Solvent Effects on Homolytic Bond Dissociation Energies of Hydroxylic Acids

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Abstract: The homolytic bond dissociation energies (BDEs) of the O−H bonds in DMSO solution for (a) phenol and a number of its derivatives, (b) three oximes, (c) three alcohols, (d) three hydroxylamines, and (e) two hydroxamic acids have been estimated by eq 1: $\mathrm{BDE}_{\mathrm{HA}} = 1.37\mathrm{p}K_{\mathrm{HA}} + 23.1E_{\mathrm{ox}}(\mathrm{A}^-) + 73.3$ kcal/mol. For most of these hydroxylic acids, the BDEs of the O−H bonds estimated by eq 1 are within ±2 kcal/mol of the literature values in nonpolar solvents or in the gas phase. There is no reason to believe, therefore, that these BDEs are "seriously in error because of failure to correct for solvent effects" as has been claimed on the basis that BDEs in highly polar solvents estimated for the O−H bond in phenol by photoacoustic calorimetry must be so corrected.

Introduction

The gas-phase homolytic bond dissociation energies (BDEs) of hydrocarbons and hydrocarbons bearing heteroatom substituents, such as substituted methanes, $\mathrm{GCH_2{-}H}$, where G is MeO, HO, PhS, $\mathrm{Me_3Si}$, Ph, $\mathrm{Me_2N}$, etc., have long been considered to provide the best estimates for the stablilities of the corresponding radicals.[1] The determination of gas-phase BDEs has been limited for experimental reasons primarily to small molecules, however. Several years ago a simple method of estimating the BDEs of H−A bonds in weak acids was developed in our laboratory. The method uses a semiempirical equation (eq 1) based on a themodynamic cycle.

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

The $\mathrm{p}K_{\mathrm{HA}}$ values in DMSO of the acids, which are accurate to ±0.2 $\mathrm{p}K_{\mathrm{HA}}$ unit, are multiplied by 1.37 to convert $\mathrm{p}K_{\mathrm{HA}}$ units to kcal/mol, and the oxidation potentials of their conjugate bases, $E_{\mathrm{ox}}(\mathrm{A}^-)$, are multiplied by 23.1 to convert eV to kcal/mol. (Henceforth kcal/mol will be abbreviated as kcal.) Although most of the oxidation potentials are irreversible, they have been found to be suitable to estimate BDEs by eq 1 that are within the usual accuracy, ±3 kcal, for BDE values. The method has been applied to estimate BDEs of acidic C−H, N−H, O−H, and S−H bonds in hundreds of weak acids, large and small, and the results have been described in more than 50 publications in the *Journal of the American Chemical Society* and the *Journal of Organic Chemistry*. For example, in one paper, estimates of the BDEs for (a) the benzylic and allylic H−C bonds in 14 hydrocarbons, (b) the acidic H−C bonds in 12 hydrocarbons bearing one or more heteroatoms, (c) the acidic H−N bonds in 5 nitrogen acids, and (d) the H−O bond in phenol and the S−H bond in thiophenol were reported.[2] For the 18 weak acids where literature (usually gas phase) BDE values were available agreement to within ±2 kcal was observed for all but three acids ($\mathrm{Ph_3C{-}H}$, PhNH−H, and PhO−H). For triphenylmethane the literature BDE value was shown to be too low by 6 kcal, and evidence was presented to suggest that the literature BDE value for aniline was also too low.[2] On the other hand, the BDEs estimated for the O−H bond in phenol and a number of its meta and para derivatives appeared to agree reasonably well with literature values, as is brought out in Table 1.

Table 1. Comparison of BDEs for Phenols

phenol	BDE[a]	BDE[b]	BDE[c]	BDE[d]	BDE[e]	BDE[f]
$\mathrm{C_6H_5OH}$	90.4 ± 1	88.3	88.3 ± 2	84 ± 1	85.6	87
$\mathrm{3\text{-}MeC_6H_4OH}$	90.0					
$\mathrm{3,5\text{-}Me_2C_6H_3OH}$	89.7					
$\mathrm{3\text{-}MeOC_6H_4OH}$	90.8					
$\mathrm{4\text{-}ClC_6H_4OH}$	90.9	89.6		84.4		
$\mathrm{4\text{-}MeC_6H_4OH}$	88.7	86.1	86.5			
4-*t*-$\mathrm{BuC_6H_4OH}$	88.7		86.5	82.1		
$\mathrm{4\text{-}PhC_6H_4OH}$	87.6		85.0			
$\mathrm{2,6\text{-}Me_2C_6H_3OH}$	85.5		85.1			
$\mathrm{4\text{-}MeOC_6H_4OH}$	84.6	82.6	84.0	78.1		
$\mathrm{4\text{-}H_2NC_6H_4OH}$	77.3	75.5				
$\mathrm{4\text{-}O^-C_6H_4OH}$	73.0	72.4				
$\mathrm{4\text{-}MeCOC_6H_4OH}$	92.8	90.8				
$\mathrm{4\text{-}NCC_6H_4OH}$	94.2	92.9				
$\mathrm{4\text{-}O_2NC_6H_4OH}$	94.7	94.2				

[a] Estimated from eq 1.[3] [b] Merenyi *et al.* from $E_{\mathrm{rd}}(\mathrm{ArO^\bullet})$ and $\mathrm{p}K_{\mathrm{HA}}$s in aqueous medium.[4] [c] Mahoney and DaRooge from rate constants for reaction of $\mathrm{ArO^\bullet}$ radicals in $\mathrm{C_6H_5Cl}$ with hydroperoxides and differences of the heats of formation of the hydroperoxides.[5] [d] Griller *et al.* from photoacoustic calorimetric measurements (solvent not specified).[6] [e] McMillen, D. F.; Golden, D. M.[1] [f] "Corrected" value in a nonpolar medium.[7]

Our BDE for phenol of 90.4 ± 1 kcal estimated by eq 1 is based on the average of the values (kcal in parentheses) for (a) the parent, H (90.4), (b) 3-Me (90.0), (c) 3,5-Me, (89.7), (d) 3-MeO (90.8), and (e) 4-Cl (90.0).[3]

Examination of Table 1 shows that there is remarkably good agreement between our BDE values and the BDEs estimated by Merenyi *et al.* for phenol and 8 of its meta and para derivatives by combining reduction potentials of phenoxyl radicals with $\mathrm{p}K_{\mathrm{HA}}$ values, both measured in aqueous solution.[4] These values were obtained by essentially the same method that we used. In the aqueous medium the $\mathrm{p}K_{\mathrm{HA}}$ for phenol is 10, i.e., 8 $\mathrm{p}K_{\mathrm{HA}}$ units (11 kcal) lower than in DMSO, but the reduction potentials of the $\mathrm{ArO^\bullet}$ radicals evidently change to

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keep pace. Our estimated BDE values are usually 1−2 kcal higher than those of Merenyi and also 1−2 kcal higher than those obtained in chlorobenzene in the careful study of Mahoney and DaRooge.[5] Our value for phenol and its 4-Cl, 4-*t*-Bu, and 4-MeO derivatives are about 5−6 kcal higher than those obtained by photoacoustic calorimetry (PAC) by Griller *et al.* (solvent unspecified)[6] and for the best gas-phase value chosen by McMillen and Golden.[1]

Recently a further extensive study of the BDE of the O−H bond in phenol has been carried out by photoacoustic calorimetry (PAC), and the BDE has been found to be solvent dependent.[7] In particular, the BDE of the PhO−H bond in both ethyl acetate and acetonitrile, which are dipolar hydrogen bond acceptor solvents like DMSO, have been found to be 95 kcal. The authors have corrected this value for solvation of the hydrogen atom (2 kcal) and hydrogen bonding of phenol to the solvent (4.7 kcal) to 88.3 kcal. Although they apparently did not carry out any PAC measurements in DMSO, they have made the reasonable assumption that the BDE, as estimated by PAC, will be 95.6 kcal in DMSO. They suggest that this value should be corrected by 2 kcal for solvation of the hydrogen atom, and by 6.6 kcal for hydrogen bonding of phenol to the DMSO solvent to give a value of 87 kcal. The authors have concluded from this study that our BDE estimated by eq 1 for the O−H bond in phenol is seriously in error because we have neglected to correct for solvent effects, and that “similar errors must be present in many other electrochemical (EC) bond energies that also were determined in polar solvents”.

It is not clear, however, to what extent the BDE for the PhO−H bond estimated by eq 1 needs to be corrected for hydrogen bonding. For example, phenol must be strongly hydrogen bonded to water in aqueous solution, yet the BDE estimated for the O−H bond for phenol in this medium by Merenyi *et al.*[4] is identical with that of Mahoney and DaRooge (88.3 kcal) in chlorobenzene. The Merenyi value is also only 1 kcal higher than the “corrected value” of Wayner *et al.* for phenol in acetonitrile or DMSO.[7] (Merenyi *et al.* estimate the solvent correction to be of the order of 2−3 kcal for their BDE in aqueous solution.)

We assume that the presumption of serious errors in other BDEs estimated by our electrochemical method refers to other O−H bonds rather than to C−H, N−H, or S−H bonds, which are known to be very weak hydrogen bond donors. We have therefore sought to compare the BDEs estimated by the EC method (eq 1) with literature BDEs in nonpolar solvents or the gas phase for the O−H bonds in (a) additional phenols, (b) oximes, (c) alcohols, (d) hydroxylamines, and (e) hydroxamic acids.

Results and Discussion

In order to make the desired comparisons of BDEs of O−H bonds estimated by eq 1 in DMSO with literature values in nonpolar solvents or the gas phase, it was necessary to find hydroxylic acids (a) with known O−H BDEs, (b) with acidities that are measurable in DMSO, and (c) with conjugate bases for which oxidation potentials can be measured by cyclic voltammetry (CV). Fortunately, we had already made measurements on several additional phenols and on several oximes where the required data were available in the literature. Acidity data, but not oxidation potential data, were also available for a number of alcohols, where the O−H BDEs were known. The BDEs of the O−H bonds in several hydroxylamines and hydroxamic acids had also been reported in the literature, but acidity and oxidation potential data were lacking. These hydroxylamines and hydroxamic acids were purchased or synthesized, and the requisite data obtained by pK_{HA} and CV measurements.

The BDEs of the O−H Bonds in Oximes. In 1992 we measured acidities and estimated the BDEs of the O−H bonds in 21 oximes.[8] Later we were surprised (and chagrined) to find a report in the earlier literature of the BDEs of the O−H bonds in three ketoximes, *t*-Bu_2C═NOH, *t*-Bu(1-Ad)C═NOH, and *t*-Bu(*i*-Pr)C═NOH, measured by a direct calorimetric method in benzene[9] that were 6.3 to 15.8 kcal lower than the BDEs we had found. This indicated that either there was something wrong with our method or the O−H bonds in the ketoximes are dramatically weakened by increasing the bulk of the alkyl groups. Fortunately, the latter turned out to be true. The BDEs estimated by eq 1 for the two oximes *t*-Bu_2C═NOH and *t*-Bu-(1-Ad)C═NOH are 82.6 and 81.7 kcal, respectively.[10] Each of these BDEs is 1.7 kcal higher than that reported in the literature. The estimates of the BDEs of oximes using eq 1 have now been extended to the O−H bond in *t*-Bu(*i*-Pr)C═NOH. It has been found to have a BDE of 86.0 kcal, i.e., 1.7 kcal higher than the literature report. Serious solvent corrections for the BDEs obtained for these oximes are obviously not needed.

The BDEs of the O−H Bonds in Additional Phenols. In earlier studies the BDEs of the O−H bonds in 2,4,6-tri-*tert*-butylphenol and α-tocopherol have been estimated by eq 1 to be 82.3 and 80.9 kcal, respectively.[11] The BDE of the O−H bond in 2,4,6-tri-*tert*-butylphenol obtained by the direct calorimetric method in benzene solution[12] is 1.1 kcal lower than our value, and that for the O−H bond in α-tocopherol estimated by kinetic measurements combined with a Polanyi-type correlation is 0.5 kcal lower.[13] Here too solvent corrections are not needed.

The BDEs of the O−H Bonds in Alcohols. The gas-phase BDEs of the O−H bonds in three alcohols (kcal in parentheses) are as follows:[1] MeOH (104.5), EtOH (104), *t*-BuOH (105). The pK_{HA} values of these alcohols are 29.1, 29.8, and 32.2, respectively.[14] It is difficult to obtain oxidation potential values for these strongly basic anions because they bond strongly with small amounts of alcohol or water, if present. But by using concentrated solutions of $CH_3SOCH_2^-K^+$ in DMSO and low concentrations of alcohol this has now been accomplished, and eq 1 has been used to obtain the results shown in Table 2.

Examination of Table 2 shows that there is no need to correct the BDEs of alcohols for solvation effects, despite their strong hydrogen-bond donor abilities.

The BDEs of the O−H Bonds in Hydroxylamines. The homolytic cleavage of the O−H bonds in hydroxylamines has aroused considerable interest because of their weakness. The

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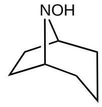
Table 2. Acidities and BDEs of Alcohols

ROH	pK_{HA}	$E_{ox}(A^-)$[c]	BDE_{HA}[d]	BDE(lit.)[e]
MeOH	29.1[a]	−0.368	104.6	104.4
EtOH	29.8[a]	−0.483	103.0	104.2
i-PrOH	30.25[a]	−0.471	103.9	104.7
t-BuOH	32.2[a]	−0.512	105.5	105.1
BzOH	27.0[b]	−0.372	101.7	

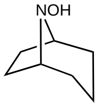
[a] Data from ref 14. [b] Data from ref 15. [c] Irreversible oxidation potentials. Measured in DMSO with 1−3 mM alcohol, 10−20 mM potassium dymsyl, and 0.1 M $Bu_4N^+PF_6^-$ electrolyte at a sweep rate of 100 mV s^{-1}, and referred to the ferrocene/ferrocenium couple. [d] BDEs estimated from pK_{HA} and $E_{ox}(A^-)$ values by eq 1. [e] Data from ref 1.

Table 3. Acidities and Homolytic Bond Dissociation Energies of Hydroxylic Acids Estimated by Eq 1

	acid	pK_{HA}[a]	$E_{ox}(A^-)$[c]	BDE_{HA}[f]
1.	Et_2NOH	29.6	−1.645	75.9
2.	*t*-Bu_2NOH	31.1	−2.070[d]	68.2
3.		32.4	−1.764[d] −1.660	77.0 79.0
4.	TMPOH	31.0	−1.997[d]	69.7
5.	PhCON(*i*-Pr)OH	18.7	−0.769[R]	81.2
6.	PhCON(*t*-Bu)OH	19.6	−0.879[R]	79.9
7.	*t*-Bu(*i*-Pr)C=NOH	25.5	−0.965[R] [e]	86.0
8.	*t*-Bu_2C=NOH	24.4[b]	−1.035[R] [e]	82.6

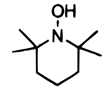
[a] Data taken from Table 5 unless otherwise indicated. [b] Data from ref 10. [c] Irreversible oxidation potentials measured in DMSO with 1 to 3 mM and 0.1 M $Bu_4N^+PF_6^-$ at a sweep rate of 100 mV s^{-1}, and referred to the ferrocene/ferrocenium couple unless otherwise indicated. Superscript R indicates reversible. [d] Reduction potential of the corresponding radical. [e] 0.1 M $Et_4N^+BF_4^-$ was used. [f] Estimated by eq 1.

Table 4. Comparison of the O−H Bond BDEs Estimated by Eq 1 and Those Obtained in the Gas Phase or in Nonpolar Solvent

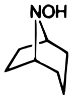
	acid	BDE_{HA}[a]	BDE(lit.)[f]	ref
1.	PhOH	90.4[b]	84−88.3 87 ± 1[g]	*i* 7
2.	α-tocopherol	80.9[c]	80.4	13
3	2,4,6-tri-*tert*-butyl phenol	82.3[c]	81.2	9
4.	Et_2NOH	75.9	69.5	18
5.	*t*-Bu_2NOH	68.2	<69.6[h]	9
6.	TMPOH	69.7	69.6	9
7.		78.0	77.0	9
8.	*t*-Bu(*i*-Pr)C=NOH	86.0	84.3	9
9.	*t*-Bu_2C=NOH	82.6	80.9	9
10.	*t*-Bu(1-Ad)C=NOH	81.7[d]	80.0	9
11.	MeOH	104.6[e]	104.5	1
12.	EtOH	103.0[e]	104	1
13.	*t*-BuOH	105.5[e]	105	1
14.	PhCON(*i*-Pr)OH	81.2	79.3	16
15.	PhCON(*t*-Bu)OH	79.9	78.0	16

[a] Data taken from Table 3 unless otherwise indicated. [b] Reference 2. [c] Reference 11. [d] Reference 10. [e] Data from Table 2. [f] Data reported in references. [g] Estimated to be the best gas-phase value described in ref 7. [h] See text. [i] Table 1.

nitroxyl radicals derived from hydroxylamines where the nitrogen atom is attached to a tertiary alkyl center such as in **1**, 2,2,6,6-tetramethyl-*N*-hydroxypiperidine (TMPOH), and **2**, *N*-hydroxylnortropane, are stable enough to allow the BDEs of their O−H bonds to be measured by a direct calorimetric method or by an equilibrium constant method for hydrogen atom transfer reactions such as eq 2.[9]

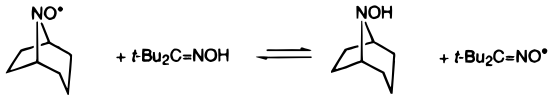


1



2

BDE (kcal) : **69.6** **77.0**



(2)

2• **3** **2** **3•**

BDE = 80.9 kcal BDE = 77 kcal

In order to make estimates of the BDEs of **1**, **2**, and *t*-Bu_2NOH by eq 1 it was necessary to measure their acidities and the oxidation potentials of their conjugate bases. This turned out to be a challenging assignment because all three acids have pK_{HA} values above 30, which requires rigid exclusion of water and oxygen. Also, these acids, in common with other hydroxylic acids, are subject to homo-hydrogen-bonding, which means that the acid bonds to its conjugate base to form a hydrogen-bond complex, $RO^-\cdots H-OR$, wherein the undissociated acid bonds more strongly to its conjugate base than to the solvent. This perturbs the equilibrium of the acid with indicator ions and can lead to erroneous pK_{HA} values. It was therefore necessary to carry out the titrations under conditions where the $[RO^-]/[ROH]$ ratio is close to unity.[14] The oxidation potentials also proved challenging to measure, but successful measurements were obtained under the conditions described to measure the CVs of alcohols. The pK_{HA} values and oxidation potentials and BDEs are given in Table 3.

Examination of Table 3 shows that estimates of BDEs for hydroxylamines **1** and **2** by eq 1 are 69.7 and 78 kcal, respectively. These values are within 1 kcal of the literature values. The BDEs of *t*-Bu_2NOH was not measured by Mahoney *et al.*, but was estimated to be several kcal lower than that of **1** (69.6 kcal).[9] Our value estimated by eq 1 is 68.2 kcal.

The BDEs of the O−H Bonds in Hydroxamic Acids. Perkins *et al.* have determined the BDEs of the O−H bonds in *N*-isopropyl- and *N*-*tert*-butylbenzohydroxamic acids,[16] which were prepared by benzoylation of the corresponding hydroxylamines:[17]

$$t\text{-BuNH}_2\text{OH}^+\text{Cl}^- + \text{PhCOCl} \xrightarrow[\text{CH}_3\text{CN}]{\text{Et}_3\text{N}} \text{PhCON}(t\text{-Bu})\text{OH}$$

The pK_{HA}s of these hydroxamic acids were measured by the overlapping indicator method. The acidities of these hydroxamic acids are close to that of phenol in DMSO, and the homo-hydrogen-bonding constants are as large as those of phenols. This would appear to make them good candidates for BDE solvent corrections caused by hydrogen bonding. The BDEs are, however, each only 1.9 kcal higher than the BDEs found in the Perkins equilibrium studies.

Summary of Comparisons with Literature BDE Values. The comparisons of BDEs of the O−H bonds in the five different hydroxylic acids described in previous sections by eq 1 with literature values measured in nonpolar solvents or the gas phase are summarized in Table 4.

With the exception of phenol itself and diethylhydroxylamine, the BDEs of all 15 of these hydroxylic acids estimated by eq 1

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are within ±2 kcal of the literature values. We have no explanation for the 6.4-kcal difference in BDE for Et_2NOH, but our value of 75.9 kcal is consistent with the BDEs of seven other R_2NOH hydroxylamines, estimated by eq 1, which fall in the range of 74−77 kcal.[19] It is clear from these comparisons that estimates of BDEs of the O−H bonds in most hydroxylic acids made by eq 1 agree remarkably well with literature values, and that there is no reason to believe that this method leads to "serious errors" as has been suggested.[7] Our value for the O−H bond in phenol of 90.4 kcal is, however, 2.1 kcal higher than the value obtained by Mahoney *et al.* in chlorobenzene,[5] and 3.4 kcal higher than the 87 kcal estimated to be the best gas phase value.[7] Furthermore, persual of the data in Table 4 shows that BDE values estimated by eq 1 are usually slightly higher than the literature values suggesting that the BDEs may be subject to small solvent effects in DMSO.

The relationship between the BDE in DMSO solution, BDE-$(HA)_s$, and the corresponding gas-phase value, $BDE(HA)_g$, can be expressed by eq 3:

$$\mathrm{BDE(HA)_s} = \mathrm{BDE(HA)_g} + \Delta H_{\mathrm{solv}}(\mathrm{H}^\bullet)_{\mathrm{s}} + \Delta H_{\mathrm{solv}}(\mathrm{A}^\bullet)_{\mathrm{s}} - \Delta H_{\mathrm{solv}}(\mathrm{HA})_{\mathrm{s}} \quad (3)$$

The BDEs of the C−H bond in carbon acids are generally assumed to be solvent independent because the last two terms in eq 3 cancel one another.[20] It is also generally agreed that the remaining $\Delta H_{\mathrm{solv}}(\mathrm{H}^\bullet)_{\mathrm{s}}$ term is small. Its value is unknown, and it is often neglected. This leaves $\mathrm{BDE(HA)_s} = \mathrm{BDE(HA)_g}$ for carbon acids, as has been observed experimentally in DMSO,[2] and also in aqueous medium.[20]

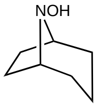
The hydrogen bond donor properties of the hydroxyl group in hydroxylic acids are likely to cause stronger bonding with the hydrogen-bond-acceptor DMSO solvent than occurs with the $A^\bullet$ radical. The BDE of the hydroxyl group will then be strengthened thereby, but the effects are smaller than estimated for the hydrogen bond energies (3−4 kcal for alcohols)[21] suggesting that solvation of the $A^\bullet$ radicals may also be involved to some extent. The hydrogen bond energy of phenol in DMSO has been estimated to be 6−7 kcal,[21] which may account for the greater difference in our BDE value in DMSO versus literature values than is observed for other hydroxylic acids.

We conclude that solvent corrections of about 2−3 kcal are needed for the BDEs of the O−H bonds in phenol and its simple derivatives as estimated by eq 1 in DMSO, and that smaller (1 to 2 kcal) solvent corrections may possibly be needed for some other hydroxylic acids. There is no evidence to indicate that "serious errors must be present in many other EC bond energies", as suggested by Wayner *et al.*[7] Solvent corrections for H−C, H−N, or H−S acids should ordinarily not be needed since the hydrogen-bonding donor abilities of these functions are weak.

Experimental Section

NMR spectra were recorded on a Gemini XL-300 (300 MHz) or XLA 400 (400 MHz) spectrometer. Melting points were measured on a Thomas Hoover capillary melting point apparatus and are uncorrected. *N*-Isopropylhydroxylamine hydrochloride, *N*-*tert*-butylhydroxylamine hydrochloride, *N*-hydroxyldiethylamine, *N*-oxyl-2,2,6,6-tetramethylpiperidine, di-*tert*-butyl nitroxide, and tropane (*N*-methyl-8-azabicyclo-[3.2.1]octane) are commercially available (Aldrich).

Table 5. Equilibrium Acidities of Hydroxylic Acids Determined by the Overlapping Indicator Method[a]

acid	indicator (pK_{In})[b]	pK_{HA}[c]	pK_{hb}[d]
Et_2NOH	DDH (29.4)	29.60 ± 0.05	3.3 ± 0.1
t-Bu_2NOH	TH (30.6)	31.15 ± 0.05	*e,f*
TMPOH	TH (30.6)	31.00 ± 0.02	*e,f*
	TH (30.6)	32.4 ± 0.1	*e,g*
PhCON(*i*-Pr)OH	CNAH (18.9)	18.70 ± 0.02	3.7 ± 0.1
PhCON(*t*-Bu)OH	2-NPANH (20.66)	19.6 ± 0.1	3.6 ± 0.1
t-Bu(*i*-Pr)C═NOH	TP2H (25.6)	25.5 ± 0.1	3.25 ± 0.03

[a] See ref 14. [b] Indicators: TH = triphenylmethane. DDH = bis(*p*-phenylphenyl)methane. MFH = 9-methylfluorene. CNAH = 4-chloro-2-nitroaniline. 2-NPANH = 2-naphthylacetonitrile. TP2H = 1,3,3-triphenylpropene. The pK_{HIn} values are given in parentheses. [c] pK_{HA} corrected for homo-H-bonding.[14] [d] Homo-H-bonding constant.[14] [e] The pK_{HA} is too high to obtain pK_{hb} values. [f] The homo-H-bonding effect was observed to be small ($pK_{hb} < 1$). [g] The homo-H-bonding effect was observed to be large ($pK_{hb} \sim 3-4$).

***N*-Hydroxy-2,2,6,6-tetramethylpiperidine** was prepared by the method of Ingold *et al.*[9] *N*-Oxyl-2,2,6,6-tetramethylpiperidine (0.78 g, 5 mmol) and 1,2-diphenylhydrazine (1.0 g, 5.8 mmol) were mixed in 5 mL of benzene under a nitrogen atomosphere. The mixture was stirred at room temperature for 20 min, then fractionally distilled to give 0.5 g (63%) of a pale yellow liquid (bp 60 °C/10τ) which solidified upon standing, mp 37−39 °C (lit.[22] mp 38−40 °C). ^{1}H NMR ($CDCl_3$): δ 1.22 (12H, s, Me), 1.56 (6H, s, CH_2), 4.03 (1H, br, OH).

***N,N*-Di-*tert*-butylhydroxylamine** was similarly prepared from di-*tert*-butyl nitroxide in 70% yield, bp 50 °C/10τ, mp 37−38 °C.[23] ^{1}H NMR (C_6D_6): δ 1.22 (18H, s, *t*-Bu), 3.97 (1H, br, OH).

***tert*-Butyl isopropyl ketoxime** was similarly prepared by a method reported earlier[10] from *tert*-butyl isopropyl ketone imine (which was obtained from a reaction of *tert*-butyllithium and isobutyronitrile) and hydroxylamine hydrochloride in 80% yield, mp 140−141 °C (lit.[24] mp 140−141 °C). ^{1}H NMR: δ 1.10 (6H, d, J = 7.1 Hz, *i*-Pr), 1.30 (9H, s, *t*-Bu), 2.59 (1H, m, CH), 8.83 (1H, s, NH).

***N*-Hydroxylnortropane**. First, a reaction of tropane with ethyl chloroformate in benzene solution[25] gave *N*-ethoxycarbonylnortropane in 95% yield, bp 109−111 °C/8τ (lit.[25] bp 122−124 °C/13τ). Then, hydrolysis of *N*-ethoxycarbonylnortropane in refluxing concentrated hydrochloric acid gave nortropane hydrochloride in 90% yield. The hydrochloride (1.5 g, 10 mmol) was dissolved in 10 mL of 1 N NaOH aqueous solution and warmed to 50 °C, then 2.0 mL of 30% hydrogen peroxide (18 mmol) and 2 mg of phosphotungstic acid were added. After the gas evolution ceased (ca. 15 min), the resulting solution was extracted with 20 mL of CH_2Cl_2 containing 1.2 g (6 mmol) of PhNHNHPh. The organic layer was dried with anhydrous K_2CO_3. After removal of the solvent, sublimation of the residue at 10 τ gave 0.6 g (48%) of *N*-hydroxynortropane, mp 114−116 °C (lit.[26] mp 118 °C). ^{1}H NMR ($CDCl_3$): δ 1.3−1.9 (10H, m), 3.44 (2H, s), 4.4 (1H, br, OH).

***N*-Oxynortropane** was prepared by the method of Ingold *et al.*[26] The reduction potential of this radical was measured successfully using the crude product.

***N*-*tert*-Butylbenzohydroxamic acid** was prepared by a revised method of Perkins *et al.*[17] Into an acetonitrile solution (10 mL) containing *N*-*tert*-butylhydroxylamine hydrochloride (0.55 g, 5 mmol) and triethylamine (2.8 mL, 20 mmol) was added dropwise an acetonitrile solution of benzoyl chloride (1.2 mL, 10 mmol). The resulting mixture was stirred overnight and then mixed with 20 mL water and extracted with CH_2Cl_2 twice (10 mL each). The organic layer was dried and the

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solvent was stripped off. The residue was dissolved in 20 mL of EtOH, then mixed with 10 mL of 1 N aqueous NaOH solution and stirred for 1 h. The resulting mixture was extracted with 5 mL of CH_2Cl_2. The aqueous layer was neutralized with 1 N aqueous hydrochloric acid to pH 7 and extracted with CH_2Cl_2 twice (10 mL each). The organic layer was dried and the solvent was stripped off. The residue was recrystalized from hexane to give 0.7 g (70%) of slightly yellow solid; mp 110−113 °C (lit.[17] mp 113 °C). ^{1}H NMR ($CDCl_3$): δ 1.33 (9H, s,*t* -Bu), 7.3−7.5 (5H, m, Ph), 8.4 (1H, br, OH).

***N*-Isopropylbenzohydroxamic acid** was similarly prepared from *N*-isopropyl-hydroxylamine hydrochloride in 67% yield; mp 87−89 °C. ^{1}H NMR ($CDCl_3$): δ 1.30 (6H, d, $J = 6.5$ Hz, *i*-Pr), 4.21 (1H, m), 7.4−7.5 (5H, m, Ph), 8.4 (1H, br, OH).

Equilibrium acidities in DMSO were determined by the overlapping indicator method as described previously.[27] The results were summarized in Table 5.

Oxidation potentials were measured by a conventional cyclic voltammetric instrument, as described previously.[3] All potentials are reported with reference to $E_{1/2}$ of the ferrocene/ferrocenium couple. Oxidation potentials of the conjugate anions of alcohols cannot be obtained with tetraethylammonium tetrafluoroborate as the supporting electrolyte because their conjugate anions form strong homo-hydrogen-bonds with the small amounts of water present, and deprotonation of the acids competes with the deprotonation of the electrolyte. When tetrabutylammonium hexafluorophosphate was used as the supporting electrolyte, this problem was not encountered for hydroxylic acids with $pK_a < 33$.

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