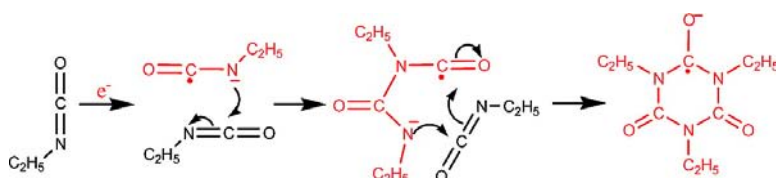


Isocyanurate Anion Radicals via Electron-Initiated Cycloaddition of Isocyanates

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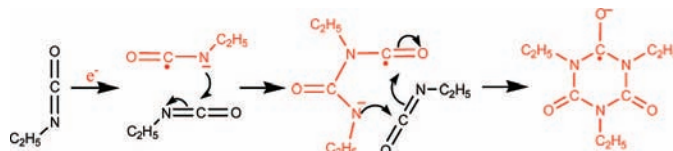
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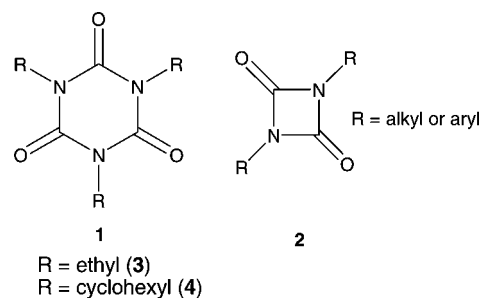
ABSTRACT



Room temperature sodium metal reductions of alkyl isocyanates lead to the rapid electron-initiated formation of alkyl isocyanurate anion radicals, which exhibit EPR coupling to only two equivalent nitrogens. Reduction of ^{13}C -enriched ethyl isocyanate reveals that the odd electron localizes in the π system of one carbonyl in the isocyanurate ring. EPR line-width alternation effects indicate that at least two stable conformers are in rapid equilibrium undergoing fast exchange.

Aromatic isocyanurates (**1**),¹ produced via the cyclotrimerization of isocyanates, have considerable commercial importance and are commonly used in polymeric blends of polyurethanes and other copolymer resins, making these materials more flame-retardant, transparent, and impact-resistant.² Isocyanate itself is often used as a precursor to the synthesis and development of new β -lactams, which are key moieties in one of the most important classes of antibiotics.³ Isocyanurates have even become significant in organosilica nanochemistry.⁴ Uretidinediones (**2**) are not as commercially important but are commonly found as a byproduct in the synthesis of isocyanurates. Despite these considerations, very little is known about the one-electron reduction of isocyanates. The only published example of an isocyanate anion radical is with methyl isocyanate, which was generated in a solid solvent matrix at 77 K using

γ -radiation.⁵ However, the one-electron reduction with these systems has not been explored under ambient conditions.



Our motivation to investigate the one-electron transfer to isocyanates is peaked by the realization that ketyls are arguably the most important and versatile class of anion radicals. In view of the tendency for isocyanates to undergo cycloaddition in the presence of Lewis acid or Lewis base catalysts,⁶ we anticipated and found such behavior upon isocyanate ketyl formation. Surprisingly, the cyclotrimer

(1) Isocyanurates are planar and considered aromatic with the nitrogen lone pairs contributing to the π system of the ring.

(2) (a) Wirpsza, Z. *Polyurethanes: Chemistry, Technology and Application*; Ellis Horwood: London, 1993. (b) Zitinkina, A. K.; Sibanova, N. A.; Tarakonov, O. G. *Russ. Chem. Rev.* **1985**, *54*, 1866. (c) Nicholas, L.; Gmitter, G. R. *J. Cell. Plast.* **1975**, *267*.

(3) (a) Fisher, J. F.; Meroueh, S. O.; Mobashery, S. *Chem. Rev.* **2005**, *105*, 395. (b) Rigby, J. H.; Brouet, J.; Burke, P. J.; Rohach, S.; Sidique, S.; Heeg, M. J. *Org. Lett.* **2006**, *8*, 3121–3123.

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anion radical produced reveals that the unpaired electron is coupled to only two ring nitrogens. This is a consequence of some interesting quantum mechanical considerations.

When a hexamethylphosphoramide (HMPA) solution containing ethyl isocyanate (C_2H_5NCO) or cyclohexyl isocyanate ($C_6H_{11}NCO$) is exposed to a freshly distilled alkali metal mirror, under high vacuum, a reddish-orange solution results that exhibits a strong EPR signal. The EPR spectrum generated from the reduction of C_2H_5NCO shows a 1:2:3:2:1 pentet that results from the unpaired electron coupled to two equivalent ^{14}N atoms ($I = 1$) with an $a_N = 1.66$ G and a g factor of 2.0046; no additional hyperfine couplings (i.e., from the CH_2 groups adjacent to these nitrogens) are observed. However, the anion radical generated from the reduction of $C_6H_{11}NCO$ exhibits a strong well-resolved pentet of triplets due to the coupling from two equivalent N atoms ($a_N = 1.634$ G) and two equivalent H atoms ($a_H = 0.14$ G) and has a similar g factor (Figure 1).⁷ The a_H 's come from

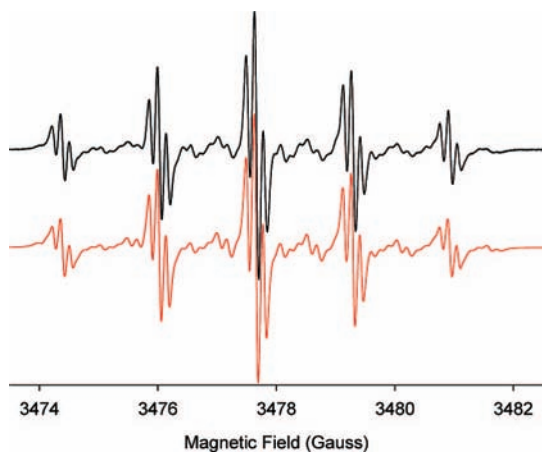


Figure 1. (Upper) X-band EPR spectrum recorded at 295 K after a HMPA solution containing $C_6H_{11}NCO$ was exposed to Na metal. (Lower) Computer simulation using a mixture of two spectra in a 1:1 ratio for the ion pair and free ion species. The free ion spectrum was generated by modulating a_N ($2 \times N$) between two states using 1.80 and 1.47 G at a rate of 1×10^8 s $^{-1}$ and $a_H = 0.14$ G ($2 \times H$). The intrinsic peak-to-peak line width (Δw_{pp}) is 0.07 G. The ion pair spectrum was generated using $a_N = 1.52$ G ($2 \times N$), $a_H = 0.152$ G ($2 \times H$), and $a_{Na} = 0.45$ G ($1 \times Na$), $\Delta w_{pp} = 0.12$ G. The spectrum for the ion pair is shifted upfield relative to the spectrum for the free ion by 0.22 G.

coupling to the hydrogens bonded to the ipso carbons on two of the cyclohexyl ring moieties. In addition, a second species is present that gives an EPR spectrum exhibiting Na hyperfine splittings from an ion pair in solution (Figure 1). This was somewhat surprising considering that ion pairing

effects are usually absent in HMPA.⁸ When the temperature of this solution is lowered to 0 °C, the ion pair species disappears.

Since the nitrogen coupling observed in the reduction of both C_2H_5NCO and $C_6H_{11}NCO$ is due to only a pair of nitrogens, our initial conclusion was that a cyclodimerization occurred and that $2^{\cdot-}$ ($R = C_2H_5$ or C_6H_{11}) had formed. However, results using ^{13}C -enriched ethyl isocyanate ($C_2H_5N^{13}CO$) revealed that a cyclotrimerization occurs upon reduction.

Enriched ^{13}C -ethyl isocyanate was synthesized from ^{13}C -propionic acid.⁹ The EPR spectrum, obtained after the reduction of $C_2H_5N^{13}CO$, reveals that the odd electron is also coupled to *three* carbonyl carbons, with $a_C = 2.41$ G ($1 \times ^{13}C$) and $a_C = 0.69$ G ($2 \times ^{13}C$) (Figure 2). Upon closer

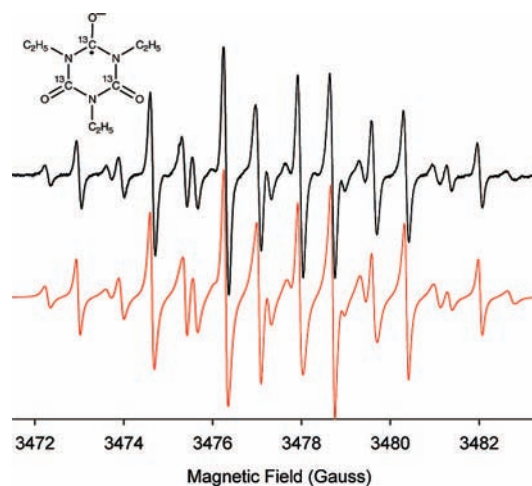


Figure 2. (Upper) X-band EPR spectrum recorded at 295 K after a HMPA solution containing $C_2H_5N^{13}CO$ was exposed to Na metal. (Lower) Computer generated simulation using $a_N = 1.66$ G ($2 \times ^{14}N$), $a_C = 2.41$ G ($1 \times ^{13}C$), and $a_C = 0.69$ G ($2 \times ^{13}C$). To simulate the line-width modulation effect, the most accurate computer simulation was generated by modulating the small a_C between two states at a rate of 4×10^6 s $^{-1}$ using 0.55 G ($2 \times ^{13}C$) and 0.83 G ($2 \times ^{13}C$). The state with $a_C = 0.55$ G is shifted downfield by 0.05 G. Δw_{pp} is 0.09 G.

inspection, we see that the triplet splitting from the two equivalent ^{13}C atoms does not exhibit the expected 1:2:1 intensity pattern. This is especially apparent when looking at the first triplet (downfield) in Figure 2. It is clear from these first three resonances that the outer lines are broadened relative to the center line. This broadening is due to a line-width alternation effect from the selective modulation of the small ^{13}C hyperfine splittings. (An expansion of this downfield region can be found in Supporting Information.)

The large difference in a_C 's for the three carbonyl carbons and the fact that coupling is observed to only two nitrogens

(8) Levin, G.; Jagur-Grodzinski, J.; Szwarc, M. *J. Am. Chem. Soc.* **1970**, *92*, 2268–2275.

(9) (a) The propionyl chloride was generated from the acid using the procedure from: Brown, H. C. *J. Am. Chem. Soc.* **1938**, *60*, 1325–1328. (b) The acid chloride was exposed to NaN_3 to generate the propionyl azide which was then heated to form the isocyanate.

(7) The g factor was measured using the perylene cation radical in concentrated sulfuric acid as an internal standard. See: (a) Segal, B. G.; Kaplan, M.; Fraenkel, G. K. *J. Chem. Phys.* **1965**, *43*, 4191. (b) Allendoerfer, R. D. *J. Chem. Phys.* **1971**, *55*, 361.

suggest either that the electron is localized in the π system of one carbonyl or that a product less symmetrical than $3^{\bullet-}$ (e.g., the third nitrogen is missing) has formed. When the reduction of C_2H_5NCO is carried out in a THF- d_8 solution, followed by reoxidation with iodine ($3C_2H_5NCO + e^- \rightarrow 3^{\bullet-} + 1/2 I_2 \rightarrow 3 + I^-$), NMR analysis reveals that **3** is the dominant product, with an 86% yield (Figure 3). The same

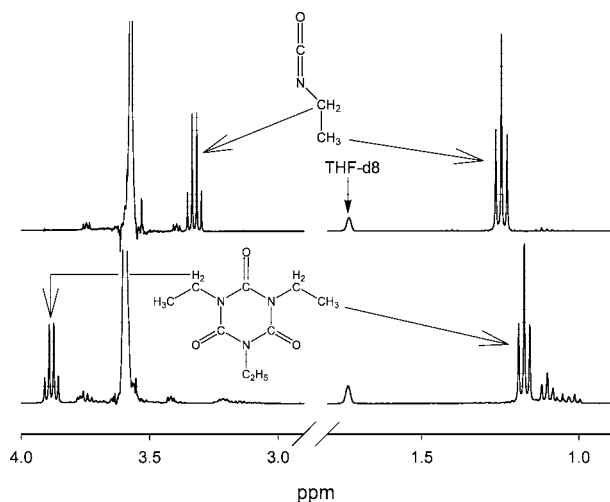


Figure 3. (Upper) 400 MHz 1H NMR spectrum of a THF- d_8 solution containing ethyl isocyanate with an excess of 18-crown-6 (~ 3.6 ppm). (Lower) 400 MHz 1H NMR spectrum of the same THF- d_8 solution after reduction of the ethyl isocyanate with Na metal followed by reoxidation with I_2 . The 18-crown-6 is needed to generate solvated electrons in THF.

procedure was carried out with the $C_6H_{11}NCO$ system, and **4** was generated with a 81% yield.¹⁰

As further confirmation that the anion radicals of **3** and **4** are generated by the electron-initiated reduction of their respective isocyanates, we synthesized **3** using known synthetic procedures.¹¹ The reduction of authentic **3** and **4** in HMPA gave the *identical* EPR spectrum as that generated by the reduction of ethyl isocyanate and cyclohexyl isocyanate, respectively. These results leave little doubt that the anion radicals of **3** and **4** form upon reduction of their isocyanate precursors.

B3LYP/6-31G* geometry optimizations for **3** and $3^{\bullet-}$ show that the gas phase anion radical is unstable relative to the neutral molecule by 40.8 kJ/mol, indicating that solvation effects are important to the stability of $3^{\bullet-}$. Despite this, we find that the predicted spin densities for the ring carbons and nitrogens correlate remarkably well with the measured coupling constants (Figure 4).¹² These calculations also

(10) (a) 1H chemical shift assignments are known. See: Tang, J.; Verkade, J. G. *J. Org. Chem.* **1994**, *59*, 4931–4938. (b) Duong, H. A.; Cross, M. J.; Louie, J. *Org. Lett.* **2004**, *6*, 4679–4681.

(11) Ovchinnikova, N. A.; Sinyakov, A. E.; Reznik, A. M.; Sakharov, S. G.; Gorbunova, Yu. E.; Mikhailov, Yu. N.; Kanishcheva, A. S.; Butskii, V. D. *Koord. Khim.* **2002**, *28*, 673–677.

(12) Calculations on **4** and $4^{\bullet-}$ give similar results, with **4** being more stable by only 33 kJ/mol; $4^{\bullet-}$ has calculated spin densities similar to those of $3^{\bullet-}$.

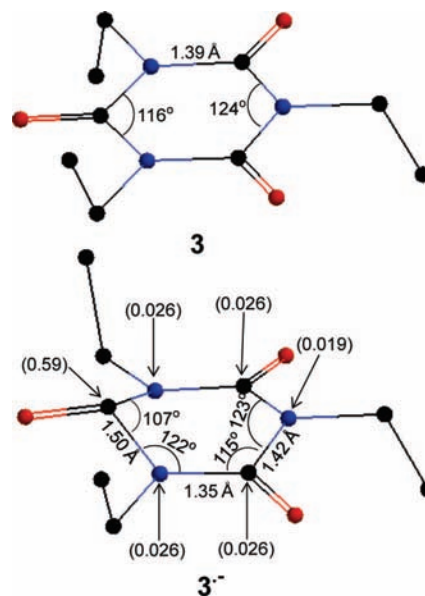


Figure 4. Geometries predicted by B3LYP/6-31G* for **3** and $3^{\bullet-}$ (carbon = black, nitrogen = blue, and oxygen = red; the hydrogens on the ethyl groups have been removed for clarity). In the isocyanurate ring of **3**, all six bond lengths are the same, all three NCN bond angles are 116° , and all three CNC bond angles are 124° . In $3^{\bullet-}$ the predicted spin densities on all ring carbon and nitrogen atoms are in parentheses. The carbonyl with high spin density is now pyramidalized, whereas the other two COs are nearly coplanar with the nitrogens.

indicate that the D_{3h} isocyanurate ring in **3** loses planarity upon electron attachment; this would imply that $3^{\bullet-}$ undergoes a first order Jahn–Teller (J-T) distortion.¹³ This distortion reduces the symmetry of the isocyanurate ring resulting in two or more conformers that differ in geometry, symmetry and spin distribution.¹³ Our calculations have found one of these conformers for which the isocyanurate ring in $3^{\bullet-}$ has a boatlike geometry (C_s symmetry) with two short and four long N–C bonds, and the carbonyl with high spin density is now pyramidalized while the other two COs remain nearly coplanar (Figure 4).¹⁴ However, the line-width effect observed in the EPR spectrum (Figure 2) suggests that a second similar, but not identical, J-T conformer of $3^{\bullet-}$ is also present.

The line-width alternation effect detected in the EPR spectrum recorded at 295 K (Figure 2) becomes more pronounced upon cooling the HMPA solution, confirming that there are indeed two J-T conformers of $3^{\bullet-}$ in equilibrium, undergoing fast exchange on the EPR time scale (see

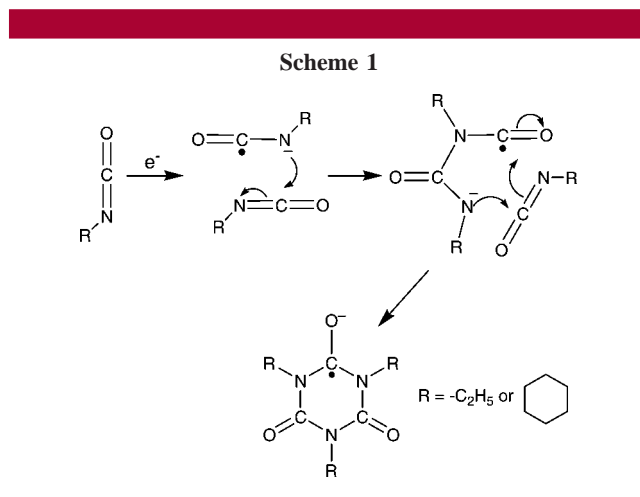
(13) For a discussion and examples of systems that undergo J-T distortion upon electron addition, see: (a) Jahn, H. A.; Teller, E. *Proc. R. Soc. London Ser. A* **1937**, *161*, 220. (b) Horvat, D. A.; Hammons, J. H.; Stevenson, C. D.; Borden, W. T. *J. Am. Chem. Soc.* **1997**, *119*, 9523–9526. (c) Kurth, T. L.; Brown, E. C.; Hattan, C. M.; Reiter, R. C.; Stevenson, C. D. *J. Phys. Chem. A* **2002**, *106*, 478–481. (d) Gerson, F.; Huber, W. *Electron Spin Resonance Spectroscopy of Organic Radicals*; Wiley-VCH: Weinheim, 2003; p 161.

(14) The symmetry assignments assigned to **3** and $3^{\bullet-}$ are of the isocyanurate ring only. DFT calculations on **4** and $4^{\bullet-}$ also show that the neutral isocyanurate ring undergoes a boatlike molecular distortion upon electron reduction.

Supporting Information).¹⁵ This fast exchange causes the pair of ¹³C's to appear magnetically equivalent. Furthermore, a small decrease in the average coupling constant for two of the ¹³C's is apparent as the solution is cooled ($a_C = 0.69$ G at 295 K and 0.65 G at 260 K). A dynamic Jahn–Teller effect explains these observations and is revealed through broadening of the EPR lines.^{13d} Although the structure and symmetry of the second conformer remain elusive, it is clear from these experiments that a more thorough quantum mechanical study is needed to fully elucidate these unique isocyanurate anion radical systems.

The larger observed ¹³C hyperfine splitting ($a_C = 2.41$ G), assigned to the carbonyl carbon with the highest calculated spin density ($\rho = 0.59$), is surprisingly small when compared to those of other ketyl anions exhibiting high spin density on the carbonyl carbon.¹⁶ For example, the carbonyl in di-*tert*-butyl ketyl has an $a_C = 52.7$ G.^{16b} Certainly there are a number of factors that will affect the value of a_C including spin density at the carbon and the degree of carbonyl bending. However a B3LYP/6-31G* calculation for di-*tert*-butyl ketyl gives nearly the same carbonyl spin density ($\rho = 0.58$) and degree of bending as in **3**^{•−}. A third important contribution to the value of a_C is any spin polarization contribution from the adjacent atoms to the π spin polarization of the carbonyl carbon. Empirically determined spin polarization constants reveal that the spin contribution to a_C , when adjacent nitrogens are present, is much smaller than the spin contribution from adjacent carbons.¹⁷ These differences account for the smaller a_C in **3**^{•−} when compared with di-*tert*-butyl ketyl.¹⁸

We propose that the mechanism for the formation of **3**^{•−} follows a path similar to that for a variety of Lewis base catalyzed reactions (Scheme 1).^{10a,19} However, in this system



the electron initiates the trimerization. Previous Lewis base or acid catalytic methods for the synthesis of alkyl isocyanurates can typically be quite slow (taking many hours) even at elevated temperatures¹⁹ and commonly yield a mixture of both **1** and **2**, often in low quantities.^{6,10b,19} This one-step method is very rapid and requires only the addition of an electron. Considering the high yield obtained for **3** and **4**, this method may prove to be a viable new one-step route for the synthesis of a host of substituted isocyanurates and enable further exploration of these unique heterocyclic anion radicals.

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Supporting Information Available: Experimental details and spectroscopic data for both isocyanurate systems. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(18) See Supporting Information for a more detailed discussion of spin polarization contribution to a_C .

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