Effects of Structural Changes on Acidities and Homolytic Bond Dissociation Energies of the N–H Bonds in Pyridones and Related Heterocycles

F. G. Bordwell,* Debra L. Singer, and A. V. Satish

Contribution from the Department of Chemistry, Northwestern University, 2145 Sheridan Road, Evanston, Illinois 60208-3113

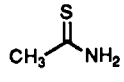
Received October 14, 1992

Abstract: Equilibrium acidities in DMSO have been obtained for the H–N (or H–O) bonds in 2-, 3-, and 4-aminopyridines, 3-hydroxypyridine, 2- and 4-pyridones, 2-piperidone, and 2-quinolone, as well as thio analogues in which the C=O bond has been replaced by C=S. Homolytic bond dissociation energies (BDEs) for the acidic H–A bonds in these molecules have been estimated by combining the pK_{HA} values with the oxidation potentials of their conjugate bases, $E_{ox}(A^-)$. The acidity order for the aminopyridines was found to be 4 > 2 > 3 whereas the BDEs of their N–H bonds decreased in the opposite order, 3 > 2 > 4. The N–H bond of 2-pyridone was found to be 9.4 pK_{HA} units (12.9 kcal/mol) more acidic than its saturated analogue, 2-piperidone, whereas its homolytic bond dissociation energy was found to be about 12 kcal/mol weaker. The 2- and 4-pyridones and 2-quinolone exhibit homo-hydrogen bonding whereas their thio analogues do not. The stabilization energy of the 2-thiopyridonyl radical was estimated to be 17 kcal/mol greater than that of the 2-pyridonyl radical, which explains the much greater ease with which esters of *N*-hydroxy-2-thiopyridone compared to esters of *N*-hydroxy-2-pyridone produce radicals in the Barton reaction.

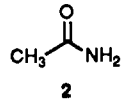
In earlier papers we have reported acidity measurements in DMSO for the N–H bonds in various types of compounds including anilines,[1] carboxamides,[2a] thiocarboxamides,[2b] and amidines[3] and for the O–H bonds in phenols[4a] and oximes.[4b] Combination of these pK_{HA} values with the oxidation potentials of the conjugate bases using eq 1, or the like, has also provided

$$\mathrm{BDE} = 1.37pK_{HA} + 23.06E_{ox}(A^-) + 73.3 \qquad (1)$$

estimates of the homolytic bond dissociation energies (BDEs) of the acidic N–H (or O–H) bonds in these compounds, which were found to agree within ±2 kcal/mol with the best gas-phase values with few exceptions.[1-4] Replacement of the C=O bond in carboxamides by a C=S bond was found to have a profound effect on both pK_{HA} and BDE. For example, the pK_{HA} of the N–H bond in thioacetamide (**1**) was found to be 18.5 in DMSO, i.e., 7 pK_{HA} units (9.6 kcal/mol) lower than that of acetamide (**2**), and the BDE of the N–H bond in thioacetamide was found to be 16 kcal/mol lower.[2b]



1
pK_{HA} = 18.5
BDE = 91 kcal/mol



2
pK_{HA} = 25.5
BDE = 107 kcal/mol

In addition, the near identity of the BDE of the N–H bond in CH_3CONH_2 with that in NH_3 indicated that the odd electron in the corresponding radical, •NH—C(Me)=O, was not delocalized into the C=O bond.[2b] This lack of resonance is in agreement with ESR data, which indicate that •N—C=O type radicals are π radicals with most of the electron density on nitrogen and very little on oxygen,[5] but it is contrary to our observation of apparent extensive delocalization in radicals of the type •C—C=O[6] and •S—C=O.[2b] There is evidence to indicate, however, that resonance in radicals of the type •O—C=O is unimportant from calculations of Borden, Davidson, and their colleagues, which show that there is no tendency in the formyl radical for the C–O bond lengths to equilibrate,[7] and from the near equivalence of the O–H bond BDEs in carboxylic acids and alcohols.[8] Recently we provided experimental support for Borden's postulate that resonance energies (REs) in allylic radicals increase as the electronegativity of the terminal atoms decreases. By examining the BDEs in appropriate models we found that the REs *appear* to increase in the following order: O=C—O•, O=C—N• (REs ≃ 0 kcal/mol) < N=N—N• (RE ≃ 5 kcal/mol) < O=C—C• (RE ≃ 10 kcal/mol) < N=C—S•, C=C—S•, C=C—C• (REs ≃ 17–22 kcal/mol).[9]

In the present paper we examine the acidities and BDEs of a number of cyclic compounds containing heteroallylic moieties of the type N=C—NH_2, O=C—NH, S=C—NH, and C=C—O—H. To the best of our knowledge, there is no information in the literature concerning the acidities or BDEs of the acidic H–A bonds for most of these compounds (aminopyridines, 3-hydroxypyridine, pyridones, thiopyridones, piperidone, thiopiperidone, and quinolone).

(1) (a) Bordwell, F. G.; Algrim, D. J. *J. Am. Chem. Soc.* **1988**, *110*, 2964–2968. (b) Cheng, J.-P., Ph.D. Dissertation, Northwestern University, 1987.
(2) (a) Bordwell, F. G.; Algrim, D. J. *J. Org. Chem.* **1976**, *41*, 2507–2508. (b) Bordwell, F. G.; Algrim, D. J.; Harrelson, J. A., Jr. *J. Am. Chem. Soc.* **1988**, *110*, 5903–5904.
(3) Bordwell, F. G.; Ji, G.-Z. *J. Am. Chem. Soc.* **1991**, *113*, 8398–8401.
(4) (a) Bordwell, F. G.; Cheng, J.-P. *J. Am. Chem. Soc.* **1991**, *113*, 1736–1743. (b) Bordwell, F. G.; Ji, G.-Z. *J. Org. Chem.* **1992**, *57*, 3019–3025. (c) Bordwell, F. G.; McCallum, R. J.; Olmstead, W. N. *J. Org. Chem.* **1984**, *49*, 1424–1427. (d) Bordwell, F. G.; Cheng, J.-P.; Ji, G.-Z.; Satish, A. V.; Zhang, X.-M. *J. Am. Chem. Soc.* **1991**, *113*, 9790–9795.
(5) (a) Danen, W. C.; Gellert, R. W. *J. Am. Chem. Soc.* **1980**, *102*, 3264–3265. (b) Sutcliffe, R.; Griller, D.; Lessard, J.; Ingold, K. U. *J. Am. Chem. Soc.* **1981**, *103*, 624–628.
(6) Bordwell, F. G.; Harrelson, J. A., Jr. *Can. J. Chem.* **1990**, *68*, 1714–1718.
(7) Feller, D.; Huyser, E. S.; Borden, W. T.; Davidson, E. R. *J. Am. Chem. Soc.* **1983**, *105*, 1459–1460. Feller, D.; Davidson, E. R.; Borden, W. T. *J. Am. Chem. Soc.* **1984**, *106*, 2513–2519.
(8) McMillen, D. F.; Golden, D. M. *Annu. Rev. Phys. Chem.* **1982**, *33*, 493–532.
(9) Bordwell, F. G.; Ji, G.-Z.; Zhang, X.-M. *J. Org. Chem.* **1991**, *56*, 5254–5256.

0002-7863/93/1515-3543$04.00/0

Table I. Acidities and Homolytic Bond Dissociation Energies (BDE) of N-H and O-H Bonds in Aminopyridines, Pyridones, Thiopyridones, and 3-Hydroxypyridine

compd	pK_{HA}[a]	$E_{ox}(A^-)$[d]	BDE[f]
aniline	30.6	-0.992	92
2-aminopyridine	27.7[b]	-1.061[e]	87[e]
3-aminopyridine	28.5[b]	-0.801[e]	94[e]
4-aminopyridine	26.5[b]	-1.091[e]	84[e]
3-hydroxypyridine	15.8[c]	0.006	95
2-piperidone	26.4	0.009	110
2-pyridone	17.0[c]	0.057	98
4-pyridone	14.8[c]	0.225	99
2-quinolone	17.6[c]	0.164	101
2-thiopiperidone	20.1	-0.415	91
2-thiopyridone	13.3	-0.454	81
4-thiopyridone	11.9	-0.339	82
2-thioquinolone	13.7	-0.367	83
phenol	18.0[c]	-0.325	90
thiophenol	10.3	-0.360	79

[a] Measured in DMSO against at least two indicators. [b] Measured by M. Van Der Puy. [c] These pK_{HA} values were corrected for homo-hydrogen bonding. [d] Measured in DMSO by cyclic voltammetry using platinum working and auxiliary electrodes and Ag/AgI reference electrode with 0.1 M Et_4NBF_4 as electrolyte. The potential range is scanned at 100 mV/s while the solution is blanketed by argon. The potentials are reported with reference to the $E_{1/2}$ of Fc/Fc^+ redox couple measured under the same conditions. The oxidations of anions are irreversible at 100 mV/s scan rate and the peak potentials are reported. [e] Measured by X.-M. Zhang. [f] In kcal/mol; calculated using eq 1.

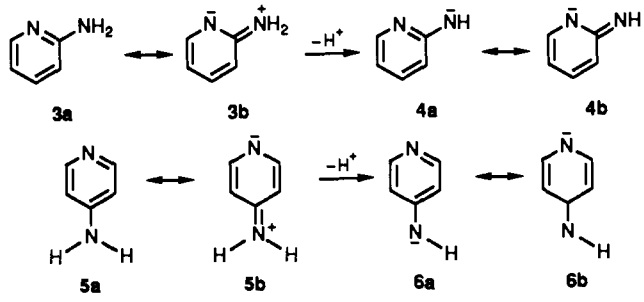
Results and Discussion

The results of acidity and BDE measurements on the types of compounds mentioned in the introduction are summarized in Table I.

Rationalization of the changes in acidities and BDEs of compounds shown in Table I that are brought about by structural changes will be made in terms of assumptions concerning the effects on the ground-state energies of the undissociated acids and the energies of the anions and radicals formed by loss of a proton or hydrogen atom. As a working hypothesis we assume that structural changes resulting in an increase in the ground-state energy of the undissociated acid will cause the acidity to increase and the BDE of the acidic C-H, N-H, or O-H bond to decrease. For example the structural change from **1** to **2** results in a large increase in ground-state energy since the C=S bond is 35 kcal/mol, or more, weaker than the C=O bond. We believe that this increase in ground-state energy is at least partially responsible for the 9.6 kcal/mol increase in the acidity of the N-H bond and the 16 kcal/mol decrease in its BDE.

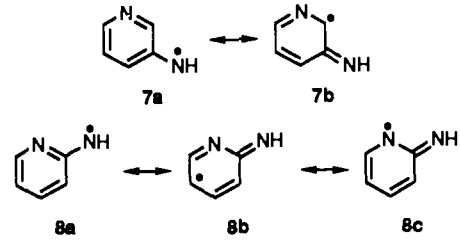
Acidities and BDEs of Aniline, Aminopyridines, and 3-Hydroxypyridine. Aniline has a pK_{HA} value of 30.6 in DMSO, which makes it more acidic than ammonia by about 10.5 pK_{HA} units (14.4 kcal/mol).[1a] This increase is believed to be caused primarily by resonance stabilization of the anilinide ion by delocalization of the negative charge into the benzene ring.[10] Examination of Table I shows that the aminopyridines are more acidic than aniline by 2.9–4.1 pK_{HA} units (4.0–5.6 kcal/mol) and that the acidities increase in the order 3 < 2 < 4. Delocalization of the charge in the pyridylamide ions is possible for all three amide ions, but the charge can be delocalized so as to reside on the nitrogen atoms in the pyridine ring only in the anions (**4** and **6**) derived from the 2- and 4-isomers (**3** and **5**). In the 3 isomer the charge can be delocalized so as to reside only on the less electronegative carbon atoms, and the 1.1 and 2.7 kcal/mol lower acidity of 3-aminopyridine than the acidities of the 2- and 4-isomers, respectively, can be rationalized in this way. The 1.1 pK unit (1.5 kcal/mol) lower acidity of 2-amino- than 4-aminopyridine may be associated with the lower ground-state energy of the neutral 2-isomer caused by less charge separation of the dipolar contributors (compare **3b** with **5b**), which is acid weakening, together with a four-electron repulsion between the lone pairs on the nitrogen atoms (compare **4** with **6**).

The acidity of 3-hydroxypyridine is 3 kcal/mol higher than that of phenol, a difference that is comparable to the higher acidity of 3-aminopyridine than aniline (2.9 kcal/mol). These effects are attributable to the electron-withdrawing field/inductive (F) effect of the sp^2 ring nitrogen atom. 3-Hydroxypyridine exhibits strong homo-H-bonding in DMSO ($\log K_{hb} = 3.5$), which is typical of phenols,[4c] whereas the aminopyridines are not homo-hydrogen bonded. (The 2- and 4-hydroxypyridines exist in DMSO entirely in the tautomeric forms of 2- and 4-pyridones,[12] and the acidities and BDEs of their N-H bonds will be discussed later.)



In earlier papers evidence has been presented to show that whereas radicals are stabilized by delocalization of the odd electron, they are destabilized by electron withdrawal.[13,14] The 2 kcal/mol higher BDE for the N-H bond in 3-aminopyridine than that in aniline can be rationalized in terms of the electron-withdrawing field/inductive (F) effect of the ring nitrogen atom overshadowing the delocalization effect in the corresponding 3-pyridylamino radical, $3\text{-}NC_5H_5NH^\bullet$ (**7**). In other words, whereas the F effect lowers the heterolytic bond dissociation energy of the N-H bond in 3-aminopyridine, relative to that in aniline, by stabilizing the corresponding anion, it raises the homolytic bond dissociation energy by destabilizing the corresponding radical.

A similar effect was observed in 3-hydroxypyridine, in which the BDE of the H-O bond was found to be 5 kcal/mol higher than that of phenol. (ΔBDE effects have been shown to be exaggerated in phenols.[4a])



(10) Calculations by Thomas have suggested that the major part of the increase in acidity of phenol, relative to cyclohexanol, is due to the positive potential of the hydrogen atoms in the initial state,[11a] but Topsom and Taft have presented evidence from gas-phase data that resonance stabilization of the anion is the principal acidifying factor.[11b] This should hold true also for aniline, relative to cyclohexylamine, where the electrostatic potential at the acidic hydrogen atom is smaller.

(11) (a) Siggel, M. R. F.; Thomas, T. D. *J. Am. Chem. Soc.* **1986**, *108*, 4360–4362. Thomas, T. D.; Carroll, T. X.; Siggel, M. R. F. *J. Org. Chem.* **1988**, *53*, 1812–1815. (b) Taft, R. W.; Koppel, I. A.; Topsom, R. D.; Anvia, F. *J. Am. Chem. Soc.* **1990**, *112*, 2047–2052.

(12) Beak, P.; Fry, S. F., Jr.; Lee, J.; Steele, F. *J. Am. Chem. Soc.* **1976**, *98*, 171–179.

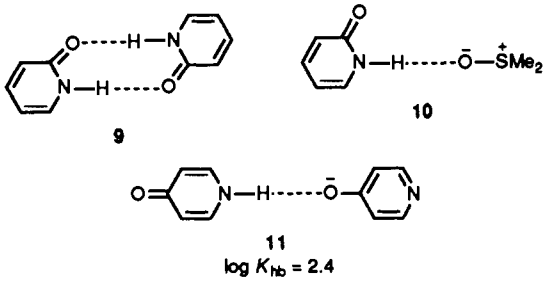
(13) Bordwell, F. G.; Zhang, X.-M. *J. Org. Chem.* **1990**, *55*, 6078–6079.

(14) Pasto, D. J. *J. Am. Chem. Soc.* **1988**, *110*, 8164–8175.

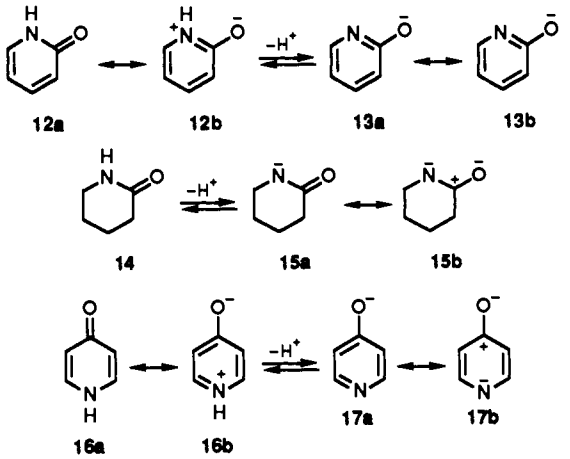
The homolytic BDEs of the N–H bonds in 2- and 4-aminopyridines are 5 and 8 kcal/mol lower, respectively, than that of the N–H bond in aniline, which suggests that delocalization so as to place the odd electron on the ring nitrogen is stabilizing the corresponding radicals (e.g., **8**). Here the delocalizing effect overshadows the destabilizing *F* effect. Other examples where stabilizing delocalizing effects overshadow destabilizing *F* effects have been observed in $C_5H_5N^{+\bullet}CHCN$ vs $Me_3N^{+\bullet}CHCN$ and like radicals.[13] The smaller *F* effect in the 4-$NC_5H_5NH^{\bullet}$ radical than in the 2-$NC_5H_5NH^{\bullet}$ radical together with the higher ground state energy of **5** than **3** (due to greater charge separation in **5b** than **3b**) may be responsible for the lower BDE of the N–H bond in 4-amino- than in 2-aminopyridine. The delocalization energies of about 5 and 8 kcal/mol for the radicals derived from 2-amino- and 4-aminopyridines, respectively, relative to aniline, are about the same as resonance energies (REs) estimated for radicals of the type PhC(=NH)N$^{\bullet}$H and N≡C—NH$^{\bullet}$, where the REs are 6 and 8 kcal/mol, respectively, relative to NH_3.[3,15]

Acidities of Pyridones, Piperidone, and Quinolone. The 2- and 4-pyridones (and thiopyridones) have been shown to exist as hydrogen-bonded dimers (e.g., **9**) in dioxane or benzene solution,[16] but in DMSO the strong H-bond acceptor properties of the solvent dictate a monomer structure (e.g., **10**).[17] Nevertheless, our acidity measurements show that homo-hydrogen bonding does occur between 2- and 4-pyridones and their conjugate bases, log K_{hb} = 3.6 and 2.4, respectively (e.g., **11**). Homo-hydrogen bonding does not ordinarily occur with N–H acids because of their low acidity and polarity.[1a] The N–H bonds in 2- and 4-pyridones are exceptional, however, in that they are more acidic than the O–H bonds in phenols, which are known to exhibit strong homo-H bonding.[18] Also, the pyridonide ions are ambident and the basic donor atom can be oxygen (**11**). The latter is evidently the determining factor since the thiopyridones, which are much more acidic than the pyridones, *fail to exhibit homo-hydrogen bonding.*

2-Pyridone (**12**) is a stronger acid than its saturated analogue 2-piperidone (**14**) by 9.4 pK_{HA} units (12.9 kcal/mol). This large difference can be explained by the aromaticity of its conjugate base (**13**), which is absent in the conjugate base of 2-piperidone (**15**).

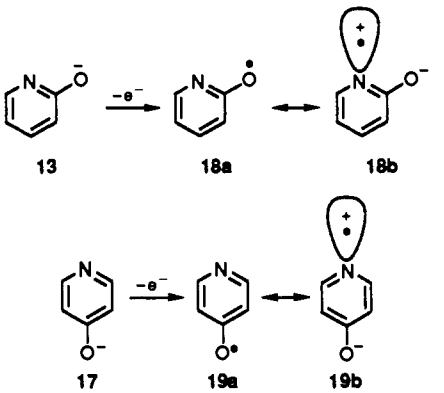


The 3 kcal/mol higher acidity of 4-pyridone (**16**) than 2-pyridone (**12**) may be attributed to a higher energy of its aromatic ground state due to more charge separation (compare **12b** and **16b**), together with repulsions between the lone pair on oxygen and nitrogen in the anions (compare **13** and **17**).



2-Quinolone (log K_{hb} = 2.7) is a weaker acid than 2-pyridone by 0.8 kcal/mol. Evidently the negative charge on the oxygen atom in the conjugate base derived from 2-quinolone is not being delocalized into the benzene ring.

BDEs of Pyridones, Piperidone, and 2-Quinolone. 2-Pyridone has a BDE 12 kcal/mol lower than its saturated analogue, 2-piperidone. Here too it appears likely that delocalization of the odd electron is responsible for the greater stability of the radical, and the marked lowering of the BDE. The radicals **18** and **19**, which are formed by loss of an electron from the aromatic conjugate bases of 2- and 4-pyridones, **13** and **17**, respectively, retain some aromaticity.

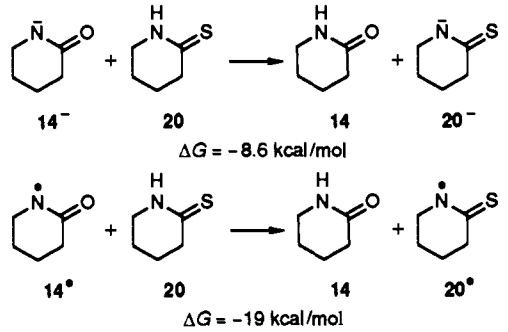


The 1 kcal/mol higher BDE for the N–H bond in 4-pyridone than that in 2-pyridone is at first sight surprising, since we have assumed that 4-pyridone has the higher ground-state energy. Ordinarily, a higher ground-state energy should lead to a lower BDE and a more stable radical. Comparison of the resonance contributors to the radicals show, however, that the aromatic contributor **18b** for the radical derived from the conjugate base of 2-pyridone is stabilized by an electrostatic interaction between the positive charge on nitrogen and the negative charge on oxygen, whereas this stabilizing factor is absent in the aromatic contributor **19b** for the radical derived from 4-pyridone. This provides a rationale for the lower BDE of the N–H bond in 2-pyridone.

The BDE data showing that the N–H bond in 2-quinolone has a 3 kcal/mol *higher* BDE than that in 2-pyridone is unexpected. One would expect fusion of a benzene ring across the e bond of 2-pyridone to *lower* the BDE if the odd electron in the corresponding radical delocalizes into the benzene ring. This is what happens when a benzene ring is fused on to phenol to give 2-naphthol, which causes a 2 kcal/mol decrease in BDE.[4a] A possible explanation is that the fused benzene ring lowers the ground-state energy of 2-quinolone, relative to that of 2-pyridone,

(15) Harrelson, J. A., Jr. Unpublished results.
(16) Krackov, M. H.; Lee, C. M.; Mautner, H. G. *J. Am. Chem. Soc.* **1965**, *87*, 892–896.
(17) Aksnes, D. W.; Kryvi, H. *Acta Chem. Scand.* **1972**, *26*, 2255–2266.
(18) Richardson, J. H.; Stephenson, L. M.; Brauman, J. I. *J. Am. Chem. Soc.* **1975**, *97*, 1160–1162.

Scheme I



by π bond delocalization, raises the BDE of the N–H bond, and destabilizes the corresponding radical.

Acidities and BDEs of 2-Thiopiperidone, 2- and 4-Thiopyridones, and 2-Thioquinolone. Examination of Table I shows that replacement of the C=O bond in 2-piperidone, 2- and 4-pyridones, and 2-quinolones by a C=S bond caused the acidities to increase by 8.6, 5.1, 4.0, and 5.3 kcal/mol, respectively. The smaller increases observed for the pyridones and quinolone than for 2-piperidone can be attributed to a leveling effect since 2-piperidone is less acidic by 12.1–15.9 kcal/mol than the pyridones and quinolone. The acidifying effects brought about by these structural changes are believed to be the result of an increase in ground-state energies of the thioamides, relative to the oxygen analogues, together with the greater ability of sulfur than oxygen to accommodate a negative charge.[20]

The effect of replacing the C=O bond by a C=S bond has a much greater effect on the ΔBDEs of the N–H bonds than on their acidities. The BDEs are 18 ± 1 kcal/mol lower for the thio analogues than for 2-piperidone, 2-pyridone, 4-pyridone, and 2-quinolone (Table I). It is noteworthy that the effect on the BDE of replacing C=O by C=S is the same for 2-piperidone (BDE = 110 kcal/mol) as for 2-pyridone (BDE 98 kcal/mol), despite a 12 kcal/mol difference in the BDEs and a marked difference in the nature of the radicals formed, i.e., an aromatic radical from 2-pyridone (**18**), and a nonaromatic radical from 2-piperidone (**14**). Evidently it is the increase in ground-state energy introduced by the replacement of the C=O bond by a C=S bond that is the dominant factor, rather than the nature of the radicals that are formed.

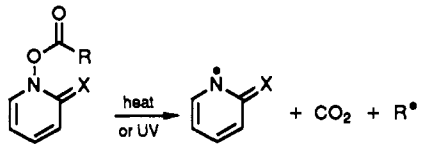
We have seen that 2-thiopiperidone has an N–H bond acidity 8.6 kcal/mol higher and a BDE for the N–H bond that is 19 kcal/mol lower than the corresponding values for 2-piperidone (**14**; Table I). The effects of replacing the C=O bond by a C=S bond on acidities and BDEs for 2- and 4-pyridones and 2-quinolone are similar, i.e., 5.1, 4.0, and 5.3 kcal/mol increases in acidities, respectively, and 18 ± 1 kcal/mol decreases in BDEs. These large thermodynamic differences in the anion and radical stabilities are illustrated in Scheme I for 2-piperidone (**14**) and 2-thiopiperidone (**20**).

A much smaller difference in thermodynamic effects on anions than on radical stabilities similar to that shown in Scheme I has been observed previously where a favorable orbital overlap to form a three-electron bond was found to stabilize a radical by 16 kcal/mol, whereas avoidance of a four-electron repulsion in the analogous anion was found to exert only about a 2.5 kcal/mol stabilizing effect.[19] This result and the present results follow what now appears to be a general rule: *thermodynamic effects in solution caused by structural changes are much greater on radicals than on analogous anions because the latter are leveled by solvation effects.*

(19) Bordwell, F. G.; Vanier, N. R.; Zhang, X.-M. *J. Am. Chem. Soc.* **1991**, *113*, 9856–9857.
(20) Bordwell, F. G.; Harrelson, J. A., Jr.; Lynch, T.-Y. *J. Org. Chem.* **1990**, *55*, 3337–3341.

In this and earlier papers the higher acidities of thiocarboxamides than carboxamides have been rationalized in terms of higher ground-state energies for the sulfur analogues and a superior ability of sulfur over oxygen to accommodate a negative charge in the anion.[2,20] The lower BDEs of the N–H bonds in the sulfur analogues can also be associated with higher ground-state energies and with a superior ability of sulfur over oxygen to accommodate spin density,[21,22] but in addition, there is reason to believe that the resonance energy (RE) of the heteroallylic moiety •N—C=S ↔ N=C—S• may be greater than that of the •N—C=O ↔ N=C—O• moiety. In fact, we estimate that the N–H bonds in carboxamides have BDEs that are within 1 or 2 kcal/mol of that of the N–H bond in ammonia, suggesting that very little or no RE is present, whereas the RE of the sulfur analogue may be much higher.[9]

Barton has developed a method of generating R• radicals from *N*-hydroxypyridone or *N*-hydroxy-2-thiopyridone esters (**21**) and has observed that the method is much more successful when X in **21** is sulfur rather than oxygen.[23] This is understandable when we consider that the radical **22** is 23 kcal/mol more stable when X = S than when X = O.



21 **22**

Summary and Conclusions

The 4–5.6 kcal/mol higher acidities in DMSO of 2-, 3-, and 4-aminopyridines than aniline are rationalized by the larger field/inductive (*F*) effect stabilizing the pyridylamide ions caused by replacing one of the =CH moieties in the benzene ring by the more electronegative =N moiety, together with delocalization of the negative charge in the pyridylamide ions. The acidity order 3 < 2 < 4 is rationalized by differences in delocalization and ground-state effects, and this type of explanation is also used to account for the N–H BDE order and size, i.e., 4-NC_5H_5NH–H (84 kcal/mol) < 2-NC_5H_5NH–H (87 kcal/mol) < PhNH–H (92 kcal/mol) < 3-NC_5H_5NH–H (94 kcal/mol). Whereas the field/inductive (*F*) effect lowers the heterolytic bond dissociation energy of the N–H bond in 3-aminopyridine, relative to that in aniline, by stabilizing the corresponding anion, it raises the homolytic N–H bond dissociation energy by destabilizing the corresponding radical. A similar effect was observed for the O–H bond in 3-hydroxypyridine, relative to that in phenol.

Homo-hydrogen bonding does not ordinarily occur with N–H acids in DMSO,[25] but 2- and 4-pyridones have log K_{hb} constants of 3.6 and 2.4, respectively, due to the unusually high acidity of their N–H bonds and particularly the possibility of an oxygen base taking part in homo-hydrogen bonding. (Thiopyridones fail to undergo homo-hydrogen bonding despite their higher acidities.)

The 11.4 kcal/mol greater effect in increasing radical than anion stabilities in 2-piperidone by replacing a C=O moiety by a C=S moiety is represented as being part of a general rule that thermodynamic effects in solution brought about by structural changes are much greater on radicals than on analogous anions because of the leveling effects of solvation on the anions. The

(21) Biddles, T.; Hudson, A.; Wiffen, J. T. *Tetrahedron* **1972**, *28*, 867–873.
(22) Griller, D.; Nonhebel, D. C.; Walton, J. C. *J. Chem. Soc., Perkin Trans. 2* **1984**, 1817–1821.
(23) Barton, D. H. R.; Blundell, P.; Jaszberenyi, J. Cs. *Tetrahedron Lett.* **1989**, 2341–2344.
(24) Zhang, X.-M.; Bordwell, F. G. *J. Am. Chem. Soc.*, in press.
(25) Bordwell, F. G.; Olmstead, W. N. *J. Org. Chem.* **1980**, *45*, 3299–3305.

results on relative anion and radical stabilities for 2- and 4-pyridones versus 2- and 4-thiopyridones also conform to this rule.

Experimental Section

General. NMR spectra were recorded on a Varian EM-390 spectrometer using $CDCl_3$ as solvent and Me_4Si as internal standard. Melting points were determined on a Thomas Hoover capillary melting point apparatus and are uncorrected. The procedure for electrochemical measurements has been described earlier.[4d] All potentials are irreversible and are reported with reference to the formal potential ($E_{1/2}$) of the ferrocene/ferrocenium couple, which is 0.875 V vs Ag/AgI in DMSO.

Materials. All compounds in Table I except 2-thiopiperidone were commercial samples. The purity of pK_{HA} samples was checked by thin-layer chromatography (on Eastman Chromatogram sheets No. 13181, silica gel with fluorescent indicator), NMR, melting point, or GLC. Commercial samples of 2-pyridone, 2-thiopyridone and 3-hydroxypyridine (Aldrich Chemical Co.) were recrystallized from benzene whereas 4-pyridone and 4-thiopyridone were distilled under reduced pressure.

2-Thiopiperidone was obtained by thionation of 2-piperidone (δ-valerolactam) using Lawesson's reagent, following the general method.[26] The product was purified by column chromatography over silica gel and recrystallized from hexane; mp 92–93 °C (lit.[27] mp 92–93 °C); the NMR spectrum was in agreement with literature[28] data.

Acknowledgment. This research was supported by the National Science Foundation. We thank the Gaylord Chemical Co., Slidell, LA 70569-1209, for a generous gift of DMSO.

(26) Scheibye, S.; Pedreson, B. S.; Lawesson, S.-O. *Bull. Soc. Chim. Belg.* **1978**, *87*, 229.
(27) Fuhrer, W.; Hobi, R.; Pfaltz, A. *Helv. Chim. Acta* **1974**, *57*, 1498–1505.
(28) Lien, E. J.; Chou, J. T.; Guadauskas, G. A. *Spectrosco. Lett.* **1972**, *5*, 293–305.