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# Electronic Structure of Persistent Radicals: Nitroxides

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The molecular and electronic structures of 10 free nitroxide radicals have been investigated by HeI/HeII photoelectron spectroscopy (UPS), DFT calculations, and comparison with the spectra of related compounds. We observe that the electronic structure of the nitroxide group is unaffected by substitution except in a carbonyl derivative where nitroxide group orbitals are noticeably stabilized. Also, we have detected small variations in the photoionization cross-sections for singlet and triplet states of cation, the states belonging to the same electron configuration. The relationship between electronic structure and radical reactivity is discussed, and an experimentally based estimate of delocalization energy of the unpaired electron is given. Some conflicting kinetic data on radical reactivity have been analyzed in view of the UPS results.

## Introduction

Many radicals are highly reactive species containing open-shell electronic configuration and an odd number of valence electrons, but some radicals are stable with lifetimes of the order of months.[1] Technological applications of stable free radicals include the biomedical field[2] (spin labels, spin traps, antioxidants), chemical synthesis (initiators in radical-chain polymerization and redox reactions), and materials chemistry[3] (building blocks for molecular-based magnetic materials). Besides the technological applications, radicals are thought to be involved in the process of aging and environmental degradation (destruction of ozone layer). Certain radicals (e.g., nitroxides studied in this work) are kinetically stabilized by the presence of bulky substituents. Stable free radicals are thus readily amenable to study by UV photoelectron spectroscopy (UPS) in combination with quantum chemical calculations.

An early study of 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) and di-*t*-Bu-nitroxide radicals[4] has been performed at single photon energy and under low resolution. Research into the electronic structure of free radicals is an active research field.[5] UPS studies have so far involved short-lived free radicals generated by pyrolysis in situ, i.e., within the spectrometer from appropriate stable precursors.[6,7] UPS spectra of short-lived radicals suffer from band overlap with precursor molecule, and only the first, low ionization energy band can usually be reliably detected. In our work, the problem does not arise because we study stable free radicals free from precursors.

## Experimental and Theoretical Methods

Compounds **1**−**9** were obtained commercially and used without further purification after checking their identity by NMR and GC measurements (Chart 1). Compound **10** was synthesized and characterized according to ref 8.

The recorded HeI/HeII photoelectron spectra of **1**−**10** were calibrated with small amounts of Xe gas which was added to the sample flow. The spectral resolution in HeI and HeII spectra was 25 and 70 meV, respectively, when measured as full-width half-maximum (fwhm) of the $^2P_{3/2}$ $Ar^+$ line. The spectra were measured at sample inlet temperatures ranging from 30 to 160 °C. These temperatures were required to obtain sufficient vapor pressures in the ionization region. The resolution in the HeII spectra was always inferior to that of the HeI, which implies that some bands which are well resolved in HeI become unresolved in the corresponding HeII spectrum. The consequence is that measured relative band intensities and intensity ratios sometimes refer to a combined intensity of two bands rather than to a single band.

The quantum chemical calculations were performed with the Gaussian 03 program[9] and employed density functional method (DFT). Full geometry optimization of the neutral radical ($^2A$ state) was performed at the UB3PW91/6-31+G(d) level using unrestricted spin wave function followed by the harmonic vibrational analysis to ensure that the calculated geometry represented a true minimum on the potential energy surface. Subsequently, single-point calculations at the UB3PW91/6-311++G(d,p) level were performed to obtain total

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(1) Parsons, A. F. *An Introduction to Free Radical Chemistry*, Blackwell Science: Oxford 2000.

(2) Kocherginsky, N.; Swartz, H. M. *Nitroxide Spin Labels, Reactions in Biology and Chemistry*, CRC Press: Boca Raton 1995.

(3) Rassat, A. *Pure Appl. Chem.* **1990,** *62*, 223.

(4) Morishima, I.; Yoshikawa, K.; Yonezawa, T.; Matsumoto, H. *Chem. Phys. Lett.* **1972**, *16*, 336.

(5) Wentrup, C. *Science* **2002**, *295*, 1846.

(6) Zheng, S.; Shijun, Z.; Meng, L.; Wang, D. *Chem. Phys. Lett.* **2003,** *369*, 180.

(7) Sun, Z.; Zheng, S.; Wang, J.; Ge, M. F.; Wang, D. *Chem. Eur. J.* **2001** *7*, 2995.

(8) Rozantsev, E. G. *Free Nitroxyl Radicals*, Plenum Press: New York, 1970; p 203.

10.1021/jo0401671 CCC: $27.50

**CHART 1**

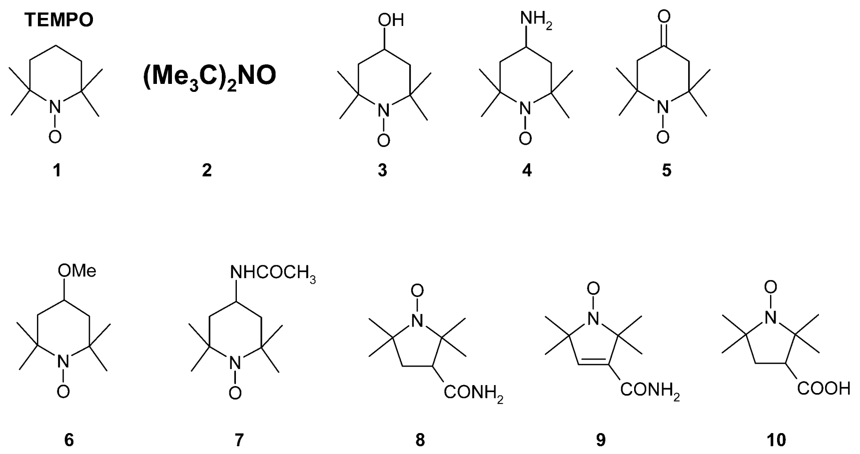

**TABLE 1. Vertical Ionization Energies ($E_i$ ± 0.05 eV), Bands, Band Assignments (MO Type), Calculated Ionization Energies of Nitroxide Bands (ΔDFT, TDDFT/eV), Ratios of Band Intensities at HeII/HeI Radiation ($RI_{exp}$), and Singlet−Triplet Energy Gaps (ΔST/eV) Where Resolvable Bands Exist**

| radical | band | $E_i$ | MO type[a] | ΔDFT/TDDFT[b] | $RI_{exp}$[c] | ΔST |
|---|---|---|---|---|---|---|
| **1** | X | 7.30 | $\pi_{NO}^*$ | 7.50 | 1.0 | |
| | A | 8.95 | $n_{NO}$(T) | *8.69* | 1.09 | 0.25 |
| | B | 9.20 | $n_{NO}$(S) | *9.5* | 0.90 | |
| **2** | X | 7.20 | $\pi_{NO}^*$ | 7.40 | 1.0 | |
| | A | 8.85 | $n_{NO}$(T) | *8.77* | 0.93 | 0.35 |
| | B | 9.20 | $n_{NO}$(S) | *9.6* | 0.98 | |
| **3** | X | 7.30 | $\pi_{NO}^*$ | 7.40 | 1.0 | |
| | A | 9.0 | $n_{NO}$(T) | *8.81* | 1.18 | 0.35 |
| | B | 9.35 | $n_{NO}$(S) | *9.6* | 1.18 | |
| | C | 10.35 | $n_{OH}$ | | | |
| **4** | X | 7.24 | $\pi_{NO}^*$ | 7.53 | 1.0 | |
| | A | 8.90 | $n_{NO}$(T) | *8.74* | 0.62 | |
| | B−C | 9.22 | $n_{NO}$(S), $n_{NH2}$ | *9.5* | 0.58 | |
| **5** | X | 7.56 | $\pi_{NO}^*$ | 7.93 | 1.0 | |
| | A | 9.27 | $n_{NO}$(T) | *9.13* | 0.75 | |
| | B−C | 9.55 | $n_{NO}$(S), $n_{CO}$ | *10.0* | 0.75 | |
| | D | 10.9 | $\pi_{CO}$ | | | |
| **6** | X | 7.25 | $\pi_{NO}^*$ | 7.56 | 1.0 | |
| | A | 8.9 | $n_{NO}$(T) | *8.77* | 0.86 | |
| | B−C | 9.6 | $n_{NO}$(S), $n_{OMe}$ | *9.5* | 0.73 | |
| **7** | X | 7.25 | $\pi_{NO}^*$ | 7.7 | 1.0 | |
| | A | 8.95 | $n_{NO}$(T) | *9.02* | 0.78 | |
| | B−D | 9.35 | $n_{NO}$(S), $n_O$, $n_N$ | 9.36, *9.8* | 0.73 | |
| **8** | X | 7.3 | $\pi_{NO}^*$ | 7.42 | 1.0 | |
| | A−B | 9.1, 9.5 | $n_{NO}$(T), $n_{NO}$(S) | *8.96, 9.78* | 0.80 | |
| | C | 9.9 | $n_{CO}$ | | 0.94 | |
| | D | 10.6 | $n_{NH2}$ | | | |
| **9** | X | 7.36 | $\pi_{NO}^*$ | 7.54 | 1.0 | |
| | A | 9.2 | $n_{NO}$(T) | *8.87* | 1.22 | |
| | B−D | 9.65, 9.95, 10.25 | $n_{NO}$(S), $n_O$, $n_N$ | *9.22* | 0.88 | |
| | E | 11.2 | $\pi_{CC}$ | | | |
| **10** | X | 7.4 | $\pi_{NO}^*$ | 7.67 | 1.0 | |
| | A | 9.2 | $n_{NO}$(T) | *9.2* | 1.16 | 0.55 |
| | B−C | 9.75 | $n_{NO}$(S), $n_{COOH}$ | *10.0* | 0.75 | |
| | D | 10.65 | $\pi_{COOH}$ | | | |

[a] Symbols S and T refer to singlet and triplet states, respectively. [b] Values in italics were obtained by TDDFT methods. [c] band intensities were measured by using asymmetric Gaussian band shapes as suggested in ref 11 and baseline correction. The variable bandwidths were in the range 0.1−0.3 eV.

energies for the $^2$A and $^1$A states of the resulting cation (Chart 2). The two energies were then subtracted to afford the value of the first vertical ionization energy (ΔDFT in Table 1). To obtain second and third ionization energies we used the TDDFT method[9] at the B3P86/6-311++G** level and calculated excitation energies for X($^1$A) → A ($^1$A) and X($^1$A) → B ($^3$A) transitions in cation (TDDFT in Table 1).

The TDDFT method was selected because it includes electron correlation while still being computationally efficient for large molecules, unlike, e.g., the CASSCF method. Also, the TDDFT method performs satisfactorily for low energy excitations (2−5 eV).[10a] The use of the B3P86 hybrid functional has been recently recommended for TDDFT studies.[10b] The calculated geometries of radicals agree well with experimental ones obtained by X-ray diffraction (Table 2), thus lending support to our choice of computational method.

To compare relative stability of the nitroxide radicals we have performed further quantum chemical calculations. In these calculations, the geometries of each radical, the corresponding hydroxy compound, ethanol, and the ethoxy radical

**CHART 2**

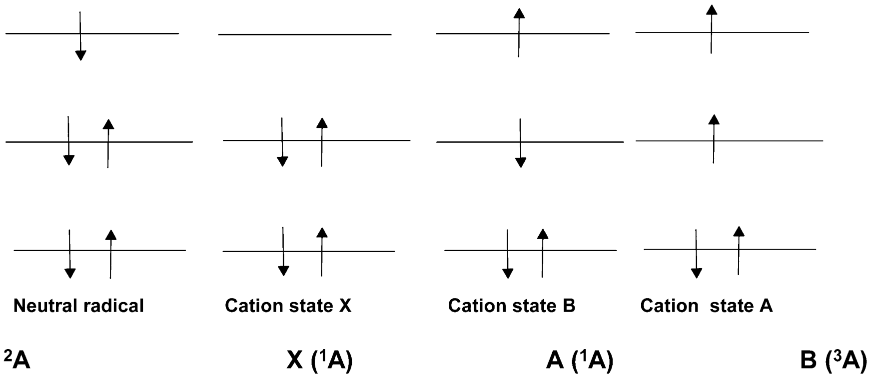

**TABLE 2. Molecular Structure Parameters for Nitroxide Radicals, Calculated at the UB3PW91/6-31+G(d) Level and Compared to X-ray Diffraction Data (*) Where Available**[a]

| radical | N−O bond/Å | C−NO bond/Å | ∠CNO/deg | ∠C(NO)C/deg |
|---|---|---|---|---|
| **1**[18] | 1.279, 1.283* | 1.496, 1.488* | 115.9, 116.7* | 124.5, 123.6* |
| **2** | 1.281 | 1.510 | 112.8 | 134.5 |
| **3** | 1.278 | 1.495 | 116 | 124.5 |
| **4** | 1.279 | 1.495 | 116 | 124.4 |
| **5**[19] | 1.278, 1.276* | 1.497, 1.488* | 115.7, 118* | 124.5, 123.5* |
| **6** | 1.278 | 1.495 | 115.9 | 124.4 |
| **7** | | | | |
| **8**[20] | 1.269, 1.268* | 1.482, 1.490* | 122.2, 122.5* | 115.8, 115.0* |
| **9** | 1.268 | 1.481 | 122.2 | 114.8 |
| **10**[21] | 1.272, 1.280* | 1.482, 1.481* | 121.8, 122.0* | 116, 116* |

[a] Superscripts indicate references to X-ray diffraction studies.

were optimized at the B3LYP/6-31+G(d) and MP2/6-31+G(d) levels. Frequency calculations were performed at the B3LYP/6-31+G(d) level and the zero-point corrections added to the B3LYP and MP2 energies. Zero-point energies were scaled by 0.98. The relative radical stabilities were estimated from the isodesmic reaction $R_2NO^\bullet + CH_3CH_2OH \rightarrow R_2NOH + CH_3CH_2O^\bullet$.

## Results and Discussion

**Electronic Structures of 1 and 2.** The analysis of the HeI/HeII photoelectron spectra is summarized in Table 1. The density of ionic states (bands) above 11 eV is large, and we have concentrated on the spectral features below this threshold in order to obtain reliable assignments.

The assignment was based on the considerations of band intensity changes in HeI and HeII spectra, DFT calculations, and comparison with the spectra of related molecules.

TEMPO is the parent compound for the series, and its electronic structure is thus of special interest. The first band (Figure 1) corresponds to ionization from the antibonding orbital located at the NO moiety ($\pi_{NO}$*). This assignment is supported by our DFT calculations and by previous work.[4] The next two bands at 8.95 and 9.2 eV correspond to ionizations from oxygen lone pair of NO group ($n_{NO}$). The cation which is created upon $n_{NO}$

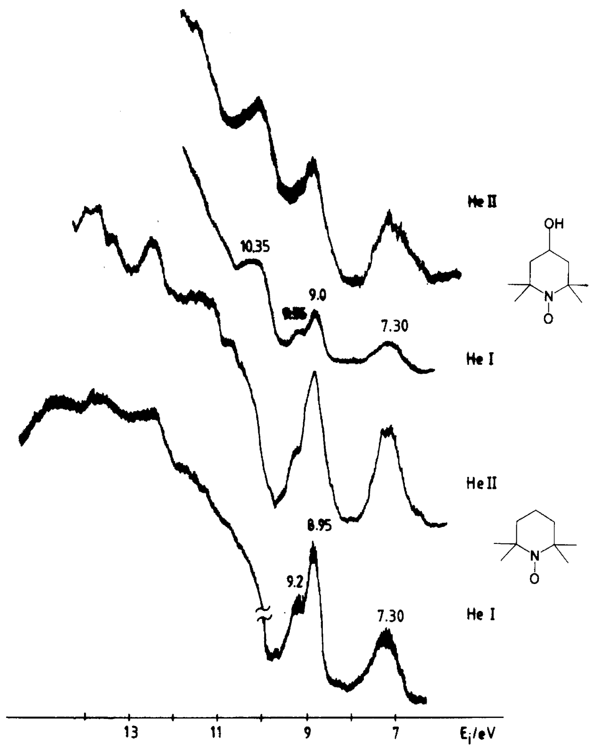

**FIGURE 1.** HeI/HeII photoelectron spectra of **1** and **3**.

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(9) *Gaussian 03, Revision B.01*, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. Gaussian, Inc., Pittsburgh, PA, 2003.

(10) (a) Zyubin, A. S.; Mebel, A. M. *J. Comput. Chem.* **2003**, *24*, 692. (b) Wiberg, K. B.; Stratmann, R. E.; Frisch, M. J. *Chem. Phys. Lett.* **1998**, *297*, 60.

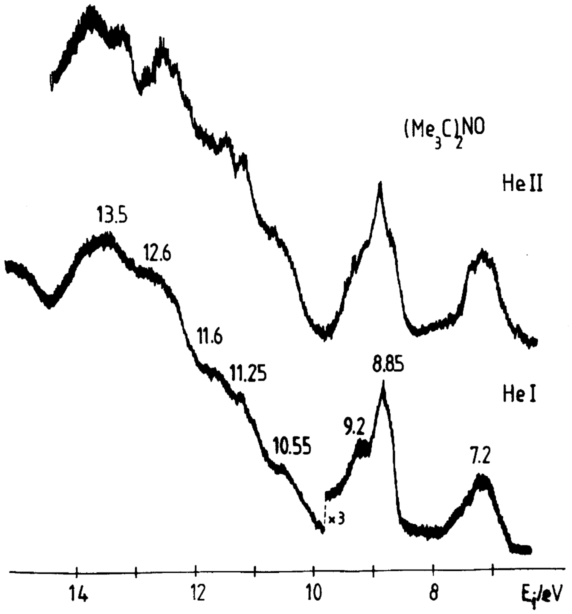

**FIGURE 2.** HeI/HeII photoelectron spectra of **2**.

ionization can exist in either the singlet or triplet state [$n_{NO}$ (T), $n_{NO}$ (S)] which gives rise to two bands with an approximately 3:1 intensity ratio (Chart 2). It is important to note that the three bands mentioned also occur in the acyclic nitroxide $(Me_3C)_2NO$ and at similar ionization energies (Figure 2). The relative intensity of the three bands varies with photon energy. This can be rationalized from their different AO characters and variation of atomic photoionization cross-section with photon energy. The HeII/HeI ratios for C2p, O2p, and N2p orbitals are 0.31, 0.64, and 0.45, respectively,[12] and suggest that nitrogen- and oxygen-containing MOs should exhibit small intensity variations as was indeed observed.

**Electronic Structures of 3−7.** The photoelectron spectra of **3**−**7** (Figures 1, 3, and 4) were interpreted with the aid of DFT calculations, HeI/HeII intensity variations, comparison with the TEMPO spectrum, and the well-established assignments for UPS spectra of related molecules. The related molecules were cyclohexanol,[13] cyclohexylamine,[14] cyclohexanone,[13] and methoxycyclohexane.[15]

In the spectrum of **3**, the first three bands are similar to the TEMPO spectrum and can be assigned to the same types of ionizations. The band at 10.35 eV can, on the basis of comparison with the spectrum of cyclohexanol, be attributed to hydroxyl oxygen lone pair ionization. In cyclohexanol the hydroxyl oxygen appears at 10.1 eV.

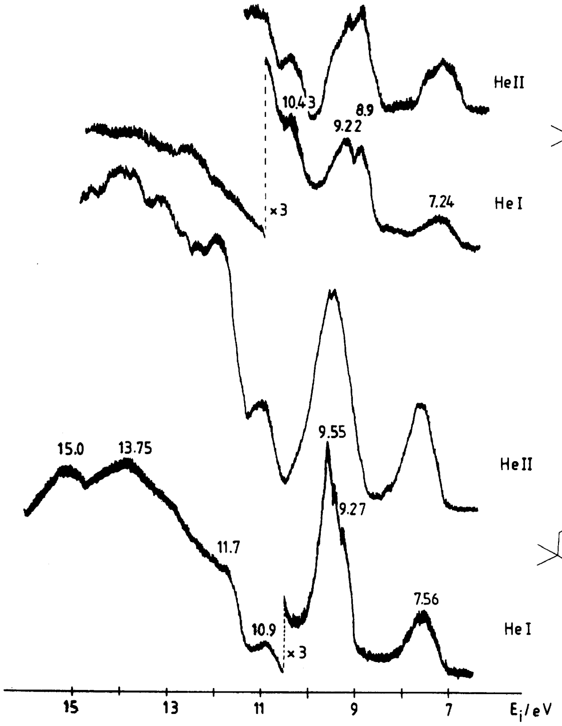

**FIGURE 3.** HeI/HeII photoelectron spectra of **4** and **5**.

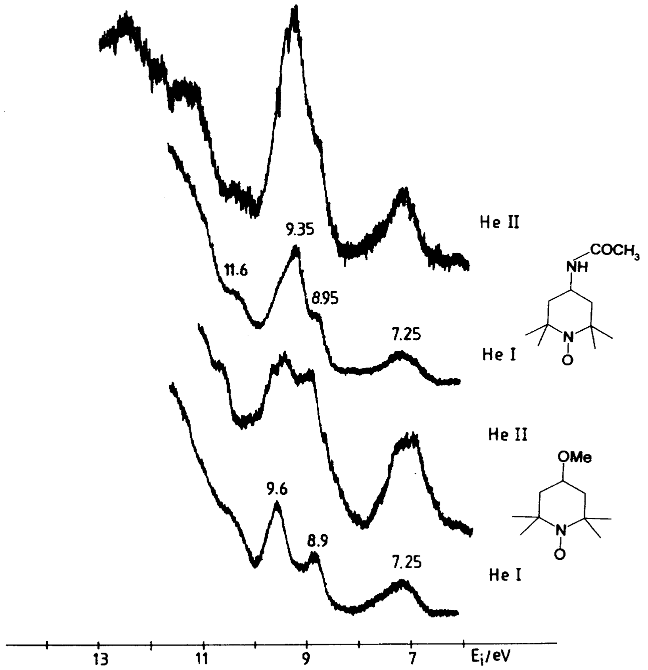

**FIGURE 4.** HeI/HeII photoelectron spectra of **6** and **7**.

The spectrum of **5** shows a 0.3 eV shift of the first band toward higher ionization energies. The overlapping bands at 9.27 and 9.55 eV contain three ionizations which can be assigned to the $n_{NO}$ singlet−triplet pair and the carbonyl oxygen lone pair which in cyclohexanone appears at 9.1 eV.

In cyclohexylamine and methoxycyclohexane, amine and oxygen lone pair energies are 8.53 and 9.22 eV, respectively. This suggests that the third band in the spectrum of **4** (at 9.22 eV) contains two ionizations: $n_{NO}$ (S) and $n_{NH2}$. Likewise, the 3rd band in **6** (at 9.6 eV) contains two ionizations: $n_{NO}$ (S) and $n_O$.

All the assignments are consistent with the order of ionic states predicted by calculations and HeII/HeI

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(11) Lichtenberger, D. L.; Copenhaver, A. S. *J. Electron Spetrosc. Relat. Phenom.* **1990**, *50*, 335.

(12) Yeh, J. J. *Atomic Calculation of Photoionization Cross-sections and Asymmetry Parameters*, Gordon and Breach: Langhorne 1993.

(13) Tian, S.-X.; Kishimoto, N.; Ohno, K. *J. Electron Spectrosc. Relat. Phenom.* **2002**, *127*, 167.

(14) Cowling, S. A.; Johnstone, R. A. W. *J. Electron Spectrosc. Relat. Phenom.* **1973**, *2*, 161.

(15) Neijzen, B. J. M.; Schmitz, R. F.; Klumpp, G. W.; de Lange, C. A. *Tetrahedron* **1975**, *31*, 875.

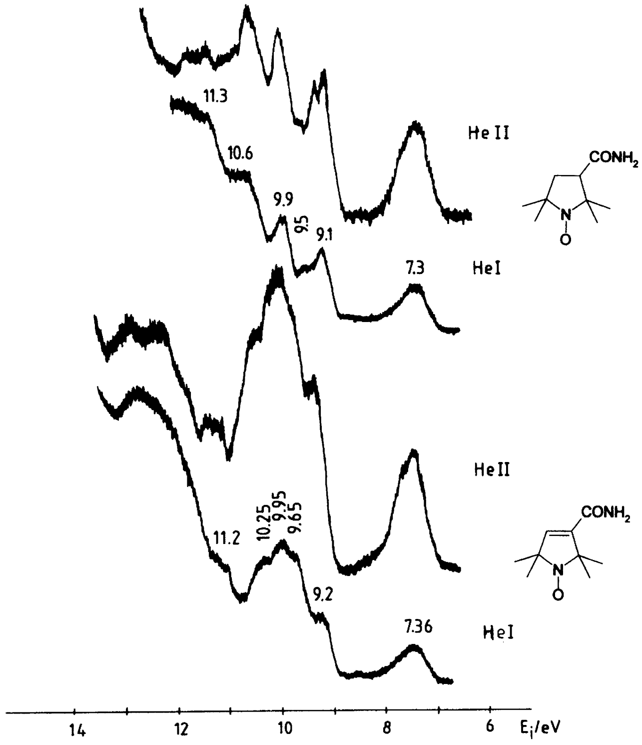


**FIGURE 5.** HeI/HeII photoelectron spectra of **8** and **9**.

intensity variations. For example, the TEMPO spectrum shows that relative intensity variations of $n_{NO}$ (S) and $n_{NO}$ (T) bands with photon energy are small and that the 3:1 ratio is maintained. However, in **4**−**7** the ratio is very different from 3:1 value and is also strongly photon energy dependent. These observations indicate that additional bands arise from orbitals localized on substituent groups.

**Electronic Structures of 8−10.** The spectra in this group (Figures 5 and 6) can be interpreted by comparison with the TEMPO spectrum and the assigned spectra of acetamide,[16] acrylamide,[17] and acetic acid.[18] The additional bands i.e., bands not belonging to $\pi_{NO}$* and $n_{NO}$ ionizations, originate from ionizations of substituent localized orbitals (amide and acetyl groups), and the relevant assignments are given in Table 1. The suggested assignments are again supported by calculations and band intensity variations.

**Relative Stability of the Nitroxide Radicals.** Is the electronic structure deduced from UPS data related to radical stabilities (RSE) and if so how? To determine RSE we calculated enthalpies of reaction of nitroxide radicals with ethanol (Table 3). At both the B3LYP and MP2 levels, the reaction energies radicals are within 20 kJ/mol of each other. This is consistent with the trend in ionization energies of nitroxide group's orbitals, which are little affected by substituents in the 4-position. Similar behavior was found in the five-membered cyclic nitroxides, despite the closer proximity of substitutents to the nitroxide group. The presence of a double bond in the ring leads to only a small difference in the nitroxide energy, which is again consistent with the insensitivity of ionization energies to substitution.

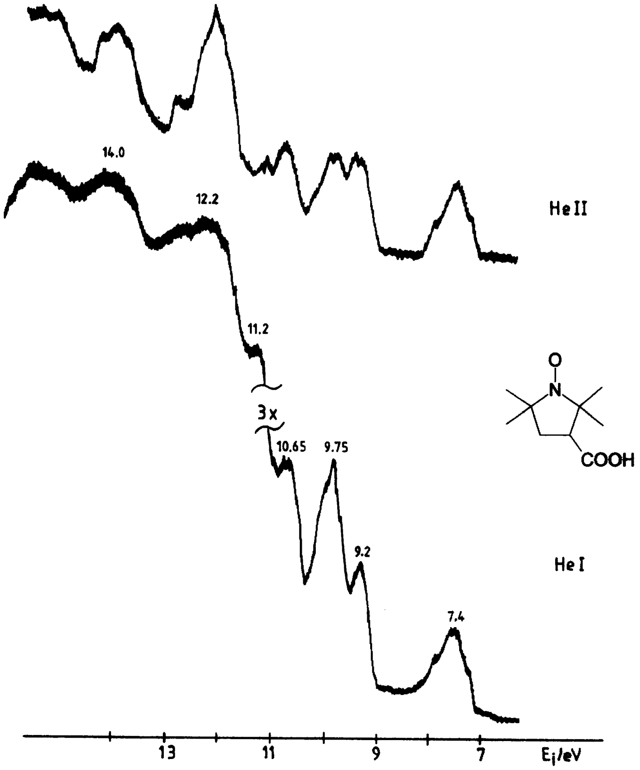


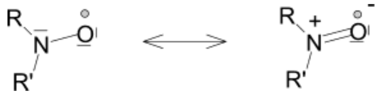
**FIGURE 6.** HeI/HeII photoelectron spectra of **10**.

**TABLE 3. Calculated Enthalpies for Reactions ($\Delta H_r$) between Nitroxide Radicals and Ethanol,[a] Chemical Reduction Rate Constants ($k_{rel}$), and Electrochemical Oxidation Potentials ($E_{1/2}$) for Nitroxide Radicals [a,b]**

| nitroxide | $\Delta H_r$/kJ mol$^{-1}$ B3LYP/6-31+G(d) | $\Delta H_r$ MP2/6-31+G(d) | $k_{rel}$[b] | $E_{1/2}^{ox}$/mV[b] |
|---|---|---|---|---|
| **1** | 157.3 | 168.6 | 0.6 | |
| **2** | 160.3 | 170.6 | | |
| **3** | 156.5 | 166.9 | 1.7 | 480 |
| **4** | 156.1 | 166.9 | 5.5 | 630 |
| **5** | 151.9 | 161.1 | 1.9 | 670 |
| **6** | 142.3 | 148.1 | | |
| **7** | 155.2 | 165.6 | | |
| **8** | 152.7 | 158.6 | 2.3 | 630 |
| **9** | 154.4 | 162.7 | 2.5 | 730 |
| **10** | 164.4 | 175.3 | 1.0 | 540 |

[a] $R2NO^{\bullet} + CH_3CH_2OH \rightarrow R_2NOH + CH_3CH_2O^{\bullet}$ (this work). [b] $k_{rel}$ is the relative, first-order rate constant for reduction of nitroxide radicals by ascorbate (from ref 29).

**Structure and Reactivity.** Nitroxide radicals have delocalization energy for the unpaired electron of approximately 120 kJ/mol[2] which can be related to the resonance structures shown below.



Also, the nitroxyl nitrogen atom is sp$^2$ hybridized. The assertion about sp$^2$ hybridization is based on their

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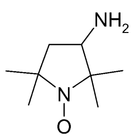
(16) Kishimoto, N.; Osada, Y.; Ohno, K. *J. Electron Spectrosc. Relat. Phenom.* **2001**, *114−116*, 183.

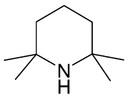
(17) Åsbrink, L.; Svensson, A.; von Niessen, W.; Bieri, G. *J. Electron Spectrosc. Relat. Phenom.* **1981**, *24*, 293.

(18) Kimura, K.; Katsumata, S.; Achiba, Y.; Yamazaki, T.; Iwata, S. *Handbook of HeI Spectra of Fundamental Organic Molecules*, Japan Scientific Societies Press: Tokyo 1981.

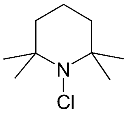
molecular structures,[19–22] all of which contain nitroxyl nitrogen in planar coordination.



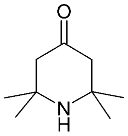
**11**



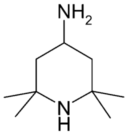
**12**



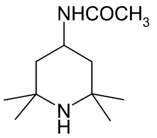
**13**



**14**



**15**



**16**

We have compared HOMO ionization energies in **1**, **12**, and **13**. N-Substitution by chlorine leads to stabilization by 0.27 eV,[23] while N-substitution by oxygen leads to destabilization of 0.73 eV. The difference between these two energies (1 eV) can then be used to estimate the delocalization energy of the NO bond, which amounts to 96.5 kJ/mol. This estimate is based on the assumption that electronegativities (and hence inductive effects) of chlorine and oxygen are comparable.[24] We suggest that the literature value of 120 kJ/mol[2] may be an overestimate. We have thus obtained the information about RSE from UPS data and compared it with the information obtained independently from thermodynamic and kinetic analysis.[2]

To understand the influence of substituents on nitroxide group we shall compare substituent-induced $\pi_{NO}$* energy shifts in radicals **5**, **4**, and **7** with corresponding $n_N$ energy shifts in piperidine analogues **14**, **15**, and **16**. (For photoelectron spectra of **15** and **16** see the Supporting Information.) The comparison reveals that substituent-induced energy shifts in piperidines for keto, amino, and amide groups amount to 0.48, 0.06, and 0.21 eV, respectively. Analogous shifts in nitroxides have values of 0.25, 0.07, and 0.06 eV, respectively. These values make it clear that substituents influence the electronic structure of NO group to only a small extent.

We shall discuss rates of reactions of radicals next. For most radical reactions activation barriers are very small; hence, the structure of transition state is less significant for determining reactivity. The properties which influence reaction rates of nitroxide radicals are steric protection (hindrance) of the nitroxide active site and the stabilization enthalpy of nitroxide group's unpaired electron. This thermodynamic stabilization is of course directly related to the electronic structure of the radical itself and thus to UPS data. We shall now examine kinetic data in order to gauge the significance (or the lack of it) of electronic structures for reactivity. The reactions of **3**, **5**, **8**, and **9** with $^{\bullet}\mathbf{CH_2OH}$ proceed at measurably different rates; the rate constants are 4.4, 7.2, 4.6, and 3.5 × $10^8$ $M^{-1}$ $s^{-1}$, respectively.[25] The electronic structure of the nitroxide group is virtually unperturbed by substitution or rings size as our UPS data show. The different rates mentioned above are thus surprising and possibly need reexamination. On the other hand, reactions of **1**, **3**, and **5** with hydroxyl radical have the same rate constants[26] (4.5 × $10^9$ $M^{-1}$ $s^{-1}$). These results suggest that in reactions of cyclic nitroxide radicals with hydroxyl radicals the electronic structure effects are not significant as can be expected from UPS analysis. However, different rates were observed in reactions of **1** and **2** with alkyl/aryl radicals. Compound **1** reacts faster than **2** with all alkyl/aryl substrates.[27] Bowry and Ingold[27] suggested, on the basis of their study which involved carbon radical substrates of different sizes, that steric protection is the dominant factor. This suggestion is in accordance with our UPS results.

What about the influence of electronic structure on reactions involving nitroxides with nonradical substrates? An extensive study of reduction rates of substituted cyclic nitroxides with ascorbate was reported by Morris et al.[28] using ESR spectroscopy. The study provided electrochemical redox potentials for these compounds (Table 3) and suggested that there was no effect of the gaseous environment (i.e., whether it is oxygen or nitrogen) on reaction rates.[28] The authors concluded that the principal factor affecting reduction rate is the type of ring on which nitroxide is located. The six-membered ring nitroxides (piperidine analogues) reacted faster than five-membered ring nitroxides (pyrrolidine analogues). This effect was explained by different accessibility of NO group to the reducing agent, i.e., steric factors being more important than the electronic structure. This is again in accordance with our UPS data. However, for a particular ring type the rates were found to correlate with inductive substituent constants, but not with substituent sizes. This would suggest that (contrary to our UPS results) electronic structure effects are more important. In other to resolve this discrepancy we consider a related kinetic study performed by ESR which involved reductions of 3-amino-2,2,5,5-tetramethylpyrrolidine-1-oxyl (**11**) and **4** with ascorbate.[29] The results obtained by Noethig-Laslo and Bobst[29] have shown the opposite trend; i.e., **11** and **4** are reduced at the same rate under nitrogen atmosphere even though they have different ring sizes. This kinetic result is in accordance with our UPS data on the electronic structures of nitroxide radicals. However, under aerobic conditions (in the air) the reduction of **4** was more than 10 times faster than of **11**. This may explain the discrepancy with Morris et al.[28] Noethig-Laslo and Bobst[29] rationalized the greater apparent stability of **11** vs **4** as being due to the slower reoxidation rate of the hydroxylamine product of **4** as compared to the hydroxylamine product of **11**.

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(19) Capiomont, P. A.; Lajzerowicz, J.; Legrand, J.-F.; Zeyen, C. *Acta Crystallogr.* **1981**, *B37*, 1557.

(20) Bordeaux, P. D.; Lajzerowicz, J. *Acta Crystallogr.* **1974**, *B30*, 790.

(21) Chion, P. B.; Lajzerowicz, J. *Acta Crystallogr.* **1975**, *B31*, 1430.

(22) Wetherington, J. B.; Ament, S. S.; Moncrief, J. W. *Acta Crystallogr.* **1974**, *B30*, 568.

(23) Bodor, N.; Kaminski, J. J.; Worley, S. D.; Colton, R. J.; Lee, H. T.; Rabalais, J. W. *J. Pharm. Sci.* **1974**, *63*, 1387.

(24) Emsley, J. *The Elements,* 3rd ed., Oxford University Press: Oxford 1998.

(25) Landolt-Bornstein, New Series, II/13c, Springer-Verlag: Berlin 1983; p.183, 218.

(26) Samuni, A.; Goldstein, S.; Russo, A.; Mitchell, J. B.; Krishna, M. C.; Neta, P. *J. Am. Chem. Soc.* **2002**, *124*, 8719.

(27) Bowry, V. W.; Ingold, K. U. *J. Am. Chem. Soc.* **1992**, *114*, 4992.

(28) Morris, S.; Sosnovsky, G.; Hui, B.; Huber, C. O.; Rao, N. U. M.; Schwartz, H. M. *J. Pharm. Sci.* **1991**, *80*, 149.

(29) Noethig-Laslo, V.; Bobst, A. M. *Croat. Chem. Acta* **1991**, *64*, 1.

We may compare further the UPS data (ionization energies) and the results of kinetic study.[28] We note that there is no correlation between electrochemical redox potentials ($E_{1/2}$) and rates ($k_{\mathrm{rel}}$) as shown in Table 3, nor is there a correlation between $E_{1/2}$ and the first ionization energies ($E_{\mathrm{i}}$) as can be seen from Tables 1 and 3. The $E_{1/2}$ values can be influenced by radical's electronic structure, solvation effects and surface effects on the electrode, but not by steric accessibility of the NO group. Oxidation potential $E_{1/2}^{\mathrm{ox}}$ can be compared to the first ionization energy ($E_{\mathrm{i}}$) since both processes involve the removal of electron from the radical species. The lack of good $E_{\mathrm{i}}$ vs $E_{1/2}^{\mathrm{ox}}$ correlation (Tables 1 and 3) indicates that solvation and surface effects are more important than electronic structure for the rate of radical's oxidation at the anode.

## Conclusion

The electronic and molecular structure of nitroxide functional group remains largely unaffected by substitution of the radical molecule. This was rationalized by the fact that HOMO ionization takes place from an orbital which is strongly localized at the nitroxide functional group.[30] This stability persists regardless of whether the radical has cyclic or acyclic structure or whether the ring size is large or small. The stability is evident from the comparison of photoelectron spectra of **1** and **2** where the energy shifts are only 0.1 eV. The only discernible shift occurs in carbonyl derivative. Comparison of the spectra of **5** and **1** reveals the 0.26 eV shift in the $\pi_{\mathrm{NO}}^*$ orbital and 0.32 eV shift in $n_{\mathrm{NO}}$ orbital. To put the observed shifts into perspective we note that nitrogen lone pair shift on going from **12** to **13** amounts to 0.48 eV.[23] There is a weak inductive effect operating between substituent and nitroxide group as can be seen from the lack of variation in NO orbital energies with the type of substituent present. Only the introduction of very strongly electron withdrawing groups significantly changes nitroxide orbital energies. For example, in $(CF_3)_2NO$ the nitroxide group ionization energies rise from 7.3 to 10.7 and from 8.95 to 12.0 eV.[31] In keto derivative **5** the change is smaller, but still discernible amounting to 0.3 eV.

We have observed small differences in band intensities of triplet−singlet split bands which reflect different photoionization cross-sections for the two electronic states of cation. This is the first time that such an observation had been made for the molecule not containing heavy atoms. This observation is worth investigating further by using high resolution, tuneable radiation source e.g. synchrotron. To the best of our knowledge no such variable photon energy studies had been performed on stable radical species to date.

We have also used our UPS data to resolve some conflicting kinetic information on rates of radical reactions and showed unambiguously that the electronic structure and electron delocalization play only a minor role in the reactions of nitroxide radicals.

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## Appendix: UPS

The assignment of the spectra of large molecules is often facilitated by measuring band intensities at various photon energies. The empirical relative intensity of each band in 7−10 eV region of the HeI or HeII spectrum was subsequently normalized to the first band i.e., the one with the lowest ionization energy. The first band was selected for normalization because it is always well defined and does show any overlap with other bands. The ratios of normalized HeII and HeI intensities were then used to calculate $\mathrm{RI}_{\mathrm{exp}} = \sigma_{\mathrm{i}}^{\mathrm{HeII}}/\sigma_{\mathrm{i}}^{\mathrm{HeI}}$ (Table 1). The band normalization was necessary because absolute band intensities could not be measured. Band intensities vary because of changing molecular photoionization cross-sections at different photon energies.

**Supporting Information Available:** Coordinates of optimized geometries and total energies for nitroxide radicals; HeI photoelectron spectra of **15** and **16**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(30) Hvistendahl, G.; Undheim, K. *Chem. Scripta* **1971**, *1*, 123.

(31) Cornford, A. B.; Frost, D. C.; Herring, F. G.; McDowell, C. A. *Faraday Discuss.* **1972**, *54*, 56.