

# Revision of the $\alpha_2^H$ value for *N,N*-dialkylhydroxylamines based on kinetic and spectroscopic measurements

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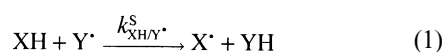
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Kinetic solvent effects on hydrogen-atom abstraction from *N,N*-diethylhydroxylamine and *N,N*-dibenzylhydroxylamine by the 2,2-diphenyl-1-picrylhydrazyl radical (DPPH<sup>•</sup>) indicated that these compounds are much weaker hydrogen-bond donors than implied by the currently accepted  $\alpha_2^H$  value of 0.453. Lower  $\alpha_2^H$  values were also obtained by monitoring 1 : 1 complex formation with two strong hydrogen-bond acceptors, HMPA and DMSO, in tetrachloromethane using IR spectroscopy. It is concluded that the  $\alpha_2^H$  value for sterically non-hindered *N,N*-dialkylhydroxylamines should be revised downward to 0.29.

## Introduction

Recent studies of solvent effects on the rates of hydrogen-atom abstraction from various substituted phenols, aniline, *tert*-butyl hydroperoxide and cyclohexane have rationalized an imposing body of kinetic data.<sup>1</sup> At ambient temperatures, kinetic solvent effects (KSEs) for the generalized reaction represented by eqn. (1) were found to be very well correlated by a simple

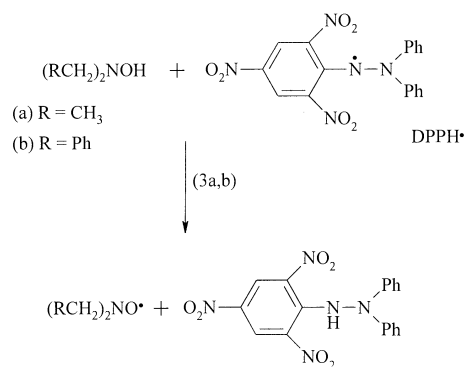


empirical equation that is based on the general, thermodynamically related scales of Abraham *et al.* for solute hydrogen-bond basicities for 1 : 1 complexes in CCl<sub>4</sub> ( $\beta_2^H$  for solvent S)<sup>2</sup> and hydrogen-bond acidities for 1 : 1 complexes in CCl<sub>4</sub> ( $\alpha_2^H$  for substrate XH).<sup>3</sup> This empirical equation is given by eqn. (2)<sup>1</sup> where  $k^{\text{S}}$  is the rate constant in solvent S and  $k^{\circ}$  is

$$\log(k_{\text{XH/Y}}^{\text{S}}/\text{dm}^3 \text{ mol}^{-1} \text{ s}^{-1}) = \log(k_{\text{XH/Y}}^{\circ}/\text{dm}^3 \text{ mol}^{-1} \text{ s}^{-1}) - 8.3\alpha_2^H\beta_2^H \quad (2)$$

the rate constant in a saturated hydrocarbon or other non-hydrogen-bond accepting solvent for which  $\beta_2^H = 0.00$ . Despite the fact that eqn. (2) uses a solute parameter,  $\beta_2^H$ , as a solvent property this equation has been found to apply to all Y<sup>•</sup> radicals that have been examined to date including *tert*-alkoxyl, peroxy, alkyl, and 2,2-diphenyl-1-picrylhydrazyl (DPPH<sup>•</sup>). The absolute reactivities of the various Y<sup>•</sup> are reflected by their  $k^{\circ}$  values. The magnitude of the KSE, *i.e.*, the sensitivity of reaction (1) to solvent effects is dependent only on the ability of XH to act as a hydrogen-bond donor (HBD) and is given by  $-8.3\alpha_2^H$ . Eqn. (2) rests on a rather limited number (12) of substrates, most of which (8) are substituted phenols. Confidence in the generality and utility of this equation would increase if it could be shown to apply to new classes of substrates. With this goal in mind, we have now determined KSEs for hydrogen-atom abstraction from two *N,N*-dialkylhydroxylamines by DPPH<sup>•</sup>, reactions (3a) and (3b) (Scheme 1).

For such compounds only one  $\alpha_2^H$  value is available,<sup>3</sup> *viz.*,  $\alpha_2^H$  [(PhCH<sub>2</sub>)<sub>2</sub>NOH] = 0.453. This is a mean value calculated<sup>3</sup> from data for 1 : 1 complex formation between (PhCH<sub>2</sub>)<sub>2</sub>NOH and three bases, diethyl ether, DMSO and triethylamine at 25 °C in



Scheme 1

CCl<sub>4</sub>.<sup>4</sup> It implies that the KSE for an *N,N*-dialkylhydroxylamine would have about half the maximum possible value [ $\alpha_2^H$  values range from 0.00 (*e.g.*, cyclohexane) to nearly 1.0 for strong acids (*e.g.*, 0.951 for CF<sub>3</sub>CO<sub>2</sub>H)]. However, in the event, the kinetic measurements indicated that  $\alpha_2^H$  was considerably smaller than 0.45 for both hydroxylamines and these lower values were confirmed by infrared spectroscopy.

## Results

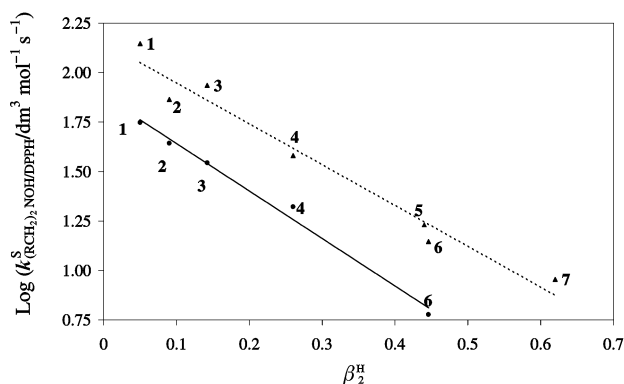
### Kinetic solvent effects on reactions 3a and 3b

The rates of these reactions were measured at ambient temperature following the rapid mixing of equal volumes of stock solutions of the DPPH<sup>•</sup> radical and the dialkylhydroxylamine in the same solvent. Initial reagent concentrations were chosen so as to have convenient reaction rates while using a large excess of hydroxylamine to ensure pseudo-first-order kinetic behavior. Typically, the DPPH<sup>•</sup> concentration was  $1 \times 10^{-4}$  mol dm<sup>-3</sup> before mixing and this was reacted with five different concentrations of the hydroxylamine (range 2.5 to  $50 \times 10^{-3}$  mol dm<sup>-3</sup> before mixing). The experimental pseudo-first-order rate constants,  $k_{\text{exptl}}^{\text{S}}$ , were determined by monitoring decay of the DPPH<sup>•</sup> at its UV band maximum (*ca.* 330 nm, solvent-dependent). Plots of  $k_{\text{exptl}}^{\text{S}}$  vs. [(RCH<sub>2</sub>)<sub>2</sub>NOH] were linear ( $r^2 > 0.99$ ) and their slopes gave the desired second-order rate constant in the chosen solvent,  $k_{(\text{RCH}_2)_2\text{NOH/DPPH}^{\bullet}}^{\text{S}}$  according to eqn. (4).

**Table 1** Absolute rate constants ( $\text{dm}^3 \text{mol}^{-1} \text{s}^{-1}$ ) for hydrogen-atom abstraction from  $(\text{CH}_3\text{CH}_2)_2\text{NOH}$  and  $(\text{PhCH}_2)_2\text{NOH}$  by the  $\text{DPPH}^\bullet$  radical in various solvents at ambient temperatures

Solvent	$\beta_2^{\text{H}}$ <sup>a</sup>	$k_{(\text{RCH}_2)_2\text{NOH/DPPH}^\bullet}^{\text{S}}$	
		R = CH <sub>3</sub>	R = Ph
Tetrachloromethane (1)	0.05 <sup>b</sup>	56	140
Chlorobenzene (2)	0.09	44	73
Benzene (3)	0.14	35	86
Anisole (4)	0.26	21	38
Acetonitrile (5)	0.44	—	17
Ethyl acetate (6)	0.45	6	14
Pyridine (7)	0.62	—	9

<sup>a</sup> From ref. 2 unless otherwise noted. <sup>b</sup> From ref. 1. The “usual” value of 0.00 does not reflect the fact that  $\text{CCl}_4$  is a weak HBA, see also ref. 5.



**Fig. 1** Plot of  $\log(k_{(\text{RCH}_2)_2\text{NOH/DPPH}^\bullet}^{\text{S}}/\text{dm}^3 \text{mol}^{-1} \text{s}^{-1})$  vs.  $\beta_2^{\text{H}}$  (solid line R = CH<sub>3</sub>, dashed line R = Ph). The numbers beside the points correspond to solvents indicated in Table 1.

$$k_{\text{expt}}^{\text{S}} = k_0^{\text{S}} + k_{(\text{RCH}_2)_2\text{NOH/DPPH}^\bullet}^{\text{S}}[(\text{RCH}_2)_2\text{NOH}] \quad (4)$$

These results are summarized in Table 1 and plots of  $\log(k_{(\text{RCH}_2)_2\text{NOH/DPPH}^\bullet}^{\text{S}}/\text{dm}^3 \text{mol}^{-1} \text{s}^{-1})$  vs. the  $\beta_2^{\text{H}}$  value of the solvent are shown in Fig. 1.

#### $a_2^{\text{H}}$ Values derived from kinetic solvent effects

The plots of  $\log(k_{(\text{RCH}_2)_2\text{NOH/DPPH}^\bullet}^{\text{S}}/\text{dm}^3 \text{mol}^{-1} \text{s}^{-1})$  vs.  $\beta_2^{\text{H}}$  for solvent S (Fig. 1) yield the following KSE eqns. (5) and (6).

$$\text{R} = \text{CH}_3; \quad \log k^{\text{S}} = 1.8_8 - 2.4_0\beta_2^{\text{H}} \quad (5)$$

$$\text{R} = \text{Ph}; \quad \log k^{\text{S}} = 2.1_6 - 2.0_7\beta_2^{\text{H}} \quad (6)$$

The intercepts in these two plots correspond to  $\log k^\circ$ , where  $k^\circ$  is the rate constant for hydrogen-atom abstraction from  $(\text{RCH}_2)_2\text{NOH}$  by  $\text{DPPH}^\bullet$  in a non-hydrogen-bond accepting solvent for which  $\beta_2^{\text{H}} = 0.00$ , such as an alkane. Unfortunately,  $k^\circ$  could not be directly measured because  $\text{DPPH}^\bullet$  is essentially insoluble in alkanes. The slopes of these two plots correspond to  $-8.3 a_2^{\text{H}}$  for the two  $(\text{RCH}_2)_2\text{NOH}$ . Thus, for diethylhydroxylamine,  $a_2^{\text{H}} = 2.4_0/8.3 = 0.28_9$  and for dibenzylhydroxylamine,  $a_2^{\text{H}} = 2.0_7/8.3 = 0.24_9$  (Table 2). This last value was so much lower than the literature value<sup>3</sup> of 0.453 that we decided that both  $a_2^{\text{H}}$  values should be determined by the usual infrared spectroscopic procedure.

#### $a_2^{\text{H}}$ Values derived from infrared spectroscopy

Because the KSE-derived  $a_2^{\text{H}}$  values for the hydroxylamines indicated that they were relatively weak HBDS we chose two

**Table 2** Values of  $a_2^{\text{H}}$  obtained for two *N,N*-dialkylhydroxylamines by KSE and IR measurements

Hydroxylamine	$a_2^{\text{H}}$ Values based on:			Mean
	KSE	IR(DMSO) <sup>a</sup>	IR(HMPA) <sup>b</sup>	
$(\text{CH}_3\text{CH}_2)_2\text{NOH}$	0.28 <sub>9</sub>	0.29 <sub>4</sub>	0.32 <sub>4</sub>	0.30 <sub>2</sub>
$(\text{PhCH}_2)_2\text{NOH}$	0.24 <sub>9</sub>	0.34 <sub>2</sub>	0.25 <sub>1</sub>	0.28 <sub>1</sub>

<sup>a</sup>  $L_{\text{DMSO}} = 1.2399$ ,  $D_{\text{DMSO}} = 0.2656$  (see ref. 3) and measured  $K^i/\text{mol}^{-1} \text{dm}^3 = 3.9_3$  and  $7.4$ , for  $(\text{CH}_3\text{CH}_2)_2\text{NOH}$  and  $(\text{PhCH}_2)_2\text{NOH}$ , respectively. <sup>b</sup>  $L_{\text{HMPA}} = 1.5693$ ,  $D_{\text{HMPA}} = 0.6287$  (see ref. 3) and measured  $K^i/\text{mol}^{-1} \text{dm}^3 = 18.1$  and  $5.3_9$  for  $(\text{CH}_3\text{CH}_2)_2\text{NOH}$  and  $(\text{PhCH}_2)_2\text{NOH}$ , respectively.

very strong hydrogen-bond acceptors (HBAs) dimethyl sulfoxide, DMSO ( $\beta_2^{\text{H}} = 0.78$ ) and hexamethylphosphoramide, HMPA ( $\beta_2^{\text{H}} = 1.00$ ) for the IR measurements. The equilibrium constant,  $K^i$  for 1 : 1 complex formation between each hydroxylamine and each base, was determined in  $\text{CCl}_4$  at ambient temperatures. The free OH fundamental stretching band at *ca.* 3600  $\text{cm}^{-1}$  obeyed the Beer–Lambert law, *i.e.*, its intensity increased linearly with increasing  $[(\text{RCH}_2)_2\text{NOH}]$  for hydroxylamine concentrations in the range  $(2\text{--}20) \times 10^{-3} \text{mol dm}^{-3}$ , indicating that there was no self-association of the hydroxylamine at these concentrations. The intensity of the free OH band was determined using a  $4.5 \times 10^{-3} \text{mol dm}^{-3}$  concentration of each hydroxylamine together with five different concentrations of each HBA over the concentration range  $(5\text{--}20) \times 10^{-3} \text{mol dm}^{-3}$ . The intensity of the free OH band gave, from the Beer–Lambert law calibration plot, the concentration of non-hydrogen-bonded hydroxylamine at each HBA concentration. The equilibrium constant for hydrogen-bond formation between the hydroxylamine and HBA was obtained from the least-squares slopes of plots of  $[(\text{RCH}_2)_2\text{NOH} \cdots \text{HBA}]_{\text{H-bonded}}/[(\text{RCH}_2)_2\text{NOH}]_{\text{free}}$  against  $[\text{HBA}]_{\text{free}}$ , *i.e.*, eqn. (7).

$$K^i = \frac{[(\text{RCH}_2)_2\text{NOH} \cdots \text{HBA}]_{\text{H-bonded}}}{[(\text{RCH}_2)_2\text{NOH}]_{\text{free}} \times [\text{HBA}]_{\text{free}}} \quad (7)$$

Values of  $a_2^{\text{H}}$  for each hydroxylamine were then calculated using the relations<sup>3</sup> given by eqns. (8) and (9) where  $L_{\text{HBA}}$  and

$$\log K^i = L_{\text{HBA}} \log K_A^{\text{H}} + D_{\text{HBA}} \quad (8)$$

$$a_2^{\text{H}} = (\log K_A^{\text{H}} + 1.1)/4.636 \quad (9)$$

$D_{\text{HBA}}$  are known constants because both DMSO and HMPA are calibrated HBAs<sup>3</sup> (see footnotes to Table 2). These  $a_2^{\text{H}}$  values are given in Table 2.

## Discussion

### Kinetics of hydrogen-atom abstraction

Dibenzylhydroxylamine is roughly twice as reactive towards the  $\text{DPPH}^\bullet$  radical as diethylhydroxylamine. There is no reason to expect any significant differences in the Arrhenius pre-exponential factors for the two reactions. The activation enthalpy for H-atom abstraction from dibenzylhydroxylamine is, therefore, presumably *ca.* 1.7  $\text{kJ mol}^{-1}$  lower than for abstraction from diethylhydroxylamine and this probably reflects a lower O–H bond dissociation enthalpy (BDE) in the former compound. The lower O–H BDE implies that the dibenzylaminoyl radical is thermodynamically stabilized relative to diethylaminoyl, a conclusion which can be justified in valence-bond terms by a small contribution from benzyl radical stabilization in canonical structures **C** which would be greatly reduced in  $(\text{CH}_3\text{CH}_2)_2\text{NO}^\bullet$  (Fig. 2).

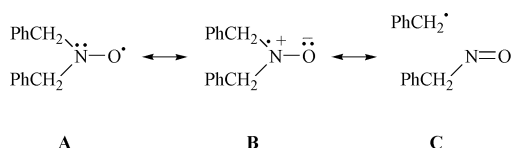


Fig. 2

Both hydroxylamines are very good hydrogen-atom donors to the DPPH<sup>•</sup> radical. Thus, in the absence of hydrogen-bonding, the  $k^{\circ}$  values are 76 and 143 dm<sup>3</sup> mol<sup>-1</sup> s<sup>-1</sup> for diethyl- and dibenzyl-hydroxylamine, respectively. For comparison, the  $k^{\circ}$  value for hydrogen-atom abstraction by DPPH<sup>•</sup> from phenol is only 0.2 dm<sup>3</sup> mol<sup>-1</sup> s<sup>-1</sup>.

### $a_2^H$ Values for hydroxylamines

Our IR-derived  $a_2^H$  values for dibenzylhydroxylamine (Table 2) may be compared with values which can be calculated from the reported<sup>4</sup> equilibrium constants for 1 : 1 complex formation in CCl<sub>4</sub> at 25 °C of this compound with three calibrated<sup>3</sup> HBAs. Thus, for diethyl ether ( $\beta_2^H = 0.45$ ),<sup>2</sup> DMSO ( $\beta_2^H = 0.78$ )<sup>2</sup> and triethylamine ( $\beta_2^H = 0.67$ )<sup>2</sup> the reported<sup>4</sup> values of  $K^1$ /mol<sup>-1</sup> dm<sup>3</sup> (with the calculated values of  $a_2^H$  in parentheses) are 2.3 (0.44), 11 (0.37) and 14 (0.46). Surprisingly, the  $K^1$  (and hence the  $a_2^H$ ) values do not correlate with the relative HBA abilities of the three bases (as given by  $\beta_2^H$ ). For the strongest base, DMSO, there is fair agreement with our own measurements (see Table 2). What of the other two bases? Abraham *et al.*<sup>3</sup> found that for a number of rather weak acids, certain acid–base combinations had to be excluded from their general scheme. Dialkylhydroxylamines are certainly weak acids and diethyl ether is one of the “excluded” bases. However, pyridine ( $\beta_2^H = 0.62$ ) is also an excluded base and yet the measured rate constant for the (PhCH<sub>2</sub>)<sub>2</sub>NOH + DPPH<sup>•</sup> reaction in pyridine falls on the line correlating log  $k^S$  with  $\beta_2^H$  (see Fig. 1). This line yields an  $a_2^H$  value compatible with those derived from our IR measurements (Table 2), despite the fact that it is based on rate constants measured in solvents having smaller  $\beta_2^H$  values than pyridine. We are therefore reluctant to believe that some dialkylhydroxylamine–base combinations exhibit special features which would exclude them from the general scheme of Abraham *et al.*<sup>3</sup> We consider it more likely that  $K^1$  values for the H-bonding of dibenzylhydroxylamine to diethyl ether and to triethylamine were overestimated, something which is easier to do with weak acid–weak base combinations than with the weak acid–strong base combinations we employed.

The KSE-derived  $a_2^H$  values for both hydroxylamines are in reasonable agreement with the values determined by IR spectroscopy (using DMSO and HMPA as the HBAs, see Table 2). There is no significant difference in the mean  $a_2^H$  values for diethyl- and dibenzyl-hydroxylamine and therefore the overall mean  $a_2^H = 0.29$  should be appropriate for the majority of sterically non-hindered *N,N*-dialkylhydroxylamines. However,  $a_2^H = 0.29$  will not be a “universal” value for all hydroxylamines. Larger, perhaps much larger,  $a_2^H$  values will apply when electron-withdrawing groups are attached to the nitrogen atom, both in ring systems such as *N*-hydroxypyrroles and *N*-hydroxyindoles and in acyclic systems such as bis(trifluoromethyl)hydroxylamine. The range of  $a_2^H$  values for hydroxylamines may even rival the range found for 4-substituted phenols, *viz.* 0.55<sub>0</sub> for 4-methoxyphenol<sup>1</sup> to 0.82<sub>4</sub> for 4-nitrophenol.<sup>3</sup> Experiments are planned to explore this important facet of hydroxylamine chemistry.

## Experimental

### Materials

*N,N*-Diethylhydroxylamine and *N,N*-dibenzylhydroxylamine were purchased from Aldrich in the purest grades available and were used without further purification. Solvents were also of the purest grades commercially available and, with the exception of CCl<sub>4</sub>, DMSO and HMPA, were deoxygenated by bubbling with nitrogen and used without purification. The tetrachloromethane used in the IR experiments was distilled from phosphorus pentoxide and great care was then taken to avoid any contact with moisture in the atmosphere. DMSO and HMPA were dried over CaH<sub>2</sub> and their purity was checked by IR spectroscopy.

### Kinetic measurements with DPPH<sup>•</sup>

The maximum of the DPPH<sup>•</sup> absorption band in the UV (*ca.* 330 nm) was determined for each solvent using a Hewlett Packard 8425A diode array spectrophotometer. Deoxygenated stock solutions of the hydroxylamine, (2.5–50) × 10<sup>-3</sup> mol dm<sup>-3</sup>, were very rapidly mixed (~1.3 × 10<sup>-3</sup> s) with equal volumes of a deoxygenated stock solution of DPPH<sup>•</sup> (1 × 10<sup>-4</sup> mol dm<sup>-3</sup>) in the same solvent using a Biosequential SX-18 MV stopped-flow reaction analyzer (Applied Photophysics). The pseudo-first-order decay of the DPPH<sup>•</sup> was monitored at its band maximum.

### IR Spectroscopic measurements

Spectra were recorded on a Midac M FTIR spectrometer using a CaF<sub>2</sub> cell with a pathlength of ~2.5 mm. Stock solutions containing 5 × 10<sup>-3</sup> mol dm<sup>-3</sup> of the hydroxylamine were prepared in tetrachloromethane which had been freshly distilled from P<sub>2</sub>O<sub>5</sub>. Aliquots of 4.5 cm<sup>3</sup> of these solutions were mixed with 0.5 cm<sup>3</sup> aliquots containing (50–200) × 10<sup>-3</sup> mol dm<sup>-3</sup> of DMSO or HMPA in the freshly distilled CCl<sub>4</sub>. The intensities of the non-hydrogen-bonded OH stretching band at *ca.* 3600 cm<sup>-1</sup> were then recorded on solutions containing 4.5 × 10<sup>-3</sup> mol dm<sup>-3</sup> hydroxylamine and five different concentrations of the HBA in the range (5–20) × 10<sup>-3</sup> mol dm<sup>-3</sup>. The equilibrium constant,  $K^1$ , for 1 : 1 complex formation between the hydroxylamine and HBA was calculated as described above. The  $a_2^H$  values were then calculated from  $K^1$ .

### Acknowledgements

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