

## Coupling of Acidities and Oxidation Potentials To Estimate Homolytic Bond Dissociation Energies and Radical Stabilization Energies

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The  $pK_{HA}$  and  $E_{ox}(A^-)$  values of 29  $\alpha$ -substituted derivatives of acetone and acetophenone have been compared with those of the parents. The  $\Delta pK_{HA}$  and  $\Delta E_{ox}(A^-)$  values are summed to obtain  $\Delta BDE$  values, which are equated with the radical stabilization energies (RSEs) of the corresponding radicals. Since the two equilibria defining  $pK_{HA}$  and  $E_{ox}(A^-)$  are linked to one another, either changes in  $pK_{HA}$  or  $E_{ox}(A^-)$  may play the major role in deciding the size of the RSEs caused by making the structural change. The largest RSE observed (21 kcal/mol) was for an  $\alpha$ -R<sub>2</sub>N substituent, which was caused almost entirely by a change in  $\Delta E_{ox}(A^-)$ . But the next largest RSE (10–11 kcal/mol) was for a Ph or a PhS substituent, which was caused largely by a decrease in  $\Delta pK_{HA}$ . Similar analyses were made for *N*-substituent effects on the RSEs of 11 derivatives of acetamide, benzamide, and benzenesulfonamide and for replacing the oxygen atom in the carboxamides by a sulfur atom. Finally, the effects of polyfluorination of hydrocarbons were shown to cause destabilization of the radicals formed by loss of a hydrogen atom from the acidic function.

### Introduction

During the past five years we have used eq 1 to estimate

$$BDE_{HA} = 1.37pK_{HA} + 23.1E_{ox}(A^-) + C \quad (1)$$

homolytic bond dissociation energies (BDEs) for the acidic H–A bonds in several hundred weak acids, HA.<sup>1</sup> We have assumed, following O'Neal and Benson and later workers in the field, that  $\Delta BDEs$ , relative to the parent in a family (e.g., H<sub>3</sub>C–H, 105 kcal/mol for the H–C bond in GCH<sub>2</sub>–H methanes) can be equated with the relative stabilization energies of the corresponding A<sup>•</sup> radicals (RSEs).<sup>2</sup> (Henceforth kcal/mol will be abbreviated as kcal.) The assumption of O'Neal and Benson has been challenged, however: (a) by R uchardt, who suggested that  $\Delta BDEs$  may be associated with destabilization of the intact molecule rather than with stabilization of the corresponding radicals,<sup>3</sup> (b) by Dust and Arnold, who concluded that since the BDE of a C–H bond is the difference in the heat of formation of the radical and the initial molecule, the effect of structural changes on BDEs cannot be attributed to the stability of the radical alone,<sup>4</sup> and (c) most importantly, by Clark and Wayner, who recently provided convincing experimental evidence to show that the size of the BDEs for the C–Br bonds in para-substituted benzyl bromides, which were measured by photoacoustic calorimetry, were associated with ground state electrostatic interactions between the polar C<sup>δ+</sup>–Br<sup>δ-</sup> bonds and the remote substituents in the intact molecule.<sup>5</sup> Also, in a recent review Sustmann and Korth have discounted the usefulness of


our  $\Delta BDEs$  in assessing the importance of "captodative" effects on the stabilities of carbon-centered radicals because ground state effects have not been taken into account.<sup>6</sup> It is important to note, however, that in our method  $\Delta BDE$  is the result of the coupling of two equilibria:  $H-A \rightleftharpoons H^+ + A^- \rightleftharpoons H^{\bullet} + A^{\bullet}$ . Therefore, the effect of changes in ground state energies in HA will be spread over two equilibria. Ordinarily these effects on acidities will be small compared to their effects on anion stabilities. As a consequence of the coupling of these equilibria, anion basicities are linked to radical stabilities as measured by  $\Delta E_{ox}(A^-)$  values. Furthermore, we have found that there is an intrinsic relationship between anion basicities ( $pK_{HA}$ ) and  $E_{ox}(A^-)$  values. Thus, in nine different families of carbon acids where BDEs remain nearly constant, e.g., 2- and 2,7-substituted fluorenes,<sup>7a</sup> triphenylmethanes (*p*-GC<sub>6</sub>H<sub>4</sub>CHPh<sub>2</sub>),<sup>7g</sup> and the like,<sup>7</sup> there is a linear correlation between  $E_{ox}(A^-)$  and  $pK_{HA}$  with a slope near unity when both axes are expressed in kcal. The  $E_{ox}(A^-)$  values become more negative as the anion basicity increases and vice versa. *This intrinsic relationship must be present also when BDE is not constant, but will then be perturbed by the presence of radical stabilizing or destabilizing effects that lead to differences in BDEs.* It is the purpose of this paper to analyze some of our data to show how the interplay between  $\Delta pK_{HA}$  and  $\Delta E_{ox}(A^-)$  values combine to give new insights into how  $\Delta BDE$  values provide measures of radical stabilities.

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**Table I.** Effects of  $\Delta pK_{HA}$  and  $\Delta E_{ox}(A^-)$  Values on  $\Delta BDEs$  for Structural Changes in Ketones<sup>a</sup>

no.	ketone	$pK_{HA}$	$\Delta pK_{HA}^b$	$\Delta E_{ox}(A^-)^c$	$\Delta BDE = RSE^d$	ref
1	CH <sub>3</sub> COCH <sub>3</sub>	36.3	(0.0)	(0.0)	(0.0)	
2	PhCH <sub>2</sub> COCH <sub>3</sub>	27.1	9.9	1.8	11.7	
3	PhCH <sub>2</sub> COCH <sub>2</sub> Ph	25.6	10.9	0.1	11.0	
4	Ph <sub>2</sub> CHCOCH <sub>3</sub>	26.5	10.9	2.1	13.0	
5	MeCH <sub>2</sub> COCH <sub>2</sub> Me	37.1	-0.6	6.4	5.8	
6	Me <sub>2</sub> CHCOCHMe <sub>2</sub>	38.6	-1.7	11.4	9.7	
7	<i>t</i> -BuCOCH <sub>3</sub>	37.9	-1.0	1.7	0.7	
8	CH <sub>3</sub> COCH <sub>2</sub> SO <sub>2</sub> Ph	17.1	19.9	-24.7	-4.8	
9	PhCOCH <sub>3</sub>	33.8	2.9	-1.5	1.4	
	PhCOCH <sub>3</sub>	33.8	(0.0)	(0.0)	(0.0)	
10	PhCOCH <sub>2</sub> CH <sub>2</sub> Ph	32.2	1.8	2.7	4.5	
11	PhCOCH <sub>2</sub> Me	33.4	0.6	4.8	5.4	
12	PhCOCHMe <sub>2</sub>	36.0	-1.5	9.1	7.5	
13	PhCO- 	36.6	-2.1	7.9	5.7	
14	PhCOCH <sub>2</sub> OMe	31.3	2.7	10.2	12.9	8
15	PhCOCH <sub>2</sub> NMe <sub>2</sub>	32.3	1.7	19.4	21.1	8
16	<i>c</i> -C <sub>6</sub> H <sub>10</sub> NCH <sub>2</sub> COPh	32.2	1.8	19.2	21.0	7c
17	<i>c</i> -C <sub>6</sub> H <sub>10</sub> NCH(Ph)COPh	29.5	5.0	12.1	17.1	7c
18	( <i>c</i> -C <sub>6</sub> H <sub>10</sub> N) <sub>2</sub> CHCOPh	35.0	-0.6	20.7	20.1	10
19	<i>c</i> -C <sub>6</sub> H <sub>9</sub> N <sup>+</sup> CH <sub>2</sub> COPh	14.6	19.4	-13.2	6.2	9
20	PhSCH <sub>2</sub> COPh	23.4	10.6	1.0	11.6	10
21	(PhS) <sub>2</sub> CHCOPh	16.6	17.9	-6.0	11.9	10
22	PhSeCH <sub>2</sub> COPh	25.5	8.5	0.2	8.7	10
23	PhCOCH <sub>2</sub> SP <sub>7</sub>	27.1	6.9	5.7	12.6	10
24	PhCOCH <sub>2</sub> SCH <sub>2</sub> Ph	26.0	8.0	4.6	12.6	10
25	PhCOCH <sub>2</sub> Ph	24.2	9.8	0.9	10.7	
26	PhCOCHPh <sub>2</sub>	25.7	8.8	1.9	10.7	
27	PhCOCH <sub>2</sub> COPh	18.3	15.7	-15.6	0.1	
28	PhCOCH <sub>2</sub> COMe	19.4	14.6	-13.3	1.3	
29	PhCOCH <sub>2</sub> CN	14.0	20.0	-16.6	3.4	
30	PhCOCH <sub>2</sub> SO <sub>2</sub> Ph	15.6	18.4	-20.5	-2.1	
31	PhCOCH <sub>2</sub> N <sup>+</sup> Me <sub>3</sub>	20.0	14.0	-17.5	-3.5	9

<sup>a</sup> Data taken from Bordwell, F. G.; Harrelson, J. A., Jr. *Can. J. Chem.* 1990, 68, 1714-1718, unless otherwise noted. All values are in kcal/mol. <sup>b</sup> Statistically corrected for the number of acidic hydrogen atoms. For example,  $\Delta pK_{HA}$  for Ph<sub>2</sub>CHCOCH<sub>3</sub> is corrected for the ratio of acidic hydrogen atoms ( $\log 6 \approx 0.77$ ) by adding  $0.77 \times 1.37 = 1.05$  kcal. <sup>c</sup> Irreversible oxidation potentials measured in DMSO relative to the Fc/Fc<sup>+</sup> couple, as described previously in ref 1. <sup>d</sup>  $\Delta BDE = RSE = \Delta pK_{HA} + \Delta E_{ox}(A^-)$ .

## Results and Discussion

An analysis of the effects of structural variations for  $\alpha$ -substituted derivatives of acetone and acetophenone on  $\Delta pK_{HA}$ ,  $\Delta E_{ox}(A^-)$ , and  $\Delta BDE$  (RSE) values is presented in Table I.

Column 3 in Table I lists the  $pK_{HA}$  values for 31 ketones (taken from the references given) multiplied by 1.37 to convert them to kcal. Column 4 gives  $\Delta pK_{HA}$  values, relative to that of a parent (acetone or acetophenone) statistically corrected for the number of acidic hydrogen atoms. Column 5 gives  $\Delta E_{ox}(A^-)$  values for the oxidation potentials of the enolate ions relative to that of the parent indicated. Column 6 gives the sum of the  $\Delta pK_{HA}$  and  $\Delta E_{ox}(A^-)$  values; the  $\Delta BDEs$  thus obtained are assumed to be equal to the stabilization energies (RSEs) of the corresponding radical, relative to that of the parent.

**$\alpha$ -Phenyl Effects on RSEs.** The second entry in Table I shows the effect of an  $\alpha$ -Ph group on the  $pK_{HA}$ ,  $E_{ox}(A^-)$ , and BDE relative to that of acetone. (The BDE of acetone is estimated to be 94 kcal by eq 1).<sup>1</sup> The  $\Delta pK_{HA}$  is 9.9 kcal and the  $\Delta E_{ox}(A^-)$  value is 1.8 kcal, leading to an RSE of 11.7 kcal. (The experimental error in these values is estimated to be about  $\pm 1$  kcal.) In view of the direct intrinsic relationship between anion basicity and  $E_{ox}(A^-)$  discussed in the introduction one would expect the decrease in basicity of the CH<sub>3</sub>COCHPh<sup>-</sup> anion relative to the CH<sub>3</sub>COCH<sub>2</sub><sup>-</sup> anion to cause a 9.9-kcal (0.429 V) shift in

$E_{ox}(A^-)$  to a more positive potential. Instead, the shift is 1.8 kcal (0.078 V) to a more negative potential. We interpret this to mean the radical is being stabilized by about 11 kcal as it is being formed on the electrode as a consequence of the odd electron being delocalized into the  $\alpha$ -phenyl ring. It follows that the effects of structural changes on  $\Delta pK_{HA}$ , as well as those on  $\Delta E_{ox}(A^-)$ , may be linked to radical stabilization and destabilization effects. Introduction of a second Ph group at the  $\alpha'$ -position (entry 3) causes a further small increase in acidity, but this is counteracted by a lesser-negative shift in  $E_{ox}(A^-)$ , and  $\Delta BDE = RSE = 11.0$  kcal). On the other hand, introduction of a second Ph group on the same carbon atom (entry 4) causes no change in acidity, but  $\Delta E_{ox}(A^-)$  increases from 0.1 to 2.1 kcal, and the net RSE increases to 13 kcal. Steric inhibition of resonance is expected to be appreciable in the Ph<sub>2</sub>CHCOCH<sub>3</sub> radical. (Note that the RSEs for the PhCH<sub>2</sub><sup>•</sup>, Ph<sub>2</sub>CH<sup>•</sup>, and Ph<sub>3</sub>C<sup>•</sup> are 17, 23, and 24 kcal, respectively.<sup>1</sup>) The  $\alpha$ -Ph effects on the  $\Delta pK_{HA}$  and  $\Delta E_{ox}(A^-)$  values of acetophenone follow the same pattern (entry 25) and add up to an RSE of ca. 10 kcal. A second  $\alpha$ -Ph (entry 26) causes a decrease in acidity but the RSE remains at about 10 kcal. These phenyl effects on the RSEs of the CH<sub>3</sub>COCH<sub>2</sub><sup>•</sup> and PhCOCH<sub>2</sub><sup>•</sup> radicals are much smaller than the 17 kcal of PhCH<sub>2</sub><sup>•</sup> vs the CH<sub>3</sub><sup>•</sup> radical, but this is expected since the CH<sub>3</sub>COCH<sub>2</sub><sup>•</sup> and PhCOCH<sub>2</sub><sup>•</sup> radicals are about 11-12 kcal more stable than the methyl radical, so we can expect a leveling effect to be operative when an  $\alpha$ -Ph group is introduced.

**$\alpha$ -Alkyl Effects on RSEs.** The RSEs of alkyl radicals based on  $\Delta BDEs$  of the C-H bonds of the corresponding hydrocarbons increase in the order (kcal): CH<sub>3</sub><sup>•</sup> (0.0) < MeCH<sub>2</sub><sup>•</sup> (7) < Me<sub>2</sub>CH<sup>•</sup> (10) < Me<sub>3</sub>C<sup>•</sup> (12).<sup>2b</sup> Examination of Table I reveals that  $\alpha$ -Me or  $\alpha$ -PhCH<sub>2</sub> substitution increases the RSEs by 4-6 kcal (entries 5, 10, and 11). A second  $\alpha$ -Me substitution causes a further increase of 2-4 kcal (entries 6 and 12), but an  $\alpha$ -cyclohexyl group (entry 13) is no more effective than a single methyl group. These radical stabilizing effects of  $\alpha$ -alkyl groups (hyperconjugation) have their origins in the changes brought about in the  $E_{ox}(A^-)$  values during formation of the radicals from the anions, since their effects on  $pK_{HA}$  are generally radical destabilizing.

**$\alpha$ -Heteroatom Effects on RSEs.** The effects of substitution of  $\alpha$ -MeO,  $\alpha$ -Me<sub>2</sub>N, or  $\alpha$ -C<sub>6</sub>H<sub>10</sub>N groups into acetophenone cause large increases in the RSEs of the corresponding radicals due almost entirely to the ability of these groups to delocalize the odd electron. Large negative shifts in  $E_{ox}(A^-)$  occur as a consequence, and these effects are augmented by small increases in acidity. The resulting RSEs, about 13 kcal for  $\alpha$ -MeO (entry 14) and about 21 kcal for R<sub>2</sub>N (entries 15 and 16) are the largest in Table I. In view of ESR evidence that the *p*-MeS group, is superior to the *p*-MeO group, or any other group, in stabilizing the benzyl radical in the  $\sigma_{\alpha}$  scale,<sup>4</sup> one might expect an  $\alpha$ -RS groups to also exert its effect primarily on  $E_{ox}(A^-)$ . But we see from Table I (entry 20) that the radical stabilizing effect of an  $\alpha$ -PhS on  $E_{ox}(A^-)$  is preempted by its acidifying effect, which is actually about 1 kcal greater than that of Ph (entry 25). Evidently, when the Ph-SCHCOPh anion is oxidized on the electrode, stabilization by PhS of the radical being formed is strong enough to cause  $E_{ox}(A^-)$  to shift to a more negative potential rather than a more positive potential. The net effect is to give the PhSCHCOPh radical an RSE of 11 kcal, about 1 kcal

greater than that for the PhCHCOPh radical, and about the same as that for the PhCOCHOMe radical. (This is consistent with other evidence indicating that  $\alpha$ -RS and  $\alpha$ -RO effects on adjacent carbon-centered radicals do not differ greatly.<sup>10</sup>) The data for  $\alpha$ -PrS and  $\alpha$ -PhCH<sub>2</sub>S acetophenones (entries 23 and 24) give an RSE in each instance of 12.5 kcal, i.e., one that is close to that for PhS, but the breakdown into  $\Delta pK_{HA}$  and  $E_{ox}(A^-)$  values is different. The  $\Delta pK_{HA}$  values for the RSCH<sub>2</sub>COPh derivatives are lower by 3.7 and 2.6 kcal, respectively, than that of PhSCH<sub>2</sub>COPh, but these lower values are compensated by more negative  $E_{ox}(A^-)$  values. The  $\Delta pK_{HA}$  and  $\Delta E_{ox}(A^-)$  values for PhSeCH<sub>2</sub>COPh (entry 22) are smaller than those for PhSCH<sub>2</sub>COPh, and the RSE is 8 kcal, rather than 11 kcal.

#### Effects of Two Donors or Two Acceptors on RSEs.

A large amount of qualitative data<sup>6</sup> and some quantitative data<sup>10</sup> have appeared in the literature regarding the enhanced stability of carbon-centered radicals wherein both a donor and an acceptor group are attached to the radical center, but relatively little information is available concerning the effects when two donor or two acceptor groups are present.<sup>10</sup> Introduction of a second *c*-C<sub>5</sub>H<sub>10</sub>N group into *c*-C<sub>5</sub>H<sub>10</sub>NCH<sub>2</sub>COPh (entry 16) causes only a 1.5-kcal shift of  $E_{ox}(A^-)$  to a more negative potential, and this is counteracted by about a 1 kcal increase in  $pK_{HA}$ . The net result is to decrease the RSE by 1 kcal. Introduction of a second  $\alpha$ -PhS group into PhSCH<sub>2</sub>COPh (entry 20) causes a further 6.6 kcal increase in acidity, but this is counteracted by a 6-kcal shift of  $E_{ox}(A^-)$  to a more positive potential, and again the net result on RSE is minimal. These effects in tertiary radicals are no doubt leveled by saturation and steric effects as is evident from the 5-kcal decrease in RSE resulting from introduction of an  $\alpha$ -Ph group into *c*-C<sub>5</sub>H<sub>10</sub>NCH<sub>2</sub>COPh (entry 17), but a similar failure to change the RSE by introduction of a second like group is also observed when two acceptor groups are present in secondary radicals. In PhCOCH<sub>2</sub>COPh (entry 27) we see that no change in RSE occurs by introduction of a second PhCO group into PhCOCH<sub>3</sub> because the 15 kcal increase in acidity is matched by a 15-kcal shift in  $E_{ox}(A^-)$  to a more positive potential. Similar effects are observed for substituting  $\alpha$ -COMe or  $\alpha$ -CN groups into PhCOCH<sub>3</sub> (entries 28 and 29); substitution of  $\alpha$ -SO<sub>2</sub>Ph groups causes radical destabilizing effects (entries 8 and 30).

**$\alpha$ -Pyridinium and  $\alpha$ -Trimethylammonium Effects on RSEs.** Introducing an  $\alpha$ -Me<sub>3</sub>N<sup>+</sup> or  $\alpha$ -PyN<sup>+</sup> group into PhCOCH<sub>3</sub> increases the acidity by about 14 and 19 kcal, respectively (entries 31 and 19). The effect of the  $\alpha$ -Me<sub>3</sub>N<sup>+</sup> group causes a 17.5-kcal shift of  $E_{ox}(A^-)$  to a more positive potential, and the net effect is about a 3.5-kcal destabilization of the radical, relative to that of the parent radical. On the other hand, the delocalizing effect of the  $\alpha$ -PyN<sup>+</sup> group on the odd electron decreases the positive shift in  $E_{ox}(A^-)$ , and the net effect on RSE is a 6-kcal stabilizing effect.

#### Effects of $\Delta pK_{HA}$ and $\Delta E_{ox}(A^-)$ Values on the RSEs of the Acidic N-H Bonds in Carboxamides, Hydrox-

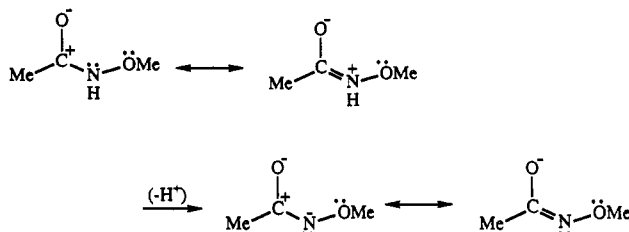
**Table II. Effects of  $\Delta pK_{HA}$  and  $\Delta E_{ox}(A^-)$  Values on  $\Delta BDE$ s for the Conversion of Carboxamides to Hydroxamic Acids, Hydrazides, and Thiocarboxamides<sup>a</sup>**

no.	carboxamide	$pK_{HA}$ (kcal)	$\Delta pK_{HA}^a$	$\Delta E_{ox}(A^-)^c$	$\Delta BDE =$ RSE <sup>d</sup>
1	CH <sub>3</sub> CONH <sub>2</sub>	34.9	(0.0)	(0.0)	(0.0)
2	CH <sub>3</sub> CONHOH	21.9	13.4	6.3	19.7
3	CH <sub>3</sub> CONHOMe	23.2	12.1	6.0	18.1
4	CH <sub>3</sub> CONHNH <sub>2</sub>	29.9	5.4	20	25.4
5	PhCONH <sub>2</sub>	32.0	3.3	-2.3	1.0
6	PhCONHOH	32.0	(0.0)	(0.0)	(0.0)
7	PhCONHOH	18.8	13.6	5.7	19.3
8	PhCONHOCH <sub>2</sub> Ph	19.6	12.8	5.2	18.0
9	PhCONHNH <sub>2</sub>	25.9	6.5	20.6	27.1
10	PhCONHNMe <sub>2</sub>	27.0	5.4	19.4	24.8
11	PhSO <sub>2</sub> NH <sub>2</sub>	22.0	(0.0)	(0.0)	(0.0)
12	PhSO <sub>2</sub> NHNH <sub>2</sub>	23.4	-1.0	26	25.0
13	PhSO <sub>2</sub> NHNMe <sub>2</sub>	21.6	0.8	22	22.8
14	CH <sub>3</sub> CONH <sub>2</sub>	34.9	(0.0)	(0.0)	(0.0)
15	CH <sub>3</sub> CONHMe	35.5	-0.2	1.5	1.3
16	CH <sub>3</sub> CONHPh	29.4	5.9	2.8	8.7
17	CH <sub>3</sub> CSNH <sub>2</sub>	25.3	10.0	6.7	16.7
18	PhCONH <sub>2</sub>	32.0	(0.0)	(0.0)	(0.0)
19	PhCSNH <sub>2</sub>	23.1	8.9	7.5	16.4

<sup>a</sup> Data taken from Bordwell, F. G.; Harrelson, J. A., Jr.; Lynch, T.-Y. *J. Org. Chem.* 1990, 55, 3337-3341; all values are in kcal/mol. <sup>b</sup> Statistically corrected for the number of acidic hydrogen atoms. <sup>c</sup> Irreversible oxidation potentials measured in DMSO relative to the Fe/Fe<sup>+</sup> couple, as described previously in ref. 1. <sup>d</sup>  $\Delta BDE = RSE = \Delta pK_{HA} + \Delta E_{ox}(A^-)$ .

**amic Acids, and Hydrazides.** Analyses of the type used for ketones in Table I are shown for carboxamides and related compounds in Table II.

**$\alpha$ -HO and  $\alpha$ -MeO Effects on RSEs of Nitrogen-Centered Radicals.** Examination of Table II shows that the 18-19 kcal decrease in BDE resulting from replacement of a hydrogen atom on nitrogen in acetamide by an OH or OCH<sub>3</sub> group (entries 1 and 2)<sup>11</sup> are caused primarily by a 12-13-kcal decrease in  $pK_{HA}$ , augmented by a 6-kcal shift to a more negative  $E_{ox}(A^-)$  potential. The large increase in N-H acidity can be associated with destabilization of the ground state of the acid caused by the enhancement of the positive charge on nitrogen resulting from attachment of the (electronegative) oxygen atom, together with the introduction of four electron repulsions between the adjacent oxygen and nitrogen atoms. These repulsions can be minimized in the anion by delocalization of the negative charge to oxygen. (This rationalization is



patterned, in part, after recent calculations showing that the higher acidity of acetic acid than that of 1-propanol is inherent in its ground state electronic properties rather than in differential effects in the product anions.<sup>12</sup>) The reduction in the basicity of the anion caused by introduction of the  $\alpha$ -OCH<sub>3</sub> group must tend to shift the  $E_{ox}(A^-)$

(8) Bordwell, F. G.; Lynch, T.-Y. *J. Am. Chem. Soc.* 1989, 111, 7558-7562.

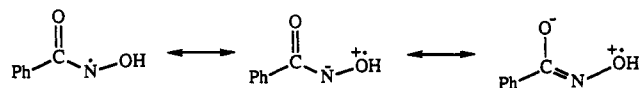
(9) See Bordwell, F. G.; Zhang, X.-M. *J. Org. Chem.* 1990, 55, 6078-6079 for other examples comparing the effects of PyN<sup>+</sup> and Me<sub>3</sub>N<sup>+</sup> groups on acidities and BDEs.

(10) Bordwell, F. G.; Zhang, X.-M.; Alnajjar, M. S. *J. Am. Chem. Soc.* 1992, 114, 7623-7629.

(11) Bordwell, F. G.; Harrelson, J. A., Jr.; Lynch, T.-Y. *J. Org. Chem.* 1990, 55, 3337-3341.

(12) (a) Siggel, M. R.; Thomas, T. D. *J. Am. Chem. Soc.* 1986, 108, 4360-4363. (b) Siggel, M. R.; Streitwieser, A.; Thomas, T. D. *J. Am. Chem. Soc.* 1988, 110, 8022-8028. (c) Taft, R. W.; Koppel, I. A.; Topsom, R. D.; Anvia, F. *J. Am. Chem. Soc.* 1990, 112, 2047-2052.

value to positive potentials, but instead, an appreciable shift to negative potentials is observed because of the powerful stabilizing effect of the hydroxyl group on the nitrogen-centered radical being formed. Similar effects are observed on introducing  $\alpha$ -OH and  $\alpha$ -OCH<sub>2</sub>Ph groups into PhCONH<sub>2</sub> (entries 7 and 8).



**$\alpha$ -H<sub>2</sub>N and  $\alpha$ -Me<sub>2</sub>N Effects on RSEs of Nitrogen-Centered Radicals.** The structural change from CH<sub>3</sub>-CONH<sub>2</sub> to CH<sub>3</sub>CONHNH<sub>2</sub> (entry 4) causes a smaller increase in acidity (5 kcal) than does OH or OR on acidity due to the much smaller electronegativity of nitrogen, but causes a much larger negative shift in the  $E_{ox}(A^-)$  value (20 kcal).<sup>11</sup> The stabilizing effect of the amino group on the carbon-centered radical PhCOCHNH<sub>2</sub> has been found to be about 9 kcal greater than that of the MeO group in the PhCOCHOMe radical (Table I). This compares nicely with the net difference in  $\Delta$ BDEs of 7 kcal between the nitrogen-centered radicals CH<sub>3</sub>CONOMe and CH<sub>3</sub>-CONNH<sub>2</sub> (entries 3 and 4). Similar effects were observed for comparable substitutions into benzamide (entries 8 and 9).

The effects of the  $\alpha$ -OH,  $\alpha$ -OCH<sub>2</sub>Ph, and  $\alpha$ -NH<sub>2</sub> groups on the  $\Delta pK_{HA}$  and  $\Delta E_{ox}(A^-)$  values in PhCONH<sub>2</sub> are within about 1 kcal of those of the  $\alpha$ -OH,  $\alpha$ -OMe, and  $\alpha$ -NH<sub>2</sub> groups in CH<sub>3</sub>CONHOH, CH<sub>3</sub>CONHOMe, and CH<sub>3</sub>-CONHNH<sub>2</sub>. The Me<sub>2</sub>N group in PhCONHNMe<sub>2</sub> causes a 2-kcal smaller effect on the BDE than does the H<sub>2</sub>N group (entries 9 and 10). The same difference was observed on the BDE for the acidic C-H bonds in the carbon acids PhCOCH<sub>2</sub>NMe<sub>2</sub> vs PhCOCH<sub>2</sub>NH<sub>2</sub>.<sup>8</sup> A comparable difference in BDEs was also observed between the acidic N-H bonds of the sulfonylhydrazides, PhSO<sub>2</sub>-NHNMe<sub>2</sub> and PhSO<sub>2</sub>-NHNH<sub>2</sub>, relative to the BDE of the N-H bond in PhSO<sub>2</sub>NH<sub>2</sub> (entries 12 and 13). Here the effects are caused almost entirely by differences in  $E_{ox}(A^-)$  values.

**N-Me and N-Ph Effects on RSEs.** The effects of substituting Me and Ph groups for a hydrogen atom of the amino group of CH<sub>3</sub>CONH<sub>2</sub> (entries 15 and 16) are similar to those observed for introducing these groups for an  $\alpha$ -hydrogen atom of acetophenone (Table I), except that they are smaller (2 and 8 vs 6 and 11 kcal, respectively). The methyl effect in the carboxamide is due primarily to a change in  $\Delta E_{ox}(A^-)$  and the Ph effect is due primarily to a change in  $\Delta pK_{HA}$ , as is true also in the acetophenone substrate.

**Effects of Replacing C=O By C=S in Carboxamides.** Replacement of the oxygen atom in the carbonyl group of CH<sub>3</sub>CONH<sub>2</sub> or PhCONH<sub>2</sub> by a sulfur atom causes about a 16-kcal decrease in BDE in each instance. Analysis shows that these effects are caused both by an increase in acidity and a negative shift in  $E_{ox}(A^-)$ . The increase in acidity can be attributed to an increase in ground state energy of about 35 kcal,<sup>13</sup> and the superior ability of sulfur relative to oxygen to accommodate a negative charge.<sup>11</sup> The shifts in the  $E_{ox}(A^-)$  values to more negative potentials are probably associated with the greater ability of sulfur relative to oxygen to accommodate an odd electron.

(13) Charton, M. In *The Chemistry of Doubly-bonded Functional Groups*; Patai, S. Ed.; Wiley: New York, 1989; Chapter 5, Table I.

**Table III. Acidities and Homolytic Bond Dissociation Energies of Carbon Acids and Their Polyfluoro Analogues**

no.	substrates	$pK_{HA}^a$	$E_{ox}(A^-)^b$	BDE <sup>c</sup>	$\Delta$ BDE = RSE/ <sup>d</sup>
1		10.35	-0.492	76.1	(0.0)
		6.1	-0.040	80.7	-4.6
2	9-C <sub>6</sub> H <sub>6</sub> FIH	17.9	-1.028	74.1	(0.0)
	9-C <sub>6</sub> F <sub>5</sub> FIH	14.75	-0.662	78.2	4.1
3	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> CN	21.9	-0.909	82.3	(0.0)
	C <sub>6</sub> F <sub>5</sub> CH <sub>2</sub> CN	15.8	-0.483	83.8	-1.5
4	(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> CHCN	17.5	-0.885	76.8	(0.0)
	(C <sub>6</sub> F <sub>5</sub> ) <sub>2</sub> CHCN	7.95	-0.106	81.7	-4.9
5	(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> CH	30.6	-1.486	80.8	(0.0)
	( <i>p</i> -HC <sub>6</sub> F <sub>4</sub> ) <sub>3</sub> CH	13.3	-0.401	82.3	-1.5
6	C <sub>6</sub> H <sub>5</sub> CH(CN)CO <sub>2</sub> Et	8.0	-0.186	80.0	(0.0)
	C <sub>6</sub> F <sub>5</sub> CH(CN)CO <sub>2</sub> Et	5.1	0.213	85.2	-5.2
7	H <sub>3</sub> CH			105 <sup>d</sup>	(0.0)
	F <sub>3</sub> CH			107 <sup>d</sup>	-2
8	C <sub>6</sub> H <sub>6</sub>			111 <sup>d</sup>	(0.0)
	C <sub>6</sub> F <sub>6</sub> H			116 <sup>d</sup>	-5
9	Me <sub>3</sub> CH			96 <sup>d</sup>	(0.0)
	(F <sub>3</sub> C) <sub>3</sub> CH			109 <sup>e</sup>	-13

<sup>a</sup> Reference 15. <sup>b</sup> Irreversible oxidation potentials measured by cyclic voltammetry in DMSO using a Pt working electrode and a Ag/AgI reference electrode. The oxidation potentials reported were referenced to the Fc/Fc<sup>+</sup> couple (0.875 V with our instrument<sup>1</sup>). <sup>c</sup> Estimated by using eq 1. <sup>d</sup> Reference 2b. <sup>e</sup> Reference 16. <sup>f</sup> The sum of  $\Delta pK_{HA}$  and  $E_{ox}(A^-)$ , or the difference in BDEs relative to the parent indicated.

**Effects of  $\Delta pK_{HA}$  and  $\Delta E_{ox}(A^-)$  on RSEs of Carbon-Centered Radicals Derived from Polyfluorohydrocarbons.** Substitution of a fluorine atom for one of the hydrogen atoms of methane decreases the BDE by 2 kcal, an effect that can be attributed to delocalization of the odd electron in the corresponding radical. The presence of three fluorine atoms in F<sub>3</sub>C-H causes an *increase* in the BDE of the C-H bond to 107 kcal,<sup>2b</sup> presumably because the destabilizing electron-withdrawing effects of the three fluorine atoms overshadow their delocalizing effects on the corresponding radical. Kinetic studies by Jiang, Li, and Wang have also led to the conclusion that whereas a single fluorine atom stabilizes an adjacent carbon-centered radical, three fluorine atoms are destabilizing.<sup>14</sup> Alternatively, it is possible that substitution of fluorine atoms for hydrogen atoms in hydrocarbons may decrease the ground-state energy of the molecule by virtue of the unusual strength of C-F bonds. Both of these rationales suggest that RSEs in radicals derived from polyfluorohydrocarbons will decrease, relative to their parents. The results of our experiments with several compounds of this type are shown in Table III.

Examination of Table III shows that 1,2,3,4,5,6,7,8-octafluoro-9-(ethoxycarbonyl)fluorene (entry 1) is 5.8 kcal more acidic than 9-(methoxycarbonyl)fluorene. According to the analyses presented in terms of  $\Delta pK_{HA}$  and  $\Delta E_{ox}(A^-)$  in the earlier sections, this decrease in the basicity of the conjugate base should result in a shift in the oxidation potential,  $E_{ox}(A^-)$ , of about 5.8/23.1 = 0.25 V to a more positive potential, unless the presence of the fluorine atoms

(14) Jiang, X.-K.; Li, X.-L.; Wang, K.-Y. *J. Org. Chem.* 1989, 54, 5648-5650.

(15) Bordwell, F. G.; Branca, J. C.; Barea, J. E.; Filler, R. *J. Org. Chem.* 1988, 53, 780-782.

(16) Evans, B. S.; Weeks, S. I.; Whittle, E. *J. Chem. Soc. Faraday Trans. 1* 1983, 79, 1471-1482.

exerts a stabilizing effect on the radicals being formed, as was usually the case for the structural changes in the ketones and carboxamides discussed in the previous sections. The  $E_{\text{ox}}(\text{A}^-)$  shift observed is actually 0.45 V (10.4 kcal) to a more positive potential, indicating that, if the fluorines do exert any radical-stabilizing effect, it is completely overshadowed by their destabilizing electron-withdrawing effect. The net effect is to increase the BDE by about 5 kcal and to destabilize the corresponding radical by this amount. The effects of 9-(pentafluorophenyl)fluorene (entry 2) on the  $\Delta pK_{\text{HA}}$  and  $\Delta E_{\text{ox}}(\text{A}^-)$  follow the same pattern and destabilize the radical by 4 kcal.

Replacing the moiety  $\text{C}_6\text{H}_5$  in  $\text{C}_6\text{H}_5\text{CH}_2\text{CN}$  by the moiety  $\text{C}_6\text{F}_5$  (entry 3) lowers the  $pK_{\text{HA}}$  by 8.36 kcal, which is expected to cause a 0.36-V positive shift in  $E_{\text{ox}}(\text{A}^-)$ . A positive shift of 0.426 V (9.8 kcal) was observed, which corresponds to a 1.5-kcal destabilization of the radical. Replacing both of the phenyl groups in  $(\text{C}_6\text{H}_5)_2\text{CHCN}$  by perfluorophenyl groups (entry 4) causes a 13-kcal decrease in  $pK_{\text{HA}}$  and an 18-kcal (0.78 V) positive shift in the  $E_{\text{ox}}(\text{A}^-)$  value, which leads to a 4.9-kcal destabilizing effect on the radical. In entry 6 replacement of a single phenyl group by a perfluorophenyl group causes only a 4-kcal decrease in  $pK_{\text{HA}}$  compared to a 8.4-kcal decrease for entry 3, but the positive shift in  $E_{\text{ox}}(\text{A}^-)$  is almost as large (9.2 vs 9.8 kcal). A possible explanation may be that, whereas the tertiary  $\text{C}_6\text{F}_5\dot{\text{C}}(\text{CN})\text{CO}_2\text{Et}$  carbanion is subject to strong steric inhibition of solvation, the secondary carbanion  $\text{C}_6\text{F}_5\dot{\text{C}}\text{HCH}_2\text{CN}$  and the corresponding radicals are not. The 1.5-kcal greater positive  $E_{\text{ox}}(\text{A}^-)$  shift than predicted by the  $pK_{\text{HA}}$  change in entry 5 is surprisingly small considering the presence of 12 fluorine atoms.

Further examples of the effects of introducing fluorine atoms on the BDEs of the C-H bonds in hydrocarbons taken from the literature are shown in entries 7-9. Note that the bond-strengthening (radical destabilizing) effects increase progressively as the number of fluorine atoms increase.

**Summary and Conclusions.** Detailed analyses of  $\Delta pK_{\text{HA}}$  and  $E_{\text{ox}}(\text{A}^-)$  values, relative to those of a parent, have been made for (a) the introduction of  $\alpha$ -substituents into acetone and acetophenone, (b) the introduction of  $N$ -substituents into carboxamides, and (c) the introduction

of fluorine substituents into a variety of hydrocarbons. Because of an inherent linear relationship between anion basicities and their oxidation potentials it is shown that either the  $\Delta pK_{\text{HA}}$  values or the  $\Delta E_{\text{ox}}(\text{A}^-)$  values, the sum of which equal  $\Delta\text{BDE}$  (or RSE), may be dominant in determining the size of the RSE. For example, the presence of an  $\alpha$ - $\text{R}_2\text{N}$  group in acetophenone leads to about a 21-kcal increase in the RSE of the corresponding radical that is due almost entirely to a shift in  $E_{\text{ox}}(\text{A}^-)$  to more negative potentials, whereas the presence of an  $\alpha$ -Ph group in acetophenone leads to about a 10-kcal increase in the RSE due almost entirely to a decrease in  $pK_{\text{HA}}$ . In both cases, however, the effects are caused by delocalization of the odd electron in the radical being generated on the electrode by the substituent. For the  $\alpha$ -Ph group this delocalizing effect on the radical negates the much lower basicity of the anion and results in a small negative shift in  $E_{\text{ox}}(\text{A}^-)$  to a more negative potential, rather than the large shift to a more positive potential than might have been expected. These analyses indicate that the  $\Delta\text{BDEs}$  being measured are giving a good report on the RSEs of the radicals being formed from anions on the electrode. The results in Table III are consistent in showing that the introduction of three or more fluorine atoms into hydrocarbons always causes appreciable strengthening of the acidic C-H bonds.

### Experimental Section

The oxidation potentials of the conjugate anions of the perfluoro compounds reported in Table III were measured by cyclic voltammetry. The working electrode (BAS) consists of 1.5-mm diameter platinum disk embedded in a cobalt glass seal. It was polished with Buehler 0.05- $\mu\text{m}$  polishing alumina or cleaned with an ultrasonic instrument, rinsed with ethanol, and dried before each run. The counter electrode was a platinum wire (BAS). The reference electrode was Ag/AgI, and the potentials reported were referenced to a ferrocenium/ferrocene couple ( $E^{1/2} = 0.875$  V vs the Ag/AgI couple).<sup>1</sup> Tetraethylammonium tetrafluoroborate was used as the supporting electrolyte.

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