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Homolytic Bond Dissociation Enthalpies of the Acidic H−A Bonds Caused by Proximate Substituents in Sets of Methyl Ketones, Carboxylic Esters, and Carboxamides Related to Changes in Ground State Energies

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Abstract: Equilibrium acidities in DMSO were measured for the N−H bonds in 15 carboxamides, and the homolytic bond dissociation enthalpies (BDEs) for these bonds were estimated. For the N−H bonds in five aliphatic carboxamides, the average pK_{HA} is 25.5 and the average BDE is 108 ± 2 kcal/mol. Equilibrium acidities in DMSO of the C−H bonds for seven sets of acids in series of the type GCH_2COCH_3, GCH_2CO_2Et, and GCH_2CONR_2 and the oxidation potentials of their conjugate bases, $E_{ox}(A^-)$, where G is H, Ph, PhS, 1,3-dithianyl, Me_3N^+, Ph_3P^+, or MeCO, are also reported. For every set, there is a progressive increase in pK_{HA} and a smaller progressive cathodic shift of $E_{ox}(A^-)$, which are associated with progressive small increases in the BDEs of the acidic C−H bonds. These increases in BDEs are believed to be associated with progressive decreases in ground state energies in the order ketone > ester > amide. These results conform to a general rule that structural changes in weak acids that decrease ground state energies will tend to increase the BDEs of acidic H−A bonds, and vice versa.

Despite the prevalence of the carboxamide function in nature, relatively little is known about either the acidities of their N−H or α-C−H bonds or the homolytic bond dissociation enthalpies (BDEs) of these bonds. In 1928, the acidity constant of acetamide was reported to be $pK_{HA} = 15.1$ in aqueous solution from conductivity measurements,[1] and this value is still cited,[2] despite long-standing evidence that acidity constants above $pK_{HA} = 12$ are difficult or impossible to measure in aqueous solution.[3] For example, the pK_{HA} value of 12.4 for the O−H bond in acetaldoxime in aqueous solution[3,4] was judged to be much too low compared to the value of 28.5 measured in DMSO.[5] If the ΔpK_{HA} value of 8 units between the acidities in H_2O and DMSO for phenol[6] is taken as a benchmark for O−H acids, the pK_{HA} of the O−H bond of acetaldoxime in aqueous solution would be about 20.5, i.e., much too high to measure. For N−H acids the difference in acidities in DMSO and aqueous solutions is smaller. For example, the ΔpK_{HA} for hydrazoic acid in DMSO vs that in H_2O is 3.2 pK_{HA} units, and the ΔpK_{HA} for trifluorosulfonamide in DMSO vs that in H_2O is 3.4 units.[7] The pK_{HA} of the N−H bond in DMSO of acetamide is 25.5,[8] and that in aqueous solution is therefore probably about 3.3 units lower, i.e., about 22.

The acidity of the C−H bond in acetamide is much too weak to measure, even in DMSO. Estimates based on extrapolations from acidities of GCH_2CONR_2 derivatives, where G = Ph, PhS, or CN, place the pK_{HA} of CH_3CONR_2 derivatives at about 34−35.[9]

The pK_{HA} values for a variety of carboxamides, hydrocarbons, and the like have been combined with the oxidation potentials of their conjugate bases, using eq 1 or the like, to obtain estimates

$$\mathrm{BDE}_{HA} = 1.37pK_{HA} + 23.1E_{ox}(A^-) + 73.3 \quad \mathrm{kcal/mol} \qquad (1)$$

of the homolytic bond dissociation enthalpies of their acidic C−H or N−H bonds.[10] In this paper, we will first present the acidities and BDEs in DMSO of the N−H bonds in a variety of carboxamides. Next we will examine some remote and proximate substituent effects in related carboxylic esters and carboxamides that lead to changes in BDEs that appear to be associated with changes in ground state energies.

Results and Discussion

Structural Effects on Acidities and BDEs of Carboxamides. Acidity and BDE data for the N−H bonds in a variety of carboxamides are summarized in Table 1. Examination of Table 1 shows that changes in the nature of the alkyl groups in RCONHR have relatively little effect on the acidities of the N−H bonds. The average acidity for entries 2−6 in Table 1 is 25.5 ± 1.4 pK_{HA} units. Formamide, the first member of the series, has an acidity 2 pK_{HA} units higher than the average.

Substitution of a Me group for one of the N−H hydrogen atoms in acetamide decreases the acidity by only 0.1 pK_{HA} unit (statistically corrected); however, a similar substitution of a *t*-Bu group for one of the N−H bonds in *t*-$BuCONH_2$ results in a 2.25 pK_{HA} unit decrease in acidity, presumably due to steric inhibition of solvation.

Introduction of an *N*-Ph group into acetamide to give acetanilide causes an increase in acidity of 4.3 pK_{HA} units, an

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Table 1. Equilibrium Acidities in DMSO and Homolytic Bond Dissociation Enthalpies for the N−H Bonds of Some Carboxamides

no.	amide	pK_{HA}[a]	$E_{ox}(A^-)$[b]	H−N BDE[c]
1	$HCONH_2$	23.45	0.135 (120)	108.5
2	CH_3CONH_2	25.5[a]	−0.025 (110)	107.5
3	Me_3CCONH_2	25.5	0.045 (72)	109
4	Et_3CCONH_2	26.0	0.00 (50)	109
5	2-piperidone	26.4	0.009 (250)	109.5
6	2-pyrrolidone	24.1	0.030 (130)	107
7	$CH_3CONHMe$	25.9	−0.092 (110)	106.5
8	Me_3CCONH-*t*-Bu	28.05	−0.055 (120)	110.5
9	$CH_3CONHC_6H_5$	21.45[a]	−0.120 (84)	100
10	$CH_3CONHC_6H_4OMe$-*p*	22.1	−0.275 (90)	99
11	$CH_3CONHC_6H_4CN$-*p*	18.6	0.119 (85)	101.5
12	$C_6H_5CONH_2$	23.35[a]	0.074 (100)	107
13	C_6H_5CONH-Ph	18.8[a]	−0.069[d]	97
14	4-$MeOC_6H_4CONH_2$	24.0		
15	3-$CF_3C_6H_4CONH_2$	21.85		

[a] Reference 8. [b] Wave widths in mV are shown in parentheses. [c] Estimated by eq 1. [d] Bordwell, F. G.; Ji, G.-Z. *J. Am. Chem. Soc.* **1991**, *113*, 8398−8401.

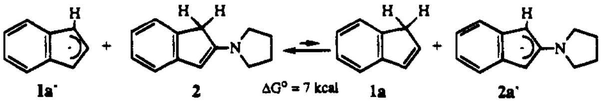
effect typical of phenyl substitutions at acidic sites, but much smaller than the effects observed for substitution of the acidic C−H bond in carbon acids, such as acetone, which is about 10 pK_{HA} units.[10a] Introduction of a *p*-MeO group into acetanilide causes a 0.6 pK_{HA} unit decrease in acidity, whereas introduction of a *p*-CN group causes a 2.9 unit increase in acidity (entries 9−11). These remote substituent effects are expected in view of the electron donor effect of *p*-MeO and electron acceptor effect of *p*-CN, which tend to destabilize and stabilize the corresponding anions, respectively. Similar substituent effects are observed on the acidity of benzamide where *N*-phenyl substitution causes a 4.8 pK_{HA} unit increase in acidity and substitution of *p*-MeO and *m*-CF_3 groups into the benzene ring cause a 0.65 pK_{HA} unit decrease and a 1.5 pK_{HA} unit increase in acidities, respectively (entries 12−15).

Further examination of Table 1 shows that the BDEs of the N−H bonds in most $RCONH_2$ carboxamides appear to fall in the range of about 106−110 kcal/mol. (Henceforth kcal/mol will be abbreviated as kcal.) The accuracy of these values is difficult to determine, however, because most cyclic voltammetric (CV) peaks for carboxamide anions are very broad. Those in Table 1 average about 100 mV, which makes the accuracy difficult to determine. A reviewer has pointed out that a peak width of 120 mV corresponds to a shift of about 140 mV (3 kcal), and that the peak width for entry 5 in Table 1 of 250 mV indicates that the potential must be shifted by at least 7 kcal, relative to E_0. Comparisons of individual N−H BDEs for carboxamides therefore cannot be made. Nevertheless, the BDEs estimated for the $RCONH_2$ carboxamides (entries 1−8 and 12 in Table 1) average 108 ± 2 kcal, and the peak widths for the CVs of two carboxamides, Me_3CCONH_2 (BDE $\simeq$ 109 kcal) and Et_3CCONH_2 (BDE $\simeq$ 109 kcal), are in the normal range (72 and 50 mV, respectively). We conclude that the BDEs for the N−H bonds in most $RCONH_2$ carboxamides are not greatly different from that in NH_3 (107−108 kcal). Substitution of one of the N−H hydrogen atoms in $RCONH_2$ carboxamides by an aryl group (entries 9, 10, 11, and 13) causes the BDE of the remaining N−H bond to decrease by about 10 kcal, which is comparable to the effects of α-Ph substitutions on the BDEs of carbon acids.[10]

Ground State Energy Effects on BDEs. In examining the effects of substituent changes on BDEs of C−H bonds in carbon acids, we have assumed that ΔBDEs, relative to that of methane, provide an estimate of radical stabilization energies (RSEs), following the generally accepted view.[11] In a recent study of *p*-substituent effects on BDE values of C−Br bonds in benzyl bromides, Clark and Wayner have interpreted their results in terms of dipole−dipole interactions between the dipole of the substituent and that of the C−Br bond that are either attractive and strengthen the bond or repulsive and weaken the bond. The ground state energies (GSEs) of the bromides were assumed to be decreased in the first instance and increased in the latter.[12] The authors suggested that similar effects might be obtained in other substrates where the reactive bond has a sizable dipole, such as phenols. Recently we have shown that the effects of most *p*-acceptor substituents on the BDEs of the O−H bonds in phenols, and also the S−H bonds in thiophenols, and the N−H bonds in anilines can indeed also be interpreted in this way.[13a] Note also that the attractive effects of the $^{\delta+}H—^{\delta-}N$ and $C^+{=}N^-$ dipoles in *p*-$CNC_6H_4NHCOCH_3$ can be considered to cause a small increase in BDE of the N−H bond, relative to that in acetanilide (compare entries 11 and 9 in Table 1), whereas the *p*-MeO group in *p*-$MeOC_6H_4NHCOCH_3$ (entry 10) causes a small decrease in the N−H BDE. If we accept these remote substituent effects on BDEs as "ground state effects", it follows that we can expect proximate substituents also to cause sizable ground state effects on BDEs.

Ground State Effects Related to Substituent Effects in Indenes. A number of authors have suggested through the years that changes in BDEs resulting from substituent changes may be subject to changes in ground state energies,[12,14] but it is usually difficult to know whether or not a decrease or increase in ground state energy has occurred, let alone identify how these changes affect the BDEs of particular bonds. Fortunately the effects of 2- and 3-substituents on the acidities and BDEs of indenes have provided a unique example where ground state effects can be evaluated for some substituents and can be related to their effects on BDEs.[15] For example, the pyrrolidino group, c-C_4H_8N, despite its donor properties, causes about a 1 kcal acidity increase when placed in the 9-position of fluorene or the α-position of acetophenone, due to its field/inductive effect, but causes a 6 kcal acidity *decrease* when placed in the 2- or 3-position of indene. The acidity decreases are due to interactions of the 2- or 3-c-C_4H_8N groups with the C=C bond in indene that stabilize the indene ground state.[15,16]

The total stabilizing ground state effect is then about 7 kcal (eq 2), which agrees well with Hine's estimate of 8.2 kcal for the C=C double-bond-stabilizing parameter of the Me_2N group.[16b] The BDE for the acidic C−H bond in 2-c-C_4H_8N-indene is estimated by eq 1 to be 83.5 kcal, which means that



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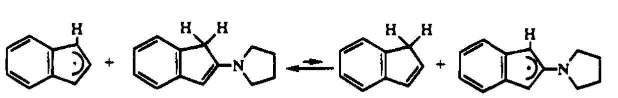
this bond is 4.8 kcal stronger than that estimated for the acidic 1-C−H bond in the parent indene (eq 2). The BDEs for 2-c-$C_5H_{10}N$, 2-c-OC_4H_8N, 2-Ph, and 2-PhS, donor-substituted indenes have also been estimated to strengthen the acidic 1-C−H bonds (by 3.8, 4.1, 0.6, and 1.5 kcal, respectively[15]).

These results show that a donor substituent, such as the pyrrolidino group at the 2-position of indene, can indirectly cause a 6.2 kcal decrease in the heterolytic bond energy (acidity) of the C−H bond in the adjacent 1-position and a 4.8 kcal increase in the homolytic enthalpy (BDE) of this bond (eqs 2 and 3).

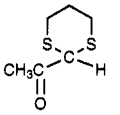
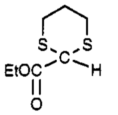
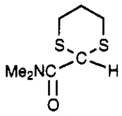


3· 4 ΔBDE = 4.8 kcal 3 4· (3)

These changes in acidity and in BDE are both clearly associated with a decrease in the ground state energy of the 2-substituted indene, relative to that of indene. The 1-C−H bond in indene is both allylic and benzylic so should be particularly susceptible to structural changes that affect its bond strength. The observation of increases in BDEs of the acidic C−H bond in indenes caused by decreases in ground state energies resulting from the introduction of donor substituents at the 2-position is believed to be an example of a general relationship between the BDEs of H−A bonds in weak acids and ground state energies. Thus, it seems reasonable to expect the following general rule to hold: structural changes that decrease ground state energies in a series of structurally related weak acids will tend to strengthen the acidic H−A bonds, causing their BDEs to increase, and structural changes that increase the ground state energies in such a series will tend to weaken the acidic H−A bonds, causing their BDEs to decrease. This rule appears to hold not only for the BDEs of remotely substituted phenols, anilines, and thiophenols[13a] but also in other instances.[13b−e] In the section that follows we apply the rule to proximate structural changes in seven weak acid series that cause changes in ground state energies and in the BDEs of acidic C−H bonds.

Application of the GSE−BDE Rule to Various Methyl Ketone−Carboxylic Ester−*N,N*-Dimethylcarboxamide Series. The structural changes resulting from the replacement of the methyl group in a methyl ketone by an OEt or NMe_2 group converts the simple ketone function into a more stable conjugated function, i.e., a carboxylic ester or carboxamide. Wheland estimated that the conjugated functions in ethyl acetate and acetamide have about the same resonance energies (16−18 kcal).[17] Theoretical calculations in the period 1987−1990 suggested, however, that resonance in carboxamides was negligible,[18a,b] but more recent calculations indicate that the π-delocalization energy in the carboxamide function is about 15 kcal,[18c] in rough agreement with Wheland's estimate. These structural changes should therefore lead to progressive decreases in the ground state energies of a series of weak acids consisting of methyl ketones, where the resonance of the methyl group with the carbonyl group is small compared to that of the OEt and NMe_2 groups in the corresponding carboxylic ethyl esters and *N,N*-dimethylcarboxamides. According to the GSE−BDE rule, these progressive decreases in ground state energies should lead to progressive increases in the BDEs of the acidic C−H bonds, assuming that the better donor properties of NMe_2 than OEt would make the carboxamides more stable than the esters. This idea has been tested by estimating the BDEs for seven sets of GCH_2COMe−GCH_2CO_2Et−GCH_2CONMe_2 combinations, where G is H, Ph, PhS, 1,3-dithianyl, Me_3N^+, Ph_3P^+, and CH_3CO. The results are summarized in Table 2.

Table 2. Effects on pK_{HA} and BDE Values in DMSO of the Replacement of Methylcarbonyl Functions in Ketones by Alkoxycarbonyl or (Dialkylamino)carbonyl Functions

no.	acid	pK_{HA}[a]	$E_{ox}(A^-)$[b]	BDE[c]
1	CH_3COCH_3	26.5	−0.674	94
2	CH_3CO_2Et	~30		~96[d]
3	CH_3CONMe_2	~35		~98[e]
4	$PhCH_2COCH_3$	19.8	−0.753	82
5	$PhCH_2CO_2Et$	22.6	−0.879	84
6	$PhCH_2CONH_2$	24.7	−0.937	85.5
7	$PhCH_2CONMe_2$	26.6	−1.023	86
8	$PhSCH_2COCH_3$	18.85	−0.649	84
9	$PhSCH_2CO_2Et$	21.2	−0.715	86
10	$PhSCH_2CONH_2$	23.0	−0.350	96.5
11	$PhSCH_2CON$-c-C_4H_8	26.1[f]	−0.961[f]	86.8
12	$PhSCH_2CONMe_2$	25.9	−0.934[f]	87.2
13		18.4[f]	−0.916[f]	77.5
14		20.9	−0.951	80.0
15		27.0	−1.094	85.0
16	$Me_3N^+CH_2COCH_3$	16.3	0.047	96.5
17	$Me_3N^+CH_2CO_2Et$	20.0	−0.141	97.5
18	$Me_3N^+CH_2CONMe_2$	24.9	−0.383	98.5
19	$Ph_3P^+CH_2COCH_3$	7.1	0.571	96.3
20	$Ph_3P^+CH_2CO_2Et$	8.50	0.553	97.7
21	$Ph_3P^+CH_2CONMe_2$	12.6[f]	0.323[f]	98.0
22	$Ph_3P^+CH_2CON$-c-C_4H_8	12.2[f]	0.278[f]	96.4
23	$CH_3COCH_2COCH_3$	13.3	+0.006	91.6
24	$CH_3COCH_2CO_2Et$	14.2	+0.005	92.9
25	$CH_3COCH_2CONMe_2$	18.2[f]	−0.230[f]	92.9

[a] Data reported in earlier publications from this laboratory unless otherwise noted. [b] Irreversible potentials measured by cyclic voltammetry under the conditions previously described and referenced to the Fc/Fc^+ couple. [c] Calculated by eq 1 unless otherwise noted. [d] Average of a value estimated by extrapolation and that for $Ph_3P^+CH_2CO_2Et$.[19] [e] Assumed to be equal to that for $Ph_3{}^+CH_2CONMe_2$. [f] This work.

Examination of the data in Table 2 shows that the BDEs of the acidic C−H bonds generally increase in the order GCH_2COMe < GCH_2CO_2Et < GCH_2CONMe_2, which is the expected order of decreasing ground state energies. The BDE order remains the same throughout Table 2 despite the variation in BDE of the parent ketone function from 77 kcal in 2-acetyl-1,3-dithiane to 96 kcal for $Ph_3P^+CH_2COMe$. The pK_{HA} and BDE data for the simplest series, acetone, ethyl acetate, and *N,N*-dimethylacetamide (entries 1−3), are not easy to obtain. Acetone alone in this series is acidic enough to be measured in DMSO. The conjugate base of ethyl acetate is unstable in

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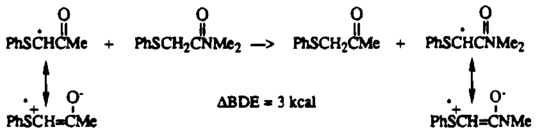
DMSO, apparently due to rapid loss of ethoxide ion, and *N,N*-dimethylacetamide is much too weak an acid to measure in DMSO. Reasonably good pK_{HA} values for CH_3CO_2Et and CH_3CONMe_2 can be obtained by extrapolation, however,[9] and the BDEs can be estimated from those for $Ph_3P^+CH_2CO_2Et$ and $Ph_3P^+CH_2CONMe_2$.[19]

Introduction of an α-Ph group (G) into acetone, ethyl acetate, acetamide, and *N,N*-dimethylacetamide (entries 4−7 in Table 2) increases their acidities to a point where all members of the series can be measured in DMSO, the oxidation potentials of the conjugate bases can be measured by cyclic voltammetry, and eq 1 can be used to estimate the BDEs. The acidities of the parent compounds are increased by an average of about 7.5 pK_{HA} units (10.3 kcal) by α-phenyl substitution, and the BDEs are decreased by about 13 kcal.

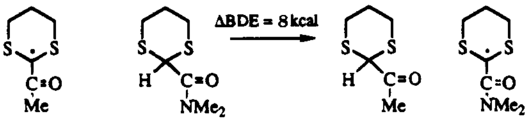
Introduction of α-phenylthio groups into acetone, ethyl acetate, and *N,N*-dimethylacetamide has effects on acidities and BDEs similar to those observed for α-phenyl substitutions. The acidities (entries 8−12 in Table 2) increase by an average of 10.6 kcal, relative to the parents, and the BDEs decrease by about 10 kcal. The effect of α-PhS in decreasing the BDE is only slightly smaller than that of an α-Ph group. Both of these effects are believed to be due to delocalization of the odd electron in the corresponding radicals by interaction with a lone pair on sulfur. In the $PhSC^{\bullet}HCOCH_3$ radical, and related radicals, the odd electron is delocalized. The ΔBDE (∼3 kcal; eq 4) for the ketone vs amide is slightly smaller than in the series where G = Ph (ΔBDE = 4 kcal).



(4)

The BDE for $PhSCH_2CONH_2$ of 96.5 kcal (entry 10) is clearly out of line with the BDEs of the acidic C−H bonds in the other substrates. For this carboxamide the more acidic hydrogen atom must be that situated on nitrogen rather than that situated on carbon.

The effect of the two sulfur atoms in weakening the acidic C−H bonds in the 2-substituted 1,3-dithianes (entries 13−15) is substantially greater (ΔBDE ≃ 8 kcal; eq 5) than for the



(5)

corresponding effects of a single PhS substituent in entries 8, 9, and 12, respectively (ΔBDE = 4 kcal). This is consistent with the effects on the BDEs observed for similar 2-benzoyl-1,3-dithianes compared to acyclic analogues of the type $(RS)_2CHCOPh$.[20] In the tertiary radicals $(RS)_2C^{\bullet}COPh$, the stereoelectronic, radical-stabilizing effects of the sulfur atoms are attenuated by crowding, which is relieved in the cyclic analogues.[20]

The effect of an α-Me_3N^+ group in increasing the acidity of acetone, ethyl acetate, and *N,N*-dimethylacetamide is slightly greater than that of either an α-Ph or α-PhS group but is due entirely to a field/inductive effect. The effect of the α-Me_3N^+ group on the BDE is, however, opposite to that of α-Ph or α-PhS, i.e., it is slightly bond strengthening. It follows that the effect of electron withdrawal on the corresponding radicals is destabilizing. (Note that the BDE of the $Me_3N^+CH_2COCH_3$ is 2.5 kcal greater than that of CH_3COCH_3.) Nevertheless, the order of effects on BDE for entries 16−18 is the same as for the other substrates. The effects of α-Ph_3P^+ groups in decreasing the pK_{HA} values are similar to those of α-Me_3N^+ groups, but much larger.[19] The effects of Ph_3P^+ on the BDEs in the ketone−ester−amide series are essentially the same as those of the Me_3N^+ group, however. The strongly acidifying CH_3CO group is weakly radical stabilizing, and the ΔBDEs along the ketone−ester−amide series are very small.

Analysis of the Effects of Structural Changes in the Ketone−Ester−Amide Series in Terms of Eq 1. According to eq 1, there are two factors determining the changes in BDEs with structural changes, namely pK_{HA} and $E_{ox}(A^-)$ values. Earlier studies have shown that, within a family of weak acids, such as meta-substituted fluorenes, increases in pK_{HA} values cause nearly equivalent shifts in $E_{ox}(A^-)$ values to more negative potentials, i.e., a 1 kcal increase in pK_{HA} causes about a 1 kcal cathodic shift in $E_{ox}(A^-)$. The frequent observation of such correlations has shown that there is an intrinsic linear relationship between pK_{HA} and $E_{ox}(A^-)$ with a slope near unity.[13d] This relationship is perturbed, however, when structural features are present that stabilize or destabilize the $A^{\bullet}$ radicals being formed. For example, points for *p*-donors, such as 3-MeO and 3-MeS in fluorenes, deviate from the linear relationship because they cause larger cathodic shifts in $E_{ox}(A^-)$ than predicted by the change in pK_{HA}. A progressive decrease in ground state energies along the series GCH_2COCH_3, GCH_2CO_2Et, GCH_2CONMe_2 also perturbs this intrinsic relationship by increasing the pK_{HA} values more than predicted by the cathodic shifts in $E_{ox}(A^-)$ values. Examination of the entries in the seven sets of data in Table 2 shows that in every instance the progressive increases in BDEs along a given series are associated with progressive increases in pK_{HA} values that are larger than the progressive cathodic increases in $E_{ox}(A^-)$ values. For example, when G is Ph, the increases in pK_{HA} values in changing from $PhCH_2COCH_3$ to $PhCH_2CO_2Et$ and $PhCH_2CONMe_2$ are 3.8 and 10.6 kcal, respectively, compared to cathodic shifts in $E_{ox}(A^-)$ values of 2.9 and 6.2 kcal, respectively.

Summary and Conclusions. Earlier results for substituted indenes provided a unique opportunity to observe the effects of structural changes on the BDEs of the acidic H−A bond of a weak acid where the effects of these structural changes on ground state energies were known. The conclusion drawn was that, as a rule, decreases in ground state energies in weak acids tend to increase the BDEs of the acidic H−A bonds, and vice versa. This rule has now been tested further. For several series of acids, GCH_2COCH_3, GCH_2CO_2Et, GCH_2CONMe_2, it was assumed that the ground state energies decreased progressively, due to increases in conjugation, as the CH_3 group in the ketone was replaced by an OEt group and then by an NMe_2 group. For seven sets of data where G was changed from H to Ph, PhS, c-$(CH_2)_3S_2CH$, Me_3N^+, Ph_3P^+, or CH_3CO, the BDEs increased progressively along the ketone−ester−amide series. This is consistent with the rule deduced in the indene series that decreases in ground state energies for a series of acids will tend to increase the BDEs of the acidic H−A bonds. The differences in BDEs are small because the changes in ground state energies are small throughout Table 2, despite overall changes in acidities that cover about 31 kcal and differences in overall BDEs that cover about 21 kcal, but the order is consistent.

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[19] Zhang, X.-M.; Bordwell, F. G. *J. Am. Chem. Soc.* **1994**, *116*, 968−972 and references cited therein.

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Experimental Section

General Procedure. NMR spectra were recorded on a Varian Gemini XL-300 or a Varian XLA 400 spectrometer. Melting points were measured on a Thomas Hoover capillary melting point apparatus and are uncorrected.

Materials. Bromoacetyl bromide was a product of Eastman Organic Chemicals, and 1,3-dithiane was obtained from Aldrich Chemical Co. The water contained in a 80% *N,N*-dimethylacetylacetamide aqueous solution (Aldrich) was removed by azeotropic distillation using cyclohexane. A pure sample of amide was obtained as a colorless liquid (bp 86−87 °C/3.0 τ) by distillation.

Bromo-*N,N*-dimethylacetamide. Gaseous dimethylamine (9.6 g, 0.21 mol) was introduced during 1 h at 0−10 °C into a 100 mL of anhydrous ether solution containing 20 g (0.1 mol) of bromoacetyl bromide. The precipitate was removed by filtration, and the solvent was evaporated. The crude product was distilled under reduced pressure, yielding 9.1 g of a colorless liquid (54%), bp 85−87 °C/1.8 τ (lit.[21] bp 63−65 °C/1 τ).

(Triphenylphosphonio)-*N,N*-dimethylacetamide Bromide. Bromo-*N,N*-dimethylacetamide (3.1 g, 19.3 mmol) was added dropwise to a 20 mL of anhydrous acetonitrile solution containing 5.0 g (19.3 mmol) of triphenylphosphine. The solution was refluxed for 2 h, the solvent was removed, and the crude product was recrystallized from acetone to give 5.2 g of colorless crystals (64% yield), mp 198−200 °C. ^{1}H NMR ($CDCl_3$): δ 2.82 (3H, s, NCH_3), 3.39 (3H, s, NCH_3), 5.53 (1H, s, CH_2CO), 5.58 (1H, s, CH_2CO), 7.5−7.9 (15H, m, Ar).

(Triphenylphosphonio)-*N,N*-dimethylacetamide Nitrate. An anhydrous acetonitrile solution (5 mL) of (triphenylphosphonio)-*N,N*-dimethylacetamide bromide (0.580 g, 1.35 mmol) was mixed with an acetonitrile solution of $AgNO_3$ (0.230 g, 1.35 mmol), and the mixture was allowed to stir for 30 min. The precipitate was removed by filtration, and the solution was diluted with 10 mL of acetone to yield 0.4 g of a crystalline solid. The crude product was purified by recrystallization from acetone/acetonitrile, mp 158−159 °C. ^{1}H NMR ($CDCl_3$): δ 2.81 (3H, s, NCH_3), 3.20 (3H, s, NCH_3), 5.23 (1H, s, CH_2CO), 5.27 (1H, s, CH_2CO), 7.5−7.9 (15H, m, Ar). Anal. Calcd for $C_{22}H_{23}N_2O_4P$: C, 64.39; H, 5.65; N, 6.83. Found: C, 64.16; H, 5.50; N, 6.90.

α-(Phenylthio)-*N,N*-dimethylacetamide.[21] Bromo-*N,N*-dimethylacetamide (1.66 g, 10 mmol) was added to a suspension of PhSNa (1.32 g, 10 mmol) in 30 mL of acetone, and the mixture was refluxed for 2 h. After the precipitate (NaBr) was removed by filtration, the solvent was removed by rotavap and the crude product was purified by distillation to give 1.2 g of a colorless liquid (60% yield), bp 157−160 °C/0.4 τ. ^{1}H NMR ($CDCl_3$): δ 2.95 (3H, s, NCH_3), 3.03 (3H, s, NCH_3), 3.75 (2H, s, CH_2CO), 7.2−7.5 (5H, m, Ar).

2-Acetyl-1,3-dithiane was prepared by the method of Seebach and Corey.[22] A hexane solution containing *n*-butyllithium (3.7 mL, 2.5 M, 9.1 mmol) was added into 40 mL of a dry THF solution containing 1.3 g (8.3 mmol) of 1,3-dithiane, and the combined solution was stirred for 30 min. The resulted lithium dithianate solution was added dropwise to 25 mL of dry ethyl acetate during 30 min at −70 to −78 °C. The solution was allowed to warm up to 0 °C, and 20 mL of a saturated ammonium chloride aqueous solution was added. The organic layer was separated and then dried by $CaCl_2$. A fractional distillation gave 0.6 g (45% yield) of a colorless liquid, bp 105−107 °C/1.8 τ. ^{1}H NMR ($CDCl_3$): δ 2.0 (2H, m, CH_2), 2.3 (3H, s, CH_3), 2.6 (2H, m), 3.15 (2H, m), 4.26 (1H, SCHS).

(Phenylthio)acetopyrrolidide. A solution containing 40 g of bromoacetyl bromide (0.2 mol) in 300 mL of diethyl ether was chilled to 0 °C. A solution containing 28 g (0.4 mol) of pyrrolidine in 50 mL of Et_2O was added dropwise. A two-phase solution was formed, and the top phase was then collected. After the removal of the solvent, 10 g of bromoacetopyrrolidide (26% yield) was obtained as a crystalline solid. In a 200 mL round-bottom flask, bromoacetopyrrolidine (5 g) and equimolar amounts of PhSH and Na_2CO_3 were mixed in 100 mL of acetone. The solution was gently refluxed for 2 h, the mixture was allowed to cool to the room temperature, and 30 mL of H_2O was added. The solution was extracted with diethyl ether, and the combined ether solution was washed with aqueous sodium bicarbonate and dried over Na_2SO_4. (Phenylthio)acetopyrrolidide (2 g, 34%) was obtained as a white solid after removal of the solvent. Further purification was carried out by a recrystallization in ethanol, mp 80−82 °C. ^{1}H NMR ($CDCl_3$); δ 1.85 (2H, m), 1.92 (2H, m), 3.46 (4H, m), 3.67 (2H, s), 7.30 (3H, m), 7.45 (m, 2H). Anal. Calcd for $C_{11}H_{15}NOS$: C, 65.12; H, 6.83; N, 6.33. Found: C, 64.95; H, 6.79; N, 6.34.

Table 3. Equilibrium Acidities Determined by the Overlapping Indicator Method

compd	HIn (pK_a)	pK_a(HA)	pK_a (av)
$C_3H_6S_2CHCOCH_3$	MCLPHF (16.8)	18.41 ± 0.06	
	MCLPHF (16.8)	18.40 ± 0.03	18.40
$Ph_3P^+CH_2CONMe_2$	ESO2FH (12.3)	12.50 ± 0.06	
	ESO2FH (12.3)	12.61 ± 0.03	12.55
$PHSCH_2CON$-c-C_4H_8	TP2H (25.6)	26.06 ± 0.06	
	TP2H (25.6)	26.15 ± 0.04	
	HB1 (26.1)	26.20 ± 0.05	26.1
$Ph_3P^+CH_2CON$-c-C_4H_8	HZFO2 (12.95)	12.13 ± 0.03	
	HZFO2 (12.95)	12.20 ± 0.04	12.1
Me_3CCONH_2	MC1PXH (26.6)	25.70 ± 0.05	
	HB1 (26.1)	25.31 ± 0.06	25.5
Me_3CCONH-*t*-Bu	PXH (27.9)	27.95 ± 0.01	
	PXH (27.9)	28.15 ± 0.02	28.05
$CH_3CONHC_6H_4OMe$-*p*	FH (22.6)	22.09 ± 0.03	
	FH (22.6)	22.12 ± 0.02	22.1
$CH_3CONHC_6H_4CH$-*p*	PFH (17.9)	18.58 ± 0.03	18.6
	CNAH (18.9)	18.61 ± 0.01	
Et_3CCONH_2	TPzH (25.6)	25.95 ± 0.02	26.0
	T-BuFH (24.35)	26.02 ± 0.01	

(Triphenylphosphonio)acetopyrrolidide Nitrate. Triphenylphosphine (8.9 g, 34 mmol) in 30 mL of diethyl ether was added to a solution of 6.55 g (34 mmol) of bromoacetopyrrolidide in 100 mL of diethyl ether, to give $Ph_3P^+CH_2CONC_4H_8Br^-$, as a white solid (13 g, 84% yield). The bromide salt (3 g) was dissolved in 20 mL of 1:1 H_2O/EtOH, and a solution containing 1 equiv of $AgNO_3$ in H_2O was added. A slight excess of $AgNO_3$ was added to ensure that all of the bromide ion was removed. The AgBr precipitate was separated by filtration, and the filtrate was treated with water to give white crystals of nitrate, mp 205 °C (dec). ^{1}H NMR ($CDCl_3$): δ 1.79 (2H, pent, CH_2), 1.91 (2H, pent, CH_2), 3.30 (2H, t, NCH_2), 3.71 (2H, t, NCH_2), 5.11 (2H, d, PCH_2), 7.4−7.8 (15H, m, PPh_3). ^{13}C NMR ($CDCl_3$): δ 23.38, 26.04, 32.37, 33.25, 46.35, 47.71, 118.72, 119.91, 128.40, 128.57, 129.87, 130.4, 131.94, 132.07, 133.70, 133.83, 134.48, 134.52, 161.70, 161.75. Anal. Calcd for $C_{24}H_{25}N_2O_4P$: C, 66.03; H, 5.78; N, 6.42. Found: C, 66.87; H, 5.90; N, 6.60.

Equilibrium Acidities. The equilibrium acidities in DMSO were determined by the overlapping indicator method as described previously.[7] The results, together with the indicator used, are summarized in Table 3.

Oxidation Potentials. The oxidation potentials were determined by conventional cyclic voltammetry as described previously.[10b] The working and auxiliary electrodes are platinum. The reference electrode is Ag/AgI, and all of the reported potentials are referenced to the ferrocene/ferrocenium (Fc/Fc$^+$) couple.

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