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# Reduction of an Hexamethylphosphoramide Degradation Product: A Diazabutadiene

**Brad D. Rose, Steven J. Peters,* Richard C. Reiter, and Cheryl D. Stevenson***

*Department of Chemistry, Illinois State University, Normal, Illinois 61790-4160*

*cdsteve@ilstu.edu; sjpeter@ilstu.edu*

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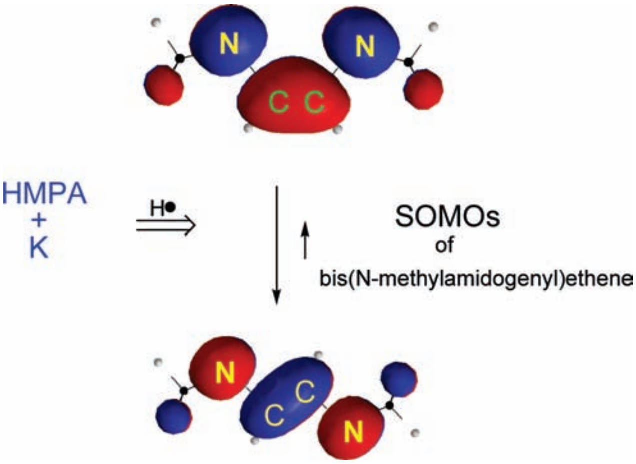
## ABSTRACT



**Alkali metal over-reduction of an electron acceptor in the presence of a hydrogen atom donor, in hexamethylphosphoramide (HMPA), results in a radical that is not simply the anion radical of the acceptor. This new species exhibits an enigmatic EPR pattern. Using $^{15}N$ and $^{2}H$ labeling studies, the "HMPA degradation product" was found to be the anion radical of *N,N′*-dimethyl-1,4-diazabutadiene. DFT calculations support this assignment and a mechanism for its formation.**

For well over a quarter century, a rather enigmatic and fleeting EPR signal (Figure 1) has been observed whenever a variety of substrates are over-reduced with alkali metals in hexamethylphosphoramide (HMPA) when in the presence of a source of hydrogen atoms.[1] This so-called "HMPA degradation product" ($\mathbf{1}^{\bullet-}$) has been observed during dehydrohalogenations prior to reduction, reduction of alkyne condensation products, etc.[1]

Since HMPA is a common solvent for anion radicals and it normally allows observation of the anion radical in the absence of ion association,[2] we recently decided to identify the underlying unknown species ($\mathbf{1}^{\bullet-}$) that gives rise to this troubling spectrum.[3] We anticipated a radical containing the P═O moiety. However, a series of isotopic labeling studies have revealed $\mathbf{1}^{\bullet-}$ to be a new example of an unligated diimine anion radical, that of *N,N′*-dimethyl-1,4-diazabutadiene.

It seemed reasonable that the slow over-reduction of a conjugated organic acid (more electrons added than

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[1] Weak versions of this spectrum were observed during over-reduction experiments in the following studies: (a) Peters, S. J.; Turk, M. R.; Kiesewetter, M. K.; Reiter, R. C.; Stevenson, C. D. *J. Am. Chem. Soc.* **2003**, *125*, 11212–11268. (b) Gard, M. N.; Kiesewetter, M. K.; Reiter, R. C.; Stevenson, C. D. *J. Am. Chem. Soc.* **2003**, *125*, 16143–16150.

[2] Ion association is absent with anion radicals in HMPA. See: (a) Levin, G.; Jagur-Grodzinski, J.; Szwarc, M. *J. Am. Chem. Soc.* **1970**, *92*, 2268–2275. (b) Stevenson, C. D.; Echegoyen, L.; Lizardi, L. R. *J. Phys. Chem.* **1972**, *76*, 1439–1442.

[3] This spectrum causes consternation, as its appearance means that you have over-reduced and can no longer observe the desired radical.

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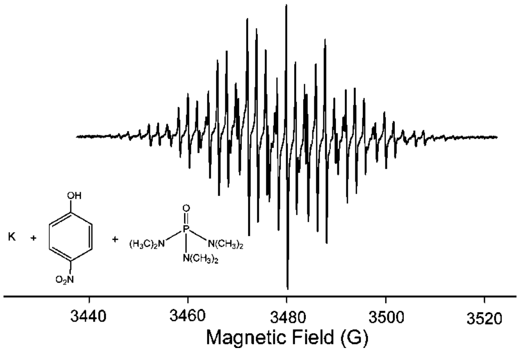

**Figure 1.** X-band EPR spectrum obtained from the potassium over-reduction of *p*-nitrophenol in HMPA. The *p*-nitrophenol simply serves as a hydrogen donor, and a wide variety of hydrogen atom donors can be used to generate the same spectrum. Weaker versions of this spectrum have been observed in many previous studies.

organic acid) of high solution electron affinity would yield desirable concentrations of this HMPA degradation product. The careful reduction of *p*-nitrophenol with a freshly distilled potassium mirror in HMPA first exhibits the known EPR pattern for the *p*-nitrophenol anion radical.[4] As the reduction proceeds past one electron transferred per $NO_2-C_6H_4-OH$ ([K] > [ *p*-nitrophenol]), H atoms are released, and this spectrum is replaced by a strong signal due to $\mathbf{1}^{\bullet-}$ (Figure 1). Even at this signal-to-noise ratio, an unambiguous interpretation is impossible, due to the multitude of possible spin combinations.

The conundrum can be resolved with isotopically labeled HMPAs, but unfortunately none are commercially available. Only a patent procedure, which is difficult to reproduce and quite cumbersome, for the synthesis of laboratory amounts has been reported.[5] Furthermore, since HMPA is a common solvent used in EPR studies, a clean simple synthetic method for isotopically labeled HMPA was developed.

Specifically, an excess of $^{15}N$-dimethylamine or perdeuterated dimethylamine was reacted with $POCl_3$ in dry THF under high vacuum conditions at ambient temperatures. After sufficient mixing time, the solution was exposed to excess ammonia. The $NH_3$ helps break up the $(CH_3)_2NH_2Cl$ precipitate to release more amine for further reaction with the $POCl_3$. After additional mixing, the excess $NH_3$ was removed and the remaining solution was dissolved in diethyl ether and filtered to remove the white salt ($NH_4Cl$). After removal of the ether, the product was distilled under reduced pressure to provide a 49% yield of labeled HMPA. The product and its purity were verified using GCMS and NMR (Figure 2).

The reduction and EPR analysis were repeated in our newly synthesized per-$^{15}N$-HMPA. Only nuclei with $I = 1/2$ can now be present, and the resulting EPR spectrum (red in Figure 3) was easy to simulate (blue in Figure 3).

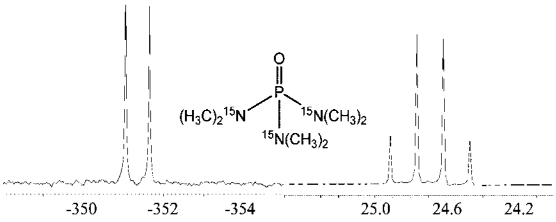

**Figure 2.** (Right) $^{31}P$ NMR $^1H$-decoupled spectrum of the $^{15}N$-labeled HMPA synthesized as described above recorded at 202.45 MHz. The chemical shift is referenced to 85% phosphoric acid at 0.0 ppm. $^1J_{15N\text{-}31P} = 29.9$ Hz. (Left) $^{15}N$ NMR spectrum of the $^{15}N$-labeled HMPA synthesized as described above recorded at 50.70 MHz. The chemical shift is referenced to nitrobenzene at $-6.0$ ppm. $^1J_{31P\text{-}15N} = 29.9$ Hz.

Indeed, three sets of $I = 1/2$ spins were found, one of which results from a group of six, presumably two methyl groups. Present also are two groups of two spins, due to $^{15}N$, $^1H$, and/or $^{31}P$.

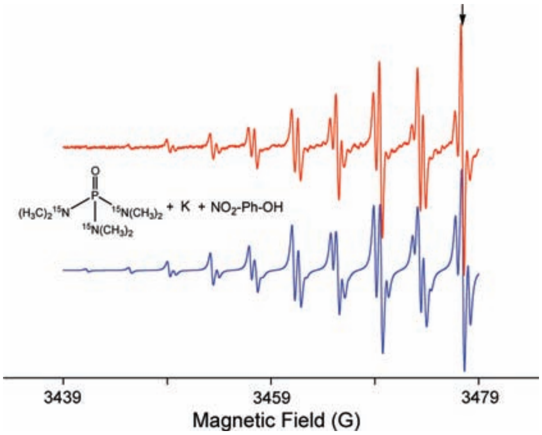

**Figure 3.** (Upper) Low-field half of the x-band EPR spectrum obtained from the K over-reduction of *p*-nitrophenol in per-$^{15}N$-HMPA. (Lower) A computer simulation using couplings of 7.870 G for six spins, 4.145 G for two spins, and 8.456 G for two spins. $I = 1/2$ for all of the nuclear spins. The arrow marks the spectral center and the $\Delta w_{pp} = 0.28$ G.

To resolve this spin ambiguity, the reduction and EPR analysis were repeated in HMPA-$d_{18}$. Surprisingly, in the deuterated solvent, only $I = 1$ spins proved to be present (see Figure 4); all of the $I = 1/2$ spins in $\mathbf{1}^{\bullet-}$ must be due to protons; and there can be no splittings from $^{31}P$.

All that was necessary to obtain the correct simulation was to determine which and how many of the $I = 1/2$ spins, from Figure 3, must be multiplied by the ratio of gyromagnetic ratios $\gamma_{2H}/\gamma_H$ or $\gamma_{14N}/\gamma_{15N}$ along with changing the spin numbers from 1/2 to 1. All possibilities were computed, and the only simulation that agrees with the empirical spectrum is shown in blue in Figure 4.

Now, simply converting the couplings from the six equivalent deuteriums of $a_D = 1.21$ to $a_H = 7.87$ G and two

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[4] Piette, L. H.; Ludwig, P.; Adams, R. N. *J. Am. Chem. Soc.* **1962**, *84*, 4212–4215.

[5] (a) Liu, R. *Huaxue Shijie* **1991**, *32*, 154–155. (b) Kenneth, G. L. *Amidation of phosphorus halides with organic amines*, US Patent 2,852,550, 1958.

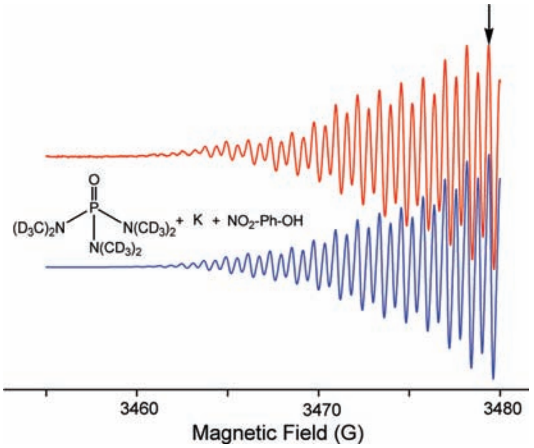


**Figure 4.** (Upper) Low-field half of the x-band EPR spectrum obtained from the K over-reduction of *p*-nitrophenol in per-deuterated-HMPA. (Lower) A computer simulation using $a_D$'s = 1.21 G (6 $^2$Hs), 0.637 G (2 $^2$Hs), and 6.01 G for two $^{14}$N's. $I = 1$ for all of the nuclear spins and the $\Delta w_{pp} = 0.20$ G. The g-tensor anisotropy effects due to the nitrogen splitting were included in the simulation. The arrow marks the spectral center.

equivalent deuteriums of $a_D = 0.637$ to $a_H = 4.15$ G and $I = 1$ to 1/2 reveals a near perfect fit (see Figure 5) to the original spectrum shown in Figure 1.

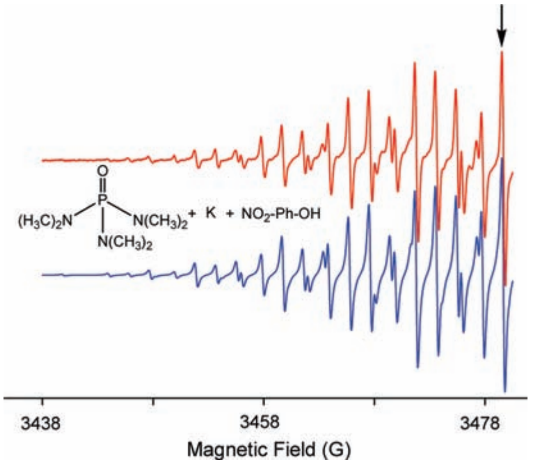


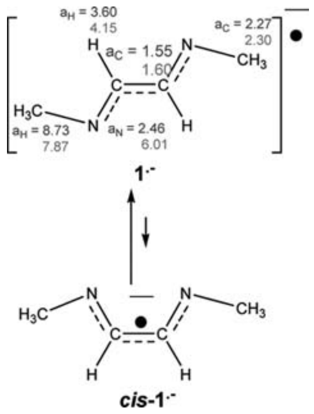
**Figure 5.** (Upper) Low-field half of the x-band EPR spectrum obtained from the potassium over-reduction of *p*-nitrophenol in isotopically natural abundance HMPA. (Lower) This spectrum was computer simulated using coupling constants of 7.870 G for six H's, 4.145 G for two H's, and 6.01 G for two $^{14}$N's. The vertical arrow marks the spectral center, and $\Delta w_{pp} = 0.25$ G.

A somewhat redundant but revealing experiment involves the use of $NO_2-C_6H_4-OD$, which expresses no incorporation of deuterium into $1^{\bullet-}$. The HMPA degradation product is composed only of atoms originating from the HMPA. We also know that ($\mathbf{1}^{\bullet-}$) is N to N conjugated, having the set of two protons on carbons (the H−N bond cannot endure under this strongly reducing environment), and it has at least a $C_2$ symmetry. These considerations provide an empirical formula of $C_2(CH_3)_2H_2N_2$.

The presence of two different groups of carbons is supported by the vertical expansion of Figure 5 (see Supporting Information) revealing splittings from two pairs of $^{13}$C nuclei with splittings of 2.17 and 2.55 G. All of this suggests that $\mathbf{1}^{\bullet-}$ is a *N*,*N*′-dimethyl-1,4-diazabutadiene anion radical.

As in the alkyl-substituted butadiene anion radicals,[6] $\mathbf{1}^{\bullet-}$ can be in the cis or trans configuration (Scheme 1); this issue can be resolved via DFT calculations.

**Scheme 1.** cis−trans Equilibrium of the Diimine Anion Radical, Lying Predominantly in the Direction of the trans Isomer



The B3LYP//6-311++G** calculation predicts the trans isomer to be of lower energy by 4.06 kcal/mol. The B3LYP//6-311++G**/EPR-III computed electron−nuclear couplings (blue) compare favorably, except for $a_N$, to the empirical values (red). Volumes have been written, and not without controversy,[7] concerning calculated $a_N$'s and the reasons for poor and good agreement with the empirical values. Interestingly, EPR-II predicts an $a_N$ of 6.11 G which is very close, but EPR-II makes poor predictions for the non-nitrogen coupling constants. EPR-III, however, predicts less than half of the empirical value of 6.01 G (see Supporting Information).

A reasonable mechanism for the initial formation of the cis configuration of $\mathbf{1}^{\bullet-}$ involves the attack of the phenolic

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(6) Gerson, F.; Hopf, H.; Merstetter, P.; Mlynek, C.; Fischer, D. *J. Am. Chem. Soc.* **1998**, *120*, 4815–4824.

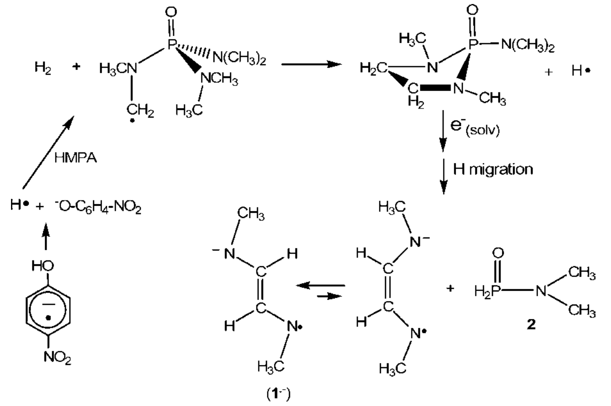
(7) (a) Hermosilla, L.; Calle, P.; Garcia de la Vega, J. M.; Sieiro, C. *J. Phys. Chem. A* **2006**, *110*, 13600–13608. (b) Engels, B. *Calculation of NMR and EPR Parameters Theory and Applications*; Kaup, M., Buhl, M., Malkin, V. G., Eds.; Wiley-VCH: Weinheim, 2004; pp 483−492. (c) Wetmore, S. D.; Boyd, R. J. *J. Phys. Chem. B* **1998**, *102*, 9332–934. (d) Bartra, R.; Giese, B.; Spichty, M.; Gescheidt, G.; Houk, K. N. *J. Phys. Chem.* **1996**, *100*, 18371–18379.

(8) (a) Wertz, J. E.; Bolton, J. R. *Electron Spin Resonance*; McGraw-Hill: New York, 1986; pp 58−60. (b) Atkins, P.; de Paula, J. *Physical Chemistry*, 7th ed.; W. H. Freeman: New York, 2002; pp 432−435. (c) See also: Wiberg, K. B.; Rablen, P. R.; Marquez, M. *J. Am. Chem. Soc.* **1992**, *114*, 8654–8668.

(9) Franz, K. D.; Dieck, T. H.; Starzewski, K. A. O.; HohMann, F. *Tetrahedron* **1975**, *31*, 1465–1469.

hydrogen atom coming from the *p*-nitrophenol upon a methyl group of the HMPA (Scheme 2). After intramolecular rearrangement and further reduction, both **1** and **2** could be formed. The fate of **2** is unknown, but it is clear that it could not persist under these highly reductive conditions.

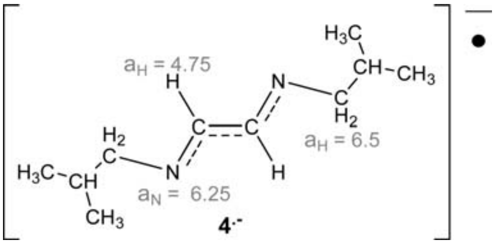
**Scheme 2.** Proposed Mechanism for the Formation of $1^{\bullet-}$



1,3-Butadiene (**3**) is the simplest conjugated hydrocarbon, and its corresponding anion radical serves as the exemplar[8a,b] and undergraduate text-book target of quantum mechanics as applied to molecular systems.[8b] After all, EPR spin density measurements reveal the quantum mechanical "location" of the odd electron in this simplest conjugated "molecular box" ($3^{\bullet-}$), and the corresponding spin densities compare quite favorably with the anachronistic Hückel theoretical approach.[8c] The simplest atomic perturbation upon $3^{\bullet-}$ amounts to the replacement of carbons with adjacent (in the Periodic Table) elements. This is the topic of some contemporary theoretical work on the neutral analogues.[8c]

The anionic aza-derivatives are, however, inherently unstable and have with one exception[9] been reported as bound ligands.[10] In this study, the anion radical of *N*,*N*′-dimethyl-1,4-diazabutadiene ($1^{\bullet-}$) appears as its solvated ion in HMPA, and its spin densities compare quite favorably with those from the DFT theoretical approach.

The anion radical of **1** has not been previously reported; however, over 30 years ago the one exception, mentioned above, involved the observation of the anion radicals of *N*,*N*′-dialkyldiimenes, where the alkyl groups are sufficiently bulky to retard polymerization. The system closest to $1^{\bullet-}$ is shown below ($4^{\bullet-}$). Even though the resolution is quite poor (see Figure 1 in ref 9), the coupling constants compare quite favorably to ours for $1^{\bullet-}$.



$4^{\bullet-}$

Presumably $1^{\bullet-}$, and a variety of its reaction products, should now be available from a simple one-pot procedure from one of the most common and useful solvents: HMPA. When radicals under reductive conditions are involved, HMPA may be more than just a solvent. Further, the synthetic procedure described for the isotopically labeled HMPA should be viable for "HMPAs" where the methyl groups are replaced with other entities extending the possible zoo of break down products. We are currently exploring this avenue.

**Acknowledgment.** We thank the National Science Foundation for MRI grant (CHE-0722385), and Steve Peters thanks the Research Corporation for support.

**Supporting Information Available:** Previously observed spectra of $1^{\bullet-}$, DFT calculation results, and the natural abundance $^{13}C$ spectral analysis. This material is available free of charge via the Internet at http://pubs.acs.org.

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(10) (a) For example, see: Tuononen, H. M.; Armstrong, A. F. *Inorg. Chem.* **2005**, *44*, 8277–8284, and references therein. (b) Schmidt, E. S.; Jockisch, A.; Schmidbaur, H. *J. Am. Chem. Soc.* **1999**, *121*, 9758–9759. (c) Andappan, M. M. S.; Nilsson, P.; von Schenck, H.; Larhed, M. *J. Org. Chem.* **2004**, *69*, 5212–5218.