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Hydride Affinities of Organic Radicals in Solution. A Comparison of Free Radicals and Carbenium Ions as Hydride Ion Acceptors

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Abstract: Hydride affinities of free radicals ($R^{\bullet}$) in solution can be obtained from a thermochemical cycle which gives rise to (i) ($-\Delta G_{\mathrm{hydride}}(R^{\bullet})_S = \Delta G_{\mathrm{hom}}(R\text{–}H)_S - F\Delta E^{\circ}{}_{\mathrm{NHE}}[(H^{\bullet}/H^-) - (R\text{–}H/R\text{–}H^{\bullet -})]_S$), in which $-\Delta G_{\mathrm{hydride}}(R^{\bullet})_S$ is equated to the difference between the free energy change of homolytic bond dissociation in solution ($\Delta G_{\mathrm{hom}}(R\text{–}H)_S$) and a term involving the standard potentials of the ($H^{\bullet}/H^-$) and ($R\text{–}H/R\text{–}H^{\bullet -}$) couples, $F\Delta E^{\circ}{}_{\mathrm{NHE}}[(H^{\bullet}/H^-) + (R\text{–}H/R\text{–}H^{\bullet -})]_S$. Substitution in (i) for $\Delta G_{\mathrm{hom}}(R\text{–}H)_S$ results in (ii) ($-\Delta G_{\mathrm{hydride}}(R^{\bullet})_S = 2.303RT(\mathrm{p}K_a)(R\text{–}H)_S + FE^{\circ}{}_{\mathrm{NHE}}[(R^{\bullet}/R^-) + (R\text{–}H/R\text{–}H^{\bullet -})]_S + C$), which equates $\Delta G_{\mathrm{hydride}}(R^{\bullet})_S$ to experimentally accessible quantities plus a constant C. For a given solvent S, C is equal to $-FE^{\circ}{}_{\mathrm{NHE}}[(H^+/H^{\bullet}) + (H^{\bullet}/H^-)]_S$, which has previously been evaluated for water, acetonitrile, and dimethyl sulfoxide. The difference in the free energy changes for heterolytic dissociation of the R–H bond in a neutral compound and the corresponding anion radical is given by (iii) ($\Delta\Delta G_{\mathrm{hydride}}(R^{\bullet} - R^+)_S = -F\Delta E^{\circ}{}_{\mathrm{NHE}}[(R\text{–}H/R\text{–}H^{\bullet -}) - (R^+/R^{\bullet})]_S$). Since the differences in standard potentials for reduction of R^+ and R–H are large, usually greater than 2 V, $\Delta\Delta G_{\mathrm{hydride}}(R^{\bullet} - R^+)_S$ will generally equal ≥ 50 kcal/mol. Equations ii and iii are applied to the reactions of 10-substituted 9-methylanthracene and substituted toluene radical anions in dimethyl sulfoxide and acetonitrile. A general relationship between $\Delta G_{\mathrm{hydride}}(R^{\bullet}\text{ or }R^+)_S$ and the electron affinity (of R–H or R^+) in solution, which arises from the near cancellation of the other terms in (ii), is discussed. Absolute values for the hydride affinities of several NAD^+ models in acetonitrile are estimated.

Introduction

The formation of π-cation or π-anion radicals from aromatic compounds is accompanied by the weakening of all σ-bonds, which sets the stage for enhanced bond cleavages. Examples of this phenomenon include (i) the dramatic lowering of the $\mathrm{p}K_a$[3] and (ii) of the C–R bond dissociation energies (BDE)[4] accompanying the formation of alkylarene radical cations ($ArCH_2R \rightarrow ArCH_2R^{+\bullet}$), (iii) the negative free energy changes of C–X heterolytic bond dissociation of phenyl halide radical anions[5] ($PhX \rightarrow PhX^{\bullet -}$), and (iv) a substantial lowering of C–H heterolytic bond dissociation energies of methylarene anion radicals[6] ($ArCH_3 \rightarrow ArCH_3^{\bullet -}$) as compared to those of the neutral molecules.

We have recently reported hydride affinities, defined as the free energy changes for reaction 1, where subscript S refers to

$$(R^+)_S + (H^-)_S \rightleftarrows (R\text{–}H)_S \qquad \Delta G_{\mathrm{hydride}}(R^+)_S \qquad (1)$$

the solvent, of a number of series of carbenium ions in acetonitrile and dimethyl sulfoxide (DMSO) solution.[7,8] The free energy changes [$\Delta G_{\mathrm{hydride}}(R^+)_S$] for reaction 1 were evaluated using eq 2, which was derived from a thermochemical cycle.[8] Reasonably good correlations were observed between $\Delta G_{\mathrm{hydride}}(R^+)_S$ and gas-phase hydride affinities as well as with $\mathrm{p}K_R$ for the ionization of carbinols in acidic solution. Ionic solvation energies estimated from $\Delta G_{\mathrm{hydride}}(R^+)_S$ and the gas-phase data are in good agreement with those estimated from ionization potentials along with electrode potentials, suggesting that little error is introduced by the necessary approximations.

$$-\Delta G_{\mathrm{hydride}}(R^+)_S = 2.303RT(\mathrm{p}K_A(R\text{–}H)_S) + FE^{\circ}{}_{\mathrm{NHE}}[(R^{\bullet}/R^-) + (R^+/R^{\bullet})]_S - FE^{\circ}{}_{\mathrm{NHE}}[(H^{\bullet}/H^-) + (H^+/H^{\bullet})]_S \quad (2)$$

Gas-phase hydride affinities[9] have proven to be a valuable source of data to compare solution calorimetric data[10] of ionization reactions to establish quantitative scales of relative carbenium ion stabilities. The hydride-transfer equilibria of NAD^+ (nicotinamide adenine dinucleotide) analogues[11] provides an example of the importance of these reactions in biochemistry.

In this work we have made estimates of hydride affinities of free radicals, defined in eq 3, and compare these to the values

$$(R^{\bullet})_S + (H^-)_S \rightleftarrows (R\text{–}H^{\bullet -})_S \qquad \Delta G_{\mathrm{hydride}}(R^{\bullet})_S \qquad (3)$$

previously reported for the corresponding carbenium ions.[8] In general, reaction 1 is energetically more favorable than (3) by

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Scheme I

	Free Energy Change
$R\text{–}H^{-} \rightleftharpoons R^{\bullet\,\prime} + H^{-}$	$-\Delta G_{hydride}(R^{+})_{s}$
$R^{\bullet} + H^{\bullet} \rightleftharpoons R\text{–}H$	$-\Delta G_{hom}(R\text{–}H)_{s}$
$R\text{–}H^{-\bullet} + H^{\bullet} \rightleftharpoons R\text{–}H + H^{-}$	$-F\Delta E^{\circ}_{NHE}[(H^{\bullet}/H^{-}) - (R\text{–}H/R\text{–}H^{-\bullet})]_{s}$

Table I. Electrode Potentials for the ($H^{+}/H^{\bullet}$) and ($H^{\bullet}/H^{-}$) Redox Couples in Water, Acetonitrile, and Dimethyl Sulfoxide

solvent	E°_{NHE}-($H^{+}/H^{\bullet}$)[a]	E°_{NHE}-($H^{\bullet}/H^{-}$)[b]	$FE^{\circ}_{NHE}[(H^{+}/H^{\bullet})$ + $(H^{\bullet}/H^{-})]$[c]
water	-2.29	0.18	-48.7
acetonitrile	-1.77	-0.60	-54.7
dimethyl sulfoxide	-2.48	-0.55	-69.9

[a] Potentials in V from ref 13. [b] Potentials in V from ref 8. [c] In kcal/mol.

≥50 kcal/mol. Studies were carried out on radicals derived from substituted toluenes and 9-methylanthracenes. The use of electrode potentials to derive experimentally inaccessible thermochemical quantities has, in recent years, become an important method in physical organic chemistry.[12]

Results and Discussion

Thermochemical Relationships. The differences in the free energy changes for heterolytic and homolytic bond dissociation can, in general, be associated with an electrode potential difference.[13] The pertinent thermochemical cycle from which $\Delta G_{hydride}(R^{\bullet})_S$ can be extracted is shown in Scheme I. Equating the free energy changes above and below the line results in eq 4.

$$-\Delta G_{hydride}(R^{\bullet})_S = \Delta G_{hom}(R\text{–}H)_S - F\Delta E^{\circ}_{NHE}[(H^{\bullet}/H^{-}) - (RH/RH^{\bullet-})]_S \quad (4)$$

$$\Delta G_{hom}(R\text{–}H)_S = 2.303RT(pK_a(R\text{–}H)_S) + F\Delta E^{\circ}_{NHE}[(R^{\bullet}/R^{-}) - (H^{+}/H^{\bullet})]_S \quad (5)$$

$$-\Delta G_{hydride}(R^{\bullet})_S = 2.303RT(pK_a(R\text{–}H)_S) + FE^{\circ}_{NHE}[(RH/RH^{\bullet-}) + (R^{\bullet}/R^{-})]_S - FE^{\circ}_{NHE}[(H^{\bullet}/H^{-}) + (H^{+}/H^{\bullet})]_S \quad (6)$$

Use of a similar thermochemical cycle[13,14] gives expression 5 for the free energy of the homolytic bond dissociation, $\Delta G_{hom}(R\text{–}H)_S$, and combination of the two equations gives (6), which allows $\Delta G_{hydride}(R^{\bullet})_S$ to be calculated using available pK_a data along with the appropriate electrode potentials. The electrode potentials for the ($H^{\bullet}/H^{-}$)[7] and the ($H^{+}/H^{\bullet}$)[13,14] couples have been evaluated in acetonitrile and in DMSO. The pertinent electrode potential data for use in these thermochemical equations are summarized in Table I.

The difference in hydride affinities of radical ($R^{\bullet}$) and cation (R^{+}), $\Delta\Delta G_{hydride}(R^{\bullet} - R^{+})_S$, is illustrated in the thermochemical cycle shown in Scheme II, which gives rise to eq 7. This

$$\Delta\Delta G_{hydride}(R^{\bullet} - R^{+})_S = -F\Delta E^{\circ}_{NHE}[(R\text{–}H/R\text{–}H^{\bullet-}) - (R^{+}/R^{\bullet})]_S \quad (7)$$

relationship shows that once $\Delta G_{hydride}(R^{+})_S$ has been determined

Scheme II

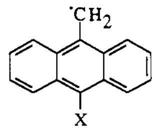
	Free Energy Change
$R\text{–}H \rightleftharpoons R^{+} + H^{-}$	$-\Delta G_{hydride}(R^{+})_{s}$
$R^{\bullet} + H^{-} \rightleftharpoons R\text{–}H^{-\bullet}$	$\Delta G_{hydride}(R^{\bullet})_{s}$
$R^{\bullet} + R\text{–}H \rightleftharpoons R^{+} + R\text{–}H^{-\bullet}$	$-F\Delta E^{\circ}_{NHE}[(R\text{–}H/R\text{–}H^{-\bullet}) - (R^{+}/R^{\bullet})]_{s}$

using eq 2, the only additional data necessary to evaluate $\Delta G_{hydride}(R^{\bullet})_S$ is the electrode potential for the $(R\text{–}H/R\text{–}H^{\bullet-})_S$ couple.

Electrode Potentials and Thermochemical Cycles. Standard electrode potentials, *i.e.* reversible or thermodynamic electrode potentials referred to the normal hydrogen electrode, are the quantities required in thermochemical cycles. These are designated as $E^{\circ}_{NHE}(ox/red)_S$, where ox and red are the oxidized and reduced species of the couple, respectively, and the subscript S designates the solvent. Experimental electrode potentials are often not reversible values. We will refer to electrode potentials derived from experimental measurements as either $E^{ox}(red)$ or $E^{red}(ox)$, depending upon which half-reaction is studied. When appropriate, $E^{\circ}_{NHE}(ox/red)$ may be equated to $E^{ox}(red)$ or $E^{red}(ox)$. In some other cases, the latter may be corrected to the pertinent $E^{\circ}_{NHE}(ox/red)$ by estimating the kinetic contributions associated with the experimental potentials.

The errors encountered upon the inappropriate use of irreversible potentials in thermochemical cycles have been discussed.[15] It should be pointed out that the errors due to kinetic potential shifts of the ($RH/RH^{\bullet-}$) and the ($R^{\bullet}/R^{-}$) couples are in opposite directions and are expected to tend to cancel one another when used in eq 6. Consequently, we believe that the error in $\Delta G_{hydride}(R^{\bullet})_S$ arising from experimental determination of electrode potentials is on the order of 1 kcal/mol.

Hydride Affinities of Arylmethyl Radicals Derived from Substituted Anthracenes. Electrode potential and pK_a data required for the determination of $\Delta G_{hydride}(R^{\bullet})_{DMSO}$ using eq 6 for free radicals of general structures **1** and **2** are gathered in Table II. The $E^{ox}_{NHE}(R^{-})$[16] and the $pK_a(R\text{–}H)$[17] are from the literature while $E^{\circ}_{NHE}(RH/RH^{\bullet-})$ values were determined in this work. The $\Delta G_{hydride}(R^{\bullet})_{DMSO}$ derived are listed in the last column. A reasonably good linear correlation was observed between $\Delta G_{hydride}(R^{\bullet})_{DMSO}$ and $pK_a(R\text{–}H)_{DMSO}$ for radicals of structure **1** ($r^2 = 0.98$) while the same plot for those of structure **2** showed considerable scatter ($r^2 = 0.72$). This could be a reflection of the fact that the substituent on **1** is remote to the reaction site while that on **2** is not. In any event, as 2.303RT-(pK_a(R–H)) (eq a in the Appendix) decreases, the corresponding $-\Delta G_{hydride}(R^{\bullet})_{DMSO}$ can be expected to increase in magnitude. The correlations of $-\Delta G_{hydride}(R^{\bullet})_{DMSO}$ with $-23.06E^{\circ}_{NHE}(RH/RH^{\bullet-})_{DMSO}$ (eq b in the Appendix) and with $-23.06E^{ox}_{NHE}(R^{-})_{DMSO}$ (eq c in the Appendix) for radicals of structure **1** are slightly better ($r^2 = 0.99$ in both cases). As both of these free energies decrease, the hydride affinities of radicals of structure **1** become more negative. The fact that all three of the experimental quantities in eq 6 correlate linearly (Table IV)



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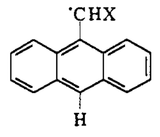

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Table II. Hydride Affinities of Radicals ($R^{\bullet}$) Derived from 10- and α-Substituted 9-Methylanthracenes in Dimethyl Sulfoxide Solution

substituent					
9-	10-	pK_a[a]	$E°_{NHE}$-$(RH/RH^{-\bullet})_S$[b]	E^{ox}_{NHE}-(R^-)[c]	$-\Delta G_{Hydride}$-$(R^{\bullet})_S$ (kcal/mol)
CH_3	H	31.1	−1.838	−0.952	48
CH_3	CH_3	31.8	−1.843	−0.978	48
CH_3	Ph	30.8	−1.761	−0.918	50
CH_3	OCH_3	31.8	−1.823	−1.000	48
CH_3	Cl	28.2	−1.644	−0.810	52
CH_3	CHO	16.6	−1.165	−0.138	63
CH_3	CN	20.0	−1.294	−0.350	59
CH_3	NO_2	13.2	−0.946	0.158	70
CH_3	COPh	22.2	−1.288	−0.391	62
CH_3	SPh	25.5	−1.565[d]	−0.651	54
CH_2NO_2	H	12.7	−1.272(irr)	0.332	66
CH_2CN	H	19.7	−1.667	−0.392	49
CH_2SPh	H	28.6	−1.531(irr)	−0.825	55
CH_2OPh	H	30.2	−1.577(irr)	−0.976	52
CH_2OCH_3	H	30.6	−1.759	−1.098	46

[a] Data reported by the Bordwell group (ref 28 and 29) and ref 30. [b] Reversible reduction potentials (in V) except when specified as irreversible (irr) in DMSO obtained at a voltage sweep rate of 1 V/s. Measurements were made relative to Fc^+/Fc and then referred to NHE. [c] Values (V) obtained on conversion of data from ref 17. [d] At 100 V/s.

Table III. Hydride Affinities of Benzyl Radicals Derived from Toluenes in Acetonitrile

substrate	pK_A[a]	$E°_{NHE}$-$(R\text{–}H/R\text{–}H^{-\bullet})$ (V)	E^{red}_{NHE}-$(R^{\cdot})$[b] (V)	$-\Delta G_{hydride}(R^{\bullet})$ (kcal/mol)
$H\text{–}C_6H_4\text{–}CH_3$	50.3	−3.21[c]	−1.19	22
p-$Me\text{–}C_6H_4\text{–}CH_3$	52.0	−3.23[c]	−1.38	19
p-$MeO\text{–}C_6H_4\text{–}CH_3$	54.4	−3.24[c]	−1.51	19
p-$Cl\text{–}C_6H_4\text{–}CH_3$	50.0	−2.56[c]	−1.16	37
p-$F\text{–}C_6H_4\text{–}CH_3$	51.4	−2.75[c]	−1.26	32
p-$NC\text{–}C_6H_4\text{–}CH_3$	40.4	−2.36	−0.53	43
p-$MeCO\text{–}C_6H_4\text{–}CH_3$	39.0	−2.03	−0.47	50
p-$O_2N\text{–}C_6H_4\text{–}CH_3$	≈29[d]	−1.09	0.12[e]	72

[a] Data obtained from the relationship for toluene, $pK_a(R\text{–}H) = \Delta G_{hom}(R\text{–}H) - FE°_{NHE}[(R^{\bullet}/R^-) - (H^+/H^{\bullet})]$, where $\Delta G_{hom}(R\text{–}H)$ = BDE(R–H) − 6 kcal/mol from ref 13 and BDE(R–H) equals 88 kcal/mol from ref 31. Other relative values from ref 18 were adjusted to the toluene value. [b] Values from ref 18. [c] See text. [d] Derived from Bordwell's[28] value of 20.4 in DMSO by adding 9 (The pK_a's of a number of acids in acetonitrile have been found to be, on average, 9 units greater than those in DMSO).[34] [d] Value from ref 8.

with $\Delta G_{hydride}(R^{\bullet})_{DMSO}$ is interesting. The slopes of the linear correlations then give the relative importance of the three processes in determining the magnitude of $\Delta G_{hydride}(R^{\bullet})_{DMSO}$. Accordingly, processes a and c appear to be slightly less important than process b in the energetics of reaction 3 of free radicals of structure **1**. The magnitudes of the slopes of reactions a and c are very nearly the same, and since the two have opposite signs, this gives rise to a near cancellation of the two effects. Thus, $\Delta G_{hydride}(R^{\bullet})_{DMSO}$ correlates with $E°_{NHE}(RH/RH^{\bullet-})_{DMSO}$ with near unit slope.

Hydride Affinities of Substituted Benzyl Radicals. Application of $pK_a(R\text{–}H)$ and electrode potential data in eq 6 resulted in the $\Delta G_{hydride}(R^{\bullet})_{MeCN}$ values for substituted benzyl radicals summarized in Table III. The $pK_a(R\text{–}H)_{MeCN}$ data are those reported by Wayner[18] adjusted[8] to account for more recent thermochemical data.[13] The reduction potentials of the first three substrates in Table III were obtained by adjusting the reduction potential of benzene[19] by the expected substituent effect.[20] It has been shown that the magnitudes of substituent effects on electrode potentials are directly dependent upon the "absolute" electrode potential[21] for the parent process.[20] The "absolute" potential for the (benzene/benzene$^{\bullet-}$) couple is equal to 1.24 V. The expected effect[20] of a methyl substituent on this process is only 13 mV. In analogous cases the effect of a methyl substituent on the ($PhCl/PhCl^{\bullet-}$) and the ($PhF/PhF^{\bullet-}$) couples amounts to only 20 mV. Thus, the maximum adjustment of $E°_{NHE}(RH/RH^{\bullet-})$ made for substituent effects on entries 1–5 in Table III was only 0.04 V, which is within the expected error of the electrode potentials. The reduction potentials of the radicals are from ref 18.

The most prominent feature of the data in Table III is the very wide range of values of $-\Delta G_{hydride}(R^{\bullet})_{MeCN}$; from 19 (*p*-$CH_3O$-) to 72 (*p*-$O_2N$-) kcal/mol. This should be compared to the much more narrow range (46–70 kcal/mol) observed for the radicals derived from anthracene derivatives in Table II. The hydride affinities for a series of radicals might be expected to correlate with Hammett σ^-. For the data in Table III, this correlation results in a Hammett ρ equal to 28 while ρ equals 13 for the corresponding correlation of data for **1** in Table II. Neither of the correlations are very good, r^2 = 0.93 and 0.96, respectively. The conclusion that can be drawn from the relative values of ρ for plots of $\Delta G_{hydride}(R^{\bullet})$ of **1** and of the substituted benzyl radicals is that the latter process is much more sensitive to substituent effects than is the former.

In view of the observation that $\Delta G_{hydride}(R^{\bullet})_{DMSO}$ of the series of anthrylmethyl radicals (**1**) depends only on $E°_{NHE}$-$(RH/RH^{\bullet-})_{DMSO}$ due to the near cancellation of the effects of $pK_a(R\text{–}H)_{DMSO}$ and $E°_{NHE}(R^{\bullet}/R^-)_{DMSO}$, comparable correlations were carried out using the data for the benzyl radicals in Table III. The correlation of $\Delta G_{hydride}(R^{\bullet})_{MeCN}$ with $E°_{NHE}$-$(RH/RH^{\bullet-})_{MeCN}$ was observed to be linear (r^2 = 0.997) with near unit slope (−1.06). Once again, the correlations involving $pK_a(R\text{–}H)_{MeCN}$ and $E°_{NHE}(R^{\bullet}/R^-)_{MeCN}$ resulted in nearly equal slopes with opposite signs, giving rise to a near cancellation of the two effects. Neither of the latter correlations were very good, r^2 = 0.91 and 0.92, respectively.

Rationale for the Near Cancellation of the Effects of Changes in $pK_a(R\text{–}H)_S$ and $E°_{NHE}(R^{\bullet}/R^-)_S$ on $\Delta G_{hydride}(R)_S$. Apparently, the structural effects giving rise to changes in $pK_a(R\text{–}H)_S$ and $E°_{NHE}(R^{\bullet}/R^-)_S$ cancel (or nearly so) when deriving $\Delta G_{hydride}(R)_S$ using either eq 2 or 6. The two free energy terms in these equations refer to reactions 8 and 9 in the directions shown. The assumption

Free Energy Change

$$R\text{–}H \rightleftharpoons R^- + H^+ \qquad 2.303RT(pK_a(R\text{–}H)_s) \qquad (8)$$

$$R^- \rightleftharpoons R^{\bullet} + e^- \qquad FE°_{NHE}(R^{\bullet}/R^-)_s \qquad (9)$$

that the importance of structural effects is dominated by effects on the stability of the charged species (R^-) leads to the prediction that the contributions of the free energy changes in reactions 8 and 9 to $\Delta G_{hydride}(R)_S$ should effectively cancel. This appears to be the case for the collective correlation of the hydride affinity data of both R^+ (Table III, ref 8) and $R^{\bullet}$ (Table III, this study) when R is substituted benzyl in acetonitrile. It is apparent from the discussion in the following section that this relationship does not hold nearly so well with the available data in DMSO, encompassing a much wider range of structures (Tables II, IV, and V in ref 8 and Table IV in this study).

Comparison of Hydride Affinities of Free Radicals with Those of the Corresponding Carbenium Ions. Application of eq 7 derived from the thermochemical cycle shown in Scheme II to the available $\Delta G_{hydride}(R^+)_S$ data[8] along with the $\Delta G_{hydride}(R^{\bullet})_S$ data reported here affords the $\Delta\Delta G_{hydride}(R^{\bullet} - R^+)_S$ listed in Table V. Again, there appears to be a distinct difference in the results for the anthryl radicals and cations as compared to those for the benzyl radicals and cations. In the case of the former, $\Delta\Delta G_{hydride}(R^{\bullet} -$

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Table IV. Dependence of Hydride Affinities of Free Radicals ($R^\bullet$) on Acid Dissociation Constants, R–H Reduction Potentials, and $R^\bullet$ Reduction Potentials

radical series	quantity correlated[a]	slope	correlation coeff[b]
anthrylmethyl (**1**)	$2.303RT(\mathrm{p}K_a)$	+0.792	0.98
anthrylmethyl (**1**)	$FE°_{NHE}(RH/RH^{-\bullet})$	–1.01	0.99
anthrylmethyl (**1**)	$FE°_{NHE}(R^\bullet/R^-)$	–0.797	0.99
benzyl	$2.303RT(\mathrm{p}K_a)$	+1.46	0.91
benzyl	$FE°_{NHE}(RH/RH^{-\bullet})$	–1.06	0.997
benzyl	$FE°_{NHE}(R^\bullet/R^-)$	–1.34	0.92

[a] All quantities in kcal/mol, $\Delta G_{hydride}(R^\bullet$ or $R^+)$ taken as the dependent variable. [b] Correlation coefficient equal to r^2 in the linear regression analysis.

Table V. Comparison of the Hydride Affinities of Cations with Those of the Corresponding Radicals

substrate	solvent	$-\Delta G_{hydride}(R^+)_S$[a] (kcal/mol)	$\Delta\Delta G_{hydride}(R^\bullet - R^+)_S$ (kcal/mol)
anthracenes			
9-CH_3, 10-H	DMSO	98	47
9-CH_3, 10-CH_3	DMSO	95	43
9-CH_3, 10-CH_3O	DMSO	91	40
9-CH_2OCH_3, 10-H	DMSO	102	54
9-CH_2OPh, 10-H	DMSO	111	56
9-CH_2SPh, 10-H	DMSO	109	51
9-CH_3, 10-Cl	DMSO	105	50
9-CH_3, 10-NO_2	DMSO	120	48
toluenes			
H–C_6H_4–CH_3	MeCN	118	93
p-Me–C_6H_4–CH_3	MeCN	112	88
p-MeO–C_6H_4–CH_3	MeCN	106	84
p-Cl–C_6H_4–CH_3	MeCN	121	82
p-F–C_6H_4-CH_3	MeCN	122	87
p-NC–C_6H_4–CH_3	MeCN	122	76
p-MeCO–C_6H_4–CH_3	MeCN	123	70
p-O_2N–C_6H_4–CH_3	MeCN	129	54

[a] Data from ref 8.

$R^+)_S$ has a nearly constant value (≈50 kcal/mol) while those for the latter vary from 54 to 93 kcal/mol. The greater range of $\Delta\Delta G_{hydride}(R^\bullet - R^+)_S$ for the substituted benzyl radicals is a reflection of the wider range of the corresponding $R^\bullet$ hydride affinities.

Equation 7, along with the observation of near unit slopes, suggests that there may be a general relationship between the hydride affinity $[\Delta G_{hydride}(R)_S]$, where R is either a carbenium ion or a free radical, and the corresponding electron affinity of either R^+ or R–H in solution. When the solvent is acetonitrile, this relationship is demonstrated in Figure 1, in which all the available $\Delta G_{hydride}(R)_S$ data, carbenium ion data from ref 8 and free radical data from this study, are plotted as a function of the electron affinities in acetonitrile, $FE°_{NHE}[(R^+/R^\bullet)$ or $(RH/RH^{\bullet-})]$. Linear regression analysis on the data results in eq 10. The $\Delta G_{hydride}(R)_{MeCN}$ data in Figure 1 encompass a range from 19 to 129 kcal/mol. It is of interest to note that the standard deviation associated with eq 10 is ±1.4 kcal/mol with a correlation coefficient of 0.999. Linear regression analysis of the available $\Delta G_{hydride}(R)_{DMSO}$ data resulted in eq 11. A unit slope was not observed in this case (0.954), the standard deviation was ±2.9 kcal/mol; and the correlation coefficient was 0.98.

$$-\Delta G_{hydride}(R)_{MeCN} = 1.01FE°_{NHE}[(R^+/R^\bullet) \text{ or } (RH/RH^{\bullet-})] + 95.8\ (\pm 1.4) \quad (10)$$

$$-\Delta G_{hydride}(R)_{DMSO} = 0.95FE°_{NHE}[(R^+/R^\bullet) \text{ or } (RH/RH^{\bullet-})] + 88.1\ (\pm 2.9) \quad (11)$$

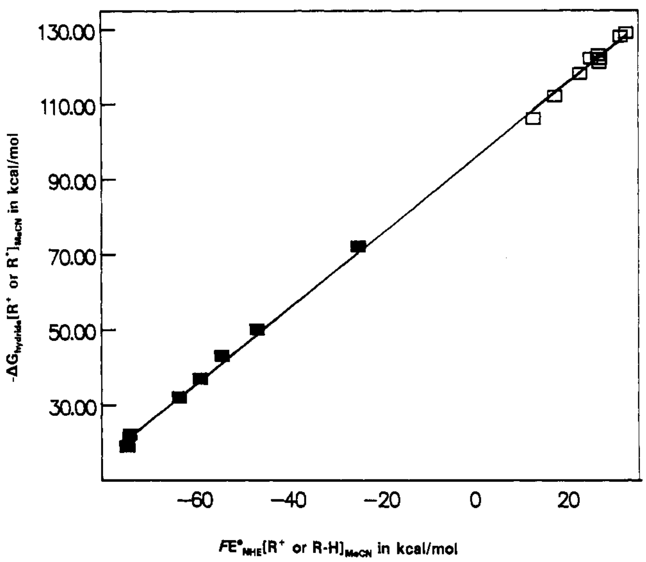
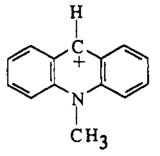


Figure 1. Plot of free energy hydride affinities for substituted benzyl cations (R^+) and radicals ($R^\bullet$) in acetonitrile as a function of the electron affinities in solution of either R^+ or R–H.

Estimation of Hydride Affinities of NAD^+ Models. Relative hydride affinities are available for NAD^+ models from equilibrium studies.[11,23] It is of considerable interest to be able to place the data for these important hydride acceptors on the absolute scale along with those for the other carbenium ions.[8] Neither the pertinent $\mathrm{p}K_a(R–H)_S$ nor the $\Delta G_{hom}(R–H)_S$ values are available for any of these models. On the other hand, $E°_{NHE}(NAD^+/NAD^\bullet)$ for cations **3**, **4**, and **5** in acetonitrile have been reported



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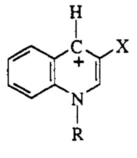

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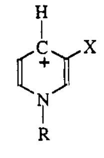

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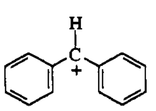
by Wayner.[24] Application of eq 10 for cation **3** results in $\Delta G_{hydride}(R^+)_{MeCN}$ equal to 92 kcal/mol. However, it must be kept in mind that eq 10 was derived from data for substituted benzyl cations and may not be applicable to **3**. In order to assess the direct applicability of eq 10, an analysis of the related secondary carbenium ions **6**, **7**, and **8** was carried out. The data



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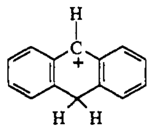

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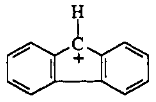

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for diphenylmethyl (**6**), 9,10-dihydroanthryl (**7**), and fluorenyl (**8**) carbenium ions are summarized in Table VI. Linear eq 10 results in deviations ranging from 4 to 9 kcal/mol from those obtained using eq 2. The smallest deviation (4 kcal/mol) was observed for **6**, which is structurally most closely related to the benzyl cations.

In view of the results presented in the previous paragraph we conclude that eq 10 is not expected to be applicable to estimate $\Delta G_{hydride}(R^+)_{MeCN}$ for the NAD^+ models. A far better estimate

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Table VI. Deviations of Hydride Affinities of Secondary Carbenium Ions in Acetonitrile from the Values Predicted by Eq 10

carbenium ion	ΔG_{hom}-(R–H)[a]	pK_a-(R–H)[b]	$E°_{NHE}$-($R^\bullet/R^-$) (V)	$E°_{NHE}$-($R^+/R^\bullet$) (V)	$-\Delta G_{hydride}(R^+)_S$ (kcal/mol)	
					eq 2	eq 10
6	79[c]	43	–0.90[e]	0.59[e]	106	110
7	72[d]	40	–0.99[f]	0.34[f]	95	104
8	76[c]	35	–0.52[e]	1.00[e]	114	119

[a] $\Delta G_{hom}(R–H) = BDE(R–H) - 6$ kcal/mol, relationship from ref 13. [b] $pK_a(R–H) = \Delta G_{hom}(R–H) - FE°_{NHE}[(R^\bullet/R^-) - (H^+/H^\bullet)]$. [c] Calculated from BDE in kcal/mol from ref 15. [d] Calculated from BDE in kcal/mol from ref 32. [e] Data from ref 18. [f] Data from ref 33.

Table VII. Hydride Affinities of NAD$^+$ Models in Acetonitrile

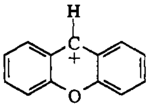
NAD$^+$ model	R	X	$-\Delta G_{hydride}(R)_{MeCN}$[a]
3			83[b]
4a	CH_3	CN	83[c]
4b	$PhCH_2$	CN	85[c]
5a	$PhCH_2$	CN	76[c]
5b	$PhCH_2$	$COCH_3$	73[c]
5c	$PhCH_2$	$CONH_2$	72[c]

[a] In kcal/mol. [b] Calculated from $\Delta G_{hydride}(\mathbf{3})_{MeCN} = \Delta G_{hydride}(\mathbf{7})_{MeCN} - F\Delta E°_{NHE}[(\mathbf{7}^+/\mathbf{7}^\bullet) - (\mathbf{3}^+/\mathbf{3}^\bullet)]$. [c] Calculated from $\Delta G_{hydride}(NAD^+)_{MeCN} = \Delta G_{hydride}(\mathbf{3})_{MeCN} + \Delta\Delta G(H^-)$ [values of $\Delta\Delta G(H^-)$ quoted in ref 24 based on data in ref 23].

is expected to result from selecting a structurally similar cation as a model for one of the NAD$^+$. Cation **7** has a ring structure similar to that of **3**, and the two differ only at the 10-position, CH_3N (**3**) *vs* CH_2 (**7**). Therefore, we estimate $\Delta G_{hydride}(\mathbf{3})_{MeCN}$ to be equal to –83 kcal/mol using eq 12. Hydride affinities for all the NAD$^+$ models for which the reduction potentials in acetonitrile have been reported[24] are summarized in Table VII.

$$\Delta G_{hydride}(\mathbf{3})_{MeCN} = \Delta G_{hydride}(\mathbf{7})_{MeCN} + F\Delta E°_{NHE}[(\mathbf{7}^+/\mathbf{7}^\bullet) - (\mathbf{3}^+/\mathbf{3}^\bullet)] \quad (12)$$

A test of the validity of eq 12 would be to apply the relationship with another model for **3**. The hydride affinity of **9** has been



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reported to be equal to 90 kcal/mol in DMSO,[8] 15 kcal/mol lower than that of **6** in the same solvent. Assuming that $\Delta\Delta G_{hydride}(\mathbf{6} - \mathbf{9})$ is the same in acetonitrile leads to a value of 91 kcal/mol for **9** in that solvent. Then applying a relationship analogous to (12) results in a value of –82 kcal/mol for $\Delta G_{hydride}(\mathbf{3})_{MeCN}$. On the basis of the use of two different model cations and relationship 12, we conclude that $\Delta G_{hydride}(\mathbf{3})_{MeCN}$ = –83 ± 2 kcal/mol.

Summary

Hydride affinities of free radicals are small, usually on the order of ≥50 kcal/mol less negative than those of the corresponding carbenium ions. There is a general relationship between $\Delta G_{hydride}(R^\bullet \text{ or } R^+)_S$ and the electron affinity of either R–H or R^+, respectively, in solution. In a closely related series consisting of both $R^\bullet$ and R^+, *i.e.* substituted benzyl radicals and cations, the slope of the linear correlation is 1.01 with a correlation coefficient of 0.999. A correlation of data from several different series of reactions in DMSO was linear, but considerable scatter was observed. It was concluded that the observation of near unit slopes arises from the near cancellation of opposing contributions from $pK_a(R–H)_S$ and $E°_{NHE}(R^\bullet/R^-)_S$ when eq 2 or 6 is used to calculate $\Delta G_{hydride}(R^+ \text{ or } R^\bullet)_S$.

Experimental Section

Materials. Reagent-grade acetonitrile was distilled from P_2O_5 under N_2 and stored over activated alumina. The purification of DMSO was carried out according to a literature procedure.[25] Tetrabutylammonium hexafluorophosphate (Aldrich) was recrystallized from CH_2Cl_2/Et_2O and vacuum-dried at 110 °C for 10 h before use. Fluorene, 9-methylanthracene, 9,10-dimethylanthracene, diphenylmethane, toluene, *p*-xylene, 4-methylanisole, 4-chlorotoluene, 4-fluorotoluene, 4-methylacetophenone, 4-tolunitrile, and 4-nitrotoluene were obtained from Aldrich and were used as received. All other compounds were prepared using published procedures or modifications of published procedures. The purity of all compounds was verified by melting point determination and spectral analysis.

Electrochemical Measurements. A standard three-electrode electrochemical cell equipped with a Teflon top was used for electrode potential measurements.[26] The working electrode was a 0.2 mm diameter Pt disk and was reconditioned by polishing with a 0.05-μm alumina suspension (Struers, Denmark) between runs. The potentials were measured at a sweep rate of 1 V/s *vs* a 0.1 M $AgClO_4$/Ag reference electrode with the ferrocenium/ferrocene redox couple as the internal standard. The counter electrode was a Pt wire.

Instrumentation and Data Handling Procedures. Cyclic and linear sweep voltammetry were performed using a JAS Instrument Systems, Model JDP-165A, potentiostat driven by a Hewlett Packard 3314A function generator. The signals were filtered with a Stanford Research Systems, Inc. Model SR640 dual channel low pass filter before recording on a Nicolet Model 310 digital oscilloscope. An IBM AT compatible personal computer was used to control the oscilloscope and the function generator *via* an IEEE interface. The current–potential curves were collected and averaged at trigger intervals selected to reduce periodic noise.[27] The averaged signals were then treated with a digital frequency domain low pass filter before numerical differentiation.

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Appendix

The equations for calculating free energy hydride affinities, (2) and (6), each involve three other quantities which may or may not depend upon each other. In order that unit slope be observed in correlations of the hydride affinities with one of these quantities, either the other two quantities must be independent of the first or a cancellation of effects must be involved. The pertinent interrelationships for eqs 2 and 6 are summarized below. The following abbreviations are used to facilitate the analysis: $H(R^+) = -\Delta G_{hydride}(R^+)_S$, $H(R^\bullet) = -\Delta G_{hydride}(R^\bullet)_S$, $K = 2.303RT(pK_a(R–H)_S)$, $E(R^+) = FE°_{NHE}(R^+/R^\bullet)_S$, $E(RH) =$

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$FE^\circ_{NHE}(RH/RH^{-\bullet})_S$, $E = FE^\circ_{NHE}(R^\bullet/R^-)_S$, and $C = -FE^\circ_{NHE}[(H^\bullet/H^-) + (H^+/H^\bullet)]_S$.

$$H(R^+) = K + E(R^\bullet) + E(R^+) + C \qquad (2)$$

$$H(R^\bullet) = K + E(R^\bullet) + E(RH) + C \qquad (6)$$

The following equations (a–f) are the first derivatives of the term on the right hand side of (2) or (6) with respect to each of the terms on the left hand sides of the equations. Each of the terms was evaluated by linear regression analysis using the pertinent data for eq 2 (ref 8) or eq 6 (Table III). The numbers in parentheses are the correlation coefficients (r^2). Of the eighteen terms, eleven are unique; some are inverses of others.

What this analysis shows is that all of the quantities in both eqn. (2) and eqn. (6) are interrelated. However, in each of the equations (a - f) linearity ($r^2 \geq 0.99$) is only observed for one of the three correlations. These correlations, shown in bold face, have near unit slope and the other two very nearly offset each other. Equation (10) is a combination of the relationships illustrated in (c) and (f) below and the plot is shown in Figure 1.

$$\underset{-0.450(0.48)}{dH(R^+)/dK} = 1 + \underset{-1.079(0.996)}{dE(R^\bullet)/dK} + \underset{-0.384(0.47)}{dE(R^+)/dK} \qquad \text{(a)}$$

$$\underset{0.435(0.52)}{dH(R^+)/dE(R^\bullet)} = \underset{-0.923(0.996)}{dK/dE(R^\bullet)} + 1 + \underset{0.370(0.51)}{dE(R^+)/dE(R^\bullet)} \qquad \text{(b)}$$

$$\underset{1.157(0.992)}{dH(R^+)/dE(R^+)} = \underset{-1.228(0.47)}{dK/dE(R^+)} + \underset{1.380(0.51)}{dE(R^\bullet)/dE(R^+)} + 1 \qquad \text{(c)}$$

$$\underset{-1.457(0.91)}{dH(R^\bullet)/dK} = \underset{-1.088(0.995)}{dE(R^\bullet)/dK} + 1 + \underset{-1.362(0.91)}{dE(RH)/dK} \qquad \text{(d)}$$

$$\underset{1.340(0.92)}{dH(R^\bullet)/dE(R^\bullet)} = \underset{-0.915(0.995)}{dK/dE(R^\bullet)} + 1 + \underset{1.248(0.90)}{dE(RH)/dE(R^\bullet)} \qquad \text{(e)}$$

$$\underset{1.064(0.997)}{dH(R^\bullet)/dE(RH)} = \underset{-0.665(0.91)}{dK/dE(RH)} + \underset{0.725(0.90)}{dE(R^\bullet)/dE(RH)} + 1 \qquad \text{(f)}$$