-1}),[58] which means that the radical cations of the dihydropyridine-type organic hydrides **XH**$^{\bullet+}$ can not only quench some very active radicals, such as O$^{\bullet}$, HO$^{\bullet}$, and HOO$^{\bullet}$, but also quench the relative stable radicals, such as $O_2^{\bullet}$, NO$^{\bullet}$, and ONNOH$^{\bullet}$ by hydrogen atom transfer. This result suggests that the radical cations of the dihydropyridine-type organic hydrides **XH**$^{\bullet+}$ all are unstable in the air.

According to the values of the enthalpy changes for the 45 **XH**$^{\bullet+}$ to release protons (7.7−13.5 kcal mol^{-1}), it is clear that the dihydropyridine-type radical cations (**XH**$^{\bullet+}$) belong to strong proton donors, the acidities of them in acetonitrile are much greater than those of some typical organic acids in acetonitrile, such as benzoic acid (pK_a = 20.1, equivalent to 27.5 kcal mol^{-1} free energy change of benzoic acid to release proton)[61] and trifluoroacetic acid (pK_a = 12.7, equivalent to 17.4 kcal mol^{-1} free energy change of trifluoroacetic acid to release proton in acetonitrile),[62] but smaller than of some inorganic acids in acetonitrile, such as HBr (pK_a = 5.5, equivalent to 7.5 kcal mol^{-1} free energy change of HBr to release proton in acetonitrile),[63] and HCl (pK_a = 8.9, equivalent to 12.2 kcal mol^{-1} free energy change of HCl to release proton in acetonitrile),[63] and H_2S (pK_a = 0.5, equivalent to 0.7 kcal mol^{-1} free energy change of H_2S to release proton in acetonitrile).[64]

In order to more intuitively compare the thermodynamic driving forces of the radical cations to release hydrogen atoms and to release protons as well as to more conveniently examine the effect of substituents at the pyridine ring on the thermodynamic driving forces of the radical cations to release hydrogen atoms and to release protons, the 19 typical radical cations of the **XH** are ranked in Figures 7 and 8 according to their corresponding values of the enthalpy changes in acetonitrile, respectively. From Figures 7 and 8, it is found that, although the substituents at the dihydropyridine ring have significant effect on the thermodynamic driving forces of the radical cations to release hydrogen atoms and to release protons, no well linear relationship can be found; the reason could be that the mechanism of the substituents effect on the thermodynamic driving forces of the radical cations to release hydrogen atoms and to release protons is quite complicated.

Since the enthalpy change values of the 45 **XH**$^{\bullet+}$ to release protons and to release hydrogen atoms all are quite larger than zero, it is conceived that the radical cations **XH**$^{\bullet+}$ in acetonitrile should be relatively stable, which means that **XH**$^{\bullet+}$ in anaerobic acetonitrile solution all could be directly detected and characterized by EPR spectroscopy under general experimental conditions.[65,66] Since the proton-donating ability of **XH**$^{\bullet+}$ is much larger than the corresponding hydrogen-atom-donating ability, it is conceivable that when the hydride transfer from the dihydropyridine-type organic hydrides were initiated by electron transfer, the possibility of proton transfer in the second reaction step should be much larger than that of the hydrogen atom transfer in the second reaction step. That is, the e−H^{+}−e sequence hydride transfer should be most likely among the various possible multistep mechanisms for the hydride transfer from the dihydropyridine-type organic hydrides (Scheme 1), if the hydride transfer were initiated by single-electron transfer.

Thermodynamic Driving Forces of the Dihydropyridine-Type Organic Hydrides (XH) and Their Neutral Pyridine-Type Radicals (X$^{\bullet}$) To Release Electrons in Acetonitrile. As is well-known, the standard oxidation potentials of the dihydropyridine-type organic hydrides (**XH**) and their neutral pyridine-type radicals (**X**$^{\bullet}$) are very important electrochemical parameters, which can be used as an indicator of the electron-donating ability of **XH** and **X**$^{\bullet}$ in solution.

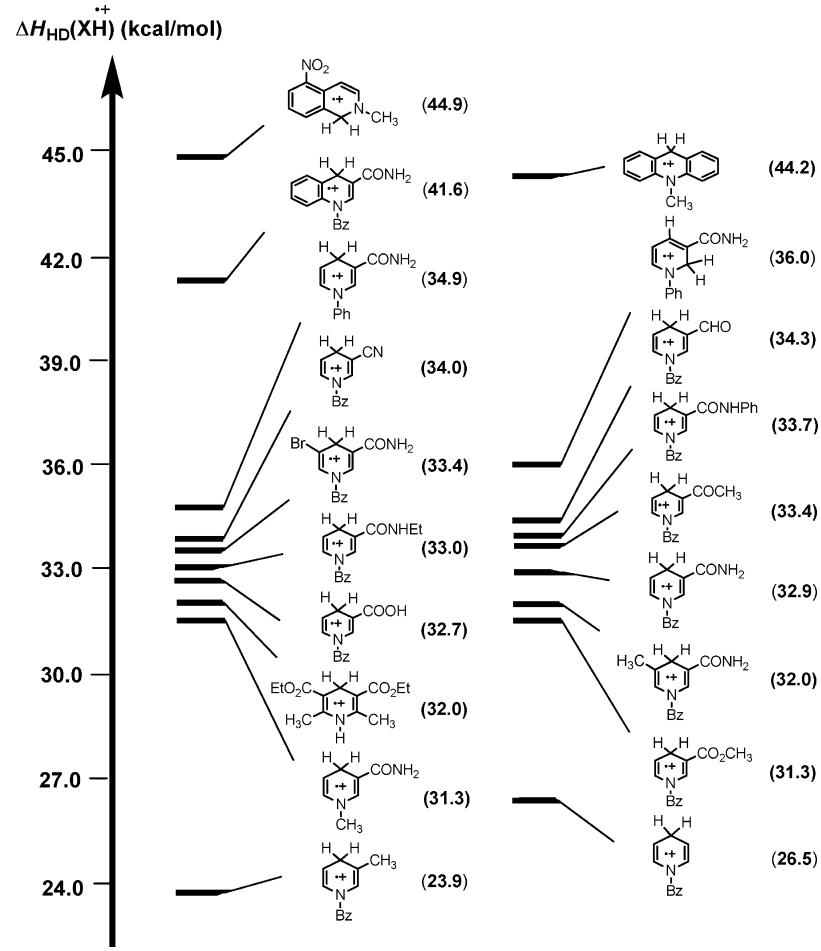


Figure 7. Comparison of thermodynamic driving forces of the corresponding radical cations ($\mathbf{XH}^{\bullet+}$) of some typical dihydropyridine-type organic hydrides to release a hydrogen atom in acetonitrile.

From column 6 in Table 2, it is found that the one-electron oxidation potentials of **XH** [$E^o(\mathbf{XH}^{0/-})$] range from −0.094 (V vs $Fc^{+/0}$) for **10H** to 0.521 (V vs $Fc^{+/0}$) for **5H** (G = p-CN). Since the one-electron oxidation potentials of the 45 **XH** all are not quite negative (generally positive than that of ferrocene), which means that the 45 **XH** all are quite weak one-electron donors. In order to intuitively compare the electron-donating abilities among the dihydropyridine-type organic hydrides and conveniently examine the effect of the substituents and the structure of the organic hydrides on the electron-donating ability, 19 typical dihydripyridine-type organic hydrides are ranked in Figure 9 according to their oxidation potentials. From Figure 9, it is clear that the electron-donating group (EDG) at the pyridine ring can increase the electron-donating ability of the organic hydrides, and the electron-withdrawing group (EWG) at the pyridine ring can decrease the electron-donating ability of the organic hydrides, but no good linear relationships were found between the oxidation potentials and the well-known substituent parameters, such as σ, σ^o, σ^+, σ^-. If the oxidation potentials of **1H**−**10H** were compared in detail, it is found that the contribution order of the substituents to the electron-donating ability of the organic hydrides is CH_3 > H > CONHEt > $CONH_2$ > CONHPh > $COCH_3$ > CO_2Et > COOH > CHO > CN. It is worth noteing that if the substituent effects on the electron-donating abilities and on the hydride-donating abilities are compared, it is found that the contribution orders of the substituents to the electron-donating ability all are not in agreement with that of the substituents to the hydride-donating ability. The difference appears in the cases of two substituents $-COCH_3$ in **2H** and −COOEt in **3H**. To the hydride-donating ability, the contribution of $-COCH_3$ (67.1 kcal mol^{-1} for **2H**) is smaller than that of −COOEt (65.8 kcal mol^{-1} for **3H**), but to the electron-donating ability, the contribution of $-COCH_3$ (0.323 V for **2H**) is larger than that of −COOEt (0.361 V for **3H**). This result suggests that **2H** and **3H** can be used together as mechanism probes to diagnose the mechanism details of quinone reduction by some organic hydrides, which have been disputed until now.

From column 7 in Table 2, it is found that the one-electron oxidation potentials of the neutral pyridine-type radicals $\mathbf{X}^{\bullet}$ [$E^o_{ox}(\mathbf{X})$] range from −0.924 (V vs $Fc^{+/0}$) for **17**$^{\bullet}$ to −1.682 (V vs $Fc^{+/0}$) for **10**$^{\bullet}$. Since the one-electron oxidation potentials of $\mathbf{X}^{\bullet}$ are quite negative values, generally more negative than −0.924 V relative to ferrocene, the neutral pyridine-type radicals ($\mathbf{X}^{\bullet}$), especially attached by electron-donating groups should belong to very strong one-electron donors. Since the oxidation potentials of $\mathbf{X}^{\bullet}$ are close to or even more negative than the reduction potential of molecular oxygen (O_2) (−1.050 V vs $Fc^{+/0}$ saturated in acetonitrile, about 3×10^{-3} M),[67] a valuable conclusion can be made that the neutral pyridine radicals ($\mathbf{X}^{\bullet}$) are impossible to exist stably in living body or in oxygenic solution. This result indicates that if we want to detect the neutral pyridine-type radicals $\mathbf{X}^{\bullet}$ during the reactions of some dihydropyridine-type organic hydrides, the oxygen must be removed completely from the reaction system. In order to more intuitively disclose the effect of structure and substituents on the electron-

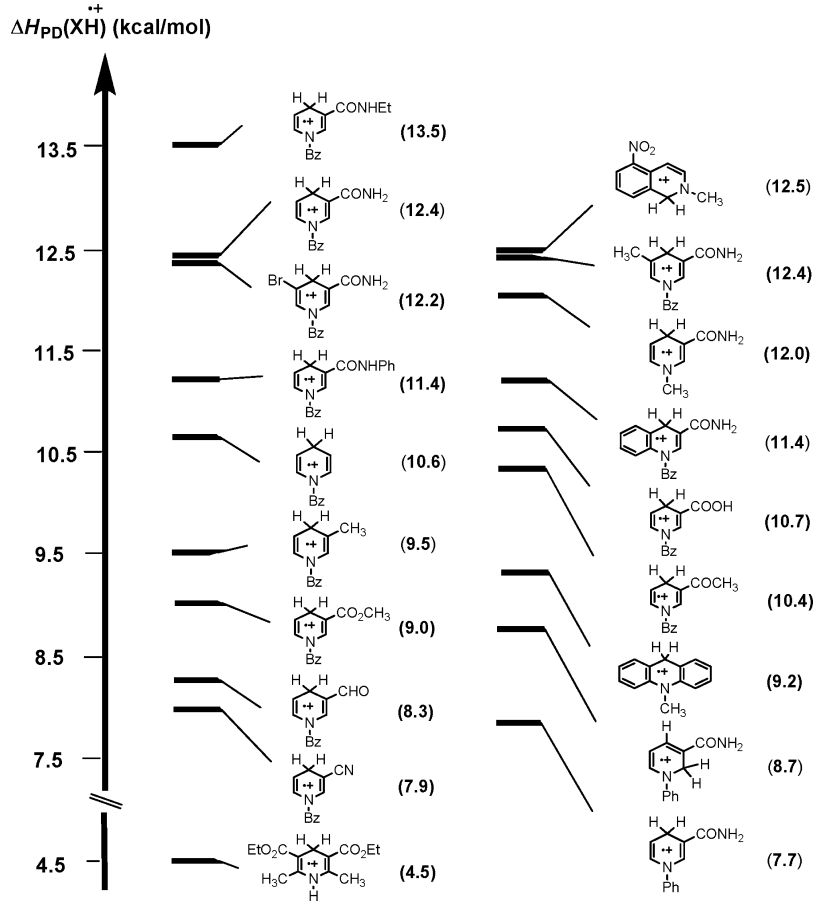
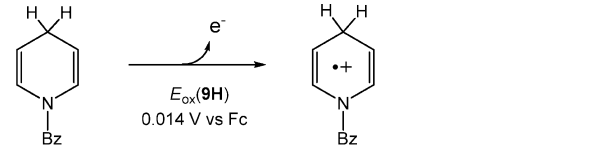


Figure 8. Comparison of thermodynamic driving forces of the corresponding radical cations ($\mathbf{XH}^{\bullet+}$) of some typical dihydropyridine-type organic hydrides to release a proton in acetonitrile.

donating abilities of $\mathbf{X}^{\bullet}$, the typical $\mathbf{X}^{\bullet}$ (**1**−**17,** G = H) are ranked in Figure 10 according to their one-electron oxidation potentials. From Figure 10, there are two orders to be found: (i) the electron-withdrawing abilities of the substituents at the pyridine ring of $\mathbf{X}^{\bullet}$ are increased in the order CH_3, < H < CONHEt < $CONH_2$ < COOH < COOEt < CONHPh < $COCH_3$ < CHO < CN; (ii) the larger the aromaticity of $\mathbf{X}^{\bullet}$, the smaller the electron-donating ability of $\mathbf{X}^{\bullet}$.

If the oxidation potentials of the neutral pyridine-type radicals ($\mathbf{X}^{\bullet}$) and their parent dihydropyridine-type organic hydrides (**XH**) were compared, it is found that the oxidation potentials of $\mathbf{X}^{\bullet}$ are more negative than that of the corresponding parent **XH** by more than 1.0 V (generally 1.0−1.7 V), which indicates that the electron-donating ability of $\mathbf{X}^{\bullet}$ is much larger than that of the corresponding parent **XH**. In order to examine the factor which makes the electron-donating ability of $\mathbf{X}^{\bullet}$ is larger than that of **XH**, the structures of **XH** and $\mathbf{XH}^{\bullet+}$ (eq 14) as well as the structures of $\mathbf{X}^{\bullet}$ and $\mathbf{X}^{+}$ (eq 15) were compared. From eq 14, it is clear that the oxidation of **XH** deals only with an electron escape from **XH**, since no new π-bond was formed in the molecule, but for the oxidation of $\mathbf{X}^{\bullet}$ (eq 15), the oxidation of $\mathbf{X}^{\bullet}$ deals not only with an electron escape from $\mathbf{X}^{\bullet}$, but also with the formation of a new π-bond in the pyridine ring. Since the formation of the new π-bond can release a large amount of energy, the electron-donating ability of $\mathbf{X}^{\bullet}$ should be much larger than that of **XH**.

If the effects of structure and substituent on the differences of oxidation potentials between $\mathbf{X}^{\bullet}$ and **XH** are examined, it is found that the substituent effect on the difference of oxidation potentials between $\mathbf{X}^{\bullet}$ and **XH** (**1H**−**15H**) is quite small, but the effect of framework structure on the difference of the oxidation potentials between $\mathbf{X}^{\bullet}$ and **XH** is quite marked (see **16H** and **17H**). Generally, the larger the aromaticity of the structure, the smaller the difference of oxidation potentials between $\mathbf{X}^{\bullet}$ and **XH**.



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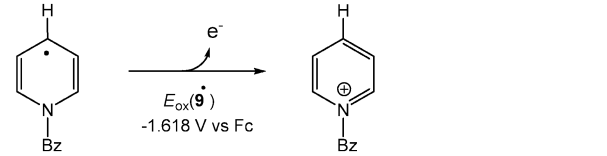

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Construction of the Thermodynamic Characteristic Graphs (TCGs) of Dihydropyridines as a "Molecule ID Card". It is well-known that the structure of the organic hydride compounds (such as a dihydropyridine) can be safely diagnosed or determined according to its some characteristic spectra, such

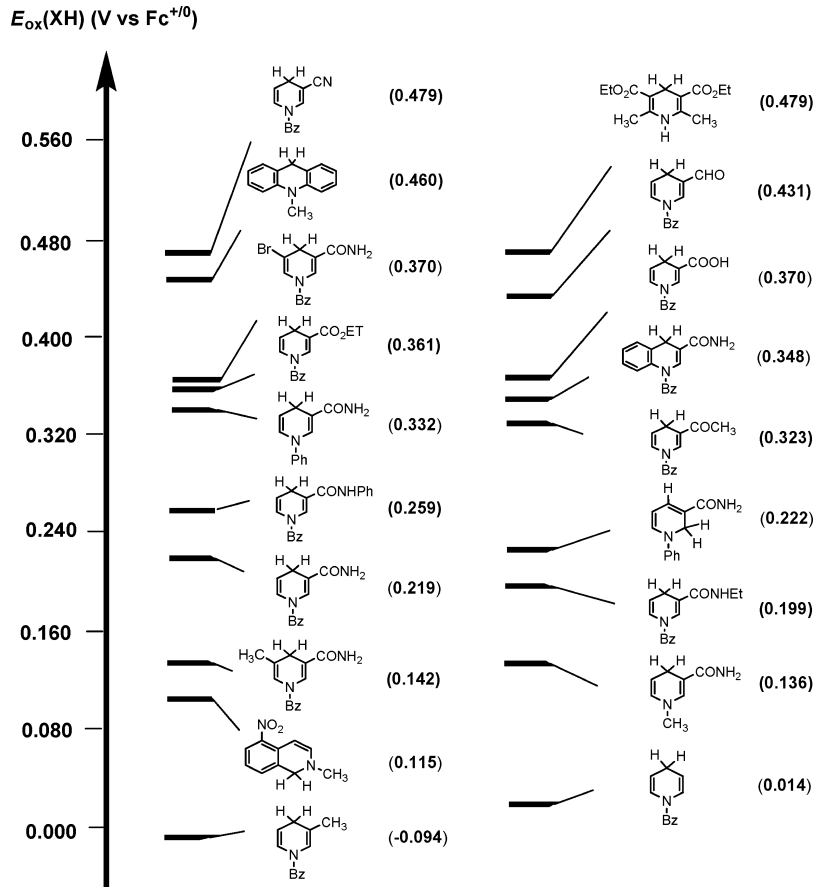


Figure 9. Comparison of thermodynamic driving forces of some typical dihydropyridine-type organic hydrides (**XH**) to release an electron in acetonitrile.

as NMR spectrum, IR spectrum, and MS. But the chemical properties of the organic hydride and its various reaction intermediates could not be directly diagnosed or determined only according to a certain spectrum or graph of the molecule until now. If a certain characteristic chemical information graph of molecule can be produced, and can be efficiently used to quantitatively diagnose or scale the characteristic chemical properties of the molecule and its various reaction intermediates, which is the case that the NMR spectrum and IR spectrum of molecule can be used to determine the molecular structure, the chemists' dream for a long time could become reality that only from the characteristic graphs of molecules one could reliably design various new desired chemical reactions, safely predict the possible products of reactions, and exactly parse the reaction mechanism. Therefore, developing a characteristic graph of molecule as a "Molecule ID Card", which contains the essential information about the chemical properties of molecules and their various reaction intermediates has been my ambition for a long time.

In Table 2, it is found that there are six primary thermodynamic parameters about the characteristic chemical or electrochemical properties of the dihydropyridines (**XH**) and their reaction intermediates ($\mathbf{XH}^{\bullet+}$ and $\mathbf{X}^{\bullet}$ and $\mathbf{X}^{+}$), which have been obtained by using the experimental method in this work. Since the sizes of proton, hydride anion, hydrogen atom, and electron are all quite small, it is conceived that the thermodynamic driving forces of the dihydropyridines and their various reaction intermediates to release hydride anions, hydrogen atoms, protons, and electrons should be the most intrinsic thermodynamic parameters to quantitatively scale the characteristic chemical properties of the dihydropyridines and their reaction intermediates, such as oxidizability, reducibility, antioxidants, hydricity, acidity, nucleophilicity, electrophilicity, and so on, which gives us one efficient access to quantitatively scale the chemical properties of dihydropyridines and especially their reaction intermediates. If the six thermodynamic parameters scaling the different chemical characters of dihydropyridines and their reaction intermediates are gathered together according to their mutual conversion to build a graph, it is clear that, for any species among the dihydropyridines and their various reaction intermediates, one can obtain three characteristic thermodynamic parameters from the graph to quantitatively diagnose the characteristic chemical properties of the species. Since this graph consists only of thermodynamic parameters of dihydropyridines and their reaction intermediates, this graph in this work is defined as *the thermodynamic characteristic graph* (TCG) of the dihydropyridines (**XH**), which can be used as a "Molecule ID Card" to quantitatively diagnose the characteristic chemical properties of the dihydropyridines and their reaction intermediates in acetonitrile solution.

Scheme 4 shows the thermodynamic characteristic graphs (TCG) of dihydropyridine **9H** as an example. It is clear that from the TCG of **9H**, three thermodynamic characteristic parameters can be obtained for each species among the species system of **9H** (including **9H**, $\mathbf{9H}^{\bullet+}$, $\mathbf{9}^{\bullet}$, and $\mathbf{9}^{+}$) (see Table 5). The three different thermodynamic parameters can be used to quantitatively describe three different characteristic chemical properties of the species at the same time. From Table 5, it is easy to make a diagnosis that **9H** is good hydride donor, the radical cation of **9H** is a good oxidant and a strong organic

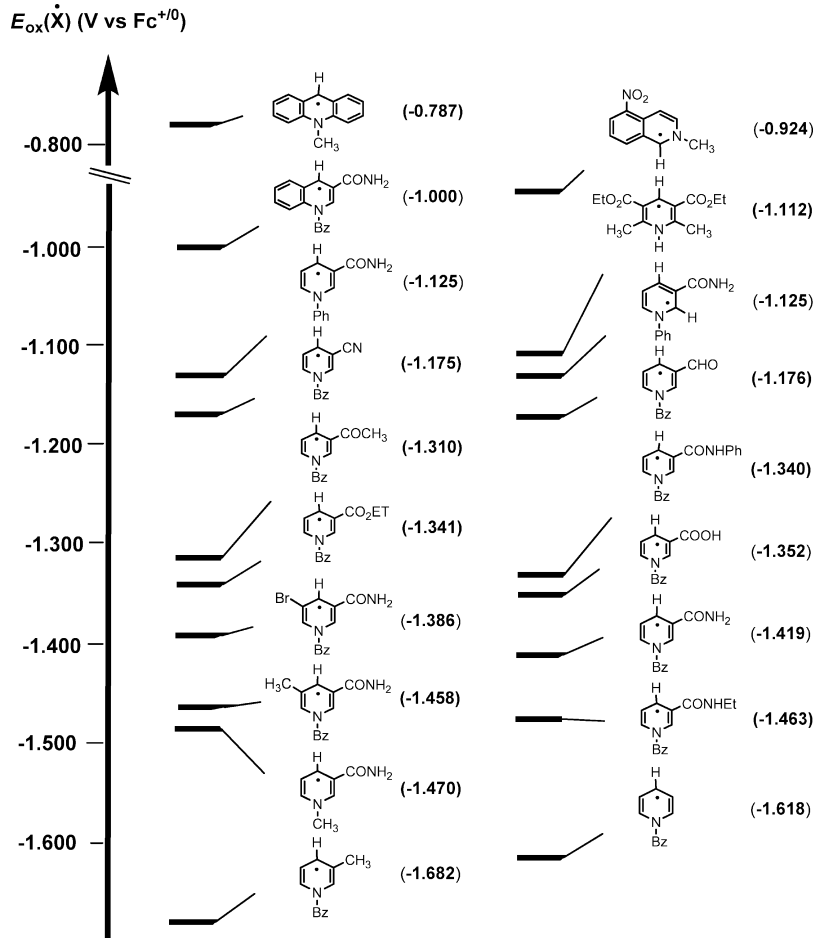
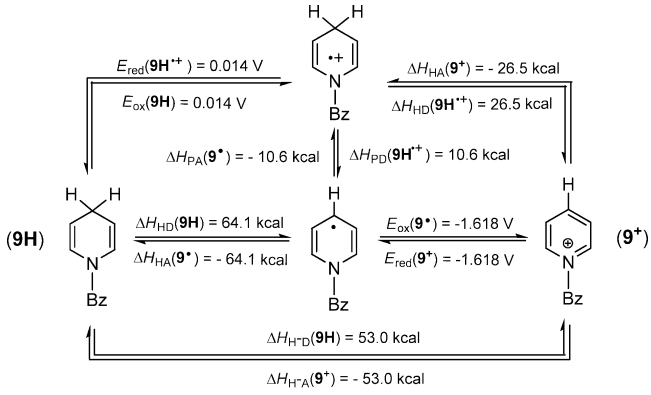


Figure 10. Comparison of thermodynamic driving forces of the corresponding pyridine-type neutral radicals (**X•**) of some typical dihydropyridine-type organic hydrides to release an electron in acetonitrile.

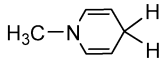
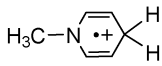
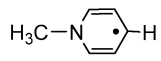
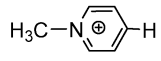
SCHEME 4: Thermodynamic Characteristic Graph (TCG) of Dihydropyridine 9H as a "Molecule ID Card"



acid, $\mathbf{9}^{\bullet}$ is a strong reductant, and $\mathbf{9}^{+}$ is a quite stable species. Evidently, the thermodynamic characteristic graph (TCG) of a molecule is a very useful chemical information memorizer of molecules, which not only can be used to diagnose the chemical characters of the dihydropyridines and their various reaction intermediates but also can be used to construct thermodynamic analysis platform to predict reaction products and analyze the reaction mechanism. In fact, this idea has been successfully applied in the diagnoses of the characteristic chemical properties of imines and their various reaction intermediates in our previous paper.[50]

Relationship between Thermodynamics and Kinetics for the Hydride Transfer from XH to AcrH$^+$. In principle, thermodynamic driving forces of **XH** to release hydride anions are only used to measure the tendency of hydride transfer from **XH**, which cannot be directly used to predict the rate of the hydride transfer. But, in fact, for most chemical reactions, the reaction rate is directly related with thermodynamic driving forces. In order to disclose the intrinsic relationship between the kinetic rate of hydride transfer and the corresponding thermodynamic driving force of hydride transfer, the dependence of the logarithm of second-order rate constant (log k_2) for hydride transfer from **XH** to AcrH$^+$ on the thermodynamic driving force of **XH** to release hydride anions in acetonitrile was examined, and the results show that, if the dihydropyridine-type organic hydrides cover the 45 **XH** (**1H**−**17H**), the linear relationship is not good, which means that the kinetic rate of hydride transfer is not only dependent on the corresponding thermodynamic enthalpy change of hydride transfer but also dependent on some other thermodynamic factors such as entropy change of **XH**. However, when the dihydropyridine-type organic hydrides are limited in **1H**−**15H** except some ones with strong electron-donating group on the pyridine ring, the linear relationship is good ($r = 0.9673$) (see Figure 11), which means that if **XH** have the same or similar fundamental structure, log k_2 of

TABLE 5: Chemical Properties of Dihydropyridine 9H and Its Various Reaction Intermediates Diagnosed According to the TCG of 9H (Scheme 4)

species	thermodynamic parameters*	diagnoses of the characteristic properties
	ΔH_{H^-D}(**9H**) = 53.0 kcal ΔH_{HD}(**9H**) = 64.1 kcal E_{ox}(**9H**) = 0.014 V	good hydride donor, strong nucleophilic agent mild hydrogen donor, mild-strong antioxidant good one-e reductant
	ΔH_{PD}(**9H**$^{+\bullet}$) = 10.6 kcal ΔH_{HD}(**9H**$^{+\bullet}$) = 26.5 kcal E_{red}(**9H**$^{+\bullet}$) = 0.014 V	strong organic acid strong hydrogen acceptor, large dimerizability good one-e oxidant
	ΔH_{PA}(**9**$^{\bullet}$) = -10.6 kcal ΔH_{HA}(**9**$^{\bullet}$) = -64.1 kcal E_{ox}(**9**$^{\bullet}$) = -1.618	weak base mild-strong hydrogen acceptorr, good antioxidant very strong one-e reductant
	ΔH_{H^-A}(**9**$^{+}$) = -53.0 kcal ΔH_{HA}(**9**$^{+}$) = -26.5kcal E_{red}(**9**$^{+}$) = -1.618 V	weak hydride acceptor, weak electrophilic agent poor hydrogen acceptor, weak antioxidant very weak one-e oxidant

* ΔH_{PA}(**9**$^{\bullet}$), ΔH_{HA}(**9**$^{\bullet}$), ΔH_{H^-A}(**9**$^{+}$), and ΔH_{HA}(**9**$^{+}$) are defined as the enthalpy changes of **9**$^{\bullet}$ to obtain proton, to obtain hydrogen atom, and the enthalpy changes of **9**$^{+}$ to obtain hydride anion and to obtain hydrogen in acetonitrile, respectively. The values are equal to the enthalpy changes of the corresponding opposite species to obtain proton, to obtain hydrogen atom and to obtain hydride anion in acetonitrile by switching the signs.

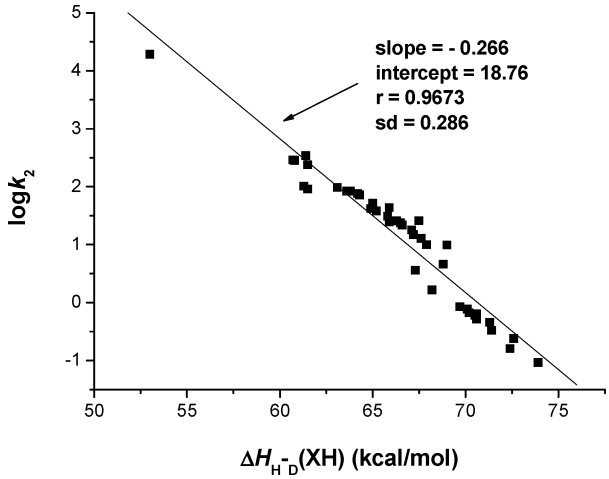


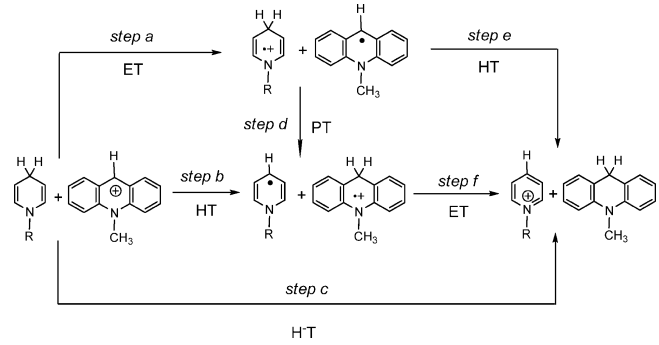
Figure 11. Relationship between log k_2 (at 25 °C) for hydride transfer from **XH** (**1H**−**15H**) to AcrH$^+$ and the enthalpy changes of **XH** to release hydride anions in acetonitrile.

the hydride transfer can be well dependent on the enthalpy changes of **XH** to release hydride anions in acetonitrile and the relationship can be expressed by eq 14. This finding suggests that for any organic hydrides with the same or similar fundamental structure, the rate of the hydride transfer may be estimated according to the corresponding thermodynamic driving forces.

$$\log k_2 = -0.266 \times \Delta H_{H^-D}(\mathbf{XH}) + 18.76 \qquad (16)$$

Thermodynamic Analysis on Mechanism Possibilities for the Hydride Transfer from XH to AcrH$^+$. Although the dihydropyridine-type organic hydrides all have quite good hydride-donating abilities and the applications as organic hydride donors have been extensively investigated, the hydride transfer mechanism to two-electron acceptor (i.e., hydride acceptor) is still a disputed question.[68,69] The focus of the controversy is whether the mechanism of the hydride transfer is one step or multistep sequence involving electron−proton−electron, electron−hydrogen, or hydrogen−electron. One of the main reasons resulting in the difficulty to elucidate the hydride transfer mechanism is that no detailed energetic data of each possible mechanistic step for the hydride transfer are available. From this work, we not only can obtain the thermodynamic driving forces of the 45 dihydropyridine-type organic hydrides to release hydride anion, hydrogen atom, and electron but also can obtain the thermodynamic driving forces of the various reaction intermediates of the 45 dihydropyridine-type organic hydrides to release hydrogen atom, proton, and electron. It is clear that according to these thermodynamic data we may construct a thermodynamic analytic platform to examine the detailed mechanistic steps of the hydride transfer. Herein we take the reaction of **XH** and AcrH$^+$ as an example (see Scheme 5). The detailed thermodynamic data on the each possible mechanistic step of the hydride transfer are summarized in Table 6.

SCHEME 5: Possible Reaction Pathways of Hydride Transfer from Dihydropyridine-Type Organic Hydrides (XH) to AcrH$^+$ in Acetonitrile



From Table 6, it is easy to find that the state energy change scales of the three initial steps (steps a, b, and c) in the four

TABLE 6: Energetics of Each Mechanistic Step of Hydride Transfer from XH to AcrH$^+$ Shown in Scheme 5

	ΔH^o (or ΔG^o)					
XH	step a[a]	step b[b]	step c[c]	step d[d]	step e[e]	step f[f]
1H						
p-CH_3O	22.9	25.7	−18.0	2.8	−40.8	−43.6
p-CH_3	23.0	26.1	−17.5	3.0	−40.5	−43.5
p-H	23.2	26.5	−16.9	3.2	−40.1	−43.3
p-F	23.3	26.5	−16.8	3.1	−40.1	−43.2
p-Cl	23.6	27.0	−16.1	3.4	−39.7	−43.1
p-CN	24.3	27.6	−14.8	3.2	−39.1	−42.3
2H						
p-CH_3O	25.1	26.4	−14.9	1.3	−40.0	−41.3
p-CH_3	25.3	26.5	−14.6	1.1	−39.9	−41.0
p-H	25.6	26.9	−14.0	1.2	−39.6	−40.8
p-F	25.7	26.9	−13.9	1.1	−39.6	−40.7
p-Cl	26.1	27.0	−13.5	0.9	−39.6	−40.5
p-CN	26.7	27.8	−12.1	1.0	−38.8	−39.8
3H						
p-CH_3O	25.9	25.9	−16.2	−0.1	−42.1	−42.0
p-CH_3	26.2	26.0	−15.9	−0.2	−42.0	−41.9
p-H	26.5	26.3	−15.3	−0.2	−41.7	−41.5
p-F	26.6	26.4	−15.2	−0.3	−41.7	−41.5
p-Cl	26.8	26.8	−14.5	0	−41.3	−41.3
p-CN	27.4	27.3	−13.2	−0.1	−40.6	−40.5
4H						
p-CH_3O	27.5	26.7	−11.4	−0.9	−38.9	−38.0
p-CH_3	27.8	26.9	−11.0	−0.9	−38.8	−37.8
p-H	28.1	27.2	−10.6	−0.9	−38.7	−37.7
p-F	28.2	27.2	−10.5	−1.0	−38.6	−37.6
p-CN	29.0	28.4	−8.5	−0.7	−37.5	−36.9
5H						
p-CH_3O	28.6	27.3	−10.9	−1.3	−39.5	−38.2
p-CH_3	28.8	27.6	−10.5	−1.3	−39.3	−38.0
p-H	29.2	28.0	−9.8	−1.3	−39.0	−37.7
p-F	29.3	28.0	−9.7	−1.4	−39.0	−37.6
p-Cl	29.6	28.7	−8.7	−0.9	−38.2	−37.3
p-CN	30.2	29.6	−7.2	−0.7	−37.3	−36.7
6H	26.7	28.3	−13.6	1.5	−40.3	−41.8
7H	22.7	27.1	−17.3	4.3	−40.0	−44.3
8H	24.1	26.4	−15.2	2.2	−39.3	−41.5
9H	18.5	19.9	−28.1	1.4	−46.5	−47.9
10H	16.0	16.4	−33.1	0.3	−49.1	−49.4
11H	21.4	24.7	−19.6	3.2	−41.0	−44.2
12H	26.7	29.7	−12.9	3.0	−39.6	−42.6
13H	25.8	24.3	−12.3	−1.5	−38.1	−36.6
14H	23.3	22.8	−13.8	−0.5	−37.0	−36.6
15H						
CH_3	21.3	24.2	−20.4	2.8	−41.7	−44.5
Et	21.3	25.2	−19.6	3.9	−40.9	−44.7
pr	21.3	24.3	−20.3	2.9	−41.5	−44.5
i-pr	21.6	25.1	−19.8	3.4	−41.4	−44.8
n-butyl	21.4	24.7	−19.7	3.3	−41.1	−44.4
16H	26.2	25.3	−8.4	−0.9	−34.6	−33.7
17H	20.8	24.8	−7.2	3.3	−28.1	−31.9

[a] Derived from the equation ΔG(step a) = $-23.06[E_{red}(AcrH^+) - E_{ox}(\mathbf{XH})]$, where $[E_{red}(AcrH^+) = -0.787$ V vs Fc,[9f] and the unit of ΔG(step a) is kcal mol^{-1}. [b] Derived from the equation ΔH(step b) = $\Delta H_{HD}(\mathbf{XH}) - \Delta H_{HD}(AcrH_2^{\bullet+})$, where $\Delta H_{HD}(AcrH_2^{\bullet+}) = 44.2$ kcal mol^{-1},[9f] and the unit of ΔH(step b) is kcal mol^{-1}. [c] Derived from the equation ΔH(step c) = $\Delta H_{H-D}(\mathbf{XH}) - \Delta H_{H-D}(AcrH_2)$, where $\Delta H_{H-D}(AcrH_2) = 81.1$ kcal mol^{-1},[35] and the unit of ΔH(step **c**) is kcal mol^{-1}. [d] Derived from the equation ΔH(step d) = $\Delta H_{PD}(\mathbf{XH}^{\bullet+}) - \Delta H_{PD}(AcrH_2^{\bullet+})$, where $\Delta H_{PD}(AcrH_2^{\bullet+}) = 9.2$ kcal/mol,[9f] and the unit of ΔH(step d) is kcal mol^{-1}. [e] Derived from the equation ΔH(step e) = $\Delta H_{HD}(\mathbf{XH}^{\bullet+}) - \Delta H_{HD}(AcrH_2)$, where $\Delta H_{HD}(AcrH_2) = 73.0$ kcal mol^{-1},[9f] and the unit of ΔH(step e) is kcal mol^{-1}. [f] Derived from the equation ΔG(step f) = $-23.06[E_{red}(AcrH_2^{\bullet+}) - E_{ox}(\mathbf{X}^{\bullet})]$, where $[E_{red}(AcrH_2^{\bullet+}) = 0.460$ V vs Fc,[9f] and the unit of ΔG(step f) is kcal mol^{-1}.

possible pathways range from 16.0 to 30.2 kcal mol^{-1} for the electron transfer (step a), from 16.4 to 29.6 kcal/mol for the hydrogen transfer (step b), and from −7.2 to −33.1 kcal/mol for the concerted hydride transfer (step c). Since the state energy changes for the concerted hydride transfer (step c) all are quite negative (more negative than −7.2 kcal mol^{-1}), and the state energy changes for the electron transfer and for hydrogen transfer all are quite positive (more positive than 16.0 kcal mol^{-1}), it is reasonable to suggest that the electron transfer process (step a) and the hydrogen transfer process (step b) all can be ruled out as the initial step for the reaction of **XH** with AcrH$^+$, and as a result, the remaining concerted hydride transfer step (step c) should be the merely reasonable pathway for the reaction of **XH** with AcrH$^+$.

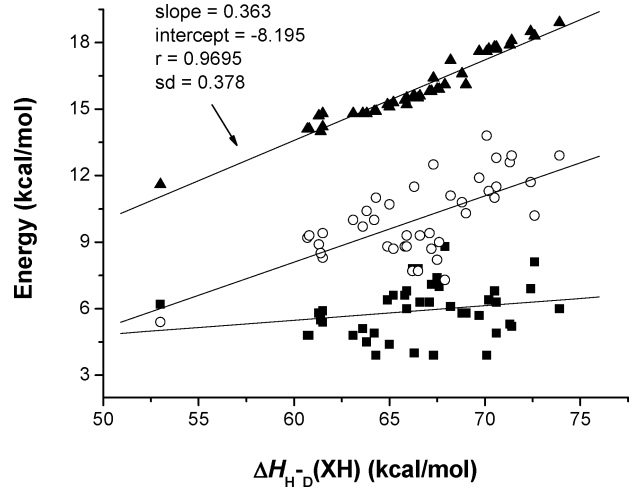


Figure 12. Plots of $\Delta G^{\ddagger}$ (▲), $\Delta H^{\ddagger}$ (■) and $-T\Delta S^{\ddagger}$ (○) for hydride transfer from **XH** to AcrH$^+$ in acetonitrile against ΔH_{H^-D}(**XH**).

In order to further verify the reaction mechanism of **XH** with AcrH$^+$, the kinetics of the reaction was examined. From Table 4, it is found that the activation free energetic scales of the reactions of **XH** with AcrH$^+$ range from 11.5 to 18.9 kcal mol^{-1}, which are much smaller than the corresponding standard state energy changes of the initial electron transfer (step a) (16.0−30.2 kcal mol^{-1}), and much smaller than the corresponding standard state energy changes of the initial hydrogen transfer (step b) (16.4−29.6 kcal mol^{-1}), but larger than the corresponding standard state energy change of the concerted hydride transfer (step c) (−7.2 to −33.1 kcal mol^{-1}). On the basis of a general *reaction law* that the activation free energy change is always larger than or at least equal to the corresponding standard state free energy change for any elemental reaction,[70] it is evident that both of the reaction steps a and b should be ruled out as the initial reaction in the reactions of **XH** with AcrH$^+$, and the only remaining step c is suitable for the reaction law (Figure 12).

By comparing the values of $\Delta H^{\ddagger}$ and $-T\Delta S^{\ddagger}$, it is found that the values of $\Delta H^{\ddagger}$ are generally much smaller than that of the corresponding $-T\Delta S^{\ddagger}$, which means that the hydride transfer from **XH** to AcrH$^+$ is mainly driven by enthalpy change of the reaction, and that is the reason that the kinetic rate of hydride transfer from **XH** to AcrH$^+$ is strongly dependent on the corresponding thermodynamic driving forces of **XH** to release hydride anion.

Conclusions

In this work, 45 dihydropyridine-type organic compounds as a class of very important organic hydride source were designed and synthesized. The thermodynamic driving forces of the 45 organic hydrides to release hydride anions, to release hydrogen atoms, and to release electrons, the thermodynamic driving

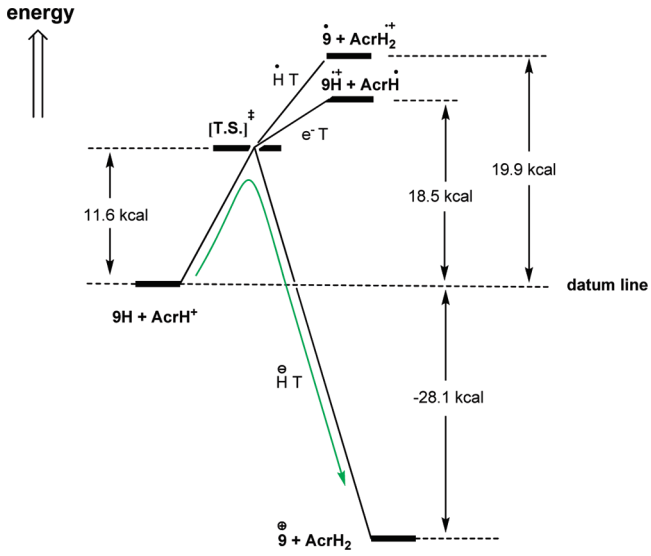


Figure 13. Comparison of state energy changes for the three possible initial steps of hydride transfer from *N*-benzyl-1,4-dihydropyridine (**9H**) to $AcrH^+$ and the activation free energy of the hydride transfer.

forces of the radical cations of the 45 dihydropyridines to release protons and to release hydrogen atoms, and the thermodynamic driving forces of the neutral pyridine-type radicals to release electrons in acetonitrile were determined by using titration calorimetry and electrochemical methods. After detailed examination of the dependence of the thermodynamic driving forces on the structure of the dihydropyridines, the dependence of the thermodynamic driving forces on the kinetics of the hydride transfer, and the thermodynamic relationship between the dihydropydines and their various reaction intermediates for their mutual conversions, the following conclusions can be made:

(1) The 45 dihydropyridine-type organic hydrides belong to strong or middle-strong organic hydride donors. The hydride-donating ability of them especially the one with strong electron-donating groups at the pyridine ring is close to or even greater than that of the well-known inorganic hydride donor, $NaBH_4$. It is evident that the 45 dihydropyridine-type organic hydrides can construct a useful organic hydride donor library that the hydride-donating abilities all are well-known. In the organic hydrides library, **10H** is the strongest hydride donor, but **16H** is the weakest hydride donor.

(2) Besides being used as good hydride source, the dihydropyridine-type organic hydrides also can be used as good hydrogen atom source. Since the hydrogen-donating abilities of the dihydropyridine-type organic compounds all are much greater than that of tocopherol (Vitamin E) (79.3 kcal mol^{-1}),[53] a well-known natural phenolic antioxidant, it is conceived that the 45 dihydropyridine-type organic hydrides can also be used as efficient antioxidants. According to the effect of the substituents at the pyridine ring on the hydrogen-donating abilities, the neutral pyridine-type radicals ($\mathbf{X}^{\bullet}$) were suggested to be electron-deficient radicals.

(3) One-electron-donating abilities of the dihydropyridine-type organic hydrides (**XH**) are generally not strong, most are smaller than that of ferrocene, which means that, when the dihydropyridine-type organic hydrides are chosen as reducing agents to reduce organic unsaturated compounds, the reductions are generally initiated by charge transfer rather than by electron transfer.

(4) The radical cations of the dihydropyridine-type organic compounds belong to strong proton donors (strong acids), and the acidities are generally much greater than that of the general neutral strong organic acids, but smaller than that of the gneral strong inorganic acids in acetonitrile.

(5) The radical cations of the dihydropyridine-type organic compounds all are strong hydrogen atom donors, and the hydrogen-donating abilities are generally greater than those of the corresponding parent **XH** by about 30−40 kcal/mol, but generally smaller than the corresponding proton-donating abilities by more than 20 kcal mol^{-1}.

(6) The pyridine-type neutral radicals ($\mathbf{X}^{\bullet}$) all are very strong one-electron donors, and the electron-donating abilities are generally greater than those of the corresponding parent **XH** by more than 1 V (equivalent to 23.06 kcal mol^{-1}), which means that when the dihydropyridine-type organic hydrides are chosen as reducing agents to reduce organic unsaturated compounds, such as ketone, aldehydes, and imines, the multistep mechanism (e−p−e) of the hydride transfer is impossible to be separated.

(7) The reason resulting in the good hydricity of the dihydropyridine-type compounds (**XH**) is that the carbon atom at 4-position in the cation $\mathbf{X}^+$ can form or partially form a new π-bond in the pyridine ring.

(8) The thermodynamic driving forces of the dihydropyridine-type compounds to release hydride anions in acetonitrile were found to be linearly well correlated with the rate of the hydride transfer from the dihydropyridine-type organic compounds to $AcrH^+$.

(9) The kinetics of hydride transfer from the dihydropyridine-type organic hydrides is generally controlled by the thermodynamic function entropy, but driven by the thermodynamic function enthalpy.

(10) The idea of a thermodynamic characteristic graph (TCG) of the dihydropyridine-type organic hydrides as an efficient "Molecule ID Card" was introduced. The TCG not only can be used to quantitatively diagnose and predict the characteristic chemical properties of the dihydropyridines but also can be used to quantitatively described the characteristic chemical properties of the reaction intermediates of the dihydropyridines, which means that the construction of TCG of compounds can create a new access to quantitatively scale the chemical activities of the reaction intermediates of organic compounds, such as radical, radical cations, radical anions, carbocations, and carbanions.

It is evident that the determination of these hard-won and fundamental thermodynamic data could not only supply a gap of the thermodynamics of the dihydropyridine-type organic hydrides as organic hydride source, but also would strongly promote the application of the dihydropyridine-type organic hydrides in the fields of organic syntheses chemistry, drug chemistry, materials chemistry, hydrogen-energy source chemistry, and many others.

In addition, it is special to point out herein that the significance of this work not only can guide experimental chemists how to choose suitable hydride donor from the dihydropyridine-type organic hydrides source as efficient organic reductants but also even more importantly can provide theoretical chemists with a lot of useful thermodynamic experimental data which is very required and indispensable to establish new and reliable theoretical approaches to estimate the thermodynamic potentials of new organic hydride source in solution.

Experimental Section

Materials. All reagents were of commercial quality from freshly opened containers or were purified before use. Reagent-grade acetonitrile was refluxed over $KMnO_4$ and K_2CO_3 for several hours and was doubly distilled over P_2O_5 under argon

before use. The commercial tetrabutylammonium hexafluorophosphate (Bu_4NPF_6, Aldrich) was recrystallized from CH_2Cl_2 and was vacuum-dried at 383 K overnight before preparation of supporting electrolyte solution. 9-Phenylxanthylium perclorate (9-phenyl-$Xn^+ClO_4^-$) and the 3-substitutent 1,4-dihydropyridines **XH** were obtained according to literature methods[10,39] and the final products were identified by ^{1}H NMR and MS.

Measurment of Redox Potentials. The electrochemical experiments were carried out by cyclic voltammetry (CV) and osteryoung square wave voltammetry (OSWV) using a BAS-100B electrochemical apparatus in deaerated acetonitrile under argon atmosphere at 298 K as described previously.[23] *n*-Bu4NPF6 (0.1M) in acetonitrile was employed as the supporting electrolyte. A standard three-electrode cell consists of a glassy carbon disk as work electrode, a platinum wire as a counter electrode, and 0.1 M AgNO3/Ag (in 0.1 M *n*-Bu4NPF6-acetonitrile) as reference electrode. The ferrocenium/ferrocene redox couple ($Fc^{+/0}$) was taken as the internal standard. The reproducibilities of the potentials were usually $\leqslant$5 mV for ionic species and $\leqslant$10 mV for neutral species.

Isothermal Titration Calorimetry (ITC). The titration experiments were performed on a CSC4200 isothermal titration calorimeter in acetonitrile at 298 K as described previously.[14b] The performance of the calorimeter was checked by measuring the standard heat of neutralization of an aqueous solution of sodium hydroxide with a standard aqueous HCl solution. The heat of reaction was determined following 10 automatic injections from a 250 μL injection syringe containing a standard solution into the reaction cell (1.30 mL) containing 1 mL other concentrated reactant. Injection volume (10 μL) were delivered 0.5s time interval with 300−350s between every two injections. The reaction heat was obtained by integration of each peak except the first.[71]

Kinetic Measurements. Kinetic measurements were carried out in acetonitrile using a stopped-flow and UV/vis spectrophotometer connected to a superthermostat circulating bath to regulate the temperature of cell compartments. The oxidation rate of **XH** by $AcrH^+ClO_4^-$ was measured at 25−45 °C by monitoring the changes of absorption of $AcrH^+ClO_4^-$ at 415 nm under pseudo-first-order conditions (**XH** in over 20-fold excess). The pseudo-first-order rate constants were then converted to k_2 by linear correlation of pseudo-first-order rate constants against the concentrations of **XH**. The activation parameters were derived from Arrhenius plots and from Eyring plots.

Acknowledgment. Financial support from the Ministry of Science and Technology of China (Grant No. 2004CB719905), the National Natural Science Foundation of China (Grant Nos. 20921120403, 20832004, 20721062, and 20672060) and the 111 Project (B06005) is gratefully acknowledged.

Supporting Information Available: Detailed synthetic routes and general preparation procedures of the 45 dihydropyridines and the detailed ^{1}H NMR data of some representative dihydropyridines. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) (a) Deno, N. C.; Peterson, J.; Saines, G. S. *Chem. Rev.* **1960**, *60*, 7, and references cited therein. (b) Ian, C.; Watt, F. *Adv. Phys. Org. Chem.* **1988**, *24*, 59.

(2) (a) Berg, J. M.; Tymoczko, J. L.; Stryer, L. *Biochemistry*, 6th ed.; W. H. Freeman: San Francisco, 2008; p 510. (b) Schomburg, D.; Schomburg, I.; Chang, A.; Stephan, D. *Enzyme Handbook*; Springer: New York, 2005; pp 43−48. (c) Birkmayer, G. *NADH: The Energizing Coenzyme*; NTC/contemporary: Lincolnwood, IL, 1998. (d) Murakami, Y.; Kikuchi, J.-I.; Hisaeda, Y.; Hayashida, O. *Chem. Rev.* **1996**, *96*, 721. (e) Stout, D. M.; Meyers, A. I. *Chem. Rev.* **1982**, *82*, 223. (f) Eisner, U.; Kuthan, J. *Chem. Rev.* **1972**, *72*, 1. (g) Bruice, T. C. *Acc. Chem. Res.* **1980**, *13*, 256. (h) Kuthan, J.; Kurfurst, A. *Ind. Eng. Chem. Prod. Res. Dev.* **1982**, *21*, 191–261.

(3) (a) Walsh, C. *Acc. Chem. Res.* **1980**, *13*, 148. (b) Walsh, C. *Acc. Chem. Res.* **1986**, *19*, 216. (c) Fitzpatrick, P. F. *Acc. Chem. Res.* **2001**, *34*, 299.

(4) Van, Q. L.; Schwarzkopf, B.; Bacher, A.; Keller, P. J.; Lee, S.; Floss, H. G. *J. Am. Chem. Soc.* **1985**, *107*, 8300.

(5) (a) Stroud, R. M.; Finer-Moore, J. S. *Biochemistry* **2003**, *42*, 239. (b) Hong, B. Y.; Haddad, M.; Maley, F.; Jensen, J. H.; Kohen, A. *J. Am. Chem. Soc.* **2006**, *128*, 5636.

(6) (a) Karrer, P. *Chem. Rev.* **1934**, *14*, 17. (b) Neta, P. *Chem. Rev.* **1972**, *72*, 533.

(7) (a) Blaedel, W. J.; Haas, R. G. *Analy Chem* **1970**, *42*, 918. (b) Srividya, N.; Ramamurthy, P.; Shanmugasundaram, P.; Ramakrishna, V. T. *J. Org. Chem.* **1996**, *61*, 5083. (c) Marcinek, A.; Adamus, J.; Huben, K.; Gebicki, J.; Bartczak, T. J.; Bednarek, P.; Bally, T. *J. Am. Chem. Soc.* **2000**, *122*, 437. (d) Gebicki, J.; Marcinek, A.; Zielonka, J. *Acc. Chem. Res.* **2004**, *37*, 379.

(8) (a) Fukuzumi, S.; Okamoto, K.; Tokuda, Y.; Gros, C.; Guilard, R. *J. Am. Chem. Soc.* **2004**, *126*, 17059. (b) Yuasa, J.; Fukuzumi, S. *J. Am. Chem. Soc.* **2006**, *128*, 14281.

(9) (a) Zhu, X.-Q.; Liu, Y.; Zhao, B.-J.; Cheng, J.-P. *J. Org. Chem.* **2001**, *66*, 370. (b) Cheng, J.-P.; Lu, Y.; Zhu, X.-Q.; Sun, Y.; Bi, F.; He, J. *J. Org. Chem.* **2000**, *65*, 3853. (c) Cheng, J.-P.; Lu, Y.; Zhu, X.-Q.; Mu, L. J. *J. Org. Chem.* **1998**, *63*, 6108. (d) Zhu, X.-Q.; Liu, Y.-C. *J. Org. Chem.* **1998**, *63*, 2786. (e) Zhu, X.-Q.; Liu, Y.-C.; Wang, H.-Y.; Wang, W. *J. Org. Chem.* **1999**, *64*, 8982. (f) Zhu, X.-Q.; Zhang, M.-T.; Yu, A.; Wang, C.-H.; Cheng, J.-P. *J. Am. Chem. Soc.* **2008**, *130*, 2501.

(10) (a) Donkersloot, M. C. A.; Buck, H. M. *J. Am. Chem. Soc.* **1981**, *103*, 6554. (b) Lamborg, M. R.; Burton, R. M.; Kaplan, N. O. *J. Am. Chem. Soc.* **1957**, *79*, 6173. (c) Anderson, A. G.; Berkelhammer, G. *J. Am. Chem. Soc.* **1957**, *79*, 992.

(11) Kreevoy, M. M.; Ostovic, D. O.; Lee, I. H.; Binder, D. A.; King, G. W. *J. Am. Chem. Soc.* **1988**, *110*, 524.

(12) (a) Zhang, X.-M.; Bordwell, F. G.; Puy, M. V. D.; Fried, H. E.; Fried, H. E. *J. Org. Chem.* **1993**, *58*, 3060. (b) Bordwell, F. G.; Gallagher, T.; Zhang, X.-M. *J. Am. Chem. Soc.* **1991**, *113*, 3495.

(13) Brotzel, F.; Mayr, H. *Org. Biomol. Chem.* **2007**, *5*, 3814.

(14) (a) Lu, Y.; Qu, F.; Zhao, Y.; Small, A. M. J.; Bradshow, J.; Moore, B. *J. Org. Chem.* 2009, ASAP DOI: 10.1021/jo9007628. (b) Lu, Y.; Qu, F.; Moore, B.; Endicott, D.; Kuester, W. *J. Org. Chem.* **2008**, *73*, 4763–4770. (c) Lu, Y.; Endicott, D.; Kuester, W. *Tetrahedron Lett.* **2007**, *48*, 6356–6358.

(15) (a) Ellis, W. W.; Raebiger, J. W.; Curtis, C. J.; Bruno, J. W.; DuBois, D. L. *J. Am. Chem. Soc.* **2004**, *126*, 2738. (b) Reichenbach-Klinke, R.; Kruppa, M.; Konig, B. *J. Am. Chem. Soc.* **2002**, *124*, 12999. (c) Bartlett, P. N.; Simon, E. *J. Am. Chem. Soc.* **2003**, *125*, 4014.

(16) (a) Powell, F. M.; Wu, S. C.; Bruice, T. C. *J. Am. Chem. Soc.* **1984**, *106*, 3850. (b) Sinha, A.; Bruice, T. C. *J. Am. Chem. Soc.* **1984**, *106*, 7291. (c) Luo, J.; Bruice, T. C. *J. Am. Chem. Soc.* **2001**, *123*, 11952.

(17) (a) Martin, N. J. A.; Ozores, L.; List, B. *J. Am. Chem. Soc.* **2007**, *129*, 8976. (b) Yang, J. W.; List, B. *Org. Let.* **2006**, *8*, 5653. (c) Martin, N. J. A.; List, B. *J. Am. Chem. Soc.* **2006**, *128*, 13368. (d) Hoffmann, S.; Nicoletti, M.; List, B. *J. Am. Chem. Soc.* **2006**, *128*, 13074. (e) Lai, C. C.; Colter, A. K. *Chem. Commun.* **1980**, 1115. (f) Andrew, T. L.; Swager, T. M. *J. Am. Chem. Soc.* **2007**, *129*, 7254.

(18) (a) Carlson, B. W.; Miller, L. L. *J. Am. Chem. Soc.* **1985**, *107*, 479. (b) Miller, L. L.; Valentine, J. R. *J. Am. Chem. Soc.* **1988**, *110*, 3982, and references therein.

(19) (a) Anne, A.; Hapiot, P.; Moiroux, J.; Neta, P.; Saveant, J.-M. *J. Am. Chem. Soc.* **1992**, *114*, 4694. (b) Anne, A.; Fraoua, S.; Grass, V.; Moiroux, J.; Saveant, J.-M. *J. Am. Chem. Soc.* **1998**, *120*, 2951. (c) Anne, A.; Fraoua, S.; Moiroux, J.; Saveant, J.-M. *J. Am. Chem. Soc.* **1996**, *118*, 3938.

(20) Pestovsky, O.; Bakac, A.; Espenson, J. H. *J. Am. Chem. Soc.* **1998**, *120*, 13422.

(21) (a) Mahoney, L. R.; DaRooge, M. A. *J. Am. Chem. Soc.* **1975**, *97*, 4722. (b) Ingold, K. U. *J. Am. Chem. Soc.* **1985**, *107*, 7053. (c) Pedulli, G. F. *J. Org. Chem.* **1996**, *61*, 9259. (d) Lucarini, M.; Pedulli, G. F. *J. Am. Chem. Soc.* **1999**, *121*, 11546.

(22) (a) Xu, H.-J.; Liu, Y.-C.; Fu, Y.; Wu, Y.-D. *Org. Lett.* **2006**, *8*, 3449. (b) Ouellet, S. G.; Tuttle, J. B.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2005**, *127*, 32.

(23) (a) Zhu, X.-Q.; Wang, H.-Y.; Wang, J.-S.; Liu, Y.-C. *J. Org. Chem.* **2001**, *66*, 344. (b) Zhang, B.; Zhu, X.-Q.; Lu, J.-Y.; He, J.-Q.; Wang, P. G.; Cheng, J.-P. *J. Org. Chem.* **2003**, *68*, 3295.

(24) (a) Hoffmann, S.; Seayad, A. M.; List, B. *Angew. Chem.* **2005**, *117*, 7590. ; *Angew. Chem., Int. Ed.* **2005**, *44*, 7424. (b) Storer, R. I.; Carrera, D. E.; Ni, Y.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2006**, *128*, 84.

(25) (a) Rueping, M.; Sugiono, E.; Azap, C.; Theissmann, T.; Bolte, M. *Org. Lett.* **2005**, *7*, 3781. (b) Rueping, M.; Antonchick, A. P.; Theissmann, T. *Angew. Chem.* **2006**, *118*, 3765; *Angew. Chem., Int. Ed.* **2006**, *45*, 3683. (c) Rueping, M.; Antonchick, A. P.; Theissmann, T. *Angew. Chem.* **2006**, *118*, 6903; *Angew. Chem., Int. Ed.* **2006**, *45*, 6751.

(26) (a) Schwarz, D. E.; Cameron, T. M.; Hay, P. J.; Scott, B. L.; Tumas, W.; Thorn, D. L. *Chem. Commun.* **2005**, *47*, 5919. (b) Zhang, D.; Wu, L. Z.; Zhou, L.; Yang, Q. Z.; Zhang, L. P.; Tung, C. H. *J. Am. Chem. Soc.* **2004**, *126*, 3440. (c) Morkovnik, A. S.; Ivakhnenko, E. P.; Bogachev, Y. G.; Tertov, B. A.; Berberova, N. T.; Okhlobystin, O. Y. *Khim. Geterotsikl. Soedin.* **1988**, *2*, 203.

(27) Heller, A. *Acc. Chem. Res.* **1990**, *23*, 128.

(28) (a) Dueymes, C.; Decout, J. L.; Peltie, P.; Fontecave, M. *Angew. Chem., Int. Ed.* **2002**, *41*, 486. (b) Yan, P.; Holman, M. W.; Robustelli, P.; Chowdhury, A.; Ishak, F. I.; Adams, D. M. *J. Phys. Chem. B* **2005**, *109*, 130. (c) Strohbach, D.; Novak, N.; Muller, S. *Angew. Chem., Int. Ed.* **2006**, *45*, 2127. (d) Trieflinger, C.; Rurack, K.; Daub, J. *Angew. Chem., Int. Ed.* **2005**, *44*, 2288.

(29) (a) Zayats, M.; Katz, E.; Willner, I. *J. Am. Chem. Soc.* **2002**, *124*, 2020. (b) Willner, I.; Blonder, R.; Buckmann, A. F. *J. Am. Chem. Soc.* **1998**, *120*, 9335. (c) Garza, L.; Jeong, G.; Liddell, P. A.; Sotomura, T.; Moore, T. A.; Moore, A. L.; Gust, D. *J. Phys. Chem. B* **2003**, *107*, 10252.

(30) Zhu, X.-Q.; Cao, L.; Liu, Y.; Yang, Y.; Lu, J.-Y.; Wang, J.-S.; Cheng, J.-P. *Chem.—Eur. J.* **2003**, *9*, 3937.

(31) (a) Gelbard, G.; Lin, J.; Roques, N. *J. Org. Chem.* **1992**, *57*, 1789. (b) Kanomata, N.; Suzuki, M.; Yoshida, M.; Nakata, T. *Angew. Chem., Int. Ed.* **1998**, *37*, 1410. (c) Mikata, Y.; Hayashi, K.; Mizukami, K.; Matsumoto, S.; Yano, S.; Yamazaki, N.; Ohno, A. *Tetrahedron Lett.* **2000**, *41*, 1035.

(32) (a) Zhu, X.-Q. Chemistry of Organic Hydride. International Conference on Hydrogen and Hydrogen Storage: Methods and Materials, Jan 3−6, 2009, Bangalore, India. (b) Zhu, X.-Q. Chemistry of Organic Hydride, the 5th Sino-US Chemistry Professor Conference, June 29−30, 2009, Lanzhou, China.

(33) (a) Chikashita, H.; Ide, H.; Itoh, K. *J. Org. Chem.* **1986**, *51*, 5400. (b) Lee, I.-S. H.; Jeoung, E. H.; Kreevoy, M. M. *J. Am. Chem. Soc.* **1997**, *119*, 2722. (c) Lee, I.-S. H.; Jeoung, E. H.; Kreevoy, M. M. *J. Am. Chem. Soc.* **2001**, *123*, 7492. (d) Lee, I.-S. H.; Ji, Y. R.; Jeoung, E. H. *J. Phys. Chem. A* **2006**, *110*, 3875. (e) Lee, I.-S. H.; Jeoung, E. H. *J. Org. Chem.* **1998**, *63*, 7275.

(34) (a) Hapiot, P.; Moiroux, J.; Savéant, J.-M. *J. Am. Chem. Soc.* **1990**, *112*, 1337. (b) Anne, A.; Moiroux, J. *J. Org. Chem.* **1990**, *55*, 4608. (c) Klippenstein, J.; Arya, P. D.; Wayner, D. M. *J. Org. Chem.* **1991**, *56*, 6736. (d) Handoo, K. L.; Cheng, J.-P.; Parker, V. D. *J. Am. Chem. Soc.* **1993**, *115*, 5067.

(35) Zhu, X.-Q.; Li, H.-R.; Li, Q.; Ai, T.; Lu, J.-Y.; Yang, Y.; Cheng, J.-P. *Chem.—Eur. J.* **2003**, *9*, 871–880.

(36) (a) Ellis, W. W.; Raebiger, J. W.; Curtis, C. J.; Bruno, J. W.; DuBois, D. L. *J. Am. Chem. Soc.* **2004**, *126*, 2738–2743. (b) Handoo, K. L.; Cheng, J.-P.; Parker, V. D. *J. Am. Chem. Soc.* **1993**, *115*, 5067.

(37) (a) Zhu, X.-Q.; Yang, Y.; Zhang, M.; Cheng, J.-P. *J. Am. Chem. Soc.* **2003**, *125*, 15298. (b) Zhu, X.-Q.; Zhang, M.; Liu, Q.-Y.; Wang, X.-X.; Zhang, J.-Y.; Cheng, J.-P. *Angew. Chem., Int. Ed.* **2006**, *45*, 3945. (c) Zhu, X.-Q.; Dai, Z.; Yu, A.; Wu, S.; Cheng, J.-P. *J. Phys. Chem. B* **2008**, *112*, 11694.

(38) (a) Anderson, A. G.; Berkelhammer, G. *J. Am. Chem. Soc.* **1957**, *80*, 992. (b) Anne, A.; Moiroux, J. *J. Org. Chem.* **1990**, *55*, 4608. (c) Wong, Y.-S.; Marazano, C.; Gnecco, D.; Hupesh, C. D. *Tetrahedron Lett.* **1994**, *35*, 707.

(39) (a) Brewster, M. E.; Simay, A.; Czako, K.; Winwood, D.; Farag, H.; Bodor, N. *J. Org. Chem.* **1989**, *54*, 3721. (b) Rotili, M. A.; Tarantino, D.; Ornaghi, D. P.; et al. *J. Med. Chem.* **2006**, *49*, 6897.

(40) Zhu, X.-Q.; Liang, H.; Zhu, Y.; Cheng, J.-P. *J. Org. Chem.* **2008**, *73*, 8403–8410.

(41) Equations 5−7 were constructed from the thermodynamic cycles (1)−(3) in Scheme 3, respectively. Note that we used the term free-energy change ΔG_{et} to replace the enthalpy change ΔH_{et} in eqs 5−7 for the electron-transfer processes. The justification of this treatment is that entropies associated with electron transfer are negligible, as verified by Arnett et al. Arnett, E. M.; Amarnath, K.; Harvey, N. G.; Cheng, J.-P. *J. Am. Chem. Soc.* **1990**, *112*, 344.

(42) Wayner, D. D. M.; Parker, V. D. *Acc. Chem. Res.* **1993**, *26*, 287.

(43) (a) O'Dea, J.; Wojciechowski, M.; Osteryoung, J. *Anal. Chem.* **1985**, *57* (4), 954–955. (b) Osteryoung, J.; O'Dea, *J. Electroanal. Chem.* **1986**, *14*, 209. (c) Osteryoung, J.; O'Dea, J. *J. Electroanal. Chem.* **1986**, *14*, 209.

(44) (a) Logan, S. R. *Fundamentals of Chemical Kinetics*; Addison Wesley Longman: London, 1996; Chapter 2, p 35. (b) Bunnett, J. F. *Investigations of Rates and Mechanisms of Reactions*, 4th ed.; Bernasconi, C. F., Ed.; John Wiley & Sons: New York, 1986; Part I, p 181.

(45) Cheng, J.-P.; Handoo, K. L.; Parker, V. D. *J. Am. Chem. Soc.* **1993**, *115*, 2655.

(46) Ciancanelli, R.; Noll, B. C.; DuBois, D. L.; DuBois, M. R. *J. Am. Chem. Soc.* **2002**, *124*, 2984.

(47) Ellis, W. W.; Raebiger, J. W.; Curtis, C. J.; Bruno, J. W.; DuBois, D. L. *J. Am. Chem. Soc.* **2004**, *126*, 2738.

(48) Curtis, C. J.; Miedaner, A.; Ellis, W. W.; DuBois, D. L. *J. Am. Chem. Soc.* **2002**, *124*, 1918.

(49) Toluene was chosen as the reference to examine the reason that makes dihydropyridines have good hydricity. The main reason is that the cation of toluene can not form additional chemical bond by electron delocalization on the plan of the cation. 1,4-Cyclohexadiene is not a suitable reference, even though the structure is similar to that of the dihydropyridines, the reason is that the cation of 1,4-cyclohexadiene can form partial additional chemical bond by electron delocalization. Pentadiene is a suitable reference, since the cation of pentadiene cannot form additional chemical bond by electron delocalization, but the relevant thermodynamic parameters (except BDE) cannot be available. In fact, if BDEs of the four compounds in acetonitrile solution—1,4-cyclohexadiene (72 kcal), pentadiene (86 kcal), toluene (90 kcal), and 1,4-dihydropyridine **9H** (64 kcal)—are examined together, it is clear that BDE of pentadiene (86 kcal) is quite closer to that of toluene (90 kcal) than 1,4-cyclohexadiene and **9H**, which means that toluene should be one of the most suitable references in this work.

(50) Zhu, X.-Q.; Liu, Q.-Y.; Chen, Q.; Mei, L.-Y. *J. Org. Chem.* **2009**, in press.

(51) Herein Pauling's standpoint about the nature of the chemical bonds was applied that, for any of polyatomic molecules which contain A−B chemical bond, the intrinsic value of A−B bond dissociation energy always keeps constant as long as the atoms A and B are given (cf. Pauling, L. *J. Am. Chem. Soc.* **1932**, *54*, 3570–3582.

(52) The main reason is that for the carbon atom at the 4-position in $\mathbf{1}^+$ it is easier to get electron from the nitrogen atom at the opposite position than the carbon atom at the corresponding position in the cation $\mathbf{16}^+$.

(53) Wayner, D. D. M.; Lusztyk, E.; Ingold, K. U. *J. Org. Soc.* **1996**, *61*, 6430.

(54) Ruscic, B.; Wagner, A. F.; Harding, L. B.; et al. *J. Phys. Chem A* **2002**, *106*, 2727.

(55) Ramond, T. D.; Blanksby, S. J.; Kato, S.; Bierhaum, V. M.; Davico, G. E.; Schwartz, R. L.; Lineberger, W. C.; Ellison, G. B. *J. Phys. Chem A* **2002**, *106*, 9641.

(56) Jonsson, M. *J. Org. Soc.* **1996**, *100*, 6814.

(57) Santos, R. M. B.; Muralha, V. S. F.; Correia, C. F.; Guedis, R. C.; Cabral, B. J. C.; Simoes, J. A. M. *J. Phys. Chem A* **2002**, *106*, 9883.

(58) Benson, S. W. *Chem. Rev.* **1978**, *78*, 23.

(59) Bordwell, F. G.; Liu, W. Z. *J. Am. Chem. Soc.* **1996**, *118*, 10819.

(60) Fisher, E. R.; Armentrout, P. B. *J. Phys. Chem.* **1990**, *94*, 43967–4398.

(61) Kolthoff, I. M., Jr.; Chantooni, M. K. *J. Phys. Chem.* **1966**, *70*, 856.

(62) Jashinski, T.; El-Harakany, A. A.; Halaka, F. G.; Sadek, H. *Croat. Chem. Acta* **1978**, *51*, 1.

(63) Kolthoff, I. M.; Bruckenstein, S., Jr.; Chantooni, M. K. *J. Am. Chem. Soc.* **1961**, *83*, 3927.

(64) Kolthoff, I. M., Jr.; Chantooni, M. K. *J. Am. Chem. Soc.* **1973**, *95*, 8539.

(65) (a) Fukuzumi, S.; Inada, O.; Suenobu, T. *J. Am. Chem. Soc.* **2002**, *124*, 14538. (b) Fukuzumi, S.; Inada, O.; Suenobu, T. *J. Am. Chem. Soc.* **2003**, *125*, 48008.

(66) Fukuzumi, S.; Tokuda, J. Y.; Etano, T.; Okamoto, T.; Otera, J. *J. Am. Chem. Soc.* **1993**, *115*, 8960.

(67) Barberger, M. D.; Liu, W.; Ford, E.; Miranda, K. M.; Switzer, C.; Fukuto, J. M.; Farmer, P.; Wink, D. A.; Houk, K. N. *Proc. Natl. Acad. Sci. U.S.A.* **2002**, *99* (17), 10958–10963.

(68) (a) Lu, Y.; Zhao, Y.; Handoo, K. L.; Parker, V. D. *Org. Biomol. Chem.* **2003**, *1*, 173–181. (b) Perrin, C. L.; Zhao, C. *Org. Biomol. Chem.* **2008**, *6*, 3349–3353. (c) Ostovic, D.; Roberts, R. M. G.; Kreevoy, M. M. *J. Am. Chem. Soc.* **1983**, *105*, 7629–7631. (d) Kreevoy, M. M.; Kotchevar, A. T. *J. Am. Chem. Soc.* **1990**, *112*, 3579–3583. (e) Lee, I.-S. H.; Jeoung, E. H.; Kreevoy, M. M. *J. Am. Chem. Soc.* **2001**, *123*, 7492–7496.

(69) (a) Miller, L. L.; Valentine, J. R. *J. Am. Chem. Soc.* **1988**, *110*, 3982, and references therein. (b) Carlson, B. W.; Miller, L. L. *J. Am. Chem. Soc.* **1985**, *107*, 479. (c) Fukuzumi, S.; Koumitsu, S.; Hironaka, K.; Tanaka, T. *J. Am. Chem. Soc.* **1987**, *109*, 305, and references therein. (d) Fukuzumi, S.; Nishizawa, N.; Tanaka, T. *J. Org. Chem.* **1984**, *49*, 3571. (e) Coleman, C. A.; Rose, J. G.; Murray, C. J. *J. Am. Chem. Soc.* **1992**, *114*, 9755.

(70) Isaacs, N. S. *Physical Organic Chemistry*, 2nd ed.; Addison Wesley Longman: London, 1995; Chapter 2.

(71) Note: typically the first injection shows less heat than expected. This is often due to diffusion across the tip of the needle or to difficulties in positioning the buret drive.

JP911137P