# Equilibrium Acidities of HA²⁺ Dications in Dimethyl Sulfoxide Solution

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A potentially general method for estimating the acidities of HA²⁺ dications in DMSO solution based on a thermodynamic cycle has been developed by combination of the equilibrium acidity of the acid ($pK_{HA}$) with its oxidation potential [$E_{ox}(HA)$], the oxidation potential of its conjugate base [$E_{ox}(A^-)$], and those of the corresponding radical [$E_{ox}(A^•)$] and radical cation [$E_{ox}(HA^{+•})$] (eq 6). The $pK_{HA^{+•}}$ values for the radical cations derived from 2,4,5-triphenylimidazole, *p*-(phenylamino)diphenylamine, and 5*H*-dibenz[*bf*]azepine (iminostilbene) by loss of an electron were found to be 1.5, 4.1, and 3.8, respectively, and the $pK_{HA^{2+}}$ values of the corresponding dications formed by loss of an electron from these radical cations were found to be -8.1, -5.7, and -7.7, respectively.

## Introduction

Equilibrium acidities of weak organic acids (eq 1) have been measured in a variety of solvents.[1] The most

$$H-A \rightleftharpoons H^+ + A^- \qquad (1)$$
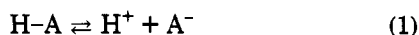
extensive acidity scale is that developed in the dipolar non-hydrogen-bond-donor ("aprotic") solvent dimethyl sulfoxide (DMSO), which now contains more than 1500 $pK_{HA}$ values for carbon, nitrogen, oxygen, and sulfur acids.[2]

Radical cations, HA⁺•, formed by removal of an electron from weak HA acids, are common reactive intermediates in chemistry.[3] Direct experimental measurement of the equilibrium acidity of a radical cation ($pK_{HA^{+•}}$) is difficult because the presence of short-lived and highly reactive radical species on both sides of eq 2 makes it difficult to

$$HA^{+•} \rightleftharpoons H^+ + A^• \qquad (2)$$

establish an equilibrium in polar solvents. The $pK_{HA^{+•}}$ values of radical cations can be estimated, however, by combination of the $pK_{HA}$ values for their precursor acids with their oxidation potentials [$E_{ox}(HA)$] and those of their conjugate bases [$E_{ox}(A^-)$], as shown in eq 3.[4] The $pK_{HA^{+•}}$ values of several hundred radical cations containing acidic C-H, N-H, O-H, or S-H bonds have been estimated in DMSO solution by using eq 3.[2,4b,5]

$$pK_{HA^{+•}} = pK_{HA} + 16.8[E_{ox}(A^-) - E_{ox}(HA)] \qquad (3)$$

Dications, HA²⁺, formed by the loss of two electrons from neutral weak HA acids, have been found to be reactive

intermediates in a number of chemical reactions,[6] but almost nothing is known about their equilibrium acidities. Experimental observations, together with theoretical calculations, have shown that the dications can exist in the gas phase or in superacid solutions, but they may be thermodynamically unstable with respect to dissociation (deprotonation) in polar solvents because of strong Columbic repulsion between the two positive charges and the extremely large solvation energy of the proton. The solvation energy of the proton in polar solvents such as water or DMSO is known to be much larger than those of other cations primarily due to its small size and large positive charge density.[7] Loss of a proton from a dication species of the type HA²⁺, eq 4, has been shown to be the principal reaction pathway in polar solvents.[8] For example, tetralkylhydrazine radical cations formed by removal of one electron from tetralkylhydrazines are generally long-lived species in solution. Removal of a second electron from the tetralkylhydrazine radical cations to give the corresponding dications results in the formation of dication species with submillisecond lifetimes, however.[6a]

The establishment of the equilibrium (eq 4) for HA²⁺ dications and direct measurement of $pK_{HA^{2+}}$ is expected

$$HA^{2+} \rightleftharpoons H^+ + A^+ \qquad (4)$$
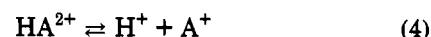
to be even more difficult than that for HA⁺• radical cations (eq 2) since dications have shorter lifetimes than those of the corresponding radical cations.[6a] Note that the A⁺ cation on the right side of eq 4 is expected to be much less stable than the corresponding A• radical in the right side of eq 2 because the A⁺ cation is formed by removal of an electron from an electron-deficient A• radical. In the present paper, we report a potentially general method for

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estimating the equilibrium acidities of dications in DMSO solution of $HA^{2+}$-type dications and apply it to determine the equilibrium acidities of the nitrogen dications derived from 2,4,5-triphenylimidazole, *p*-(phenylamino)diphenylamine, and 5*H*-dibenz[*bf*]azepine (iminostilbene).
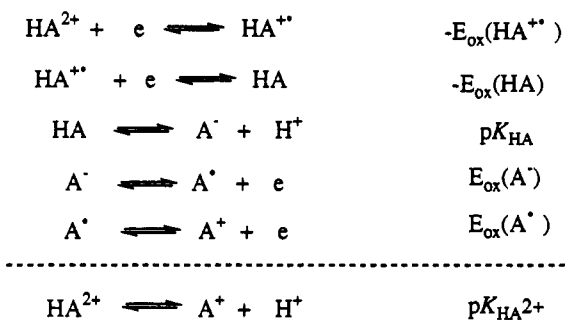
## Results and Discussion

**Thermodynamic Cycles.** According to the law put forth by Hess in 1840, the total enthalpy for a given chemical reaction is the same regardless of the reaction pathways by which the reaction takes place.[9] Application of Hess's Law during the subsequent century and a half has made it possible to determine various thermodynamic quantities that are inaccessible experimentally.[9,10] Similarly, eq 5, which is based on a thermodynamic cycle, can be used to estimate homolytic bond dissociation enthalpies (BDEs) of the acidic H–A bonds in HA weak acids that are difficult, if not impossible, to measure by experimental methods.

$$BDE_{HA} = 1.37pK_{HA} + 23.1E_{ox}(A^-) + 73.3 \quad (5)$$

The $BDE_{HA}$s estimated by eq 5 have been shown to be in remarkably good agreement ($\pm 2$ kcal/mol) with the best available gas-phase literature BDEs.[11]

A thermodynamic cycle can also be designed to estimate the equilibrium acidities of $HA^{2+}$ dications, as shown in Scheme 1.

### Scheme 1

| | | |
|---|---|---|
| $HA^{2+} + e \rightleftharpoons HA^{+\cdot}$ | | $-E_{ox}(HA^{+\cdot})$ |
| $HA^{+\cdot} + e \rightleftharpoons HA$ | | $-E_{ox}(HA)$ |
| $HA \rightleftharpoons A^- + H^+$ | | $pK_{HA}$ |
| $A^- \rightleftharpoons A^\cdot + e$ | | $E_{ox}(A^-)$ |
| $A^\cdot \rightleftharpoons A^+ + e$ | | $E_{ox}(A^\cdot)$ |

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$$HA^{2+} \rightleftharpoons A^+ + H^+ \qquad pK_{HA^{2+}}$$

Equation 6 is a summation of the terms shown on the right side of the equations in Scheme 1. The constant

$$pK_{HA^{2+}} = pK_{HA} + 16.8[E_{ox}(A^-) - E_{ox}(HA) +$$
$$E_{ox}(A^\cdot) - E_{ox}(HA^{+\cdot})] \quad (6)$$

16.8 (23.1/1.37) converts the related oxidation potentials in volts into $pK_{HA}$ units. To the best of our knowledge, this is the first method to determine the equilibrium acidities of dications from thermodynamic quantities alone. The first three terms on the right side of eq 6 are

identical with the terms on the right side of eq 3. Therefore, eq 6 can be simplified to eq 7. Equation 7 shows that the

$$pK_{HA^{2+}} = pK_{HA^{+\cdot}} + 16.8 [E_{ox}(A^\cdot) - E_{ox}(HA^{+\cdot})] \quad (7)$$

determination of a $pK_{HA^{2+}}$ value requires measurements of the oxidation potentials of the corresponding $A^\cdot$ radical and $HA^{+\cdot}$ radical cation, together with an estimate of the $pK_{HA^{+\cdot}}$ value of the corresponding radical cation.[4]
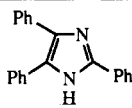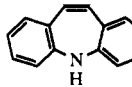
**Equilibrium Acidities of the Dications Derived from 2,4,5-Triphenylimidazole, *p*-(Phenylamino)-diphenylamine, and 5*H*-Dibenz[*bf*]azepine in DMSO Solution.** The equilibrium acidities of organic weak acids in DMSO solution can be determined accurately by a titration method,[2] and their oxidation potentials and those of the corresponding conjugate anions, $A^-$, are readily measured by the cyclic voltammetry. Most of these oxidation potentials measured by conventional cyclic voltammetry (scan rate: 100 mV/s) are irreversible, however.[5,10,11] This means that the oxidation potentials of the corresponding $A^\cdot$ radicals forming $A^+$ cations and the corresponding $HA^{+\cdot}$ radical cations forming $HA^{2+}$ dications, which are needed to estimate $HA^{2+}$ acidities, cannot be measured by conventional cyclic voltammetry (CV). But, when the $A^\cdot$ radicals formed by oxidation of $A^-$ anions on the electrode surface have sufficiently long lifetimes it is possible to determine both $E_{ox}(A^-)$ and $E_{ox}(A^\cdot)$ by a single CV measurement even at a conventional scan rate (100 mV/s).[10a,12] Also, a number of nitrogen radical cations are stable enough to be further oxidized to the corresponding dications on an electrode surface at 100 mV/s,[6a,b,e,12] including those in the present study. The equilibrium acidities of the neutral weak acids and the related oxidation potentials needed for the determination of $pK_{HA^{2+}}$ values for 2,4,5-triphenylimidazole, *p*-(phenylamino)diphenylamine, and 5*H*-dibenz[*bf*]azepine were measured and are summarized in Table 1. The equilibrium acidities of the radical cations and dications derived from these nitrogen acids determined by using of eq 3 and 6, respectively, are included in Table 1 for comparison.

Examination of Table 1 shows that removal of an electron from 2,4,5-triphenylimidazole to form the corresponding radical cation is accompanied by a decrease in $pK_a$ from 15.5 to 1.5, i.e., 14 $pK_a$ units. Decreases of 21.5 and 22.3 $pK_a$ units were also observed for *p*-(phenylamino)diphenylamine and iminostilbene, respectively. The latter two decreases are remarkably similar to the 22, 24, and 26 $pK_a$ unit decreases observed by removal of one of the lone pair electrons from thiophenol, aniline, and phenol, respectively, to form the corresponding radical cations.[5c] Removal of one electron from toluene to form the corresponding radical cation is accompanied by a much greater decrease in $pK_a$ (63 units) because the electron must come from the $\pi$ electron system, which disrupts the aromaticity (Scheme 2).

In Scheme 3 loss of the electron from 2,4,5-triphenylimidazole is pictured as coming from the lone pair on the $sp^2$ nitrogen, rather than from the $sp^3$ nitrogen, since loss of an electron from the $sp^3$ nitrogen bearing the hydrogen atom would disrupt the 6-$\pi$ electron aromaticity of the imidazole ring. The relatively small decrease in

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**Table 1. Equilibrium Acidities of 2,3,5-Triphenylimidazole, *p*-(Phenylamino)diphenylamine, 5*H*-Dibenzo[*b*,*f*]azepine, and the Corresponding Radical Cations and Dications in Dimethyl Sulfoxide (DMSO) Solution**

| compounds | $pK_{HA}{}^a$ | $E_{ox}(HA)^c$ | $E_{ox}(HA^{+\cdot})^d$ | $E_{ox}(A^-)^e$ | $E_{ox}(A^{\cdot})^g$ | $pK_{HA^{+\cdot}}{}^i$ | $pK_{HA^{2+}}{}^j$ |
|---|---|---|---|---|---|---|---|
| (2,3,5-triphenylimidazole structure) | 15.5 | 0.616 | 0.953 | −0.217 | 0.380 | 1.5 | −8.1 |
| *p*-PhNHC₆H₄NHPh | 25.6$^b$ | 0.044 | 0.492 | −1.234 | −0.092 | 4.1 | −5.7 |
| (dibenzazepine structure) | 26.1 | 0.268 | 0.810 | −1.030$^f$ | 0.130$^h$ | 3.8 | −7.7 |

$^a$ In $pK_{HA}$ units; equilibrium acidities taken from ref 2 unless otherwise indicated. $^b$ Taken from ref 5f. $^c$ In volts; reversible oxidation potentials of the neutral weak acids measured in DMSO solution by cyclic voltammetry (CV).[5] $E_{1/2}$ is reported and referenced to the ferrocene/ferrocenium (Fc/Fc⁺) couple.[11a] $^d$ In volts; irreversible oxidation potentials of the radical cations measured in acetonitrile solution.[14] The $E_p$ is reported. $^e$ In volts; reversible oxidation potentials of the conjugate anions measured in DMSO solution. The $E_{1/2}$ values are reported and referenced to the Fc/Fc⁺ couple.[11a] $^f$ Measured by a fast-scan CV[15] and referenced to the ferrocene/ferrocenium (Fc/Fc⁺) couple.[11a] $^g$ In volts; irreversible oxidation potentials of the radicals derived from the corresponding conjugate anions by oxidation in DMSO solution unless otherwise indicated. Ep is reported. $^h$ Reversible oxidation potential measured in DMSO by a fast-scan CV.[15] $^i$ In $pK_{HA}$ units; estimated by using eq 3. $^j$ In $pK_{HA}$ units; estimated by using eq 6 or eq 7.

**Scheme 2**
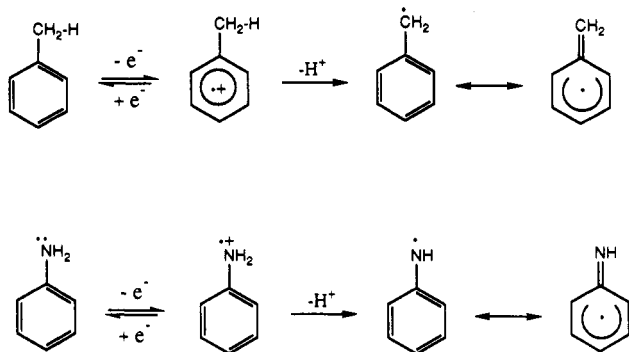


$pK_a$ (14 units) is a consequence of the generation of the positive charge in the radical cation **1** on an atom remote from the acidic site rather than at the acidic site as occurs for the radical cations derived from *p*-PhNHC₆H₄NHPh or iminostilbene (**3** and **5**, respectively). (Note also that removal of an electron from the lone pair on the nitrogen atom of the *p*-Me₂N group in *p*-dimethylaminophenol to form the corresponding radical cation results in a decrease in $pK_a$ of only 13.5 units, compared to 26.1 units for removal of one electron from the lone pair on the oxygen atom of phenol.[5e])

Removal of an electron from the radical cations (**1**, **3**, and **5**) derived from 2,4,5-triphenylimidazole, *p*-PhNHC₆H₄NHPh, and iminostilbene results in further decreases in $pK_a$ of 9.6, 9.8, and 11.5 units, respectively. In dication **2** the plus charges can be placed on each of the two nitrogen atoms, and that on the sp² nitrogen atom can be delocalized to some extent into the phenyl ring at C-2. In dication **4** the plus charges can reside on the two nitrogen atoms and the odd electrons can be delocalized into the phenyl rings. In dication **6** one positive charge and one odd electron can reside on nitrogen, and the second positive charge and odd electron can reside on carbon and can be delocalized into the benzene rings.

These dications are strongly acidic, but no doubt less so than those derived from tetraalkyldiazenium dications, where the two positive charges are on adjacent nitrogen atoms,[6a,e] and far less acidic than the estimates of $pK_a$ values for the dications derived from (*p*-methoxyphenyl)-diphenylmethane and triphenylmethane of −57 and −72, respectively.[13]

**Summary and Conclusions.** A potentially general method of estimating the acidities of HA²⁺-type dications has been developed by a combination of the equilibrium acidities of weak acids ($pK_{HA}$) with the oxidation potential of the acid, HA, and those of the corresponding A⁻ anions, A⁻ radicals, and HA⁺⁻ radical cations. The important feature of this method is that *all terms required by eq 6 are thermodynamic quantities*. The method has a limited application, however, because it is difficult to measure the oxidation potentials of the radicals [$E_{ox}(A^{\cdot})$] and of the radical cations [$E_{ox}(HA^{+\cdot})$] by conventional cyclic voltammetry. For example, many carbon radicals stabilized by adjacent amino groups,[10a,b] and oxygen radicals derived from 2,6-di-*tert*-butyl-4-substituted phenols,[10c] are stable enough to be oxidized further to dications by conventional cyclic voltammetry at 100 mV/s, but the corresponding radical cations are very unstable as judged by their large negative $pK_{HA^{+\cdot}}$ values.[10a–c] This instability prevents the measurements of the oxidation potentials of the radical cation to the dication. The acids in Table 1 are the only ones we have examined to data that permit all oxidation potentials to be measured by conventional cyclic voltammetric techniques, but we anticipate finding additional examples.
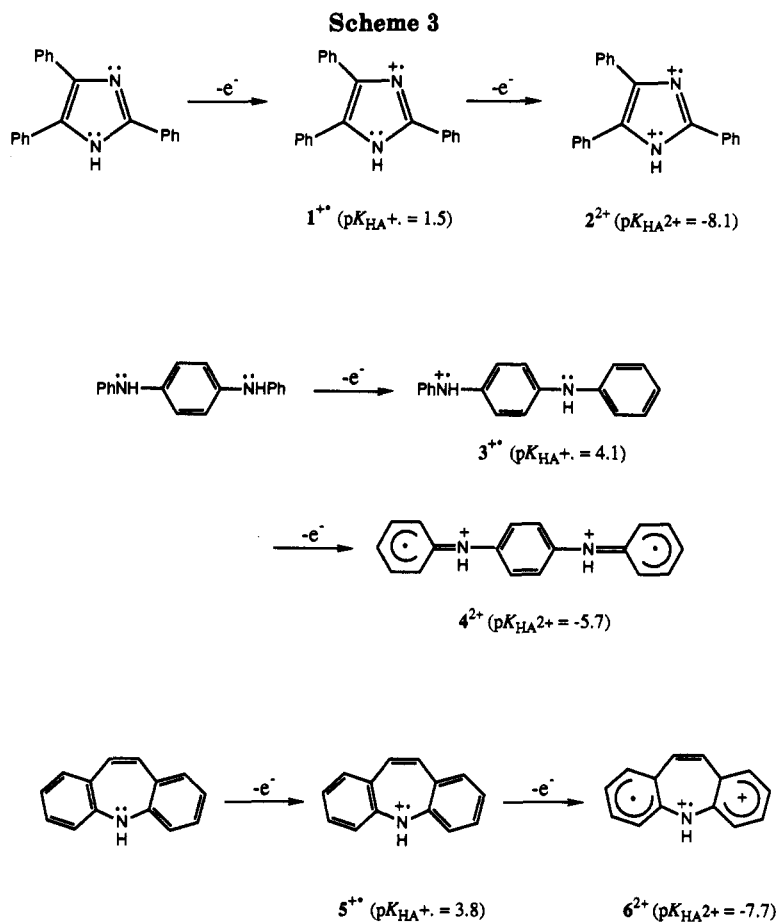
**Experimental Section**

**Materials.** 2,4,5-Triphenylimidazole, *p*-(phenylamino)diphenylamine, and 5*H*-dibenz[*bf*]azepine (iminostilbene) were commercial samples from Aldrich Chemical Co. The purity and identity of each sample was confirmed by spectral analysis and melting points.

The equilibrium acidities of the neutral weak acids in DMSO solution were measured by the overlapping indicator titration method as described previously.[2] The oxidation potentials were measured by a conventional cyclic voltammetric instrument, as described previously.[5,10,11] The working electrode (BAS) consists of a 1.5-mm diameter platinum disk embedded in a cobalt glass seal. It was polished with a 0.05-μm Fisher polishing aluminum or cleaned with ultrasonic instrument and rinsed with ethanol and dried before each run. The counter electrode was platinum wire (BAS). The reference electrode was Ag/AgI, and the reported oxidation potentials were referenced to ferrocene/ferrocenium couple ($E_{1/2}$ = 0.875 V vs the Ag/AgI couple in our instrument).[11a]

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(14) Cheng[14a] has shown that the oxidation potentials of several hundred weak acids and their conjugate anions measured in acetonitrile solution are usually in good agreement (±50 mV) with those measured in DMSO solution. (a) Cheng, J.-P. Ph.D. Dissertation, Northwestern University, Evanston, IL, 1987.

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**Scheme 3**



$1^{+\bullet}$ ($pK_{HA}+. = 1.5$)    $2^{2+}$ ($pK_{HA}2+ = -8.1$)

$3^{+\bullet}$ ($pK_{HA}+. = 4.1$)

$4^{2+}$ ($pK_{HA}2+ = -5.7$)

$5^{+\bullet}$ ($pK_{HA}+. = 3.8$)    $6^{2+}$ ($pK_{HA}2+ = -7.7$)

Tetraethylammonium tetrafluoroborate was used as the supporting electrolyte. The $pK_{HA}$ measurement and all electrochemical experiments were carried out under an argon atmosphere.