# Use of the Point Dipole Approximation for Nitroxide Biradicals

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**Abstract:** The dipolar splitting parameter $D$ has been determined for five nitroxide biradicals in order to test the point-dipole approximation for electron–electron dipolar interactions. Calculation of $D$ using the point-dipole approximation or a distributed dipole approximation does not give a satisfactory fit to the data, with errors as large as 23.9% for the point-dipole approximation and 14.4% for the distributed dipole approximation. An equation is presented which enables the calculation of $D$ to 3.2%. The data imply that $\zeta_N \approx 1$ and that the nitroxide biradicals are approximately 70% in the triplet state.

Nitroxide biradicals have elicited interest as structural probes in biological systems. One of the more interesting potential uses of nitroxide biradicals is the determination of molecular scale distances by utilization of the distance dependence of the electron dipole–dipole interaction. If the point-dipole approximation is used[1] for calculating nitroxide–nitroxide distances, it must be assumed that $\zeta_N = 1.0$ and that the biradical is a pure triplet state. We chose to approach this problem by synthesizing relatively rigid nitroxide biradicals and directly comparing the distances calculated from the point-dipole approximation with the actual distances. In an earlier paper we reported the x-ray crystallographic structure for one such biradical (2) and the nitroxide–nitroxide distance calculated from the point-dipole approximation.[2] Subsequently, Rohde et al. confirmed our x-ray data and reached the same conclusions as we did earlier as to the most stable conformation of 2 and the value of dipolar splitting parameter $D$.[3] We have synthesized three new rigid nitroxide biradicals (3–5) and report new data on a fourth (6), for which x-ray data are also available[4] in order to test the point-dipole approximation.

## Experimental Section

ESR spectra were run on a Varian E-3 ESR spectrometer equipped with a variable temperature control. Rigid glass spectra were obtained in diethyl ether:isopentane:ethanol (5:3:2), toluene, or ethanol at −196 °C.

**The dinitroxide of cholestan-3-one (1)** was prepared as described by Keana and Dinerstein.[1]

**1,4-Bis(4',4'-dimethyloxazolidin-N-oxyl)cyclohexane (2)** was prepared by refluxing 1.0 g of cyclohexane-1,4-dione[5] for one week with 18.0 g of 2-amino-2-methyl-1-propanol and 0.1 g of p-toluenesulfonic acid in 100 ml of toluene using a Dean Stark trap. The reaction mixture was extracted three times with 100 ml of 10% sodium bicarbonate and dried over magnesium sulfate, and the solvent was removed in vacuo. The residue was dissolved in 100 ml of cold ether. A cold solution of 3.0 g of m-chloroperbenzoic acid was added dropwise. The reaction mixture was allowed to warm to room temperature and left overnight. The yellow solution was extracted with 50 ml of 10% sodium bicarbonate and then with water until the washings were neutral. The dinitroxide was isolated by preparative thin-layer chromatography, to give 192 mg (13%): mp 218–219 °C; calcd $m/e$ 284.1735, obsd $m/e$ 284.1752. The structure has been confirmed by x-ray crystallography,[2] with the two N-oxyl groups trans diequatorial.

**cis-2,7-Decalindione.** A solution of 1.0 g of $\Delta^{1,9}$-octalin-2,7-dione[6] in 0.5 g of tert-butyl alcohol and 10 ml of ether was added to a solution of 25 ml of liquid ammonia and 0.5 g of lithium metal. After 3 h the reaction was quenched with solid ammonium chloride and the ammonia was allowed to evaporate. The residue was dissolved in 25 ml of cold acetone and oxidized at 0 °C with excess 8 N chromic acid.[7] The excess oxidant was destroyed with 2-propanol. The resulting mixture was partitioned between water and ether. The ether layer was dried and the residue recrystallized

from hexane to give cis-2,7-decalindione; mp 63–65 °C (lit.[8] 62–64 °C); calcd $m/e$ 166.0993; obsd $m/e$ 166.1009.

**2,7-Bis(4',4'-dimethyloxazolin-N-oxyl)-cis-decalin (3)** was prepared from 100 mg of cis-2,7-decalindione by the same method as for 2, to give 38 mg (18%): mp 119–120 °C; calcd $m/e$ 338.2205; obsd $m/e$ 338.2178.

**2,6-Bis(4',4'-dimethyloxazolin-N-oxyl)-trans-decalin (4)** was prepared from 300 mg of trans-2,6-decalindione[9] by the same method as for 2, to give 67 mg (11%): mp 191–192 °C; calcd $m/e$ 338.2205; obsd $m/e$ 338.2194.

**1,5-Bis(4',4'-dimethyloxazolin-N-oxyl)-trans-decalin (5)** was prepared from 1.0 g of trans-1,5-decalindione[10] by the same method as for 2, to give 301 mg (15%): calcd $m/e$ 338.2205; obsd $m/e$ 338.2205.

**Bis(2,2,5,5-tetramethyl-3-pyrrolidon-N-oxyl)diazine (6)** was prepared by the method of Dupeyre et al.[11]

## Results

The series of five nitroxide biradicals synthesized here (2–6) are relatively rigid, with the detailed x-ray structure being available for 2[2] and 6.[4]

From our x-ray crystallographic structure determination[2] we found that 2 is trans diequatorial with respect to the



1

2

3

4

5

6
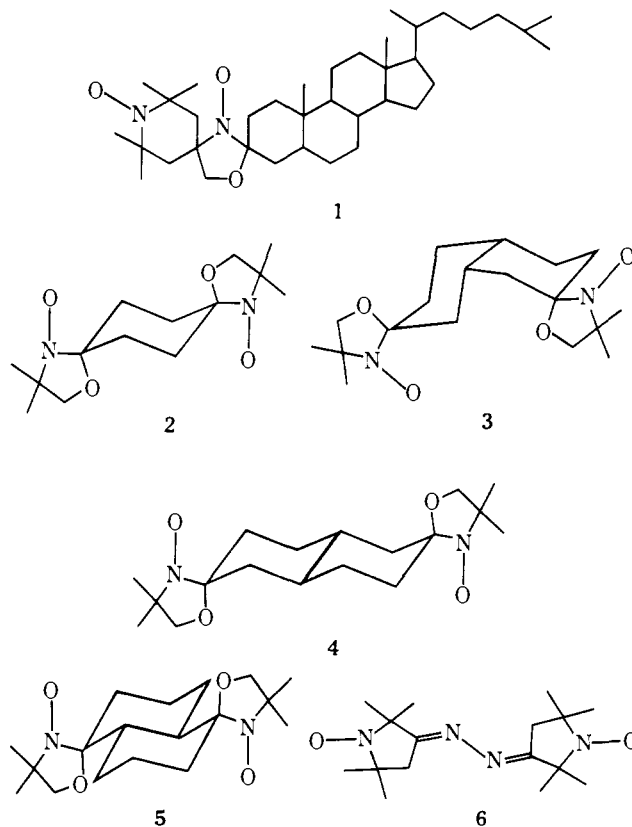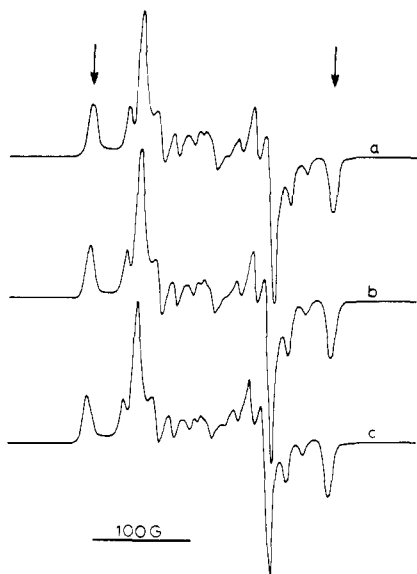
Figure 1. ESR spectra of biradical 2 in a rigid glass of (a) diethyl ether:isopentane:ethanol, (b) ethanol, and (c) toluene at −196 °C. The maximum splitting 2D is indicated by the arrows.
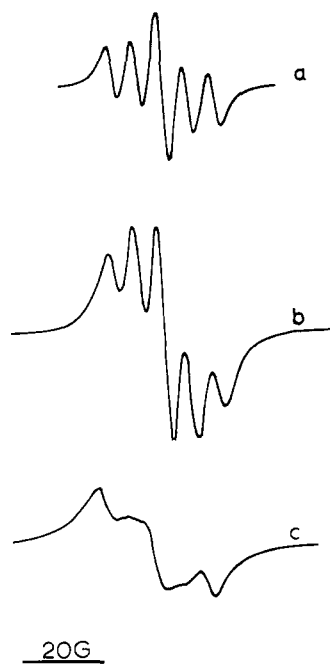


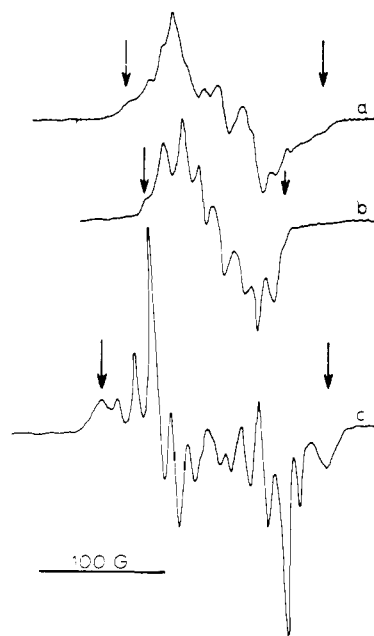Figure 2. ESR spectra of (a) 6, (b) 2, and (c) 1 at room temperature.



Figure 3. Rigid glass ESR spectrum of 1 at −196 °C.



Figure 4. Rigid glass ESR spectra of (a) 3, (b) 4, and (c) 5 at −196 °C.
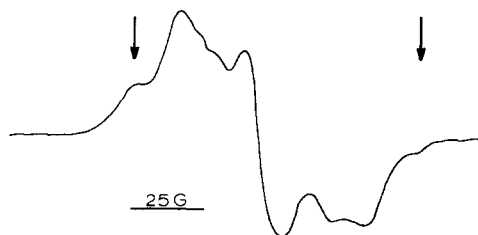


Figure 5. Rigid glass ESR spectrum of 6 at −196 °C.

N–O groups. This was also found to be the case in a more recent study by Rohde et al.[3] Rohde et al. also examined 2 by ESR in a rigid glass and in a doped crystalline powder of the diamine precursor to 2. Their rigid glass data agree closely with our earlier determination.[2] In their crystalline powder study a trace of the diaxial conformation was also observed. Michon and Rassat[12] have also concluded that 2 is trans diequatorial. The rigid glass ESR spectrum of 2 is the same in toluene, ether:isopentane:ethanol, and absolute ethanol, showing that the polarity of the solvent has little effect on the conformation (Figure 1). Although the yield of 2 was relatively low, it is highly probable that none of the cis isomer was formed since: (a) all of the free-radical products can be accounted for as either 2 or monoradicals; (b) on preparative thin-layer chromatography the only biradical found was 2 (as little as 0.1% of the cis isomer could have been detected); and (c) space-filling models of the cis

isomer show that it should be highly strained. The cyclohexane ring of 2 is in a normal chair conformation, and all bond lengths and bond angles are normal.[2]

The structural data for 2 allow us to assign structures to 3–5 as being the isomers with equatorial N–O groups. Since the bond angles and bond lengths of the cyclohexane ring of 2 are normal, it is possible to calculate the nitrogen to nitrogen and oxygen to oxygen distances of 3–5 accurately with a computer. X-ray data are available to use directly for similar calculations on 2 and 6.

The ESR spectra at room temperature of 1, 2, and 6 are shown in Figure 2, while the rigid glass spectra of 1–6 are shown in Figures 1 and 3–5. The dipolar splittings D in gauss are given in Table I.
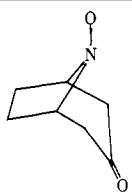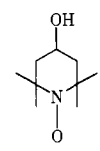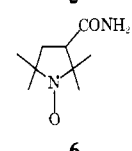
## Discussion

Nitroxide biradicals have been proposed as tools for distance determinations in biological systems[1,3,13] since the di-

**Table I.** Dipolar Splitting Parameters for Nitroxide

| Compd | $D \pm 2$, G | Compd | $D \pm 2$, G |
|-------|------|-------|------|
| 1 | 228 | 4 | 53[a] |
| 2 | 120 | 5 | 92 |
| 3 | 81 | 6 | 51[a] |

[a] Error ±5 G.

**Table II.** The Angle of the N–O Bond to the CNC Plane for Several Nitroxides

| Nitroxide | Ref | Angle, deg |
|-----------|-----|------------|
|  | 15 | 30 |
|  | 16, 17 | 16 |
| **2** | 2 | 2 |
|  | 18 | 0 |
| **6** | 4 | 0 |

polar splitting $D$ should be proportional to $\langle 1/r^3 \rangle$ where $r$ is the distance between the unpaired electrons (eq 1).[13]

$$2D = 3g^2\beta^2 \langle 1/r^3 \rangle \tag{1}$$

Since $\langle 1/r^3 \rangle$ is an average over all possible electronic positions, $D$ will change if the delocalization of the unpaired electron in the N–O bond changes.

The angle that the N–O bond makes with the CNC plane varys considerably with different types of nitroxides (Table II). For pyrrolidine and oxazolidine nitroxides the N–O bond lies in the CNC plane, and so the hybridization of the nitrogen is close to $sp^2$. Since it is likely that the unpaired electron resides principally in the nonbonding nitrogen orbital, the unpaired electron will effectively be on a p orbital. The p orbital should have overlap with the nonbonding oxygen orbitals thereby delocalizing the unpaired electron. For piperidine and bicyclic nitroxides the nonbonding nitrogen orbital has more $sp^3$ character. This should have two effects on the delocalization of the unpaired electron. Since the orbital has more s character there should be more spin density at the nitrogen nucleus, giving a larger value for $a_N$, which is experimentally found to be the case.[14] The degree of overlap with the nonbonding oxygen orbitals should be different and so should the delocalization of the unpaired electron.

The principal goal of this research was to determine the accuracy of the point-dipole approximation in calculating nitroxide–nitroxide distances.

The accuracy of the point-dipole approximation in determining nitroxide–nitroxide distances depends on several factors: (1) the delocalization of the unpaired electrons, (2) whether the degree of delocalization depends on the nitroxide–nitroxide distance and the angle between the N–O bonds, and (3) the fraction of nitroxide–nitroxide pairs in the triplet state.

**Table III.** Calculations of the Dipolar Splitting Constant Using the Point-Dipole Approximation

| Compd | $r_{NN}$, Å | $D_{obsd}$, G | $D_{calcd}$,[a] G | $\Delta D$, G[b] |
|-------|------|------|------|------|
| 2 | 5.75[c] | 120 | 146 | 26 |
| 3 | 6.69[d] | 81 | 93 | 12 |
| 4 | 8.12[d] | 53 | 52 | -1 |
| 5 | 6.25[d] | 92 | 114 | 22 |
| 6 | 7.90[c] | 51 | 56 | 5 |

[a] $D_{calcd}$ is from eq 2 and the nitrogen to nitrogen nitroxide distance. [b] $\Delta D = D_{calcd} - D_{obsd}$. [c] From x-ray structure determination. [d] From x-ray data for **2** assuming the decalin band lengths and angles to be the same as for the cyclohexane ring to **2**. The assumption is justified by the fact that the cyclohexane ring of **2** is in a normal chair conformation with normal bond angles and lengths.[2]

**Table IV.** Parameters for Calculation of the Dipolar Splitting Constant Using a Distributed Dipole Approximation

| Compd | $\varsigma_N$[a] | $\theta_{max}$, deg | $\phi$,[c] deg | $\phi_0$,[b,c] deg |
|-------|------|------|------|------|
| 2 | 0.64 | 6.24 | 115.80 | 109.56 |
| 3 | 0.74 | 4.35 | 89.10, 146.83 | 89.10, 146.83 |
| 4 | 1.00 | 0.00 | 118.89 | 114.54 |
| 5 | 0.61 | 6.21 | 111.68 | 105.47 |
| 6 | 0.86 | 0.35 | 166.82 | 166.47 |

[a] From Figure 8. [b] $\phi$ for $\theta = 0$. [c] For **2** and **4–6** $\theta_{NO} = \theta_{NO'}$ so there is only one value for $\phi$.

In Table III is shown a comparison of the experimental dipolar splitting $D_{obsd}$ and $D_{calcd}$ from eq 2. As can be seen
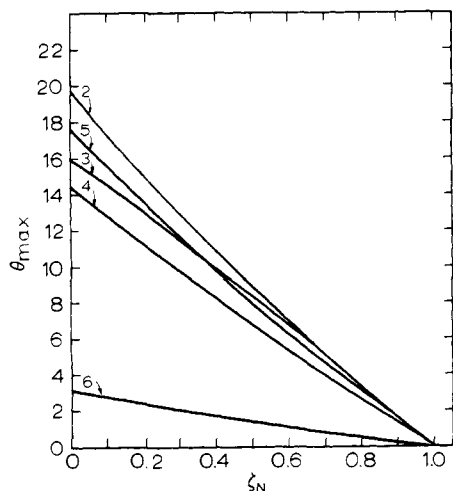
$$D_{calcd} = \tfrac{3}{2}g^2\beta/r^3 \tag{2}$$

$D_{calcd}$ is systematically higher than $D_{obsd}$. The disagreement increases as $r_{NN}$ decreases. For **2** the discrepancy is 26 G, which is an error of 22%. This large error cannot be due to experimental error in $r_{NN}$ since it comes from a precise x-ray structural determination.[2] If these differences are a result of errors inherent in the point-dipole approximation then the calculations should be improved by using a distributed dipole approximation. The simplest approach is to assume the unpaired spin density is distributed between the nitrogen and the oxygen of the nitroxyl group. For compounds **2** and **4–6** both N–O groups lie in the same plane. For **3** the angular deviation of the NO groups, the least-squares plane is 6.7°. This is a small distortion, and so for calculations on **3** it was assumed that the two NO groups are in the same plane. The angles and bond lengths used for calculations on **3** were obtained from a projection of the two N–O groups onto the least-squares plane. For the distributed dipole approximation described above $D_{calcd}$ is given by eq 3,

$$D_{calcd} = \tfrac{3}{4}g^2\beta^2 \left| \frac{\varsigma_N^2(1 - 3\cos^2\theta)}{r_{NN}^3} \right.$$
$$+ \frac{\varsigma_N\varsigma_O(1 - 3\cos^2[\theta + \theta_{NO}])}{r_{NO}^3}$$
$$+ \frac{\varsigma_N\varsigma_O(1 - 3\cos^2[\theta + \theta_{NO'}])}{r_{NO'}^3}$$
$$\left. + \frac{\varsigma_O^2(1 - 3\cos^2[\theta + \theta_{OO}])}{r_{OO}^3} \right| \tag{3}$$

where $\varsigma_N$ and $\varsigma_O$ are the unpaired electron densities on nitrogen and oxygen, respectively. The quantities $\theta$, $\theta_{NO}$, $\theta_{NO'}$, $\theta_{OO}$, $r_{NN}$, $r_{NO}$, $r_{NO'}$, and $r_{OO}$ are defined in Figure 6. To compare $D_{calcd}$ from eq 3 with $D_{obsd}$, $D_{calcd}$ must be maximized with respect to $\theta$ to obtain $D_{max}$ and $\theta_{max}$. Both $D_{max}$ and $\theta_{max}$ depend on $\varsigma_N$.
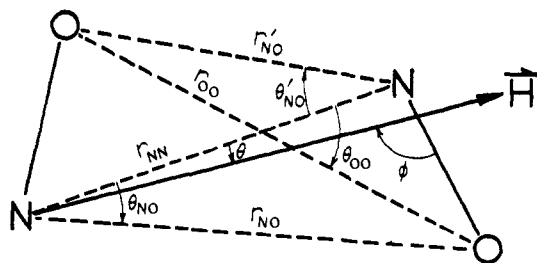
Figure 6. The geometry of the N–O groups in the nitroxide biradicals with respect to the magnetic field direction H.



Figure 7. Plot of $\zeta_N$ vs. $\theta_{max}$.



Figure 8. Plot of $\zeta_N$ vs. $D_{max}$. The $D_{obsd}$ are indicated by ($\bullet$).



Figure 9. Plots of the point-dipole approximation (- - -), the distributed dipole approximation (O), eq 4 (—), and the experimental values of $D$ ($\bullet$).
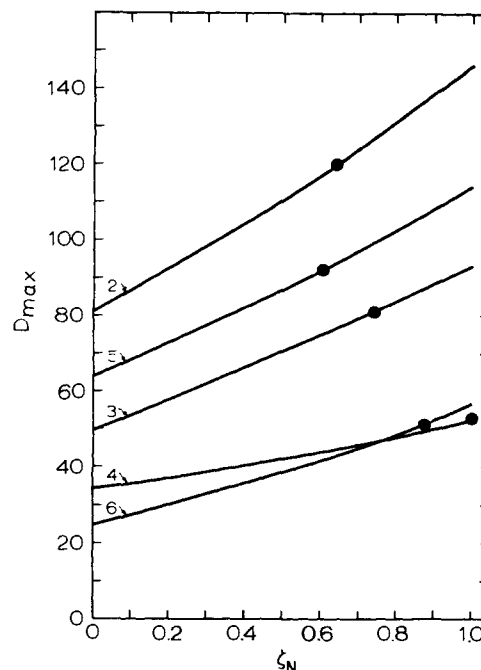
In Figures 7 and 8 $\zeta_N$ is plotted vs. $\theta_{max}$ and $D_{max}$, respectively, for 2–6. There is no unique value of $\zeta_N$ which gives good agreement between $D_{max}$ from eq 3 and $D_{obsd}$. The best value of $\zeta_N$ varies from 0.61 to 1.00, depending on the compound (Table IV and Figure 8). These calculations suggest that the distribution of the unpaired spin density is strongly dependent on the nitroxide–nitroxide distance and/or angle. However, $a_N$, the isotropic hyperfine splitting constant, is the same for 2 and 6 (Figure 2), which represent the distance extremes in this study. The angle between the N–O bonds is also quite different in these two cases (Table IV). Since any change in $\zeta_N$ should give a change in $a_N$ it is highly unlikely that $\zeta_N$ is different for these two compounds. Neither the point-dipole approximation nor a simple distributed dipole approximation give a satisfactory correlation between the observed and calculated dipolar splitting.

In another approach the least-squares line for $D_{obsd}$ vs. $1/r_{NN}^3$ was determined (eq 4). The least-squares line and the experimental data are shown in Figure 9. The fit to the
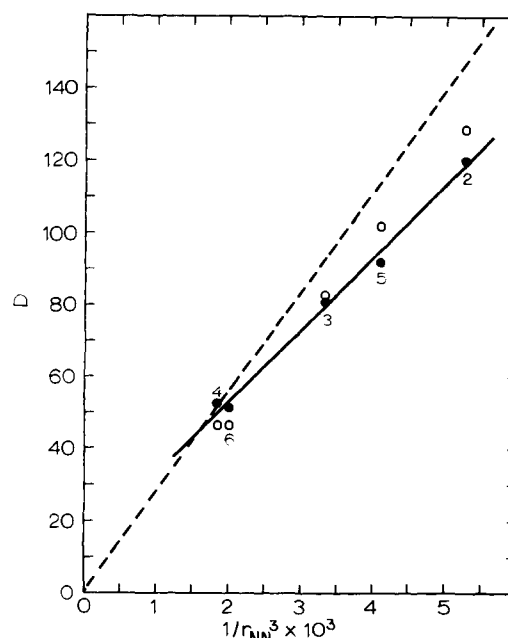
$$D_{obsd} = 12.74 + 2.009 \times 10^4/r_{NN}^3 \qquad (4)$$

straight line is exceptionally good, with a coefficient of determination of 0.996. Using $D_{obsd}$ and eq 4, the average deviation between the calculated and observed values of $r_{NN}$ is 1.4%. The largest deviation is for 4 (2.3%). If eq 4 is used to calculate $D$ from $r_{NN}$ the average deviation between calculated and experimental values is 3.2% and the largest deviation is 5.2% (4). If the average value of $\zeta_N$ from Table IV ($\zeta_{N,av} = 0.77$) is used to determine $D_{calcd}$ in eq 3, the average deviation between the calculated and experimental values of $D$ is 7.8% and the largest deviation is 11.3% (4). For the point-dipole approximation the average deviation is 14.4% and the largest deviation is 23.9% (5).

Compounds 2, 4, and 5 have very similar geometry, with $\phi_0$, the angle between the line connecting the nitroxide ni-

trogen and the N–O bond, being near 110°, and so they should fall on a good straight line for a plot of $D$ vs. $1/r_{NN}^3$ regardless of whether $D$ is orientation dependent. However, 3 and 6 have considerably different geometries. For 3, one N–O group is approximately perpendicular to the N to N line while the other N–O group makes an angle of 146.83°. For 6 the N–O groups are almost parallel to the N to N line. Therefore if $\zeta_N$ is significantly less than one, compounds 3 and 6 should not fall on the same line as 2, 4, and 5, since for $\zeta_N < 1$, $D$ will be orientation dependent. However, all five compounds fall on a good straight line (eq 4), and so $\zeta_N \approx 1.0$ and the point-dipole approximation should be completely satisfactory. It is not. The experimental and calculated values of $D$ differ by 21.7 and 23.9% for 2 and 5,

respectively. The distributed dipole approximation requires that $\zeta_N$ vary considerably from compound to compound for the best fit. The average value of $\zeta_N = 0.77$ gives a small improvement over the point-dipole approximation. However, such a value for $\zeta_N$ is inconsistent with the fact that compounds **3** and **6**, which have different geometries for the N–O groups than **2, 4** and **5**, all fall on an extremely good least-squares line for a plot of $D_{obsd}$ vs. $1/r_{NN}^3$.

These difficulties can be resolved if, for the distance range examined here (5.7–8.1 Å), the nitroxide biradicals are not 100% in the triplet state. The slope of eq 4 implies that the nitroxide biradicals are 72% in the triplet state and 28% in the singlet state. For $r_{NN} > 8.1$ Å the fraction in the triplet state should increase, thereby increasing the slope of the plot of $D_{obsd}$ vs. $1/r_{NN}^3$. Ultimately the curve should pass through the origin of the plot. For $r_{NN} < 5.7$ Å the fraction of molecules in the triplet state should decrease, with the slope of the $D_{obsd}$ vs. $1/r_{NN}^3$ also decreasing. Consequently, eq 4 will give the *upper* limit for $r_{NN}$ for $r_{NN} <$ 5.7 Å ($D_{obsd} > 121$ G) and lower limit for $r_{NN} > 8.1$ Å ($D_{obsd} < 50$ G).

Assuming that the compounds used in this study are a reasonable sample of nitroxide biradicals, eq 4 can be used to calculate $r_{NN}$ with an average error of 1.4% for 5.7 Å $\leq r_{NN} \leq 8.1$ Å (121 G $\geq D_{obsd} \geq 50$ G). A dipolar splitting of 50 G is the practical lower limit for which $D_{obsd}$ can be accurately determined (Figures 4b and 5), and so distances between nitroxides more than 8 Å apart cannot be readily determined by ESR.

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# Photoionization Mass Spectrometry of 2-Fluoropropane and 2,2-Difluoropropane. A Novel Determination of the Proton Affinity of Vinyl Fluoride and 1,1-Difluoroethylene

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**Abstract:** Photoionization efficiency curves for the parent and abundant fragment ions from 2-fluoropropane and 2,2-difluoropropane are reported in the energy region between threshold and 13 eV. For 2-fluoropropane an adiabatic ionization potential of 11.08 ± 0.02 eV is determined, with appearance thresholds of 11.23 ± 0.03, 11.53 ± 0.03, and 11.75 ± 0.03 eV for the fragment ions $(CH_3)_2CF^+$, $CH_2CHF^+$, and $CH_3CHF^+$, respectively. For 2,2-difluoropropane an adiabatic ionization potential of 11.42 ± 0.02 eV is determined, with appearance thresholds of 11.57 ± 0.03 and 11.81 ± 0.03 eV for the fragment ions $CH_2CF_2^+$ and $CH_3CF_2^+$, respectively. These data are interpreted in terms of the thermochemistry of the neutrals and ions involved. From the difference in thresholds for the loss of $CH_4$ and $CH_3$, a thermochemical cycle yields the proton affinities of vinyl fluoride (173.6 kcal/mol) and 1,1 difluoroethylene (174.8 kcal/mol), independent of the heats of formation of any neutral species.

There have been several recent studies of gas-phase acid-base chemistry which provide insight into the thermochemistry of organic molecules and ions containing fluorine. Fluoride transfer reactions between substituted carbonium ions have been shown to be fast, providing relative $R^+$-$F^-$ heterolytic bond energies and hence heats of formation of fluorine-substituted cations.[2–4] Proton affinities of fluoroethylenes have been measured, yielding heats of formation of the corresponding conjugate acids, which are fluorinated ethyl cations.[5] The enthalpy of formation of $CF_2$ and the difluoromethyl cation have been interrelated by studying proton transfer reactions involving $CF_2H^+$.[6] Thermochemical data for fluorine-substituted anions have been derived from studies of the reactions of $F^-$ and other bases with fluoroalkenes[7] and fluoroalkanes[8] in the gas phase. A factor hindering interpretation of experimental results in these studies is the lack of thermo-chemical data for molecules and ions containing fluorine. This in part can be attributed to experimental difficulties associated with making accurate calorimetric measurements involving fluorinated species. Thus it is not surprising that previous studies[2,3,6] have uncovered inconsistencies which can be resolved only if the heats of formation used for neutral species are considered to be in error.

Although systematic studies of photoionization efficiencies have been reported for parent and fragment ions derived from lower alkanes,[9] ketones,[10] and alcohols,[11] none of the alkyl fluorides have been studied except methyl fluoride.[12] In view of the ability of photoionization mass spectrometry to determine accurate appearance potentials for fragmentation processes, we have undertaken a series of studies in our laboratories directed at providing more precise thermochemical data for fluorine-substituted neutrals and ions. We wish to report