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Equilibrium acidities and homolytic bond dissociation enthalpies of *m*- and *p*-substituted benzaldoximes and phenyl methyl ketoximes

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ABSTRACT: The equilibrium acidities in DMSO of nine *p*- and *m*-substituted benzaldoximes and eight *p*-substituted phenyl methyl ketoximes were measured. Estimates of the homolytic bond dissociation energies (BDEs) of the acidic O—H bonds in these compounds were made by combination of their pK_{HA} values with the oxidation potentials of their conjugate bases, $E_{ox}(A^-)$, using the equation BDE = $1.37pK_{HA} + 23.06E_{ox}(A^-) + 73.3$ kcal (1 kcal = 4.184 KJ). Plots of $E_{ox}(A^-)$ vs pK_{HA} for *p*-substituted benzaldoximes and *p*-substituted phenyl methyl ketoximes were linear with slopes near unity. Consequently, as required by the above equation, the BDEs estimated for the O—H bonds in these oximes were constant, being 88.3 ± 0.3 and 89.2 ± 0.4 kcal, respectively. © 1998 John Wiley & Sons, Ltd.

KEYWORDS: equilibrium acidities; homolytic bond dissociation enthalpies; benzaldoximes; phenyl methyl ketoximes

INTRODUCTION

Our earlier acidity measurements on aliphatic oximes in DMSO revealed that the pK_{HA} values in aqueous solution are merely lower limits and that the real values in water must be 3–6.5 pK_{HA} units higher. For example, the acidity of acetaldoxime in DMSO is 8.5 pK_{HA} units higher than that of benzaldoxime, whereas that reported in water is only 1 pK_{HA} unit higher.[1]

The homolytic bond dissociation energies (BDEs) for the O—H bonds in oximes in DMSO estimated by the equation

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

Where E_{ox} (A^-) are the oxidation potentials of their conjugate bases. Equation (1) is based on a thermodynamic cycle originally devised by Brauman and coworkers[2] to estimate BDEs from gas-phase acidities, electron affinities and ionization potentials. In 1983, Friedrich[3] showed that equation (1) could be used to obtain the first and the second BDEs of the O—H bonds in hydroquinone and a value of the last term (C) in equation (1) of 56.8 kcal (1 kcal = 4.184 kJ) was used.[4] In the period from 1988 to data, using an empirically based $C = 56$ kcal vs NHE or latter its equivalent $C = 73.3$ vs Fc^+/Fc, hundreds of BDEs have been estimated from equation (1) in our laboratory. The BDEs generally agree with literature values to within ± 3 kcal or better.[4] In 1991, Parker *et al.*[5] obtained C values of 73.5 and 75.8 and independently derived BDEs.

The BDEs of only a few oximes had been determined prior to our studies.[1] A direct calorimetric method has been devised, however, that can be used if the radicals formed from the oximes are stable for many hours in concentrated solution at room temperature and undergo clean, rapid, exothermic and reversible reactions with a suitable hydrogen donor. These stringent requirements were found to be met for the iminoxy radicals derived from three oximes, *t*-Bu(*i*-Pr)C=NOH, *t*-Bu_2C=NOH, *t*-Bu(1-Ad)C=NOH, for which BDEs of the O—H bonds were found to be 84.3 ± 3, 80.9 ± 3 and 80.0 ± 3 kcal mol^{-1}, respectively.[6] These values are smaller than the BDE values for the O—H bonds in Me_2C=NOH, or Et_2C=NOH estimated by equation (1) by as much as 18 kcal mol^{-1} [1] (henceforth kcal mol^{-1} will be abbreviated as kcal). This cast serious doubt on our method, but a check of the BDEs of the O—H bonds in *t*-Bu_2C=NOH and *t*-Bu(1-Ad)C=NOH by estimates using equation (1) gave 82.6 and 81.7 kcal, respectively, in good agreement with the values obtained calorimetrically.[7] This result showed that the O—H bond energies in oximes were highly sensitive to the bulk of the substituents attached to carbon.

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The estimates of the BDEs of the O—H bonds in oximes by equation (1) were next extended to substituted benzaldoximes and phenyl methyl ketoximes in our laboratory and (independently) at Nankai University. In the meantime, an extensive study of the BDE of the O—H bond in phenol was carried out by photoacoustic calorimetry (PAC), which showed that it was solvent dependent.[8] In both ethyl acetate and acetonitrile, which are dipolar hydrogen bond acceptor solvents like DMSO, the PAC BDEs of PhO—H were both found to be 95 kcal. The authors corrected this value for solvation of the hydrogen atom (2 kcal) and hydrogen bonding of phenol to the solvent (4.7 kcal) to give BDE = 88.3 kcal, which agrees well with literature values for phenol: (a) 88.3 kcal [from $E_{rd}(PhO^{\bullet})$] and pK_{HA} in aqueous medium,[9] (b) 88.3 ± 2 kcal from rate constants for $PhO^{\bullet}$ radical,[10] (c) 84 ± 1 kcal from PAC measurements (solvent not specified)[11] and (d) 85.6 kcal from gas-phase measurements.[12] [Our average value for the O—H bond in PhOH estimated from equation (1) is 90.4 ± 1 kcal, an average of (a) the parent H (90.4 kcal),(b) 3-Me (90.0 kcal),(c) 3.5-diMe (89.7 kcal), (d) 3-MeO (90.8 kcal) and (e) 4-Cl (90.0 kcal).[13] The authors assumed that the PAC BDE value for PhO—H in DMSO would also be about 95 kcal, and would need to be corrected for solvation. They concluded that the BDE estimated for the O—H bond in phenol by equation (1) is seriously in error because no correction was made for solvent effects and that '*Similar errors must be present in many other electrochemical bond energies that also were determined in polar solvents.*' This would presumably apply to our estimates by equation (1) for PhCH=NOH and PhC(Me)=NOH and their derivatives in DMSO since the BDEs of the O—H bonds for the parents are estimated from equation (1) to be close to that of PhOH, i.e. 88.1 and 88.4 kcal, respectively.

RESULTS AND DISCUSSION

Equilibrium acidities (pK_{HA}) and homolytic bond dissociation enthalpies (BDEs) of *m*- and *p*-substituted benzaldoximes and phenyl methyl ketoximes

Equilibrium acidities (pK_{HA}) in DMSO for *m*- and *p*-substituted benzaldoximes, together with the oxidation potentials of their conjugate anions and estimates of the BDEs of their O—H bonds by using equation (1), are summarized in Table 1.

Table 1. Equilibrium acidities and homolytic bond dissociation energies of the acidic O—H bonds in *p*-substituted benzaldoximes $p\text{-}GC_6H_4CH{=}NOH$ in DMSO

No.	G	pK_{HA}[a,b]	$E_{OX}(A^-)$[c,b]	BDE[d]	ΔBDE
1	4-MeO	20.8	−0.608	87.8	−0.3
2	4-Me	20.6	−0.585	88.0	−0.1
3	H	20.2	−0.559	88.1	(0.0)
4	4-Cl	19.3	−0.520	87.8	−0.3
5	4-Br	19.2	−0.520	87.6	−0.5
6	$4\text{-}CF_3$	18.6	−0.471	87.9	−0.2
7	4-CN	18.0	−0.440	87.8	−0.3
8	$3\text{-}NO_2$	17.7[e]	−0.390	88.6	0.5
9	$4\text{-}NO_2$	17.3	−0.371	88.4	0.3

[a] In pK_{HA} units; equilibrium acidities were measured in DMSO solution by the overlapping indicator method or the standard acid method.[14] The values for benzaldoxime and its 4-MeO, 4-Me and 4-NO_2 derivatives agree to within ±0.3 unit with those in Ref. 1.

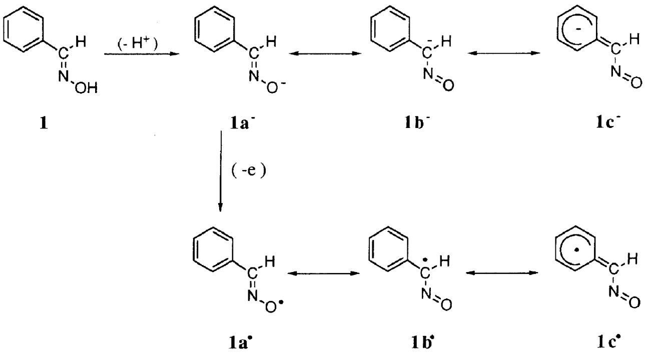
[b] Measured at Nankai University.

[c] In volts; irreversible oxidation potentials of the conjugate bases were measured by CV in DMSO solution, and referenced to the ferrocenium / ferrocene couple.

[d] In kcal mol^{-1}, estimated by using equation (1).

[e] Measured at Northwestern University.

Considering that (a) there are appreciable substituent effects on both pK_{HA} and BDE values when the methyl group in acetaldoxime ($CH_3CH{=}NOH$) is replaced by a phenyl group (11.6 and 8.0 kcal, respectively) and (b) the pK_{HA} and BDE values of PhCH=NOH are close to those of phenol, one might expect that *p*-acceptor substituents would cause appreciable increases in the acidities of the acidic O—H bonds by stabilizing the anions (**1a**$^-$ ↔ **1b**$^-$ ↔ **1c**$^-$), and that *p*-donor substituents would cause appreciable decreases in the BDEs of the O—H bond because of their stabilizing effects on the corresponding radicals.



Examination of Table 1 shows, however, that all the acidities of the benzaldoximes fall within a narrow range of 3.5 pK_{HA} units, from a pK_{HA} of 17.3 for *p*-NO_2 to 20.8 for *p*-MeO, and the BDE values remain constant, averaging 88.3 ± 0.3 kcal for the series of benzaldoximes. This is in sharp contrast to the large substituent effects observed in *p*-substituted phenols, where a *p*-NO_2 group enhances the acidity by 7.2 pK_{HA} units and increases the BDE by 4.8 kcal and a *p*-MeO group decreases the acidity by 1.1 pK_{HA} units and decreases the BDE by 5.3 kcal.[13] These differences are understandable when one consider that the appreciable substituent effects on both pK_{HA} and BDE values caused by the phenyl substitution for the methyl group in $CH_3CH{=}NOH$ take place as the result of *proximate* substitution effects, whereas the negligible substituent effects on BDEs in the

p-$GC_6H_4CH{=}NOH$ series are due to *remote* substituent effects, and (b) the relatively large substituent effects on BDEs in the p-GC_6H_4OH series are probably due to the ground-state energy effects involving the neutral compounds, which are caused by the dipole–dipole interactions between the *para* substituents and the polar O—H bond in the p-substituted phenols,[15] whereas in the p-$GC_6H_4CH{=}NOH$ series this kind of interaction should be greatly attenuated owing to the longer distance between the *para* substituents and the polar O—H bond. Note also that even though the single electron on oxygen in the corresponding radicals derived from p-$GC_6H_4CH{=}NOH$ can be delocalized to the α-carbon atom, the effect of the p-G group is attenuated owing to the relatively lower spin density on the α-carbon atom compared with that on the α-oxygen atom in the p-substituted phenols. Furthermore, the small substituent effect on BDEs finds precedent in the results obtained for a substantial number of carbon acid families where the effects of remote substituents on BDEs of the acidic C—H bonds are small, and the BDEs of the acidic H—A bonds are often constant to within ± 2 kcal or less.[15]

Examination of the pK_{HA}, $E_{ox}(A^-)$ and BDE values for p-$GC_6H_4C(Me){=}NOH$ ketoximes revealed strikingly similar behavior (Table 2) and the substituent effects can be interpreted similarly.

A Hammett plot of the pK_{HA} values of eight p-substituted benzaldoximes is linear with a slope of 3.2, with σ_p values rather than σ_p- values for p-NO_2 and p-CN points (Figure 1).[16]

These results indicate that the negative charge in the anion remains primarily on oxygen with little or no delocalization to the benzene ring or carbon atom, as would be expected from contributors **1b**$^-$ and **1c**$^-$. Also, the effects of substituents on the oxidation potentials of the conjugate anions are small and mirror almost exactly the changes in pK_{HA}. In other words, there is a linear relationship between $E_{ox}(A^-)$ and pK_{HA} with a slope near unity (0.93) when both axes are expressed in kcal (Figure 2).

Linear relationship with slopes near unity have been observed previously for plots of $E_{ox}(A^-)$ vs pK_{HA} in a variety of weak acid families. For example, the BDEs of the acidic C—H bonds in 12 m-substituted fluorenes (2-G and 2,7-diG substituents) are estimated to be 79.5 ± 0.3 kcal,[17] and those of the benzylic C—H bonds in 14 $GC_6H_4CH_2CN$ acetonitriles (omitting 4-Me_2N) are estimated to be 8 ± 1.[18] This behavior is consistent with an intrinsic 1:1 linear relationship between anion basicity and anion oxidation potentials.[19] It requires that the BDEs of the acidic C—H bonds in the series be essentially constant. The linear plot for $E_{ox}(A^-)$ vs pK_{HA} for p-substituted phenyl methyl ketoximes provides a striking example (Figure 3).

Table 2. Equilibrium acidities and homolytic bond dissociation energies of the acidic O—H bonds in methyl p-substituted ketoximes p-$GC_6H_4C(Me){=}NOH$ in DMSO

No.	G	pK_{HA}[a,b]	$E_{ox}(A^-)$[c,b]	BDE[d]	ΔBDE
1	4-MeO	22.0	−0.629	88.9	0.5
2	4-Me	21.7	−0.609	89.0	0.6
3	H	21.1[e]	−0.598	88.4	(0.0)
4	4-Cl	20.5	−0.539	89.0	0.6
5	4-Br	20.5	−0.537	89.0	0.6
6	4-CF_3	19.5	−0.483	88.9	0.5
7	4-CN	18.9	−0.450	88.8	0.4
8	4-NO_2	18.2	−0.407	88.8	0.4

[a] In pK_{HA} units; equilibrium acidities were measured in DMSO solution by the overlapping indicator method or the standard acid method.[14]

[b] Measured at Nankai University.

[c] In volts; irreversible oxidation potentials of the conjugate bases were measured by CV in DMSO solution, and referenced to the ferrocenium/ferrocene couple.

[d] In kacl mol^{-1}, estimated by using equation (1).

[e] Measured at Northwestern University.

Tables 1 and 2 show that the BDEs of the ketoximes averaged about 1.5 kcal greater than those of the benzaldehyde oximes. In the benzaldoximes there was a slight increase in the BDEs as the substituents became more electron withdrawing. The BDEs of the O—H bonds in the parents, PhCH=NOH and PhC(Me)=NOH, are within experimental error of one another (88.1 and 88.4 kcal, respectively) and that of PhOH (90.4 kcal). There is, of course, no evidence for or against a solvent effect on these BDEs because of the absence of literature values to be used for comparison. The BDE values of the benzaldoximes and methyl phenyl ketoximes are in the same region (69–85 kcal) as those for four hydroxylamines, two hydroxamic acids, three phenols, and three oximes estimated by equation (1) that were found to agree to within ±2 kcal with the best literature values.

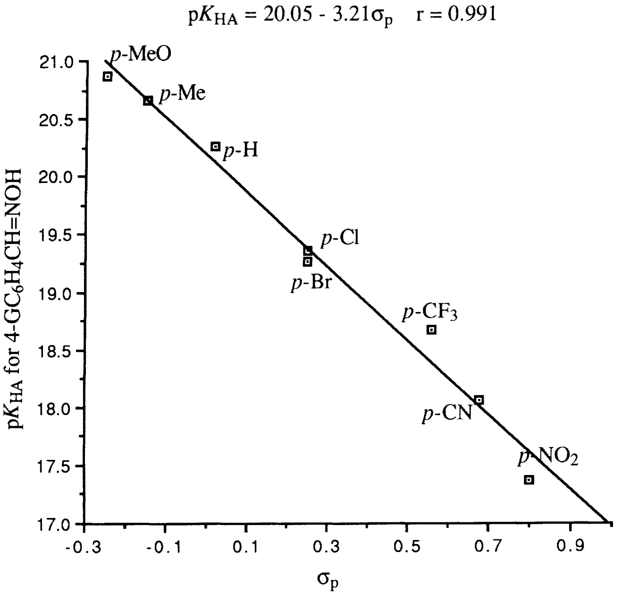


Figure 1. Hammett plot of the pK_{HA} values for p-$GC_6H_4CH{=}NOH$ versus σ_p constants

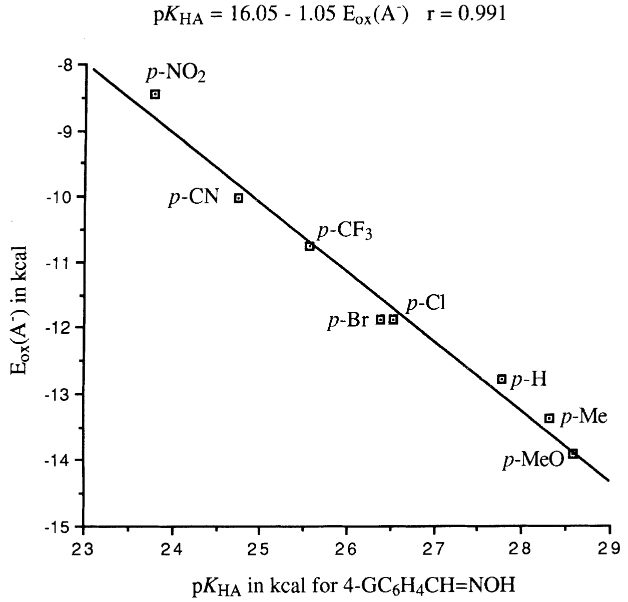


Figure 2. Plot of $E_{ox}(A^-)$ versus pK_{HA} for p-$GC_6H_4CH{=}NOH$

These BDE values tend to be slightly higher than the literature values, however, which may be due to small solvent effects.

Table 3. Equilibrium acidities of p-substituted benzaldoximes p-$GC_6H_4CH{=}NOH$ and methyl p-substituted ketoximes p-$GC_6H_4C(Me){=}NOH$ in DMSO

Weak acid	HIn[a,b]	pK_{HIn}	$pK_{HA} \pm SD$[c]
p-$GC_6H_4CH{=}NOH$:			
4-MeO	2NPANH	20.66	20.80 ± 0.01
4-Me	2NPANH	20.66	20.62 ± 0.02
H	2NPANH	20.66	20.21 ± 0.01
4-Cl	CNAH	18.9	19.25 ± 0.03
4-Br	CNAH	18.9	19.20 ± 0.04
$4\text{-}CF_3$	CNAH	18.9	18.61 ± 0.03
4-CN	PFH	17.9	18.07 ± 0.05
$3\text{-}NO_2$	DPANH	17.5	17.73 ± 0.02
$4\text{-}NO_2$	DPANH	17.5	17.30 ± 0.05
p-$GC_6H_4CH(Me){=}NOH$:			
4-MeO	FH	22.6	21.98 ± 0.01
4-Me	FH	22.6	21.71 ± 0.06
H	2NPANH	20.66	21.05 ± 0.04
4-Cl	2NPANH	20.66	20.48 ± 0.02
4-Br	2NPANH	20.66	20.48 ± 0.01
$4\text{-}CF_3$	CNAH	18.9	19.50 ± 0.05
4-CN	CNAH	18.9	18.88 ± 0.00
$4\text{-}NO_2$	DPANH	17.5	18.18 ± 0.07

[a] HIn (indicator).

[b] 2NPANH=2-naphthylacetonitrile; CNAH=4-chloro-2-nitroaniline; PFH=9-phenylfluorene; DPANH=diphenylacetonitrile pK_{HA} measured by standard acid method and dimsyl was quenched by dibenzyl sulfone; FH=fluorene.

[c] Two runs were made for the pK_{HA} measurement.

EXPERIMENTAL

p-Substituted benzaldoximes and p-substituted phenyl methyl ketoximes were prepared according to the method of Vogel.[20] They were purified by distillation for liquids and recrystallization for solids, and checked for purity by ^1H NMR spectroscopy and their physical properties.

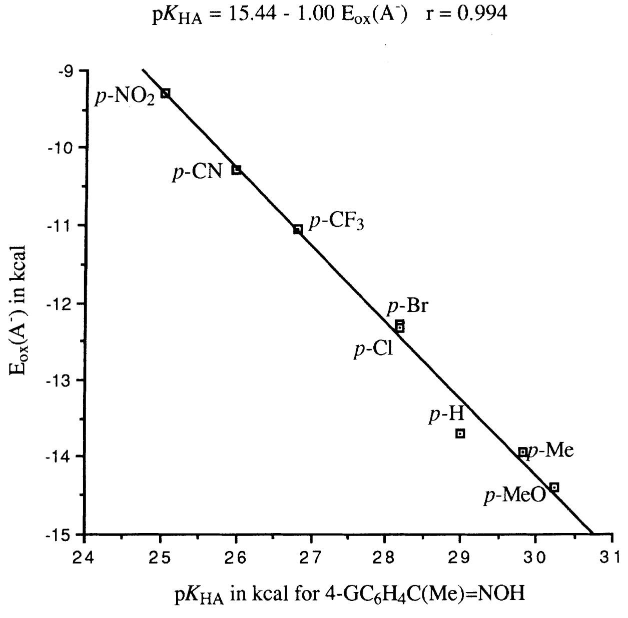


Figure 3. Plot of $E_{ox}(A^-)$ versus pK_{HA} for p-$GC_6H_4CH(Me){=}NOH$

The equilibrium acidities were measured in DMSO by either the overlapping indicator method or the standard acid method as reported previously.[14] The results, together with the indicators or standard acids used, are summarized in Table 3.

The oxidation potentials of the conjugate bases were measured by cyclic voltammetry (CV) in DMSO. The working electrode (BAS) consists of a 1.5 mm diameter platinum disk embedded in a cobalt glass seal. It was polished with a 0.05 mm Fischer polishing aluminum 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 reported potentials were referenced to the ferrocenium/ferrocene (Fc^+/Fc) couple. Tetraethylammonium tetrafluoroborate was used as the supporting electrolyte. All electrochemical experiments were carried out under an argon atmosphere.

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