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Hydride, Hydrogen Atom, Proton, and Electron Transfer Driving Forces of Various Five-Membered Heterocyclic Organic Hydrides and Their Reaction Intermediates in Acetonitrile

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Abstract: The enthalpy changes of 47 five-membered heterocyclic compounds (**ZH**) [33 substituted 2,3-dihydro-2-phenylbenzo[d]imidazoles (**1H–5H**), 9 substituted 2,3-dihydro-2-phenylbenzo[d]thiazoles (**6H**), and 5 substituted 2,3-dihydro-2-phenylbenzo[d]oxazoles (**7H**)] as a class of very important organic hydride donors to release hydride anion were determined by using titration calorimetry. The result shows that the enthalpy change scale of the 47 **ZH** in acetonitrile ranges from 49.0 to 93.4 kcal/mol. Such a long energy scale evidently shows that the 47 **ZH** can construct a large and useful library of organic hydride donors, which can provide various organic hydride donors that the hydride-releasing enthalpies are known. The enthalpy changes of the 47 **ZH** to release hydrogen atom and the 47 **ZH**^{•+} to release proton and hydrogen atom were also evaluated by using relative thermodynamic cycles according to Hess' law. The results show: (1) the enthalpy change scale of the 47 **ZH** to release hydrogen atom covers a range from 71.8 to 91.4 kcal/mol, indicating that the 47 **ZH** all should be weak hydrogen atom donors. (2) The enthalpy change scales of the 47 **ZH**^{•+} to release proton and to release hydrogen atom range from 17.5 to 25.7 and from 27.2 to 52.4 kcal/mol, respectively, implying that the proton-donating abilities of **ZH**^{•+} are generally quite larger than the corresponding hydrogen atom-donating abilities. The standard redox potentials of the 47 **ZH** and the 47 corresponding salts (**Z**⁺) were measured by using cyclic voltammetry (CV) and Osteryoung square wave voltammetry (OSWV), the results display that the standard oxidation potential scale of **ZH** ranges from −0.254 to −0.002 V for **1H–5H** and from 0.310 to 0.638 V for **6H–7H**, implying that **1H–5H** should be strong one-electron reducing agents and **6H–7H** should be weak one-electron reducing agents; the standard reduction potential scale of **Z**⁺ ranges from −1.832 to −2.200 V for **1**⁺–**5**⁺ and from −1.052 to −1.483 V for **6**⁺–**7**⁺, meaning that **1**⁺–**5**⁺ belong to very weak one-electron oxidation agents. The energies of the intramolecular hydrogen bond in **3H**, **3H**^{•+}, and **3**[•] with a hydroxyl group at ortho-position on the 2-phenyl ring were estimated by using experimental method, the results disclose that the hydrogen bond energy is 3.2, 2.8–3.0, and 3.9–4.0 kcal/mol for **3H**, **3H**^{•+}, and **3**[•] in acetonitrile, respectively, which is favorable for hydrogen atom transfer but unfavorable for hydride transfer from **3H**. The relative effective charges on the active center in **ZH**, **ZH**^{•+}, **Z**[•], and **Z**⁺, which is an efficient measurement of electrophilicity or nucleophilicity as well as dimerizing ability of a chemical species, were estimated by using experimental method; the results indicate that **1**[•]–**5**[•] belong to electron-sufficient carbon-radicals, **6**[•]–**7**[•] belong to electron-deficient carbon radicals, they are all difficult to dimerize, and that **1**⁺–**5**⁺ belong to weak electrophilic agents, **6**⁺–**7**⁺ belong to strong electrophilic agents. All these information disclosed in this work could not only supply a gap of the chemical thermodynamics of the five-membered heterocyclic compounds as organic hydride donors, but also strongly promote the fast development of the chemistry and applications of the five-membered heterocyclic organic hydrides.

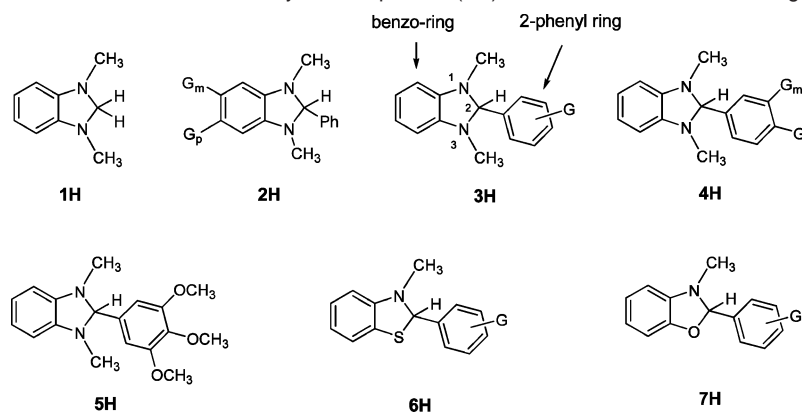
Introduction

Organic hydride donors are one class of very important organic compounds that can provide hydride anions in chemical and biochemical reactions.¹ Because naturally produced organic hydride donors, such as NAD(P)H,² FADH₂,³ tetrahydrofolate,⁴ and ascorbic acid (Vitamine C),⁵ play very important roles in

the processes of biological reductions and bio-antioxidations, the chemistry and biochemistry of naturally produced organic hydride donors have been a focus of interest for many chemists and biochemists in the past several decades.⁶ Recently, man-made organic hydride donors have been also attracting extensive

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Scheme 1. Structures of the 47 Five-Membered Heterocyclic Compounds (**ZH**) Examined in This Work as Organic Hydride Donors^a

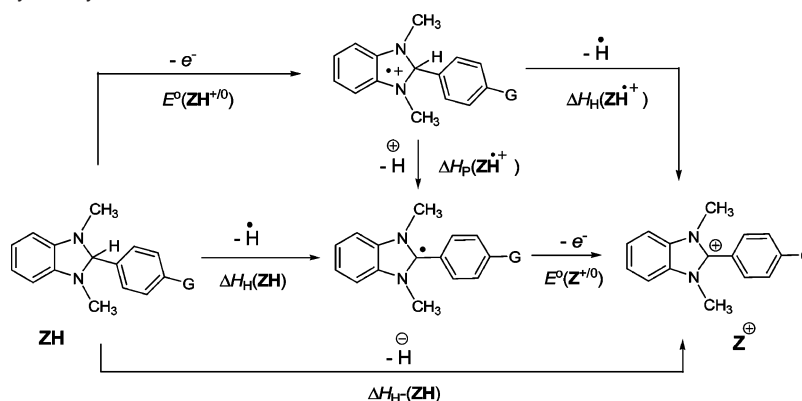
^a **2H**: G_p = OMe, Me, H, Cl, CF_3 ; G_m = H, Me. **3H**: G = p -NMe₂, p -OH, p -MeO, p -Me, p -H, p -Cl, p -Br, p -CF₃, p -CN, p -NO₂, m -MeO, m -Me, m -Cl, m -Br, m -NO₂, o -Me, o -Cl, o -OH. **4H**: G_m = MeO, NO₂, Me, F, Br, Cl; G_p = MeO, Me, F, Cl. **6H**: G = p -MeO, p -Me, p -H, p -F, p -Cl, p -Br, m -MeO, m -Me, m -Cl. **7H**: G = p -MeO, p -Me, p -H, p -Cl, p -Br.

and increasing attention of chemists and biochemists and many important man-made organic hydride donors have been designed and synthesized. Among all the kinds of man-made organic hydride donors, five-membered heterocyclic compounds, such as 2,3-dihydrobenzo[d]imidazoles (**1H**–**5H**), 2,3-dihydrobenzo[d]thiazoles (**6H**), and 2,3-dihydrobenzo[d]oxazoles (**7H**)^{7–13} (Scheme 1) and some six-membered heterocyclic compounds, such as 1-benzyl-1,4-dihydronicotinamide (BNAH), Hantzsch ester (HEH), and 9,10-dihydroacridine (AcrH₂),^{14–24} have

received the much attention of chemists and biochemists. The main reason is that these man-made heterocyclic compounds have many important chemical properties and quite extensive applications, such as, as models of some natural organic hydride donors to examine the thermodynamics, kinetics and mechanisms of the hydride transfer in vivo;^{14–24} as organic reducing agents to efficiently reduce various olefins, aldehydes, ketones, epoxy compounds, organic halides, and imides for organic synthesis;^{25–28} as hydrogen-stored materials to release hydrogen gas by reacting with protonic acids;²⁹ as functional molecules to construct various molecule devices;^{30–33} and as various

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Scheme 2. Possible Pathways of Hydride Transfer from **ZH**



molecular probes to explore the essence of living phenomena,^{34–35} etc. However, by systematically examining the past publications on the chemistry of the man-made five-membered and six-membered heterocyclic compounds as organic hydride donors, it is found that although the applications of the five-membered heterocyclic compounds in chemistry are as extensive as those of the six-membered heterocyclic compounds, the studies of the thermodynamics, kinetics and mechanisms of the five-membered heterocyclic compounds to release hydride anion are quite poorer than those on the six-membered heterocyclic compounds. Especially, rather scant attention has been paid to the detailed thermodynamic analysis on the course of the hydride transfer from the five-membered heterocyclic compounds. In fact, no paper was found to report the determination of the thermodynamic driving forces of the five-membered heterocyclic compounds as organic hydride donors to release hydride anion in solution so far, the key reason could be that these important thermodynamic data are difficult to be experimentally measured. Because hydride and hydrogen atom transfer from **ZH**, and proton and hydride atom transfer from **ZH**⁺ as well as electron transfer from **ZH** and **Z**[•] are often involved in the course of the hydride transfer from the five-membered heterocyclic compounds (Scheme 2),³⁶ it is evident that the thermodynamic driving forces of **ZH** to release a hydride anion and a hydrogen atom, **ZH**⁺ to release a proton and a hydrogen atom, **ZH** to release an electron, and **Z**⁺ to capture an electron in solution all should be very important and urgently required for chemists and biochemists not only to thoroughly elucidate the detailed mechanism of the hydride transfer from the five-membered heterocyclic compounds but also to scientifically design and synthesize new desired five-membered heterocyclic compounds as organic hydride donors. Therefore, the determination of hydride, hydrogen atom, proton, and electron-transfer driving forces of various five-membered heterocyclic organic hydrides and their reaction intermediates in solution has been a strategic goal in our research program for a long time. In this paper, five contributions can be provided: (1) Forty-seven five-membered heterocyclic compounds with N, S, and O as the heteroatoms

(ZH in Scheme 1) were designed and synthesized according to convenient synthetic strategies. (2) Standard electrochemical characterizations of the 47 five-membered heterocyclic compounds and their corresponding salts were examined by using the electrochemical methods of CV (cyclic voltammetry) and OSWV (Osteryoung square wave voltammetry), respectively. (3) The thermodynamic driving forces of the 47 five-membered heterocyclic compounds to release hydride and to release hydrogen atom in acetonitrile were determined by using titration calorimetry and electrochemical method. (4) The thermodynamic driving forces of the 47 $\text{ZH}^{+\bullet}$ to release proton and to release hydrogen atom in acetonitrile were estimated quantitatively by using thermodynamic cycle method according to Hess' law. (5) The intramolecular hydrogen bond energies in ZH , $\text{ZH}^{+\bullet}$, and Z^{\bullet} were exactly estimated by using the experimental method. (6) Distribution of effective charge on the five-membered heterocycles in ZH , $\text{ZH}^{+\bullet}$, Z^{\bullet} , and Z^{+} was evaluated by using Hammett-type linear free energy analyses and examining EPR spectra of the related radical cations. It is clear that the determination and quantitative estimation of these important thermodynamic parameters would not only supply a gap of the chemical thermodynamics of the five-membered heterocyclic compounds as organic hydride donors but also strongly promote the fast development of the chemistry and applications of the five-membered heterocyclic compounds.

Results

Forty-seven five-membered heterocyclic compounds with N, S, and O as the heteroatoms (**ZH**) shown in Scheme 1 were synthesized in this work according to conventional and convenient synthetic strategies, and the target products were identified by ^1H NMR and MS; the detailed synthetic routes are provided in the Supporting Information. Redox potentials of the 47 **ZH** and their corresponding salts (**Z** $^{+}$) were determined in acetonitrile by using two electrochemical methods CV and OSWV (Figures 1 and 2, respectively); the detailed experimental results are summarized in Table 1. The molar enthalpy changes (ΔH_f) of hydride transfer from the organic hydride donors **1H**–**5H** to *N*-methylacridinium ($\text{AcrH}^{+}\text{ClO}_4^{-}$) (eq 3) and from **3H** ($G = \text{H}$) to the corresponding salts of **6H**–**7H** (**6** $^{+}$ –**7** $^{+}$) were measured in acetonitrile by using titration calorimetry (Figure 3); the detailed experimental results are also listed in Table 1. ESR spectra of the radical cations **3H** $^{+\bullet}$ ($G = \text{H}$) and the 2-deuterated **3H** $^{+\bullet}$ (**3D** $^{+\bullet}$) were recorded in acetonitrile at low temperature by following the reactions of **3H** or **3D** with Fe-

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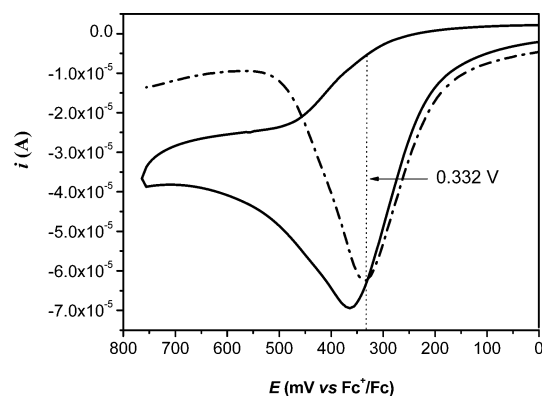


Figure 1. Cyclic voltammetry (CV) and Osteryoung square wave voltammetry (OSWV) of **6H** ($G = H$) in deaerated acetonitrile containing 0.1 M $n\text{-Bu}_4\text{NPF}_6$ as supporting electrolyte. The full line: CV graph (sweep rate = 0.1 V/s), the dashed line: OSWV graph.

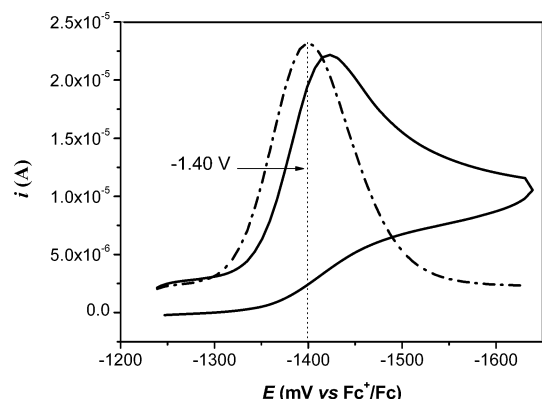


Figure 2. CV and OSWV of **6⁺** ($G = H$) in deaerated acetonitrile containing 0.1 M $n\text{-Bu}_4\text{NPF}_6$ as supporting electrolyte. The full line: CV graph (sweep rate = 0.1V/s), the dashed line: OSWV graph.

(bpy)₃³⁺ in deaerated acetonitrile; the detailed EPR spectra and the corresponding computer simulation spectra are shown in Figure 4.

The thermodynamic driving force of the five-membered heterocyclic compounds (**ZH**) to release hydride anion in acetonitrile, in this work, is defined as the enthalpy changes of the organic hydride donors to release hydride anion in acetonitrile (eqs 1 and 2). The determination of the enthalpy changes of the 47 **ZH** to release hydride anion in acetonitrile were performed according to two different experimental strategies: For the strong organic hydride donors (**1H–5H**), the enthalpy changes in acetonitrile can be obtained according to eq 4, which were formed from hydride exchange reactions of **1H–5H** with the strong hydride acceptor $N\text{-methylacridinium}$ ($\text{AcrH}^+\text{ClO}_4^-$) (eq 3) in acetonitrile. In eq 4, ΔH_r is the enthalpy change of the reaction (eq 3) in acetonitrile, which can be determined by using titration calorimetry (see Figure 3); $\Delta H_{\text{H}^-}(\text{AcrH}_2)$ is the enthalpy change of 9,10-dihydroacridine (AcrH_2) to release a hydride in acetonitrile, which is available from our previous work.³⁷ For the weak organic hydride donors (**6H–7H**), the enthalpy changes of them to release hydride in acetonitrile can be obtained from eq 6, which was formed according to another hydride exchange reaction of the corresponding salts of **6H–7H** (**6⁺–7⁺**) with the strong organic hydride donor **3H** ($G = H$)

Table 1. Reaction Enthalpy Changes of **1H–5H** with $\text{AcrH}^+\text{ClO}_4^-$ and of **6⁺–7⁺** with **3H** ($G = H$) as well as the Redox Potentials of Relative Species in Acetonitrile Together with the Redox Potentials of Some Well-Known Six-Membered Heterocyclic Organic Hydride Donors and the Corresponding Salts for Comparison

hydrides (ZH)		ΔH_f^a	$E_{\text{ox}}(\text{ZH}^{+/0})^b$		$E_{\text{red}}(\text{Z}^{+/0})^b$	
			CV	OSWV	CV	OSWV
			1H			
		−31.6	−0.145	−0.179	−2.217	−2.173
			2H			
<i>p</i> -OCH ₃	<i>m</i> -H	−31.4	−0.221	−0.254	−2.121	−2.094
<i>p</i> -Me	<i>m</i> -H	−30.1	−0.135	−0.161	−2.109	−2.077
<i>p</i> -Cl	<i>m</i> -H	−22.9	0.020	−0.002	−1.984	−1.962
<i>p</i> -CF ₃	<i>m</i> -H	−19.2	0.158	0.118	−1.923	−1.894
<i>p</i> -Me	<i>m</i> -Me	−32.1	−0.201	−0.238	−2.150	−2.126
			3H			
<i>p</i> -NMe ₂		−30.5	−0.126	−0.167	−2.235	−2.200
<i>p</i> -OH		−28.5	−0.090	−0.123	−2.128	−2.097
<i>p</i> -MeO		−28.2	−0.075	−0.120	−2.122	−2.074
<i>p</i> -Me		−27.7	−0.058	−0.111	−2.091	−2.056
<i>p</i> -H		−27.0	−0.068	−0.103	−2.055	−2.024
<i>p</i> -Cl		−25.9	−0.035	−0.079	−1.978	−1.948
<i>p</i> -Br		−25.9	−0.036	−0.078	−1.985	−1.950
<i>p</i> -CF ₃		−24.6	−0.010	−0.055	−1.923	−1.888
<i>p</i> -CN		−24.4	−0.004	−0.043	−1.891	−1.860
<i>p</i> -NO ₂		−24.0	0.005	−0.035	−1.863	−1.832
<i>m</i> -MeO		−26.5	−0.045	−0.088	−2.022	−1.984
<i>m</i> -Me		−27.3	−0.060	−0.103	−2.068	−2.028
<i>m</i> -Cl		−25.5	−0.024	−0.067	−1.962	−1.927
<i>m</i> -Br		−25.4	−0.023	−0.066	−1.960	−1.922
<i>m</i> -NO ₂		−24.2	0.004	−0.035	−1.883	−1.848
<i>o</i> -Me		−29.7	−0.067	−0.123	−2.114	−2.074
<i>o</i> -Cl		−27.9	−0.042	−0.089	−1.981	−1.962
<i>o</i> -OH		−27.3	−0.061	−0.117	−1.958	−1.943
			4H			
<i>p</i> -MeO	<i>m</i> -NO ₂	−25.2	−0.024	−0.050	−1.944	−1.903
<i>p</i> -MeO	<i>m</i> -Br	−26.5	−0.052	−0.091	−2.024	−1.985
<i>p</i> -MeO	<i>m</i> -MeO	−27.6	−0.086	−0.121	−2.085	−2.055
<i>p</i> -Me	<i>m</i> -Me	−28.0	−0.092	−0.125	−2.110	−2.076
<i>p</i> -F	<i>m</i> -F	−25.4	−0.021	−0.052	−1.948	−1.918
<i>p</i> -F	<i>m</i> -Br	−25.1	−0.013	−0.048	−1.930	−1.900
<i>p</i> -Cl	<i>m</i> -F	−24.7	−0.003	−0.042	−1.917	−1.886
<i>p</i> -Cl	<i>m</i> -Cl	−24.5	−0.011	−0.041	−1.910	−1.877
			5H			
		−27.1	−0.074	−0.111	−2.069	−2.030
			6H			
<i>p</i> -MeO		−15.8	0.342	0.310	−1.516	−1.483
<i>p</i> -Me		−16.9	0.350	0.319	−1.483	−1.453
<i>p</i> -H		−18.9	0.365	0.332	−1.430	−1.400
<i>p</i> -F		−19.6	0.372	0.338	−1.405	−1.379
<i>p</i> -Cl		−21.5	0.395	0.362	−1.362	−1.327
<i>p</i> -Br		−21.6	0.396	0.360	−1.360	−1.326
<i>m</i> -MeO		−20.3	0.384	0.350	−1.395	−1.360
<i>m</i> -Me		−18.0	0.365	0.329	−1.453	−1.422
<i>m</i> -Cl		−22.8	0.400	0.365	−1.318	−1.286
			7H			
<i>p</i> -MeO		−34.1	0.516	0.478	−1.209	−1.175
<i>p</i> -Me		−35.1	0.544	0.510	−1.185	−1.149
<i>p</i> -H		−37.0	0.595	0.564	−1.141	−1.111
<i>p</i> -Cl		−39.2	0.669	0.638	−1.087	−1.052
<i>p</i> -Br		−39.0	0.671	0.636	−1.089	−1.057
			References			
BNAH			0.260	0.219	−1.448	−1.419
HEH			0.509	0.479	−1.144	−1.112
AcrH ₂			0.493	0.460	−0.817	−0.787

^a ΔH_r was obtained from the reaction heats of eqs 3 and 5 by switching the sign; the latter were measured by titration calorimetry in acetonitrile at 298 K. The data, given in kcal/mol, were average values of at least three independent runs. The reproducibility is ± 0.5 kcal/mol. ^b Measured by CV and OSWV methods in acetonitrile at 298 K, the unit in volts vs Fc^+/Fc^0 and reproducible to 5 mV or better.

(37) (a) Zhu, X.-Q.; Zhang, M.; Liu, Q.-Y.; Wang, X.-X.; Zhang, J.-Y.; Cheng, J.-P. *Angew. Chem., Int. Ed.* **2006**, *45*, 3954. (b) Zhu, X.-Q.; Li, H.-R.; Li, Q.; Ai, T.; Lu, J.-Y.; Yang, Y.; Cheng, J.-P. *Chem.-Eur. J.* **2003**, *9*, 871.

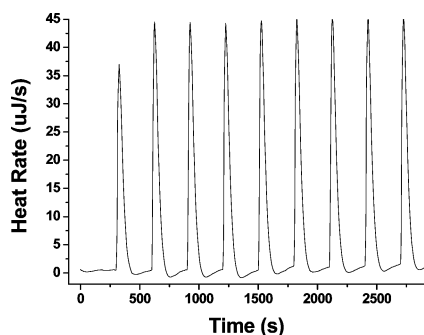
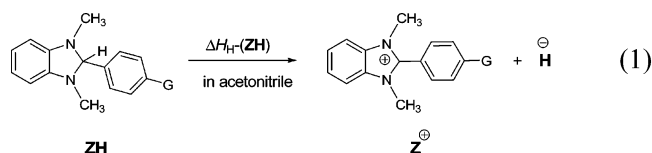
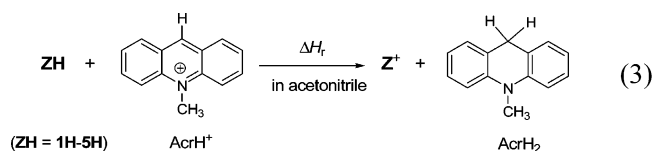


Figure 3. Isothermal titration calorimetry (ITC) for the reaction heat of **3H** ($G = H$) with N -methylacridinium ($\text{AcrH}^+\text{ClO}_4^-$) in acetonitrile at 298 K. Titration was conducted by adding $10\ \mu\text{L}$ of $\text{AcrH}^+\text{ClO}_4^-$ (2.0 mM) every 300 s into the acetonitrile containing the **3H** (ca. 10.0 mM).

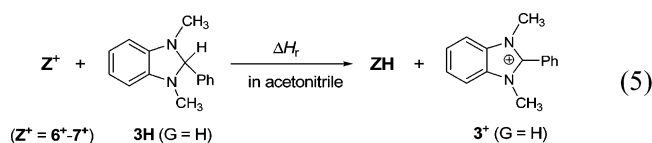
(eq 5). In the eq 6, ΔH_f is the enthalpy change of the reaction (eq 5) in acetonitrile, which can be determined by using titration calorimetry; $\Delta H_H^-(\mathbf{3H})$ is the enthalpy change of **3H** ($G = H$) to release a hydride in acetonitrile, which can be available from this work. The detailed enthalpy change values of the 47 **ZH** to release hydride in acetonitrile are summarized in Table 2.



$$\Delta H_H^-(\text{ZH}) = H_f(\text{Z}^+) + H_f(\text{H}^-) - H_f(\text{ZH}) \quad (2)$$



$$\Delta H_H^-(\text{ZH}) = \Delta H_H^-(\text{AcrH}_2) + \Delta H_f \quad (4)$$



$$\Delta H_H^-(\text{ZH}) = \Delta H_H^-(\mathbf{3H}) - \Delta H_f \quad (6)$$

The thermodynamic driving forces of **ZH** to release hydrogen atom and the thermodynamic driving forces of **ZH**⁺ to release proton and to release hydrogen atom in acetonitrile are also defined as the corresponding enthalpy changes of **ZH** to release a hydrogen atom and of **ZH**⁺ to release a proton and to release a hydrogen atom in acetonitrile, respectively. It is evident that these enthalpy change values can be used to measure hydrogen-donating abilities of **ZH** and proton-donating abilities and hydrogen-donating abilities of **ZH**⁺. To obtain the enthalpy change values of the 47 **ZH** to release a hydrogen atom in acetonitrile and the enthalpy change values of the 47 **ZH**⁺ to release a proton and to release a hydrogen atom in acetonitrile, three thermodynamic cycles were constructed according to the chemical process of **ZH** to release an hydride anion in acetonitrile (Scheme 3). From the three thermodynamic cycles,

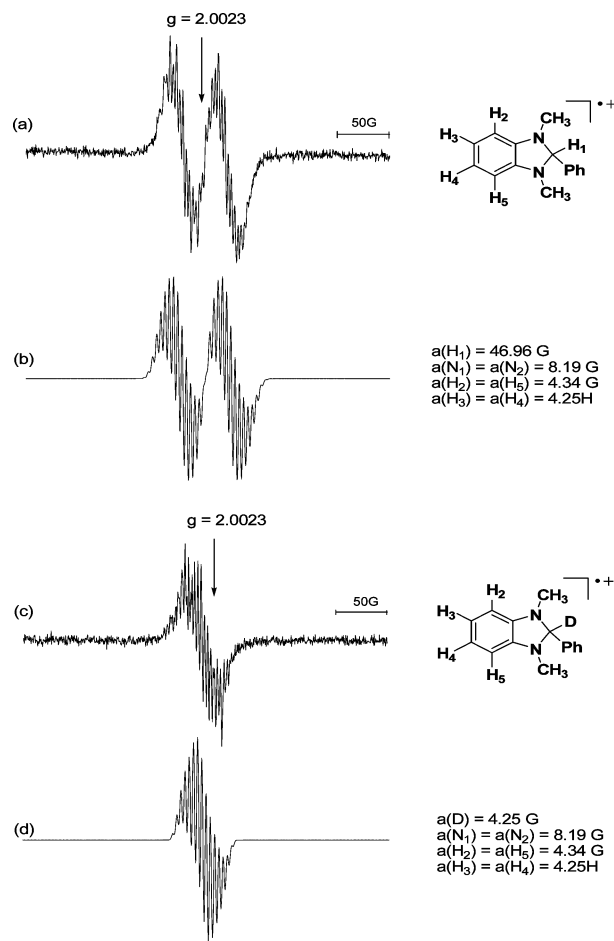


Figure 4. (a) ESR spectrum of **3H**⁺• ($G = H$) generated by oxidation of **3H** ($G = H$) (7.5×10^{-3} M) with $\text{Fe}(\text{bpy})_3^{3+}$ (1.0×10^{-2} M) in deaerated MeCN at 233 K and (b) computer simulation spectrum with the hfc values. (c) ESR spectrum of **3D**⁺• ($G = H$) generated by oxidation of **3D** ($G = H$) (9.5×10^{-3} M) with $\text{Fe}(\text{bpy})_3^{3+}$ (1.0×10^{-2} M) in deaerated MeCN at 233 K and (d) computer simulation spectrum with the hfc values.

eqs 7–9³⁸ were formed according to Hess' law, respectively. In eqs 7–9, $\Delta H_H^-(\text{ZH})$ and $\Delta H_H(\text{ZH})$ are the enthalpy changes of **ZH** to release a hydride anion in acetonitrile and to release a neutral hydrogen atom in acetonitrile, respectively; the $\Delta H_P(\text{ZH}^+)$ and $\Delta H_H(\text{ZH}^+)$ are the enthalpy changes of **ZH**⁺ to release a proton in acetonitrile and to release a neutral hydrogen atom in acetonitrile, respectively; $E^\circ(\text{Z}^{+/0})$, $E^\circ(\text{ZH}^{+/0})$, $E^\circ(\text{H}^{0/-})$, and $E^\circ(\text{H}^{+/0})$ are the standard redox potentials of **Z**⁺, **ZH**, **H**⁺, and **H**⁻ in acetonitrile, respectively. Evidently, it is not difficult to obtain the enthalpy changes of **ZH** to release a neutral hydrogen atom in acetonitrile and the enthalpy changes of **ZH**⁺ to release a proton and to release a neutral hydrogen atom in acetonitrile, if only $\Delta H_H^-(\text{ZH})$, $E^\circ(\text{Z}^{+/0})$, $E^\circ(\text{ZH}^{+/0})$, $E^\circ(\text{H}^{0/-})$ and $E^\circ(\text{H}^{+/0})$ are available. In fact, $\Delta H_H^-(\text{ZH})$ can be available from the above work (Table 1), the standard redox potentials of $E^\circ(\text{H}^{0/-})$ and $E^\circ(\text{H}^{+/0})$ can be obtained from literature,³⁹ $E^\circ(\text{Z}^{+/0})$ and $E^\circ(\text{ZH}^{+/0})$ can be obtained from experimental

(38) Equations 7, 8, and 9 were constructed from the thermodynamic cycles (I), (II), and (III) in Scheme, 3, respectively. Note that we used the term free-energy change ΔG_{et} to replace the enthalpy change ΔH_{et} in eqs 7–9 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.

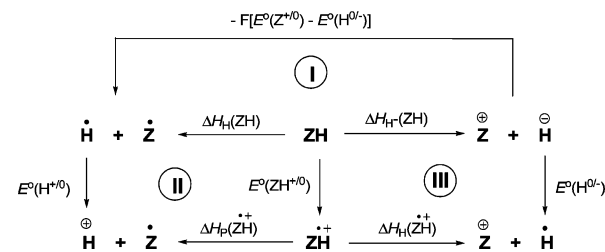
(39) Wayner, D. D. M.; Parker, V. D. *Acc. Chem. Res.* **1993**, *26*, 287.

Table 2. Enthalpy Changes of **ZH** to Release a Hydride Anion and to Release a Neutral Hydrogen Atom as well as the Enthalpy Changes of **ZH⁺** to Release a Proton and to Release a Neutral Hydrogen Atom in Acetonitrile (kcal mol⁻¹)^a Together with the Corresponding Values of Some Well-Known Six-Membered Heterocyclic Organic Hydride Donors for Comparison

hydrides (ZH)		$\Delta H_{\text{H}}^-(\text{ZH})^b$	$\Delta H_{\text{H}}(\text{ZH})^c$	$\Delta H_{\text{P}}(\text{ZH}^{+\bullet})^c$	$\Delta H_{\text{H}}(\text{ZH}^{+\bullet})^c$
1H		49.5	73.4	24.1	27.2
2H					
<i>p</i> -OCH ₃	<i>m</i> -H	49.7	71.8	24.4	29.3
<i>p</i> -Me	<i>m</i> -H	51.0	72.7	23.3	28.6
<i>p</i> -Cl	<i>m</i> -H	58.2	77.2	24.0	32.0
<i>p</i> -CF ₃	<i>m</i> -H	61.9	79.4	23.4	32.9
<i>p</i> -Me	<i>m</i> -Me	49.0	71.8	24.1	28.2
3H					
<i>p</i> -NMe ₂		50.6	75.1	25.7	28.2
<i>p</i> -OH		52.6	74.8	24.3	29.2
<i>p</i> -MeO		52.9	74.5	24.0	29.4
<i>p</i> -Me		53.4	74.6	23.9	29.7
<i>p</i> -H		54.1	74.6	23.7	30.2
<i>p</i> -Cl		55.2	73.9	22.5	30.8
<i>p</i> -Br		55.2	74.0	22.5	30.8
<i>p</i> -CF ₃		56.5	73.8	21.9	31.5
<i>p</i> -CN		56.7	73.4	21.1	31.4
<i>p</i> -NO ₂		57.1	73.1	20.7	31.7
<i>m</i> -MeO		54.6	74.2	22.9	30.4
<i>m</i> -Me		53.8	74.4	23.5	29.9
<i>m</i> -Cl		55.6	73.8	22.1	30.9
<i>m</i> -Br		55.7	73.8	22.1	31.0
<i>m</i> -NO ₂		56.9	73.3	20.9	31.5
<i>o</i> -Me		51.4	73.0	22.6	28.0
<i>o</i> -Cl		53.2	72.2	21.1	29.1
<i>o</i> -OH		53.8	72.4	21.9	30.3
4H					
<i>p</i> -MeO	<i>m</i> -NO ₂	55.9	73.6	21.5	30.8
<i>p</i> -MeO	<i>m</i> -Br	54.6	74.2	23.0	30.5
<i>p</i> -MeO	<i>m</i> -MeO	53.5	74.7	24.2	30.0
<i>p</i> -Me	<i>m</i> -Me	53.1	74.8	24.4	29.7
<i>p</i> -F	<i>m</i> -F	55.7	73.7	21.7	30.7
<i>p</i> -F	<i>m</i> -Br	56.0	73.6	21.5	30.9
<i>p</i> -Cl	<i>m</i> -F	56.4	73.7	21.4	31.1
<i>p</i> -Cl	<i>m</i> -Cl	56.6	73.7	21.4	31.3
5H		54.0	74.6	23.9	30.3
6H					
<i>p</i> -MeO		69.9	77.9	17.5	36.5
<i>p</i> -Me		71.0	78.3	17.7	37.4
<i>p</i> -H		73.0	79.1	18.2	39.1
<i>p</i> -F		73.7	79.3	18.2	39.7
<i>p</i> -Cl		75.6	80.0	18.4	41.0
<i>p</i> -Br		75.7	80.1	18.5	41.1
<i>m</i> -MeO		74.4	79.5	18.2	40.1
<i>m</i> -Me		72.1	78.7	17.8	38.3
<i>m</i> -Cl		76.9	80.3	18.7	42.2
7H					
<i>p</i> -MeO		88.3	89.2	24.9	51.0
<i>p</i> -Me		89.3	89.6	24.6	51.3
<i>p</i> -H		91.2	90.6	24.3	51.9
<i>p</i> -Cl		93.4	91.4	23.5	52.4
<i>p</i> -Br		93.2	91.4	23.4	52.3
References^d					
BNAH		64.2	70.7	12.4	32.9
HEH		69.3	68.7	4.5	32.0
AcrH ₂		81.1	73.0	9.2	44.2

^a See reference 40. Relative uncertainties were estimated to be smaller than or close to 1 kcal/mol in each case. ^b $\Delta H_{\text{H}}^-(\text{ZH})$ values of **1H**–**5H** and **6H**–**7H** were estimated from eqs 4 and 6, respectively, taking $\Delta H_{\text{H}}^-(\text{AcrH}_2) = 81.1 \text{ kcal mol}^{-1}$ from ref 37b. ^c $\Delta H_{\text{H}}(\text{ZH})$, $\Delta H_{\text{P}}(\text{ZH}^{+\bullet})$, and $\Delta H_{\text{H}}(\text{ZH}^{+\bullet})$ were estimated from eqs 7–9, respectively, taking $E^\circ(\text{H}^{+/0}) = -2.307 \text{ (V vs Fc}^{+/0})$, $E^\circ(\text{H}^{0/-}) = -1.137 \text{ (V vs Fc}^{+/0})$ (Fc = ferrocene),³⁹ and choosing the redox potentials of **ZH** and **Z⁺** measured by OSWV method (Table 1) as $E^\circ(\text{ZH}^{+/0})$ and $E^\circ(\text{Z}^{+/0})$, because the values from OSWV are closer to the corresponding standard redox potentials than the values from CV in this work. ^d Values are derived from ref 37c after revision according to the remeasured redox potentials of the six-membered heterocyclic organic hydride donors and the corresponding salts in acetonitrile by using Osteryoung square wave voltammetry (OSWV), because OSWV has been verified in this work to be more exact for evaluating the standard one-electron redox potentials of analyte with irreversible electrochemical processes than CV. The remeasured oxidation potentials of the six-membered heterocyclic organic hydride donors are 0.219, 0.479, and 0.460 V (vs Fc^{+/0}) for BNAH, HEH, and AcrH₂, respectively; the remeasured reduction potentials of the corresponding salts in acetonitrile are -1.419, -1.112, and -0.787 V (vs Fc^{+/0}) for BNA⁺, HE⁺, and AcrH⁺, respectively (see Supporting Information).

Scheme 3. Three Thermodynamic Cycles Were Constructed on the Basis of the Heterolytic C₂–H Bond Dissociation Process of **ZH**



measurements (Table 1). The detailed values of $\Delta H_{\text{H}}(\text{ZH})$, $\Delta H_{\text{P}}(\text{ZH}^{+\bullet})$ and $\Delta H_{\text{H}}(\text{ZH}^{+\bullet})$ for the 47 five-membered heterocyclic compounds in acetonitrile are also summarized in Table 2.

$$\Delta H_{\text{H}}(\text{ZH}) = \Delta H_{\text{H}}^-(\text{ZH}) - F[E^\circ(\text{Z}^{+/0}) - E^\circ(\text{H}^{0/-})] \quad (7)$$

$$\Delta H_{\text{P}}(\text{ZH}^{+\bullet}) = \Delta H_{\text{H}}(\text{ZH}) - F[E^\circ(\text{ZH}^{+/0}) - E^\circ(\text{H}^{+/0})] \quad (8)$$

$$\Delta H_{\text{H}}(\text{ZH}^{+\bullet}) = \Delta H_{\text{H}}^-(\text{ZH}) - F[E^\circ(\text{ZH}^{+/0}) - E^\circ(\text{H}^{0/-})] \quad (9)$$

Discussion

Enthalpy Change Scales of ZH to Release Hydride. From the second column in Table 2, it is clear that the enthalpy changes of the 47 five-membered heterocyclic compounds (**ZH**) as organic hydride donors range from 49.0 kcal/mol for **2H** ($G_{\text{p}} = G_{\text{m}} = \text{CH}_3$) to 93.4 kcal/mol for **7H** ($G = \text{p-Cl}$). Such a long enthalpy change scale evidently shows that the 47 **ZH** can construct a large and useful library of organic hydride donors, which can provide various organic reducing agents, the enthalpy change values of which are known for chemists to choose in organic syntheses. In the library of organic hydride donors, **2H** ($G_{\text{p}} = G_{\text{m}} = \text{CH}_3$) is the strongest organic hydride donor. To examine the effect of heteroatoms on the five-member ring in the organic hydrides on the hydride-donating abilities, the 47 five-membered heterocyclic organic hydrides (**ZH**) may be grouped into three categories according to the nature of the heteroatoms in the five-membered ring: 2,3-dihydrobenzo[d]-imidazole series with two nitrogen atoms as the heteroatoms (**1H**–**5H**), 2,3-dihydrobenzo[d]thiazole series with S and N as the heteroatoms (**6H**), and 2,3-dihydrobenzo[d]oxazole series with O and N as the heteroatoms (**7H**). Simple comparison of the enthalpy change scales of the three series of the organic hydride donors to release hydride anion clearly shows that the enthalpy change values increase in the order: **1H**–**5H** (49.0–57.1 kcal/mol) < **6H** (69.9–76.9 kcal/mol) < **7H** (88.3–93.4 kcal/mol), which means that the hydride-donating abilities of **ZH** should decrease in the order: 2,3-dihydrobenzo[d]imidazoles > 2,3-dihydrobenzo[d]thiazoles > 2,3-dihydrobenzo[d]oxazoles. The main reason could be that the aromatic properties of the corresponding hydride-removed products (**Z⁺**) decrease in the order: benzo[d]imidazoliums (**1⁺**–**5⁺**) > benzo[d]thiazoliums (**6⁺**) > benzo[d]oxazoliums (**7⁺**).⁴¹ If the $\Delta H_{\text{H}}^-(\text{ZH})$ values of **ZH** are compared with those of some well-known

(40) It is suggested to use the energetic data herewith in a relative sense for the purpose of comparison within family. This is because the electrode potentials were measured under irreversible conditions and some uncertainties in the absolute data were involved (possibly by a few tenths millivolts). For a recommended way to correct an irreversible potential to a reversible value, please see ref 39.

(41) Chen, Z.; Wannere, C. S.; Corminboeuf, C.; Puchta, R.; Schleyer, P. von R. *Chem. Rev.* **2005**, *105*, 3842.

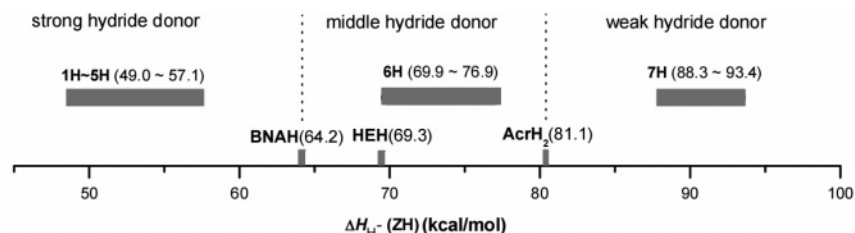


Figure 5. Comparison of hydride donating abilities of **ZH** with BNAH, HEH, and AcrH₂.

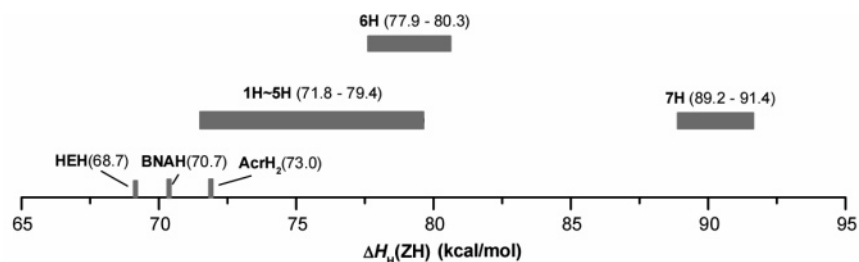


Figure 6. Comparison of hydrogen atom donating abilities between **ZH** and NADH models: BNAH, HEH, and AcrH₂.

NADH models BNAH, HEH, and AcrH₂ in acetonitrile (see Figure 5), it is found that (i) the hydride-donating abilities of **1H–5H** (49.0–57.1 kcal/mol) are not only far larger than that of Hantzsch ester (HEH) (69.3 kcal/mol) but also larger than that of BNAH (64.2 kcal/mol); (ii) the hydride-donating abilities of **6H** (69.9–76.9 kcal/mol) is smaller than that of HEH, but larger than that of AcrH₂ (81.1 kcal/mol); (iii) the hydride-donating abilities of **7H** (88.3–93.4 kcal/mol) is much smaller than that of AcrH₂. Because BNAH is a well-known strong organic hydride donor, HEH is a well-known middle-strong organic hydride donor, and AcrH₂ is a well-known weak organic hydride donor, we can suggest that **1H–5H** should be due to strong organic hydride donors; generally, these organic hydride donors can be chosen as good organic reducing agents for organic syntheses; **6H** belongs to middle-strong or weak organic hydride donors. The applications of these organic hydrides should be limited as an efficient organic reducing agents for organic syntheses; **7H** belongs to very weak organic hydride donors, which generally are not suitable to be chosen as organic reducing agents for organic syntheses, but the corresponding salts (**7**⁺) should be good hydride acceptors for organic syntheses. In fact, many 2,3-dihydrobenzo[d]imidazoles (**1H–5H**) have been extensively used as organic reducing agents in organic syntheses.^{6–8}

Enthalpy Change Scales of ZH to Release Hydrogen Atom. From the third column in Table 2, it is clear that the enthalpy change scale of the 47 **ZH** in acetonitrile ranges from 71.8 to 79.4 kcal/mol for **1H–5H**, from 77.9 to 80.3 kcal/mol for **6H** and from 89.2 to 91.4 kcal/mol for **7H**. Because $\Delta H_H(\text{ZH})$ of **1H–5H** are smaller than those of the corresponding **6H**, and the latter are smaller than that of the corresponding **7H**, it is clear that the hydrogen-donating abilities of the 47 **ZH** decrease in the order **1H–5H** > **6H** > **7H** when the substituent is the same. If the $\Delta H_H(\text{ZH})$ values of **ZH** were compared with those of the NADH models BNAH, HEH, and AcrH₂ in acetonitrile (see Figure 6) and with that of fluorene (Fl-H) (82.1 kcal/mol in dimethyl sulfoxide),⁴² a well-known authentic reference of C–H BDE, the following conclusions

can be drawn: (i) The hydrogen-donating abilities of **1H–5H** (71.8–79.4 kcal/mol) are smaller than those of BNAH (70.7 kcal/mol) and HEH (68.7 kcal/mol), but some of them, especially those with electron-donating groups, are larger than AcrH₂ in acetonitrile (73.0 kcal/mol), which indicates that **1H–5H**, especially those with electron-donating groups, would be not only excellent organic hydride donors but also moderate hydrogen-atom donors, which has been supported by many experiments.^{7–10} (ii) The hydrogen-donating abilities of **6H** (77.9–80.3 kcal/mol) are not only quite smaller than those of BNAH and HEH but also quite smaller than that of AcrH₂, which indicates that **6H** are not good hydrogen-atom donors. However, because the hydrogen-donating abilities of **6H** are quite larger than that of Fl–H in DMSO, **6H** could be also used as the source of hydrogen atoms like **1H–5H** when the reaction temperature is high or to meet a stronger hydrogen atom acceptor during the reactions. (iii) **7H** is not a good source of hydrogen atom, because the $\Delta H_H(\text{7H})$ (89.2–91.4 kcal/mol) is not only much larger than that of AcrH₂ but also much larger than that of Fl–H in DMSO, indicating that **7H** cannot be used as the source of hydrogen atoms in general thermal reactions.

Enthalpy Change Scales of ZH⁺ to Release Proton and to Release Hydrogen Atom. As stated in the introduction section, the hydride transfer from the five-membered heterocyclic compounds **ZH** generally were initiated by one-electron transfer;^{8,9} an incipient radical cation intermediate **ZH^{•+}** should be formed, from which proton transfer or hydrogen-atom transfer is believed to follow in the second reaction step. Therefore, it is necessary to evaluate and compare the enthalpy changes of **ZH^{•+}** to release proton and to release hydrogen atom. From columns 4 and 5 in Table 2, we found that the enthalpy change scale of the 47 **ZH^{•+}** to release proton in acetonitrile ranges from 18.9 to 25.7 kcal/mol for **1H^{•+}–5H^{•+}**, from 17.5 to 18.7 kcal/mol for **6H^{•+}**, and from 23.4 to 24.9 kcal/mol for **7H^{•+}**. The enthalpy change scale of the 47 **ZH^{•+}** to release a hydrogen atom in acetonitrile ranges from 24.2 to 31.7 kcal/mol for **1H^{•+}–5H^{•+}**, from 36.5 to 43.2 kcal/mol for **6H^{•+}**, and from 51.0 to 52.4 kcal/mol for **7H^{•+}**. These results clearly show that as to the proton-donating abilities of **ZH^{•+}**, **6H^{•+}** is the strongest among the three classes of **ZH^{•+}** (**1H^{•+}–5H^{•+}**, **6H^{•+}**, and **7H^{•+}**);

(42) (a) Zhang, X.-M.; Bordwell, F. G. *J. Am. Chem. Soc.* **1992**, *114*, 9787. (b) Parker, V. D. *J. Am. Chem. Soc.* **1992**, *114*, 7458.

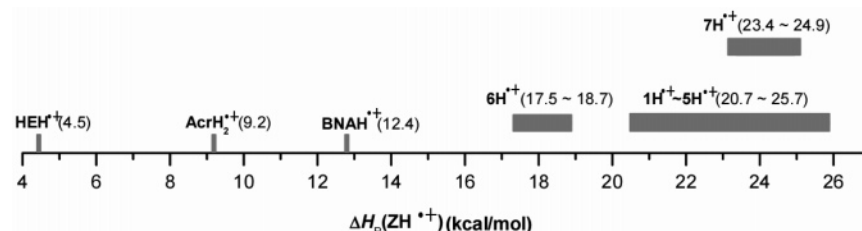


Figure 7. Comparison of proton donating abilities between $\text{ZH}^{+\bullet}$ and $\text{NADH}^{+\bullet}$ models: $\text{BNAH}^{+\bullet}$, $\text{HEH}^{+\bullet}$, and $\text{AcrH}_2^{+\bullet}$.

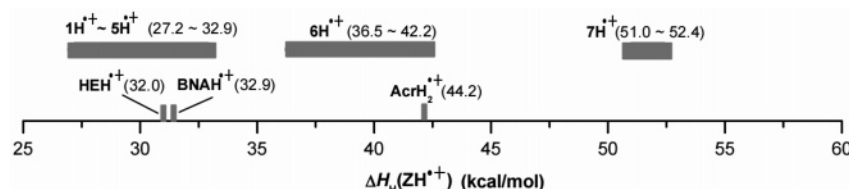


Figure 8. Comparison of hydrogen atom donating abilities between $\text{ZH}^{+\bullet}$ and $\text{NADH}^{+\bullet}$ models: $\text{BNAH}^{+\bullet}$, $\text{HEH}^{+\bullet}$, and $\text{AcrH}_2^{+\bullet}$.

but as to the hydrogen atom-donating abilities of $\text{ZH}^{+\bullet}$, $1\text{H}^{+\bullet}-5\text{H}^{+\bullet}$ is the strongest among the three classes of $\text{ZH}^{+\bullet}$.

If the $\Delta H_p(\text{ZH})^{+\bullet}$ of $\text{ZH}^{+\bullet}$ in acetonitrile were compared with those of $\text{NADH}^{+\bullet}$ models $\text{BNAH}^{+\bullet}$, $\text{HEH}^{+\bullet}$, and $\text{AcrH}_2^{+\bullet}$ in acetonitrile (12.4, 4.5, and 9.2 kcal/mol for $\text{BNAH}^{+\bullet}$, $\text{HEH}^{+\bullet}$, and $\text{AcrH}_2^{+\bullet}$, respectively) (see Figure 7), it is found that the $\Delta H_p(\text{ZH})^{+\bullet}$ of the 47 $\text{ZH}^{+\bullet}$ all are much larger than those of the $\text{NADH}^{+\bullet}$ models, which indicates that the acidities of the 47 $\text{ZH}^{+\bullet}$ should be much smaller than those of the $\text{NADH}^{+\bullet}$ models. However, by comparing $\Delta H_H(\text{ZH})^{+\bullet}$ of the 47 $\text{ZH}^{+\bullet}$ with $\Delta H_H(\text{NADH})^{+\bullet}$ of the $\text{NADH}^{+\bullet}$ models $\text{BNAH}^{+\bullet}$, $\text{HEH}^{+\bullet}$, and $\text{AcrH}_2^{+\bullet}$ (32.9, 32.0, and 44.2 kcal/mol for $\text{BNAH}^{+\bullet}$, $\text{HEH}^{+\bullet}$, and $\text{AcrH}_2^{+\bullet}$, respectively) (see Figure 8), it is found that the hydrogen-releasing abilities of $1\text{H}^{+\bullet}-5\text{H}^{+\bullet}$ are larger than or close to those of $\text{BNAH}^{+\bullet}$ and $\text{HEH}^{+\bullet}$ but much larger than that of $\text{AcrH}_2^{+\bullet}$, the hydrogen-donating abilities of $6\text{H}^{+\bullet}$ are slight larger than or close to that of $\text{AcrH}_2^{+\bullet}$, whereas the hydrogen-donating abilities of $7\text{H}^{+\bullet}$ are much smaller than that of $\text{AcrH}_2^{+\bullet}$. Because none of the enthalpy change values of the 47 $\text{ZH}^{+\bullet}$ to release proton and to release hydrogen atom are quite small, it is reasonable to predict that $\text{ZH}^{+\bullet}$ like $\text{BNAH}^{+\bullet}$ ⁴³ and $\text{AcrH}_2^{+\bullet}$ ⁴⁴ in acetonitrile solution could be directly detected and characterized by EPR spectroscopy under general experimental condition.⁴⁵

Standard Redox Potentials of ZH and Z^+ . As is well-known, the standard redox potentials of ZH and the corresponding salts (Z^+) are very important electrochemical parameters of ZH and Z^+ , which can be used as an indicator of the electron-donating ability of ZH and the electron-gaining ability of Z^+ . In this work, the oxidation potentials of the 47 ZH and the reduction potentials of the corresponding 47 salts Z^+ in acetonitrile were determined by CV and OSWV, respectively (see Table 1). Because the CV technique can only provide irreversible oxidation or reduction peak potentials for most of the 47 ZH and for all of the 47 Z^+ , the redox peak potentials of ZH and Z^+ derived from CV are not exactly equal to the

corresponding standard redox potentials of ZH and Z^+ . According to the structural character of CV graphs and the fundamentals of the CV technique,⁴⁶ generally the difference should be ca. 30 mV, that is, the irreversible oxidation peak potentials of ZH derived from CV are smaller than the corresponding standard oxidation potentials of ZH (i.e., the corresponding half wave oxidation potentials of ZH) by ca. 30 mV, and the irreversible reduction peak potentials of Z^+ derived from CV are larger than the corresponding standard reduction potentials of Z^+ (i.e., the corresponding half wave reduction potentials of Z^+) by ca. 30 mV. To obtain accurate standard redox potentials of ZH and Z^+ , OSWV was used to measure the redox potentials of ZH and Z^+ , because it was identified that the OSWV technique can provide a stable and accurate current response as an indicator of electrochemical property of analyte under conditions that complicate conventional CV methods.⁴⁷ From Table 1, it is found that for the oxidation potentials of 47 ZH , the results derived from OSWV are generally smaller than the corresponding results derived from CV by ca. 30 mV, but for the reduction potentials of 47 Z^+ , the results derived from OSWV are generally larger than the corresponding results derived from CV by ca. 30 mV, indicating that the values derived from OSWV should be much closer to the corresponding standard redox potentials of ZH and Z^+ than those derived from CV according to the structural character of CV graphs and theoretic prediction mentioned above. To further verify the OSWV measurements, the change of the oxidation wave of 2H ($\text{G} = \text{CF}_3$), which can display a good reversible oxidation wave in the conventional CV graph, especially at fast sweep rate (1000 mV/s), was examined by using CV and OSWV when pyridine as a base was added into the solution (see Figure 9). In Figure 9, it is clear that when the base was introduced into the solution, the oxidation wave of the 2H in CV tends to become irreversible and the position of the oxidation wave peak markedly moves from left to right, but the oxidation wave peak of the 2H in OSWV remains at the primary position and is just equal to the half wave potential of the 2H in CV graph, which indicates that the results derived from OSWV should be more

(43) (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.

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

(45) In general, if bond dissociation energy of a chemical species is larger than 6–8 kcal/mol, the chemical species could exist with a detectable amount at room temperature.

(46) Bard, A. J.; Faulkner, L. R. *Electrochemical methods fundamental and Applications*, 2nd ed.; John Wiley & Sons: New York, 2003.

(47) (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. J.; O'Dea, J. *Electroanal. Chem.* **1986**, *14*, 209.

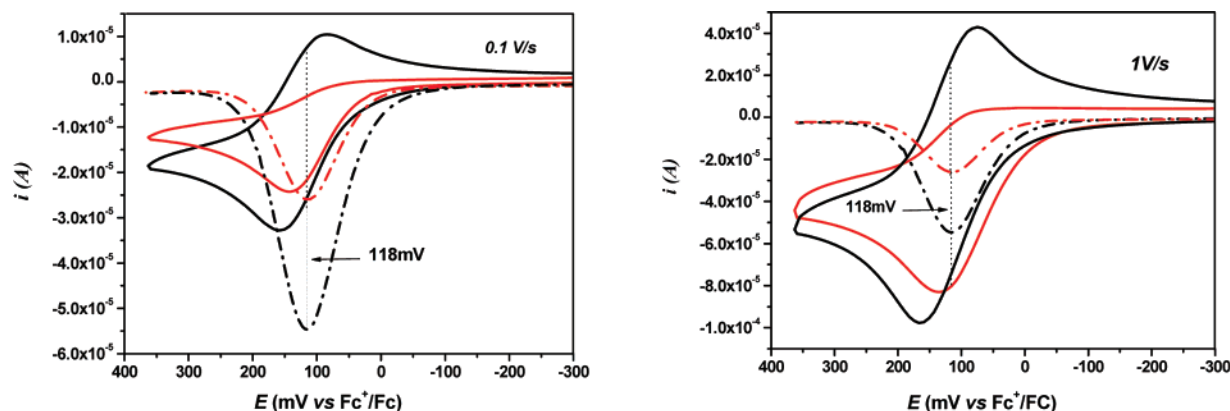


Figure 9. CV and OSWV of **2H** ($G = CF_3$) in acetonitrile + 0.1 M TBAPF₆. Black full line: CV graph (no pyridine added), red full line: CV graph in the presence of pyridine (1.2 mM); black dashed line: OSWV graph (no pyridine added), red dashed line: OSWV graph in the presence of pyridine (1.2 mM).

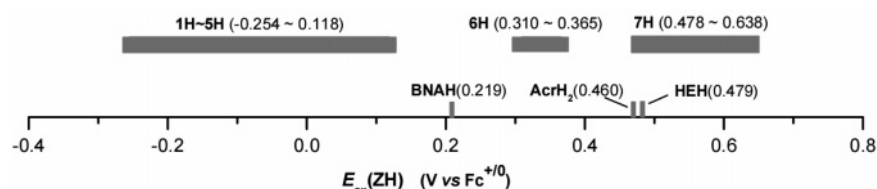


Figure 10. Comparison of one-electron donating abilities between **ZH** and NADH models: BNAH, HEH, and AcrH₂.

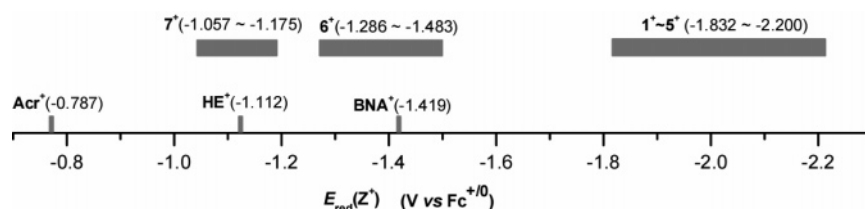


Figure 11. Comparison of one-electron gaining abilities between **Z⁺** and NAD⁺ models: BNA⁺, HE⁺, and AcrH⁺.

reliable and more accurate as the standard redox potentials of **ZH** and **Z⁺** in this work. So, in the following discussion about the electron-donating abilities of **ZH** and the electron-gaining abilities of **Z⁺**, the results from OSWV will be used as the standard redox potentials of **ZH** and **Z⁺**.

Concerning the electron-donating abilities of **ZH** as one-electron reductants, from Table 1, it is clear that the standard oxidation potential scale of **ZH** covers from -0.254 to 0.118 V for **1H–5H**, from 0.310 to 0.365 V for **6H** and from 0.478 to 0.638 V for **7H**, which indicates that the electron-donating abilities of **ZH** decrease in the order: 2,3-dihydrobenzo[d]-imidazoles **1H–5H** > 2,3-dihydrobenzo[d]thiazoles **6H** > 2,3-dihydrobenzo[d]oxazoles **7H**. Comparison of the one-electron oxidation potentials of the five-membered heterocyclic compounds **ZH** with those of the well-known six-membered heterocyclic organic hydrides BNAH (0.219 V vs $Fc^{+/0}$),⁴⁸ HEH (0.479 V vs $Fc^{+/0}$),⁴⁸ and AcrH₂ (0.460 V vs $Fc^{+/0}$)⁴⁸ (Figure 10) shows that electron-donating abilities of **1H–5H** are not only quite larger than those of HEH and AcrH₂ but also even larger than that of BNAH, which indicates that **1H–5H** should be strong one-electron donors.⁸ As to the five-membered heterocyclic compounds with sulfur and nitrogen as the heteroatoms (**6H**), the electron-donating abilities are significantly smaller than that of BNAH but larger than those of HEH and AcrH₂, which means that **6H** should be due to the middle strong one-electron donors. However, as to the five-membered het-

erocyclic compounds with oxygen and nitrogen as the heteroatoms (**7H**), the electron-donating abilities are not only smaller than BNAH, but also even smaller than HEH and AcrH₂, suggesting that **7H** should be very poor one-electron donors and cannot be used as efficient one-electron reducing agent.

Concerning the electron-gaining abilities of **Z⁺** as one-electron oxidants, from Table 1, it is found that the one-electron reduction potentials of **Z⁺** range from -1.832 to -2.200 V for **1⁺–5⁺**, from -1.286 to -1.483 V for **6⁺** and from -1.052 to -1.175 V for **7⁺**, which suggests that the electron-gaining abilities of **Z⁺** generally increase in the order: **1⁺–5⁺** (-1.832 to -2.200 V) < **6⁺** (-1.286 to -1.483 V) < **7⁺** (-1.052 to -1.175 V). Comparison of the reduction potentials of **Z⁺** and the well-known NAD⁺ models BNA⁺ (-1.419 V),⁴⁸ diethyl 1-hydro-2,6-dimethylpyridine-3,5-dicarboxylate cation (HE⁺) (-1.112 V),⁴⁸ and AcrH⁺ (-0.787 V)⁴⁸ (Figure 11) clearly shows that the one-electron oxidizabilities of **1⁺–5⁺** are not only much smaller than those of HE⁺ and AcrH⁺ but also smaller than that of BNA⁺; the one-electron oxidizabilities of **6⁺** are smaller than those of HE⁺ and AcrH⁺ but larger than or close to BNA⁺; the one-electron oxidizabilities of **7⁺** are smaller than that of AcrH⁺, larger than that of BNA⁺, and larger than or close to that of HE⁺. Because the one-electron reduction potentials of **Z⁺** all are quite negative (-1.052 to -2.200 V vs $Fc^{+/0}$), much more negative than that of the well-known one-electron oxidant ferrocenium (Fc^{+}), the latter is often used as a reference of one-electron oxidants (0.000 V); the one-electron

(48) Determined in this work by using OSWV method.

oxidizabilities of Z^+ , particularly, 1^+-5^+ should be very weak, which means that the reduced forms of Z^+ (Z^\bullet), especially $1^\bullet-5^\bullet$, should be very strong one-electron reductants. By comparing the one-electron oxidation potentials between Z^\bullet and the corresponding ZH , it is found that one-electron oxidation potentials of Z^\bullet are generally more negative than those of the corresponding ZH by -2 V for $1^\bullet-5^\bullet$, -1 V for 6^\bullet , and -0.5 V for 7^\bullet . Such a large difference of the oxidation potentials between Z^\bullet and ZH , especially between $1^\bullet-5^\bullet$ and $1H-5H$ suggests that the free radicals Z^\bullet , in particular $1^\bullet-5^\bullet$, cannot exist as a detectable reaction intermediate during the hydride transfer from $1H-5H$, especially at room temperature. In fact, none of the neutral free radicals $1^\bullet-7^\bullet$ has been directly detected and characterized by EPR spectroscopy until now.

Effect of the Substituents at Para- and Meta-Positions on the Enthalpy Changes and the Redox Potentials. From Tables 1 and 2, it is clear that the enthalpy change values of ZH and $ZH^{+\bullet}$ and the redox potentials of ZH and Z^+ all are strongly dependent on the nature and the position of substituents. To elucidate the relations of the nature of substituents with the enthalpy changes and the redox potentials, the effects of the remote substituents at *p*- and *m*-positions (G_p and G_m) were examined on the $\Delta H_H^-(ZH)$ and $\Delta H_H(ZH)$ of ZH (**2H**, **3H-5H**, **6H**, and **7H**), on the $\Delta H_p(ZH)^{+\bullet}$ and $\Delta H_H(ZH)^{+\bullet}$ of $ZH^{+\bullet}$ (**2H** $^{+\bullet}$, **3H** $^{+\bullet}-5H$ $^{+\bullet}$, **6H** $^{+\bullet}$, and **7H** $^{+\bullet}$), as well as on the $E_{ox}^-(ZH)$ of ZH (**2H**, **3H-5H**, **6H**, and **7H**) and on the $E_{red}(Z^+)$ of Z^+ (**2** $^+$, **3** $^+-5$ $^+$, **6** $^+$, and **7** $^+$), respectively; the results in Figures S1–S6 (Supporting Information) show that the $\Delta H_H^-(ZH)$, $\Delta H_H(ZH)$, $\Delta H_p(ZH)^{+\bullet}$, $\Delta H_H(ZH)^{+\bullet}$, $E_{ox}(ZH)$, and $E_{red}(Z^+)$ of the 24 chemical and electrochemical processes all are linearly dependent on the sum of Hammett substituent parameters σ_p and σ_m with very good correlation coefficients, which indicates that the Hammett linear free energy relationship holds in the 24 chemical and electrochemical processes as well as the concerted effects of multiple substituents at para- and meta-positions have good linear additivity on the enthalpy changes and the redox potentials. From the slopes and the intercepts of the 24 straight lines, the corresponding 24 mathematical formulas (eqs 10–33) can be easily derived. Evidently, for any one- or multi-substituted at para- and/or meta-position five-membered heterocyclic compounds ZH (**2H**, **3H-5H**, **6H**, and **7H**) and the corresponding radical cations, $ZH^{+\bullet}$ (**2H** $^{+\bullet}$, **3H** $^{+\bullet}-5H$ $^{+\bullet}$, **6H** $^{+\bullet}$, and **7H** $^{+\bullet}$), it is not difficult to safely estimate the values of the corresponding $\Delta H_H^-(ZH)$, $\Delta H_H(ZH)$, $\Delta H_p(ZH)^{+\bullet}$, and $\Delta H_H(ZH)^{+\bullet}$ according to eqs 10–25, as long as the corresponding Hammett substituent parameters (σ) are available and the standard deviation of the estimations is less than ± 0.25 kcal/mol. In the same way, for any one- or multi-substituted at para- and/or meta-position five-membered heterocyclic compounds ZH (**2H**, **3H-5H**, **6H**, and **7H**) as well as the corresponding salts Z^+ (**2** $^+$, **3** $^+-5$ $^+$, **6** $^+$, and **7** $^+$), the values of the corresponding redox potentials can also be reliably estimated from eqs 26–33, respectively, if only the corresponding Hammett substituent parameters are available and the standard deviation of the estimations is less than 25 mV. Because the family of the five-membered heterocyclic compounds as organic hydride donors is very large, and most of Hammett substituent parameters of various substituents located at the para- and meta-positions are easily obtained from literature,⁴⁹ it is evident that

the 24 formulas should have a very extensive application in the prediction of the related thermodynamic driving forces of the various five-membered heterocyclic compounds and their reaction intermediates to release or capture hydride, hydrogen atom, proton, and electron.

$$\Delta H_H^-(ZH) = 16.1 \sum(\sigma_p + \sigma_m) + 53.7 \text{ for } \mathbf{2H} \quad (10)$$

$$\Delta H_H^-(ZH) = 4.1 \sum(\sigma_p + \sigma_m) + 54.1 \text{ for } \mathbf{3H-5H} \quad (11)$$

$$\Delta H_H^-(ZH) = 11.2 \sum(\sigma_p + \sigma_m) + 73.0 \text{ for } \mathbf{6H} \quad (12)$$

$$\Delta H_H^-(ZH) = 12.5 \sum(\sigma_p + \sigma_m) + 91.2 \text{ for } \mathbf{7H} \quad (13)$$

$$\Delta H_H(ZH) = 9.8 \sum(\sigma_p + \sigma_m) + 74.4 \text{ for } \mathbf{2H} \quad (14)$$

$$\Delta H_H(ZH) = -1.3 \sum(\sigma_p + \sigma_m) + 74.3 \text{ for } \mathbf{3H-5H} \quad (15)$$

$$\Delta H_H(ZH) = 4.0 \sum(\sigma_p + \sigma_m) + 79.0 \text{ for } \mathbf{6H} \quad (16)$$

$$\Delta H_H(ZH) = 7.0 \sum(\sigma_p + \sigma_m) + 90.6 \text{ for } \mathbf{7H} \quad (17)$$

$$\Delta H_p(ZH^{+\bullet}) = -0.6 \sum(\sigma_p + \sigma_m) + 23.8 \text{ for } \mathbf{2H}^{+\bullet} \quad (18)$$

$$\Delta H_p(ZH^{+\bullet}) = -3.3 \sum(\sigma_p + \sigma_m) + 23.3 \text{ for } \mathbf{3H}^{+\bullet}-\mathbf{5H}^{+\bullet} \quad (19)$$

$$\Delta H_p(ZH^{+\bullet}) = 1.9 \sum(\sigma_p + \sigma_m) + 18.0 \text{ for } \mathbf{6H}^{+\bullet} \quad (20)$$

$$\Delta H_p(ZH^{+\bullet}) = -0.4 \sum(\sigma_p + \sigma_m) + 24.3 \text{ for } \mathbf{7H}^{+\bullet} \quad (21)$$

$$\Delta H_H(ZH^{+\bullet}) = 5.7 \sum(\sigma_p + \sigma_m) + 30.1 \text{ for } \mathbf{2H}^{+\bullet} \quad (22)$$

$$\Delta H_H(ZH^{+\bullet}) = 2.1 \sum(\sigma_p + \sigma_m) + 30.1 \text{ for } \mathbf{3H}^{+\bullet}-\mathbf{5H}^{+\bullet} \quad (23)$$

$$\Delta H_H(ZH^{+\bullet}) = 9.0 \sum(\sigma_p + \sigma_m) + 39.0 \text{ for } \mathbf{6H}^{+\bullet} \quad (24)$$

$$\Delta H_H(ZH^{+\bullet}) = 5.2 \sum(\sigma_p + \sigma_m) + 51.9 \text{ for } \mathbf{7H}^{+\bullet} \quad (25)$$

$$E_{ox}(ZH) = 0.4496 \sum(\sigma_p + \sigma_m) - 0.1134 \text{ for } \mathbf{2H} \quad (26)$$

$$E_{ox}(ZH) = 0.0887 \sum(\sigma_p + \sigma_m) - 0.0979 \text{ for } \mathbf{3H-5H} \quad (27)$$

$$E_{ox}(ZH) = 0.0947 \sum(\sigma_p + \sigma_m) + 0.3353 \text{ for } \mathbf{6H} \quad (28)$$

$$E_{ox}(ZH) = 0.3178 \sum(\sigma_p + \sigma_m) + 0.5637 \text{ for } \mathbf{7H} \quad (29)$$

$$E_{red}(Z^+) = 0.2733 \sum(\sigma_p + \sigma_m) - 2.0336 \text{ for } \mathbf{2}^+ \quad (30)$$

$$E_{red}(Z^+) = 0.2334 \sum(\sigma_p + \sigma_m) - 2.0138 \text{ for } \mathbf{3}^+-\mathbf{5}^+ \quad (31)$$

$$E_{red}(Z^+) = 0.3118 \sum(\sigma_p + \sigma_m) - 1.3991 \text{ for } \mathbf{6}^+ \quad (32)$$

$$E_{red}(Z^+) = 0.2394 \sum(\sigma_p + \sigma_m) - 1.1096 \text{ for } \mathbf{7}^+ \quad (33)$$

Effect of Substituents at Ortho-Position on the Enthalpy Changes of ZH and $ZH^{+\bullet}$. From Tables 1 and 2, it is also found that three ortho-substituted five-membered heterocyclic compounds **3H** ($G = o\text{-CH}_3$, $o\text{-Cl}$, and $o\text{-OH}$) are listed. Because a substituent at ortho-positions generally contains more information about steric effect than that at para- or meta-positions, we made a comparison of the effect of substituents at ortho-position and those at para-position on the enthalpy changes of **3H** and **3H** $^{+\bullet}$. The purpose is to elucidate the steric effect of substituents and the intramolecular hydrogen bond on the enthalpy changes of ZH to release hydride and to release hydrogen atom and

(49) Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165.

Table 3. Comparison of Driving Force of Ortho-substituted **3H** with the Para-Substituted Isomers as Well as of the Ortho-substituted **3H**⁺ with the Para-Substituted Isomers

G	$\Delta H_{\text{H}}^-(\mathbf{3H})^a$			$\Delta H_{\text{H}}(\mathbf{3H})^a$			$\Delta H_{\text{P}}(\mathbf{3H}^{+\bullet})^a$			$\Delta H_{\text{H}}(\mathbf{3H}^{+\bullet})^a$		
	ρ^b	σ^b	Δ^c	ρ^b	σ^b	Δ^c	ρ^b	σ^b	Δ^c	ρ^b	σ^b	Δ^c
CH ₃	53.4	51.4	2.0	74.6	73.0	1.6	23.9	22.6	1.3	29.7	28.0	1.7
Cl	55.2	53.2	2.0	73.9	72.2	1.7	22.5	21.1	1.4	30.8	29.1	1.7
OH	52.6	53.8	-1.2	74.8	72.4	2.4	24.3	21.9	2.4	29.2	30.3	-1.1

^a Unit is kcal/mol. ^b From Table 2. ^c $\Delta = \Delta H(\text{p-isomer}) - \Delta H(\text{o-isomer})$.

ZH⁺ to release proton and to release hydrogen atom. Table 3 shows a comparison of the enthalpy changes of the three ortho-substituted **3H** with the corresponding three para-substituted isomers to release hydride and to release hydrogen atom as well as the enthalpy changes of the three ortho-substituted **3H**⁺ with the corresponding three para-substituted isomers to release proton and to release hydrogen atom. From Table 3, it is found that when the substituent (G) is CH₃ and Cl, as compared with the substituents at para-position, the substituents at ortho-position make the $\Delta H_{\text{H}}^-(\mathbf{3H})$, $\Delta H_{\text{H}}(\mathbf{3H})$, $\Delta H_{\text{P}}(\mathbf{3H}^{+\bullet})$, and $\Delta H_{\text{H}}(\mathbf{3H}^{+\bullet})$ become smaller by 2.0, 1.6, 1.3, and 1.7 kcal/mol for CH₃, and by 2.0, 1.6, 1.4, and 1.7 kcal/mol for Cl, respectively, which suggested that the substituents at ortho-positions are in favor of dissociation of C₂–H bond and (C₂–H)⁺ bond in **3H** and **3H**⁺. The main reason is that the steric effect of the substituents at the ortho-positions is larger than that at the para-position, which makes the molecular state energy increase. But, if the substituent is hydroxyl group (OH), the $\Delta H_{\text{H}}^-(\mathbf{3H})$ of the ortho-substituted isomer is larger than that of the corresponding para-substituted isomer by 1.2 kcal/mol. The reason could be that the hydroxyl group at the ortho-position can form intramolecular hydrogen bond with the nitrogen atom in the five-membered ring to make the ortho-substituted isomer to be stabler than the para-substituted isomer, which has been verified by the ¹H NMR spectrum of ortho-hydroxyl **3H** in CD₃CN (Figure 12). Because the steric effect of hydroxyl group at ortho-position is close to the steric effect of methyl group ($E_s = 0.00$)⁵⁰ and chlorine atom ($E_s = 0.07$),⁵⁰ and the positively charged nitrogen atoms in the ortho-hydroxyl **3**⁺ are not able to form intramolecular hydrogen bond with the proton in the OH group due to the static repulsion, which can be confirmed by the ¹H NMR spectrum of ortho-hydroxyl **3**⁺ in CD₃CN (Figure 12) and Wuest' work,⁵¹ it is safe that the energy of the intramolecular hydrogen bond in the ortho-hydroxyl **3H** can be estimated according to the difference of the enthalpy changes between the ortho-hydroxyl **3H** and the para-hydroxyl **3H** to release a hydride and the difference of the enthalpy changes between the ortho-methyl **3H** and the para-methyl **3H** or between the ortho-chloro **3H** and the para-chloro **3H** to release a hydride, i.e., the energy of the intramolecular hydrogen bond in the ortho-hydroxyl **3H** should be equal to the difference of the enthalpy changes between the ortho-hydroxyl **3H** and the para-hydroxyl **3H** to release a hydride reduced by the difference of the enthalpy changes between the ortho-methyl **3H** and the para-methyl **3H** or between the ortho-chloro **3H** and the para-chloro **3H** to release a hydride. The result is 3.2 kcal/mol. By using the similar method, the energies of the intramolecular hydrogen bond in

the neutral radical **3**[•] (o-OH) and in the radical cation **3H**⁺• (o-OH) also can be estimated to be 3.9–4.0 and 2.8–3.0 kcal/mol, respectively (Scheme 6). By simply comparing the energy magnitude of hydrogen bond in **3H** and **3**[•] (shown in Scheme 6), it is clear that the formation of the intramolecular hydrogen bond in **3H** is unfavorable for the escape of hydride anion from **3H** but is in favor of the escape of hydrogen atom from **3H**, because the energy of hydrogen bond in **3**[•] is larger than that in **3H**. In the same way, because the energy of hydrogen bond in **3**[•] is larger than that in **3H**⁺, it is conceivable that the formation of the intramolecular hydrogen bond in **3H** is not in favor of the escape of hydrogen atom from **3H**⁺ but in favor of the escape of proton from **3H**⁺ (Scheme 4).

Estimation of the Effective Charge Distribution on the Five-Membered Ring in ZH, ZH⁺, Z[•], and Z⁺. Because the hydride transfer from **ZH** is generally initiated by electron transfer in the course of **ZH** reductions, **ZH**⁺ and **Z**[•] should be two classes of very important reaction intermediates; however, very little information about the structure and the effective charge distribution is available. The main reason is that these important reaction intermediates are generally too unstable to be isolated from the reaction system for the special examination. Because the effective charge density on the active center in reaction intermediates can be used as an efficient measurement of the electrophilicity or nucleophilicity as well as the dimerizing ability of the reaction intermediates, it is necessary to estimate the effective charge on the active center in **ZH**, **ZH**⁺, **Z**[•], and **Z**⁺. To reasonably estimate relative effective charge on the active center in **ZH**, **ZH**⁺, **Z**[•], and **Z**⁺, the method of Hammett-type linear free energy analysis on the dependencies of $\Delta H_{\text{H}}^-(\mathbf{ZH})$, $\Delta H_{\text{H}}(\mathbf{ZH})$, $\Delta H_{\text{P}}(\mathbf{ZH}^{+\bullet})$, and $\Delta H_{\text{H}}(\mathbf{ZH}^{+\bullet})$ on the substituent constant (σ) (see Figures S1–S4 in Supporting Information) was used herein, due to the fact that the Hammett linear free-energy relationship analysis can provide a very efficient access to estimate the effective charge distribution.⁵² First, the estimation was carried out on the system of **7H**. From Figures S1–S4, it is clear that the enthalpy changes of **7H** to release hydride anion and to release neutral hydrogen atom as well as the enthalpy changes of **7H**⁺ to release a proton and to release a neutral hydrogen atom all are excellently linearly dependent on the sum of Hammett substituent parameters σ_{p} and σ_{m} with line slopes of 12.54 and 6.98 for **7H** to release a hydride and to release a neutral hydrogen atom, respectively, and with line slopes of -0.35 and 5.22 for **7H**⁺ to release a proton and to release a neutral hydrogen atom, respectively, which means that the Hammett linear free energy relationship holds in the four chemical processes. According to the root cause of the Hammett substituent effect, it is conceived that the sign of the line slope values reflects an increase or decrease of the effective charge on the C(2) atom in the oxazole ring and the magnitude of the line slope values is a measurement of the effective charge change on the C(2) atom during the corresponding four reaction processes. To quantitatively evaluate the relative effective charge changes on the C(2) atom during the four different reaction processes, we defined that the effective

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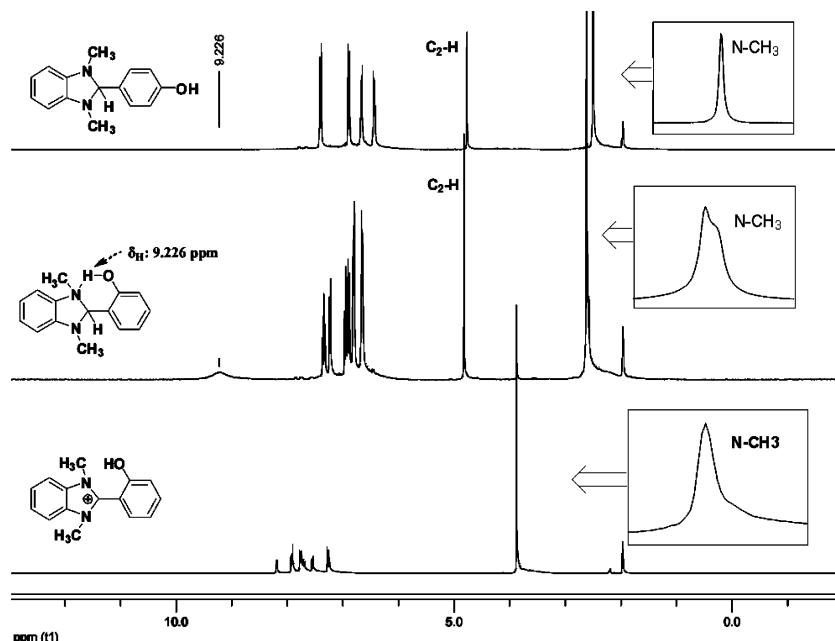
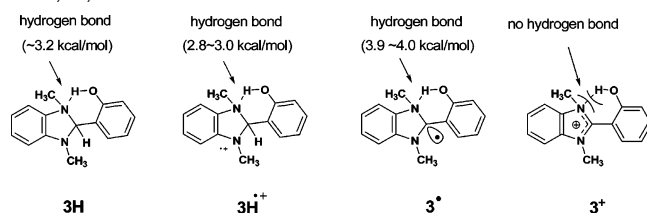


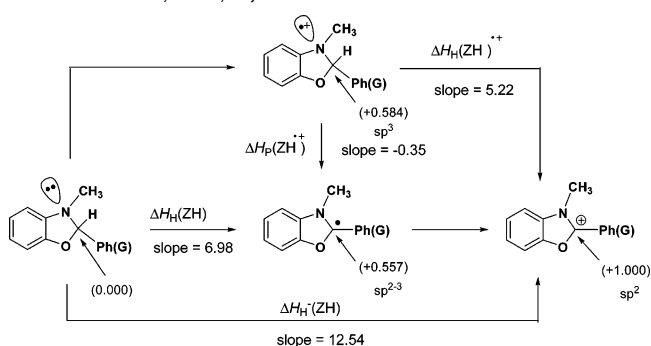
Figure 12. Comparison of the ^1H NMR spectra of ortho-hydroxyl 3H , ortho-hydroxyl 3H^+ , and para-hydroxyl 3H in CD_3CN .

Scheme 4. Comparison of Intramolecular Hydrogen Bond in 3H , 3H^+ , 3^+ , and 3^+



charge on the C(2) atom in 7H is zero and the effective charge on the carbon atom in 7^+ is positive one (+1.000) according to Lewis electron structures of 7H and 7^+ . This definition indicates that the slope value of 12.54 for 7H to release a hydride anion is equivalent to positive effective charge increase of one unit on the C(2) atom in going from 7H to 7^+ . According to this relationship, it is easy to deduce that the line slope of 6.98 for 7H to release a neutral hydrogen atom is equivalent to a positive effective charge increase of 0.557 on the C(2) atom in going from 7H to 7^+ . Because the effective charge on the carbon atom in 7H has been defined as zero, the effective charge on the C(2) atom in 7^+ should be +0.557. Similarly, because the line slopes of 5.22 for 7H^+ to release a neutral hydrogen atom is equivalent to a positive effective charge increase of 0.416 on the C(2) atom in going from 7H^+ to 7^+ , the effective charge on the C(2) atom in 7H^+ can be deduced to be +0.584 according to effective charge of positive one on the carbon atom in 7^+ defined above. In fact, this result can be also estimated from the line slope of -0.35 for 7H^+ to release a proton within experimental error according to the effective charge of 0.557 on the C(2) atom in 7^+ ascertained above. The details of the relative effective charge on the C(2) atom in 7H and its various reaction intermediates are shown in Scheme 5. Second, the estimation was carried out for the system of 6H . From Figures 7–10, it is also found that the line slopes of the enthalpy changes of 6H to release hydride anion and to release neutral hydrogen atom are 11.24 and 3.99 and the line slopes of the enthalpy changes of 6H^+ to release a proton and a neutral hydrogen atom are 1.87 and 8.99. Because the slope value of 12.54 is equivalent to an effective positive

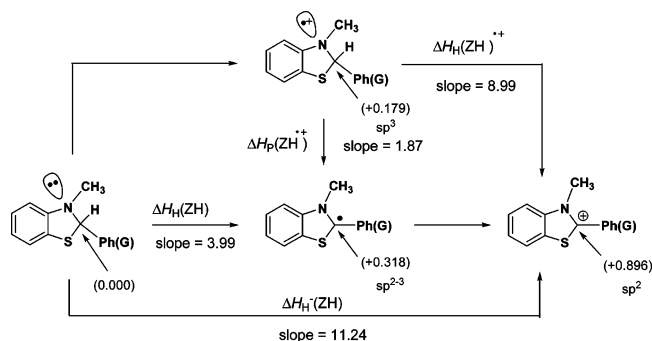
Scheme 5. Relative Effective Charge on the Carbon Atom at 2-Position in 7H , 7H^+ , 7^+ , and 7^+ in Acetonitrile



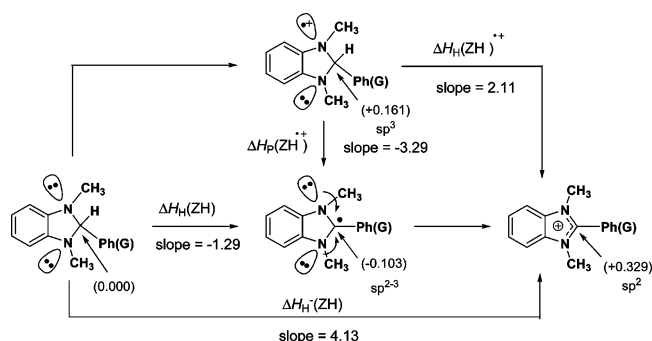
charge increase of one unit on the C(2) atom, which has been ascertained above in the system of 7H , the slope value of 11.24 for 6H to release a hydride anion should be equivalent to a positive effective charge increase of 0.896 on the C(2) atom in going from 6H to 6^+ .⁵³ If the effective charge on the C(2) atom in 6H is defined to be zero,⁵⁴ the effective charge on the C(2) atom in 6^+ should be +0.896. According to the effective charge on the C(2) atom in 6^+ (+0.896) and the line slopes of the enthalpy changes of 6H^+ to release a proton and a neutral hydrogen atom (1.87 and 8.99, respectively), the effective charges on the C(2) atom in 6H^+ and 6^+ were estimated to be

- (53) To make the effective charge on the C(2) atom in the system of 6H be directly comparable with that in the system of 8H , the line slope of 8H to release hydride anion was also used as a criterion of effective positive charge increase of one unit in the system of 6H .
- (54) Relative to the defined effective charge of the C(2) atom in 8H (0.000), the effective charge on the C(2) atom in 6H could not be exactly equal to zero (slightly smaller than zero in principle), but the difference should be very small and may be negligible because many papers show that the Hammett substituent effect on the stability of neutral molecules except neutral free radicals is much smaller than that on the stability of the corresponding charged species, which means that the effective charge on neutral molecule could not be quite large [cf: (a) Wiberg, K. B. *J. Org. Chem.* **2002**, 67, 4787. (b) Zhang, H. Y.; Sun, Y. M.; Wang, X. L. *J. Org. Chem.* **2002**, 67, 2709. (c) Fu, Y.; Liu, L.; Lin, B. L.; Mou, Y.; Cheng, Y. H.; Guo, Q. X. *J. Org. Chem.* **2003**, 68, 4657. (d) Pratt, D. A.; DiLabio, G. A.; Valgimigli, L. V.; Pedulli, G. F.; Ingold, K. U. *J. Am. Chem. Soc.* **2002**, 124, 11085. (e) Pratt, D. A.; DiLabio, G. A.; Mulder, P.; Ingold, K. U. *Acc. Chem. Res.* **2004**, 37, 334.]

Scheme 6. Relative Effective Charge on the Carbon Atom at 2-Position in **6H**, **6H⁺**, **6[•]**, and **6⁺** in Acetonitrile



Scheme 7. Relative Effective Charge on the Carbon Atom at 2-Position in **3H-5H**, **3H⁺-5H⁺**, **3⁻-5⁻**, and **3⁺-5⁺** in Acetonitrile



+0.179 and +0.318, respectively (Scheme 6). Similarly, the relative effective charge on the C(2) atom in **3H–5H**, **3H⁺–5H⁺**, **3[•]–5[•]**, and in **3⁺–5⁺** are also easily estimated according to the line slopes of related enthalpy changes, when the effective charge on the C(2) atom in **3H–5H** was defined as zero. The detailed results are shown in Scheme 7.

From Schemes 5–7, it is clear that the relative effective charges of the C(2) atom in \mathbf{Z}^+ are +0.329 for $\mathbf{3}^+ - \mathbf{5}^+$, +0.896 for $\mathbf{6}^+$, and +1.000 for $\mathbf{7}^+$, which means that $\mathbf{7}^+$ and $\mathbf{6}^+$ should be very strong electrophilic agents, whereas $\mathbf{3}^+ - \mathbf{5}^+$ should be quite weak electrophilic species. The reason leading to the much smaller effective positive charge on the C(2) atom in $\mathbf{3}^+ - \mathbf{5}^+$ is that the inductive effect of the nitrogen group $\text{N}(\text{Me})\text{C}_6\text{H}_5$ ($F = 0.25$)⁵⁵ in $\mathbf{3}^+ - \mathbf{5}^+$ on the C(2) atom is quite smaller than that of the sulfur group SC_6H_5 ($F = 0.30$)⁴⁹ in $\mathbf{6}^+$ and that of the oxygen group OC_6H_5 ($F = 0.37$)⁴⁹ in $\mathbf{7}^+$, and at the same time, the resonance effect of the nitrogen group $\text{N}(\text{Me})\text{C}_6\text{H}_5$ ($R = -0.55$)⁵⁶ on the C(2) atom is much more negative than that of the sulfur group SC_6H_5 ($R = -0.23$)⁵⁰ and that of the oxygen group OC_6H_5 ($R = -0.40$)⁴⁹, both of the two effects makes the effective positive charge of the C(2) atom in $\mathbf{3}^+ - \mathbf{5}^+$ be much smaller than those in $\mathbf{7}^+$ and in $\mathbf{6}^+$. Concerning the effective charge of the C(2) atom in \mathbf{ZH}^+ , it is found that the effective charge on the C(2) atom in $\mathbf{3H}^+ - \mathbf{5H}^+$ (+0.161) is slightly smaller than that in $\mathbf{6H}^+$ (+0.179) but much smaller than that in $\mathbf{7H}^+$ (+0.584). According to the inductive parameters (F) of $\text{N}(\text{Me})\text{C}_6\text{H}_5$ ($F = 0.25$)⁵⁵, SC_6H_5 ($F = 0.30$), and OC_6H_5 ($F = 0.37$), and the sp^3 hybridized state and the tetrahedral

orientation of the C(2) atom orbits in $\mathbf{ZH}^{+\bullet}$, it seems likely that the effects of heteroatoms in the five-membered ring on the effective charge of the C(2) atom in $\mathbf{ZH}^{+\bullet}$ were performed only by the static inductive pathway. However, by comparing the value difference of the inductive parameters (F) among N(Me)-C₆H₅, SC₆H₅ and OC₆H₅ with the corresponding value difference of the effective charge on the C(2) atom in $\mathbf{3H}^{+\bullet}$ – $\mathbf{5H}^{+\bullet}$ (+0.161), $\mathbf{6H}^{+\bullet}$ (+0.179), and $\mathbf{7H}^{+\bullet}$ (+0.584) in detail, it is found that the value changes of the inductive parameters of N(Me)C₆H₅, SC₆H₅, and OC₆H₅ are not in agreement with the change of the corresponding relative effective charges on the C(2) atom, which means that the effects of heteroatom groups in the five-membered ring on the effective charge of the C(2) atom in $\mathbf{ZH}^{+\bullet}$ could include other unknown effects except inductive effect. From Schemes 5–7, we also found that the C(2) atom carries the effective charges of +0.557 in $\mathbf{7}^{\bullet}$, +0.318 in $\mathbf{6}^{\bullet}$, and –0.103 in $\mathbf{3}^{\bullet}$ – $\mathbf{5}^{\bullet}$, which indicates that $\mathbf{3}^{\bullet}$ – $\mathbf{5}^{\bullet}$ are due to electron-sufficient free radicals and have somewhat nucleophilicity, but $\mathbf{6}^{\bullet}$ and $\mathbf{7}^{\bullet}$ are due to electron-deficient free radicals and have good electrophilicity. As is well-known, carbon radicals are generally sp² hybridized;⁵⁷ if the C(2) atom in \mathbf{Z}^{\bullet} were purely sp² hybridized as in the case of \mathbf{Z}^{+} , the positive charge on the C(2) atom in $\mathbf{6}^{\bullet}$ should be +0.499 rather than +0.318. If the carbon atom in \mathbf{Z}^{\bullet} were purely sp³ hybridized as in the case of $\mathbf{ZH}^{+\bullet}$, the charges on the carbon atom in $\mathbf{6}^{\bullet}$ and in $\mathbf{3}^{\bullet}$ – $\mathbf{5}^{\bullet}$ should be +0.170 and +0.152 rather than +0.318 and –0.103, respectively. It is evident that the C(2) atom in \mathbf{Z}^{\bullet} should be hybridized between sp² and sp³ (sp^{2–3}).

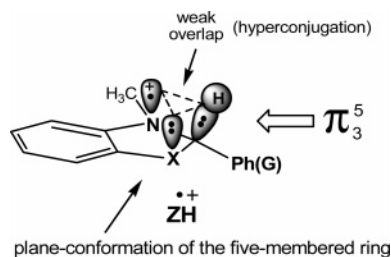
To quantitatively evaluate the contribution of inductive effect and resonance effect of the heteroatom groups in the five-membered heterocyclic compounds toward the relative effective charge on the C(2) atom in \mathbf{ZH}^+ , \mathbf{Z}^* , and \mathbf{Z}^+ , and predict the effect of other heteroatom groups except NMePh, PhS, and PhO on the relative effective charge on the C(2) atom in \mathbf{ZH}^+ , \mathbf{Z}^* , and \mathbf{Z}^+ , the binary correlation plots of the relative effective charges of the C(2) atom in \mathbf{ZH}^+ , \mathbf{Z}^* , and \mathbf{Z}^+ against the inductive parameter (F) and resonance parameter (R) of the heteroatom groups [N(Me)C₆H₅, SC₆H₅, and OC₆H₅] were made (see Figures S7–S9 in Supporting Information). From the ratio of F to R in the horizontal ordinates and each value of the inductive parameter (F) and the resonance parameter (R) of the three heteroatom groups, the relative contributions of the inductive effect and the resonance effect to the formation of the effective charge at the C(2) atom in \mathbf{ZH}^+ , \mathbf{Z}^* , and \mathbf{Z}^+ can be estimated. The results show that the relative contribution of the inductive effect and the resonance effect is: 76.1 and 23.9% for $3\mathbf{H}^+ - 5\mathbf{H}^+$, 90.1 and 9.9% for $6\mathbf{H}^+$, 86.6 and 13.4% for $7\mathbf{H}^+$; 78.6 and -21.4% for $3^* - 5^*$, 91.3 and -8.7% for 6^* , 88.2 and -9.9% for 7^* ; 62.7 and -37.3% for $3^+ - 5^+$, 82.8 and -17.2% for 6^+ , 77.4 and -22.6% for 7^+ , respectively. From those results, it is worth generalizing the following three points: (i) The effective charges of the C(2) atom are mainly derived from the contributions of the inductive effect of the heteroatoms. (ii) The contribution of the resonance effect on the effective charge on the C(2) in \mathbf{Z}^+ is larger than that in \mathbf{Z}^* , the main reason could be that in \mathbf{Z}^+ , the C(2) atom is purely sp² hybridized and trigonal, which makes the carbon atom more favorably interact with the two vicinal heteroatoms by “reso-

(55) Derived from the addition of the F -value of NHC_6H_5 (0.22)⁴⁸ and the difference (0.03) of F -values between $\text{N}(\text{Me})\text{COMe}$ (0.34)⁴⁸ and NHCOMe (0.31)⁴⁸ according to Benson's additivity of static effects.

(56) Derived from the addition of the R -value of NHC_6H_5 (-0.78)⁴⁸ and the difference (0.23) of R -values between N(Me)COMe (-0.08)⁴⁸ and NH-COMe (-0.31)⁵¹ according to the additivity of static effects.

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Scheme 8. Hyperconjugation of the σ -Bond between the C(2) and the Bonded Hydrogen Atom with the Two Heteroatoms in $\text{ZH}^{+\bullet}$



nance fashion". (iii) In $\text{ZH}^{+\bullet}$, the resonance contribution of the heteroatoms to the effective positive charge of the C(2) atom is positive rather than negative, which means that the resonance effect of the heteroatom groups in $\text{ZH}^{+\bullet}$ makes the effective charge on the C(2) atom become somewhat more positive unlike in the cases of Z^+ and Z^\bullet . The reason could be that the hyperconjugation of the σ -bond between the C(2) atom and the bonded hydrogen atom with the two heteroatoms can form a conjugated five π -electrons system with three centers due to the plane-conformation of the five-membered ring in $\text{ZH}^{+\bullet}$ known from the computer calculation (Supporting Information), which lessens the outside electron cloud of the C(2) atom donated by the bonded hydrogen atom (Scheme 8). It should be specially mentioned herein that for any other five-membered organic compounds (YH) like ZH , the effective charges on the C(2) atom in $\text{YH}^{+\bullet}$, Y^\bullet , and Y^+ could be also evaluated from the slopes and the intercepts of the corresponding dual-correlation plot lines, if only the inductive parameter (F) and resonance parameter (R) of the heteroatom groups can be safely and accurately available. Furthermore, from the obtained the effective charges on the C(2) atom in $\text{YH}^{+\bullet}$, Y^\bullet , and Y^+ , the corresponding enthalpy changes of YH to release a hydride anion and to release a hydrogen atom as well as $\text{YH}^{+\bullet}$ to release a proton and to release a hydrogen atom may be also estimated, respectively, according to the dependence of the enthalpy changes on the corresponding effective charge changes described above.

From the analysis on the relative effective charge on the C(2) atom stated above, it can be derived that the C(2) atom in $3\text{H}^{+\bullet}$ – $5\text{H}^{+\bullet}$ only carries rather small positive charge (+0.161), implying that the single electron should appear mainly on the nitrogen atoms at 1- and 3-positions, that is, the center of the radical spin in $3\text{H}^{+\bullet}$ – $5\text{H}^{+\bullet}$ should be located at two nitrogen atoms at 1- and 3-positions. Because the hydrogen atom at the C(2) position has very strong acidity [$\Delta H_p(3\text{H}^{+\bullet}$ – $5\text{H}^{+\bullet}) < 25.7$ kcal/mol] and located at the β -position of the radical spin center, it can be inferred that the hyperfine coupling constant (hfc) of the hydrogen atom at the C(2) position should be extremely large.

To verify the above inference and further support the estimation of the effective charge on the C(2) atom shown in Schemes 5–7, the ESR spectra of $3\text{H}^{+\bullet}$ ($G = \text{H}$) and its 2-deuterated isotope isomer $3\text{D}^{+\bullet}$ were detected for the first time in the electron-transfer oxidation of 3H ($G = \text{H}$) and its 2-deuterated substitute 3D with $\text{Fe}(\text{bpy})_3^{3+}$ and the hyperfine coupling constants (hfc) are determined by comparison of the observed spectra with the computer-simulated spectra as shown in Figure 5. From Figure 5, it is clear that when the hydrogen atom at the C(2) position was not substituted by deuterium atom, the ESR spectrum was split into two sets of peaks, the hyperfine

coupling constant (hfc) is 46.96 G. But, if the hydrogen atom at the C(2) position was substituted by deuterium atom, the splitting of the spectrum disappears and one set of peaks was formed, which indicates that the large hfc value (46.96 G) may be safely assigned to the proton at the C(2) position,⁵⁸ since hyperfine coupling constant (hfc) of deuterium is far smaller than that of proton.⁵⁹ Evidently, this experimental result not only elucidates the single-electron spin structure of $3\text{H}^{+\bullet}$ – $5\text{H}^{+\bullet}$ but also lends support to the estimation of the relative effective charge on the five-membered ring in $\text{ZH}^{+\bullet}$, Z^\bullet , and Z^+ .

Conclusions

In this work, 47 important five-membered heterocyclic compounds (ZH) as organic hydride donors were designed and synthesized. Enthalpy changes of the 47 organic hydride donors to release a hydride and to release a neutral hydrogen atom and their radical cations ($\text{ZH}^{+\bullet}$) to release a proton and to release a neutral hydrogen atom in acetonitrile were estimated by using the experimental method. The standard oxidation potentials of the 47 organic hydride donors (ZH) and the standard reduction potentials of the corresponding 47 salts (Z^+) were examined by using CV and OSWV methods, respectively. After analyses on the determined enthalpy change scale and the determined redox potential scale and the detailed examination of the remote substituents effects on the enthalpy changes and on the redox potentials, the following valuable conclusions can be made:

(1) The five-membered heterolytic compounds with two nitrogen atoms as the heteroatoms (1H – 5H) are the strong organic hydride donors; the hydride donating abilities are generally larger than that of the model of NADH (BNAH). Most of them can be used as good organic reducing agents in organic syntheses. The five-membered heterocyclic compounds with nitrogen and sulfur or oxygen as the heteroatoms (6H and 7H) should be weak organic hydride donors; the hydride-donating abilities are generally smaller than that of HEH. Most of them generally cannot be chosen as organic reducing agents for organic syntheses. However, their corresponding salts can be used as good hydride acceptors.

(2) The five-membered heterocyclic compounds ZH belong to weak organic hydrogen-atom donors. The hydrogen-atom donating abilities are generally smaller than those of the NADH models (BNAH, HEH), but larger than that of fluorene (Fl–H). Because the enthalpy changes of 1H – 5H and 6H to release hydrogen atoms are significantly smaller than that of tocopherol, a natural phenolic antioxidant, 1H – 6H should be good antioxidants, but 7H is not good.

(3) The proton-donating abilities (acidities) of the 47 radical cations $\text{ZH}^{+\bullet}$ are much smaller than those of the NADH⁺ models (BNAH⁺, HEH⁺, and AcrH₂⁺). But the hydrogen-atom donating abilities of $\text{ZH}^{+\bullet}$ are close to or slightly larger than those of the NADH⁺ models.

(4) The five-membered heterocyclic compounds 1H – 5H belong to the strong one-electron reducing agents, the one-

(58) The hyperfine coupling constant (hfc) of the proton at the C(2) in the $3\text{H}^{+\bullet}$ (46.96 G) is slightly smaller than that of the proton at the C(4) in BNAH⁺ (53.0 G);⁴⁴ the main reason is that the acidity of the proton at the C(2) in the $3\text{H}^{+\bullet}$ [$\Delta H_p(3\text{H}^{+\bullet}) = 23.7$ kcal/mol] is smaller than that of the proton at the C(4) in BNAH [$\Delta H_p(\text{BNAH}^{+\bullet}) = 12.4$ kcal/mol] (see Table 2).

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electron reducing powers are generally larger than that of ferrocene. The five-membered heterocyclic compounds **6H**–**7H** are due to the weak one-electron reducing agents; the one-electron reducing powers are generally smaller than or close to those of the NADH models (BNAH, HEH, and AcrH₂). The salts of **ZH** should belong to very weak one-electron oxidation agents, the one-electron oxidation powers of **1**⁺–**5**⁺ are generally much smaller than NAD⁺ and its models.

(5) The substituent effects hold excellent Hammett linear free energy relationships on the enthalpy changes of **ZH** to release hydride and to release hydrogen atom, and on the enthalpy changes of **ZH**^{•+} to release proton and to release hydrogen atom as well as on the redox potentials of **ZH** and **Z**^{•+}, respectively. Meanwhile, the substituent effects also have good additive properties for various substituents; the total effect of the various substituents is equal to the sum of individual substituent effects except for the substituent at ortho-position.

(6) On the $\Delta H_{\text{H}}^-(\text{ZH})$, $\Delta H_{\text{H}}(\text{ZH}^{•+})$, and $E_{\text{ox}}(\text{ZH})$, the effect of the substituents at the benzo-ring is larger than that at the 2-phenyl ring and the signals of the two effects are same (positive for both); on the $\Delta H_{\text{H}}(\text{ZH})$, the effect of the substituents at the benzo-ring is larger than that at the 2-phenyl ring, but the signals of the two effects are opposed (positive for the substituent at the benzo-ring, negative for the substituent at the 2-phenyl ring); on the $\Delta H_{\text{P}}(\text{ZH}^{•+})$, the effect of the substituents at the benzo-ring is smaller than that at the 2-phenyl ring and the signals of the two effects are same (negative for both); on the $E_{\text{red}}(\text{Z}^{•+})$, the effect of the substituents at the benzo-ring is close to that at the 2-phenyl ring and the signals of the two effects are same (positive for both).

(7) The substituent with large size at the ortho-position is in favor of the C₂–H bond and (C₂–H)^{•+} bond dissociation in **ZH** and **ZH**^{•+} due to steric effect.

(8) The energies of intramolecular hydrogen bond in the five-membered heterocyclic compounds **3H**, **3H**^{•+}, **3**[•], and **3**⁺ with a hydroxyl group at the ortho-position in the 2-phenyl ring were estimated by using experimental method for the first time. The results show that the hydrogen bond energy is 3.2, 2.8–3.0, 3.9–4.0, and 0.0 kcal/mol in **3H** (G = *o*-OH), **3H**^{•+} (G = *o*-OH), **3**[•] (G = *o*-OH), and **3**⁺ (G = *o*-OH), respectively. The energy difference of the hydrogen bond between **ZH** and **Z**^{•+} as well as **Z**^{•+} can lead **ZH** more difficult to release hydride anion but easier to release a hydrogen atom. At the same time, the energy difference of the hydrogen bond between **ZH**^{•+} and **Z**^{•+} as well as **Z**^{•+} can lead **ZH**^{•+} to being more difficult to release a hydrogen atom but easier to release a proton.

(9) The relative effective charges on the C(2) atom in the carboniums **Z**⁺ were estimated; the results are +1.000 for **7**⁺, +0.896 for **6**⁺, and +0.329 for **3**⁺–**5**⁺, indicating that the electrophilicity of the C(2) atom in **3**⁺–**5**⁺ should be much weaker than that of the C(2) atom in **7**⁺ and in **6**⁺. The aromatic stabilization energies of benzo[d]imidazolium **3**⁺–**5**⁺ are generally larger than those of benzo[d]thiazolium **6**⁺ and benzo[d]-oxazolium **7**⁺ by 18.9 and 37.1 kcal/mol, respectively.

(10) The relative effective charge on the C(2) atom in the neutral radicals **Z**[•] were estimated; the results show that the C(2) atom carries –0.103 in **3**[•]–**5**[•], +0.318 in **6**[•], and +0.557 in **7**[•], which means that the radical center C(2) atom in **1**[•]–**5**[•] is electron-sufficient, but the radical center C(2) atom in **6**[•]–**7**[•] is electron-deficient. Because the radical center C(2) atom in **Z**[•]

carries a certain extent of positive or negative charge, it can be predicted that the neutral radicals **Z**[•] formed from **ZH** could be quite difficult to dimerize, unlike in the cases of the NAD[•] models (BNA[•] and AcrH[•]) formed from the NADH models ((BNAH and AcrH₂). In fact, no report has been found about the dimerization of the radical **Z**[•] until now.

(11) Radical cation **3H**^{•+} (G = H) was characterized by ESR spectrum for the first time.

Experimental Section

Materials. All reagents were of commercial quality from freshly opened containers or were purified before use. Reagent grade acetonitrile was refluxed over KMnO₄ and K₂CO₃ for several hours and was doubly distilled over P₂O₅ under argon before use. The commercial tetrabutylammonium hexafluorophosphate (Bu₄NPF₆, Aldrich) was recrystallized from CH₂Cl₂ and was vacuum-dried at 110 °C overnight before preparation of supporting electrolyte solution. *N*-Methylacridinium (AcrH⁺ClO₄[–]) was obtained from the exchange of Na⁺ClO₄[–] with AcrH⁺I[–] in hot water; the latter was prepared according to literature methods.⁶⁰ Forty-eight five-membered heterocyclic compounds with N, S, and O as the heteroatoms (**ZH** in Scheme 1) were synthesized according to conventional synthetic strategies, and the final products were identified by ¹H NMR and MS; the detailed synthetic routes are provided in the Supporting Information.

ESR Detection Experiments. The ESR measurements were performed on a Bruker-EMX EPR spectrometer. The deaerated MeCN solution of **3H** (G = H) (8.0 × 10^{–3} M) or 2-deuterated **3H** (G = H) and the deaerated MeCN solution of Fe(bpy)₃³⁺ (1.0 × 10^{–2} M) under an atmospheric pressure of argon were mixed in a flat ESR cell by using a JEOL ES-EMCNT1 rapid mixing flow apparatus. The flow rate was 1.9 cm³ s^{–1}, and the mixing time before reaching the ESR cell is about 500 ms. The ESR spectra were recorded under non-saturating microwave power conditions. The magnitude of modulation was chosen to optimize the resolution and the signal-to-noise (S/N) ratio of the observed spectra. The *g* value and hyperfine splitting constants (hfc) were calibrated by using a Mn²⁺ marker.

Measurement of Redox Potentials. The electrochemical experiments were carried out by CV and OSWV using a BAS-100B electrochemical apparatus in deaerated acetonitrile under argon atmosphere at 298 K as described previously.⁶¹ *n*-Bu₄NPF₆ (0.1 M) 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⁺/Fc) was taken as the internal standard. The reproducibilities of the potentials were usually ≤5 mV for ionic species and ≤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.⁶² 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. Data points were collected every 2 s. The heat of reaction was determined following 10 automatic injections from a 250 μL injection syringe containing a standard solution (2 mM) into the reaction cell (1.30 mL) containing 1 mL of other concentrated reactant (~10 mM). Injection volumes (10 μL) were delivered in 0.5 s time intervals with 300–450 s between every two injections. The reaction heat was obtained by integration of each peak except the first.

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Supporting Information Available: Detailed synthetic routes and general preparation procedures of the 47 five-membered heterocyclic compounds (**ZH**) as well as some representative ^1H NMR spectra of **ZH** and **Z**⁺, the optimized conformations and the absolute energies (in Hartrees) of **3H** (G = H) and its

radical cation **3H**^{•+} together with a reference to the program we used to carry out the calculations. Plots of $\Delta H_{\text{H}}^-(\text{ZH})$, $\Delta H_{\text{H}}(\text{ZH})$, $\Delta H_{\text{P}}(\text{ZH}^{+\bullet})$, and $\Delta H_{\text{H}}(\text{ZH}^{+\bullet})$, as well as $E_{\text{ox}}(\text{ZH})$ and $E_{\text{red}}(\text{Z}^+)$, against the sum of Hammett substituent parameters σ_{p} and σ_{m} . Dual-correlations of the effective charge on the C(2) in **ZH**^{•+}, **Z**[•], and **Z**⁺ with inductive and resonance parameters (F and R) of the groups: N(Me)C₆H₅, SC₆H₅, and OC₆H₅. CV and OSWV graphs of some representative **ZH** and **Z**⁺ as well as BNAH, HEH, AcrH₂, and the corresponding salts. Derivation of eqs 4 and 6. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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